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It's All a Matter of Taste: Gustatory Processing and Ingestive Decisions

by Christian H. Lemon, PhD

A strong taste preference for caloric sweets can guide dietary choices associated with the occurrence of many health problems including diabetes and obesity.

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Abstract

This paper reviews the physiology of taste processing and ingestive decisions.

Introduction

The appetitive taste sensation of "sweet" is pleasant, rewarding and serves a primary function of signaling the availability of calories in food. Neural circuits for sweet taste likely evolved to allow organisms to detect calories in the environment and balance their caloric intake against energy needs. Here we will discuss some principles of taste system organization and how neural circuitry for appetitive tastes is positioned to guide food preferences and intake behaviors.

General Organization of the Taste System

Taste is one of the chemical senses, which include smell (olfaction) and the chemically sensitive neural pathways of the somatosensory (trigeminal) system. These senses evolved to allow organisms to react appropriately to environmental chemicals involved with, for example, communication and reproduction, and also for the detection of nutrients and toxins in potential food sources. This later function is largely handled by your sense of taste (also known as gustation), which assumes the critical role of a guardian to the internal milieu. How a substance tastes to you plays a large role in determining whether or not you'll ingest that substance and subsequently incorporate it into your body. Toxins taste "bitter" to humans and are avoided whereas "sweetness" is pleasurable and is associated with the presence of calories in the stimulus source (of course, artificial sweeteners are designed to taste sweet without calories). Lower animals, such as rodents, also show avoidance of bitter tastes and acceptance and preference for sweet-tasting stimuli. Sweet taste likely evolved as pleasurable to entice organisms to consume foods containing calories, which are necessary for survival.

Other taste percepts include the traditional "salty" and "sour" and a more recently described sensation know as "umami". Umami is a Japanese word referring to the "savory" or "meaty" taste of certain amino acid stimuli, such as monosodium glutamate (MSG). The concept of only four or five

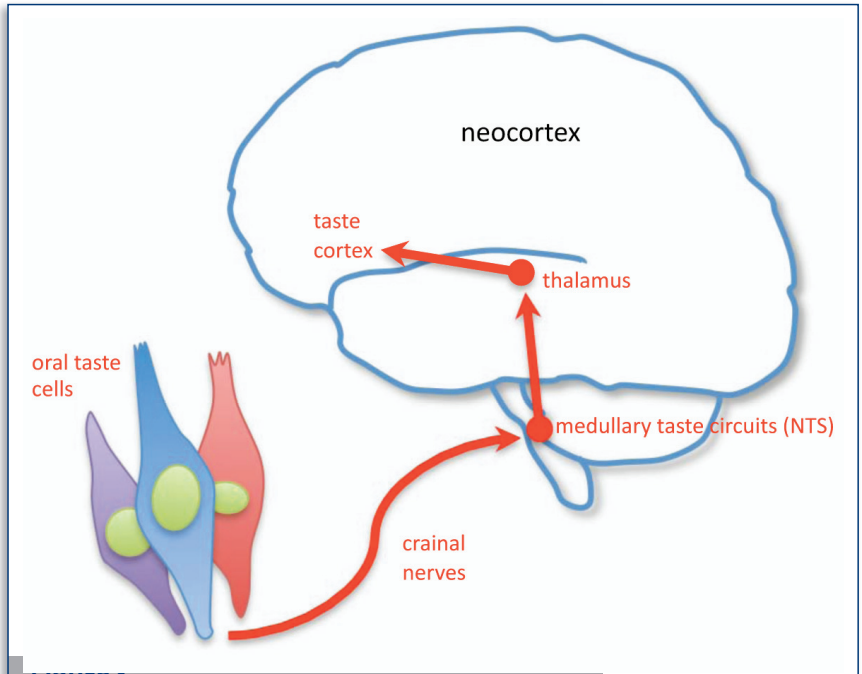

Figure 1
A portion of the gustatory pathway in the human brain. Information from taste receptor cells in the mouth is relayed to the nucleus of the solitary tract (NTS) in the medulla. Taste neurons in the NTS send projections to the thalamus, which in turn routes gustatory information to taste cortex.

basic taste categories has, at times, been a subject of some debate in the field of gustation. Some taste researchers have argued that there may be subtleties and variations in perceptual quality within a taste category, rendering not five possible taste sensations but a continuum of different taste possibilities.[1] Along this line, rodents, heavily used in taste research, trained to perform in a taste discrimination task can perceive differences between the oral sensations of the sugars sucrose and maltose[2], which would be classified as only sweet under the strict "five-taste" model. Nonetheless, it is reasonable to use the concept of basic taste qualities to assign general meaning to and categorize the overall percepts evoked by taste stimuli.

