Diffusion Tensor Imaging with Free Water Elimination Reveal Compounded Brain Microstructural Injury in People with HIV who Use Marijuana

Teddy Salan[1], Fernando M Moradel Cano[2], Dario N Ayala[2], Ranya Marrakchi El Fellah[3], Eva Widerstrom-Noga[4], Suresh Pallikkuth[5], Denise Vidot[3], Allan E Rodriguez[2], Robert L Cook[6], Varan Govind[1]

[1]Department of Radiology, [2]Division of Infectious Diseases, Department of Medicine, [3]School of Nursing and Health Studies, [4]Department of Neurological Surgery, [5]Department of Microbiology and Immunology, Miller School of Medicine, University of Miami, Miami, Florida, United States,
[6]Department of Epidemiology, College of Public Health and Health Professions & College of Medicine, University of Florida, Gainesville, Florida, United States

Background

HIV infection is associated with chronic neuroinflammation and microstructural injury in people with HIV (PWH).[1] On the other hand, the effect of chronic cannabis use on brain tissue microstructure is less established,[2] with some studies showing that cannabis does not negatively affect white matter (WM) microstructure. However, these findings were dependent on age, frequency/duration and mode of administration.

Aim

The goal of this study is to evaluate the effect of HIV infection and cannabis use on brain microstructure using multi-shell diffusion tensor imaging (DTI) and diffusion kurtosis imaging (DKI) with free-water elimination (FWE).

Methods

Recruitment Site: UM/JMH HIV Clinic & Herbal Heart Study

Eligibility Criteria:
- Age between 18 and 50 years
- No MRI contraindications
- No primary psychiatric or neurological conditions
- Cannabis use (CB+) within the past month

Total Sample Size: 93 participants
- Males: n=47
- Females: n=46
- Mean age: 36 years (SD = 7.7)
- HIV status: HIV+ (n=48) HIV- (n=45)

Group Classification for DTI analysis:
- *HIV+CB+* (n=14) *HIV-CB+* (n=12)
- *HIV+CB-* (n=7) *HIV-CB-* (n=10)

DTI Acquisition and processing:
- The MRI protocol included multi-shell diffusion-weighted (DW) MRI (b = 1000/2000 s/mm2; 30 gradient directions)
- DWI data were processed using FSL[3] and Dipy[4] to obtain DTI metrics: fractional anisotropy (FA), mean-axial- and radial-diffusivities (MD, AD, RD); DKI metrics: kurtosis FA (kFA), mean-, axial-, and radial-kurtosis (MK, AK, RK); and FWE-DTI metrics: FWE-FA, FWE-MD, FWE-AD, FWE-RD, and free water fraction (f_{FW}) (**Figure 1**).

Analysis

- Each of the DTI/DKI/FWE metrics were evaluated at 33 WM regions-of-interest (ROI) obtained from the JHU-MNI-type2 atlas[5] covering the whole brain. (**Figure 2**)
- At each ROI, we performed non-parametric two-way ANOVA to find the effect of HIV and cannabis on DTI/DKI/FWE metrics.
- Analysis performed with R, significance at p<0.05, uncorrected in this preliminary analysis)

