Brain Struct Funct (2010) 214:551–561
DOI 10.1007/s00429-010-0266-9

REVIEW

Taste representation in the human insula

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Received: 25 February 2010 / Accepted: 21 April 2010 / Published online: 29 May 2010

Abstract The sense of taste exists so that organisms can detect potential nutrients and toxins. Despite the fact that this ability is of critical importance to all species there appear to be significant interspecies differences in gustatory organization. For example, monkeys and humans lack a pontine taste relay, which is a critical relay underlying taste and feeding behavior in rodents. In addition, and of particular relevance to this special issue, the primary taste cortex appears to be located further caudally in the insular cortex in humans compared to in monkeys. The primary aim of this paper is to review the evidence that supports this possibility. It is also suggested that one parsimonious explanation for this apparent interspecies differences is that if, as Craig suggests, the far anterior insular cortex is newly evolved and unique to humans, then the human taste cortex may only appear to be located further caudally because it is no longer the anterior-most section of insular cortex. In addition to discussing the location of taste representation in human insular cortex, evidence is presented to support the possibility that this region is better conceptualized as an integrated oral sensory region that plays role in feeding behavior, rather than as unimodal sensory cortex.

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Keywords Taste · Insula · fMRI · PET · Neuroimaging · Primary taste cortex · Interspecies differences

Introduction

Taste includes the sensations of sweet, sour, salty, bitter, savory, and possibly fat and metallic taste, for which the transduction mechanisms remain unknown or incompletely characterized. Organisms have evolved the ability to detect taste, not to identify food, which is primarily a function of the visual and olfactory systems (Small 2008), but rather to identify potential nutrients and toxins. For example, sweet signals energy in the form of calories, salty signals electrolytes, sour signals low pH, savory (umami) signals proteins, and bitter sensation evolved to detect poisonous substances (Scott and Plata-Salaman 1991). Flavor, on the other hand, refers to perceptions such as raspberry, coffee and chocolate, to name but a few favorites, which depend upon the integration of taste, somatosensory, and retronasal olfactory inputs.

Although, the variability of gustatory sensations appears narrow when compared to the world of flavor, this situation reflects the elegance of evolution rather than any physiological limitation of the system. For example, organisms have evolved many structurally variable bitter receptors to cope with the existence of a diverse array of poisonous substances (Chandrashekar et al. 2000, 2006; Kinnamon 2000). However, despite the variability, the physical outcome is the same and so too is the perceptual signal and the affective response it evokes. Newborns readily reject bitter tasting substances (Steiner et al. 2001), and with very few exceptions, pure bitter stimuli remain universally disliked throughout the lifespan (Hill et al. 1986; Glendinning 1994). The opposite pattern is

observed with sweet, which for many thousands of years faithfully signaled the presence of energy in the form of carbohydrates. Thus, whereas flavor preferences for foods such as kimchi, vegemite and poutine are learned, there exists a very stable, though not immutable (Hill et al. 1986; Hill and Przekop 1988; Glendinning 1994), relationship between the taste quality, its physiological significance, and the affective reaction that it will evoke. As such, physiological significance plays a major role in the organization of the gustatory sense (Chang and Scott 1984; Scott and Mark 1987; Scott and Plata-Salaman 1999).

Interspecies differences in the taste pathway

Given the collective importance of being able to sense nutrients and toxins across all species it seems reasonable to imagine that taste anatomy and physiology would be highly conserved. Remarkably, this is not the case (Small and Scott 2009). In rodents taste information is conveyed by cranial nerves 7, 9, and 10 to the nucleus of the solitary tract (NTS) (Norgren and Leonard 1971; Norgren 1990). From here the majority of taste neurons project to the pontine parabrachial nucleus (PBN) (Cho et al. 2002). At the level of the PBN the rodent gustatory pathway bifurcates into two pathways: a ventral "affective" projection to the hypothalamus, central gray, ventral striatum, bed nucleus of the stria terminalis and amygdala and a dorsal "sensory" pathway, which first synapses in the thalamus and then the agranular and dysgranular insular gustatory cortex (Norgren and Leonard 1971; Norgren 1976, 1984, 1990; Kosar et al. 1986).

