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The orbitofrontal cortex and beyond: From affect to decision-making

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ABSTRACT

The orbitofrontal cortex represents the reward or affective value of primary reinforcers including taste, touch, texture, and face expression. It learns to associate other stimuli with these to produce representations of the expected reward value for visual, auditory, and abstract stimuli including monetary reward value. The orbitofrontal cortex thus plays a key role in emotion, by representing the goals for action. The learning process is stimulus-reinforcer association learning. Negative reward prediction error neurons are related to this affective learning. Activations in the orbitofrontal cortex correlate with the subjective emotional experience of affective stimuli, and damage to the orbitofrontal cortex impairs emotion-related learning, emotional behaviour, and subjective affective state. With an origin from beyond the orbitofrontal cortex, top-down attention to affect modulates orbitofrontal cortex representations, and attention to intensity modulates representations in earlier cortical areas of the physical properties of stimuli. Top-down word-level cognitive inputs can bias affective representations in the orbitofrontal cortex, providing a mechanism for cognition to influence emotion. Whereas the orbitofrontal cortex provides a representation of reward or affective value on a continuous scale, areas beyond the orbitofrontal cortex such as the medial prefrontal cortex area 10 are involved in binary decision-making when a choice must be made. For this decision-making, the orbitofrontal cortex provides a representation of each specific reward in a common currency.

Contents

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Abbreviations: BOLD, blood oxygenation level-dependent; BPD, Borderline Personality Disorder; fMRI, functional magnetic resonance imaging.

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1. Introduction

The functions of the orbitofrontal cortex and how it relates to areas to which it is connected are considered here, based on its connections, neurophysiology, activation in functional neuroimaging studies, and on the effects of damage to the orbitofrontal cortex. Activity in the orbitofrontal cortex is compared to that in the areas that project to it, and to the activity in the areas to which it projects. This enables us to develop a theme of how sensory representations in the input regions are transformed into reward-related representations in the orbitofrontal cortex important in affective value and emotion, and then to representations used to make decisions (choices) based on reward value in areas beyond the orbitofrontal cortex to which it projects. We also describe new evidence for how top-down cognitive and attentional inputs coming from beyond the orbitofrontal cortex to the orbitofrontal cortex can influence the affective representations in the orbitofrontal cortex, showing how cognition descends down into the emotional system in the brain to influence what we feel.

The focus is on humans and macaques, because there are many topological, cytoarchitectural, and probably connectional similarities between macaques and humans with respect to the orbitofrontal cortex (see Fig. 1 and Carmichael and Price, 1994; Kringelbach and Rolls, 2004; Öngür and Price, 2000; Petrides and Pandya, 1995; 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, 2007c, 2008e; 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, 2005; Rolls and Scott, 2003). To understand the functions of the orbitofrontal cortex in humans, the majority of the studies described here were therefore performed with macaques or with humans.

Evidence from the connections, effects of damage, single neuron recording, functional neuroimaging, and computational neuroscience is all necessary in order to understand cortical function, and evidence from all these approaches is included in this review. Single neuron responses are essential for understanding the nature of the representation in a cortical area, for each neuron contributes in a different way to the ensemble encoding of stimuli, with each neuron having a different profile of tuning to a subset of the stimuli to provide high capacity and good generalization (see examples in Figs. 3 and 5), and the properties of exactly what is represented (such as which aspects of taste, texture, smell, face, touch, etc. are independently represented) only being measurable by comparing the responses of single neurons (Rolls, 2008e). The use of information theory to determine what is represented by neurons about stimuli or events in the world by using the mutual information between the stimuli and the neuronal responses is a rigorous way to analyse this, as has been described elsewhere (Rolls, 2008e), and shows that most of the information in the responses of neurons in cortical areas during behaviour and with attention is carried by the number of spikes in a short interval of 20–50 ms, rather than by any stimulus-dependent synchronization or temporal encoding (Aggelopoulos et al., 2005; Rolls, 2008e: Appendix on information theory and neuronal encoding). Evidence at this neuronal level is needed to provide the basis for computational theories of brain function, which need to specify what is encoded by the computing elements of the brain between which information is exchanged, the neurons (Rolls, 2008e). Functional neuroimaging studies are valuable for allowing aspects of human brain function to be analysed, including for example some of the top-down effects of attention and cognition on sensory and reward processing that are described below.

