

Flavor: Brain processing

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6.1 Introduction

A diagram of the taste and related olfactory, somatosensory, and visual pathways in primates is shown in Fig. 6.1. Neurophysiological studies in primates provide a foundation for understanding taste, olfactory, and flavor processing and neuroimaging in humans, for investigations of the tuning of individual neurons provide the fundamental information about how these stimuli are encoded in different brain areas, using a sparse distributed representation in which each neuron is tuned differently to other neurons (Kadohisa et al., 2005; Rolls, 2008a, 2015c; Rolls et al., 2010a; Rolls and Treves, 2011). Studies in nonhuman primates are especially relevant (Rolls, 2014a, 2015a,b), for the taste pathways in primates proceed via the thalamus to the taste cortex, whereas in rodents there is a pontine taste area which has direct subcortical connections (Small and Scott, 2009); effects of satiety are found peripherally in the nucleus of the solitary tract in rodents (Rolls and Scott, 2003; Scott and Small, 2009; Rolls, 2015b); and rodents do not have the major part of the primate (including human) orbitofrontal cortex, the granular part (Wise, 2008; Rolls, 2014a).

6.2 Flavor processing in the primate brain

6.2.1 Taste processing

6.2.1.1 Pathways

A diagram of the taste and related olfactory, somatosensory, and visual pathways in primates is shown in Fig. 6.1. The multimodal convergence that enables single neurons to respond to different combinations of taste, olfactory, texture, temperature, and visual inputs to represent different flavors produced often by new combinations of sensory input is a theme of recent research that will be described.

6.2.1.2 The primary taste cortex

Rolls and colleagues have shown (Rolls, 2015b) that the primary taste cortex in the primate anterior insula and adjoining frontal operculum contains not only taste neurons tuned to sweet, salt, bitter, sour (Scott et al., 1986; Yaxley et al., 1990; Rolls and Scott, 2003), and umami as exemplified by monosodium glutamate (Baylis and Rolls, 1991; Rolls et al., 1996b), but also other neurons that encode oral

