Hunger signals, including those from endogenous cannabinoids, mapped in the brain

March 23 2022, by Aran Sullivan

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Cannabis is well-known for having an effect on eating behaviors. However, how the natural cannabinoid molecules found in the body regulate feeding and eating is not well researched. Now Masoud Ghamari-Langroudi, research assistant professor of molecular physiology and biophysics, research assistant professor of pharmacology

and faculty affiliate at the Warren Center for Neuroscience Drug Discovery, and his lab have discovered how endogenous cannabinoids, those made by the body, modulate the "feeding cells" in the brain to regulate body weight.

In this study, Ghamari-Langroudi expands on his previous work involving MC4 receptors, which are crucial in regulating energy homeostasis, the balance of energy intake and expenditure in the body. MC4 receptors respond to cannabinoid molecules, whether they are naturally in the body or from drugs such as cannabis. His lab used a variety of techniques, including behavioral studies, gene expression analysis, hormone assays and electrophysiology techniques, to map the brain circuits associated with cannabinoids and eating behavior.

"We describe here how endogenous cannabinoids produced in the hypothalamus—a brain region important in homeostasis—can 'fine tune' the activity of the MC4 receptor feeding cells," Ghamari-Langroudi said.

"There has been a sharp increase in obesity and anorexia in recent years," Ghamari-Langroudi said. "We hope our research will offer an understanding of how feeding behavior is regulated, which can also be an avenue to develop therapeutics."

MC4 receptors are implicated in a variety of disordered eating behaviors, including obesity and anorexia, making the Food and Drug Administration particularly interested in targeting them as a therapeutic tactic against associated disorders. The drugs that have been developed so far have adverse effects, including high blood pressure, according to Ghamari-Langroudi. "This novel finding of regulation of MC4R neurons could potentially provide therapeutic tools to target energy homeostasis without the unwanted effects observed by current MC4R targeting drugs," he said.

Ghamari-Langroudi and his lab plan to continue this research to obtain an even clearer map of the neural circuits described in this study. They also hope to eventually find additional potential targets within this circuitry to understand and treat disordered eating.

More information: Yu Yong et al, Endogenous cannabinoids are required for MC4R-mediated control of energy homeostasis, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2015990118

Provided by Vanderbilt University