

Neural Integration of Taste, Smell, Oral Texture, and Visual Modalities

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46.1 INTRODUCTION

46.1.1 Introduction and Overview

The aims of this chapter are to describe how taste, olfactory, visual, oral sensory, and other sensory inputs are combined in the brain, how a representation of reward value is produced, and how cognition and selective attention influence this processing.

Complementary neuronal recordings in primates, and functional neuroimaging in humans, show that the primary taste cortex in the anterior insula provides separate and combined representations of the taste, temperature, and texture (including fat texture) of food in the mouth independently of hunger and thus of reward value and pleasantness. One synapse on, in the orbitofrontal cortex, these sensory inputs are for some neurons combined by associative learning with olfactory and visual inputs, and these neurons encode food reward in that they only respond to food when hungry, and in that activations correlate with subjective pleasantness. Cognitive factors, including word-level descriptions, and selective attention to affective value, modulate the representation of the reward value of taste and olfactory stimuli in the orbitofrontal cortex and a region to which it projects, the anterior cingulate cortex, a tertiary taste cortical area. The food reward representations formed in this way play an important role in the control of appetite, food intake. Individual differences in these reward representations may contribute to obesity.

46.1.2 Food Reward and Appetite

A reason why it is important to understand the brain systems for food reward is that the reward value of food (i.e., whether we will work for a food), measures our appetite for a food, and whether we will eat a food. Thus normally we want food (will work for it, and will eat it) when we like it. “We want because we like”: the goal value, the food reward value, makes us want it. For example, neurons in the orbitofrontal cortex and lateral hypothalamus described below respond to the reward value of a food when it is, for example, shown, and these neuronal responses predict whether that food will be eaten (Rolls, 1981, 2005a, 2014; Rolls et al., 1986, 1989). Similarly, in a whole series of studies on sensory-specific satiety in humans based on these discoveries, the reported pleasantness in humans of a food is closely correlated with whether it will then be eaten, and even with how much is eaten (Rolls et al., 1981b, 1983b, 1984). The situation when it has been suggested that wanting is not a result of liking (Berridge et al., 2009), is when behavior becomes a habit. A habit is a stimulus-response type of behavior that is no longer under control of the goal, but is under the control of an overlearned conditioned stimulus (Rolls, 2005a, 2014). The concept here is that food reward normally drives appetite and eating, and it is therefore important to understand the brain mechanisms involved in food reward, in order to understand the control of appetite and food intake.

46.1.3 Investigations in Primates including Humans

The focus of the approach taken here is on complementary neurophysiological investigations in macaques and functional neuroimaging in humans. There are a number of reasons for this focus.

First, there are major anatomical differences in the neural processing of taste in rodents and primates (Rolls and Scott, 2003; Scott and Small, 2009; Small and Scott, 2009). In rodents (and also in primates) taste information is conveyed by cranial nerves 7, 9, and 10 to the rostral part of the nucleus of the solitary tract (NTS) (Norgren and Leonard, 1971; Norgren and Leonard, 1973; Norgren, 1990) (see Figure 46.1). However, although in primates the NTS projects to the taste thalamus and thus to the cortex (Figure 46.1), in rodents the majority of NTS taste neurons responding to stimulation of the taste receptors of the anterior tongue project to the ipsilateral medial aspect of the pontine parabrachial nucleus (PbN), the rodent “pontine taste area” (Cho et al., 2002; Small and Scott, 2009). The remainder project to adjacent regions of the medulla. From the PbN the rodent gustatory pathway bifurcates into two pathways: (1) a ventral “affective” projection to the hypothalamus, central gray, ventral striatum, bed nucleus of the stria terminalis and amygdala; and (2) a dorsal “sensory” pathway, which first synapses in the thalamus and then the agranular and dysgranular insular gustatory cortex (Norgren and Leonard, 1971; Norgren, 1974, 1976, 1990). These regions, in turn, project back to the PbN in rodents to sculpt the gustatory code and guide complex feeding behaviors (Norgren, 1976; Di Lorenzo, 1990; Norgren, 1990; Li et al., 2002; Lundy and Norgren, 2004).

In contrast, in primates (including humans) there is strong evidence to indicate that the PbN gustatory relay is absent (Small and Scott, 2009): (1) Second-order gustatory projections that arise from rostral NTS appear not to synapse in the PbN and instead join the central tegmental tract and project directly to the taste thalamus in primates (Beckstead et al., 1980; Pritchard et al., 1989); (2) Despite several attempts, no one has successfully isolated taste responses in the monkey PbN (Norgren, 1990; Small and Scott, 2009) (the latter cite Ralph Norgren, personal communication and Tom Pritchard, personal communication); (3) In monkeys the projection arising from the PbN does not terminate in the region of ventral basal thalamus that contains gustatory responsive neurons (Pritchard et al., 1989).

Second, a functional difference of rodent taste processing from that of primates is that physical and chemical signals of satiety have been shown to reduce the taste responsiveness of neurons in the nucleus in the solitary tract, and the pontine taste area, of the rat, with decreases in the order of 30%, as follows (Rolls and Scott, 2003; Scott and Small, 2009). Gastric distension by air or with 0.3 M

NaCl suppress responses in the NTS, with the greatest effect on glucose (Gleen and Erickson, 1976). Intravenous infusions of 0.5 g/kg glucose (Giza and Scott, 1983), 0.5 U/kg insulin (Giza and Scott, 1987b), and 40 µg/kg glucagon (Giza et al., 1993), all cause reductions in taste responsiveness to glucose in the NTS. The intraduodenal infusion of lipids causes a decline in taste responsiveness in the PbN, with the bulk of the suppression borne by glucose cells (Hajnal et al., 1999). The loss of signal that would otherwise be evoked by hedonically positive tastes implies that the reward value that sustains feeding is reduced at the brainstem level, making termination of a meal more likely (Giza et al., 1992). Further, if taste activity in NTS is affected by the rat’s nutritional state, then intensity judgements in rats should change with satiety. There is evidence that they do. Rats with conditioned aversions to 1.0 M glucose show decreasing acceptance of glucose solutions as their concentrations approach 1.0 M. This acceptance gradient can be compared between euglycemic rats and those made hyperglycemic through intravenous injections (Scott and Giza, 1987). Hyperglycemic rats showed greater acceptance at all concentrations from 0.6 to 2.0 M glucose, indicating that they perceived these stimuli to be less intense than did conditioned rats with no glucose load (Giza and Scott, 1987a).

In contrast, in primates, the reward value of taste is represented in the orbitofrontal cortex in that the responses of orbitofrontal taste neurons are modulated by hunger in just the same way as is the reward value or palatability of a taste. In particular, it has been shown that orbitofrontal cortex taste neurons stop responding to the taste of a food with which a monkey is fed to satiety, and that this parallels the decline in the acceptability of the food (Rolls et al., 1989; Critchley and Rolls, 1996c). In contrast, the representation of taste in the primary taste cortex of primates (Scott et al., 1986; Yaxley et al., 1990) is not modulated by hunger (Rolls et al., 1988; Yaxley et al., 1988). Thus in the primary taste cortex of primates (and at earlier stages of taste processing including the nucleus of the solitary tract (Yaxley et al., 1985)), the reward value of taste is not represented, and instead the identity of the taste is represented (Rolls, 2014).

