How does the brain know what the tongue knows?

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Each taste, from sweet to salty, is sensed by a unique set of neurons in the brains of mice, new research reveals. The findings demonstrate that neurons that respond to specific tastes are arranged discretely in what the scientists call a "gustotopic map." This is the first map that shows how taste is represented in the mammalian brain.

There's no mistaking the sweetness of a ripe peach for the saltiness of a potato chip – in part due to highly specialized, selectively-tuned cells in the tongue that detect each unique taste. Now, Howard Hughes Medical Institute and NIH scientists have added to our understanding of how we perceive taste, showing that four of our basic tastes—sweet, bitter, salty, and "umami," or savory—are also processed by distinct areas of the brain. The researchers published their work in the September 2, 2011, issue of the journal *Science*.

"This work further reveals coding in the taste system via labeled lines, and it exposes the basic logic for the brain representation of the last of the classical five senses," said Howard Hughes Medical Institute investigator Charles S. Zuker, who is at Columbia University College of Physicians and Surgeons.

"The way that we perceive the sensory world has been something that's fascinated humanity throughout our whole existence," says Nicholas J. P. Ryba of the National Institute of Dental and Craniofacial Research, who collaborated with Zuker on the new study. "What is a taste, really? It's the firing of a set of neurons in the brain, and that's what we want to understand."

In the past, researchers had measured the electrical activity of small clusters of neurons to see which areas of a mouse's brain were activated by different tastes. In those experiments, the areas responding to different tastes seemed to blend together, and scientists therefore concluded that neurons appeared to process all tastes broadly.

Zuker, Ryba, and other collaborators had previously identified unique taste receptors and taste receptor cells for each taste – uncovering a "one taste, one cell class" coding scheme. Activating these receptor cells triggered innate behaviors in mice: attraction to sweet, umami, and low salt and aversion to bitter, sour, and high salt. With this clear link between taste and "hardwired" behaviors, the researchers wondered why different tastes would be processed by the same neurons in the brain. They suspected that the previous experiments had missed something. So Xiaoke Chen, a postdoctoral associate in Zuker's lab tried a powerful new technique, called two-photon calcium imaging, to determine which neurons responded when an animal is exposed to different taste qualities.

When a neuron is activated, it releases a wave of calcium throughout the cell. So the level of calcium can serve as a proxy for measuring activation of neurons. The researchers injected dye into the neurons of mice that made those cells light up with fluorescence every time calcium was released. Then, they looked at the brains of the mice under high-powered microscopes that allowed them to watch hundreds of nerve cells at a time deep within the brain of mice. When a cell was activated, the researchers saw it fluoresce. This allowed them to monitor the activity of large ensembles of cells, as opposed to previous methods, which tracked only a few cells at a time. They observed that when a mouse is given something bitter to taste, or the receptors on its tongue that sense bitter are stimulated, many neurons in one small, specific area of the brain light up. When the mouse is given something salty, an area a few millimeters away is activated. Each taste corresponded to a different hotspot in the brain. None of the areas overlapped—in fact, there was space between all of them.

"The idea of maps in the brain is one that has been found in other senses," says Ryba. "But in those cases the brain maps correspond to external maps." Different frequencies of sound activate different sets of neurons, for example. In the case of these auditory neurons, the map is arranged in order of frequency, from the lowest to the highest. Visual neurons are found in an arrangement that mimics the field of vision sensed by the eyes. However, taste offers no preexisting arrangement before reaching the brain; furthermore, the receptors for all tastes are found randomly throughout the tongue—thus the spatial organization of taste neurons into a topographic brain map is all the more surprising.

Zuker says that now the team has discovered a brain map for taste qualities, they next want to uncover "how taste combines with other sensory inputs like olfaction and texture, and the internal state—hunger and expectation, for example—to choreograph flavor, taste memories, and taste behaviors."

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