MICROSTRUCTURAL MRI CHANGES ASSOCIATED WITH COGNITIVE IMPAIRMENT IN CONTROLLED HIV

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BACKGROUND

- Despite cART, cognitive impairment and brain MRI abnormalities are still prevalent in people with HIV (PWH).
- Diffusion tensor imaging (DTI) can be used to detect microstructural changes in both white matter (WM) and grey matter (GM), and it may be possible to detect subtle and early changes prior to neurocognitive decline.
- These microstructural changes can be measured using Fractional Anisotropy (FA) and Mean Diffusivity (MD).
- In this cross-sectional study **we investigated integrity of the brain parenchyma in virologically controlled PWH (HIV+) and socio-demographically similar control subjects (HIV-).**

METHODS

- 134 patients with **fully suppressed HIV-infection on ART for >12months** and 48 socio-demographically similar control subjects (HIV-) infection were enrolled in a natural history study at the NIH.
- All participants underwent 3T MRI which included DTI at 2mm isotropic resolution and 30 diffusion directions, a comprehensive battery of NP testing, and clinical evaluation.
- DTI measures were calculated using TORTOISEv3 software, including DIFF PREP, DIFF CALC, and DR BUDDI.
- **Fractional anisotropy (FA) and mean diffusivity (MD) were determined from various regions of interest (ROIs)**.
- The neuropsychological battery included evaluations of attention/working memory, executive function, information processing, verbal fluency, learning, psychomotor and memories domains.
- Results from the neuropsychological battery were standardized into T-scores (mean=50, standard deviation=10) and demographically corrected using population-specific normative scores to obtain an overall score, with higher scores indicating better cognitive function.
- We analyzed group differences of FA and MD in various ROIs and conducted **linear regressions with NP testing and DTI adjusted for age and sex.**

	Controls (n=48)	HIV+ (n=134)	P-value
Age (years), mean (SD)	50.2 (10.1)	50.5 (9.1)	0.83
Sex (Male) n (%)	24 (50.0)	93 (69.4)	0.02
Race (African American, n (%)	32 (66.7)	79 (59.7)	0.40
Hx of cocaine abuse, n (%)	8 (17)	50 (38)	0.01
Plasma HIV RNA <50 c/mL, n (%)	-	132 (98.5)*	-
CD4 count (cells/μL), mean (SD)	-	641 (306)	-
Nadir CD4 <200 cells/μL, n (%)	-	72 (59.8)	-

Table 1. Characteristics of study participants. *All participants (n=134) had a viral load <200 c/mL

DTI showed that both white and grey matter were more abnormal in the HIV+ group compared to HIV- controls, with the grey matter abnormalities more clearly associated with current neuropsychological outcomes.

RESULTS

- The **HIV+ group showed higher MD (more abnormal) and lower FA (also more abnormal) in various WM ROIs** including cerebral WM (MD p=0.02, FA p=0.02) compared to HIV- controls.

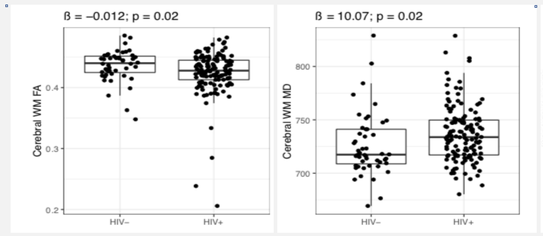


Figure 1. Linear regression of FA of cerebral white matter by HIV status adjusted for age and sex.

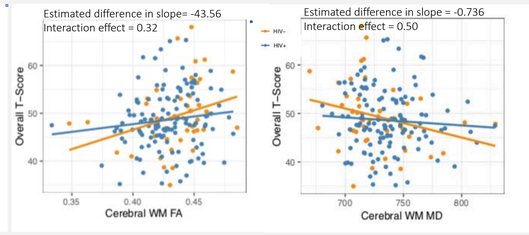


Figure 2. Plot of MD and FA of Cerebral WM by measure of cognitive function (Overall T-score).

- However, the **white matter abnormalities were not associated with cognition** in the HIV+ group (p=0.38 for overall T-score).
- Instead, it was the **grey matter abnormalities that were associated with worse cognition** including overall T-score (0.03), memory (p=0.02), and information processing (p=0.03).

	Control slope	Control p-value	HIV slope	HIV p-value
Attention Working Memory	-1.66	0.20	-0.65	0.47
Executive Functioning	-0.62	0.64	-1.56	0.11
Information Processing	-1.51	0.25	-1.53	0.03
Verbal Fluency	-1.80	0.25	-1.16	0.19
Learning	-1.38	0.24	-1.04	0.19
Psychomotor	-1.77	0.15	-1.32	0.08
Memory	-1.43	0.22	-1.79	0.02
OVERALL T-SCORE	-2.34	0.15	-2.41	0.03

Table 2. Linear regression adjusted for age and sex between the MD of the cerebral cortex and neuropsychological outcomes by domain in the HIV+ and HIV- groups.