2. Connections

Part of the background for understanding neuronal responses in the orbitofrontal cortex is the anatomical connections of the orbitofrontal cortex (Barbas, 1995; Carmichael and Price, 1994, 1995; Öngür and Price, 2000; Pandya and Yeterian, 1996; Petrides and Pandya, 1995; Price, 2006, 2007). A schematic diagram that helps to show the stage of processing in different sensory streams of the orbitofrontal cortex is provided in Fig. 2. Conceptually, the orbitofrontal cortex can be thought of as receiving from the ends of each modality-specific "what" cortical pathway.

Rolls et al. (1990) discovered a taste area with taste-responsive neurons in the lateral part of the macaque orbitofrontal cortex, and showed anatomically 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 (Critchley and Rolls, 1996c; Pritchard et al., 2005; Rolls, 2008d; Rolls and Baylis, 1994; Rolls et al., 1996a).

In the mid-orbitofrontal cortex, there is an area with olfactory neurons (Rolls and Baylis, 1994) and anatomically, there are direct connections from the primary olfactory cortex, pyriform cortex, to area 13 a of the posterior orbitofrontal cortex, which in turn has onward projections to a middle part of the orbitofrontal cortex (area 13) (Barbas, 1993; Carmichael et al., 1994; Morecraft et al., 1992; Price, 2007; Price et al., 1991) (see Fig. 1).

Thorpe et al. (1983) found neurons with visual responses in the orbitofrontal cortex, and anatomically, visual inputs reach the

