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Study may offer answers for treating depression in alcoholics

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A study by researchers at Vanderbilt University Medical Center is offering a glimmer of hope to alcoholics who find it hard to remain sober because their abstinence is hounded by stubborn, difficult-to-treat depression.

Using an anesthetic drug that also has antidepressant properties, and another drug that raises levels of a mood-enhancing natural chemical in the brain, the researchers found that they could alleviate depressive-like symptoms in a mouse model of alcoholism.

The findings, published online this month in the journal *Neuropsychopharmacology*, could set the stage for development of novel treatments for mood and anxiety disorders that are induced by withdrawal from alcohol.

Depression is highly associated with alcohol abuse disorders. Yet before these findings can be applied to humans, "much work remains to be done," said senior author Danny Winder, Ph.D., professor of Molecular Physiology and Biophysics and of Psychiatry.

Clinical studies in which both conditions have been treated at the same time are "woefully lacking," he and his colleagues wrote. In addition, commonly used antidepressants called selective serotonin reuptake inhibitors (SSRI) are not very effective in this population.

The Vanderbilt researchers validated a previously established mouse

model in which the animals exhibit depression-like behavior following withdrawal of alcohol.

They then tested ketamine, an anesthetic drug that blocks the NMDA receptor in the brain and which has been shown to have rapid and long-lasting antidepressant effects in humans. When the mice were given ketamine, the depressive symptoms were reversed.

The researchers also tested the effect of raising brain levels of an endocannabinoid called 2-AG by blocking the enzyme monoacylglycerol (MAG) lipase. Endocannabinoids are naturally produced chemical messengers that have been implicated in depression and anxiety-like behavior.

A previous Vanderbilt study found that raising 2-AG levels with an MAG lipase inhibitor reduced stress-induced anxiety-like behaviors in mice. In the current study, treatment with a MAG lipase inhibitor had a similar effect to ketamine in reversing depressive symptoms after alcohol withdrawal.

"We are excited to pursue the role of the endocannabinoid system further," Winder said. But clinical use of ligands (compounds) that bind endogenous cannabinoid receptors is still in its infancy, he said.

Provided by Vanderbilt University Medical Center