Taste and Smell

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Taste and Smell

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chemosensory systems Biological systems that detect soluble and volatile chemicals.
gustatory Related to taste.
olfactory Related to smell.
pheromone Chemical that, when emitted by members of a species, will affect the behavior or physiology of other members of that species.
taste bud Cluster of 80–150 specialized epithelial cells; responsible for the initial events of taste reception.
umami Savory taste; basic taste quality elicited by monosodium glutamate.
vomeronasal organ Sensory organ specialized to detect pheromones in certain animals.

Chemosensory systems, of which taste and smell are specialized forms, detect both soluble and volatile chemicals. The senses of taste and olfaction can affect social behaviors, including feeding, territoriality, and mating. Taste and smell are also used in selection and evaluation of flavor and in avoidance of potentially harmful compounds. Through the cephalic phase of digestion, taste also affects certain exocrine and endocrine secretions, thus affecting nutrition and metabolism and the overall quality of life.

OVERVIEW OF TASTE AND SMELL

All animals respond to various chemicals in nature; not all chemicals, however, are detected exclusively by chemosensory taste and smell systems. Painful, irritating, and pungent chemicals, for example, are also detected by the trigeminal system, and chemicals associated with sexual and social signals (pheromones) are detected by the vomeronasal organ in certain animals. Although the vomeronasal organ is physically present in humans, its functionality is controversial (see further).

Receptors for taste and olfaction are located at the entry port of each governing system, i.e., the gastrointestinal tract for taste and the respiratory tract for olfaction. Unlike other sensory systems, the taste and olfaction sensory systems have specialized peripheral chemosensory receptors that interact with the soluble and volatile chemicals that are subsequently rejected, ingested, or inhaled. Intake of chemicals can be either beneficial or harmful, and taste and smell are important discriminatory screening mechanisms for avoiding potentially harmful chemicals.

PERIPHERAL ORGANIZATION OF THE TASTE SYSTEM

The peripheral gustatory system is exposed to a variety of physical, chemical, and biological insults. Extremely hot, cold, irritating, acidic, and nonsterile stimuli may have damaging effects on the peripheral taste receptor system. Therefore, the gustatory system evolved as a rapidly renewing specialized epithelial system. This is in contradistinction to most other sensory systems, including olfaction, in which stimuli are detected by sensory neurons.

Structures that are involved in peripheral taste reception, in decreasing order of size, are the taste papillae, taste buds, receptor cells, and taste receptor proteins. Taste papillae are visible with the unaided eye and are located throughout the oral cavity on the tongue, palate, pharynx, and epiglottis. There are four major types of gustatory papillae: circumvallate, foliate, fungiform, and taste stripes (from the original German *geschmaksstreifen*). However, the most abundant papillae on the tongue, the filiform papillae, are nongustatory (Fig. 1). These are prone to overgrowth, staining (especially with coffee and food dyes), or excessive shedding, which impart a white, coffee-brown, or raspberry appearance, respectively.

Of the gustatory papillae, the circumvallate papillae are located in a V-shaped array in the posterior third of the tongue. In humans, there are between 3 and 13 circumvallate papillae, and their number varies in other animals: rats and mice have only one, whereas cows may have as many as 25. Symmetrically located on the lateral posterior side of the tongue are the foliate papillae, which are pocket-shaped invaginations lined with taste buds. Distributed over a large surface area, the mushroom-shaped fungiform papillae cover the anterior dorsal surface of the tongue. The number of

