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The Future for Olfactory Research

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During the past 20 years or so, both our appreciation for the importance of the sense of smell and our understanding of basic mechanisms involved have increased to a remarkable degree. This has particularly been the case during the last five years.

Heightened Interest in Olfactory Research

This increase in interest in the sense of smell has, for example, been fostered by, and reflected in, increased interest by national media such as *The National Geographic*, the television program NOVA, and countless news stories in newspapers and magazines, and on radio and television. The public seems newly fascinated by the world of scent.

In the scientific community too, it is no longer just a few who devote their research lives to the study of olfaction. A growing scientific organization, the Association for Chemoreception Sciences founded about 15 years ago, holds an annual meeting that serves as a forum for discussing new research.

The founding of the Monell Chemical Senses Center, nearly 25 years ago, was an important stimulus to increased scientific interest. As the first and still the only organization exclusively devoted to basic research on the chemical senses—taste, smell, trigeminal chemosensation—the Center provides a home for scientists to work in an interdisciplinary setting. The Center also sets major research goals, one of which is to unravel the mysteries of the sense

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of smell, from its cellular basis to its social psychological impact on behavior.

Several factors have been responsible for drawing more and more scientists into research in olfaction. The Monell Center is one factor. Traditionally, the Center actively recruits post-doctoral level scientists who have degrees in other areas, for example, biochemistry, nutrition and developmental biology. Many of these individuals, trained at Monell, have remained in olfactory research.

Another factor is the Fragrance Research Fund, which makes a policy of encouraging scientists who are not primarily trained in olfactory research to compete for olfactory research funds. Both the Fragrance Research Fund and the Monell Center have helped to bring new perspectives to the field.

Finally, I believe that the very excitement of the field combined with marvelous new technical developments in biomedical science have served to attract top scientists from other fields into olfactory research. The two winners of the Scientific Sense of Smell Award represent two such individuals (see "Effects of Fragrance on Humans" on page 4) and there are many more. It is apparent that the science of olfaction is no longer a backwater, but instead is in the forefront of biomedical research.

Current Areas of Olfactory Research

Why is olfactory research so interesting to scientists? Here are just a few of the reasons.

Role in human behavior: We are learning that odors play a much greater role in human behavior than previously thought. This is exemplified in several of the presentations at the symposium preceding the "Sense of Smell Award" ceremony (see "Effects of Fragrance on Humans" on page 4). I would only add that it is now known that odors are intricately involved in the mother-infant bonding and in very early learning about flavor, a key component of which is odor. There is a very real possibility that pheromones—that is, odors known in animals to regulate reproductive physiology and behavior—also affect humans. This is a very active research area now and one that we should closely follow.

Model for brain functions: A second reason for the surge in scientific study of olfaction is the recognition that this system may provide an excellent model for study of how the brain functions. The way the olfactory system processes odors at the level of the olfactory bulb—the first way-station after the actual receptors—is providing scientists with a relatively simple system to investigate processing of sensory information using modern neurophysiological and computational techniques. Similarly, the transductive processes—how odors are recognized by receptors and how that recognition is turned into a neural signal—are now known to have many similarities to transductive processes elsewhere such as in vision and neural transmission, increasing the generality of research findings.

A pathway to the brain: A third reason for this heightened interest of biomedical scientists in the sense of smell, however, derives from several of the olfactory system properties that are unique rather than common. The cilia of the primary neurons—which contain the receptors—are formally a portion of the central nervous system. Essentially, a small bit of the brain extends out into the upper nasal airway, exposed to the outside environment. This provides scientists with a unique opportunity to easily study living central nervous system tissue by merely taking small biopsies rather than using much more invasive techniques. Some of my colleagues at Monell are routinely doing this now. Their goal is to understand the cellular mechanisms of human olfaction both in health and in such degenerative diseases as Alzheimer's.

