

Longitudinal Alterations of white matter microstructure in Lecanemab-treated patients with mild cognitive impairment and early Alzheimer's Disease

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KEY TAKE AWAY:

- After Lecanemab treatment, the treatment group showed significant increases in MD, AxD, and RD alongside decreased FA in key fiber tracts (e.g., corpus callosum, anterior commissure, left SLF-II), indicating repair of white matter microstructural damage.
- The spatial distribution patterns of these diffusion changes suggest that Lecanemab’s effects involve myelin repair, axonal abnormality correction, and edema alleviation, offering imaging-based clues for monitoring therapeutic response.

BACKGROUND

RESULTS

CONCLUSIONS

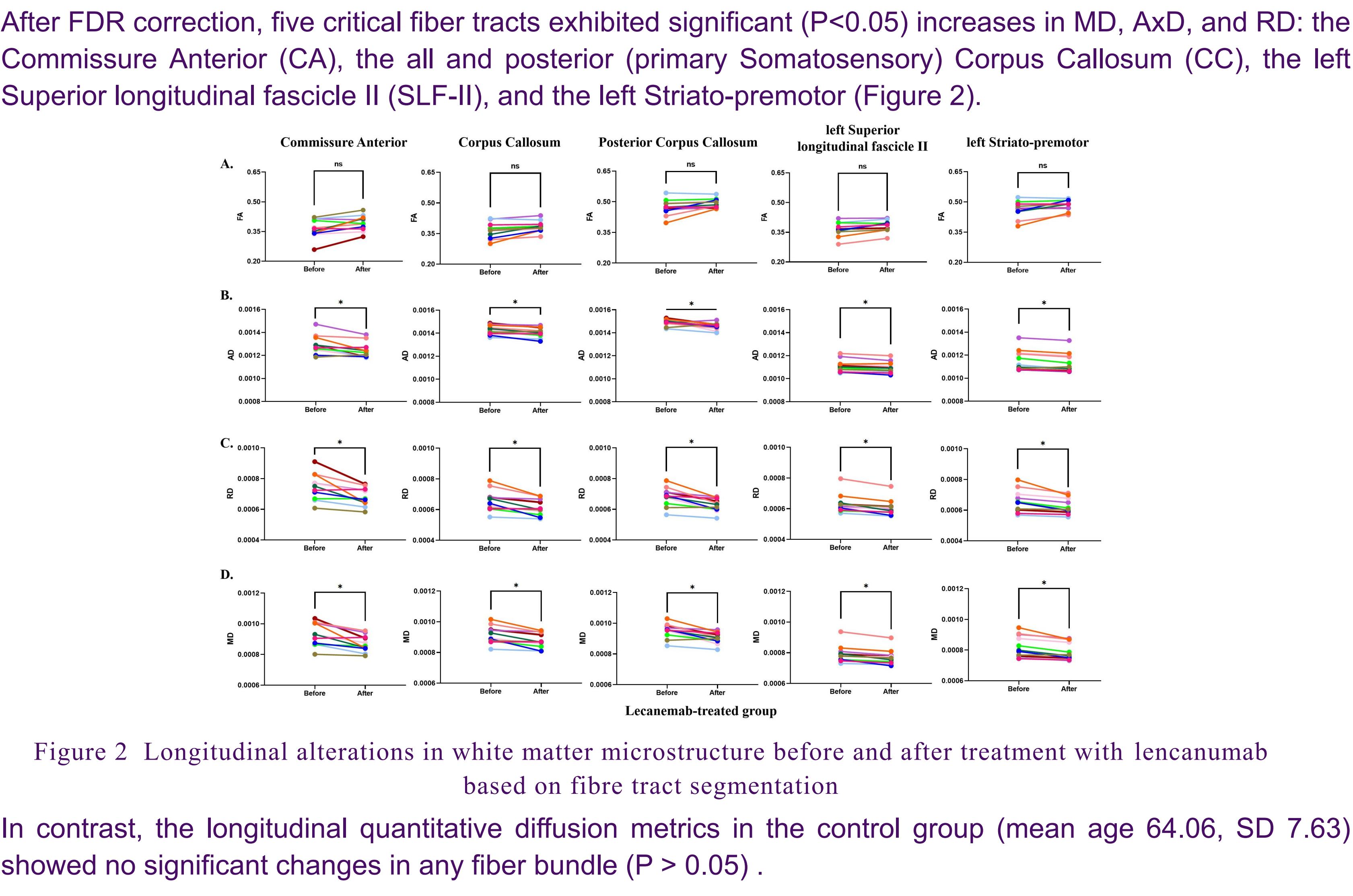
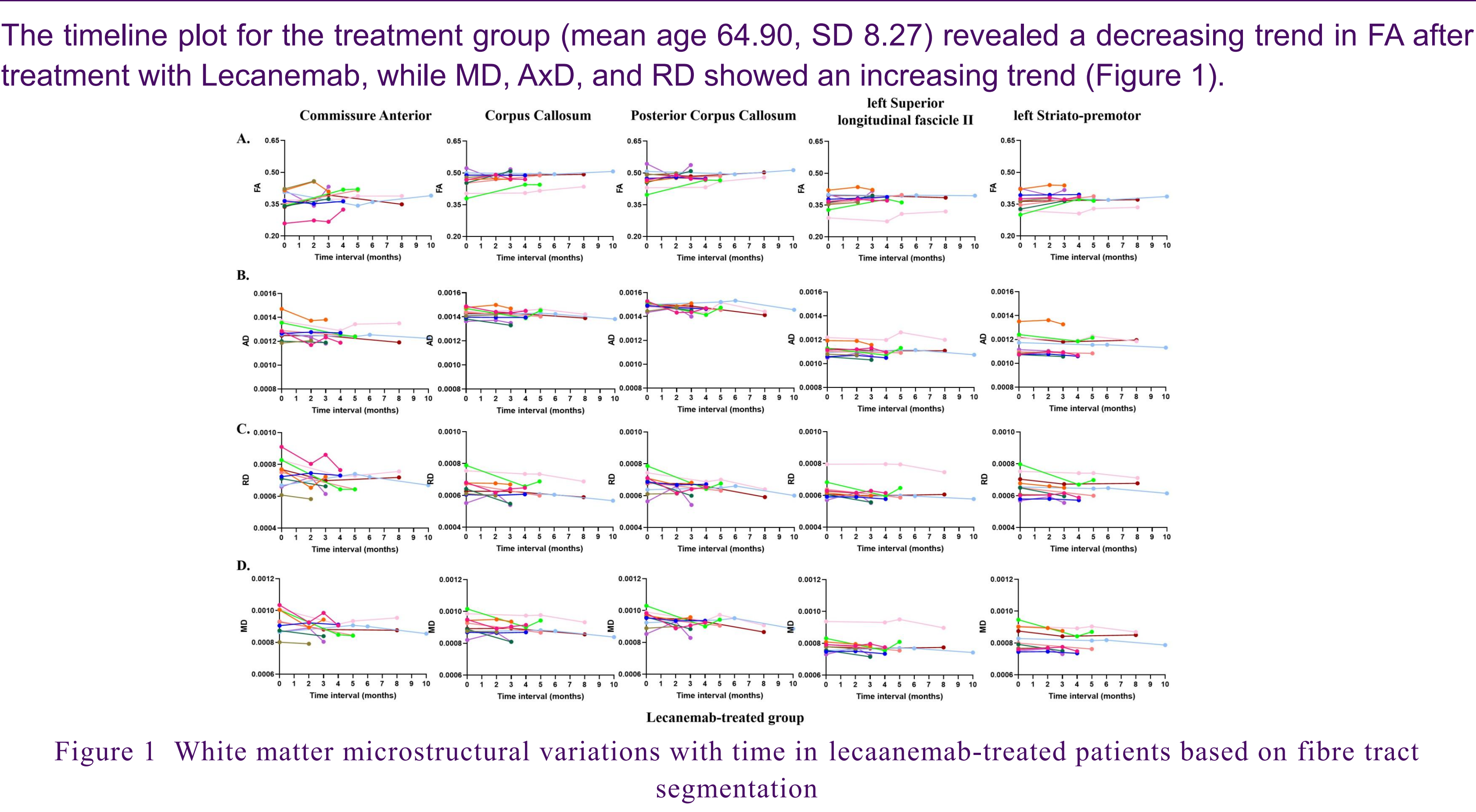
Alzheimer's disease (AD) is characterized by progressive neurodegeneration, including reduced white matter (WM) integrity [1-2]. Its hallmark amyloid β (A β) deposits and tau pathology induce axonal degeneration, myelin destruction, and neuroinflammation, leading to abnormal diffusion indices in critical fiber tracts [3]. This disrupts whole-brain network connectivity and accelerates cognitive decline. Lecanemab, a monoclonal antibody targeting A β , has demonstrated clinical efficacy [4-5], but its effects on WM microstructure remain poorly understood. This study is aim to investigate the effects of lecanemab treatment on white matter microstructural integrity in patients with mild cognitive impairment (MCI) and early AD using diffusion tensor imaging (DTI) tractography with automated fiber tract segmentation.

