

Ptau217 Prediction Of Cognitive Change In Late Life - A Latent Change Modeling Study

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Introduction

- Plasma phosphorylated tau 217 (pTau217) is a promising, scalable, minimally invasive blood-based biomarker of Alzheimer's disease (AD) pathology (Mattsson-Carlgrén et al., 2020).
- pTau217 is correlated with amyloid and tau PET and clinical diagnosis, and is increasingly used to index AD pathology.
- Its **domain-specific** associations with cognitive change in *preclinical* stages remain poorly characterized; most studies use global composites (mPACC, MMSE).

Aim. Test bidirectional associations between pTau217 and ~6-year change across **five cognitive domains** in older men, and assess whether pTau217 change is associated with cognitive change.

Methods

Sample

- N = 1,261** community-dwelling men, waves 3 & 4 of the *Vietnam Era Twin Study of Aging (VETSA)* (Kremen et al., 2019).
- Plasma + cognition at **age 68** (baseline; 2016–2019; n=1,196) and **age 73** (2021–2024; n=941); mean interval **5.63 yrs** (SD=0.60).
- ~80% reported no combat exposure; at study entry similar to U.S. men of the same age cohort.

Measures

- Cognition:** factor scores for 5 domains — executive function, verbal fluency, episodic memory, processing speed, visuospatial ability — standardized to wave-1 means/SDs (higher = better).
- pTau217:** ALZpath assay on Quanterix Simoa HD-X (USC ATRI Biomarker Core). Box–Cox transformed across waves; site and storage time regressed out within wave (umx) (Castro-de-Araujo et al., 2025).