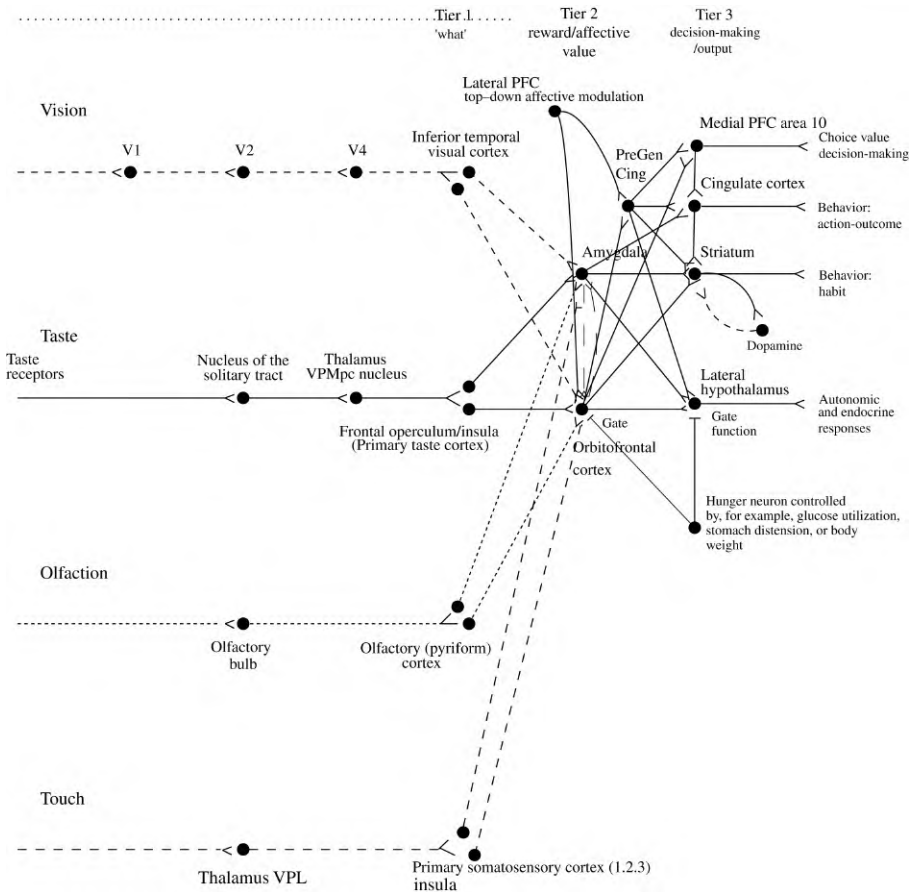


Figure 6.1 Schematic diagram showing some of the gustatory, olfactory, visual, and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex, and the secondary olfactory cortex, are within the orbitofrontal cortex. V1, primary visual cortex; V4, visual cortical area V4; PreGen Cing, pregenual cingulate cortex. “Gate” refers to the finding that inputs such as the taste, smell, and sight of food in some brain regions only produce effects when hunger is present (Rolls, 2005a). Tier 1, the column of brain regions including and below the inferior temporal visual cortex represents brain regions in which “what” stimulus is present is made explicit in the neuronal representation, but not its reward or affective value which are represented in the next tier of brain regions (Tier 2), the orbitofrontal cortex and amygdala, and in the anterior cingulate cortex. In Tier 3 areas beyond these, such as medial prefrontal cortex area 10, choices or decisions about reward value are taken, with the mechanisms described elsewhere (Rolls, 2008b, 2014a; Rolls and Deco, 2010). Top-down control of affective response systems by cognition and by selective attention from the dorsolateral prefrontal cortex is also indicated. Medial PFC area 10, medial prefrontal cortex area 10; VPMpc, ventralposteromedial thalamic nucleus.

somatosensory stimuli including viscosity, fat texture, temperature, and capsaicin (Verhagen et al., 2004). Some neurons in the primary taste cortex respond to particular combinations of taste and oral texture stimuli, but do not respond to olfactory stimuli, or visual stimuli such as the sight of food (Verhagen et al., 2004). Neurons in the primary taste cortex do not represent the reward value of taste, that is, the appetite for a food, in that their firing is not decreased to zero by feeding the taste to satiety (Rolls et al., 1988; Yaxley et al., 1988; Rolls, 2015b).

6.2.1.3 *The secondary taste cortex*

A secondary cortical taste area in primates was discovered by Rolls et al. (1990) in the orbitofrontal cortex, extending several millimeter in front of the primary taste cortex. Different neurons in this region respond not only to each of the four classical prototypical tastes sweet, salt, bitter, and sour (Rolls, 1997; Rolls and Scott, 2003), but also to umami tastants such as glutamate (which is present in many natural foods such as tomatoes, mushrooms, and milk) (Baylis and Rolls, 1991) and inosine monophosphate (which is present in meat, and some fish such as tuna) (Rolls et al., 1996b). This evidence, taken together with the identification of glutamate taste receptors (Zhao et al., 2003; Maruyama et al., 2006), leads to the view that there are five prototypical types of taste information channels, with umami contributing, often in combination with corresponding olfactory inputs (Rolls et al., 1998; McCabe and Rolls, 2007; Rolls, 2009), to the flavor of protein. In addition, other neurons respond to water, and others to somatosensory stimuli including astringency, as exemplified by tannic acid (Critchley and Rolls, 1996b), and capsaicin (Rolls et al., 2003b; Kadohisa et al., 2004). Taste responses are found in a large mediolateral extent of the orbitofrontal cortex (Critchley and Rolls, 1996b; Pritchard et al., 2005; Rolls, 2008a, 2015a; Rolls and Grabenhorst, 2008).

6.2.1.4 *The pleasantness of the taste of food, sensory-specific satiety, and the effects of variety on food intake*

The modulation of the reward value of a sensory stimulus such as the taste of food by motivational state, for example, hunger, is one important way in which motivational behavior is controlled (Rolls, 2014b). The subjective correlate of this modulation is that food tastes pleasant when hungry, and tastes hedonically neutral when it has been eaten to satiety. Following Edmund Rolls' discovery of sensory-specific satiety revealed by the selective reduction in the responses of lateral hypothalamic neurons to a food eaten to satiety (Rolls, 1981; Rolls et al., 1986), it has been shown that this is implemented in a region that projects to the hypothalamus, the orbitofrontal (secondary taste) cortex, for the taste, odor, and sight of food (Rolls et al., 1989; Critchley and Rolls, 1996a; Rolls, 2015a).

This evidence shows that the reduced acceptance of food that occurs when food is eaten to satiety, the reduction in the pleasantness of its taste and flavor, and the effects of variety to increase food intake (Cabanac, 1971; Rolls and Rolls, 1977, 1982, 1997; Rolls et al., 1981a,b, 1982, 1983b,c, 1984; Rolls and Hetherington, 1989; Hetherington, 2007), are produced in the orbitofrontal cortex, but not at earlier stages of processing where the responses reflect factors such as the intensity of the taste, which is little

affected by satiety (Rolls et al., 1983a; Rolls and Grabenhorst, 2008; Rolls, 2015a). In addition to providing an implementation of sensory-specific satiety (probably by habituation of the synaptic afferents to orbitofrontal neurons with a time course of the order of the length of a course of a meal), it is likely that visceral and other satiety-related signals reach the orbitofrontal cortex, as indicated in Fig. 6.1 (from the nucleus of the solitary tract, via thalamic and possibly hypothalamic nuclei), and there modulate the representation of food, resulting in an output that reflects the reward (or appetitive) value of each food (Rolls, 2014a).