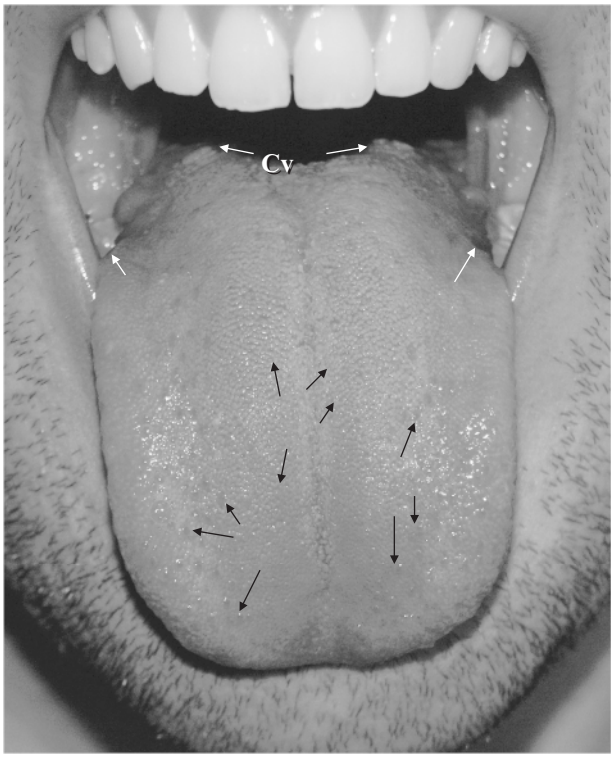

FIGURE 1 Human tongue. The dorsal surface of the tongue has four types of papillae: fungiform (Fu), nongustatory filiform (Fi), circumvallate (Cv), and foliate (Fo). Foliate papillae are not visible.

fungiform papillae in humans varies from 50 to 200. Finally, the taste stripes are located on both sides of the palatal midline at the borderline of the soft and hard palates.

The different taste papillae contain varying numbers of taste buds. For instance, in humans, the circumvallate papillae contain 100–200 taste buds, the foliate papillae have 320–2950 buds, and the fungiform papillae have 1–10 taste buds. The taste bud is the functional unit of the sense of taste. It is onion-shaped and contains 50–100 continuously maturing taste receptors and supporting taste cells (Fig. 2). Over 95% of the taste bud is shielded from the oral cavity by tight junctions, the structures that are responsible for the epithelial barrier. Only the apical portions of a few taste cells are exposed to the oral cavity through a 3- to 5-μm-wide opening, the taste pore (Fig. 3).

Unlike components of any other sensory system, taste cells have a rapid turnover rate of 10.5 days. The progenitor cells, the basal cells, are located at the base of the taste bud. As cells continuously grow and mature, they move from the basal area of the bud toward the taste pore. At any given time, the taste pore may contain the apical tips of 8–10 taste cells. The resident time of these 8–10 cells is as brief as a few hours, before they are shed into the oral cavity and washed away by saliva. This rapid turnover of cells, characteristic of many epithelial cells (e.g., certain cells lining the small intestine), means that the exposed taste receptor cells used for lunch are not the same as those used for dinner.

TASTE RECEPTORS, SIGNAL TRANSDUCTION, AND GUSTATORY PROCESSING

Generally, gustatory stimuli interact first with specific protein receptors on the apical, exposed surface of the taste receptor cells. This interaction then leads to changes in ion flux across the taste receptor cell membrane. The resulting depolarization induces release of neurotransmitter from the receptor cell to the nerve fiber innervating the cell. Changes in the firing rate of this innervating nerve are conveyed to specific regions of the central nervous system, where the taste message is decoded into a perceptual modality. During the past 5 years, a variety of taste receptor candidates—ion channels, ligand-gated channels, enzymes, and G-protein-coupled receptors (GPCRs)—have been identified for

FIGURE 2 Taste cells. (A) Transmission (phase contrast) photomicrograph of a single mouse taste cell. (B and C) Scanning electron micrographs of dissociated mouse taste cells. Bars = 10 μm. Some contaminating tissue is attached to the taste cell in B. Reproduced from Spielman *et al.* (1989) with permission from Elsevier Science.

