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

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Background:

- Cognitive impairment among older HIV+ individuals could be due to HIV itself, vascular disease or the early onset of Alzheimer's disease.
- Amyloid deposition, a hallmark of Alzheimer's can be detected by brain position emission tomography (PET) imaging.
- A previous PET study using another marker of amyloid, [^{11}C] Pittsburgh B compound (PIB), in 16 HIV+ subjects (age: mean (SD) =46 (3) years) with normal cognition (69%) and HIV-associated neurocognitive disorder (HAND) (31%) did not show increased [^{11}C-PIB] uptake.

Objective:

- To determine whether abnormal amyloid deposits measured by PET [^{18}F] AV-45 is present in older HIV+ individuals > age 50 years, and is increased in HIV+ individuals with symptomatic HAND (mild neurocognitive disorder (MND) and dementia), compared to asymptomatic HAND [asymptomatic neurocognitive impairment (ANI) and normal cognition].

Methods:

- 25 HIV+ individuals (age: mean (SD) =59.9 (6.0) years) and 6 HIV- individuals (age: mean (SD) = 61.9 (9.3) received neurological evaluations including neuropsychological testing, functional assessments and high resolution research tomography (HRRT) PET [^{18}F] AV-45 imaging.
- AV-45 uptake was evaluated by qualitative (clinical read) and quantitative analysis.
- AV-45 uptake was measured by cerebellum standardized uptake value (SUVR) in 17 cortical and subcortical regions, and compared 1) by HIV serostatus, and 2) between HIV+ individuals with and without symptomatic HAND, using the Wilcoxon test.

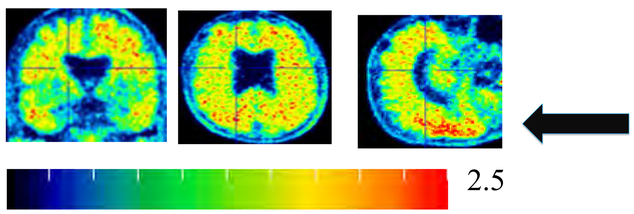
Results: Demographics stratified by HIV and HAND status

	HIV-	HIV+	HIV+ Normal Cognition	ANI	MND	Dementia
(n)	11	30	5	8	9	7
Age-years [Mean SD)]	61.9 (9.3)	59.9 (6.0)	56.5 (2.9)	64.1 (7.5)	60.0 (4.9)	58.0 (5.3)
Education-years [Mean (SD)]	15.3 (2.0)	14.6 (2.6)	15.7 (1.6)	15.0 (2.8)	13.9 (2.6)	14.0 (3.0)
Gender -% male	90.9	73.3	100	50.0	66.7	85.7
CD4 count [Mean (SD)]	--	652.1 (329.1)	675.2 (378.3)	664.0 (227.4)	641.6 (437.8)	632.3 (294.7)
Plasma HIV RNA-% Undetectable->20	N/A	90.0	100	87.5	88.9	85.7

- There were no differences in demographics stratified by HIV and HAND status

Standardized uptake value ratio 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



Effect of HIV serostatus on AV-45 uptake

- 3/30 (10%) of HIV+ individuals had increased AV-45 uptake by qualitative analysis.
- 3/11 (27%) HIV- individuals had increased AV-45 uptake by qualitative analysis.
- There was no difference in the frequency of increased AV-45 uptake among HIV- and HIV+ individuals by qualitative or quantitative analysis .

SUVR regional uptake stratified by HAND status in HIV+ individuals

	Normal	ANI	MND	Dementia
n	5	8	9	7
Hippocampus	**1.10**	**1.18**	**1.24**	**1.28**
Basal ganglia	**1.46**	**1.58**	**1.65**	**1.61**
Frontal white matter	2.49	2.43	2.59	2.51
Orbitofrontal	1.03	1.37	1.31	1.33
Parietal	1.38	1.37	1.31	1.33
Occipital	1.39	1.49	1.43	1.40

Quantitative Regional AV-45 uptake stratified by HAND stage:

- HIV+ individuals with HAND had a trend for increased AV-45 uptake in the hippocampus [mean (SD) =1.23 (0.19)] and basal ganglia [mean (SD)= 1.61 (0.27)] compared to HIV+ individuals with normal cognition [Hippocampus [mean (SD)1.10 (0.12) (p = 0.17), basal ganglia mean (SD) =1.46 (0.08) (p =0.08)].
- HIV+ individuals with symptomatic HAND (MND and dementia) had a trend for increased AV-45 uptake in the hippocampus [mean (SD) = 1.26 (0.15)] and basal ganglia [mean (SD)= 1.63 (0.25)], compared to HIV+ individuals with ANI/normal cognition [hippocampus mean (SD) = 1.15 (0.19), (p= 0.079), basal ganglia mean (SD) =1.55 (0.27), (p =0.065)].

Discussion:

- Amyloid deposition as measured by PET AV-45 uptake is increased in a minority (10%) of HIV+ individuals > age 50.
- PET scans with increased amyloid were seen in HIV+ individuals who were age 55-64 which is an age range, which is unusual for an HIV- individuals to have increased uptake, raising the possibility of increased amyloid at an earlier age among HIV+ individuals compared to HIV- individuals.
- By quantitative analysis, HIV+ individuals do not have increased uptake in posterior cortical regions which are abnormal in individuals with Alzheimer's disease.
- HIV+ individuals with HAND have trends for increased amyloid uptake in the hippocampus and basal ganglia which are specific regions which could contribute to cognitive deficits (memory, psychomotor slowing) in individuals with HAND.

Conclusion:

- Amyloid deposition is increased in a minority of HIV+ individuals > age 50.
- Additional studies are need to determine if HIV+ individuals have increased amyloid uptake at an age earlier than HIV- individuals, and whether HIV+ individuals with HAND have increased amyloid uptake in specific regions compared to HIV+ individuals without HAND.

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