Hunger and hormones determine food's appeal

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(Medical Xpress) -- It's been said that there are two kinds of eating: eating to survive, or satisfy hunger, and eating for pleasure. The pathways in the brain that control each urge have been studied independently. But now, research by Howard Hughes Medical Institute investigator Jeffrey M. Friedman of Rockefeller University provides evidence that the two pathways are closely intertwined.

By activating regions of the brain linked to food-related pleasure, Friedman and colleagues discovered how the brain mediates the link between food preferences and hunger. Their findings were published online November 13, 2011, in the journal Nature Neuroscience.

Appetite based on hunger, Friedman discovered in the 1990s, is mediated in part by a hormone called leptin. When a mouse loses weight or is food-deprived, leptin levels fall, leading to an increase of food intake. Likewise, leptin levels rise in an animal after weight gain with a corresponding reduction of food intake. The available evidence further indicates that leptin plays the same role in humans.

Other researchers have shown that when people are eating, the brain's so-called reward center is involved. Eating a food that tastes good—such as sugar— is known to activate that area's dopamine (DA) neurons, which are also turned on by other pleasurable stimuli such as sex and cocaine.

Friedman and his colleague Ana Domingos suspected that changes in leptin concentration might affect these pathways in the brain and thus

influence how much one likes food. The high reward value of sugar and other pleasurable foods presents an obvious challenge to dieters, and understanding leptin's effects on eating for pleasure might suggest opportunities to intervene with potential therapies that reduce food cravings and diminish the risk of diet relapse, Domingos says.

Friedman and Domingos wanted to investigate these questions in mice. To do so, they needed to find a way to ask a mouse how much it liked sugar.

"If I put a can of Coke, orange soda, or Diet Coke in front of you, you could taste them and tell me which you liked best," says Friedman. "You can't do that with an animal."

So Friedman and Domingos collaborated with HHMI early career scientist Karl Deisseroth at Stanford University, who has developed a way to use a laser beam to turn on subsets of neurons at any time in the brain of a living mouse brain. Friedman and Domingos engineered mice so that DA neurons were activated when the laser was switched on by consuming liquids at a sipper, which tracks the number of licks an animal takes. By allowing the mice to control the activation of the DA neurons by licking, the researchers could get the mouse to like the associated drink. Then, they could determine whether that artificial activation of the reward pathway overpowered the reward signals the animal received from eating certain nutrients at a different sipper. Friedman and Domingos call the choice between self-induced activation of dopamine neurons or a sweetener such as sucrose an assay for "liking."

With the system in place, the scientists exposed mice to different pairs of three different drinks: one with sucrose—natural table sugar; one with the artificial sweetener sucralose; and one with water. Normally, mice will prefer sucrose over sucralose and both sweeteners over water. But

when the mice drank the water, the laser was switched on, activating their DA neurons and sending a reward signal to the animal's brain. In the first choice between sucrose and laser, the mice still preferred sucrose to the water coupled to laser—suggesting that it naturally provides more reward than that conferred by direct activation of dopamine neurons. In contrast, the mice demonstrated no preference between water accompanied by the laser activation and sucralose.

When sucralose and sucrose are pitted against each other, mice choose the natural, calorie-containing sucrose the majority of the time. But when Friedman and his colleagues engineered the laser to turn on DA neurons when the mice drank sucralose, the mice began to prefer the artificial drink, sipping from the sucralose 84 percent of the time, indicating that the extra DA activation had shifted an animal's preference from sucrose to sucralose.

Domingos says the findings help explain why, according to the US Department of Agriculture, natural sweeteners have consistently outsold artificial sweeteners ever since artificial sweeteners were introduced in 1947. "This experiment shows that we prefer sugar to artificial sweeteners because of sugar's actions in the brain, not only in the tongue. When we artificially add those actions to sucralose, then animals will like the artificial sweetener more," she says. To test whether levels of leptin affect hedonic reactions to sugar, Friedman's team repeated the experiments in mice that had been deprived of food for 24 hours. The hungry mice no longer preferred the combination of sucralose and DA activation to sucrose. Instead, they drank sucrose 93 percent of the time.

To determine whether the increased liking of sugar was really due to low leptin levels, the scientists next injected leptin into food-deprived mice. The animals once again preferred the sucralose and DA activation, drinking the artificial sweetener 69 percent of the time.

The switch in preferences, says Friedman, suggests that leptin levels affect how strong a role the DA system has in mediating food preferences. When an animal is food-deprived, with lower levels of leptin, the reward value of food with calories—sucrose—is higher than that of sucralose accompanied by DA activation. Leptin reversed this effect: when the hormone was high, the animal liked sugar less, indicating its reward value had decreased. Friedman points out that further studies will be needed to determine how and where the nutrient value of sucrose is sensed.

“Some people eat because they’re hungry, and other people eat because they like eating,” says Friedman. “And what this says is that in a sense they’re part of the same integrated pathway. This provides experimental evidence that -- similar to what we all know from our experience -- when you’re hungry, you like food more.” Having an assay to show this in animals provides an opportunity to further delineate these pathways.

Next, Friedman and Domingos plan to try activating smaller subsets of DA neurons to test which neurons are associated with sucrose and sucralose specifically. The experimental setup of combining neuron activation with food preferences can also answer other questions.

“This is a new assay to measure how much an animal likes a particular nutrient,” says Friedman. “It can be applied to lots of other situations—we can now ask the same questions of fat or protein that we asked for sucrose and sucralose. Or test whether an animal has a liking for particular nutrients that it is deficient in.”

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