An Odor is Not Worth a Thousand Words: From Multidimensional Odors to Unidimensional Odor Objects

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Abstract

Olfaction is often referred to as a multidimensional sense. It is multidimensional in that ~1000 different receptor types, each tuned to particular odor aspects, together contribute to the olfactory percept. In humans, however, this percept is nearly unidimensional. Humans can detect and discriminate countless odorants, but can identify few by name. The one thing humans can and do invariably say about an odor is whether it is pleasant or not. We argue that this hedonic determination is the key function of olfaction. Thus, the boundaries of an odor object are determined by its pleasantness, which—unlike something material and more like an emotion—remains poorly delineated with words.

Contents

THE MECHANISMS OF SMELL

In this article, we first briefly review the mechanisms and neural substrates that together underlie the perception of smell. Because we make a claim on the human psychology of smell, we detail evidence obtained from humans rather than from other animals wherever possible. We review several lines of evidence that together bring us to suggest a novel definition for odor objects. We propose that odor objects, unlike visual objects, reflect a combination of molecules in the external world combined with an internal state of emotion and homeostasis that together generate a given pleasantness that is itself the odor object.

OLFACTION STARTS WITH A SNIFF

Sniffs are not inconsequential to the eventual olfactory percept (Kepecs et al. 2006, Mainland & Sobel 2006, Schoenfeld & Cleland 2006) that they influence in at least two ways. First, sniffs influence the quantity and quality of the molecules perceived. How sniffs influence odor quantity is plainly evident: The more vigorous the sniff, the more odor molecules are delivered to the olfactory system. Consistent with this, and similar to other senses subserved by a sensory-motor apparatus, an olfactomotor system can modify sniffs within ~160 ms of odorant onset (Johnson et al. 2003) in order to optimize detection threshold (Sobel et al. 2000) and maintain olfactory constancy (Teghtsoonian & Teghtsoonian 1984). In turn, the way in which sniffs influence odor quality is more complicated: Odorant molecules can differ in their sorption, namely their tendency to cross the olfactory mucosa (Mozell & Jagodowicz 1973). Furthermore, sorption interacts with sniff airflow rate to produce varying patterns of activity across the olfactory mucosa (Kent et al. 1996). In simple terms, this is because higher rates of airflow will favor high sorption, and lower airflow will favor low sorption (Mozell et al. 1991). Thus, a given sniff airflow rate will optimize perception for particular odorants as a reflection of their sorption. Furthermore, because mammals have a different rate of airflow in each nostril during a given sniff (Gilbert & Rosenwasser 1987, Principato & Ozenberger 1970), each nostril is therefore optimized for slightly different odorants. In other words, a typical mammalian sniff provides the brain with two simultaneous slightly offset images of the olfactory world (Sobel et al. 1999).

In addition to influencing the quantity and quality of the molecules perceived, the second influence of sniffs on olfaction is through driving neural activity patterns throughout the olfactory system. This is evident in clean-air sniff-induced activity at the olfactory epithelium (Grosmaitre et al. 2007), bulb (Adrian 1942), and cortex (Sobel et al. 1998, Zelano et al. 2005). The exact manner by which sniff-induced neural activity influences the eventual olfactory percept remains unclear. Finally, considering the importance of sniffing, it is noteworthy that much of our notion on function within the olfactory system was obtained through experiments in anesthetized rodents that were not sniffing. In our view, this may have significantly affected our notion of processing in this system.

Once an odor is sniffed, it is processed within an olfactory neuroanatomy that has been remarkably conserved in mammals (Ache & Young 2005) and consists of three primary processing stages: epithelium, bulb, and cortex.

OLFACTORY EPITHELIUM

Transduction of an odorant molecule starts with its transport to the olfactory epithelium by sniffing. In humans, the epithelia are located bilaterally ~7 cm up the nasal passage, lining the cribriform plate and extending to the nasal turbinates (Clerico et al. 2003). Here the odorant molecules cross a mucous membrane through a process that combines passive diffusion and possibly active transport (Pelosi 2001, Pevsner et al. 1985) in order to then bind with transmembrane G-protein-coupled olfactory receptors at the ciliated end of olfactory receptor neurons (Nakamura & Gold 1987, Pace et al. 1985). The mammalian olfactory receptor repertoire contains ~1000 different receptor types (Buck & Axel 1991). Each olfactory receptor neuron expresses only one (Chess et al. 1994, Nef et al. 1992, Ressler et al. 1993, Strotmann et al. 1992, Vassar et al. 1993) or two (Goldman et al. 2005) of these receptor types, and the ~1000 types are distributed at unknown proportions across millions of olfactory receptor neurons. Genetic analysis has suggested that humans functionally express ~350 of these receptor types (Glusman et al. 2001), within ~12 million olfactory receptor neurons (Moran et al. 1982). It is currently held that each receptor type can bind with a number of different odorants, and each odorant can bind with a number of different receptor types, thus generating a potentially massive combinatorial space for coding smell (Breer 2003, Firestein 2001). The bipolar sensory neurons, which continuously regenerate throughout the life span (Graziadei et al. 1979, Graziadei & Monti Graziadei 1983), can be considered "transition neurons" between the peripheral nervous system and central nervous system (Doucette 1991). They send one dendrite-like process to the olfactory epithelium, and the other axon-like process joins the olfactory nerve bundle (cranial nerve I) to cross through the cribriform plate and synapse at specialized neuropoil termed "glomeruli" on the surface of the ipsilateral olfactory bulb (**Figure 1**). The epithelium is obviously a key structure in olfaction, and damage to the human epithelium can lead to anosmia (a complete loss of smell) (Dalton 2004, Doty & Mishra 2001).

OLFACTORY BULB

The path from epithelium to bulb entails a striking case of neural convergence whereby all neurons expressing the same type of receptor converge to one of two mirror-glomeruli in the olfactory bulb (Mombaerts et al. 1996, Ressler et al. 1994, Tsuboi et al. 1999, Vassar et al. 1994). The result of this connectivity, whereby each glomerulus now "represents" one receptor type, is a stereotyped map where odor identity can be represented in the spatiotemporal patterns of glomerular activation (Cleland et al. 2007, Leon & Johnson 2003). Within the glomeruli, the receptor axons contact dendrites of either mitral or tufted output neurons and periglomerular interneurons. The mitral and tufted cell axons join to form the lateral olfactory tract that is the output from the

bulb to the ipsilateral primary olfactory cortex in the ventral portions of the temporal lobe (**Figure 1**). Consistent with its key role in formation of the olfactory percept, the olfactory bulb receives more afferents from cortex than efferents to cortex (Kay & Freeman 1998). This suggests the olfactory bulb as a candidate site for much of the extensive contextual influences on olfactory perception (Kay & Freeman 1998), a major topic that is discussed later in this review. Finally, considering the prominent position of the olfactory bulb in the stream of olfactory processing, a series of studies that found only minimal olfactory impairments following extensive olfactory-bulb lesions remains puzzling (Slotnick & Bisulco 2003).

Epithelium-to-bulb connectivity was uncovered mostly in rodents. Considering this rule of convergence, whereby all receptor neurons expressing a particular receptor type converge on the same glomerulus, combined with the expectation of ~350 functional olfactory receptor types expressed in humans (Glusman et al. 2001), one might predict that the human olfactory bulb would have about 700 glomeruli. However, the few studies that addressed this in human tissue identified nearly eightfold the number of expected glomeruli (Maresh et al. 2008). Thus, the rules underlying the organization of the human olfactory bulb and its relation to the epithelium may be slightly different than are the rules in rodents.

Nevertheless, the human olfactory bulb plays a key role in odor processing. Undeveloped olfactory bulbs are associated with anosmia (MacColl et al. 2002), and reduced bulb volume is associated with poor olfactory detection and discrimination (Buschhuter et al. 2008).

