

THE HUMAN NERVOUS SYSTEM

THIRD EDITION

Edited by

JÜRGEN K. MAI

*Institute for Anatomy, Heinrich-Heine University Düsseldorf,
Düsseldorf, Germany*

GEORGE PAXINOS

Neuroscience Research Australia, Sydney, Australia



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The Emotional Systems

Edmund T Rolls

Oxford Centre for Computational Neuroscience, Oxford, UK

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s0010

EMOTIONS DEFINED, AND AN ANATOMICAL FRAMEWORK

p0010

A very useful working definition of emotions is that they are states elicited by instrumental reinforcers (Weiskrantz, 1968; Gray, 1975; Rolls, 2005). Instrumental reinforcers are rewards and punishers that are obtained as a result of an action instrumental in gaining the reward or avoiding the punisher. For the purposes of this chapter a positive reinforcer or reward can be defined as a stimulus that the animal will work to obtain, and a punisher as a stimulus that will reduce the probability

of an action on which it is contingent or that an animal will work to avoid or escape (Rolls, 2005).

This approach is supported by the following. First, the definition is conceptually acceptable, in that it is difficult to think of exceptions to the rule that instrumental reinforcers are associated with emotional states, and to the rule that emotional states are produced by instrumental reinforcers (Rolls, 2005). Second, the definition is powerful in an evolutionary and explanatory sense, in that the functions of emotion can be conceived of as related to processes involved in obtaining goals, and in states that are produced when goals are received.

Indeed, my evolutionary Darwinian account states that the adaptive value of rewards and punishers is that they are gene-specified goals for action, and that it is much more effective for genes to specify rewards and punishers, the goals for action, than to attempt to specify actions. Examples of such primary (i.e. unlearned or gene-specified) reinforcers include the taste of food, pain, stimuli that promote reproductive success, and face expression (Rolls, 2005). Other stimuli become secondary reinforcers by learned associations with primary reinforcers in parts of the brain involved in emotion such as the orbitofrontal cortex and amygdala. An example is the sight of food. Third, this approach provides a principled way to analyse the brain mechanisms of emotion, by examination of where in the brain stimuli are represented by their reinforcement value. Forth, this approach maps well onto the anatomy of the brain. As will be shown in this chapter, the structures in Figure 38.1 up to and including the column with the inferior temporal visual cortex at the top are involved in producing representations of objects that are independent of their reward value: i.e. representations of “what” objects are present. Structures in the column of Figure 38.1 that includes the orbitofrontal cortex and amygdala represent the reward or punisher, that is the affective, value of stimuli. Fifth, there are good reasons for the separation of “what” and emotional processing in the brain: the reward value of an object can change very rapidly, for example when a food is eaten to satiety it is no longer rewarding, and when associative learning leads for example to a person becoming associated with a large reward. But we do not wish at the same time to no longer recognize the food or person, as we might for example learn where a food is located even if we are not hungry at the time so that the food is not rewarding when it is seen. Sixth, the approach leads to a clear understanding of emotion as a state elicited by a reinforcing goal, and motivation as a state (such as hunger) when we are trying to obtain a goal (in this case food). Seventh, and again an important anatomical point, after reward value is represented on a continuous scale in the orbitofrontal cortex, pregenual cingulate cortex, and amygdala, we may need to make a choice on a particular trial about whether to perform actions for one reward or for a different one, and the choice between rewards involves a separate stage of and type of processing in the hierarchy in areas such as the medial prefrontal cortex area 10 (Figure 38.1). Eighth, and again an important anatomical point, there are different routes from affective representations to different types of output, including action, habit, and autonomic, as shown in Figure 38.1. Ninth, humans’ ratings of the subjective emotional value of stimuli are directly related to activations in the emotional tier structures of Figure 38.1 (the orbitofrontal and pregenual cingulate

cortices, and the amygdala). Tenth, damage to the emotional tier structures of Figure 38.1 alter humans’ behavior to emotional stimuli, and decrease their ratings of their own subjective emotional states, as will be described later (Rolls, 2005).

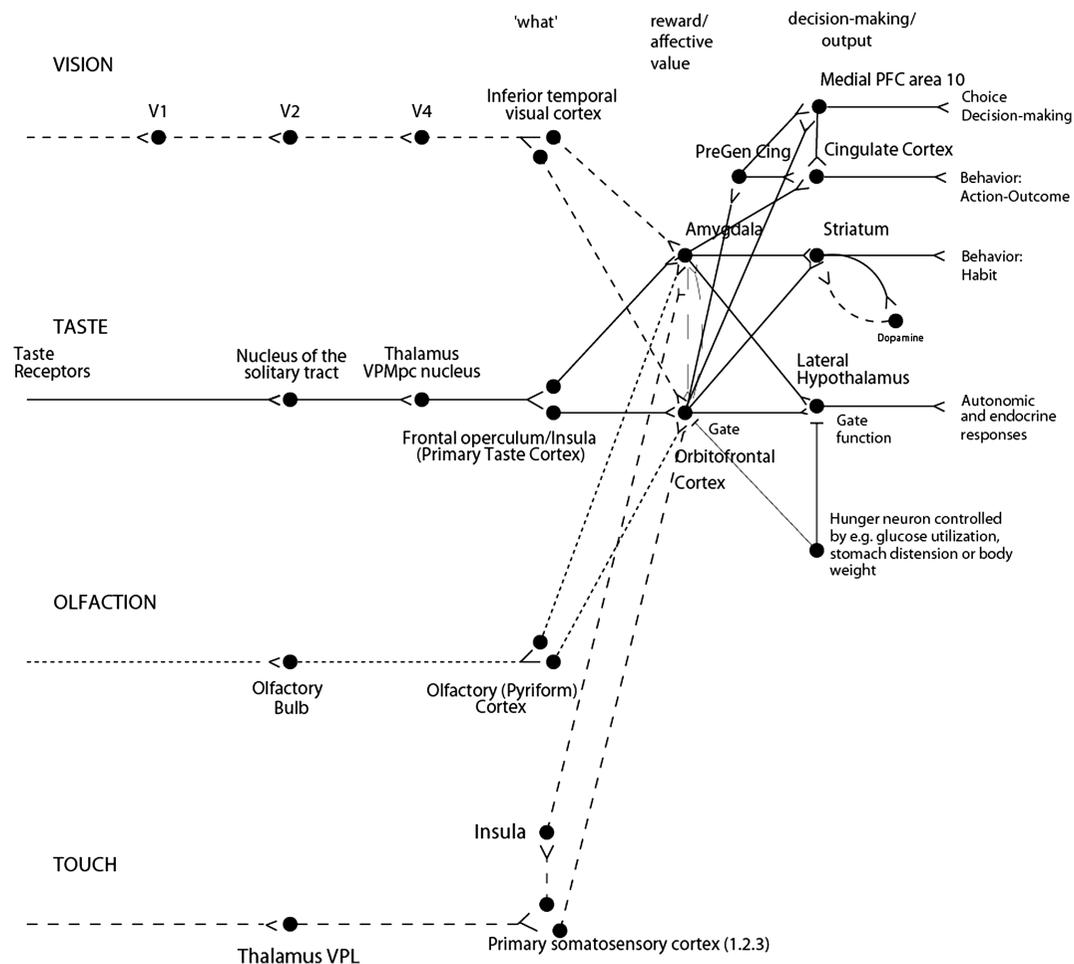
With this introduction and anatomical framework, we now consider in more detail some of the brain structures involved in emotion, and at the same time contrast them with the structures that in terms of connectivity and function precede them and succeed them in the anatomical and functional hierarchy moving from left to right in Figure 38.1.

The focus is on humans and macaques, because there are many topological, cytoarchitectural, and probably connectational similarities between macaques and humans with respect to the orbitofrontal cortex (Figure 38.1, and Carmichael and Price, 1994; Petrides and Pandya, 1995; Öngür and Price, 2000; Kringelbach and Rolls, 2004; Price, 2006, 2007). This brain region may be less well developed in rodents. Moreover, the orbitofrontal cortex receives visual information in primates from the inferior temporal visual cortex, which is a highly developed area for primate vision enabling invariant visual object recognition (Rolls, 2000a, 2007a, 2008c; Rolls and Deco, 2002; Rolls and Stringer, 2006), and which provides visual inputs used in the primate orbitofrontal cortex for one-trial object-reward association reversal learning, and for representing face expression and identity. Further, even the taste system of primates and rodents may be different, with obligatory processing from the nucleus of the solitary tract via the thalamus to the cortex in primates, but a subcortical pathway in rodents via a pontine taste area to the amygdala, and differences in where satiety influences taste responsive neurons in primates and rodents (Norgren, 1984; Rolls and Scott, 2003; Rolls, 2005). To understand the functions of the orbitofrontal cortex and connected areas in humans, the majority of the studies described here were therefore performed with macaques or with humans.

THE ORBITOFRONTAL CORTEX

Connections

Maps of the architectonic areas in the orbitofrontal cortex and medial prefrontal cortex are shown in Figure 38.2 for humans (above) and monkeys (below) (Carmichael and Price, 1994; Öngür et al., 2003). The anatomical connections of the orbitofrontal cortex (Carmichael and Price, 1994, 1995; Barbas, 1995; Petrides and Pandya, 1995; Pandya and Yeterian, 1996; Öngür and Price, 2000; Price, 2006, 2007) include the following (see also Chapters 26 and 34). Conceptually, the



