

U.S. Department of Veterans Affairs

Veterans Health Administration Parkinson's Disease Research, Education & Clinical Centers 

 NATIONAL VA PARKINSON'S DISEASE

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 Education · Collaboration · Advocacy

# THE TRANSMITTER

### May 2025

### **Article Reviews**

Prepared by: Megan Super, MD-Fellow; Sara Berman, MD-Fellow; & Joaquin Vizcarra, MD-Fellow ~ Philadelphia PADRECC

#### Artificial Intelligence-Based Virtual Assistant for the Diagnostic Approach of Chronic Ataxias

AI tools are becoming increasingly popular in medicine and other fields. This article presents the development and validation of an AI-powered virtual assistant (VA) designed to aid in diagnosing chronic ataxias—a group of over 300 rare and often genetically heterogeneous diseases. The VA, developed using structured decision trees and large language models (LLMs), was tested on 453 published clinical cases representing 151 causes of chronic ataxia. It achieved a diagnostic accuracy of 90.9%, significantly outperforming 21 neurologists (18.3%) and GPT-4 (19.4%). However, this result is likely misleading given their definition of accuracy which meant the correct diagnosis was included in the differential. The VA created a differential list with a mean number of diagnoses of  $21.3 \pm 11.1$  per clinical case as opposed to  $4.6 \pm 2.6$  from neurologists and  $7.3 \pm 1.7$  by GPT-4. This significant difference in the number of differentials generated likely accounts for the higher diagnostic accuracy found with the VA. When comparing the ratio of correct diagnoses to total diagnoses given, the VA performed similarly to neurologists with a 4.2% accuracy score vs 4.0% for the neurologists. Unlike GPT-4, which produced 7 data hallucinations and 83.6% of all incorrect diagnoses, the VA showed no such errors. The study concludes that this AI tool provides a fast, accurate, and consistent diagnostic aid, especially useful in resource-limited settings, and may be scalable to other neurological and nonneurological diseases. However, more work is needed before such an assistant is useful in a real-world clinical setting.

Mov Disord. 2025 May; 40(5); https://pubmed.ncbi.nlm.nih.gov/40119570/

#### Loneliness in Parkinson's disease: Subjective experience overshadows objective motor impairment

This study found that loneliness is a major issue for people with Parkinson's disease (PD), affecting over 60% of 178 individuals with PD surveyed. Interestingly, how lonely someone feels isn't strongly linked to how severe their physical symptoms are, but rather to how much the disease affects their daily life, their mental health (especially depression), and the size of their social network. Men with PD tended to feel more emotionally lonely, possibly due to losing close confidants. The results suggest that helping

people with PD feel less lonely-by addressing depression and improving social connections-could also help them function better in daily life, regardless of how advanced their physical symptoms are.

*Parkinsonism Relat Disord*. 2025 May 10;136:107867. doi: 10.1016/j.parkreldis.2025.107867. Epub ahead of print. PMID: 40378710. <u>https://pubmed.ncbi.nlm.nih.gov/40378710/</u>

#### Distinct Longitudinal Clinical-Neuroanatomical Trajectories in Parkinson's Disease Clinical Subtypes: Insight toward Precision Medicine

In a long-term follow-up of 421 people with early Parkinson's disease enrolled in the PPMI study—each tracked for an average of 8.2 years—researchers identified three distinct clinical subtypes at baseline: mild motor-predominant (223 individuals), intermediate (146), and diffuse-malignant (52). Over time, those in the diffuse-malignant group experienced a markedly steeper decline: their motor scores worsened more rapidly (P = 0.007), and they showed greater deterioration in both cognitive function and the ability to carry out everyday tasks (both P < 0.0001), even after accounting for age and use of levodopa.

A subset of 128 patients and 60 healthy controls underwent repeated MRI scans, which revealed that individuals in the diffuse-malignant subtype also accumulated brain atrophy at a faster rate—particularly in the precuneus, the temporal and fusiform gyri, and the cerebellum (corrected P < 0.05). In contrast, the mild motor-predominant and intermediate groups followed much slower and more localized patterns of change. Together, these findings underscore that Parkinson's disease does not follow a single, uniform course; rather, each subtype appears to reflect a different pathophysiological pathway. Recognizing these patterns early on could help clinicians tailor treatments to the specific trajectory each patient is likely to follow.

*Mov Disord*. 2025 May 26. doi: 10.1002/mds.30229 *Online ahead of print* <u>https://movementdisorders.onlinelibrary.wiley.com/doi/epdf/10.1002/mds.30229</u>

## **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/June. 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 treatment strategies, new medications and other procedures, and other clinical issues to improve patient care and outcomes across the national PADRECCs service area. It also serves to provide clinical support to the PADRECC Associated Sites by focusing on procedures and measures to standardize clinical care across the PADRECC network.

