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Amyloid uptake by PET imaging in older HIV+ individuals with cognitive impairment

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Background:

- More than 7.5% of HIV+ individuals on antiretroviral therapy > age 50 years die from non-HIV related causes, suggesting that the causes of cognitive impairment among old HIV+ individuals may overlap with causes among elderly HIV- individuals (*e.g.*, Alzheimer's disease, stroke***).***[1]
- HIV infection leads to pre-mature aging in multiple organ systems *(e.g.*, heart, liver, kidney, bone, endocrine).[2]
- Position envision tomography (PET) with [^{18}F] AV-45 detects amyloid deposition, a pathological hallmark of Alzheimer's disease.
- In a previous study[3], HIV+ individuals without cognitive impairment (69%) and all <age 60 years, did not have increased amyloid uptake as measured by another radioligand (PIB).

Objective:

- To determine if amyloid uptake measured by PET [^{18}F]AV-45 is increased in older individuals > age 50 years:1) stratified by HIV serostatus, 2) stratified by HIV- associated neurocognitive disorder (HAND) stage among HIV+ individuals, and 3) increased at an earlier age in HIV+ individuals compared to HIV- individuals.

Methods:

- 48 HIV+ and 25 HIV- individuals (age > 50 years received neurological evaluations including neuropsychological testing, functional assessments and high resolution research tomography (HRRT) PET [^{18}F] AV-45 imaging.
- AV-45 uptake was measured by cerebellum standardized uptake value ratios (SUVR) in 17 cortical and subcortical regions.
- Global and regional cortical uptake was compared 1) by serostatus (entire cohort), 2) by HAND stage (among HIV+'s only) and 3) stratified by age decade comparing HIV+ and HIV- individuals in their 50's, 60's and 70's using the Kruskal-Wallis rank test.
- Regions examined included the global cortex, prefrontal, orbitofrontal. superior frontal, lateral temporal, mesial temporal, hippocampus, anterior cingulate, posterior cingulate, parietal, occipital cortex, precuneus, frontal white matter, centrum semiovale, caudate, putamen, basal ganglia, thalamus, midbrain and pons.

Results: Demographics stratified by HIV and HAND status

	HIV-	HIV+	HIV+ Normal Cognition	ANI	MND	Dementia
(n)	25	48	13	12	12	11
Age-years [Mean SD)]	63.6 (7.6)	59.3* (5.2)	61.4 (7.4)	62.1 (6.8)	60.8 (4.7)	57.5 (5.0)
Education-years [Mean (SD]	16.0 (0.55)	14.5* (0.43)	16.1 (2.9)	14.9 (2.8)	14.1 (2.6)	13.9 (2.9)
Gender – % male	88	72	92	58	58	73
Race- % Caucasian	76	42*	62	33	33	36
CD4 count [Mean (SD)]	--	674 (320)	706 (294)	571 (239)	713 (410)	706 (334)
Plasma HIV RNA-% Undetectable-<20	N/A	92	92	92	92	91

*p <0.05, ANI-asymptomatic neurocognitive impairment, MND- mild neurocognitive disorder

- HIV+ individuals were younger (p=0.006), less educated (p=0.034), and less likely to be Caucasian (p=0.0.022) compared to HIV- individuals.

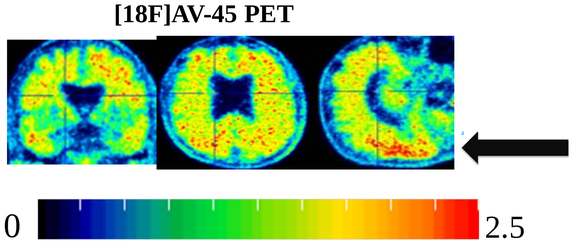
Age decade stratified by serostatus

Age (mean)	50-59	60-69	≥70
HIV+	24	23	1
HIV-	8	10	7*

- More HIV- individuals were age ≥ 70 than HIV+ individuals.

Standardized uptake value ratio (SUVR) generated from 20 min scans (50-70 min post tracer injection) dynamic [18F]AV-45 PET

Positive Amyloid uptake in a 64 year old HIV+ individual with ANI



SUVR global and regional uptake stratified by HIV serostatus

- 7/51 (14%) of HIV+ individuals had higher uptake by qualitative analysis
- 4/24 (17%) of HIV- individuals had higher uptake by qualitative analysis
- There were no differences in median(IQR) global or regional cortical uptake stratified by serostatus (HIV+ global SUVR=1.41 (1.26, 1.56), HIV- SUVR=1.40 (1.22, 1.56)

SUVR global and regional uptake stratified by HAND stage

- There were no differences in median(IQR) global or regional cortical uptake stratified by HAND stage [Global SUVR for HIV+ individuals with normal cognition=1.47 (1.23, 1.54), ANI=1.37 (1.19, 1.54), MND=1.50 (1.29, 1.70), dementia=1.35 (1.16, 1.48)]

SUVR global and regional uptake stratified by decade

Age (years)	50-59	60-69	≥ 70
HIV+	1.48	1.35	1.26
HIV-	1.32	1.41	1.58

- HIV+ individuals age 50-59 had the highest global cortical uptake, whereas global cortical increased with age for HIV- individuals
- HIV+ individuals age 50-59 were more likely to have elevated global cortical uptake (defined as SUVR > 1.40) than HIV- individuals age 50-59 (HIV+ 65%, HIV- 25%, p=0.044).

SUVR regional uptake by HIV serostatus and decade

Age (years)	50-59		60-69	
	HIV+	HIV-	HIV+	HIV-
Prefrontal	1.48	1.28*	1.32	1.40
Superior frontal	1.48	1.26*	1.38	1.44
Posterior Cingulate	1.62	1.43*	1.48	1.63
Parietal	1.61	1.34*	1.38	1.43
Precuneus	1.52	1.28*	1.38	1.32
Putamen	1.47	1.28*	1.38	1.42

* p < 0.05

- HIV+ individuals age 50-59 had higher uptake in prefrontal, superior frontal, posterior cingulate, parietal cortex, precuneus, and putamen compared to HIV- individuals age 50-59.
- There were no differences in regional uptake for HIV+ and HIV- individuals age 60-69.

Discussion

- Amyloid deposition as measured by PET AV-45 uptake is higher in a minority (14%) of HIV+ individuals > age 50.
- HIV- individuals in our study were older than HIV+ individuals.
- Overall in our study there were no differences in global or regional uptake stratified by serostatus (comparing HIV+ and HIV- individuals only), possibly due to differences in demographics.
- HIV+ individuals age 50-59 had higher global and regional uptake compared to age-matched HIV- individuals suggestive of increased amyloid uptake at an earlier age, *i.e.*, premature aging in the brain in HIV+ individuals.
- The increased amyloid uptake in HIV+ individuals age 50-59 was not associated with worsening cognition, suggesting an increased future risk for Alzheimer's disease (*i.e.*, pre-clinical Alzheimer's disease).

Conclusion

- Amyloid deposition by PET imaging is higher in a minority of HIV+ individuals > age 50.
- Amyloid deposition may occur at an earlier age in HIV+ individuals > age 50 compared to age matched HIV-individuals suggestive of premature aging in the brain.
- However, higher amyloid deposition did not correlate with cognitive impairment in HIV+ individuals in their 50's.
- Further longitudinal studies of PET amyloid imaging and cognition in older HIV+ individuals are warranted.

Acknowledgements

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