Watching brains on acid using an MRI

Enlarge / LSD blotter paper

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What exactly happens in a brain when it is hit by a hallucinogen? Lots of drugs have effects that are obvious extensions of our normal body processes; they raise moods, dull pain, or boost our energy. But hallucinogens are notable for giving their users experiences that are anything but normal.

Now, a team of Swiss researchers has used MRI imaging to follow the brain as it’s under the influence of acid. And their results support the idea that hallucinogens cause the breakdown of the system that helps the brain keep track of which information is coming from the real world and which is generated by the brain itself.

Cortex overload

The brain receives a steady flow of information, some from the outside world, some from the body, and some generated by its internal thought processes. Your brain has to essentially decide which of it to take seriously and raise to the level of consciousness, which to monitor subconsciously, and which to discard. Hallucinations, whether due to drugs or mental disorders, appear to involve a breakdown in this information

processing.

We have some idea of the different brain structures responsible for this processing. The cerebral cortex appears critical for consciousness, perception, and attention, for example. The thalamus also appears to be involved in consciousness and helps relay sensory signals to other areas of the brain. Based on this and additional research, neuroscientists have proposed that the thalamus acts as a gatekeeper for sensory information flowing into the cortex.

In this model, hallucinogens suppress this gatekeeping function. As a consequence, the cortex gets overwhelmed by information and starts losing track of information, leading to a flood of intense sensations and other cognitive disruptions. The idea is consistent with a lot of data we have, but it's an extremely difficult idea to test. After all, people using hallucinogens aren't reliable witnesses to anything, much less their internal brain state.

To get at this question, the researchers behind the new work got ahold of a healthy supply of LSD and an MRI machine. These were combined with a technique that was developed relatively recently called dynamic causal modeling.

Functional meets causal

Normally, functional MRI (fMRI) imaging involves getting someone to perform a task and then comparing the brain's activity during the task to its resting activity. This method is great if you want to isolate a specific process, but it's not especially useful if you want to identify global changes in brain activity, like those caused by LSD.

In this work, however, the researchers focused on the brain's activity in two resting states: with and without acid. Even when seemingly doing nothing, our brain experiences waves of activity. Some brain regions signal independently of each

other, while others have linked activity—one region's firing triggers another's. Since there's so much going on in the brain, it's tough to tell these situations apart.

That's where dynamic causal modeling comes in. It involves researchers making a predictive model and then having an algorithm see whether real-world data can fit the model by tweaking the strength of the connections in it. While it's a complicated process, you can think of it as a way of checking whether the firing we see during normal brain activity is consistent with the connections we think are present in the brain.

To do the comparison, the researchers used three different conditions: a group of control subjects, a group that had taken LSD, and a group that took both LSD and a second drug. LSD, as it turns out, binds to a lot of proteins in the brain, including multiple receptors for serotonin and dopamine. The additional drug in these experiments, called Ketanserin, blocks just one of the serotonin receptors. But that's enough to block most of the subjective experiences of being on acid. So while we might expect LSD to change a lot of activity that isn't relevant to its hallucinogenic effects, the combination of the two drugs should help us identify which of these changes is most relevant to the issue at hand.

The researchers' model testing identified a number of changes driven by LSD that aren't altered by Ketanserin, suggesting they're not central to the hallucinations. And it identified another set of connections that appeared to be critical to the hallucinogenic effects.

Gatekeeper or organizer?

Overall, these effects were consistent with the model, in which the thalamus acts as a gatekeeper for the cerebral cortex. But instead of a general flooding of the cortex, they found that a limited number of specific regions saw increased

activity. This suggests the states induced by hallucinogens are distinct from states like anesthesia and sleep, which lead to widespread changes in the cortex. To some extent, this is a “duh!” finding, given that you can hold conversations with people on acid. But it’s an important finding for future studies that want to further tease out how hallucinogens work.

Of course, LSD isn’t the only hallucinogen out there; other studies have looked at ayahuasca and psilocybin. These results are generally consistent with the ones reported here but have also suggested that psychedelic drugs may simply lead to a disorganization of signaling within the brain. And at our current level of understanding, it’s not possible to distinguish between these two models.

Which of course means that the folks in Zurich are going to be lining up additional volunteers to take some acid and find out if it makes sitting in an MRI tube entertaining.

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