The importance of cortical processing of taste in primates, first for identity and intensity in the primary taste cortex, and then for reward value in the orbitofrontal cortex, is that both types of representation need to be interfaced to visual and other processing that requires cortical computation. For example, it may have adaptive value to be able to represent exactly what taste is present, and to link it by learning to the sight and location of the source of the taste, even when hunger and reward is not being produced, so that the source of that taste can be found in future, when it may have reward value. In line with cortical processing to dominate the processing of taste in primates, there is no

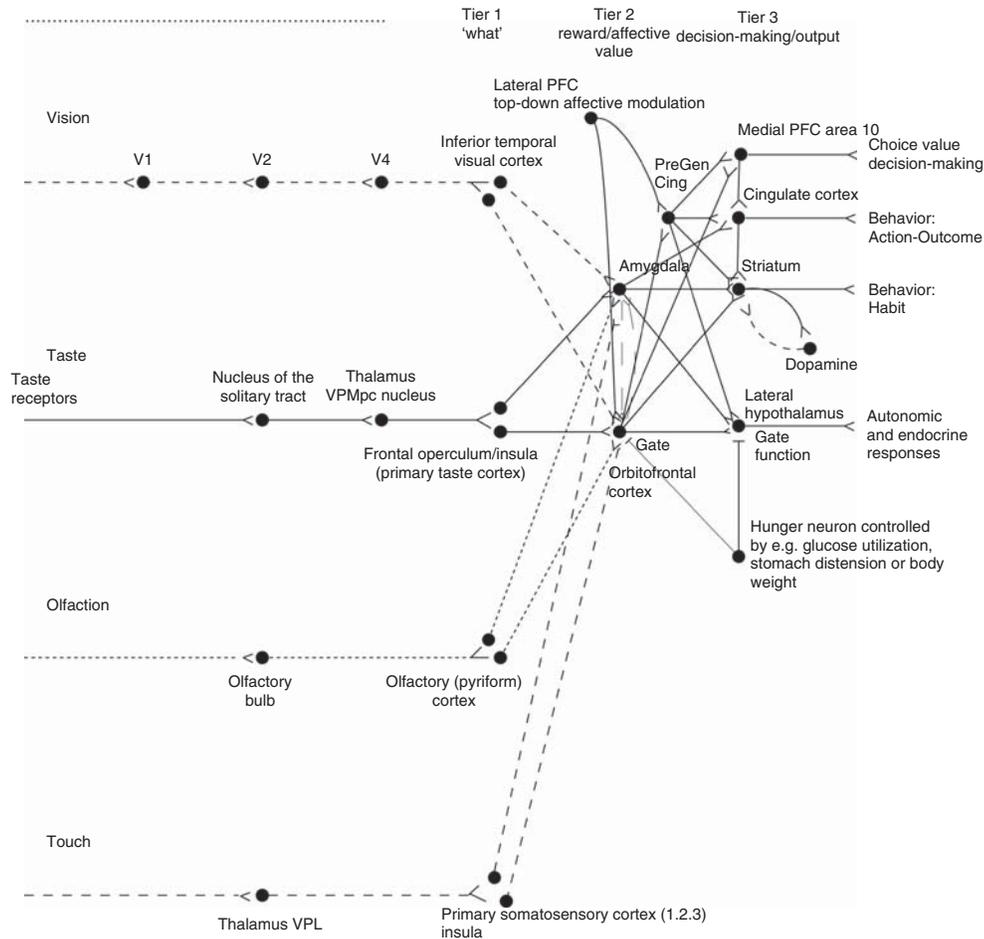


Figure 46.1 Schematic diagram showing some of the gustatory, olfactory, visual and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex, and the secondary olfactory cortex, are within the orbitofrontal cortex. 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, 2008a; Rolls and Deco, 2010; Rolls, 2014). 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.

modulation of taste responsiveness at or before the primary taste cortex, and the pathways for taste are directly from the nucleus of the solitary tract in the brainstem to the taste thalamus and then to the taste cortex (Figure 46.1) (Rolls, 2014).

The implication is that taste, and the closely related olfactory and visual processing that contribute to food reward, are much more difficult to understand in rodents than in primates, partly because there is less segregation of “what” (identity and intensity) from hedonic processing in rodents, and partly because of the more serial hierarchical processing in primates (Figure 46.1).

Third, the prefrontal cortex (and for that matter the temporal lobe visual cortical areas) have also undergone great development in primates, and one part of the prefrontal cortex, the orbitofrontal cortex, is very little developed in rodents, yet is one of the major brain areas involved in taste and olfactory processing, and emotion and motivation, in primates including humans. Indeed, it has been argued (on the basis of cytoarchitecture, connections, and functions) that the granular prefrontal cortex is a primate innovation, and the implication of the argument is that any areas that might be termed orbitofrontal cortex in rats (Schoenbaum et al., 2009) are homologous only

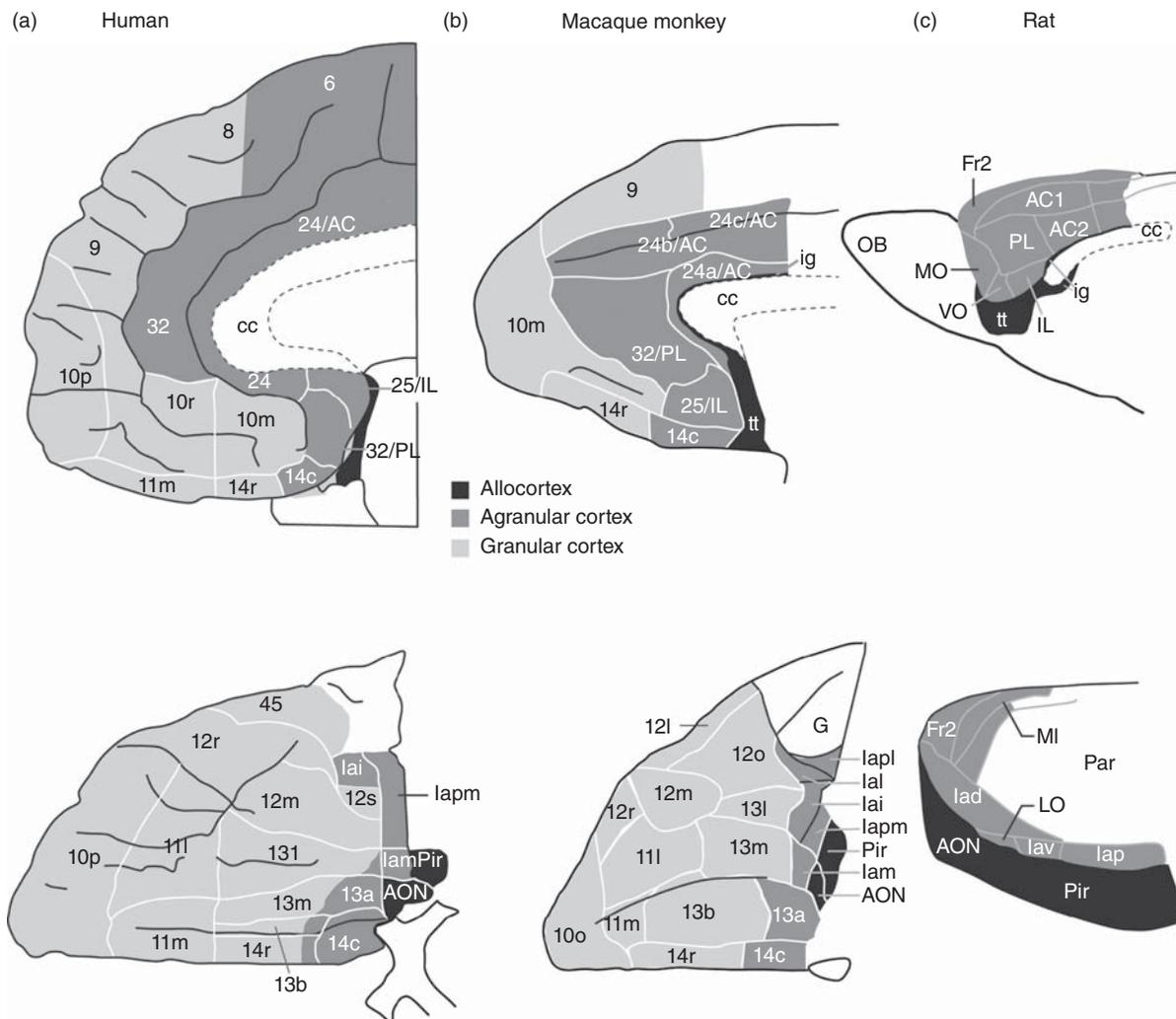


Figure 46.2 Comparison of the orbitofrontal (below) and medial prefrontal (above) cortical areas in humans, macaque monkeys, and rats. (a) Medial (top) and orbital (bottom) areas of the human frontal cortex (Öngür et al. (2003)). (b) Medial (top) and orbital (bottom) areas of the macaque frontal cortex (Carmichael and Price (1994)). (c) Medial (top) and lateral (bottom) areas of rat frontal cortex (Palomero-Gallagher and Zilles (2004)). Rostral is to the left in all drawings. Top row: dorsal is up in all drawings. Bottom row: in (a) and (b), lateral is up; in (c), dorsal is up. Not to scale. Abbreviations: AC, anterior cingulate cortex; AON, anterior olfactory ‘nucleus’; cc, corpus callosum; Fr2 second frontal area; Ia, agranular insular cortex; ig, induseum griseum; IL, infralimbic cortex; LO, lateral orbital cortex; MO, medial orbital cortex; OB, olfactory bulb; Pr, piriform (olfactory) cortex; PL, prelimbic cortex; tt, tenia tecta; VO, ventral orbital cortex; Subdivisions of areas are labelled caudal (c); inferior (i), lateral (l), medial (m); orbital (o), posterior or polar (p), rostral (r), or by arbitrary designation (a, b). Reproduced with permission from Passingham and Wise (2012). *The Neurobiology of the Prefrontal Cortex*. Oxford University Press: Oxford.

