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Background

- Lecanemab, an anti-amyloid beta ($A\beta$) antibody, is the first FDA-approved therapy for early Alzheimer's disease (AD). This study aimed to investigate its clinical efficacy, track the dynamic trajectory of plasma biomarkers, and explore the correlation between biomarker changes and clinical outcomes in patients with early AD.

Methods

- Study design:** A multicenter, prospective observational cohort study.
- Participants:** Patients with early AD receiving lecanemab were consecutively enrolled from 30 tertiary hospitals in Northwest China (July 2024–November 2025).
- Follow-up visits:** Baseline (V0), 3 months (V1), 6 months (V2), 9 months (V3).
- Plasma biomarker detection:** Electrochemiluminescence assay was used to measure $A\beta$ 1-40, $A\beta$ 1-42, p-tau181, p-tau217, GFAP, and NFL.
- Clinical assessments:** Cognitive and global function were evaluated via MMSE, CDR-SB, ADAS-cog, and ADCS-ADL.
- Statistical analysis:** Repeated measures ANOVA, linear mixed models and multiple linear regression were applied to analyze biomarker dynamics and their correlations with clinical outcomes.

Results

- A total of 54 patients with early AD were included; 64.8% were female, and 61.1% were APOE ϵ 4 carriers.
- 40 patients completed the V1 visit, 24 completed the V2 visit, and 12 completed the V3 visit. Baseline plasma GFAP levels were positively correlated with years of education ($r=0.326$, $P=0.019$).
- Plasma p-tau181 and the p-tau181/ $A\beta$ 42 ratio were negatively correlated with MMSE scores ($P < 0.05$), while plasma $A\beta$ 1-40 and $A\beta$ 1-42 were negatively correlated with ADAS-cog scores ($P < 0.05$), suggesting these markers are associated with the degree of cognitive impairment.

- Following lecanemab treatment, plasma $A\beta$ 1-40 and $A\beta$ 1-42 levels showed an upward trend, while GFAP, p-tau181, and the p-tau181/ $A\beta$ 42 ratio showed a general downward trend. Significant changes in most markers were observed as early as 3 months after treatment initiation ($P < 0.05$) (Figure 1).

