Aβ38 in the brains of patients with sporadic and familial Alzheimer's disease and transgenic mouse models.

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Research question and background

The pathogenesis of Alzheimer's disease (AD) is believed to be closely dependent on deposits of neurotoxic amyloid β-peptide (Aβ) which become abundantly present throughout the central nervous system in advanced stages of the disease. The different Aβ-peptides existing are generated by subsequent cleavage of the amyloid precursor protein (A□PP) and may vary in length and differ at their C-terminus. Despite extensive studies on the most prevalent species Aβ40 and Aβ42, Aβ-peptides with other C-termini such as Aβ38 have not received much attention yet.

Methods and tissues used

Immunohistochemistry, brain material from Netherlands Brain Bank as well as from Uppsala and Helsinki.

Results and conclusion

In the present study we used a highly specific and sensitive antiserum against Aβ38 to analyze the distribution of this Abeta species in cases of sporadic and familial AD, as well as in the brains of a series of established transgenic AD mouse models. We found Aβ38 to be present as vascular deposits in the brains of the majority of sporadic AD cases, whereas it is largely absent in non-demented control cases. Aβ38-positive extracellular plaques were virtually limited to familial cases.

Interestingly we observed Aβ38-positive plaques not only among familial cases due to APP mutations, but also in cases of familial AD caused by presenilin (PSEN) mutations. Furthermore we demonstrate that Aβ38 deposits in the form of extracellular plaques are common in several AD transgenic mouse models carrying either only A□PP, or combinations of APP, PSEN1 and Tau transgenes.