

This study seeks to understand how low blood pressure when standing, known as orthostatic hypotension (OH), affects cognitive performance and hemodynamics (e.g., how blood flows through your blood vessels) in people with Parkinson's disease.

The Challenge

Low blood pressure when upright, known as orthostatic hypotension (OH), occurs in 30-50% of people with Parkinson disease (PD). OH is associated with worse cognition in PD and could be a treatable risk factor for cognitive dysfunction. However, the mechanisms of this association remain unclear.

The Approach

This research project seeks to determine how OH affects positional cognitive performance and brain blood flow in persons with PD. In this study, participants with PD with and without OH undergo repeated cognitive testing while laying down and while upright on a tilt table. During cognitive testing, blood pressure is measured continuously and simultaneously while measuring hemodynamics using novel optical neuroimaging technology: functional near-infrared spectroscopy (fNIRS). To understand the mechanisms behind OH and worse cognitive functioning in PD, we are examining the relationship between blood pressure, cognitive performance, and hemodynamics comparing groups with and without OH while laying down and while upright.

The Impact

When complete, this project will provide new information on how blood pressure, brain blood flow, and cognitive changes are connected in people with PD. Understanding how OH affects hemodynamics and cognitive skills could help us understand if OH directly contributes to chronic cognitive dysfunction. We anticipate that these findings will help guide treatment targets for OH in PD and encourage further longitudinal studies to explore whether treating OH can improve cognitive function or prevent its worsening in individuals with PD.

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RESEARCH HIGHLIGHTS

These research highlights are based on preliminary findings of this research study:

- In the 8 participants with OH, we found a significant strong positive relationship between baseline systolic blood pressure at 3 minutes upright and performance on a verbal fluency letter test when upright, where lower systolic blood pressure at baseline correlated with poorer cognitive performance.
- The 8 participants with OH had poorer performance on the cognitive test while upright compared to laying down.
- We found that in preliminary analyses of the neuroimaging data in 4 participants with OH, neural efficiency (a measure of mental effort) during the cognitive test was lower while upright compared to laying down.

Key Benefits



CLINICAL

Diagnostic Procedures – *Potential*

The findings will improve understanding of the association between cognitive impairment in PD and hemodynamic biomarkers. This data will inform a potential mechanism for how OH impacts cognitive function and brain blood flow in PD.



COMMUNITY

Disease Prevention and Reduction- *Potential*

The knowledge gained from this project will facilitate clinical decision-making by advancing understanding of when to initiate therapy for OH and how aggressively to treat OH to minimize episodes of low blood flow to the brain and associated cognitive dysfunction while avoiding harm from commonly associated supine hypertension (i.e., high blood pressure when lying down).



The Team:

- Katherine Longardner, MD (Primary Investigator/KL2 Scholar) is an Assistant Clinical Professor in the UCSD Department of Neurosciences.
- Irene Litvan, MD, MSc, FAAN, FANA, (Primary Mentor) is a Professor in the UCSD Department of Neurosciences.
- David Salmon, PhD (Co-Mentor) is a Professor in the UCSD Department of Neurosciences.
- Roy Freeman, MD (Co-Mentor) is a Professor of Neurology at Harvard School of Medicine in Boston, MA.
- Kurtulus Izzetoglu, PhD (Co-Mentor) is an Associate Professor in the School of Biomedical Engineering, Science and Health Systems at Drexel University in Philadelphia, PA.
- Dawn Schiehser, PhD (Co-Mentor) is a Professor in the UCSD Department of Psychiatry and is a clinical neuropsychologist and researcher at the VA San Diego.
- Michael Skipworth, BS is the UCSD clinical research coordinator for this project

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