#### Recent agenda items have included:

- 1. Parkinson's KinetiGraph (PKG): practice and protocol use in the PADRECCs
- 2. **Vyalev:** subcutaneous continuous infusion therapy practice and protocol use in the PADRECCs

3. The Parkinson's Neurogastroenterology Clinic Model at OHSU: Presentation by Dr.

Delaram Safarpour and Dr. Sarah Diamond describing the OHSU model of interdisciplinary PD/GI care for PD.

### **Education Committee**

- **PADRECC/ILEAD Webinars:** 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 provided for the <u>live</u> webinars. Check out the following link for a list of past webinars: <u>Movement Disorders Series Parkinson's Disease Research</u>, <u>Education and Clinical Centers (va.gov)</u>
- **PD Hospital Safety Training Presentation:** Developed a short grab and go presentation for VA CLC, CNH and Veteran State Home staff to improve the care of Veterans with PD who reside there. Committee is currently piloting locally. Philly, Richmond & San Fransico PADRECCs presented to their local State Veteran Homes with positive feedback.
- The Parkinson's Foundation/VHA Partnership: This committee serves as point of contact for partnership activities.
  - The 2024/2025 PF Veteran Webinar Series is underway.
  - VA Professionals Survey- developed to gain a sense of VA Clinicians' PD education needs/resources. Emailed to PADRECC & PAS sites in May.
- VA Annie Mobile App Protocol for PD: Developing a protocol that will be available nationwide to provide educational messages related to PD and will link to specific resources such as exercise videos, informational PDFs and websites. Currently in the piloting phase.
- **Parkinson's Disease Rehab-Community of Practice on Microsoft Teams-** Collaboration with rehabilitation subject matter experts across the VA with interest in PD to develop this COP to address and enhance rehabilitation care for Veterans with PD and similar conditions. The goal of the platform is to share evidence-based knowledge to inform PD-specific rehabilitation practices, provide access to up-to-date resources, program success and opportunities for improvement. All are welcome to join:

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• **PADRECC Transmitter:** This committee continues to assemble and distribute this *e*-newsletter every other month.

# Philadelphia PADRECC Associated Site Updates

#### Albany Stratton VA Medical Center PAS Director: Octavian Adam, MD

The Albany Stratton VA Medical Center is in the early stages of a study investigating color vision (CV) deficiencies related to Parkinson's disease (PD). Previous research suggests PD-related CV deficiencies occur years or even decades before clinical diagnosis of PD. However, these CV deficiencies are subtle,

making them difficult to detect. With support from the NIH's National Institute of Biomedical Imaging and Bioengineering, we are comparing the effectiveness of multiple types of color vision assessments for detecting these deficiencies, including a new high-precision and fully automatic brain-computer interface (BCI)-based assessment. If successful, accurate detection of PD-related CV deficiencies will improve Veteran (and non-Veteran) health by enabling earlier identification of PD, more precise monitoring of disease progression, and better evaluation of the effectiveness of treatments. For more information, please contact the study's PI, James Norton at james.norton1@va.gov.

#### **Pittsburgh VA Healthcare System** PAS Director: Edward A. Burton, MD, DPhil, FRCP

#### **Recently published article in Nature Communications -- September 2024**

#### A zebrafish model of progressive supranuclear palsy suggests new approaches to treatment

Progressive supranuclear palsy (PSP) is a neurodegenerative disease characterized pathologically by accumulation of Tau protein in neurons and glia, along with loss of neurons and synapses, and activation of microglia. Clinically, PSP can present in several different ways, including a variant that mimics Parkinson's disease, and another called Richardson syndrome in which prominent balance, swallowing and eye movement deficits occur. Currently, there is no treatment that prevents PSP from progressing (although some of the symptoms can be relieved) and most patients die from complications of the disease within a decade of onset.

The aim of our work is to develop effective treatments for PSP. To do this, we generated a model that allows us to test a large number of possible treatment approaches very quickly. Zebrafish share 70% of their genes with humans (closer to 90% if analysis is restricted to genes implicated in human diseases) and, as vertebrates, zebrafish brain structure and function – including regulation of movement by dopamine neurons – is also very similar to ours. An extensive collection of tools allows researchers to add or remove genes from the zebrafish genome efficiently, and since a pair of adult zebrafish can produce 50 - 100 offspring every week or two, it is possible to breed large numbers of tiny larval fish that can be screened rapidly to find rare biological events. As a result of these factors, zebrafish are commonly used as a laboratory animal model in neuroscience and genetics.