In the primate, taste information is also carried to the NTS by cranial nerves 7, 9, and 10 (Beckstead and Norgren 1979). However, second-order gustatory projections that arise from the NTS do not synapse in the PBN. Instead, they project directly to the taste thalamus (Beckstead et al. 1980; Pritchard et al. 2000). Likewise, in humans functional magnetic resonance imaging (fMRI) has been used to demonstrate responses in the PBN to hand grip, Valsalva maneuver, and inspiration, but not to tongue contraction or taste stimulation, which instead elicit responses in the NTS (Topolovec et al. 2004). Thus in humans and in monkeys there appears to be no PBN taste relay and no bifurcation of taste inputs into discrete sensory and affective pathways. The functional implications of this dramatic interspecies difference remain relatively unexplored but likely include fundamental differences in the ways in which sensory signals influence feeding behavior (Scott and Small 2009; Small and Scott 2009).

Interspecies differences in the cortical representation of taste

Of greater relevance to the topic of this special issue is that there also appears to be, at first glance, a significant interspecies difference in cortical representation of taste between human and non-human primates. More specifically, the primary efferent projection from the taste thalamus in the monkey is located in ipsilateral insular/opercular cortex adjacent to the superior limiting sulcus (far anterior insula and overlying frontal operculum) and extending rostrally to the caudolateral orbitofrontal cortex (OFC) (Mufson and Mesulam 1984; Ogawa et al. 1985; Pritchard et al. 1986). A second, less extensive, projection terminates in areas 3a, 3b, 2, and 1 along the lateral margin of the precentral gyrus (Pritchard et al. 1986). Thus according to a strictly anatomical definition there are two primary taste cortices in monkeys, with the anterior insula and overlying operculum being the dominant region. In humans, neuroimaging studies of taste implicate a much more extensive insula/opercular involvement than would be expected based on monkey work, which notably seems to exclude the far anterior region of insular cortex. In an early review of human taste cortex we first noted the variability in taste evoked responses across studies and suggested that there were multiple gustatory representations, including (1) the mid dorsal insula and overlying operculum at the junction of frontal and parietal lobes, (2) anterior dorsal insula and overlying frontal operculum and (3) ventral insula. We also suggested that the first two regions roughly correspond to the two anatomical projections observed in non-human primates; however, it was clear that the anterior cluster did not extend into the most rostral and dorsal region of the anterior insula (Small et al. 1999; Fig. 1).

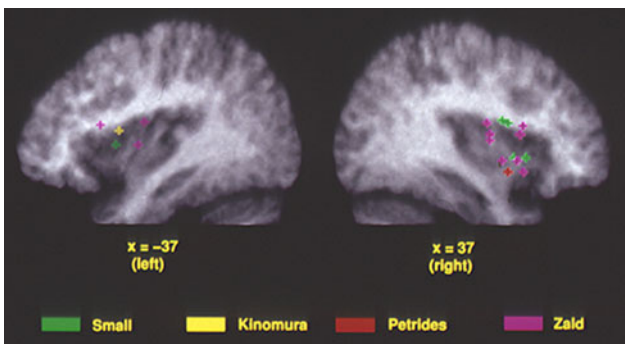

Fig. 1 Meta-analysis of early PET studies of taste. *Left* and *right* sagittal sections of the human brain showing the peaks from early PET neuroimaging studies of taste illustrated as *crosses* and *color coded* according the laboratory or study from which they were generated (Kinomura et al. 1994; Petrides et al. 1996; Small et al. 1997a, 1997b; Zald et al. 1998). $x = 37$ and -37 refers to MNI coordinate at which the sagittal sections are displayed. Modified from Small et al. (1999)

More recently, Verhagen and colleagues conducted a second meta-analysis of taste (and olfactory) responses and again noted that taste (and olfactory) activations extended essentially the whole length of the insula and overlying operculum (Verhagen and Engelen 2006).

Determining which of these multiple taste-responsive regions represents primary taste cortex in the human has been the subject of considerable study and debate. Based on magnetoencephalography data showing that the parietal operculum is the first region activated during presentation of the taste stimulus Ogawa, Kobayakawa and their colleagues have argued that human primary taste cortex is in the parietal operculum (Kobayakawa et al. 1996, 1999; Ogawa et al. 2005). We have suggested (Small 2006) that although provocative, this conclusion must be viewed cautiously, as it is inconsistent with primate gustatory organization, and the known connectivity of the posterior insula with somatosensory and auditory, but not gustatory and olfactory systems (Mesulam and Mufson 1982).