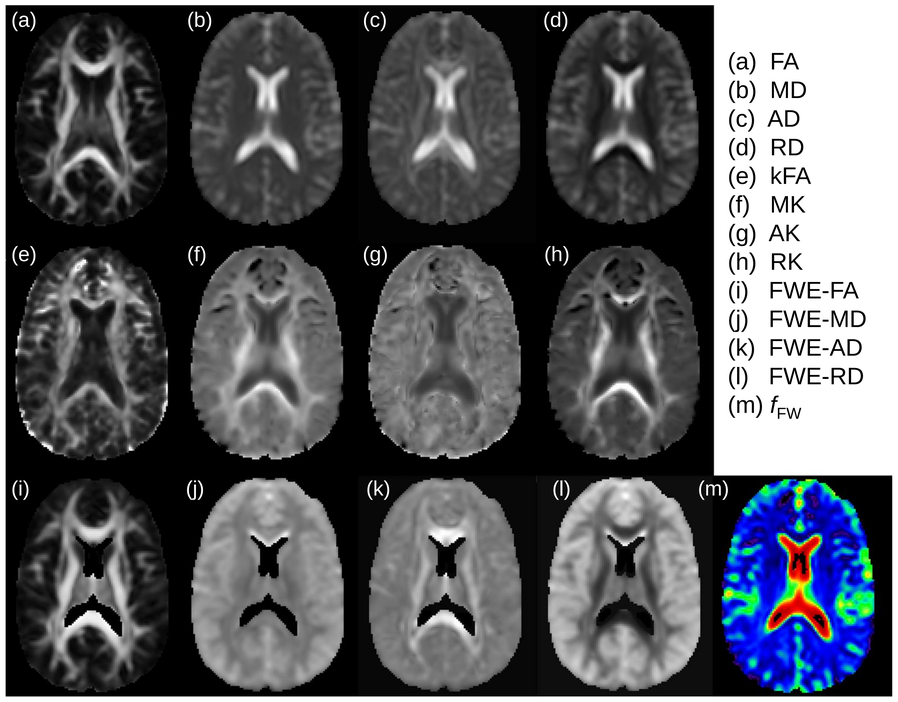

Figure 1: Axial slices showing the respective DTI (a-d), DKI (e-h), and FWE-DTI (i-m) maps obtained from a healthy control subject (HIV-CB-).

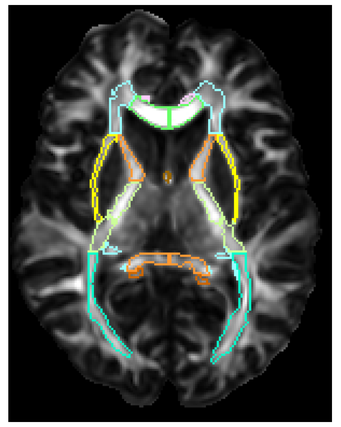

Figure 2: Axial slice of the JHU-MNI FA template image highlighting the location of the white matter (WM) regions of interest (ROI).

The original JHU-MNI-type2 atlas contains 66 WM ROIs from both the left and right side of the brain which were combined into 33 ROIs for our analysis.

