Cannabis Use is Associated with Reduced Brain Integrity in Persons with HIV

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BACKGROUND

- Cannabis (CB) use is increasing nationwide due to legal changes and widespread commercialization
- People with HIV (PWH) are more likely to use CB versus people without HIV (PWoH)
- To date, data on the effects of CB use on cognition in PWH are mixed and few studies incorporate measures of structural brain integrity

METHODS

- 2x2 design classifying PWoH and PWH (viral load <200 copies/mL) participants as CB user (CB+) or non-user (CB-) based on self-reported use
  - CB+: average of ≥3 days/week for past ≥12 months
  - CB-: no use ever, or <10 times total in lifetime
- Regular use in past 12 months of substances other than CB, alcohol, or tobacco exclusionary
  - Current moderate or severe Alcohol Use Disorder, as defined by DSM-5 criteria, also exclusionary
- All participants completed:
  - Questionnaires assessing lifetime (LT) and recent (past 30 days) CB use (Kreek-McHugh-Schluger-Kellogg scale; KMSK)
  - Cognitive testing in the domains of Learning, Delayed Recall, Executive Functioning (EF), Psychomotor Speed (PM), and Language. Raw test scores were converted to demographically-adjusted domain Z-scores.
  - Urine sample to measure 14 common metabolites of CB
  - 3T magnetic resonance imaging (MRI) scan to compute regional brain volumes and cortical thickness (CT) measures from Freesurfer 5.3.
- General linear models assessed affects of HIV, CB use, and their interaction on cognition, brain volumes and CT.
- Regression analyses assessed relationships between LT or recent use, urine CB metabolites, cognition, and neuroimaging metrics in PWH compared to PWoH.
- Analyses were adjusted for age, sex, race, education level, and other lifetime substance use (tobacco, alcohol, and cocaine KMSK scores; reported use of other substances was minimal)

Table 1. Demographic and substance use characteristics by group

	PWoH/CB- N=49	PWoH/CB+ N=37	PWH/CB- N=38	PWH/CB+ N=49	P-value
Age (years; M ± SD)	41.4 ± 15.2	39.2 ± 13.7	50.8 ± 12.3	48.0 ± 12.6	<.001
Sex (% Male)	43%	41%	66%	67%	.013
Education (years; M ± SD)	15.1 ± 1.9	14.3 ± 2.6	13.4 ± 2.6	13.0 ± 1.7	<.001
Race (%AA)	36%	43%	55%	71%	.002
Recent CD4 T-cell count, median (IQR)	N/A	N/A	706 (481, 941)	600 (435, 854)	0.77
Recent CD4/CD8 ratio; median [IQR])	N/A	N/A	0.90 (0.62, 1.32)	0.99 (0.61, 1.42)	0.74
30-day CB KMSK (M ± SD)	0.3 ± 1.2	8.2 ± 1.9	0.3 ± 1.1	9.2 ± 1.8	<.001
Lifetime CB KMSK (M ± SD)	1.9 ± 3.1	11.1 ± 3.0	3.7 ± 4.0	11.6 ± 3.4	<.001
Lifetime Alcohol KMSK (M ± SD)	5.0 ± 3.6	7.3 ± 3.8	5.1 ± 4.4	6.5 ± 4.1	0.02
Lifetime Tobacco KMSK (M ± SD)	1.0 ± 2.4	4.7 ± 4.7	5.2 ± 5.3	7.1 ± 4.5	0.01
Lifetime Cocaine KMSK (M ± SD)	0.4 ± 2.3	1.2 ± 3.1	2.4 ± 4.4	2.8 ± 5.6	0.01
Urine THC-COOH (ng/mL)	N/A	15.2± 15.3	N/A	22.5 ± 29.9	0.20
Urine THC-COOH-gluc (ng/ML)	N/A	866.5 ± 1148.2	N/A	785.7 ± 1018.7	0.58

RESULTS

- PWoH were younger, more educated, and had less LT tobacco use than PWH.
- PWH/CB- and PWH/CB+ groups did not differ on any demographic or substance use measures, except for recent and LT CB use (**Table 1**)
- PWoH/CB+ and PWH/CB+ groups did not significantly differ on any measures of current or past CB use
- Outcomes by group:
  - PWH had worse cognitive performance across all cognitive domains except Language (p-values <.05); with no significant effect of CB use (p-values >.05)
  - Frontal lobe volume was significantly smaller in both CB+ groups compared to CB- (p=.01), with no HIVxCB interaction (p>.05).
  - CB use was significantly associated with cortical thinning in the frontal lobe **(Figure 1),** temporal lobe, cingulate, and global CT in PWH, but not in PWoH

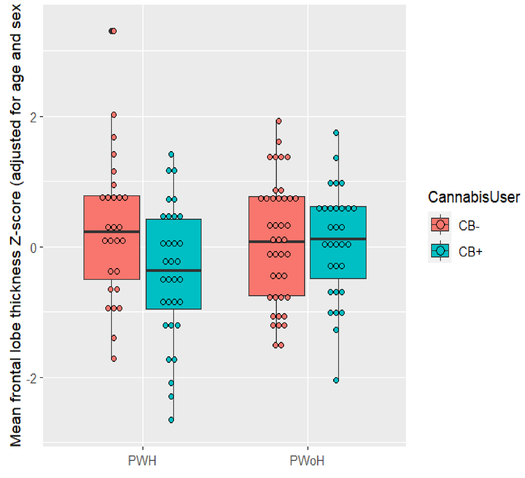


Figure 1. Frontal lobe cortical thickness values were significantly lower in CB users compared to non-users within PWH; there was no effect of CB use within PWoH.

RESULTS continued

- Greater LT CB use associated with worse Delayed Recall performance across all participants (p=.02)
- Greater LT CB use significantly associated with smaller frontal, temporal, hippocampal, and gray matter volumes; and globally reduced CT values, in PWH only (p-values <.01) (**Figure 2**)
- Greater recent CB use associated with widespread reduced cortical volumes and CT, particularly in frontal lobe regions, in PWH only (p-values <.01)
- Higher urine levels of THC-COO-gluc was related to reduced frontal volumes for all participants (PWoH and PWH) (p=.03).

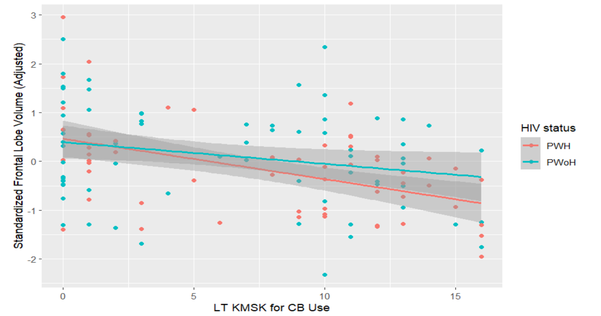


Figure 2. Higher reported LT use of CB on the KMSK significantly associated with small frontal lobe volumes in PWH, but not PWoH.

CONCLUSIONS

- LT and recent CB use were detrimental to structural brain integrity, particularly in frontal and temporal regions, with relationships primarily observed in PWH only compared to PWoH.
- Recent CB use did not impact cognitive performance in this study, although greater LT use associated with worse recall (memory) regardless of HIV status.
- PWH should be cautioned about the potential long-term effects of CB use on brain health.
- Future analyses might consider the role of other factors, such as inflammation, in understanding how CB use may impact brain integrity.

ADDITIONAL KEY INFORMATION

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