

Integrating Lifestyle, Clinical Features, and Neuroinflammation in Alzheimer's disease and Related Disorders

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Key findings: Peripheral and neuroinflammation markers show distinct links to neurodegeneration and cognition; multiple mechanisms, rather than a single dominant process, underlie cognitive decline in aging and dementia.

INTRODUCTION

- Inflammation is a key biological process implicated in neurodegeneration^{1,2}.
- Peripheral inflammation (IL-6) and neuroinflammation (GFAP) may influence cognition through overlapping or independent pathways².
- It is unclear whether IL-6 affects brain pathology via neuroinflammation or through parallel systemic mechanisms.
- We examined how lifestyle, clinical factors, IL-6, and GFAP relate to neurodegeneration and cognition in group of aging adults with and without cognitive impairment and dementia .

METHODS

Variables	Details
Participants	N = 591 adults from the COMPASS-ND ³ cohort Diagnostic groups: CU, SCI, MCI, V-MCI, AD, Mixed
Peripheral Inflammation	IL-6
Neuroinflammation	GFAP (astrocytic reactivity)
Neurodegeneration	pTau181, NfL, Aβ42/40, White matter volume
Clinical & Lifestyle Factors	BMI, comorbidities, sleep, nutrition
Cognition	MoCA
Analysis	Age adjusted structural equation model (SEM); General linear model (GLM) plots are presented to illustrate continuous relationships

RESULTS

Inflammation Predictors	Neurodegeneration	Cognition
IL-6 ↑ with age, BMI, comorbidities	IL-6 & GFAP → pTau181, NfL	MoCA associated with IL-6, GFAP, pTau181, NfL, Aβ42/40
GFAP ↑ with age; ↓ with BMI, linked to more sleep	GFAP → Aβ42/40	Indirect effects from IL-6 and GFAP to MoCA via pTau181 & NfL
IL-6 did not predict GFAP → independent pathways		