Petrides and Pandya performed a comparative cytoarchitectonic study of the human and monkey brain and identified a closer correspondence in the architectonic features of the anterodorsal insula and adjacent frontal opercular cortex and suggested that this region corresponded to primary taste cortex in both species. In humans, as in monkeys, this region is located within the cortex of the horizontal ramus of the Sylvian fissure with the rostral limit defined by the end of the ramus (Petrides and Pandya 1994). However, while many neuroimaging studies report activation in the anterior insula and overlying operculum; and some conclude that there is a good correspondence between primary taste cortex in monkeys and humans (Rolls 2007), in our own studies we have been impressed by the lack of consistent activation in the far anterior region. For example, in our more recent fMRI paper we compared the average response to sweet, sour, and salty taste to the average response to an artificial saliva solution, that had little or no taste, and isolated responses within the caudal-most part of the anterior insula, as well as in the anterior ventral insula (Bender et al. 2009; Fig. 2). Moreover, in their own PET study Frey, Petrides and their colleagues, observed taste-elicited responses in multiple regions of insula and overlying operculum, but not in any region of anterior insula and overlying frontal operculum (Frey and Petrides 1999; Fig. 2).

There are multiple reasons why the precise location of primary taste cortex in humans remains so elusive. First, taste sensations co-occur with multiple other oral sensory experiences, which are co-localized with taste. For example, the primate primary gustatory cortex contains nearly as many somatosensory-specific as taste-specific neurons, in addition to bimodal neurons responding to both

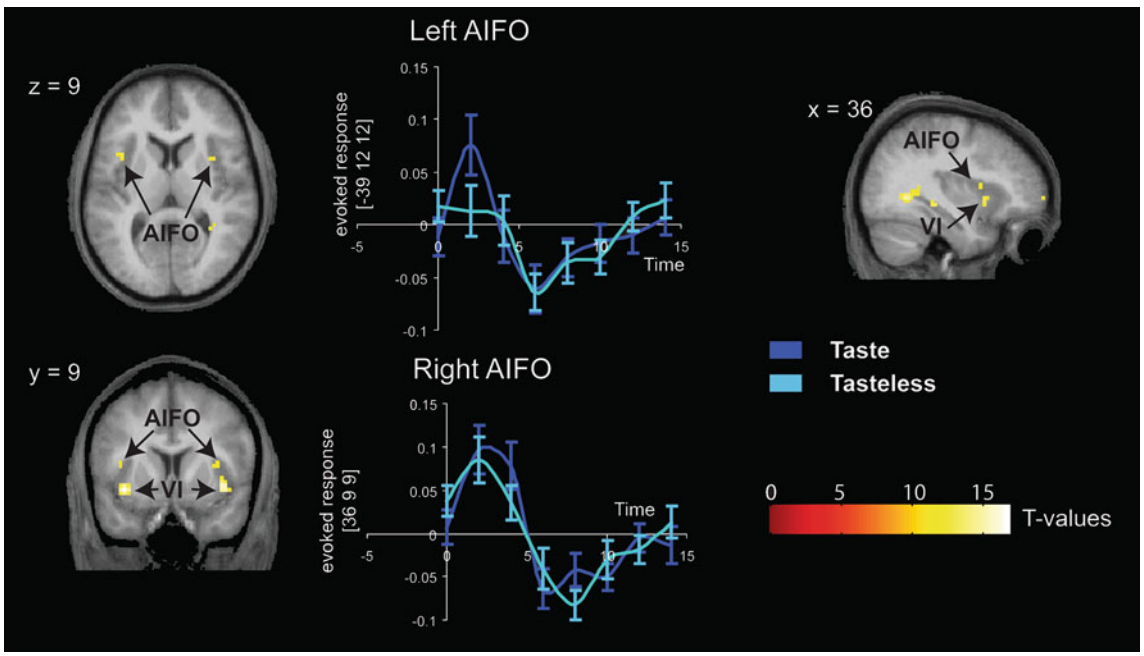

Fig. 2 Insular response to taste collapsed across tastants and tasks. Average insular responses in 15 healthy individuals to taste solutions (sweet + sour + salty) versus an artificial saliva solution collapsed across several different task conditions (detecting taste, judging pleasantness, judging quality) adapted from Bender et al. (2009). AIFO refers to the anterior insula and overlying frontal operculum but note that this response is in the caudal-most section of the anterior insula. VI refers to ventral anterior insula. The graphs display the time series data with the average responses over subjects (± SEM) extracted from the peak voxels on the *y* axis and the hemodynamic response estimated from the fist eigenvariate at each TR (2 s) in peristimulus time from the onset of the event on the *x* axis. The data were estimated based on the finite impulse response model. The *color bar* represents the *t* values and the *t*-map image was thresholded at $P < 0.001$ uncorrected

somatosensory and taste stimulation (Yamamoto et al. 1985; Smith-Swintosky et al. 1991; Plata-Salaman et al. 1992, 1996; Kadohisa et al. 2004). Thus, activation in response to a taste stimulus may well be caused by co-stimulation of oral somatosensation. Second, the problem of isolating the taste signal in fMRI studies is further confounded by the fact that taste cells are actually the minority in taste cortex. Single unit recording studies estimate that only 5–10% of neurons in the primate primary taste area respond to taste (Scott and Plata-Salaman 1999). Third, different neuroimaging studies employ different task designs that may, or may not require active evaluation, and subtle differences in tasks appear to be associated with variability in response (Bender et al. 2009; Fig. 4).

