

Kidney Function Influences Blood-Based Alzheimer's Disease Biomarkers Largely Independent of Cognitive Status

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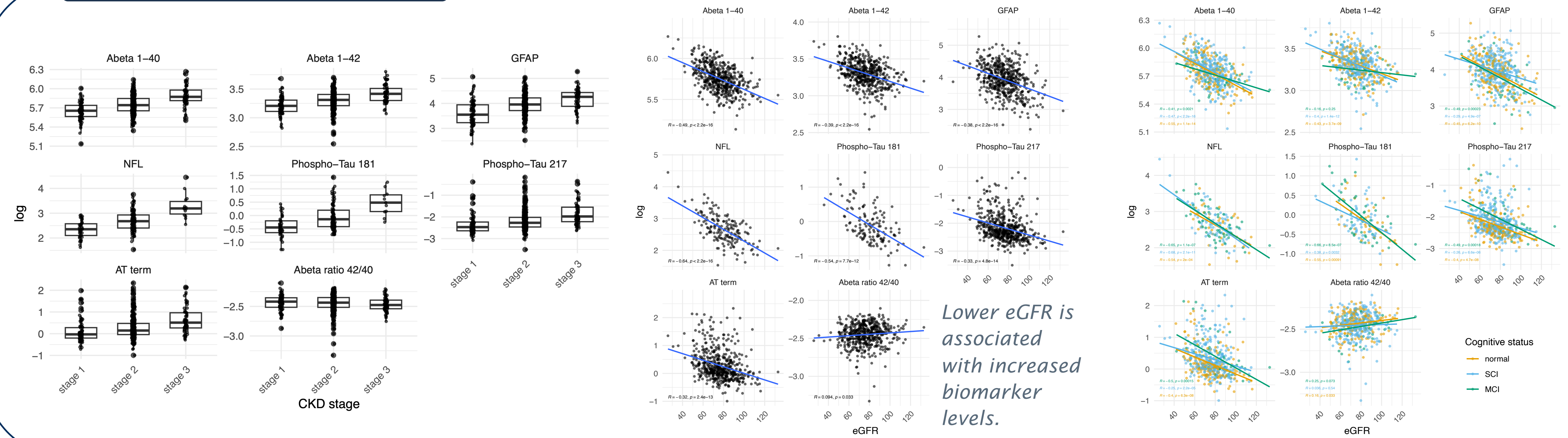
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Background

- Blood-based biomarkers are increasingly incorporated into the clinical evaluation of Alzheimer's disease (AD).
- Reduced kidney function may alter circulating biomarker concentrations, complicating interpretation.
- Understanding how chronic kidney disease (CKD) affects plasma AD biomarkers and whether these effects depend on cognition is essential for clinical use.
- Aim.** To investigate associations between CKD stage, plasma AD biomarkers, and cognition.

Results



Methods

Participants. Cross-sectional analysis of **579 individuals** with normal cognition, subjective cognitive impairment (SCI), or mild cognitive impairment (MCI). See Table 1 for demographics.

Table 1. Demographics

	Normal	SCI	MCI	P Value
N (total: 559)	190	334	55	
Age	68.2 (41-91)	69.0 (40-94)	64.5 (40-84)	<.001
Sex (f/m)	102/88	165/169	28/27	0.64
Education	16.0 (10-20)	15.0 (8-20)	13.0 (10-18)	<.001
BMI	25.6 (18.5-35.5)	25.4 (19.9-43.0)	28.6 (16.5-40.6)	<.001
MMSE	30.0 (26-30)	29.0 (25-30)	28.0 (24-30)	<.001
PACC5	0.14 ± 0.6	0.00 ± 0.6	-0.88 ± 0.5	<.001
CKD				
Stage 1 (eGFR: > 90 mL/min/1.73 m ²)	30	44	14	
Stage 2 (eGFR: 60-89 mL/min/1.73 m ²)	123	237	34	
Stage 3 (eGFR: 30-59 mL/min/1.73 m ²)	31	42	6	
APOE				
E2/E2 (1.4%)	0	4	1	
E2/E3 (13.5%)	21	34	10	
E2/E4 (3.4%)	6	3	5	
E3/E3 (58.8%)	111	191	26	
E3/E4 (22.3%)	29	63	9	
E4/E4 (0.7%)	2	6	1	