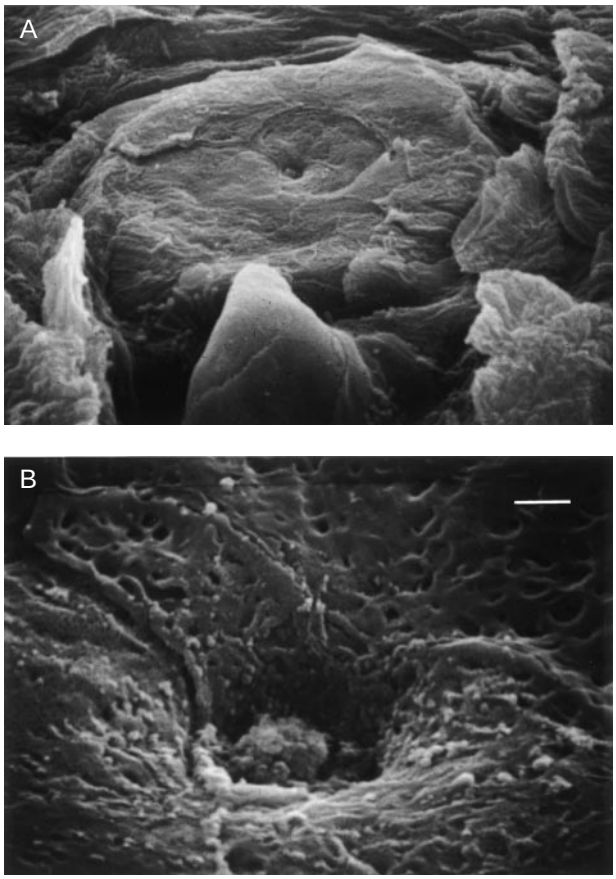

FIGURE 3 Taste pore. (A) Scanning electron micrograph of a rat fungiform papilla. The central pit represents the taste pore. (B) High-power scanning electron micrograph of the taste pore shown in A. Bar = 1 μm. Reproduced from Spielman and Brand (1997) with permission from Elsevier Science.

the five basic taste qualities: sweet, bitter, sour, salty, and savory (or umami, the amino acid taste of monosodium glutamate).

Sweet Taste

Sweet taste in humans is elicited by a variety of compounds, including sugars and sugar derivatives, D-amino acids, some of the small L-amino acids (glycine and L-alanine), and artificial sweeteners (such as cyclamate, saccharine, aspartame, sucralose, and very high-potency sweeteners). Recent evidence suggests that GPCRs are responsible for detecting sugars. A candidate sweet receptor, the T1R3, was cloned and found to be functional only as a heterodimer with a previously cloned receptor, the T1R2. Both are expressed in about 20% of the taste cells located in the posterior, lateral, and anterior taste buds of the tongue. The mechanism by which sweet taste is transduced has been previously elucidated. T1R3/T1R2 receptors couple through an increase in cGMP and activation of a cyclic-nucleotide-gated channel that leads to depolarization through calcium influx. Interestingly, artificial sweeteners use a different pathway, similar to many bitter compounds.

Bitter Taste

Detection of potentially harmful, even toxic, compounds is one of the primary roles of bitter taste. This gustatory stimulus is represented by a large and diverse array of compounds, ranging from ions (potassium) to complex artificial (denatonium) or naturally occurring compounds (caffeine, strychnine, quinine). Because of its potential survival benefit, bitter taste has the lowest detection threshold of all taste qualities, the largest known set of taste receptors, and is assumed to have the most diverse set of mechanisms of signal transduction.

Similar to sweet taste, bitter taste transduction involves primarily GPCRs as cell surface binding sites for many bitter stimulants. A family of 40–80 membrane-associated bitter taste receptors, termed T2Rs, was recently identified in rodents and humans. In humans, T2Rs are encoded in 24 genes located on three chromosomes. It is assumed, although not yet tested, that all T2Rs are bitter responsive. Bitter taste receptors apparently are coupled through gustducin, a taste tissue-enriched G protein α subunit, and associated β3 and γ13 subunits to the cyclic nucleotide and the phosphoinositide signal transduction pathways. Gustducin activates one or more phosphodiesterases, reducing the levels of cyclic nucleotides (cAMP and cGMP), leading to opening of a cyclic nucleotide-gated cation channel and depolarization. The β3/γ13 also activates phospholipase C-β2, which releases two second messengers, inositol trisphosphate (IP_3) and diacylglycerol (DAG). The former releases intracellular calcium, leading to cell depolarization. The specifics of the interplay between these two second messengers, the reduction of cyclic nucleotides, and the increase of IP_3 and DAG are not known; nor is it obvious which is the leading event in depolarization.

