Chem. Percept.
DOI 10.1007/s12078-008-9017-1

Perceptual and Neural Plasticity of Odor Quality Coding in the Human Brain

Jay A. Gottfried

Received: 28 November 2007 / Accepted: 26 March 2008
© 2008 Springer Science + Business Media, LLC

Abstract Current neurobiological models of odor perception tend to emphasize the "bottom-up" contributions of odorant chemistry in determining the perceptual features of an odor. However, increasing research suggests that "top-down" effects related to learning and experience play equally important roles in human olfactory perception, implying that a given set of olfactory receptors activated by an odorant does not neatly map onto a given odor percept. Rather, odor perception may rely on more synthetic mechanisms subserved by higher order brain regions. This review article focuses on the modulatory effects of learning, context, and experience on human odor perception. Recent psychophysical and neuroimaging work from our laboratory indicates that sensory-specific information about odor quality is not static within human piriform and orbitofrontal cortices but can be rapidly updated by mere sensory exposure. This experience-dependent neural plasticity parallels behavioral improvements in odor perception, providing direct evidence for the role of learning in shaping neural representations of odor quality in the human brain.

Keywords Experience · Human Brain · Neural Plasticity · Odor · Olfaction · Orbitofrontal Cortex · Piriform Cortex · Olfactory Perceptual Learning · Smell

---

J. A. Gottfried (✉)
Cognitive Neurology & Alzheimer's Disease Center,
Northwestern University Feinberg School of Medicine,
320 E. Superior St., Searle 11-453,
Chicago, IL 60611, USA
e-mail: j-gottfried@northwestern.edu

Abbreviations

PET	positron emission tomography
fMRI	functional magnetic resonance
OFC	orbitofrontal cortex

Introduction

An old merchant marine ship known as The Raven is said to be haunted, for successive captains have all met an unseemly and inexplicable demise. The crew mutters about an awful smell aboard the ship, an "odor of death," that always heralds the captain's last gasp. Enter Lamont Cranston (alias *The Shadow*) and his friendly companion Margo Lane who agree to investigate the strange goings-on. By using his hypnotic powers to cloud the seamen's minds, The Shadow is soon able to identify and apprehend the villain. Light, playful dialogue between Margo and Lamont, as he demystifies the circumstances surrounding the odor of death, brings the story to a satisfying conclusion:

> Margo Lane: But what about that odor? That hideous odor of death?
>
> Lamont Cranston: That was nothing more than a few basic chemicals placed in the ventilator. Our *imagination* provided the so-called odor of death.
>
> Margo Lane: Hmm…simple enough.
>
> –Transcript from *The Shadow* radio program (Shadow, 19 October 1941)

As this brief glimpse of American cultural history aptly demonstrates, the notion that human olfactory perception is under the spell of context, expectation, and experience is an old one. Many of us have experienced a bland glass of red wine suddenly transforming into an “odiferous vernal celebration of blueberry, sawdust, and horse-mane” (or something to that effect) after a few trifling comments from a self-appointed wine expert. These anecdotal examples highlight the fundamental malleability of odor object perception.

The above considerations have far-reaching implications for neurobiological theories of odor perception. The idea that “top-down” factors such as learning, context, and experience can help define percepts of smells (Wilson and Stevenson 2003; Stevenson and Wilson 2007) provides an alternative (though less often acknowledged) perspective on odor processing, complementing “bottom-up” olfactory models that have focused on odorant chemistry. Recent work in non-human animals has shown that chemical determinants of an odorous molecule (such as molecular functional group or carbon-chain length) are encoded as discrete patches or clusters within glomeruli of the olfactory bulb, and it has been suggested that odor identity is represented in the combination of bulbar activity patterns elicited by each of an odorant’s unique chemical features (for recent reviews, see Mori et al. 2006; Johnson and Leon 2007). Interestingly, several rodent studies have demonstrated a relationship between these chemistry-based bulb “maps” and odor perception, as indexed via behavioral paradigms of olfactory habituation or discrimination learning (Linster et al. 2001; Cleland et al. 2002; Ho et al. 2006; Youngentob and Schwob 2006). For example, behaviorally indistinguishable odor enantiomers (mirror-image molecules) evoke highly overlapping spatial patterns in the olfactory bulb, whereas behaviorally discriminable enantiomers evoke statistically distinct patterns (Linster et al. 2001). There is also evidence in humans for an influence of odorant chemistry on perceived odor valence (Khan et al. 2007) and on functional magnetic resonance imaging (fMRI) responses in anterior piriform cortex (Gottfried et al. 2006; Li et al. 2006), suggesting that human olfactory brain regions have direct access to information about an odorant’s chemical attributes and can extract this information to guide certain forms of odor perception.

