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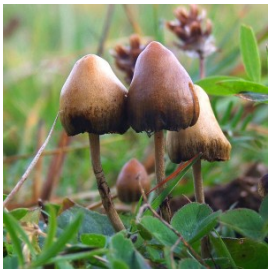
The Scicurious Brain: This is your brain on psilocybin

By Scicurious | February 8, 2012

This is a paper which is not quite what it's cracked up to be. Because while it does, indeed, have great pictures of your brain on drugs, it doesn't really go any further than that. It *doesn't explore why these changes are occurring or what they say about the functions of psilocybin*. So while it provides some nice correlations, the causation is still lacking.



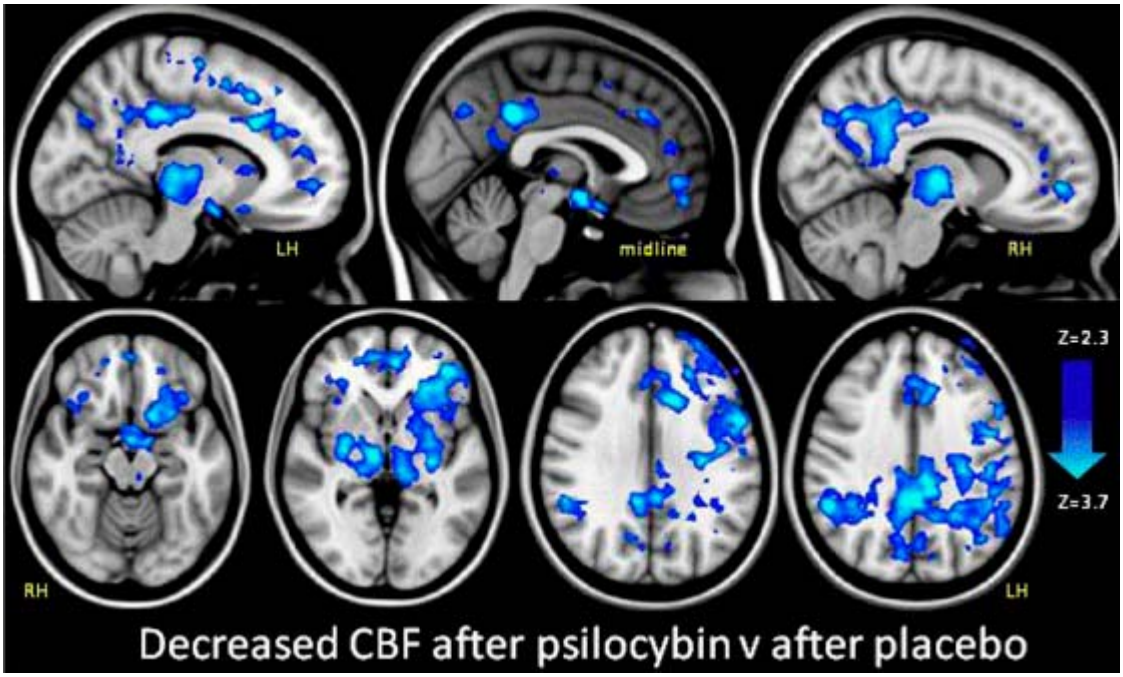
Carhart-Harris et al. "Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin" PNAS, 2012.

There are several hundred references to studies on psilocybin on Pubmed. We know that it is classified as a hallucinogen and has high affinity for the serotonin 2A type of receptor (through which it is thought to have its sensory distorting effects). We know how its metabolized, what dose related effects and subjective effects can be. But no one had ever put people on psilocybin into an fMRI and looked at the results.