Sour Taste

Sour taste quality, similar to bitter taste, is a protective/warning system. It indicates the protons of acids. Protons may have a local effect on oral soft and hard tissues or a systemic effect when acidity indicates spoiled food. Several protein candidates have been implicated in sour taste transduction, including amiloride-sensitive epithelial sodium channels

(ENaCs), proton-gated channels [mammalian degenerin 1 (MDEG1), K^+ channels], hyperpolarization-activated cyclic nucleotide-gated channels (HCNs), H^+-gated ion channels, and the acid-sensing ion channels (ASICs). A variety of mechanisms may be associated with these channels, indicating the potential complexity of this taste quality. Generally, all potential mechanisms lead to an increase in intracellular positive charge that results in direct depolarization. Some of these mechanisms are supported by behavioral studies using the channel blocker, amiloride, which was shown to reduce aversion to acids in some species (the hamster, for example). The specific signal transduction mechanisms for most of these receptors remain to be elucidated.

Humans have a characteristic strong facial grimace, a "sour face," when exposed to sour stimuli. The grimace induces a strong contraction of facial muscles, which channels saliva onto the surface of the tongue. The mechanisms of salivation and tasting are tightly linked, and sour taste is the strongest salivary stimulant. With increasing salivary flow rates, higher levels of bicarbonates are secreted, which leads to buffering of the acid protons, protecting oral tissue from damage.

Salty Taste

Similar to sour taste, salty taste represents ions. Unlike sourness, however, saltiness is an essential indicator of minerals and serves as a monitor for ion homeostasis. The most important representative of this taste stimulant is sodium chloride. In rodents, an amiloride-sensitive epithelial sodium channel detects sodium chloride; the chloride appears to be mediated by a paracellular mechanism. In humans, the ENaC is less prominent and additional mechanisms not yet identified may be involved.

Umami (Amino Acid) Taste

Umami, from the Japanese word for "delicious" (*umai*), describes a taste quality specific for monosodium glutamate (MSG). This taste is synergistically enhanced in the presence of 5′ ribonucleotides, especially inosine 5′-monophosphate (IMP) and guanosine 5′-monophosphate (GMP). MSG and glutamate, the excitatory neurotransmitter, are almost identical. It was, therefore, reasonable to expect that their receptors might be related. Indeed, a truncated form of the brain glutamate receptor, mGluR4, was found in the taste system and is one of a number of candidate receptors for umami. The signal transduction mechanism for umami using the mGluR4 receptor is assumed to be similar to that in brain, a reduction in the level of cAMP leading to a closure of an unspecified cation conductance. One problem with this mechanism is that the mGluR4 receptors are generally inhibitory. Because tasting MSG likely requires an excitatory response from the taste cell, the actual role that an inhibitory receptor such as mGluR4 plays in transduction of the taste of MSG is questionable.

A completely different receptor type for MSG has been recently proposed, one that has little homology with other known glutamate receptors. This receptor is a dimer of two of the receptor proteins of the T1R family, namely, T1R1/T1R3. Note that this dimer is similar to the proposed sweet receptor, except that one monomer of the dimer pair is different. For sweet taste, the dimer is T1R2/T1R3. One interesting feature of the T1R1/T1R3 receptor for MSG is that its activity toward glutamate is enhanced by the ribonucleotides. This synergism between glutamate and the ribonucleotides is a hallmark of umami taste, and the observation that the T1R1/T1R3 dimer is enhanced by IMP lends credence to the suggestion that T1R1/T1R3 is the major receptor for umami taste. Japanese cuisine has taken advantage of appropriate combinations of foods to maximize this synergistic effect. The combination of pork, chicken, black mushrooms, sea bream, etc., which contain nucleotides, and tomatoes, cauliflower, celery, carrots, and mushrooms, which are rich in MSG, lead to an enhanced taste for glutamate via this synergistic culinary effect.

Other Tastes

In aquatic animals, other amino acids act as taste stimulants. The catfish, for instance, shows sensitivity to L-arginine, L-alanine, and glycine. The L-arginine receptor is a ligand-gated nonselective cation channel and is primarily located on the barbel, a tactile process located on the lip of the catfish.

