

## **How humans distinguish between smells: A biological, molecular and psychological investigation into olfactory function**

### Overview

Teaching introductory chemistry to middle school students may often prove to be a frustrating task. The new concepts can be abstract and therefore difficult for students to visualize and comprehend. Of all the science disciplines that I have taught, I have found that chemistry requires more of my creative input to keep the lessons inquiry based and hold the students' interest. So the question became: is there a way to teach middle school students chemistry with a theme that will hold their attention and what would intrigue them and spark their interest?

The idea of the chemistry of smells came to me while teaching after lunch one afternoon. The room seemed to be filled with a variety of distinctive middle school aromas ranging from fragrant body spray deodorants and colognes to perspiration and/or stink bombs. As this was a topic I thought all middle school students could relate to, I decided to investigate the connection between smells and chemistry and teach the introductory chemistry unit with this new theme. I also thought this topic would allow for the integration of interdisciplinary lessons such as anatomy and physiology.

In order to successfully create the chemistry of smells unit, I had to first understand how humans were able to detect odors. Although students think that the nose simply smells an odor, the process is actually quite a complicated one. It was not until 1991, when a groundbreaking paper by Richard Axel and Linda Buck was published, that the mystery behind the olfactory system was revealed. An odorant molecule does indeed travel into the nose, but its journey does not stop there. Inside the nose, the molecule attaches to an olfactory nerve cell which in turn sends signals to the brain and the odor is sensed. Although the receptor site model was a breakthrough, there are still many concepts not fully understood by scientists and as a result there is still significant research being conducted. For example, scientists are researching exactly how the olfactory cortex decodes information once it receives signals from the olfactory bulb (Axel, 2006).

My capstone project took a turn in a new direction after an interview with Dr. Charles Wysocki of the Monell Chemical Senses Center in Philadelphia. He suggested that I research the branch of odor studies being conducted on human odor perception. It

was fascinating to read the various studies that were researched in the connection between memory and smell, commonly known as Proustian memories. This phenomenon is described as a powerful memory which is elicited in the presence of a particular odor and unique to an individual. For example, the whiff of a certain perfume may elicit a powerful memory to one person and simply smell pleasant to another. Research has been conducted in many areas of this field including the connection between behavior and smell and the effects of personality disorders on the olfactory system.

The pedagogy piece consists of a two week unit focusing on the chemistry of smells. It incorporates a variety of inquiry based and hands-on activities that allow students to investigate basic chemistry concepts while also learning about the olfactory system. The final assessment requires students to synthesize all of the information they have learned throughout the unit by conducting an authentic scientific study and then presenting their findings to the class at a symposium.

My capstone project has afforded me the opportunity to take a unit that was good and make it even better. By incorporating the theme of smell, I hope that the students will be even more engaged and more excited about learning chemistry concepts such as atoms, molecules and chemical bonding. In addition, they should also benefit from the interdisciplinary lessons and gain experience in conducting their own authentic research study.

