Plasma Aβ42/Aβ40 ratios are not reduced in older people living with HIV

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BACKGROUND

- It is unclear whether people with HIV (PWH) are at higher risk for age-related neurodegenerative disorder (e.g. Alzheimer disease (AD)), and if so, how to differentiate HIV-related neurocognitive impairment from AD.
- The plasma Aβ42/Aβ40 ratio is a clinically-available blood biomarker test for brain amyloidosis.
- The plasma Aβ42/Aβ40 ratio can also be used to calculated the Amyloid Probability Score (APS), which additionally incorporates age and apolipoprotein proteotype into a risk score for brain amyloidosis.
- These measures have not yet been fully examined in older PWH with and without cognitive impairment.

METHODS

- 66 PWH with undetectable viral load (<50 copies/mL) ;195 people without HIV (PWoH)
- All participants completed a blood draw and magnetic resonance imaging scan
- The plasma Aβ42/Aβ40 ratio and APS were obtained using liquid chromatography-tandem mass spectrometry method (PrecivityAD ® by C_2N Diagnostics, St. Louis, MO)
- Cognitive status was assessed with cognitive battery in PWH, and with the Clinical Dementia Rating (CDR) scale in PWoH
  - Cognitively normal PWoH (PWoH_CN) *n*=138
  - PWoH with symptomatic AD (PWoH_AD) *n*=57
  - Cognitively normal PWH (PWH_CN) *n*=43
  - Cognitively impaired PWH (PWH_CI) *n*=23
- General linear models assessed group differences in plasma Aβ42/Aβ40 ratio (age, sex, race, APOE4 covariates) and APS (sex, race covariates)
- Regression analyses assessed relationships between Aβ42/Aβ40 ratios or APS and cognitive domain Z-scores, HIV clinical characteristics, and hippocampus volumes.

The **plasma Aβ42/Aβ40 ratio**, a blood based biomarker for brain amyloid in Alzheimer's disease, is **not abnormal** in older, cognitively-normal or cognitively-impaired people with HIV when compared to similarly-aged, cognitively normal people without HIV.

Table 1. Participant demographic and clinical characteristics

	PWoH_CN n=138	PWoH_AD n=57	PWH_CN n=43	PWH_CI n=23	P-value
Age (years; M ± SD)	57.0 ± 6.9*	66.2 ± 5.7	57.3 ± 5.6*	55.5 ± 4.8*	<.001
Sex (% Male)	46%	61%	77%^	83%^	<.001
Education (years; M ± SD)	16.0 ± 4.8	15.2 ± 2.7	13.4 ±2.1*^	13.0 ± 2.9*^	<.001
Race (%AA)	43%*	7%	63%*	70%*	<.001
Recent CD4 T-cell count, median (IQR)	N/A	N/A	639 (444, 898)	580 (362, 771)	0.1
Nadir CD4 T-cell count, median (IQR)	N/A	N/A	190 (17, 275)	54 (24, 300)	0.89
Recent CD8 T-cell count, median (IQR)	N/A	N/A	867 (606, 1116)	1011 (559, 1085)	0.97
CD4/CD8 ratio, median (IQR)	N/A	N/A	0.7 (0.5, 0.9)	0.7 (0.3, 1.2)	0.19
Duration of HIV infection (months; median [IQR])	N/A	N/A	240 (126, 288)	300 (204, 372)	0.08

* indicates significant difference from PWoH_AD group (p<.05); ^ indicates significant difference from PWoH_CN group (p<.05)

RESULTS

- Plasma Aβ42/Aβ40 ratio and APS significantly differed between groups (*p*<.001). Pairwise comparisons revealed significantly lower Aβ42/Aβ40 ratios and higher APS values in the PWoH_AD group compared to the other 3 groups (*p*-values<.01), with no other significant differences **(Fig 1).**

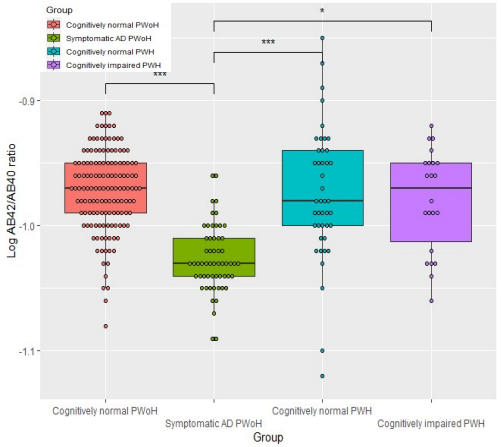

Figure 1. Log-transformed Aβ42/Aβ40 ratios by group.

RESULTS

- Lower plasma Aβ42/Aβ40 ratio (*p*=.003) and higher APS (*p*=.009) associated with smaller hippocampal volumes only in PWoH AD **(Fig 2).**
- Neither plasma Aβ42/Aβ40 ratio nor APS associated with cognitive domain Z-scores or HIV clinical characteristics in PWH.

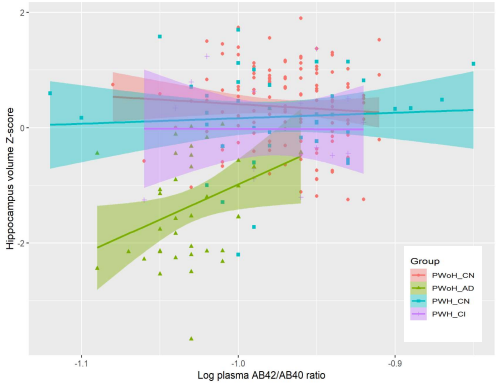

Figure 2. Plasma Aβ42/Aβ40 ratios associated with hippocampus volumes in PWoH_AD.

CONCLUSIONS

- Plasma Aβ42/Aβ40 ratios and APS, markers of brain amyloidosis, are not significantly altered in older PWH, regardless of degree of cognitive impairment, compared to similarly-aged PWoH_CN.
- The plasma Aβ42/Aβ40 ratio could serve as a screening tool for AD and may help differentiate effects of HIV from AD within PWH

ADDITIONAL KEY INFORMATION

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