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Effects Of Perinatal HIV-infection On The Cortical Thickness In Young Adulthood

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BACKGROUND

Brain atrophy has been observed in perinatally HIV-infected patients (PHIV) despite initiation on combined antiretroviral treatment (cART)[1]. Findings have included lower volumes and thinner cortices[2-5] when compared to healthy controls but different results have been presented by other authors[6, 7]. We aimed to analyze CT and brain volumes of immunovirological stable PHIV youths whose daily lives are not limited.

METHODS

A total of 25 PHIV patients and 25 healthy controls (HIV-) matched by age, sex, level of education and socioeconomic status underwent a MRI scan. CAT12 toolbox was used to extract CT values from T1w images using parcellations from two atlases Human Connectome Project multi-modal parcellation (HCP-MMP1) and Desikan–Killiany atlas (DK40). Mean thickness values for all ROIs in both atlases were compared between PHIV and HIV- with a two-independent-samples t-test including age and gender as covariates. To measure regional brain volumes native segmented images were parceled in ROI according to the Neuromorphometrics atlas and tissue volumes (mm^3) and normalized by the total intracranial volume for each subject.

Assessments for psychopathological symptoms and neurocognitive status were conducted.

RESULTS (I)

Sample characteristics

Sociodemographic, psychological and cognitive variables	PHIV	HIV-	P value
Sex (female) (%, n)	60% (15)	60% (15)	1.000
Age at assessment (%, n)	20.60 (3.16)	20.40 (2.84)	0.815
Level of education (%, n)			
Low	70.8% (17)	63.6% (14)	0.294
Medium	16.7% (4)	4.5% (1)	
High	12.5% (3)	31.8% (7)	
Annual Income (%, n)			
<12.000 €	21.7% (5)	26.1% (6)	0.175
12.000-16.000 €	26.1% (6)	34.8% (8)	
16.000-26.000 €	26% (6)	21.4% (7)	
26.001-30.000 €	17.4% (4)	8.7% (2)	
> 30.000 €	8.7% (2)	0% (0)	
Caucasian (%, n)	76% (19)	52% (13)	0.080
STAI-STATE	21.22(12.99)	15.45 (11.45)	0.246
STAI-TRAIT	23.70(12.40)	21.45(11.41)	0.657
BDI	10.17 (9.60)	10.05 (9.67)	0.918
Fluid Intelligence (z score)	-0.12 (0.73)	0.24 (0.66)	0.059
EFZ-10 (z score)	0.26 (0.44)	0.17 (0.51)	0.515

Imunovirological variables	
Age at HIV diagnosis (years)	0.50 [0.24-3.44]
CDC Stage C3	10 (40%)
Encephalopathy	3 (12%)
Nadir CD4 (Cells/mm3)	249 [84-343]
Nadir CD4 (%)	11.9 [5-17]
CD4 count (cells/mm3)	687 [497-830]
CD4 count (%)	32.7 [30-39]
CD4/CD8	0.99 [0.69-1.42]
Age at treatment onset (years)	1.4 [0.3-4.2]
Age at onset on cART (years)	2.3 [1.4-5.4]
Total time with cART	17.1 [14.8-18.5]
Number of cART regimens	7 [5-9]
Patients with uVL	21 (84%)
Time with uVL(years)	10.8 [6.8-13.1]
VL in detectable (cop/ml)	416 [185-530]
Type of CART	
– 2 NRTIs + 1 NNRTI	3 (12%)
– 2 NRTIs + 1 PI	3 (12%)
– 2 NRTIs + 1 II	9 (36%)
– 1 PI + 1 II	3 (12%)
– Other combinations	7 (28%)

Despite good control of HIV infection for 10 years and no differences in neurocognitive evaluation, HIV vertically infected patients showed thinner cortices of the *temporal, orbito-frontal* and *occipital lobes and* ***lower* *right amygdala and left putamen* ***volumes****.***

RESULTS (II)

Cortical Thickness (CT)

Between-group differences in thickness were found according to both atlases. First, HCP-MMP1, where individuals with HIV showed significantly thinner cortices in left and right Ventral Visual Complex (VVC) and in the right Piriform (Pir) cortex (Table 1, Figure 1). Secondly, results using Desikan–Killiany atlas (DK40), revealed a significant reduction in thickness across left and right fusiform gyrus, left and right lateral-orbitofrontal gyrus and right pars orbitalis (Table 2, Figure 2). The opposite contrast (PHIV > HIV-) did not show any significant difference.

