Do psychedelic substances have long-term effects on cognitive functions?
A naturalistic and ecologically valid online study

Research plan

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Background

Psychedelics and cognition

- Executive functions (EF) are crucial in goal-directed behavior such as planning, academic performance, and self-control
- EF are top-down control processes (Miller & Cohen, 2001)
- Psychedelics acutely harm EF (e.g., Pokorny et al., 2020)

Do psychedelics have long-term effects on cognition?

- Psychedelics have long-term effects on, e.g., creativity and divergent thinking (Mason et al., 2019)
- They act on $5HT_{2A}$-receptors and PCC which are central for EF (Barrett et al., 2020; Leech & Sharp, 2014)
- **Regular ayahuasca use has been associated with better EF (Bouso et al., 2012)**

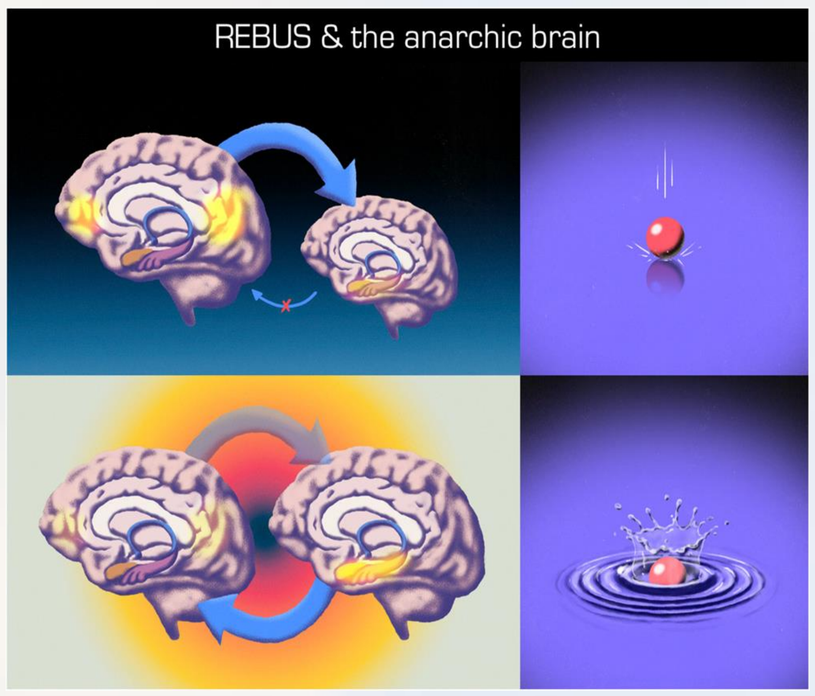

Figure 1. Theoretical premise: the REBUS model of psychedelics (Carhart-Harris & Friston, 2019). Psychedelics relax high-level priors and increase bottom-up processing. Such effects could be reflected in EF performance, where top-down control is essential.

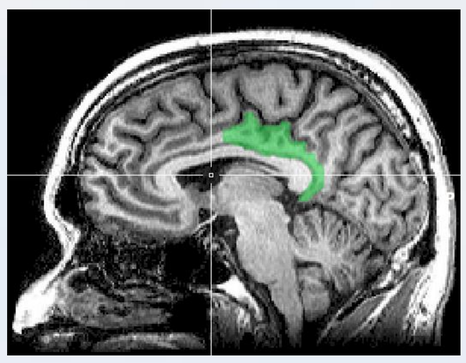

Figure 2. Bouso et al. (2015) found differences in cortical thickness in posterior cingulate cortex (PCC) between regular ayahuasca users and matched controls. PCC is central in EF.

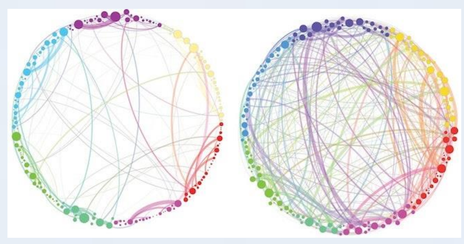

Figure 3. Psychedelics produce their effects by increasing functional brain connectivity. Connectivity on placebo on the left, psilocybin on the right (Petri et al., 2014)

Implementation

1. Analysis of an existing dataset: Associations between psychedelics use and EF
2. Two new experiments: Cross-sectional and longitudinal

Background variables

- E.g., age, SES, gender, previous drug use, openness to experience, conscientiousness, conservatism, meditation experience

Mediating variables

- Depth of the experience (ASCs or MEQ30)

Dependent variabels

- Classical cognitive tests: Simon (inhibition), Antisaccade (attention), N-back (working memory), Colour-Shape (flexibility), Posner cueing (exogenous vs. endogenous attention)
- An ecologically valid 3D game EPELI that runs on the browser, enabling rich, real-time data
- Psychological well-being, etc.