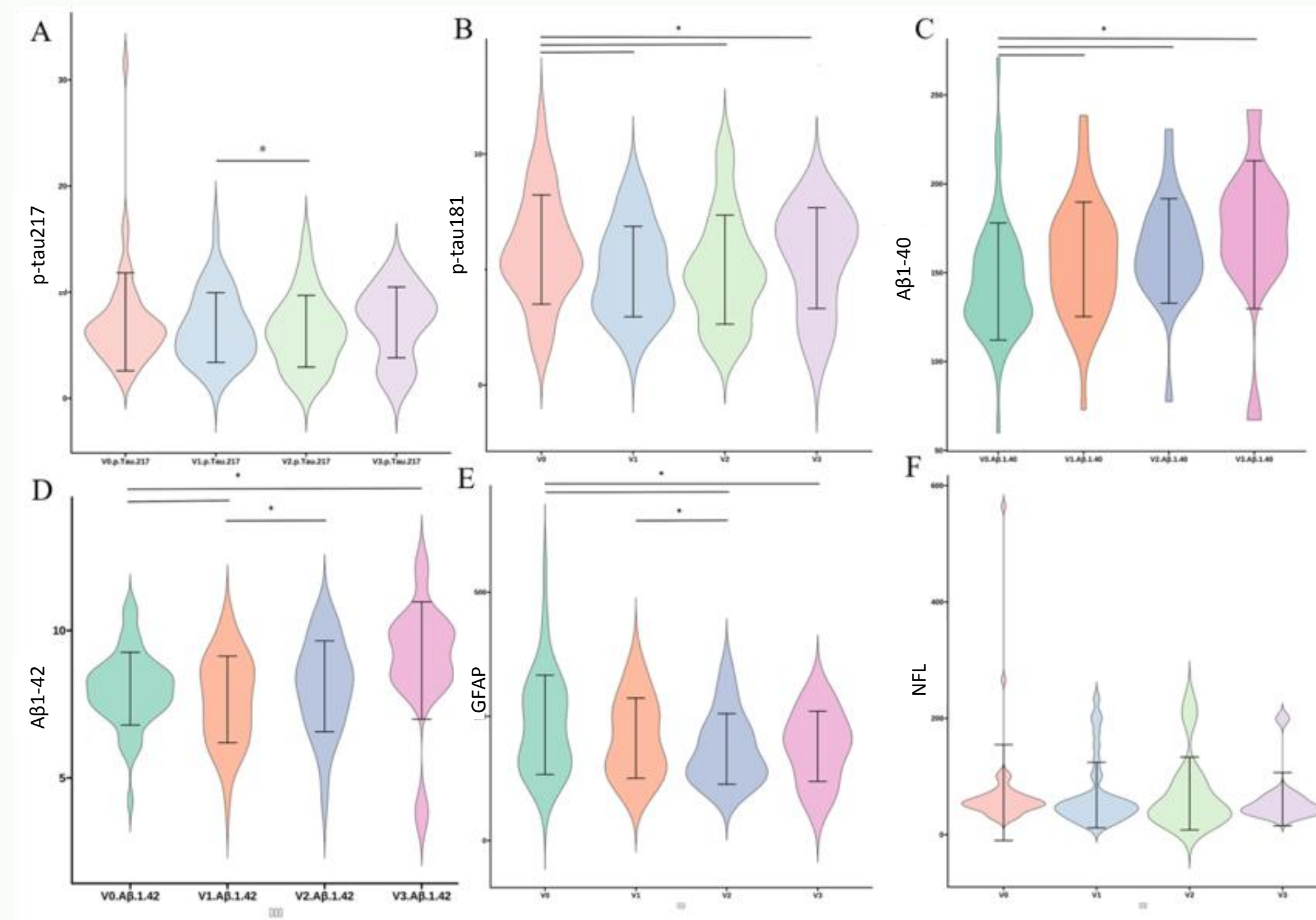


Figure 1. Dynamic changes in plasma biomarkers.

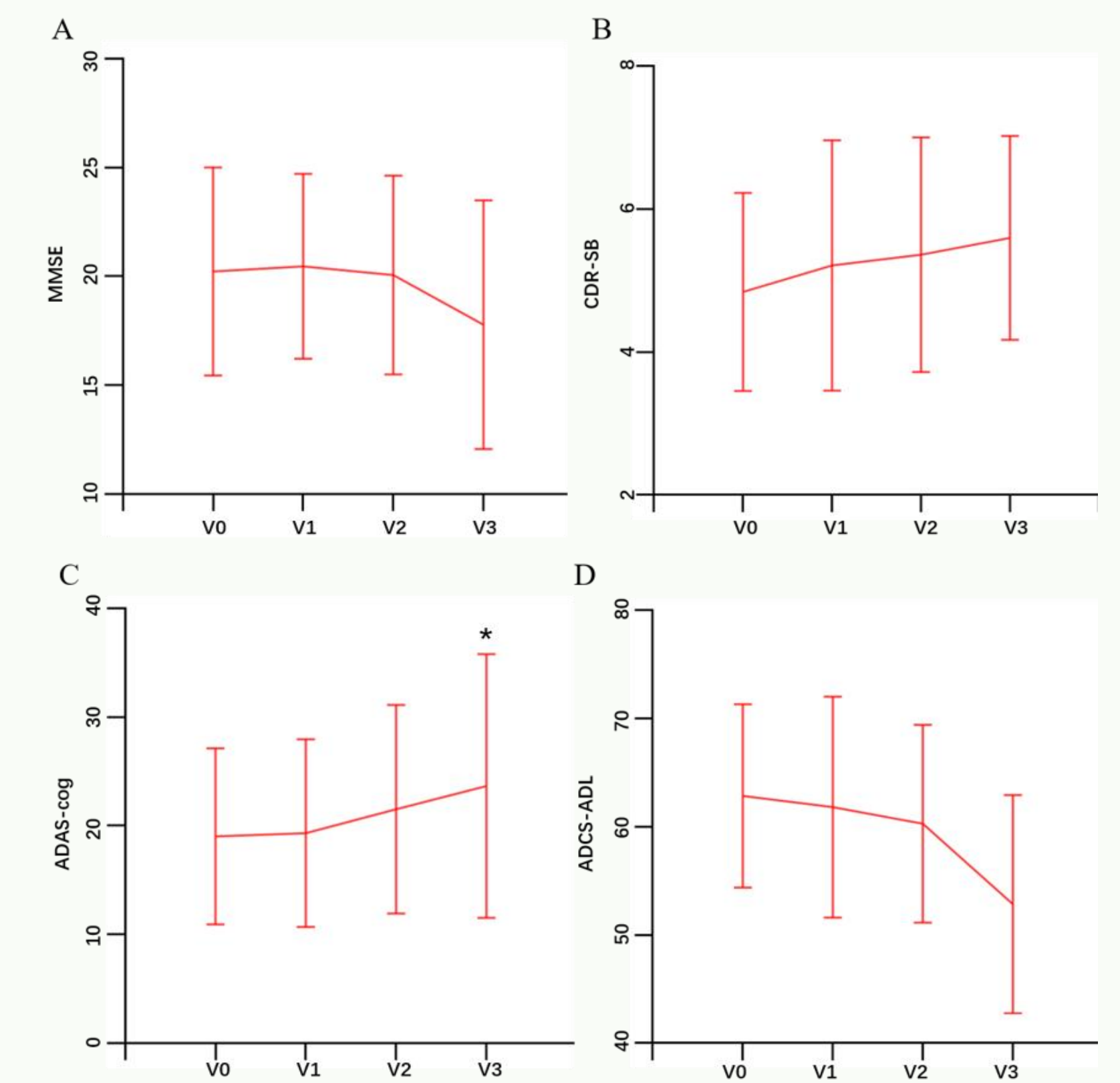


Figure 2. Changes in clinical functional scales.

