Poster 0459

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Beneficial Effects of Cannabis on Blood Brain Barrier and Inflammation in HIV

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Objective

Could cannabis use in PLWH ameliorate neuroinflammation and blood-brain barrier damage?

Background & Significance

HIV infection leads to:

- Upregulation of urokinase plasminogen activator (uPA), a matrix-degrading proteolytic enzyme, and its receptor, uPAR, disrupting the basal lamina around cerebral capillaries
- Increased permeability of the blood-brain barrier (BBB)
- Higher cerebrospinal fluid (CSF)-to-serum albumin ratio (CSAR)
- Neuroinflammation - Elevated concentrations of soluble CD14 (sCD14), a marker of microbial translocation and cellular activation, and CXCL-10, a mediator of T lymphocyte and monocyte activation and chemoattraction in CSF

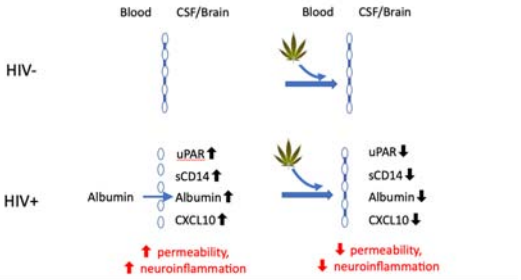
Cannabis is commonly used among persons living with HIV (PLWH) and:

- Stabilizes BBB in animal models
- Has anti-inflammatory effects in vitro

Hypothesis

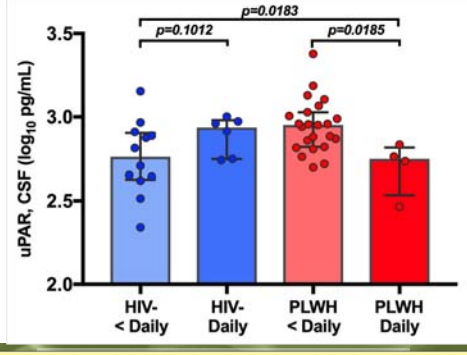
More frequent recent cannabis use in PLWH, but not HIV-, will be associated with lower CSF uPAR, CSAR and neuroinflammation

Fig 1. Model of Blood-brain/CSF barrier before and after cannabis



Results

Fig 2. Interaction between HIV and cannabis use frequency as regards CSF uPAR. PLWH who used cannabis daily had lower CSF uPAR levels than those who did not, while the same did not hold for HIV- participants (interaction p=0.005)



Methods

- PLWH and HIV- current cannabis users (current users selected to reduce the influence of confounding factors).
- Self-reported frequency of cannabis use over the past month*
- Urine toxicology for THC
- BBB permeability markers: CSF soluble uPAR (suPAR), CSF to Serum Albumin Ratio (CSAR)
- Neuroinflammation: CSF soluble CD14 (sCD14), CXCL-10
- Statistical Analyses: Regression and t-tests

Cannabis users in the past month N = 75

HIV- N = 30

HIV+ N = 45

Table. Demographics and CSF parameters	HIV-	HIV+	p
N	30	45	
Days CAN used past month – median (IQR)	9.5 (1.75, 30)	9.0 (9, 30)	ns
Age – mean (SD)	37.6 14.1	41.1 12.7	ns
Men – N (%)	25 (83%)	45 (100%)	ns
CSF Albumin mg/dL - mean (SD)	12.2 (6.4)	17.4 (8.1)	0.029
CSAR – mean (SD)	2.8 (1 .4)	3.8 (1 .7)	0.049

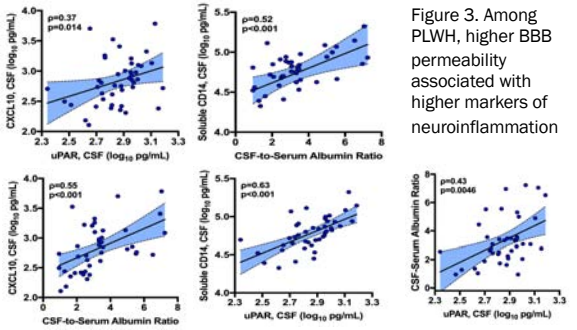


Figure 3. Among PLWH, higher BBB permeability associated with higher markers of neuroinflammation

Results Summary

- Significant interaction between HIV and cannabis use frequency (total days over the past month)
- More frequent use of cannabis was associated with lower concentrations of uPAR in CSF in PLWH (p=0.022) but not in HIV- (p = 0.34).
- Similar, but non-statistically significant relationship for CSAR
- Increased blood-brain barrier permeability related to neuroinflammation
- In PLWH, higher CSF uPAR correlated with higher CSAR (rho=0.47; p<0.001), and more inflammation [higher concentrations of CXCL-10 (p=0.003) and sCD14 (p<0.0001)]
- Self-reported cannabis use frequency strongly related to urine toxicology (data not shown)
- Sex differences could not be evaluated due to the small number of women included

Conclusions

- Recent more frequent cannabis use may have a beneficial impact on HIV-associated BBB injury and neuroinflammation.
- Since BBB and neuroinflammation lead to HIV-associated CNS injury, cannabinoids may have therapeutic benefits in the CNS

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