The Flavor of Aging

The ability to smell and taste breaks down with age, diminishing quality of life and impeding good nutrition. Researchers are beginning to understand why these senses falter. Improved techniques and experimental methods promise to lend new insights, perhaps revealing ways to make aging easier to swallow.

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(Published 24 March 2004)

For the elderly, food turns bland and odors fade. Aging’s undermining of the chemical senses makes meals uninspiring and sidetracks healthy eating habits. The changes also dampen awareness of spoiled food or malodorous—and potentially noxious—chemicals. Researchers are gaining a clearer view of how aging takes a toll on the senses of smell and taste, and they are hoping to find ways to revive them. Scientists are also investigating why neurodegenerative diseases often cripple the sense of smell and whether that failing might presage dementia.

Bite some Châteaubriand and sip a Bordeaux—chemical excitement will swirl in your nose and mouth. Salts, acids, and sugars tickle taste buds, and fragrances waft into your nose, teasing olfactory neurons. Nerves relay those events to the brain, which identifies flavors and smells: the tangy horseradish sauce, the fruit, oak, or licorice flavors of the wine. As people age, however, their olfactory palate weakens and warps.

Deficits in the senses of smell and taste might not be as deadly as other afflictions of aging, such as heart disease or diabetes, but they can profoundly diminish quality of life. “Older people don’t experience the same pleasure from food,” says psychobiologist Charles Wysocki of the Monell Chemical Senses Center in Philadelphia. A resulting dampened appetite can lead to poor nutrition and unhealthy weight loss; changes in the senses of smell and taste can also render a person oblivious to dangers marked by foul odors or flavors. Researchers are delving into why the systems deteriorate, and future investigations might unearth ways to keep old people enjoying the spice of life.

Better Living Through Chemistry

The senses of smell and taste allow organisms to sample their chemical surroundings. Taste buds principally monitor four types of compounds: salty, sweet, sour, and bitter. The system regulates intake of molecules that are important for life, such as sugars and salts, and helps creatures avoid toxic ones, which are typically bitter. Researchers debate the existence of a fifth class of taste—umami, sometimes translated from the Japanese as “savory,” which detects the presence of chemicals such as MSG. In the mouth, molecules of each type cling to different receptor proteins that coat the surface of taste bud cells on the tongue. These cells connect with neurons that tell the brain whether the mouth is licking a lollipop or gulping salt water.

Whereas the sense of taste concentrates on a discrete set of chemical categories, the sense of smell discriminates among a far wider range. Humans can distinguish perhaps 10,000 different odors; creatures with a more refined nose—dogs, for instance—can pick out many more, and at lower concentrations. Dogs carry approximately double the number of different kinds of receptors that humans do and boast larger olfactory bulbs, reflecting a greater number of olfactory neurons. The key to smell’s breadth is a collection of subtly different receptor proteins that, like antibodies in the immune system, grab particular chemical structures. Thousands of olfactory neurons stretch from the top inner surface of the nose to the olfactory bulb in the brain; each neuron carries one type of receptor protein that sparks a signal when it grabs an odor molecule. An odor molecule sticks to multiple types of receptor proteins, hence activating a constellation of neurons.

Sensing circuitry. Odor molecules enter the nose and travel to its upper surface, where they bind receptor proteins and activate neurons. Salty, bitter, sweet, and sour molecules from food stick to receptor cells in taste buds, which spark adjoining neurons. Both smell and taste neurons send signals to brain centers that process sensory information.
The olfactory bulb integrates the pattern of nerve firing and relays the information to brain centers that influence behavior, emotion, and learning.

**A Bitter Pill**

These chemical-sensing systems falter with age, however, and lasagna starts tasting like oatmeal. Experiments over the last several decades have revealed that younger people register lower concentrations of sugar or salt than do older people. But concerns about the methods employed in that work have spurred researchers to reexamine whether their conclusions apply to real life. Such studies typically used much lower concentrations than a person normally consumes at the dinner table; the age-related changes detected in the lab might not alter a person’s daily experience. Taste sensitivity varies dramatically among individuals, further confounding results. “There’s a serious measurement problem,” says geneticiSage Beverly Cowart of Monell. “We’ve got to be scrupulous about every single conclusion we’ve come to.”

Researchers are now testing a range of quantities of taste molecules rather than keying in on the low end. In addition, they try to equate responses among individuals by asking subjects to match the magnitude of their reactions to other sensations, such as comparing taste intensity to sound volume. Although the second sensation might also change with age, researchers can get a more meaningful gauge of taste response in different people by assessing multiple variables simultaneously, says Bartoshuk.

