Increased amygdala responses to emotional faces after psilocybin for treatment-resistant depression

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What is the amygdala?

The amygdala is a small, ancient region of the mammalian brain known to be important in evaluating the emotional significance of different kinds of stimuli. This includes those that might represent a threat, have social significance or a reward value – it decides if something is pleasurable or aversive, and induces the fight-or-flight response if a fear-inducing stimuli is detected.

Why are we studying it?

The amygdala plays an important role in mental health. For example, it is overly active in depressed people in response to sad stimuli, but under-active in response to positive ones. This may explain the negative or fearful perception of the world in depressed individuals.

Our *Beckley/Imperial Research Programme* has already shown that psilocybin is a promising therapeutic tool for treatment-resistant depression. The present study aimed at developing our understanding of the neurobiological mechanisms underlying these positive effects, with a particular focus on the amygdala.

What did we do?

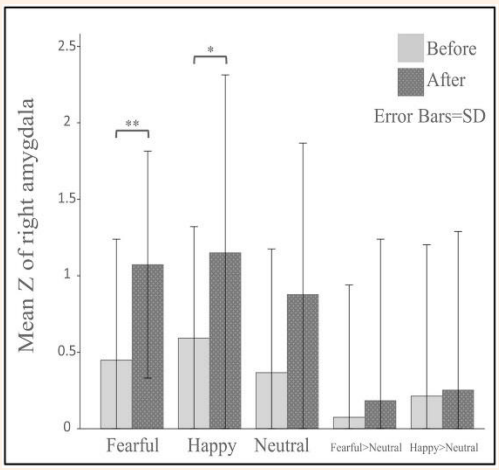
- 19 patients with moderate to severe treatment-resistant depression received two separate doses of psilocybin (10mg and 25mg, orally) 7 days apart.
- Each participant underwent two fMRI scans, one at baseline, before treatment, and the other on the morning after the higher-dose session. During the scans, participants passively viewed pictures of fearful, neutral, or happy faces.
- Patients completed surveys for 5 weeks following treatment to measure their levels of anxiety and depression, and the relationship between these measures and changes in brain function were analysed.

Examples of Fearful, Neutral, and Happy faces from the Karolinska Directed Emotional Faces set, similar to those used in this study.

What did we find?

- We found that psilocybin increased the activity of the right amygdala in response to emotional, but not neutral, faces.
- Additionally, positive clinical outcomes (i.e., reduction in depression scores) correlated with an increased amygdala response to fearful faces – those patients that had the greatest neural response to these stimuli were those that experienced the greatest antidepressant effect.

The right amygdala showed significantly increased activation during emotional stimuli



Activity in the right amygdala while viewing fearful, neutral, and happy faces, before and after psilocybin-assisted therapy (and ** indicate significant differences)*

Why is this important?

Psilocybin-assisted therapy was associated with increased amygdala responses to emotional stimuli, an opposite effect to previous findings with SSRIs. This suggests fundamental differences in these treatments' therapeutic mechanisms, with SSRIs mitigating negative emotions and psilocybin allowing patients to confront and work through them. Based on the present results, we propose that psilocybin with psychological support is a treatment approach that potentially revives emotional responsiveness in depression, enabling patients to reconnect with their emotions.

About the research team

Amanda Feilding is the founder and director of the Beckley Foundation. She and David Nutt are Co-Directors of the *Beckley/Imperial Research Programme*. Robin Carhart-Harris is the Programme's principal investigator. Leor Roseman, who conducted this study, is a PhD student at Imperial College London.