Results

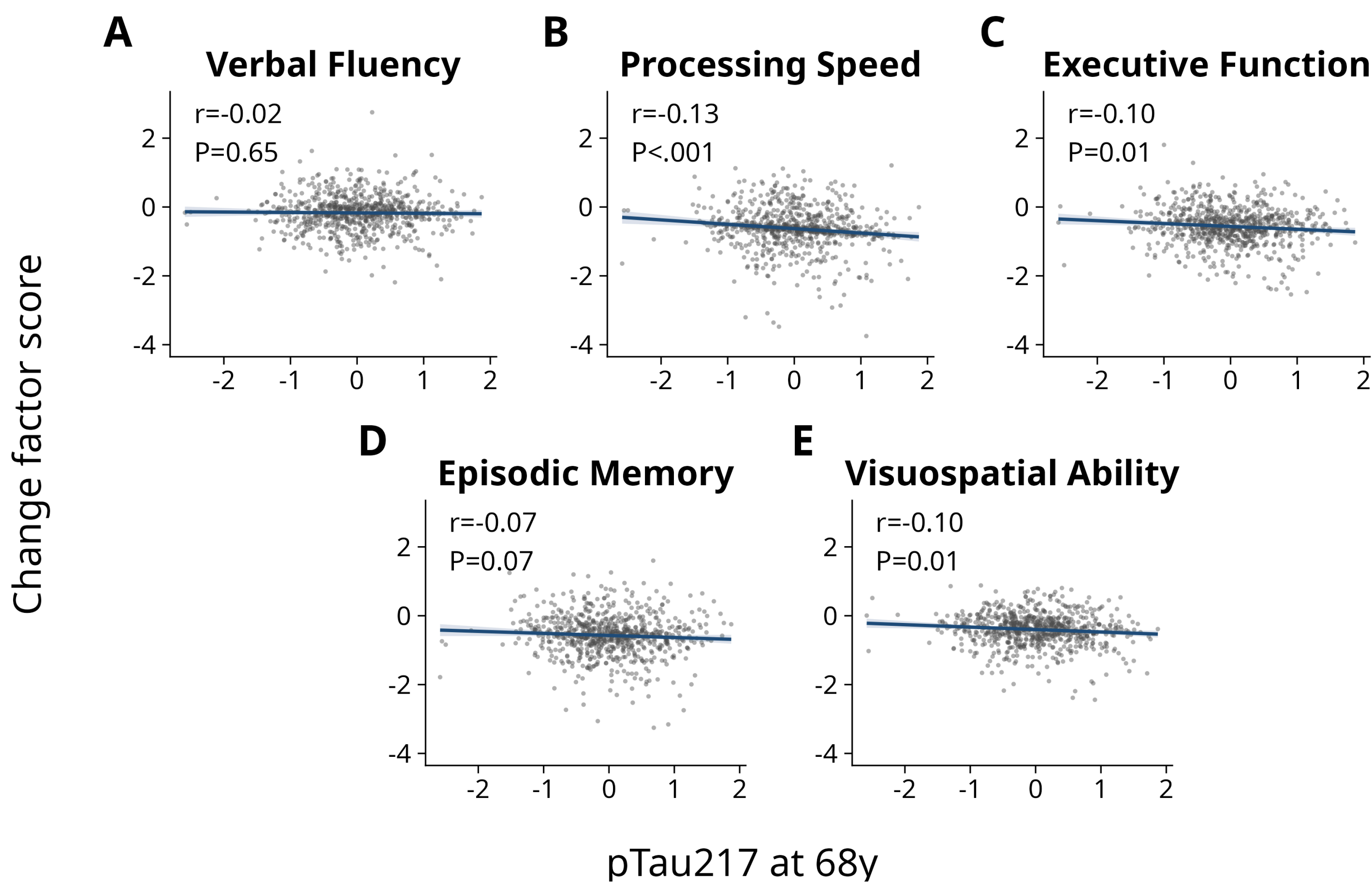


Figure 1: Post-hoc regression of pTau217 on cognitive change scores (parameter σ_{y2} in Figure 2).

Table 2. Standardized LCSM coefficients [95% CI]. *FDR $q < 0.05$.

Domain	γ_1 (pTau→ Δ Cog)	γ_2 (Cog→ Δ pTau)	Baseline cor.	Change cor.
Executive function	-0.08 [-0.16, 0.00]	-0.05 [-0.14, 0.03]	-0.02 [-0.10, 0.06]	-0.13 [-0.20, -0.05]*
Verbal fluency	-0.03 [-0.11, 0.05]	-0.07 [-0.16, 0.01]	0.00 [-0.08, 0.08]	-0.06 [-0.13, 0.02]
Episodic memory	-0.06 [-0.15, 0.02]	-0.10 [-0.19, -0.01]	-0.01 [-0.09, 0.07]	-0.09 [-0.17, -0.02]*
Processing speed	-0.12 [-0.20, -0.04]*	-0.04 [-0.12, 0.05]	-0.03 [-0.11, 0.05]	-0.12 [-0.20, -0.04]*
Visuospatial ability	-0.09 [-0.17, -0.02]*	-0.06 [-0.15, 0.02]	-0.02 [-0.10, 0.05]	-0.13 [-0.20, -0.06]*