On the other hand, it would be overly optimistic to assume that an aromatic aldehyde, a saturated polyester, or a heterocyclic furan should inevitably yield the smell of hawthorn, quince, or baked bread. Indeed, olfactory psychophysics research has shown that structure and function are anything but predictable when it comes to olfactory perception (Polak 1973; Cain and Polak 1992). If the exact same volatile odorous molecule can evoke manifold different odor percepts, even within the same individual and even in a short span of time, then it is evident that odor quality (i.e., the character or identity of a smell emanating from an odorous object) is not a straightforward outcome of physical attributes (Wilson and Stevenson 2006). Indeed, a recent olfactory fMRI cross-adaptation study from our laboratory indicates that odorant structure and perceived odor quality are encoded in separable subregions of the human primary olfactory (piriform) cortex (Gottfried et al. 2006). By using a set of odorants that systematically varied in molecular functional group (aldehyde or alcohol) and perceptual quality (lemon or vegetable smell), we were able to dissociate these two factors within a single experimental design. Cross-adapting fMRI responses were identified to functional group (but not quality) in anterior piriform subregions and to odor quality (but not group) in posterior piriform subregions (Gottfried et al. 2006). Notably, the presence of odor quality codes in posterior piriform cortex was independent of any simple structural configuration, raising the possibility that synthetic, integrative mechanisms underlie the neural organization of odor objects (Wilson and Stevenson 2003; Wilson et al. 2003), likely established through perceptual learning, sensory context, and semantic experience.

The remainder of this article reviews the role of learning, context, and experience in modulating human odor perception, at both the behavioral and neural levels, with some emphasis on our own research (Li et al. 2006) involving olfactory perceptual learning in the human brain.

Perceptual Plasticity of Human Olfactory Processing

Much evidence suggests that there is marked ambiguity in human olfactory discrimination. This curious feature distinguishes the olfactory system from other sensory modalities, perceptions of which (e.g., visual or auditory) tend to be more dependably anchored to the physical environment. On the other hand, the inherent ambiguity in odor perception probably makes it more susceptible to the modulatory effects of learning and experience, which, for a sensory system designed to form associations with biologically relevant events (such as foods, predators, and mates), would have distinct evolutionary advantages.

On the basis of human psychophysical studies, it has been known for many years that identification of single odors is poor, but improves when relevant semantic (e.g., verbal) labels are available (Cain 1979). Even basic aspects of olfactory processing are strongly modulated by visual, perceptual, and cognitive factors. Dalton has shown that the adaptation (fatigue) of odor perception is affected by whether subjects are told the odor is healthy or hazardous (Dalton 1996). Color has been found to interact with perceived odor intensity (Zellner and Kautz 1990; Gilbert et al. 1996; Zellner and Whitten 1999). Odor intensity and pleasantness are enhanced by cultural experience (Ayabe-Kanamura et al. 1998) and by knowledge of the odor’s source (Distel and Hudson 2001). In a clever study by Herz and von Clef (2001), subjects were presented a series of odors in combination with either positive or negative labels. As an example, the odor of violet leaf was paired on alternate trials with the word “cucumber” or with the word “mildew.” Pleasantness ratings of these odors were significantly and profoundly affected by the attached verbal context. From these studies, one is tempted to infer that the ambiguous nature of odor perception helps to place the sense of smell under the powerful sway of both external (sensory) and internal (cognitive) factors.

One of the more scandalous experiments was a wine-tasting study conducted at the University of Bordeaux (Morrot et al. 2001) where 54 enology students provided a series of odor descriptions for red wines (e.g., chicory, prune, cherry) and white wines (e.g., honey, grapefruit, lemon). Following this part of the study, a white wine was surreptitiously colored with odorless, tasteless red dye without the subjects’ knowledge. As a result, subjects consistently described the “red” white wine using language typically reserved for red wine and avoided the use of white wine terms. Thus, in the absence of appropriate visual information, wine odor had minimal impact on olfactory discrimination, and despite “expertise” among the wine students, the visual contextual cue dominated. These examples suggest that interactions between olfactory and other sensory modalities may contribute to effective odor perception and that the experience of a smell is heavily regulated by accompanying sensory, semantic, and verbal cues.

The power of suggestion (as a contextual cue) also plays an equally important role in odor perception. A classroom of students was convinced that a bottle filled with distilled water actually contained a “strong and peculiar” odor that slowly spread from the front to the back of the room (Slosson 1899). When a radio station informed its listeners that a certain auditory tone would recreate the physiological experience of a “pleasant country smell,” many people reported perceiving such an odor (O’Mahony 1978). Learning and experience are also critical in olfactory identification and discrimination (reviewed in Wilson and Stevenson 2003). Taken together, these findings indicate that an individual’s olfactory viewpoint is considerably shaped by higher order operations, likely to be mediated via central olfactory processes. It is even fair to say that context and experience effectively weave olfactory illusions, whereby one’s perception of an odor can be altered depending on the surrounding circumstances.

Neural Plasticity of Human Olfactory Processing

Initial human olfactory imaging studies [including positron emission tomography (PET) and fMRI] were designed to delineate which areas of the brain are responsive to different odors (Zatorre et al. 1992; Zald and Pardo 1997; Sobel et al. 1998). These investigations confirmed and extended much of what had been established from animal and human (lesion) studies that when subjects smell an odor, brain activity is triggered in the primary olfactory (piriform) cortex and the amygdala in the medial temporal lobes and in the orbitofrontal cortex (OFC) situated at the basal frontal part of the brain. Interestingly, each of these areas including piriform cortex, amygdala, and OFC is considered to be part of the extended “reptilian” brain or limbic cortex, critical for controlling emotion, memory, and behavior. Thus, the anatomical and functional evidence support the idea that odors engage those very brain regions that are essential to survival.