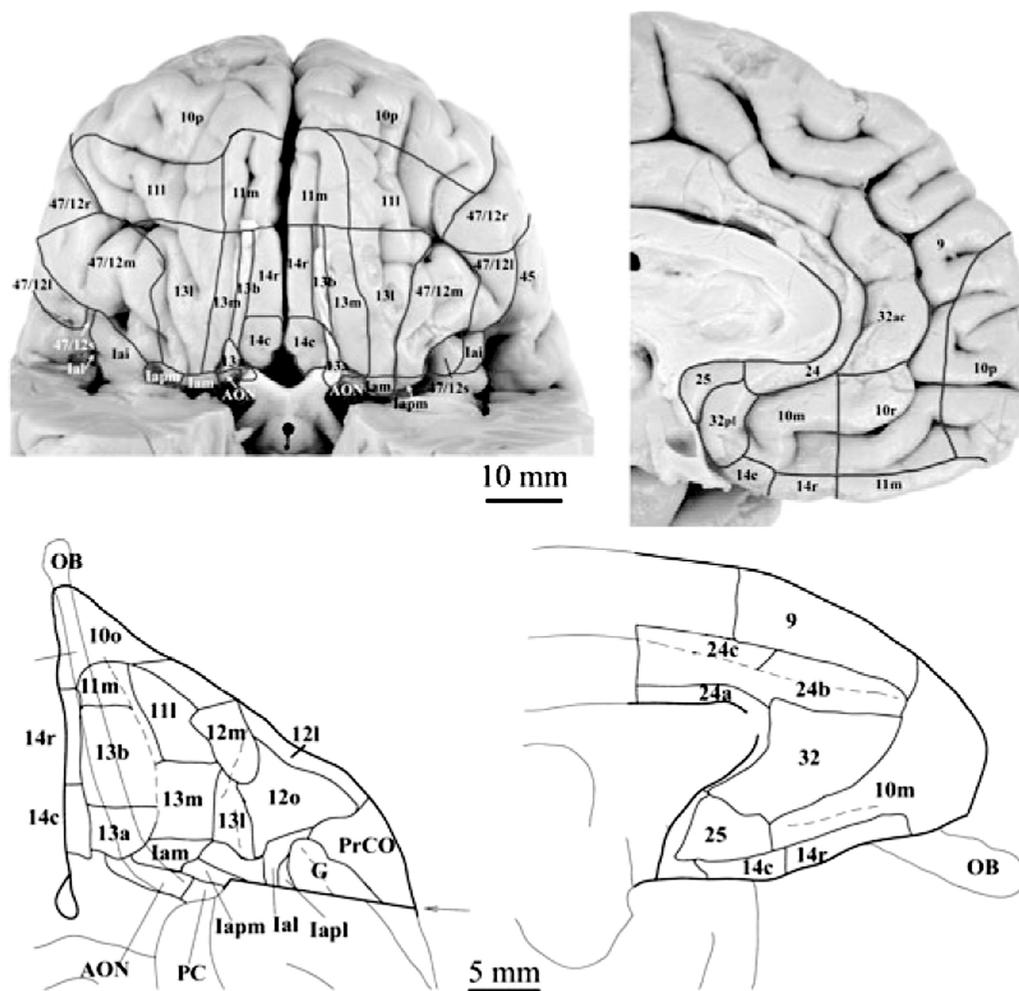
f0010 **FIGURE 38.1** Schematic diagram showing some of the gustatory, olfactory, visual and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex, and the secondary olfactory cortex, are within the orbitofrontal cortex. V1, primary visual cortex; V4, visual cortical area V4; PreGen Cing, pregenual cingulate cortex; PFC, prefrontal 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, 2005). 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. The reward or affective value is represented in the next tier of brain regions, the orbitofrontal cortex and amygdala. The next tier of brain regions is involved in choices based on reward value, and in different types of output to behavior.

orbitofrontal cortex can be thought of as receiving from the ends of each modality-specific "what" cortical pathway as shown in Figure 38.1, and this functional connectivity is emphasized in the following.

p0035 Rolls et al. (1990) discovered a taste area with taste-responsive neurons in the lateral part of the macaque orbitofrontal cortex, and showed anatomically with horseradish peroxidase pathway tracing from a neurophysiologically identified area that this was the secondary taste cortex in that it receives a major projection from the primary taste cortex (Baylis et al., 1995). This region projects on to more anterior areas of the orbitofrontal cortex (Baylis et al., 1995). Taste neurons are also found more medially (Rolls and Baylis, 1994; Critchley and Rolls, 1996c; Rolls et al., 1996a; Pritchard et al., 2005; Rolls, 2008b).

In the mid orbitofrontal cortex, there is an area with p0040 olfactory neurons (Rolls and Baylis, 1994) and anatomically, there are direct connections from the primary olfactory cortex, pyriform cortex, to area 13a of the posterior orbitofrontal cortex, which in turn has onward projections to a middle part of the orbitofrontal cortex (area 13) (Price et al., 1991; Morecraft et al., 1992; Barbas, 1993; Carmichael et al., 1994; Price, 2007) (Figure 38.1).

Thorpe et al. (1983) found neurons with visual p0045 responses in the orbitofrontal cortex, and anatomically, visual inputs reach the orbitofrontal cortex directly from the inferior temporal cortex (where object and face identity are represented (Rolls, 2007a, 2008c)), the cortex in the superior temporal sulcus (where face expression and gesture are represented (Hasselmo et al., 1989)), and the temporal pole cortex (see Barbas,



f0015 **FIGURE 38.2** Maps of architectonic areas in the orbitofrontal cortex and medial prefrontal cortex of humans (above) and monkeys (below). AON, anterior olfactory nucleus; G, primary gustatory cortex; lai, lal, lam, lapm, subdivisions of the agranular insular cortex; OB, olfactory bulb; PC, pyriform cortex; PrCO, precentral opercular area. After Öngür et al. (2003) and Carmichael and Price (1994), reprinted from the *Journal of Comparative Neurology* with permission of John Wiley & Sons, Inc.

1988, 1993, 1995; Barbas and Pandya, 1989; Seltzer and Pandya, 1989; Morecraft et al., 1992; Carmichael and Price, 1995). There are corresponding auditory inputs (Barbas, 1988, 1993; Romanski et al., 1999; Romanski and Goldman-Rakic, 2001; Rolls et al., 2006).

p0050 Some neurons in the orbitofrontal cortex respond to oral somatosensory stimuli such as the texture of food (Rolls et al., 1999, 2003c), and anatomically there are inputs to the orbitofrontal cortex from somatosensory cortical areas 1, 2 and SII in the frontal and pericentral operculum, and from the insula (Barbas, 1988; Carmichael and Price, 1995). The caudal orbitofrontal cortex receives inputs from the amygdala (Price et al., 1991). The orbitofrontal cortex also receives inputs via the mediodorsal nucleus of the thalamus, pars magnocellularis, which itself receives afferents from temporal lobe structures such as the prepyriform (olfactory) cortex, amygdala, and inferior temporal cortex (see Öngür

and Price, 2000). These connections provide some routes via which the responses of orbitofrontal cortex neurons can be produced. Within the orbitofrontal cortex, there are many intrinsic connections (Öngür and Price, 2000), and these may be part of what enables many orbitofrontal cortex neurons to have multimodal responses, as described below and elsewhere (Rolls, 2005, 2008b,c; Rolls and Grabenhorst, 2008).

The orbitofrontal cortex projects back to temporal p0055 lobe areas such as the amygdala (Barbas, 2007). The orbitofrontal cortex also has projections to the cingulate cortex (Carmichael and Price, 1996; Price, 2006), the ventral striatum (Ferry et al., 2000) and head of the caudate nucleus (Kemp and Powell, 1970; Haber et al., 2006), medial prefrontal cortex area 10 (Price, 2007), entorhinal and perirhinal cortex (Barbas, 2007; Insausti, et al., 1987) providing a route for reward information to reach the hippocampus (Rolls and Xiang, 2005; Rolls,

2010a), preoptic region and lateral hypothalamus (where neurons respond to the sight and taste of food, and show sensory-specific satiety (Burton et al., 1976; Rolls et al., 1976)), and the ventral tegmental area (Nauta, 1964; Johnson et al., 1968), and these connections provide some routes via which the orbitofrontal cortex can influence behavior (Rolls, 2005) and memory (Rolls and Xiang, 2005; Rolls, 2008c, 2010a).

s0025 **Effects of Damage to the Orbitofrontal Cortex on Emotion and Emotion-Related Learning**

p0060 Part of the evidence on the functions of the orbitofrontal cortex in emotion comes from the effect of lesions of the orbitofrontal cortex. Macaques with lesions of the orbitofrontal cortex are impaired at tasks that involve learning about which stimuli are rewarding and which are not, and are especially impaired at altering behavior when reinforcement contingencies change. The monkeys may respond when responses are inappropriate, e.g., no longer rewarded, or may respond to a non-rewarded stimulus. For example, monkeys with orbitofrontal damage are impaired on Go/NoGo task performance in that they Go on the NoGo trials (Iversen and Mishkin, 1970); in an object reversal task in that they respond to the object which was formerly rewarded with food; and in extinction in that they continue to respond to an object which is no longer rewarded (Butter, 1969; Jones and Mishkin, 1972; Izquierdo and Murray, 2004; Izquierdo et al., 2004; Murray and Izquierdo, 2007). There is some evidence for dissociation of function within the orbitofrontal cortex, in that lesions to the inferior convexity produce the Go/NoGo and object reversal deficits, whereas damage to the caudal orbitofrontal cortex produces the extinction deficit (Rosenkilde, 1979). Sensory-specific satiety (a method of reward devaluation in which a food is fed to satiety), which is implemented neuronally in the orbitofrontal cortex (Rolls et al., 1989), is impaired by orbitofrontal cortex lesions (Murray and Izquierdo, 2007). Rapid associations between visual stimuli and reinforcers such as taste, and the rapid reversal of these associations, is an important function of the orbitofrontal cortex (Thorpe et al., 1983; Rolls et al., 1996b; Rolls, 2005). Consistent with this, in humans rapid reversal is impaired by orbitofrontal cortex damage (Rolls et al., 1994; Fellows and Farah, 2003; Hornak et al., 2004; Rolls and Grabenhorst, 2008).

p0065 It is suggested that difficulty in processing reinforcers, and especially in rapid visual discrimination reversal learning, underlies some of the impairments in emotion produced by damage to the orbitofrontal cortex (Rolls, 2005). In humans, euphoria, irresponsibility, lack of affect, and impulsiveness can follow frontal lobe damage (Damasio, 1994; Rolls, 1999a; Kolb and

Whishaw, 2003), particularly orbitofrontal cortex damage (Hornak et al., 1994, 1996, 2003; Rolls, 1999a, 2005; Berlin et al., 2004, 2005). These emotional changes may be related at least in part to a failure to rapidly update the reinforcement associations of stimuli when the contingencies are changed as in a visual discrimination reversal task (Rolls et al., 1994; Rolls, 1999b, 2005; Fellows and Farah, 2003; Berlin et al., 2004; Hornak et al., 2004; Fellows, 2007). Similar mechanisms may contribute at least in part to the poor performance of humans with ventromedial prefrontal cortex damage on the Iowa Gambling Task (Bechara et al., 2000; Maia and McClelland, 2004).