Additional taste qualities exist. Fats have been recently found to act on taste cells, in addition to stimulating the trigeminal system. In particular, some free fatty acids activate taste cells through a potassium channel blockage. Water and metallic tastes have also been proposed as distinct, although nontraditional, taste qualities.

Signal Transduction and Processing

Taste receptor cells, similar to neurons, exhibit action potentials in response to gustatory signal transduction, leading to release of neurotransmitters. The receptor cells synapse with first-order neurons at the taste bud level. Gustatory information is carried for central processing by three cranial nerves: the VIIth,

or facial (of which the chorda tympani and greater superficial petrosal branches innervate the anterior two-thirds of the tongue and palate), the IXth, or glossopharyngeal (innervating the foliate and circumvallate papillae), and the Xth, or vagus (innervating the base of the tongue, epiglottis, and pharynx). Pain and thermal and tactile information, crucial for food detection and appreciation, are carried by the maxillary and mandibular branches of the Vth or trigeminal nerve.

Although it has been assumed for many years that specific regions of the tongue are tuned for specific taste qualities, it is now clear that all three gustatory nerves carry all taste stimuli. Even single nerve fibers may be broadly tuned to carry information about multiple types of gustatory stimuli. Gustatory information carried by the three cranial nerves is passed on to the nucleus of the solitary tract in the medulla oblongata. From there, information is sent to the ventral posteromedial thalamus and eventually to the gustatory cortex in the lower tip of the parietal lobe.

PERIPHERAL ORGANIZATION OF THE OLFACTORY SYSTEM

The sense of smell, although generally not considered as important as some of the other senses, allows human beings to detect thousands of odors in their environment. The nasal cavity is divided by the septum, and humans have three folds, or turbinates, in the dorsal part on each side. Sensory neurons are located predominantly on the superior turbinate and to a lesser extent on the middle turbinate and the septum, whereas nonsensory epithelium lines the other areas. The sensory portion of the olfactory mucosa contains several cell types. Olfactory receptor neurons (ORNs) are the cells that detect chemical stimuli. They are bipolar neurons with a dendritic process ending in an apical swelling called an olfactory knob, which is exposed to the outside world, and an axon that projects through the cribriform plate into the olfactory bulb. The olfactory knob carries either cilia or microvilli, which contain the receptor molecules that detect odors and the elements of signal transduction pathways that convert the binding of odor molecules into electrical signals. Other cells in the sensory area of the olfactory mucosa are sustentacular cells (also called supporting cells), which surround sensory neurons and produce part of the mucus that covers the epithelium and basal cells; the basal cells are immature precursor cells for ORNs and give the olfactory neuroepithelium the ability to regenerate after injury. There also is a constant turnover of ORNs, with new cells arising from dividing basal cells, then maturing into functional receptor neurons, and finally dying and being resorbed. The life span of ORNs varies but is in the range of 30 to 90 days. The nonsensory areas of the mucosa contain respiratory cells that possess motile cilia at their exposed apical ends. Ciliary movement generates a continuous retrograde flow of mucus toward the throat. Bowman glands, scattered throughout the epithelium, produce mucus. The mucus contains odorant-binding proteins, which are lipocalins, having relatively low molecular weight and high affinity for odorant molecules. Although several potential roles for odorant-binding proteins have been proposed, including transport of odorant to and/or from receptors, facilitation of odor binding to receptors, termination of receptor binding of odorant, and detoxification of the mucosa, none of these functions has been clearly established.

OLFACTORY RECEPTORS AND SIGNAL TRANSDUCTION

To detect and distinguish thousands of different odorant molecules, the nose needs a large number of different receptors. In the early 1990s, a large family of genes that encoded apparent receptor molecules was identified in olfactory tissue. These receptors, similar to sweet and most bitter receptors, possess seven transmembrane domains that contain conserved sequences and a highly variable exposed region that is believed to be the ligand-binding site. More recently, some of these proteins have been confirmed to be odorant receptors by functional expression in cell systems such as *Xenopus* oocytes and immortalized cell lines. About 1000 different members of this family of receptors have been predicted for the mouse, one of the first and best studied mammalian models of olfaction. For humans, 350 functional olfactory receptor genes have been identified and cloned. It appears that humans have a large number of pseudogenes, which have high similarities with the nucleotide sequences encoding functional receptors but contain mutations that lead to nonfunctional proteins.

