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Introduction: molecular mechanism of olfaction

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The appropriate interplay of an organism with its surroundings depends on the detection capacity of its sensory systems. The relative importance of the various sensory modalities, such as vision, olfaction and audition, in providing relevant information varies between the different species, but each sensory system significantly contributes to the input information processed in the brain. The sense of smell and its capacity to detect small extraneous molecules is of critical importance for most animals; detection of odorous cues significantly contributes to the identification and evaluation of food, territories, predators and reproductive partners. In fact, the olfactory system is a highly specialized chemodetector capable of recognizing certain odorous compounds at concentration as low as a few parts per trillion. It is able to distinguish myriads of chemical compounds; it may sense almost any volatile chemical it encounters. On the other hand, the olfactory system is also involved in detecting pheromones, very distinct compounds released by conspecific animals which elicit innate behaviors, thus regulating social and sexual interactions of animal populations. This dual task of sensing general odors and specific pheromones is accomplished by segregated sets of different sensory neurons and distinct neural pathways. General odorants are detected by sensory neurons residing in the olfactory epithelium of the nasal cavity which convey odor signals via the main olfactory bulb to high brain centers. Pheromones are recognized by sensory neurons in the vomeronasal organ which are connected to the accessory olfactory bulb; pheromone signals are transmitted to the amygdala and hypothalamus.

In both chemosensory systems, initiation of odor sensing is mediated by distinct families of olfactory receptors each encoded by a multigene family. They are all members of the heptahelical, G-protein-coupled receptor superfamily. Upon activation, these receptors elicit a cascade of transduction events that ultimately lead to an increase in membrane conductance. The resulting generator potential is converted to a distinct frequency of action potentials which are conveyed via the axon to the olfactory bulb. Thus, reception of odor signals and conversion into the language of the nervous system is based on complex cascades of biochemical and electrophysiological processes. The convergent results from experimental studies of the last few years employing modern biological techniques have deciphered some of the principles and mechanisms underlying the flow of information from odor molecules to the neuronal activity of olfactory sensory neurons and its processing in the brain. In this issue European scientists highlight various aspects of olfactory signaling, ranging from perireceptor events and signal transduction to the principles of odor coding and pheromone reception.

Terrestrial vertebrates smell volatile, primarily hydrophobic molecules. These airborne compounds have to cross the aqueous fluid of mucus covering the chemosensory epithelium of the nose before reaching the chemoreceptive membrane of their olfactory receptor neurons (ORNs). Small soluble proteins within the nasal mucus that bind odorous molecules, named odorant binding proteins (OBPs), may facilitate the transfer across this barrier. Their relatedness to a family of proteins (lipocalins) that transport hydrophobic molecules through other fluid compartments towards their targets seems to support this concept. In his review, P. Pelosi summarizes the current knowledge about the features of OBPs from different vertebrate species. By combining novel structural data, binding properties of OBPs and expression patterns for OBP subtypes, he also outlines the view that OBPs, rather than being shuttles for general odor molecules, may instead be primarily involved in the reception of pheromones.

Upon interaction with the chemosensory structures of olfactory neurons, the sensory cilia, odorants elicit an electrical response. In his article S. Frings reviews the current view about the mechanisms underlying the process of chemoelectrical transduction, i.e. how the chemical signal of an odorant is transduced into an electrical response of an olfactory sensory neuron. The author focuses on the cyclic AMP pathway and takes a detailed look at two key players in this process, the cyclic nucleotide-gated cation channel and the Ca^{+}-activated Cl^{-}-channel, which in a concerted action generate the receptor potential. The paper then examines the central role of calcium in the signaling process, emphasizing the dual function of calcium, first, its role in generating the electrical response, and second, in terminating the transduction cascade.

Detection and discrimination of odor molecules is supposed to be based on the specific interaction of odorants only with those olfactory neurons which are equipped with appropriate receptor types in their ciliary membrane. One of the central questions in olfaction is how the brain extracts information about the stimulus from the responses of distinct subpopulations of sensory neurons. Since olfactory cues do not contain any spatial information, it has been hypothesized that the olfactory system may use spatial activity patterns to encode the quality of odors. The paper by S. Korsching evaluates the spatial patterns observed at different levels of the odor processing cascade. Possible implications of topographic patterns of olfactory receptor expression in the olfactory epithelium are reviewed. The main focus is on odorant-induced activity patterns in the olfactory bulb, the first relay station in the brain. Recent work has led to the concept that a spatial map of glomerular activity in the olfactory bulb is a major determinant for encoding odor quality. The functional implications of temporal activity patterns of higher-order neurons for odor information processing are considered.

A prerequisite for precise transmission of odor signal into the brain and thus for reliable processing of odor information is the correct wiring of the ORN axons with their appropriate targets in the olfactory bulb. Previous studies monitoring activity patterns in the olfactory bulb upon odorant stimulation suggest that cells responding to the same odorant may synapse onto the same target cells in the brain. The paper by J. Strotmann reviews the recent work demonstrating that sensory neurons expressing the same receptor type in fact project to the same glomeruli. Current views about how these precise patterns of connectivity might be established, i.e. which cell types and molecules may contribute to guiding and targeting axons to their correct positions, is discussed. The wiring patterns of the main olfactory epithelium are compared with those found for the vomeronasal organ neurons projecting into the accessory bulb. The obviously different principles may be of fundamental importance for a distinct information processing of odor and pheromone signals.

The olfactory system exhibits a remarkable degree of dynamics. The sensory cells, real nerve cells, have only a limited life-span but are replaced throughout adulthood by progenitor cells originating from the basal region of the epithelium. Despite this constant turnover, the topography of axonal projections apparently is maintained. In their paper, L. Astic and D. Saucier review the results of deafferentation studies which revealed first insights into the mechanisms underlying morphological reestablishment as well as functional reorganization of the olfactory system.

The vomeronasal organ (VNO) is a chemosensory system located in a tubular structure at the base of the nasal cavity; it is thus distinctly separated from the main olfactory epithelium and occurs in most amphibia, reptiles and nonprimate mammals. The VNO is supposed to be specialized for the detection of conspecific chemicals, pheromones. In his contribution P. Brennan highlights the nature of vomeronasal stimuli and the functional role of the VNO in mediating behavioral and physiological responses. The recent progress in deciphering the mechanisms and principles which underlie processing and coding of vomeronasal information is particularly emphasized.

Although our understanding of olfaction is far from complete, due to the enormous progress made in various fields of chemosensory research, the sense of smell is less mysterious currently a rather exciting area of contemporary research.