6.2.2 The representation of flavor: convergence of olfactory, taste, and visual inputs in the orbitofrontal cortex

Taste and olfactory pathways are brought together in the orbitofrontal cortex where flavor is formed by learned associations at the neuronal level between these inputs (Fig. 6.1) (Rolls and Baylis, 1994; Critchley and Rolls, 1996c; Rolls et al., 1996a; Verhagen et al., 2004; Rolls, 2011d, 2014a). Visual inputs also become associated by learning in the orbitofrontal cortex with the taste of food to represent the sight of food, and contribute to flavor (Thorpe et al., 1983; Rolls, 1996). The visual and olfactory, as well as the taste inputs, represent the reward value of the food, as shown by sensory-specific satiety effects (Critchley and Rolls, 1996a).

6.2.3 The texture of food, including fat texture

Some orbitofrontal cortex neurons have oral texture-related responses that encode parametrically the viscosity of food in the mouth (shown using a methyl cellulose series in the range 1–10,000 cP), others independently encode the particulate quality of food in the mouth, produced quantitatively, for example, by adding 20–100 μm microspheres to methyl cellulose (Rolls et al., 2003b), and others encode the oral texture of fat (Rolls et al., 1999; Verhagen et al., 2003; Rolls, 2011c, 2015a) as illustrated in Fig. 6.2. Somatosensory signals that transmit information about capsaicin (chili) and astringency are also reflected in neuronal activity in these cortical areas (Critchley and Rolls, 1996b; Kadohisa et al., 2004, 2005).

In addition, we have shown that some neurons in the orbitofrontal cortex reflect the temperature of substances in the mouth, and that this temperature information is represented independently of other sensory inputs by some neurons, and in combination with taste or texture by other neurons (Kadohisa et al., 2004, 2005).

6.3 Flavor processing in the human brain: functional neuroimaging

6.3.1 Taste

In humans, it has been shown (Rolls, 2012b, 2014a, 2015c,a, 2016a) in neuroimaging studies using functional Magnetic Resonance Imaging (fMRI) that taste activates an

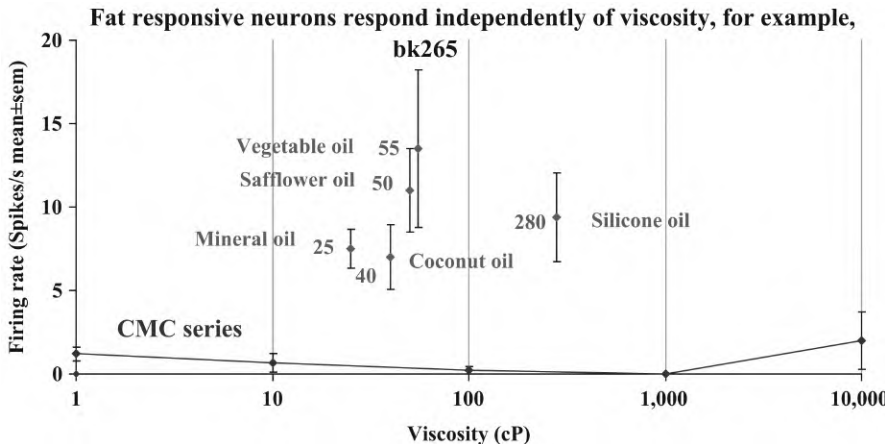


Figure 6.2 A neuron in the primate orbitofrontal cortex responding to the texture of fat in the mouth, independently of viscosity. The cell (bk265) increased its firing rate to a range of fats and oils (the viscosity of which is shown in centipoise). The information that reaches this type of neuron is independent of a viscosity sensing channel, in that the neuron did not respond to the methyl cellulose (CMC) viscosity series. The neuron responded to the texture rather than the chemical structure of the fat, in that it also responded to silicone oil ($(\text{Si}(\text{CH}_3)_2\text{O})_n$) and paraffin (mineral) oil (hydrocarbon). Some of these neurons have taste inputs.

Source: After Verhagen et al. (2003).

area of the anterior insula/frontal operculum, which is probably the primary taste cortex (O'Doherty et al., 2001; de Araujo et al., 2003b; Small, 2010; Rolls, 2015b), and part of the orbitofrontal cortex, which is probably the secondary taste cortex (Francis et al., 1999; O'Doherty et al., 2001; de Araujo et al., 2003b; Rolls, 2005b, 2008a). We pioneered the use of a tasteless control with the same ionic constituents as saliva (O'Doherty et al., 2001; de Araujo et al., 2003b), as water can activate some neurons in cortical taste areas (Rolls et al., 1990) and can activate the taste cortex (de Araujo et al., 2003b). Within individual subjects, separate areas of the orbitofrontal cortex are activated by sweet (pleasant) and by salt (unpleasant) tastes (O'Doherty et al., 2001).

The primary taste cortex in the anterior insula of humans represents the identity and intensity of taste in that activations there correlate with the subjective intensity of the taste, and the orbitofrontal and anterior cingulate cortex represents the reward value of taste, in that activations there correlate with the subjective pleasantness of taste (Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a; Rolls, 2015a,b) (Fig. 6.3).

