

Baseline Regional Tau PET Stratifies Short-Term Cognitive and MRI Trajectories in a Real-World Chinese Cohort Receiving Lecanemab



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Lecanemab exposure was associated with slower CDR-SB worsening. The apparent hippocampal difference attenuated after baseline tau adjustment, while regional tau independently predicted cognitive and structural trajectories.

INTRODUCTION

RESULTS

CONCLUSIONS

- Anti-amyloid therapy slows clinical decline in early Alzheimer’s disease, but individual trajectories remain heterogeneous¹.
- Tau PET provides prognostic information beyond amyloid PET and structural MRI², and combined amyloid/tau positivity identifies individuals at high risk of future cognitive decline³.
- We therefore examined whether regional baseline tau predicted cognitive and structural trajectories and explained apparent group differences during lecanemab exposure.

METHODS

- We retrospectively studied 50 lecanemab-treated patients and 52 untreated patients with longitudinal cognition and/or MRI.
- Time zero was defined as treatment initiation in the lecanemab group and the baseline assessment in the untreated group. Baseline tau PET was available for all 50 treated participants and 36 untreated participants.
- Regional tau burden was quantified in five CenTauR ROIs⁴⁻⁵. Temporoparietal CenTauRz represented neocortical tau⁶.
- MRI measures were derived using FreeSurfer’s longitudinal processing stream⁷.
- Linear mixed-effects models tested group×time and tau×time interactions, adjusting for age, sex, education, APOE ε4, and eTIV for MRI outcomes. FDR correction was applied within prespecified test families.

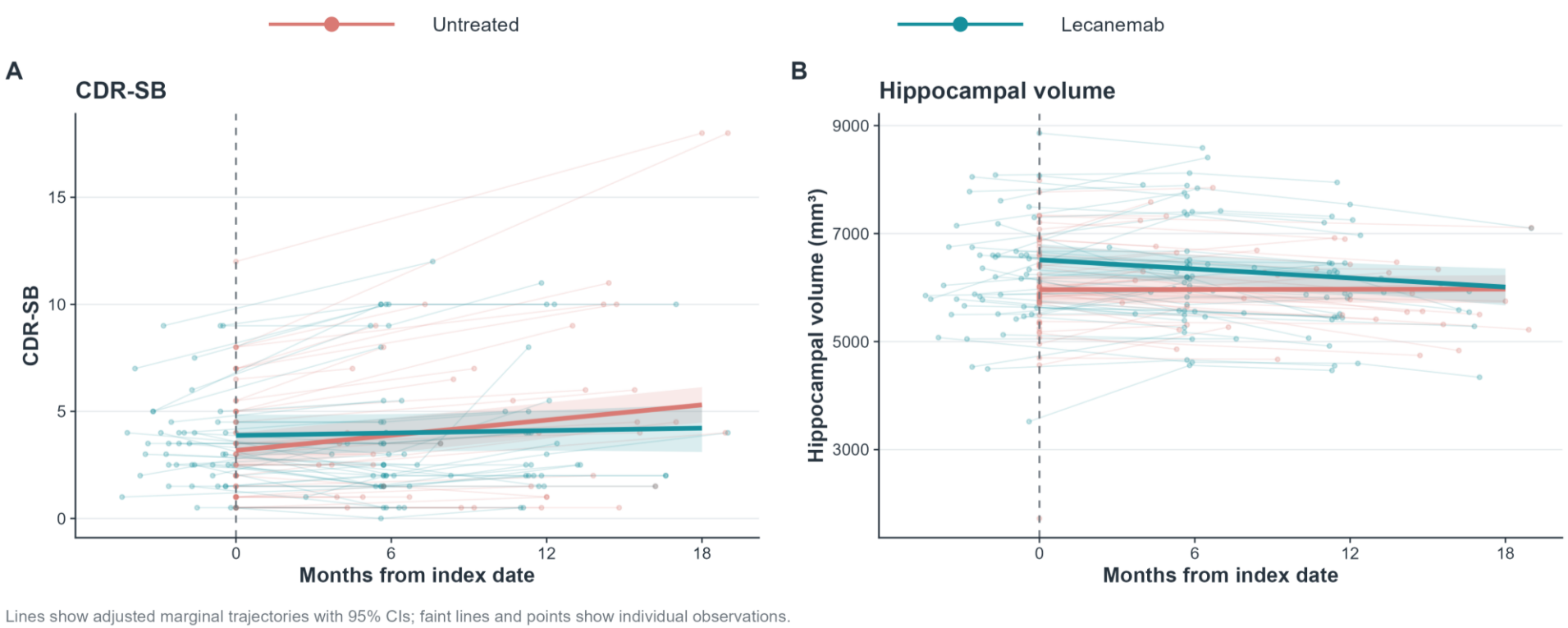
Table1. Demographic and clinical characteristics of study participants

