Reduced error-related default mode network deactivations linked with HIV and medication management

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Introduction
- Both recreational and medical cannabis (CB) use are prevalent among individuals with HIV.
- Evidence links both HIV & CB use with functional alterations in brain regions thought to contribute to error processing & error awareness
  - Insula
  - Dorsal medial prefrontal cortex (dmPFC)
- Regions comprising the default mode network (DMN)
- Error processing may have critical implications for clinically relevant medication management behaviors and antiviral therapy (ART) adherence.
- As such we utilized an error awareness task (EAT) to probe error processing and awareness related brain activity in regions of interest and assess separate and interactive HIV & CB effects on such activity.

Study purpose: 1. Characterize error processing and error awareness related brain activity, 2. assess separate and interactive HIV and CB-related group effects on such activity, and 3. delineate relationships between altered error processing brain function, cognitive functioning, and medication management abilities.

Results: Error-Related Activity

1. Insula
2. dmPFC

A. 1. al
B. t-value

1. Error vs. correct task-effect brain activity. A) Increased activity during error trials was observed notably in the 1 bilateral anterior insula and 2 dmPFC. B) Increased error-related activity in the anterior insula was correlated with better cognitive control in the task (fewer errors).

Results: Awareness-Related Activity

1. Insula
2. PCC

A. 1. al
B. t-value

1. Aware vs. unaware error task-effect brain activity. A) Increased activity during aware error trials was observed in the 1 bilateral insulae. In contrast, during unaware errors, we observed reduced deactivation in the 2 bilateral PCC. B) More PCC deactivation following aware (vs. unaware) errors correlated with fewer self-reported cognitive failures.

Results: Group-Effect

1. PCC
2. mPFC

A. 1. al
B. t-value

1. HIV main effect on error-related brain activity and associations with cognitive failures and medication management abilities. Significant HIV main effect on error vs. correct brain activity. A) PLWH vs. HIV- participants displayed less PCC and mPFC deactivation following errors, but did not differ in activity on correct trials. B) Among HIV participants, more error-related PCC deactivation was linked with fewer errors whereas among PLWH, the opposite pattern was observed such that more PCC deactivation was linked with more errors. C) Enhanced error-related PCC deactivations were associated with better medication management across both HIV groups. D) PCC deactivation mediated the effect of HIV status on medication management such that PLWH displayed reduced error-related PCC deactivation which, in turn, was associated with poorer MMT performance.

Conclusions
- Our results demonstrate insufficient error-related DMN suppression linked with HIV and associated with clinically-relevant consequences for medication management behaviors.
- Certain HIV-associated neurocognitive alterations may stem from a reduced ability to disengage task irrelevant mental operations that ultimately hinders error processing, and behavioral adaptation.
- May provide heuristic value for strategies to improve medication adherence.

Takeaway message: Outcomes indicate reduced error-related DMN suppression among PLWH that is critically linked to medication management abilities.

Methods
- Participants: 103 individuals stratified by HIV-serostatus and chronic cannabis use history
  - HIV data: Six 5.5-min EAT runs (EPI); one T1-weighted structural
  - MRT processing: Following preprocessing (FMRIPREP), data was entered into subject-level GLMs to assess 1 cognitive control/failure related activity with a [NoGo > GoGo-correct] contrast, and [2] error awareness activity with a [NoGo-Aware > GoGo-Unaware] contrast. Whole-brain one-sample t-tests assessed task-effects across full sample.
  - MRT group-level analysis: To assess group differences in error-related and awareness-related activity we performed, 2(HIV+ vs. HIV-) x 2(CB+ vs. CB-) ANCOVAs (controlling for sex, age, IQ) utilizing AFNI's 3dsvm program.
  - Cognitive-behavioral measures: We assessed linear relationships between altered error-related brain function and 1 objective cognitive failures (frequency of NoGo errors in the EAT), 2 subjective, self-reported cognitive failures (Cognitive Failures Questionnaire [CFQ] total scores), and 3 Revised Medication Management Test (MMT-R) performance.