A "SENSE" OF ATTRACTION

The Role of Pheromones in Behavior

By Lauren Schumacher

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Walking down the street, you pass by someone to whom you are immediately drawn. You've never met this person before, yet you feel a tangible attraction. Did you glimpse an appealing smile? Hear a sonorous voice? Catch a scent that reminded you of an old fling? Or could you have picked up on cues impossible to recognize on a conscious level?

Recent research, including work done in the lab of the Harvard Higgins Professor of Molecular and Cellular Biology, Catherine Dulac, has demonstrated that chemical signals known as pheromones play a crucial role in attraction and courtship for many mammals (1). Scientists are just beginning to understand how pheromones affect behavior. Some studies suggest that even people's behavior may be influenced by pheromones although we are not aware of their effects.

What are Pheromones?

Pheromones are chemicals secreted by an individual, for instance through sweat, which convey information to other members of the same species who can instinctively interpret these signals (2). Pheromones are similar to smells in how they are detected, but instead of processing them as smells, they are processed as signals that can communicate messages such as aggression, identity, territory possession, and reproductive interest (3).

Research on rodents indicates that pheromones can be detected by both the main olfactory system and the accessory olfactory system (2) (Figure 1). In the main olfactory system, inhaled pheromones, as well as other odors, pass into the nasal cavity to the olfactory epithelium. In the olfactory epithelium, they bind to specific odorant receptor proteins, activating attached olfactory receptor neurons that send electrical signals to the main olfactory bulbs which are then relayed to the olfactory cortex for further processing (3). Interestingly, in the olfactory cortex, some neurons are stimulated only by combinations of certain odors and not the individual chemicals in the mix, treating mixtures like a distinct scent (4).

Other, often less volatile, pheromones are detected by the accessory olfactory system in rodents. In this case, pheromones enter the vomeronasal organ (VNO) in the nasal septum and bind to vomeronasal sensory neurons which send signals to the accessory olfactory bulb. Unlike in the main olfactory system, the integration

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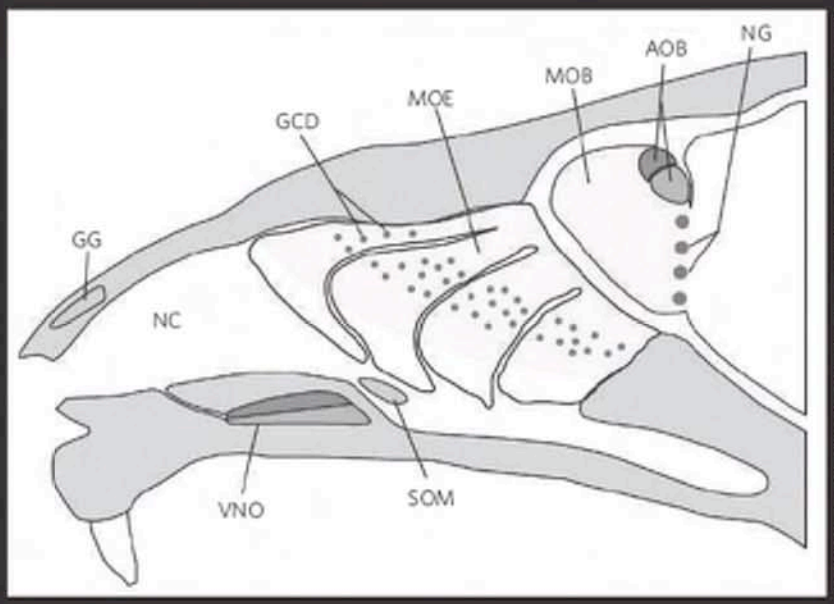
Mouse Olfactory Systems



Brennan, Peter A. and Keverne, Peter A. and Frank Zufall. "Pheromonal communication in vertebrates." Nature 444, 308-315 (15 Nov 2006).