An increasing number of fMRI studies have begun to show that odor processing in the human brain is powerfully modified by sensory, emotional, associative, and cognitive experience. Put differently, one and the same odor may provoke a different brain response depending on the surrounding events. In one of the first fMRI studies of this kind, O’Doherty et al. (2000) showed that appetite and motivational state could influence sensory-specific odor responses in human OFC. On alternating fMRI blocks, healthy participants were presented with banana or vanilla odor both before and after a lunch of bananas until they became sated for this item. As a result of this manipulation, the neural activity evoked by the banana odor (but not the vanilla odor) was selectively diminished in OFC, indicating that this brain region was sensitive to how rewarding the banana stimulus was at any given time (it is unlikely that the OFC effect was due to sensory habituation, as perceptual ratings of odor intensity did not significantly differ from pre- to post-satiety for either odor stimulus). Other studies in the gustatory domain have shown similar effects. Responses in human OFC decrease as chocolate (a complex food stimulus with prominent olfactory components) is consumed to satiety (Small et al. 2001) and also occur when subjects drink a flavorful food liquid (either tomato juice or chocolate milk) until they are sated (Kringelbach et al. 2003).

Odor responses in the brain are also highly malleable when smells are presented with other sensory cues. An early PET study by Small et al. (1997) evaluated sensory processing in response to odors, tastes, and combinations of odors and tastes that either matched (e.g., strawberry odorant with a sweet sucrose tastant) or mismatched (e.g., strawberry odorant with a salty sodium chloride tastant). These investigators found that combined odor–taste stimuli elicited reduced PET activity in olfactory and gustatory brain regions. Moreover, they found greater brain activity in the amygdala and the basal forebrain when these combinations mismatched (vs. matched) in quality. These results provided early evidence that multisensory context can influence the neural processing evoked by smells. An fMRI variation of this study (Small et al. 2004) in which smells were delivered retronasally (via the mouth) rather than orthonasally (via the nose) also demonstrated multisensory odor–taste integration within OFC and nearby regions in the insula and anterior cingulate cortex.

Using a different fMRI paradigm, Gottfried and Dolan (2003) showed that visual information also modifies odor-dependent activity in OFC. The primary aim of this study was to characterize mechanisms underlying visual modulation of olfactory perception. Using a simple odor detection task, we demonstrated that olfactory detection was faster and more accurate when odors appeared in the context of semantically congruent visual cues. So, for example, subjects were able to detect the smell of rose more quickly and more accurately when it was presented in combination with a congruent image (e.g., the picture of a flower) as opposed to an incongruent image (e.g., the picture of a bus). Then, by comparing fMRI data between the congruent and incongruent smell–picture conditions, we identified the neural correlates of this behavioral effect: activity was increased in OFC and in the hippocampus. These data confirm that the exact same sensory input can evoke different brain responses depending on whether it was experienced in a semantically appropriate context.

Similar results of sensory context on odor processing in OFC have been demonstrated with combinations of odors and tastes, as mentioned above (Small et al. 2004), and with combinations of odors and verbal labels (de Araujo et al. 2005). In this latter study, the perceived pleasantness of a test odor (combination of sweaty-smelling isovaleric acid + cheddar cheese flavor) was rated higher when accompanied by the visual word label, “cheddar cheese,” than when accompanied by the word label, “body odor.” Analysis of the fMRI data revealed greater activation in OFC and cingulate cortex to the test odor when it was labeled “cheddar cheese” than when it was labeled “body odor,” and this effect correlated with pleasantness ratings to the test odor. Together, the 2003 odor–picture study by Gottfried and Dolan and the 2005 odor–word study by de Araujo et al. help to underscore the idea that prior experience and sensory context have a marked impact on the processing of olfactory information. Such mechanisms may also help to resolve the inherent ambiguity in olfactory perception and optimize odor-directed behaviors.

Olfactory Perceptual Learning in the Human Brain

Often sensory exposure, even in the absence of explicit training, is sufficient to modify sensory perception. William James, one of the founders of American psychology, was among the first to discuss this unique form of learning in his *Principles of Psychology* (James 1890), punctuating his observations with a number of colorful personages, including an enophile who could distinguish between the upper and lower halves of Madeira wine by its flavor, a blind woman who could sort the washed linen of institutionalized patients by the smell of their clothes, and an agricultural inspector who could identify the geographical source of a sack of flour by touch. Notwithstanding the possibility that these special perceptual abilities may have been present at birth, their talents nicely showcase the phenomenon of “perceptual learning” (James 1890; Gibson and Walk 1956; Gibson 1991; Goldstone 1998; Gilbert et al. 2001; Fahle and Poggio 2002) in which sensory experience induces meaningful changes in behavior and brain function.

Perceptual learning has been studied most commonly in the visual system. For example, mere visual exposure to scribbled pictures (doodles) results in subjects being better able to differentiate among related pictures, generating doodle “expertise” (Gibson and Walk 1956). It has become clear that the same principles hold in the olfactory domain. Repeated presentations of an odor reduce olfactory detection thresholds (Stevens and O’Connell 1995; Dalton et al. 2002) and can even boost olfactory sensitivity in subjects seemingly anosmic to the steroid androstenone (Wysocki et al. 1989; Mainland et al. 2002). Exposure to wine (Owen and Machamer 1979) or beer (Peron and Allen 1988) is sufficient to improve sensitivity toward stimuli whose chief sensory property is olfactory. Experience and familiarity significantly enhance odor perception and odor quality discrimination of odor mixtures (Rabin 1988; Rabin and Cain 1989; Jehl et al. 1995), while exposure to odor mixtures alters the perceived quality of the individual components (Stevenson 2001). Many of these studies provide examples of stimulus “differentiation,” an important mechanism of perceptual learning in which experience refines sensory perception through differentiation of stimulus features, dimensions, or categories (Gibson 1991; Goldstone 1998; Schyns et al. 1998).