It is noteworthy that when humans talk about how food tastes we are usually referring to a food's flavor. Even though we may ascribe a particular taste to a food, flavor technically involves the perception that is due to an interaction between the smell, tactile (touch, texture), temperature and taste properties of that food when it is in the mouth. In precise terms, taste originates from the interaction of chemicals dissolved in saliva with oral taste receptor cells, which in turn engage neural pathways mediating taste sensation (See Figure 1).

Taste receptor cells have an apical, stimulus-sensing end facing the inside of the mouth and a basal end embedded in the oral epithelium that houses machinery allowing them to communicate with other taste cells or nerve terminals. Taste receptor cells can change the electrical potential of their membrane in response to taste stimulation but are usually not classified as neurons, as taste cells do not possess axons. Taste receptor cells rely on synaptic connections with the fibers of cranial nerves to carry their messages to the brain. This arrangement is advantageous considering that throughout life there is continual turnover and replacement of oral taste cells, which generally have a lifespan of 9 to 10 days on average. Thus, one could intuit that if a taste cell synaptically coupled to an afferent nerve dies off a new one can take its place at this synapse and quickly reestablish communication with the brain, without having to rewire an axon from the periphery to the appropriate brain location.

In humans and other mammals, taste cells are clumped together into onion-shaped structures called taste buds. Each bud houses 50 to 100 or so cells, including taste cells and possible supporting cells. Taste buds are found in various regions of the oral cavity, including on the tongue and the soft palate on the roof of the mouth. The cellular membrane of the apical, stimulus-sensing portion of a taste receptor cell expresses proteins that are capable of interacting with taste chemicals - these membrane proteins are the actual taste receptor molecules. Through this stimulus-receptor interaction taste cells covert the chemical energy of a sapid substance into an electro-chemical neural message that is readable by the nervous system – a process known as gustatory transduction.

From what we currently know there are two basic types of taste receptors: ion channels and seven-transmembrane spanning G-protein-coupled receptors (GPCRs). Cations in sodium salts (Na^+) and protons (H^+) in acidic (sour) stimuli are

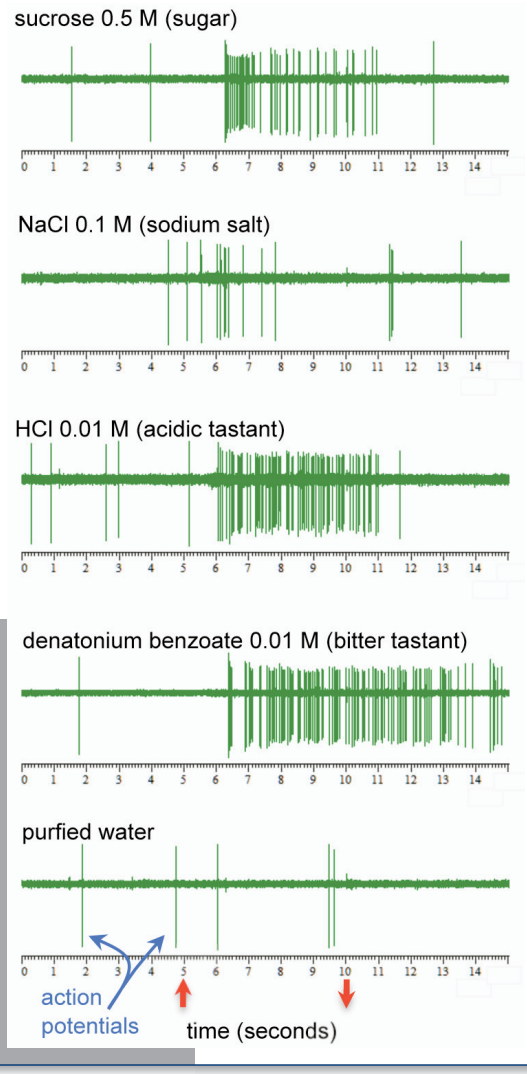

Figure 2
Electrophysiological responses to different types of taste stimuli measured from one taste neuron in the nucleus of the solitary tract (NTS) of an anesthetized mouse. Each trace was taken from a digital oscilloscope, which measures voltage (y-axis) against time (x-axis). The large vertical deflections along each trace are single action potentials generated by the neuron. Stimuli were flowed into the mouth and over the tongue, and each stimulus presentation trial was 15 seconds long. A trial began by flowing purified water into the oral cavity. At 5 seconds into each trial, the flow was switched from purified water to a stimulus dissolved in purified water. The upward arrow below the x-axis for the bottom trace denotes the stimulus onset at 5 seconds; the stimulus that evoked each response is indicated above each trace. The downward arrow indicates when the stimulus was rinsed from the mouth using water, which occurred at 10 seconds. Note that the response to the bitter tastant lingers after the stimulus flow stops. Also observe that these traces were all measured from the same neuron. As shown in this figure, some taste neurons in the brain can respond to stimuli that have very different tastes. Other cells (not shown) can show more selectivity to stimuli of a single taste quality class.

