A Cognitive Development Model of the Effects of Psychedelics

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Background

- Classic psychedelic drugs cause non-ordinary states of consciousness with visual effects, transcendence of time and space, awe, universal connection, and ineffability[1]
- **Psilocybin** ("magic mushrooms") treats clinical conditions, including depression, anxiety, PTSD, addiction, migraines, eating disorders, etc.[2]

What is the mechanism?

- Theories informed by neuroimaging suggest increases in neural plasticity, but do not explain changes in subjective cognitive experience[3]
- Conditions most responsive to psilocybin are characterized by pathologically rigid mental models, suggesting a role for cognitive flexibility.
- **Current aim:** Apply a cognitive development model to understand the clinical benefits of psilocybin in adults

Cognitive flexibility

- Adults treated with psilocybin have neural similarities with children[4]
  - Increased plasticity and global connectivity
  - Decreased connectivity in default mode network and frontal regions
- Using children as a proxy psilocybin group, we make specific predictions for how psilocybin could cause cognitive flexibility

What Features Allow Children to be More Cognitively Flexible?

1. More diffuse exogenous attention[5]
   - Adults selectively attend to goal-relevant aspects of a task and ignore goal-irrelevant ones
   - Children have diffuse allocation of attentional resources
   - Tested with a change detection task
2. Less biased by prior knowledge[6]
   - Adults have strong priors that are resistant to revision
   - Children flexibly update their current theories in response to counterevidence
   - Tested with a causal inference task
3. Employ global, exploratory, search strategies[7]
   - Adults privilege efficiency and utility maximization, using exploitive search strategies
   - Children engage in directed and systematic exploration, even when incurring costs, using exploratory search strategies
   - Tested with a novel serial production task (SPT) with dynamic constraints, spatially correlated multi-armed bandit, and approach-avoid task

Pilot Study Design (n=9)

- Data collected from participants in a clinical trial examining **psilocybin** vs niacin **placebo** for chronic phantom limb pain
- All task data collected 1 day after dosing

Psilocybin (n=5)

- Mean age = 41, 3 female, 3 white, 4 prior use

Placebo (n=4)

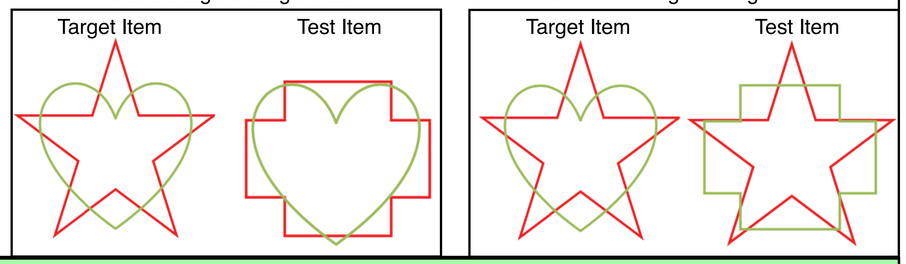
- Mean age = 31.25, 1 female, 3 white, 3 prior use

Pilot Results

- No effect of **psilocybin** on exogenous attention
- **Psilocybin** reduces strength of prior beliefs
- **Psilocybin** results in broader, exploratory, search, which may be associated with analgesia
- Ongoing data collection for n=30 (15 per condition)

Experiment 1: Change Detection Accuracy[5]

- Participants cued to one of two overlapping shapes
- A target image is shown, followed by a test item where the cued or un-cued shape changes
- Children have higher change detection accuracy for un-cued shapes
- **Results: No difference in change detection accuracy following psilocybin**