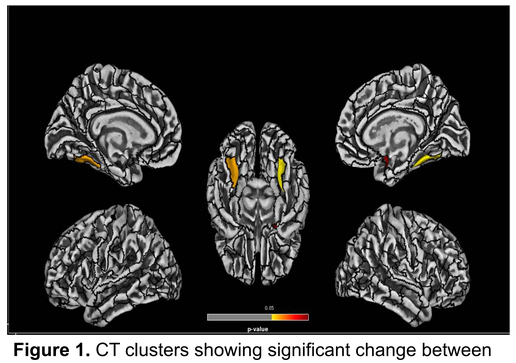


Figure 1. CT clusters showing significant change between pediatric HIV patients and healthy controls according to HCP MMP1 atlas parcellation (HIV->PHIV; p<0.05, Holm-Bonferroni corrected).

Table 1. Between group comparison on CT using HCP-MMP1 HIV- > PHIV

P-value	T-value	Ze-Value	Hemisphere	HCP_MMP1
0.0333072	4.06722	3.73931	L	L-VVC
0.0124165	4.37718	3.98109	R	R-Pir
0.045473	3.96701	3.65958	R	R-VVC

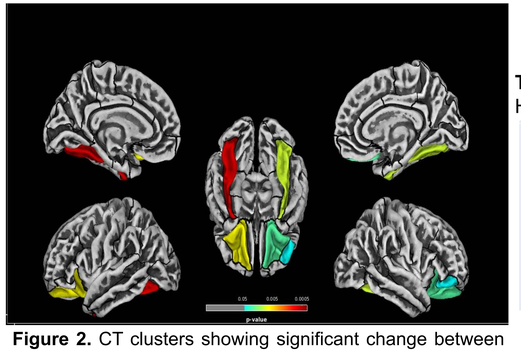


Figure 2. CT clusters showing significant change between pediatric HIV patients and healthy controls according to DK40 atlas parcellation (HIV->PHIV; p< 0.05, Holm-Bonferroni corrected).

Table 2. Between group comparison on cortical thickness using DK40 HIV- > PHIV

P-value	T-value	Ze-Value	Hemisphere	Aparc_DK40
0.0006886	4.76698	4.27483	L	L-fusiform
0.0065198	4.06872	3.7405	L	L-lateralorbitofrontal
0.0095448	3.94246	3.63993	R	R-fusiform
0.0246956	3.62703	3.38345	R	R-lateralorbitofrontal
0.0472847	3.40276	3.19657	R	R-parsorbitalis

RESULTS (III)

Basal Ganglia Volumes

Regarding basal ganglia volumes, according to the Neuromorphometrics atlas, PHIV patients showed lower right amygdala (B=-0,352, p=0,012) and left putamen (B=-0,339, p=0,017) volumes when compared with HIV-. No differences were observed between groups for total grey matter, total white matter, total intracranial volume or cerebrospinal fluid.

Within the PHIV group, higher CD4 count was associated with higher volumes in right putamen (B=0,00000038, p=0,045) and increasing age of cART initiation and lower NADIR was associated with larger volumes in left accumbens (B=0,0000046, p=0,033; B=-0,00000008, p=0,045, respectively).

CONCLUSIONS

Despite good control of HIV infection for 10 years and no differences in neurocognitive evaluation, HIV vertically infected patients showed thinner cortices of the temporal, orbito-frontal and occipital lobes. These results support the need to perform complementary neuroimaging studies that could help to detect more subtle neuro-alterations not observed by psychometric evaluations. Moreover, longitudinal follow-up would be important to determine the HIV impact on brain thickness in PHIV patients during adulthood and if these findings will have a clinical expression in the future.

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ADDITIONAL KEY INFORMATION

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