Capitalizing upon the ability of attention to modulate early sensory cortex, we attempted to isolate gustatory "baseline shifts" to help identify early gustatory cortex. Baseline shifts refer to the ability of selective attention to alter the responsivity of early sensory cortex so that the region becomes more sensitive to incoming sensory signals and thus increase sensitivity in the service of goal-directed behavior (Kanwisher and Wojciulik 2000). As such, trying to hear in the absence of sound, see in the absence of visual inputs, or smell in the absence of odor, all activate respective primary cortical regions (Hopfinger et al. 2000; Zelano et al. 2005; Voisin et al. 2006). We therefore reasoned that trying to taste in the absence of taste should increase the response of primary taste cortex (Veldhuizen et al. 2007). In our study subjects received taste and tasteless solutions and were either asked to try to detect whether a taste was present or to taste passively while undergoing fMRI. In addition, because we were concerned that subjects might try to detect a taste even though they were asked not to, we informed the subject about the identity of the solution in half of the passive trials. This created three conditions. In condition *detect* subjects heard "detect" and then "liquid", then received the stimulus, and finally pressed a button to indicate whether or not a taste was present. Condition *passive uninformed* was identical to *detect* except that subjects heard "randomly press" instead of "detect" and then randomly pressed a button following delivery of the solution. The *passive informed* conditioned differed from *detect* not only in the attentional component, indicated by the instruction (i.e. "randomly press" rather than "detect"), but also in expectation, since subjects heard "taste" or "tasteless", depending upon what was subsequently delivered, rather than "liquid". Analyses focused on the tasteless trials. When we compared *detect* to *passive informed* we saw activation in parietal operculum, mid dorsal insula and overlying operculum, and far anterior dorsal insula and overlying operculum. However, when we performed the more closely matched contrast (*detect* vs. *passive uniformed*), the parietal operculum and mid dorsal insular responses remained significant but the far anterior insular response disappeared. We therefore concluded that there was evidence for baseline shifts in the parietal operculum and mid dorsal insula and overlying operculum but not in the far anterior dorsal insula, which instead appeared sensitive to expectation rather than selective attention. Although, not conclusive, these results again support the notion that primary taste cortex is located more caudally in humans than in monkeys. They also suggest that activations in the far anterior dorsal regions of the insula are related to higher-order processes like expectation rather than basic sensory representation of taste (Fig. 3).

In summary, although the debate over the primary insular representation of taste in humans remains unresolved there is converging evidence that it is located further caudally in the human compared to the monkey insular cortex. Given the precedent for profound interspecies differences in the gustatory neuroaxis in primates compared to rodents it is possible that the location of taste cortex in humans "migrated" further posteriorly. However, a more parsimonious explanation is that if, as Craig (2009) suggests, the far anterior insular cortex is newly evolved and unique to humans, then the human taste cortex may only appear to be located further caudally because it is no longer in the anterior-most section of insular cortex.

Functions of the human insular gustatory cortex

The primary perceptual dimensions of taste include quality, intensity, and affective value. In addition to coding these

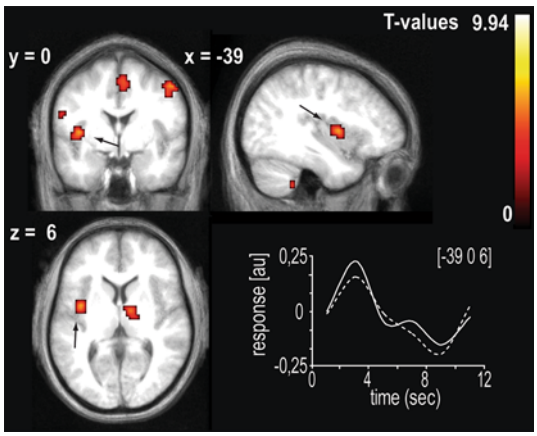

Fig. 3 Location of insular baseline shift resulting from attention to taste. Average insular response from 14 healthy subjects evoked when attempting to detect a taste in a tasteless solution versus passively sampling the tasteless solution (adapted from Veldhuizen et al. 2007). *x*, *y* and *z* values represent MNI coordinates for the sagittal, coronal and axial planes. The time series *graphs* represent extracted response in arbitrary units (*au*) on the *y* axis plotted over time in seconds on the *x* axis. The *solid line* represents response in *detect* and the *dashed line* the response in *passive uniformed*. The *color bar* represents the *t* values and the *t*-map image was thresholded at $P < 0.001$ uncorrected