Figure 1. The main and accessory mouse olfactory systems: In the main olfactory system, inhaled pheromones, as well as other odors, pass into the nasal cavity (NC) to the main olfactory epithelium (MOE) where they bind to specific odorant receptor proteins, activating attached olfactory receptor neurons which send electrical signals to the main olfactory bulbs (MOB) which are then relayed to the olfactory cortex for further processing. Less volatile pheromones enter the vomeronasal organ (VNO) in the nasal septum and bind to vomeronasal sensory neurons which send signals to the accessory olfactory bulb (AOB).

of multiple odors into one signal in the accessory olfactory system begins in the accessory olfactory bulb, rather than the olfactory cortex (5). While adult humans have a VNO, they do not appear to have an accessory olfactory bulb and seem to process all odors through the main olfactory system (2).

Role of Pheromones in Behavior

Pheromones can be grouped into three general categories based on function. Releaser pheromones induce immediate responses; for instance, releaser pheromones from a male mouse may elicit aggression from other male mice or they may attract a female one. Primer pheromones have a more gradual effect, often influencing a more general state of the individual sensing the pheromones, for example, by encouraging the onset of puberty or the duration of the ovulatory phase of the menstrual cycle. The third category consists of signaler pheromones. These pheromones communicate information, such as the gender, sexual receptiveness, or genetic closeness, of the pheromone releaser. A given pheromone can act in a manner falling under more than one of the categories, based on whether the recipient is male or female (2). The effect of pheromones depends both on the compound released as well as on who receives the signals.

Recent research has revealed that pheromones can affect behavior in mammals even more than previously thought. Dulac and colleagues have shown that pheromones play a key role in dictating mouse sexual behaviors. Mutant male mice unable to detect pheromones with the VNO were attracted to females and males, and attempted to mate with both genders (1). Female mice unable to detect certain pheromones, because of either the same genetic mutation or due to surgical removal of the VNO, were not only unable to tell males and females apart, but also exhibited male mating behaviors. When introduced to new mice of either gender, these females solicited and mounted them in the same manner as males. This indicates that the ability of female mice to detect pheromones is essential to female mating behaviors (6). In these mice, the very behaviors that mark them as female apparently depend on pheromonal cues.

