Immune Activation, and Neurocognition in Ugandan Adolescents living with HIV

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BACKGROUND

- Immune activation is associated with neurocognitive problems in virally suppressed adults living with HIV.
- Less is known about this relationship in adolescents with perinatally acquired HIV (PHIV) residing in low-income countries with high burdens of PHIV. We examined this relationship in Ugandan adolescents with PHIV.
- Our objectives were
  - 1) To evaluate neurocognition using NeuroScreen (NS) in PHIV compared to HIV uninfected children (HIV-) in Uganda
  - 2) To investigate the relationship between inflammation and immune activation and neurocognition

METHODS

Study design: cross sectional analysis of data from an observational cohort of PHIV and HIV- children cohort prospectively enrolled at the JCRC in Kampala, Uganda

Subjects:

HIV+: children living with perinatally acquired HIV aged 10-18 years years, on stable ART for at least 6 months with HIV-1 RNA< 400 copies/mL.

- **HIV-**: HIV unexposed uninfected children age and gender matched.

Neurocognition:

- NeuroScreen (tablet-based neurocognitive tests, Figure 1)

Plasma Biomarkers:

- Plasma markers of systemic inflammation: hsCRP, IL6
- Plasma markers of monocyte activation: sCD14 and sCD163
- Plasma marker of oxidized lipids: oxLDL

Cellular markers of monocyte and T cell activation:

- T cells phenotyped by flow cytometry: co-expression of CD38 and HLA-DR
- Monocytes phenotyped by flow cytometry: expression of CD14 and CD16

Statistical Analysis

- Control based test z-score and overall z score were calculated
- Person correlations to examine associations between test performance and biomarkers

In this cohort from Uganda, PHIV on ART with viral suppression have evidence of worse neurocognition which correlated with monocyte and T cell activation.

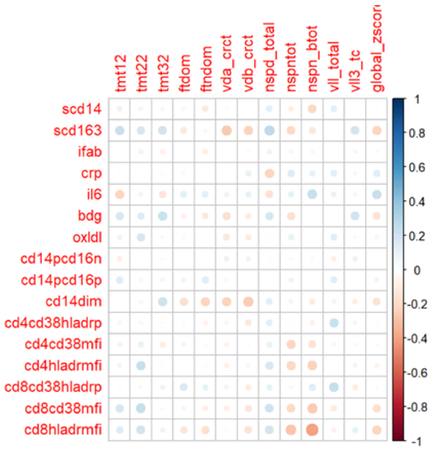
RESULTS

- Compared to controls, global z-scores were lower among the PHIV group (p=0.05), and significantly worse on executive functioning and delayed recall tests (Figure 2).
- Heatmap of correlation between biomarkers and test performance for all participants is highlighted in Figure 3.
- Monocyte activation significantly correlated with worse test performance:
  - sCD163 with worse global z-score;
  - sCD163 and non-classical monocytes with worse attention, processing speed, and motor speed.
- T-cell activation was significantly associated with worse performance on learning, working memory, and executive functioning tests.
- Similar associations were found by study arm, though among controls, T-cell activation and worse delayed recall were also significantly correlated (r=0.32, p=0.02)

Table 1: Baseline Characteristics

	PHIV n=28	HIV- N=54	p
Age (years)	15.53	14.88	0.26
Female sex (%)	11 (39)	22 (41)	1
HIV Variables			
Viral load < 20 copies/mL (%)	24 (86%)		
CD4 nadir (cells/µL)	619.50		
CD4 cell count (cells/µL)	988		
ART Duration (years)	9.88		

FIGURE 3: CORRELATION BETWEEN BIOMARKERS AND NS FOR ALL PARTICIPANTS



T cells and monocyte represent % lymphocytes and % monocytes
BDG: Beta-d-glucan (pg/mL), hsCRP: high sensitivity C reactive protein (ng/mL),
IFAB-P: intestinal fatty acid binding protein (pg/mL),
IL-6: interleukin 6 (pg/mL), oxLDL: oxidized LDL,
sCD14 and 163: soluble CD14 and soluble CD163 (pg/mL)

TMT1.2 and 2.2: Trail Making Completion Time
Ftdom Ftndom: Finger tapping dominant hand and non dominant hand
Vda and vdb crct: Visual Discrimination Correct responses
NSPD tot: Numer speed total time
NSPNtot: Number Span Forward
NPSPN btot: Number Span Backwards
VLL total: Verbal list learning total score
VLL 3-tc: Verbal list learning delayed recall total score

CONCLUSIONS

- PHIV with virologic suppression on ART showed evidence of worse neurocognition
- Monocyte and T cell activation correlated with worse neurocognition in Ugandan adolescents with PHIV
- Controls also showed similar associations
- More research is needed to understand this relationship and its mechanisms in adolescents in the global South.

FIGURE 1: NEUROSCREEN

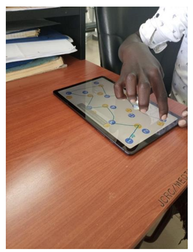
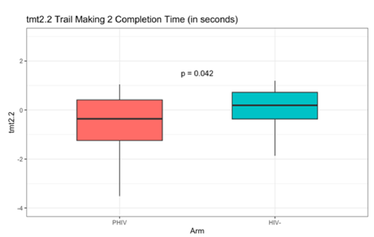
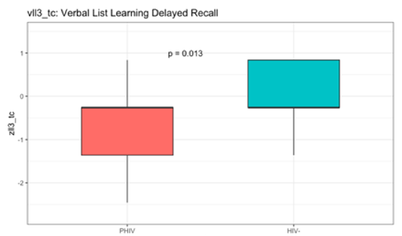
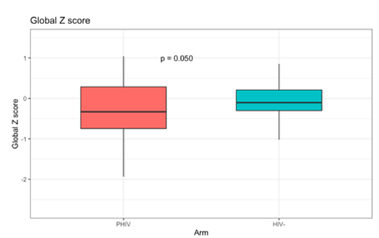


FIGURE 2: NS COMPARISON BETWEEN GROUPS







ADDITIONAL KEY INFORMATION

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