Analysis of BACE1 expression and substrate processing in early and late stage Alzheimer's disease

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Research question and background

Alzheimer's disease (AD) is characterized by the accumulation of amyloid plaques, which are predominantly composed of amyloid beta-peptide (Abeta)[1]. Two principal physiological pathways either prevent or promote Aβ generation from its precursor (amyloid precursor protein; APP) in a competitive manner. Modulation of the amyloidogenic pathway is currently exploited by anti-Abeta therapeutic strategies. Although APP processing has been studied in great detail, unknown proteolytic events appear to hinder stoichiometric analyses of APP metabolism in vivo. We now identified higher molecular weight C-terminal fragments of APP (CTF-eta in addition to the long-known alpha- and beta-secretase (a disintegrin and metalloproteinase; ADAM10 and beta-site APP cleaving enzyme 1; BACE1) generated CTF-alpha and CTF-beta. Eta secretase were identified as members of the family of matrix-metalloproteases (MMPs). We are investigating MMP expression and BACE1 expression and compare it to the processing pattern of known substrates like APP.

Methods and tissues used

The tissue is investigated by Western blot analysis for changes in secretase expression and in changes of substrate processing comparing AD samples to healthy controls.

Results and conclusion

No results are published so far. The Investigation is ongoing.