to the agranular parts of the primate orbitofrontal cortex (shaded mid gray in Figure 46.2), that is to areas 13a, 14c, and the agranular insular areas labelled Ia in Figure 46.2 (Passingham and Wise, 2012). It follows from that argument that for most areas of the orbitofrontal and medial prefrontal cortex in humans and macaques (those shaded light gray in Figure 46.2), special consideration must be given to research in macaques and humans. As shown in Figure 46.2, there may be no cortical area in rodents that is homologous to most of the primate including human

orbitofrontal cortex (Preuss, 1995; Wise, 2008; Passingham and Wise, 2012).

46.2 TASTE PROCESSING IN THE PRIMATE BRAIN

46.2.1 Pathways

A diagram of the taste and related olfactory, somatosensory, and visual pathways in primates is shown in Figure 46.1.

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 that will be addressed.

46.2.2 The Insular Primary Taste Cortex

Rolls and colleagues have shown 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; Scott and Plata-Salaman, 1999; 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 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).

Parts of the insula can be activated by visual stimuli related to disgust, such as a face expression of disgust (Phillips et al., 2004), and this could reflect the fact that parts of the insula are part of the visceral efferent system involved in autonomic responses (Critchley, 2005) (and may even overlap partly with the taste-responsive areas (Simmons et al., 2013)).

46.2.3 The Secondary Taste Cortex in the Orbitofrontal Cortex

A secondary cortical taste area in primates was discovered by Rolls and colleagues (Thorpe et al., 1983; Rolls et al., 1989; Rolls et al., 1990) in the orbitofrontal cortex, extending several mm in front of the primary taste cortex. This is defined as a secondary cortical taste area, for it receives direct inputs from the primary taste cortex, as shown by a combined neurophysiological and anatomical pathway tracing investigation (Baylis et al., 1995). Different neurons in this region respond not only to each of the four classical prototypical tastes sweet, salt, bitter, and sour (Rolls et al., 1990, 2003a; Rolls, 1997; Verhagen et al., 2003; Kadohisa et al., 2005b), 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, 2009a), to the flavor of protein. In addition, other neurons respond to water (Rolls et al., 1990), and others to somatosensory stimuli including astringency as exemplified by tannic acid (Critchley and Rolls, 1996a), and capsaicin (Rolls et al., 2003a; Kadohisa et al., 2004).

Some of the coding principles are illustrated by the two neurons shown in Figure 46.3. The two neurons each

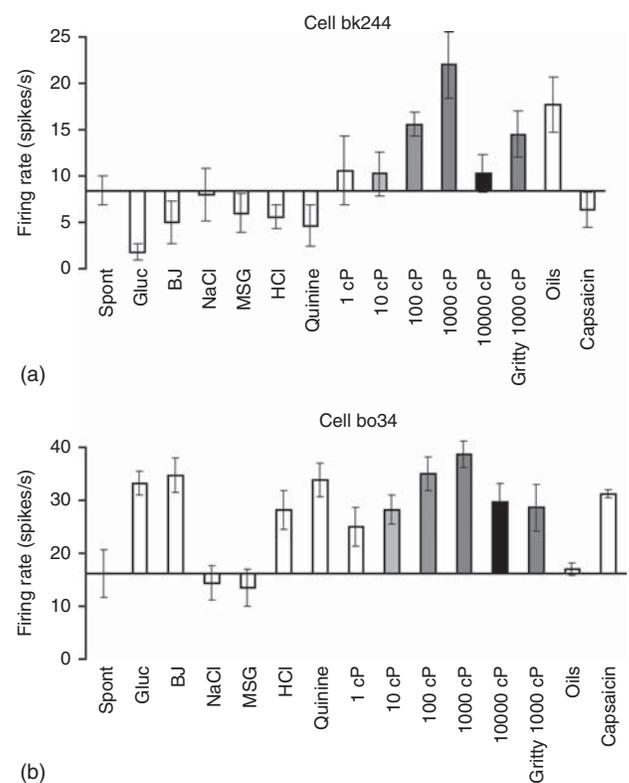


Figure 46.3 Taste and oral somatosensory inputs to orbitofrontal cortex neurons. (a) Firing rates (mean \pm sem) of viscosity-sensitive neuron bk244 which did not have taste responses, in that it did not respond differentially to the different taste stimuli. The firing rates are shown to the viscosity series (carboxymethylcellulose 1 – 10,000 centiPoise, to the gritty stimulus (1,000 cP carboxymethylcellulose with Fillite microspheres), to the taste stimuli 1 M glucose (Gluc), 0.1 M NaCl, 0.1 M MSG, 0.01 M HCl and 0.001 M QuinineHCl, and to fruit juice (BJ). Spont = spontaneous firing rate. (b) Firing rates (mean \pm sem) of viscosity-sensitive neuron bo34 which had no response to the oils (mineral oil, vegetable oil, safflower oil and coconut oil, which have viscosities that are all close to 50 cP). The neuron did not respond to the gritty stimulus in a way that was unexpected given the viscosity of the stimulus, was taste tuned, and did respond to capsaicin. (After Rolls, Verhagen and Kadohisa, 2003).

have their independent tuning to the set of stimuli. It is this independent tuning or coding that underlies the ability of the brain to represent the exact nature of a stimulus or event, and this applies to taste in addition to other sensory modalities (Rolls et al., 2010d; Rolls and Treves, 2011). The encoding of information in the brain can of course not be captured by functional neuroimaging, because that takes an average of the activity of tens of thousands of neurons, whereas each neuron conveys information that is to a considerable extent independent of the information encoded by other neurons (Rolls et al., 2009; Rolls et al., 2010d; Rolls and Treves, 2011).

Taste responses are found in a large mediolateral extent of the orbitofrontal cortex (Critchley and Rolls, 1996a; Pritchard et al., 2005; Rolls, 2008b; Rolls and Grabenhorst, 2008). Indeed, taste neurons have been shown to extend throughout area 13 in a region that is approximately 7–12 mm from the midline (Rolls and Baylis, 1994; Critchley and Rolls, 1996a; Rolls et al., 1996b; Rolls, 2008b), the exact area in which Pritchard et al. (2005) also found a population of taste neurons (see Figure 46.3 with cytoarchitectonic areas indicated after Carmichael and Price, 1994; Öngür and Price, 2000; Petrides and Pandya, 2001; Öngür et al., 2003). We showed in our previous studies that these taste neurons extend from approximately 4 mm anterior to the clinoid process of the sphenoid bone to 12 mm anterior. Pritchard et al. (2005) focused their investigation on a region 5–9 mm anterior to the sphenoid.) Although Pritchard et al. (2005) commented that in their study there was a good proportion of taste neurons in this area, we, in comparing the proportions of taste neurons in different parts of the orbitofrontal cortex extending out laterally through area 12, find similar proportions of taste neurons throughout this mediolateral extent (from 7 mm to 20 mm lateral) (Rolls et al., 1989, 1990, 1996b, 2003a; Rolls and Baylis, 1994; Critchley and Rolls, 1996a; Verhagen et al., 2003; Kadohisa et al., 2004, 2005b). Moreover, even in area 13m, in the region 7–12 mm lateral where Pritchard et al., (2005) found taste neurons, we know that many other properties are represented, including oral texture as exemplified by astringency and fat texture (Critchley and Rolls, 1996a; Rolls et al., 1999); and olfactory properties (Critchley and Rolls, 1996b, c; Rolls et al., 1996) which can become associated by learning with taste stimuli (Rolls et al., 1996c). Thus area 13m contains taste, oral texture, and olfactory representations. Some of these cells are multimodal in these modalities (Rolls and Baylis, 1994; Critchley and Rolls, 1996a; Rolls et al., 1996c), and the majority of these neurons have their responses to taste and/or olfactory stimuli modulated by hunger (Critchley and Rolls, 1996c). In a more recent investigation, Rolls,

Verhagen, Gabbott, and Kadohisa measured the responses of 1753 neurons in rhesus macaques, and found taste neurons in the mid and medial orbitofrontal cortex region extending to within approximately 7 mm of the midline in area 13m, but very few in the more medial areas 10, 14, and 25, as illustrated in Figure 46.4 (Rolls, 2008b).

