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LETTER TO THE EDITOR

Human Pheromone Detection by the Vomeronasal Organ: Unnecessary for Mate Selection?

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Abstract

Recently, Foltan and Sedy proposed a hypothesis stating that the adult human VNO is integral to the prevention of inappropriate mate selection. In this commentary, we address the authors' assumption that humans have a functional VNO, that pheromones are detected exclusively by the VNO, and that human pheromones are responsible for negative stimuli during mate selection. After examining the published literature on human vomeronasal function, we argue that their hypothesis is critically flawed. We offer a brief review of the adult human VNO in support of our argument.

Key words: behavior, human, pheromone, vomeronasal

A recent paper proposes the hypothesis that the human vomeronasal organ (VNO) provides crucial inhibitory chemosensory information that discourages mating between ''inappropriate'' partners (Foltan and Sedy 2009). New information about human chemical communication would be exciting; unfortunately, the authors provide no data to support their hypothesis aside from an anecdotal personal observation. The authors also poorly cite research articles. For example, the section titled ''How the VNO influences human behavior'' presents only rodent data without any accompanying comparisons to human behavior. The authors discuss the crucial role that an ion channel, canonical transient receptor potential 2 (TRPC2), plays in rodent VNO function without mentioning that the human *trpc2* is a non-protein-producing pseudogene (Wes et al. 1995; Liman and Innan 2003). Although significant, these points alone do not invalidate the hypothesis. We argue that this hypothesis is critically flawed due to the following: first, the authors disregard data that suggest that the adult human VNO is nonfunctional; second, the authors assume that every ''scent of a pheromone nature'' is detected by the VNO; third, they argue that every human pheromone triggers an ''inhibitory feedback mechanism'' crucial for the ''involuntary ability to exclude inappropriate mates'' and therefore encouraging commitment to an existing mate.

The Le Forte I surgery performed by the authors is a surgery of the midface that repositions the maxilla for proper alignment with the mandible (Perciaccante and Bays 2004). The surgery involves separating the maxilla from the surrounding bones and some of the associated soft tissues, including removing a portion of the nasal septum and mucosa (Perciaccante and Bays 2004). It is during this step that Foltan and Sedy (2009) claim to damage the VNO and the ''supplying nerve.'' The authors then contradict this statement by acknowledging that the human VNO does not look like a ''classical'' sensory organ and that there is no VNO nerve.

The adult human VNO has been repeatedly reviewed as nonfunctional (Keverne 1999; Meredith 2001; Wysocki and Preti 2004). Physical and histological examination of the human VNO suggests that this organ contains few neurons, consists mostly of epithelial cells, and has no sensory function (Johnson et al. 1985). Specifically, most cells within the adult human VNO express keratin proteins, markers of epithelial cells (Trotier et al. 2000; Witt et al. 2002). No cells express olfactory marker protein, a hallmark of mature olfactory neurons (Monti-Graziadei et al. 1977; Trotier et al. 2000; Witt et al. 2002). No cells have synaptic contacts (Trotier et al. 2000) and few if any cells express S-100, a marker of glia and nerve bundles (Trotier et al. 2000; Witt et al. 2002). Additionally, there is no evidence for a nerve

connecting to or from the VNO (Trotier et al. 2000; Witt et al. 2002).

Chemosensory cues that meet the authors' definition of a pheromone are not detected exclusively by the VNO. The mouse's main olfactory system does not receive sensory input from the VNO; yet, it responds to social signals (Lin et al. 2005; Kang et al. 2009). Multiple signaling pathways within the main olfactory epithelium (MOE) mediate this sensitivity (Wang et al. 2006; Leinders-Zufall et al. 2007; Lin et al. 2007). Importantly, human perception of the putative pheromone androstadienone does not require VNO stimulation (Knecht et al. 2003), though brain activation by androstadienone and another putative human pheromone, estratetraenol, is dependent upon access to the MOE (Savic et al. 2009). Therefore, the authors' assumption of total loss of chemosensory communication by putative pheromones following VNO ablation is not supported in the literature.

The VNO-independent mechanism by which these steroidal compounds stimulate the central nervous system is undefined. The possibilities include diffusion into the blood stream via nasal capillaries, direct access to the cerebral spinal fluid via movement across the cribriform plate (Hanson and Frey 2008), and receptor activation in the MOE. Receptor activation in the MOE is supported by a brain imaging study that demonstrates a short latency between sniffing and brain activation and the requirement of an accessible MOE (Savic et al. 2009). Additionally, a putative human homologue to the rodent vomeronasal receptors is expressed in the MOE (Rodriguez et al. 2000) and can be activated by odorants in vitro (Shirokova et al. 2008). These data are not conclusive, and more studies are needed on the role of the MOE in human pheromone sensation.

Our last concern centers on the pheromone's presumed effect on human behavior. The authors suggest that human pheromones exclusively provide "negative stimuli" that provoke "an involuntary response." As to the first point, we are unsure as to the conceptual framework in which mating stimuli that eventually block mating would be produced, released, and conserved within a population. In this hypothesis, how are the senders of such stimuli able to mate and thus raise their own fitness level? That is, the pheromone producers must successfully mate—apparently against great odds—in order for this communication system to be maintained. Second, the authors provide no evidence that human pheromones are negative stimuli. Putative human pheromones do not appear to stimulate a "negative" response. On the contrary, published evidence suggests that putative human pheromones inhibit decreases in positive mood (Jacob and Mcclintock 2000; Jacob et al. 2002; Wyart et al. 2007). Therefore, the authors' assumption that all pheromonal communication produces a negative effect during mate selection is not supported.

In our view, the hypothesis proposed by Foltan and Sedy (2009) that the human VNO provides crucial inhibitory chemosensory information preventing inappropriate mating is unsound. They provide no data to support their claim, and the cited research literature is mischaracterized. They acknowledge that it is generally agreed that the human VNO is nonfunctional but contend it is crucial for normal human social behavior. They assume that all putative pheromonal communication requires the VNO, where the research literature clearly demonstrates that suspected pheromones can activate both the main and accessory olfactory systems. The authors assert that human pheromonal communication provides negative information, and in doing so, they disregard the data on human pheromonal function that suggests that human pheromones have positive effects.

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