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Megan Niehaus
menzx8@umsystem.edu

Julie Mannarino
julie.mannarino@mimh.edu

Jacob Bolzenius
bolzeniusj@umsl.edu

Tori Frerichs
vrf44z@mail.umsl.edu

Robert Paul
robert.paul@mimh.edu

Cognition and Inflammation in Youth with Perinatal HIV

Megan Niehaus,[1,2] Kyaw Linn,[3] Julie Mannarino,[2] Jacob Bolzenius,[2] Tori Frerichs,[1,2] Soe Mar,[4] Robert Paul[1,2]

[1]Department of Psychological Sciences, University of Missouri – St. Louis, [2]Precision Health Research Core, Missouri Institute of Mental Health, [3]Pediatric Neurology Unit, Yangon Children's Hospital, [4]Department of Pediatric Neurology, Washington University in St. Louis

Introduction

Background:

- Approximately 90% of those with perinatally acquired HIV (PHIV) reside in low- or middle-income countries (LMICs) where antiretroviral therapy (ART) is less accessible.
- Cognitive difficulties are commonly observed among youth with PHIV compared to uninfected peers
- In contrast to research on chronic HIV among adults, variance in cognitive profiles among youth with PHIV is likely attributable to an array of psychosocial and immune stressors present during critical developmental periods, rather than HIV disease mechanisms.
- Relationships between inflammatory markers and neurodevelopmental delays among youth with PHIV have not been well examined.

Study Aim:

- To identify inflammatory correlates of cognitive performance among youth with PHIV residing in orphanages in Yangon, Myanmar.

Methods

Participants:

- A total of 149 individuals (105 PHIV, 44 without HIV) residing in private orphanages in the same region of Yangon, Myanmar were included in the analysis.
- Individuals were between the ages of 9 and 19 and had been residing at the orphanage for at least 6 months.
- Youth with PHIV had been on ART for at least 6 months.
- Exclusion criteria included neurodevelopmental disorders, non-HIV chronic medical conditions, and acute illness at the time of enrollment.

Measures:

- Demographics, health and family history, and psychosocial factors (e.g., education, nutrition, recreational activity) .
- Neurocognitive performance was assessed using a 17-test battery covering 6 cognitive domains (i.e., Executive Function, Learning, Memory, Psychomotor/Processing Speed, Visuospatial, and Gross Motor).
  - Battery was designed to optimize translation between English and Burmese.
- Inflammatory markers (i.e., CD14, CD163, CRP, neopterin, TNF-α, and IL-6), which were log10 transformed due to positively skewed distributions.

Statistical Analyses:

- Differences in demographic and clinical/health indices were identified between serostatus groups using independent samples t-tests and chi-square tests.
- ANCOVAs (i.e., biomarkers) and MANCOVAs (i.e., cognition) were computed to compare serostatus groups accounting for demographic and clinical/health group differences.

Table 1. Demographic and HIV clinical characteristics at enrollment.

Variable	PHIV (n=105)	HIV- (n=44)
Current Age, M (SD)	12.88 (2.22)*	13.95 (1.29)*
Sex (% male)	52 (50.0%)	17 (38.6)
Number of Months Residing in Orphanage, M (SD)	82.85 (33.76)*	63.70 (27.85)*
Grade, M (SD)	5.19 (2.32)*	7.11 (1.47)*
HIV Tropism, n (%)		
X4	20 (47.6%)	-
R5	22 (52.4%)	-
Age at HIV Diagnosis, M (SD)	6.87 (4.83)	-
Nadir CD4+ T-cell count, Median (IQR)	733 (381-1083)	-
Current CD4+ T-cell count, Median (IQR)	729 (565-1026)	798 (690-905)
HIV Viral Load, n (%) undetectable	85 (81.7%)	-
Previous Opportunistic Infection, n (%)	38 (37.3%)	-
Father's Cause of Death, n (%)		
HIV	34 (32.7%)	0 (0%)
Unknown	68 (65.4%)	8 (50.0%)
Father Still Alive	2 (1.9%)	8 (50.0%)
Mother's Cause of Death, n (%)		
HIV	31 (30.1%)	0 (0%)
Unknown	69 (67.0%)	8 (50.0%)
Mother Still Alive	3 (2.9%)	8 (50.0%)

*$p < .01$

Results

Table 2. Performance on cognitive tests.

Domain	Test	PHIV (n=105)	HIV- (n=44)
Executive Function	Color Trails 2	161.36 (54.66)**	118.17 (39.02)**
	Digit Span Forward	8.74 (2.99)	8.88 (2.37)
	Digit Span Backward	4.35 (1.76)	5.37 (1.71)
	Animal Fluency	16.69 (6.10)	16.16 (4.34)
	Food Fluency	14.28 (5.48)	13.79 (4.03)
Learning	HVLT-R Total Learning	21.59 (5.46)**	26.05 (4.04)**
	BVMT-R Total Learning	20.52 (9.53)**	27.82 (5.27)**
Memory	HVLT-R Delayed Recall	8.22 (2.63)	9.77 (1.74)
	BVMT-R Delayed Recall	8.95 (3.45)*	11.23 (1.09)*
Psychomotor / Processing Speed	Grooved Pegboard-Dominant	73.44 (22.08)	64.07 (18.03)
	Grooved Pegboard-Nondominant	81.17 (31.28)	69.69 (10.25)
	Color Trails 1	90.00 (44.69)	63.40 (20.52)
	Trails A	67.53 (36.34)*	44.18 (13.10)*
	Digit Symbol	32.43 (11.25)**	46.86 (8.02)**
	Symbol Search	22.23 (7.07)**	28.32 (5.49)**
Visuospatial	Block Design	27.50 (16.68)**	42.23 (14.31)**
	Beery VMI	18.58 (4.12)**	22.05 (1.79)**
Gross Motor	Timed Gait	13.82 (3.40)	13.09 (2.75)

*Note: Data represent M(SD); *p < .05, **p < .01*

Figure. Partial correlations between cognitive performance and inflammatory markers.