The outcomes of such studies have inspired researchers to refine old ideas. For instance, some tastes remain relatively robust over the human life span, whereas others fade. Although the elderly might not detect the low concentrations of sugar that tickle a younger person’s taste buds, the two groups react similarly to higher concentrations. At moderate concentrations, salt sensation appears to decline with age, however, and bitter response drops profoundly.

Anecdotal reports suggest that such age-related alterations can perturb eating habits or impair health. But no one knows how often diminished taste or smell sensitivity leads to health problems. Insensitivity to bitterness might render older people more likely to eat spoiled food or ingest poisons, says psychologist Beverly Cowart of Monell. And some researchers hypothesize that loss of bitter sensitivity might indirectly hamper healthy eating. The mouth contains a second sensory network—called the trigeminal system—that responds to touch and pain. It detects the burn of chili peppers or the creaminess of fat, for instance. Taste nerves feed back to this system and shut it down; losing this clamp over time might alter fat intake, says Bartoshuk. “We know that women tend to like fat more with age,” she says. “Is that because bitter [taste] is lost?” Her work supports that idea. For instance, people with an unusually sharp sense of taste—so-called supertasters—generally like fat less than other people do, whereas individuals who have lost taste perception from injury enjoy it. “The sensory changes with age are interesting,” says Bartoshuk. However, she doesn’t understand why people who detect fat easily crave it. “The question is, do they change food preferences?”

Early research on smell also indicated a decline in that sense. In a classic 1986 study, for instance, researchers sent scratch-and-sniff cards to *National Geographic* readers. They asked people to identify each of six odors and quantify its intensity; more than a million people responded. People lose the ability to detect odors only after age 70, the data revealed. But the sense of smell dwindles even in middle age: Individuals in their late 50s rated smells lower in intensity than did younger people, and they frequently identified odors incorrectly. One possible health implication was immediately clear: Older people missed the stinky sulfur compound added to natural gas and found it less offensive, suggesting that the elderly might not recognize dangerous gas leaks. Supporting that idea, almost twice as many individuals with smell impairments suffer accidents such as ingesting spoiled food, burning pans on the stove, or ignoring gas leaks, according to work published 15 March in *Archives of Otolaryngology—Head and Neck Surgery*.

Recent studies have bolstered this view of a general decline in the sense of smell with age. “There’s pretty substantial evidence for smell loss with aging,” says nutritionist Valerie Duffy of the University of Connecticut School of Allied Health in Storrs, “and recent studies suggest that there’s more loss out there than we ever expected.” For instance, the sense of smell wanes in more than 60% of people over age 80, according to a study by Claire Murphy, a cognitive neuroscientist at San Diego State University in California, published in the *Journal of the American Medical Association* in 2002.

Researchers don’t know whether all odors become less fragrant, or whether older people miss certain smells but notice others. The problem is that the vast majority of studies use only a few odors. People recognize too many fragrances for researchers to test them all; scientists keep experiments manageable by probing only a few smells. In addition, researchers typically rely on subjects to identify smells, which reflects not only odor detection but also memory recall. To tackle these issues, neurophysiologist Nancy Rawson of Monell says that researchers have begun using techniques such as magnetic resonance imaging to monitor neural activity in brain smell centers directly, thus circumventing memory deficits. And because study subjects don’t have to identify odors—which adds to the tedium of an experiment—such approaches might allow testing of more compounds.

**Flavor Saver**

Advances in smell-circuit studies might allow scientists to delve deeper into how the sense of smell changes, but the more burning question is why. “We don’t really know the mechanism of smell...
loss and why it’s occurring with age,” says Duffy. Unlike most other brain cells, olfactory neurons die and are replaced frequently throughout an organism’s life. Malfunctions in that process might hamper the sense of smell in the aged. For instance, older people typically carry fewer olfactory neurons than younger people do, and olfactory tissue in the nose is supplanted by other types of skin cells with age. That observation suggests that older people lose the capacity to maintain smell-detecting cells. Taste receptor cells also die and regenerate throughout life, and the relatively robust taste response—compared with that of smell—in the elderly might reflect a more vigorous replacement system. Sweet cells might bounce back faster than do bitter cells, posits Bartoshuk, although further experiments are needed to test that idea.

Researchers don’t know whether cells expire faster in the elderly, or whether replacement cells don’t step in as quickly, but some studies implicate rampant cell death. For instance, olfactory neurons in old rats produce larger quantities of molecules that spur cell suicide than do neurons from young rats, according to work by Robert Kern, an olfactory dysfunction researcher at Northwestern University in Chicago, and colleagues published in January 2004 in Laryngoscope.

