Biomarker predicts cognitive decline in Alzheimer's disease

September 9 2021, by Marla Paul

Credit: CC0 Public Domain

A biomarker in the brain predicts future cognitive decline in patients with the language form of Alzheimer's disease (AD), reports a new Northwestern Medicine study.

Northwestern Medicine scientists discovered the buildup of tau protein in the brain predicts the amount of future cognitive decline over one year in individuals with AD. The study measured used a newer type of positron emission tomography (PET) imaging that shows the location of toxic tau protein in the brain.

"Our new research shows tau PET imaging biomarkers can predict

future decline in individuals with primary progressive aphasia due to AD," said senior study author Emily Rogalski, associate director of Northwestern's Mesulam Center for Cognitive Neurology and Alzheimer's Disease. "These tau-based biomarkers may help predict the pace of progression of the disease and be important for early detection. They may eventually help us treat AD before we see symptoms."

The higher the level of the bad form of tau in the brain, the worse a person's cognitive performance, the study showed. The more tau protein a person had in a specific region of their brain, the more likely they were to have worse cognition a year later. The study also found the higher the level of tau, the more atrophy was occurring across the brain.

The study was published Sept. 8 in *Alzheimer's and Dementia*.

Early diagnosis of AD is important because the Food & Drug Administration recently approved Biogen's Aduhelm (aducanumab) to treat patients in the disease's mild stages, and other drugs are in the development pipeline.

"The presence and level of these biomarkers might give us a picture of how aggressive the disease is going to be, providing important markers necessary for precision-medicine interventions," said lead author Adam Martersteck. He conducted the research as a neuroscience graduate student at Northwestern University Feinberg School of Medicine and now is a postdoctoral fellow at the University of California Berkeley.

The study was among the first to show the amount of tau pathology in the brain predicts subsequent cognitive decline over time.

The individuals in the study had Progressive Primary Aphasia (PPA), which is often caused by an early-onset form of AD. In PPA, the parts of the brain that control language and speech degenerate.

"It's important to show that AD in primary progressive aphasia is similar to the more common late-onset AD that causes memory problems, so that participants with PPA can be included in clinical trials and offered all the same opportunities," Martersteck said.

The finding about predictive decline from tau pathology is also applicable to more common forms of AD in which memory loss is the primary symptom. One theory is that toxic forms of AD accumulate and then trigger events resulting in brain cell degeneration. This research supports this theory.

Participants from around the country were seen locally or flown to Chicago for MRI, tau PET imaging and cognitive testing at Northwestern's Mesulam Center for Cognitive Neurology and Alzheimer's Disease. The 19 participants all had been diagnosed with PPA.

As a growing proportion of Americans age, the prevalence of AD is expected to rise. An estimated 50 million people worldwide and 6 million in the U.S. have AD, with those numbers expected to triple in the next 30 years.

In the study, scientists measured toxic tau at baseline and tested participants on their ability to name objects. Participants returned a year later and were tested again on their ability to name objects. The more tau they had in the left anterior temporal lobe on PET imaging, the more likely they were to have worse cognition and a decline in their naming.

"The next steps for the research are to determine if these measurements are reliable at the individual level to guide prognosis and intervention targets," Rogalski said. "We know some individuals with PPA progress more rapidly than others, but factors driving fast versus slow progression have been difficult to ascertain. Reliable biomarkers are one key to

solving this conundrum."

More information: Adam Martersteck et al, Relationships among tau burden, atrophy, age, and naming in the aphasic variant of Alzheimer's disease, *Alzheimer's & Dementia* (2021). DOI: 10.1002/alz.12445

Provided by Northwestern University