

Correlations between Alzheimer's Disease and Inflammatory Plasma Biomarkers in Virologically Suppressed Older People with HIV

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BACKGROUND

- Plasma-based biomarkers offer a promising and accessible approach for detecting Alzheimer's disease (AD), including in older people with HIV (PWH).
- Emerging evidence in the general population suggests that systemic inflammation may contribute to AD-related biomarker changes, but data in PWH remain limited.
- We previously demonstrated that elevated plasma p-tau217 and GFAP predict cognitive decline in this population.

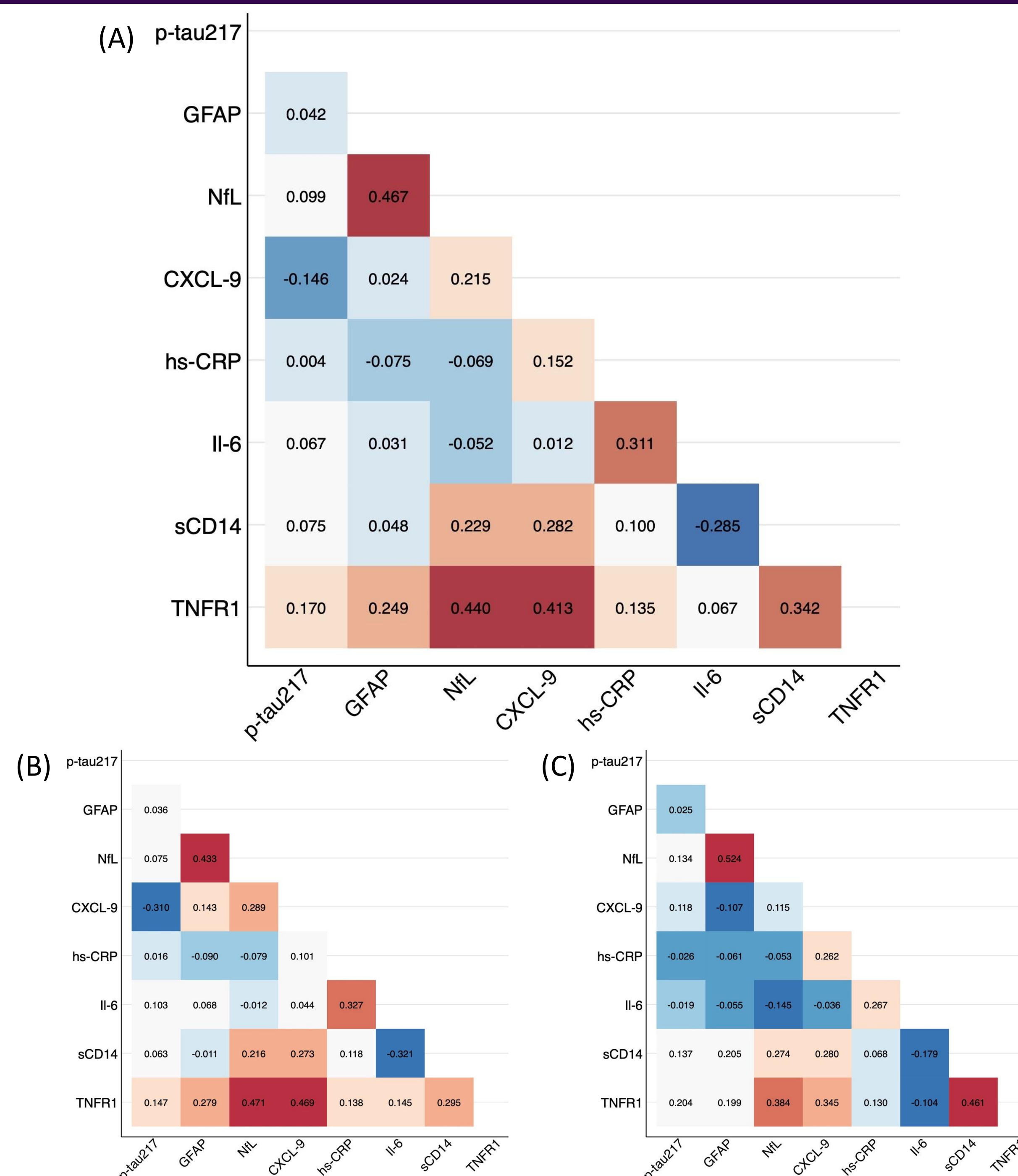
OBJECTIVE

- To examine correlations between AD-related and inflammatory plasma biomarkers among older PWH.

