

A newly characterized form of tau may be involved in initiating Alzheimer's disease

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The tau protein accumulates in abnormal shapes in the brains of individuals with Alzheimer's disease (AD), but the early steps of tau misfolding and aggregation are unknown.

A team led by investigators at Massachusetts General Hospital (MGH) and Boston Children's Hospital, recently used advanced proteomics methods to identify a new soluble form of tau that may be involved in these initiating steps.

In their work, which is published in the journal [Brain](#), senior authors Bradley T. Hyman, MD, Ph.D., and Judith A. Steen, Ph.D., and their colleagues used methods including [mass spectroscopy](#) to evaluate various forms of tau present in [brain](#) tissue samples from AD patients, compared with samples from healthy controls.

Mass spectroscopy measures the mass-to-charge ratio of molecules in a sample to determine their structure and [chemical properties](#).

The experiments revealed that in the brains of AD patients, a soluble form of tau is not present in the classical tau aggregates but has many of the same toxic properties.

Characterization of this form of tau by mass spectroscopy by first author Mukesh Kumar, Ph.D. in Steen's lab at Boston Children's FM Kirby Neurobiology Center showed that it is similar to, but seemingly a forme fruste of, the insoluble tau that is found in Alzheimer's disease aggregates at a [molecular level](#).

In medicine, forme fruste (a French term meaning "a crude or unfinished form") is an atypical or attenuated manifestation of a clinical condition.

"This suggests that the soluble tau may be an earlier step in the process that ultimately leads to neurodegeneration, providing new information about potentially how to target that species," say Hyman and Steen.

"We hope to gain additional understanding of the conformation of the

aqueous form of tau that has pathological properties in order to uncover its mechanisms of action, and to design agents that can block it."

More information: Mukesh Kumar et al, Alzheimer proteopathic tau seeds are biochemically a forme fruste of mature paired helical filaments, *Brain* (2024). [DOI: 10.1093/brain/awad378](https://doi.org/10.1093/brain/awad378)

Provided by Massachusetts General Hospital

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