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STANFORD RESEARCH UPDATE (September 2023)

Dr. Carla Abdelnour Ruiz, MD, PhD
Postdoctoral Scholar
Sue Berghoff LBD Research Fellow
Stanford Medicine-Poston Lab

Dr. Abdelnour Ruiz's research is focused on using a blood marker called plasma pTau181 to identify Alzheimer's disease pathology in patients with a clinical diagnosis of Lewy body disease. These diseases—Alzheimer's disease and Lewy body disease—are the most common "neurodegenerative" causes of cognitive impairment and dementia in the elderly. Sometimes, they occur together in the same person, and this co-occurrence has been associated with a more rapid decline in cognitive abilities.

In this study, Dr. Abdelnour Ruiz has discovered that the pTau181 marker found in blood (plasma) can accurately detect the presence of Alzheimer's disease pathology in people with a Lewy body disease diagnosis. Furthermore, she has found that the levels of plasma pTau181 in a person's blood can predict how well they will perform in daily tasks and how their memory and thinking abilities may change over time. In patients with Lewy body disease who already have cognitive problems, the initial levels of plasma pTau181 can foretell the rate at which their daily functioning may decline. This can help doctors anticipate the challenges their patients will face in years to come.

In addition to this, changes in plasma pTau181 levels over a two-year period have been linked to specific cognitive functions. A faster increase in these levels can be associated with problems in areas like memory, attention, and executive function.

PROGRESS THROUGH RESEARCH

Going beyond diagnosis and prognosis, this research has important implications for clinical trials aimed at developing new treatments. By using blood markers like plasma pTau181 in people with Lewy body disease… experimental treatments can be tested on the right people at the right time, increasing the chances of finding effective therapies.

The significance of this research goes beyond diagnosis and prognosis. It has important implications for clinical trials aimed at developing new treatments. By using blood markers like plasma pTau181 in people with Lewy body disease, researchers can select those who are likely to experience a more rapid decline, as well as analyze the treatment response accounting for the presence of concurrent Alzheimer's disease pathology[1]. This means that experimental treatments can be tested on the right people at the right time, increasing the chances of finding effective therapies.

With this in mind, Dr. Abdelnour Ruiz has contributed to this field through a recent paper that reviewed randomized clinical trials (RCTs) in Dementia with Lewy bodies (DLB)[2]. In this comprehensive analysis, the authors examined 40 trials involving 25 different agents, including both symptomatic treatments and disease-modifying therapies (DMTs) for DLB. The authors found a recent trend of including participants at the early stages, although more than half of active clinical trials still aim to enroll mild to moderate dementia patients. Additionally, repurposed agents make up a significant portion of clinical trials, comprising 65% of the ongoing efforts. However, they also found some challenges: the need for disease-specific outcome measures and biomarkers, and the need to improve representation of global and diverse populations.

In summary, this research highlights the use of a blood test for early detection, personalized care, and more successful clinical trials in people with Lewy body disease.

References:

1. Gibson LL, Abdelnour C, Chong J, Ballard C, Aarsland D. Clinical trials in dementia with Lewy bodies: the evolving concept of co-pathologies, patient selection and biomarkers. *Curr Opin Neurol*. Jun 28 2023; doi:10.1097/WCO.0000000000001173
2. Abdelnour C, Gonzalez MC, Gibson LL, et al. Dementia with Lewy Bodies Drug Therapies in Clinical Trials: Systematic Review up to 2022. *Neurology and Therapy*. 2023; doi:10.1007/s40120-023-00467-8

Dr. Carla Abdelnour Ruiz received her medical degree at the Central University of Venezuela, completed her neurology residency training at the University Hospital Príncipe de Asturias in Spain, and conducted her doctorate in Medicine at the Autonomous University of Barcelona working with Drs. Dag Aarsland, Javier Pagonabarraga and Jaime Kulisevsky. As a Sue Berghoff LBD Research Fellow, she is investigating the impact of different comorbidities in the clinical presentation, cognitive profile, and disease progression of Lewy body disease. Additional study includes the biological underpinnings of prodromal Lewy body disease to identify potential biomarkers for diagnosis and prognosis. She was a steering committee member of the European Dementia with Lewy bodies board member of LBDA.

