# New insights into tau proteins in people living with ALS

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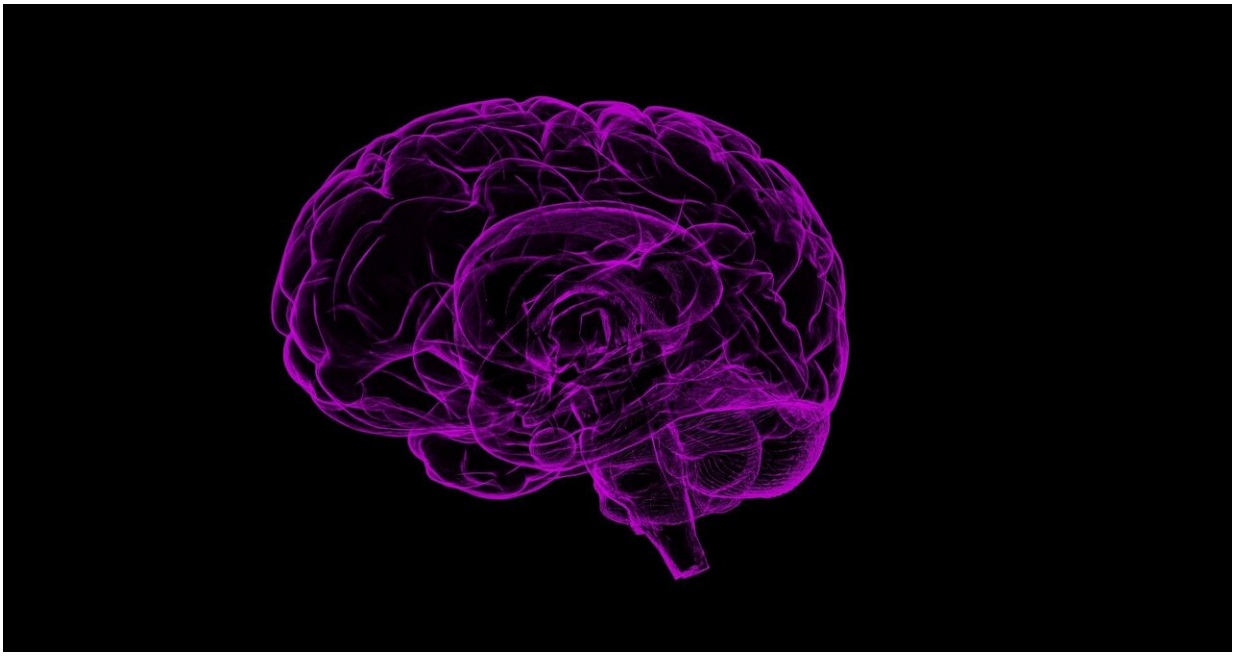

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A team led by investigators at Massachusetts General Hospital (MGH) has shown that people living with amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, who carry a mutation in the *C9orf72* gene exhibit elevated levels of tau and phosphorylated tau protein in the motor cortex region of the brain. The research, which is published in *Brain Pathology*, also identified new genetic mutations in the tau gene and revealed that the ratio of different forms of tau protein may be an indicator of disease

progression in ALS.

"This study focused on tau, a protein that is critical for stabilizing the structure of nerve cells and has been implicated in Alzheimer's disease, and whether it plays a role in ALS pathogenesis as it can form aggregates and lead to cellular dysfunction in a number of neurodegenerative disorders," says senior author Ghazaleh Sadri-Vakili, Ph.D., director of the NeuroEpigenetics Laboratory at the MassGeneral Institute for Neurodegenerative Disease and the Sean M. Healey and AMG Center for ALS at Mass General.

Using post-mortem brain samples from people with ALS, the researchers discovered that tau and one of its phosphorylated forms are increased in the brains of patients whose cells carry a mutation in the *C9orf72* gene that was linked to ALS and dementia 10 years ago. "We also identified new genetic mutations in the tau gene that are specific to ALS and may have functional consequences that may exacerbate disease onset or progression," says Sadri-Vakili.

To determine if tau protein is a viable biomarker for ALS, the team measured tau and its phosphorylated form in cerebrospinal fluid from people living with ALS. The investigators demonstrated that increases in these particular forms of tau protein in patients' cerebrospinal fluid correlated with disease progression. Therefore, tau levels—and specifically the ratio between tau and the phosphorylated form of the tau protein—might help clinicians predict patients' rate of disease progression. "These findings are exciting as there is an unmet and urgent need for disease biomarkers in ALS," notes Sadri-Vakili.

**More information:** Tiziana Petrozziello et al, Novel genetic variants in MAPT and alterations in tau phosphorylation in amyotrophic lateral sclerosis post-mortem motor cortex and cerebrospinal fluid, *Brain Pathology* (2021). DOI: 10.1111/bpa.13035

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