## Introduction

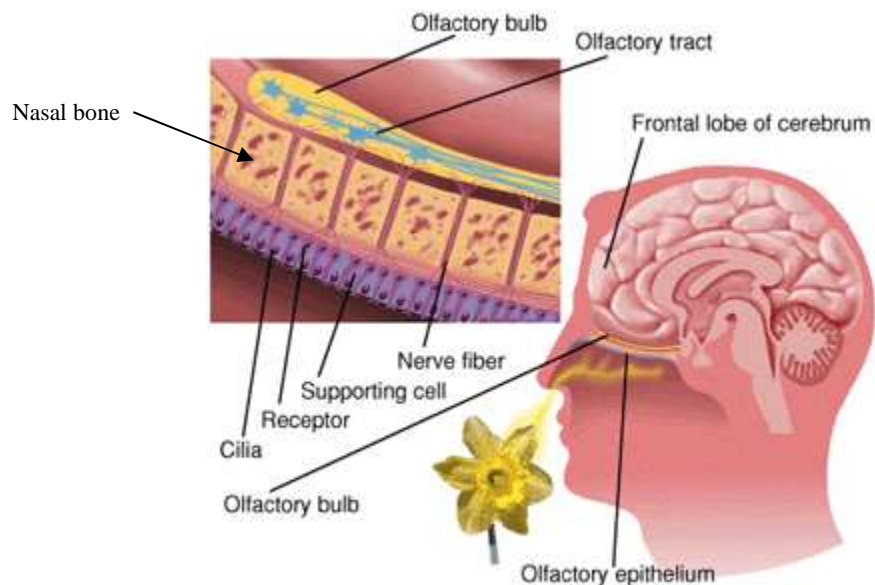
In the world of studying odor, there is an intersection of cultural, historical, behavioral and scientific observations. Researchers have taken a multidisciplinary approach in order to fully understand the entire picture of how and why humans detect aromas as being pleasant or unpleasant. Recent attempts by the US military to create a “stink bomb” have proved unsuccessful. The military could not find a single odor that proved to be repulsive when described by a variety of ethnic groups (Dilkes, Dalton & Beauchamp, 1999). Why is this? What makes one human perceive an odor as pleasant while others do not? In order to understand how humans smell, research involving the complex, and not entirely understood, mechanisms of the olfactory system were studied along with current psychological studies. Many scientists believe that humans learn how to smell based on their past experiences. A quintessential example of this idea was demonstrated in a study conducted by Cain and Johnson (1978). The researchers conducted their study in both Britain and the United States. Participants were asked to rate the pleasantness of the smell of wintergreen. The participants in the United States gave the aroma one of the highest ratings, while participants in Britain gave it one of the lowest. This discrepancy can be explained by their past experiences with the wintergreen aroma. In Britain, wintergreen was often associated with medicine and typically connected to a negative experience. In the United States, wintergreen scents were associated with candy and often related to a positive experience. This example illustrates the complexity and interconnectedness of the phenomena related to sensing and interpreting odors. My project attempts to shed light on the fundamentals of a few of these phenomena.

## Anatomy of the Nose and Brain

Prior to discussing the physiology of the olfactory system, the basic anatomy of the nose and brain should be understood (see Figure 1). When humans breathe in air, it travels through the nasal passages which are lined with mucus membranes. These mucus membranes aid in filtering out unwanted particles from the inhaled air and secrete a mucus layer that lines the nasal passage (Krogh, 2005). The olfactory epithelium is a specific area of the mucus membrane that houses the olfactory nerve cells, and is located

at the top of the nasal cavity (Axel, 2006). Olfactory nerve cells, also referred to as neurons or receptor cells, transmit olfactory information to the brain upon being triggered by an odorant molecule in the inhaled air. Neurons are made up of three main parts called the dendrite, the cell body and the axon.

The dendrite of the olfactory receptor cell is capped by numerous hair-like cilia. It is in these cilia that the receptor proteins are expressed. At the opposite end of the cell body, the axons, long thin projections of each neuron, extend up through the nasal bone to a part of the brain called the olfactory bulb (Axel and Buck, 1991). The olfactory bulb is the area of the brain that conducts initial processing of odor information. This process takes place in structures called glomeruli. One glomerulus houses tens of thousands of axons from the receptor cells as well as dendrites from other neurons that then connect the olfactory bulb to the other regions of the brain (Axel, 2006). The axons of these cells transfer information by traveling via the olfactory tract to other parts of the brain, in particular the limbic system. The limbic system includes the amygdala, the hypothalamus and the hippocampus. The amygdala, which synapses directly with the olfactory nerve, is critical for emotional associative learning, as it is the part of the brain that is associated with emotion, primarily fear. It is essential for human olfactory memory in particular. The hippocampus and hypothalamus regions of the brain are associated with both emotion and memory.



