

Intranasal ketamine confers rapid antidepressant effect in depression

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A research team from the Icahn School of Medicine at Mount Sinai published the first controlled evidence showing that an intranasal ketamine spray conferred an unusually rapid antidepressant effect—within 24 hours—and was well tolerated in patients with treatment-resistant major depressive disorder. This is the first study to show benefits with an intranasal formulation of ketamine. Results from the study were published online in the peer-reviewed journal *Biological Psychiatry* on April 2, 2014.

Of 18 patients completing two treatment days with ketamine or saline, eight met response criteria to ketamine within 24 hours versus one on saline. Ketamine proved safe with minimal dissociative effects or changes in hemodynamic dimensions.

The study randomized 20 patients with [major depressive disorder](#) to ketamine (a single 50 mg dose) or saline in a double-blind, crossover study. Change in depression severity was measured using the Montgomery-Asberg Depression Rating Scale. Secondary outcomes included the durability of response, changes in self-reports of depression, anxiety, and the proportion of responders.

"One of the primary effects of ketamine in the brain is to block the NMDA [N-methyl-d-aspartate] glutamate receptor," said James W. Murrough, MD, principal investigator of the study, and Assistant Professor of Psychiatry and Neuroscience, and Associate Director of the Mood and Anxiety Disorders Program at the Icahn School of Medicine at Mount Sinai. "There is an urgent clinical need for new treatments for depression with novel mechanisms of action. With further research and development, this could lay the groundwork for using NMDA targeted treatments for major depressive disorder."

"We found intranasal ketamine to be well tolerated with few side effects," said Kyle Lapidus, MD, PhD, Assistant Professor of Psychiatry, at the Icahn

School of Medicine at Mount Sinai.

One of the most common NMDA receptor antagonists, ketamine is an FDA-approved anesthetic. It has been used in animals and humans for years. Ketamine has also been a drug of abuse and can lead to untoward psychiatric or cognitive problems when misused. In low doses, ketamine shows promise in providing rapid relief of depression, with tolerable side effects.

Study co-author Dennis S. Charney, MD, Anne and Joel Ehrenkranz Dean of the Icahn School of Medicine at Mount Sinai and President for Academic Affairs for the Mount Sinai Health System, and a world expert on the neurobiology and treatment of mood disorders, said: "What we have here is a proof of concept study and we consider the results very promising. We hope to see this line of research further developed so that we have more treatments to offer patients with severe, difficult-to-treat major depressive disorder."

Going forward, the Mount Sinai research team hopes to examine the mechanism of action, dose ranging, and use functional brain imaging to further elucidate how ketamine works.

Provided by The Mount Sinai Hospital

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