features of pure taste stimuli, the gustatory system must integrate with the other oral sensory modalities to produce flavor percepts, and with homeostatic systems to guide feeding behavior. There is evidence that the human insular taste regions play a role in all of these functions. However, there are three caveats to keep in mind in considering the functional organization taste cortex in humans. First, it is likely that most functions require network interactions that extend beyond the insula/operculum (Small et al. 1997b). Second, the so-called insular taste areas are heteromodal, with neighboring cells responding to sensations, behaviors and states associated with flavor and feeding (Scott and Plata-Salaman 1999). Third, the spatial and temporal resolution afforded by human lesion studies and functional neuroimaging are likely not adequate to resolve critical signals, such as the temporal code for sensory-specific responses to the somatosensory, chemosensory and hedonic components of tastants (Katz et al. 2002; Katz 2005).

Quality

Although there is clear evidence that taste receptor cells form dedicated channels that code a single taste quality (Chandrashekar et al. 2006, 2010), the existence of this "labeled line" coding in the central nervous system is debated (Smith and Scott 2003; Lemon and Katz 2007; Tomchik et al. 2007). Chief amongst the evidence cited against labeled line coding is the fact that primate insular taste cortex neurons are rather broadly tuned. In other words, taste-responsive neurons in the monkey taste cortex generally respond to more than one taste quality (Scott and Plata-Salaman 1991, 1999). There is also little evidence for chemotopy in monkey taste cortex, with responses to all tastes relatively interspersed. However, there are several reports of spatially segregated responses to different taste qualities in rodents (Sugita and Shiba 2005; Accolla et al. 2007), primates (Scott and Plata-Salaman 1999) and humans (Small et al. 2003; Schoenfeld et al. 2004). What is currently not clear is whether these "chemotopic" responses reflect quality coding, or the coding of another related dimension, such as physiological significance, pleasantness, or intensity (Veldhuizen et al. 2008). For example, it is possible to isolate discrete responses in the rodent NTS (Chang and Scott 1984) and gustatory cortex (Accolla and Carleton 2008) to sweet and bitter tastes, but this distinction dissolves if an aversion is conditioned to the sweet taste-indicating that basis for the segregation is physiological significance rather than quality.

Irrespective of whether chemotopy exists, or whether the quality code is conveyed as labeled line, or across a pattern of activity, it is clear that human insular taste cortex contributes to quality coding. Lesions encompassing the primary taste cortex impair taste quality perception (Pritchard et al. 1999). Similarly, asking subjects to judge taste quality during fMRI scanning specifically recruits this region, especially in the left hemisphere (Bender et al. 2009; Fig. 4).

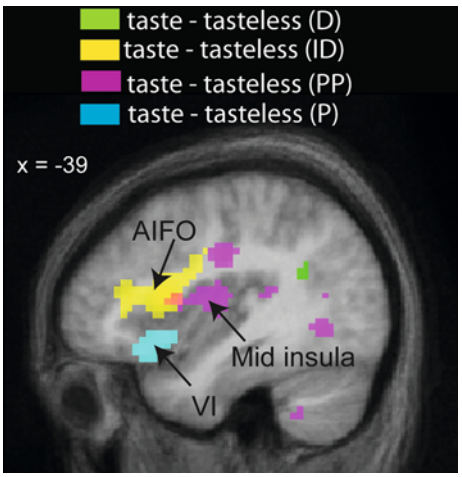

Fig. 4 Taste–tasteless as a function of task in the insula. The results of a group analysis of 15 healthy right handed subjects who participated in an experiment designed to test for the presence of functional specialization in gustatory cortex (adapted from Bender et al. 2009). The sagittal brain section depicts the location of response isolated in the contrast of taste–tasteless for each of four conditions (*ID* identification, *PP* perceived pleasantness, *P* passive, *D* detect) color coded and superimposed upon the mean anatomical image. The SPM *t*-maps were thresholded at $P < 0.005$ for the purpose of illustration. *Bar graphs* depict the average percept signal change over subjects (± SEM) of the neural response at the peak voxel indicated by the *black arrow* (*y* axis) for taste and tasteless across the four tasks. The *color key* is located at the *bottom* of the figure

In sum, insular cortex appears to contribute to taste quality coding in humans; however, although there appears to be some evidence of segregated responses within gustatory cortex, it is not clear whether this reflects chemotopic organization or physiological significance. It is also not clear whether chemotopic organization exists in human taste cortex but on a spatial, or temporal (Di Lorenzo 2003) scale not accessible with traditional functional neuroimaging methodology.

