

Cortical gray–white matter contrast alterations precede amyloid- β positivity and macrostructural changes in older adults without dementia

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Abstract:

INTRODUCTION: Early Alzheimer's disease (AD) involves subtle cortical changes that may precede atrophy. Magnetic resonance imaging (MRI) microstructural markers may detect earlier pathology than classical morphometry.

METHODS: We analyzed cross-sectional MRI and amyloid- β (A β) positron emission tomography (PET) data from 1323 non-demented AMYPAD participants. Cortical volume, thickness, gray–white matter contrast (GWC), and mean diffusivity (MD) were related to global A β burden and estimated time to A β -positivity using regression, correlation, and change-point analyses.

RESULTS: Microstructural measures showed stronger age associations than macrostructural measures, whereas all measures were unaffected by apolipoprotein E (APOE) - ϵ 4 carriership. GWC and MD showed minimal overlap with volume and thickness. Higher A β burden was most strongly associated with reduced GWC and cortical thinning. Change-point analyses showed GWC alterations preceded A β -positivity by several years.

DISCUSSION: Cortical microstructural MRI, particularly GWC, changes earlier than atrophy and may serve as an early in vivo marker of AD pathology.

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