46.2.4 The Anterior Cingulate Cortex: A Tertiary Taste Cortical Area

The orbitofrontal cortex, including the extensive areas where taste neurons noted above are found, projects to the pregenual cingulate cortex area 32 (Carmichael and Price, 1996). Human imaging studies have shown that reward-related stimuli, such as the taste of sucrose and the texture of oral fat, activate the pregenual cingulate cortex (de Araujo and Rolls, 2004; Rolls, 2005a; Rolls and Grabenhorst, 2008; Rolls, 2009b; Grabenhorst and Rolls, 2011). However, little is known at the neuronal level of whether the responses of single neurons in the pregenual cingulate cortex are tuned to taste stimuli and respond differentially to different taste stimuli. Rolls, Gabbott, Verhagen, and Kadohisa therefore recorded from single neurons in the macaque pregenual cingulate cortex, in order to obtain evidence on these issues (Rolls et al., 2008b).

The responses of a pregenual cingulate cortex neuron with taste responses are shown in Figure 46.5. The neuron increased its firing rate primarily to glucose, fruit juice and cream, with some response to the oily texture of silicone oil, to monosodium glutamate, and to quinine. When the macaque was fed to satiety with glucose, the neuron showed a sensory-specific decrease in its response to the taste of glucose (Rolls, 2008b).

The data for the pregenual cingulate cortex and adjacent areas were obtained by Rolls, Gabbott, Verhagen, and Kadohisa (Rolls, 2008b) in two rhesus macaques in recordings that extended from approximately 10 mm anterior with respect to the sphenoid reference to approximately 13 mm anterior, with the recording sites of the neurons shown in Figure 46.6 (Rolls, 2008b). As shown, most of these neurons were in area 32, with one taste neuron in area 10. Although a small proportion of the neurons were classified as responding to taste, this proportion is not out of line with the proportion of taste neurons recorded with identical techniques in the same laboratory in the primary taste cortex in the macaque anterior insula and adjoining frontal opercular cortex. Of the 12 responsive neurons in the medial wall cortex, 11 had best responses to sweet stimuli (glucose and/or fruit juice, as illustrated in Figure 46.5), and one had best responses to quinine and NaCl. The spontaneous firing rates of neurons in the

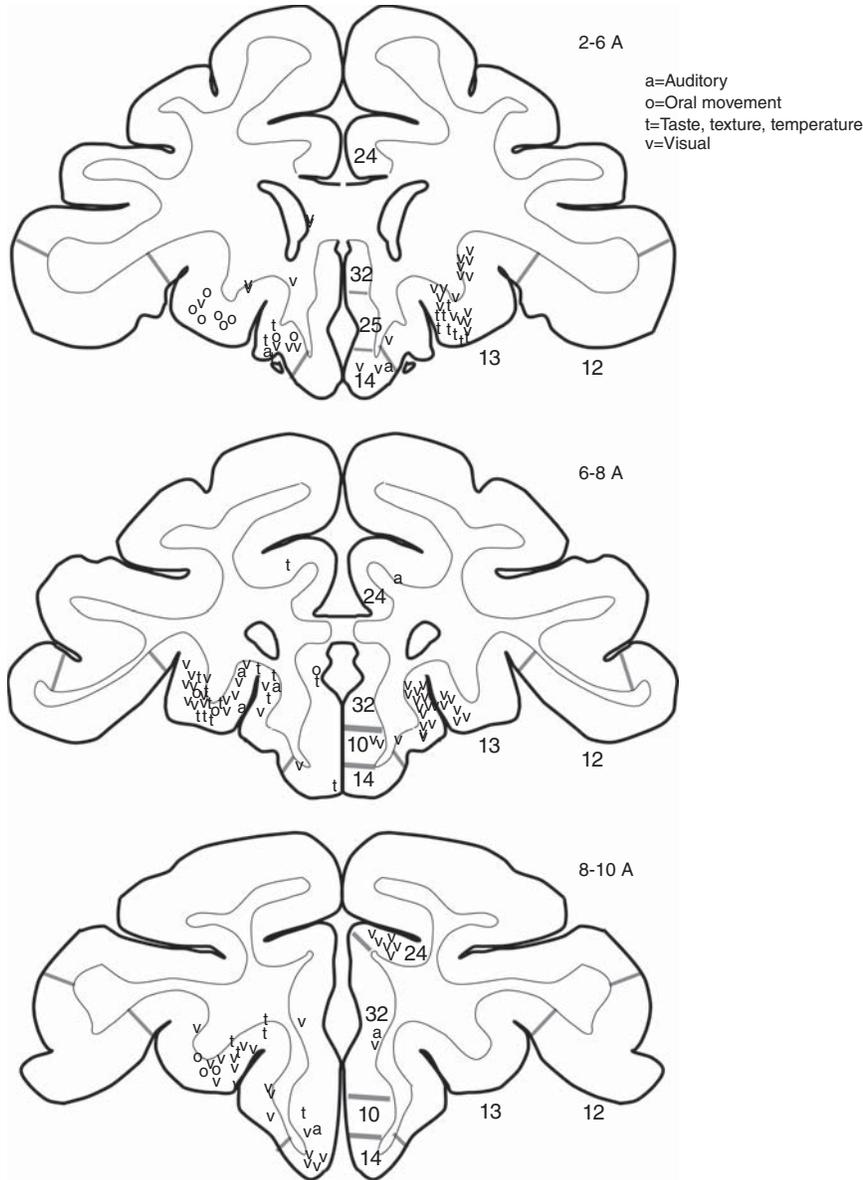


Figure 46.4 The reconstructed positions of the neurons in the medial orbitofrontal cortex with different types of response, with the cytoarchitectonic boundaries determined after Carmichael and Price (1994). The neurons within different planes at distances in mm anterior (a) to the sphenoid reference point are shown on the coronal sections. (Data from Rolls, Verhagen, Gabbott and Kadohisa, 2008; see Rolls, 2008b).

pregenual cingulate cortex were typically in the range 0–5 spikes/s, which increased significantly to 20–30 spikes/s when the neurons were responding selectively to specific taste stimuli.

The presence of a neuronal representation of a primary (unlearned) reinforcer, taste, in the pregenual cingulate cortex is of importance for understanding the functions more generally of the anterior cingulate cortex in complex reward-related learning (Amiez et al., 2006), and in action selection (Grabenhorst and Rolls, 2011; Rushworth et al., 2011), for this evidence shows that primary rewards are represented in at least one part of the anterior cingulate cortex – the pregenual cingulate cortex area 32 (Rolls, 2008b; Rolls, 2009b). Neurons responding to fruit juice used as a

reinforcer in saccade countermanding have been found in the dorsal part of the anterior cingulate sulcus area 24c (Ito et al., 2003), and the pregenual cingulate cortex provides a source of inputs to area 24 (Carmichael and Price, 1996). Indeed, establishing that the pregenual cingulate cortex contains a representation of a primary reinforcer, in this case a taste, is of importance more generally in relation to understanding the functions of the pregenual cingulate cortex in emotion (Rolls and Grabenhorst, 2008; Rolls, 2009b; Grabenhorst and Rolls, 2011), in that for example some disorders of emotion in humans produced by anterior cingulate damage include deficits in responding to what are probably other primary reinforcers, face and voice expression (Hornak et al., 2003; Rolls, 2005a, 2014).