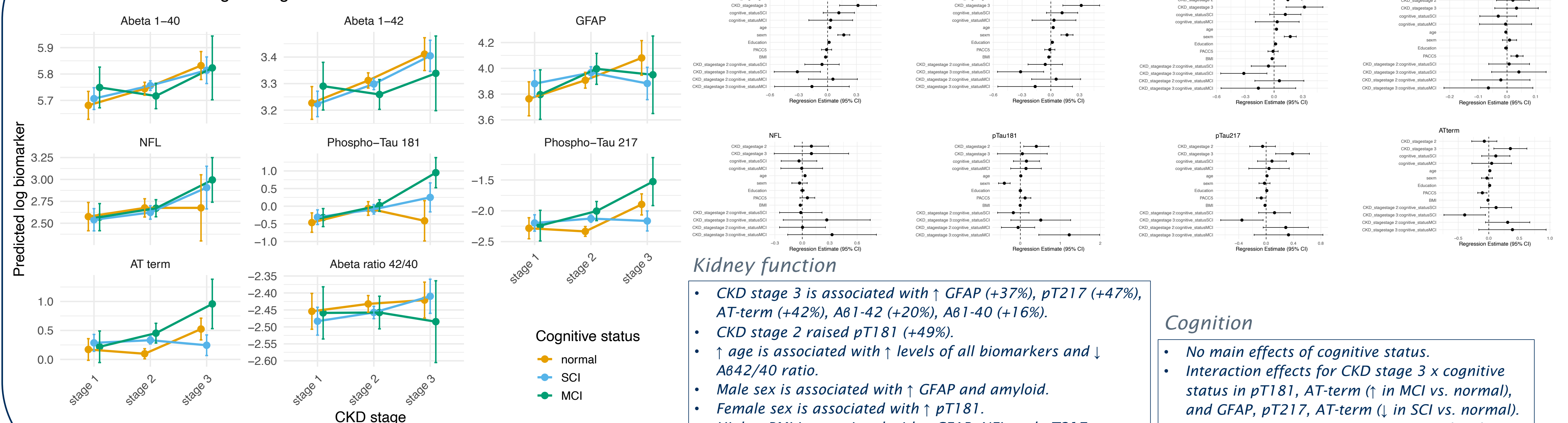
Biomarkers. Plasma GFAP, NFL, phospho-tau (pT181, pT217), amyloid-β (Aβ₁₋₄₀, Aβ₁₋₄₂, ratio), and a composite amyloid-tau ratio (AT-term: Aβ₄₀/42×pT217).

Blood. eGFR was used to categorize participants into CKD stage 1-3 (Table 1).

Models. Linear regression on log-transformed biomarkers with CKD stage, cognitive status, and their interaction, adjusted for age, sex, education, PACC5, and BMI.

Results

Interaction: CKD stage × cognitive status



Kidney function

- CKD stage 3 is associated with ↑ GFAP (+37%), pT217 (+47%), AT-term (+42%), Aβ1-42 (+20%), Aβ1-40 (+16%).
- CKD stage 2 raised pT181 (+49%).
- ↑ age is associated with ↑ levels of all biomarkers and ↓ Aβ42/40 ratio.
- Male sex is associated with ↑ GFAP and amyloid.
- Female sex is associated with ↑ pT181.
- Higher BMI is associated with ↓ GFAP, NFL and pT217.
- Aβ42/40 ratio was insensitive to CKD.

Cognition

- No main effects of cognitive status.
- Interaction effects for CKD stage 3 × cognitive status in pT181, AT-term (↑ in MCI vs. normal), and GFAP, pT217, AT-term (↓ in SCI vs. normal).
- PACC5: Better memory was associated with ↑ Abeta ratio, ↓ pTau217 and ↓ AT term.

TAKE HOME

- Kidney function has a clinically relevant impact on multiple blood-based AD biomarkers, particularly astroglial (GFAP), tau (pT217, pT181, AT-term) and amyloid (but not on the ratio).
- CKD effects were broadly consistent across cognitive groups, though some stage 3 interactions reached nominal significance (e.g., higher pT181 in MCI).
- Renal function, along with age, sex, and BMI should be accounted for when interpreting plasma AD biomarkers in clinical practice.