The most extensively documented signal transduction mechanism in ORNs involves the second messenger molecule cAMP. Binding of an odorant to a receptor molecule leads to the activation of a GTP-binding protein (G protein); an ORN-specific G protein, G_{olf}, has been identified. Activation of G proteins causes dissociation of the α subunit from the $\beta\gamma$ subunit complex. The α subunit activates the enzyme adenylyl cyclase, which converts ATP into the second messenger cAMP. cAMP in turn activates nonselective cation channels, resulting in depolarization of the receptor

neuron and leading to generation of action potentials. Calcium ions constitute a major component of the depolarizing current through the cAMP-activated channels, and the transient rise in intracellular calcium activates a second conductance through chloride channels, which amplifies the depolarization of the cell because internal chloride is unusually high in ORNs.

Several additional messenger molecules have been implicated in signal transduction in ORNs, either as part of different transduction pathways or as modulators of the cAMP cascade. These substances include cGMP, 1,4,5-inositol trisphosphate, nitric oxide (NO), and carbon monoxide (CO), although their exact contributions to signal transduction remains controversial.

OLFACTORY BULB AND HIGHER CENTERS

Depolarization of ORNs by odors leads to the generation of action potentials, which travel along the axons that form the olfactory nerve projecting to the olfactory bulb. The axon terminals form synapses with mitral and tufted cells in the outer layer of the olfactory bulb, in discrete structures called glomeruli (Fig. 4). Mitral and tufted cells are output neurons, sending their axons to the next center in the brain. Several ORNs project onto one output neuron (convergence), and it has been shown that ORNs express only one or very few olfactory receptor molecules and that all ORNs that have the same receptors project to the same one or two glomeruli in the bulb. There are local interneurons, called periglomerular cells, that make synapses with the output neurons within a glomerulus. These dendrodendritic synapses are reciprocal, with synaptic neurotransmitter release sites on both sides of the synaptic cleft. Release of neurotransmitter from the output neuron side has an excitatory effect on the periglomerular cell, whereas release of neurotransmitter from the periglomerular cell is inhibitory to the output neurons. Activation of these synapses can result in lateral inhibition that is similar to that observed in the retina. In deeper layers of the bulb, a second population of local interneurons, the granule cells, forms the same type of dendrodendritic synapses with secondary dendrites of output neurons. The interneurons are believed to play an important role in the processing of olfactory information.

The signals are finally sent via the axons of the output neurons, which form the olfactory tracts, to higher centers of the brain, including parts of the limbic system and the orbitofrontal cortex, where the integration of olfactory information with inputs from other sensory systems, including taste, takes place.

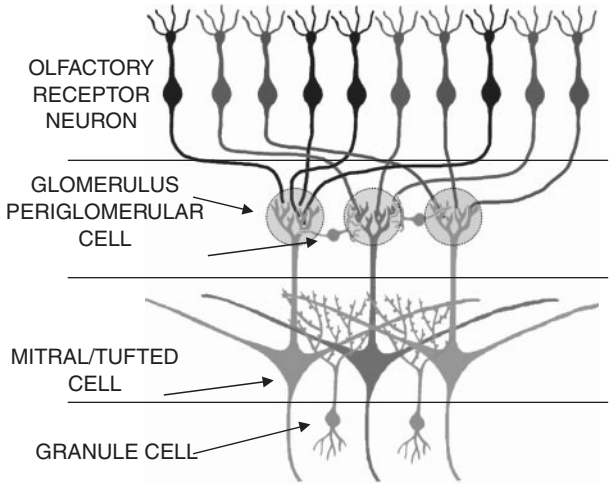

FIGURE 4 Organization of the olfactory bulb. Olfactory receptor neurons form synapses with dendrites of mitral and tufted cells in glomeruli located in the outer layer of the olfactory bulb. Local interneurons, called periglomerular cells, make dendrodendritic synapses with mitral/tufted cells in adjacent glomeruli. Another set of interneurons, granule cells, form dendrodendritic synapses with mitral/tufted cells in the deeper layer of the bulb. The color coding illustrates the fact that receptor neurons expressing the same receptor molecules project to the same glomeruli in the olfactory bulb. Courtesy of Graeme Lowe, Monell Chemical Senses Center, Philadelphia.