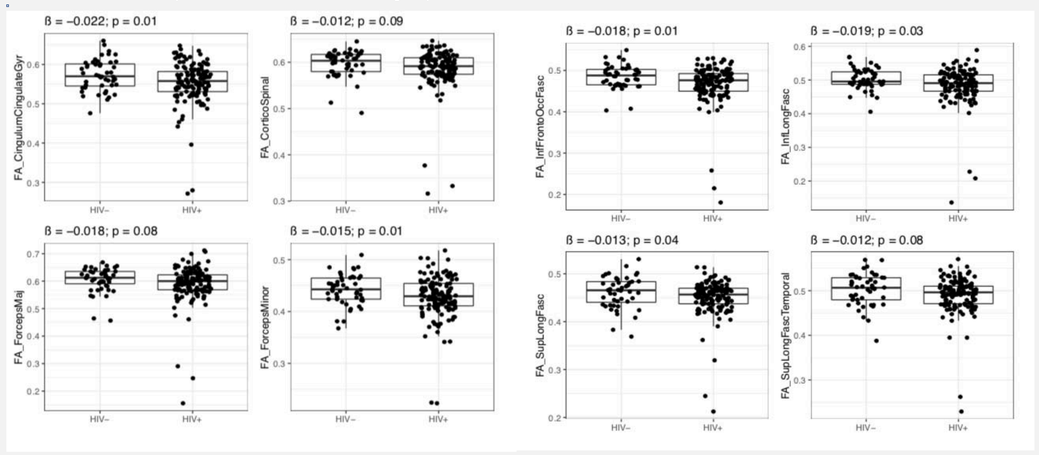


Figure 3. FA of white matter tracts by HIV status adjusted for age and sex. The FA of the Cingulum Cingulate Gyrus, Forceps Minor, Inferior Fronto-Occipital Fasciculus, Inferior Longitudinal Fasciculus, and Superior Longitudinal Fasciculus were significantly lower in the HIV+ group (p=0.01, p=0.01, p=0.01, p=0.03, and p=0.04, respectively) compared to the HIV- group.

RESULTS CONTINUED

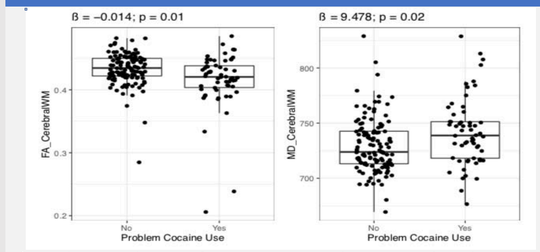


Figure 4. Linear regression of Cerebral WM by self-reported history of cocaine abuse, adjusted for age and sex, independent of HIV status.

- Independent of HIV status, those with a history of cocaine abuse showed lower FA (p=0.01) and higher MD (p=0.02) in the cerebral white matter than those without.

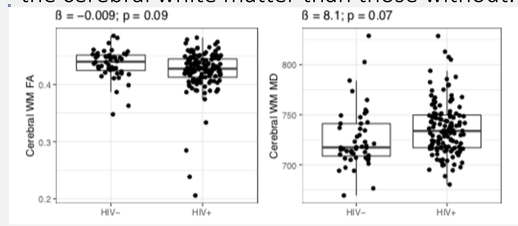


Figure 5. Linear regression of Cerebral WM by HIV status adjusted for age, sex, and self-reported history of cocaine abuse.

- Adjusting for age, sex, and history of cocaine, FA was still lower, and MD was still higher in the HIV group .
- However, cocaine use is somewhat a confounder of the relationship between HIV and DTI parameters.

CONCLUSIONS

- DTI detected microstructural abnormalities in numerous brain parenchymal ROIs of HIV+ compared to HIV- controls.
- These changes are present even despite sustained virologic suppression with long-term ART.
- Both WM and GM were abnormal in the HIV+ groups, with the GM abnormalities more clearly associated with current NP outcomes in this cross-sectional study.
- Past cocaine abuse may be a contributing factor to changes seen in the white matter.

FUTURE DIRECTIONS

- Further investigate potential cofounding variables such as history of drug use.
- Investigate outliers to determine any significant clinical outcomes or phenotypic groups.
- Serial MRIs and NP testing with this cohort will evaluate whether the WM abnormalities are also associated with NP outcomes in the future.

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