

Associations between Metabolic Comorbidities and Plasma Biomarkers across Neurodegenerative Diseases



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- ↑ p-tau217 is consistently associated with impaired renal clearance across studies
- Confounding by BMI/Medication use may have led to paradoxical inverse relationships between NFL & Hyperlipidemia, and GFAP and DM/HbA1c seen in our study

INTRODUCTION METHODS RESULTS CONCLUSIONS

- Plasma biomarkers have demonstrated clinical utility in the differential diagnosis of Alzheimer’s disease and are of increasing importance in other neurocognitive disorders.
- **AIM:** to study the effect of metabolic comorbidities on plasma biomarker concentrations in a transdiagnostic research cohort.

- N=376 participants recruited from the Oxford Memory Clinic and the FAST study (AD=90, LBD=16, CBS=7, FTD=14, MCI=24, SCD=36, controls=189).
- p-tau217, Aβ42/40 ratio, GFAP, NFL, PRDX6 and ACHE measured using the Alamar NULISA CNS Panel.
- Hypertension, diabetes, hyperlipidemia, chronic kidney disease and concurrent medication coded from medical records. BMI, blood pressure, HbA1c, serum creatinine and HDL cholesterol were available or imputed in a subset of participants.
- Linear regression used to study associations between biomarkers and comorbidities/clinical parameters, controlling for age, sex and education. Sensitivity analyses controlled for BMI and concurrent medication respectively.

- Kidney disease and serum Cr associated with ↑p-tau217, while serum creatinine only associated with ↑ACHE (Figure 1).
- Hyperlipidemia inversely associated with NFL and ACHE, but sensitivity analyses including BMI these were attenuated [NFL ($\beta_{\text{Hyperlipidemia+}}=-0.31, p=0.20$), ACHE ($\beta_{\text{Hyperlipidemia+}}=-0.064, p=0.84$)].
- ↑ HDLC inversely associated with PRDX6. This remained significant when adjusting for BMI ($\beta_{\text{HDLc}}=-0.31, p=0.20$) but attenuated after excluding participants on concurrent statin therapy ($\beta_{\text{HDLc}}=-0.051, p=0.13$).
- Diabetes and HbA1c inversely associated with GFAP; this association remained significant when the model adjusted for BMI ($\beta_{\text{HbA1c}}=-0.097, p=0.004$) but attenuated after excluding participants with glucose-lowering therapy ($\beta_{\text{HbA1c}}=-0.053, p=0.08$).

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- Kidney impairment was associated with ↑ p-tau217 and ACHE, consistent with the effect of impaired renal clearance.
- Paradoxically, inverse relationships between neurodegenerative biomarkers and dyslipidemia, and between GFAP and diabetes were seen. Confounding by higher BMI (leading to a dilutional effect on plasma biomarkers) or medication use may account for this.