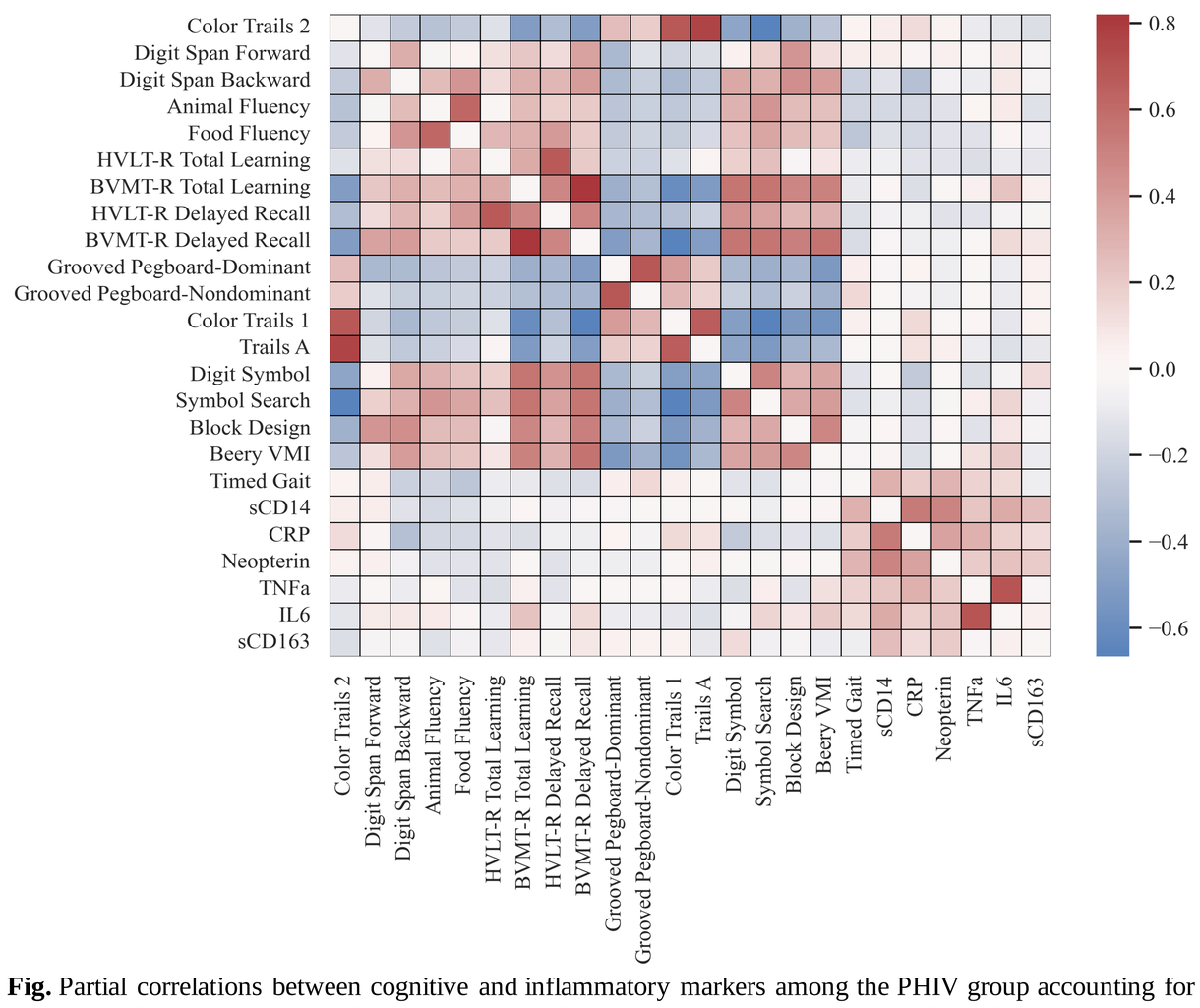

Fig. Partial correlations between cognitive and inflammatory markers among the PHIV group accounting for age and grade. Significant correlations were noted between CRP and Digit Span Backward (r=-.306, p<.01), CRP and Digit Symbol (r=-.252, p<.05), sCD14 and Timed Gait (r=.305, p<.01), and neopterin and Timed Gait (r=.290, p<.05).

Discussion

Summary

- We observed several moderate strength relationships between cognitive performance and inflammatory markers among youth with PHIV.
- Findings provide support for the hypothesis that non-HIV-specific biomarkers may yield explanatory value for variations in cognitive performance among youth with PHIV.

Future Directions:

- Longitudinal assessments are needed to characterize continued changes in relationships between cognitive function and peripheral inflammation as youth with PHIV advance toward adulthood
- Further evaluation of psychosocial factors that confer increased risk or protective status for these individuals have potential to identify therapeutic options