METHODS

This study included 11 patients diagnosed with MCI or early AD who received intravenous infusions of lecanemab every two weeks. Additionally, the study also included 18 patients with MCI or early AD who were matched for age and education level with the treatment group but didn't receive any anti-A β therapy, as the control group. All participants underwent at least two magnetic resonance imaging (MRI) scans in 0 to 10 months period.

All imaging was performed using a 3T MRI scanner according to standardized protocols. The analysis of DTI data was conducted as follow: DTI data preprocess (MRtrix), reconstruction and automated 72 fiber bundle segmentation (<https://github.com/MIC-DKFZ/TractSeg>). Ultimately, quantitative diffusion metrics include were extracted including fractional anisotropy (FA), mean diffusivity (MD), axial (AxD) and radial (RD) diffusivity along the segmented tracts.

Longitudinal changes were analyzed using paired t-tests or non-parametric tests, depending on the distribution of the data. Then, false discovery rate (FDR) correction (p<0.05) identified significant microstructural changes.



Lecanemab can improve AD-induced damage in white matter microstructure, repair myelin damage, axonal abnormalities, and tissue oedema. The fibers spatial distribution characteristics of these changes reflect the complex interplay between AD pathology and therapeutic effects, potentially providing partial imaging-based evidence for monitoring the therapeutic efficacy of lecanemab. Further investigations integrating multi-modal neuroimaging and biomarkers are warranted to elucidate the mechanisms underlying these microstructural alterations and their clinical implications.

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