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Odor/taste integration and the perception of flavor

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Abstract Perceptions of the flavors of foods or beverages reflect information derived from multiple sensory afferents, including gustatory, olfactory, and somatosensory fibers. Although flavor perception therefore arises from the central integration of multiple sensory inputs, it is possible to distinguish the different modalities contributing to flavor, especially when attention is drawn to particular sensory characteristics. Nevertheless, our experiences of the flavor of a food or beverage are also simultaneously of an overall unitary perception. Research aimed at understanding the mechanisms behind this integrated flavor perception is, for the most part, relatively recent. However, psychophysical, neuroimaging and neurophysiological studies on cross-modal sensory interactions involved in flavor perception have started to provide an understanding of the integrated activity of sensory systems that generate such unitary perceptions, and hence the mechanisms by which these signals are “functionally united when anatomically separated”. Here we review this recent research on odor/taste integration, and propose a model of flavor processing that depends on prior experience with the particular combination of sensory inputs, temporal and spatial concurrence, and attentional allocation. We propose that flavor perception depends upon neural processes occurring in chemosensory regions of the brain, including the anterior insula, frontal operculum, orbitofrontal cortex and anterior cingulate cortex, as well as upon the interaction of this

chemosensory “flavor network” with other heteromodal regions including the posterior parietal cortex and possibly the ventral lateral prefrontal cortex.

Multisensory integration

Integration of information from physiologically distinct sensory modalities is a general property of the mammalian nervous system (Gibson 1966; Marks 1991; Stein and Meredith 1993). Its purpose may be to enhance the detection or identification of stimuli, particularly in those cases where a single sensory modality provides ambiguous, incomplete, or low perceptibility information. Integration across sensory modalities is reflected in the presence of multimodal neurons that receive converging sensory information. Multimodal neurons, such as those found in the superior colliculus (Meredith and Stein 1986) may respond specifically to combinations of different sensory inputs, or sensory-specific neurons may be responsive to modulation by other sensory modalities (Meredith and Stein 1983; Meredith and Stein 1986; Stein and Meredith 1993; Calvert et al. 1998). Evidence for multimodal integration comes from the supra-additive responses of such neurons to multimodal stimulation, relative to unimodal inputs (Meredith and Stein 1983; Meredith and Stein 1986). This neural enhancement is then reflected behaviorally in responses to multimodal stimuli. For example, Stein et al. (1988) showed supra-additive enhancement of accuracy of behavioral responses in cats to visual stimuli through simultaneous presentation of auditory tones, even when the tones presented unimodally were irrelevant to the task.

Supra-additive responses to audio-visual stimuli have also been documented in the human using neuroimaging techniques such as functional magnetic resonance imaging (fMRI), positron emission tomography (PET), and evoked related potential (ERP) mapping (Calvert et al.

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1997, 1999, 2000, 2001; Lewis et al. 2000; Macaluso et al. 2000; Bushara et al. 2001; Calvert 2001; Laurienti et al. 2002; Bushara et al. 2003; Calvert and Campbell 2003; Lewald and Guski 2003; McDonald et al. 2003). One advantage of these methods is that they enable observation of processing across many regions, if not the entire brain, so that it is possible to measure simultaneous activity in different cortical zones. In a review of the neuroimaging literature on audio-visual integration Calvert (2001) highlighted the involvement of several heteromodal cortical zones in multisensory integration, including the superior temporal sulcus and the posterior parietal cortex, which she proposed were specialized in enhancing identification and localization, respectively. The role of sensory-specific cortex in cross-modal integration is a subject of current debate (Calvert et al. 1999; Fort et al. 2002; Laurienti et al. 2002; Bushara et al. 2003). Many studies show enhanced activity in sensory-specific regions when one stimulus enhances detection or recognition of another (Calvert et al. 1999; Giard and Peronnet 1999; Macaluso and Driver 2001). Other studies show response depression during bimodal presentations (Lewis et al. 2000; Laurienti et al. 2002; Bushara et al. 2003). What is clear is that modulation of sensory-specific cortex appears to be a key aspect of sensory integration and this indicates that multisensory integration relies not only upon multimodal neurons but also upon the information coded across networks of unimodal neurons.

Odor/taste integration

Much of the human psychophysical evidence for integration of odors and tastes is derived from data showing interactions between these distinct modalities when they are experienced in mixtures—that is, as part of a flavor. A commonly reported effect is the ability of food odors such as strawberry or vanilla to enhance sweetness when added to solutions of a tastant like sucrose (Frank and Byram 1988; Frank et al. 1989, 1993; Bingham et al. 1990; Cliff and Noble 1990; Clark and Lawless 1994; Prescott 1999; Stevenson et al. 1999). These increases in taste intensity are not mediated by chemical interactions between the odorant and tastant, since preventing odor volatiles from reaching olfactory receptors (for example, by closing the external nares during tasting) abolishes the effect. The odorants are also typically tasteless when experienced alone in solution. Moreover, rather than resulting from either a general sensory summation, or being related to the chemical compounds used, the effects are specific to the taste and odor *qualities*. Frank and Byram (1988) showed that *strawberry*, but not *peanut butter*, odor enhanced the sweetness of sucrose; conversely, saltiness was not enhanced by *strawberry* odor. Odor-induced taste enhancement has been interpreted, in a similar fashion to such multimodal effects in other modalities, as a reflection of integrated cross-modal activity, in this

case reflecting the perception of flavor as a discrete, functional sense (Prescott 1999, 2004).

Neuroimaging studies of olfaction, gustation, and flavor are beginning to isolate a network of regions that are likely responsible for taste/odor integration, and hence flavor perception. Independent presentation of a tastant or an odorant produces overlapping activation in regions of the insula and operculum (Small et al. 1999; Savic et al. 2000; Cerf-Ducastel and Murphy 2001; Cerf-Ducastel et al. 2001; Poellinger et al. 2001), the orbitofrontal cortex (OFC) (Zatorre et al. 1992; Small et al. 1997a, b; Zald and Pardo 1997; Sobel et al. 1998; Zald et al. 1998; Francis et al. 1999; Small et al. 1999; O'Doherty et al. 2000; Savic et al. 2000; O'Doherty et al. 2001; Poellinger et al. 2001), and the anterior cingulate cortex (Zald and Pardo 1997; Zald et al. 1998; O'Doherty et al. 2000; Savic et al. 2000; Small et al. 2001; de Araujo et al. 2003; Royet et al. 2003; Small et al. 2003) (Fig. 1). The insula, operculum, OFC and anterior cingulate cortex are also sensitive to somatosensory stimulation of the oral cavity (Pardo et al. 1997; Cerf-Ducastel et al. 2001; de Araujo and Rolls 2004). Similarly, single-cell recording studies in monkeys have identified taste and smell-responsive cells in the insula/operculum (Scott and Plata-Salaman 1999) and OFC (Rolls and Baylis 1994; Rolls et al. 1996b). The presence of unimodal representation of taste, odor, and oral touch in the insula, frontal operculum, and OFC of the human and nonhuman primate suggests that these regions play a key role in integrating the disparate sensory inputs that give rise to the flavor perception. Chemosensory responses in the monkey anterior cingulate cortex have yet to be investigated but the consistency of responses in this region to taste and oral somatosensation (Small et al. 2003; de Araujo and Rolls 2004; Small et al. 2004) in humans is highly suggestive of a role in flavor processing.

