

## Study suggests region of prefrontal cortex impacted by ketamine

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One 10 ml vial of 1000 mg ketamine. Credit: Psychonaught/Wikipedia

(Medical Xpress)—A team of researchers working at Yale University



has found that a region of the brain's prefrontal cortex known as the infralimbic prefrontal cortex (IL-PFC) appears to be the part of the brain involved that reacts to ketamine, causing relief of depression symptoms. In their paper published in *Proceedings of the National Academy of Sciences*, the team describes how they tested the impact of ketamine on neural activity in the IL-PFC and what they learned in the process.

Ketamine is a well known drug, partly because it has been used in some instances to successfully treat depression in patients (very quickly) that did not respond to any other medication or treatment, partly because it has hit the underground as a popular illicit drug (due to the hallucinations it can cause), and partly because of its use as a date rape drug. Despite its widespread renown, scientists still do not really understand how it does what it does to the human brain. To learn more, the researchers with this new effort focused on its impact on the IL-PFC, a region of the brain that has in the past been associated with emotional responses.

To better understand what happens when Ketamine is introduced into the brain, the researchers watched neural and behavioral activity as Ketamine was introduced indirectly (via the blood) and directly into rat brains. They found that deactivating neural activity in the IL-PFC prior to administering the drug caused a halt to systematic effects and injecting the drug directly into the IL-PFC caused the systematic effects to come about, suggesting that the IL-PFC is the region of the brain that is most impacted by the drug. The team found also that stimulating the same region optogenetically resulted in the same systematic effects as injection of ketamine. In addition, the researchers found that use of ketamine caused an increase in the number of synapses in the IL-PFC, suggesting the drug had a long term or even permanent impact on the brain.

Taken together, the results show, the team suggests, that other



alternatives to ketamine for use in treating depression might be found that do not have the harmful side effects. The team plans to continue their research, hoping to better understand how it is that ketamine causes the observed changes in <u>neural activity</u> in the IL-PFC.

**More information:** Optogenetic stimulation of infralimbic PFC reproduces ketamine's rapid and sustained antidepressant actions, Manabu Fuchikami, *PNAS*, <u>DOI: 10.1073/pnas.1414728112</u>

## **Abstract**

Ketamine produces rapid and sustained antidepressant actions in depressed patients, but the precise cellular mechanisms underlying these effects have not been identified. Here we determined if modulation of neuronal activity in the infralimbic prefrontal cortex (IL-PFC) underlies the antidepressant and anxiolytic actions of ketamine. We found that neuronal inactivation of the IL-PFC completely blocked the antidepressant and anxiolytic effects of systemic ketamine in rodent models and that ketamine microinfusion into IL-PFC reproduced these behavioral actions of systemic ketamine. We also found that optogenetic stimulation of the IL-PFC produced rapid and long-lasting antidepressant and anxiolytic effects and that these effects are associated with increased number and function of spine synapses of layer V pyramidal neurons. The results demonstrate that ketamine infusions or optogenetic stimulation of IL-PFC are sufficient to produce long-lasting antidepressant behavioral and synaptic responses similar to the effects of systemic ketamine administration.

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