

New Compound Improves Obesity-Related Health Complications

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(PhysOrg.com) -- An experimental compound appears to improve metabolic abnormalities associated with obesity, according to a preliminary study led by researchers at the National Institutes of Health. A report of the study, which was conducted with obese mice, appears online today in the *Journal of Clinical Investigation*.

"This is a promising early step toward a treatment for some of the serious health consequences of [obesity](#)," says Kenneth R. Warren, Ph.D., acting director of the National Institute on Alcohol Abuse and Alcoholism (NIAAA), part of the NIH.

"Our results suggest that this compound could perhaps provide clinical benefits for obese individuals without the liabilities seen thus far with similar compounds," adds senior author and NIAAA Scientific Director, George Kunos, M.D., Ph.D.

Previous studies have shown that similar compounds block the activity of endocannabinoids, natural messengers in the body that are chemically similar to the active compound in marijuana, and help regulate many biological functions. These compounds can help promote weight loss and improve metabolic complications of obesity, such as diabetes and insulin resistance, changes in blood lipid composition, and fatty liver. However, the clinical advancement of such compounds has been stymied by behavioral side effects associated with their use, such as anxiety, depression and suicidal thoughts.

Dr. Kunos and first author Joseph Tam, D.D.S., Ph.D., of the NIAAA Laboratory of Physiologic Studies, collaborated with a team of scientists within and outside NIH to investigate a compound designed to avoid those side effects while preserving the beneficial effects of blocking endocannabinoid activity.

"Endocannabinoid receptors are present in the brain, as well as in peripheral tissues including the liver, skeletal muscles, pancreas, and fatty tissues," explained Dr. Kunos. "Activation of peripheral endocannabinoid receptors contributes to obesity-related metabolic and hormonal abnormalities."

The researchers reasoned that a compound that is unable to penetrate into the brain would selectively block the activity of endocannabinoid receptors in peripheral tissues, and therefore might alleviate metabolic and hormonal problems related to obesity. All while avoiding the behavioral problems that result from blocking endocannabinoid receptors in the brain.

They developed such a compound, tested it in obese mice, and found that the mice showed improvements in glucose regulation, fatty liver, and plasma lipid profiles. They also found that the compound did not affect behavioral responses, such as cannabinoid-induced immobility and hypothermia, that are mediated by endocannabinoid receptors in the brain, and that it reduced weight in mice with diet-induced obesity by about 12 percent, but did not affect weight in mice with a genetic predisposition for obesity.

"These preliminary findings are very encouraging and warrant further testing of this compound as a potential pharmacotherapy for the metabolic syndrome associated with obesity," said Dr. Tam.

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