

Supplementary Material

Patients with Mild Cognitive Impairment stratified by baseline blood plasma pTau217 show differences in CANTAB-assessed cognitive decline

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References

1. Kaula AJ *et al.* *Alzheimer's Dement.* 2025;21:e108841.
2. Haraldsen IH *et al.* *Front Neurobot.* 2024;17:1289406.

Supplementary methods

pTau217 assay

- pTau217 concentration was measured on 25 µL blood plasma samples with MSD S-PLEX Tau (pT217) kit (K151APFS; Mesoscale Discovery) on the MESO QuickPlex SQ 120MM instrument (MSD) according to the kit protocol (Mesoscale Discovery, 2024).

Cognitive assessments

- Participants completed digital cognitive assessments on a tablet using Cambridge Neuropsychological Test Automated Battery (CANTAB).
- The tests in this battery included Delayed Matching to Sample (DMS), Paired Associates Learning (PAL), Rapid Visual information Processing (RVP), Pattern Recognition Memory (PRM), Spatial Working Memory (SWM).
- One outcome measure from each task was selected for analysis:
 - DMS percent correct all delayed
 - PAL first attempt memory score
 - RVP A-prime (sensitivity to target)
 - PRM percent correct delayed recall
 - SWM between errors stages 4–8.

- This analysis also included two novel reaction time (RT) measures from PAL:
 - PAL median first attempt reaction time
 - PAL fastest correct reaction time

Statistical analyses

- Participants with complete data for pTau217 and CANTAB data for at least three time points were included in the analyses.
- All statistical analyses were performed using Python (3.12.12) in Jupiter notebook (7.4.6). All analyses were performed in a secure analytical environment. All *p*-values were two-tailed, and the significance level was $\alpha = .05$
- Associations between baseline plasma pTau217 and cognitive trajectories were investigated using linear mixed effect (LME) models conducted individually with each selected CANTAB measure as response variable.
- pTau217 was split into three severity groups (low, ≤ 3 pg/mL; intermediate, >3 – <6 pg/mL; high, ≥ 6 pg/mL) based on guided literature cutoffs for the assay.¹
- pTau217 groups, time point, site, age, sex and education were included as fixed effects.
- Participants were grouped with random intercept and slopes. The interaction between time and pTau217 was included to investigate the effect on rate of cognitive change. Age and education variables were centred around the mean.
- Cognitive trajectories were visualized stratified by pTau217 group, with cognitive scores adjusted for age, sex and education.
- Group means were plotted across timepoints with 95% confidence intervals using bootstrapping (sample = 1000).

Supplementary references

1. Kivisäkk P *et al. Sci Rep.* 2024;14:629.