*Figure 1.* The receptor proteins are expressed in the cilia. The receptors are activated when odorant molecules bind to them and signals are sent to the olfactory bulb and eventually higher regions of the brain. Adapted from prenhall.com (1999).

### Breakthrough Description of Mechanism for Odor Discrimination

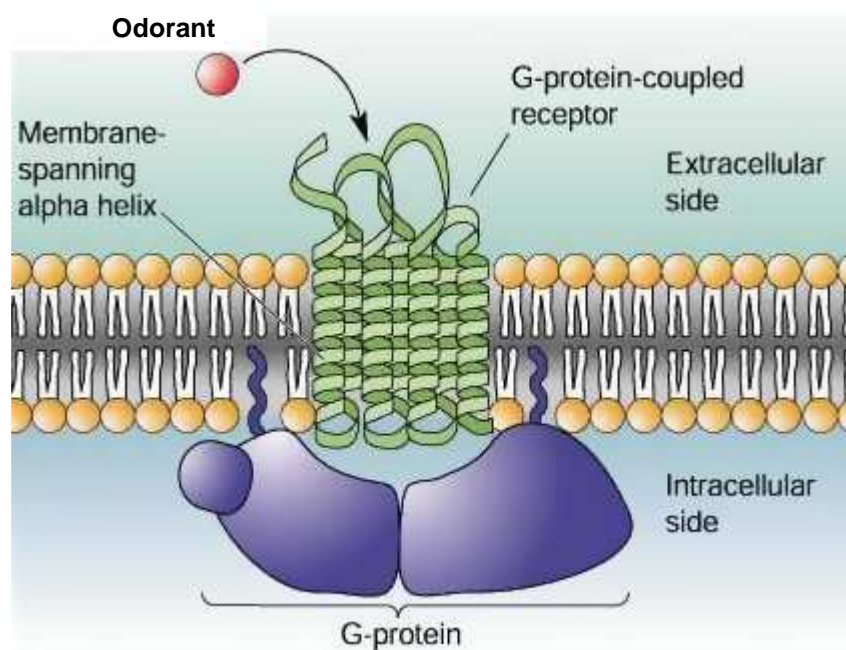
In 1991, a groundbreaking paper was published by Richard Axel, a professor at Columbia University as well as an investigator at the Howard Hughes Medical Institute, and Linda Buck who, at the time, was a post doctoral fellow in the Axel lab and is now a professor at the Fred Hutchinson Cancer Research Center. Axel and Buck were awarded the Nobel Prize in 2004 for their studies detailing how the mouse olfactory system works. Because of the technical difficulty involved in studying receptor proteins, the pair chose to study the genes that code for them instead. All neuron cells contain a copy of all of a human's genes. The neurons in the olfactory system do not utilize all of the genes; only certain ones are expressed, or used to create the corresponding proteins. This occurs when the DNA is transcribed into mRNA in the nucleus. The mRNA then leaves the nucleus and travels to the rest of the cell, specifically the ribosomes. In the ribosomes, the mRNA is read and proteins are created. It was much less difficult for Axel and Buck to isolate the mRNA from the cell and convert it to DNA than to sort through all of the genes located in one cell. From the DNA created in the lab, the researchers used the Polymerase Chain Reaction (PCR) to amplify the particular regions of DNA that corresponded to odorant receptor genes, and then obtained these genes' sequences to determine which of the 1300 odorant receptors a particular mouse neuron may have (Axel, 2006). The newly created DNA was derived from a single neuron, which had already been tested for its response to a range of odorants. Because they only found one type of receptor mRNA in each neuron they tested, they concluded that each neuron must only feature one type of receptor.