OLFACTORY CORTEX

By current definition, primary olfactory cortex consists of all brain regions that receive direct input from the mitral and tufted cell axons of the olfactory bulb (Allison 1954; Carmichael et al. 1994; de Olmos et al. 1978; Haberly 2001; Price 1973, 1987, 1990; Shipley 1995). These comprise most of the paleocortex, including (by order along the olfactory tract) the anterior olfactory cortex (also referred to as the anterior olfactory nucleus) (Brunjes et al. 2005), the ventral tenia tecta, anterior hippocampal continuation and indiusium griseum, the olfactory tubercle, piriform cortex, the anterior cortical nucleus of the amygdala, the periamygdaloid cortex, and the rostral entorhinal cortex (Carmichael et al. 1994). This definition of primary olfactory cortex as "all regions that receive direct input from the olfactory bulb" has recently been reevaluated, primarily because the definition is unhelpful when considering function (Cleland & Linster 2003, Haberly 2001, Sobel et al. 2003). One cannot assign *a function* to primary olfactory cortex when primary olfactory cortex is a label legitimately applied to a large proportion of the mammalian brain. With this in mind, there has been a growing tendency to use the term "primary olfactory cortex" for piriform cortex alone. Piriform cortex, the largest component of primary olfactory cortex in mammals, lies along the olfactory tract at the junction of temporal and frontal lobes and continues onto the dorsomedial aspect of the temporal lobe. Beyond these primary regions, olfactory information is projected throughout the brain, most prominently to orbitofrontal gyri and the insular cortex (Small & Prescott 2005).

The specific functional roles of human primary olfactory cortex remain poorly understood. Lesion studies have implicated primary olfactory cortex in odor discrimination (Zatorre & Jones-Gotman 1991), odor memory (Rausch et al. 1977), odor identification (Jones-Gotman & Zatorre 1988), and olfactory learning (Dade et al. 2002). The interesting aspect of this list is the faculty not listed, namely, we know of no reports on complete anosmia following focal cortical lesions in humans. In other words, we know of no olfactory equivalent to cortical blindness.

Imaging studies have implicated primary cortex in various olfactory tasks: Odor intensity coding, where, as a rule, increased intensity was associated with increased activation (Anderson et al. 2003; Rolls et al. 2003, 2008;

Royet et al. 2001; Winston et al. 2005); pleasantness coding, where, as a rule, reduced pleasantness was associated with increased activation (Anderson et al. 2003, Gottfried et al. 2002, Grabenhorst et al. 2007, Rolls et al. 2003, Royet et al. 2000, Zald & Pardo 1997); familiarity coding, where, as a rule, increased familiarity was associated with increased activation regardless of task (Qureshy et al. 2000, Royet et al. 1999, Savic & Berglund 2004); olfactory attention, whereby a gating function has been ascribed to piriform cortex (Rolls et al. 2008, Zelano et al. 2005); and olfactory memory, whereby piriform cortex functioned as an olfactory analogue of the visuospatial sketchpad where odors were reflected in ongoing activity during active maintenance (Dade et al. 1998, 2001; Savic et al. 2000; Zelano et al. 2009) (**Figure 2**).

One study directly explored the role of primary olfactory cortex in odor identity coding. In order to determine whether the piriform cortex encodes information about perceptual or structural determinants of odor, lemon-like and vegetable-like odorants that contained alcohol or aldehyde functional groups were presented in a functional magnetic resonance imaging (fMRI) cross-adaptation paradigm. A double dissociation in odor coding was revealed. Posterior piriform coded odor quality, and anterior piriform coded odor structure, in this case, functional group (Gottfried et al. 2006).

Two overriding aspects to the anatomy of olfaction have been highlighted as unique among the distal senses. The first is that olfaction is the only sense in which information does not propagate from periphery to cortex through the thalamus. As noted, olfactory information goes from epithelium to bulb to cortex, without a thalamic relay. Piriform cortex then projects to orbitofrontal cortex both directly and, through a thalamic path, indirectly. The functional significance of this thalamic path remains unclear, although it may play a role in olfactory attention (Plailly et al. 2008).

The second unique aspect of olfactory neuroanatomy is its ipsilateral unilateral connectivity. Most anatomical evidence suggests that each epithelium projects to its ipsilateral bulb that in turn projects to its ipsilateral primary cortex (Powell et al. 1965). That said, recent functional evidence in both rodents (Cross et al. 2006, McBride & Slotnick 1997, Wilson 1997) and humans (Porter et al. 2005, Savic & Gulyas 2000) suggests apparently equal levels of ipsilateral and contralateral functional connectivity from nostril to cortex, thus rendering the question of laterality less clear.

The above neuroanatomy is the substrate of human olfaction. Using this substrate, humans can perform tasks that are on one hand astonishingly keen, yet on the other hand astonishingly dull. Here we detail both ends of performance.

HUMANS ARE ASTONISHINGLY GOOD AT ODOR DETECTION AND DISCRIMINATION

Humans possess an extraordinary, if underappreciated, sense of smell (Shepherd 2004, Zelano & Sobel 2005). Nowhere is this more evident than in odor detection (**Figure 3*A***). The odorant ethyl mercaptan, which is often added to propane as a warning agent, can be detected at concentrations below 1 part per billion (ppb) and perhaps as low as 0.2 ppb (Whisman et al. 1978). This is equivalent to approximately three drops of odorant within an Olympic-size swimming pool—given two pools, a human could detect by smell which pool contained the three drops of odorant. Extremely low detection thresholds have been reported for the odorants d-limonene and ozone as well (Cain et al. 2007). Finally, a report by the Japan Sanitation Center (Nagata & Takeuchi 1990) suggested humans can detect isoamyl mercaptan at 0.77 parts per trillion! This, to our knowledge, is the lowest reported human detection threshold.

Feats of detection are not limited to the olfaction lab. For example, consumers detected an off-odor in mineral water bottles that was undetected by the modern analytical in-line detection devices that were supposed to reject contaminated bottles (Widen et al. 2005). Humans not only are inherently good at odor detection, but they also can