Taste, Olfaction, Flavor, Oral Texture, and Oral Temperature Reward Value in the Orbitofrontal Cortex

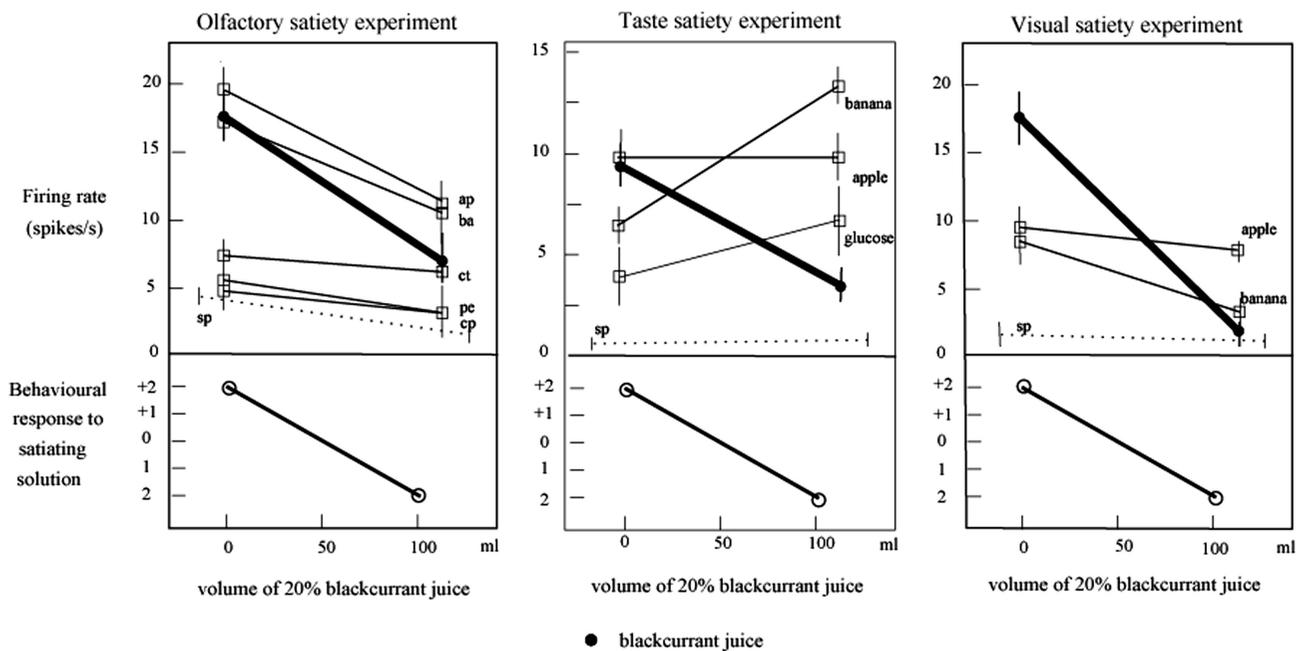
s0030

Taste and Oral Texture

s0035

p0070 One of the discoveries that has helped us to understand the functions of the orbitofrontal cortex in behavior is that it contains a major cortical representation of taste (see Rolls et al., 1990; Rolls, 1995, 1997; Rolls and Scott, 2003; Kadohisa et al., 2005a) (cf. Figure 38.1). Given that taste can act as a primary reinforcer, that is without learning as a reward or punisher, we now have the start for a fundamental understanding of the function of the orbitofrontal cortex in stimulus-reinforcer association learning (Rolls, 1999a, 2004, 2005, 2008c). We know how one class of primary reinforcers reaches and is represented in the orbitofrontal cortex. A representation of primary reinforcers is essential for a system that is involved in learning associations between previously neutral stimuli and primary reinforcers, e.g. between the sight of an object, and its taste.

p0075 The representation in the orbitofrontal cortex (shown by analysing the responses of single neurons in macaques) is for the majority of neurons the reward value of taste (Rolls et al., 1990, 1996a, 1998; Baylis and Rolls, 1991; Rolls, 1995, 1997, 2000c; Rolls and Scott, 2003; Kadohisa et al., 2005a) and oral texture including viscosity (Rolls et al., 2003c), fat texture (Rolls et al., 1999; Verhagen et al., 2003), and astringency as exemplified by tannic acid (Critchley and Rolls, 1996c). The evidence for this is that the responses of orbitofrontal taste neurons are modulated by hunger (as is the reward value or palatability of a taste). In particular, it has been shown that orbitofrontal cortex taste neurons gradually stop responding to the taste of a food as the monkey is fed to satiety (Rolls et al., 1989, 1996a). The example shown in Figure 38.3 is of a single neuron with taste, olfactory, and visual responses to food, and the neuronal responses elicited through all these sensory modalities showed a decrease. The decrease is



[AQ2]
f0020

FIGURE 38.3 Multimodal orbitofrontal cortex neuron with sensory-specific satiety-related responses to visual, taste and olfactory sensory inputs. The responses are shown 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). *After Critchley and Rolls (1996a).*

relatively specific to the food eaten to satiety, and the responses of these neurons are thus very closely related to sensory-specific satiety. In contrast, the representation of taste in the primary taste cortex (Scott et al., 1986; Yaxley et al., 1990) is not modulated by hunger (Rolls et al., 1988; Yaxley et al., 1988). Thus in the primate including human primary taste cortex, the reward value of taste is not represented, and instead the identity and intensity of the taste are represented (Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a; Rolls, 2005, 2008c).

p0080

Additional evidence that the reward value of food is represented in the orbitofrontal cortex is that monkeys work for electrical stimulation of this brain region if they are hungry, but not if they are satiated (Mora et al., 1979; Rolls, 2005). Further, neurons in the orbitofrontal cortex are activated from many brain-stimulation reward sites (Mora et al., 1980; Rolls et al., 1980). Thus there is clear evidence that it is the reward value of taste that is represented in the orbitofrontal cortex (see further Rolls, 1999a, 2000d, 2005), and this is further supported by the finding that feeding to satiety decreases the activation of the human orbitofrontal cortex to the food eaten to satiety in a sensory-specific way (Kringelbach et al., 2003). Some orbitofrontal cortex neurons respond to the “taste” of water in the mouth (Rolls et al., 1990), and their responses occur only when thirsty and not when satiated (Rolls et al., 1989); and correspondingly in humans the subjective pleasantness or affective value

of the taste of water in the mouth is represented in the orbitofrontal cortex (de Araujo et al., 2003b). This is part of the evidence for the separation of a “what” tier of processing, which in this case is the primary taste cortex, from a reward and affect-related representation in the orbitofrontal cortex tier of processing, as shown in Figure 38.1.

Functional neuroimaging studies in humans have p0085 shown that the most medial part of the human orbitofrontal cortex is activated by taste, oral texture, and olfactory stimuli (Francis et al., 1999; O’Doherty et al., 2000; Small et al., 2001, 2005; de Araujo et al., 2003a,c, 2005; Rolls et al., 2003a; de Araujo and Rolls, 2004; Gottfried et al., 2006; McCabe and Rolls, 2007; Rolls and McCabe, 2007), and that the activations correlate with ratings of subjective pleasantness and so are in the domain of affective representations (Kringelbach and Rolls, 2004; Rolls, 2005). This most medial part of the human orbitofrontal cortex may have moved medially when compared with the representation in macaques, probably because of the extensive development of the dorsolateral prefrontal cortex in humans (Rolls, 2008b; Rolls and Grabenhorst, 2008). Affectively pleasant stimuli are often represented medially, and unpleasant or aversive stimuli laterally, in the human orbitofrontal cortex. Evidence consistent with this has been found for taste (O’Doherty et al., 2001; de Araujo et al., 2003a), pleasant touch (Francis et al., 1999; Rolls et al., 2003b), and pleasant vs. aversive olfactory stimuli (Francis et al., 1999; O’Doherty et al., 2000;

Rolls, 2000d; Rolls et al., 2003a; see further Kringelbach and Rolls, 2004).

s0040 **An Olfactory Reward Representation in the Orbitofrontal Cortex**

p0090 For 35% of orbitofrontal cortex olfactory neurons, the odors to which a neuron responded were influenced by the taste value (glucose or saline) with which the odor was associated (Critchley and Rolls, 1996b). Thus the odor representation for 35% of orbitofrontal neurons appeared to be built by olfactory-to-taste association learning. This possibility was confirmed by reversing the taste with which an odor was associated in the reversal of an olfactory discrimination task. It was found that 68% of the sample of neurons analysed altered the way in which they responded to odor when the taste reinforcement association of the odor was reversed (Rolls et al., 1996b). The olfactory-to-taste reversal was quite slow, both neurophysiologically and behaviorally, often requiring 20–80 trials, consistent with the need for some stability of flavor representations formed by a combination of odor and taste inputs.

p0095 To analyse the nature of the olfactory representation in the orbitofrontal cortex, Critchley and Rolls (1996a) measured the responses of olfactory neurons that responded to food while they fed the monkey to satiety. They found that the majority of orbitofrontal olfactory neurons decreased their responses to the odor of the food with which the monkey was fed to satiety (see example in Figure 38.3). Thus for these neurons, the reward value of the odor is what is represented in the orbitofrontal cortex (cf. Rolls and Rolls, 1997), and this parallels the changes in the relative pleasantness of different foods after a food is eaten to satiety (Rolls et al., 1981a,b, 1997; see Rolls, 1999a, 2000d, 2005). The subjective pleasantness or reward or affective value of odor is represented in the orbitofrontal cortex, in that feeding the humans to satiety decreases the activation found to the odor of that food, and this effect is relatively specific to the food eaten in the meal (Francis et al., 1999)

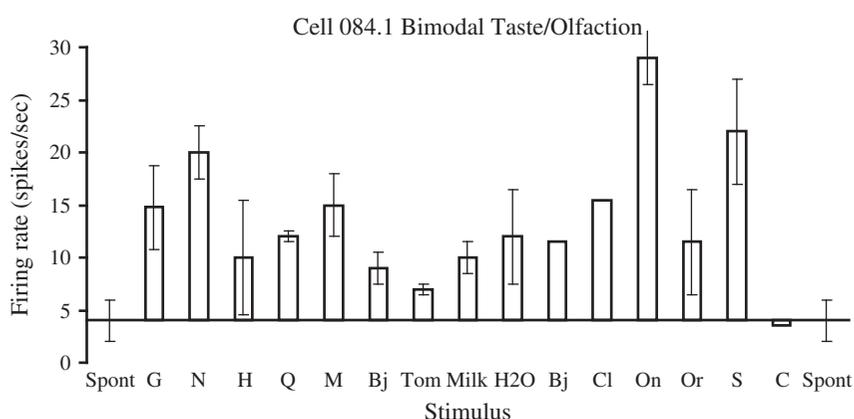
(cf. Morris and Dolan, 2001; O'Doherty et al., 2000). Further, the human medial orbitofrontal cortex has activation that is related to the subjective pleasantness of a set of odors, and a more lateral area has activation that is related to the degree of subjective unpleasantness of odors (Rolls et al., 2003a). A functional magnetic resonance imaging (fMRI) investigation in humans showed that whereas in the orbitofrontal cortex the pleasantness vs unpleasantness of odors is represented, this was not the case in primary olfactory cortical areas, where instead the activations reflected the intensity of the odors (Rolls et al., 2003a), providing a further example of the hierarchy of "what" followed by reward processing shown in Figure 38.1.

s0045 **Convergence of Taste and Olfactory Inputs in the Orbitofrontal Cortex: the Representation of Flavor**

p0100 In the orbitofrontal cortex, not only unimodal taste neurons, but also unimodal olfactory neurons are found. In addition some single neurons respond to both gustatory and olfactory stimuli, often with correspondence between the two modalities (Rolls and Baylis, 1994) (cf. Figure 38.4). It is probably here in the orbitofrontal cortex of primates including humans that these two modalities converge to produce the representation of flavor (Rolls and Baylis, 1994; de Araujo et al., 2003c), for neurons in the primary taste cortex in the insular/frontal opercular cortex do not respond to olfactory (or visual) stimuli (Verhagen et al., 2004).

