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Inflammation and cognition associations in young adults with perinatal HIV exposure and/or infection

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— BACKGROUND —

- Children with perinatal HIV exposure, particularly those with HIV infection, are at risk for worse cognitive outcomes compared to unexposed children.
- Inflammation is a potential risk factor for worse cognitive outcomes in populations with HIV, but no studies have evaluated this association within young adults with perinatal HIV (YAPHIV) or perinatal HIV exposure but uninfected (YAPHEU).
- We evaluated the association between inflammatory biomarkers and NIH Toolbox cognitive outcomes in YAPHIV and YAPHEU.

— METHODS —

- Participants with available plasma samples and NIH Toolbox cognitive scores at entry into the PHACS AMP Up study, as of April 1, 2022
- Participants were subdivided into three groups:
  - YAPHIV who experienced a Stage 3 event
  - YAPHIV who had not experienced a Stage 3 event
  - YAPHEU
- A Stage 3 event was being diagnosed with an opportunistic infection.
- Principal Component Analysis (PCA) was used to derive PCA factors from biomarkers for:
  - Monocyte activation (sCD14, sCD163),
  - Acute phase inflammation (CRP, fibrinogen, TNF-a)
  - Proinflammatory/Th1/Th17 cytokines (IFN-γ , IL-1β, IL-2, IL-12p70, IL-17a)
  - Anti-inflammatory/Th2 cytokines (IL-4, IL-6, IL-10)
  - Homeostasis (GM-CSF, Fractalkine).
- We computed Pearson correlations of individual log-transformed biomarkers and four PCA factors with Composite Standard Scores for Total, Fluid (e.g., processing speed, executive functions), and Crystallized Cognition (e.g., word knowledge), separately by HIV status.

— RESULTS —

- Of the 765 participants in AMP UP, 638 had available plasma samples and NIH Toolbox scores
- YAPHIV: n=521, mean age 22.7 (SD:4.2) years
  - 135 YAPHIV had a Stage 3 event
- YAPHEU: n=117, mean age 19.0 (SD:1.4) years were included.

Cognition was **weakly correlated** with measured inflammatory biomarkers, with different patterns in YAPHEU and YAPHIV with and without history of severe disease

— RESULTS —

Table: Pearson correlations of principal component scores of log-transformed biomarkers with NIHT age-corrected composite scores by HIV status

		Fluid Composite Score				Crystalized Composite Score				Total Composite Score			
Component		YAPHEU n=106	YAPHIV n=499	YAPHIV with CDC Stage 3 event n=130	YAPHIV without CDC Stage 3 event n=366	YAPHEU n=116	YAPHIV n=509	YAPHIV with CDC Stage 3 event n=132	YAPHIV without CDC Stage 3 event n=374	YAPHEU n=106	YAPHIV n=491	YAPHIV with CDC Stage 3 event n=128	YAPHIV without CDC Stage 3 event n=360
Component 1	Correlation	0.188	-0.020	0.093	-0.074	-0.106	-0.047	-0.022	-0.061	0.028	-0.034	0.053	-0.077
	95% CI	(-0.003, 0.365)	(-0.108, 0.068)	(-0.081, 0.261)	(-0.175, 0.028)	(-0.283, 0.078)	(-0.133, 0.041)	(-0.192, 0.150)	(-0.161, 0.041)	(-0.163, 0.218)	(-0.122, 0.055)	(-0.121, 0.225)	(-0.178, 0.027)
Component 2	Correlation	-0.030	0.019	-0.121	0.051	-0.067	0.033	0.011	0.032	-0.029	0.019	-0.071	0.035
	95% CI	(-0.220, 0.162)	(-0.069, 0.106)	(-0.287, 0.052)	(-0.052, 0.152)	(-0.246, 0.117)	(-0.054, 0.119)	(-0.160, 0.181)	(-0.069, 0.133)	(-0.218, 0.163)	(-0.070, 0.107)	(-0.242, 0.103)	(-0.068, 0.138)
Component 3	Correlation	0.058	-0.104	-0.116	-0.096	0.013	-0.068	-0.073	-0.064	0.053	-0.100	-0.105	-0.095
	95% CI	(-0.135, 0.246)	(-0.190, -0.017)	(-0.283, 0.057)	(-0.197, 0.007)	(-0.170, 0.195)	(-0.154, 0.019)	(-0.241, 0.099)	(-0.164, 0.038)	(-0.139, 0.242)	(-0.186, -0.011)	(-0.274, 0.069)	(-0.196, 0.009)
Component 4	Correlation	-0.043	-0.044	0.072	-0.079	-0.007	-0.019	0.030	-0.026	-0.072	-0.038	0.072	-0.065
	95% CI	(-0.232, 0.149)	(-0.132, 0.044)	(-0.102, 0.241)	(-0.180, 0.024)	(-0.189, 0.175)	(-0.105, 0.068)	(-0.142, 0.200)	(-0.127, 0.076)	(-0.260, 0.120)	(-0.126, 0.051)	(-0.103, 0.243)	(-0.167, 0.039)

-Biomarkers listed have the highest loading for each component:

- ***Component 1- IFN-γ, IL-12p70, IL-1β, IL-2, IL-17a, Fractalkine, and GM-CSF***
- ***Component 2- IL-4, IL-6, IL-10***
- ***Component 3- CRP, Fibrinogen, sCD14***
- ***Component 4- TNF-α, sCD163***

-95% CI: 95% confidence interval of correlation which was obtained based on Fisher's Z transformation.

— Summary of Results —

- YAPHIV with a Stage 3 event had the lowest mean Fluid Cognition and Total Cognition scores and YAPHIV-without a Stage 3 event had the highest mean Fluid Cognition and Total Cognition scores amongst all groups.
- The biomarkers types that loaded onto each Principal Component (PC) were as follows:
  - PC1 contained biomarkers with proinflammatory (Th1/Th17 cytokines) and homeostatic functions
  - PC2 contained biomarkers with anti-inflammatory and Th2 functions
  - PC3 and PC 4 contained biomarkers of acute phase inflammation and monocyte activation
- In YAPHEU, Principal Component (PC) 1 was weakly positively correlated with Fluid Cognition and weakly negatively correlated with Crystallized Cognition.
- In YAPHIV, PC 3 was weakly negatively correlated with Fluid Cognition and Total Cognition.
- In YAPHIV with a CDC Stage 3 event, PC 3 was also weakly negatively correlated with Fluid and Total Cognition, and PC2 was weakly negatively associated with Fluid Cognition

| CONCLUSIONS |

- PCA factor scores were weakly correlated with cognition measures, with different patterns in YAPHEU (Pro-inflammatory/Th1/Th17 cytokines and Homeostasis) and YAPHIV (monocyte and acute inflammation), with additional differentiation in YAPHIV with a history of a CDC Stage 3 event
- Further research is needed to understand the role of inflammatory profiles, perinatal HIV exposure or infection, and other factors in cognition.

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