



Neuroinformatics and
Brain Connectivity Lab

Independent and interacting effects of HIV infection and cannabis use on insular functional connectivity

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Introduction

Lagging behind rapid changes to state laws, societal views, and medical practice is scientific investigation of cannabis's impact on the brain, especially among individuals living with HIV/AIDS where use is prevalent^{1,2}. Although possessing therapeutic potential³, chronic cannabis use is linked with neurobehavioral deficits⁴ and neurobiological alterations⁵. These consequences are particularly relevant to HIV+ patients as HIV infection also carries liability for alterations in brain and behavior. While the combined impact of HIV and cannabis on brain function has received little attention⁶, research assessing each condition independently implicates the insula and anterior cingulate cortex (ACC) as regions of interest. Here, we focus on the insula, a critical node in the neurocircuitry of addiction, that has been linked with clinically-relevant symptoms such as diminished error processing, poor decision-making, drug craving, and relapse, all of which may contribute to issues in HIV management or disease transmission. To characterize the independent and combined impact of HIV and cannabis on the functional integrity of the insula, we utilized seed-based resting-state functional connectivity (rsFC) assessments interrogating bilateral insular subregions among a participant sample stratified by HIV-serostatus (HIV+ vs. HIV-) and cannabis use (CB+ vs. CB-).

Methods

Resting-State fMRI: To identify alterations in functional circuits

- fMRI resting-state data (8-min) from 73 participants (21 HIV+/CB+, 19 HIV+/CB-, 21 HIV-/CB+, 12 HIV-/CB-).
- Pre-processing and analyses performed in FSL and AFNI.
 - Motion-correction, ICA-AROMA, WM/CSF nuisance regression, band-pass filtering, smoothing.
- Separate assessments for left and right anterior, middle, and posterior insula seeds.
- For each seed, whole-brain 2 (HIV) x 2 (CB) between-subjects ANOVAs were performed.

Meta-Analytic Decoding: To characterize potential behavioral implications of circuit alterations

- Searched BrainMap database for experiments reporting coordinate in ROI
 - Activations only; Healthy control populations only
- Functional Decoding: Considered behavioral Domain and Paradigm Class
 - Forward Inference Analysis: Likelihood that a given construct activated this brain region
 - Reverse Inference Analysis: Probability that this brain region is associated with a given construct

