Alzheimer's disease markers could be identified through protein water mobility

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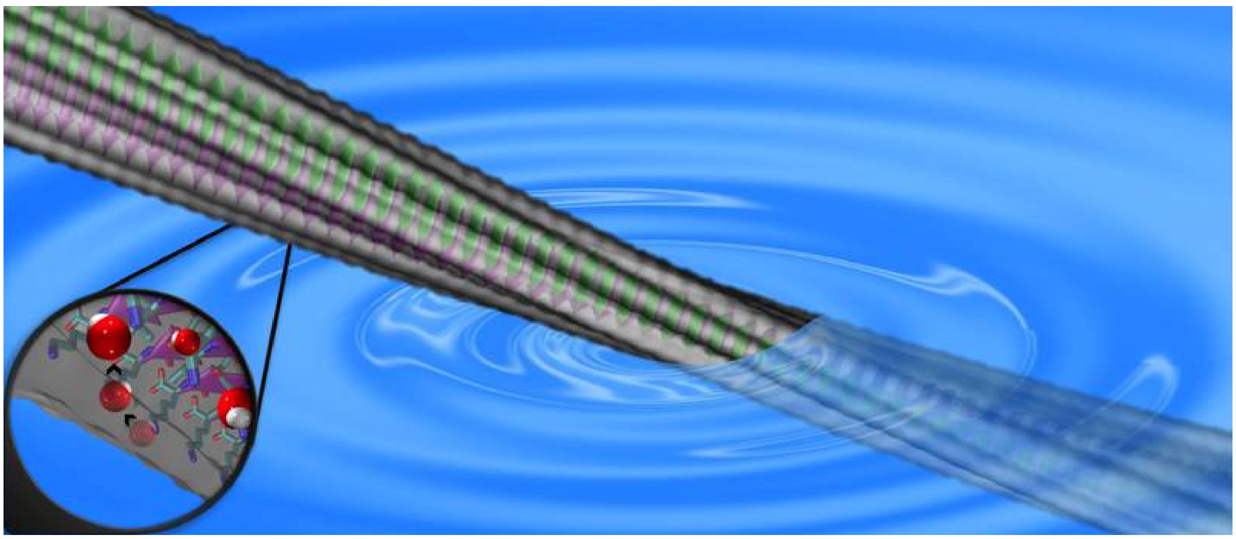

Protein fiber formation is modulated by the surrounding solvent. The knowledge of hydration water properties helps to gain insight into the fibrillation processes and might assist the development of new diagnostic strategies. Credit: IBS /Y.Fichou

A study of water mobility on the surface of tau protein fibres has been conducted by a global team of scientists using neutron scattering experiments at the Institut Laue-Langevin (ILL) in Grenoble, France and the Jülich Centre for Neutron Science at the Heinz Maier-Leibnitz-Zentrum (MLZ) in Garching, Germany. The team, led by IBS scientists, found water mobility on the surface of tau protein fibres is increased;

the findings, reported in *PNAS* (*Proceedings of the National Academy of Sciences* of the United States of America), suggest that the movement of water molecules could be a marker for the presence of amyloid tau fibres and contribute to the detection of Alzheimer's disease.

The accumulation of individual tau protein molecules into amyloid fibres occurs in a variety of neuro-degenerative diseases, damaging the neurons and preventing effective cognitive functions and mental abilities. "Amyloid fibres develop as the intrinsically disordered individual tau proteins aggregate, forming a fibre core surrounded by a so-called 'fuzzy coat'", explains Dr. Jacques-Philippe Colletier, a co-author on the study. "These pathological fibres develop early on in Alzheimer's disease and understanding the mechanism by which tau aggregates is integral to understanding the disease's development and progression."

The team measured and compared the mobility of water molecules on the surface of non-aggregated tau monomers and tau fibres. This was done by carrying out neutron scattering experiments on tau that had been deuterated (whereby all hydrogen atoms are replaced by atoms of its isotope deuterium) at the ILL and the MLZ, international research centres at the leading edge of neutron science and technology that provided the high flux of neutrons needed to probe and record the dynamics of water molecules on the surface of tau. Fibre formation was triggered by adding heparane sulphate which was also deuterated, a technique developed at the Institut de Biologie Structurale (IBS) in Grenoble.

Dr Martin Weik, also a co-author on the study, said: "This study perfectly illustrates the benefits of using neutrons in probing the dynamics of biological samples. This spectroscopic technique allowed us to measure the mobility of water molecules on tau surfaces with high accuracy."

Protein deuteration was used to largely mask the neutron scattering signal of the proteins themselves, and focus instead on the signal from the water molecules on the protein surfaces. Drs Yann Fichou and Giorgio Schirò of the research team were surprised to observe that the amyloid fibres formed after tau aggregation showed enhanced water mobility in their vicinity compared to non-aggregated tau proteins, and explained the additional steps taken. "The experimental result was further refined by carrying out molecular dynamics simulations, suggesting that it is the mobility of water on the surface of the 'fuzzy coat' of tau sticking out of the fibre core that is increased."

The ensemble of results suggests that methodologies sensitive to the diffusion of water, such as diffusion magnetic resonance imaging, could be used to detect increased water mobility in Alzheimer-diseased brains.

More information: "Hydration water mobility is enhanced around tau amyloid fibers." *PNAS*, DOI: 10.1073/pnas.1422824112

Provided by Institut Laue-Langevin

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