Until Axel and Buck published their study, very little was known about how humans perceived and recognized a wide variety of odorants. Prior to their work, scientists knew that mammals could discriminate between odorants, but the mechanism remained a mystery. One hypothesis to explain the large number of detectable aromas was that there could also be a large number of receptors that could react with a single or small number of odorants. That would mean that there would have to be upwards of 10,000 different odorant receptors in order for humans to smell all of the odors that they are capable of smelling. Alternatively, there could be a small number of odorant receptors that could recognize a large number of odorants, by being less selective in how closely

the odorants must match the binding site (Axel and Buck, 1991). Axel and Buck believed that members of a large multigene family encoded the individual odorant receptors, but their results suggest a large family of distinct odorant receptors.

### Physiology of the Olfactory System






Odorant molecules in the air we breathe travel into the nasal passage. The molecules become trapped within the mucus layer, giving them access to millions of neurons inside the nose. The odorant molecules then come in contact with G-protein coupled receptor proteins (Figure 2) that are located on the end of the cilia (Axel, 2006). When the receptor proteins interact with the odorant molecules, there is a structural change in the receptor proteins, which induces change in the associated G-proteins. This initiates the process that eventually leads to the transmission of the electrical pulses along the olfactory sensory axon (Axel, 2006). The cascade of events begins with generation of cyclic AMP, leading to an increase of calcium in the cell. The increase in calcium leads to a depolarization of sensory neurons and as a result they become more positively charged. When the threshold is reached, an action potential is fired off. The signal then travels through the axon that extends to the olfactory bulb region of the brain.



*Figure 2.* The odorant binds to the G-protein coupled receptor located on the neural cell membrane, initiating the cascade of events that leads to an action potential. Adapted from [www.csuci.edu](http://www.csuci.edu) (2005).

The particular axons that are activated depend upon which receptor protein is targeted. Each cell produces only one type of receptor protein. In humans, there are approximately 350 different types of receptor proteins produced (Axel, 2006). In other mammals, such as mice, the number of different receptor proteins could be upwards of 1000 (Axel, 2006). Because there are millions of neurons in olfactory bulb, there must be a duplication of many of the types of receptor proteins. In other words, there are thousands of each of the 350 types of receptor proteins found within the human nose. If the system worked like a lock and key, where only one receptor protein fit with a specific odorant molecule, we would only be able to smell 350 different odorant molecules. However, it has been determined that humans can smell upwards of 10,000 different smells. How is this possible?

Although each receptor protein contains a similar segment inside the membrane, the regions on the outside of the membrane must be different in order to bind to different odorants. Since we can smell far more than 350 odorants, the inference is that specific odorant molecules must be able to activate more than one series of protein receptors. Dr. Charles Wysocki of the Monell Chemical Senses Center in Philadelphia compared this concept to keys on a piano (personal communication, July 3, 2007). He explained that each key may represent a receptor protein, the player's fingers the odor molecule, and the sound produced would be the perceived smell. The player's fingers could play the same keys as well as combinations of keys, or chords. There are many more combinations of keys than just keys alone. Figure 3 depicts how one odorant molecule may be detected by one or more odorant receptors. Each combination will elicit a specific odor perception within the brain, just as striking a combination of keys on a piano will produce a specific sound. Receptor proteins must be able to accept many different kinds of odorant molecules and one odorant can bond to one receptor. In other words, the number of molecules that each odorant receptor can detect is finite. Each odor molecule may bind to several different receptors and therefore has a unique combination of odorant receptors that may range from one (lone piano key) to several (a chord). Different chemical structures, therefore, will activate a different combination of odor receptors.

Odorant receptors	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Description
<b>A</b> 					●										rancid, sour, goat-like
<b>B</b> 		●				●									sweet, herbal, woody
<b>C</b> 	●			●	●		●			●	●				rancid, sour, sweaty
<b>D</b> 		●			●	●									violet, sweet, woody
<b>E</b> 	●			●	●		●	●		●	●	●			rancid, sour, repulsive
<b>F</b> 				●	●		●			●					sweet, orange, rose
<b>G</b> 	●			●	●		●	●		●		●		●	waxy, cheese, nut-like
<b>H</b> 				●	●		●			●		●			fresh, rose, oily floral

MODIFIED AFTER LINDA BUCK AND COLLEAGUES IN CELL VOL 96, MARCH 5, 1999

Figure 3. Odorants are detected by a combination of odorant receptors which elicit a wide variety of odor perceptions within the brain. Reproduced from [www.nobleprize.org](http://www.nobleprize.org) (2004).

