Plasma Inflammation is Associated With Brain Cellularity in Diffusion-Based Spectral Imaging in HIV

592

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BACKGROUND

- Elevated levels of inflammation and neurodegeneration in the brain and periphery are associated with worse brain health outcomes in persons without HIV (PWoH)[1]
- People with HIV (PWH) have greater peripheral inflammation and neurodegeneration that may make them more vulnerable to elevated brain inflammation and alterations in brain white matter[2]
- Diffusion-based spectral imaging (DBSI) derived global cellularity (GC) is associated with activated microglia and may be used as a measure of brain inflammation[3]
- This study examines the association between plasma measures of inflammation, neurodegeneration, and brain measures of inflammation in PWH compared to PWoH

METHODS

- 222 PWH (77% male) and 45 PWoH (56% male) all age ≥ 30 years
- PWH had a viral load ≤ 200 copies/mL
- All participants underwent DBSI in a 3T MRI scanner, and the diffusion-weighted signal corresponding to cellularity was extracted both regionally and globally using established pipelines
- All participants completed a blood draw to obtain inflammatory and neurodegenerative markers of interest: CD14-CD16+ monocytes, CD14+CD16+ (proinflammatory monocyte), CD14+CD16- (classical monocyte with proinflammatory properties), sCD163 (anti-inflammatory), sCD14 (proinflammatory), glial fibrillary acidic protein (GFAP), and neurofilament light chain (NfL)
- Regression analyses were performed with age and sex included as covariates

	PWoH (n=45)	PWH (n=222)	P-value
Age (years; M ± SD)	51.4 ± 13.0	54.9 ± 9.04	<0.05
Sex (% male)	56%	77%	N/A
Race (% African American)	55.6%	60.8%	N/A
Education (years; M ± SD)	14.6 ± 2.86	13.3 ± 2.45	<0.01
Recent CD4 T-cell Count, median (IQR)	N/A	620 (416, 824)	N/A
CD14+CD16- (%; median [IQR])	79.6 (72.5, 86.7)	84.9 (78.7, 91.1)	<0.01
Plasma sCD163 (ng/mL; median [IQR])	623 (325.5, 920.5)	798 (488.5, 1107.5)	<0.05
Global Cellularity, mean ± SD	0.0600 ± 0.0111	0.0891 ± 0.0201	<0.001

Table 1. Demographic and Clinical Characteristics.
M = mean, SD = standard deviation, IQR = interquartile range

Increased age, percent of classical monocyte CD14+CD16-, and reduced anti-inflammatory sCD163 are associated with higher brain cellularity in PWH.

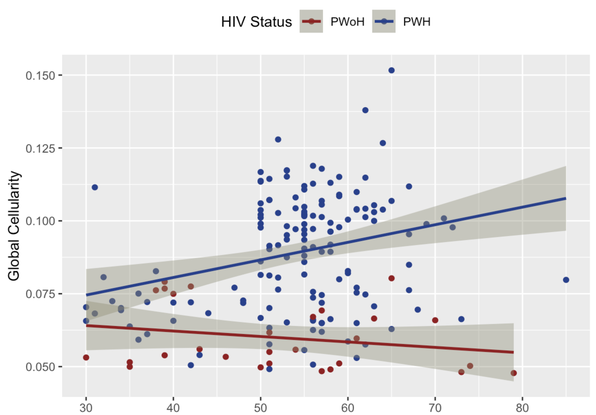


Figure 1. GC as a function of age.

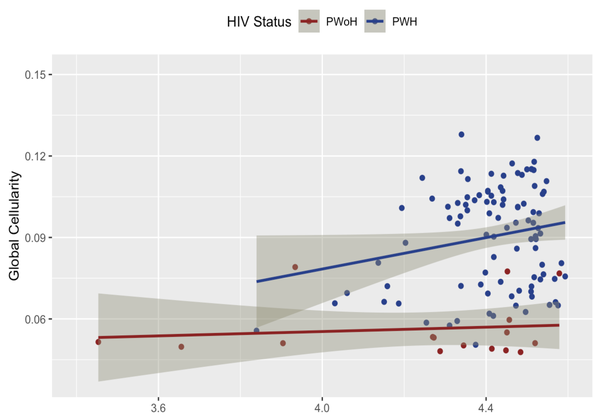


Figure 2. GC as a function of plasma percent of CD14+CD16-.

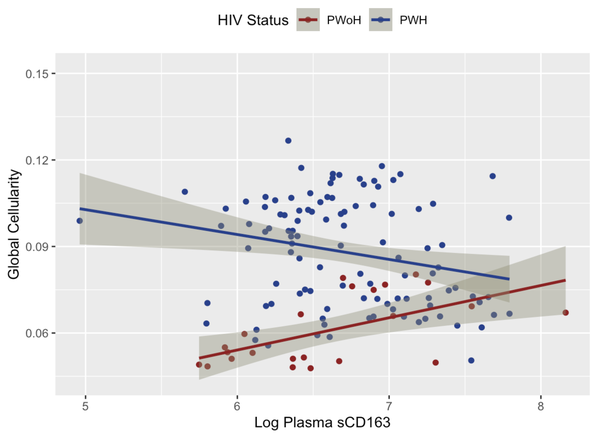


Figure 3. GC as a function of plasma sCD163.

RESULTS

- PWH had a significantly higher GC compared with PWoH ($p < 0.001$)
- Increasing age was significantly associated with increased GC in PWH ($p < 0.001$), but there was no association in PWoH (Figure 1)
- PWoH and PWH combined inflammatory markers and cells:
  - Percent of CD14+CD16- monocytes were significantly associated with GC when both PWH and PWoH were combined ($p < 0.01$), but only close to significance within each group (Figure 2)

RESULTS CONTINUED

- PWH only inflammatory markers and cells:
  - Elevated percent of CD14+CD16- monocytes showed a trend level with increased GC ($p < 0.08$) (Figure 2)
  - Elevated plasma sCD163 was significantly associated with lower GC ($p < 0.05$) (Figure 3)
- PWoH only inflammatory markers and cells:
  - Elevated percent of CD14+CD16- monocytes displayed a positive trend with increased GC ($p < 0.09$) (Figure 2)
  - Elevated sCD163 was significantly associated with increased GC ($p < 0.01$) (Figure 3)
- GFAP and NfL were not associated with any changes in GC in either PWH or PWoH

CONCLUSIONS

- With CD14+CD16- classical monocytes having proinflammatory properties and sCD163 inflammatory marker cells being anti-inflammatory, the trends seen in PWH suggest that DBSI cellularity may be uniquely sensitive to detecting central inflammatory processes happening in PWH
- Monocytes and peripheral markers of inflammation may provide better insight into or predict brain inflammation in PWH
- Further analysis of other groups of inflammatory markers (C-reactive protein and cytokines) and regional cellularity values would provide a more complete understanding of the interaction between peripheral inflammatory processes and GC

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