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SUE BERGHOFF LBD RESEARCH FELLOWSHIP
2022 Research Updates

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A variety of proteins exist in the brain and perform essential brain functions. However, when certain proteins misfold or clump together to form abnormal deposits in the brain, it can lead to neurodegenerative diseases and dementia.

Traditionally, neurodegenerative dementias have been classified based on the particular type of protein deposits found in the brain. And yet when studying the brain tissues of people who died with dementia, what researchers often see under the microscope are abnormal deposits of more than one protein.

Lewy body diseases (LBD) are characterized by abnormal deposits of a protein called alpha-synuclein.

Frequently, people with LBD can also have amyloid and tau protein deposits, which are associated with Alzheimer's disease. In these cases, people can experience worse performance on cognitive tests, more wide-ranging clinical characteristics, and shorter survival. It is possible that they could have different responses to treatments, or benefit from therapies targeting amyloid or tau proteins.

Therefore, it is important to study people with Lewy body diseases, who might also have Alzheimer's disease-related protein deposits, to understand how the presence of these other proteins influences clinical presentation, disease progression, and treatment response.

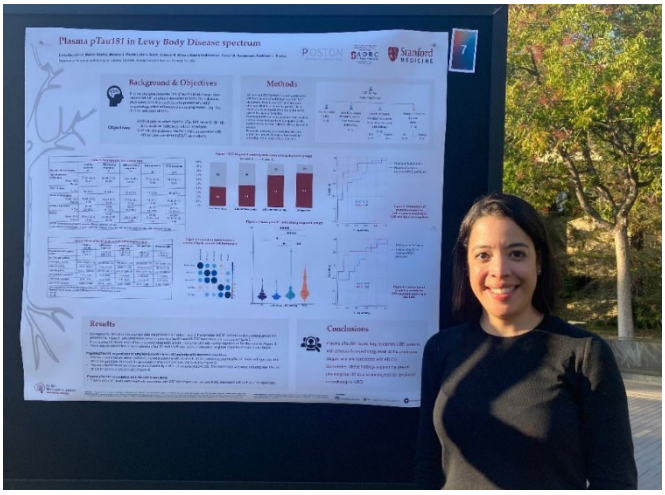
Amyloid and tau deposits can be identified with biomarkers including positron emission tomography (PET) brain imaging, and analysis of cerebrospinal fluid (CSF) obtained with a lumbar puncture. These biomarkers are very useful, but there is a need to develop more easily obtained and less expense biomarkers that can be performed on larger numbers of people.

Recent technology advances have allowed researchers to obtain biomarker information from blood. These 'blood-based' biomarkers are being used to study amyloid and tau proteins. In our research center at Stanford, we have analyzed a blood-based biomarker called plasma p-tau181 and found that it can identify people with Alzheimer's disease, who are shown to have abnormal deposits of amyloid and tau proteins when measured with CSF and PET imaging. Now we are studying plasma p-tau181 in people with Lewy body diseases.

In a recent study, we determined whether plasma p-tau181 was able to identify Alzheimer's disease-related proteins in people with Lewy body diseases who have cognitive impairment. For example:

- mild cognitive impairment due to Lewy bodies
- dementia with Lewy bodies
- Parkinson's disease with mild cognitive impairment
- Parkinson's disease with dementia

We found that plasma p-tau181 was able to identify Alzheimer's disease-related proteins in some people with Lewy body diseases and cognitive impairment.



Our results indicate that plasma p-tau181 might be a useful screening tool to identify Alzheimer's disease-related proteins in people with Lewy body diseases. This has several potential implications.

- Researchers can apply this biomarker in larger populations with less access to sophisticated tools to analyze CSF or PET imaging, or to patients with contraindications for these procedures.
- This blood-based biomarker is also easier to measure repeatedly over the course of the disease.
- It might also be able to identify subgroups of people, who might have different responses to treatments.

Soon we plan to analyze how plasma p-tau181 levels change over time in people with Lewy body diseases, and to study whether these changes can be related to worsening cognitive or motor performance longitudinally.

Dr. Joe Winer, PhD
Postdoctoral Scholar
Sleep & Circadian Studies Center
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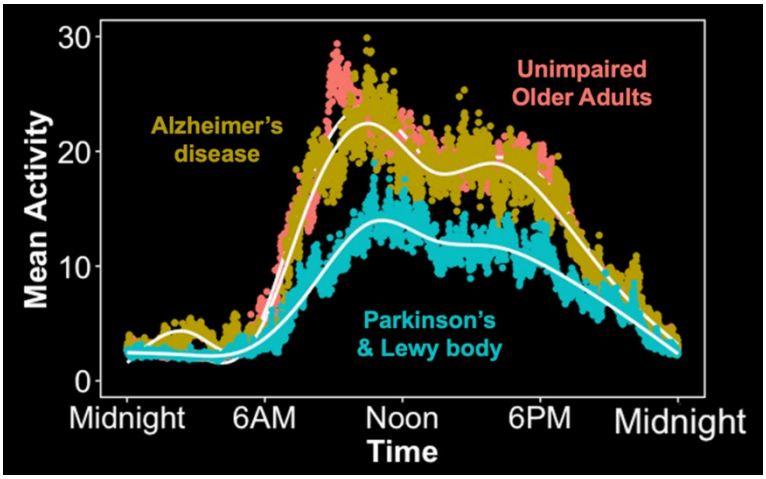
Scientific studies have shown that fluctuating cognition and REM sleep behavior disorder are symptomatic of Lewy body dementias. It is encouraging to follow the work of Dr. Joe Winer and others at Stanford as they investigate the impact of sleep and physical activity on neurodegenerative disease progression.

In Fall 2021, Dr. Winer began using movement-sensing watches, also known as actigraphy watches, to record patterns of physical activity and sleep in participants in the Stanford Healthy Brain Aging Study.

Thus far, researchers have collected actigraphy data from over 150 individuals, including people with Parkinson's disease and Lewy body dementias. From the actigraphy watches the research team can measure levels of real-world activity, sleep duration, and sleep quality; and then investigate how these factors are affected across neurodegenerative diseases.



Because the Stanford Healthy Brain Aging Study collects data from research participants annually, the research team will be able to determine whether better sleep health and increased physical activity are associated with Parkinson's disease and Lewy body dementia symptoms progressing more slowly over time.

The graph above shows activity levels across an average 24-hour day for people with Parkinson's disease or Lewy body dementia, as well as in people with Alzheimer's disease, and unimpaired older adults

As the graph illustrates, there is a clear difference in daytime activity levels (from 6am to midnight) in individuals with Parkinson's disease or Lewy body dementias versus individuals with Alzheimer's disease, and unimpaired older adults.

Researchers are working to understand what causes these 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.

Dr. Winer studies sleep in the lab 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.

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

https://www.berghoff-foundation.org/lbd-research

https://med.stanford.edu/poston-lab/research.html