

LSD, a future anti-anxiety pill?

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The craze for psychedelics used for therapeutic purposes is real. However, the scientific evidence supporting their effectiveness and explaining their mode of action in treating mental health disorders is still very thin. A new study led by Dr. Gabriella Gobbi, a senior scientist in the Brain Repair and Integrative Neuroscience (BRaIN) Program at the Research Institute of the McGill University Health Centre (RI-MUHC), sheds light on previously unexplained neurobiological mechanisms by

which LSD is believed to relieve anxiety.

While preliminary studies suggested that psychotherapy-assisted microdosing was effective in alleviating anxiety and [depressive symptoms](#) in people with severe psychiatric or neurological problems, the biological mechanisms underlying these effects had remained unclear to date. The study conducted by Dr. Gobbi's team demonstrates for the first time that regular administration of low doses of LSD ([lysergic acid diethylamide](#)) reduces anxiety symptoms through neurobiological mechanisms that are similar to some commonly prescribed classes of antidepressants and anxiolytics : [selective serotonin reuptake inhibitors](#) (SSRIs). SSRIs are better known by their trade names: Prozac, Zoloft, Celexa, Cipralex, etc.

"Our lack of knowledge of the biological processes associated with psychedelic drugs hinders the development of potential new treatments," says Dr. Gabriella Gobbi, also a Professor and Head of the Neurobiological Psychiatry Unit in the Department of Psychiatry at McGill University. "Understanding the mechanisms of action and efficacy of psychedelics will allow us to develop a more precise indication of hallucinogenic drugs for psychiatric and neurological diseases," she says.

The study, which was published today in the journal *Neuropsychopharmacology*, was conducted in collaboration with researchers in psychiatry at McGill University, as well as researchers in neuroscience at Vita Salute San Raffaele University and in Pharmaceutical and Pharmacological Sciences at the University of Padua, Italy.

Neurobiological mechanisms under the microscope

According to the results of the study, the use of LSD increases the

nervous transmission of serotonin, also called 5-hydroxytryptamine (5-HT). Serotonin is a neurotransmitter that plays an essential role in the state of well-being. It has been shown that prolonged periods of stress result in a decrease in the activity of the neurons that transmit serotonin (5-HT neurons). Like the SSRI antidepressants, LSD is believed to desensitize the receptors, which decrease the electrical activity of serotonin on these neurons, thereby stimulating them to release more serotonin.

Dr. Gobbi's study also found that low doses of LSD promoted the formation of new dendritic spines in rodents. These spines are the branches of neurons that are responsible for transmitting the electrical signal to the nerve cell body. "We have shown that LSD can rebuild these branches that are 'dismantled' due to stress. This is a sign of brain plasticity," explains Dr. Danilo De Gregorio, who is today an Assistant Professor of Pharmacology at San Raffaele University in Milan and first author of the study.

The research team evaluated the administration of low doses of LSD over a period of seven days on a group of mouse models subjected to chronic stress conditions. Repeated doses showed optimal results in decreasing anxiety-like behaviors caused by stress. More studies are needed to demonstrate the drug effectiveness for depressive and anxiety disorders in humans and the inherent mechanisms of action.

Another study by Dr. Gobbi, published in 2016, had already shown that low doses of LSD affected only the nerve transmission of serotonin while higher doses affected the dopamine system, causing the psychotic effects.

"I began my research on psychedelics several years ago out of personal curiosity. How is it possible that a simple drug can change your state of mind so profoundly? What is its mechanism of action? To my surprise,

this research is now in the spotlight," says Dr. Gobbi. The next step for her team will be to evaluate the mechanisms of action of other psychedelic substances, such as psilocybin (an active component of magic mushrooms) and ketamine.

Caution and patience are required

There have been no major advances in [psychiatric care](#) in the last decade. It is essential to develop new therapeutic alternatives, because for a proportion of people with serious mental health problems, current treatments are not working. LSD, psilocybin, ayahuasca and MDMA are among the drugs that are being developed to treat various psychiatric disorders such as anxiety, depression, post-traumatic stress disorder and addiction, as well as certain neurodegenerative diseases. Health Canada authorized the use of [psychedelic drugs](#) in a very strict clinical setting last January.

However, there is still a long way to go, says Dr. Gobbi. "Interest in LSD stems from its ability to influence serotonin levels and produce feelings of happiness, confidence and empathy as well as improvement of social behavior. However, more studies are needed to identify safe and effective therapeutic uses, as psychedelics can cause psychosis and neurotoxic effects," says the researcher, who warns the public about the dangers of self-medicating with illegal drugs.

More information: Danilo De Gregorio et al, Repeated lysergic acid diethylamide (LSD) reverses stress-induced anxiety-like behavior, cortical synaptogenesis deficits and serotonergic neurotransmission decline, *Neuropsychopharmacology* (2022). [DOI: 10.1038/s41386-022-01301-9](https://doi.org/10.1038/s41386-022-01301-9)

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