

FSU researcher testing safety of low-dose ketamine to treat depression

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([HTTPS://NEWS.FSU.EDU/NEWS/HEALTH-MEDICINE/2018/10/30/FSU-RESEARCHER-TESTING-SAFETY-OF-LOW-DOSE-KETAMINE-TO-TREAT-DEPRESSION/](https://news.fsu.edu/news/health-medicine/2018/10/30/fsu-researcher-testing-safety-of-low-dose-ketamine-to-treat-depression/)) | 10:04 AM | SHARE:



► Mohammed Kabbaj, professor in the Department of Biomedical Sciences. (Credit: Colin Hackley)

People who get no depression relief from Prozac-type medicines have found a fast-acting substitute in a drug called ketamine. But is it safe? The National Institutes of Health has awarded a Florida State University researcher nearly \$2 million to investigate ketamine, which some have called a wonder drug.

Over the next five years, College of Medicine researcher Mohamed Kabbaj and his lab will seek answers to these and other questions: Is ketamine addictive when administered in low doses? In what ways does it affect females and males differently? How does it interact with alcohol?

“Hopefully, by the end of these five years we’ll have more information for psychiatrists to decide whether ketamine can be safely prescribed for suicidal patients and for patients who do not respond to classic antidepressant treatment,” said Kabbaj, a professor in the Department of Biomedical Sciences.

Ketamine was developed in the 1960s as an anesthetic to replace PCP, which was giving patients hallucinations and other so-called “dissociative effects.” In the last decade, psychiatrists discovered that ketamine in low doses also worked remarkably fast to relieve the symptoms of depression and reverse thoughts of suicide.

“A lot of clinics have popped up around the country treating depression and bipolar disorder with repeated infusions of ketamine,” Kabbaj said. “But no studies have been done to look into the safety of these treatments related to ketamine’s potential addictive and cognitive effects.”

In large doses, ketamine (called “special K” and other names on the street) is abused by people seeking a quick high. With that dosage, side effects include addiction. Kabbaj’s goal is to find out whether low doses of ketamine also are addictive and determine the mechanisms of ketamine’s actions at both high and low doses in both sexes.

Kabbaj’s previous studies, also funded by the NIH, demonstrated sex differences in ketamine’s antidepressant effects. Women require much lower doses than men to get those benefits.

“We’re also going to determine which brain areas are implicated in ketamine’s addictive properties at low and high doses,” he said. “Our work will focus on the nucleus accumbens, an area that is associated with reward and behavioral reinforcement.”

The release of dopamine in this brain area, in response to ketamine administration, leads to activation of two populations of neurons that express either dopamine D1 receptors or dopamine D2 receptors. This project, Kabbaj said, will try to assess the role of those neuron populations in ketamine’s addictive effects.

Since a large population of depressed patients abuse alcohol, another aim of this study is to examine the interaction between ketamine, depression and alcohol in male and female subjects.

“If you have a patient who drinks alcohol and you give him ketamine, is it safe?” Kabbaj asked.

“What is the interaction between ketamine and alcohol?”

“Women metabolize alcohol much more slowly than men and are more prone to depression. Ketamine and alcohol share some similarities in their mode of action in the brain, so it is critical to examine the ketamine-alcohol interaction in both sexes.”

Some of ketamine’s effects on drinking alcohol might be therapeutic, he said.

“There are some studies now showing that ketamine can reduce alcohol drinking,” he said. “Our study will directly test these interactions and examine the potential mechanisms behind them.”

Kabbaj is one of many researchers trying to learn more about this promising drug.

“It’s a very hot topic right now,” he said. “Soon we’ll know what ketamine is doing, in terms of the molecular and cellular mechanisms mediating its fast-acting antidepressant properties. So maybe we can develop other drugs that act similarly but without causing dissociative effects and leading to addiction.”

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