These neurophysiological studies of taste and smell highlight an important difference between chemosensory and visual and auditory cortical representations. In contrast to primary representation of vision and audition, which occurs in unimodal neocortex, early representation of both taste and smell occurs in heteromodal regions of the limbic and paralimbic brain. This suggests that compared to audio-visual integration, taste-odor integration occurs at earlier stages of processing and is likely to be influenced by experience and affective factors such as the physiological significance of a given stimulus, since learning and affective processing are the primary functions of this cortical zone (Mesulam 1998). The possibility of very early cortical integration of the sensory components of flavor is consistent with the fact that taste perception is almost always accompanied by oral somatosensation and retronasal olfaction.

Rolls and colleagues (Rolls and Baylis 1994; Rolls et al. 1996a, 1999; Verhagen et al. 2003) have performed a series of studies in which gustatory, olfactory, visual, and oral somatosensory stimuli were presented to awake behaving monkeys and responses were recorded from

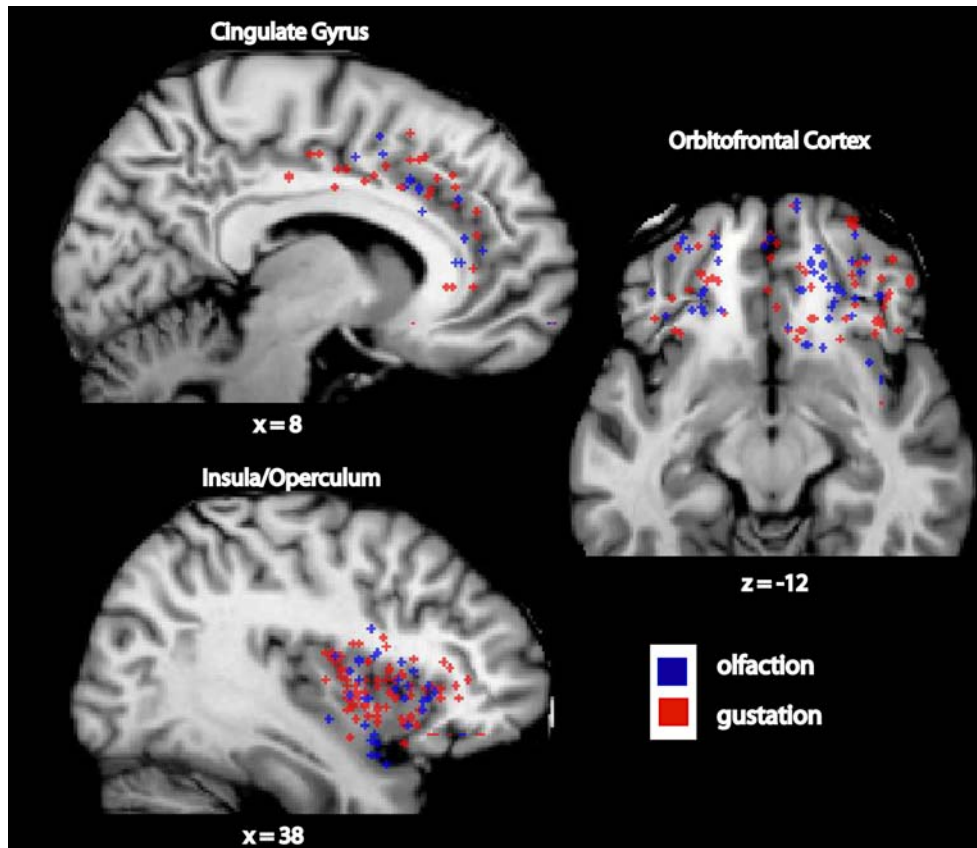


Fig. 1 Images showing activation foci (*peaks*) reported in studies of gustatory (*red*) and olfactory (*blue*) stimulation in the anterior cingulate cortex (*top left sagittal section*), insula/operculum (*bottom left sagittal section*) and orbitofrontal cortex (*right axial section*). To collect the studies the following search terms were entered into MEDLINE: (1) taste AND fMRI, (2) taste AND PET, (3) gustation AND fMRI, (4) gustation AND PET, (5) olfaction and fMRI, (6) olfaction AND PET, (7) smell AND fMRI, (8) smell AND PET. Studies were excluded if (1) Talairach or MNI coordinates were not reported; (2) subjects were not right handed; (3) subjects were not young healthy adults; (4) stimuli had an olfactory *and* a gustatory component (e.g. a food or drink); (5) stimuli were not chemical (e.g. electric taste; imagery). Activation foci were included only if they were produced by an analysis in which a stimulus was compared to a baseline or if the analysis compared or correlated a perceptual attribute (intensity, pleasantness) of a taste or a smell stimulus. Activation foci were not included if they were generated by an analysis aimed at isolating a cognitive variable (e.g. short term versus long term olfactory memory). This produced a total of 18 olfactory (Zatorre et al. 1992; Zald and Pardo 1997; Fulbright et al. 1998; Royet et al. 1999, 2003; Qureshy et al. 2000; Royet et al. 2000; Savic and Gulyas 2000; Savic et al. 2000; Zatorre et al. 2000; Bengtsson et al. 2001; Cerf-Ducastel and Murphy 2001; Poellinger et al. 2001; Gottfried et al. 2002a, b; Zald et al. 2002; Anderson et al. 2003; Rolls et al. 2003; Kringelbach et al. 2004) and 12 gustatory (Kinomura et al. 1994; Kringelbach et al. 2004; Small et al. 1997a, b, 2003, 2004; Zald et al. 1998, 2002; Frey and Petrides 1999; O'Doherty et al. 2001, 2002; de Araujo et al. 2003) studies. In the anterior cingulate there were 28 taste foci and 14 smell foci. In the orbitofrontal cortex there were

