# Dose-dependent changes in global brain activity and functional connectivity following exposure to psilocybin: a BOLD MRI study in awake rats

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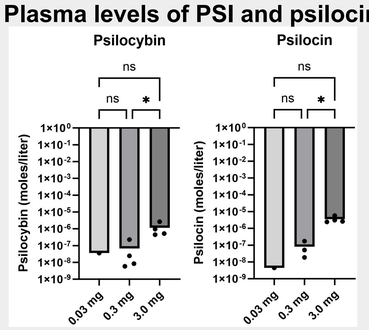
## Background, Rationale & Approach

**Amidst the War on Drugs in 1971, the United Nations classified psilocybin (PSI) and other psychedelic drugs as Schedule 1 substances. However, in the past decade, there has been a resurgence of scientific interest in PSI. Small clinical trials report promising results in treating MDD, end-of-life distress, PTSD, and alcoholism. Animal studies report that low doses of PSI act through 5HT2a receptors to decrease anxiety and promote prosocial behavior, while higher doses also alter dopaminergic signaling, causing cognitive dysfunction. How does PSI alter brain neural circuitry to affect behavior? To address this question, we used BOLD imaging to follow changes in brain activity in male and female rats exposed to PSI**

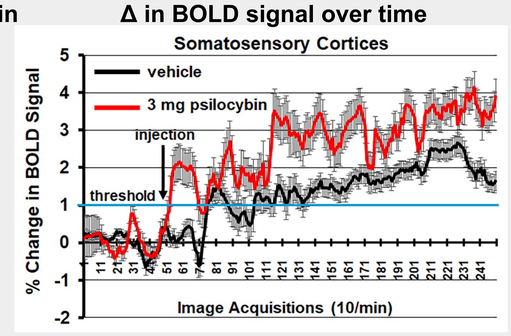
## Experimental Design

**Female and male rats were given IP injections of vehicle or psilocybin in doses of 0.03, 0.3, and 3.0 mg/kg while fully awake during the imaging session. Changes in BOLD signal were recorded over a 25 min window. Approximately 35 min post injection data for resting state functional connectivity were collected. All data were registered to rat 3D MRI atlas with 173 brain regions providing site-specific changes in global brain activity and changes in functional connectivity. Experiments were conducted under dim red illumination between 10:00 hrs and 18:00 hrs to avoid the transitions between the L-D dark cycles. Blood was assayed for PSI and psilocin 30 min post injection.**