We also found activation of the human amygdala by the taste of glucose (Francis et al., 1999). Extending this study, O'Doherty et al. (2001) showed that the human amygdala was as much activated by the affectively pleasant taste of glucose as by the affectively negative taste of NaCl, and thus provided evidence that the human amygdala is not especially involved in processing aversive, as compared to rewarding, stimuli. Zald et al. (1998, 2002) also showed that the amygdala, as well as the orbitofrontal cortex, responds to aversive (eg, quinine) and to sucrose taste stimuli.

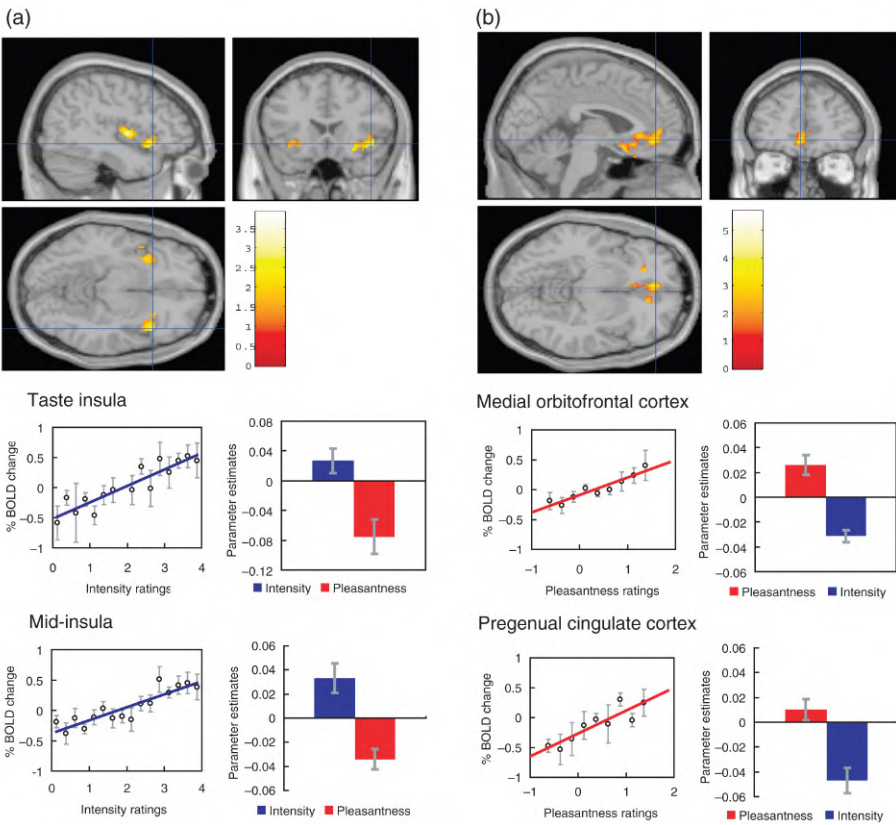


Figure 6.3 Effect of paying attention to the pleasantness versus the intensity of a taste stimulus. (a) Top: a significant difference related to the taste period was found in the taste insula at $[42\ 18\ -14]$ $z = 2.42$ $p < 0.05$ (indicated by the cursor) and in the mid insula at $[40\ -2\ 4]$ $z = 3.03$ $p < 0.025$. Middle: taste insula. Right: the parameter estimates (mean \pm sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the taste insula $t = 4.5$, $df = 10$, $p = 0.001$. Left: the correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate ($r = 0.91$, $df = 14$, $p \ll 0.001$). Bottom: mid insula. Right: the parameter estimates (mean \pm sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the mid insula $t = 5.02$, $df = 10$, $p = 0.001$. Left: the correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate ($r = 0.89$, $df = 15$, $p \ll 0.001$). The taste stimulus, monosodium glutamate, was identical on all trials. (b) Top: a significant difference related to the taste period was found in the medial orbitofrontal cortex at $[-6\ 14\ -20]$ $z = 3.81$ $p < 0.003$ (toward the back of the area of activation shown) and in the pregenual cingulate cortex at $[-4\ 46\ -8]$ $z = 2.90$ $p < 0.04$ (at the cursor). Middle: medial orbitofrontal cortex. Right: the parameter estimates (mean \pm sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the orbitofrontal cortex $t = 3.81$, $df = 10$, $p = 0.003$. Left: the correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate ($r = 0.89$, $df = 15$, $p \ll 0.001$). The taste stimulus, monosodium glutamate, was identical on all trials.

Umami taste stimuli, of which an exemplar is monosodium glutamate (MSG) and which capture what is described as the taste of protein, activate the insular (primary), orbitofrontal (secondary), and anterior cingulate (tertiary; [Rolls, 2008a](#)) taste cortical areas ([de Araujo et al., 2003a](#)). When the nucleotide 0.005 M inosine 5'-monophosphate (IMP) was added to MSG (0.05 M), the BOLD (blood oxygenation-level dependent) signal in an anterior part of the orbitofrontal cortex showed supralinear additivity, and this may reflect the subjective enhancement of umami taste that has been described when IMP is added to MSG ([Rolls, 2009](#)). The supralinear additivity refers to a greater activation to the combined stimulus MSG + IMP than to the sum of the activations to MSG and IMP presented separately. This evidence that the effect of the combination is greater than the sum of its parts indicates an interaction between the parts to form, in this case, an especially potent taste of umami, which is part of what can make a food taste delicious ([Rolls, 2009](#)). Overall, these results illustrate that the responses of the brain can reflect inputs produced by particular combinations of sensory stimuli with supralinear activations, and that the combination of sensory stimuli may be especially represented in particular brain regions, and may help to make the food pleasant.