56 taste foci and 49 smell foci. In the insula there were 72 taste foci and 36 smell foci. The standardized proportional MNI stereotaxic coordinates representing each of the activation peaks were plotted onto a high resolution MRI image from a single subject who did not participate in any of the studies. In order to display the activation foci relative to one another, the stereotaxic coordinates corresponding to the plane of interest were averaged so that peaks could be plotted onto a single MRI section that would be most representative of the group of foci. In the sagittal plane peaks were collapsed across hemisphere. Thus, all left and right hemisphere peaks are plotted according to their anterior–posterior position (*y*-value) and inferior–superior position (*z*-value) on the average sagittal plane from the group, which represents the left–right position (*x*-value). A similar procedure was followed for the insula/opercular *peaks*. For the orbitofrontal cortex the anterior–posterior position and *left–right* position was used to plot peaks onto the average axial plane, which represents the inferior–superior position. The average *x*-value (*sagittal plane*) for the insula was 38, the average *x*-value for the anterior cingulate was 8 and the average *z*-value (*axial plane*) for the orbitofrontal cortex was –12. The three plots clearly show that chemosensory stimuli activate a variety of regions within the insula, anterior cingulate, and orbitofrontal cortex and that much of these regions is responsive to both gustatory and olfactory stimulation. However, visual inspection of the plots suggests that taste stimuli tend to activate the caudal and lateral orbitofrontal cortex; whereas olfactory stimuli do not (especially in the right hemisphere). In contrast, olfactory stimuli tend to activate the ventral most insular region, which is continuous with primary olfactory cortex; whereas gustatory stimuli do not

neurons located in the caudal OFC, extending into the ventral insula. They identified unimodal taste, smell, visual, fat, and texture cells that were interspersed with multimodal cells that responded to independent stimu-

lation of two or more modalities. Interestingly the strongest responses were often observed to multimodal stimuli, such as blackcurrant juice compared to unimodal stimuli such as glucose or banana odor. However,

because simultaneous presentation of two unimodal inputs was not compared to independent presentation of these same inputs it is not known if the responses to the multimodal stimuli were supra-additive and thus comparable to the audio-visual multimodal cells identified in the superior colliculus of the cat (Stein 1998).

In the human, several neuroimaging studies have been performed where unimodal stimulation with a taste or an odor were compared to bimodal (simultaneous) presentation of the same tastes and odors (Small et al. 1997a, b, 2004; de Araujo et al. 2003). Consistent with the results discussed above, De Araujo et al. (2003)

reported activation in the frontal operculum, ventral insula/caudal OFC, amygdala, and anterior cingulate cortex to unimodal stimulation with either a taste or an odor and to bimodal stimulation with a taste/odor mixture. A study by Small et al. (2004) using a similar design also found activity in frontal operculum, ventral insula/caudal OFC, and anterior cingulate cortex to a taste/odor mixture; but in this study the response was supra-additive, in that greater activity was observed when the subjects received a taste/odor mixture compared to the summed neural activation evoked by independent stimulation with the taste and the odor components (Fig. 2). Thus, although the integration appeared to be stronger in the Small et al. (2004) study, both studies highlight the importance of these regions in flavor processing. Importantly, the ventral insula/caudal OFC region is likely analogous to the area where multimodal neurons were reported in monkeys by Rolls and Baylis (1994). Additional areas also showed supra-additive responses, but not consistently in both studies. Only De Araujo et al. (2003) observed a supra-additive response in the anterior OFC, whereas Small et al. (2004) reported supra-additive responses in the ventral lateral prefrontal cortex, dorsal insula, and posterior parietal cortex that were not reported by De Araujo et al. (2003). Future studies are clearly needed to determine the role for these regions in taste/odor integration but it is noteworthy that the posterior parietal cortex activation is in a similar region (intraparietal sulcus) that Calvert (2001) outlined as important in audio-visual integration and may indicate that there are common mechanisms devoted to sensory integration across all modalities.

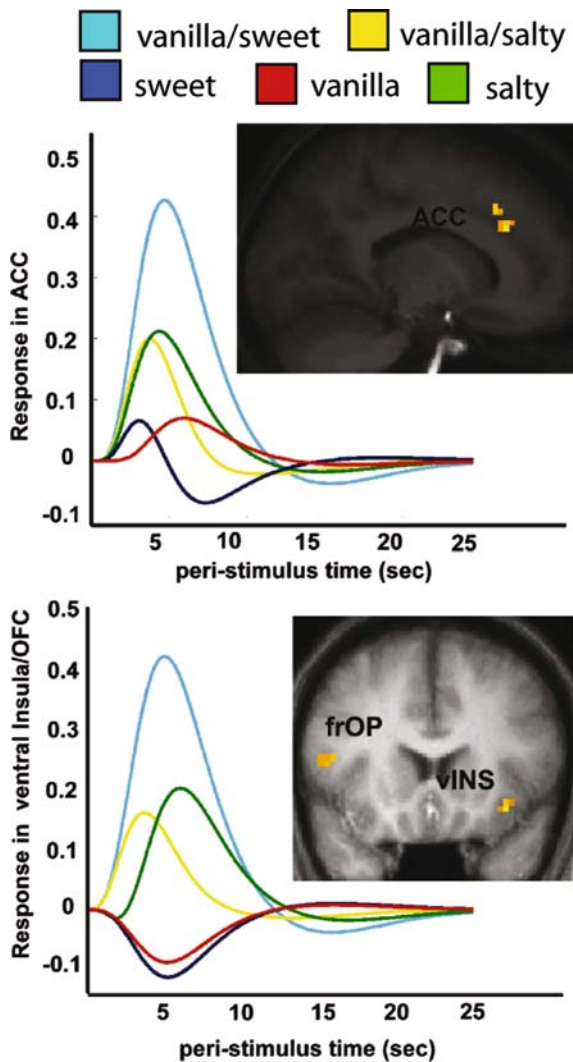


Fig. 2 Super-additive responses in the anterior cingulate cortex (ACC) and ventral insula/caudal OFC (vINS) in a group random effects analysis of a congruent taste/odor solution compared to the summed activity of its constituents (Small et al. 2004). The congruent solution consisted of sweet/vanilla. A salty/vanilla solution was also made to represent the incongruent taste/odor combination. In the graphs the response to the congruent taste/odor mixture = turquoise; incongruent taste/odor mixture = yellow; vanillin in solution = red; sucrose in solution = blue; and saline solution = green. y-Axis = response in arbitrary units. x-Axis = peri-stimulus time in seconds

