Göteborg, 2021

CEREBROSPINAL FLUID BIOMARKERS AND COGNITION IN OLDER ADULTS

Akademisk avhandling som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Europa, Wallenberg Centrum, Medicinaregatan 20A, Göteborg, den 12 maj, klockan 9:00.

av Maya Arvidsson Rådestig

Fakultetsopponent:
Professor Emeritus David Smith
Department of Pharmacology
University of Oxford
Storbritannien

Avhandlingen baseras på följande delarbeten

I. M Arvidsson Rådestig, J Skoog, H Zetterberg, J Kern, A Zettergren, S Sacuiu, M Waern, H Wetterberg, K Blennow, I Skoog, S Kern. Cognitive Performance and Cerebrospinal Fluid Markers in Preclinical Alzheimer's Disease: Results from the Gothenburg H70 Birth Cohort Studies.
Journal of Alzheimer's disease 2021; 79 (2021) 225–235

II. M Arvidsson Rådestig, J Skoog, H Zetterberg, T Skillbäck, A Zettergren, T Rydberg Sterner, M Mellqvist Fässberg, S Sacuiu, M Waern, H Wetterberg, K Blennow, I Skoog, S Kern. Cognition in older adults with elevated CSF neurofilament light and neurogranin – a H70 cross-sectional study.
Manuscript.

III. M Arvidsson Rådestig, I Skoog, T Skillbäck, H Zetterberg, J Kern, A Zettergren, U Andreasson, H Wetterberg, S Kern, MD, K Blennow. Cerebrospinal fluid biomarkers of axonal and synaptic degeneration in a population-based sample.
Manuscript.

På grund av rådande nationella restriktioner att minska smittspridning av covid-19 är disputationen öppen för allmänheten via live-streaming. Länk kommer att läggas ut på institutionens hemsida.

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR NEUROVETENSKAP OCH FYSIOLOGI

GÖTEBORGS UNIVERSITET

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CEREBROSPINAL FLUID BIOMARKERS AND COGNITION IN OLDER ADULTS

Maya Arvidsson Rådestig

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Abstract

Alzheimer's disease (AD) is the most common type of dementia. The cause of the disease is unknown, but a substantial amount of evidence suggest that the disease is started by an imbalance in the production and clearance of the protein amyloid-β, which then starts a cascade of neurodegenerative events leading to cognitive symptoms. Biomarkers in cerebrospinal fluid (CSF, amyloid-β and tau) reflecting the pathological changes in AD can be seen as early as 10-20 years before the clinical diagnosis. Pathological levels of the known CSF AD biomarkers in cognitively normal individuals can be seen frequently in older adults and this is called preclinical AD. This thesis explores different CSF biomarkers for AD and cognition in older adults in the preclinical phase of AD using a research framework classification system for preclinical AD- the so called ATN system. Study I explores cognition in older adults with preclinical AD, using the ATN classification system. We investigated the hypothesis that individuals with positive AD biomarkers would have lower cognitive test scores than those without biomarkers, and we show this for some tests primarily in the memory domain. However, the groups with and without biomarkers performed similarly in most tests. Study II investigates the relationship between cognition and the neurodegeneration biomarker neurofilament light protein (NfL) and the synaptic degeneration biomarker neurogranin (Ng). We investigated the hypothesis that individuals with high levels of the biomarkers NfL and Ng would have subtle cognitive decline compared to those with normal levels of these biomarkers. We found that this was true in a few cognitive tests, however, in most of the tests the groups with and without high levels of NfL and Ng performed similarly. Study III investigates the levels of the biomarkers NfL and Ng in the ATN groups in cognitively normal older adults. We found that individuals with neurodegeneration (tau pathology) had higher levels of NfL and Ng, but we did not find any difference in NfL or Ng levels in participants with amyloid pathology compared to those without amyloid pathology. This suggests that older adults with T-tau pathology have increased axonal and synaptic damage. In conclusion, the results from this thesis suggest that the known CSF biomarkers for AD and synaptic and neurodegeneration could be valuable biomarkers in the earliest phase of AD.

Keywords: preclinical Alzheimer's disease, cerebrospinal fluid, biomarkers, cognition

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