### Plasma levels of PSI and psilocin




### Δ in BOLD signal over time

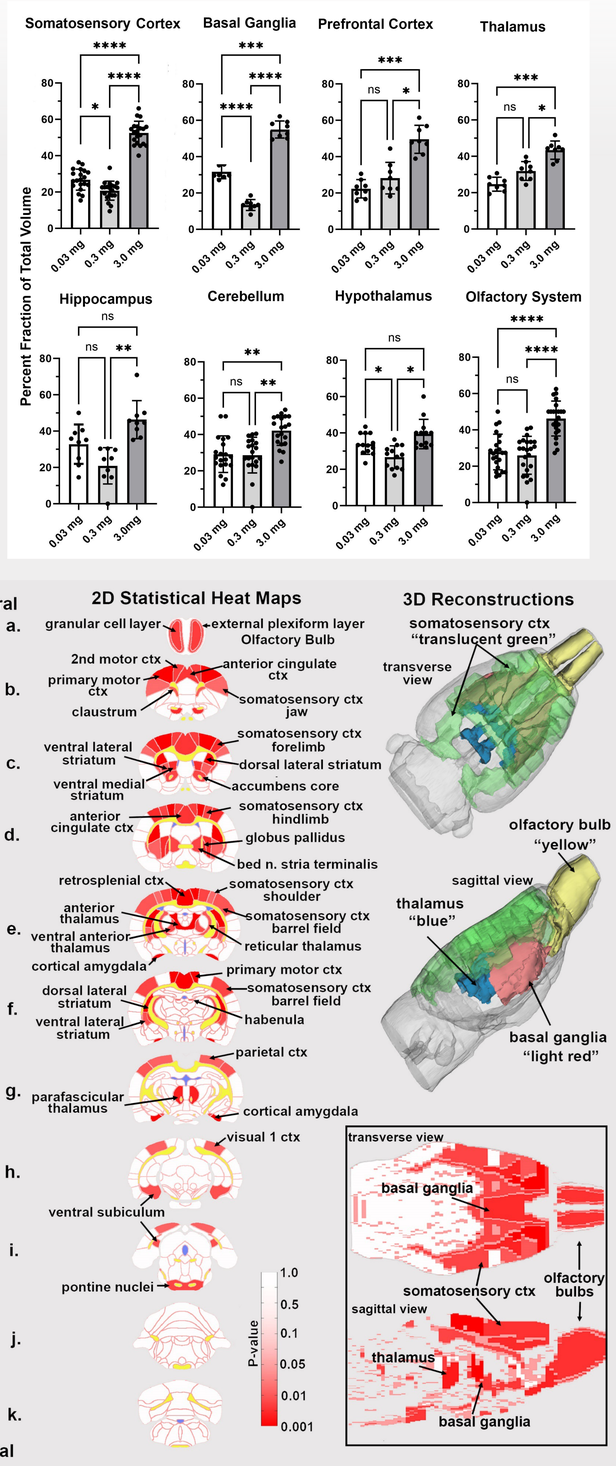



## Summary

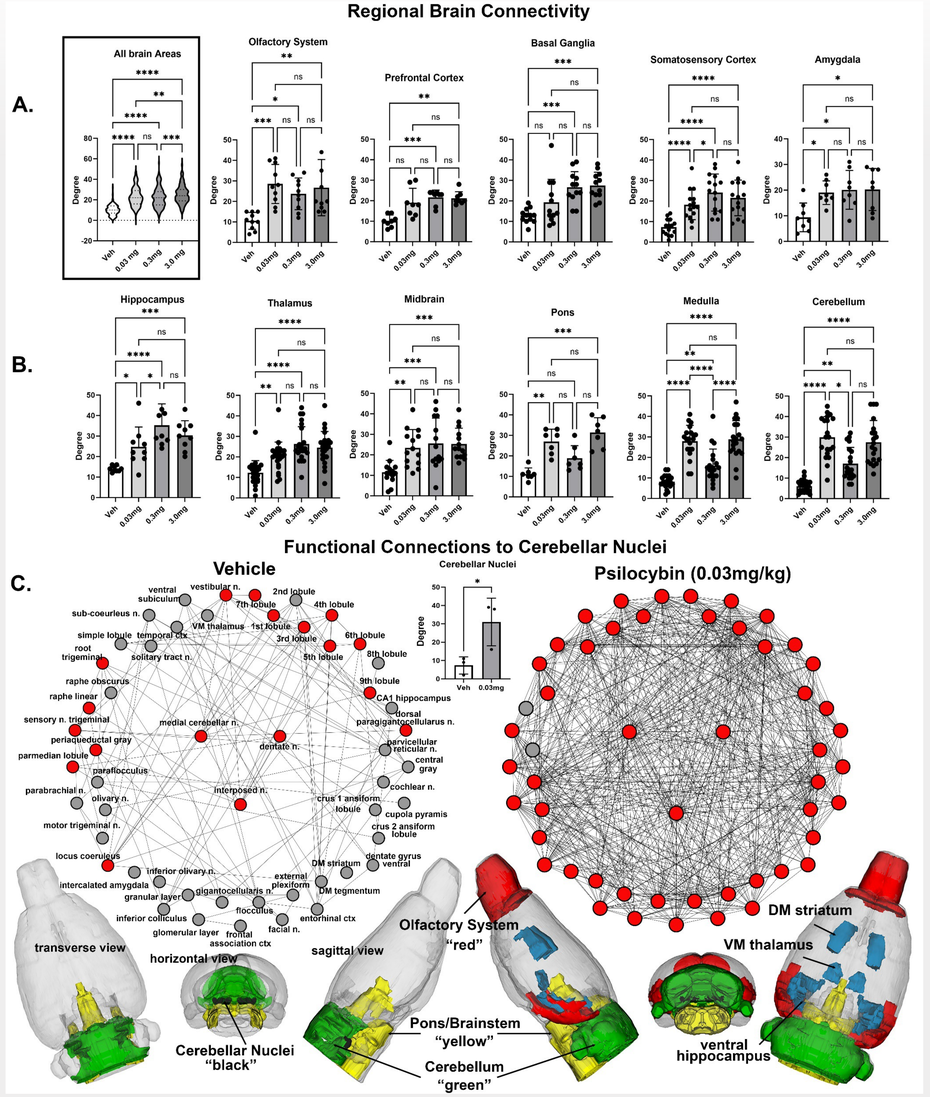
**To the best of our knowledge this is the first phMRI study in animals or humans to show a dose-dependent change in BOLD signal in response to PSI. To make these data more relevant to the human condition, imaging was performed while male and female rats were fully awake without the confound of anesthesia and during the dark phase of L-D cycle when rats are normally active. There was a dose-dependent increase in BOLD signal in much of the forebrain, basal ganglia and somatosensory cortex and a global dose-dependent increase in functional connectivity.**

## Results

### BOLD Pharmacological Functional MRI




### BOLD Resting State Functional MRI




## Ongoing Research

- **Ketanserin treatment to parse out the role of 5HT2a receptor**
- **Normal light-dark cycle to see the influence of circadian timing**
- **Brain and plasma lipidomics to assess changes in endocannabinoid system**
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## Acknowledgement

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National Institute on Drug Abuse
Advancing Addiction Science