Göteborg, 2020

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

Akademisk avhandling

Som för avläggande av medicinsk doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal **Arvid Carlsson**, Medicinaregatan 3, den fredag den **13 november 2020**, klockan **9:00**

av Eleni Gkanatsiou

Fakultetsopponent:

Stefan Lichtenhaler, professor

Technical University Munich, Germany

Avhandlingen baseras på följande delarbeten

I. Murray CE, Gami-Patel P, **Gkanatsiou E**, Brinkmalm G, Portelius E, Wirths O, Heywood W, Blennow K, Ghiso J, Holton JL, Mills K, Zetterberg H, Revesz T, Lashley T. The presubiculum is preserved from neurodegenerative changes in Alzheimer's disease. Acta Neuropathol Commun. 2018 Jul 20;6(1):62

II. **Gkanatsiou E**, Portelius E, Toomey CE, Blennow K, Zetterberg H, Lashley T, Brinkmalm G. A distinct brain beta amyloid signature in cerebral amyloid angiopathy compared to Alzheimer's disease Neurosci Lett. 2019 May 14;701:125-131.

III. **Gkanatsiou E**, Sahlin C, Portelius E, Johannesson M, Söderberg L, Fälting J, Basun H, Möller C, Odergren T, Zetterberg H, Blennow K, Lannfelt L, Brinkmalm G. Characterization of monomeric and soluble aggregated Aβ in Down's syndrome and Alzheimer's disease brains. Submitted

IV. **Gkanatsiou E**, Nilsson J, Toomey C, Vrillon A, Kvartsberg H, Portelius E, Zetterberg H, Blennow K, Brinkmalm A, Lashley T, Brinkmalm G. Amyloid pathology and synaptic loss in pathological aging. Manuscript

V. **Gkanatsiou E**, Hansen D, Portelius E, Nilsson J, Zetterberg H, Blennow K, Warner T, Lashley T, Brinkmalm G. Exploring amyloid beta peptides in Parkinson's disease dementia and dementia with Lewy bodies. Manuscript

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR NEUROVETENSKAP OCH FYSIOLOGI

GÖTEBORGS UNIVERSITET

Göteborg, 2020

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

Eleni Gkanatsiou

Department of Psychiatry and Neurochemistry, Institute of Neuroscience and physiology, Sahlgrenska academy at the University of Gothenburg, Sweden

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

ISBN: 978-91-8009-060-5 (PRINT) http://hdl.handle.net/2077/65140
ISBN: 978-91-8009-061-2 (PDF)