

“Olfaction: Smell of Change in the Air” with Richard Doty

Transcript of Cerebrum Podcast



Guest: Richard L. Doty, Ph.D. is the director of the University of Pennsylvania’s Smell and Taste Center and the inventor of the University of Pennsylvania Smell Identification Test (UPSIT), a standardized olfactory test heralded as the olfactory equivalent to the eye chart. Dr. Doty is editor of the *Handbook of Olfaction and Gustation*, the largest collection of basic, clinical, and applied knowledge on the chemical senses ever compiled in one volume. He is an author or co-author of over 400 professional publications. His most recent books are *The Neurology of Olfaction*, co-authored by Christopher Hawkes and *The Great Pheromone Myth*. Among his awards are the James A. Shannon Award from the National Institutes of Health (1996), the Olfactory Research Fund’s Scientific Sense of Smell Award (2000), the William Osler Patient-Oriented Research Award from the University of Pennsylvania (2003), and the Association for Chemoreception Science’s Max Mozell Award for Outstanding Achievement in the Chemical Senses (2005).

Host: Bill Glovin serves as editor of *Cerebrum* and the *Cerebrum Anthology: Emerging Issues in Brain Science*. He is also executive editor of the Dana Press and *Brain in the News*. Prior to joining the Dana Foundation, Mr. Glovin was senior editor of *Rutgers Magazine* and editor of *Rutgers Focus*. He has served as managing editor of *New Jersey Success*, editor of *New Jersey Business* magazine, and as a staff writer at *The Record* newspaper in Hackensack, NJ. Mr. Glovin has won 20 writing awards from the Society of Professional Journalists of New Jersey and the Council for Advancement and Support of Education. He has a B.A. in Journalism from George Washington University.

Bill Glovin: Hi, and welcome to this month's *Cerebrum* Podcast. I'm *Cerebrum* editor, Bill Glovin, and I've hosted these podcasts for about a year now. It's been quite a learning curve for me. Initially, I used to conduct Q & A's with our *Cerebrum* authors but thought it would be easier for people to just hear our authors explain the article topic in their own words. I hope you're finding these *Cerebrum* podcasts useful, and you can always feel free to give me feedback at bglovin@dana.org. You can also find all our podcasts at dana.org/multimedia/podcasts and can subscribe to Cerebrum articles and podcasts by simply going to dana.org/cerebrum/archives and typing in your email address.

This month's podcast guest is Richard L. Doty, author of our most recent *Cerebrum* article, [Olfaction: Smell of Change in the Air](#). Dr. Doty is a giant in the world of smell research, and we're quite lucky to have him. He is director of the University of Pennsylvania Smell and Taste Center and the inventor of the University of Pennsylvania's smell identification test, which is sort of the olfactory equivalent to the art chart. He's also the editor of *The Handbook of Olfaction and Gustation*, the largest volume of clinical and applied knowledge on chemical sensors ever compiled in one volume.

Dr. Doty first got me juiced about olfaction a few years ago when he spoke at a presentation at the Rubin Museum in New York. That was about a new app being developed to bring all kinds of smells into your home, workplace, and car. During that talk, he briefly hit on olfaction's potential to detect and treat various neurological disorders and smell's considerable impact on mood and behavior and how olfaction research has lagged behind other research areas but is quickly catching up. I pestered Dr. Doty to write an article for us on olfaction ever since, peppering his email box several times, and his scheduled finally allowed him to take it on. We're thrilled to have him on the phone with us. Welcome, Dr. Doty. Let's begin with is smell something that we develop as infants, or is it partly genetic, or both? Or do we even know the answer?

Richard L. Doty: Well, certainly the smell receptors that we have at the top of the nose, which number around 10 billion, are present at birth so babies can smell most things, if not all things. Indeed, there's evidence that smelling can occur in the womb and that the receptors are active at that time. Having said that, much of what we know is that we'll develop identification or our abilities to identify odors as we grow older. Although, by the time we're four or five years of age, we know most of the major smells that we come upon. So there may be some development during life, but certainly smell is well-formed at the time of birth.