p0105 The importance of the combination of taste and smell for producing affectively pleasant and rewarding representations of sensory stimuli is exemplified by findings with umami, the delicious taste or flavor that is associated with combinations of components that include meat, fish, milk, tomatoes, and mushrooms, all of which are rich in umami-related substances such as glutamate or inosine 5' monophosphate. Umami taste is produced by glutamate acting on a fifth taste system (Chaudhari et al., 2000; Zhao et al., 2003; Maruyama et al., 2006). However, glutamate presented

[AQ3]



f0025 **FIGURE 38.4** The responses of a bimodal single neuron with taste and olfactory responses recorded in the caudolateral orbitofrontal cortex. G, 1 M glucose; N, 0.1 M NaCl; H, 0.01 M HCl; Q, 0.001 M quinine HCl; M, 0.1 M monosodium glutamate; Bj, 20% blackcurrant juice; Tom, tomato juice; B, banana odor; Cl, clove oil odor; On, onion odor; Or, orange odor; S, salmon odor; C, control no-odor presentation. The mean responses \pm sem are shown. The neuron responded best to the tastes of NaCl and monosodium glutamate and to the odors of onion and salmon. After Rolls and Baylis (1994).

alone as a taste stimulus is not highly pleasant, and does not act synergistically with other tastes (sweet, salt, bitter, and sour). However, when glutamate is given in combination with a consonant, savory, odor (vegetable), the resulting flavor can be much more pleasant (McCabe and Rolls, 2007). We showed using functional brain imaging with fMRI that this glutamate taste and savory odor combination produced much greater activation of the medial orbitofrontal cortex and pregenual cingulate cortex than the sum of the activations by the taste and olfactory components presented separately (McCabe and Rolls, 2007). Supra-linear effects were much less (and significantly less) evident for sodium chloride and vegetable odor. Further, activations in these brain regions were correlated with the subjective pleasantness and fullness of the flavor, and with the consonance of the taste and olfactory components. Supra-linear effects of glutamate taste and savory odor were not found in the insular primary taste cortex. We thus proposed that glutamate acts by the non-linear effects it can produce when combined with a consonant odor in multimodal cortical taste-olfactory convergence regions. We suggested that umami can be thought of as a rich and delicious flavor that is produced by a combination of glutamate taste and a consonant savory odor. Glutamate is thus a flavor enhancer because of the way that it can combine supra-linearly with consonant odors in cortical areas where the taste and olfactory pathways converge far beyond the receptors (McCabe and Rolls, 2007).

a physical parameter that varies with the slickness of fat) (Verhagen et al., 2003); that other orbitofrontal cortex neurons encode the viscosity of the texture in the mouth (with some neurons tuned to viscosity, and others showing increasing or decrease firing rates as viscosity increases) (Rolls et al., 2003c); and that other neurons have responses that indicate the presence of texture stimuli (such as grittiness and capsaicin) in the mouth independently of viscosity and slickness (Rolls et al., 2003c). Ensemble (i.e. population, distributed) encoding of all these variables is found. In a complementary human functional neuroimaging study, it has been shown that activation of parts of the orbitofrontal cortex, primary taste cortex, and mid-insular somatosensory region posterior to the insular taste cortex have activations that are related to the viscosity of what is in the mouth, and that there is in addition a medial prefrontal/cingulate area where the mouth feel of fat is represented (de Araujo and Rolls, 2004). Moreover, the subjective pleasantness of fat is represented in the orbitofrontal cortex and a region to which it projects, the pregenual cingulate cortex (Grabenhorst et al., 2009).

An overlapping population of orbitofrontal cortex neurons represents the temperature of what is in the mouth (Kadohisa et al., 2004), and this is supported by a human fMRI study (Guest et al., 2007).

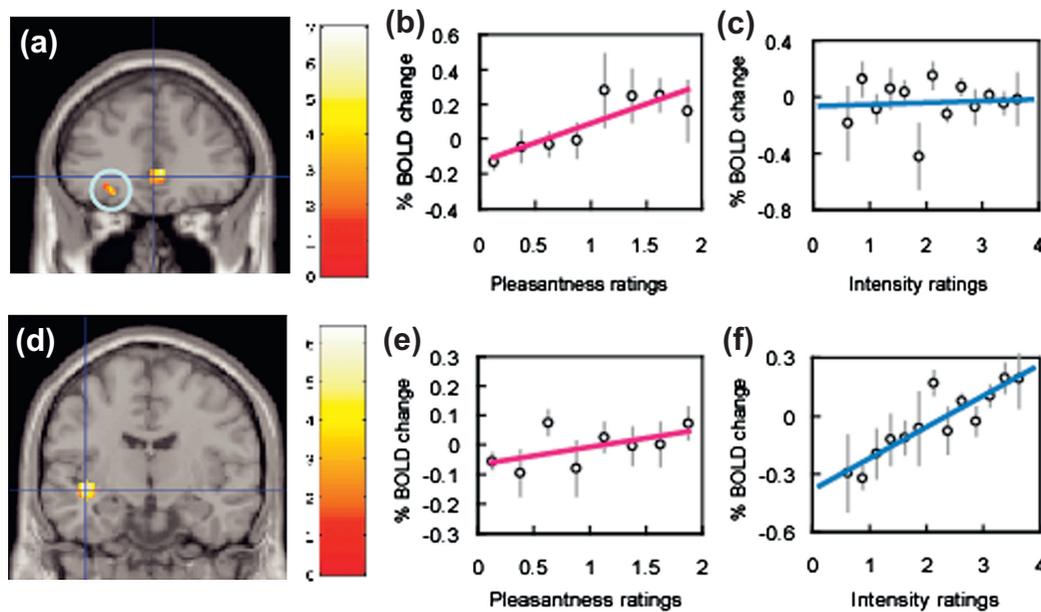
Somatosensory and Temperature Inputs to the Orbitofrontal Cortex, and Affective Value

In addition to these oral somatosensory inputs to the orbitofrontal cortex, there are also somatosensory inputs from other parts of the body, and indeed an fMRI investigation we have performed in humans indicates that pleasant and painful touch stimuli to the hand produce greater activation of the orbitofrontal cortex relative to the somatosensory cortex than do affectively neutral stimuli (Francis et al., 1999; Rolls et al., 2003b). In an fMRI investigation in humans, it was found that the mid-orbitofrontal and pregenual cingulate cortex and a region to which they project, the ventral striatum, have activations that are correlated with the subjective pleasantness ratings made to warm (41°C) and cold (12°C) stimuli, and combinations of warm and cold stimuli, applied to the hand (Rolls et al., 2008b) (Figure 38.5a–c). Activations in the lateral and some more anterior parts of the orbitofrontal cortex were correlated with the unpleasantness of the stimuli. In contrast, activations in the somatosensory cortex and ventral posterior insula were correlated with the intensity but not the pleasantness of the thermal stimuli (Figure 38.5d–f). Further, cognitive modulators of affective value such as the description of cream being rubbed on the arm as “rich and

s0050 **Oral Texture and Temperature**

p0110 A population of orbitofrontal neurons responds when a fatty food such as cream is in the mouth. These neurons can also be activated by pure fat such as glyceryl trioleate, and by non-fat substances with a fat-like texture such as paraffin oil (hydrocarbon) and silicone oil (Si(CH₃)₂O)_n. These neurons thus provide information by somatosensory pathways that a fatty food is in the mouth (Rolls et al., 1999). These inputs are perceived as pleasant when hungry, because of the utility of ingestion of foods that are likely to contain essential fatty acids and to have a high calorific value (Rolls, 2005). Satiety produced by eating a fatty food, cream, can decrease the responses of orbitofrontal cortex neurons to the texture of fat in the mouth (Rolls et al., 1999).

p0115 We have shown that the orbitofrontal cortex receives inputs from a number of different oral texture channels, which together provide a rich sensory representation of what is in the mouth. Using a set of stimuli in which viscosity was systematically altered (carboxymethylcellulose with viscosity in the range 10–10 000 centiPoise), we have shown that some orbitofrontal cortex neurons encode fat texture independently of viscosity (by



f0030 **FIGURE 38.5** Representation of the pleasantness but not intensity of thermal stimuli in the orbitofrontal cortex (top), and of the intensity but not the pleasantness in the mid ventral (somatosensory) insular cortex (bottom). (a) SPM analysis showing a correlation in the mid orbitofrontal cortex (blue circle) at $[-26\ 38\ -10]$ between the BOLD signal and the pleasantness ratings of for thermal stimuli. Correlations are also shown in the pregenual cingulate cortex. For this mid orbitofrontal cortex region, (b) shows the positive correlation between the subjective pleasantness ratings and the BOLD signal ($r = 0.84$, $df = 7$, $p < 0.01$), and (c) shows that there is no correlation between the subjective intensity ratings and the BOLD signal ($r = 0.07$, $df = 12$, $p = 0.8$). (d) SPM analysis showing a correlation with intensity in the posterior ventral insula with peak at $[-40\ -10\ -8]$ between the BOLD signal and the intensity ratings for the for thermal stimuli. For this ventral insula cortex region, (e) shows no correlation between the subjective pleasantness ratings and the BOLD signal ($r = 0.56$, $df = 7$, $p = 0.15$), and (f) shows a positive correlation between the subjective intensity ratings and the BOLD signal ($r = 0.89$, $df = 12$, $p < 0.001$). After Rolls et al. (2008c).

moisturizing" increase activations to the sight of rubbing of the arm in the orbitofrontal and pregenual cingulate cortex, and increased correlations there with the subjectively rated pleasantness of the touch (McCabe et al., 2008).

p0130 A principle thus appears to be that processing related to the affective value and associated subjective emotional experience of thermal stimuli that are important for survival is performed in different brain areas to those where activations are related to sensory properties of the stimuli such as their intensity. This conclusion appears to be the case for processing in a number of sensory modalities, including taste (Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a) and olfaction (Anderson et al., 2003; Rolls et al., 2003a; Grabenhorst et al., 2007), and the finding with such prototypical stimuli as warm and cold (Rolls et al., 2008b) provides strong support for this principle (Figure 38.1).

p0135 Non-glabrous skin such as that on the forearm contains C fibre tactile afferents that respond to light moving touch (Olausson et al., 2002). The orbitofrontal cortex is implicated in some of the affectively pleasant aspects of touch that may be mediated through C fibre tactile afferents, in that it is activated more by light touch to the forearm than by light touch to the glabrous skin (palm) of the hand (McCabe et al., 2008).