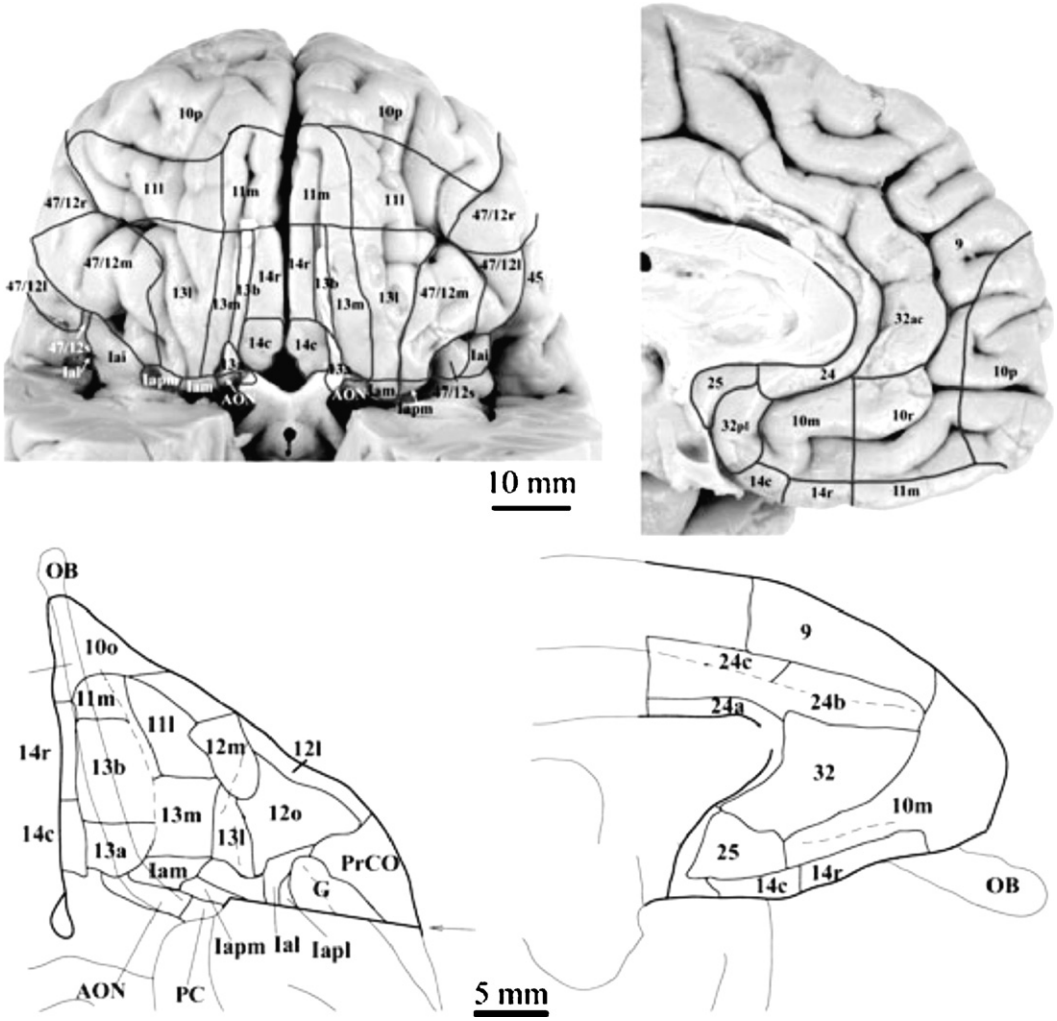

Fig. 1. Maps of architectonic areas in the orbitofrontal cortex and medial prefrontal cortex of humans (above) and monkeys (below). AON: anterior olfactory nucleus; G: primary gustatory cortex; Iai, Ial, Iam, Iapm: subdivisions of the agranular insular cortex; OB: olfactory bulb; PC: pyriform cortex; PrCO: precentral opercular area. Reproduced from Öngür et al. (2003), and Carmichael and Price (1994), reprinted from the Journal of Comparative Neurology with permission of John Wiley & Sons, Inc.

orbitofrontal cortex directly from the inferior temporal cortex (where object and face identity are represented, Rolls, 2007c, 2008e), the cortex in the superior temporal sulcus (where face expression and gesture are represented, Hasselmo et al., 1989), and the temporal pole (see Barbas, 1988, 1993, 1995; Barbas and Pandya, 1989; Carmichael and Price, 1995; Morecraft et al., 1992; Seltzer and Pandya, 1989). There are corresponding auditory inputs (Barbas, 1988, 1993; Rolls et al., 2006; Romanski and Goldman-Rakic, 2001; Romanski et al., 1999).

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, 2008e).

The orbitofrontal cortex projects back to temporal 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 (Haber et al., 2006; Kemp and Powell, 1970), 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), 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 (Johnson et al., 1968; Nauta, 1964), and these connections provide some routes via which the orbitofrontal cortex can influence behaviour (Rolls, 2005) and memory (Rolls and Xiang, 2005).

3. Effects of damage to the orbitofrontal cortex

Part of the evidence on the functions of the orbitofrontal cortex comes from the effect of lesions of the orbitofrontal cortex. Macaques with lesions of the orbitofrontal cortex are impaired at