Moreover, these olfactory neurons are among the very few brain structures that regenerate. Usually when a brain neuron dies, it is not replaced. This is not the case for olfactory neurons. Why? What properties do they have that allows regeneration? These questions are of great interest to many scientists interested in brain function and particularly those who are developing strategies to help individuals

Effects of Fragrance on Humans

1992 Sense of Smell Award winners were John Stabenau of Neiman Marcus (left), Dr. Linda Buck of Harvard Medical School (second from left), and Dr. Richard Axel of the Howard Hughes Medical Institute and Columbia University (second from right). Also pictured above are Fragrance Research Fund officers Annette Green, vice president, and Dr. Jack Mausner, president, who presented the awards.

An oral report on the topic "Living Well With Your Sense of Smell" was presented prior to the Fragrance Research Fund's 9th Annual Sense of Smell Awards Ceremony at the Plaza Hotel in New York on November 4, 1992. Dr. Gary Beauchamp, director and president, Monell Chemical Senses Center, moderated a distinguished panel who reported on recent developments in understanding the effects of fragrance on human moods and activities.

Dr. Howard Ehrlichman, Professor of Psychology, Queens College, reported on the results of his research supported by the Fund and discussed how his work strongly suggests that the effect of odor on people's emotional states is real and that it can be demonstrated in rigorous scientific studies. Dr. Ehrlichman found that people who smelled a pleasant odor (almond) recalled relatively more happy memories and fewer unhappy memories than those who smelled an unpleasant odor (pyridine). Dr. Ehrlichman is convinced that the results of these studies demonstrate that real psychological changes occur when people smell pleasant or unpleasant odors. And since these studies were conducted under very sterile laboratory conditions, it was suggested that in the real world the impact of odors may be greater.

Mary Kliauga, Director, Bureau of Chemistry & Environmental Studies, Good Housekeeping Institute, described a study of the effects of fragrance on the performance of proofreaders. It was revealed that the accuracy of participating proofreaders was significantly better when they worked in a room in which fragrances (lavender or peppermint) were diffused throughout the room, as compared to when they worked in a room with no fragrance at all.

Dr. Craig Warren, Vice President and Director, Organoleptic Research, International Flavors and Fragrances, Inc., presented the provocative results of IFF's research on measuring the mood benefits of fragrance. He defined eight major moods (happiness, sensuality, relaxation, stimulation, irritation, stress, depression and apathy) and used charts to show the effect fragrance has on those moods.

Dr. Beauchamp then provided a review of the present state of olfactory research and reviewed areas that he believes will be developed in the near future by the many people now actively pursuing olfactory research and by the increasing number of research centers. (See accompanying article.)

In the evening following the symposium, Dr. Jack Mausner, Senior Vice President, Research and Development, Chanel, Inc. and President of the Fragrance Research Fund, presented this year's Scientific Sense of Smell Award to Dr. Linda Buck, Assistant Professor at Harvard Medical School, and Dr. Richard Axel, Investigator at the Howard Hughes Medical Institute and Higgins Professor at Columbia University, in recognition of their recent discovery of the family of smell genes. As a result of this discovery, scientists can now develop new knowledge about how odors are detected and how the brain interprets odor signals. Mausner also presented a Retail Sense of Smell Award to Neiman Marcus; the award was accepted by John Stabenau, Vice President and Divisional Merchandise Manager, Cosmetics, Neiman Marcus.

recover from damage to their brains—for example, stroke victims.

The fact that the olfactory nerve is exposed to the outside environment allows it to act as a direct pathway to the brain. This raises the possibility that substances might be transported up the nerve and thereby enter other portions of the brain. The earliest symptoms of some human degenerative diseases seem to involve olfactory function and structure. For example, early stage Alzheimer's patients exhibit a diminished sense of smell and the distinctive tangles and plaques seen at patient autopsy are prominent in olfactory areas of the brain. It has been speculated—I emphasize that remains only a speculation now—that some causative or stimulatory agent related to this disease could move up the olfactory axon and into the central portion of the brain.

The sense of smell provides a direct pathway to the brain in another way as well. Perhaps more than any other sense, odor information goes directly to the parts of the brain involved in emotion. For many mammals, odors are the most potent of sensory cues; they guide the search for mates, avoidance of predators, recognition of offspring and interaction with the world around them. This is not as true for humans, but the emotive power of scent remains potent. Thus, the study of emotion will surely profit from increases in our knowledge of olfaction.

