Using new technique, researchers make surprising discoveries about how flies' brains respond to tastes

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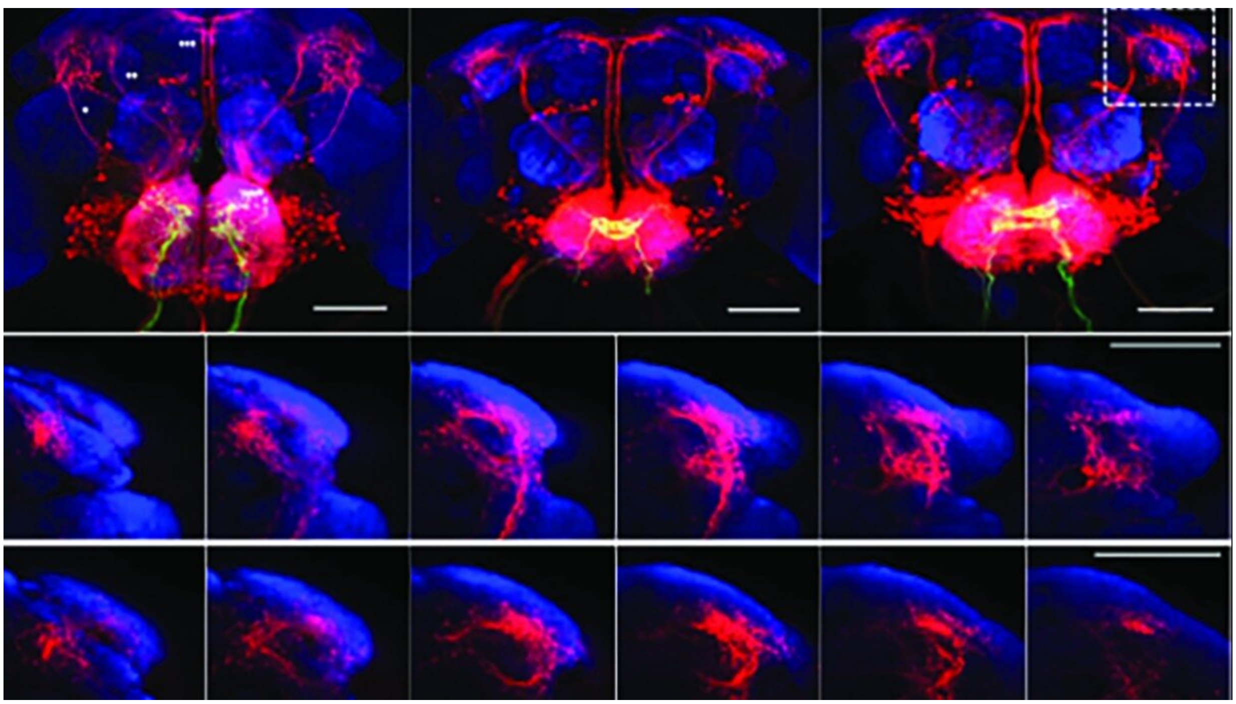

A new imaging technique called trans-Tango(activity), developed by researchers with the Brown's Carney Institute for Brain Science, reveals how specific neurons in brain circuits of fruit flies respond to stimuli such as sweet and bitter tastes. Credit: Gilad Barnea

Taste matters to fruit flies, just as it does to humans: like people, the flies tend to seek out and consume sweet-tasting foods and reject foods that taste bitter. However, little is known about how sweet and bitter tastes are represented by the brain circuits that link sensation to behavior.

In a new study published in *Current Biology*, researchers at Brown University described how they developed a new imaging technique and used it to map the neural activity of fruit flies in response to sweet and bitter tastes.

"These results show that the way fly brains encode the taste of food is more complex than we had anticipated," said study author Nathaniel Snell, who earned his Ph.D. in neuroscience from Brown in 2021 and conducted the research as part of his thesis.