Pheromonal Induction of Neurogenesis

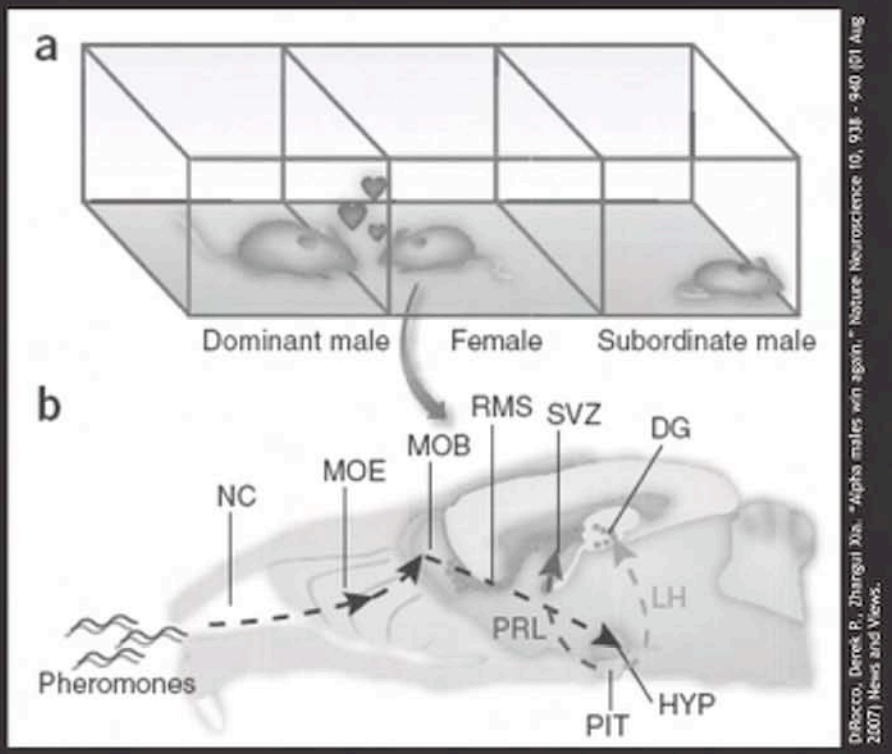


Figure 2. The mechanism of pheromonal influence on female mate preferences: Dominant male sex pheromones are detected by the main olfactory system of female mice. The olfactory bulb (MOB) then sends signals to the hypothalamus (HYP) which releases LH and prolactin (PRL) which stimulate neurogenesis (indicated in green) in the hippocampus and olfactory bulb. This neurogenesis then leads to females' stronger attraction to dominant males.

How do Pheromones Work?

From these experiments, it is clear that, at least in some species, pheromones influence behavior. How they do so is not well understood in most cases. However, some recent research has revealed that, at least in the case of mate preference, pheromones may act by stimulating neurogenesis, the creation of new neurons. Normal female mice demonstrate a strong preference for mating with dominant males. This inclination is thought to be based on the female's memories, created through neurogenesis, of the dominant male's sex pheromones (7).

To test whether these memories were a product of pheromone-induced neurogenesis, scientists exposed female mice to the bedding of dominant males, subordinate males, castrated males (which lack sex pheromones), and females, as well as bedding scented with other odors such as coconut (8) (Figure 2). They found that females exposed to dominant male pheromones had significantly higher levels of neurogenesis, in both the olfactory bulb and hippocampus (an area of the brain important for long term memory), than females exposed to any of the other odors. The researchers concluded that this indicates that neurogenesis in these areas of the female brain occurs specifically in response to the sex pheromones of dominant males (Figure 3). Furthermore, female mice whose main olfactory epithelium was disabled showed no preference for dominant males over subordinate ones, revealing that this pheromone-based selection is mediated by the main olfactory system. Likewise, when neurogenesis was blocked in females they mated equally with dominant and subordinate males.

When female mice are exposed to dominant male sex pheromones, their production of two hormones, luteinizing hormone (LH) and prolactin, also increases (7). To examine whether these hormones play a role in pheromone-induced neurogenesis, Mak *et al.* looked at neurogenesis in female knock-out mice with non-functional LH or prolactin receptors. The females without LH receptors had no pheromone-stimulated neurogenesis in the hippocampus, and females without prolactin receptors lacked neurogenesis in the olfactory bulb (8). Together, this research suggests a mechanism of pheromonal action which begins with detection of dominant male sex pheromones by the main olfactory system of female mice. The olfactory bulb then sends signals to the hypothala-

mus which releases LH and prolactin which stimulate neurogenesis in the hippocampus and olfactory bulb. This neurogenesis then leads to females' stronger attraction to dominant males (8). These findings show one manner in which pheromones may influence behavior; however, the ways that most other pheromones may affect behavior remain to be fully characterized.

Pheromones in People

Much controversy surrounds the question of whether people are affected by pheromones since humans do not appear to have a functional accessory olfactory system and many of the pheromones observed in other species are sensed by this system (7). This makes the recent results of Mak *et al.* especially exciting because the pheromonal pathway they elucidated is detected by the main olfactory system. Since people do have a functional main olfactory system, it is conceivable that humans may also be influenced by pheromones detected by their main olfactory epithelium, similar to how the sexual preference of mice is processed in the study by Mak *et al.* described above.

In addition, scientists have found evidence that pheromones do affect human behavior. One candidate for a human pheromone is androstadienone, a volatile compound found on the skin and hair of men, released by sweat. This compound induces activity in women's olfactory systems. It also has noticeable affects on their behavior. Women exposed to androstadienone become more relaxed and content (9).