Visual Inputs to the Orbitofrontal Cortex, Visual Stimulus-Reinforcement Association Learning and Reversal, and Negative Reward Prediction Error Neurons

s0060

We have been able to show that there is a major visual p0140 input to many neurons in the orbitofrontal cortex, and that what is represented by these neurons is in many cases the reinforcement association of visual stimuli. The visual input is from the ventral, temporal lobe, visual stream concerned with "what" object is being seen (see Rolls, 2000a; Rolls and Deco, 2002). Many neurons in these temporal cortex visual areas have responses to objects or faces that are invariant with respect to size, position on the retina, and even view (Rolls, 2000a, 2007a, 2008a,c, 2009c; Rolls and Deco, 2002; Rolls and Stringer, 2006), making these neurons ideal as an input to a system that may learn about the reinforcement association properties of objects and faces, for after a single learning trial, the learning then generalizes correctly to other views etc. (see Rolls, 2000a, 2005 2008c; Rolls and Deco, 2002). Using this object-related information, orbitofrontal cortex visual neurons frequently respond differentially to objects or images depending on their reward association (Thorpe et al., 1983; Rolls et al., 1996b). The primary reinforcer

that has been used is taste, and correlates of visual to taste association learning have been demonstrated in the human orbitofrontal cortex with fMRI (O'Doherty et al., 2002). Many of these neurons show visual-taste reversal in one or a very few trials. (In a visual discrimination task, they will reverse the stimulus to which they respond, from for example, a triangle to a square, in one trial when the taste delivered for a behavioral response to that stimulus is reversed (Thorpe et al., 1983)). This reversal learning probably occurs in the orbitofrontal cortex, for it does not occur one synapse earlier in the visual inferior temporal cortex (Rolls et al., 1977), and it is in the orbitofrontal cortex that there is convergence of visual and taste pathways onto the same single neurons (Thorpe et al., 1983; Rolls and Baylis, 1994; Rolls et al., 1996b).

p0145 The probable mechanism for this learning is an associative modification of synapses conveying visual input onto taste-responsive neurons, implementing a pattern association network (Rolls and Treves, 1998; Rolls and Deco, 2002; Rolls, 2005, 2008c), with the reversal facilitated by a rule for which stimulus is currently rewarded held in short-term memory (Deco and Rolls, 2005c).

p0150 The visual and olfactory neurons in primates that respond to the sight or smell of stimuli that are primary reinforcers such as taste clearly signal an expectation of reward that is based on previous stimulus-reinforcement associations (Thorpe et al., 1983; Rolls et al., 1996b). So do the conditional reward neurons (Thorpe et al., 1983; Rolls et al., 1996b; Rolls and Grabenhorst, 2008). With visual-taste association learning and reversal in primates, in which the orbitofrontal cortex neurons and the behavior can change in one trial (Thorpe et al., 1983; Rolls et al., 1996b), the changing responses of the orbitofrontal cortex neurons can contribute to the reversed behavior, a view of course supported by the impaired reversal learning produced in primates including humans by orbitofrontal cortex damage (e.g. Rolls et al., 1994; Fellows and Farah, 2003; Berlin et al., 2004; Hornak et al., 2004).

p0155 To analyse the nature of the visual representation of food-related stimuli in the orbitofrontal cortex, Critchley and Rolls (1996a) measured the responses of neurons that responded to the sight of food while they fed the monkey to satiety. They found that the majority of orbitofrontal visual food-related neurons decreased their responses to the sight of the food with which the monkey was fed to satiety (see example in Figure 38.3). Thus for these neurons, the reward value of the sight of food is what is represented in the orbitofrontal cortex.

p0160 In addition to these neurons that encode the reward association of visual stimuli, other, "error," neurons in the orbitofrontal cortex detect non-reward, in that they respond for example when an expected reward is not obtained when a visual discrimination task is reversed

(Thorpe et al., 1983), or when reward is no longer made available in a visual discrimination task. These may be called "negative reward prediction error neurons" (Rolls and Grabenhorst, 2008). Evidence that there may be similar error neurons in the human orbitofrontal cortex is that in a model of social learning, orbitofrontal cortex activation occurred in a visual discrimination reversal task at the time when the face of one person no longer was associated with a smile, but became associated with an angry expression, indicating on such error trials that reversal of choice to the other individual's face should occur (Kringelbach and Rolls, 2003).

The orbitofrontal cortex negative reward prediction error neurons respond to a mismatch between the reward expected and the reward that is obtained. Both signals are represented in the orbitofrontal cortex, in the form of for example neurons that respond to the sight of a learned reinforcer such as the sight of a stimulus paired with taste, and neurons that respond to the primary reinforcer, the taste (or texture or temperature). The orbitofrontal cortex is the probable brain region for this computation, because both the signals required to compute negative reward prediction error are present in the orbitofrontal cortex, so are the negative reward prediction error neurons, and lesions of the orbitofrontal cortex impair tasks such as visual discrimination reversal in which this type of negative reward prediction error is needed (see above).

It may be noted that the dopamine neurons in the midbrain may not be able to provide a good representation of negative reward prediction error, because their spontaneous firing rates are so low (Schultz, 2004) that much further reduction would provide only a small signal. In any case, the dopamine neurons would not appear to be in a position to compute a negative reward prediction error, as they are not known to receive inputs that signal expected reward, and the actual reward (outcome) that is obtained, and indeed do not represent the reward obtained (or "outcome"), in that they stop responding to a taste reward outcome if it is predictable. Although dopamine neurons do appear to represent a positive reward prediction error signal (responding if a greater than expected reward is obtained; Schultz, 2004, 2006), they do not appear to have the signals required to compute this, that is, the expected reward, and the reward outcome obtained, so even a positive reward prediction error must be computed elsewhere. The orbitofrontal cortex does contain representations of these two signals, the expected reward and the reward outcome, and has projections to the ventral striatum, which in turn projects to the region of the midbrain dopamine neurons, and so this is one possible pathway along which the firing of positive reward prediction error might be computed (Figure 38.1). Consistent with

this, activations in parts of the human ventral striatum are related to positive reward prediction error (Hare et al., 2008; Rolls et al., 2008c). Thus the dopamine projections to the prefrontal cortex and other areas are not likely to convey information about reward to the prefrontal cortex, which instead is likely to be decoded by the neurons in the orbitofrontal cortex that represent primary reinforcers, and the orbitofrontal cortex neurons that learn associations of other stimuli to the primary reinforcers to represent expected value (Thorpe et al., 1983; Rolls et al., 1996b, 2008c; Rolls, 2008c). Although it has been suggested that the firing of dopamine neurons may reflect the earliest signal in a task that indicates reward and could be used as a reward prediction error signal during learning (see Schultz, 2006; Schultz et al., 2000), it is likely, partly on the basis of the above evidence, though an interesting topic for future investigation, that any error information to which dopamine neurons fire originates from representations in the orbitofrontal cortex that encode expected value and reward outcome, and which connect to the ventral striatum (Rolls, 2005, 2008c, 2009b).

p0175 In responding when the reward obtained is less than that expected, the orbitofrontal cortex negative reward prediction error neurons are working in a domain that is related to the sensory inputs being received (expected reward and reward obtained). There are also error neurons in the anterior cingulate cortex that respond when errors are made (Niki and Watanabe, 1979), or when rewards are reduced (Shima and Tanji, 1998; and in similar imaging studies, Bush et al., 2002). Some of these neurons may be influenced by the projections from the orbitofrontal cortex, and reflect a mismatch between the reward expected and the reward that is obtained. However, some error neurons in the anterior cingulate cortex may reflect errors that arise when particular behavioral responses or actions are in error, and this type of error may be important in helping an action system to correct itself, rather than, as in the orbitofrontal cortex, a reward prediction system about stimuli needs to be corrected. Consistent with this, many studies provide evidence that errors made in many tasks activate the anterior/midcingulate cortex, whereas tasks with response conflict activate the superior frontal gyrus (Rushworth et al., 2004; Matsumoto et al., 2007; Rushworth and Behrens, 2008; Vogt, 2009).

s0065 Face-Selective Processing in the Orbitofrontal Cortex

p0180 Another type of visual information represented in the orbitofrontal cortex is information about faces. There is a population of orbitofrontal neurons that respond in many ways similar to those in the temporal cortical visual areas (Rolls, 1984, 1992a, 1996, 2000a, 2007a,

2008a,c; Rolls and Deco, 2002). The orbitofrontal face-responsive neurons, first observed by Thorpe et al. (1983), then by Rolls et al. (2006), tend to respond with longer latencies than temporal lobe neurons (140–200 ms typically, compared to 80–100 ms); also convey information about which face is being seen, by having different responses to different faces; and are typically rather harder to activate strongly than temporal cortical face-selective neurons, in that many of them respond much better to real faces than to two-dimensional images of faces on a video monitor (cf. Rolls and Baylis, 1986). Some of the orbitofrontal cortex face-selective neurons are responsive to face expression, gesture, or movement (Rolls et al., 2006). The findings are consistent with the likelihood that these neurons are activated via the inputs from the temporal cortical visual areas in which face-selective neurons are found (Figure 38.1). The significance of the neurons is likely to be related to the fact that faces convey information that is important in social reinforcement in at least two ways that could be implemented by these neurons. The first is that some may encode face expression (Rolls et al., 2006) (cf. Hasselmo et al., 1989), which can indicate reinforcement. The second way is that they encode information about which individual is present (Rolls et al., 2006), which by stimulus-reinforcement association learning is important in evaluating and utilizing learned reinforcing inputs in social situations, e.g., about the current reinforcement value as decoded by stimulus-reinforcement association, to a particular individual.

This system has also been shown to be present in p0185 humans. For example, Kringelbach and Rolls (2003) showed that activation of a part of the human orbitofrontal cortex occurs during a face discrimination reversal task. In the task, the faces of two different individuals are shown, and when the correct face is selected, the expression turns into a smile. (The expression turns to angry if the wrong face is selected.) After a period of correct performance, the contingencies reverse, and the other face must be selected to obtain a smile expression as a reinforcer. It was found that activation of a part of the orbitofrontal cortex occurred specifically in relation to the reversal, that is when a formerly correct face was chosen, but an angry face expression was obtained. In a control task, it was shown that the activations were not related just to showing an angry face expression. Thus in humans, there is a part of the orbitofrontal cortex that responds selectively in relation to face expression specifically when it indicates that behavior should change, and this activation is error-related (Kringelbach and Rolls, 2003) and occurs when the error neurons in the orbitofrontal cortex become active (Thorpe et al., 1983).