Notably, despite growing behavioral evidence for olfactory perceptual learning, how this form of learning updates odor quality codes in the human brain is unknown. Recent work by Dr. Wen Li and colleagues in my laboratory (Li et al. 2006) has specifically explored which brain areas mediate experience-induced behavioral changes in odor expertise. To this end, we combined fMRI techniques with an olfactory habituation paradigm (Wilson 2000a, b, 2003) to test whether prolonged olfactory exposure (as a simple form of perceptual learning) would modify neural representations of odor quality in areas previously implicated in coding of this perceptual feature, including piriform cortex (Gottfried et al. 2006; Kadohisa and Wilson 2006) and OFC (Schoenbaum and Eichenbaum 1995; Savic et al. 2000; Royet et al. 2001; Dade et al. 2002; Gottfried et al. 2006). Moreover, in parallel to the neural effects, we hypothesized that odor experience would facilitate perceptual differentiation between odorants sharing critical qualitative or molecular attributes.

Subjects took part in three fMRI scanning sessions. During pre-habituation, they repeatedly smelled four odorants: a target (TG) odorant destined for habituation; a quality-related (QR) odorant; a functional-group related (GR) odorant; and an unrelated (CT) odorant. During the habituation session, subjects smelled the TG stimulus continuously for a period of 3.5 min. The post-habituation session was identical to pre-habituation. Thus, by measuring odorant-evoked neural activity both before (pre) and after (post) TG habituation, we were able to assess how sensory experience updates fMRI representations of odor quality and odorant structure.

We found that from pre- to post-habituation, there was experience-dependent response enhancement in both piriform and orbitofrontal cortices, which even preceded behavioral changes in odor discrimination. In posterior piriform cortex (Fig. 1a), neural activity elicited by the quality-related odorant increased from pre- to post-habituation; in olfactory OFC (Fig. 1b), increased activation was seen in response to both the quality-related and the functional group-related odorants. In parallel to these neural effects, subject-specific similarity ratings of odor quality decreased (indicating more dissimilar) from pre- to post-habituation for the pair of odorants related in perceptual quality, and they also decreased for the odorant pair related in chemical structure. The implication is that sensory experience with the TG odorant successfully enhanced the discriminative capacity (or expertise) for odorants similar in perceptual quality or structure. For example, subjects exposed for 3.5 min to R-carvone (a minty ketone) became mint “experts,” and they simultaneously became experts at distinguishing among ketone-bearing odorants.

Finally, to demonstrate whether there was a predictive relationship between the magnitude of response change in OFC (or piriform cortex) and the behavioral improvement in perceptual learning, we performed a correlation analysis by regressing subject-specific changes in neural activity (post- minus pre-habituation) against changes in odor quality similarity (post minus pre). In olfactory OFC, there was a significant correlation between neural and behavioral indices of learning (Fig. 2). No such effect was observed in piriform cortex. These additional results suggest that OFC is a critical locus for guiding experience-dependent behavioral improvements in odor expertise. The role of OFC in helping to orchestrate olfactory perceptual learning may

