Anti-convulsant drug significantly reduced major depression symptoms

November 1 2018

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Researchers from the Icahn School of Medicine at Mount Sinai found that patients with Major Depressive Disorder (MDD) exhibited a significant reduction of depressive symptoms after being treated with ezogabine, an FDA approved drug used to treat seizures.

After treatment, patients showed a 45 percent reduction in depression, a

significant reduction in anhedonia, the inability to feel pleasure; and a significant increase in resilience.

This is the first study to suggest that ezogabine, part of a class of drugs known as potassium channel openers, may have an antidepressant affect in humans.

The review will be published online on Thursday November 1st, in *Molecular Psychiatry*.

Major depressive disorder (MDD) impacts 15 million Americans and is the leading cause of disability, yet current treatments possess limited efficacy. A new therapeutic direction is emerging from the increased understanding of natural resilience as an active stress-coping process. It is known that potassium channels in the brain's reward system are an active mediator of resilience.

In a previous study, the Mount Sinai research team tested ezogabine, also known as retigabine, a potassium channel opener, in mice. They found that that ezogabine had significant antidepressant effects in the mice, expressed by two common measures in rodents: increased social interactions and preferences for natural rewards.

In this study, 18 medication free individuals with MDD experiencing a major depressive episode received up to 900 mg of ezogabine daily during 10 weeks in an open label study to determine if the drug significantly engaged their reward system. Resting state functional magnetic resonance imaging data revealing the connectivity of the reward system were collected at baseline and post-treatment to reexamine brain reward circuitry. After treatment with ezogabine, subjects exhibited a significant reduction of depressive symptoms measured by the the change in connectivity of their reward system.

"The results of this study are exciting because we haven't had a new medicine to treat depression in decades," said the study's senior author, James Murrough, MD, Ph.D., Director of the Mood and Anxiety Disorders Program at the Icahn School of Medicine at Mount Sinai. "Most antidepressants are in the same class of drugs and work by increasing serotonin. Our research suggests a different molecular target that works through other brain mechanisms and could be helpful for patents."

The research team at Mount Sinai is currently conducting a larger multi-site double blind trial of ezogabine in patients with depression funded by the National Institute of Mental Health to further determine its efficacy in treating depression.

"We know that patients with depression become depressed for different reasons, and we've been stuck in a one size fits all treatment for a long time," said Dr. Murrough. "A new class of medicines could give us an opportunity to treat patients based on the specific underlying cause of their disease."

Provided by The Mount Sinai Hospital