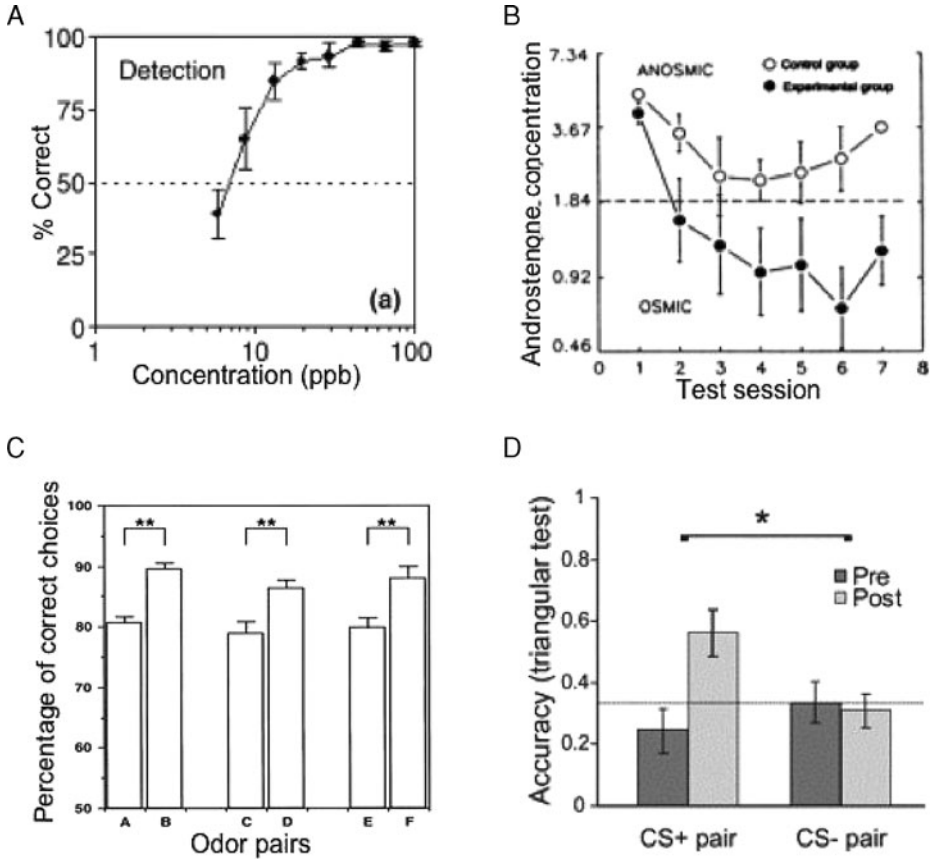

Figure 3

Keen human odor detection and discrimination. (*A*) Correct detection of ozone corrected for guessing (averages ± SEM). The is significantly beyond the 50% chance level by ~10 parts per billion (ppb) (adapted from Cain et al. 2007). (*B*) Androstenone detection thresholds declined in an exposed group, but not in an unexposed group. The dashed line represents the functional definition of androstenone anosmia (adapted from Wysocki et al. 1989). (*C*) Discrimination between similar odorants: *column A*, odor pairs that involved two hexenols; *column B*, odor pairs that involved a hexanol and a hexenol; *column C*, odor pairs that involved two *cis*-hexenols; *column D*, odor pairs that involved two trans-hexenols; *column E*, odor pairs that involved hexenols sharing the same geometry but differing in the position of the double bond by only one carbon atom; and *column F*, odor pairs that involved hexenols sharing the same geometry but differing in the position of the double bond by two carbon atoms (adapted from Laska 2005). (*D*) Odor discrimination accuracy was at chance (dashed line) for CS+ and CS− pairs before conditioning, but selectively improved for the CS+ pair after conditioning. Error bars, ±SEM (adapted from Li et al. 2008).

improve with practice. Repeated exposure to an odorant leads to enhanced olfactory sensitivity and decreased detection thresholds for a number of different odorants (Cain & Gent 1991, Dalton et al. 2002, Engen & Bosack 1969) (**Figure 3*B***). Furthermore, humans who were completely unable to detect the odor of androstenone developed the ability to detect it after repeated exposure (Wysocki et al. 1989). There is an ongoing debate as to the point of plasticity underlying these improvements in olfaction with exposure or practice. A study with androstenone-anosmic mice (mice unable to detect androstenone despite otherwise intact olfaction) found evidence in favor of epithelial rather than cortical plasticity. Exposure

of a surgically disconnected androstenone-anosmic mouse epithelium to androstenone enabled later androstenone-detection once the epithelium-to-bulb projection regenerated in those mice (Yee & Wysocki 2001). In other words, events at the isolated epithelium gave rise to behavioral plasticity. An additional study measured electrical evoked responses (EOGs) stemming from the human olfactory epithelium concurrent with an androstenone exposure paradigm and found changes in the EOG pattern with lowered detection thresholds, leading the authors to conclude that an epithelial modification occurred over time (Wang et al. 2004). In contrast, in favor of cortical plasticity, systematically exposing only one nostril of human androstenone anosmics to androstenone led to improved detection in both the exposed and the unexposed nostril (Mainland et al. 2002). This suggests that plasticity occurred at a substrate common to both nostrils, namely cortex. A conclusion consistent with all the data is that exposure may induce changes at both the peripheral and central levels. Repeated exposure may indeed lead to increased expression of receptors at the epithelial level (Yee & Wysocki 2001) and to an increased ability of the brain to make sense of what was a previously senseless message (Mainland et al. 2002). The recent identification of the specific human olfactory receptor that is primarily responsible for the detection of androstenone (Keller et al. 2007) may now enable a more direct investigation of this question.

Humans are not only good at detecting odorants, they are also good at discriminating one odorant from another, either in terms of concentration or molecular identity. Humans can discriminate between two odorants that differ in concentration by as little as 7% (the olfactory "just noticeable difference") (Cain 1977), and even smaller changes in the relative proportion of a component in a mixture can change the perception of the mixture (Le Berre et al. 2008). Humans can also discriminate the smallest alterations in molecular structure, such as between odorants equal in number of carbons but differing in functional group (Laska et al. 2000) or equal in functional group but differing in chain length by one carbon only (Laska & Freyer 1997) (**Figure 3*C***). Moreover, humans are able to discriminate between various pairs of enantiomers (mirror-image molecules) such as (+) and (−) carvone. Still, discrimination is not always easy. Humans fail to discriminate some enantiomer pairs (Laska & Teubner 1999), unfamiliar odors are harder to discriminate than familiar odors (Mingo & Stevenson 2007), and the ability to discriminate the number of odorants in a mixture is limited to four (Laing & Glemarec 1992), even when the odors are "poor blending" odors (Livermore & Laing 1998).

In turn, like odor detection, odor discrimination can improve with learning and practice (Rabin 1988). Increased familiarization was associated with a decrease in discrimination errors of initially unfamiliar odors (Jehl et al. 1995). Odor enantiomers that were initially indiscriminable became discriminable after one of the enantiomers was associated with an electric shock (Li et al. 2008) (**Figure 3*D***). Subjects working in perfume retail outlets were significantly better at odor discrimination compared with subjects not working in such odorous environments (Hummel et al. 2004), and wine tasters were superior to naive controls at odor discrimination (Bende & Nordin 1997).

Whereas discrimination between common molecules in the laboratory is outstanding, it may be even better between molecules that are ecologically meaningful. For example, human participants could use smell to discriminate their own T-shirt from 100 identical T-shirts worn by others for 24 hours (Lord & Kasprzak 1989). If the latter sounds more like an olfactory feat of a dog, a separate amusing study found that humans can in fact discriminate their pet dog from other dogs using smell alone (i.e., the humans smelled the dogs. . .) (Wells & Hepper 2000). More ecologically relevant, however, is that human mothers could discriminate between the smell of their baby and other babies (Porter et al. 1983), five- to eight-year-old children could discriminate between the smell of their three- to four-year-old siblings and

other children (Porter & Moore 1981), and nine-year-old children could discriminate between the smells of their close friends (Mallet & Schaal 1998). Many of these discriminations are achieved despite low confidence or awareness (Lundstrom et al. 2008). Furthermore, these discriminatory powers may be innate: Babies can discriminate the smell of their breast-feeding mothers from other mothers by six days after birth (Macfarelane 1975, Schaal et al. 1980), and newborn babies cry less when exposed to the odor of amniotic fluid (which was present in the intrauterine environment) than to the odor of their mother's breasts (Varendi et al. 1998). Breast-feeding infants, at approximately two weeks of age, discriminated between their mother's axillary odor and odors produced by either nonparturient or unfamiliar lactating women (Cernoch & Porter 1985).