Also prompted by the neuronal recording evidence of p0190 face and auditory neurons in the orbitofrontal cortex

(Rolls et al., 2006), it has further been shown that there are impairments in the identification of facial and vocal emotional expression in a group of patients with ventral frontal lobe damage who had socially inappropriate behavior (Hornak et al., 1996). The expression identification impairments could occur independently of perceptual impairments in facial recognition, voice discrimination, or environmental sound recognition. Poor performance on both expression tests was correlated with the degree of alteration of emotional experience reported by the patients. There was also a strong positive correlation between the degree of altered emotional experience and the severity of the behavioral problems (e.g. disinhibition) found in these patients (Hornak et al., 1996). A comparison group of patients with brain damage outside the ventral frontal lobe region, without these behavioral problems, was unimpaired on the face expression identification test, was significantly less impaired at vocal expression identification, and reported little subjective emotional change (Hornak et al., 1996). It has further been shown that patients with discrete surgical lesions of restricted parts of the orbitofrontal cortex may have face and/or voice expression identification impairments, and these are likely to contribute to their difficulties in social situations (Hornak et al., 2003).

s0070 **Top-Down Effects of Cognition and Attention on Taste, Olfactory, Flavor, Somatosensory, and Visual Processing: Cognitive Enhancement of the Value of Affective Stimuli**

p0195 How does cognition influence affective value? How does cognition influence the way that we feel emotionally? Do cognition and emotion interact in regions that are high in the brain's hierarchy of processing, for example in areas where language processing occurs, or do cognitive influences descend down anatomically to influence the first regions that represent the affective value of stimuli?

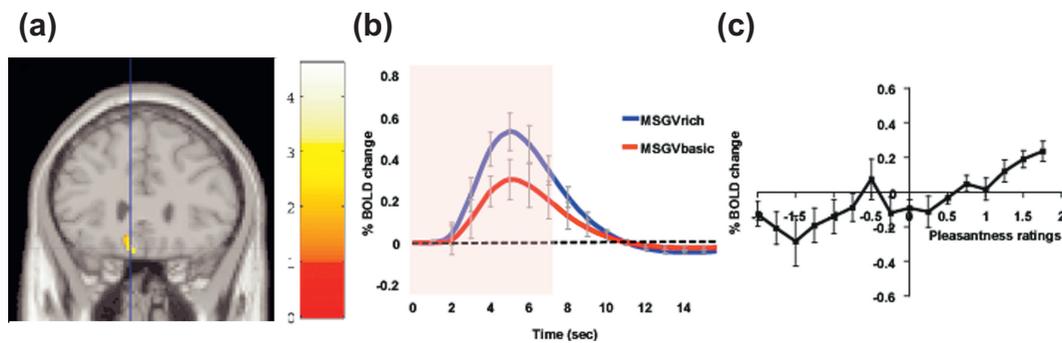
p0200 An fMRI study to address these fundamental issues in brain design has shown that cognitive effects can reach down into the human orbitofrontal cortex and influence activations produced by odors (de Araujo et al., 2005). In this study, a standard test odor, isovaleric acid with a small amount of cheese flavor, was delivered through an olfactometer. (The odor alone, like the odor of brie, might have been interpreted as pleasant, or perhaps as unpleasant.) On some trials the test odor was accompanied with the visually presented word label "cheddar cheese," and on other trials with the word label "body odor." It was found that the activation in the medial orbitofrontal cortex to the standard test odor was much greater when the word label was cheddar cheese than when it was body odor. (Controls

with clean air were run to show that the effect could not be accounted for by the word label alone.) Moreover, the word labels influenced the subjective pleasantness ratings to the test odor, and the changing pleasantness ratings were correlated with the activations in the human medial orbitofrontal cortex. Part of the interest and importance of this finding is that it shows that cognitive influences, originating here purely at the word level, can reach down and modulate activations in the first stage of cortical processing that represents the affective value of sensory stimuli (de Araujo et al., 2005; Rolls, 2005).

Also important is how cognition influences the affective brain representations of the taste and flavor of a food. This is important not only for understanding top-down influences in the brain, but also in relation to the topical issues of appetite control and obesity (Rolls, 2007b,c, 2010b, 2011). In an fMRI study it was shown that activations related to the affective value of umami taste and flavor (as shown by correlations with pleasantness ratings) in the orbitofrontal cortex were modulated by word-level descriptors (e.g. "rich and delicious flavor") (Grabenhorst et al., 2008a) (Figure 38.6). Affect-related activations to taste were modulated in a region that receives from the orbitofrontal cortex, the pregenual cingulate cortex, and to taste and flavor in another region that receives from the orbitofrontal cortex, the ventral striatum. Affect-related cognitive modulations were not found in the insular taste cortex, where the intensity but not the pleasantness of the taste was represented. Thus the top-down language-level cognitive effects reach far down into the earliest cortical areas that represent the appetitive value of taste and flavor. This is an important way anatomically in which cognition influences the neural mechanisms that control appetite.

When we see a person being touched, we may empathize the feelings being produced by the touch. Interestingly, cognitive modulation of this effect can be produced. When subjects were informed by word labels that a cream seen being rubbed onto the forearm was a "Rich moisturizing cream" vs "Basic cream," these cognitive labels influenced activations in the orbitofrontal/pregenual cingulate cortex and ventral striatum to the sight of touch and their correlations with the pleasantness ratings (McCabe et al., 2008). Some evidence for top-down cognitive modulation of the effects produced by the subject being rubbed with the cream was found in brain regions such as the orbitofrontal and pregenual cingulate cortex and ventral striatum, but some effects were found in other brain regions, perhaps reflecting backprojections from the orbitofrontal cortex (McCabe et al., 2008).

What may be a fundamental principle of how top-down attention can influence affective vs non-affective



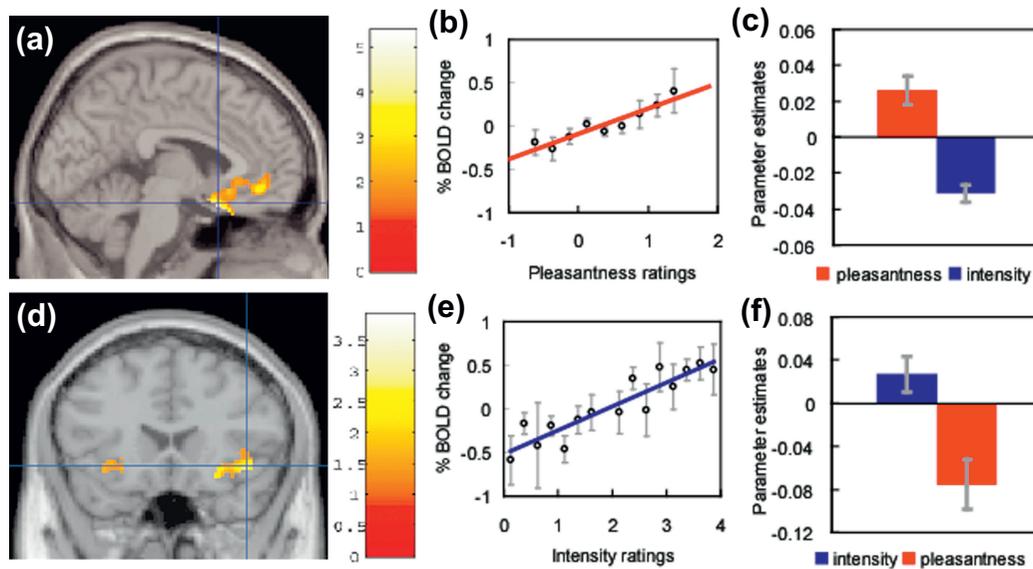
f0035 **FIGURE 38.6** Cognitive modulation of affective representations in the medial orbitofrontal cortex. (a) The medial orbitofrontal cortex was more strongly activated when the flavor stimulus was labeled “rich and delicious flavor” (MSGVrich) than when it was labeled “boiled vegetable water” (MSGVbasic) ([-8 28 -20]). (b) The timecourse of the BOLD signals for the two conditions. The means across subjects \pm sem are shown. (c) The BOLD signal in the medial orbitofrontal cortex was correlated with the subjective pleasantness ratings of taste and flavor (mean across subjects \pm sem, $r = 0.86$, $p < 0.001$). After Grabenhorst et al. (2008a).

processing has recently been discovered. For an identical taste stimulus, paying attention to pleasantness activated some brain systems, and paying attention to intensity, which reflected the physical and not the affective properties of the stimulus, activated other brain systems (Grabenhorst and Rolls, 2008). In an fMRI investigation, when subjects were instructed to remember and rate the pleasantness of a taste stimulus, 0.1 M monosodium glutamate, activations were greater in the medial orbitofrontal and pregenual cingulate cortex than when subjects were instructed to remember and rate the intensity of the taste (Figure 38.7a–c). When the subjects were instructed to remember and rate the intensity, activations were greater in the insular taste cortex (Figure 38.7d–f). Thus, depending on the context in which tastes are presented and whether affect is relevant, the brain responds to a taste differently. These findings show that when attention is paid to affective value, the brain systems engaged to represent the sensory stimulus of taste are different from those engaged when attention is directed to the physical properties of a stimulus such as its intensity. This differential biasing of brain regions engaged in processing a sensory stimulus depending on whether the attentional demand is for affect-related vs more sensory-related processing may be an important aspect of cognition and attention. This has many implications for understanding attentional effects to affective value not only on taste, but also on other sensory stimuli.

p0220 Indeed, the concept has been validated in the olfactory system too. In an fMRI investigation, when subjects were instructed to remember and rate the pleasantness of a jasmine odor, activations were greater in the medial orbitofrontal and pregenual cingulate cortex than when subjects were instructed to remember and rate the intensity of the odor (Rolls et al., 2008a). When the subjects were instructed to remember and rate the intensity, activations were greater in the inferior frontal gyrus.

These top-down effects occurred not only during odor delivery, but started in a preparation period after the instruction before odor delivery, and continued after termination of the odor in a short-term memory period. Thus, depending on the context in which odors are presented and whether affect is relevant, the brain prepares itself, responds to, and remembers an odor differently. These findings show that when attention is paid to affective value, the brain systems engaged to prepare for, represent, and remember a sensory stimulus are different from those engaged when attention is directed to the physical properties of a stimulus such as its intensity. This differential biasing 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 important for understanding how the context can influence how we process stimuli that may have affective properties, how different people may respond differently to stimuli if they process the stimuli in different ways, and more generally, how attentional set can influence the processing of affective stimuli by influencing processing in for example the orbitofrontal cortex and related areas.

