For Fruit Flies, Food Experience Can Alter Taste Preferences

If you've ever wondered how you learn to like a food you dislike, a new study conducted by UC Santa Barbara's Craig Montell, Duggan Professor of Neuroscience in the Department of Molecular, Cellular, and Developmental Biology, may offer an answer. The work addresses a central question in neurobiology — how experience can alter animal behavior. The research, published in *Nature Neuroscience*, was conducted by Montell's team, which includes lead author Yali Zhang, Rakesh Raghuwanshi and Wei Shen.

Among the most widely observed, but poorly understood modifiable behavioral phenomena is that dietary experience can alter taste preferences. This is essential for survival, since animals from insects to humans have to respond to a changing food environment. Alterations in taste are well known in humans, as people from the Far East have different taste preferences than people from the West. Individuals who move from one culture to another typically learn to accept the local foods, some of which were originally aversive.

Using the fruit fly, Drosophila melanogaster, as an animal model, the researchers unraveled a mechanism to explain how animals modify their taste preferences. "This study was inspired by trying to understand how it is an animal learns to like foods they didn't like before," said Montell. "We want to understand taste proclivity because it is a universal behavior in all animals."
The researchers focused on camphor, an aversive but safe food additive. Historically, camphor has been used as a main flavoring ingredient for many desserts, including ice cream. They found that fruit flies learn to consume camphor-containing foods if they are fed long-term on a camphor diet. The same was not true of aversive, toxic tastants such as quinine or strychnine.

The alterations occurred through a mechanism involving changes in the animal's peripheral gustatory receptor neurons (GRNs), which occur within hairlike structures called sensilla. Of particular importance, Montell's team defined the cellular and molecular basis for the taste plasticity.

Long-term camphor exposure — for a fruit fly that lives only about two months this is only a few days — caused a reduction in the response by the Transient Receptor Potential-Like (TRPL) channel, a directly camphor-activated channel that brings ions such as calcium into the cell. For humans this might translate to mean that repeated exposure to disliked food over a period of weeks or months may result in the eventual acceptance of that food.

The fruit flies' reduced distaste for camphor occurred through a mechanism that involves the degradation of the TRPL protein by an enzyme called E3 ubiquitin ligase, or Ube3a, which targets specific protein substrates for degradation. Following the decline in TRPL, there was also a decrease in synaptic connections, but that was not sufficient to cause the taste adaptation. "We don't know what's activating the Ube3a, but it's tantalizing to speculate that it is calcium regulated," said Montell. "We think it's a combination of the decline in TRPL levels and the decrease in synaptic connections that together cause the change in behavior.

"We not only found that ubiquination is important and leads to degradation, but we also discovered that mutations in Ube3a prevent this taste plasticity," he continued. "This is because in the absence of Ube3a, TRPL is not ubiquinated so it is not degraded. This underscores that it's the decline in the TRPL levels that underlie this mechanism."

An interesting phenomenon was the reversibility of the process of accepting camphor as a food additive. The decline in TRPL levels and synaptic connections that accompany the flies' increased acceptance of camphor reverse after returning the flies long-term to a camphor-free diet.
Montell and his team surmise that the calcium influx resulting from increased activity of TRPL in the presence of camphor leads to increased internalization of the channel. "Then the ubiquin ligase itself might somehow get activated," he said. "Understanding that mechanism is one question for the future."

These findings not only show the molecular and cellular pathway that controls how diet changes taste proclivity in an animal, but also suggest a general neural mechanism underlying food experience-induced changes in taste preferences in other animals, including mammals. "Our work raises the possibility that reversible changes in taste receptor cells, as a result of long-term exposure to a specific diet, could contribute to a similar type of phenomenon in humans," concluded Montell. "If we come to understand this really well, someday it could be harnessed by the food industry."

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