More recent research conducted by Malnic, Hirono, Sato and Buck (1999) supports three important points regarding the theory of combinatorial receptor codes described above. To identify the odorant receptors that recognize specific odors, the researchers used calcium imaging and single-cell RT-PCR. The study used four types of odorants that included carboxylic acids with straight carbon chains (ranging from 4-9 carbon atoms), corresponding aliphatic alcohols, bromocarboxylic acids and dicarboxylic acids. There were a total of 24 individual odorants tested. To identify which receptors responded to the specific odorants, olfactory neurons from mice were first placed on cover slips and loaded with fura-2, a dye that when added to cells responds to ultraviolet light when bound to calcium. When the neurons respond to odorants, there is an increase in intracellular calcium that can be detected with an ultraviolet light (calcium imaging). After the calcium imaging, a two-step single cell RT-PCR procedure was implemented to identify odorant receptor genes expressed by individual neurons (Malnic, *et al.*, 1999). Of the 647 mouse olfactory neurons that were tested, 98 responded to at least one of the test odorants during calcium imaging. From that subset, receptor cDNAs were obtained using RT-PCR from 14 of 47 neurons tested.

The mechanisms that explain how mammals discriminate between odors can be broken down into three categories. The first is that a single receptor can recognize



multiple odorants. Malnic, *et al.* (1999) discovered that approximately 86 percent of the neurons where odorant receptors were identified were tested and found to recognize only one test odorant, but an average of four odorants per receptor was determined. Their research showed that both structure and functional group were important. Patterns were detected in the length of the odorant molecule's carbon chain. For example, some of the odorant receptors were able to recognize odorants possessing seven to nine carbon atoms while other odorant receptor recognized odorant molecules with carbon chains of five through seven (Malnic, *et al.*, 1999). One of the 47 odorant receptors recognized odorant molecules possessing carbon chains of all lengths (Malnic, *et al.*, 1999). None of the odorant receptors were able to recognize all four classes of odorant molecules.

The second key point supported by Malnic, *et al.* (1999) is that each single odorant is recognized by multiple receptors. Eleven of the seventeen odorants that were recognized by at least one receptor in the mouse neurons tests were able to be recognized by two or more of the odorant receptors (Malnic, *et al.*, 1999). This demonstrates that odorants are capable of binding to more than one receptor. It was also determined that odorant receptors that were highly genetically related or nearly identical would recognize the same odorant.

The research conducted by Malnic, *et al.* (1999) also supported the idea that different odorants are recognized by a distinct combination of receptors. Each odorant receptor may recognize multiple odorants; however all of the odorants were recognized by a specific combination of odorant receptors. For example, eight of the odorant receptors that recognized bromooctanoic acid also recognized other odorants, but none of the other odorants tested were recognized by the identical combination of eight odorant receptors (Malnic, *et al.*, 1999). Each of the odorants tested were recognized by their own unique combinations of odorant receptors.

Although the olfactory nerve cells are distributed randomly throughout the olfactory epithelium, all of the same type of olfactory neurons' axons meet in the same glomerulus in the olfactory bulb (Axel, 2006). These axons then excite the mitral nerve cells, and that signal is forwarded to the limbic parts of the brain as described in an earlier section.