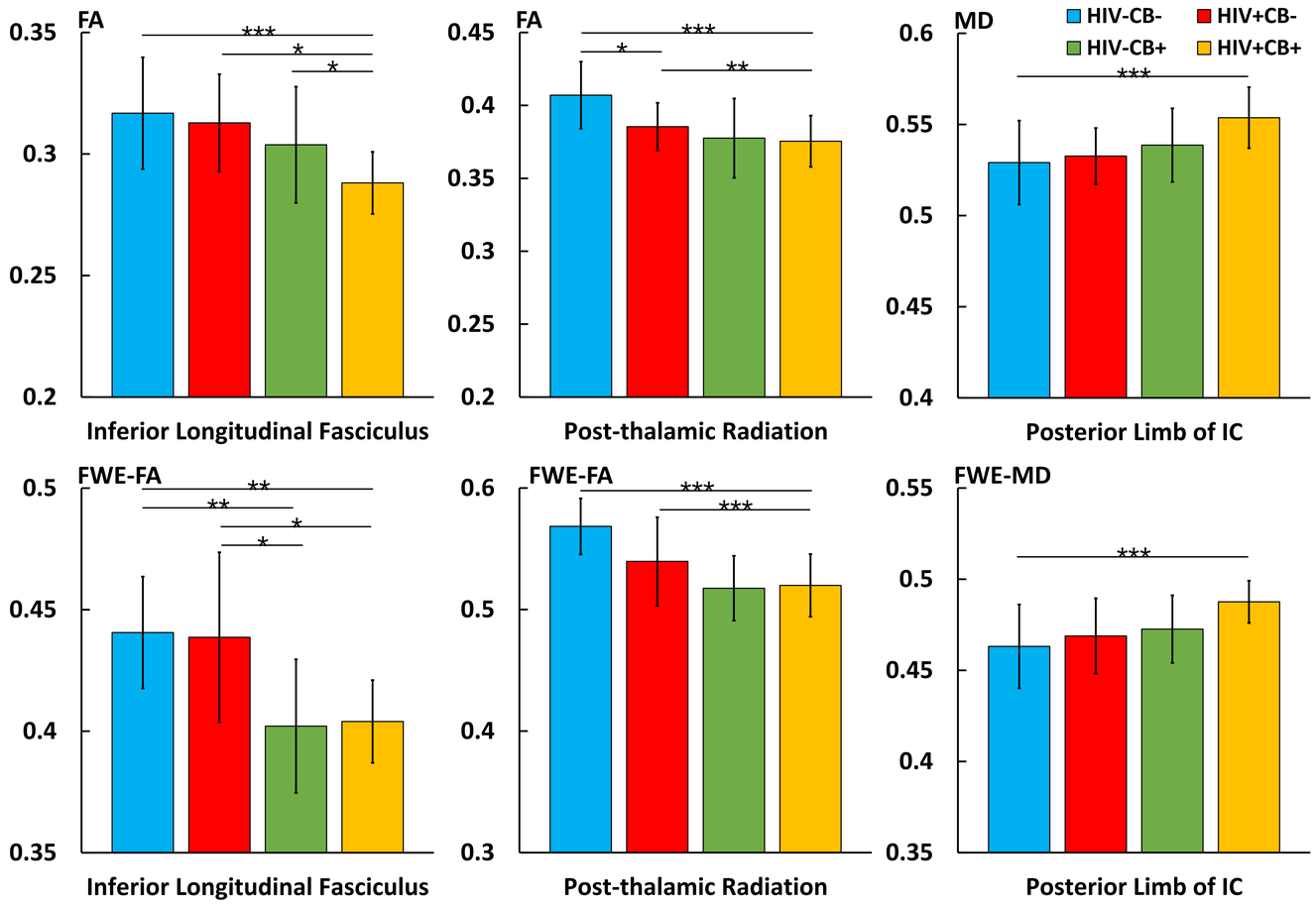

Figure 3: Group comparisons of FA, MD, FWE-FA and FWE-MD values in the Inferior Longitudinal Fasciculus, Post-thalamic radiation, and Posterior limb of the Internal capsule. (*p<0.05, **p<0.01, ***p<0.001)

Results

- Results from DTI metrics showed extensive WM injury (lower FA and higher MD, AD, and RD) in HIV+CB+, HIV+CB- and HIV-CB+ subjects relative to controls (HIV-CB-) (**Figure 3**).
- The most widespread injury was observed among HIV+CB+ subjects, with few significant differences between HIV+CB- and HIV-CB+ groups.
- The most affected ROIs were the inferior and superior longitudinal fasciculus, and post-thalamic radiation (**Figure 3**).
- Identical results were found with FWE-DTI metrics including f_{FW}, while differences in DKI metrics were not significant (**Figure 4**).

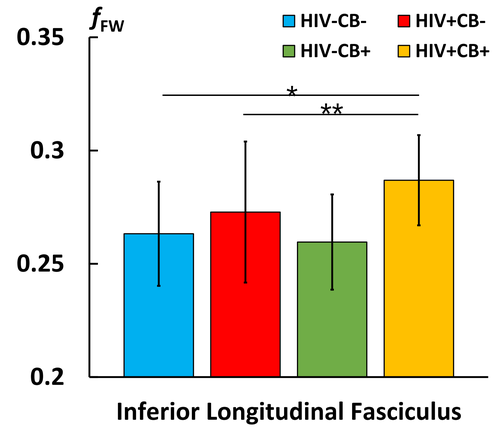

Figure 4: Group comparisons of f_{FW} in the Inferior Longitudinal Fasciculus.

Conclusions

- Our results show that cannabis consumption can intensify white matter injury in PWH, as shown by the lower FA and higher diffusivities in HIV+CB+ subjects compared to all other groups, while HIV+CB- and HIV-CB+ had comparable measurements.
- Higher f_{FW} also suggests higher inflammation in HIV+CB+, which may be a driving factor for the associated WM injury.

Limitations and Future Analysis

The current analysis did not examine the effect of relevant co-variates such as BMI, sex, frequency, duration and mode of cannabis administration, and use of other drugs.

In our study, we have also collected blood samples from each subject to analysis THC and CBD and other cannabinoid metabolites levels in blood. In future analyses, we will associate these measurements with neuroimaging outcomes.

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Email: txs785@med.miami.edu

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