Role of experience in odor/taste integration

A distinctive characteristic of odor/taste integration is that for enhancement effects to occur, the odor and taste components need to be perceptually congruent, or similar (Frank et al. 1991; Schifferstein and Verlegh 1996; van der Klaauw and Frank 1996). Thus, the degree of enhancement produced by an odor for a particular taste was found to be significantly correlated with ratings of the perceived similarity of the odorant and tastant (Frank et al. 1991). Perceptual congruency is most evident in the observation that some odors, when sniffed, elicit descriptions of qualities that are more usually associated with basic taste qualities (Burdach et al. 1984; Dravnieks 1985). These descriptions appear to have many of the qualities of synesthesia, in which a stimulus in one sensory modality reliably elicits a consistent corresponding stimulus in another modality (Stevenson et al. 1998; Martino and Marks 2000; Cytowic 2002). However, in contrast to synaesthetic phenomena across other sensory modalities, the possession of taste properties by odors is almost universal, particularly in the case of commonly consumed foods, e.g. the sweet smell of honey and the sour smell of vinegar. Such smelled taste qualities have been found to

be significant predictors of the extent to which an odor will modify the perception of a tastant in solution (Stevenson et al. 1999; Nguyen et al. 2002).

The importance of congruency is also shown in other psychophysical and behavioral demonstrations of odor/taste interactions. Dalton et al. (2000) demonstrated that orthonasal (i.e. sniffed) detection thresholds for an odorant were significantly reduced while subjects held a taste in the mouth, but only if the taste was perceptually congruent. Similar findings of an increased sensitivity to tastes at threshold level in the presence of, or immediately following the sniffing of, a congruent odor have also been reported (Djordjevic et al. 2003; Prescott 2004). Odor/taste integration has also been implicated in reports of cross-modal influences on the processing speed of chemosensory information. Simultaneous orthonasal presentation of congruent odors was found to reduce taste recognition reaction times, relative to incongruent pairs (White and Prescott 2001).

Physiological indices also reveal a strong influence of perceptual congruency. In studies of brain event-related potentials, latencies to odors were significantly shorter, and amplitudes greater, when presented with congruent but not incongruent tastes (Welge-Lüssen et al. 2004). Supra-additive responses observed in neuroimaging studies (De Araujo et al. 2003; Small et al. 2004) were in response to congruent taste/odor mixtures. Small et al. (2004) reported that the posterior parietal cortex, frontal operculum, anterior cingulate cortex, dorsal insula, and ventral insula/caudal OFC responded significantly more to a congruent taste/odor mixture (sucrose/vanillin) versus an incongruent taste/odor mixture (saline/vanillin) and that these same regions were not activated by comparison of the incongruent mixture with the sum of its parts (Fig. 2). Interestingly, a small supra-additive response was observed in an adjacent region of ventral insula to the incongruent mixture. Small et al. (2004) proposed that this activity reflected the convergence of two familiar unimodal stimuli (salty and vanilla) into an unfamiliar mixture and suggested that the activation may indicate that the region is important for flavor learning. Consistent with this proposal, Sakai and colleagues noted that bilateral ablation of the insula (or prefrontal cortex) disrupted taste-odor association learning in rats (Sakai and Imada 2003).

Hence, a significant number of findings, from studies using a variety of behavioral and physiological approaches tend to point to the ability of qualities in one chemosensory modality to enhance responses to qualities in another. Many of these findings underline the importance of perceptual congruency in enhancement, and this is consistent with the fact that multimodal neurons in the caudal OFC will respond only if the taste, odor, or visual stimulus is congruent across modalities. For example, a cell will respond to glucose, blackcurrant juice, the sight of the syringe that delivered the blackcurrant juice and fruity odors, but not to salty, onion odor, fishy odor, or the site of pliers (Rolls and Bayliss 1994). However, as noted above, as in non-chemosen-

sory systems, there is evidence that enhancement as a result of odor/taste integration can occur without congruency (Small et al. 2004). There is also recent psychophysical evidence of this, with a replication of the Dalton et al. (2000) sub-threshold integration study showing similar sensitivity enhancements for both congruent and incongruent odor/taste pairs (Delwiche and Heffelfinger 2003). Certainly, the existence of enhancement effects due to perceptual congruency is not necessarily incompatible with a multi-sensory integration of odors and tastes that is independent of experience. Perceptual congruency may be a phenomenon that arises as a result of multisensory integration of odors and tastes following repeated pairing.

How do taste-related odor qualities develop? Several groups have emphasized the importance of associative learning. For example, Rolls and colleagues (Rolls and Bayliss 1994; Rolls 1997) have argued that bimodal taste/odor neurons developed from unimodal neurons, which originally responded only to olfactory information, through learning of appropriate combinations of signals during repeated co-exposure of particular tastes with odors. Similarly, Frank and Byram (1988) proposed that odors take on taste qualities through frequent co-occurrence with particular tastes. Many food-related odors are seldom, if ever, experienced in the mouth without an accompanying taste. Given that combinations of specific tastes with specific odors are relatively invariant for most foods and beverages (at least within cultures), this is a plausible explanation. In Western cultures, we are unlikely, for example, to very often consume combinations such as vanilla odor and saltiness, or chicken odor and sweetness, whereas if we exchange these tastes and odors, the combinations are much more familiar. Consistent with this, it has been reported that French and Vietnamese vary in their judgments of the extent to which given odors and tastes are seen as congruent (Nguyen et al. 2002).

An associative learning explanation for the origins of odor "taste" properties was confirmed in a series of experiments (Stevenson et al. 1995, 1998) in which relatively novel odors, initially low in smelled sweetness and sourness when sniffed, were repeatedly paired with either sweet (sucrose) or sour (citric acid) tastes in solution. Following co-exposure in a series of mock discrimination tasks in which subjects were asked to pick the odd sample out of three identical odor/taste pairs, the odors were rated significantly higher in smelled sweetness or sourness, depending on the taste with which they were paired. In addition, odors associated with one quality (e.g. sweetness) also decreased in the extent to which they possessed the other quality (e.g. smelled sourness). This appears to be a very rapid and enduring process. Recent research has indicated that as little as a single co-exposure with a sweet taste can render a novel odor sweeter smelling (Prescott et al. 2004). In addition, the effect does not diminish over time, even when the odor is repeatedly experienced without the taste (Stevenson et al. 2000).

