

Longitudinal Structural Neuroimaging Study of Lecanemab in Early Alzheimer’s Disease: A Subfield Analysis of Hippocampal and Amygdalar Volumes



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Background	METHODS	RESULTS	CONCLUSIONS
Lecanemab, a novel anti-amyloid-β monoclonal antibody, has been shown to slow clinical progression in early Alzheimer’s disease (AD). However, its effects on brain structure, particularly the dynamic volumetric changes in hippocampal and amygdalar subfields, remain unclear. This study aimed to longitudinally assess the volumetric changes in the whole brain and hippocampal-amygdalar subregions at 3, 6, and 12 months after lecanemab treatment using high-resolution MRI.	This longitudinal observational study included patients with early AD receiving standard lecanemab therapy. 3D-T1 weighted MRI scans were performed at baseline, 3, 6, and 12 months. Automated segmentation software (e.g., FreeSurfer) was used to calculate total intracranial volume (eTIV), total gray matter volume (TotalGM), and the volumes of the whole hippocampus and amygdala, along with their anatomical subfields (e.g., hippocampal head/body, CA1-4, dentate gyrus, basolateral, lateral nuclei, etc.) bilaterally. Finally, changes in volume from baseline at each time point were analyzed.	A total of 179 patients were included. The eTIV showed no significant change at any time point ($P>0.05$), indicating measurement stability. The rate of decline in total brain volume was significantly slowed at 6 months ($P=0.013$) and 12 months ($P=0.011$) compared to baseline. Hippocampal volumetric changes exhibited significant time- and subfield-specific effects: the rate of volume loss in the left whole hippocampus and several key subfields (e.g., hippocampal body, CA1-body, GC-ML-DG-body) showed significant attenuation starting at 6 months (P values from <0.001 to 0.028), with some effects persisting at 12 months. A similar trend was observed in the right hippocampus, though significance in some subfields emerged later. Atrophy in specific amygdalar nuclei (e.g., left cortical nucleus) was also significantly slowed after 6 months.	Lecanemab treatment significantly attenuates the rate of whole-brain and specific hippocampal subfield (notably the body) atrophy in early AD patients after 6 months, with some protective effects sustained at 12 months. Hippocampal subfields respond heterogeneously to treatment, with the left hippocampal body and dentate gyrus potentially serving as sensitive indicators. This study provides direct structural neuroimaging evidence for the neuroprotective effect of lecanemab.