What happens to the signals from the odorant receptors once they reach the higher areas of the brain? There is not a full understanding yet as to how the information received from the odorant receptors are represented in the olfactory cortex, nor is it understood how the individual components of odor codes are decoded to detect the perception of an odor (Malnic, *et al.*, 1999). Although researchers know that signals from the olfactory neurons ultimately reach areas of the brain such as the amygdala and hypothalamus, it is not know if those areas receive the information as a whole, or if the signals are “routed” out to different areas depending upon the code.

### Molecular basis for pleasant and unpleasant odors

What allows humans to detect a smell as being pleasant? Is there a commonality between the structure of odorant molecules that smell pleasant and those that smell unpleasant? One group of chemical compounds that have typically been associated with pleasant smells is esters. Many esters have distinctive odors and as a result have been used in artificial flavorings and fragrances. Recognizable smells may include citrus odors such as pineapple, cherry, and raspberry. Other pleasant smells, such as lavender, cinnamon and peppermint are also examples of esters. There are also some esters that could be classified as unpleasant, such as airplane glue, nail polish remover and model paint.

Carboxylic acids are very polar compounds due to the presence of hydrogen bonding sites. Many carboxylic compounds, especially those with low molecular weights and therefore high volatility, are associated with unpleasant odors. Molecules with higher molecular weights do not exist in the gaseous state, but instead in the solid state and therefore we are unable to detect their odor. Examples of carboxylic acids with unpleasant odors are butyric acid, which is the odor associated with gas gangrene and rancid butter, acetic acid (vinegar) and formic acid which is used by ants as a defense compound (Denniston, Topping & Caret, 2007). However, carboxylic acids are also be associated with the aromas of strong cheeses such as Parmigiano-Reggiano, which some people perceive to be an excellent cheese with a pleasant aroma.

There are several factors that may influence molecular codes and odor perception. The first is that a small change in the structure of a molecule may result in a

dramatic change in the way mammals perceive the odor. The change of a functional group may result in the perception of two very different odors. For example, the carboxylic acids listed above were described as unpleasant using terms such as rancid or repulsive while alcohols with the same chain length were described as pleasant using terms such as herbal or flower-like. Malnic *et al.* (1999) compared the odorant receptors that recognized acids and alcohols with the same carbon chain and found that while some of the odorant receptors recognized both, they were recognized by different combinations of odorant receptors. This research suggests that changes in the perceived quality of the odorant where the structure has been altered may be a direct result of changes in the receptor codes (Malnic *et al.*, 1999).

Another factor influencing perceived odor may be the concentration of the odorant molecules. Some odorants may be perceived in various different ways depending on the concentration. An example of this is thioterpineol, which can smell very different at various concentrations. At a low concentration, this odorant may be perceived as a tropical fruit. At a slightly higher concentration, it may be perceived as having a grapefruit-like odor and at an even higher concentration it may be described as having a garbage-like smell. A change in concentration will change the receptor codes and therefore a change in the perceived smell (Malnic *et al.*, 1999), perhaps based on weaker binding to some of the receptors that make up the odorant's code. In addition, some odorants can be detected at lower concentrations than other odorants. This may be explained by research indicating that the complexity of the odorant code may relate to how easily it is detected (Malnic *et al.*, 1999). The size of the code may also relate to difficulty in human detection of certain smells. If an odor is recognized by one odorant receptor and there was a gene mutation in which that receptor was nonexistent, that odor would not be able to be detected.

#### Why do humans perceive the same odors differently?

Both neurological and behavioral studies have been conducted regarding odor-evoked memories. Although neurological testing involves using scientific technology such as positron emission tomography (PET) and magnetic resonance imaging (MRI), many of the behavioral studies conducted are based on more subjective measures. This is

mainly due to the difficulty in controlling the quality of the odorants in the laboratory setting. Both the exact amounts of odor presented to subjects as well as the way the odors are presented must be controlled in precise and reproducible ways (Herz, 2000).