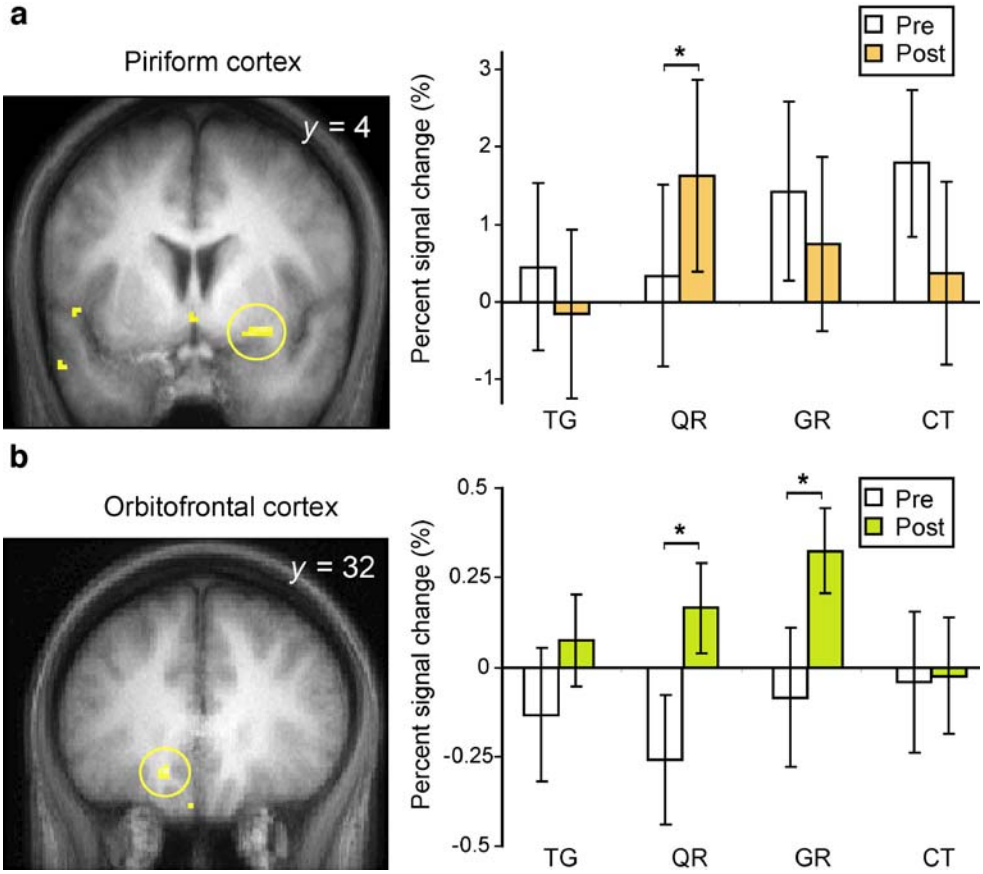

Fig. 1 Learning-induced neural plasticity in olfactory areas of the human brain. **a** In posterior piriform cortex, continuous exposure to the target odorant (*TG*) enhances neural activity from pre- to post-habituation in response to the quality-related odorant (*QR*), but not to the functional group-related odorant (*GR*) or the unrelated control odorant (*CT*). **b** In orbitofrontal cortex, TG exposure enhances neural activity in response to both the QR and GR odorants. Brain activations are overlaid on coronal sections of a T1-weighted MRI scan (display threshold, $p<0.001$ uncorrected). Error bars indicate mean± SEM. *$p<0.05$ corrected for small volume (reprinted and modified from Neuron, vol. 52, W. Li, E. Luxenberg, T. Parrish, J.A. Gottfried, Learning to smell the roses: experience-dependent neural plasticity in human piriform and orbitofrontal cortices, pp 1097–1108, Copyright 2006, with permission from Elsevier)

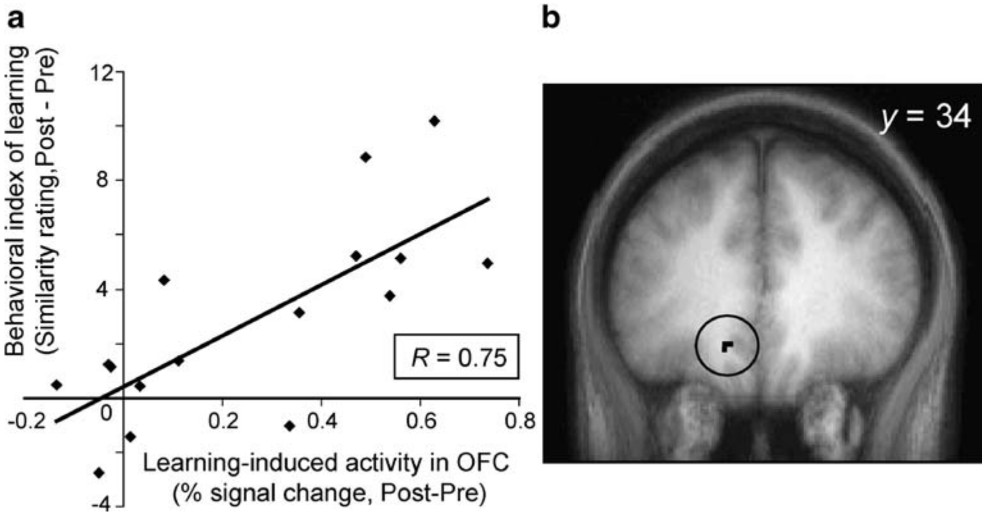

Fig. 2 Experience-dependent plasticity in orbitofrontal cortex is predictive of olfactory perceptual learning. This subject-wise regression analysis indicates that the magnitude of learning-induced response enhancement in orbitofrontal cortex (*OFC*) directly correlates with the degree of learning-induced perceptual odor expertise, as indexed via behavioral ratings of odor quality similarity (post- minus pre-exposure). Each *black diamond* represents a different subject (reprinted and modified from Neuron, vol. 52, W. Li, E. Luxenberg, T. Parrish, J.A. Gottfried, Learning to smell the roses: experience-dependent neural plasticity in human piriform and orbitofrontal cortices, pp 1097–1108, Copyright 2006, with permission from Elsevier)

reflect its highly integrative anatomical organization, involving dense and reciprocal connectivity with limbic emotional brain networks (Carmichael and Price 1995). To the extent that it is the afferent input (and efferent output) that distinguishes OFC from other regions of prefrontal cortex (PFC; Goldman-Rakic 1987), orbital PFC would be particularly suited for mediating emotional (and olfactory) expertise, whereas dorsolateral PFC (with a different set of inputs and outputs) would be better equipped to mediate higher order cognitive expertise.

It is interesting to note that fMRI signal increases in the human brain are commonly observed in non-olfactory studies of perceptual learning (Gauthier et al. 1999; Furmanski and Engel 2000; Gauthier et al. 2000; Schwartz et al. 2002; Sigman et al. 2005). For example, perceptual training for novel, unfamiliar visual objects (greebles) was associated both with increased neural activity in fusiform and occipital cortices and with enhanced greeble recognition during a sequential matching task (Gauthier et al. 1999). Similar regional patterns of fMRI activation were observed when ornithologists viewed pictures of birds (but not cars) and when automobile enthusiasts viewed pictures of cars (but not birds; Gauthier et al. 2000). Such findings suggest that areas of higher order visual association cortex help facilitate visual object categorization and expertise, raising the possibility that higher order olfactory brain areas described here (piriform cortex and OFC) have a similar functional role in category learning, configural coding, and subordinate-level discrimination of "odor objects."