Importantly, these effects appear to have a strong perceptual reality, since they are independent of changes in liking for the odors or awareness of which odors, and tastes were paired (Stevenson et al. 1995, 1998). There is also evidence that taste qualities in odors (e.g. smelled sweetness) may often be functionally equivalent to those same qualities experienced as tastants. Thus, the ability of taste qualities in odors to influence taste perceptions has recently been extended to include suppression of taste intensity by incongruent or novel odors (Prescott 1999; see Fig. 3), while Stevenson et al. (1999) showed that a sweet-smelling odor not only enhanced the sweetness of sucrose in solution but also suppressed the sourness of a citric acid solution. This latter effect corresponds to those interactions seen in binary taste mixtures, in which it is similarly found that sweetness generally suppresses sourness (McBurney and Bartoshuk 1973).

Like the acquisition of taste qualities by odors, the ability of these odors to influence taste perceptions has also been shown to be a function of associative learning. Odors that initially either had either no impact on sucrose sweetness or actually suppressed sweetness were both found to enhance sweetness following an exposure phase of repeated pairings with sucrose in solution (Prescott 1999). Figure 3 shows the differing impact of odors that vary in familiarity or initial smelled sweetness on the sweetness of sucrose when combined in a mixture. This variation is postulated to originate in different degree of prior association with sweet tastes. Note that following experimental exposure together with sucrose, there is significant change in the ability of low familiarity and/or low sweetness odors to modify sucrose sweetness.

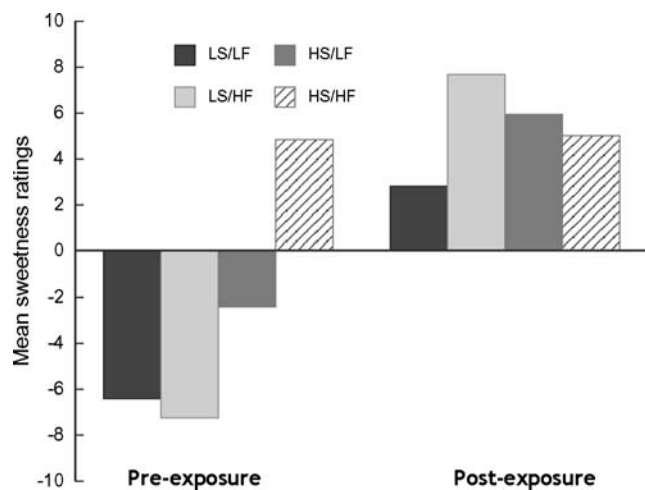


Fig. 3 Ratings of the tasted sweetness of odor/sucrose mixtures, relative to sucrose alone, showing initial suppression of sucrose sweetness by odors low in smelled sweetness (*LS*) but varying in familiarity (*LF* low familiarity; *HF* high familiarity), and enhancement by a sweet-smelling, familiar odor (*HS/HF*). After subjects received repeated exposures of the odors and sucrose together as solutions, sweetness enhancement is additionally shown by two odors (*LS/HF*; *HS/LF*). Reprinted from Prescott (1999), with permission from Elsevier

Other behavioral effects noted above, such as the impact of odors on measures of reaction time to name tastes (White and Prescott 2002) and on sub-threshold odor/taste integration (Breslin et al. 2003), have also recently been shown to be subject to learning effects, in that they occurred only following specific odor/taste pairings.

Current explanations of taste qualities in odors and their impact on tastes in mixtures (McBurney 1986; Frank et al. 1991, 1993; Stevenson et al. 1995; Schifferstein and Verlegh 1996) propose that the interactions between odors and tastes occur as a result of emerging perceptual congruency, which arises out of associative processes. This reflects a central encoding of these elements as dimensions of the same compound stimulus—a flavor—in which qualities such as sweetness (whether associated with a tastant or an odor) are perceptually combined. It is this co-encoding of the odor and taste as a flavor in memory that determines the subsequent interactions of the elements of the flavor.

One account (Stevenson and Boakes 2004) proposes that experiencing a novel odor involves comparison with memories of previously encountered odors. If in the initial experience of the odor it is paired with a taste, a configural (unitary) stimulus is encoded in memory. Subsequently, sniffing the odor alone will evoke the most similar odor memory, that is, a flavor, which will include both the odor and the taste component. Thus, for example, sniffing caramel odor activates memorial representations of caramel flavors, which includes a significant sweet component. This results either in perceptions of smelled taste properties such as sweetness or, in the case of a mixture, a perceptual combination of the memorial odor representation with the physically present taste in solution. In other words, perceptions are being constructed from a combination of both “real” tastes and taste properties of the odor that are encoded in memory. Such explanations are consistent with data showing that memorial representations of chemosensory qualities can combine with physically present stimuli to produce mixtures that show very similar psychophysical interactions to those of identical combinations of physically present qualities. These “mental mixtures” have been demonstrated with combinations of different tastes (Stevenson and Prescott 1997), odors (Algom and Cain 1991), as well as odor/taste mixtures (Algom et al. 1993). In a direct test of this type of explanation, a recent study in which a sweet tastant was combined with either sniffed or imagined odors found essentially equivalent patterns of odor/taste interactions—primarily suppression by an incongruent odor—in both conditions (Djordjevic et al. 2004). However, cross-modal enhancement and supra-additive neural responses occur in other sensory modalities without the existence of common perceptual experiences across modalities. As noted earlier, there is evidence that this may be true for chemosensory systems as well (Delwiche and Heffelfinger 2003; Small et al. 2004), indicating that while memorial processes may be an important aspect of flavor perception, multisensory integration of odors and

tastes may also occur independently of prior experience, most likely facilitated by common spatial and temporal properties (see below).

If the acquisition of taste-like properties by odors reflects associative learning, then it is reasonable to predict that odors that elicit taste perceptions develop the ability to activate gustatory neurons, either as a direct function of the olfactory perception or as a result of a reactivation of a flavor memory. It would then follow that food odors should preferentially activate gustatory regions of the brain such as the junction of the dorsal insula with the frontal operculum, which is thought to represent the primary gustatory area (Scott and Plata-Salaman 1999; Small et al. 1999). To test this hypothesis, Leger et al. (2003) used fMRI to compare brain response to a food odor (chocolate) with the responses to three non-food odors (lavender, butanol, and farnesol). As predicted, greater activity was observed in the primary gustatory region to the chocolate compared to all other odors. In addition, activation in the hypothalamus was only observed during retronasal experience of the chocolate odor, indicating that mode of olfactory delivery (i.e. orthonasal versus retronasal olfaction) may interact differently with food versus non-food odors.