THE VOMERONASAL ORGAN

The vomeronasal organ (VNO) is an important sensory system in many vertebrates, particularly in mammalian species (rodents, cats, and horses, among others). It is often described as the sensory system that detects pheromones, or, in a more general sense, "social odors," a notion that has been supported for several animals and stimuli. However, it is important to note that in some cases pheromone function can be exerted through the main olfactory organ and that some volatile stimuli that are not considered behaviorally relevant can be detected by sensory neurons of the VNO.

The presence of a functional VNO in humans and the existence of human pheromones are among the most intensely debated questions in the field of olfaction. Anatomical studies have described the presence of a VNO in almost all subjects, although the organ varies greatly in size and shape among individuals and even within the nostrils in an individual. Some groups have found bipolar receptor-like cells in the area of the human VNO and electrical activity has been recorded on stimulation with derivatives of human hormones. However, no evidence has been found for an axonal connection with the olfactory bulb or other parts of

the brain. Genes that show significant homology with receptor genes isolated from rodent VNOs have been identified and found to be expressed in the olfactory mucosa of humans. Although many are pseudogenes, some appear to code for a functional receptor molecule. These receptors have not yet been isolated and their ligands are unknown.

The literature contains reports of physiological effects (synchronization of menstrual cycle) as well as behavioral effects of human scents that suggest the existence of pheromone-like substances in humans, most likely associated with apocrine secretions of the skin. With a VNO that appears nonfunctional because of its lack of neuronal connections, such stimuli might be detected with the olfactory mucosa.

INTERACTION OF TASTE, SMELL, AND OTHER SENSORY SYSTEMS

Several sensory systems must be activated to enjoy food. Gustatory, olfactory, and somatosensory (temperature, touch, and pain) systems are activated by chemical ingredients in food, dependent in part on the quality of the food. Each sensory system contributes to provide part of the overall sensation called flavor.

The absence of only one sensory system may significantly affect the pleasure of eating. For instance, individuals with an upper respiratory infection may experience a decrease in their sense of smell, and therefore a reduction in the appreciation of flavor. This can often be confused with a loss of taste. Indeed, 9 out of 10 patients complaining of loss of taste turn out to have a smell disorder. The relative ease with which the olfactory system can become compromised can be traced back to the anatomy of the olfactory system. With inhalation, the olfactory neurons, which have a slow rate of renewal, are directly exposed to potentially toxic agents. In addition, the olfactory nerve is prone to physical damage. This combination, along with frequent obstructions of the upper respiratory pathway, is a major reason why olfactory factors are the main cause of chemosensory disorders.

Texture, temperature, and carbonation (which induces mild pain) of food also affect taste and smell. The fat content of potato chips and cream cheese, the temperature of ice cream, the carbonation and temperature of beer, and the spicy nature of certain foods all contribute to the overall enjoyment of eating. Most foods are appreciated slightly below body temperature (36°C). This maximizes the emission of volatile compounds that are sensed by the olfactory system after swallowing. Other foods, such as ice cream and beer, are best at lower temperatures (closer to 4°C), whereas tea and coffee are most appreciated slightly above body temperature.

SUMMARY

A variety of chemicals act on taste and smell. The primary binding sites for these stimuli are a large number of recently identified cell surface receptors that are coupled with diverse signal transduction mechanisms. Taste and smell interact with other sensory systems, in particular those for perceiving temperature, texture, and pain. Together, they provide an overall assessment of the chemosensory and somatosensory properties of food.

See Also the Following Articles

Digestion, Overview • Salivary Glands, Physiology

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