It is now commonly accepted, through the results of various experiments, that there is a connection between emotion, memory and smell. During the experiments, two aspects of memory were focused on most frequently: accuracy and emotion. Accuracy was defined as the detail and precision to which the event is recalled whereas emotionality was defined as the quality and/or intensity of the emotional accompaniment (Herz, 2000). During the course of the experiments, odor was not found to be any more or less powerful than any of the other senses such as sight, touch or hearing. In other words, odor was just as effective at evoking a memory as when a subject saw a picture of the object, touched the object, or heard the name of the object. Where odor-elicited memories differed from those elicited by the other senses was emotionality. Subjects were able to describe more emotions when presented with olfactory cues than when using their other senses.

Additional experiments conducted by Rachel Herz support these findings. In 2004, she studied the emotional qualities of memories evoked by three specific cue items (a campfire, fresh-cut grass and popcorn). The sensory cues (olfactory, visual or auditory) were introduced to the subjects after the initial memory was recalled. This was to ensure that memories evoked by subjects were not influenced by the memory cue itself. In this study, subjects were first given a verbal cue (e.g. the word campfire). They were then asked to think of a person, place or event from their past, defined as an autobiographical memory and then rate it on a variety of dimensions (Herz, 2004). These included emotionality, vividness, evocativeness, and specificity. Subjects were then exposed to visual, auditory and olfactory cues, such as a picture of a campfire or the smell of the campfire. They were then asked to rate the memory again using the same four scales. This method was thought to produce more reliable data, as the emotional quality cited by the subjects would be due to the processes occurring during the sensory recollection and not memory selection (Herz, 2004). Results from this study showed that odor-evoked memories elicited the most emotional responses.

Herz (2005) also hypothesized that odor and emotionality were linked due to a learned behavior and believed that the process was twofold. First the emotion that occurs during the time that the odor is perceived becomes associated with that odor. Second, re-exposure to the odor can then elicit that emotion and therefore have an effect on mood. Emotional odor-associative learning demonstrates how humans can smell the same odor but may either like or dislike that odor based on past experiences. Several studies have supported this hypothesis (Dilks *et al.*, 1999; Cain and Johnson, 1978; Herz, 2004).

Herz and Epple (1999) tested how ambient odors associated to odors influenced cognitive performance in children. A group of five-year-old children were given a maze that could not be solved and thereby induced a feeling of frustration or failure. While experimenting with the maze, the children experienced either one of two fragrances that were agreed upon by adults to smell pleasant, or no odor at all. After experiencing the maze and odor, the children were then given a break and then a cognitive performance test. The room where the children took the test was scented with the same odor they experienced during the maze activity, a different odor or no odor at all. The test consisted of a worksheet that had forty puppies, twenty of which were missing their tail. The children were instructed to identify the puppies that were missing their tail within a ten second time period. The children were judged on emotion based on facial expressions and verbal remarks. Children who performed the cognitive test under the same conditions under which they conducted the maze activity had lower scores, regardless of which odor, or lack thereof, they had been exposed to. Results supported the hypothesis that emotional experience can become conditioned to odor and influence behavior (Herz & Epple, 1999). It also supports the view that humans can learn to associate a specific smell with an emotion or experience. In this case, the children associated a specific smell with failure or frustration and when exposed to that same odor again, it elicited similar emotions.

A recent publication reported the effect of emotional stimulation on olfactory sensitivity and odor judgment (Pollatos, Kopietz, Linn, Albrecht, Sakar, Anzinger, Schandry & Wiesmann, 2007). This research differed from previous research because it looked at the effects of emotion on olfaction instead of the effects of olfaction on emotion. In this study, subjects were exposed to emotional stimuli that consisted of a

series of pictures. The pictures were categorized as pleasant, unpleasant or neutral by the subjects using a scale of one through nine, with one being very unpleasant and nine being very pleasant. Subjects were then exposed to two of the pictures for five seconds. At that time, the participants' eyes were covered and they were exposed to the various odors. They were then asked to rate the odor in terms of both pleasantness and intensity. The results showed that viewing pleasant pictures prior to a smell evoked a feeling of perceived pleasantness while viewing negative pictures prior to a smell brought about feelings of unpleasantness. The emotional state did not affect perception of odor intensity, although men experienced higher intensity ratings across all emotional states. In sum, this study showed that a negative emotional state accompanied unpleasant odor perception and that a positive emotional state accompanied pleasant odor perception.

