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In mice, a high-fat, high-sugar diet remodels the microbiome and endocannabinoid system

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Weight gain and diet have long been known to shuffle the population of gut microbes. More recently, studies have also connected weight gain and diet to changes in the intestinal endocannabinoid system (eCB), a complex network of metabolites and receptors that help regulate appetite and metabolism, among other chores. A new study in *mSystems*, an open-access journal of the American Society for Microbiology, investigates the relationship between microbiota and the eCB system.

The two systems change in parallel in response to dietary changes, but their relationship to each other isn't well understood. "We have data that shows if we change the endocannabinoid system [as through genetic modification], we can modulate the microbiota," says scientist Alain Veilleux at Laval University in Quebec, Canada. "And if we modulate the gut microbiota, like by using probiotics, we see that the endocannabinoid system is also altered. They have a kind of bi-directional relationship." It's not clear if one changes first in response to a high-fat, high-sugar diet, he says.

This week in *mSystems*, Veilleux and his colleagues report on these findings and others from a new study designed to investigate the relationship between the microbiota and the eCB system in the small intestine and cecum. Using experiments conducted on mice that were fed a diet high in sugar and fat for two months, the researchers identified, for the first time, potential interactions between the specific bacterial genera and the eCB system.

Notably, several of those connected changes were observable in some parts of the small intestine almost immediately after beginning the experiment. "The gut microbiota and eCB system had similar profiles after three days that they had after 60 days," says Veilleux. As early as three days after feeding, the researchers found that decreased abundances of bacterial genera including Barnesiella, Defluviitalea, and Eubacterium, corresponded to simultaneous upticks in a few molecules that modulate eCB activity.

Scientists first began to probe the eCB system in the 1980s with investigations designed to look for the body's receptors for tetrahydrocannabinol, or THC, the primary psychoactive ingredient in cannabis. In the decades since then, subsequent studies have shown a significant role for endocannabinoids in a variety of bodily functions, including sleep, immunity, appetite, and mood.

At Laval, Veilleux's research focuses on the functions of the small intestine in metabolic diseases. For the new study, he collaborated with researcher Vincenzo Di Marzo, also at Laval, whose lab focuses on understanding the "Microbiome-Endocannabinoidome Axis," with the goal of finding new medical treatments for conditions related to metabolism.

Veilleux says the new findings, which reveal some connections between these two influential systems, can help them move toward that goal. "Our study helps us focus more on what happens when we change the diet," he says. Ultimately, "we want to make it possible to design better nutritional or pharmaceutical strategies to prevent or correct the alterations we see, and to help treat metabolic complications."

More information: Sébastien Lacroix et al, Rapid and Concomitant Gut Microbiota and Endocannabinoidome Response to Diet-Induced Obesity in Mice, *mSystems* (2019). DOI: 10.1128/mSystems.00407-19