

Magic Mushrooms: A New Frontier in Mental Health

Nicolas Viulet¹, Josh Poulin^{1,2}, Ashley Liu¹, Sean Nestor^{1,2}

¹University of Toronto, ²Sunnybrook Health Science Centre

INTRODUCTION

Major Depressive Disorder (MDD) disrupts communication between mood-related brain networks, such as the default mode (DMN), salience (SN), limbic, and cognitive control (CCN) networks¹. Assessing connectivity between and within brain networks quantifies this disrupted communication.

Variable connectivity between mood-related brain networks contributes to the diverse symptom presentation in MDD. For instance, increased DMN connectivity may drive negative self-referential thought³, while reduced amygdala-somatomotor connectivity is linked to decreased physical activity⁴. The widespread impact across brain regions and the diverse symptoms it causes make MDD particularly difficult to treat effectively.

Psilocybin, the psychoactive component of "magic mushrooms", has recently surfaced as a potential alternative to treating MDD⁵, especially given the varying efficacy of traditional antidepressants^{1,6}.

Despite the growing popularity of psilocybin use for MDD clinical trials and related neuroimaging analyses, few studies have used neuroimaging data to determine the impact of psilocybin on different mood-related brain networks in both depressed patients and healthy controls.

RESEARCH QUESTION

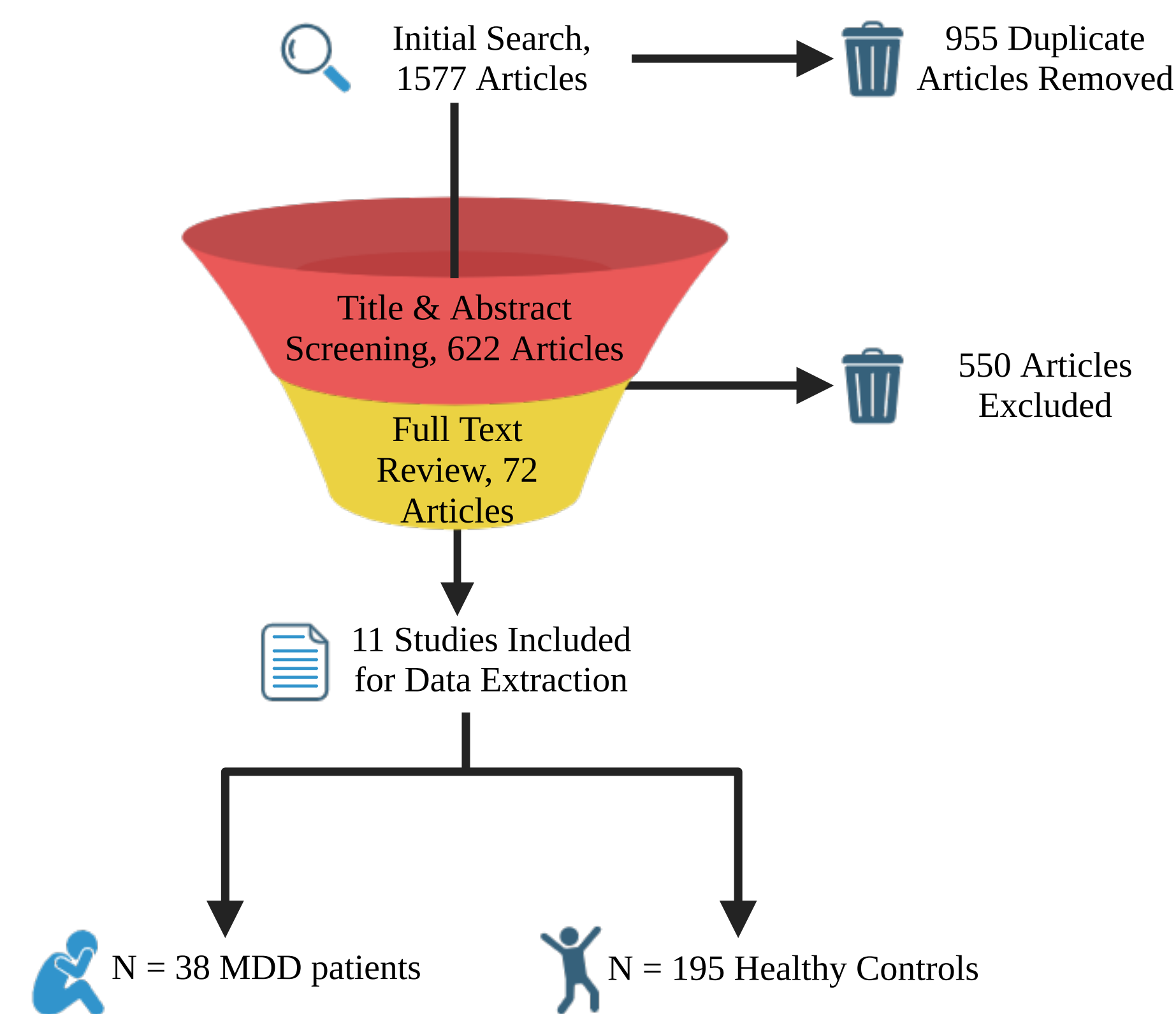
What changes in connectivity consistently occur in mood-related brain networks following psilocybin administration in depressed patients and healthy controls?