Role of temporal and spatial synchrony in odor/taste integration

Studies of visual, auditory, and somatosensory systems have highlighted the importance of spatial and/or temporal contiguity in facilitating cross-modal sensory integration (Calvert et al. 1998; Stein 1998; Driver and Spence 2000). The importance of temporal and spatial factors lie in their ability to influence whether or not sensory inputs are perceived as arising from a common event or object or as two separate events or objects. In the superior colliculus the receptive fields of multisensory neurons are in spatial register with one another, and by determining the spatial correspondence of receptive fields over a large population of neurons, each representation in the structure can be “mapped” in another modality’s spatial coordinates (Stein 1998). This physiology promotes unitary perceptions and enables the sensory capture of one modality by another. For example, while watching television the actors’ voices are perceived to emanate from their lips even though the sound actually originates from speakers on the side of the screen. However, this “capture” of the auditory information by the visual input only occurs if there is relatively little delay between the audio and video track.

Likewise, temporal and spatial contiguity may be crucial determinants of odor/taste integration because they promote perception of disparate taste, odor, and oral somatosensations as a common object—a food. Akin to the example of visual capture of auditory information presented above, there is a well-known olfactory location illusion, in which retronasal perception of odors is universally interpreted as originating in

the mouth, rather than the nose (“oral capture”). The illusion is so powerful that odors are often mistaken for “tastes” (Murphy et al. 1977; Rozin 1982). For example, loss of retronasal olfactory inputs causes the “taste” of foods to change during a head cold. It has been argued that the illusion served to bring taste and odor into a common spatial registry to facilitate integration (Rozin 1982; Green 2002; Small et al. 2004). It is currently unknown if the effect is mediated primarily by gustatory or somatosensory (or both) signals, although the demonstration that somatosensory stimulation can “capture” taste by determining its perceived spatial locus is relevant in this regard (Todrank and Bartoshuk 1991; Green 2002).

The illusion appears to depend on *both* the spatial and temporal contiguity of the discrete sensory inputs. Von Bekesy (1964; see Fig. 4) emphasized the importance of temporal factors by showing that the perceived location of an odor (mouth versus nose) and the extent to which an odor and taste were perceived as one sensation or two could be manipulated by varying the time delay between the presentation of the odor and taste. With a time delay of zero (simultaneous presentation), the apparent locus of the odor was the back of the mouth and the odor/taste mixture was perceived as a single entity. When the odor preceded the taste, the sensation was perceived as originating in the nose; when the taste preceded the odor, the sensation was located on the tongue tip. Consistent with this, Sakai et al. (2001) demonstrated that odor-induced taste enhancement can occur whether the odor is presented orthonasally (sniffed) or retronasally (in mouth), providing that the odor and taste are presented simultaneously.

Other evidence for the role of spatial or temporal contiguity in odor/taste integration comes from the

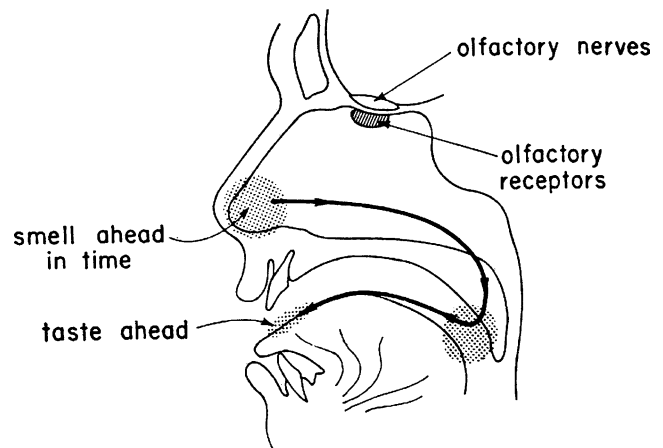


Fig. 4 Temporal and spatial determinants of odor/taste integration. “Combination of smell and taste into a single sensation. A varying time difference between the stimuli moves the locus of sensation from the tip of the nose back to the throat and forward again to the tip of the tongue.” Reprinted (including caption in italics) from von Bekesy (1964), with permission from The American Physiological Society

animal learning literature. Rescorla (1980) demonstrated in rats that simultaneous, rather than successive, presentation of an odor and taste results in more effective conditioning of rats to respond uniquely to a compound stimulus, rather than to its separate elements. More recently, it has been shown that odors can potentiate taste aversions but only if the odor is delivered in the same apparent spatial location, that is, retronasally (Slotnick et al. 1997). This latter finding, in particular, highlights the probable importance of the functional meaning of sensory stimuli in determining how they are processed by the brain. For example, pairing an odor with gastrointestinal illness is unlikely to be adaptive if the odor was not associated with a food (Rozin 1982). Such principles appear to be reflected in neural processing of odor signals. In humans, deactivations in the insula, operculum, caudal OFC, and anterior cingulate cortex have been reported following simultaneous delivery of an orthonasally presented odor with a taste (Small et al. 1997a, b), even though the stimuli were congruent (e.g. sweet with strawberry odor) (Fig. 5). This result is in striking contrast to the super-additive responses observed in these same regions when odors are given retronasally. Taken together, the data suggest that the more likely a taste and odor are perceived as originating

from a common object/source, the greater the ability of one component to influence the other and the greater the likelihood that integrative events will occur such as enhancement and super-additive neural responses.

Role of attention in odor/taste integration

In addition to being mediated both by experience and temporal/spatial contiguity, odor/taste integration appears to be modulated by attention. A general finding across sensory modalities is that responses to a particular modality can be enhanced by the presence of signals in another modality that focus attention to the response modality. For example, visual cues to attend to likely upcoming olfactory stimuli improved response accuracy to those stimuli (Spence et al. 2000, 2001). The relatively few examinations of such effects *within* multimodal chemosensory stimuli provide mixed findings. A recent study of attentional manipulations during a discrimination task involving the elements of a congruent odor/taste pair (vanillin/sucrose) demonstrated the poor ability of subjects to selectively attend to the odor component when it had to be distinguished from the compound stimulus, as compared to when it was

