

## Ketamine improved bipolar depression within minutes

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Bipolar disorder is a serious and debilitating condition where individuals experience severe swings in mood between mania and depression. The episodes of low or elevated mood can last days or months, and the risk of suicide is high.

Antidepressants are commonly prescribed to treat or prevent the <u>depressive episodes</u>, but they are not universally effective. Many patients still continue to experience periods of depression even while being treated, and many patients must try several different types of <u>antidepressants</u> before finding one that works for them. In addition, it may take several weeks of treatment before a patient begins to feel relief from the drug's effects.

For these reasons, better treatments for depression are desperately needed. A new study in <u>Biological Psychiatry</u> this week confirms that scientists may have found one in a drug called ketamine.

A group of researchers at the National Institute of Mental Health, led by Dr. Carlos Zarate, previously found that a single dose of ketamine produced rapid antidepressant effects in <u>depressed patients</u> with <u>bipolar disorder</u>. They have now replicated that finding in an independent group of depressed patients, also with bipolar disorder. Replication is an important component of the scientific method, as it helps ensure that the initial finding wasn't accidental and can be repeated.

In this new study, they administered a single dose of ketamine and a single dose of placebo to a group of patients on two different days, two weeks apart. The patients were then carefully monitored and repeatedly completed ratings to 'score' their depressive symptoms and suicidal thoughts.

When the patients received ketamine, their depression symptoms significantly improved within 40 minutes, and remained improved over 3 days. Overall, 79% of the patients improved with

ketamine, but 0% reported improvement when they received placebo.

Importantly, and for the first time in a group of patients with bipolar depression, they also found that ketamine significantly reduced <u>suicidal</u> thoughts. These antisuicidal effects also occurred within one hour. Considering that bipolar disorder is one of the most lethal of all psychiatric disorders, these study findings could have a major impact on public health.

"Our finding that a single infusion of ketamine produces rapid antidepressant and antisuicidal effects within one hour and that is fairly sustained is truly exciting," Dr. Zarate commented. "We think that these findings are of true importance given that we only have a few treatments approved for acute bipolar depression, and none of them have this rapid onset of action; they usually take weeks or longer to have comparable antidepressant effects as ketamine does."

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist, which means that it works by blocking the actions of NMDA. Dr. Zarate added, "Importantly, confirmation that blocking the NMDA receptor complex is involved in generating rapid antidepressant and antisuicidal effects offers an avenue for developing the next generation of treatments for depression that are radically different than existing ones."

More information: The article is "Replication of Ketamine's Antidepressant Efficacy in Bipolar Depression: A Randomized Controlled Add-On Trial" by Carlos A. Zarate Jr., Nancy E. Brutsche, Lobna Ibrahim, Jose Franco-Chaves, Nancy Diazgranados, Anibal Cravchik, Jessica Selter, Craig A. Marquardt, Victoria Liberty, and David A. Luckenbaugh (doi: 10.1016/j.biopsych.2011.12.010). The article appears in *Biological Psychiatry*, Volume 71, Issue 11 (June 1, 2012)



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