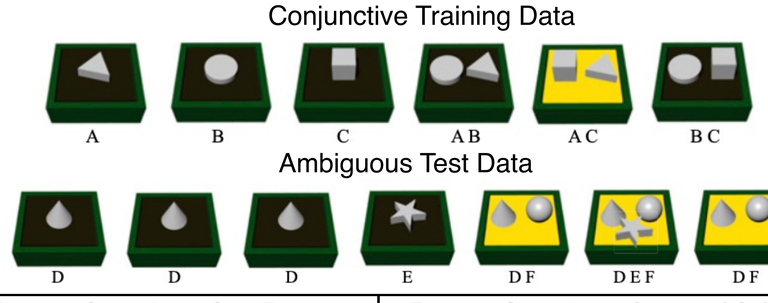


Experiment 2: Changing Strength of Priors[6]

- Adults have strong prior beliefs that causes are disjunctive and fail to revise their beliefs in the face of counterevidence
- Children share these beliefs but show less bias. When shown evidence for a conjunctive cause, they revise their belief.

Prediction: If participants are less biased by their priors, they will pick the hypothesis that best explains their data:

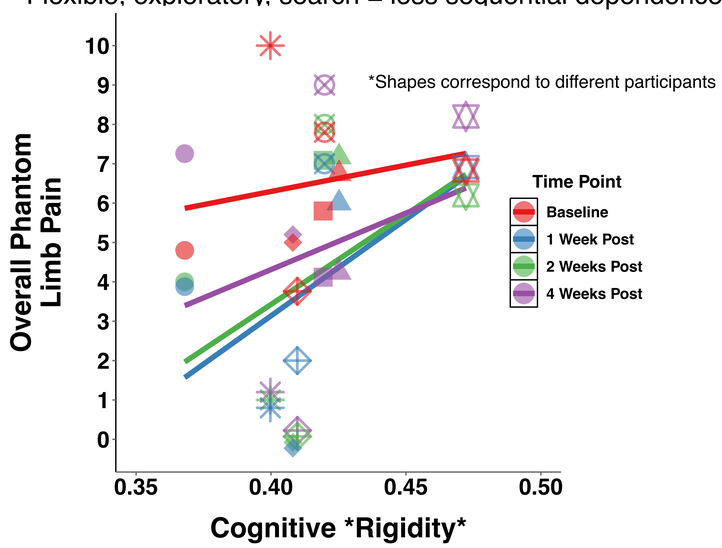
1. Identify object D as a Blicket
2. Choose multiple objects to activate the machine

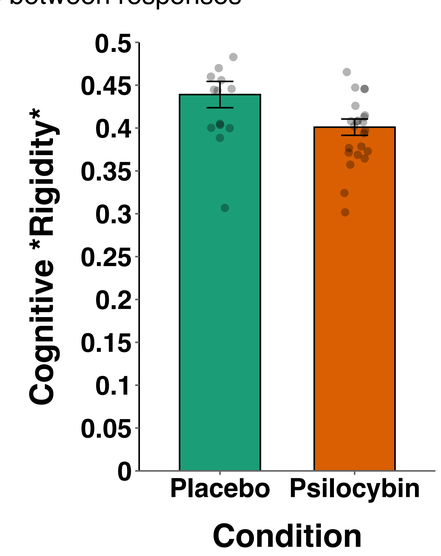


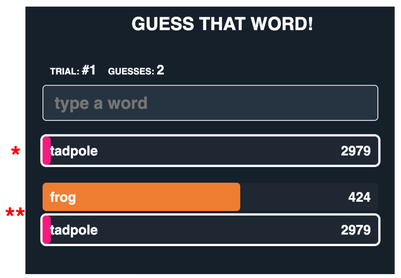
Proportion choosing D as a blicket:	Proportion choosing multiple objects to activate machine:
Placebo: 0 / 4	Placebo: 1 / 4
Psilocybin: 2 / 5	Psilocybin: 5 / 5

Experiment 3: Changing Search Strategies

- On each trial participants guess a secret target word
- After guessing, they receive feedback on the closeness rank of their guess to the target based on semantic similarity to the target
- Rigid, exploitive, search = more sequential dependence between responses
- Flexible, exploratory, search = less sequential dependence between responses







***Most recent guess**
****Guess history**

After each guess, participants are informed of how close that guess is to the target.

The history of guesses from that trial and their closeness rank remain visible.

References

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