Cannabis and Brain Metabolism in People Living with HIV: Insights from Neuroimaging and Gut-Immune Research

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BACKGROUND

Despite the effectiveness of antiretroviral therapy (ART), individuals living with HIV (PLWH) still face ongoing neuroinflammation and immune activation, primarily caused by viral reservoirs located in the brain, spleen, gut mucosa, bone marrow, and other tissues [1]. In the central nervous system, the blood-brain barrier (BBB) poses a significant challenge by limiting both antiretroviral drug penetration and immune cell access, thereby allowing HIV to persist in the brain [2]. PLWH frequently use cannabis to manage symptoms such as chronic pain, appetite loss, and mood disturbances. Beyond symptom relief, there is growing interest in its potential anti-inflammatory and neuroprotective effects, which are thought to be mediated through the Endocannabinoid System (ECS) [3]. While preliminary studies suggest that cannabis may confer neuroprotective benefits, its overall impact on brain health—both directly, as observed through neuroimaging, and indirectly, via modulation of gut-immune pathways—remains insufficiently understood [4,5].

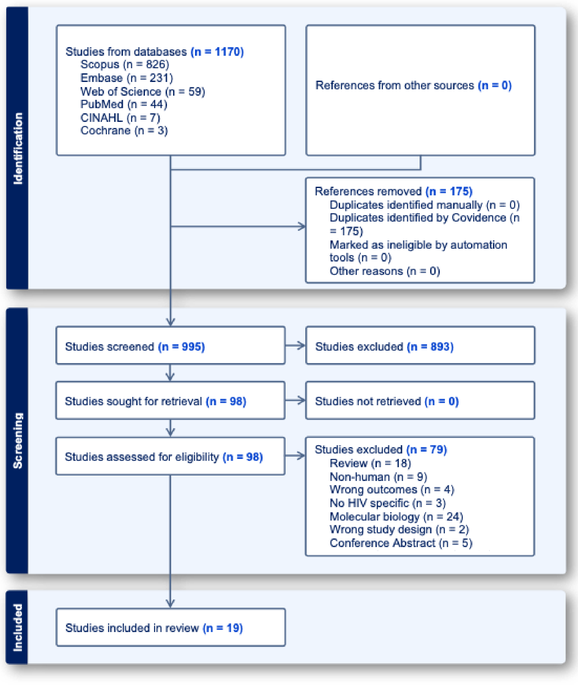
OBJECTIVES

This scoping review combines insights from neuroimaging and gut-immune studies to evaluate cannabis's influence on neurocognitive health in PLWH.

METHODS

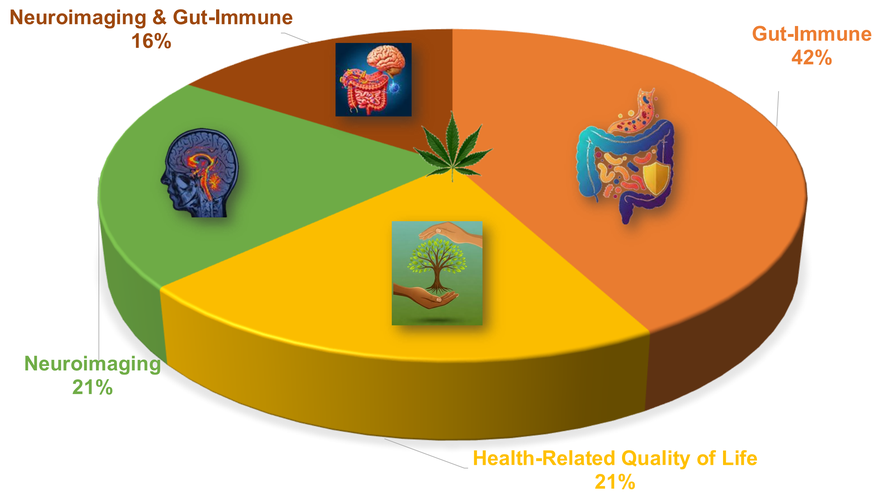
A comprehensive search of PubMed, Embase, CINAHL, Cochrane, and Web of Science databases from inception through December 2024 followed PRISMA guidelines. Key search terms included "cannabis," "neuroimaging," "gut-immune dysfunction," and "HIV." References were managed using Zotero®, and Covidence® streamlined the screening of titles, abstracts, and full-text articles. Eligible studies examined cannabis use, neuroimaging outcomes (e.g., Magnetic Resonance Imaging, MRI), and gut-immune biomarkers (e.g., microbiota composition, C-reactive protein). Data extraction and thematic organization were performed in Microsoft Excel®.

Figure 1. PRISMA Flow Diagram



RESULTS

Figure 2. Included studies categorized by outcome



Gut-Immune Outcomes: Studies examining inflammatory markers, microbiota, or immune function.
Neuroimaging Outcomes: Brain imaging studies to assess structural or functional brain differences.
HRQoL: Studies assessing self-reported physical, mental, or social well-being.
Neuroimaging and Gut-Immune: Some studies addressed both outcome domains.