Intensity

In monkeys, intensity response functions generated from taste-responsive cells conform to the slopes reported in human psychophysical experiments of perceived intensity (Smith-Swintosky et al. 1991). In humans changes in suprathreshold taste intensity occurs following insular lesions (Pritchard et al. 1999; Mak et al. 2005) and *bold* responses to a various taste stimuli increase as a function of concentration in the precise region we propose represents

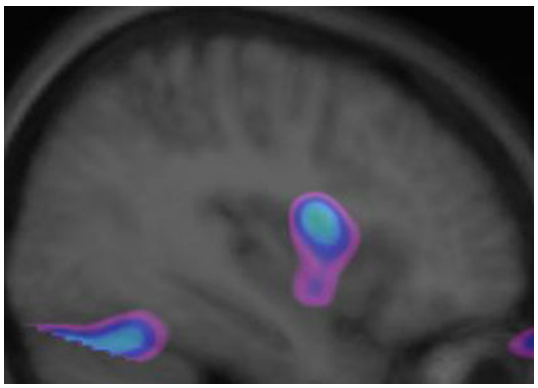

Fig. 5 Modulation of insular response to chocolate by eating to beyond satiety. The results from a group analysis ($n = 9$) of the correlation between pleasantness ratings provided following each of seven 1-min PET scans measuring regional cerebral blood flow during the savoring of a piece of Lindt© chocolate. The sagittal section shows the region of insular cortex that responded to changes in pleasantness as a function of eating to beyond satiety. Adapted from Small et al. (2001)

primary taste cortex (Small et al. 2003). Therefore, there is clear and consistent evidence that the human and monkey primary taste cortex codes perceived intensity.

Affective value, perceived pleasantness and physiological significance

Taste responses in insular cortex appear sensitive to a number of functions that reflect value coding, including variations in perceived pleasantness (Small et al. 2003), internal state (Small et al. 2001; Smeets et al. 2006; Haase et al. 2009), and modulation of value or pleasantness by manipulation of expectations and beliefs (Berns et al. 2001, Nitschke et al. 2006). For example, we found that response in the primary taste cortex correlated with changes in the perceived pleasantness of chocolate as it was eaten to beyond satiety (Fig. 5). More recently, modulation of insular responses to a pure taste by internal state was demonstrated by Haase et al. (2009). Both findings suggest that homeostatic signals may modify responses in primary taste cortex in order to reduce pleasantness and thereby promote meal termination.

Interestingly, and consistent with the above findings, the physiological state of hunger activates a complex network of brain regions that includes not only the hypothalamus but also the insular and orbitofrontal cortices; on the other hand, satiation is associated with increased neuronal activity in more dorsal regions of prefrontal, but not insular cortex (Del Parigi et al. 2002). These studies therefore provide evidence that, in humans, the insular cortex regions including its chemosensory aspect display heightened levels of activity during states of nutritional deficit. Consistent with a role for the insular cortex in homeostatic regulation, Tataranni et al. (1999) found that insular cortex activity at rest correlates positively with plasma insulin concentrations.

In an elegant demonstration of cognitive influences on insular affective processing of taste, Nitschke et al. 2006 found that when cue-based expectancies were manipulated in such a way as to mislead subjects into believing that the upcoming taste would be less unpleasant than it actually was, the responses in the insular cortex were likewise blunted (Fig. 6). Similarly, Berns et al. (2001) found that insular responses to juice or water were maximal for the unpredicted and preferred solutions, suggesting that temporal expectancies and preferences interact to drive responses.