Future Areas of Olfactory Research

What will be coming in the 21st century? This is very difficult to predict, particularly given the pace of research progress, but I will take this opportunity to speculate a bit. But, before I do, I need to emphasize a very important point here: Real progress in this area will only come through rigorous scientific investigation. Unverifiable results of research studies, secret results and marketing material masquerading as science will slow rather than enhance progress. Progress will be driven by real science not pseudoscience.

I believe we will soon have a fairly clear understanding of the major features of how odors are recognized and how they are classified (using the natural receptor-based classification scheme). For example, we will know whether perceptually similar but discriminably different odors, such as those described as woody or green or musky, share a class of receptor proteins as suggested by some of the work of Buck and Axel, the winners of the Sense of Smell Award. An understanding of the mechanism of olfaction should enable us to predict the odors of new compounds, to create new odors, and to modify responses to odors. For example, it may be possible to effectively and specifically mask offending odors while enhancing pleasant ones.

We may, in the future, begin to understand what factors permit the olfactory neurons to regenerate and why this regenerative process apparently declines with age. On average, people lose olfactory sensitivity as they age. An understanding of this process should provide the scientific knowledge necessary to stimulate regeneration of olfactory neurons. Already, research at Monell indicates that mere exposure to an odor can increase sensitivity to it. We should soon understand the molecular basis for this. Research of this kind could also provide scientists with the ability to restore function to other brain structures. This would be a magnificent discovery with obvious far-reaching implications.

As the interface between the brain and the outside chemical environment, we may discover that the olfactory system is particularly sensitive to changes in that environment. For example, changes in the sense of smell may turn out to be an early warning system for changes in the composition of the atmosphere. Ideas like this are being considered in Biosphere II, the long-term experiment in human isolation taking place in Arizona.

By learning how olfaction works, we should be able to develop biologically-based detector devices of extreme sensitivity. All of us who work in olfaction know that the sophisticated instruments developed to measure very small amounts of chemicals, such as gas chromatographs and mass spectrometers, pale in their sensitivity to even the human nose, much less the nose of a dog. Further knowledge will permit us to use the principles of olfaction to do such things as define a human's olfactory fingerprint (a signature of individual identity as distinctive as any known),

detect minute amounts of contaminants in everything from foods to our atmosphere, and aid in a variety of medical tasks such as disease diagnosis. For example, we have evidence that female animals possessing viruses which will cause mammary tumors at a future time produce a distinctive odor before any clinical signs of the tumors are evident. Thus, odor could serve as a powerful diagnostic tool, particularly when we have devices sensitive enough to routinely monitor it.

In the future, we will know much more about how odors alter human mood and performance. This knowledge should stimulate progress in such diverse areas as creation of better work environments, heightening the quality of life in the elderly and the ill, reaching out to the mentally disturbed, and strengthening the emotional ties among individuals.

Some of my own research involves how odor experience very early in life may influence flavor choices and social interactions. We know from animal studies that the sense of smell begins working even before birth. Odors in amniotic fluid can be detected and animals can learn about them. Odors in human breast milk transmit information to the infant, perhaps—again analogous to some non-human studies—resulting in the formation of life-long preferences and aversions. The ability of certain odors to elicit strong emotional response may, in part, result from these very early associations. In child rearing, I believe we will likely come to see that an olfactory-rich early environment is as important as a visually- and auditorily-rich early environment.

All of this should become much clearer during this decade. I foresee the importance of olfactory research increasing.

For whatever reasons, until relatively recently the fascination with the sense of smell was the province of the perfumer, the novelist and essayist, and the occasional scientist. This has now changed and we are in for some big discoveries and, almost certainly, some big surprises as well. As Lewis Thomas, Chairman of the Board of Directors of the Monell Center, has said: "We might fairly gauge the future of biological science, centuries ahead, by estimating the time it will take to reach a complete, comprehensive understanding of odor. It may not seem a profound enough problem to dominate all the life sciences, but it contains, piece by piece, all the mysteries."

References

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