Table 1. Characteristics of Selected Studies

Study	Sample	Design	Main Finding	Mechanistic Interpretation
Gut-Immune Outcomes				
Ellis et al., 2020	56 (35 PLWH, 21 HIV−)	Cross-sectional	Recent cannabis use is associated with reduced levels of CSF and plasma inflammation.	Cannabis has the potential to diminish microglial activation through CB2 signaling.
Okafor et al., 2024	107 sexual minority men with HIV	Cross-sectional	Intensive cannabis use is associated with reduced plasma levels of LBP.	Cannabis possesses the potential to enhance the integrity of the gut barrier, thereby reducing microbial invasion.
Neuroimaging Outcomes				
Christopher-Hayes et al., 2021	81 (40 PLWH, 41 controls)	Cross-sectional	Cannabis has normalized the elevated gamma activity observed in PLWH.	Cannabis has the potential to mitigate neuroinflammation and enhance sensory processing.
Murdoch et al., 2023	110 PLWH	Cross-sectional	Cannabis is not directly associated with the NCI; biomarkers have been identified as predictive factors for cognition.	Cannabis may affect brain connectivity and metabolomics (e.g., glycine, LPC).
Gut-immune & Neuroimaging Outcomes				
Kallianpur et al., 2020	107 participants: 52 HIV+ and 55 HIV−	Cross-sectional	A. Recent cannabis use correlated with diminished RSFC. B. Prolonged use correlated with reduced volumes in several brain regions. C. Recent use correlated with increased caudate and white matter volumes, enhanced executive function, and reduced inflammatory markers.	Cannabis may have neurotoxic and neuroprotective effects in HIV. Prolonged use can lead to brain atrophy, while frequent or recent use may lower inflammation and CD14+CD16++ monocytes that aid HIV neuroinvasion.
Health-Related Quality of Life Outcomes				
Bahji et al., 2022	2,515 PLWH on ART	Longitudinal cohort	Cannabis use was initially associated with increased viral load, but this association disappeared after adjusting for confounding factors.	Behavioral factors, such as adherence to ART, may mediate effects; however, there is no direct virologic impact.
Barre et al., 2024	79 PLWH with undetectable viral load	RCT	Twice-daily CBD oil had no major effect on HRQoL in virologically suppressed PWH but positively impacted physical health functioning.	CBD has the potential to exhibit short-term neuromodulatory or anti-inflammatory effects.

Abbreviation. HIV: Human Immunodeficiency Virus, PLWH: People Living With HIV, ART/cART: (Combination) Antiretroviral Therapy, CSF: Cerebrospinal Fluid, CB2: Cannabinoid Receptor Type 2, LBP: Lipopolysaccharide-Binding Protein, MEG: Magnetoencephalography, MRI: Magnetic Resonance Imaging, NCI: Neurocognitive Impairment, LPC: lysophosphatidylcholine, RSFC: Resting-State Functional Connectivity, ART: Antiretroviral Therapy, RCT: Randomized Clinical Trial, HRQoL: Health Related Quality of Life, CBD: Cannabidiol.

DISCUSSION

Of the 9 studies analyzed, cannabis shows beneficial and adverse effects on brain metabolism and immune function in PLWH.

Immune-metabolic studies show:
- Lower levels of monocyte activation and microbial translocation markers (Okafor et al., 2020).
- Potential anti-inflammatory effects via CB2 receptor pathways (Ellis et al., 2020).

Neuroimaging studies reveal:
- Cannabis may normalize abnormal gamma activity (Christopher-Hayes et al., 2021).
- Recent use may reduce resting-state connectivity, while prolonged use is linked to atrophy (Kallianpur et al., 2020).

Cognitive outcomes are mixed:
- No direct link to cognitive decline (Murdoch et al., 2023).

Quality of life (QoL) findings are inconsistent:
- Short-term improvements (Bahji et al., 2022) vs. no significant effects (Barre et al., 2024).

CONCLUSIONS

Cannabis may influence brain metabolism and immune function in PLWH through:
- Neuroinflammation modulation
- Neurotransmitter system regulation
- Gut-immune axis interaction

Neuroimaging suggests potential benefits in:
- Neural connectivity
- Immune regulation

Effects are more favorable with frequent or recent use.
However, outcomes vary by:
- Frequency and duration of use
- Individual health status

HRQoL impact remains inconclusive.

WHAT MORE CAN BE DONE BETTER?

🧠 Explore Dose-Response Effects
Examine how different frequencies, durations, and amounts of cannabis use impact brain structure and neurocognitive function among PLWH.

🌿 Differentiate Cannabinoid Effects
Explore the unique effects of THC and CBD on neuroinflammation, cognitive processes, and brain metabolism.

🧬 Study the Gut-Brain Axis
Evaluate the impact of cannabis-induced changes in the gut microbiome on neuroinflammation and cognitive outcomes.

🧪 Identify and Validate Biomarkers
Develop and validate reliable immune and metabolic biomarkers to monitor the effects of cannabis on brain and systemic health.

🫓 Design Rigorous Clinical Trials
Conduct RCTs to assess the therapeutic potential of cannabinoid-based interventions for neurocognitive symptoms and inflammation in PLWH.

REFERENCES

[1] Churchill et al. (2016), *Nature Reviews. Microbiology*, *14*(1): 55–60. [2] Osborne et al. (2020), *Trends Neurosci*, 43(9): 695 – 708. [3] Okafor et al. (2017), *Drug Alcohol Abuse,* 43(1):103-110. [4] Morais et al. (2021), *Nat. Rev. Microbiol.* 19, 241–255. [5] Mwangala et al. (2018), *AAS Open Res.* 1:28.
Included papers upon request.

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