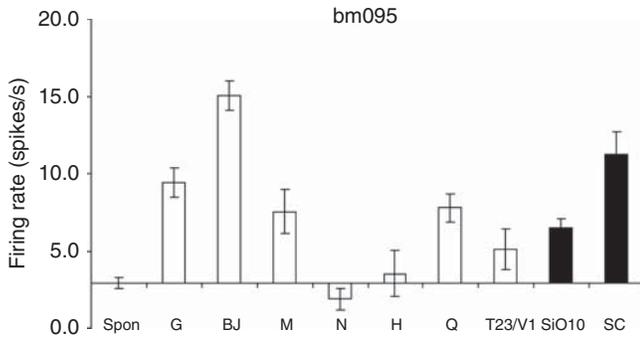


Figure 46.5 Responses of a pregenua cingulate cortex neuron (bm095) with differential responses to tastes and oral fat texture stimuli. The mean (\pm sem) firing rate responses to each stimulus calculated in a 5 s period over several trials are shown. The spontaneous (Spon) firing rate of 3 spikes/s is shown by the horizontal line, with the responses indicated relative to this line. The taste stimuli were 1 M glucose (G), blackcurrant fruit juice (BJ), 0.1 M NaCl (N), 0.1 M MSG (M), 0.01 M HCl (H) and 0.001 M QuinineHCl (Q); water (T23/V1); single cream (SC); and silicone oil with a viscosity of 10 cP (SiO10). The neuron had significantly different responses to the different stimuli as shown by a one-way ANOVA ($F[9,46]=17.7$, $p<10^{-10}$). (Data from Rolls, Gabbott, Verhagen, and Kadohisa; see Rolls, 2008b).

46.2.5 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, 2005a, 2007, 2014). 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 by neurons 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, 1996c) (Figure 46.7).

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 Hetherington, 1989; Rolls and Rolls, 1977, 1982, 1997; Rolls et al., 1981a, b, 1982, 1983a, b, 1984; Hetherington, 2007), are produced in the primate orbitofrontal cortex, but not at earlier stages of processing

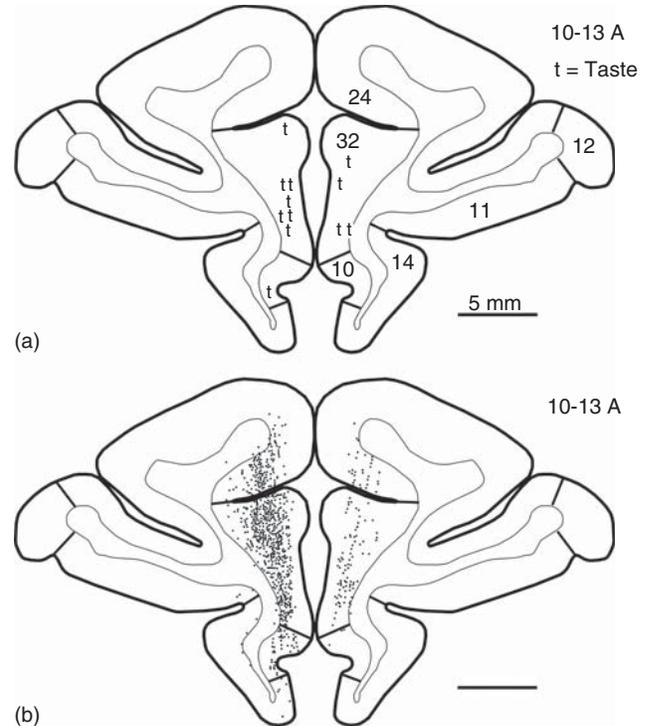


Figure 46.6 The reconstructed positions of the anterior cingulate neurons with taste (t) responses, together with the cytoarchitectonic boundaries determined by Carmichael and Price (1994). Most (11/12) of the taste neurons were in the pregenual cingulate cortex (area 32), as shown. The neurons are shown on a coronal section at 12 mm anterior (a) to the sphenoid reference point. The recording sites were reconstructed using X-radiographs made on every track and subsequent histology using the methods described by Rolls et al., (2003a). (b). The locations of all the 749 neurons recorded in the anterior cingulate region in this study are indicated to show the regions sampled. (Data from Rolls, Gabbott, Verhagen, and Kadohisa; see Rolls, 2008b).

including the insular-opercular primary taste cortex (Rolls et al., 1988; Yaxley et al., 1988) and the nucleus of the solitary tract (Yaxley et al., 1985), where the responses reflect factors such as the intensity of the taste, which is little affected by satiety (Rolls et al., 1983c; Rolls and Grabenhorst, 2008). In addition to providing an implementation of sensory-specific satiety (probably by adaptation 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 Figure 46.1) (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, 2014).

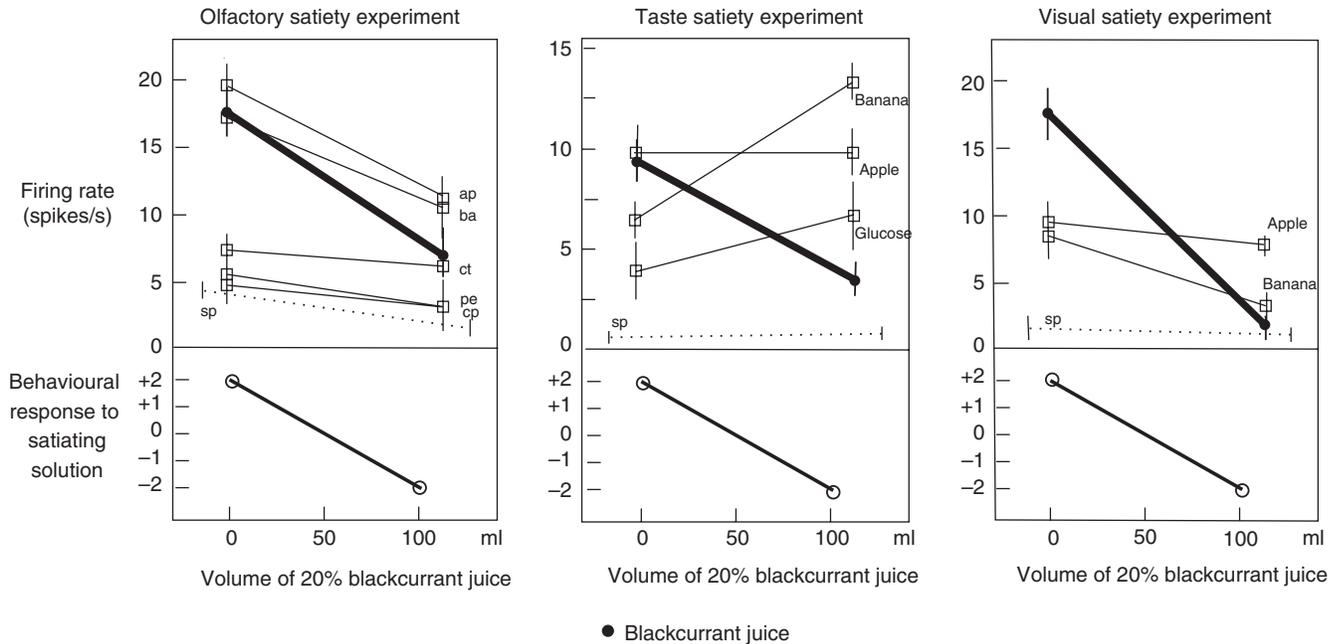


Figure 46.7 Orbitofrontal cortex neuron with visual, olfactory and taste responses, showing the responses before and after feeding to satiety with blackcurrant juice. The solid circles show the responses to blackcurrant juice. The olfactory stimuli included apple (ap), banana (ba), citral (ct), phenylethanol (pe), and caprylic acid (cp). The spontaneous firing rate of the neuron is shown (sp). The taste panel is for the flavor of food in the mouth. Below the neuronal response data for each experiment, the behavioral measure of the acceptance or rejection of the solution on a scale from +2 to -2 is shown. The values shown are the mean firing rate and its s.e. (After Critchley and Rolls, 1996c).

