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## Research Reveals How the Tongue Tastes Carbonation



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Sip a bottle of sparkling water, and your enjoyment comes not just from the bubbly fizz, but also from the slightly sour taste of carbonation. Now, a research team led by Howard Hughes Medical Institute investigator Charles S. Zuker and Nicholas J. P. Ryba at the National Institute of Dental and Craniofacial Research has learned just how the taste of carbonation is perceived.

The research also explains how certain medications taken to prevent altitude sickness can interfere with one's ability to taste carbonation – the so-called “champagne blues” described by many mountain climbers.

The findings are reported in the October 16, 2009, issue of the journal *Science*.

Though it has been known that mammals have several systems for detecting and responding to carbon dioxide -- including those involved in smell and pain perception, as well as taste -- the molecular mechanisms underlying those abilities were poorly understood. Zuker and Ryba were particularly interested in the role that taste plays in the perception of carbonation because they had previously identified receptors for four of the five tastes: sweet, sour, bitter, and umami (savory taste). Their earlier research had also shown that each of the five basic tastes in the tongue is mediated by dedicated taste receptor cells.

In the experiments reported in *Science*, lead author Jayaram Chandrashekar at the University of California, San Diego and coworkers first confirmed that the mammalian taste system could respond to stimulation with carbon dioxide. They did this by recording activity from one of the major nerves that innervate taste receptor cells in the tongue, while stimulating the tongue with club soda, gaseous carbon dioxide, and carbon dioxide dissolved in a neutral buffer solution.

Then, to home in on the particular taste cells involved in sensing carbon dioxide, the researchers turned to mice that had been genetically engineered to lack receptor cells for specific tastes. Mice that lacked sour-sensing cells showed no response to carbon dioxide; those that lacked sweet-sensing or umami-sensing cells, but had functional sour-sensing cells, did respond. The results of these experiments suggested that sour-sensing cells are necessary for carbon dioxide detection. Going a step further, the team identified the main carbon dioxide sensor in the taste system: a membrane tethered carbonic anhydrase enzyme (called Car4) that is expressed on the surface of sour-sensing cells. Mutant mice that lack Car4 are barely able to detect and respond to carbon dioxide.

The discovery that carbonic anhydrases are the substrate for tasting carbonation explains the phenomenon of “champagne blues,” the disappointment experienced by some mountain climbers who crack open the bubbly to celebrate reaching a summit only to find that it tastes like dishwater.

“It turns out that high-altitude mountaineers often take carbonic anhydrase inhibitors to combat acute mountain sickness,” Zuker said, who recently moved to Columbia University from UCSD. “When they do that, they block carbonic anhydrase in the tongue, so they're no longer able to taste the carbonation in champagne.”

The researchers' final step was to dissect the process even more finely, pinpointing the neural signal that screams “carbonation” to the taste system. By manipulating synaptic activity from sour-sensing cells, Chandrashekar showed that when he specifically blocked activity from sour cells, all taste responses to carbonation were abolished.

With the question of how we taste carbon dioxide answered, another question still remains: Why do we need the ability to taste carbonation? Surely evolution didn't anticipate the invention of soft drinks. One notion is that the capacity evolved as a way of recognizing and avoiding fermenting foods, but Zuker favors another explanation.

“It's most likely that the principal function of the enzyme Car4 is something very different, such as maintaining the pH balance, and health, of our taste buds,” Zuker said.

Zuker notes that the main goal of his group's taste research is to understand how the brain encodes and decodes sensory stimuli – how the world is represented in the brain.

“We’re using the taste system as a platform to answer this difficult question,” Zuker said. “At the input end, we need to figure out how the tongue knows what it’s tasting – what are the basic tastes, how are the cells organized, and what are the encoding properties for taste and flavor. At the other end, we need to understand how the cortex takes information from our peripheral senses and transforms it into a percept, an internal representation of the outside world.”

In addition to Zuker, Ryba and Chandrashekar, the team included David Yarmolinsky and Yuki Oka of UCSD; Lars von Buchholtz of the National Institute of Dental and Craniofacial Research; and William Sly of St. Louis University School of Medicine.