Figure 4. Floorplan of the EPELI apartment (left), where the participant conducts tasks, given by "Vincent" (right). EPELI yields rich real-time behavioral data that can be used to track, e.g., triggering of attention to salient cues (bottom-up processing). EPELI has been validated on children (Seesjärvi et al., 2021) and an adult version is currently being validated in a large-scale experiment, funded by Academy of Finland.

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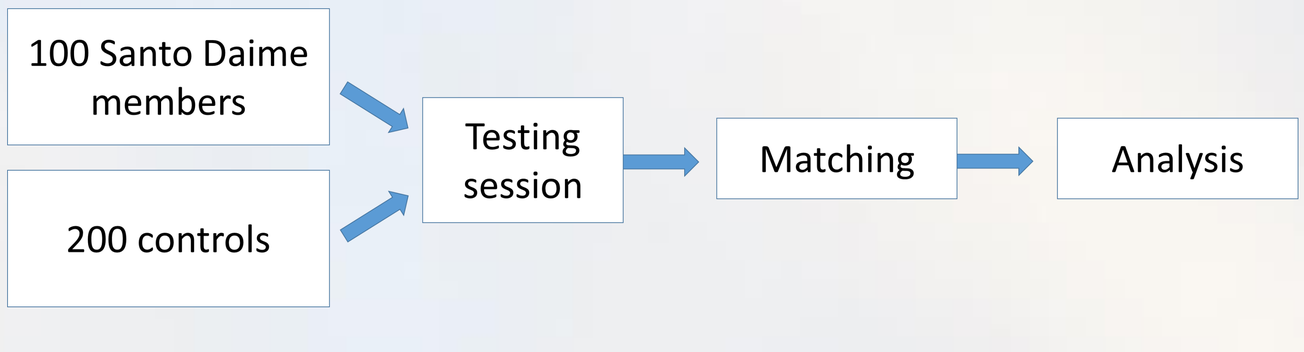

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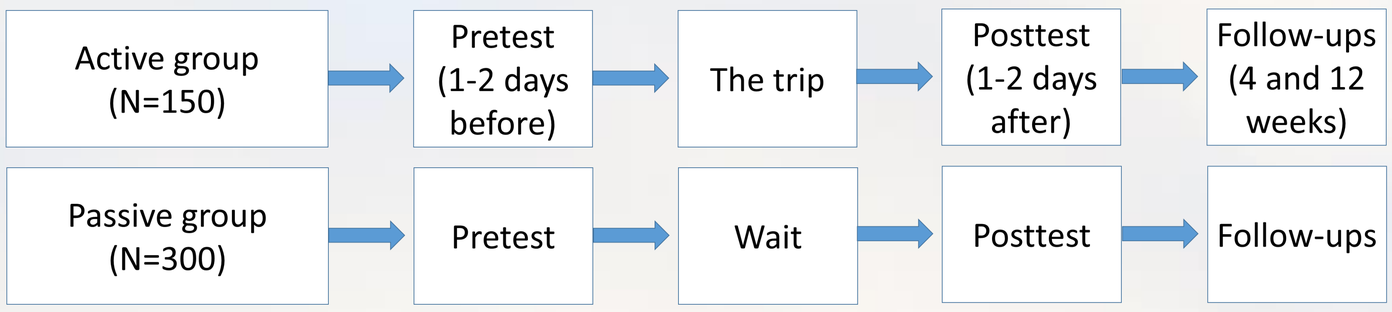

Figure 6. A) Cross-sectional setup on Santo Daime ayahuasca users vs. matched controls, tested online. B) Longitudinal setup through psychedelicsurvey.com. Persons planning to undergo a psychedelic trip register on the platform and specify the date of their trip. The system sends them links to the tests at the appropriate days. Passive control participants perform the tests on similar intervals.

A) **B)**

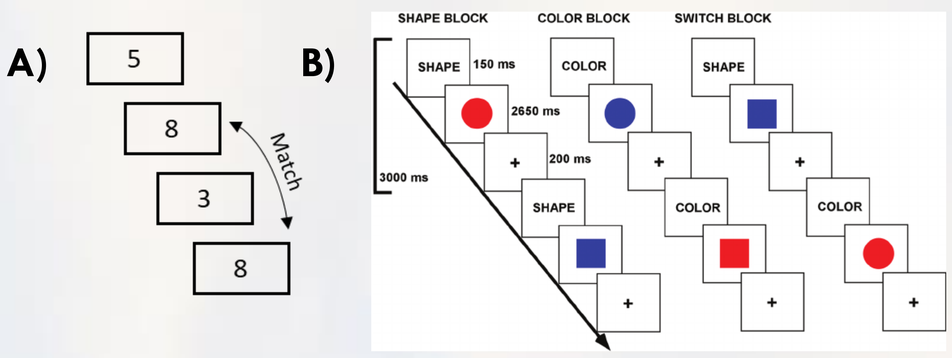

Figure 5. Examples of classical cognitive tests. In n-back (A), the subject must decide if the stimulus is the same as *n* trials ago. In the color-shape task (B) the subject must categorize either the color or shape of the stimulus, depending on cue.

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