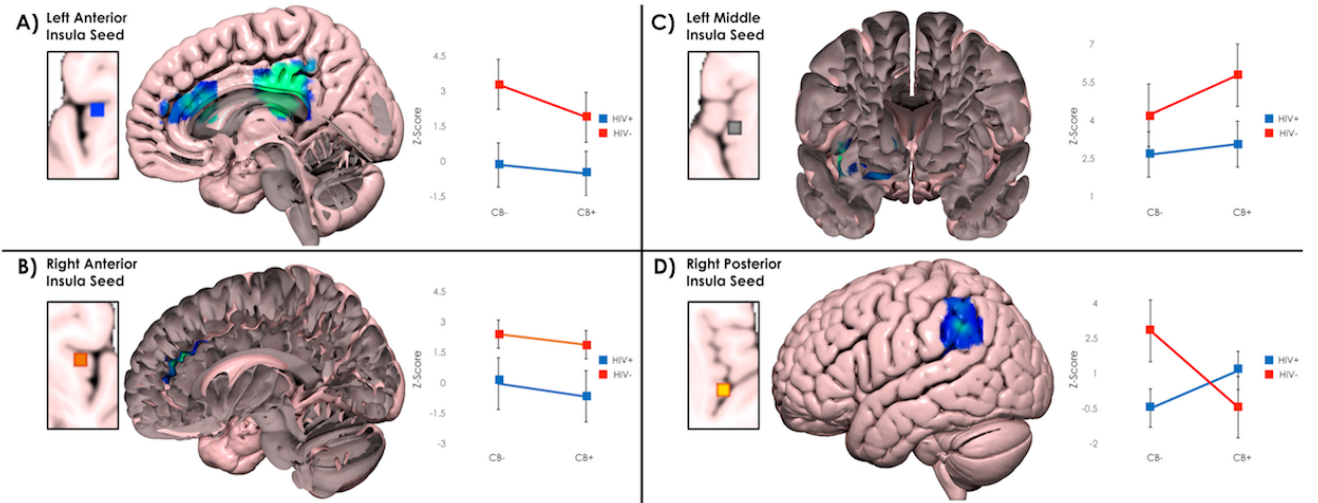


Figure 1. Insula rsFC Results: (A) The left anterior insula demonstrated significantly less connectivity to the anterior and posterior cingulates (ACC/PCC) in individuals with HIV. (B) The right anterior insula demonstrated significantly less connectivity to the right medial frontal gyrus (RMFG) in individuals with HIV. (C) The left middle insula showed less rsFC with the left striatal cortex (LVS) in individuals with HIV. (D) The right posterior insula demonstrated an interaction effect between HIV and CB in the left inferior parietal lobule (LIPL). Specifically, among HIV- participants, left posterior insula rsFC to the LIPL was decreased among cannabis users; however, among HIV+ participants, such rsFC was increased among cannabis users.

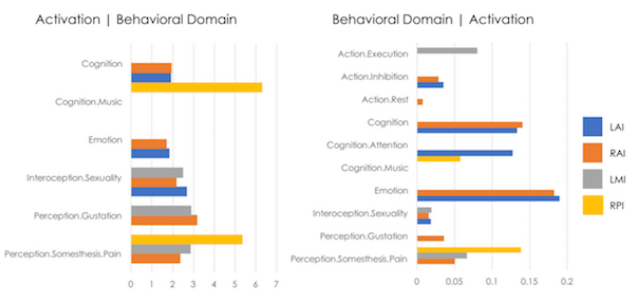


Figure 2. Behavioral Domain Decoding: Forward and reverse inference analyses yielded significant behaviors that may be impacted by the independent and combined effects of HIV and cannabis use in the circuit alterations in Figure 1. (LAI: Left Anterior Insula; RAI: Right Anterior Insula; LMI: Left Middle Insula; RPI: Right Posterior Insula)

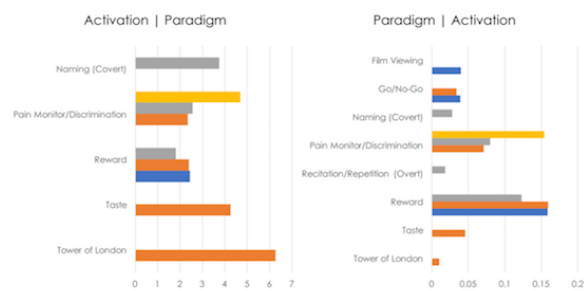


Figure 3. Paradigm Decoding: Forward and reverse inference analyses yielded significant task-related processes that may be impacted by the independent and combined effects of HIV and cannabis use in the circuit alterations in Figure 1. (LAI: Left Anterior Insula; RAI: Right Anterior Insula; LMI: Left Middle Insula; RPI: Right Posterior Insula)

Discussion

- **rsFC results:** Main effects of HIV were identified indicative of HIV-related alterations in the insula's rsFC with cortical and sub-cortical regions. An interaction effect between HIV diagnosis and cannabis use was identified between the right posterior insula and left inferior parietal lobule, indicating a possible mediating effect of cannabis.
- **Functional Decoding:** These insula-centered circuits contribute to a variety of mental processes, including cognition, emotion, attention, interoception, pain, reward, inhibition, and perceptual processes. The circuit between the right posterior insula and the left inferior parietal lobule is negatively affected by HIV but may be mediated by cannabis, and is associated with pain, attention, and perception.
- **Conclusions:** We identified alterations in insula-centric rsFC associated with HIV in frontal, striatal, and cingulate regions which are generally consistent with accounts of HIV-related fronto-striatal dysfunction. Interestingly, cannabis use among HIV+ individuals appeared, to some degree, to "normalize" insula-parietal connectivity. Elucidating the impact of HIV and cannabis on the brain is important for providing patients, healthcare providers, and policymakers with scientific information allowing for informed decision-making regarding its use.

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