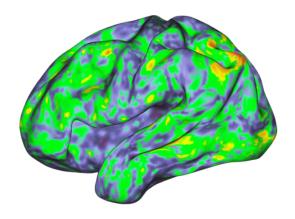
The New York Times: This Is Literally Your Brain On Drugs

By <u>Andrew Jacobs</u>



A small new study shows reactions in the brain in people who were given psilocybin in a controlled setting. If you had to come up with a groovy visualization of the human brain on psychedelic drugs, it might look something like this.

The image, as it happens, comes from dozens of brain scans produced by researchers at Washington University School of Medicine in St. Louis who gave psilocybin, the compound in "magic mushrooms," to participants in a study before sending them into a functional M.R.I. scanner.

The kaleidoscopic whirl of colors they recorded is essentially a heat map of brain changes, with the red, orange and yellow hues reflecting a significant departure from normal activity patterns. The blues and greens reflect normal brain activity that occurs in the so-called functional networks, the neural communication pathways that connect different regions of the brain.

The scans, published Wednesday in the journal Nature, offer a rare glimpse into the wild neural storm associated with mindaltering drugs. Researchers say they could provide a potential road map for understanding how psychedelic compounds like psilocybin, LSD and MDMA can lead to

lasting relief from depression, anxiety and other mental health disorders.

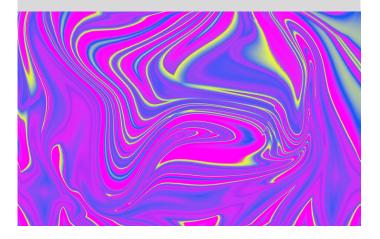
"Psilocybin, in contrast to any other drug we've tested, has this massive effect on the whole brain that was pretty unexpected," said Dr. Nico Dosenbach, a professor of neurology at Washington University and a senior author of the study. "It was quite shocking when we saw the effect size."

The study included seven healthy adults who were given either a single dose of psilocybin or a placebo in the form of methylphenidate, the generic version of the stimulant Ritalin. Each participant underwent a total of 18 brain scans, taken before, during and after the initial dosing.

Four participants returned six months later for an additional psilocybin session.

Although the scans of those given methylphenidate showed acute changes in brain activity patterns, the neural disruption among those who took psilocybin was three times greater, the study found.

Much of that disruption occurred in parts of the brain involved in introspective thinking, like daydreaming and remembering. Those areas help individuals define their sense of self.



Perhaps more surprising were the scans taken days and weeks later. They showed that the brains of those who took psilocybin had largely returned to normal, but there remained a small and significant change suggesting that the drug's effects remained long after psilocybin had left the individual's body.

Ramaekers, professor Dr. Jan a psychopharmacology at Maastricht University in the Netherlands who was not involved in the study, said the scans showing that the drug had lingering effects correlated with anecdotal evidence suggesting that the benefits of some psychedelic therapies were not permanent. "Treatments with psilocybin, even though they are effective, don't last forever," he said. "At some point, they need to be done again."

Dr. Joshua Siegel, a neuroscientist and lead author of the study, said psilocybin appeared to disrupt the brain's default mode network, an interconnected set of areas ordinarily active when the brain is not focused on anything in particular. By contrast, the default mode network remained stable in the participants who received the methylphenidate.

"The activity in these networks became much more disorganized, and boundaries between the networks essentially evaporated," Dr. Siegel said.

He used the analogy of the synchronized stadium wave to explain the phenomenon. In normal day-to-day activity, millions of neurons work in synchrony but when a psychedelic like psilocybin washes over the brain, those neurons start firing off in a chaotic fusillade. "It's like having thousands of stadium fans randomly raise their hands," he said.



Ceyda Sayali, a cognitive neuroscientist at the <u>Center for Psychedelic and Consciousness Research</u> at Johns Hopkins University who was not involved with the study, said she was struck by the images that showed a marked change when participants on psilocybin were asked to answer simple questions that forced them to focus on what was happening around them. The requests, known in the field as grounding, can briefly draw participants out of their psychedelic reverie.

In this case, the sudden jolt of reality was reflected in scans that showed a brief calming of brain activity. "This is something that has never been shown before," she said.

Dr. Siegel said the scrambled brain activity was most likely a driver of neuroplasticity, the brain's ability to form new ways of thinking and a hallmark of how psychedelic medicine can help patients break destructive thought patterns. "It almost makes you a different person, so to speak," he said.



The study, he and others say, lends weight to the notion that the psychedelic experience — the intense visualizations, the distortions of time and space, and the detachment from self — is an essential part of the therapeutic process. While such a hypothesis might seem self-evident, it is not universally accepted among psychedelic researchers, some of whom are working to develop new compounds that provide the benefits of psychedelic drugs without the disorienting effects.

Dr. Siegel said he thought the results might also serve to counter a theory promoted by some researchers that places an outsize role on the placebo effect, given that a significant percentage of participants in psychedelic studies traditionally report improvements to their mental health despite the fact that they did not receive a psychoactive drug.

"Being able to show a neurobiological mechanism that says, hey, this is actually affecting the brain, gives more meat to the argument that this not just placebo effect," he said. "It shows that these drugs are creating lasting change to the brain."