Conclusions

Many of the articles appearing in this Special Issue center on the role of multisensory integration in the formation of flavor perception, which in turn formed the main theme of a 2-day symposium at the 2007 American Chemical Society (ACS) meeting in Boston (upon which these articles are based). While the present review paper does not directly focus on sensory interactions across smell, taste, touch, and temperature, its emphasis fits squarely with the idea that the assembly of chemosensory percepts is highly dependent on non-olfactory (extra-olfactory) factors. These factors, including context, memory, learning, and experience, serve much in the same way that multisensory cues serve to shape the perception of odor objects.

As discussed above, even basic sensory exposure to a single odor is sufficient to modify how olfactory areas of the brain (including posterior piriform cortex and OFC) process smells, and these experience-dependent brain changes lead to observed behavioral improvements in odor perception and discrimination. It is worth speculating that the capacity for learning-induced neural plasticity in olfactory cortices governs the general development of human olfactory perception. This mechanism may underlie the acquisition of fine-grained percepts that distinguish, for example, the smell of *Rosa damascena* (Bulgarian rose) from that of *Rosa centifolia* (rose Maroc), such that we are able to discriminate thousands, if not tens of thousands, of different smells in the environment.

The demonstration of training-induced expertise in odor quality differentiation is somewhat at odds with the relative *absence* of training effects on odor mixture discrimination, even among wine experts who have difficulty distinguishing more than three components in an odor mixture (Laing and Francis 1989; Livermore and Laing 1996). A possible resolution to this paradox may be that odor mixture identification depends on analytical, elemental processing, which the human brain may be rather poor at implementing (so that identifying components in an odor mixture is little improved by training), whereas experience-induced changes in odor quality discrimination may rely more on integrative, configural (synthetic) processing, which the human brain is much better able to execute. These contrasting studies nevertheless illustrate some of the constraints on olfactory expertise and emphasize the point that not all aspects of olfactory perception are equally honed by experience.

The corollary to these arguments is a simple one: how an odorant's quality is perceived is a product not only of its underlying "chemistry" but also of personal, idiosyncratic experience. Presuming (perhaps unfairly) that many audience members at the ACS symposium had extensive training in analytical, biochemical, inorganic, organic, and/or physical chemistry, one goal of my presentation was to highlight some of the alternative, or complementary, mechanisms of odor coding that operate in concert with chemical (labeled-line, data-driven) models of odor perception. In all likelihood, these two mechanisms act in concert to allow a balance between structural and perceptual levels of olfactory processing and may even provide unique functional advantages depending on the needs of an organism. For example, labeled-lines communicating information about odorant chemical attributes in the olfactory bulb could ensure rapid access of biologically relevant odor stimuli to downstream brain areas mediating behaviors critical for survival. In contrast, more distributed, integrative information about odor perceptual quality in piriform cortex and OFC could serve as a neural template or pattern (Freeman 1979; Haberly 1985; Haberly and Bower 1989) for guiding higher order aspects of odor perception, memory, and recall.

In summary, it is increasingly evident that the perception of odor objects is a synthetic process requiring the incorporation of past information, present context, and future expectations. Our own data directly show that the same invariant chemical input can evoke different brain responses in posterior piriform and orbitofrontal cortices, suggesting that neural representations of odor are not static, predetermined, or predictable but are flexibly updated by experience. Such observations should also have important implications for how brains ensure perceptual constancy in spite of great variance in the olfactory environment (see Wilson and Stevenson 2006), and, at a more applied level, how odor-design chemists (e.g., food scientists and perfumers) hope to ensure perceptual constancy in spite of great subjective variance in human olfactory experience.

Acknowledgments I would like to thank P. Breslin and J.V. Leland for conference organization, members of the Gottfried lab including J. Howard, W. Li, and J. Plailly for their olfactory expertise, C. Costa-Price and C.W. Price for timely nourishment, and H. Zankel for support.

References

Ayabe-Kanamura S, Schicker I, Laska M, Hudson R, Distel H, Kobayakawa T, Saito S (1998) Differences in perception of everyday odors: a Japanese–German cross-cultural study. Chem Senses 23(1):31–38

Cain WS (1979) To know with the nose: keys to odor identification. Science 203:467–470

Cain WS, Polak EH (1992) Olfactory adaptation as an aspect of odor similarity. Chem Senses 17:481–491

Carmichael ST, Price JL (1995) Limbic connections of the orbital and medial prefrontal cortex in macaque monkeys. J Comp Neurol 363(4):615–641

Cleland TA, Morse A, Yue EL, Linster C (2002) Behavioral models of odor similarity. Behav Neurosci 116(2):222–231

Dade LA, Zatorre RJ, Jones-Gotman M (2002) Olfactory learning: convergent findings from lesion and brain imaging studies in humans. Brain 125(Pt 1):86–101

Dalton P (1996) Odor perception and beliefs about risk. Chem Senses 21(4):447–458

Dalton P, Doolittle N, Breslin PA (2002) Gender-specific induction of enhanced sensitivity to odors. Nat Neurosci 5(3):199–200

de Araujo IE, Rolls ET, Velazco MI, Margot C, Cayeux I (2005) Cognitive modulation of olfactory processing. Neuron 46 (4):671–679

Distel H, Hudson R (2001) Judgement of odor intensity is influenced by subjects' knowledge of the odor source. Chem Senses 26 (3):247–251