6.3.2 Odor

In humans, in addition to activation of the pyriform (olfactory) cortex ([Zald and Pardo, 1997](#); [Sobel et al., 2000](#); [Poellinger et al., 2001](#)), there is strong and consistent activation of the orbitofrontal cortex by olfactory stimuli ([Zatorre et al., 1992](#); [Francis et al., 1999](#); [Rolls et al., 2003a](#)). This region appears to represent the pleasantness of odor, as shown by a sensory-specific satiety experiment with banana versus vanilla odor ([O'Doherty et al., 2000](#)), and this has been confirmed by [Gottfried et al.](#) (personal communication, see [Gottfried, 2015](#)), who also showed that activations in the pyriform (primary olfactory) cortex were not decreased by odor devaluation by satiety. Further, pleasant odors tend to activate the medial, and unpleasant odors the more lateral, orbitofrontal cortex ([Rolls et al., 2003a](#)), adding to the evidence that it is a principle that there is a hedonic map in the orbitofrontal cortex, and also in the anterior cingulate cortex, which receives inputs from the orbitofrontal cortex ([Rolls and Grabenhorst, 2008](#); [Grabenhorst and Rolls, 2011](#)). The primary olfactory (pyriform) cortex represents the identity and intensity of odor in that activations there correlate with the subjective intensity of the odor, and the orbitofrontal and anterior cingulate cortex represents the reward value of odor, in that activations there correlate with the subjective pleasantness

◀ **Figure 6.3** (cont.) $t = 7.27$, $df = 11$, $p < 10^{-4}$. Left: the correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate ($r = 0.94$, $df = 8$, $p \ll 0.001$). Bottom: pregenual cingulate cortex. Conventions as given earlier. Right: the parameter estimates were significantly different for the pregenual cingulate cortex $t = 8.70$, $df = 11$, $p < 10^{-5}$. Left: the correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate ($r = 0.89$, $df = 8$, $p = 0.001$). The taste stimulus, 0.1 M monosodium glutamate, was identical on all trials.
 Source: After [Grabenhorst and Rolls \(2008\)](#).

(medially) or unpleasantness (laterally) of odor (Rolls et al., 2003a, 2008, 2009; Grabenhorst et al., 2007; Rolls and Grabenhorst, 2008; Grabenhorst and Rolls, 2011).

6.3.3 Olfactory-taste convergence to represent flavor, and the influence of satiety on flavor representations

Taste and olfactory conjunction analyses, and the measurement of supradditive effects indicating convergence and interactions, showed convergence for taste (sucrose) and odor (strawberry) in the orbitofrontal and anterior cingulate cortex, and activations in these regions were correlated with the pleasantness ratings given by the participants (de Araujo et al., 2003c; Small et al., 2004; Small and Prescott, 2005). These results provide evidence on the neural substrate for the convergence of taste and olfactory stimuli to produce flavor in humans, and on where the pleasantness of flavor is represented in the human brain. The first region where the effects of this convergence are found is in an agranular part of what cytoarchitecturally is the insula (Ia) that is topologically found in the posterior orbitofrontal cortex, though it is anterior to the insular taste cortex, and posterior to the granular orbitofrontal cortex (Fig. 6.3) (de Araujo et al., 2003c).

McCabe and Rolls (2007) have shown that the convergence of taste and olfactory information appears to be important for the delicious flavor of umami. They showed that, when glutamate is given in combination with a consonant, savory, odor (vegetable), the resulting flavor can be much more pleasant than the glutamate taste or vegetable odor alone, and that this reflected activations in the pregenual cingulate cortex and medial orbitofrontal cortex. The principle is that certain sensory combinations can produce very pleasant food stimuli, which may, of course, be important in driving food intake; and that these combinations are formed in the brain, far beyond the taste or olfactory receptors (Rolls, 2009).

To assess how satiety influences the brain activations to a whole food which produces taste, olfactory, and texture stimulation, we measured brain activation by whole foods before and after the food is eaten to satiety. The foods eaten to satiety were either chocolate milk, or tomato juice. A decrease in activation by the food eaten to satiety relative to the other food was found in the orbitofrontal cortex (Kringelbach et al., 2003), but not in the primary taste cortex. This study provided evidence that the pleasantness of the flavor of food, and sensory-specific satiety which is an important component of appetite and the control of food intake (Rolls, 2014a) are represented in the orbitofrontal cortex.