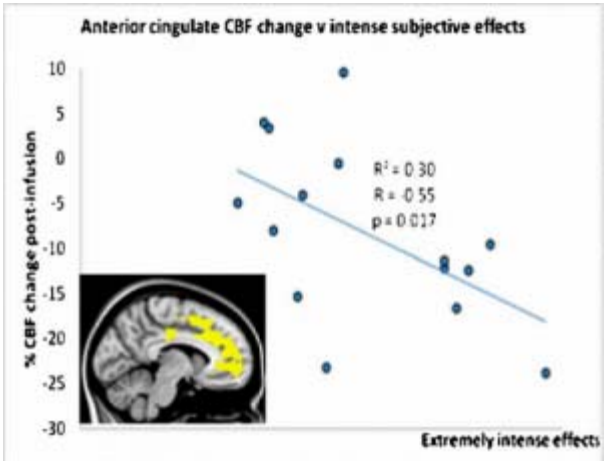
fMRI is functional magnetic resonance imaging, a technique which can measure brain activity by measuring the changes in blood flow to different areas of the brain over time. Keep in mind, though, that this techniques has its limitations. It measures changes in blood flow, and can tell you where and when those changes are occurring. But that is all. There's some debate over how correlated these changes really are with what activities are taking place, and what the changes themselves really mean for various aspects of function.

For this experiment, the authors put 15 subjects in an fMRI, and did studies using BOLD (measures of blood oxygenation), and ASL (arterial spin labeling, which also measures blood flow, but not oxygenation) while the participants were under the influence of

psilocybin or placebo. They using i.v. injections of psilocybin instead of the usual oral route of administration, in an effort to get the results in real time. And they got some very pretty pictures.



What this shows are areas of decreased blood flow, relative to placebo, in various areas of the brain while the participants were on psilocybin. The areas of greatest decrease included the cingulate cortex, the thalamus, and medial prefrontal cortex. The *thalamus is involved in a lot of relays and processing from one area of the brain to another, while the cingulate cortex is involved in emotional processing, and the medial prefrontal cortex in higher executive function.*



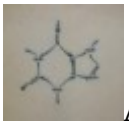
As you can see here, there was a negative correlation between the blood flow to these areas and the intensity of the subjective experience by the subjects, so the lower the blood flow, the more intense the subjective experience.

This is all well and good. But unfortunately, I think…that was ALL. The authors spoke somewhat about the "pharmaco-physiological interaction", but while that's very intense sounding, what it actually means it that the drug is affecting your brain, which is not exactly big news. They also hypothesized that these blood flow changes enable "a state of unconstrained cognition", but which blood flow changes? And via what mechanism? Does simply reducing blood flow in these regions induce subjective effects that feel like psilocybin? Does free and wild "unconstrained" thinking involve decreases in blood flow in these areas? What about serotonin receptors in these areas? Psilocybin is a strong agonist of serotonin 2A receptors, and the authors **hypothesize** that the effects of psilocybin on these areas of the brain are through the actions of serotonin 2A receptors on GABA neurons, reducing brain activity in these areas. But **they have no evidence for this,** they did not give a serotonin 2A antagonist to try and block the decreases in blood flow, or a GABA antagonist to try and block the subjective effects. While some of these effects couldn't necessarily be done in humans (like the decreases in blood flow in specific regions), several of them could have been (using a serotonin 2A antagonist or a GABA antagonist).

So while psilocybin is bound to grab people's interests, and ideas about "unconstrained cognition" may grab imaginations, this does nothing to address a mechanism, and without it, it's only a picture of your brain on drugs.

EDIT: To be clear (since the commenters point out that I wasn't), *I do not think this study is BAD. It's small and incremental. But not BAD (though I think the interpretation leaves something to be desired).* What I find rather odd about this paper is that it is small and incremental…but it's published in *PNAS, one of the bigger journals in the field (the level "below" Cell, Nature, and Science)*. In a journal like PNAS, *one usually expects to see mechanism, an effort at finding out WHY*. This is a picture of your brain on drugs, and while nice, doesn't show anything about why the drug is producing these effects or how the effects are occurring. **So I was surprised, and somewhat confused to see it in PNAS**. Is it because of the drug involved and the potential controversy? Or is there something about this publication that I've missed? I don't know. But I was, and am, surprised.

Carhart-Harris, R., Erritzoe, D., Williams, T., Stone, J., Reed, L., Colasanti, A., Tyacke, R., Leech, R., Malizia, A., Murphy, K., Hobden, P., Evans, J., Feilding, A., Wise, R., & Nutt, D. (2012). From the Cover: Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin *Proceedings of the National Academy of Sciences, 109* (6), 2138-2143 DOI: 10.1073/pnas.1119598109

 **About the Author:** Scicurious is a PhD in Physiology, and is currently a postdoc in biomedical research. She loves the brain. And so should you. Follow on Twitter @Scicurious.