Bill Glovin: Tell us why smell and taste are so closely aligned.

Richard L. Doty: When we think of taste in an anatomic or a physiological sense, we think of the taste buds. The taste buds signify only sweet, sour, bitter, salty, and something called umami or savory. There's a possibility also, that metallic and some other slight different tastes are present through taste buds. Most of what we think of as tastes are really flavors, dependent upon the sense of smell. When you eat food, the molecules go from the food stuff up to the back of the nasal cavity, that is the nasal pharynx, to the olfactory receptors at the top of the nose. And that's what determines the flavor or what we in common vernacular think of as taste for most substances like chocolate, strawberry, raspberry, steak sauce, pizza; all these kinds of sensations are really smell mediated through that means.

You can test yourself and show this for yourself if you hold your nose shut and put coffee in your mouth. You'll notice the bitterness and the sweetness of the coffee, but you also notice the coffee sensation. As soon as you open up the nose, immediately the coffee sensation appears. The same with chocolate. Put a piece of chocolate in your mouth with your nose clamped shut, and you won't notice the chocolate sensation. As soon as you unclamp your nose, then the chocolate taste, if you will, comes through. That's because by closing off your nasal passage, you're closing off the passage of the oral cavity up to the back of the nasal cavity.

Bill Glovin: Well, I like broccoli, but you may hate broccoli. I like white wine, but you prefer red, or you might like an IPA type beer and I find it too bitter. What makes us so different?

Richard L. Doty: Well, a lot of things. Certainly, in terms of sweet, sour, bitter, salty we differ in terms of the types of receptors that are present. Some people can taste extremely bitter things or see bitter substances as very intense, whereas some people don't notice bitterness of what other people find bitter. Or a substance that other people find to be bitter. So, there are genetic causes of that. They're certain genes that dictate bitterness and our perception of bitterness. So, in many instances there are genetic determinants of our sensation that we perceive through the taste buds.

Also, in the olfactory system, there are big differences as best as we can tell, on individuals for their sensitivity to a number of chemicals. For example, hydrogen cyanide, which is a very poisonous substance, there's a certain percentage of the population that can't smell that. Those aren't the people that die. Studies show that those are the people with very low levels that cannot detect it. Some chemicals called amines have a fishy odor. Some people can smell them, other people can't. Those people who can smell these substances will tend to avoid very fishy-tasting fish, whereas those who can't will find these fish very, very tasty.

Bill Glovin: Olfactory receptor cells are present throughout the body in the lungs, heart, thyroid, kidneys, etc. That seems strange. Why is that?

Richard L. Doty: Well, I think there's a family of receptors that originally identified in the olfactory area on the cilia of the olfactory receptor cells. The assumption was made that that was their only function, but as people explored it more, they find the same types of receptors throughout the body. So, in a way, it's a bit of a misnomer to call them olfactory receptors now that we know they're present all over the body. They're really chemo receptors that happen to have first been identified within the olfactory system.

Bill Glovin: Smell is critical to so many things. They say that, even when choosing a mate, smell plays a huge part. Marketers now use it to sell things. And as you point out, smell is a way to alert us to danger. Can you hypothesize as to why, for example animals, have a superior sense of smell to humans?

Richard L. Doty: Yes. Interestingly enough, some animals that we think are superior to humans actually aren't superior. For example, the mouse. We can detect many tentacles at the same levels of concentrations as a mouse. The number one exception, of course, is the dog and many carnivores. In the case of the dog, you have many more receptor cells at the top of the nose, more cilia, which are the extensions that extend out from those cells and contain the receptor sites, and also larger brain areas associated with smelling. For example, in the dog, if you calculate the surface area of their cilia that contain the receptors, it's on the order of

about one and a half times the surface area of the whole body. In the human, that same calculation indicates the receptor area to be only about seven square inches. So, you certainly have anatomical and physiological differences between species that dictate, to a large degree, these differences in the ability to smell.

