

# Possible biological function for the Alzheimer protein amyloid-beta

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A new study from Karolinska Institutet shows that amyloid- $\beta$ -peptides, which are thought to be toxic and a suspected cause of Alzheimer's disease, actually have a biological function. The discovery, which is published in the journal *Brain*, can help to explain why the so-called cholinergic signal systems are the first to be damaged on the onset of the disease.

Research on amyloid- $\beta$ -peptides in Alzheimer's disease has mainly been based on their presumed toxicity and causal role in the development of the disease. At the early stages of development, Alzheimer's disease particularly affects cholinergic signalling via the [neurotransmitter acetylcholine](#), but why this is the case is still unknown.

The present study indicates that amyloid- $\beta$  has a physiological function and influences the balance of acetylcholine in the brain. What the researchers have discovered is that amyloid- $\beta$  forms particular complexes that they call BA $\beta$ AC (BChE/AChE/A $\beta$ /ApoE complex). The complexes contain two different enzymes that break down acetylcholine at the synapses between [nerve cells](#) or between nerve cells and [glial cells](#).

"When amyloid- $\beta$  binds to them, the enzymes become hyperactive, and the neurotransmitter acetylcholine breaks down more rapidly," says principal investigator, Dr Taher Darreh-Shori at Karolinska Institutet's Department of Neurobiology, Care Sciences and Society. "This could, in turn, change the functional status of the brain's neuroglial cells, such as

astrocytes and oligodendrocytes."

Surprised the team

Another find, which surprised the team, concerns apolipoprotein-e4 (ApoE4), which is the best confirmed genetic risk factor for Alzheimer's. It is not known how ApoE increases the risk of [disease](#), but previous research has linked ApoE to the accumulation of amyloid- $\beta$  plaque in the brains of Alzheimer's patients.

"Our results show that ApoE keeps amyloid- $\beta$  soluble in the form of amyloid-ApoE complexes, which leads to the accumulation of reactive BA $\beta$ A complexes," says Dr Darreh-Shori. "High levels of ApoE seem to have a pathological effect on this mechanism, which could cause the cholinergic nerve pathways characteristic of Alzheimer's to degrade."

He and his co-researchers will now study whether the BA $\beta$ A complexes differ between the brains of Alzheimer's patients and healthy people, and if it is possible to cancel their effect.

The study was financed by grants from several bodies, including the Åhlén Foundation, the Dementia Foundation of the Swedish Dementia Association, the Olle Engkvist Foundation and the Åke Wiberg Foundation.

**More information:** Rajnish Kumar et al. Amyloid- $\beta$  peptides act as allosteric modulator of cholinergic signalling through formation of soluble BA $\beta$ ACs, *Brain* (2015). [DOI: 10.1093/brain/awv318](https://doi.org/10.1093/brain/awv318)

Provided by Karolinska Institutet

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