White matter microstructure disruption in early stage amyloid pathology

Lyduine E. Collij, Silvia Ingala, Herwin Top, Viktor Wottschel, Kristine E. Stickney, Jori Tomasse,n Elles Konijnenberg, Mara ten Kate, Carole Sudre, Isadora Lopes Alves, Maqsood M. Yaqub, Alle Meije Wink, Dennis Van 't Ent, Philip Schelten,s Bart N.M. van Berckel, Pieter Jelle Visser, Frederik Barkhof, Anouk Den Braber

Abstract:

Introduction: Amyloid beta (Aβ) accumulation is the first pathological hallmark of Alzheimer's disease (AD), and it is associated with altered white matter (WM) microstructure. We aimed to investigate this relationship at a regional level in a cognitively unimpaired cohort.

Methods: We included 179 individuals from the European Medical Information Framework for AD (EMIF-AD) preclinAD study, who underwent diffusion magnetic resonance (MR) to determine tract-level fractional anisotropy (FA); mean, radial, and axial diffusivity (MD/RD/AxD); and dynamic [18F]flutemetamol) positron emission tomography (PET) imaging to assess amyloid burden.

Results: Regression analyses showed a non-linear relationship between regional amyloid burden and WM microstructure. Low amyloid burden was associated with increased FA and decreased MD/RD/AxD, followed by decreased FA and increased MD/RD/AxD upon higher amyloid burden. The strongest association was observed between amyloid burden in the precuneus and body of the corpus callosum (CC) FA and diffusivity (MD/RD) measures. In addition, amyloid burden in the anterior cingulate cortex strongly related to AxD and RD measures in the genu CC.

Discussion: Early amyloid deposition is associated with changes in WM microstructure. The non-linear relationship might reflect multiple stages of axonal damage.

Published: 1 April 2021

Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring

https://doi.org/10.1002/dad2.12124