P026 Analysis of Amyloid-β Peptide Composition in Amyloid Deposits in Human Alzheimer's Disease Brains and in Transgenic Mice

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The composition of amyloid-β (Aβ) peptides in plaques and vascular amyloid were studied using a combination of laser dissection microscopy followed by urea-based SDS-PAGE and Western Blot. The approach enabled the specific collection of single compact or diffuse plaques from human and murine brains and for analysis of the constituent Aβ species. We detected Aβ 1-40 as the main component in compact human plaques, with low amounts of Aβ 1-42. Amyloid deposits isolated from cortical vessels of a patient with cerebral amyloid angiopathy (CAA) contains predominantly Aβ 1-40. In contrast, diffuse human plaques predominantly consist of Aβ 1-42 with minor amounts of Aβ 1-40. In comparison, compact plaques of transgenic PS2APP mice showed mainly Aβ 1-40 and in addition also smaller amounts of Aβ 1-42 and the C-terminal truncated fragments Aβ 1-37, Aβ 1-38 and Aβ 1-39 were found. In diffuse plaques of transgenic mice Aβ 1-42 and/or Aβ 1-38 was identified.
Considering that Aβ 1-42 is far more prone to aggregation than Aβ 1-40, our results strongly support the concept that diffuse plaques would be the first morphologically detectable deposits, followed by the subsequent accrual of Aβ 1-40 and the formation of compact plaques.