Medical Neuroscience | Tutorial Notes

Chemical Senses—Overview & Olfaction

MAP TO NEUROSCIENCE CORE CONCEPTS[1]

NCC1. The brain is the body's most complex organ.

NCC3. Genetically determined circuits are the foundation of the nervous system.

LEARNING OBJECTIVES

After study of the assigned learning materials, the student will:

1. Characterize the peripheral and central organization of the olfactory system.
2. Discuss sensory transduction in olfactory receptor cells.
3. Describe information coding in the olfactory system.

TUTORIAL OUTLINE

I. Overview of the chemical senses

   A. special sensory systems in the face—in the nose, mouth and eyes—are capable of detecting minute quantities of chemical molecules in the environment

      1. airborne molecules give rise to:

         a. **olfactory** (smell) sensations via the olfactory system; and

         b. **noxious** (nociceptive) sensations in the oral and nasal cavities, and in the corneas and conjunctiva of the eyes via the trigeminal chemosensory system

      2. ingested (mostly water-soluble) molecules give rise to **gustatory** (taste) sensations via the gustatory system

   B. the chemical senses provide a wealth of information across multiple domains of human behavior; they provide important cues that are relevant to:

      1. nutrition (palatable and desirable foods and drink; unpalatable or potentially harmful foods and drink)

      2. physiological functions (visceral motor activities, reproductive cycles, infant-paternal behavior)

      3. social interactions (self and others)

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[1] Visit **BrainFacts.org** for *Neuroscience Core Concepts* (©2012 Society for Neuroscience) that offer fundamental principles about the brain and nervous system, the most complex living structure known in the universe.

4. safety (harmful volatile chemicals in the environment)

5. even hedonic rewards (attractive perfumes, flower scents, pleasurable food tastes, human pheromones?)

C. thus, the chemical senses can be powerful sources of motivation that can profoundly influence human (and animal) behavior

II. Organization of the olfactory system

A. anatomical overview (see **Figure 15.1**[2])

1. airborne molecules, called **odorants**, enter the nasal cavity (passively or during active sniffing) where they diffuse through a layer of mucus and interact with **olfactory receptor neurons** in the **olfactory epithelium**

2. the axons that arise from the receptors cells project through the cribriform plate and synapse in the **olfactory bulb**, which is a telencephalic structure connected to the olfactory cortex by the **lateral olfactory tract** (despite its appearance, this is not a nerve!)

3. the projections neurons of the olfactory bulb, called **mitral cells**, send their axons to the **olfactory cortex**, which is comprised of a large set of cortical areas in the ventral-medial surface of the forebrain, including:

a. piriform cortex (in junction of temporal lobe and posterior frontal lobe)

b. olfactory tubercle (actually, part of the ventral striatum)

c. cortical divisions of the amygdala

d. entorhinal cortex (part of the hippocampal formation in parahippocampal gyrus)

4. different parts of the olfactory cortex are extensively interconnected and many parts project to other cortical and subcortical regions, including the thalamus, hypothalamus and the orbital-medial prefrontal cortex

5. two exceptional aspects of organization worth noting:

a. the olfactory system is the one sensory system that *does not* relay information through the thalamus before reaching the cortex

b. the olfactory cortex has *no* (known) map of the sensory environment or the sensory epithelium

B. sensory transduction

1. at the apical end of olfactory receptor neurons, there are olfactory cilia that extend into a thick layer of mucus (see **Figure 15.7A**)

2. odorants bind to specific molecular receptors located in the plasma membrane of the cilia

3. a sequence of molecular reactions lead to the depolarization of the olfactory receptor neuron and the generation of a receptor potential (see **Figure 15.11**)

[2] Figure references to Purves et al., *Neuroscience, 5th Ed.*, Sinauer Assoc., Inc., 2012. [click here]

a. odorant binding activates an olfactory-specific G-protein (G_{olf}, a member of the 7-transmembrane, G-protein linked receptor family)

b. activated G-proteins, in turn, activate an olfactory-specific adenylate cyclase, which increases the production of cAMP

c. cAMP opens cation-selective ion channels that allow influx of Na^+ and Ca^{++}; this leads to the depolarization of the receptor neuron

d. activation of a Ca^{++}-gated, Cl^- conductance allows for the efflux of Cl^- and further adds to the depolarization

e. if threshold is reached, then action potentials are generated at the base of the receptor neuron and transmitted to the olfactory bulb via the olfactory nerve (cranial nerve I)

4. olfactory receptor neurons **adapt** in the continued presence of an odorant (a familiar experience to all)

a. Ca^{++} binds to calmodulin (CAM) and the Ca^{++}-CAM complex interacts with the cation-selective channel and reduces its sensitivity to cAMP

b. removal of Ca^{++} via the Na^+/Ca^{++} exchanger reduces the intracellular concentration of Ca^{++} ; this reduces the receptor potential