HUMANS ARE ASTONISHINGLY BAD AT ODOR IDENTIFICATION AND NAMING

Whereas humans underestimate their detection and discrimination abilities, they overestimate their ability to identify and name odors (Cain et al. 1998, Jonsson et al. 2005, Jonsson & Olsson 2003, Lawless & Engen 1977) (**Figure 4**). This inability is subjectively striking when revealed to those who don't study olfactory psychophysics and hence appreciate it as fact. For example, in an effort to describe the eventual point of this review to a family member, author NS asked this family member to close her eyes, and then held in front of her nose a jar of peanut butter, which he asked her to name. This adult "subject," who despite eating peanut butter every day is otherwise neurologically intact, could not identify or name the odor. When she opened her eyes, she was astonished at her inability to name this odor that was otherwise so familiar. Because this inability is key to the main suggestion later made in this review, we invite the reader to conduct a similar "experiment" on him/herself, or friends and family, using the refrigerator as a relatively safe source for odorants. The outcome is always striking. Indeed, humans are unable to name by smell at least 50% of the odorous household items they use daily (Cain 1979, de Wijk et al. 1995, Lawless & Engen 1977). The dissociation between knowledge about an odor concurrent with inability to name it is evident already at childhood. When smelling dangerous household products, children correctly named 15% of the odors, but correctly rated edibility of 79% of the same odors (De Wijk & Cain 1994a). Finally, the poor odor-name bond is symmetrical—matching a name to an odor was as difficult as matching an odor to a name (Olsson & Jonsson 2008).

Like detection and discrimination, naming ability improves when odor familiarity increases (Homewood & Stevenson 2001) and further improves with explicit practice. Five practice sessions of naming 80 odorants resulted in a shift from 36 to 61 correctly named (Cain 1979). The ability to name odors increases significantly when rather than free recall, subjects can choose between alternative labels. Even for common odors such as banana, licorice, and clove, performance in cued identification far exceeded that in free identification (de Wijk & Cain 1994b). Because of this, the benchmark test used for scoring olfactory identification is not a free recall test, but rather a four-alternative forced-choice test. The University of Pennsylvania Smell Identification Test (Doty et al. 1984a,b) consists of 40 microencapsulated odorants that subjects have to scratch and sniff. For each odorant, the task is to choose from four alternative labels the one that best describes each odor. This test is one of the only "norms" in olfaction research and has been used to characterize an olfactory impairment in numerous diseases (Doty 2005).

To conclude, humans are bad at naming an odor, especially if they don't have labels to choose from. This difficulty may reflect a form of competition between language and olfaction over common neural substrates (Lorig 1999), or it may reflect a fundamental aspect of odor objects that renders them particularly difficult to name. This possibility is considered later.

VERBAL AND VISUAL INFLUENCE ON ODOR PERCEPTION

Humans are very good at detecting an odorant but are poor at naming it. The poor ability to name odors using olfactory information alone renders the process of odor naming and identification highly susceptible to interference from other modalities. For example, in one study, odorants were presented with an explicitly described source as either synthetic ("this is a synthetic rotten egg") or natural ("this is natural rose"). When pleasant odors were labeled "natural," they were rated as more familiar than when labeled "synthetic" (Herz 2003). Similarly, when an isovaleric and butyric acid mixture was labeled "parmesan cheese," it was rated as more familiar than when labeled "vomit" (Herz & von Clef 2001). In another experiment, each odor was presented three times under different names that referred to either a pleasant, unpleasant, or neutral odor source. For example, the odorant pyridine was presented with the label "sea weed," "rotten fish" or "fifty-three." Odorants were rated as more intense when presented with unpleasant names than with neutral or pleasant names (Djordjevic et al. 2008).

Visual information, particularly color, also affects odor characteristics. When a white wine was artificially colored red with an odorless dye, a panel of 54 expert tasters shifted to using olfactory characteristics of red wine in order to describe the concoction (Morrot et al. 2001). Odor solutions were also rated as smelling more intense when colored than when colorless (Zellner & Kautz 1990). Furthermore, a cherry-flavored drink colored orange was perceived as smelling orange flavored (Dubose et al. 1980), and when it was colored red, subjects performed better at identifying the solution by smell than when they performed the task blindfolded or when a lemon-flavored drink was colored red (Zellner et al. 1991). Additionally, olfactory detection was faster and more accurate when odors appeared in the context of visual cues that were semantically congruent (vanillin odor—picture of ice cream) as compared with incongruent (vanillin odor—picture of bread) (Gottfried & Dolan 2003).

This susceptibility in odor perception extends to ecological odors as well. For example, when a label "participant's baby's name" or "someone else's baby" was added correctly to a diaper, mothers rated their own baby's diaper as less displeasing. However, when the diapers were mislabeled, no difference in pleasantness was rated (Case et al. 2006). Thus, verbal labels inverted the percept of an odor. This inversion was evident not only in perception, but also in brain activity. In an fMRI experiment, subjects smelled an odor mixture that was composed of isovaleric acid and cheddar cheese flavor. The mixture was labeled on different trials as "cheddar cheese" or "body odor," and as a control, delivery of clean air was paired with the same labels. Brain regions involved in pleasantness representation were significantly more activated by odor and by clean air when labeled "cheddar cheese" than when labeled "body odor" (de Araujo et al. 2005). The influence of nonolfactory and especially verbal information on olfactory identification can be seen as facilitating a process of olfactory pattern completion or constancy (Stevenson & Boakes 2003); this is discussed in more detail below.

PLEASANTNESS AS THE PRIMARY AXIS OF OLFACTORY PERCEPTION

The studies cited above demonstrate that humans are good at detecting and discriminating smells but are poor at naming them, and humans readily change the name or label they apply to an odor as a reflection of interference from language or vision. However, humans consistently and rapidly apply to an odor verbal labels identifying its pleasantness.

Odorant pleasantness was the primary aspect of odor spontaneously used by subjects in olfactory discrimination tasks (Schiffman 1974), and odorant pleasantness was the primary criterion spontaneously used by subjects to combine odorants into groups (Berglund et al. 1973, Schiffman et al. 1977). When using

large numbers of verbal descriptors to describe odorants, pleasantness repeatedly emerged as the primary dimension in multidimensional analyses of the resultant descriptor space (Khan et al. 2007, Moskowitz & Barbe 1977, Zarzo 2008). Studies with newborns suggested that at least some aspects of olfactory pleasantness may be innate (Soussignan et al. 1997, Steiner 1979). For example, neonates' behavioral markers of disgust (wrinkling nose, raising upper lip) discriminated between vanillin judged as being pleasant and butyric acid judged as being unpleasant by adult raters (Soussignan et al. 1997). Moreover, there is agreement in the assessments of pleasantness by adults and children for various pure odorants (Schmidt & Beauchamp 1988) and personal odors (Mallet & Schaal 1998). Interestingly, fathers and daughters, and brothers and sisters, rated each other's odor as unpleasant, a phenomenon that has been considered in the context of a mechanism for incest avoidance (Weisfeld et al. 2003). The primacy of pleasantness is further borne out in the physiological responses to odors. Pleasant and unpleasant odorants were evaluated at different speeds (Bensafi et al. 2002a) and generated different autonomic responses (Bensafi et al. 2002b). Furthermore, pleasant and unpleasant odorants are appraised by dissociable neural substrates, as evidenced in both electrophysiological recordings (Alaoui-Ismaili et al. 1997, Kobal et al. 1992, Masago et al. 2001, Pause & Krauel 2000) and functional neuroimaging studies (Anderson et al. 2003, Gottfried et al. 2002, Grabenhorst et al. 2007, Rolls et al. 2003, Royet et al. 2000, Zald & Pardo 1997). The task most frequently used to test brain representation of odor pleasantness was to present subjects with a set of pleasant and unpleasant odorants and ask them to rate odor pleasantness. These tasks consistently revealed orbitofrontal cortex involvement in representing odor pleasantness (Anderson et al. 2003, Rolls et al. 2003, Royet et al. 2001). More specifically, pleasant odors increased activation in posterior medial orbitofrontal cortex, and unpleasant odors increased activation in the lateral orbitofrontal cortex (Gottfried et al. 2002, Grabenhorst et al. 2007, Rolls et al. 2003). In addition, there was evidence for the separate and simultaneous representation of positive (in medial orbitofrontal cortex) and negative (in dorsal anterior cingulate and mid-orbitofrontal cortex) hedonic value of a mixture that was composed of one pleasant and one unpleasant odorant (Grabenhorst et al. 2007). Odor pleasantness was also reflected in piriform cortex (Zelano et al. 2007). Additional regions that have been implicated in odor pleasantness processing are anterior cingulate, ventral insula, superior frontal gyrus, and motor area BA 8 (Fulbright et al. 1998; Gottfried et al. 2002; Rolls et al. 2003, 2008; Royet et al. 2000, 2003; Winston et al. 2005; Zelano et al. 2007). Increased activity for odor hedonic judgments was also evident in primary visual areas (Royet et al. 2001), suggesting that rating odor pleasantness may involve visual imagery of the odor source.