Characteristic	Untreated (n = 52)	Lecanemab (n = 50)	P-value
Age, years	66.9 ± 9.4	65.7 ± 9.5	0.511
Female sex, n (%)	31 (59.6%)	33 (66.0%)	0.544
Education, years	11.0 ± 4.0	12.3 ± 3.9	0.102
APOE ε4 carrier, n (%)	27 (51.9%)	33 (66.0%)	0.164
MCI (CDR global 0.5), n (%)	35 (67.3%)	37 (74.0%)	0.518
MMSE	21.1 ± 5.3	19.5 ± 6.5	0.172
MoCA	15.3 ± 5.9	14.2 ± 6.3	0.352
CDR-SB	3.37 ± 2.54	3.61 ± 2.30	0.611
Baseline tau PET available, n (%)	36 (69.2%)	50 (100%)	
Universal CenTauRz	11.13 ± 9.20	12.39 ± 9.40	0.536
Frontal CenTauRz	8.25 ± 8.55	8.80 ± 8.61	0.769
Mesial temporal CenTauRz	7.13 ± 2.99	7.88 ± 4.21	0.339
Meta-temporal CenTauRz	10.32 ± 6.95	12.12 ± 8.37	0.283
Temporoparietal CenTauRz	11.79 ± 10.04	13.12 ± 10.01	0.548
Cognitive baseline + follow-up, n (%)	52 (100%)	46 (92.0%)	
MRI baseline + follow-up, n (%)	52 (100%)	50 (100%)	

Values are mean ± SD or n (%). Tau summaries: untreated n=36; lecanemab n=50. P values use Welch t tests or Fisher exact tests.

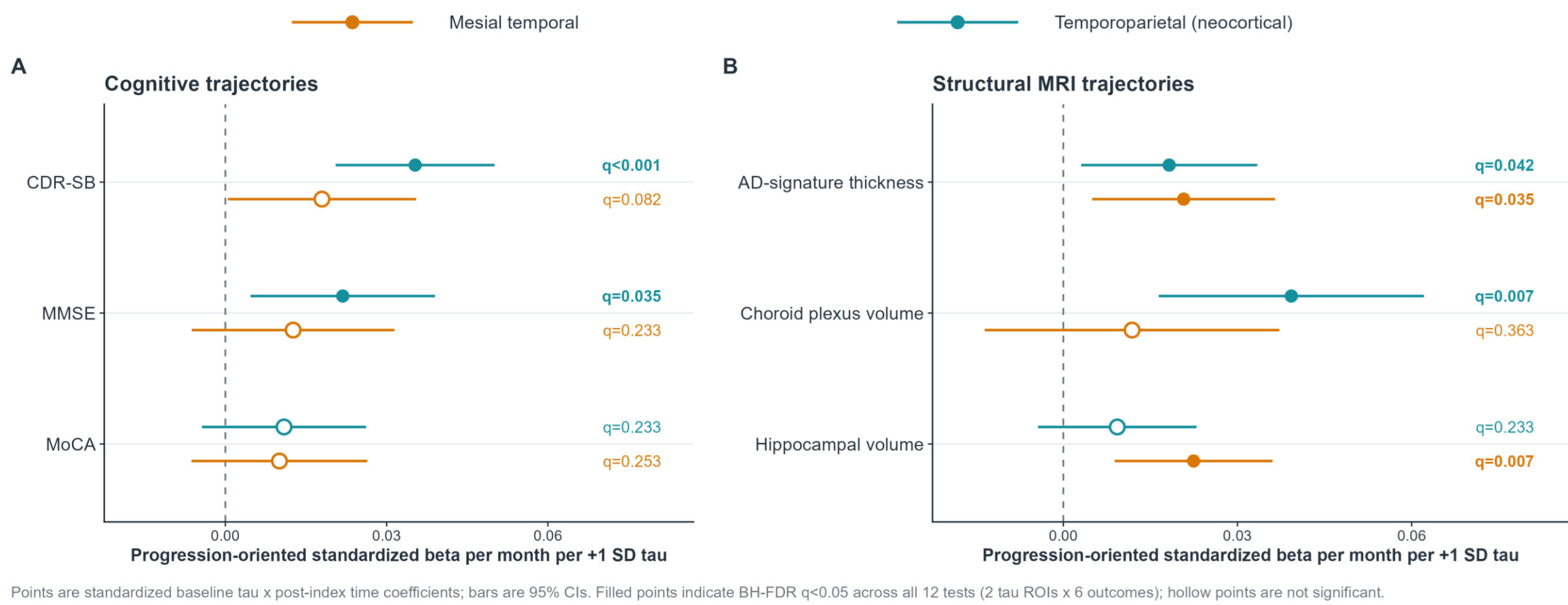
- The cohorts were comparable at baseline across demographic, clinical, and all five regional tau burden; tau PET was available for 36/52 untreated and 50/50 lecanemab-treated participants.

