

## The Chemical Senses

The chemical senses, olfaction and taste in many ways are one of the most important sensing systems in the body. They permit the individual to identify noxious odors in the environment, (e.g. smoke), and to be attracted to members of the species. The taste mechanism permits the individual to identify salt, sweet, sour, bitter and toxic materials in the food and in concert with the olfactory system is most important for setting our feeding behavior.

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### **Introduction**

#### **Rhinencephalon**

The neurologist Paul Broca in the later half of the 19th century initially designated all of the structures on the medial surface of the cerebral hemisphere the "great limbic lobe." This region, due to its strong olfactory input, was also designated the rhinencephalon.

The olfactory portion of the brain (rhinencephalon, or archipallium) comprises much of the telencephalon in fish, amphibians, and most mammals. In mammals the presence of a large olfactory lobe adjacent to the hippocampus was once considered to be evidence of the important olfactory functions of these regions. However, when a comparative neuroanatomist examined the brains of sea mammals that had rudimentary olfactory apparatus, e.g., dolphins and whales, a large hippocampus suggested other-than-olfactory functions for this region.

In 1937, Papez proposed that olfactory input was not the prime input for this region, and the experiments of Kluver and Bucy (1937) and Bucy (1952 and 1958) demonstrated the behavioral deficits seen after lesions in this zone. More recently, it has been shown that in primates only a small portion of the limbic lobe is purely olfactory: the olfactory bulb, olfactory tract, olfactory tubercle, pyriform cortex of the uncus, and corticoamygdaloid nuclei (Fig. 22-2). The other portions--hippocampal formation, fornix, parahippocampal gyrus, and cingulate gyrus--are now known to be the cortical regions of the limbic system (Fulton, 1953; Green, 1958; Papez, 1958; Scheer, 1963; Isaacson, 1982).

### **Emotional Brain**

Since the initial observations of Kluver and Bucy (1937) and Papez (1937), which localized emotions in the telencephalon, many other investigators have added information concerning the localization of behavior. We now know that many cortical and subcortical regions are incorporated in the "emotional brain."

Different investigators have coined different terms to succinctly describe the limbic system, particularly the visceral, vital, or emotional brain. The term "visceral brain" would seem appropriate since much of our emotional response is characterized by specific responses in the viscera (Fulton, 1953). On the other hand, the importance of the emotional response for the self-

preservation of the individual and the perpetuation of the species has led other investigators to call this region the "vital brain" (MacLean, 1955). The term used most commonly by investigators and the one used in this chapter is limbic lobe (limbus = margin) because the involved region is located on the medial margin of the cerebrum and surrounds the brain stem as it enters the diencephalon.

By describing a large region of the brain as being devoted to the emotions. We can separate the entire central nervous system into a "somatic brain," which controls the external environment through the skeletal muscles, and an "emotional brain," which controls the internal environment through the control of smooth muscles and glands. Our discussion of this region begins with the olfactory system and continues into the Limbic System

## **Olfactory System**

### **Olfactory Nerve (fig 22-1)**

The olfactory nerve (cranial nerve I) originates from the uppermost portions of both nasal fossae, which occupy the mucous membrane covering the superior nasal conchae and adjacent septum. The mucous membrane is attached to the walls of the nasal septum which in this region is formed by the ethmoid bone.

### **Olfactory Receptors**

The 100 million or more bipolar receptor cells are embedded in sustentacular cells. The dendrites of the receptor cells are short and ciliated. The cilia are embedded in the odor-absorbing secretion that forms the mucosa and is secreted by the Bowman glands. The olfactory receptor cells are constantly being replaced by new cells from the basal layer. All of the axons

from the olfactory neuroreceptor cells are unmyelinated. They gather together into about 20 bundles (fila olfactoria), which then pass through openings in the cribriform plate of the ethmoid bone.

