Novel Blood Test Tracks Alzheimer's Progression

— MTBR-tau243 biomarker linked with tau PET and cognitive performance

by Judy George, Deputy Managing Editor, MedPage Today
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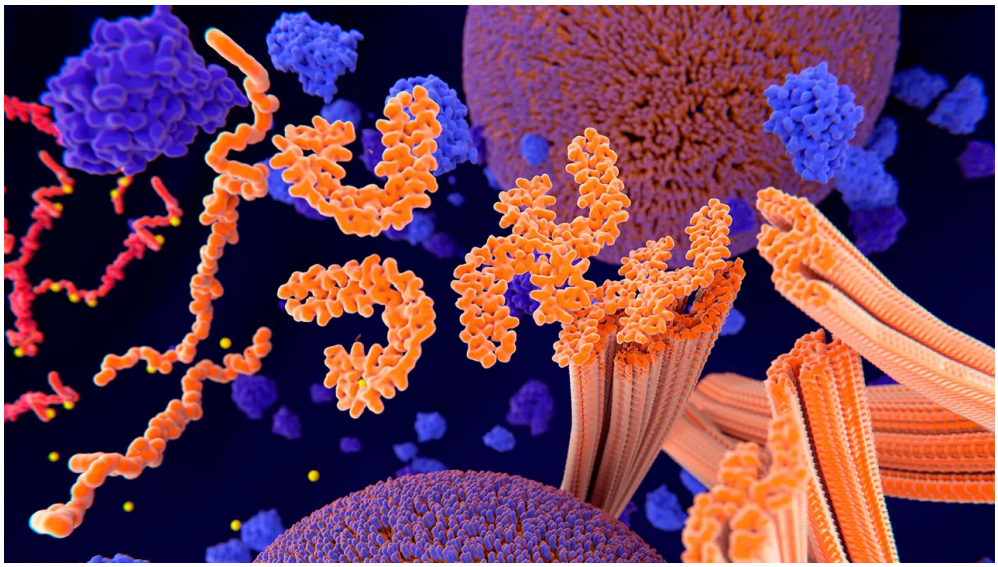

Key Takeaways

- A new blood-based test reflected Alzheimer's tau tangle pathology.
- The assay measured a new plasma tau species known as endogenously cleaved MTBR-tau243.
- The test distinguished various stages of Alzheimer's and separated it from non-Alzheimer's tauopathies.

A novel plasma-based assay was more strongly associated with tau tangle pathology in Alzheimer's disease than other established blood biomarkers, researchers said.

The assay measured a new plasma tau species known as endogenously cleaved, microtubule-binding region containing residue 243 (MTBR-tau243), which specifically reflected tau tangle pathology, reported Randall Bateman, MD, of Washington University School of Medicine in St. Louis, and co-authors.

Plasma MTBR-tau243 was associated with tau PET binding (β=0.72, R^2=0.56) and cognitive performance (β=0.60, R^2=0.40), outperforming other markers like phosphorylated tau 217 (p-tau217) and p-tau205, Bateman and colleagues said in *Nature Medicine*.

The assay was tested in three cohorts. It distinguished between early- versus later-stage Alzheimer's disease and separated Alzheimer's disease from non-Alzheimer's tauopathies.

The results suggested that plasma MTBR-tau243 could help estimate the tauopathy load in Alzheimer's disease, improving diagnostic evaluations of Alzheimer's in clinical practice and monitoring the efficacy of tau-targeted therapies in clinical trials, the researchers noted.

"This blood test clearly identifies Alzheimer's tau tangles, which is our best biomarker measure of Alzheimer's symptoms and dementia," Bateman said in a statement. The test also provides a good indication about whether a patient's symptoms are due to Alzheimer's or another disorder, he noted.

Insoluble tau aggregates within neurofibrillary tangles are a defining feature of Alzheimer's disease and closely correlate with clinical symptoms. In earlier research, Bateman and colleagues showed that the MTBR-tau243 in cerebrospinal fluid (CSF) was a specific biomarker of tau aggregate pathology. The current study extended this analysis to plasma.

The researchers tested the assay in two pilot cohorts: a sample of 55 people in the Knight Alzheimer Disease Research Center (ADRC) at Washington University, and a group of 108 people from the Swedish BioFINDER-2 cohort. They validated the assay in a larger cohort of 739 people from the Swedish BioFINDER-2 study.

In both pilot cohorts, plasma MTBR-tau243 levels were significantly increased in Alzheimer's disease dementia compared with mild cognitive impairment or very mild Alzheimer's dementia. Plasma MTBR-tau243 levels also were strongly correlated with CSF levels in the BioFINDER-2 (Spearman's ρ=0.92, P<0.001) and the Knight ADRC (Spearman's ρ=0.79, P<0.001) groups.

The validation cohort included people with Alzheimer's disease, Parkinson's disease, Lewy body dementia, progressive supranuclear palsy (PSP) or corticobasal syndrome (CBS), vascular dementia,

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frontotemporal dementia (FTD), and others. Plasma MTBR-tau243 levels were not elevated in non-Alzheimer's tauopathies; levels in people with PSP or CBS and FTD were similar to those in controls.

Among amyloid-positive participants, plasma MTBR-tau243 consistently demonstrated a significantly higher area under the curve (AUC) compared with p-tau217 and p-tau205 across nearly all tau PET regions. Plasma p-tau217, however, outperformed MTBR-tau243 (AUC 0.97 vs 0.80*)* in predicting amyloid positivity across all participants.

"I believe we will use blood-based p-tau217 to determine whether an individual has Alzheimer's disease, but MTBR-tau243 will be a highly valuable complement in both clinical settings and research trials," noted co-author Oskar Hansson, MD, PhD, of Lund University in Sweden.

"When both of these biomarkers are positive, the likelihood that Alzheimer's is the underlying cause of a person's cognitive symptoms increases significantly, compared to when only p-tau217 is abnormal," he said. "This distinction is crucial for selecting the most appropriate treatment for each patient."

Study limitations include the relatively large volume of plasma (1.5 ml) needed for this first version of the MTBR-tau243 assay, Bateman and co-authors said. Plasma MTBR-tau243 should be further validated in larger populations, including people with higher frequencies of other neurodegenerative or psychiatric diseases, medical comorbidities, and those with a wider range of race and ethnicity.

Judy George covers neurology and neuroscience news for MedPage Today, writing about brain aging, Alzheimer's, dementia, MS, rare diseases, epilepsy, autism, headache, stroke, Parkinson's, ALS, concussion, CTE, sleep, pain, and more. Follow

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Disclosures

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Co-authors reported relationships with nonprofit groups, pharmaceutical companies, and other entities. Hansson also is a part-time remote employee of Eli Lilly.

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