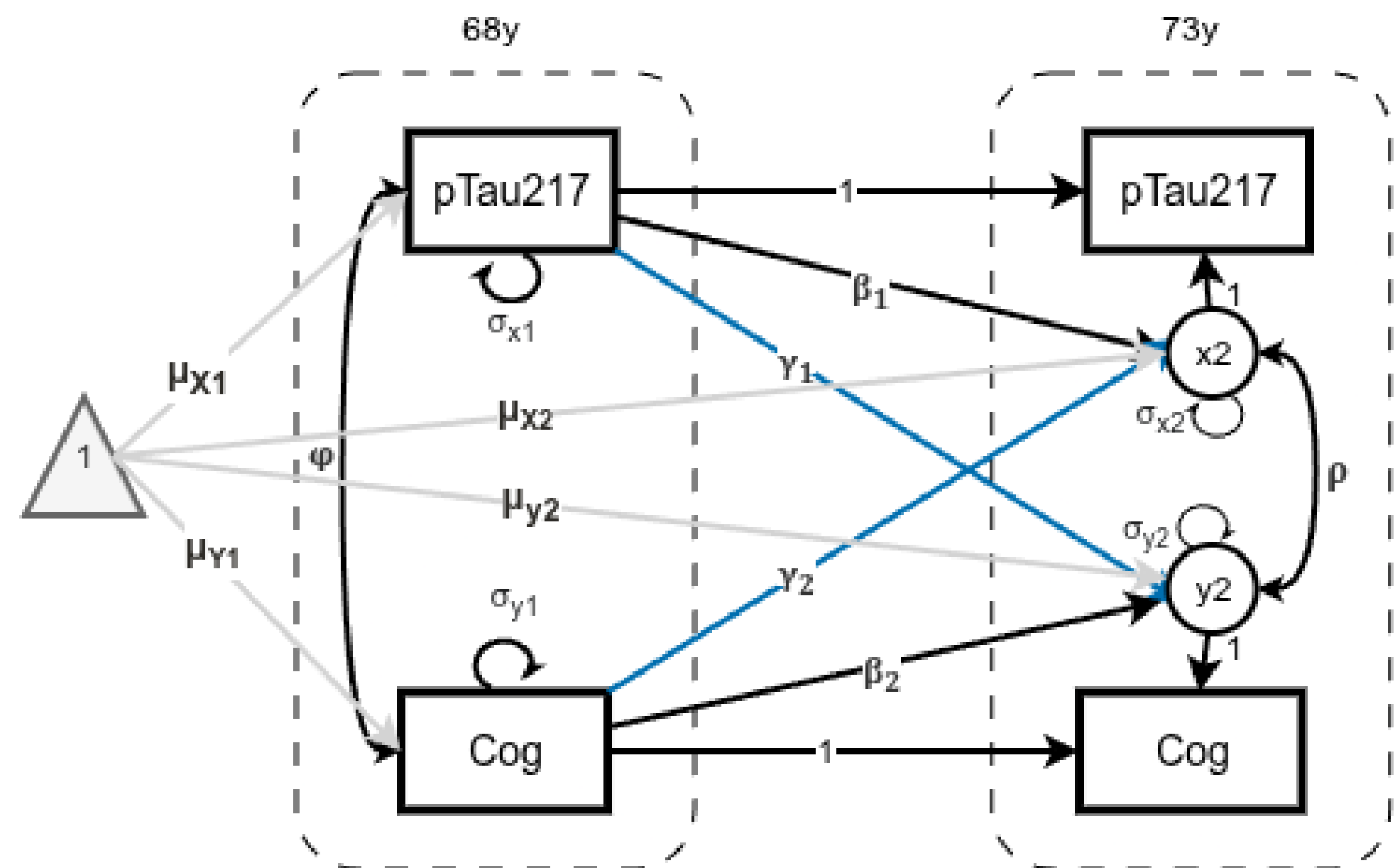


Figure 2: Bivariate latent change score model.

Table 1. Descriptive characteristics. Cognitive scores are z-scores standardized to the wave-1 VETSA sample.

	Age 68	Age 73
N	1,196	941
Age, mean (SD)	67.6 (2.5)	73.1 (2.6)
Education, mean (SD)	13.9 (2.1)	14.0 (2.1)
MCI, N (%)	213 (17.8)	178 (18.9)
pTau217, mean (SD) pg/mL	0.48 (0.28)	0.61 (0.41)
Executive function	-0.76 (0.92)	-1.09 (0.95)
Verbal fluency	-0.31 (1.00)	-0.37 (1.01)
Episodic memory	-0.44 (1.09)	-0.87 (1.13)
Processing speed	-0.99 (1.09)	-1.44 (1.22)
Visuospatial ability	-0.71 (0.94)	-0.88 (0.89)

Conclusion

- From late midlife to early old age, **plasma pTau217 change tracked cognitive change in 4 of 5 domains** (all but verbal fluency), supporting its use to monitor disease progression.
- A **single early (age 68) pTau217** measure predicted ~6-year decline most reliably in **processing speed** and **visuospatial ability**.

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