### **Olfactory Discrimination**

Vertebrates with a well-developed sense of smell are called macrosmatic, while those with a poorly developed sense of smell are called microsmatic. Dogs and cats are macrosmatic animals, while humans and all of the great apes are microsmatic. In the dog and cat about 15 % of their brain is taken up with olfaction while in us it is minute. So it is not surprising that the dog and cat can smell so much better than we can. Nevertheless, we can still distinguish thousands of different odors, and a multibilliondollar industry has developed to stimulate our olfactory system. In fact, many people have built careers on their olfactory acuity (wine and coffee sniffers and perfumers). Many blind or deaf people have such a refined sense of smell that they can detect subtle changes in their environment.

In all other sensory systems, such as vision and audition, it is possible to speak in terms of a basic measuring system, but in the olfactory system, the degree of smell is a subjective matter. So only general rules for smell can be listed. In order for humans to detect an odor, it must have some degree of volatility and lipid and water solubility. These qualities are necessary for the odorant to reach the superior portion of the nasal conchae and penetrate the aqueous mucous membrane, which contains the odor-receptant cilia. Only certain regions of the mucosa appear to respond to any olfactory stimuli, and most olfactory cells are sensitive to many different stimuli.

The following seems to best explain the transduction of the olfactory signal (Burchell, 1991; Dionne, 1988; Kauer, 1988, 2001; Lazard, 1989). The odorant enters the mucous membrane and contacts the cilia on the neuroepithelial cell, where it reaches a receptor. The receptor stimulates adenylate cyclase interaction with  $G_s$  proteins specific to olfactory cells and produces cAMP which binds to the cation channel and generates the neuronal response. In addition, odorants may bind to an olfactory-binding protein in the mucous membrane, which concentrates the odorant and moves it to the neuroepithelial cilia where transduction can then begin. The odorant is inactivated in the endoplasmic reticulum.

The olfactory-binding protein enables the system to present the stimulus to the neuroepithelium and then inactivate the stimulus, which is released from the neuroepithelial cell into the vasculature or olfactory mucosa. Kauer (1988) demonstrated in a magnificent series of studies that real-time imaging of neural activity in the olfactory bulb of the salamander can be demonstrated using voltage-sensitive dye recordings. These studies demonstrate that each odorant has a different onset latency, different magnitude, and different activation pattern in cells in the olfactory bulb.

Recent studies with in situ hybridization of five different odorant receptor mRNA have shown that axons from neurons responsive to a given receptor converge mostly on a very few glomeruli in the olfactory bulb in a bilaterally symmetrical way (Vassar et al., 1994). This data shows that a given odorant will produce a response in only a restricted number of glomeruli, and demonstrates that the olfactory system, just as other sensory systems, uses spatial segregation to identify the specific stimulus.

### **Olfactory Central Connections (Fig 22-2)**

**Olfactory Bulb.** The olfactory bulb lies on the cribriform plates and upon microscopic inspection is seen to consist of six layers from outside in as follows:

- Olfactory nerve layer
- Glomerular layer
- External granular layer
- Molecular layer
- Mitral cell layer
- Internal granular layer.

**Olfactory Nerve Layer.** The unmyelinated olfactory axons from the olfactory mucosa carried in by the rootlets from cranial nerve I, form the most external layer of the bulb. The nerve fibers form a plexus in the olfactory mucosa covering the superior nasal conchae. These unmyelinated fibers gather into about 20 bundles, which pierce the cribriform plate of the ethmoid bone.

**Glomerular Layer.** The olfactory nerves synapse with dendrites of mitral cells and tufted cells in the subjacent glomerular layer. The axons of 20 to 30 thousand bipolar olfactory cells terminate in one glomerulus. In addition, the axons of multiple mitral cells and tufted cells also converge on a single glomerulus. This summation of olfactory information permits a high sensitivity to odoriferous substances.

**External Granular Layer.** The external granular layer is deep to the glomerular layer. It consists of small multipolar cells and their dendrites enter the glomeruli.

**Molecular Layer.** The wide molecular layer consists of dendrites of mitral cells and includes tufted cells.

**Mitral Cell Layer.** This layer consists of the cell bodies of the mitral (bishop's cap) cells, which are the largest neurons in the olfactory bulb. Their dendrites form synapses in the glomerular layers, and their axons form most of the olfactory stria. (These cells are one of the magnificent examples of nerve specificity in the central nervous system, as shown by the Golgi neuronal method).