In our study (<u>https://www.nature.com/articles/s41467-024-52173-0</u>), we added the human Tau gene to the zebrafish genome, to generate zebrafish that make human Tau protein in their brains. Tau zebrafish developed difficulty moving, abnormal eye movements, loss of neurons and synapses, microglial activation, deposits of human Tau protein, and impaired survival, replicating many key features of PSP. The severe movement deficit could be detected automatically using software to analyze a video stream of zebrafish swimming in small wells. We tested 147 different drug-like small molecules for activity in preventing abnormal motor function in Tau zebrafish, by adding each compound to the water and then analyzing a video steam to detect movement abnormalities. One of the compounds rescued swimming movements and also prolonged the survival of Tau zebrafish, by preventing microglia from removing synapses from neuronal circuits (which happens in the presence of Tau accumulation). The molecular mechanism involves inhibiting a nuclear protein, Brd4, that is also expressed in human, rat, and mouse

microglia. The compound showed a similar effect in a rat model, suggesting that our observations are conserved across vertebrate species.

We are currently working to determine whether a derivative of this Brd4 inhibitor could be useful as a treatment for PSP, and to understand the mechanism of action in more detail. The new zebrafish model will be useful for other drug development studies in PSP, because it can be used to test new compounds rapidly, identifying the most promising candidates to prioritize for evaluation in more complex and time-consuming models.



The picture **shows** the head region of a Tau zebrafish viewed from above. The zebrafish picture was taken by light microscopy (black and white) then a fluorescence image, showing brain neurons containing human Tau (yellow-red color scale), was superimposed.

#### West Haven VA Medical Center (Connecticut) PAS Director: Diana Richardson, MD

#### Multidiscipline Comprehensive Parkinson's Syndrome Therapeutics and Education Program: VA Centric Care for Veteran's at Risk of Frailty

Neurology: Diana Richardson, MD Physical Therapy: Annie Valentino Upson, PT, DPT Speech Pathology: Sonia Mehta, MS, CCC-SLP Speech Pathology: Andrea Bodin, MS, CCC-SLP Nursing: Ancy Nellik, RN

The Parkinson's Disease Associated Site offers a comprehensive program across discipline designed for the management and education of patients with chronic neurodegenerative conditions such as Parkinson's Disease, Atypical Parkinsonian Syndromes, Dementia and Frailty. An additional focus is caring for Veteran's with toxin related neurological conditions.

#### Neurology

Neurological care provided by a Movement Disorder Specialist. Individualized care is provided from initial work-up to diagnosis to management and support. The neurology clinic service as a referral to the allied health services such as Physical Therapy, Speech Pathology, Occupational Therapy and Pharmacy. An additional component for patient and caregiver education and Toxin related support groups is also incorporated for encouraging the active participation of patients in their care.

#### **Physical Therapy**

The VACT Physical Therapy program is comprehensive. Assessment and treatment of a variety of symptoms affecting mobility. It also serves as a referral and recommendation service to medical providers for at risk patient who may require VNA for a Home Safety evaluation or Occupational Therapy for additional adaptive equipment or other treatment modalities.

#### **PT Fall Prevention Program**

This clinic is open to all patients receiving care at VACT. Patients are referred from Primary Care, Orthopedics, Neurology, and Movement Disorder Clinic. Patients may also self-refer as physical therapy is direct access. Once the patient is referred, a comprehensive physical therapy assessment is completed with specific orthopedic and neurological examinations including pain, flexibility, strength, balance, posture, transfer ability and gait on level, incline and stairs. The PT Fall Prevention Clinic is combined with an education program sponsored by VACT Hospital Education, Neurology and the Rehabilitation and Physical Medicine departments.

#### **Speech Pathology**

Speech-Language Pathology Services at the VACT provides comprehensive management for patients with neurological disease. Our program provides evaluation and treatment for: swallowing changes; voice, speech & communication changes; and cognitive changes. We also have several specialized programs that are being offered for patients with Parkinson's Disease/Parkinsonian Syndromes. These include:

- SPEAK OUT! Program: Our program offers "Speak Out!" individual and group sessions. Therapy is led by trained and certified speech-language pathologists. Individual sessions are completed one-to-one either in person or virtually. Following completion of the individual program, groups are a key part of helping patients maintain their skills. They consist of weekly group therapy sessions where individuals with Parkinson's, along with their speech-language pathologists, practice SPEAK OUT! exercises and strategies to improve their voice, speech, and communication.
- Cognitive Health Series: This is a five-part series for patients and families that provides education regarding cognitive changes in PD and reviewed functional strategies and resources. The series is led by a trained speech-language pathologist with a clinical specialty in cognitive and communicative disorders. This series integrates mental health providers and offers a group setting for patients and families to share their experience and learn functional tools for better living. Take home materials and resources are provided in each session, follow-up options for one-to-one individualized therapy are also available.