sensed by passage of these elements through ion channels on taste receptor cells.[3,4] On the other hand, appetitive sweet and umami and aversive bitter tastants are transduced by GPCRs. The binding of an appetitive or aversive tastant to a GPCR triggers the activation of a second messenger chemical cascade inside taste cells that can culminate in the release of neurotransmitter.

The GPCRs underlying sweet and umami taste are composed of proteins from a recently discovered class of taste receptors known as T1r. There are three known members of this receptor protein family: T1r1 (short for "taste receptor type 1, member 1"), T1r2 and T1r3. The latter protein, T1r3, is critical for both sweet and umami taste.[5,6] The T1r3 protein forms a receptor complex with its counterpart protein T1r2 to act as a functional taste receptor sensitive to a broad range of sweet stimuli, including sugars and artificial sweeteners. On the other hand, T1r3 combines with T1r1 to operate as an umami taste receptor. T1r receptors sense only appetitive taste stimuli. Bitter stimuli are transduced by a different class of receptors known as T2r, of which there are about 30 or so known members.[7]

Molecular data indicate that the receptors for sweet, umami and bitter stimuli are found in non-overlapping populations of taste cells in the mouth.[6,8] This has lead to some speculation that taste receptor cells are sensitive to only single types of taste stimuli (e.g., there are "sweet cells", "bitter cells", etc.). However, not all of the functional data on taste receptor cells support this conclusion and this issue is controversial.[9,10]

Most people are familiar with the classic "taste map" of the tongue, showing segregation of receptors for different taste qualities to different tongue regions. Some versions of this mapping posit that the sweet sensitive region of the tongue is on the anterior tip, salty is sensed on the front sides, sour is sensed on the backsides of the tongue and bitter is detected exclusively on the posterior tongue. Although sometimes still finding its way into modern textbook chapters on taste, the tongue map, which is based on old data, is incorrect: taste receptors mediating different taste qualities can be found on multiple regions of the tongue. For example, the T1r3 taste receptor involved with sweet and umami taste is found on the anterior and posterior tongue.[11] The posterior tongue is usually reserved exclusively for bitter stimuli on the

classic tongue map. What is more, application of bitter stimuli to the anterior tongue produces strong activation of taste circuitry in the brain[12] – this would arise only if there were bitter taste receptors at the front of the tongue. Behavioral studies in rodents show that disrupting the nerve innervating taste receptors on the anterior tongue disrupts the ability of rats to detect bitter stimuli, suggesting that the anterior tongue is critically involved in bitter taste perception.[13]

Information from oral taste cells is relayed by fibers of the facial (cranial nerve VII), glossopharyngeal (IX) and vagus (X) nerves to a vast network of neurons and nuclei in the brain. It is in the brain that messages from taste receptors are read out and converted to perceptual and behavioral responses. Taste information arrives in the central nervous system (CNS) at the level of the medulla, in the nucleus of the solitary tract (usually abbreviated as NTS for its Latin name, nucleus tractus solitarius). Nerve fibers innervating different regions of the mouth are mapped to the NTS in an orderly fashion, with fibers supplying sensation to the anterior tongue terminating in more forward regions of gustatory NTS and fibers from the rear of the tongue terminating in posterior regions of the nucleus. This "topography" appears to be a common organizing principle in sensory systems. Orderly mappings of body to brain are also seen in, for example, the somatosensory system, where neighboring regions of the body are systematically represented along neighboring regions of somatosensory cortex.

Taste circuitry in NTS plays a pivotal role in gustatory processing. It is in the NTS that information from oral taste receptors is formatted and encoded for transmission to higher CNS nuclei involved in flavor perceptions, affective (hedonic) responding, and the control of hunger. The NTS also maintains connections with local brain stem circuitry mediating oral motor responses to taste stimuli and, thus, likely plays a role in guiding appetitive intake and aversive rejection oral responses to tastants.