46.2.6 The Representation of Flavor: Convergence of Olfactory, Taste, and Visual Inputs in the Orbitofrontal Cortex and Related Areas Including the Amygdala and Hippocampus

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 (see Figure 46.1) (Rolls and Baylis, 1994; Critchley and Rolls, 1996b; Rolls et al., 1996). 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 et al., 1996c). 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, 1996c). Olfactory-to-taste associative learning by these orbitofrontal cortex neurons may take 30–40 trials to reverse in an olfactory-to-taste discrimination task, and this may help to make a flavor stable (Rolls et al., 1996c). Olfactory neurons are found in a considerable anterior-posterior extent of the primate orbitofrontal cortex, extending far into areas 11 and 14 (Rolls and Baylis, 1994; Critchley and Rolls, 1996b, c; Rolls et al., 1996c, 1996), and are not restricted to a

posterior region as some have thought (Gottfried and Zald, 2005).

Visual-to-taste association learning and its reversal by neurons in the orbitofrontal cortex can take place in as little as one trial (Thorpe et al., 1983; Rolls et al., 1996c; Deco and Rolls, 2005a). This has clear adaptive value in enabling particular foods with a good or bad taste to be learned and recognized quickly, important in foraging and in food selection for ingestion. The visual inputs reach the orbitofrontal cortex from the inferior temporal visual cortex, where neurons respond to objects independently of their reward value (e.g., taste), as shown by satiety and reversal learning tests (Rolls et al., 1977; Rolls, 2008a, 2012c). The visual-to-taste associations are thus learned in the orbitofrontal cortex (Rolls, 2014). These visual–taste neurons thus respond to expected value (and in humans different orbitofrontal cortex neurons signal expected monetary value (Rolls et al., 2008a)).

Different neurons in the orbitofrontal cortex respond when a visually signalled expected taste reward is not obtained, that is, to negative reward prediction error (Thorpe et al., 1983; Rolls and Grabenhorst, 2008). There is evidence that dopamine neurons in the ventral tegmentum respond to positive reward prediction error (Schultz, 2007), and as such, they do not respond to taste reward (Rolls,

2014). The inputs to the dopamine neurons may originate from structures such as the orbitofrontal cortex, where expected value, reward outcome (e.g., taste), and negative reward prediction error are represented (Rolls, 2014).

The amygdala also contains neurons that respond to taste and oral texture (Sanghera et al., 1979; Scott et al., 1993; Kadohisa et al., 2005b, 2005a). Some neurons in the primate amygdala respond to visual stimuli associated with reinforcers such as taste, but do not reflect the reinforcing properties very specifically, do not rapidly learn and reverse visual-to-taste associations, and are much less affected by reward devaluation by feeding to satiety than are orbitofrontal cortex neurons (Sanghera et al., 1979; Yan and Scott, 1996; Kadohisa et al., 2005a, b; Wilson and Rolls, 2005; Rolls, 2014). The primate orbitofrontal cortex appears to be much more closely involved in flexible (rapidly learned, and affected by reward devaluation) representations than is the primate amygdala (Rolls, 2014).

The primate hippocampus contains neurons that respond to the sight of locations in spatial scenes where taste rewards are found, but not to the sight of objects associated with taste reward (Rolls and Xiang, 2005), and this is part of the evidence for understanding the functions of the hippocampus in episodic memory (Rolls, 2008a, 2010b).

46.2.7 The Texture of Food, Including Fat Texture

46.2.7.1 Viscosity, Particulate Quality, and Astringency. 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 centiPoise), and 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., 2003a) (see Figure 46.3). Somatosensory signals that transmit information about capsaicin (chilli) and astringency are also reflected in neuronal activity in these cortical areas (Critchley and Rolls, 1996a; Kadohisa et al., 2004, 2005b).

46.2.7.2 Oral Fat Texture. Texture in the mouth is an important indicator of whether *fat* is present in a food, which is important not only as a high value energy source, but also as a potential source of essential fatty acids. In the orbitofrontal cortex, Rolls, Critchley et al., (1999) have found a population of neurons that responds when fat is in the mouth. The fat-related responses of these neurons are produced at least in part by the texture of the food rather than by chemical receptors sensitive to certain chemicals, in that such neurons typically respond not only to foods such as cream and milk containing fat, but also to paraffin oil (which is a pure hydrocarbon) and to silicone oil [$\text{Si}(\text{CH}_3)_2\text{O}_n$]. Moreover, the texture channels through which these fat-sensitive neurons are activated are separate from viscosity sensitive channels, in that the responses of these neurons cannot be predicted by the viscosity of the oral stimuli, as illustrated in Figure 46.8 (Verhagen et al., 2003; Rolls, 2011a). The responses of these oral fat-encoding neurons are not related to free fatty acids such as linoleic or lauric acid (Verhagen et al., 2003; Kadohisa et al., 2005b; Rolls, 2011a), and the fat responsiveness of these primate orbitofrontal cortex

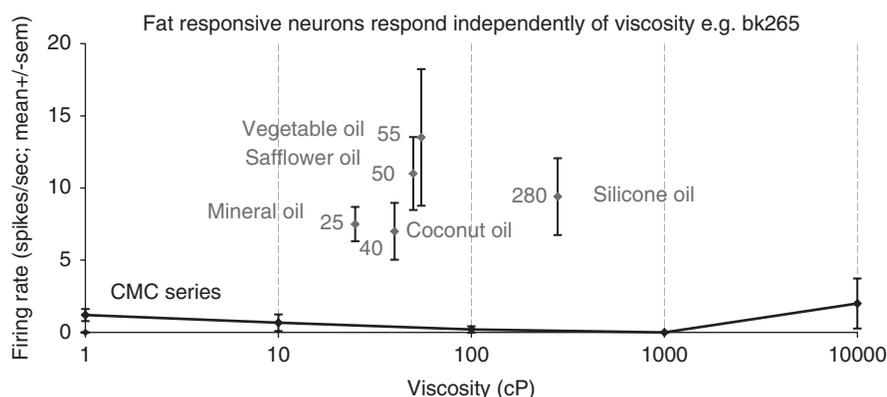


Figure 46.8 A neuron in the primate orbitofrontal cortex responding to the texture of fat in the mouth independently of viscosity. The cell (bk265) increased its firing rate to a range of fats and oils (the viscosity of which is shown in centipoise). The information that reaches this type of neuron is 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. (After Verhagen, Rolls and Kadohisa, 2003).

neurons is therefore not related to fatty acid sensing (Gilbertson et al., 1997; Gilbertson, 1998), but instead to oral texture sensing (Rolls, 2011a; Rolls, 2012b). This has I believe very important implications for the development of foods with the mouth feel of fat, but low energy content (Rolls, 2011a, 2012b). A few neurons do have responses to linoleic and/or lauric acid, but these neurons do not respond to fat in the mouth, and may reflect the bad taste that rancid fats may have (Verhagen et al., 2003; Rolls, 2011a). Some of the fat texture-related orbitofrontal cortex neurons do though have convergent inputs from the chemical senses, in that in addition to taste inputs, some of these neurons respond to the odour associated with a fat, such as the odour of cream (Rolls et al., 1999). Feeding to satiety with fat (e.g., cream) decreases the responses of these neurons to zero on the food eaten to satiety, but if the neuron receives a taste input from for example glucose taste, that is not decreased by feeding to satiety with cream (Rolls et al., 1999). Thus there is a representation of the macronutrient fat in this brain area, and the activation produced by fat is reduced by eating fat to satiety.

Fat texture, oral viscosity, and temperature, for some neurons in combination with taste, are represented in the macaque primary taste cortex in the rostral insula and adjoining frontal operculum (Verhagen et al., 2004), which provides a route for this information to reach the orbitofrontal cortex.

These oral sensory properties of food, and also the sight and smell of food, are also represented in the primate amygdala (Rolls, 2000; Rolls and Scott, 2003; Kadohisa et al., 2005a, 2005b). Interestingly, the responses of these amygdala neurons do not correlate well with the preferences of the macaques for the oral stimuli (Kadohisa et al., 2005b), and feeding to satiety does not produce the large reduction in the responses of amygdala neurons to food (Rolls, 2000; Rolls and Scott, 2003) that is typical of orbitofrontal cortex neurons.

46.2.7.3 Oral Temperature. In addition, we have shown that some neurons in the insular cortex, orbitofrontal cortex, and amygdala 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, 2005a, b; Verhagen et al., 2004). Somatosensory signals that transmit information about capsaicin (chili) are also reflected in neuronal activity in these brain areas (Kadohisa et al., 2004, 2005b). Activations in the human orbitofrontal and insular taste cortex also reflect oral temperature (Guest et al., 2007).