Fahle M, Poggio T (2002) Perceptual learning. MIT Press, Cambridge, MA

Freeman WJ (1979) EEG analysis gives model of neuronal template-matching mechanism for sensory search with olfactory bulb. Biol Cybern 35(4):221–234

Furmanski CS, Engel SA (2000) Perceptual learning in object recognition: object specificity and size invariance. Vis Res 40 (5):473–484

Gauthier I, Tarr MJ, Anderson AW, Skudlarski P, Gore JC (1999) Activation of the middle fusiform 'face area' increases with expertise in recognizing novel objects. Nat Neurosci 2(6):568– 573

Gauthier I, Skudlarski P, Gore JC, Anderson AW (2000) Expertise for cars and birds recruits brain areas involved in face recognition. Nat Neurosci 3(2):191–197

Gibson EJ (1991) An odyssey in learning and perception. MIT Press, Cambridge, MA

Gibson EJ, Walk RD (1956) The effect of prolonged exposure to visually presented patterns on learning to discriminate them. J Comp Physiol Psychol 49(3):239–242

Gilbert AN, Martin R, Kemp SE (1996) Cross-modal correspondence between vision and olfaction: the color of smells. Am J Psychol 109(3):335–351

Gilbert CD, Sigman M, Crist RE (2001) The neural basis of perceptual learning. Neuron 31(5):681–697

Goldman-Rakic PS (1987) Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In: Plum F (ed) Handbook of physiology, volume V. The nervous system, higher functions of the brain. American Physiological Society, Bethesda, MD, pp 373–417

Goldstone RL (1998) Perceptual learning. Annu Rev Psychol 49:585–612

Gottfried JA, Dolan RJ (2003) The nose smells what the eye sees: crossmodal visual facilitation of human olfactory perception. Neuron 39(2):375–386

Gottfried JA, Winston JS, Dolan RJ (2006) Dissociable codes of odor quality and odorant structure in human piriform cortex. Neuron 49(3):467–479

Haberly LB (1985) Neuronal circuitry in olfactory cortex: anatomy and functional implications. Chem Senses 10:219–238

Haberly LB, Bower JM (1989) Olfactory cortex: model circuit for study of associative memory? Trends Neurosci 12(7):258–264

Herz RS, von Clef J (2001) The influence of verbal labeling on the perception of odors: evidence for olfactory illusions? Perception 30(3):381–391

Ho SL, Johnson BA, Chen AL, Leon M (2006) Differential responses to branched and unsaturated aliphatic hydrocarbons in the rat olfactory system. J Comp Neurol 499(4):519–532

James W (1890) The principles of psychology. Henry Holt & Co., New York

Jehl C, Royet JP, Holley A (1995) Odor discrimination and recognition memory as a function of familiarization. Percept Psychophys 57(7):1002–1011

Johnson BA, Leon M (2007) Chemotopic odorant coding in a mammalian olfactory system. J Comp Neurol 503(1):1–34

Kadohisa M, Wilson DA (2006) Separate encoding of identity and similarity of complex familiar odors in piriform cortex. Proc Natl Acad Sci U S A 103(41):15206–15211

Khan RM, Luk CH, Flinker A, Aggarwal A, Lapid H, Haddad R, Sobel N (2007) Predicting odor pleasantness from odorant structure: pleasantness as a reflection of the physical world. J Neurosci 27(37):10015–10023

Kringelbach ML, O'Doherty J, Rolls ET, Andrews C (2003) Activation of the human orbitofrontal cortex to a liquid food stimulus is correlated with subjective pleasantness. Cerebral Cortex 13:1064–1071

Laing DG, Francis GW (1989) The capacity of humans to identify odors in mixtures. Physiol Behav 46(5):809–814

Li W, Luxenberg E, Parrish T, Gottfried JA (2006) Learning to smell the roses: experience-dependent neural plasticity in human piriform and orbitofrontal cortices. Neuron 52(6):1097–1108

Linster C, Johnson BA, Yue E, Morse A, Xu Z, Hingco EE, Choi Y, Choi M, Messiha A, Leon M (2001) Perceptual correlates of neural representations evoked by odorant enantiomers. J Neurosci 21(24):9837–9843

Livermore A, Laing DG (1996) Influence of training and experience on the perception of multicomponent odor mixtures. J Exp Psychol Hum Percept Perform 22(2):267–277

Mainland JD, Bremner EA, Young N, Johnson BN, Khan RM, Bensafi M, Sobel N (2002) Olfactory plasticity: one nostril knows what the other learns. Nature 419(6909):802

Mori K, Takahashi YK, Igarashi KM, Yamaguchi M (2006) Maps of odorant molecular features in the Mammalian olfactory bulb. Physiol Rev 86(2):409–433

Morrot G, Brochet F, Dubourdieu D (2001) The color of odors. Brain Lang 79(2):309–320

O'Doherty J, Rolls ET, Francis S, Bowtell R, McGlone F, Kobal G, Renner B, Ahne G (2000) Sensory-specific satiety-related olfactory activation of the human orbitofrontal cortex. Neuroreport 11 (4):893–897

O'Mahony M (1978) Smell illusions and suggestion: reports of smell contingent on tones played on television and radio. Chem Senses Flavor 3:183–189

Owen DH, Machamer PK (1979) Bias-free improvement in wine discrimination. Perception 8(2):199–209