C. olfactory coding & perception

1. odorant-receptor interactions

a. humans are sensitive to odorants in the nanomolar to millimolar concentration ranges

i. small changes in molecular structure can lead to major changes in perception (e.g., D-carvone smells like rye, but L-carvone smells like spearmint)

ii. the quality of an odor evoked by an odorant depends on its concentration (e.g., low concentrations of indole smell like a floral bouquet, but high concentrations smell putrid)

iii. most natural odors are a complex mixture of a least several odorants at different concentrations

b. some individuals lack certain genes that encode particular olfactory receptors and are anosmic for certain odorants

2. the “logic” of olfactory coding

a. different odors activate molecularly and spatially distinct subsets of olfactory receptor neurons (ORNs) in the olfactory epithelium

i. different olfactory receptor genes are expressed in subsets of ORNs that are distributed in bilaterally symmetrical zones of the olfactory epithelium

ii. however, most ORNs expresses only one allele of about 400 olfactory receptor genes

- some olfactory receptor proteins are activated by just one type of odorant molecule
- but others are activated by a number of different odorant molecules
- thus, there is a "combinatorial code" (rather than a labeled-line code) of olfactory receptors, with receptor encoding the molecular shape of odorants

b. convergence of ORN axons in the olfactory bulb

  i. the principle cells of the olfactory bulb, called **mitral cells**, send dendrites into complexes of synapses (neuropil) called **glomeruli** (see **Figure 15.14D**)

  ii. each glomerulus receives input from about 25,000 ORNs, with each of these ORNs expressing the same olfactory receptor protein!

  - this remarkable convergence may maximize the fidelity and sensitivity of odorant detection

  iii. all the ORNs that express the same olfactory receptor allele converge onto a small subset of bilaterally symmetrical glomeruli in the two olfactory bulbs

  iv. each glomerulus also contains synaptic connections of additional cell types in the olfactory bulb, including tufted cells, periglomerular cells and granule cells

  - granule cells are thought to mediate lateral inhibitory connections across mitral cells
  - granule cells may participate in plasticity of neural circuits in the olfactory bulb

c. to solve the problem of coding complex odors, the olfactory bulb employs a **sparse coding** mechanism, with a relatively small number of glomeruli activated by a subset of dominant molecular shapes that may be present in complex odors

d. temporal coding in the olfactory cortex

  i. the convergence of molecular information in the olfactory bulb is apparently lost in the projections of mitral cells to the olfactory cortex

  - a single odorant produces activation in neurons that are broadly distributed across the olfactory cortex
  - mitral cells that receive input from the same glomerulus make synaptic connections with neurons throughout a large extent of the olfactory cortex

ii. thus, in the absence of an obvious spatial code and a map of the olfactory epithelium in the olfactory cortex, olfactory perception is likely based upon a *temporal code*

iii. central olfactory structures oscillate (i.e., firing nearly synchronous patterns of action potentials) when particular odorants are presented

3. physiological effects of odorants

   a. olfactory information reaches a variety of integrative centers in the forebrain that allow olfactory cues to influence cognitive, visceral, emotional and homeostatic behaviors

      i. the piriform cortex sends input to the orbital-medial prefrontal cortex (see **Figure 15.1C**), where multimodal input related to complex stimuli—such as food—becomes integrated

      ii. the piriform cortex also projects to the mediodorsal thalamic nucleus, which projects to the prefrontal cortex, including the dorsal-lateral sector where olfactory signals may be used to guide working memory (e.g., search or tracking behavior)

      iii. olfactory projections to the entorhinal cortex (parahippocampal gyrus) are implicated in olfactory based memory acquisition and memory recall

   b. in many species (possible including humans), species-specific odorants called pheromones play an important role in influencing social interactions and reproductive behavior (although humans lack a vomeronasal organ, which tranduces pheromone signals in most mammals)

   c. the ability to detect and discriminate odors normally decreases with age (see **Figure 15.5B**)

   d. the ability to detect and discriminate odors may be lost following traumatic head injury, if the axons of CN I are severed by movement of the brain relative to the cribiform plate (see **Figure 15.1A-B**)

      i. however, some olfactory function may recover with the regrowth of ORN axons to the olfactory bulb

      ii. ORNs normally undergo a cycle of degeneration and replacement by new ORNS that differentiate from a population of neuronal stem cells from among the basal cells in the olfactory epithelium (see **Figure 15.7A**)

      iii. regeneration of ORNs, regrowth of ORN axons to the olfactory bulb, specific targeting of ORN axons to the correct glomeruli, and plasticity in central olfactory circuits may not be 100% efficient, so olfactory perception may remain permanently altered following recovery from head trauma

STUDY QUESTION

Which of the following statements concerning the encoding of olfactory signals is most accurate?

A. Most olfactory receptor neurons express a large number of different olfactory receptor genes.

B. There is a "labeled-line code" connecting the olfactory epithelium to the olfactory bulb, with a 1-to-1 mapping of olfactory receptor neurons to glomeruli.

C. There is a "combinatorial code" operating in the olfactory cortex, since individual cortical neurons respond selectively to just one odorant.

D. Central olfactory structures operate using a "temporal code", since nearly synchronous oscillations in neural activity are broadly distributed when particular odorants are presented.