STANFORD RESEARCH UPDATE (October 2023)

SUSAN & CHARLES BERGHOFF *foundation*

Dr. Joe Winer, PhD

Postdoctoral Scholar

Sleep & Circadian Studies Center

Stanford Neurology & Neurological Sciences

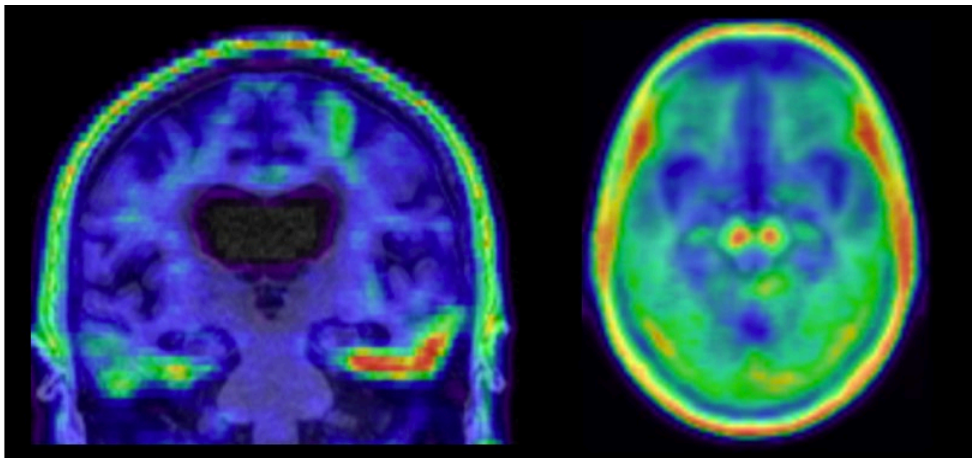
Dr. Joe Winer studies sleep using polysomnography and in real life using actigraphy and questionnaires. He also uses neuroimaging methods like MRI and PET to see how changes in sleep are associated with the early signs of neurological disease. He is currently working on two projects related to biomarkers in Lewy body disease.

First, he is utilizing wearable devices to record 24-hour patterns of activity in people with and without Lewy body disease. These data will help us understand how sleep and physical activity differ in people with Lewy body disease, and how sleep-wake patterns change at different stages of the disease. By relating these “real life” activity recordings to other biomarkers collected by the Poston Lab (such as neuroimaging, cerebrospinal fluid or CSF, and blood), Dr. Winer hopes to develop markers of disease progression that could be extracted from common wearable devices (such as FitBit or Apple Watch).

In our data collected at Stanford, we have learned that individuals with Lewy body disease have lower daytime activity levels and more fragmented patterns of activity relative to older adults without Lewy body disease. By applying the same analysis techniques to a dataset of over 80,000 older adults, we found that people with lower daytime and 24-hour activity levels were at greater risk for progressing to Parkinson’s disease. We also found that people with isolated REM sleep behavior disorder, an early stage of Lewy body disease, also showed this pattern of lower activity levels.

“Our findings support an emerging idea that wearable technology can be used to detect Lewy body disease early, which will be helpful for clinical trials targeting early stages of disease.”

Dr. Winer’s second line of research uses PET imaging to look at levels of amyloid and tau—brain proteins involved in Alzheimer’s disease. There is an increasing appreciation that many people with cognitive impairment or dementia frequently have more than one disease, i.e., Alzheimer’s disease and Lewy body disease. By collecting amyloid and tau PET scans from people with Lewy body disease, we hope to understand how co-occurring Alzheimer’s disease may contribute to patients’ cognitive and behavioral symptoms.



The image on the left shows a tau PET scan from an individual with dementia with Lewy bodies. In the temporal lobes of the brain, green and red indicate that tau tangles are present.
The image on the right shows two bright spots in the midbrain, highlighting the substantia nigra, an area that is critically important in Lewy body disease.

Our findings so far suggest that people with Lewy body disease have less tau protein accumulation compared to people with Alzheimer's disease, but that when these tau proteins are present, they are related to worse cognitive symptoms. PET imaging can also be used to measure dopamine cell loss in the substantia nigra, a region that is critically important in Lewy body disease.

"This information will be very important for future clinical trials since people with multiple types of neurodegenerative diseases will need to receive specialized treatments."

Researchers are working to understand what causes changes in daytime activity levels, and to determine if these changes can be used as a disease-specific biomarker. It is worthwhile to note the importance of developing such a biomarker, which has the potential to be easily and inexpensively applied across a large population to obtain significant measurable data over the course of longitudinal studies.

We proudly partner with Poston Lab at Stanford University to provide Continuing Medical Education and through the Sue Berghoff LBD Research Fellowship Fund.

www.berghoff-foundation.org/lbd-research