

Ketamine rapidly improves cognitive function, making those in suicidal crisis less likely to harm themselves

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

Ketamine, a drug used to treat mood disorders and severe depression, improved the thinking and reasoning of those who expressed thoughts of killing themselves within 24 hours, according to a Columbia University study.

Published today in the *Journal of Clinical Psychiatry*, the study found that one dose of [ketamine](#) not only reduced the severity of depression in people with suicide ideation, many of whom had not responded to other antidepressants, but also made them feel safer and less likely to harm themselves because it rapidly diminished their suicidal ideation.

"We found that suicidal ideation is not just related simply to severity of depression," said J. John Mann, MD, senior author and the Paul Janssen Professor of Translational Neuroscience (in Psychiatry and in Radiology) at Columbia University. "There are other reasons, including cognitive improvements that are related to a decline in suicidal ideation and thereby make those who are suicidal safer."

When they began the five-year trials, Columbia researchers knew that anesthetic ketamine, in much lower doses where it has no anesthetic effect, rapidly reduced depressive symptoms and suicidal ideation in some patients. But they wanted to obtain a better understanding of the mechanisms behind this effect and decided to examine the drug's impact on neurocognitive performance.

Study found improved cognition appeared quickly

Researchers followed 78 participants suffering with major depressive disorder and clinically significant suicidal ideation and found that a standard dose of ketamine given intravenously produced a rapid improvement of suicidal thoughts in some individuals, and part of this improvement was correlated with and improvement in problem-solving and thinking more clearly. This improvement in neurocognition—and

suicidal ideation—occurred even when some of these individuals did not show comparable improvement in depressive symptoms.

"Our study helped us gain a better understanding of how ketamine works in the brain and how quickly it can improve distorted thinking," said Ravi. N. Shah, MD, Chief Innovation Officer, Columbia Psychiatry. "Being able to think more clearly can make someone feel less suicidal."

The study compared the effects of intravenously administered ketamine—not yet approved by the FDA but provided off-label at treatment centers throughout the country—to midazolam, a sedative prescribed for anxiety and depression. It found greater cognitive improvements in thinking and reasoning in those who were given the ketamine.

Suicidal thinking diminished for six weeks with one ketamine treatment

Participants in the study who responded positively to the ketamine treatment continued to do well for up to six weeks after they were given an initial infusion in conjunction with other antidepressants that were tailored to the needs of each specific patient.

Suicide is the third leading cause of death for those ages 10-34 and the 10th leading cause of death overall in the United States. Dr. Mann said since 90 percent of those who die by suicide in the U.S. have a psychiatric illness and 60 percent of those people suffer a major depressive episode before a suicide attempt, it would be a major benefit if ketamine could be used to lessen suicidal risk.

Approved by the Food and Drug Administration for medical use in 1970, ketamine was first used as an anesthetic to treat injured soldiers during in the Vietnam War, but it soon became notorious as a party drug,

nicknamed Special K, used illicitly in clubs for its hallucinogenic and dissociative effects.

But research into the drug's potential as a treatment for depression and antidote to suicidal thoughts continued, and in 2019 the FDA approved intra-nasal spray esketamine, derived from ketamine, to be used in conjunction with an oral depressant in adults with treatment-resistant depression.

Ketamine is clearly changing functioning of important neurotransmitter systems in many key areas of the brain, and further study of ketamine and other drugs like it could lead to new mental health treatments, the researchers said. However, more research is needed to determine why some people respond to ketamine—which alters the release of glutamate that regulates much of the nervous system and helps the brain rewire itself by creating new connections and pathways—and other patients do not.

Since neuropsychological risks of long-term repeated ketamine treatments are unknown, researchers said further study is needed. Designing rapid-acting antidepressants like ketamine without the side effects of "tripping" or out-of-body experiences that could be taken in pill form at home instead of in a clinical setting, is also important, Mann said.

More information: John G. Keilp et al, Effects of Ketamine Versus Midazolam on Neurocognition at 24 Hours in Depressed Patients With Suicidal Ideation, *JCP* (2021). www.psychiatrist.com/jcp/depre...h-suicidal-ideation/

Trial: clinicaltrials.gov/ct2/show/NCT01700829

Provided by Columbia University Irving Medical Center

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