Gamma oscillations coordinate food seeking

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Credit: Claudia Knorr, FMP.

Food seeking is a crucial survival instinct. However, until recently, little was known about how the brain regulates this behavior. Scientists at the Leibniz-Institut für Molekulare Pharmakologie (FMP) and NeuroCure Cluster of Excellence in Berlin discovered a neuronal circuit which regulates the hypothalamus and activates food seeking in mice. Surprisingly, this neural mechanism appeared to utilize gamma oscillations, and does not depend on hunger. Optogenetics techniques shed light on the behavioral function of this circuit. The findings allow for better understanding of the mechanisms of feeding behavior, and could lead to development of innovative therapies to treat eating disorders. These results have been published in the scientific journal *Nature*.

It is pretty normal that thoughts often revolve around food, even when you are not hungry. Food-seeking behavior, an instinct crucial for survival of our ancestors during hunting and gathering, leads us in the 21st century to a fridge or the supermarket. This behavior fascinates scientists as well, as impairments in this drive can be linked with eating disorders like anorexia nervosa. To understand how this behavior is organized, scientists study its neuronal mechanisms.

Gamma oscillations organize communication in hypothalamus

Gamma oscillations, occurring at a rate of 30 to 90 cycles per second, are waves of neural activity known to support major cognitive functions, including memory, attention and cognitive flexibility. Until recently, it was not known whether and how these processes regulate vital behaviours including food-seeking. A team of researchers led by Tatiana Korotkova and Alexey Ponomarenko at the FMP Institute/ NeuroCure Cluster of Excellence in Berlin found that the brain features a mechanism that directly informs the hypothalamus about cognitive processing using gamma oscillations as a common language.

"Together with scientists in the U.S. and the U.K., we characterized this pathway at multiple levels, from anatomical connections to excitability of individual cells," says Tatiana Korotkova, describing their study published in the scientific journal *Nature*.

Optogenetics helped to shed light on neuronal mechanisms

To study this neuronal circuit, researchers used optogenetics, a novel method that allows activation of specific connections in the brain using light. Researchers found gamma oscillations in the lateral hypothalamus and its major gateway, the lateral septum, and noted that this brain rhythm increases as a mouse seeks food. "It was impressive to see that gamma oscillations had such a pronounced effect in LH, which was previously thought to respond mainly to chemical/hormonal signaling," explains Ph.D. student Marta Carus. In the study, replay of these oscillations in the brain, using optogenetics, led to food seeking.

Food seeking independent of food consumption

Remarkably, during gamma synchronization of this brain circuit, animals checked the food location even if they were not hungry. However, they did not consume more food than usual. Activation of this pathway also assisted in cognitively demanding situations, when the mouse had to find food using previous experience. The prefrontal cortex, a brain region that coordinates goal-directed behavior, was important for this. "Finding suitable food in the wild is tricky and time-consuming," says Tatiana Korotkova. "It's probably too late to start searching for food when an animal is already hungry, if it has no idea about what nutritional resources are available where. This circuit possibly makes us pay specific attention to food sources, such as spotting restaurants when exploring a new town, or regularly checking the fridge contents in our own kitchen."

Researchers further managed to translate parts of the code used during gamma oscillations for communication in this neural pathway. Activity of many neurons in the lateral hypothalamus depends on presence of food: while some neurons are active close to food, others are preferentially active distantly from the food location. Researchers found that during gamma oscillations feeding-related cells are activated separately from feeding-unrelated cells with high temporal precision. "Preferential and selective control of feeding-related cells by rhythmic inputs to hypothalamus demonstrates a beautiful interaction of structure and function in the brain" says Alexey Ponomarenko. "Here we see how fast synchronization, combined with a precise information transfer between brain regions and cells types, drives behaviors crucial for survival."

A disconnect between food-seeking behavior and metabolic needs is a symptom of many eating disorders, ranging from anorexia to obesity. There is still a long way to go for the development of effective medications, however, understanding of neuronal mechanisms which regulate feeding may lead to development of innovative therapies.

More information: Marta Carus-Cadavieco et al. Gamma oscillations organize top-down signalling to hypothalamus and enable food seeking, *Nature* (2017). DOI: 10.1038/nature21066

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