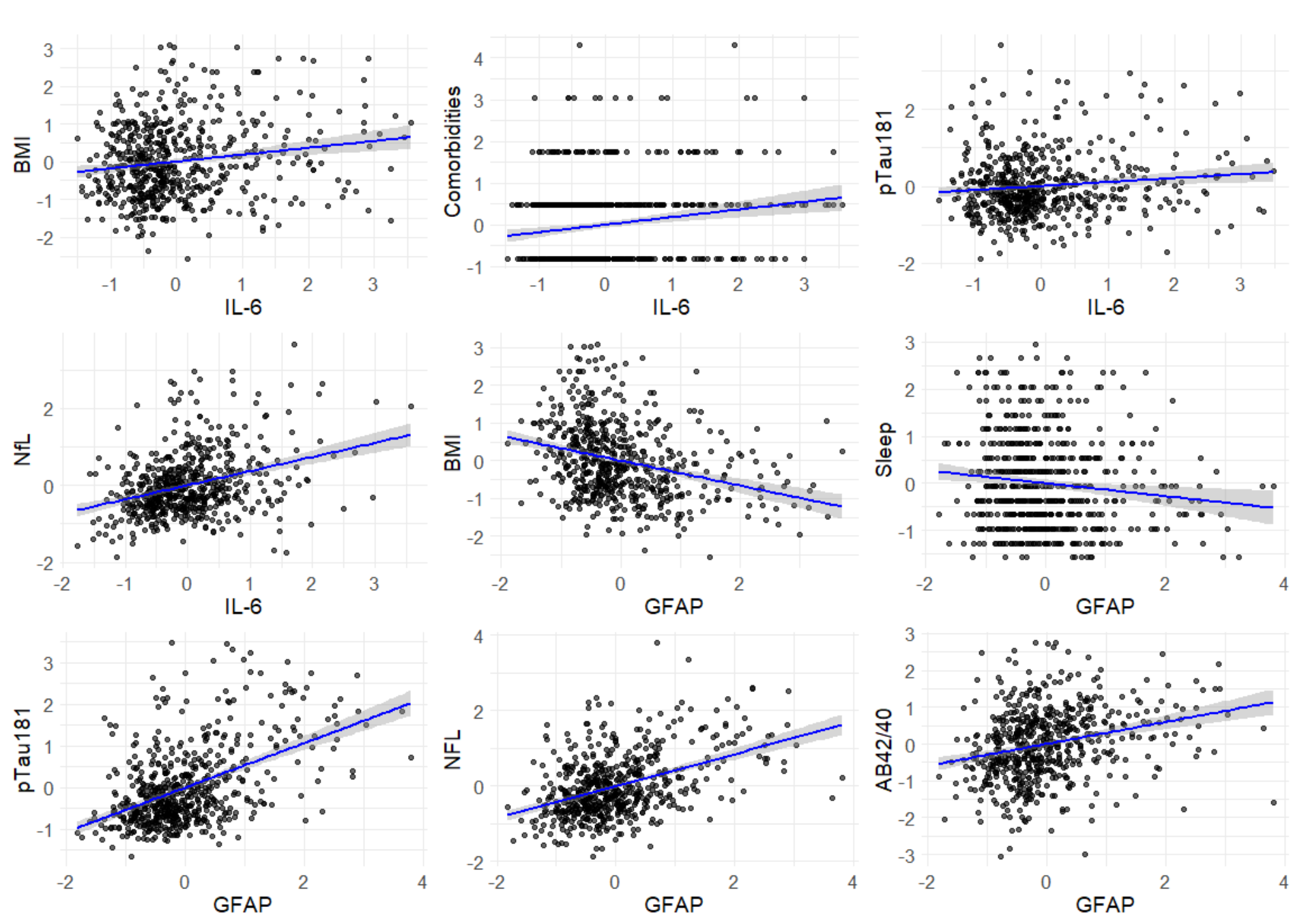


Figure 2. Significant relationships of IL-6 and GFAP with demographic, clinical features, and neuropathology biomarkers.

CONCLUSION

- Both IL-6 and GFAP contribute to neurodegeneration and cognitive decline.
- IL-6 and GFAP operate through partially independent pathways, not a single cascade.
- Neurodegeneration (pTau181, NfL) is a key mediator linking inflammation to cognition.
- Cognitive impairment reflected multiple interacting pathologies, reinforcing the view that multiple mechanisms, rather than a single dominant process, underlie cognitive decline in aging and dementia.

REFERENCES

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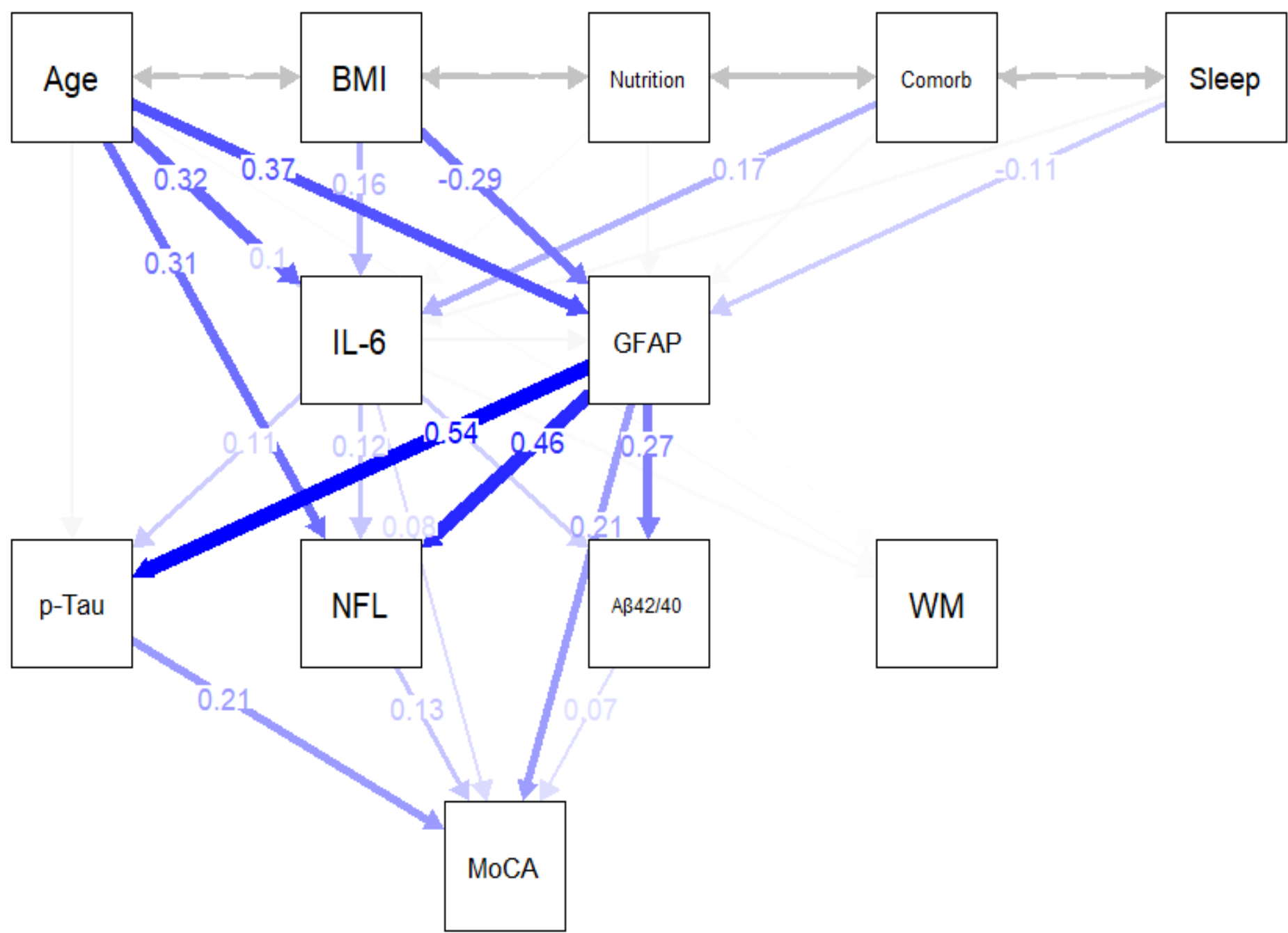