Anyone who owns a dog realizes that they seem to dream in terms of smell, as they'll wake you up barking at something and sniffing while they're dreaming. Presumably, they can think or conceptualize, perhaps, in terms of smells, where it's very rare, or almost impossible for people to do that. So, it's a complicated issue, but it stems from the receptors all the way up to the areas of the brain.

Bill Glovin: It makes sense that pleasant smells might improve your mood and maybe make you less depressed, but can you explain how smell might help to predict Parkinson's and Alzheimer's?

Richard L. Doty: Well, we now know from empirical testing that smell loss can occur very early on in both Alzheimer's and Parkinson's diseases. In the case of Alzheimer's disease, smell loss often occurs in the so-called mild cognitive impairment period. Those individuals who have smell loss early on and that early stage of dementia will be more likely to go on to have a diagnosis, ultimately, of Alzheimer's disease. In the case of Parkinson's disease, the same situation applies. That is, smell loss occurs very early on in the disease process, indeed in some cases ten, fifteen years before the motor dysfunction occurs. We think the reason for that, in the case of Parkinson's disease, is the fact that damage to the olfactory area in a region called the olfactory bulb occurs very early on in the disease process.

Certain pathological indices we call Lewy bodies, and alpha synuclein related anomalies occur within that structure early on, long before these pathologies appear in the motor system. And in the case of Alzheimer's disease, pathologies seem to appear in the olfactory system prior to the cortex and regions where there is known to be cognitive dysfunction. So, there are really anatomical and physiological reasons why smell dysfunction occurs early on in these disease processes.

Having said that, a study that we published in *Lancet Neurology* recently, we probed the idea that perhaps there's something even earlier than the disease-specific pathology that I just mentioned. Looking at certain areas of the brain and their damage early in the disease, various diseases and the varying degrees of damage to those areas suggest that acetylcholine and some neurotransmitter deficiencies may be the root cause of the smell loss associated with a wide variety of neurological disorders. This is a little far out, in terms of the way people think about these things, but that's a hypothesis that we're eagerly pursuing at the present time.

Bill Glovin: Does olfaction get the kind of NIH funding that it needs?

Richard L. Doty: Well, like many areas, it certainly does not. Most physicians do not even bother to test smell, ask about it, it's not common in most neurological evaluations, so it's never been a major component of medical books and so on until relatively recently. Even now, it's not a major component. But certainly it shows up on the chapters on olfaction now in most major medical books. Certainly, from the funding point of view, it doesn't receive that much attention. Additionally, physicians can't get reimbursed for giving smell tests from insurance companies and so on, so therefore there is no incentive financial for physicians to spend time testing their patients for smell. I think if that reversed itself, it would become like vision and hearing, those kinds of tests, would be very uniform in medical centers and in doctor's offices, but currently that is unfortunately not the case.

Bill Glovin: Is there anything that you do or you can do or other people are doing to try to kind of enlighten funders and other medical colleagues as to the importance of olfaction?

Richard L. Doty: Well, I think the medical literature, certainly those that follow it or are involved in the neurological literature in the textbook, but certainly also the ear, nose, and throat literature, there's massive amounts of evidence of the importance of sense of smell in the everyday life of people as well as markers for these predetermined diseases, for example. So, it's getting out there more and more and more, it's just that funding agencies are constrained. The whole world of medicine is changing dramatically in terms of molecular biology and genetics, so the expansion that's occurring in knowledge is not being paralleled by the expansion in funding, unfortunately.

You know we're on the verge of curing various kinds of cancers. That's really exciting, but the funding, unfortunately, is not there in these areas like it should be. And, of course, the government under the current administration, is talking about cutting back funding across the board, so it's really unfortunate, because we're at the verge of real exciting advances in olfaction and taste that will have medical implications for all of the future.

Bill Glovin: Do you see more young researchers in this area?