The principle thus appears to be that top-down attentional and cognitive effects on affective value influence representations selectively in cortical areas that process the affective value and associated subjective emotional experience of taste (Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a) and olfactory (Anderson et al., 2003; Rolls et al., 2003a; Grabenhorst et al., 2007) stimuli in brain regions such as the orbitofrontal cortex; whereas top-down attentional and cognitive effects on intensity influence representations in brain areas that process the intensity and identity of the stimulus such as the primary taste and olfactory cortical areas (Anderson et al., 2003; Rolls et al., 2003a; Grabenhorst and Rolls, 2008; Grabenhorst et al., 2007, 2008a). This is computationally appropriate in top-down models of attention



f0040 **FIGURE 38.7** Effects of attention to the pleasantness vs the intensity of a taste stimulus (0.1 M monosodium glutamate, which was identical on all trials). Top: The contrast paying attention to pleasantness – paying attention to intensity. (a) A significant difference was found in the medial orbitofrontal cortex at $[-6\ 14\ -20]$ (at the cursor) which extended forward into the pregenual cingulate cortex (at $[-4\ 46\ -8]$). (b) The activations (% BOLD change) were correlated with the subjective pleasantness ratings in the medial orbitofrontal cortex. ($r = 0.94$, $df = 8$, $p < 0.001$). (c) The parameter estimates (mean \pm sem across subjects) for the medial orbitofrontal cortex activations for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different ($p < 10^{-4}$). Bottom: The contrast paying attention to intensity – paying attention to pleasantness. (d) A significant difference was found in the taste insula at $[42\ 18\ -14]$ (indicated by the cursor). (e) The activations (% BOLD change) were correlated with the subjective intensity ratings in the taste insula medial orbitofrontal cortex. ($r = 0.89$, $df = 15$, $p < 0.001$). (f) The parameter estimates (mean \pm sem across subjects) for the taste insula for the conditions of paying attention to intensity or to pleasantness. The parameter estimates were significantly different ($p < 0.001$). After Grabenhorst and Rolls (2008).

(Rolls and Deco, 2002; Deco and Rolls, 2005a; Rolls, 2008c).

p0230 To investigate the anatomical source of the top-down modulatory effects on attentional processing, we utilized fMRI psychophysiological interaction connectivity analyses (Friston et al., 1997) with taste stimuli when attention was being paid to the pleasantness or to the intensity (Grabenhorst and Rolls, 2010). We showed that in the anterior lateral prefrontal cortex at $Y = 53$ mm the correlation with activity in orbitofrontal cortex and pregenual cingulate cortex seed regions was greater when attention was to pleasantness compared to when attention was to intensity. Conversely, we showed that in a more posterior region of lateral prefrontal cortex at $Y = 34$ mm the correlation with activity in the anterior insula seed region was greater when attention was to intensity compared to when attention was to pleasantness. We proposed a biased activation theory of selective attention to account for the findings (Figure 38.8a) (Grabenhorst and Rolls, 2010), and contrasted this with a biased competition (Desimone and Duncan, 1995; Rolls and Deco, 2002; Deco and Rolls, 2005b; Rolls, 2008c,d) theory of selective attention (Figure 38.8b).

p0235 Individual differences in these reward and top-down attentional effects, and their relation to some

psychiatric symptoms, are described elsewhere (Rolls and Grabenhorst, 2008).

A Representation of Novel Visual Stimuli in the Orbitofrontal Cortex s0075

A population of neurons has been discovered in the p0240 primate orbitofrontal cortex that responds to novel but not familiar visual stimuli, and takes typically a few trials to habituate (Rolls et al., 2005). The memories implemented by these neurons last for at least 24 hours. Exactly what role these neurons have in memory is not yet known, but there are connections from the area in which these neurons are recorded to the temporal lobe, and activations in a corresponding orbitofrontal cortex area in humans are found when new visual stimuli must be encoded in memory (Frey and Petrides, 2002, 2003; Petrides, 2007).

THE AMYGDALA

s0080

The connections of the amygdala are described in p0245 Chapter XX and by Rolls (2005), and are similar in [AQ1] many respects to those of the orbitofrontal cortex

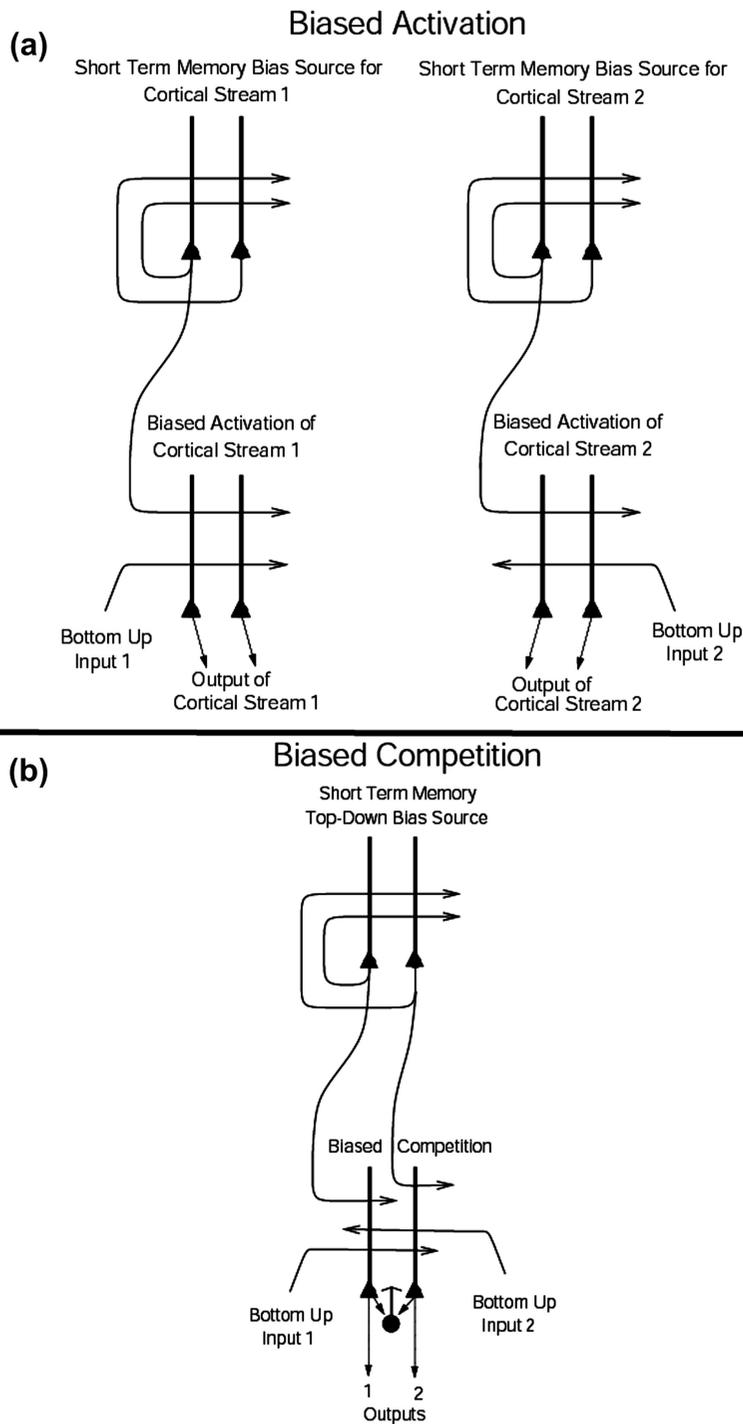


FIGURE 38.8 (a) Biased activation. The short-term memory systems that provide the source of the top-down activations may be separate (as shown), or could be a single network with different attractor states for the different selective attention conditions. The top-down short-term memory systems hold what is being paid attention to active by continuing firing in an attractor state, and bias separately either cortical processing system 1, or cortical processing system 2. This weak top-down bias interacts with the bottom-up input to the cortical stream and produces an increase of activity that can be supralinear (Deco and Rolls, 2005b). Thus the selective activation of separate cortical processing streams can occur. In the example, stream 1 might process the affective value of a stimulus, and stream 2 might process the intensity and physical properties of the stimulus. The outputs of these separate processing streams then must enter a competition system, which could be for example a cortical attractor decision-making network that makes choices between the two streams, with the choice biased by the activations in the separate streams. (b) Biased competition. There is usually a single attractor network that can enter different attractor states to provide the source of the top-down bias (as shown). If it is a single network, there can be competition within the short-term memory attractor states, implemented through the local GABA inhibitory neurons. The top-down continuing firing of one of the attractor states then biases in a top-down process some of the neurons in a cortical area to respond more to one than the other of the bottom-up inputs, with competition implemented through the GABA inhibitory neurons (symbolized by a filled circle) which make feedback inhibitory connections onto the pyramidal cells (symbolized by a triangle) in the cortical area. The thick vertical lines above the pyramidal cells are the dendrites. The axons are shown with thin lines and the excitatory connections by arrowheads. *After Grabenhorst and Rolls (2010).*

(Figure 38.1). The amygdala has for long been implicated in emotion (Davis, 1992, 1994; LeDoux, 1996, 2000; Rolls, 2005), and contains neurons related to taste, odor, the sight of reinforcers, and faces (Leonard et al., 1985; Rolls, 1992b, 2000b; Kadohisa et al., 2005a,b).

p0250

However, the amygdala is a structure that appears early in evolution, before the orbitofrontal cortex, and

although important in emotion in rodents, may be less important in primates including humans, in which it is in many ways overshadowed by the orbitofrontal cortex. Part of the anatomical basis for this may be that the orbitofrontal cortex, as a cortical structure, naturally finds its place in the cortical hierarchy, and can perform a number of computational functions better, including holding

items in short-term memory, and reversal learning, because of its highly developed neocortical recurrent collateral design (Rolls, 2005, 2008c). For example, with respect to the primate amygdala, the evidence is that any reversal of neurons in a visual discrimination reversal is relatively slow, if occurring taking tens of trials (Sanghera et al., 1979; Paton et al., 2006), and so the amygdala appears to make a less important contribution than the orbitofrontal cortex. Further, lesions in the primate amygdala appear to produce less marked changes in emotional behavior and learning than those in rodents (e.g. Antoniadis et al., 2009).

p0255 Further, the greater importance of the orbitofrontal cortex in emotion in humans is emphasized by a comparison with the effects of bilateral amygdala damage in humans, which although producing demonstrable deficits in face processing (Adolphs et al., 2005; Spezio et al., 2007), decision-making with linked autonomic deficits (Bechara et al., 1999; Brand et al., 2007), and autonomic conditioning (Phelps and LeDoux, 2005), may not (in contrast with the orbitofrontal cortex) produce major changes in emotion that are readily apparent in everyday behavior (Phelps and LeDoux, 2005; Rolls, 2008c; Seymour and Dolan, 2008). A comparison of the roles of the amygdala and orbitofrontal cortex in emotion is provided elsewhere (Rolls, 2005).

s0085 THE PREGENUAL CINGULATE CORTEX

p0260 The orbitofrontal cortex projects to the pregenual cingulate cortex (Carmichael and Price, 1996; Price, 2006), and both these areas have reward and punishment value representations that correlate on a continuous scale with the subjective pleasantness/unpleasantness ratings of olfactory (Rolls et al., 1996b, 2003a; Anderson et al., 2003; Grabenhorst et al., 2007), taste (Rolls et al., 1989; Small et al., 2003; Grabenhorst et al., 2008a; Rolls, 2008b), somatosensory (Rolls et al., 2003b), temperature (Guest et al., 2007), visual (O'Doherty et al., 2003), monetary (O'Doherty et al., 2001; Knutson et al., 2007), and social stimuli (Hornak et al., 2003; Kringelbach and Rolls, 2003; Moll et al., 2006; Spitzer et al., 2007) (see further Bush et al., 2000; Rolls, 2009a). Indeed, the pregenual cingulate cortex may be identified *inter alia* as a tertiary cortical taste area (Rolls, 2008b).