In addition, several studies have reported differential connectivity between insular taste-responsive cortex (including the primary region) and other key feeding or

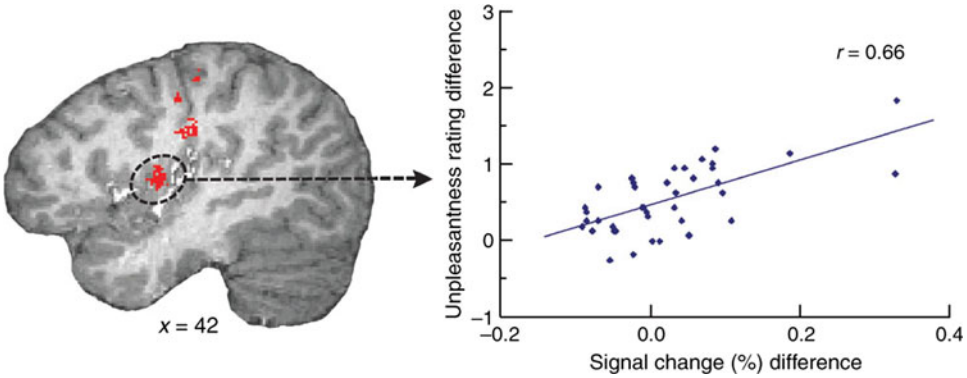

Fig. 6 Response in the insular cortex is correlated with pleasantness ratings that are modulated by expectation. *Circled* right insula and operculum cluster for which activation was correlated with taste ratings. This taste was rated as less unpleasant when it followed the mildly aversive cue than when it followed the highly aversive cue by individuals who had greater reductions in activation of this area for the highly aversive taste following the mildly aversive cue compared to when the same taste followed the highly aversive cue. The partial correlation removing the variance associated with baseline differences for the first 3 s of each trial was 0.62. Reproduced from Nitschke et al. (2006) with permission from the authors

reward regions as a function of the physiological significance of the intra-oral stimulus (Rudenga et al. 2010) or whether subjects perform an affective evaluation of a taste stimulus compared to a tasteless baseline stimulus (Bender et al. 2009). Thus, although some authors remain unconvinced that the primary taste cortex is sensitive to value (Rolls 2007), we believe that there is sufficient converging evidence from a variety of experimental designs and laboratories to draw this conclusion and to speculate that a major function of this affective influence is to help guide feeding behavior.

Functional specialization

Given the multiple regions of taste-responsive cortex, and the multiple dimensions to which insular taste responses are sensitive, it seems reasonable to speculate that specialization of function could exist across these regions. This possibility was investigated by Bender and colleagues who asked subjects to sample pure taste solutions passively or while judging the presence or absence of a taste, the quality of the taste, or its pleasantness (Bender et al. 2009). A large region of bilateral anterior (but not far anterior) insular cortex was identified that responded to taste versus tasteless irrespective of the task; however, there were variations in the precise location of the response as a function of the task the subject was asked to perform (Fig. 4). This suggests that attending to different aspects of the taste stimulus influences the location of the taste response. However, direct comparisons between the tasks only provided weak support for the possibility of functional specialization, with a trend emerging in the dorsal insula and operculum suggesting preferential response during quality identification. In contrast, functional connectivity analyses clearly supported the possibility for functional specialization between regions, with connectivity between the insula and amygdala greatest during passive versus active evaluation, and connectivity between the insula and OFC maximal during pleasantness evaluation of taste.

In summary, although there are multiple insula and opercular taste-responsive regions, there is as yet no clear indication for functional specialization. Rather these regions, as assayed with traditional fMRI techniques, appear sensitive to many features of gustatory stimuli. In contrast, evidence for functional specialization emerges when considering network interactions, and when moving beyond the insula and operculum. For example, taste responses in the OFC are clearly influenced by perceived pleasantness (Zald et al. 1998; Kringelbach et al. 2003), but appear relatively insensitive to intensity (Small et al. 2003).

Flavor

Taste sensations almost always co-occur with other intra-oral sensations during eating and drinking. Therefore, it is critical to consider taste processing within the context of flavor perception. Two illusions conspire to bring taste, retronasal olfaction, and touch into a common spatial register and hence facilitate the fusing of these discrete sensations into a single perception, which we then falsely attribute to the gustatory sense (Small 2008; Small and Green 2010b). The first illusion causes gustatory stimulation, which depends upon transduction from taste receptor cells located in discrete regions of the tongue, to appear to originate from the site of somatosensory stimulation—even if it is devoid of taste receptor cells (Green 2002). This illusion represents the "capture" of taste by touch (Green 2002). The second illusion is the olfactory localization illusion, which causes olfactory stimulation to appear to originate from the mouth despite the fact that transduction occurs in the nasal epithelium (Murphy et al. 1977). Together, these two mechanisms of illusory co-localization reflect an ability of the central nervous system to rapidly integrate segregated inputs arising from the oral cavity to form the representation of a single flavor percept (Small 2009; Small and Green 2010a).

