

ORDER OUT OF ODORS: IT ALL MAKES SCENTS, CENTS, SENSE

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Ah, the scent of roasting chestnuts and pungent pine needles, the whiff of spices in hot mulled wine. For flashbacks of yuletides past, nothing beats the power of holiday fragrances and odors, scientists say - not even silver bells' ding-a-ling or visions of sugar plums

The potent scent-memory link has long figured in literature, psychology and marketing. But only recently have scientists begun cracking the biologic code that enables us to detect and remember as many as 10,000 different odors. Also getting renewed attention is how mental representations of odors connect with memory and feelings.

"Your first reaction to a smell is emotional," says Dr. Alan R.

Hirsch, a Chicago neurologist specializing in smell and taste disorders. "We `think' smells differently than we do other sensory modalities.

"More than any other sensations, odors are particularly effective in inducing a vivid recall of an entire scene or episode from the past," Hirsch adds. He mentioned the most celebrated literary example, Proust's "Remembrance of Things Past," in which the aroma of a teatime cookie prompted a torrent of memories of his childhood in the French countryside.

Individuals respond differently to odors, Hirsch says, but some scents seem to speak the same language to almost everyone. In a study of people's fondest scent-memories, he found that many people associated the smell of baked goods with happy recollections of home and family.

Hirsch, neurological director of the Smell and Taste Treatment and Research Foundation in Chicago, said that a supermarket in which researchers released a fresh-baked scent reported that bakery sales jumped threefold. The potential for using odor as a motivational tool has not been lost on retailers, he says.

There is now a synthetic "new car" odorant that dealers use to give potential buyers a good feeling about their vehicles. And stores in the lingerie chain Victoria's Secret, according to Hirsch, are infused with a special floral potpourri scent that is supposed to "lift the spirits" of shoppers as they mull the purchase of a \$150 silk camisole.

The scientific impasse that had stymied understanding of odor perception began to crumble in 1991 when neuroscientists Linda Buck and Richard Axel at Columbia University's medical school found the first genes for odor receptors. As the work unfolded, they found there were many more - at least 100, perhaps 1,000 - than are involved in any of our other senses. Genes for identifying odors make up fully 1 percent of the human genetic blueprint, Buck and Axel's work suggests.

Before the gene discovery by Buck, who is now at Harvard Medical

School, and Axel, scientists had debated contrasting notions of how the nose could deal with the many thousands of odors wafting about in the world.

Some basics were already in the textbooks. Air breathed into the upper nasal passages flows across the moist membranes lining the nose. Embedded in the membranes are 10 million to 100 million sensory nerve cells. The knoblike ends of these cells are equipped with proteins called receptors, shaped so that they link up with odor molecules that match them.

When a receptor recognizes and captures a specific fragrance molecule, the interaction creates a coded message that is sent via electrical signals through long, threadlike fibers extending from the sensory cells to switching centers on the bottom of the brain, called the olfactory bulbs.

The input from the millions of sensory cells in the nose creates an electrical pattern in the olfactory bulbs, which act like a switching station. From there, the messages containing coded smell information are relayed to various parts of the brain. Many of the nerve pathways lead to the temporal lobe, which stores memories, while others connect with the most ancient parts of the brain that deal in the traffic of emotions, sex, appetite and survival behavior.

This wiring diagram helps explain why odors so directly affect memory and emotion. Research is continuing to find relationships between odors and mental states such as depression, migraine, hallucinations and degenerative disease.

But the big question facing researchers like Buck and Axel was: How many different kinds of sensors would be needed to identify 10,000

different scents? Was it likely that evolution had provided one type of receptor for every potential type of odor molecule? To many researchers, that seemed unlikely - not to mention inefficient.

At the other extreme, the system might work like color vision, which has only three types of receptors, for red, blue and green light. So the eye really "sees" only three colors of light - it is the brain that makes the infinite blends we interpret as all the varying shades in the world.

In experiments described by others as "elegant," Buck and Axel found a "family" of at least 100, and perhaps 1,000, different genes that cause nasal cells to make odor receptors. There may be one type of receptor for each gene, or - though this is not yet known - genes may be able to shuffle parts of themselves to create more than one receptor per gene.

Whatever the answer turns out to be, Buck says, "I was rather surprised and delighted" to discover the large gene family. "I really had felt that if you could actually find the receptors, and get your hands on the genes, you would have a very powerful tool" for exploring the entire sense of smell.

With this new information, scientists have taken a long stride toward explaining how we can smell cinnamon and cloves, the smoke of a roaring wood fire, wet wool and tree resin and all the other holiday fragrances.

But there is more than popular culture or retail profits at stake in the olfactory research. An estimated 2 million Americans have smell and taste disorders, Hirsch says. The sense of smell declines with age, and neurodegenerative diseases like Alzheimer's disease and amyotrophic lateral sclerosis, or ALS, can cause loss of the ability to smell. Brain diseases, strokes and tumors can blot out one's ability to smell.

The gene discoveries could have therapeutic implications, Hirsch says, such as treatments for taste and smell disorders, and giving clues to the presence of genes causing diseases that have loss of smell as a symptom.

Rare individuals have no sense of smell from birth, perhaps the result of a missing or mutated gene belonging to the large group of genes discovered last year by Buck and Axel.

And Buck points out one final but striking possibility: The nerve cells involved with smelling are the only ones in the central nervous system that die and replace themselves. With so much hope for brain-damaged and spinal-cord-injury patients riding on efforts to regenerate nerves, the investigation of smell could one day help rebuild shattered lives.

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