What causes cells to die in droves isn’t clear, but infection might deplete the senses. Kern’s team notes that humans with sinus infections also show elevated quantities of suicide markers in their olfactory neurons. Viruses have airborne access to olfactory neurons, and a lifetime’s worth of exposure might cripple olfactory cells in the elderly. Rodent studies support that idea: Animals raised in pathogen-free environments maintain their sense of smell to a greater extent than do less-coddled creatures. Olfactory neurons are exposed to airborne toxic particles as well, which might also kill smell cells faster than they can be replaced.

The neurons that do remain malfunction, further work suggests. Rawson has examined olfactory neurons from humans of different ages and found that older neurons become promiscuous: Each formerly selective neuron fires in response to disparate compounds. A young person’s cell might respond to rose but not lilac or vanilla, she says, but an older person’s might spark in the presence of either rose or vanilla. “When cells become sloppy, they may be sending misinformation to the brain,” says Wysocki. “Many older people complain about their odor environment because everything smells funny.”

Rawson doesn’t know why olfactory neurons misfire, but one idea is that the cells start producing more than one type of receptor. A complicated regulatory circuit, elucidated in a study published in January 2004 in the Proceedings of the National Academy of Sciences, ensures that a healthy cell produces only one kind of receptor. Age might somehow loosen that system. Passing years might also perturb the signal relays inside of neurons, says Rawson; perhaps neurons fire inappropriately when a molecule sticks only fleetingly to a receptor protein. Researchers should compare which genes are active in old and young cells to address these questions, she says. Analyzing differences in protein profiles will also advance the effort, but researchers will need new methods to take that approach: Nose biopsies provide enough material to look at genes, says Rawson, but not enough to examine proteins, at least using current techniques.

Uncovering the glitches that deaden senses might also help address another key issue: whether damage from infection or injury alone quells the senses of smell and taste or whether more general biological processes, many of which change with age, contribute as well. For instance, the immune system stumbles in the aged (see “Immunity Challenge”), and a weakened defense against infection might render olfactory cells especially susceptible to infection-induced damage. And scientists have noted differences in the senses of taste and smell between men and women, hinting at sex-based biological programs, perhaps mediated by hormones, that alter those senses. Women maintain their sense of smell longer than men do and perform better on smell tests at all ages. Hormones apparently influence the sense of taste, too: Pregnant women are often especially averse
to bitter compounds, perhaps as a mechanism to avoid chemicals that might harm a growing fetus. The means by which hormones influence the sense of taste isn’t clear. But taste cells contain estrogen receptors, and estrogen fluctuations might influence how they work or how long they live.

**Whiff of Trouble**

Other studies suggest that diseases of the aging brain cripple the senses. The sense of smell flags in Alzheimer’s disease (AD) and Parkinson’s disease; it’s one of the earliest symptoms of the affliction, says Murphy. The smell system might be particularly susceptible to neurodegeneration. For instance, human brain regions that process olfactory information accumulate the plaques that characterize AD earlier than other sites do. And rodents that produce abundant quantities of the AD-triggering protein tau lose their sense of smell, according to a study by Richard Doty, a smell and taste researcher at the University of Pennsylvania Medical Center in Philadelphia, published online 4 March in *Brain Research*.

Murphy’s group is investigating the possibility of using smell deficiencies as an early warning sign of AD. That effort is complicated by the fact that most elderly people exhibit decreased smell prowess, but Murphy says that a smell screen could assist in early diagnosis because AD patients have a far weaker sense of smell than do older people who don’t have the illness. “The difference in magnitude is really highly significant,” she says.

That difference might permit early detection, but it also raises the question of whether AD and age cripple the sense of smell in the same way. To address that issue, Murphy and her colleagues are pinning down the brain regions that dim during aging. In a *Brain Research* study published in September 2003, Murphy and her colleagues used magnetic resonance imaging to assess brain activity in individuals exposed to various odors. In younger people, three brain regions that process smell lit up more brightly than they did in older subjects. Future studies on AD patients should reveal whether similar areas fade in those individuals, or whether other brain regions show diminished responses to smell. Murphy also says she’s curious whether healthy older people recruit new brain areas to help process smell information when normal circuitry fails.

Researchers will continue to tease apart how aging depletes the senses of smell and taste while sniffing for ways to salvage the systems. Many doctors don’t take loss of the sense of smell or taste as seriously as other, more deadly conditions, such as heart disease, says Rawson. As a consequence, research in the field doesn’t receive as much attention and few treatment options have emerged. “Right now, it’s ‘Tough luck. It might come back or it might not, but there’s nothing we can do,’” she says. As researchers gain new knowledge about aging senses, they might cook up ways to help the elderly continue to relish life’s flavors.

R. John Davenport is an associate editor of SAGE KE. Because he works alone, it doesn’t matter that he can’t smell his dirty socks.

**References**