

Accelerated Regional Brain Volume Trajectories Differentiate Alzheimer’s Disease From Normal Aging And Mild Cognitive Impairment

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Accelerated regional brain atrophy clearly differentiates Alzheimer’s disease from normal aging and MCI — the left hippocampus and inferior lateral ventricle show the steepest, most distinctive longitudinal trajectories in AD.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Alzheimer’s disease (AD) is associated with progressive regional brain degeneration. Longitudinal brain volume changes may better reflect disease progression than cross-sectional measures. This study examined whether brain volume changes are faster in AD compared to cognitively normal (CN) aging and mild cognitive impairment (MCI). Linear mixed-effects models were applied separately for each region, including group, time, group×time interaction, age, sex, and intracranial volume as fixed effects, with subject-specific random intercepts and slopes	Structural MRI data from 230 participants were analyzed, including AD (n = 65; 45 females), CN (n = 79; 38 females), and MCI (n = 86; 23 females). Brain volumes were extracted for 216 cortical and subcortical regions using DLMUSE, a deep learning-based brain segmentation method. Six regions known to be vulnerable in AD were selected for longitudinal analysis: left hippocampus, left inferior lateral ventricle, left posterior cingulate gyrus, left parahippocampal gyrus, left entorhinal cortex, and left precuneus. Analyses were performed using jamovi (GAMLj) and R, and estimated marginal means were used to visualize group-specific trajectories.	Clear differences in longitudinal brain volume trajectories were observed across diagnostic groups. In the left hippocampus, AD showed the fastest rate of change (β = +78.8 units/year), with significantly slower changes in CN (p < 0.001) and MCI (p = 0.021). The left inferior lateral ventricle demonstrated marked expansion in AD (β = +740.3 units/year), distinguishing AD from normal aging (p = 0.048). Supporting regions within the default mode network and medial temporal lobe also showed accelerated atrophy in AD, including the posterior cingulate gyrus and parahippocampal gyrus (both p < 0.05). Across all examined regions, MCI exhibited intermediate trajectories, while CN showed relative longitudinal stability.	Accelerated regional brain volume trajectories clearly differentiate Alzheimer’s disease from normal aging and mild cognitive impairment. These findings highlight the value of longitudinal, region-specific measures as sensitive markers of disease progression. Including Random effects along with fixed effects in the linear mixed model helps to avoid under/overestimate of parameters , and give reliable interpretation of results Future work will extend this approach to all extracted brain regions to provide a comprehensive map of longitudinal neurodegeneration in AD.	1. Davatzikos C, et al. DLMUSE: deep learning-based brain region segmentation for large-scale neuroimaging studies. 2. Jack CR Jr, et al. The Alzheimer’s Disease Neuroimaging Initiative (ADNI): MRI methods. J Magn Reson Imaging. 2008. 3. Bates D, et al. Fitting linear mixed-effects models using lme4. J Stat Softw. 2015.
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