Plasma Inflammatory Biomarkers Link to Worse Cognition Among Africans with HIV

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Background:

- Nearly two-thirds of people with HIV (PWH) reside in Africa.[1]
- HIV-associated neurocognitive disorder (HAND) affects 30-40% of PWH in the region.[2]
- Even with suppressed viremia, PWH display abnormal levels of biomarkers of innate and adaptive immune activation.[2-5]
- Many studies on inflammation and cognitive performance lack robust sample sizes and focus on high-income global regions.

Aim:

- Examine the link between chronic inflammation and cognitive performance among a robust sample size in SSA.

Participants:

Retrospective cross-sectional analysis of 2737 participants [473 people without HIV (PWoH), 1393 suppressed PWH, 871 unsuppressed PWH] with concurrent neuropsychological testing. Enrollment data included blood collection and medical history.

Table 1: Demographic characteristics by group at enrollment visit (n=2737)

	HIV Uninfected (n=473), (17%)	Suppressed PWH (n= 1393), (51%)	Unsuppressed PWH (n= 871), (32%)	p-value
Sex, female	262 (55%)	805 (58%)	532 (61%)	0.103
Age, mean (SD; range minimum-maximum)	37.1 (10.4; 18.1-68.9)	41.5 (10.2; 18.8-76.0)	37.1 (10.2; 18.2-72.5)	**< 0.001**
Education				**0.034**
Some primary school or less	150 (32%)	475 (34%)	309 (35%)	
Completed primary school or some secondary school	192 (41%)	510 (37%)	345 (40%)	-
Completed secondary school or some vocational school or some post-secondary school	97 (21%)	314 (23%)	146 (17%)	-
Completed post-secondary school or vocational school	34 (7%)	94 (7%)	71 (8%)	-
Ability to read and write	443 (94%)	1270 (91%)	768 (88%)	**0.003**
Employed, by self-report	195 (41%)	545 (39%)	425 (49%)	**< 0.001**
NPZ mean (SD)	0.02 (0.64)	-0.20 (0.77)	-0.26 (0.73)	**< 0.001**
HIV disease characteristics†	-			**< 0.001**
CD4 count, mean (SD)		469.7 (254.7)	343.2 (250.0)	
Log10 Plasma HIV RNA, mean (SD)	-	0.8 (0.9)	4.6 (0.8)	**< 0.001**
Virally suppressed (<1000 copies/mL)	-	1393 (100%)	0 (0%)	**< 0.001**

Methods:

- **Plasma biomarker** levels quantified via Luminex/ELISA: CXCL10 (IP-10), CCL2 (MCP-1), sCD163, sCD25 (IL-2R alpha)
- Standardized, demographically-adjusted neuropsychological (NP) test performance analyzed; composite z-score (**NPZ**) averaged AVLT trials 1-5, AVLT delayed recall, Action Fluency, Trails A, and Grooved Pegboard

Statistical Analysis:

- Multivariable linear regressions used to analyze associations between NPZ and inflammatory markers with covariates: age, sex, education (plasma HIV RNA level and CD4 included with PWH group comparisons)
- Secondary analyses examined relationships between individual cognitive tests and inflammatory markers

Results:

Increasing levels of CCL2, sCD25, and CXCL10 are associated with lower (worse) NPZ in PWH.

Table 2: Primary model biomarker-NPZ associations

Biomarker	Coefficient	SE	p-value
CCL2	-0.101	0.041	**0.015**
sCD25	-0.228	0.048	**<0.001**
CXCL10	-0.207	0.039	**<0.001**
sCD163	-0.053	0.054	0.327

Table 3: Biomarker-NPZ association by group

	PWoH			Suppressed PWH			Unsuppressed PWH		
Biomarker	Coefficient	SE	p-value	Coefficient	SE	p-value	Coefficient	SE	p-value
CCL2	0.072	0.095	0.450	-0.151	0.060	**0.012**	-0.085	0.071	0.234
sCD25	-0.146	0.108	0.175	-0.269	0.073	**<0.001**	-0.195	0.079	**0.014**
CXCL10	-0.039	0.098	0.691	-0.243	0.063	**<0.001**	-0.210	0.058	**<0.001**

Table 2: Increasing levels of CCL2, sCD25, and CXCL10 are associated with lower (worse) NPZ.

- Increasing biomarker levels of CCL2, sCD25, and CXCL10 were associated with lower (**worse**) **NPZ**.
- Additional **significant covariates** included:
  - Educational attainment (β= 0.308 average, p<0.001)
  - Grouping variable, which differentiates PWoH, suppressed PWH, and unsuppressed PWH (β= -0.208 average, p<0.001)

Table 3: Elevated CCL2, sCD25, and CXCL10 correlate with lower NPZ in suppressed and unsuppressed PWH.

- Subgroup analyses demonstrated an association between **CCL2** and NPZ (β= -0.151, p=0.012) in the **suppressed** PWH group only
- For **sCD25**, the suppressed PWH group had a stronger association with NPZ (β= -0.269, p<0.001) compared to the unsuppressed group
- We found a stronger association between NPZ and **CXCL10** within the suppressed PWH group (β= -0.243, p<0.001) compared to the unsuppressed
- We identified **no associations** between biomarkers and NPZ in **PWoH**.

Results (continued):

Biomarker distributions by group

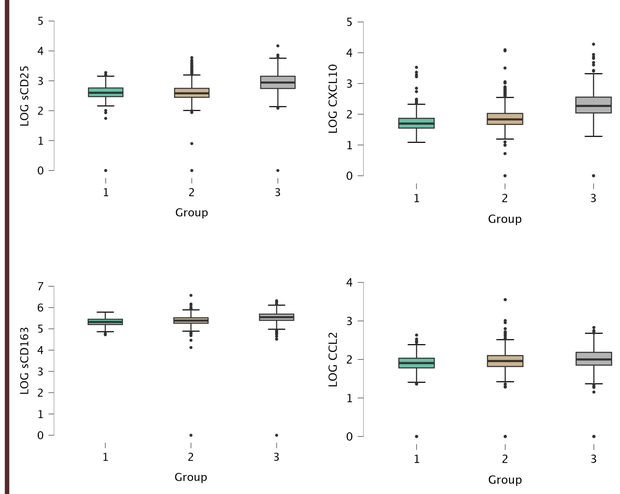


Figure 1: Biomarker distributions by group (1= PWoH, 2= suppressed PWH, 3= unsuppressed PWH).

PWoH exhibited lower levels of all the plasma inflammatory markers compared to the PWH (**p<0.001**). As expected, PWH with unsuppressed viremia exhibited the highest levels of all plasma inflammatory markers.

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Conclusions:

- In this cohort from East Africa, **inflammatory markers** among **PWH** were associated with **worse** cognitive performance, even among those with suppressed plasma viral load.
- **Grooved Pegboard** displayed the strongest associations with biomarkers (CCL2 β=-0.309, sCD25 β=-0.537, and CXCL10 β=-0.316, p<0.01).
- Relationships between **sCD163** levels and cognitive performance were not significant

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