6.3.4 Oral viscosity and fat texture

The viscosity of food in the mouth is represented in the human primary taste cortex (in the anterior insula), and also in a midinsular area that is not taste cortex, but which represents oral somatosensory stimuli (de Araujo and Rolls, 2004). Oral viscosity is also represented in the human orbitofrontal and perigenual cingulate cortices, and it is notable that the perigenual cingulate cortex, an area in which many pleasant stimuli are represented, is strongly activated by the texture of fat in the mouth, and also by oral sucrose (de Araujo and Rolls, 2004). We have shown that the pleasantness and reward value of fat texture is represented in the midorbitofrontal and anterior cingulate cortex,

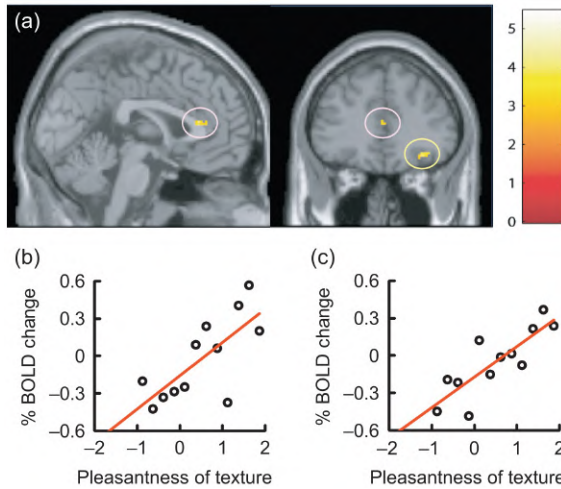


Figure 6.4 Brain regions in which the activations were correlated with the subjective pleasantness of fat texture. Mid-orbitofrontal cortex ($[32\ 34\ -14]$ $z = 3.38$ $p = 0.013$) [(a), yellow circle, (c) showing the relation between the % change in the BOLD signal and the rating of the pleasantness of the texture], and anterior cingulate cortex ($[2\ 30\ 14]$ $z = 3.22$ $p = 0.016$) [(a) pink circles, and (b)].

Source: After [Grabenhorst et al. \(2010\)](#).

where activations are correlated with the subjective pleasantness of oral fat texture ([Rolls, 2009, 2010b; Grabenhorst et al., 2010](#)) (Fig. 6.4). This provides a foundation for studies of whether activations in the fat reward system are heightened in people who tend to become obese ([Rolls, 2012b](#)). Interestingly, high fat stimuli with a pleasant flavor increase the coupling of activations between the orbitofrontal cortex and somatosensory cortex, suggesting a role for the somatosensory cortex in processing the sensory properties of food in the mouth ([Grabenhorst and Rolls, 2014](#)).

6.3.5 The sight of food

[O'Doherty et al. \(2002\)](#) showed that visual stimuli associated with the taste of glucose activated the orbitofrontal cortex and some connected areas, consistent with the primate neurophysiology. [Simmons et al. \(2005\)](#) found that showing pictures of foods, compared to pictures of places, can also activate the orbitofrontal cortex. Similarly, the orbitofrontal cortex and connected areas were also found to be activated after presentation of food stimuli to food-deprived subjects ([Wang et al., 2004](#)).

6.3.6 Top-down cognitive effects on taste, olfactory, and flavor processing

To what extent does cognition influence the hedonics of food-related stimuli, and how far down into the sensory system does the cognitive influence reach? To address this, we

performed an fMRI investigation in which the delivery of a standard test odor (isovaleric acid combined with cheddar cheese odor, presented orthonasally using an olfactometer) was paired with a descriptor word on a screen, which on different trials was “Cheddar cheese” or “Body odor.” Participants rated the affective value of the test odor as significantly more pleasant when labeled “Cheddar Cheese” than when labeled “Body odor;” and these effects reflected activations in the medial orbitofrontal cortex (OFC)/rostral anterior cingulate cortex (ACC) that had correlations with the pleasantness ratings (de Araujo et al., 2005). The implication is that cognitive factors can have profound effects on our responses to the hedonic and sensory properties of food, in that these effects are manifest quite far down into sensory and hedonic processing (in the orbitofrontal cortex, Fig. 6.1), so that hedonic representations of odors are affected (de Araujo et al., 2005).

Similar cognitive effects and mechanisms have now been found for the taste and flavor of food, where the cognitive word level descriptor was, for example, “rich delicious flavor;” and activations to flavor were increased in the orbitofrontal cortex and regions to which it projects, including the pregenual cingulate cortex and ventral striatum, but were not influenced in the insular primary taste cortex where activations reflected the intensity (concentration) of the stimuli (Grabenhorst et al., 2008a) (Fig. 6.5).

6.3.7 Effects of selective attention to affective value versus intensity on representations of taste, olfactory, and flavor processing

We have found that with taste, flavor, and olfactory food-related stimuli, selective attention to pleasantness modulates representations in the orbitofrontal cortex (Fig. 6.3), whereas selective attention to intensity modulates activations in areas such as the primary taste cortex (Grabenhorst and Rolls, 2008; Rolls et al., 2008). Thus, depending on the context in which tastes and odors are presented, and whether affect is relevant, the brain responds to a taste, odor, or flavor differently. These findings show that when attention is paid to affective value, the brain systems engaged to represent the stimulus are different from those engaged when attention is directed to the physical properties of a stimulus, such as its intensity.