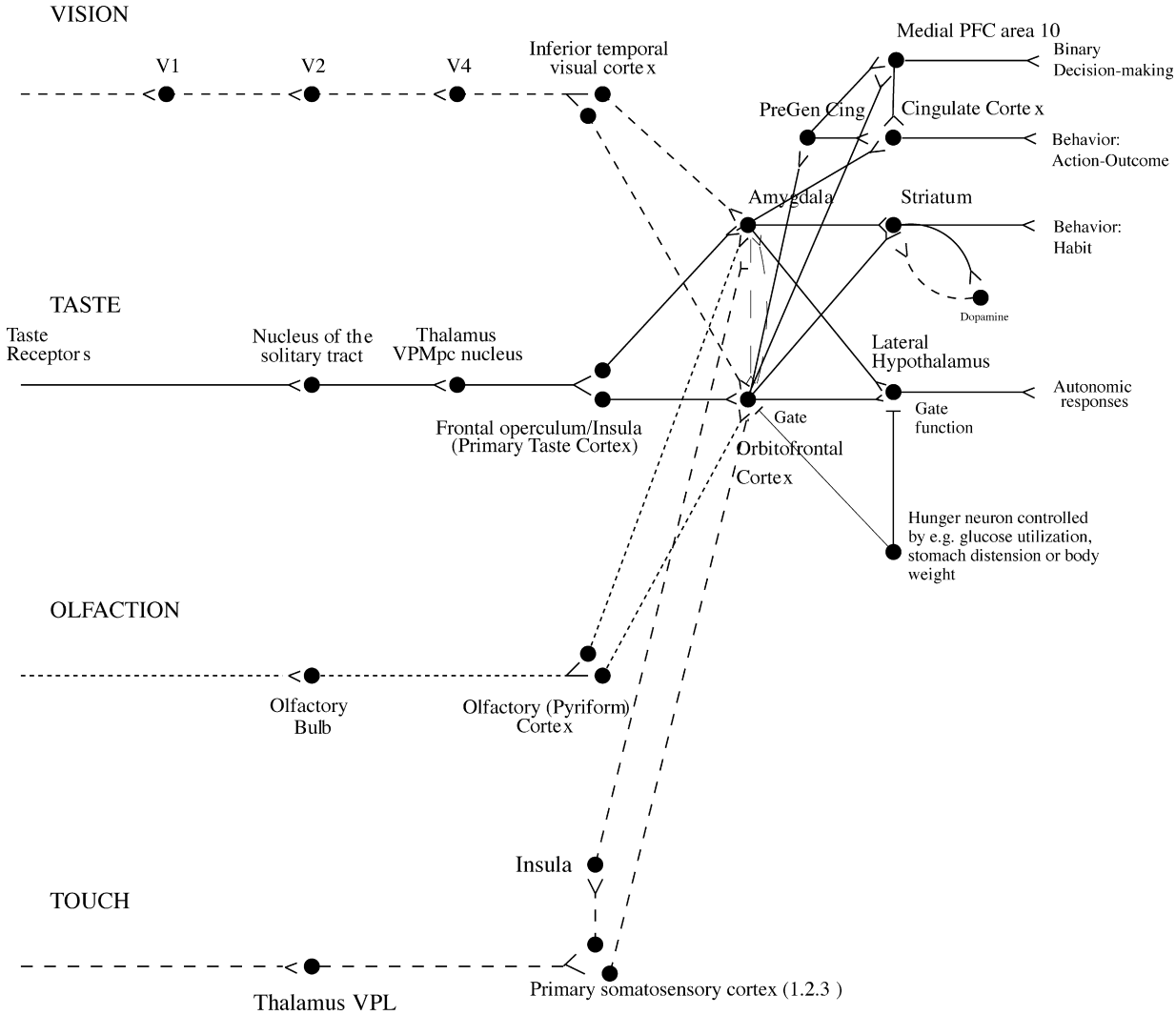

Fig. 2. Schematic diagram showing some of the gustatory, olfactory, visual and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex, and the secondary olfactory cortex, are within the orbitofrontal cortex. V1: 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, 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 which are represented in the next tier of brain regions, the orbitofrontal cortex and amygdala, and in areas beyond these.

tasks that involve learning about which stimuli are rewarding and which are not, and are especially impaired at altering behaviour 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; Izquierdo and Murray, 2004; Izquierdo et al., 2004; Jones and Mishkin, 1972; 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). When investigating the neuronal basis of stimulus-reinforcer association learning in the orbitofrontal cortex, a visual stimulus is shown, and is associated with the delivery of a sweet taste if a lick response is made (Rolls et al., 1996b; Thorpe et al., 1983). This is thus an association directly between a visual stimulus and a primary reinforcer, the taste. It would be interesting to see this measure of direct stimulus-to-primary-reinforcer association learning tested after orbitofrontal lesions in primates including humans. The rationale for this suggestion is that taste, a primary reinforcer, has a major representation in the orbitofrontal cortex, visual inputs reach the orbitofrontal cortex, and some visual neurons learn the visual-to-taste association very rapidly, in one trial. It therefore is a hypothesis that the rapid acquisition of these associations is implemented in the orbitofrontal cortex, although the amygdala is another region that could implement the acquisition, if not the rapid reversal, of these associations. However, when visual stimulus discrimination and reversal are tested, the association of the visual stimulus is not usually to the primary reinforcer, e.g., the taste, but could be to another secondary reinforcer, such as the

sound of a food dispenser, or a message stating that one has won money, and the acquisition may not be impaired by orbitofrontal cortex damage (Hornak et al., 2004; Rolls et al., 1994), though reversal is (Fellows and Farah, 2003; Hornak et al., 2004; Rolls et al., 1994). For these reasons, it would be useful to test whether the acquisition of stimulus to primary reinforcer associations is impaired by damage to the orbitofrontal cortex. Fellows and Farah (2007) did show that the choices of pictures of foods were noisy (variable) in patients with ventromedial prefrontal cortex damage, and this might reflect impairment of a system involved in learning or processing associations of stimuli with primary reinforcers such as flavor.

