Regionally Specific Cortical Thinning in HIV+ Patients in the cART era

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Background

HIV infection and its treatment affect the brain directly and indirectly, and can lead to **HIV-associated neurocognitive disorders**. Existing neuroimaging work has found evidence of brain volume loss in HIV+ patients, mainly in **subcortical structures**. However, the methods used to date may miss **subtle cortical volume changes**.

Research Objective

The primary objective of this study was to **characterize the nature and extent of regional cortical thickness reductions** in HIV+ patients, who were on stable cART with good current viral suppression, **using cortical modeling.**

Methods

Subjects:

- **133 HIV+** and **58 HIV-** participants
- **T1-weighted brain MRI** and a **standard battery of neuropsychological testing** (Hopkins Learning Test-Revised, Digit-Symbol Modalities Test and Trail-Making Tests A&B) administered to all participants.

Image Pre-processing:

- Image intensity non-uniformity correction [1]
- Intensity range normalization (0-100) [2]
- Linear registration to the ICBM152 brain template [3]
- Tissue classification [4]

Cortical Modeling:

- **Fast Accurate Cortical Extraction** [5] extracted cortical surface and measured cortical thickness.
- Homologous cortical regions **non-linearly registered** to **ICBM152 cortical template.**
- Vertex-wise linear regression analysis correlated **cortical thickness estimates** against **HIV status, nadir CD4+ cell counts, current CD4+ cell counts, viral load** and **NPZ-4.**

	HIV+ (n=133)	HIV- (n=58)	*p* value
Demographics			
Mean age (years old)	47.8 ± 12.2	42.6 ± 12.3	**0.01**
Sex (% Male)	64	55	0.27
Education (years)	14.4 ± 2.8	15.2 ± 2.1	**0.02**
Ethnicity			0.25
% African American	69	58	
% Caucasian	29	42	
% Other	2	0	
Medical and Neuropsychological			
Duration of HIV infection (months)	135 ± 99	NA	NA
% receiving cART	90	NA	NA
CPE Score	6.73 ± 3.06	NA	NA
NPZ-4 Score	-0.85 ± 1.27	-0.14 ± 0.91	**< 0.001**
Laboratory			
Median CD4 (cells/μL) (Quartiles)	520 (267, 711)	NA	NA
Median nadir CD4 (cells/μL) (Quartiles)	189 (40, 319)	NA	NA
Median Log Plasma Viral Load (copies/mL) (Quartiles)	1.31 (1.30, 1.94)	NA	NA
% Virologically Suppressed (<50 copies/mL)	72	NA	NA

Table 1: Demographics and clinical characteristics of participants.

Results

- **HIV+ patients** performed **worse** than **HIV- individuals** on **neuropsychological testing** (***p* < 0.001**).
- The cortex was **0.2–0.4 mm** thinner **bilaterally** in the **lateral temporal** and **frontal cortices**, as well as **posterior cingulate** and **orbitofrontal cortex**, in HIV+ patients.
- **Lower NPZ-4 scores** associated with **thinner cortex** in **left lateral temporal pole**, **left inferior occipital**, **right lateral occipital** and **right inferior frontal cortices**, in HIV+ patients.
- No relationship between **cortical thinning** and **measures of current or past immune status**, in HIV+ patients.

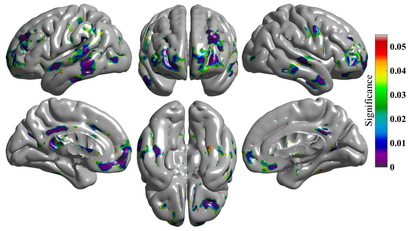

Figure 1: Significant cortical thickness reductions in HIV+ patients compared to HIV- individuals

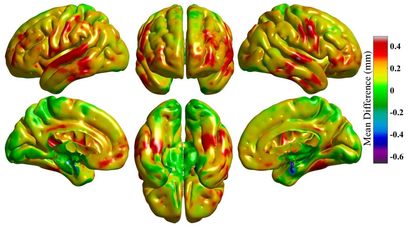

Figure 2: Average cortical thickness difference between HIV+ and HIV- groups

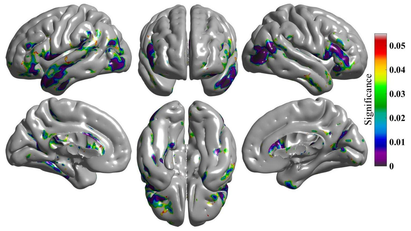

Figure 3: Cortical thickness reductions associated with poorer neuropsychological test scores in HIV+ patients

Discussion

- This was the **first study** to use **cortical modeling** on a **large sample of HIV+ patients with full viral suppression** in the majority.
- **Regionally specific cortical thinning** observed in **HIV+ patients** compared to a **demographically similar HIV- group**, despite good current viral suppression.
- **Even well-controlled infection** has an impact on **cortical thickness** and **cognitive performance,** perhaps related to **CNS viral reservoir** or **cART neurotoxicity**.
- To validate these results and disentangle the effects on the brain from other confounders, **longitudinal studies** are required.

Acknowledgements

Funding from McGill University, NSERC CGS-M and CIHR Team Grant (TCO-125272).

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