Just as significant as the researchers' findings is the method they used, said Gilad Barnea, a professor of neuroscience at Brown's Warren Alpert Medical School and director of the Center for the Neurobiology of Cells and Circuits at the University's Carney Institute for Brain Science.

To learn more about the brain processes that govern the flies' reaction to taste sensations, Barnea, Snell and a group of graduate and undergraduate students in Barnea's lab developed a new imaging technique called "trans-Tango(activity)." This is an adaptation of trans-Tango, a versatile technology invented by the Barnea lab that is used to trace neural circuits in the brain. Barnea said trans-Tango(activity) takes the understanding to a new level by revealing how specific neurons in the circuits respond to stimuli.

The brain response to stimuli is like a relay, Barnea explained: The "stick" passes from one neuron to the next, and then to the next, and so on. Previous techniques could identify a neuron with the stick, but not who gave the stick to that neuron.

"Trans-Tango(activity) allowed us to selectively look at the second-order neurons in the circuit, so we could focus on how they responded to sweet and bitter tastes," Barnea said.

Because the reaction to sweet and bitter tastes is so different, the researchers' expectation was that the neural activity along the circuits mediating those reactions would be entirely disparate as well, he said. But trans-Tango(activity) revealed some overlap of neural activity already in second-order neurons in these circuits in response to the two tastes.

Barnea said that some of the results may show how flies know to avoid a particular rotten, poisonous or otherwise bad section of a food, for example. Overall, he said that the study findings underscore the importance of the sophisticated and refined processes of taste.

"You have to remember that eating, or feeding, is an activity where you—whether you are a fly or a human—cannot make mistakes," he said. "If you consume something bad for you, it can be detrimental. Anyone who has ever paid dearly after eating a bad mussel can confirm this. So the ability to know to avoid certain foods, or even certain areas or parts of food, is important for the survival of the species."

One finding was especially intriguing to Barnea not because of what it said about survival, but what it potentially revealed about pleasure. The second-order neurons responded to bitter tastes not just when the tastes were presented, but also when they were removed. Surprisingly, Barnea and his colleagues found some overlap in activity when the bitter was removed and the sweet was presented.

Barnea said this reminded him of the concept of "aponia," which in ancient Greek means "the absence of pain," and was regarded by the Epicurean philosophers to be the height of pleasure.

"The fact that we see a neuron that responds both to the removal of the 'bad' stimulus—bitter taste—and to the presentation of the 'good' stimulus—sweet taste—is biologically reminiscent of this philosophical concept," said Barnea, who added that future research will further explore this response.

As to why insects' sense of taste matters to humans, who may experience taste differently, Barnea referred to the insects who find humans to be particularly attractive: "Understanding what drives gustatory and olfactory behaviors in mosquitoes, for example, is very important in learning how to decrease their effect on humans," he said. "Our study may add one small piece to that large puzzle."

The study shows how a research question can provide impetus to develop a new scientific technique that can then be used to answer new research questions—and vice versa.

"We believe that trans-Tango(activity) can be a useful tool not only for studying how the sense of taste works, but for understanding neural circuits in general," Snell said. "Sensory neurons encode many different kinds of information about the world, and figuring out how this information is relayed, transformed or integrated as it travels from peripheral to deeper layers of a neural circuit is a central question in neuroscience. Trans-Tango(activity) is perfectly poised to be able to answer such questions."

It took Barnea more than 20 years to develop trans-Tango to the point where it could be used successfully in fruit flies, he said, yet only five years for the team to develop and publish trans-Tango(activity)—and additional adaptations are currently in the works.

"The more we use the technology, the better it gets, and the more we can learn from it, and the more questions we can apply it to," Barnea said.

More information: Nathaniel J. Snell et al, Complex representation of taste quality by second-order gustatory neurons in Drosophila, *Current Biology* (2022). DOI: 10.1016/j.cub.2022.07.048

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