Amyloid-β PET Positivity Among Cognitively Impaired People with HIV Over Age 60

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Background:

- As the median age of people with HIV (PWH) rises, distinguishing prodromal Alzheimer's disease (AD) from HIV-associated neurocognitive disorder (HAND) has become a pressing clinical challenge.[1]
- Positron emission tomography (PET) studies, employing radiotracers measuring levels of Aβ plaques and neurofibrillary tangles *in vivo*, offer the potential to improve diagnostic accuracy of AD in PWH and differentiate disease pathology from HAND.[2]

Objective:

Primary Aim:

- We sought to characterize the frequency of amyloid-PET positivity among older cognitively impaired PWH compared to cognitively normal people without HIV (PWoH).

Secondary Aim:

- We examined the neuropsychological profiles of the PWH group by amyloid-PET status, cross-sectionally and longitudinally.

Participants:

- Retrospective cross-sectional analysis of 74 PWH, enrolled in a parent study that employed Amyloid-PET to exclude AD, and 65 PWoH, enrolled in a longitudinal cohort examining aging and cognition.
- All PWH included were deemed to have a phenotype typical of HAND, classified as having mild neurocognitive disorder (MND) based on clinical acumen using the Frascati (2007) criteria and exhibiting a CDR of 0.5
- All PWH were on cART treatment with suppressed plasma HIV RNA (<200 cp/mL), who self-reported cognitive symptoms.
- All PWoH completed comprehensive neurobehavioral evaluation and were determined to be clinically normal and with a CDR global score of 0.

Table 1: Demographic characteristics for all participants (n= 139)

	Cognitively impaired PWH (n=74), (%)	Cognitively normal PWoH (n=65), (%)	*p*-value
Age (years), mean (SD)	67 (5.16)	69 (5.86)	0.080
Education (years), mean (SD)	16.2 (2.05)	17.4 (2.09)	<0.001**
Male, n (%)	70 (94.6%)	47 (72.3%)	<0.001**
Non-Hispanic White, n (%)	55 (74.3%)	54 (83.1%)	0.211
Risk for HIV, MSM only (%)	62 (83.78%)	-	-
HIV disease characteristics CD4 count, mean (SD)[1]	629.23 (284.72)	-	-
cART-naïve	0 (0%)	-	-
On cART	74 (100%)	-	-
CDR, n (% 0.5)	74 (100%)	0 (0%)	<0.001**

[1] The CD4 count is missing for one PET- participant from the PWH group.

Methods:

Imaging Measures:

- T1-weighted MRI was conducted on Siemens Prisma Fit 3-Tesla scanner. Amyloid-PET ([18F]Florbetapir) was obtained on a GE Discovery STE/VCT PET/CT scanner.
- Processed scans were visually read as positive or negative for the presence of amyloid plaque pathology by trained and certified neurologists, following FDA-approved visual read guidelines.

Neuropsychological Measures:

- Participants underwent a 90-minute standardized neuropsychological testing battery at baseline and yearly follow-up visits, examining learning and memory, language, executive function, speed of information processing, motor/manual dexterity, and sensory-perceptual

Statistical Analysis :

- T-tests for continuous outcomes and chi-squared tests for categorical outcomes to characterize differences between the groups of PWH and PWoH and PET positive and PET negative PWH
- Amyloid-PET positivity was described as a percentage of cases in each group.
- Individual analyses of covariance (ANCOVAs) compared the neuropsychological profiles of amyloid-PET positive and negative PWH at baseline, adjusting for years of education and age.
- For longitudinal comparisons, cognitive change was calculated as the difference in z-scores between baseline and follow-up testing divided by the inter-assessment interval in years (mean= 2.26, SD= 0.73). ANCOVAs performed examined rate of cognitive change by group with same adjustments.

Results:

Demographic Characteristics:

- PWH group consisted predominantly of males (95% vs. 72%, p<0.001), with a majority self-reporting non-Hispanic white ethnicity (74% vs. 83%, p=0.211).
- PWoH group reported higher levels of educational attainment (17.4 vs. 16.2 years, p<0.001).

Primary Finding: Cognitively impaired PWH did not have an increased rate of amyloid positivity, as measured by [18F]Florbetapir, compared to cognitively normal PWoH.

- Compared to the group of PWoH, the group of cognitively impaired PWH had a lower rate of PET+.
- Secondary Finding: No significant differences were found in the change in neuropsychological performance at baseline or over time between the amyloid PET+ PWH and amyloid PET- PWH

Table 2: Frequency of Amyloid-PET Positivity in PWH

	Cognitively impaired PWH (n=74)	Cognitively normal PWoH (n=65)	*p*-value
PET+, n (%)	6 (8.11)	14 (21.54)	0.026*
PET-, n (%)	68 (91.89)	51 (78.46)	-

Discussion/Limitations:

- Outcome, particularly lower rate in PWH, may be related to restrictive enrollment criteria employed by the HIV parent study, which required that the pattern of cognitive impairment be typical of HAND
- 2 individuals with progressive memory/executive functioning dominant profiles did not meet enrollment criteria for this study scan. They were referred for clinical evaluations and later found to have CSF biomarkers consistent with AD

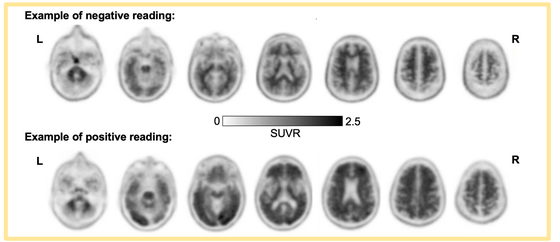


Figure 1: General examples of PET+ versus PET- readings: PET+ results reveal an increased cortical-to-cerebellum standardized uptake value ratio (SUVr)

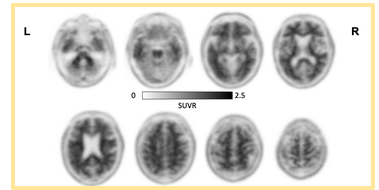


Figure 2: Specific example of Amyloid-PET ([18F]Florbetapir) positive result in person with HIV.

References and Acknowledgements:

1. Milanini B, Valcour V. Differentiating HIV-Associated Neurocognitive Disorders From Alzheimer's Disease: an Emerging Issue in Geriatric NeuroHIV. *Curr HIV/AIDS Rep*. 2017;14(4):123-132.
2. Rubin LH, Sundermann EE, Moore DJ. The current understanding of overlap between characteristics of HIV-associated neurocognitive disorders and Alzheimer's disease. J Neurovirol. 2019;25(5):661-672.

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Conclusions:

- Cognitively impaired PWH did not show increased frequency of amyloid positivity relative to cognitively normal PWoH
- Among PWH, cognitive performance did not differ by amyloid-PET status in analyses of cross-sectional baseline and longitudinal performance.