The role of the amygdala in odor pleasantness processing is controversial. Whereas some studies reported increased amygdala activation for unpleasant versus pleasant odors (Gottfried et al. 2002, Royet et al. 2003, Zald & Pardo 1997), another study suggested that amygdala activation may preferentially reflect the intensity rather than the valence of odors (Anderson et al. 2003). An alternative consistent with all the data is that the amygdala does not preferentially respond to intensity or valence per se, but rather to a combination of the two (Winston et al. 2005). When valence was held constant, the amygdala responded robustly to odor intensity for pleasant and unpleasant smells but did not similarly respond for neutral smells. In turn, when intensity was held constant (at high concentrations), the amygdala was preferentially activated by positive and negative valence but not by neutral valence.

Finally, odor pleasantness is paramount not only when considering odor perception or odorant-induced brain activation, but also emerges when considering odor molecules alone. Khan et al. (2007) applied principal components analysis to more than 1600 molecular features of more than 1500 odorants to

identify the principal physicochemical axis of odor space. They found that the resultant axis, the first principal component of molecular structure, i.e., the axis that best explains the variance in odor structure, was significantly correlated to the perception of odorant pleasantness. This implies that pleasantness is indeed "written into" the molecular structure of odors. Uncovering this relationship allowed Khan et al. (2007) to predict the pleasantness of novel molecules based on their structure alone (**Figure 5*A***). Furthermore, Haddad et al. (2008a) later demonstrated that this axis can be used as an odorant metric that explains a large portion of the variance in neural activity across a wide range of species (**Figure 5*B***) (Haddad et al. 2008b). Critically, this same metric later predicted behavioral preferences not only in humans but in mice as well (**Figure 5*C***) (Mandairon et al. 2009). Taken together, these lines of evidence combine to highlight pleasantness as the principal perceptual axis of smell (**Figure 5*D***).

All that said, pleasantness does not explain all the variance in olfactory perception, nor does physicochemical structure explain all the variance in pleasantness. For example, odor pleasantness is dependent on odor intensity (Doty 1975, Henion 1971, Moskowitz et al. 1976) and familiarity (Delplanque et al. 2008, Distel et al. 1999, Distel & Hudson 2001, Jellinek & Koster 1983), and it varies across individuals and cultures (Ayabe-Kanamura et al. 1998, Moncrieff 1966, Pangborn 1975, Wysocki et al. 1991) as well as within individuals over time (Cain & Johnson 1978, Hudson 1999). Finally, despite its perceptual primacy, the perception of odorant pleasantness, like other odor aspects, can also be significantly influenced by visual and verbal information. Thus, in the previously described studies where a verbal or visual label altered odor intensity, familiarity, identity, and brain activity, the visual and verbal labels similarly influenced pleasantness (Case et al. 2006, de Araujo et al. 2005, Herz 2003, Herz & von Clef 2001).

Taken together, findings indicate that humans are good at detecting and discriminating odorants but bad at naming odorants, and the one label they readily apply to an odor is its pleasantness. This label is reflected in human behavior and neurophysiology, and, critically, it reflects the axis that best explains the variance within the structure of molecules that have a smell. If an odor primarily denotes pleasantness, than what is an odor object? For example, what is the odor object "banana"? Or in fact, is there an odor object "banana"?

DEFINING ODOR OBJECTS

> It seemed that this poor ignorant Monarch—as he called himself—was persuaded that the Straight Line which he called his Kingdom, and in which he passed his existence, constituted the whole of the world, and indeed the whole of Space.
>
> *FlatLand, A Romance of Many Dimensions*
>
> Edwin A. Abbott, 1884

The *Merriam-Webster* definition for object is:

> ***a:*** something material that may be perceived by the senses; ***b:*** something that when viewed stirs a particular emotion.

Most previous considerations of olfactory objects used the above definition ***a*** of an object. Akin to the visual object "banana," the olfactory object "banana" was considered as an amalgamation of molecules that can be separated from the background molecules to stand out as an object reflecting something material—a banana.

In contrast, we propose that the above definition ***b*** is the more appropriate framework for defining odor objects. We suggest that an odor object is the integration of the odor's inherent pleasantness (Khan et al. 2007) with the subjective state at the moment of coding: mood, hunger, fear, etc. Therefore, an odor object is not the odor of the banana but rather an integration of the pleasantness of the banana odor with the subjective state at which it was encountered. Thus, whereas by our definition banana odor when you are hungry is a different object from banana odor when you are satiated, according to definition ***a***, these are the same object—banana.

Similarly, according to our definition, milk odor and sour-milk odor are completely different olfactory objects because they differ in their perceived pleasantness, whereas according to definition ***a***, these are the same object—milk. On the other hand, by our definition, if grapes and melon have exactly the same pleasantness for a specific person, then olfactory-wise, grapes and melon are the same object for that person. Below, we consider this point of view within four arguments.

ARGUMENT 1: AN ODOR OBJECT IS A GIVEN PLEASANTNESS

The primary function of olfaction can be viewed as to signal approach or withdrawal. This signal is best represented by pleasantness. Approach is the proper response to an edible food, a safe environment, or a fertile mate, and they all indeed generally smell pleasant. Withdrawal is the proper response to a poison or a predator, and they indeed generally smell unpleasant. In other words, because approach and withdrawal is the realm of olfaction, the language of olfaction is pleasantness, and an olfactory object is a given pleasantness.

If olfaction can tell us only about an odor's given pleasantness, then how can we know, for example, that a given odor is "strawberry"? The immediate answer to this is that usually we cannot know. As reviewed above, presented with an odor alone, humans usually fail to spontaneously provide the odor with a label. They do, however, provide a label under two conditions: What we here call the "olfactory laymen condition"—when offered alternative names (either verbally or visually), or more rarely under what we here call the "olfactory expert condition"—when an odor name is spontaneously generated. Our explanation for the laymen solution is that even through limited experience and learning, we have learned to link the given pleasantness of strawberry to a particular visual image, a particular context, and a particular name. Thus, once our nose puts us "in the ballpark" in terms of the exact pleasantness, we can complete the task by linking this pleasantness to one of a few optional solutions when offered, as long as one option will be significantly closer than the others in terms of pleasantness. In turn, the olfactory expert solution is to become so incredibly refined through experience and learning that the resolution on the pleasantness scale is fine enough to determine a strawberry by the molecular input alone. In other words, we claim that there is a pleasantness score nearly unique to strawberry, shared by only very few, if any, olfactory objects in the world, that will then smell exactly like strawberry. A simplistic analogy can be made using color. Imagine you perceived only color when visually inspecting a strawberry. Asked to identify what the "red" was, you would probably fail. Yet if you were asked whether the "red" was a strawberry, banana, or lemon, you would choose strawberry based on your previous experience. Humans can discriminate millions of colors. Now imagine that you spend your life picking strawberries, and you have learned the very unique shade of red that is shared by strawberries and only very few, if any, additional objects. If presented with this unique color, you may indeed spontaneously identify it as strawberry, not raspberry or Ferrari. In other words, even with a unidimensional scale, you could become very refined at identifying discrete objects, especially if this unidimensional scale were made of the relative inputs of 1000 (olfaction) rather than 3 (vision) different types of receptors. An ultimate unidimensional representation can explain the high level of olfactory performance retained following lesions to the olfactory bulb (Slotnick & Bisulco 2003). If the end representation of olfactory objects were multidimensional, then losing parts of the olfactory bulb would entail losing dimensions of the object, resulting in a different object. In contrast, if the representation is unidimensional, losing parts of the olfactory bulb will merely generate an impoverished object but not a different one.