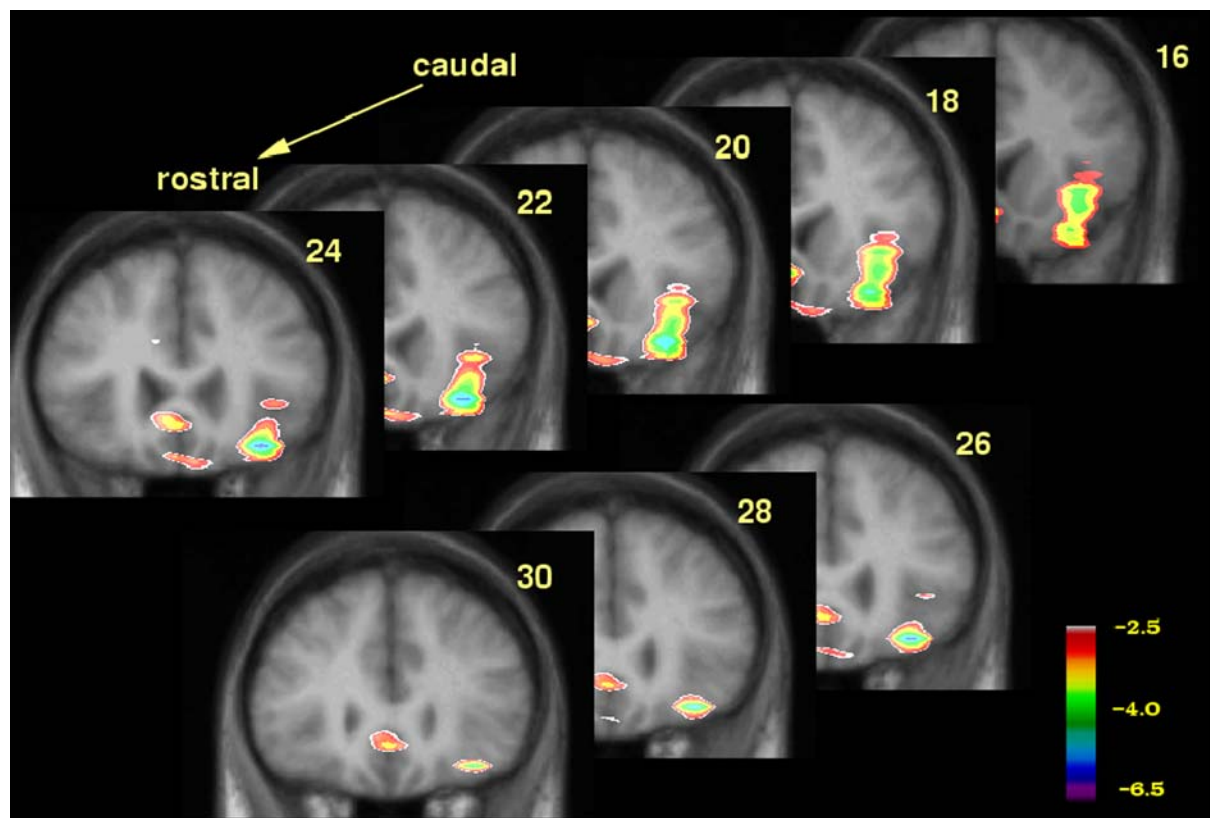


Fig. 5 Coronal sections illustrating deactivation in the insula and caudal OFC resulting from simultaneous presentation of odors on long-handled cotton swabs and tastants on tongue shaped filter papers versus independent presentation of the tastants (Small et al. 1997a, b). Numbers in the *top right corner* indicate the Talairach coordinate in the coronal plane, i.e. “y.” Color bar indicates *t*-

values. Areas of *color* indicate regions where unimodal taste stimulation resulted in greater activity than bimodal taste/odor stimulation. These suppressive effects likely resulted from the spatial disparity of the odor and taste stimuli or divided attention caused by the awareness that the components originated from separate sources

discriminated from water. In contrast, the taste alone was more easily discriminated from the odor/taste compound (Marks and Ashkenazi 2004). Similarly, Laing et al. (2002) have shown that subjects are better at identifying single tastes in taste/taste mixtures than they are at identifying odors in mixtures with a single odor component and one or more taste components. These findings highlight the unitary nature of the flavor perception and also suggest that when odors and tastes are sufficiently integrated as flavors, they are resistant to attentional manipulations.

However, in contrast, it has been repeatedly demonstrated that asking subjects to rate or attend to the different qualities within a flavor, tends to eliminate enhancement effects (Frank et al. 1993; Clark and Lawless 1994; van der Klaauw and Frank 1996). These data suggest that the way in which attention is allocated to the elements within a flavor stimulus may either compromise or facilitate integrative processes, a phenomenon that has been explained in terms of a distinction between analytical and synthetic perceptual processes (Prescott 2004). The blending of odors to form entirely new odors is a *synthetic* interaction (analogous to the blending of colors), while the mixing of tastes is typically seen as an *analytic* process, because individual taste qualities do not fuse to form new qualities and, like simultaneous auditory tones, can be distinguished from one another in mixtures. The data on the impact of attention on odor/taste interactions suggest that whether an odor/taste mixture is perceived analytically as the individual elements or synthetically as a flavor is determined by the perceptual “boundaries” that the subject sets for a given complex stimulus, which in turn will reflect the attentional focus demanded in the task (Frank et al. 1993; Frank 2003). In the case of an odor/taste mixture in which the elements are perceptually congruent, combining those elements is essentially optional. Multiple ratings of appropriate attributes force an analytical approach, whereas a single rating of a sensory quality that can apply to both the odor and taste (e.g. the tasted sweetness of sucrose and the smelled sweetness of strawberry odor) encourages synthesis of the common quality from both sensory modalities. These effects of instructional sets on attention are analogous to those seen in studies of cross-modal integration of vision and hearing. Melara et al. (1992), for example, showed that focusing on the overall similarity of visual or auditory stimulus pairs, representing different stimulus dimensions, versus focusing on their component dimensions, could influence whether the pairs were treated as interacting or separable dimensions (Garner 1974), respectively.

The impact of attentional modulation on the extent to which odors and tastes initially become integrated into flavor (as shown by increased perceptually similarity), as well as any subsequent influence of those odors on tastes in solution, was recently investigated by manipulating the perceptual strategy used (analytic versus synthetic) during the co-exposure of novel odors

and a sweet tastant (Prescott et al. 2004). While simple co-exposure was sufficient to produce sweeter smelling odors, only when the elements were treated as a synthetic whole during this exposure did the odors subsequently enhance sweetness in solution. In contrast, an analytical exposure strategy that emphasized the distinctiveness of the elements was found to inhibit the ability of the odor to influence tastes in solution (see Fig. 6). These data are therefore analogous to those showing the role of focused attention in binding visual features to form recognizable objects (Treisman 1999). In the case of flavor, binding different modalities may serve the biologically imperative function of ensuring adequate identification of foods prior to ingestion (Gibson 1966).