METHODS

- PWH aged ≥50 years with plasma HIV RNA <50 copies/mL from the HIV-NAT 006 cohort—an ongoing cohort of adults living with HIV in Bangkok, Thailand—were included.
- Plasma biomarkers were measured cross-sectionally using samples collected at the same study visit as cognitive assessments. These include:
 - AD biomarkers:
 - Phosphorylated tau 217 (p-tau217)
 - Glial fibrillary acidic protein (GFAP)
 - Neurofilament light chain (NfL)
 - Inflammatory biomarkers:
 - Chemokine (C-X-C motif) ligand 9 (CXCL9)
 - High-sensitivity C-reactive protein (hs-CRP)
 - Interleukin-6 (IL-6)
 - Soluble CD14 (sCD14)
 - Tumor necrosis factor receptor 1 (TNFR1)
- All biomarker values were log-transformed.
- Cognitive function was assessed using the Thai-validated Montreal Cognitive Assessment (MoCA), with scores ≥25 considered normal.

Systemic inflammatory markers (CXCL-9, sCD14, and TNFR1) were positively associated with AD-related biomarkers (GFAP and NfL), with stronger correlations among virally suppressed PWH aged ≥50 with lower cognitive performance.



RESULTS

- 255 PWH aged ≥50 years were included (**Table**)
- Correlations between AD and inflammatory biomarkers (**Figure A**)
 - GFAP: TNFR1 ($r = 0.249$, $p < 0.001$)
 - NfL: CXCL-9 ($r = 0.215$, $p = 0.001$), sCD14 ($r = 0.229$, $p = 0.001$), TNFR1 ($r = 0.440$, $p < 0.001$)
 - p-tau217: Statistically significant but weak correlations with CXCL-9, and TNFR1 (all $|r| < 0.2$)
- Correlations varied by cognitive status: Stronger correlations between CXCL-9 and TNFR1 with GFAP and NfL among PWH with MoCA scores <25 (**Figure B and C**).

	Overall (N=255)	MoCA <25 (N=156)	MoCA ≥25 (N=99)	<i>p</i>
Age, y	54.3 (51.8–59.1)	54.8 (52.1–60.4)	53.9 (51.3–57.1)	0.023
Sex: Female	94 (36.9%)	25 (25.3%)	69 (44.2%)	0.002
Education: >6 years	194 (76.1%)	91 (91.9%)	103 (66.0%)	<0.001
BMI, kg/m ²	23.0 (20.6–25.0)	22.8 (20.0, 24.4)	23.2 (20.9, 25.5)	0.15
Smoker	35 (13.7%)	17 (17.2%)	18 (11.5%)	0.20
Alcohol consumption	26 (10.2%)	9 (9.1%)	17 (10.9%)	0.64
DM	41 (16.1%)	15 (15.2%)	26 (16.7%)	0.75
HT	109 (42.7%)	42 (42.4%)	67 (42.9%)	0.93
Depression	18 (7.1%)	6 (6.1%)	12 (7.7%)	0.62
HIV duration, y	18.7 (15.3–21.0)	18.0 (15.0–20.8)	19.0 (15.8–21.2)	0.22
Nadir CD4 <200	144 (56.5%)	59 (59.6%)	85 (54.5%)	0.42
Current CD4	624.0 (491.0–803.0)	648.0 (467.0–797.0)	623.0 (496.0–811.5)	0.70
Current ART				
NNRTI	167 (65.5%)	66 (66.7%)	101 (64.7%)	0.75
PI	99 (38.8%)	34 (34.3%)	65 (41.7%)	0.24
INSTI	12 (4.7%)	5 (5.1%)	7 (4.5%)	>0.999

Continuous data are shown as median (IQR).

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; DM, diabetes mellitus; HT, hypertension; INSTI, Integrase strand transfer inhibitor; NNRTI, Non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor

CONCLUSION

- These findings support a potential link between systemic inflammation and AD-related biomarkers in virally suppressed older PWH.
- Longitudinal studies are warranted to clarify the role of these inflammatory pathways in the trajectories of cognitive function among this population.