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CLINICAL UTILITY OF β-AMYLOID PET IMAGING IN PEOPLE LIVING WITH HIV WITH COGNITIVE SYMPTOMS

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Background

- Clinically significant HIV-associated neurocognitive disorders (HAND) remain common with reported prevalence rates ranging between 15 to 50% in PLWH on effective cART
- Amyloid imaging using β-amyloid PET tracers such as [^{18}F]Florbetaben (FBB) for clinical use allow the *in vivo* detection or exclusion of β-amyloid plaques, which have the potential to help clinicians to distinguished those with HAND from those at risk of or with AD
- The aim of this study was to determine the clinical utility of FBB in PLWH with cognitive symptoms, and to examine changes in diagnostics, diagnostic confidence and management as a result of FBB imaging.

Methods

- Imaging with FBB PET was performed in 20 patients with cognitive concerns about dementia attending the HIV memory clinic (Orange Clinic) for assessment at the Royal Sussex County Hospital in Brighton, UK between June 2017 and February 2018
- Neuropsychological testing was carried out using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Plasma neurofilament light protein, plasma Aβ40, Aβ42 and CSF Aβ42, tau, and HIV RNA were obtained.
- FBB PET images were assessed visually by three readers blinded to the clinical diagnosis, and quantitatively by obtaining a composite cortical to cerebellar cortex standardized uptake value ratio (SUVR). FBB SUVR from 10 age-matched healthy controls were compared to SUVR of PLWH.

Results

- Patient demographics and clinical parameters for people with HIV are presented in **Table 1**. 13 patients also gave consent for CSF examination. All patients had CSF HIV RNA <40 copies/mL
- Before amyloid PET was available to the memory clinic team 14 (70%) patients had objective cognitive impairment on neurocognitive testing based on the Frascati criteria including two with a working diagnosis AD.

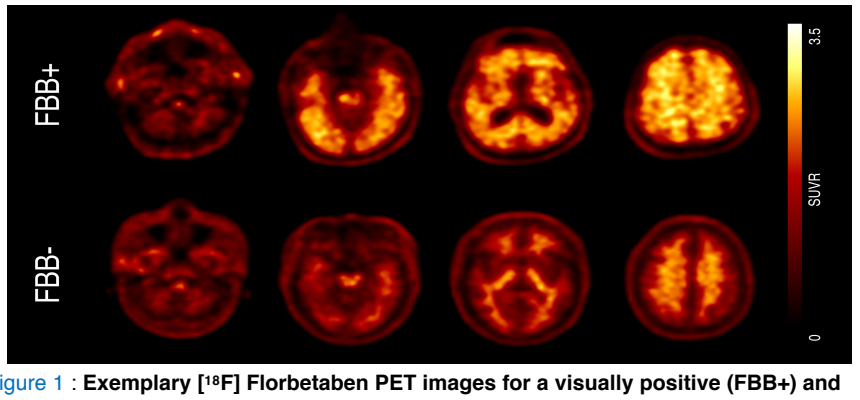

Figure 1 : **Exemplary [^{18}F] Florbetaben PET images for a visually positive (FBB+) and negative (FBB) scan**

Amyloid binding in PLWH

- No significant differences in composite SUVR between PLWH and controls were observed (PLWH mean (SD): 1.18 (0.03) vs. 1.16 (0.009), p=0.37). (Figure 1). Increased composite SUVR was associated with being on protease inhibitor therapy (F=4.6; p=0.024). No other associations between SUVR and other clinical or biomarker parameters were observed.

Variable (n=20)	Total
Demographic variables	
Median (IQR) age in years	60 (43-79)
Male (%)	19 (95)
White (%)	18 (90)
Black African (%)	2 (10)
HIV clinical data	
Time since HIV diagnosis; median (IQR) in years	19 (1-34)
Duration of cART (years)	13 (1-23)
VL<40 copies /ml (%)	20 (100)
Nadir CD4 counts (cells/µL)	268 (13-642)
Current CD4 count (cells/µL)	682 (74-1056)
CD4:CD8 ratio	0.78 (0.05-2.5)
On cART (%)	20 (100)
PI based regimen (%)	9 (45)
NNRTI based regimen (%)	9 (45)
INSTI based regimen (%)	2 (10)
Blood biomarkers	
NFL (pg/mL); median (IQR)	12 (3-38)
Aβ42 (pg/mL)	17 (11-24)
Aβ40 (pg/mL)	266 (181-364)
Aβ42/Aβ40	0.06 (0.05-0.07)

Table 1: **Demographic characteristics**

- Four patients were reported FBB+ visually. Regionally, the highest SUVR for all four patients was observed in the posterior cingulate, superior temporal and frontal superior lobe. (Table 2).
- Amyloid PET results contributed to a change in diagnosis for five patients (25%). Diagnoses changed more often because of a positive PET result (4 out of 20 [20%]) and a a change in patient treatment for five patients (25%). The patient treatment plan altered more often in patients with a positive (4 of 20 [20%]) scan than for those with a negative scan (1 out of 20)

Age	Gender	Clinical diagnosis	Composite SUVR	Visual PET diagnosis	Plasma Aβ42/Aβ40 ratio	CSF Aβ40/tau ratio	NFL (Pg/mL)
60	Female	Mild cognitive impairment	1.31	Positive	0.062	1.79	7.20
79	Male	Mild cognitive impairment	1.81	Positive	0.065	1.53	24
68	Male	Dementia suspected AD	1.41	Positive	0.05	0.98	9.4
62	Male	Dementia suspected AD	1.27	Positive	0.066	3.8	29

Table 2: **Individual characteristics for FBB+ patients**

Conclusion

- **Our data suggest that amyloid imaging has potential additional value in assessment of people with HIV with cognitive impairment, improving diagnostic accuracy and optimising treatment.**
- **As the HIV population is ageing, prospective studies evaluating the discriminatory ability and capacity of amyloid imaging to detect the early stages of AD in people living with HIV are warranted.**