**Internal Granular Layer.** This deepest layer contains stellate-shaped neurons and the axons from the mitral and tufted cells, which form the olfactory tract.

A wide overlap of layers exists because the axon collaterals from the mitral and tufted cells extend throughout the bulb. Adrian (1950) noted that each mitral cell is most sensitive to one class of odoriferous substances. Kauer (1991) discovered coding in the olfactory bulb, with each odor activating a different group of nerve cells. Inhibitory dendrodendritic synapses in the glomeruli and on the mitral cells help to regulate the response to specific odors (Reese and Shephard, 1972). The evidence points to discrimination between odors in the bulb itself, with more complex discrimination and recognition found in the olfactory cortex (the pyriform cortex).

**Olfactory Stria.** As previously noted the primary axons in the olfactory system originate from the olfactory receptor cells in the nasal fossae. The secondary axons originate from the mitral and tufted cells and pass posteriorly as the olfactory stalk, enter the base of the hemisphere, and divide into the lateral, medial, and intermedial olfactory stria (Table 1). The place where the olfactory tract enters the ventral surface of the telencephalon and divides is called the olfactory trigone; posterior to the trigone is the *anterior perforated substance* (olfactory tubercle), which is characterized in the gross brain by small perforations resulting from the removal of small penetrating blood vessels that are part of the anterior cerebral circulation.

**TABLE 1. SITES OF TERMINATION OF OLFACTORY STRIA:**

1. intermediate stria -- olfactory tubercle.
  2. medial olfactory stria -- septal region and via the anterior commissure into the opposite olfactory bulb.
  3. lateral olfactory stria -- olfactory cortex of the uncus and corticomedial amygdaloid nuclei.
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### **Regeneration of odorant receptor neurons.**

The olfactory epithelium and (gustatory epithelium) can be regenerated after injury. As the cells in the epithelium die they are normally replaced and with an injury to the olfactory nerve the pace of renewal is accelerated. With the regeneration of the receptor cells and depending on the number of the odorant receptors surviving the specific functions of any olfactory receptor neurons may be unaffected (J. Schwob. 2002. Anatomical Record 269: 33-49)



### **Dysfunction in the Olfactory System.**

If a person has a head cold, food will taste bland because of the inability to smell. The loss of smell, or anosmia, can also result from trauma or compression of the olfactory nerves, from tumors in the floor of the anterior and middle cranial fossa, or tumors involving any portion of the frontal lobe overlying the olfactory system. Viral infections may reach the olfactory cortex on the medial surface of the temporal lobe through the olfactory system and produce viral encephalitis. Other evidence suggests that one of the early changes in Alzheimer's senile dementia is a detectable drop-off in the sensitivity of the olfactory

Tumors or injury to either uncus produces "uncinate fits in which the patient has an olfactory hallucination, with associated visual hallucinations and altered emotion and behavior .

On rare occasions, this includes violent behavior (See Mark and Ervin, 1970 ).

### **Olfactory-Limbic Interactions**

In these days of air pollution one sometimes wishes we were free of olfactory senses. However, the olfactory system is necessary for our survival as individuals and as a species. For example, the aroma of food stimulates salivation and the desire to eat; musky pheromones stimulate or enhance sexual arousal; unpleasant aromas produce nausea, vomiting, and tearing; and the strong odor of smoke produces fear.

### **Vomernasal Organ and Pheromones-The accessory Olfactory System.**

The vomernasal organ (of Jacobson) is found in the medial wall of the nasal septum below the nasopalatine recess and is a blind pouch that connects to the surface through an orifice. This organ is supplied by branches of the olfactory nerve and has an epithelium

similar to that found in the olfactory mucosa. Recent studies have demonstrated that this organ is sensitive to pheromones, messenger substances between individuals. These substances act like hormones however they are not secreted into the blood but instead are secreted by one individual of a species and recognized through chemoreception by another member of the same species. The best studied pheromones have been in the insect community with prime examples being the queen substance of bees and sexual attraction in butterflies (Steinberg, Taylor and Haglund, 1994). How this signaling mechanism is used by the human species is still a subject of much lively discussion.