Our notion of an odor object that does not correspond to a visual object contrasts with

ideas developed by Richardson & Zucco (1989) and Stevenson & Wilson (2007), who likened olfactory objects to visual objects. Stevenson & Wilson (2007) proposed that an odor object differs from a visual object in that the former reflects synthetic processing. Yet they further detailed that olfactory objects are the result of a pattern-matching system that recognizes discrete sets of spatial and temporal olfactory features and that the object is dissociated from its background by rapid central adaptation (Stevenson & Wilson 2007). They wrote, "Most odours are composed of 10s or 100s of volatile components, yet they are perceived as unitary perceptual events against a continually shifting olfactory background." We agree that a pattern-matching system that recognizes discrete sets of spatial and temporal olfactory features indeed exists; however, the pattern matching is not for the odor of the physical object but rather is for the overall pleasantness. We suggest that the odor of the physical object, and the background odor, are perceived as a unitary perceptual event, and their separation is dependent on additional nonolfactory sensory information and context.

Because our hypothesis and the current prevalent hypotheses on odor objects and their separation from background are clearly opposed, we propose a simple experiment that juxtaposes these two approaches. Blindfolded subjects could be presented with two olfactory objects, one edible and one inedible, placed simultaneously side-by-side in front of their nose (for example, a bar of chocolate and a used diaper). Subjects would be informed that there are two objects in front of them, and they would be asked to determine their edibility. According to the notion of objects akin to visual objects that can be separated from the odor background (Stevenson & Wilson 2007), subjects should say, "one item is edible and the other is not." In contrast, according to our theory, whereby the entire landscape would form one odor object, subjects would give only one answer: either both objects are edible, or both are inedible (we presume that subjects will refer to two objects rather than only one because they were explicitly informed of their presence; otherwise, we expect blindfolded subjects to perceive only one object spontaneously).

ARGUMENT 2: A GIVEN PLEASANTNESS IS THE COMBINATION OF EXTERNAL AND INTERNAL FACTORS

This argument is of course not novel on its own, yet it forms a critical component of our novel definition of olfactory objects (**Figure 6**). Cabanac (1971) proposed the word "alliesthesia" to describe a condition where a given external stimulus can be perceived as either pleasant or unpleasant depending upon signals coming from inside the body. Both hunger and ambient temperature have been studied as contexts for olfactory alliesthesia.

Fasting subjects initially rated the smell of orange syrup as pleasant but shifted its rating to unpleasant following glucose ingestion (Cabanac et al. 1973). Similarly, hunger or satiety modulated the hedonic facial responses to milk in three-day-old neonates (Soussignan et al. 1999).

The immediate effects of changes in environmental temperature on odor pleasantness ratings were studied to examine the influence of temperature on metabolic reserves (Russek et al. 1979). As expected, at 40°C hungry subjects rated alimentary odors as less pleasant than at 20°C. However, temperature had no influence on the perceived pleasantness of nonalimentary odors.

In an fMRI study aimed at revealing the brain mechanisms underlying olfactory alliesthesia, subjects were scanned with two food odors and then scanned again after eating one of the odor-corresponding foods to satiety (O'Doherty et al. 2000). The representation of the satiated food changed in the orbitofrontal region, namely secondary olfactory cortex. In other words, an internal state (in this case, satiety) influenced the olfactory representation in the brain.

ARGUMENT 3: THE INTERNAL SIGNALS ARE ANALOGOUS TO THE DIFFERENT VIEW ANGLES IN VISION

Humans are able to view an object from different angles yet still know that it is the same object. This phenomenon of visual invariance, which is demonstrated by mental rotation (Shepard & Metzler 1971), is based on multiple representations of the image viewed from various points (Edelman 1999). We propose that the different internal states that modulate overall pleasantness in olfaction are analogous to the different viewing angles in vision, and the ability to perceive an olfactory object as constant despite changing internal states reflects a form of olfactory mental rotation. Furthermore, we predict that if an internal state shifts beyond a certain threshold, the object will no longer be perceived as the same. There are many examples of shifts in olfactory perception as a function of shifts in internal state, such as shifts in olfaction across the menstrual cycle (Navarrete-Palacios et al. 2003) and in pregnancy (Nordin et al. 2004), shifts in olfaction associated with depression (Pollatos et al. 2007), and shifts in olfaction associated with hunger (Cabanac et al. 1973). This prediction could be tested in an experiment that would introduce two groups of subjects, one hungry and one satiated, to a novel food with a novel odor (for example, a carambola, also called starfruit). In this model, the two groups would learn two different odors: "hungry carambola" and "satiated carambola." Subjects would then later be tested at various levels of hunger/satiety for identification of the smell of carambola in a four-alternative forced-choice paradigm, and their reaction time would be measured. We predict that reaction time would correlate with hunger/satiety and, critically, that the direction of this correlation for subjects who learned the odor "hungry carambola" would be opposite that of those who learned the odor "satiated carambola." Of course, modality controls, such as a picture of the fruit, would need to be used in order to address the possibility of state-dependent learning, regardless of our theory (Tulving 1983).

ARGUMENT 4: ODOR IS A "SENSORY EMOTION"

We define an odor object as the combination of its external molecular components and internal state components. In agreement with most models of odor perception, given an olfactory stimulus, we expect the olfactory system to generate a form of pattern completion. Thus, given the external component of the stimulus, the system may attempt to complete the pattern by generating the internal component. Hence, the well-known tendency of odors to elicit emotions (Chu & Downes 2002, Epple & Herz 1999, Herz et al. 2004, Herz 2004, Herz & Cupchik 1995, Herz & Schooler 2002, Kirk-Smith et al. 1983) may merely be a form of olfactory object constancy and pattern completion. The ability of food odors to generate hunger or nausea may similarly be olfactory object constancy and pattern completion. For example, under our definition of olfactory object, the smell of steak when you are satiated is a different object from the smell of steak when you are hungry. The molecules of steak alone are a partial stimulus. Thus, the system will try to complete the object by generating the appropriate accompanying internal state. Thus, if you are slightly hungry, the better fit and more appropriate pattern completion will be for the odor object "hungry steak," and the smell will indeed generate hunger. In turn, if you are slightly satiated, then the better fit and the more appropriate pattern completion will be for the odor object "satiated steak," and the smell will generate nausea.

Indeed, odors not only elicit mood and emotion (Chu & Downes 2002, Diego et al. 1998, Epple & Herz 1999, Herz et al. 2004, Herz 2004, Herz & Cupchik 1995, Herz & Schooler 2002, Kirk-Smith et al. 1983, Knasko 1995, Lehrner et al. 2005, Weber & Heuberger 2008), but odor perception also shares many common characteristics with mood and emotion.

First, they share a common neural substrate, namely the limbic system, which is the neural substrate of emotion (LeDoux 2007) and largely corresponds to primary and secondary olfactory cortex, most notably amygdala and orbitofrontal cortex, respectively (Price 1987, 1990; Rolls 2004).