46.3 IMAGING STUDIES IN HUMANS

46.3.1 Taste

In humans it has been shown in neuroimaging studies using functional Magnetic Resonance Imaging (fMRI) that taste activates an 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), 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, 2008b). 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) (Figure 46.9).

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, respond to aversive (e.g., quinine) and to sucrose taste stimuli.

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, 2008b)) 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, 2009a). (The supra-linear additivity refers to a greater activation to the combined

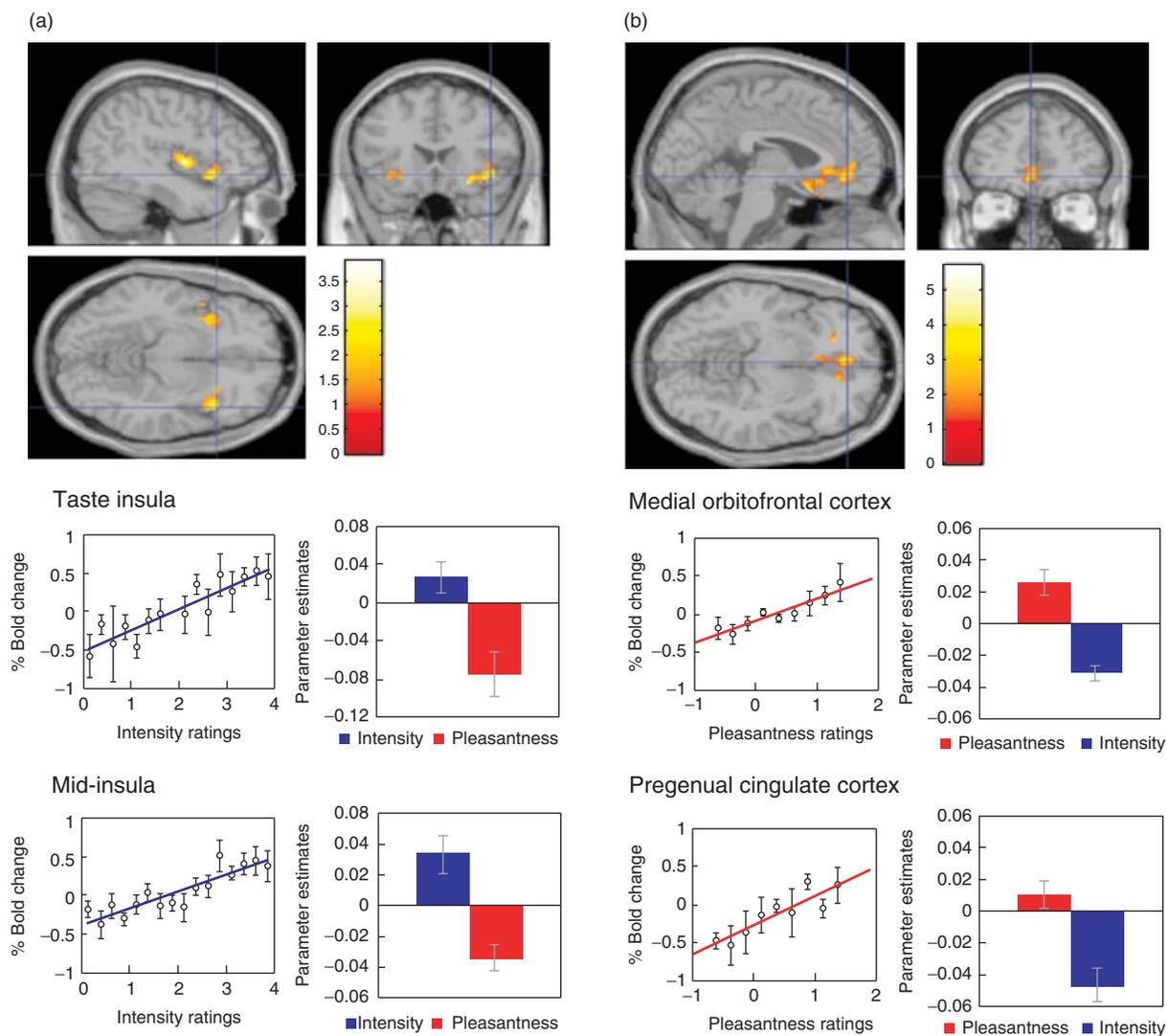


Figure 46.9 Effect of paying attention to the pleasantness vs the intensity of a taste stimulus. (a) Top: A significant difference related to the taste period was found in the taste insula at $[42\ 18\ -14]$ $z=2.42$ $p<0.05$ (indicated by the cursor) and in the mid insula at $[40\ -2\ 4]$ $z=3.03$ $p<0.025$. 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 $[-6\ 14\ -20]$ $z=3.81$, $p<0.003$ (towards 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 $t=7.27$, $df=11$, $p<10^{-4}$. 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 above. 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. (After Grabenhorst and Rolls, 2008). (See plate section for color version.)

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, 2009a.) 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.

46.3.2 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., 2003b). This region appears to represent the pleasantness of odor, as shown by a sensory-specific satiety experiment with banana vs vanilla odor (O'Doherty et al., 2000), and this has been confirmed by Gottfried et al. (personal communication, see Gottfried, 2013), 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., 2003b), 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 (medially) or unpleasantness (laterally) of odor (Rolls et al., 2003b, 2008c, 2009; Grabenhorst et al., 2007; Rolls and Grabenhorst, 2008; Rolls et al., 2008c; Rolls et al., 2009; Grabenhorst and Rolls, 2011).

46.3.3 Olfactory-Taste Convergence to Represent Flavor, and the Influence of Satiety on Flavor Representations

Taste and olfactory conjunction analyses, and the measurement of supraditive 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 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, at Y=15) 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 (see Figure 46.2) (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 odour 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, 2009a).

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, are represented in the orbitofrontal cortex.

46.3.4 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 mid-insular 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 mid-orbitofrontal and anterior cingulate cortex, where activations are correlated with the subjective pleasantness of oral fat texture (Rolls, 2009a; Grabenhorst

