Scientists pinpoint brain cells that delay first bite of food

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The parasubthalamic neurons sensitive to binge eating, shown in red, reduce the eagerness of mice to start eating. Credit: Scripps Research

Do you grab a fork and take a first bite of cake, or say no and walk away? Our motivation to eat is driven by a complex web of cells in the brain that use signals from within the body, as well as sensory information about the food in front of us, to determine our behaviors.
Now, Scripps Research scientists have identified a group of neurons in a small and understudied region of the brain—the parasubthalamic nucleus (PSTN)—that controls when an animal decides to take a first bite of food.

In the study, titled "The parasubthalamic nucleus refeeding ensemble delays feeding initiation and hastens water drinking" published in Molecular Psychiatry on July 4, 2024, the team set out to selectively manipulate a group of PSTN cells that dial up their activity during periods of binge-eating. Other scientists have observed that many PSTN cells become active following a large meal, but the team wondered how these cells might influence appetite.

"In our study, we used a technique that let us turn on cells in the mouse brain that were activated by a specific experience—in this case, binge-eating," says Jeff Dunning, Ph.D., a staff scientist at Scripps Research and first author of the new paper. "Once we have captured this ensemble of PSTN cells, we can turn them on like a light switch and watch what happens to the animals' eating and drinking."

The research team found that the ensemble of cells sensitive to binge-eating were capable of drastically changing the behavior of mice. Hungry mice normally start chowing down on food quickly once it becomes available to them. But when researchers turned on this ensemble of PSTN cells, mice were much slower to begin eating and, surprisingly, much faster to drink water.

"Our results tell us that this specific group of PSTN cells guide the early stages of hunger-driven decision making, before eating actually occurs," says Dunning. "The effect on water drinking is somewhat counterintuitive, but it might be related to prandial thirst—the phenomenon whereby thirst gets stimulated as soon as we start eating."
By manipulating even smaller sets of cells within the PSTN, the team pieced apart exactly which groups of cells were responsible for the delayed eating and accelerated drinking. They also discovered that yet another group of PSTN cells drives a different effect, urging the mice to eat more sweet foods.

"Altogether, these results reveal that PSTN neurons exert a complex combination of functions," says senior author Candice Contet, Ph.D., associate professor in the Department of Molecular Medicine at Scripps Research.

"Several studies had previously shown that PSTN activity can limit the amount of food eaten, but the fact that certain PSTN neurons control the onset of feeding or drinking, or even promote the consumption of food 'treats,' is entirely novel."

Contet, Dunning and colleagues think that their findings may have relevance for eating disorders where people have either too much or not enough control over the initiation of feeding—the decision to succumb to that first bite or wait longer.

Beyond food and water, similar mechanisms may be at play in the loss of control over the consumption of rewarding substances such as drugs of abuse, which the team is currently investigating.


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