Damage to the caudal orbitofrontal cortex in the monkey also produces emotional changes (e.g., decreased aggression to humans and to stimuli such as a snake and a doll), and a reduced tendency to reject foods such as meat (Butter et al., 1969, 1970; Butter and Snyder, 1972; Murray and Izquierdo, 2007) or to display the normal preference ranking for different foods (Baylis and Gaffan, 1991). In humans, euphoria, irresponsibility, lack of affect, and impulsiveness can follow frontal lobe damage (Damasio, 1994; Kolb and Whishaw, 2003; Rolls, 1999a), particularly orbitofrontal damage (Berlin et al., 2004, 2005; Hornak et al., 1996, 2003; Rolls, 1999a, 2005; Rolls et al., 1994), and the human literature is considered further below. 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 (Fellows and Farah, 2003; Hornak et al., 2004; Rolls, 1999b, 2005; Rolls et al., 1994). 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).

Lesions more laterally, in for example the inferior convexity, can influence tasks in which objects must be remembered for short periods, e.g., delayed matching to sample and delayed matching to non-sample tasks (Kowalska et al., 1991; Mishkin and Manning, 1978; Passingham, 1975), and neurons in this region may help to implement this visual object short-term memory by holding the representation active during the delay period (Rao et al., 1997; Rosenkilde et al., 1981; Wilson et al., 1993). Whether this inferior convexity area is specifically involved in a short-term object memory (separately from a short-term spatial memory) is not yet clear (Rao et al., 1997; Rolls, 2008e). It should be noted that this short-term memory system for objects (which receives inputs from the temporal lobe visual cortical areas in which objects are represented) may be partly separate from the short-term memory system in the dorsolateral part of the prefrontal cortex, which is more concerned with spatial short-term memories and delayed oculomotor responses (Funahashi et al., 1989; Takeda and Funahashi, 2002), consistent with its inputs from the parietal cortex (Rolls, 2008e; Rolls and Deco, 2002).

4. Taste, olfaction, flavor, oral texture, temperature: a set of rewarding stimuli

4.1. Taste: a primary reinforcer

One of the discoveries that have helped us to understand the functions of the orbitofrontal cortex in behaviour is that it contains a major cortical representation of taste (see Kadohisa et al., 2005; Rolls, 1995, 1997; Rolls and Scott, 2003; Rolls et al., 1990) (cf. Fig. 2). 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, 2004a, 2005, 2008e). 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.

The representation (shown by analysing the responses of single neurons in macaques) of taste in the orbitofrontal cortex includes robust representations of the prototypical tastes sweet, salt, bitter and sour (Rolls et al., 1990), but also separate representations of the "taste" of water (Rolls et al., 1990), and of protein or umami as exemplified by monosodium glutamate (Baylis and Rolls, 1991; Rolls, 2000d) and inosine monophosphate (Rolls et al., 1996a, 1998). An example of an orbitofrontal cortex neuron with different responses to different taste stimuli is shown in Fig. 3b. As will be described below, some neurons have taste-only responses, and others respond to a variety of oral somatosensory stimuli, including for some neurons viscosity (Rolls et al., 2003c), fat texture (Rolls et al., 1999; Verhagen et al., 2003), and for other neurons astringency as exemplified by tannic acid (Critchley and Rolls, 1996c). There are analogous data for distributed coding in rats of oral sensory including gustatory stimuli (Simon et al., 2006).

The nature of the representation of taste in the orbitofrontal cortex is that for the majority of neurons the reward value of the