It is currently unknown whether the insula plays a role in the oral referral illusions. We have suggested that the somatomotor mouth area, located in the operculum, plays a critical role in the binding of the oral senses because this region is preferentially responsive to retronasally sensed odors that are referred to the mouth (Small et al. 2005). Irrespective of whether insula contributes to referral, it is clear that the human primary taste cortex is sensitive to oral touch, texture and temperature. There are robust responses to oral somatosensory inputs (Cerf-Ducastel et al. 2001). Activation produced by a tasteless viscous stimulus (carboxymethylcellulose) is proportional to the log of its viscosity (de Araujo and Rolls 2004), and variations in the temperature of distilled water results in alterations of responses in primary taste cortex (Guest et al. 2007). As such, de Araujo and Simon suggest that the insular taste cortex is better conceptualized as supporting an integrated oral system (De Araujo and Simon 2009).

Although, single unit recording studies in monkeys have identified olfactory responses in primary taste cortex (Scott et al. 1986; Yaxley et al. 1990; Scott and Plata-Salaman 1999), and human imaging studies of olfaction frequently report responses in primary taste cortex (Verhagen and Engelen 2006), the few studies that have investigated response to tastes and odors in the same individuals, suggest that taste and odor information are integrated further ventrally with the anterior insula(de Araujo et al. 2003; Small et al. 2004). de Araujo and colleagues showed

overlapping responses in the anterior ventral insula to odors and to tastes (de Araujo et al. 2003; Small et al. 2004) and Small and colleagues identified supra-additive responses during the perception of a congruent taste–odor pair in this region (Small et al. 2004). These two findings suggest that flavor percepts, which depend critically on olfactory inputs for identification, are formed in the anterior ventral insula. However, it is important to remember that olfactory responses are observed in other regions of insular cortex, including primary taste cortex and overlying operculum. Moreover, a patient study reported taste and olfactory changes following an insular lesion that did not infringe upon the anterior ventral region (Mak et al. 2005). Therefore it is possible, and even likely that flavor perception depends upon a distributed network that includes multiple insular and as well as orbital regions.

Food

Although humans retain the ability to use their noses to navigate to food sources (Porter et al. 2007), foods are generally identified and acquired by sight. It is therefore not surprising that the sight or mere thought of food is sufficient to activate insular taste cortex (Pelchat et al. 2004; Simmons et al. 2005). Using fMRI, Simmons et al. (2005) had subjects view pictures of appetizing foods and, for comparison, pictures of locations. Compared to "location pictures" that also activate the visual pathway, food appearance specifically activates gustatory processing areas including the insular and opercular cortices. Importantly, the locations of the activations reported were highly coincidental with those known to be activated by prototypical tastants (Simmons et al. 2005). These results are consistent with an earlier demonstration that (visual and olfactory) food presentation of favorite foods was sufficient to significantly increase metabolism in the whole brain as detected by PET imaging, with largest changes observed in the anterior insular and orbitofrontal cortices (Wang et al. 2004). Insular responses to the sight and thought of food may also be modulated by internal state (Hinton et al. 2004; Malik et al. 2008a). For example, Malik and colleagues demonstrated that insular responses to pictures of foods decrease with satiety and then increase following intravenous infusions of ghrelin (Malik et al. 2008b), an orexigenic gut hormone (Tschop et al. 2000). Additionally obese relative to lean individuals also show greater insular responses to pictures of high calorie foods (Rothemund et al. 2007) and to the anticipated as well as actual ingestion of milkshake (Stice et al. 2008) indicating that individual variations in insular responses to food and food cues may be associated with variations in intake.

General summary

The sense of taste evolved to allow the detection of key nutrients and toxins. Although the range of perceptual responses computed by the gustatory system is relatively narrow this selective repertoire is characterized by innate and stable relationships with affective responses. This simple, yet elegant, system is then complimented by flavor preference formation, which in contrast to taste, is highly dependent upon experience. Thus organisms can sample novel foods in the environment and, based upon taste inputs, determine whether to ingest those containing potential nutrients. Subsequently, based upon post-ingestive effects predicted by the sense of taste (Sclafani 2004), the affective response to the flavor of that specific food is formed. The human insular "gustatory" cortex reflects the basic function of taste. The region, which is located in the caudal-most section of the anterior dorsal insula and extending into the mid-insular region, is sensitive not only to basic features of pure taste stimuli but also to stimulation of other intra-oral sensations and to fluctuations in internal state. As such, it likely plays a key role not only in taste but also in flavor perception and feeding regulation.

Acknowledgment This work was supported by NIH NIDCD R01 6706-04.

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