Some research has specifically targeted the effect of not only emotion, but also specific personality characteristics, such as anxiety or neurosis, on olfactory perception. In other words, do humans who are classified as anxious or neurotic perceive odors differently than those who are not? It is currently believed that those individuals are more sensitive to unpleasant stimuli in general, whether it is auditory, visual or taste. Chen and Dalton (2005) specifically investigated the olfactory senses by using emotionally toned film clips to evoke emotional states prior to exposing subjects to pleasant, unpleasant or neutral odors. Subjects categorized their emotional state as happy, sad, negative/hostile, fearful, and neutral and then rated that emotion on a scale from 0-4 (0= not at all, 1=a little, 2= moderately, 3=quite a bit, 4= extremely). They were also asked to rate the intensity of the odor on a scale of 1-9 (1= extremely mild, 9= extremely strong). Personality was measured by standard scales. Neuroticism and introversion used the Eysenck Personality Questionnaire Revised- Short (EPQ-RS) (Eysenck and Eysenck, 1994) and anxiety used the Taylor Manifest Anxiety Scale (TMAS) (Taylor, 1953). Results from this study showed these personality characteristics did not directly influence olfactory experience; however, it did affect the olfactory intensity. The neurotic and/or anxious subjects were more responsive to both pleasant and unpleasant odors. Women in this category perceived the odors as stronger while men in this category detected them faster (compared with neutral odors). This study shows that the personality of a human may affect why humans may perceive the same odor differently.

In addition to behavioral studies, there is also neuroimaging evidence to support that odors are more emotional and evoke stronger memories than other senses such as sight, hearing or taste. Hertz, *et al.* reported on a study in 2004 to investigate the emotional potency of odor-evoked memories. Functional magnetic resonance imaging (fMRI) was used to view the brain, specifically the amygdala and hippocampal regions because they were thought to play a crucial role in recall of odor-evoked emotion (Hertz, *et al.* 2004). Subjects were interviewed prior to the scans and asked to describe a perfume that they associated with a memory. Subjects who described a positive, autobiographical visual and odor-evoked memory were chosen for the test. At the scanning procedure, the perfume that the subject described was infused into the scanning chamber. In addition to the perfume, three other sensory stimuli including a control visual, control odor, and an experimental visual were presented to the subjects. Results from the fMRI scans showed that significantly greater activation occurred in the amygdala and hippocampal complex when the subjects were exposed the perfume they described compared with the other three stimuli. This study supported the anatomical and behavioral research that there is a strong connection between the olfactory system and the amygdala and hippocampal regions of the brain which play a large role in emotion and memory.

### Conclusion

The olfactory system and its mechanisms are topics of active research. Although there has been significant experimental evidence to support both physiological and psychological hypotheses regarding the mechanisms and roles of olfaction, there is still much to be learned about mammalian odor detection. For example, what role do pheromones play in behavioral and physiological responses in animals? How do the experiences of emotion and memory differ in people who lack a sense of smell, a condition known as anosmia, from a person with a fully functioning olfactory system? How does the olfactory cortex decode the signals it receives from the olfactory bulb? These and other questions may be investigated as new technologies, such as the fMRI scans, become more commonplace in studying odor. Understanding the complex olfactory system is important because it allows scientists to better understand the connection between the brain and a familiar, everyday function such as the sense of

smell. The olfactory system has proved to be an intriguing area to investigate the crossroads of several branches of science and may hold the key to unlocking elusive mysteries about the human brain.

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