Brain region mediates pleasure of eating

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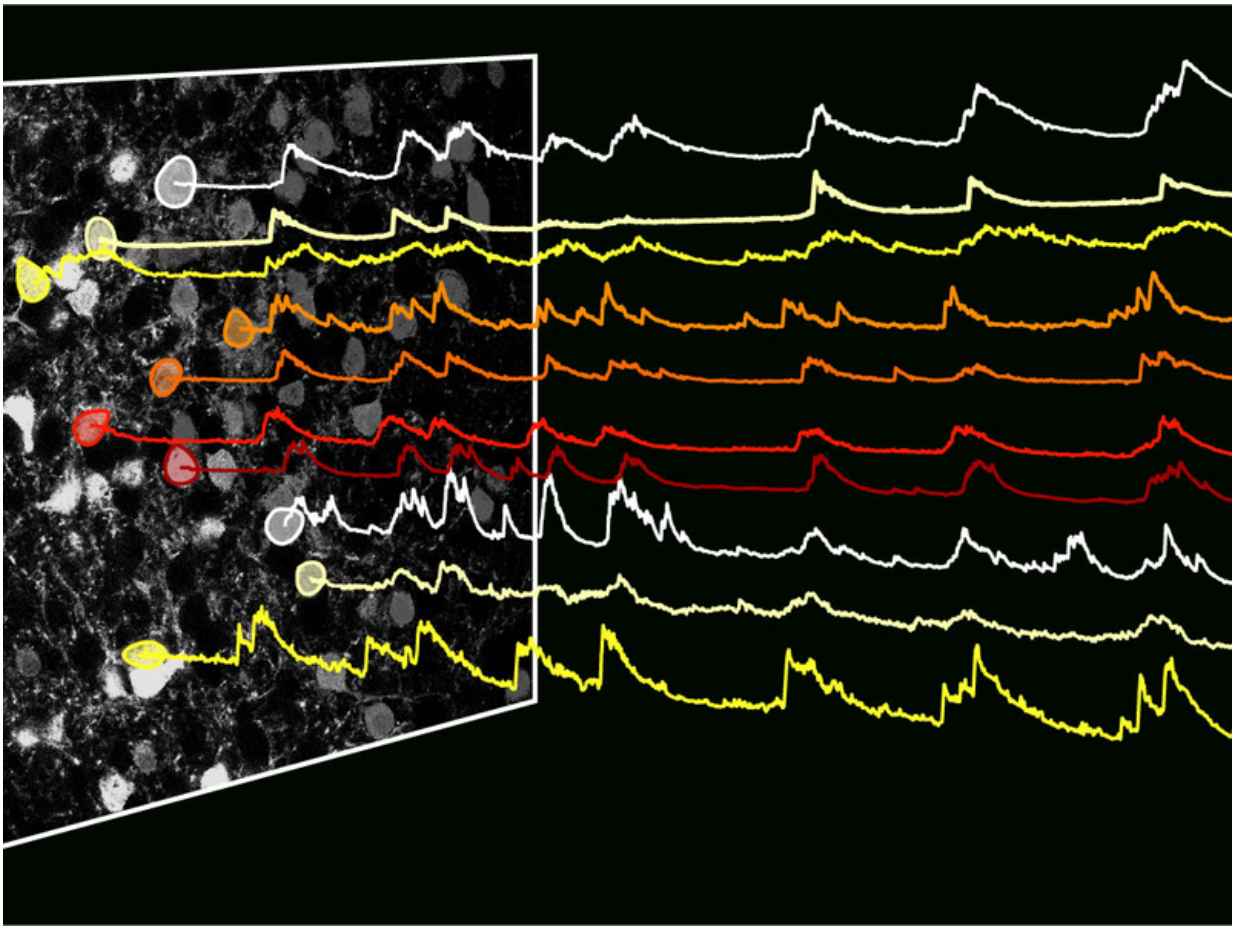

HTR2a-expressing neurons in the mouse amygdala are active during eating (peaks in the activity) to promote food consumption. (Activity patterns of individual cells are shown in different colours). Credit: MPI for Neurobiology/ Douglass & Kucukdereli

Providing the body with food is essential for survival. But even when full, we can still take pleasure in eating. Researchers at the Max Planck Institute of Neurobiology in Martinsried and the Friedrich Miescher Institute in Basel have characterized a type of neuron in the amygdala of the mouse brain that is involved in making eating rewarding. When given the choice, mice choose to activate these amygdala neurons. Artificially activating these neurons increases food intake even when the mice are not hungry. The neurobiologists have identified the neuronal circuitry underlying this behavior, raising the possibility that there could be cells with a similar function in the human brain.