The Neural Processing of Appetitive Tastes

During tasting, gustatory-sensitive neurons in the NTS sound off with a series of electrical pulses (action potentials) to identify and represent the kind of taste stimulus in the mouth (See Figure 2). These electrical pulses are the basis of the language of the nervous system and different taste stimuli will evoke different trains of pulses across NTS taste cells. The patterns of pulses evoked by appetitive sweet stimuli are unique to sweets, allowing the brain to recognize the presence of sweet stimuli and compute the appropriate reaction to these substances.

If a substance tastes sweet, it is safe to eat and likely contains calories. Thus, sweet taste circuitry is positioned to play an influential role on the decision process to ingest calories. It follows then that the intensity of sweet taste responses in NTS neurons is sensitive to the satiety state of an organism – the frequency of the neural pulses to sweets can be adjusted by the brain depending on the animals need for the nutritional content of the stimulus. Hyperglycemia following intravenous infusion of the caloric monosaccharide glucose reduces taste responses to glucose (which tastes sweet) in rodent NTS neurons by an average of 43%.[14] This hyperglycemia-induced reduction in neural taste sensitivity is somewhat selective for sweet stimuli, with responses to salty, acidic and bitter stimuli much less or not at all affected by this manipulation. The observed decrement in neural sensitivity is accompanied by a selective reduction in the perceived intensity of glucose in rats receiving an intravenous glucose load.[15] Therefore, neural taste responses to sugars are decreased when blood sugar levels are elevated, accompanied by a reduction in the intensity perception of glucose. Intravenous infusion of other satiety factors, including insulin and pancreatic glucagon, can also decrease taste responses in the NTS glucose.[16] What is more, gastric loading (i.e., being full) can also down-regulate the responsiveness of NTS neurons to taste stimulation.[17] All of these factors contributing to satiety decrease neural sensitivity to the appetitive taste properties of nutritive stimuli at a time when the animal does not immediately require calories. The modulation of sweet taste circuitry by satiety signals reflects the operation of a system playing a critical role in the decision process to ingest caloric stimuli.

Further links between taste processing and the control of caloric intake have arisen from molecular biological studies of taste receptors in mice. Because their genome is well understood, mice are a powerful tool for genetic research and it is now possible to engineer mice with selective deficiencies of genes for taste receptors. This is

accomplished by deleting the gene for that receptor from the mouse's genome and replacing it with a non-functional gene. Mice generated in this manner are commonly known as receptor "knockout" mice and they can be made to differ from their control mice only at a single gene of interest. Two groups of researchers have generated T1r3 taste receptor knockout mice.[5,6]

Remember, T1r3 is a critical subunit of the T1r taste receptors for appetitive sweet stimuli. The background (control) strain of mouse from which the T1r3 knockouts were derived, commonly known as "black-six" mice, show an avid preference for water sweetened with sucrose; they'll typically drink large quantities of sugar water on a daily basis if given the opportunity to do so. However, black-six mice engineered to carry a non-functional T1r3 allele (T1r3 knockout mice) show no preference for moderate concentrations of sucrose solutions in a two bottle choice test against water.[5] This loss of sweet preference in T1r3 knockout mice persists using experimental paradigms that attempt to mitigate post-absorptive effects and target how oral sensory processes, like taste, are guiding intake behavior towards sucrose.[6] What is more, neurophysiological investigations in T1r3 knockout mice show that the absence of this receptor causes a reorganization of neural networks that process sweet taste. Although abundant in control black-six mice, NTS taste neurons responding preferentially to sweet stimuli do not develop in T1r3 knockout mice[18] coinciding with the loss of sweet preference in these animals. These data could indicate that in mice ingestive decisions about caloric stimuli are heavily contributed by taste.

Given these associations between taste processing, satiety factors and intake behavior, it is possible that variation in the neural substrates for taste may contribute to variable patterns of food intake. Thus, a preference such as a "sweet tooth" could be contributed in part by one's sensitivity to sweet taste and the reinforcement derived from this perception. A strong preference for caloric sweets can guide dietary choices associated with the occurrence of many health problems in humans, including diabetes and obesity. Whether or not obese humans are more sensitive to the tastes of caloric stimuli than lean individuals is not clear, as data on this topic are contradictory.[19] However, recent work in rodents relating obesity to the neural processing of sweet taste shows some differences between obese and lean control rats in the ways that central taste neurons respond to sweets.[20] Further delineating relationships between the neural processing of sweet taste, body mass and intake behaviors will be critical for understanding how our sense of taste impacts and shapes our health and well being.

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Disclosure

None reported.