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Systemic Immune-Inflammation Index Links to Slower Psychomotor Speed in Older People with HIV

Crystal X. Wang[1,2], Raymond Jones[3], Evelyn Iriarte[4], Jun Yeong Byun[5], Kristen D. Krause[6], Casey D. Xavier Hall[7], Ronald J. Ellis[1,2,8], Mariana Cherner[1,2], Suzi Hong[1], David J. Moore[1,2], Scott L. Letendre[1,2,9], Jennifer E. Iudicello[1,2]

[1]Department of Psychiatry, University of California, San Diego, La Jolla, CA, USA; [2]HIV Neurobehavioral Research Program; [3]Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA; [4]College of Nursing, University of Colorado Anschutz Medical Campus, Aurora, CO, USA; [5]School of Nursing, University of Alabama at Birmingham, Birmingham, AL, USA; [6]Department of Urban-Global Public Health, Rutgers School of Public Health, Newark, NJ, USA; [7]Center of Population Science for Health Equity, College of Nursing, Florida State University, Tallahassee, FL, USA; [8]Department of Neurosciences, University of California, San Diego, CA, USA; [9]Department of Infectious Disease, University of California, San Diego, CA, USA

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Background & Significance

- **Chronic immune activation and inflammation** persist even in treated PWH and contribute to **neurocognitive impairment**[1,2], particularly in older adults. However, more research is needed.[3]
- The **Systemic Immune Inflammation Index (SII)** is a novel biomarker of inflammation that can be calculated from routine complete blood count.
  - The SII has prognostic value as an indicator of immune activation and systemic inflammation across chronic disease conditions[4,5], though few have examined its utility in PWH.[6]
  - Furthermore, no published studies have examined its relationship with neurocognitive outcomes in PWH.
- This study aimed to examine the **relationship between the SII and neurocognitive outcomes** and whether this relationship would **differ in older versus younger PWH**.

Method

Participants

- Participants were 1,867 PWH from cohort studies at the UCSD HIV Neurobehavioral Research Program (HNRP) who completed neuropsychological testing and blood draws.

Measures

- **Inflammation:** Measured with the SII, which is calculated from complete blood counts[4]
- **Neurocognition:** Assessed using demographically adjusted T-scores across 7 domains, and global cognition (higher T-score = better performance; See **Table 1**)
- **Age:** Dichotomized as older (>50) or younger (<50)
- **Covariates:** Sex, nadir and current CD4, antiretroviral therapy (ART) use, viral suppression (e.g., plasma viral load <50 copies/mL), and estimated duration of HIV infection were controlled for in all models

Hypotheses

Hypothesis 1

The SII will be associated with poorer global and domain-specific neurocognition.

Hypothesis 2

Age and inflammation will interact, such that worse inflammation will more strongly associate with poorer neurocognition in older than younger PWH.

The **Systemic Immune-Inflammation Index** was associated with worse neurocognition in people with HIV (PWH), and with psychomotor slowing in older but not younger PWH, highlighting its clinical utility as an inflammatory biomarker for identifying brain health disorders in PWH

$$SII = \frac{\text{Neutrophil count X Platelet count}}{\text{Lymphocyte count}}$$

Table 1. Participant characteristics by group

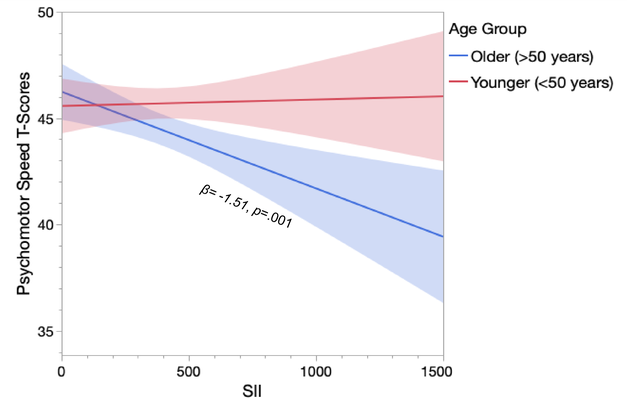
	Older PWH (>50 years; n=850)	Younger PWH (<50 years; n=1017)	*p*-value[a]
Sociodemographic Characteristics			
Age	58.40	40.40	**<.01**
Sex (male)[a]	81.4%	79.59%	.07
Education (years)[b]	13.47	12.52	**<.01**
Race/ethnicity (White)[a]	50.94%	39.82%	**<.01**
HIV Disease Characteristics			
AIDS[a]	72.37%	60.36%	**<.01**
Nadir CD4[c]	120	178	**<.01**
Current CD4[c]	537	463	**<.01**
Duration of infection (years)[c]	20	11	**<.01**
on ART[a]	88.20%	75.59%	**<.01**
Detectable plasma RNA[a,d]	23.86%	39.36%	**<.01**
Inflammation			
SII scores[c]	399.65	401.41	.89
Neurocognition (T-scores)[b]			
Global cognition	46.57	46.70	.72
Verbal fluency	48.71	48.49	.61
Executive Functioning	46.63	47.11	.29
Processing Speed	48.35	48.94	.19
Learning	44.07	43.56	.27
Recall	45.19	45.63	.35
Working Memory	46.59	46.13	.28
Motor Speed	44.44	45.67	**.02**

Note. Group differences are results of independent samples t-tests, or Chi-Square tests; [a]values represent percentages [b]values represent means [c]values represent medians [d]among those on ART; AIDS=Acquired Immune Deficiency Syndrome; RNA=ribonucleic acid

Results

- Across all participants, the **SII was associated with lower global cognition** (β = -.44, *SE* = .18, *p* = .013), which was driven by lower scores in the verbal fluency, processing speed, learning, and recall domains.
- **There was a significant age x SII interaction for psychomotor speed** (β = -.73, *SE* = -.316, *p* = .022)**,** such that greater inflammation was associated with worse psychomotor functioning for older PWH (β = -1.51, *SE* = .470, *p* = .001) but not younger PWH (*p* > .10; **Figure 1**).
  - The SII-psychomotor functioning association remained significant in a subgroup of **virally suppressed older PWH** (N = 606; β = -1.15, *SE* = .525, *p* = .029).
- No age x SII interactions emerged for global cognition or any other neurocognitive domains.

Figure 1. Interactive Effects of Age and SII on psychomotor speed



Conclusions

- **The SII was associated with poorer performance in multiple neurocognitive domains**, and globally in both younger and older PWH.
- The effects of the SII were **moderated by age for psychomotor speed**, demonstrating the **utility of the SII** in identifying psychomotor decline in older PWH.
- Results highlight the importance of **inflammation as a treatment target to improve neurocognition** in PWH, especially in older PWH.
- Future studies should examine **causal relationships** between the SII and neurocognitive impairment in PWH across the lifespan, and the potential for **anti-inflammation interventions to improve neurocognition in PWH, especially in older PWH.**

References [1]Ellis et al., 2020 [2]Saloner., 2021 [3]Aberg., 2016; [4]Hu et al., 2014; [5]Cui et al., 2023; [6]Wang et al., 2024

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Contact: crwang@health.ucsd.edu