

Interrelationships Among Plasma pTau217, GFAP, and Neurofilament Light Chain in African American Older Adults

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BACKGROUND

- Plasma biomarkers, such as phosphorylated tau 217 (pTau217), glial fibrillary acidic protein (GFAP), and neurofilament light chain (NfL), are increasingly used to characterize Alzheimer's disease (AD) pathology and neurodegeneration.
- The biological and systemic factors driving variability in these biomarkers remain incompletely understood in African American older adults.
- This population is disproportionately affected by AD and by comorbid vascular and metabolic conditions.
- We examined demographic, inflammatory, renal, and lipid factors as candidate predictors of each plasma biomarker.

RESULTS

- pTau217 model explained 42.3% of variance, higher NfL, higher GFAP, female sex, and lower eGFR were independent predictors.
- GFAP model explained 48.9% of variance. NfL, older age, sex, pTau217, and BUN contributed independently.
- NfL model explained 49.5% of variance. pTau217, reduced eGFR, GFAP, sex, and cholesterol contributed independently.
- Inflammatory markers did not enter any final regression model.
- Renal function indices consistently contributed to biomarker variability, independent of neurodegenerative and demographic factors.

CONCLUSIONS

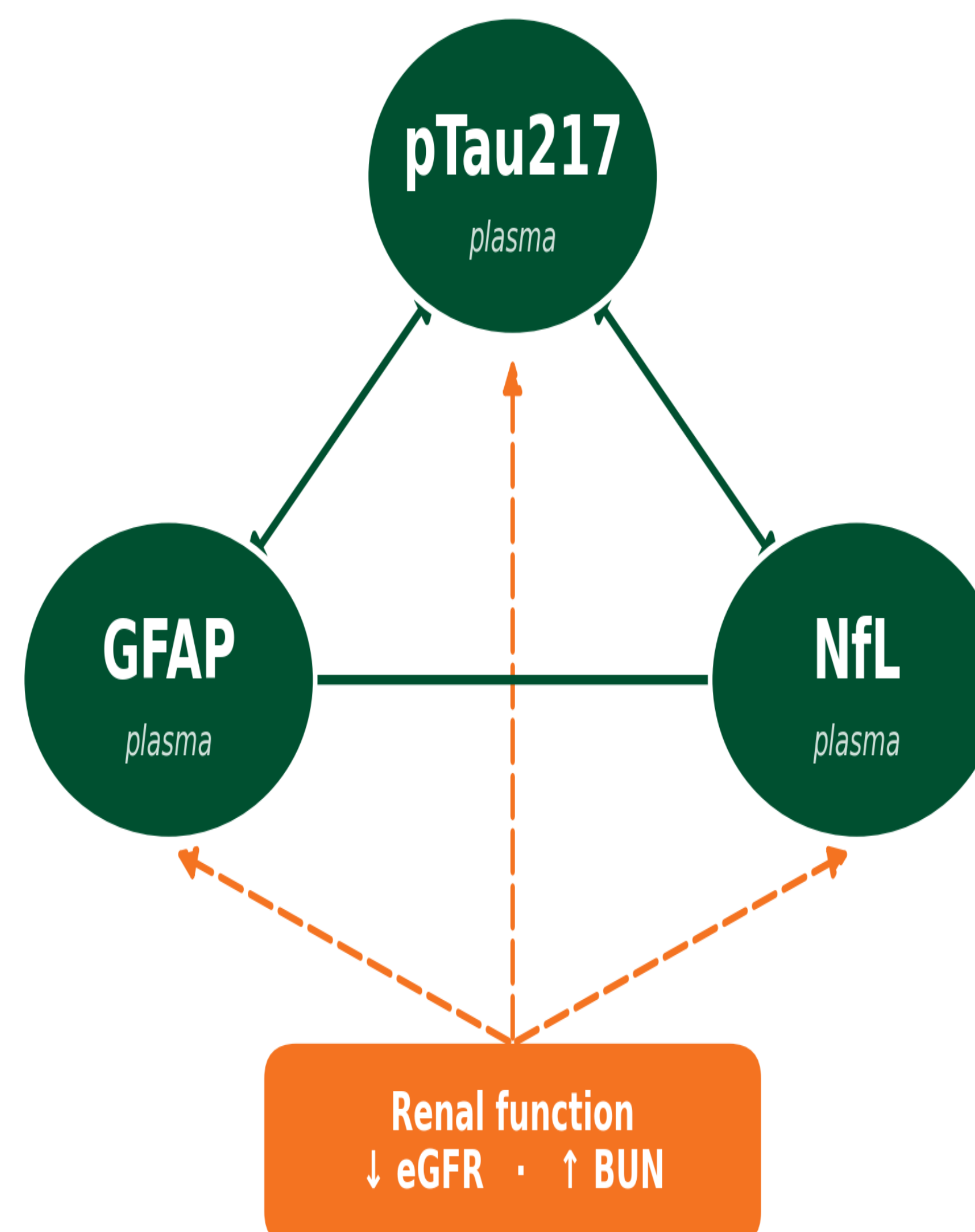
- Plasma pTau217, GFAP, and NfL show strong interrelationships, reflecting convergent influences of tau pathology, astroglial activation, and neuroaxonal injury.
- Renal function independently contributes to circulating biomarker concentrations, alongside neurodegenerative and demographic factors.
- Peripheral clearance and metabolic factors should be considered when interpreting plasma AD biomarkers in this population.
- Integrated frameworks incorporating neurological and systemic factors may improve risk assessment and biomarker interpretation in underrepresented groups.

METHODS

- 149 African American older adults were evaluated.
- Peripheral blood was collected by standard venipuncture; plasma was separated by centrifugation and stored at -80°C until analysis.
- Plasma pTau217, GFAP, and NfL were quantified using ultrasensitive Single molecule array (Simoa) immunoassays.
- Biomarker concentrations were $\log_{10}$ -transformed to satisfy assumptions for parametric analyses.
- Candidate predictors examined included demographic variables (age and sex), inflammatory markers (ASC, caspase-1, and IL-18), renal indices (eGFR, BUN, and creatinine), and lipid profiles (total cholesterol, triglycerides, HDL, and LDL).
- Stepwise multiple regression analyses identified the independent predictors of each plasma biomarker.

BIOMARKER INTERRELATIONSHIPS

Convergent influences on plasma AD biomarkers



Outcome	R ²	Independent predictors (in order of entry)
Plasma pTau217	42.3%	↑ NfL, ↑ GFAP, female sex, ↓ eGFR
Plasma GFAP	48.9%	NfL, older age, sex, pTau217, BUN
Plasma NfL	49.5%	pTau217, ↓ eGFR, GFAP, sex, cholesterol

Table 1. Independent Predictors by Model

REFERENCES

