

Plasma phosphorylated tau signature in preclinical Alzheimer’s disease

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In preclinical Alzheimer’s disease, amyloid-related plasma pTau changes were phosphorylation-site specific

- pTau217 was the strongest diagnostic and longitudinal marker
- pTau205 showed limited amyloid-related utility
- Cognitive associations differed by phosphorylation site and amyloid status

INTRODUCTION

METHODS

RESULTS

CONCLUSIONS

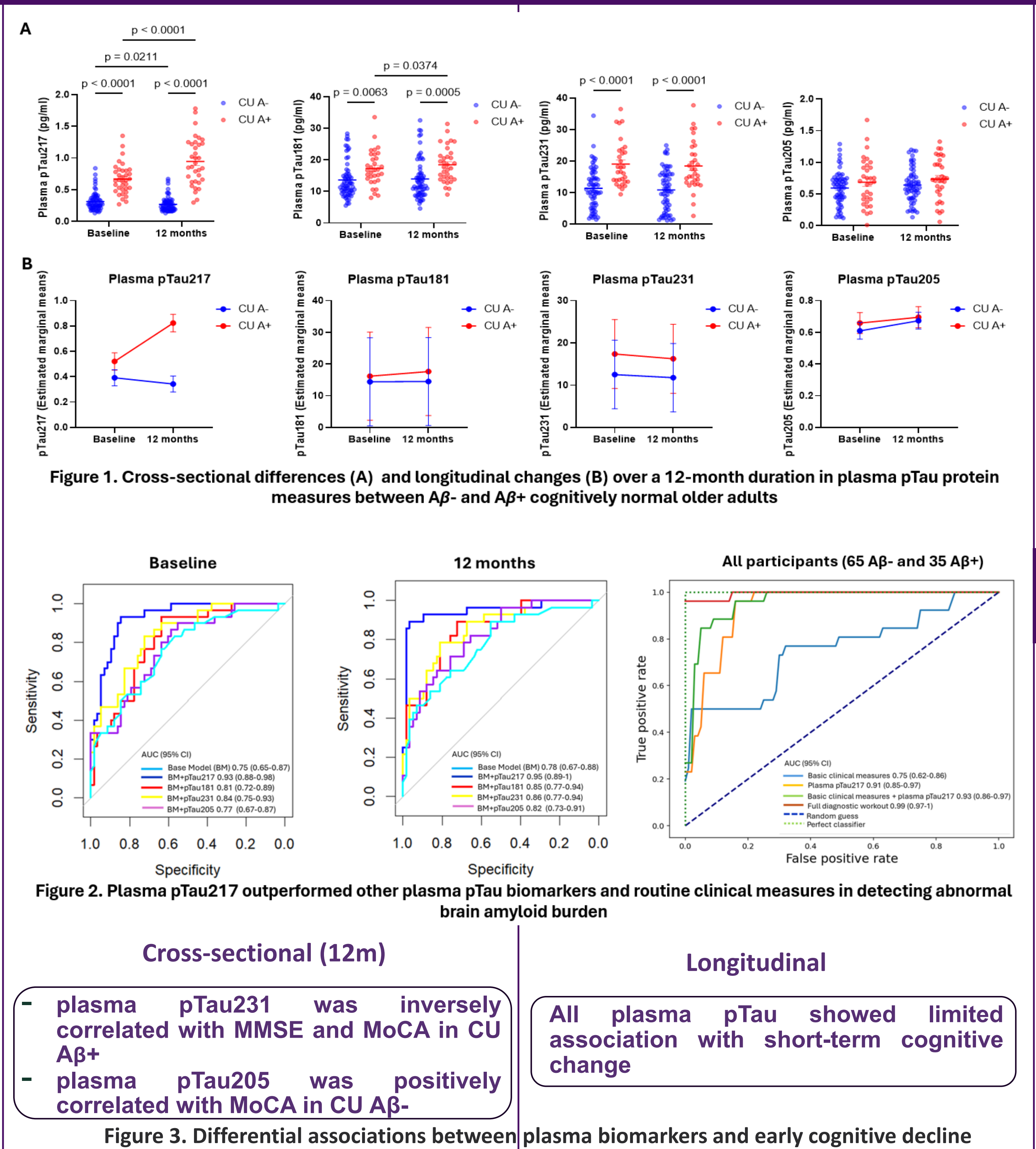
Plasma pTau biomarkers targeting different phosphorylation sites may capture distinct stages of early Alzheimer’s disease (AD) pathology.

Although pTau181 and pTau231 are established blood biomarkers^{1,2}, pTau217 and pTau205 may offer greater sensitivity to early pathological change^{3,4}. Their comparative diagnostic and longitudinal utility in preclinical AD remains insufficiently understood.

Aim: To compare the diagnostic and longitudinal associations of plasma pTau217, pTau205, pTau181, and pTau231 with amyloid burden and cognitive performance in cognitively unimpaired older adults

KARVIAH
Cognitively unimpaired (CU)
60-90 years old

Statistical analysis: Linear models (repeated measures) to compare continuous variables between Aβ- and Aβ+ groups corrected for age, sex, eGFR and APOE ε4. Spearman correlation to investigate correlations between continuous variables. Logistic regression with Aβ-/+ as response was used to evaluate ROC curve. All analyses and data visualization were carried out using IBM SPSS (v29), GraphPad Prism (v10) or R (v4.0.3).



Plasma biomarker	Amyloid-related pattern	Cognitive association
pTau217	Strongest cross-sectional, longitudinal amyloid-related change and diagnostic performance	No significant association with short-term cognitive change
pTau231	Strong cross-sectional amyloid discrimination	Higher pTau231 associated with poorer cognition in CU Aβ+ individuals
pTau181	Modest cross-sectional amyloid discrimination	No clear cognitive association observed
pTau205	Limited amyloid-related utility	Higher pTau205 associated with better cognition in CU Aβ- individuals

- Overall, plasma pTau showed distinct amyloid-related patterns and tau phosphorylation-site specificity in AD pathology
- These findings highlight the diagnostic and longitudinal monitoring properties of plasma pTau217 for preclinical AD.

REFERENCES

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