Researchers investigate the amyloid-beta peptide behind Alzheimer's

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Oleg N. Antzutkin, professor in chemistry of interfaces, at Luleå University of Technology. Credit: Maria Aberg

Using solid-state nuclear magnetic resonance (NMR) spectroscopy, researchers at Luleå University of Technology in collaboration with Warwick University in the UK for the first time in the world managed to analyse hydrogen bonds in tiny fibrils of Amyloid-beta peptide , which probably causes Alzheimer's disease. Thanks to these new results, there is a successful method avaliable – for analysis of structure of Amyloid-beta peptides in their most toxic form, that is, when they are most dangerous for the brain neurons.

"This is a very important step in research on Alzheimer's disease at a molecular level," says Oleg N. Antzutkin, professor in chemistry of interfaces, at Luleå University of Technology.

Until a few years ago scientists believed that amyloid plaques in the brain directly cause Alzheimer's disease. This is because very large amounts of plaques in the brain of Alzheimer´s patients are usually found. Since the activity of our brain is greatest in the regions responsible for short-term memory, there most of the amyloid plaques were found. Here is also usually where Alzheimer's disease is first noticed, in the form of reduced short-term memory. However, it seems to be that Amyloid plaque are rather a residual of something worse.

Now we know that it is a precursor of amyloid plaques, Amyloid-beta peptide that causes nerve cell death in Alzheimer's patient's brain. When Amyloid-beta, forms small aggregates, oligomers, ie before the peptide clumps together into plaques, it is as most toxic to brain neurons. This has been shown in test tube experiments.

However, the molecular structure of these tiny oligomers of Amyloid-beta peptide, is yet unknown today. Therefore, it is difficult to design antibodies or drugs to hit the right targets and be able to eliminate or block these toxic oligomers, before they cause Alzheimer's disease.

A successful method to solve these molecular structures has not been availiable, until now:

"Now we have a method, which can be employed to identify the specific hydrogen bonds in Amyloid-beta fibrils and therefore to distinguish between different supramolecular structures of Amyloid-beta fibrils. Previous methods have not been able to directly probe these hydrogen bonds. Using our method, it will soon be possible to study hydrogen bonds in key fragments of toxic oligomers that will assist solving their supramolecular structures. What we managed to do now, is an important step towards the full structural characterization of oligomers," says Oleg N. Antzutkin.

Luleå University of Technology has already started a collaboration on the latter topic with professor Torleif Härd´s group at the Swedish University of Agricultural Sciences in Uppsala, with Warwick University and Aarhus University.

By examining hydrogen bonds in Amyloid-beta

fibrils and oligomers, with the aid of nuclear magnetic resonance, professor Oleg N. Antzutkin and his research team has developed a method that provides a real opportunity to design a terminator or blocker of Amyloid-beta aggregates, before they become the most toxic for nerve cells and cause Alzheimer's disease.

About 80,000 Swedes per year diagnosed with Alzheimer's disease that is a severe dementia. The drugs available today can not cure the disease, only alleviate the symptoms.

Hydrogen bonds are essential in stabilisation of molecular and supramolecular structures in biological systems. Via REAPDOR solid state NMR spectroscopy professor Oleg N. Antzutkin and his group, has succeeded in measuring distances between the magnetic isotopes 15N and 17O in the amino groups and carbonyl groups, respectively, in Amyloid-beta fibrils. Simply stated, 15N NMR signal from specifically 15N and 17O enriched amino acids is decreasing, when 15N and 17O are in a near spatial vicinity from each other, that indicates a hydrogen bond.

More information: Antzutkin, O. Hydrogen Bonding in Alzheimer's Amyloid-beta Fibrils probed by 15N {17O} REAPDOR Solid-State NMR Spectroscopy. *Angewandte Chemie International Edition*. onlinelibrary.wiley.com/doi/10 … e.201203595/abstract

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