Second, pleasantness is the principal dimension of perception in both emotion (Fontaine et al. 2007) and olfaction (Khan et al. 2007).

Third, the combination of superior detection and discrimination concurrent with inferior verbalization is common to emotion and olfaction. For olfaction, this has been extensively detailed above; for emotion, a trivial example is that of love: We can all detect it and discriminate it from other emotions yet mostly fail to describe it in words (Levine 2005).

Fourth, odors and emotions share a similar status in memory in that both are not subject to recall, given that both are not subject to imagery. Olfactory imagery has been a topic of debate (Stevenson & Case 2005). In our view, what is mentally recreated during efforts of olfactory imagery is a given pleasantness. This is consistent with olfactory imagery-related activation of the olfactomotor system (Bensafi et al. 2003) and olfactory imagery-related activation of the brain (Bensafi et al. 2007). Thus, when trying to imagine the odor of strawberry, one can mentally recreate a low-acuity version of the pleasantness of strawberry. However, several objects may share the low-acuity pleasantness of strawberry, and hence this remains an impoverished form of imagery.

CONCLUSION

In this review, we have seen that the functional neuroanatomy of olfaction is highly conserved across mammals. Humans are poor at odor naming but, similar to other mammals, are keen at odor detection and discrimination. With poor access to language, the principal axis of human odor perception remains odor pleasantness.

Furthermore, we propose that poor odor naming reflects the unique nature of odor objects which, unlike visual objects, consist of an external component made of molecules and an internal component of emotional and homeostatic state that together generate a given pleasantness. This given pleasantness is the object. In summary, and echoing the quotation at the beginning of this section, we view olfaction as FlatLand (Abbott 1884), a realm in which unidimensional representations provide a wealth of information that—when augmented with multisensory and contextual information, both external and internal—generates the richness of smell. We highlight several lines of evidence that support this hypothesis, and propose novel experiments wherever the current literature did not provide data that either support or negate our ideas. We submit that our definition of odor objects, although far removed from current notions, is in fact consistent with much of the physiological and psychological data, that it explains several previously unexplained phenomena in olfaction, and most critically, that it is testable.

DISCLOSURE STATEMENT

The authors are not aware of any biases that might be perceived as affecting the objectivity of this review.

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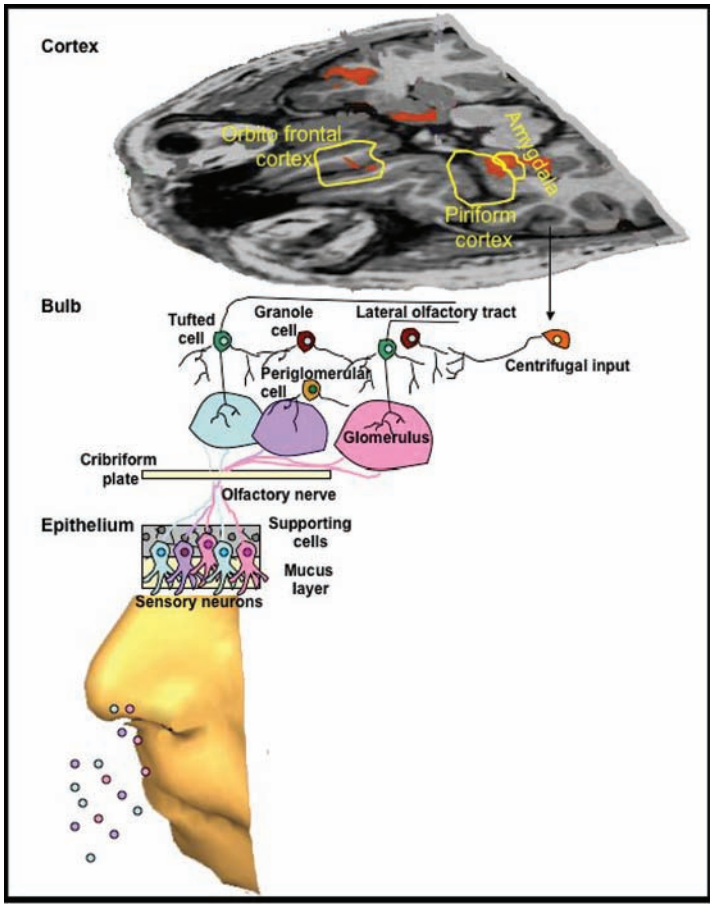

Figure 1

The olfactory neuroanatomy. Odor molecules are transported, by sniffing, to the olfactory epithelium, where they cross a mucus membrane to then bind with olfactory receptors. A neural signal is then transmitted through the olfactory nerve to the olfactory bulb. Following extensive bulbar processing resulting from interbulb, intrabulb, and cortex-to-bulb projections, the resultant signal is then projected via the lateral olfactory tract to primary olfactory cortex (piriform and amygdala are highlighted in the figure) and from there to secondary olfactory cortex (medial orbitofrontal cortex is highlighted in the figure).

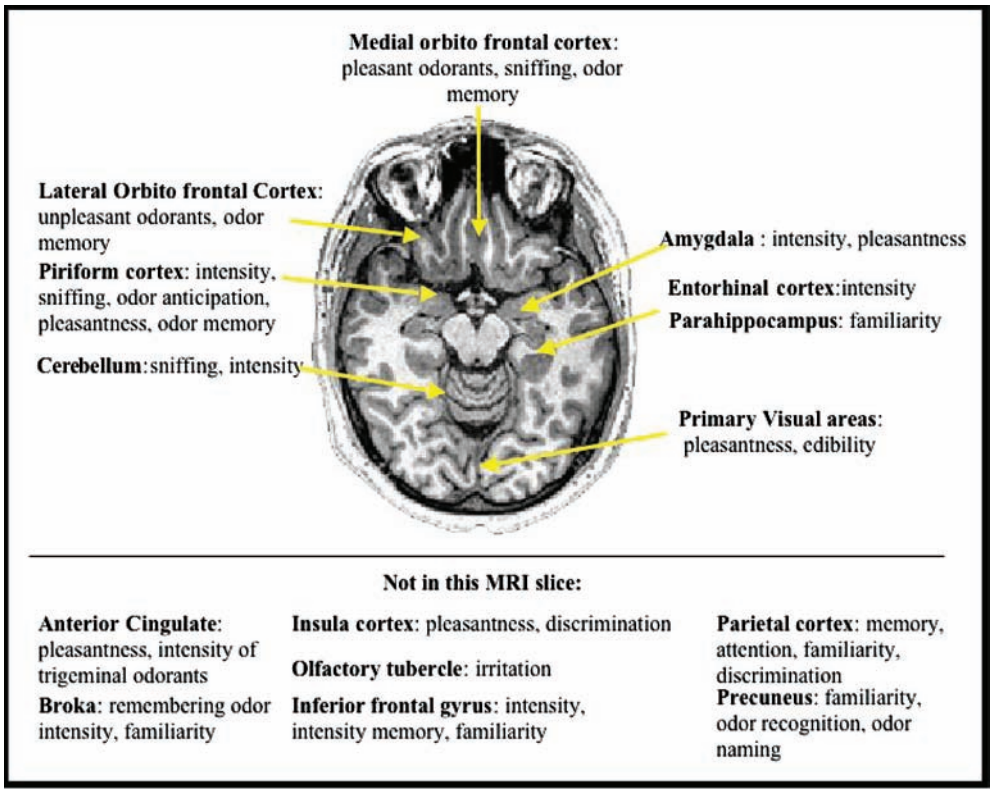

Figure 2

One magnetic resonance imaging slice captures most cortical regions implicated in olfaction. In other words, olfaction can be thought of as a ventral brain network. That said, several nonventral cortical areas have also been implicated in several olfactory tasks.