Peron RM, Allen GL (1988) Attempts to train novices for beer flavor discrimination: a matter of taste. J Gen Psych 115 (4):403–418

Polak EH (1973) Multiple profile-multiple receptor site model for vertebrate olfaction. J Theor Biol 245:175–184

Rabin MD (1988) Experience facilitates olfactory quality discrimination. Percept Psychophys 44(6):532–540

Rabin MD, Cain WS (1989) Attention and learning in the perception of odor mixtures. In: Laing DG, Cain WS, McBride RL, Ache BW (eds) Perception of complex smells and tastes. Academic, Sydney, pp 173–178

Royet JP, Hudry J, Zald DH, Godinot D, Gregoire MC, Lavenne F, Costes N, Holley A (2001) Functional neuroanatomy of different olfactory judgments. Neuroimage 13(3):506–519

Savic I, Gulyas B, Larsson M, Roland P (2000) Olfactory functions are mediated by parallel and hierarchical processing. Neuron 26 (3):735–745

Schoenbaum G, Eichenbaum H (1995) Information coding in the rodent prefrontal cortex. I. Single-neuron activity in orbitofrontal cortex compared with that in pyriform cortex. J Neurophysiol 74 (2):733–750

Schwartz S, Maquet P, Frith C (2002) Neural correlates of perceptual learning: a functional MRI study of visual texture discrimination. Proc Natl Acad Sci U S A 99(26):17137–17142

Schyns PG, Goldstone RL, Thibaut JP (1998) The development of features in object concepts. Behav Brain Sci 21(1):1–17 discussion 17–54

Sigman M, Pan H, Yang Y, Stern E, Silbersweig D, Gilbert CD (2005) Top-down reorganization of activity in the visual pathway after learning a shape identification task. Neuron 46(5):823–835

Slosson EE (1899) A lecture experiment in hallucinations. Psychol Rev 6:407–408

Small DM, Jones-Gotman M, Zatorre RJ, Petrides M, Evans AC (1997) Flavor processing: more than the sum of its parts. Neuroreport 8(18):3913–3917

Small DM, Voss J, Mak YE, Simmons KB, Parrish T, Gitelman D (2004) Experience-dependent neural integration of taste and smell in the human brain. J Neurophysiol 92(3):1892–1903

Small DM, Zatorre RJ, Dagher A, Evans AC, Jones-Gotman M (2001) Changes in brain activity related to eating chocolate: from pleasure to aversion. Brain 124(Pt 9):1720–1733

Sobel N, Prabhakaran V, Desmond JE, Glover GH, Goode RL, Sullivan EV, Gabrieli JD (1998) Sniffing and smelling: separate subsystems in the human olfactory cortex. Nature 392(6673):282–286

Stevens DA, O'Connell RJ (1995) Enhanced sensitivity to androstenone following regular exposure to pemenone. Chem Senses 20 (4):413–419

Stevenson RJ (2001) Associative learning and odor quality perception: how sniffing an odor mixture can alter the smell of its parts. Learn Motiv 32:154–177

Stevenson RJ, Wilson DA (2007) Odour perception: an object-recognition approach. Perception 36(12):1821–1833

The Shadow Radio Program, from the episode. "The Hoodoo Ship," originally broadcast on The Mutual Network (19 October 1941). Available at: http://ia351440.us.archive.org/1/items/The-Shadow/1941.10.19_Hoodoo_Ship.mp3. Accessed 13 August 2007

Wilson DA (2000a) Comparison of odor receptive field plasticity in the rat olfactory bulb and anterior piriform cortex. J Neurophysiol 84(6):3036–3042

Wilson DA (2000b) Odor specificity of habituation in the rat anterior piriform cortex. J Neurophysiol 83(1):139–145

Wilson DA (2003) Rapid, experience-induced enhancement in odorant discrimination by anterior piriform cortex neurons. J Neurophysiol 90:65–72

Wilson DA, Stevenson RJ (2003) The fundamental role of memory in olfactory perception. Trends Neurosci 26(5):243–247

Wilson DA, Stevenson RJ (2006) Learning to smell: olfactory perception from neurobiology to behavior. The Johns Hopkins University Press, Baltimore, MD

Wilson DA, Sullivan RM, Doty RL (2003) Sensory physiology of central olfactory pathways. Handbook of olfaction and gustation. Marcel Dekker, New York, pp 181–201

Wysocki CJ, Dorries KM, Beauchamp GK (1989) Ability to perceive androstenone can be acquired by ostensibly anosmic people. Proc Natl Acad Sci U S A 86(20):7976–7978

Youngentob SL, Schwob JE (2006) Odorant identification and quality perception following methyl bromide-induced lesions of the olfactory epithelium. Behav Neurosci 120(6):1346–1355

Zald DH, Pardo JV (1997) Emotion, olfaction, and the human amygdala: amygdala activation during aversive olfactory stimulation. Proc Natl Acad Sci U S A 94(8):4119–4124

Zatorre RJ, Jones-Gotman M, Evans AC, Meyer E (1992) Functional localization and lateralization of human olfactory cortex. Nature 360(6402):339–340

Zellner DA, Kautz MA (1990) Color affects perceived odor intensity. J Exp Psychol Hum Percept Perform 16(2):391–397

Zellner DA, Whitten LA (1999) The effect of color intensity and appropriateness on color-induced odor enhancement. Am J Psychol 112(4):585–604