To date, the influence of attention on taste/odor integration has not been studied systematically at the physiological level. However, indirect evidence for the importance of attention on neural integration of tastes and odors comes from an early PET study of flavor processing (Small et al. 1997a, b). In the study odors were presented on long-handled cotton swabs and tastes on tongue-shaped filter papers. During bimodal stimulation subjects were required to open their mouth to receive the taste and simultaneously sniff the end of the

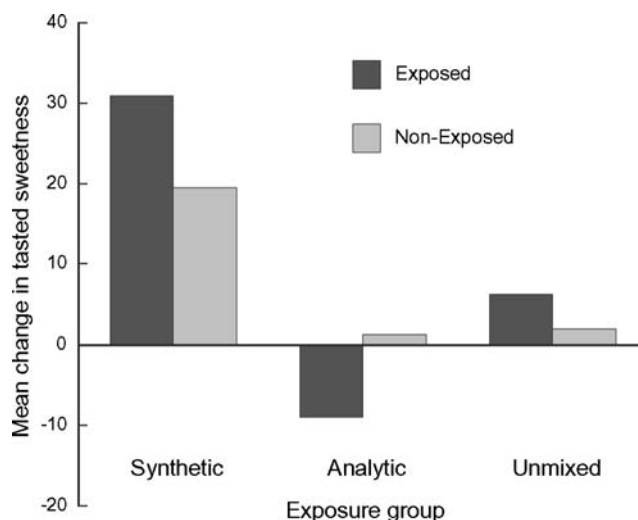


Fig. 6 The impact of sweet-smelling odors on perception of tastes depends on perceiving the mixture as a whole flavor. Changes in the ratings of the tasted sweetness of mixtures of sucrose and (initially) novel odors, relative to sucrose alone, for groups exposed to these mixtures under different attentional conditions. A significant increase in mixture sweetness was present for the group using a *synthetic* attentional strategy that emphasized the unitary nature of the elements as a flavor, but not for the groups in which the elements were either attended to as separate elements (*analytic*) or in which the elements were never combined as a mixture (*unmixed*). The “non-exposed” odors had actually been exposed together with sucrose on one occasion—at the pre-test, in which the initial ability of these odors to influence sweetness was assessed. This modest degree of exposure of the odor plus sucrose was shown to produce sweeter-smelling odors, irrespective of exposure group. Reprinted from Prescott et al. (2004), by permission of Oxford University Press

cotton swab. Not only was the odor delivered orthonasally, the subject was also well aware that the odor and taste derived from separate objects. Thus the experimenters had inadvertently created a situation that maximized the possibility of divided attention between the modalities, which resulted in suppression in cortical chemosensory regions in the comparison of the bimodal versus the unimodal conditions (Fig. 5).

Asymmetrical sensory involvement in flavor processing

Recent studies of gustatory, olfactory, and flavor processing has elucidated a list of regions that are likely important in taste/odor integration including the insula, operculum, caudal OFC and anterior cingulate cortex. These regions represent primary, secondary, and tertiary gustatory areas, and secondary and tertiary olfactory areas of the brain. Notably, absent from this list is the piriform cortex, which represents the primary olfactory area in the human (Zatorre et al. 1992; Sobel et al. 2000). This is because although olfactory responses have been isolated in the insula and operculum, which includes primary gustatory cortex, tastes do not appear to activate the piriform region (Scott et al. 1986; Yaxley et al. 1988, 1990; Kinomura et al. 1994; Small et al. 1997a, 1997b; Cerf et al. 1998; Zald et al. 1998, 2002; Frey and Petrides 1999; Kobayakawa et al. 1999; Scott and Plata-Salaman 1999; O'Doherty et al. 2001). This asymmetrical relationship is also present in perceptual experiences. Taste perception is almost always accompanied by olfactory and oral somatosensory perception in the context of feeding, whereas olfaction often occurs outside the context of feeding. Furthermore, while there is ample evidence to support the acquisition of taste-like properties by odors, there have been no reports of the acquisition of odor-like properties by tastes. Therefore it is possible that, like visual organization, in which there are specialized regions for processing specific classes of visual stimuli (e.g. the fusiform face area or the parahippocampal place area; Epstein and Kanwisher 1998; Mesulam 1998), the olfactory system may be comprised of several subsystems, only one of which is specialized for flavor processing. This sort of division may not be present in gustatory organization because taste perceptions are always relevant to flavor processing by virtue of the fact that such perceptions require a stimulus to be in the mouth.

Asymmetrical involvement of gustatory and olfactory regions in flavor processing is also supported by negative results from neuroimaging studies of taste/odor integration. First, in the PET study by Small and colleagues (Small et al. 1997a, b) the piriform region was immune to effects of divided attention resulting either from the spatial disparity of the odor and the taste or the knowledge that the stimuli originated from two separate sources. Second, neither of the taste-odor integration studies reported super-additive effects in the piriform cortex (de Araujo et al. 2003; Small et al. 2004).

Summary

In the model of flavor processing that we have outlined here, the neural substrates of a unitary flavor percept are built over time by repeated experience of sensory phenomenon appearing to originate from the oral cavity. Thus the focus is not on which sensory inputs are necessary for a stimulus to be considered a flavor but rather on the fact that they are perceived to originate in the mouth. The anterior insula, frontal operculum, OFC, and anterior cingulate cortex are proposed as the key nodes of this "flavor network". The model also posits that there are several factors that influence whether or not disparate inputs are perceived as coming from a common source. These include previous experience with the particular combination of sensory inputs, temporal and spatial concurrence, and attentional allocation. From this it also follows that although the formation of the flavor percept is dependent upon multisensory integration, the system can subsequently be engaged by unimodal stimulation. Finally, it is proposed that there is asymmetric contribution of olfaction and gustation to flavor such that only retronasally perceived odors (via the mouth) and odors previously experienced with taste (irrespective of mode of delivery) engage the flavor system. This notion is in partial agreement with Rozin (1982), who argued that olfaction is a dual sense modality because it contributes to perception of external and internal objects (via orthonasal and retronasal olfaction, respectively). However, our model differs from Rozin's (1982) because we also argue that, as a result of taste/retronasal odor association learning, orthonasally perceived odors may also engage the system. This proposal does not negate the possibility that retronasally perceived odors differentially engage other brain circuitry by, for example, activating homeostatic mechanisms related to feeding. Thus, we propose that flavor represents a functional sensory system with inputs from somatosensation, gustation, and olfaction where the key is the meaning of the sensation rather than its precise organ or site of origin. This concept of flavor recalls Gibson's (1966) ecological approach in which perceptual systems are defined by function, rather than tied to the organ of transduction.

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