The amygdala in the brain plays a key role in emotional responses, decision-making and association of events with emotions like fear or pleasure. In recent years, it has become apparent that this brain region also plays a role in eating behavior. Researchers at the California Institute of Technology have previously shown that activating a certain type of neurons in the amygdala (known as PKC-delta neurons) causes mice to stop eating. "If the mice eat something which has gone bad, for example, activity of these cells causes them to immediately stop eating," explains Rüdiger Klein, Director at the Max Planck Institute of Neurobiology. "I found this study on 'anorexia neurons' in the amygdala fascinating," says Klein, "so when three doctoral students with very different methodological backgrounds came to me, I proposed them to work on the amygdala project. Their task was to find out whether there are neurons that are involved in positively regulating food consumption." With this task in mind, the group focused on a different population of amygdala cells named HTR2a neurons."

Specializing in behavior, electrophysiology and anatomy, the three doctoral students were able to provide insight into HTR2a cell function from a range of angles. "It was a very collaborative project," recalls Amelia Douglass, one of the three lead authors of the study, which was published in *Nature Neuroscience*. "We frequently sat down together,

went through the results and then built on them, applying new cutting-edge methods in the process." Using this approach, the young researchers gradually discovered the role of the previously unstudied HTR2a amygdala cells and identified the neural circuitry involved. "Basically we showed that HTR2a cells have a positive effect on food consumption in mice, and that the mice like it when these cells are active," says Douglass.

Artificially activating HTR2a amygdala cells caused the mice to eat for longer. This effect was particularly pronounced when the mice were already full. In another experiment, the mice were able to activate HTR2a cells themselves with an optical fiber by pressing a switch with their snout. "It was clear that the mice liked having active HTR2a cells – they could not leave the switch alone," says second lead author Hakan Kucukdereli. "When we specifically ablated only the HTR2a cells, the mice continued to eat regularly and did not lose weight in the long term, and when we inactivated the cells the mice did not eat as much of appetizing food even if they were hungry".

Together with their colleagues from the Friedrich Miescher Institute in Basel, the team was able to show that HTR2a cell activity increases only once the mice start to eat, and not when the mice are presented with cues that food is about to be dispensed. The results suggest that HTR2a cells encourage ongoing food consumption by exerting a positive effect on factors such as taste and palatability. The importance of HTR2a cells in modulating food's rewarding properties is illustrated by a further experiment. Simply by activating the HTR2a cells, the researchers were able to condition mice to prefer a specific taste that was initially less preferred.

HTR2a cells thus appear to increase the 'value' of the food. When they analyzed the neuronal network, the researchers found that HTR2a amygdala cells had synaptic connections with the nearby PKC-delta cells

and that the two cell types were mutually inhibitory. The neurobiologists hypothesize that these two cell types are part of a regulatory mechanism. "Eating something bad activates PKC-delta cells, thus inhibiting the HTR2a cells, causing the animals to stop," notes Marion Ponserre, the third lead author. "By contrast, eating something delicious activates HTR2a cells, thus inhibiting PKC-delta cells, causing food consumption to be linked to reward." "Our results point to the existence of such associations, but there are still a lot of unanswered questions," notes Rüdiger Klein. "Certainly we have a good starting point for investigating the links between food consumption, emotional state and the reward system." The researchers also hypothesize that malfunctions in these amygdala circuits could result in extreme eating behaviors. "There are likely to be similar cells and circuits in the human brain, and this could also be an interesting area of research for helping people with eating disorders."

More information: Amelia M Douglass et al. Central amygdala circuits modulate food consumption through a positive-valence mechanism, *Nature Neuroscience* (2017). DOI: 10.1038/nn.4623

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