Figure2. Adjusted longitudinal trajectories by treatment group



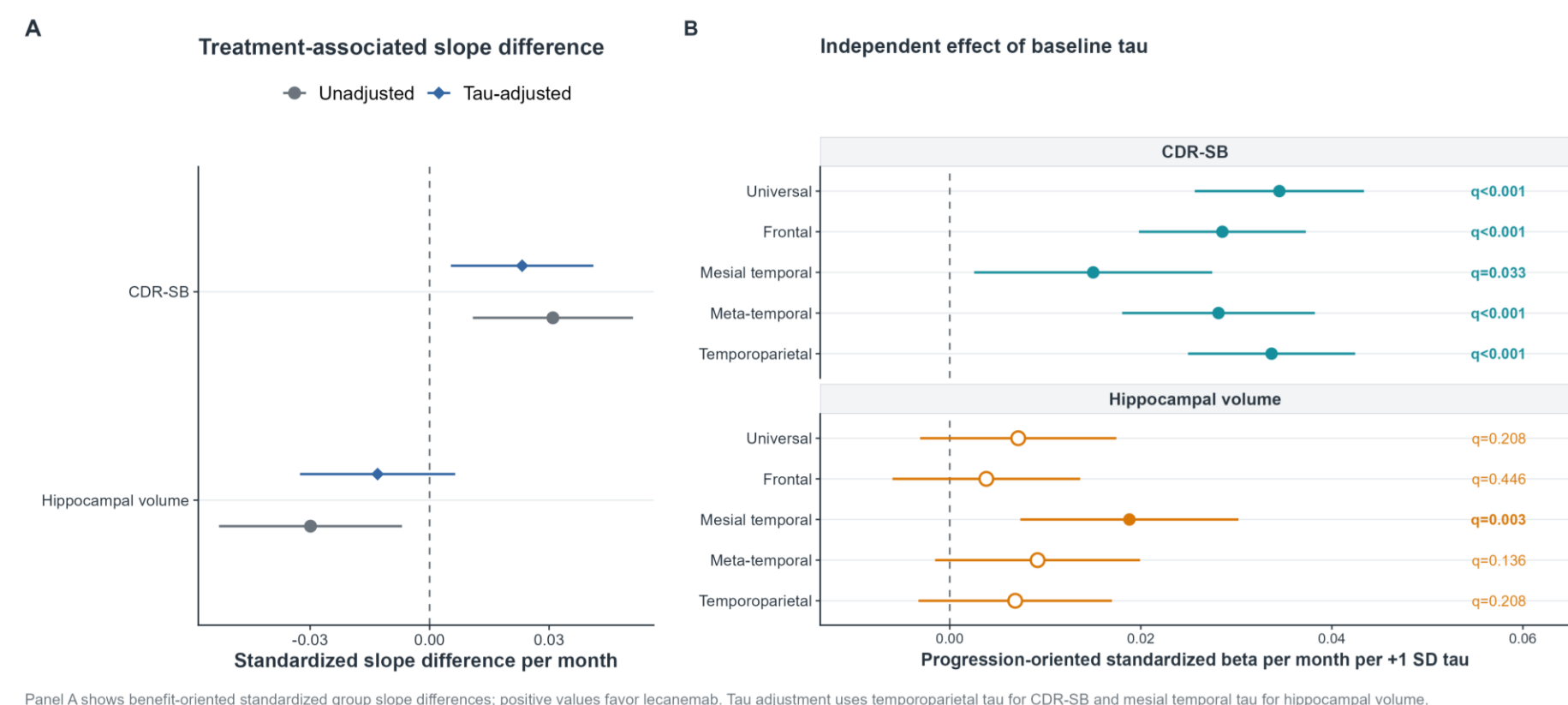
- Lecanemab exposure was associated with slower CDR-SB worsening but faster unadjusted hippocampal volume loss.

Figure1. Association between baseline tau topography and cognitive /structural MRI trajectories in participants with lecanemab treatment



- Neocortical tau was associated with worsening of CDR-SB, MMSE, and choroid plexus trajectories, whereas mesial temporal tau was related to hippocampal loss; both associated with AD-signature cortical thinning.

Figure3. Baseline tau attenuates the group difference in hippocampal volume change



- The hippocampal group difference attenuated after tau adjustment, whereas the CDR-SB association persisted; tau effects were region- and outcome-specific.

- Real-world lecanemab exposure was associated with slower CDR-SB worsening.
- The apparent hippocampal disadvantage attenuated after baseline tau adjustment, indicating that structural group comparisons are sensitive to baseline disease burden.
- Regional tau PET may improve prognostic stratification, although nonrandomized data do not establish treatment causality.

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