HYPOTHESIS

Psilocybin administration will lead to a reduction in within-network connectivity in mood-related brain networks (e.g., DMN, salience, limbic) and an increase in between-network connectivity from pre- to post-administration in both depressed patients and healthy controls.

METHODS

Article Selection Pipeline



Inclusion Criteria

- Studies on depressed (Major depressive disorder and Persistent depressive disorder, and treatment-resistant depression) adult or healthy adult humans (≥ 18 years old)
- Reporting of MNI or Talairach coordinates in standard space
- Randomized clinical trials (RCTs), open-label trials, observational studies
- Studies involving administration of psilocybin.
- Studies including neuroimaging outcomes reporting changes in regional brain activity or network functional connectivity

Exclusion Criteria

- Literature reviews and meta-analyses
- Studies with no neuroimaging data
- Studies where psilocybin is combined with other psychedelics without separate analyses
- Preclinical/animal studies

PRELIMINARY RESULTS

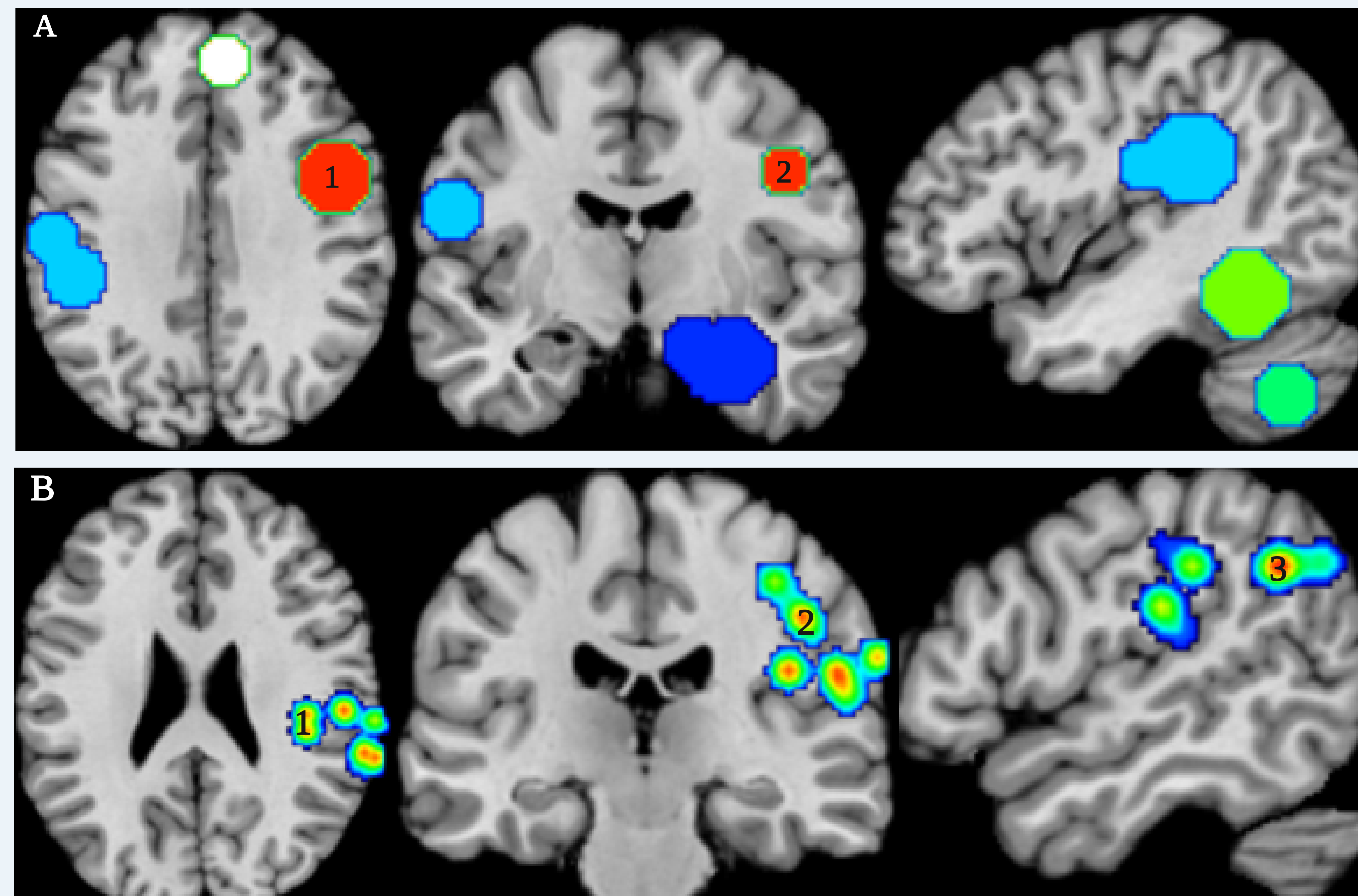


Fig 1. Images created using GingerALE and visualized via MangoGUI. Cluster-level FWE (threshold permutations = 10000, $p < .05$) analysis of peak coordinates of psilocybin activation was done for the 11 studies included in data extraction; the coordinates were collected from depressed patient and healthy control studies. Areas with warm color are suggest strong convergence of activation for the given population. (Axial, Coronal, and Sagittal View)
A) Significant clusters from depressed patients extracted from 11 coordinates. 1. Inferior frontal gyrus, precentral gyrus, insula 2. Pre-central gyrus
B) Significant clusters from healthy controls extracted from 101 coordinates. 1. Insula 2. Post-central gyrus 3. Inferior Parietal Lobe

DISCUSSION

Preliminary Findings on Brain Activation:

- Analyses indicate that both depressed patients and healthy controls exhibit activation in the **insula**, a region integral to emotional processing and self-awareness.
- Distinct activation patterns emerge in other areas:
Precentral Gyrus: Primarily activated in depressed patients, suggesting alterations in motor function or planning.
Postcentral Gyrus: Predominantly activated in healthy controls, indicating standard sensory processing.

Implications for Neural Connectivity:

- The overlapping activation in the insula across both groups may point to shared neural pathways involved in emotional regulation.
- Distinct activations in the precentral and postcentral gyri could reflect differences in sensorimotor integration between depressed individuals and healthy controls.

Potential Therapeutic Targets:

Identified brain regions may serve as targets for therapeutic intervention using psilocybin.

Note: These findings are preliminary, and further analyses are necessary.

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7. Created in <https://BioRender.com>