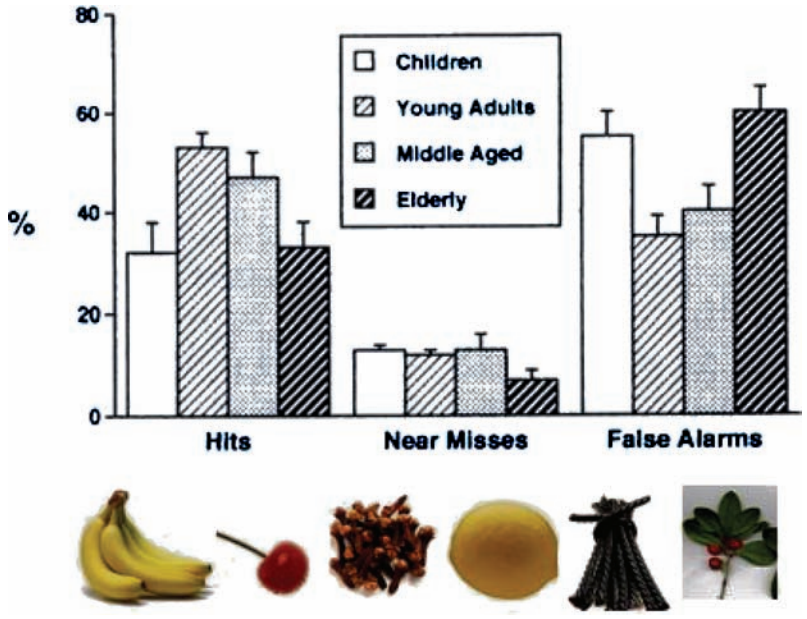

Figure 4

Poor human odor identification and naming. Percent correct (hits), near-miss, and far-miss (false alarms) identification (±SEM) for children, young adults, middle-aged, and elderly persons (from de Wijk & Cain 1994a). Images represent the odor sources used in this experiment: banana, cherry, cloves, lemon, licorice, and wintergreen.

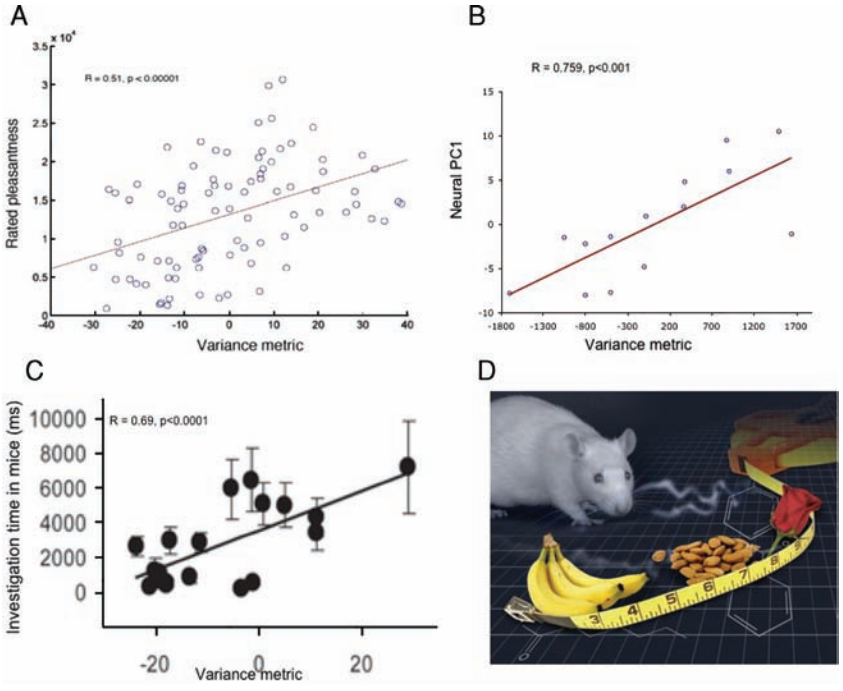

Figure 5

Pleasantness as the principal dimension of smell. (*A*) Khan et al. (2007) found that the first principal component of molecular structure (PC1), referred to as the variance metric, predicted the pleasantness of 90 different odorants as assessed by 20 subjects (adapted from Haddad et al 2008b). (*B*) The PC1 (variance metric) predicted the difference in neural activity at mouse olfactory receptor neurons (mouse data from Sato et al. 1994; correlation explained in Haddad et al. 2008a). (*C*) The PC1 (variance metric) predicted behavioral preferences in mice (adapted from Mandairon et al. 2009). (*D*) A graphic illustration of the notion of an olfactory metric that we argue reflects the axis of maximal variance in odor structure and the axis of pleasantness in perception (from Haddad et al. 2008b).

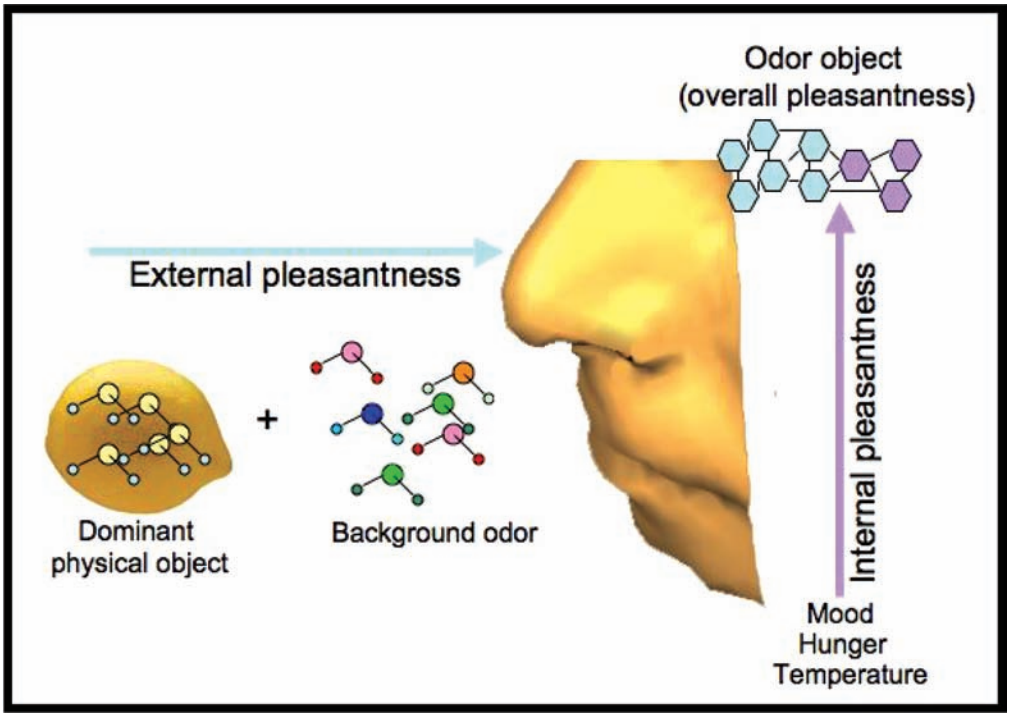

Figure 6

Definition of odor objects. We suggest that an odor object is the integration of the external odor pleasantness with the internal pleasantness. The external pleasantness is the combined pleasantness of the odor emanated from the dominant source of odor (physical object) together with the background odor (*blue hexagons*). The internal pleasantness is the subjective state at the moment of coding: mood, hunger, fear, temperature, etc. (*purple hexagons*). Brain odor-object representation is the overall pleasantness (*blue* and *purple hexagons* combined). Thus, we argue that given an external stimulus similar to the blue hexagons alone, the brain may try to complete the pattern by generating the appropriate purple hexagons, namely an emotion or homeostatic state.