The brain region that provides the top-down modulation by attention of the orbitofrontal cortex appears to be the lateral prefrontal cortex, as shown by PPI (psychophysiological interaction) analyses (Grabenhorst and Rolls, 2010), and by Granger causality analyses (Ge et al., 2012; Luo et al., 2013). The mechanism probably involves a weak top-down biased competition effect on the taste and olfactory processing (Desimone and Duncan, 1995; Deco and Rolls, 2005; Rolls, 2008b). Because whole streams of cortical processing are influenced (orbitofrontal and cingulate cortex, and even their coupling to the primary taste cortex, by pleasantness-related processing; and insular taste cortex and the midinsula by intensity-related processing; see Grabenhorst and Rolls, 2010; Luo et al., 2013), the process has been described as a biased activation model of attention (Grabenhorst and Rolls, 2010; Rolls, 2013).

This differential biasing by prefrontal cortex attentional mechanisms (Grabenhorst and Rolls, 2010; Ge et al., 2012) of brain regions engaged in processing a sensory

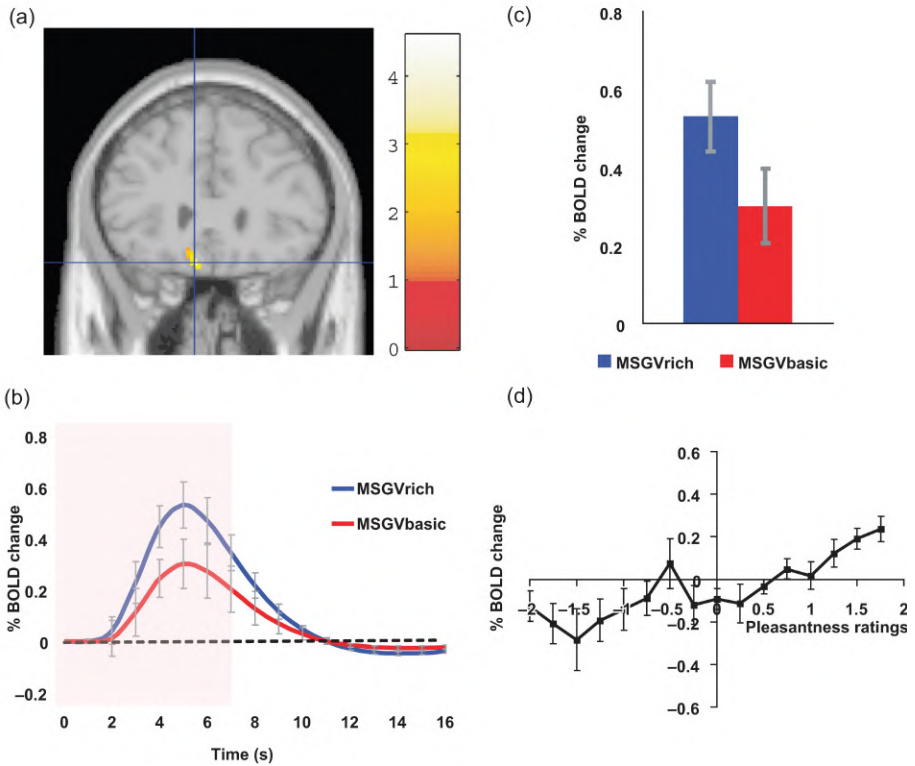


Figure 6.5 Cognitive modulation of flavor reward processing in the brain. (a) The medial orbitofrontal cortex was more strongly activated when a flavor stimulus was labeled “rich and delicious flavor” (MSGVrich) than when it was labeled “boiled vegetable water” (MSGVbasic) ([-8 28 -20]). (The flavor stimulus, MSGV, was the taste 0.1 M MSG + 0.005 M inosine 5’monophosphate combined with a consonant 0.4% vegetable odor.) (b) The timecourse of the BOLD signals for the two conditions. (c) The peak values of the BOLD signal (mean across subjects \pm sem) were significantly different ($t = 3.06$, $df = 11$, $p = 0.01$). (d) The BOLD signal in the medial orbitofrontal cortex was correlated with the subjective pleasantness ratings of taste and flavor, as shown by the SPM analysis, and as illustrated (mean across subjects \pm sem, $r = 0.86$, $p < 0.001$).
 Source: After [Grabenhorst et al. \(2008a\)](#).

stimulus depending on whether the cognitive demand is for affect-related versus more sensory-related processing may be an important aspect of cognition and attention which have implications for how strongly the reward system is driven by food, and thus for eating and the control of appetite ([Grabenhorst and Rolls, 2008, 2011](#); [Rolls et al., 2008](#); [Rolls, 2012b](#)). The top-down modulations of processing have many implications for investigations of taste, olfactory, and other sensory processing, and for the development of new food and perfumery products.

