Revealing the complex nature of amyloid beta and its relation to dementia

Akademisk avhandling

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SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR NEUROVETENSKAP OCH FYSIOLOGI
Revealing the complex nature of amyloid beta and its relation to dementia

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Abstract
Alzheimer disease (AD) is the most common type of dementia and characterized by the accumulation of amyloid plaques in the extracellular space of the brain parenchyma. Amyloid plaques consist of amyloid beta peptides (Aβ). Amyloid pathology can also be involved in other types of dementia, either as a driving force or as a coexisting pathology. In this thesis was the Aβ peptide content in relation to different amyloid deposits, types of dementia and regions investigated with the goal to improve our understanding of amyloid pathology in dementia. To analyse Aβ peptides, a hybrid immunoprecipitation - mass spectrometry method was used. The studies presented here reveal a different Aβ peptide pattern in individuals with amyloid pathology, but cognitively unaffected, compared with AD patients, who suffer from cognitive decline. Moreover, vascular Aβ contribution, due to cerebral amyloid angiopathy, differs from amyloid plaque Aβ contribution. For other groups with plaque pathology, such as Down syndrome, dementia with Lewy bodies, and Parkinson’s disease dementia, there are minor differences in the Aβ peptide pattern compared with AD. In this work, the Aβ content of the protofibril/oligomeric forms, a major anti-amyloid therapeutical target, is also revealed. This thesis can be the beginning of a deeper understanding of the complex nature of amyloid pathology and its contribution to dementia.

Keywords: Amyloid beta, dementia, Alzheimer’s disease, cerebral amyloid angiopathy, Down syndrome, pathological ageing, dementia with Lewy bodies, Parkinson’s disease dementia, mass spectrometry