- In the overall population, MMSE, CDR-SB, ADAS-cog, and ADCS-ADL scores remained generally stable during the follow-up period. Only ADAS-cog scores showed a significant increase from baseline at 9 months of treatment ($P < 0.05$) (Figure 2).

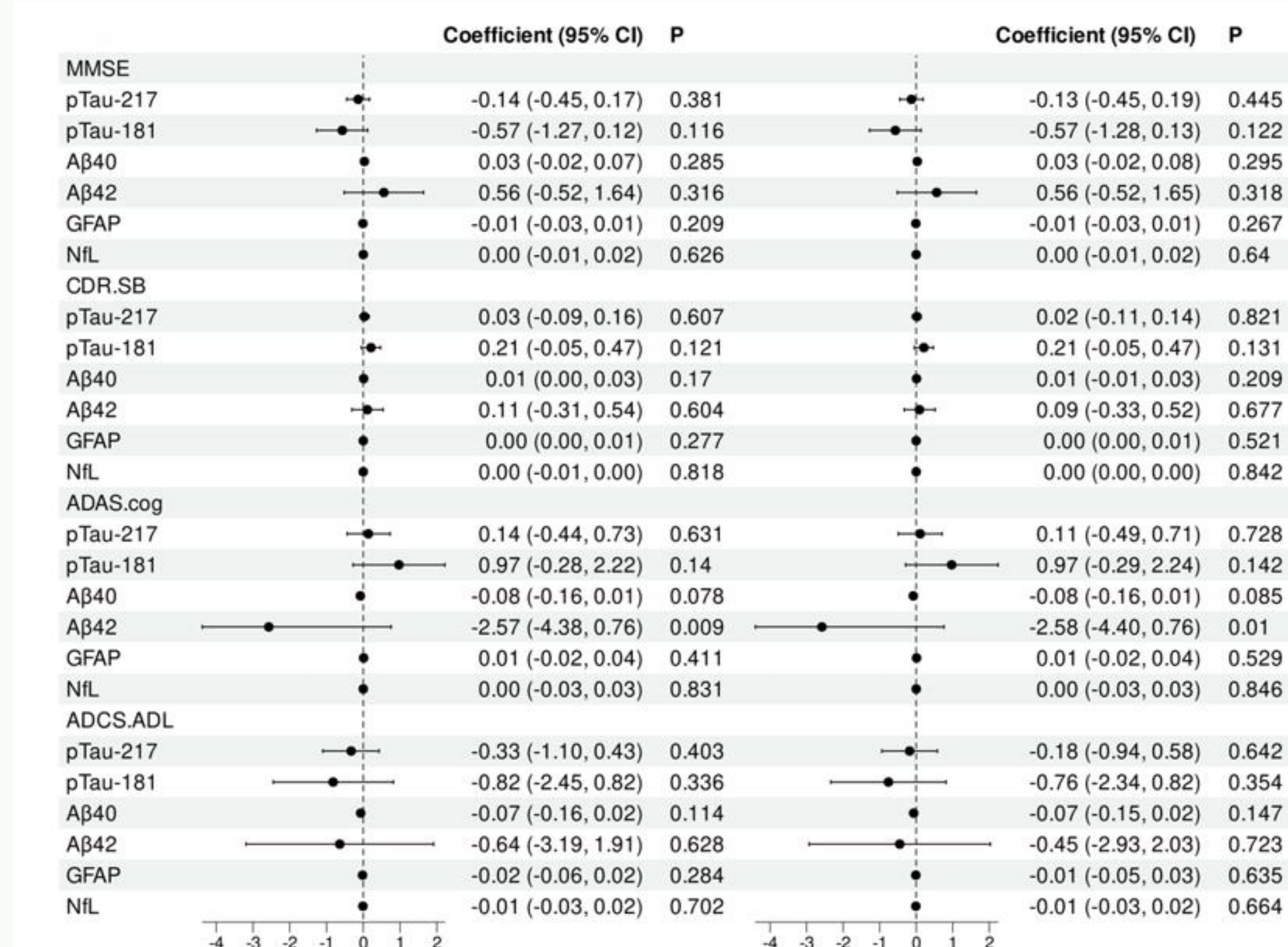


Figure 3. Correlations between baseline biomarkers and clinical outcome changes

- Lower baseline plasma $A\beta$ 42 levels were associated with a greater increase in ADAS-cog scores after 9 months of lecanemab treatment ($P < 0.01$). Other plasma biomarkers (p-tau217, p-tau181, GFAP, NFL) showed no significant association with changes in cognitive or functional outcomes (Figure 3).

Conclusions

- Cognitive function remained stable after 9 months of lecanemab treatment.
- At 3 months post-treatment, plasma $A\beta$ 1-40 increased, whereas GFAP and p-tau181 decreased.
- Lower baseline $A\beta$ 1-42 was associated with cognitive decline at 9 months. Changes in plasma biomarkers were not significantly correlated with changes in cognitive or functional outcomes.