Richard L. Doty: Not necessarily, unfortunately. There are so many interesting areas of medicine to go into, and certainly in the measurement field, what we call psychophysics, that has not attracted as many researchers as we'd like to see, but all we can do is continue to emphasize the importance of these senses, and hopefully more people will be interested in pursuing research careers in these areas.

Bill Glovin: And what is the international climate like for this research? Is it more prevalent in the United States, or maybe elsewhere?

Richard L. Doty: It's more prevalent, unfortunately, at least at the clinical level, in Europe as well as in Japan, than in the United States. Proportionately more clinicians are

administering small tests and so on and so on. We're certainly leaders, but the number of publications coming out in the European Union, for example, on olfaction per capita are much higher than what we have here in the United States.

Bill Glovin: When I saw you at that Rubin event a couple of years ago, in terms of development of that app that would deliver different smells digitally, has that happened yet or is it close to happening?

Richard L. Doty: I haven't been abreast of that as much. So far, I haven't seen that it's taken off particularly. Over the years, there've been many attempts to try to present odor into public spaces, into cars and homes and so on. In fact, the classic examples were in theaters where they would have smells come out during a movie depicting odors at the time of certain events in the movie. Many of these haven't been that successful. I think partly because people differ in terms of their preferences for odors and what some people like is an odor other people don't like. So, it's been difficult, but there are certainly circumscribed situations where that is being done and can be done, but I think only the future will tell if this is going to take off as viable commercial entities.

Bill Glovin: I remember when I worked at Rutgers, I did a piece on a marketing professor at Rutgers-Camden that was involved in olfaction in terms of marketing. It did seem like a lot of retailers were very interested in it.

Richard L. Doty: Yes. I think there are certain situations where odors play a very good role. I mean, if you have a chocolate factory or a chocolate stand or you're a restaurant and you put chocolate out for the smell, it does attract people. Certain odors are useful in that regard. So, increasing appetite. People maybe almost unconsciously appreciating smells that are coming out. Most of us maybe walk down the street and smell bread from the bread factory or whatever, and it's attracted us. So I think there are instances where that can be useful, and that there are cases where it's been tried out at casinos and things like this to see if they get increased gambling behavior. Things like that. Whether these efforts have been sustained and have proved to be that useful is another story. But certainly there have been many attempts to try this sort of thing.

Bill Glovin: Is there anything I left out that you care to mention or you think is important?

Richard L. Doty: Well, I think it's important to realize that odors not only are critical for determining the flavor of foods and beverages, but for our safety. If you don't have a sense of smell, you are much more likely to die in the next three years, if you're an older person, for example. That study that we did, and others have done, we did a very nice study with individuals at Columbia University and made a joint effort, so we know that odors play a very important role in that regards. Safety is critical.

US armed forces, now, if you can't smell, at least according to the medical regulation, you're not allowed into the armed forces. So they view odors as important. Presumably because of poisonous gases, or war gases. Also, if you're in an aircraft and can't smell a burning electrical wire or can't smell fire, or you're on a ship and the same thing happens, then you're at peril.

We all take these senses for granted, that is the sense of smell, in particular, and yet when we lose it, it becomes very important. We lose weight or gain weight, depending on how we treat the situation. Many people no longer want to go out to dinner, and they don't enjoy hearing their friends talk about how good a meal is. So it has all kinds of implications for everyday life when these senses go awry.

Bill Glovin: Well, this is certainly a fascinating subject, and I very much appreciate all your wisdom that you bring to it, and I want to just thank you again for the wonderful article. It's been great.

Richard L. Doty: Well thank you. I really enjoyed writing that piece, then I enjoyed working with you and want to thank you, as well.

Bill Glovin: And that wraps up this month's *Cerebrum* Podcast. Join us next month when we talk about the fascinating and ever-evolving world of brain stimulation with Alvaro Pascual-Leone, author of "The Illusion of the Perfect Brain Enhancer." Dr. Pascual-Leone is a professor of neurology and an associate dean for clinical and translational research at Harvard Medical School. I'm editor, Bill Glovin, and thanks for being with us.