Figure 1. SEM pathways linking lifestyle/clinical features to inflammation, neurodegeneration, and cognition. Values represent standardized coefficients.

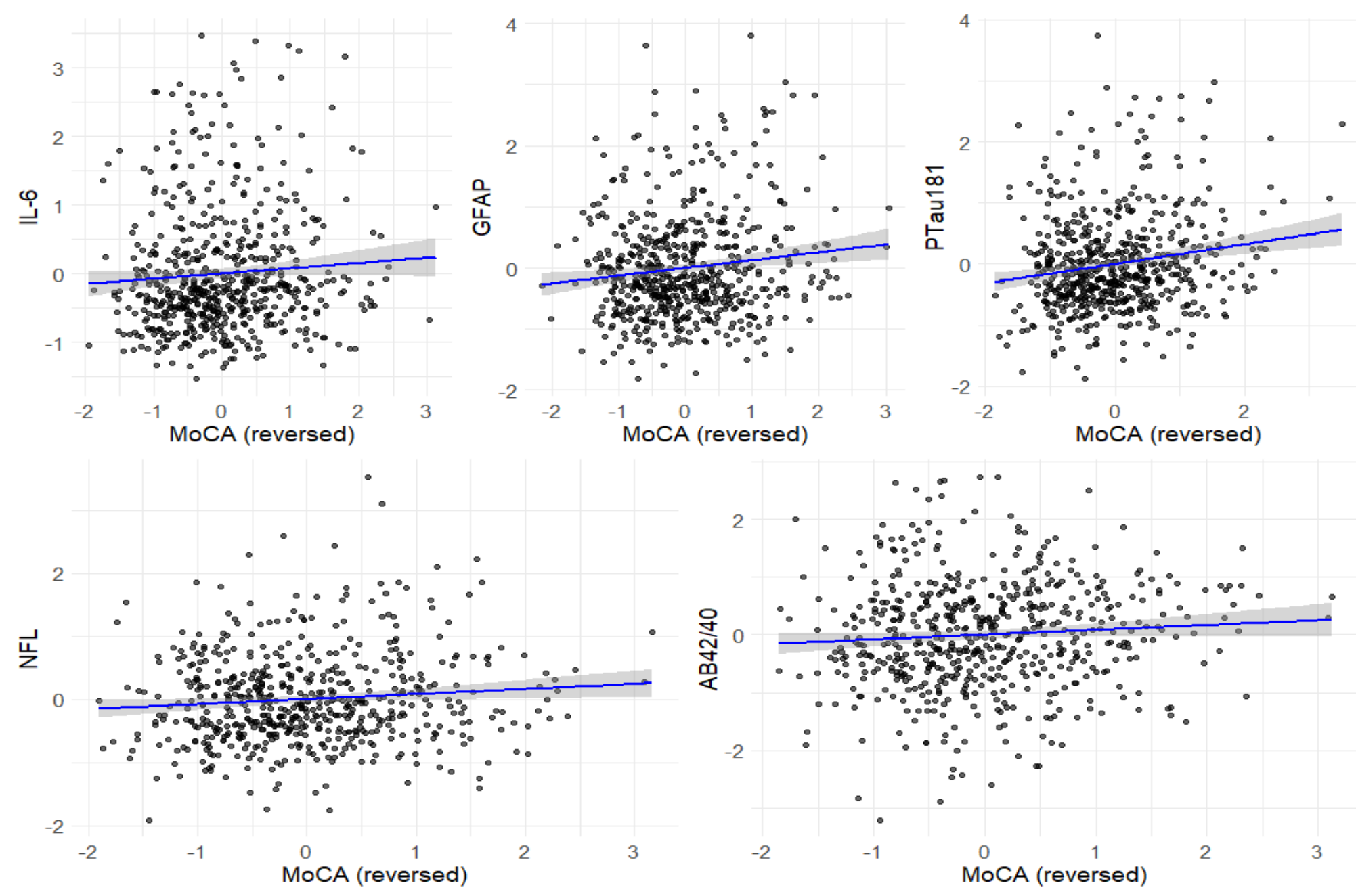


Figure 3. Significant relationships between MoCA scores, inflammation, and neuropathology biomarkers.