



THE TRANSMITTER

September 2016

Article Review

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Association of traumatic brain injury with late-life neurodegenerative conditions and neuropathologic findings. A history of traumatic brain injury is often elicited in veterans, but its role in development of parkinsonism is controversial. This large scale prospective cohort study analyzed data from the Religious Orders Study (ROS), the Memory and Aging Project (MAP), and the Adult Changes in Thought Study. Self-reported history of TBI when subjects were nondemented was indexed. Clinical outcomes studied included AD, PD, and all causes of dementia in all three cohorts, as well as incident MCI and progression of parkinsonism in ROS and MAP. TBI with loss of consciousness was associated with risk for Lewy body pathology on autopsy, progression of parkinsonism, and PD, TBI with LOC was not associated with dementia, AD, neuritic plaques, or neurofibrillary tangles. Limitations of the study include the small PD sample size and the use of self-reported TBI rather than that verified in the medical record; nonetheless, verification of the findings in three independent cohorts supports the careful surveillance of persons with TBI for incident PD.

JAMA Neurol. 2016. Sep; 73 (9): 1062. <https://www.ncbi.nlm.nih.gov/pubmed/27400367>

Tau positron emission tomographic imaging in the Lewy body diseases. Clinical and pathological studies have implicated concurrent amyloid and tau pathology along with Lewy changes in the cognitive decline seen in Parkinson disease with dementia (PDD) and in dementia with Lewy bodies (DLB). Molecular imaging has associated cortical amyloid pathology with some cases of PD and PDD, and high levels of beta-amyloid are observed in most cases of DLB. This small cross sectional study used clinical and cognitive testing data, as well as amyloid ($[^{11}\text{C}]\text{PiB}$) and tau ($[^{18}\text{F}]\text{AV-1451}$) PET to evaluate the relationship between amyloid, tau, and cognitive decline in patients with Lewy body diseases (9 PD with normal cognition, 8 PD with impaired cognition, and 7 DLB). The authors observed higher tau deposition in the inferior temporal gyrus and precuneus in PDD and DLB, which correlated with cognitive impairment; but no such relationship in healthy controls or unimpaired PD. The amount of tau detected varied widely among participants, especially in DLB. Nonetheless, the pattern of distribution in PDD and DLB was consistent and was reminiscent of that observed in AD. These findings suggest that similar pathogenic mechanisms may underlie tau accumulation in DLB and AD.

JAMA Neurol. 2016. Sep 19 (epub ahead of print). <https://www.ncbi.nlm.nih.gov/pubmed/27654968>

Pathological alpha-synuclein transmission initiated by binding lymphocyte-activated gene 3. The cell-to-cell spread of alpha-synuclein, a major constituent of Lewy bodies in PD and DLB, is thought to share some features with the spread of prions, and this has been demonstrated in animal models of PD. The spread of alpha-synuclein pathology into experimental fetal brain grafts that had been implanted in PD suggests that similar spread occurs in humans. However, the mechanisms by which alpha-synuclein spreads from cell to cell remain unclear. In this paper, scientists led by Ted Dawson from Hopkins screened a library of transmembrane proteins to identify those that preferentially bind pathological alpha-synuclein. They found that the cell surface lymphocyte-activated gene 3 (LAG-3) can mediate the uptake and export of alpha-synuclein fibrils in cell cultures and brain extracts. Alpha-synuclein-induced lesions and behaviors were ameliorated in animals lacking LAG-3. LAG3 is best characterized as an immune player, and its expression in brain is not high. Further work will be necessary to validate the interaction of LAG-3 and alpha-synuclein; nonetheless, these data are the first to identify LAG-3 as a promising therapeutic target for PD.

Committee Activities

Clinical Care Committee

- **Rotation of Committee Chair:** Leadership for the clinical care committee rotates amongst the PADRECCs. The Southwest 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. 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 first audioconference for FY 17 will be held on **November 10, 2016** "*Cholinergic Function and PD*" by Kathy Chung, MD Northwest/Portland 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.

- **2016 National VA PD Consortium Meeting:** This meeting was held in Portland, OR on September 19th, 2016, one day before the World Parkinson's Congress. Approximately 45 PADRECC and Consortium members attended the meeting. Presentations included: gastrointestinal disorders and PD, nutritional considerations, Duopa therapy, Camp Lejeune and PD, mobile apps, telehealth, palliative care, drug-induced Parkinsonism, Cholinergic function and PD, mindfulness, DBS update, and management of psychiatric complications of PD. The meeting also included poster and case presentations as well as time for networking. Presentations from the meeting will be available on the National website soon.
- **World Parkinson's Congress 2016-Portland:** The PADRECC & National VA PD Consortium were organizational partners of the WPC and had an exhibit table providing information on the care available at the VA for Veterans with PD and how to apply for VA care. Many PADRECC staff and Consortium members attended this conference and several were speakers and/or poster presenters.
- **Education Needs Assessment:** An education needs assessment was disseminated to Consortium Members in order to steer future education initiatives of this committee. Responses are being analyzed and the committee will explore potential projects to meet the needs expressed by Consortium Members. We thank you for taking the time to complete the short survey.
- **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.

Dates to Remember

November 10, 2016

EES/PADRECC Movement Disorders Series

Topic: Cholinergic Function and PD

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

January 12, 2017

EES/PADRECC Movement Disorders Series

Topic: Yoga & Mindfulness

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

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: TBA

<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/>