6.4 Beyond the reward value of flavor to decision-making

Representations of the reward value of food, and their subjective correlate the pleasantness of food, are fundamental in determining appetite, and processes such as economic decision-making (Rolls, 2005a, 2014a; Padoa-Schioppa, 2011; Padoa-Schioppa and Cai, 2011). But after the reward evaluation, a decision has to be made about whether to seek for and consume the reward. We are now starting to understand how the brain takes decisions as described in *The Noisy Brain* (Rolls and Deco, 2010) and *Emotion and Decision-Making Explained* (Rolls, 2014a), and this has implications for whether a reward of a particular value will be selected (Rolls, 2008b, 2011b, 2014a; Rolls and Grabenhorst, 2008; Rolls and Deco, 2010; Grabenhorst and Rolls, 2011; Deco et al., 2013).

A tier of processing beyond the orbitofrontal cortex, in the medial prefrontal cortex area 10, becomes engaged when choices are made between odor stimuli based on their pleasantness (Grabenhorst et al., 2008b; Rolls et al., 2010b,c,d) (tier 3 in Fig. 6.1). The choices are made by a local attractor network in which the winning attractor represents the decision, with each possible attractor representing a different choice, and each attractor receiving inputs that reflect the evidence for that choice. The attractor network is formed in a part of the cerebral cortex by strengthening of the recurrent collateral excitatory synapses between nearby pyramidal cells. One group of neurons with strengthened synapses between its members can form a stable attractor with high firing rates, which competes through inhibitory interneurons with other possible attractors formed by other groups of excitatory neurons (Rolls, 2008b, 2010a). The word attractor refers to the fact that inexact inputs are attracted to one of the states of high firing specified by the synaptic connections between the different groups of neurons. The result in this nonlinear system is that one population of neurons that forms one of the possible attractor states wins, and this implements a mechanism for decision-making with one winner (Rolls, 2008b, 2014a, 2016b; Wang, 2008; Rolls and Deco, 2010; Deco et al., 2013). The decisions are probabilistic, as they reflect the noise in the competitive nonlinear decision-making process that is introduced by the random spiking times of neurons for a given mean rate that reflect a Poisson process (Rolls and Deco, 2010; Rolls et al., 2010b). The costs of each reward need to be subtracted from the value of each reward to produce a net reward value for each available reward, before the decision is taken (Rolls, 2008b, 2014a; Rolls and Grabenhorst, 2008; Grabenhorst and Rolls, 2011). The reasoning or rational system with its long-term goals (introducing evidence such as “scientific studies have shown that fish oils rich in omega-3 may reduce the probability of Alzheimer’s disease”) then competes with the rewards such as the pleasant flavor of food (which are gene-specified (Rolls, 2005a, 2014a), though subject to conditioned effects (Booth, 1985; Rolls, 2014a)) in a further decision process which may itself be subject to noise (Rolls, 2008b, 2014a; Rolls and Deco, 2010). This can be described as a choice between the selfish phenotype (standing for phenotype) and the selfish gene (Rolls, 2011b, 2012a, 2014a). In this context, the findings described here that the cognitive system can have a top-down influence on the reward system, including the flavor reward system, are important advances in our understanding of how these decisions are reached.

6.5 Synthesis

These investigations show that a principle of brain function is that representations of the reward/hedonic value and pleasantness of sensory, including food-related, stimuli are formed separately from representations of what the stimuli are. The pleasantness/reward value is represented in areas such as the orbitofrontal cortex and pregenual cingulate cortex, and it is here that hunger/satiety signals modulate the representations of food to make them implement reward. The satiety signals that help in this modulation may reach the orbitofrontal cortex from the hypothalamus (Rolls, 2016a), and, in turn, the orbitofrontal cortex projects to the hypothalamus where neurons are found that respond to the sight, smell, and taste of food, if hunger is present (Rolls and Grabenhorst, 2008; Rolls, 2014a). We have seen previously some of the principles that help to make the food pleasant, including particular combinations of taste, olfactory, texture, visual, and cognitive inputs.

A hypothesis is developed elsewhere that obesity is associated in part with overstimulation of these reward systems by very rewarding combinations of taste, odor, texture, visual, and cognitive inputs that together produce the flavor of food (Rolls, 2005a, 2011a, 2012b, 2014a, 2015a, 2016a).

Acknowledgments

This research was supported by the Medical Research Council. The participation of many colleagues in the studies cited is sincerely acknowledged. They include Ivan de Araujo, Gordon Baylis, Leslie Baylis, Hugo Critchley, Paul Gabbott, Fabian Grabenhorst, Mikiko Kadohisa, Morten Kringelbach, Christian Margot, Francis McGlone, John O'Doherty, Barbara Rolls, Juliet Rolls, Thomas Scott, Zenon Sienkiewicz, Simon Thorpe, Maria Ines Velazco, Justus Verhagen, and Simon Yaxley.

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