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OLFACTION PRIMER: HOW SMELL WORKS

WHAT IS OLFACTION?

The world contains millions – probably trillions – of smells, which are combinations of chemical odorants. Because of genes, culture, beliefs and experience, people often react differently to the same odor. Few odors smell good or bad to everyone.

The olfactory system can detect and identify thousands of *odorants.* Odorants are small molecules that easily evaporate and become airborne. When we breathe or sniff the air, odorants are drawn into our nose, entering a complex system of nasal passages. Lining a portion of these passages is the *olfactory epithelium*, a thin sheet of mucus-coated sensory tissue. Odorants settle into the mucus, making contact with *olfactory receptor cells*. This starts a process that translates the physical/chemical characteristics of odorant molecules into the sensation of odor.

The olfactory epithelium contains millions of olfactory receptor cells, which are nerve cells that connect directly to the brain. Each receptor cell has thin threadlike projections (*olfactory cilia*), which float in the mucus. Olfactory cilia contain the molecular machinery for detecting the arrival of odorants, and for generating an electrical signal to be sent to the brain.

Odorant molecules are detected and recognized by *olfactory receptors* in the cilia's membrane. The first step in odor recognition involves selective *binding* of odorants to one or more olfactory receptors. The human nose probably contains several hundred different types of olfactory receptors. Animals with a highly developed sense of smell - such as dog, rat, or cat - may have over a thousand different receptor types.

When an odorant molecule binds with a receptor, it triggers a biochemical chain reaction inside the receptor cell. The end result is a shift of the cell's electrical charge. This shift causes the receptor cell – which is also a nerve cell - to fire off a series of electrical pulses, which are sent to the brain along a thin nerve fiber known as an *axon*. Axons from the millions of olfactory receptors cells in the nose bundle together to form the *olfactory nerve*.

The olfactory receptor cells have several unique properties. First, a remarkable characteristic of these sensory cells is that they regularly regenerate, which makes them a valuable model for nerve cell regeneration. Secondly, they are the only nerve cells related to the central nervous system that are accessible for study outside the brain. The olfactory receptor nerve cells can be easily biopsied in humans, giving us the capability to study these cells and how they function across different populations.

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ODOR CODING IN THE BRAIN – How Do We Identify Specific Odors?

Olfactory receptor cells in the nose send their electrical messages via the olfactory nerve to the *olfactory bulb***,** the brain's first processing station for odor information. Millions of receptor cells, each containing one of approximately 400 possible olfactory receptor types, are scattered randomly throughout the nose. A given molecule can activate more than one receptor and any given receptor type can respond to more than one molecule. Nerve axons from these cells reorganize as they travel to the olfactory bulb, where the nerve endings gather to form tiny spheres called *glomeruli*. Each *glomerulus* receives axons from nose cells containing the same kind of receptor.

The hundreds of glomeruli resemble an electronic switchboard. Any particular odorant may activate several different receptors, causing the switchboard to 'light up' in unique patterns. These complex patterns provide the raw information for the brain to interpret. The olfactory bulb processes these patterns and distributes the information to the rest of the brain, where additional coding takes place.

From the olfactory bulb, odor information travels directly to the *limbic system*, an ancient part of the brain involved with emotion and memory. Other connections go to olfactory cortex, where thought processes take place. Cross-connections between cortex and the limbic system may be essential in forming lifelong, emotionally-laden, olfactory memories. Olfactory information also travels to orbitofrontal cortex, which receives input from other sensory systems. Researchers now are investigating how the brain combines information to know that a certain set of odorants is a tomato… or a wet dog… or your baby.

THE CHEMICAL SENSES ACROSS THE LIFESPAN

The chemical senses influence our lives in different ways at different ages. Infants and young children need to learn what foods are safe to eat. Even before birth, information about specific flavors of mothers' diets passes to infants through amniotic fluid. This very early learning continues after birth through flavors in breast milk.

At the other end of the lifespan, olfaction is the chemical sense most affected by aging. Older people have more trouble detecting odors and find it harder to tell one odor from another. Because flavor is largely determined by olfaction, this decrease in the ability to smell can affect food preferences and even nutritional status of older adults.

ANOSMIA: IMAGINE LIFE WITHOUT SMELL

Over six million Americans and many more individuals worldwide suffer from anosmia, the lack of a sense of smell. Monell recently announced *A Sense of Hope: The Monell Anosmia Project*, a three-year $1.5M campaign to support a research and advocacy program focused on anosmia. The research goal is to identify the biological causes of smell loss in order to develop potential treatment approaches for this under-recognized invisible disability.

Our initial research project focuses on understanding how healthy human smell receptor cells might be regenerated from specialized stem cells and then transplanted into anosmic patients. Additional projects will be announced in the coming year. Visit www.monell.org/anosmiahope to learn more about anosmia.

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