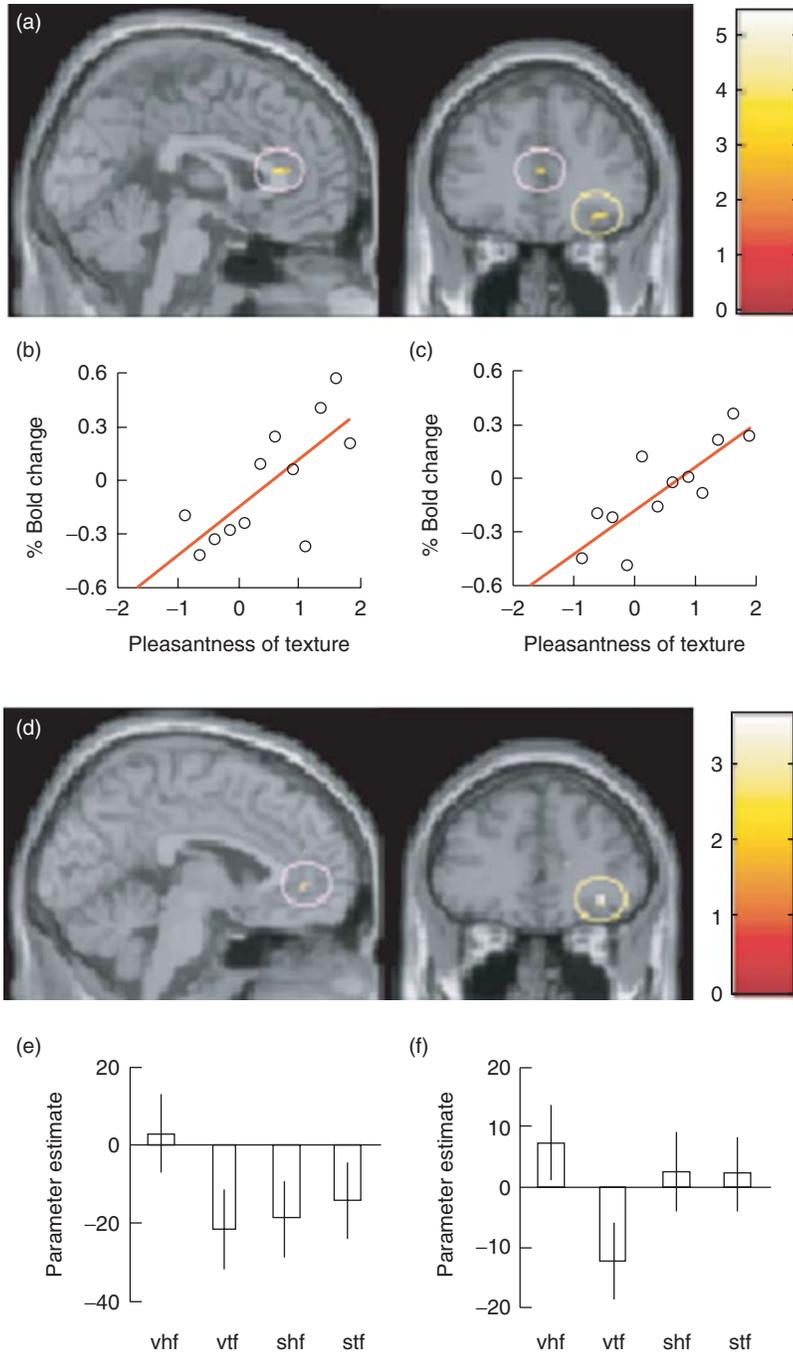


Figure 46.10 Brain regions in which the activations were correlated with the subjective pleasantness of fat texture: Mid-orbitofrontal cortex ([32 34–14] $z=3.38$ $p=0.013$) (a, yellow circle, c showing the relation between the % change in the BOLD signal and the rating of the pleasantness of the texture) and anterior cingulate cortex ([2 30 14] $z=3.22$, $p=0.016$) (a, pink circles, and b). (After Grabenhorst et al., 2010). (See plate section for color version.)

et al., 2010; Rolls, 2010a) (Figure 46.10). This provides a foundation for studies of whether activations in the fat reward system are heightened in people who tend to become obese (Rolls, 2012a). 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, 2013).

46.3.5 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, Martin and Barsalou (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).

46.3.6 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 odour, 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 odour,” 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, see Figure 46.1), 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) (see Figure 46.11).

46.3.7 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 (see Figure 46.9), whereas selective attention to intensity modulates activations in areas such as the primary taste cortex (Grabenhorst and Rolls, 2008; Rolls et al., 2008c). 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 source of 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, 2005b; Rolls, 2008a). 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 mid-insula by intensity-related processing (Grabenhorst and Rolls, 2010; Luo et al., 2013), the process has been described as a biased activation model of attention (Grabenhorst and Rolls, 2010).

This differential biasing by prefrontal cortex attentional mechanisms (Grabenhorst and Rolls, 2010; Ge et al., 2012) of brain regions engaged in processing a sensory stimulus depending on whether the cognitive demand is for affect-related vs 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; Rolls et al., 2008c; Grabenhorst and Rolls, 2011; Rolls, 2012a). 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.

46.3.8 Beyond Reward Value 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; Padoa-Schioppa, 2011; Padoa-Schioppa and Cai, 2011; Rolls, 2014). 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 this has implications for whether a reward of a particular value will be selected (Rolls, 2008a; Rolls and Grabenhorst, 2008; Rolls and Deco, 2010; Grabenhorst and Rolls, 2011; Rolls, 2011b; Deco et al., 2013; Rolls, 2014).

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, a; Rolls et al., 2010c) (tier 3 in Figure 46.1).

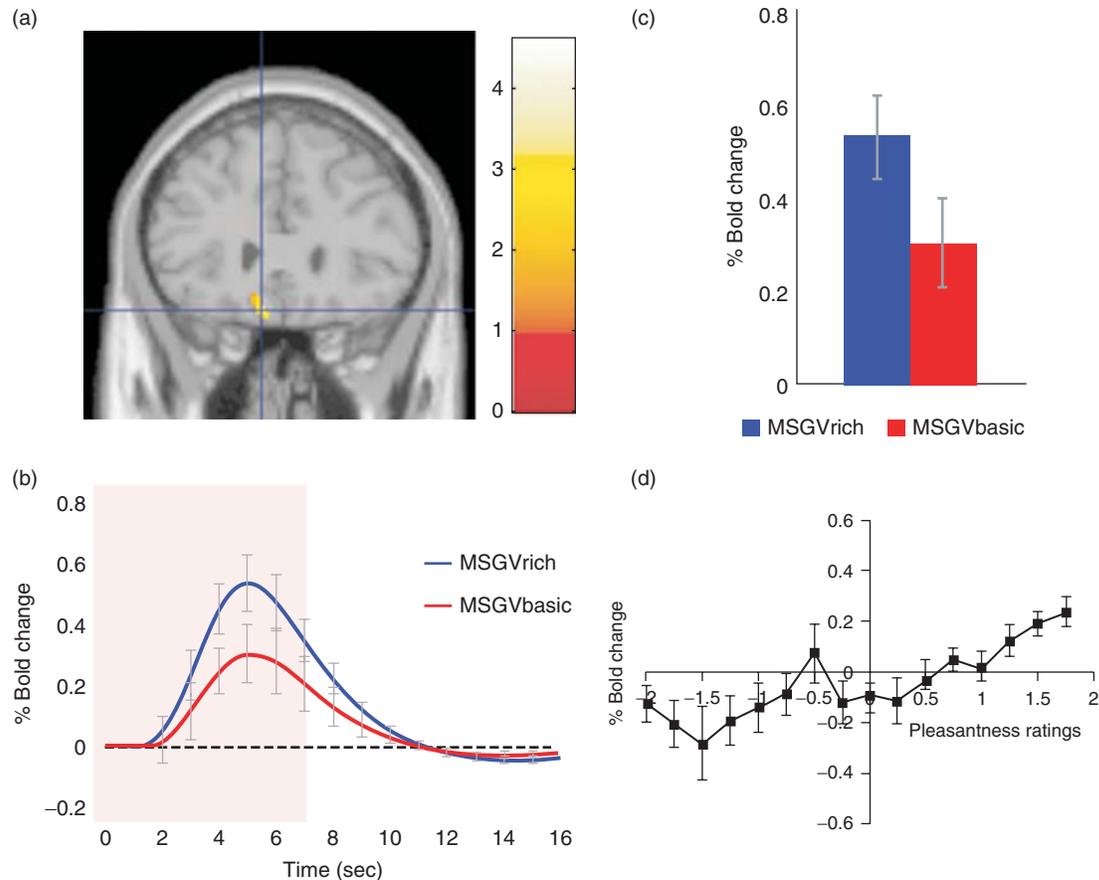


Figure 46.11 Cognitive modulation of flavor reward processing in the brain. (a). The medial orbitofrontal cortex was more strongly activated when a flavor stimulus was labelled “rich and delicious flavor” (MSGVrich) than when it was labelled “boiled vegetable water” (MSGVbasic) ([-8 28–20]). (The flavor 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, $r=0.86$, $p<0.001$). (After Grabenhorst, Rolls and Bilderbeck, 2008 (Grabenhorst et al., 2008a)). (See plate section for color version.)

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, 2008a, 2010c). The word attractor refers to the fact that inexact inputs are attracted to one of the states of high firing that are specified by the synaptic connections between the different groups of neurons. The result in this non-linear system is that one attractor wins, and this implements a mechanism for decision making with one winner

(Rolls, 2008a; Wang, 2008; Rolls and Deco, 2010; Deco et al., 2013).) The decisions are probabilistic as they reflect the noise in the competitive non-linear 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., 2010a). 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, 2008a; 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, 2014), though subject to conditioned effects

(Booth, 1985; Rolls, 2005a)) in a further decision process which may itself be subject to noise (Rolls, 2005a, 2008a; Rolls and Deco, 2010). This can be described as a choice between the selfish phenotype (standing for phenotype) and the selfish gene (Rolls, 2011b, 2012d, 2014). In this context, the findings described in this paper that the cognitive system can have a top-down influence on the reward system are important advances in our understanding of how these decisions are reached.

46.4 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, 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, 2014). We have seen above 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 (Rolls, 2005a, 2011c, 2012a, 2014).

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