p0265 We may ask why, if the activations in the orbitofrontal cortex and the pregenual cingulate cortex are somewhat similar in their continuous representations of reward or affective value, are there these two different areas? A suggestion I make is that the orbitofrontal cortex is the region that computes the rewards, expected rewards, etc, and updates these rapidly when the reinforcement contingencies change, based on its inputs about primary

reinforcers from the primary taste cortex (Baylis et al., 1995), the primary olfactory cortex (Carmichael, Clugnet et al., 1994), the somatosensory cortex (Morecraft et al., 1992), etc. The orbitofrontal cortex makes explicit in its representations the reward value, based on these inputs, and in a situation where reward value is not represented at the previous tier, but instead where the representation is about the physical properties of the stimuli, their intensity, etc. (Rolls et al., 2003b, 2008b; Small et al., 2003; Grabenhorst et al., 2007, 2008a; Grabenhorst and Rolls, 2008) (Figure 38.1). The orbitofrontal cortex computes the expected value of previously neutral stimuli, and updates these representations rapidly when the reinforcement contingencies change, as described in this review. Thus the orbitofrontal cortex is the computer of reward magnitude and expected reward value. It can thus represent outcomes, and expected outcomes, but it does not represent actions such as motor responses or movements. It is suggested that the representations of outcomes, and expected outcomes, are projected from the orbitofrontal cortex to the pregenual cingulate cortex, as the cingulate cortex has longitudinal connections which allows this outcome information to be linked to the information about actions that is represented in the midcingulate cortex, and that the outcome information derived from the orbitofrontal cortex can contribute to action-outcome learning implemented in the cingulate cortex (Rushworth et al., 2007a,b; Rolls, 2008c). Although the anterior cingulate cortex is activated in relation to autonomic function (Critchley et al., 2004), its functions clearly extend much beyond this, as shown also for example by the emotional changes that follow damage to the anterior cingulate cortex and related areas in humans (Hornak et al., 2003).

BEYOND THE ORBITOFRONTAL CORTEX s0090 TO CHOICE DECISION-MAKING

In the neurophysiological studies described above, p0270 we have found that neuronal activity is related to the reward value of sensory stimuli, and how these change when reward contingencies change, but is not related to the details of actions that are being performed, such as mouth or arm movements (Rolls, 2005, 2008c). Wallis (2007) and Padoa-Schioppa and Assad (2006) have obtained evidence that supports this. An implication is that the orbitofrontal cortex represents the reward, affective (or, operationally, goal) value of a stimulus. Further, this value representation is on a continuous scale, as shown by the gradual decrease in orbitofrontal cortex neuronal responses to taste, olfactory and visual rewarding stimuli during feeding to satiety (Rolls et al., 1989, 1996a, 1999; Critchley and Rolls, 1996a). Consistently, in humans the BOLD activations in

different parts of the orbitofrontal cortex are continuously related to subjective pleasantness ratings of taste (de Araujo et al., 2003b; Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a), olfactory (Grabenhorst et al., 2007), flavor (Kringelbach et al., 2003; McCabe and Rolls, 2007; Grabenhorst et al., 2008a; Plassmann et al., 2008), oral temperature (Guest et al., 2007), hand temperature (Rolls et al., 2008b), and face beauty (O'Doherty et al., 2003) stimuli, and to monetary reward value (O'Doherty et al., 2001), as shown by correlation analyses. An implication of these findings is that the orbitofrontal cortex may contribute to decision-making by representing on a continuous scale the value of each reward, with, as shown by the single neuron neurophysiology, different subsets of neurons for each different particular reward. It is of course essential to represent each reward separately, in order to make decisions about and between rewards, and separate representations (using distributed encoding (Rolls, 2008c)) of different rewards are present in the orbitofrontal cortex (Rolls and Grabenhorst, 2008).

p0275 Clearly a representation of reward magnitude, expected reward, and even the subjective utility of a reward is an important input to a decision-making process, and the orbitofrontal cortex (with the ventromedial prefrontal area), appears to provide this information (Rolls et al., 2008c). When making a decision between two rewards, or whether to work for a reward that has an associated cost, it is important that the exact value of each reward is represented and enters the decision-making process. However, when a decision is reached, a system is needed that can make a (for example binary) choice, so that on one trial the decision might be reward 1, and on another trial reward 2, so that a particular action can be taken. For the evaluation, the neural activity needs to represent a stimulus in a way that continuously and faithfully represents the affective value of the stimulus, and this could be present independently of whether a binary choice decision is being made or not. On the other hand, when a binary (choice) decision must be reached, a neural system is needed that does not continuously represent the affective value of the stimulus, but which instead falls into a binary state, in which for example the high firing of some neurons represents one decision (i.e. choice), and the high firing of other neurons represents a different choice. Processes such as this transition from spontaneous firing to a binary state of firing of neurons (fast vs slow) are known to occur in some premotor and related areas such as the macaque ventral premotor cortex when decisions are taken, about in this case which vibrotactile stimulus to choose (Romo et al., 2004; de Lafuente and Romo, 2006; Rolls and Deco, 2010). It has been proposed that there may be a similar choice system, in the medial prefrontal cortex area 10, that becomes engaged when

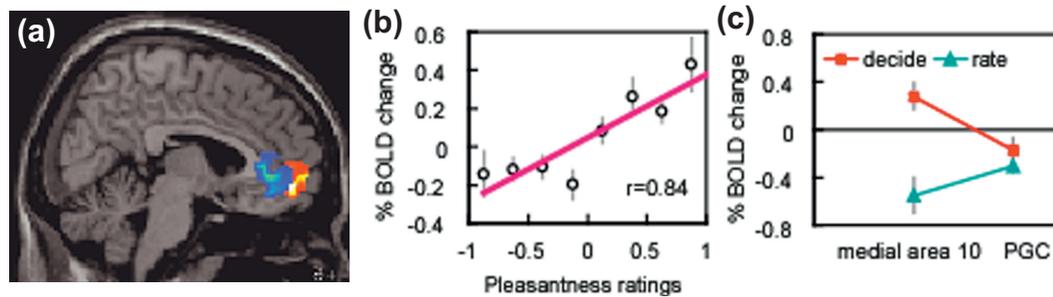
choice decisions are between rewards, or about rewards with which there is an associated cost (Rolls, 2008c). This proposal has been investigated as follows.

To investigate whether representing the affective p0280 value of a reward on a continuous scale may occur before and separately from making a binary, for example yes–no, decision about whether to choose the reward, Grabenhorst et al (2008b) used fMRI to measure activations produced by pleasant warm, unpleasant cold, and affectively complex combinations of these stimuli applied to the hand. On some trials the affective value was rated on a continuous scale, and on different trials a yes–no (binary choice) decision was made about whether the stimulus should be repeated in future. Activations that were continuously related to the pleasantness ratings and which were not influenced when a binary (choice) decision was made were found in the orbitofrontal and pregenual cingulate cortex, implicating these regions in the continuous representation of affective value. In the study with warm and cold stimuli, and mixtures of them, decision-making contrasted with just rating the affective stimuli revealed activations in the medial prefrontal cortex area 10, implicating this area in choice decision making (Grabenhorst et al., 2008b) (Figure 38.9).

Support for a contribution of medial prefrontal cortex p0285 area 10 to taking binary (choice) decisions comes from a fMRI study in which two odors were separated by a delay, with instructions on different trials to decide which odor was more pleasant, or more intense, or to rate the pleasantness and intensity of the second odor on a continuous scale without making a binary (choice) decision. Activations in the medial prefrontal cortex area 10, and in regions to which it projects including the anterior cingulate cortex and insula, were higher when binary choice decisions were being made compared to ratings on a continuous scale, further implicating these regions in binary decision-making (Rolls et al., 2010a–c).

Consistent with these findings, patients with medial p0290 prefrontal cortex lesions are impaired in a decision-making shopping task, as reflected for example by visits to previously visited locations (Shallice and Burgess, 1991; Burgess, 2000; Burgess et al., 2007). In another imaging study, area 10 activation has been related to moral decision-making (Heekeren et al., 2005).

The implications are that the orbitofrontal cortex, p0295 and the pregenual cingulate cortex to which it projects, are involved in making decisions primarily by representing reward value on a continuous scale. The evidence we describe indicates that another tier of processing beyond the affective value stages becomes engaged in relation to taking binary (choice) decisions, and these areas include the medial prefrontal cortex area 10 (Figure 38.1) (Rolls and Grabenhorst, 2008; Grabenhorst and Rolls, 2011). Having separable systems



f0050 **FIGURE 38.9** Pregenual cingulate cortex vs medial area 10 in decision-making. (a) A contrast of all trials on which decisions were made vs all trials on which ratings were made between thermal stimuli showed a significant effect in the medial prefrontal cortex area 10, as indicated in red ([6 54–8]). This contrast showed no significant difference in the pregenual cingulate cortex, although here, as shown in blue, there was a strong and significant correlation with the pleasantness ratings ([4 38–2]). (b) The % BOLD signal in the pregenual cingulate cortex was correlated with the pleasantness ratings on the trials on which ratings were made ($r=0.84$, $df=7$, $p=0.005$). (c) Compares the activations (mean \pm sem) in medial area 10 with those in the pregenual cingulate cortex (PGC) for decision and rating trials. There was a significant interaction ($p=0.015$). After Grabenhorst et al. (2008b).

anatomically for these types of processing appears to be computationally appropriate. For at the same time that one brain system is entering a binary decision state, that on this trial the choice is probabilistically one or another, in a way that could be implemented by the settling of an attractor network into one of its two or more high firing rate attractor states each representing a choice (Wang, 2002; Deco and Rolls, 2006; Rolls, 2008c; Rolls and Deco, 2010), another brain system (involving the orbitofrontal and pregenual cingulate cortex) can still be representing faithfully the reward or affective value of the stimuli on a continuous scale (Grabenhorst and Rolls, 2011).

p0300 We may note that the orbitofrontal cortex, being concerned especially with making explicit in the firing rate the representations of reinforcers, provides a brain region where different reinforcers can be compared by competition implemented by lateral inhibition. This is thus a brain area for the selection of a goal or affective state. If we consider areas to which the orbitofrontal cortex projects, such as the ventral striatum and quite large parts of the dorsal striatum (Haber et al., 2006), then it is likely that the rewards can be brought together with other representations, such as of behavioral responses, as part of a system involved in more than just affective value, including interfacing stimuli to responses (Rolls, 2005, 2008c).

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