Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin

Carhart-Harris RL., Erritzoe D, Feilding A, Nutt D, *et al.*

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What is this study about?

This study is among the first to use brain imaging to look at **what happens in the brain after a dose of psilocybin** (the active substance in 'magic mushrooms'). The results hint at what underlies psilocybin's psychedelic – and possibly therapeutic – effects.

Why did we do this study?

We have known for a long time, from observation and a wealth of studies in the '50s and '60s, that psilocybin has psychedelic ('mind-manifesting') effects that can be harnessed for therapeutic purposes. However, very few studies have examined **what it does to the brain,** and what changes in brain activity are associated with the changes in consciousness.

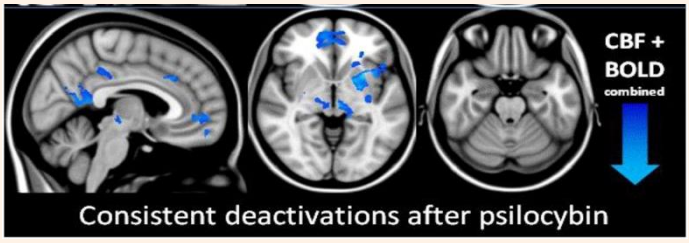
What did we do?

We scanned 2 groups of healthy volunteers after giving them psilocybin (2 mg IV) and, on a separate day, placebo (saline)

- 2 mg IV are comparable with ~15 mg oral, which is considered a moderate dose
- The first group (15 people) was scanned using a technique called **ASL** = arterial spin labelling = an MRI method to measure **blood flow** within the brain
- The second group (15 people) was scanned using a technique called resting-state **BOLD =** blood-oxygen level dependent MRI = a method to measure **blood oxygenation** within the brain
- The idea behind both scans is that brain regions that are more active need more oxygen and therefore get more blood delivered to them
- **Resting-state** refers to the fact that subjects were lying still with their eyes closed while being scanned

What did we find?

1. DECREASED BLOOD FLOW (ASL) and ACTIVITY (BOLD) in certain (overlapping) regions of the brain



- The regions in blue show where **blood flow and brain activity were lower** after psilocybin than placebo
  - Note: no region showed *greater* blood flow/activity
- This decrease was highly unexpected!
  - It was commonly assumed that the rich psychedelic experience would be associated with greater brain activity
  - An earlier PET study had shown *increased* activity
  - It could be that our study measures the early effects after psilocybin while PET measured the later effects (PET scans last 120 min, ours ~12 min)
- The regions are known to be 'hubs,' i.e. highly interconnected with other brain regions.

2. A CORRELATION between decreased blood flow and intensity of effects

In all the regions in blue, there was a relationship with the intensity of psilocybin effects reported by subjects, such that those who reported the most intense effects were those showing the greatest decrease in blood flow.

3. A CHANGE IN FUNCTIONAL CONNECTIONS between certain brain regions

- We did a 'functional connectivity analysis' = a method to test for similar activity patterns across different brain regions (suggesting the regions 'work together')
- Under normal circumstances, the medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC) – both part of the **Default Mode Network** – are 'functionally coupled' (their activity patterns correlate)
- Under psilocybin, **this functional coupling decreased**
- **This suggests that the Default Mode Network is disrupted under psilocybin**

Enter the Default Mode Network

The **Default Mode Network (DMN)** is a network of brain regions that plays a role in consciousness and high-level constructs such as the self or 'ego.' DMN regions are highly interconnected 'hubs' that are critical for information transfer across the brain. As such, the DMN serves as a central orchestrator or conductor of global brain function, which explains why its de-activation has such a profound effect on consciousness.

Why is this important?

- This study gives the **most detailed account to date on how the psychedelic state is produced in the brain**
- The results suggest decreased activity and connectivity in the brain's connector hubs, permitting an **unconstrained style of cognition**
- Importantly, this study **formed the basis for the MRC-funded 'psilocybin for depression' trial**, as mPFC activity and connectivity are known to be elevated in depression
- The decreased mPFC activity/connectivity seen here suggests a biological mechanism for the previously reported increases in well-being and openness and decreased depression in cancer patients after psilocybin

About the research team

Amanda Feilding is the founder and director of the Beckley Foundation. She and David Nutt co-direct the *Beckley/Imperial Research Programme*. Robin Carhart-Harris is the Programme's lead investigator.