Editorial

Making Sense of Scent

Most of us involved in scholarship of some kind like to think we're rational creatures and pretty much understand what makes us feel and act the way we do. We'd like to believe that we're aware of all the reasons for the decisions we make, our moods, and even our attraction to (or repulsion for) the people around us. But often lately, after researching some new aspect of neurobiology, I wonder how much of anything we do is really entirely under our conscious control. It's obvious that we're at least in part at the mercy of forces of which we're not even aware. The more we learn, the more it's clear that a thousand elements outside ourselves impact behavior, interacting with our genes, our hormones, our age, and, remarkably, our experiences. Take, for example, the power of odors. For Proust, the aroma of madeleines opened the door of reverie.[1] For others, the smell of the ocean unlocks memories of vacations by the sea; for a newborn nuzzling his mother's breast, her unique scent envelops and comforts him. Andy Warhol understood the power of olfaction to hardwire memory: "I switch perfumes all the time. If I've been wearing one perfume for 3 months, I force myself to give it up, even if I still feel like wearing it, so whenever I smell it again it will always remind me of those 3 months. I never go back to wearing it again; it becomes part of my permanent smell collection."[2]

Lest you think that Proust and Warhol's powerful rushes of emotion associated with odor came from some spiritual center, let me tell you that the real source is quite concrete: the memory for emotional events comes from the amygdala, the almond-shaped spot in the brain we use to form emotional memory. Furthermore, we're not all as exquisitely fine-tuned in this regard as was Proust: our individual capacity for emotionally enhanced memory depends on the gene that produces the α 2B-adrenergic receptor (ADRA2B) in the amygdala.[3] These very charged remembrances of things past (to borrow Marcel Proust's phrase) aren't always pleasant. ADRA2B is a very important gene: people with a deletion variant are more likely to reexperience traumatic events. Neurobiologists have explained the intensity of emotional memories, pointing out that these memories have a "flashbulb" quality, "as if they were photographically etched in the brain."[4] A number of arousing phenomena are all intertwined in the event: sympathetic arousal, the action of the amygdala, increased attention, and amplified perception. The science has even reached the media: a recent episode of the television show *Boston Legal* concerned a proposal to give propanalol to a young woman—because of the drug's blocking action of the sympathetic nervous system—so that she would have a muted memory of being raped. Happily for the pleasant rush of emotionally charged memories, age doesn't impair their recall[5]; even when we can't remember where we left our glasses or car keys, a whiff of a baking biscuit can trigger the memory of an especially pleasant breakfast shared decades ago with a beloved sibling.

The odors we're aware of, which are processed by special receptors in our main olfactory epithelium, are relayed to the olfactory cortex and then sent to higher sensory centers in the brain for processing. But there's a whole different category of olfactory stimuli of which we're largely unaware and which take a distinctly different pathway through the brain. These are the powerful chemicals or odorants called *pheromones*, chemicals produced in the skin, vaginal secretions, feces, semen, and urine that play a variety of important roles in our biological economy—some of them literally life changing. Receptors for pheromones are a specialized subpopulation of olfactory cells located in the vomeronasal organ (VNO), first described in other species but a variant of which is now known to exist in humans. Some pheromones are called *primers* and affect hormone production: male pheromones reduce prolactin levels and increase luteinizing hormone secretion; female pheromones increase prolactin secretion. Group-housed female mice exhibit a suppression of estrus, but estrus can be induced by pheromones from the male; puberty in

female mice is accelerated by male pheromones.[6] Other pheromones are called *releaser* or *signaling communicators* and are responsible for mating behaviors, aggression, maternal care, and infant–mother recognition. Halpern[6] summarized a fascinating series of descriptions of how animals propel odorants from the external world and deliver them to the VNO (snakes flick their tongues to pitch pheromones past the cells of the VNO, bulls compress their tongues against the hard palate to maintain contact between their nose and the cow's vulva during sexual play, and, one of my favorites, the gorilla's facial grimacing, involving head extension, upper lip retraction, baring of the gum, and opening the mouth, which all serve to enlarge the openings of the VNO).

Should we feel that all of this rather unsophisticated behavior is beneath us and only applies to less-evolved forms of life, scientists like Martha McClintock beg to differ: "Recent, still controversial reports suggest that chemosensory communication may occur in humans via a residual vomeronasal organ and that chemosensory/hormonal interactions also operate in humans."[7]

Other investigators have definite opinions about the power of pheromones in our lives, especially our sexual lives. Cutler et al[8] studied the impact of a synthesized human male pheromone on 38 heterosexual men and found that the treated group increased at least 6 kinds of sociosexual behaviors, which prompted a significant increase in episodes of sexual contact with women, but not, interestingly, more episodes of masturbation. McClintock herself found that pheromones excreted during the late follicular phase from the axillae of healthy women accelerated the preovulatory surge of luteinizing hormone of other women and helped synchronize menstrual cycles in women housed together.[9] Other pheromones can modulate mood: 2 are of particular interest because they stimulated mood in women (who could not detect any odor when exposed to the pheromone) but depressed it in men.[10] Savic et al[11] have shown with positron emission tomography and functional magnetic resonance imaging scans that smelling both of these pheromones activated the human brain, even in nonodorous concentrations. The pattern of activation was gender specific and also noteworthy, because homosexual men and heterosexual women displayed the same pattern of activation, in contrast to that of heterosexual men.

Just to reinforce the notion that our choice of a mate may well be influenced by things beyond our conscious control, Rantala et al[12] reported that, at least in beetles, pheromones signal male immunocompetence and broadcast a male's superior ability to resist parasites and infection to prospecting female beetles. In another report of how pheromones can guide us to a more desirable mate, vertebrates could distinguish major histocompatibility complex types by processing pheromones.[13] The debate about how acute our sense of smell is, and which odors we can actually detect, is ongoing. Giorgi et al[14] found 2 gene families in humans similar to those that encode pheromone receptors in rats, but the investigators believe that the human variants may not be functional. Still, provocative data continue to accrue, enough to convince me that we have a more extensive impact on each other than we are aware of. Preti et al[15] found that women who smelled men's underarm secretions advanced the onset of the next peak of luteinizing hormone and experienced reduced tension and increased relaxation.

Apparently, what we find visually attractive goes hand in hand with desirable pheromones. Cornwall et al[16] noted a strong correlation between men's ratings of a female pheromone (1,3,5(10),16-estratetraen-3-ol) and their preferences for feminine face shapes; women showed the same congruence of choice, giving high marks to the male pheromone (5α-androst-16-en-3-one) and masculinity in men's face shapes. Thornhill and Gangestad[17] found that the body scent of men with superior body bilateral symmetry is rated more attractive by normally ovulating women.

When all is said and done, the nose and the pathways along which it sends odorants to the brain are crucially involved in what we feel, what we remember, and even how we behave, particularly sexually. We don't just choose a pretty face. Odors, only some of which we're aware of, play an important part in what attracts us to one another and how we feel in the company of others. Napoleon's admonition to Josephine not to bathe for 3 days because he was coming home wasn't without merit. The huge evolutionary

machine has equipped us to make better choices of a mate sometimes in spite of ourselves. Although there are forces like pheromones that operate covertly to prompt our choices, they seem engineered to act in our best interests…or at least in the best interests of our offspring. As we understand more about how odors—both those perceived and those that we don't consciously register—affect behavior, all kinds of therapeutic opportunities will unfold. Certainly, the new science adds a dimension to the comment that so many lovers make, "the chemistry between us is fantastic," even if we're not fully conscious of precisely why.

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