Another possible pheromone is a chemical that indicates a person's major histocompatibility (MHC) gene. The allele, or version, of MHC which an individual man has appears to affect women's opinions of his scent. Women, given a choice of fabrics with male body scents on them, preferred the scent of men with MHC alleles similar to their own, over the scent of men with identical or completely different MHC alleles (10). Interestingly, they did not recognize the scent as human and based their choice on the pleasantness of the smell, rather than the familiarity, implying that pheromones associated with MHC alleles affected the women's emotional, rather than cognitive, processing (10).

Although the role of pheromones in human behavior is still controversial, the evidence is growing that pheromones may play a part in attraction between people. So next time you feel drawn to that stranger on the street, keep in mind that it may not just be the eyes, the laugh, or something else you consciously perceive, but also the high androstadienone levels, the similarity of their MHC or other traits imperceptibly discerned by you through pheromonal signaling. Whether the message is worth pursuing is still up to you. H

—Lauren Schumacher '10 is a Molecular and Cellular Biology concentrator in Leverett House.

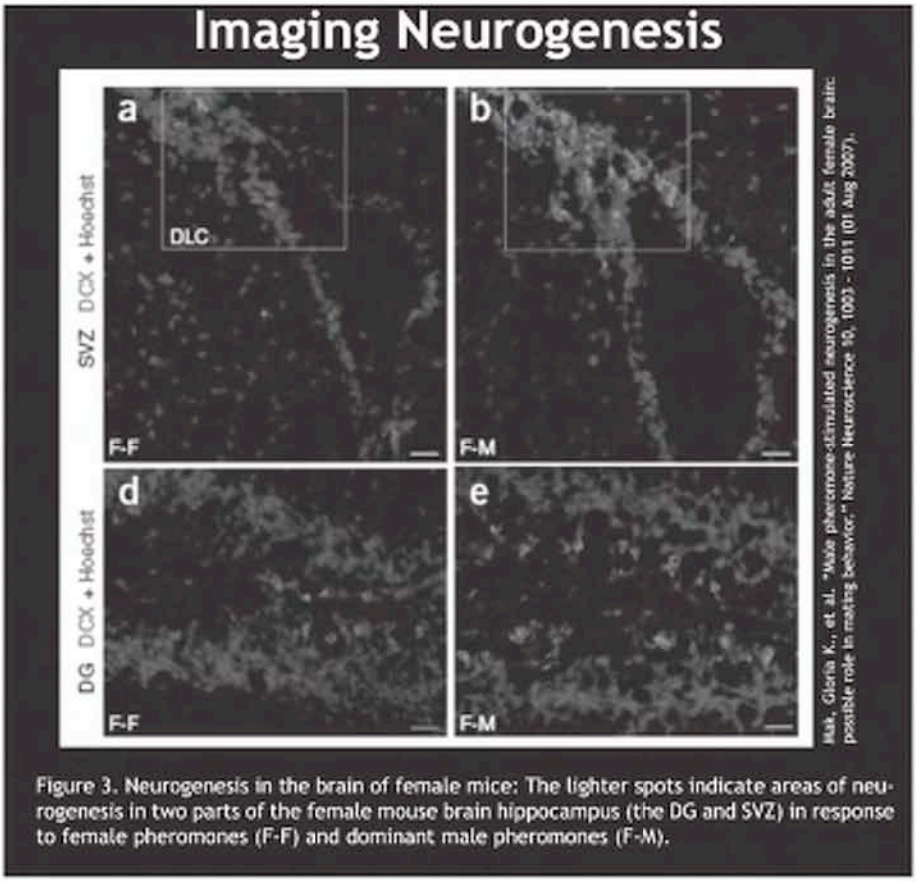


Figure 3. Neurogenesis in the brain of female mice: The lighter spots indicate areas of neurogenesis in two parts of the female mouse brain hippocampus (the DG and SVZ) in response to female pheromones (F-F) and dominant male pheromones (F-M).

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