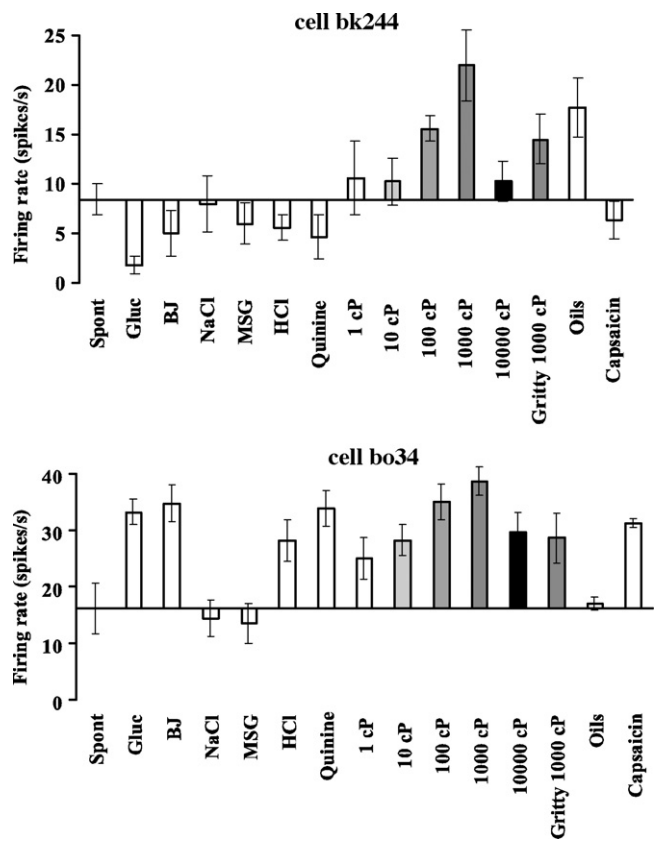

Fig. 3. Oral somatosensory and taste inputs to orbitofrontal cortex neurons. Above. Firing rates (mean ± S.E.M.) of viscosity-sensitive neuron bk244 which did not have taste responses, in that it did not respond differentially to the different taste stimuli. The firing rates are shown to the viscosity series, to the gritty stimulus (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. Below. Firing rates (mean ± S.E.M.) of viscosity-sensitive neuron bo34 which had no response to the oils (mineral oil, vegetable oil, safflower oil and coconut oil, which have viscosities which 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 (Verhagen et al., 2003).

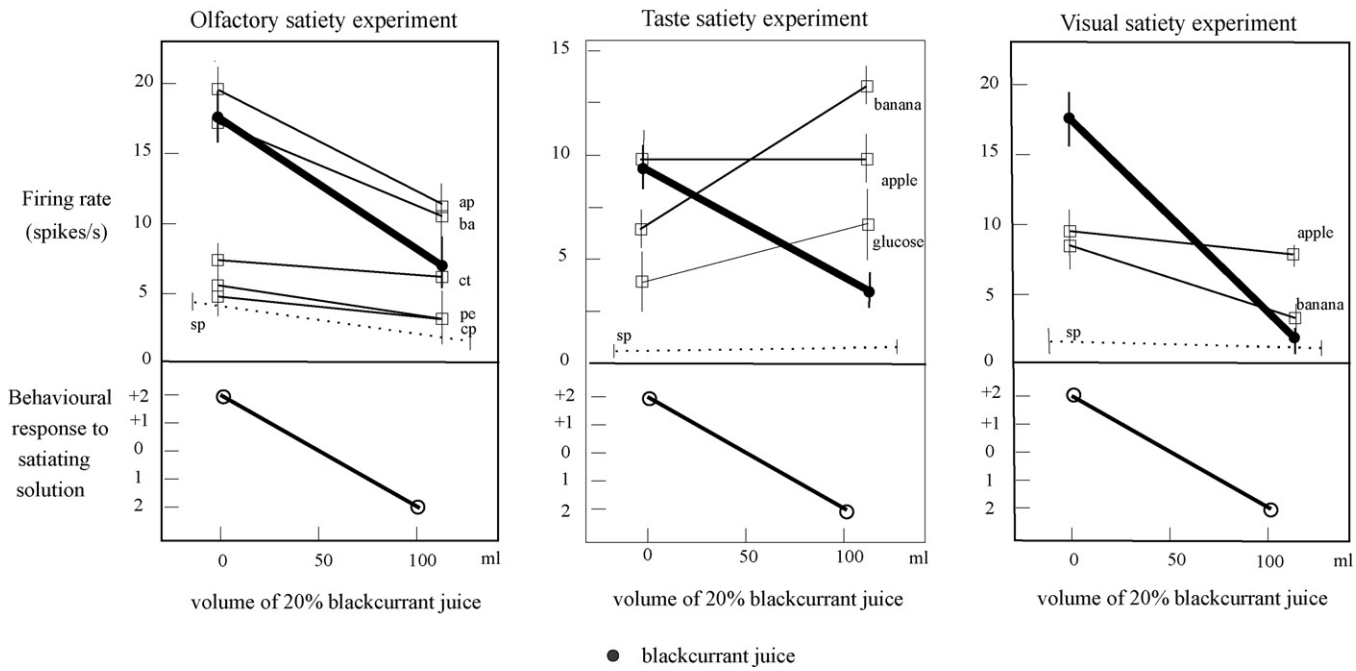

Fig. 4. Multimodal orbitofrontal cortex neuron with sensory-specific satiety-related responses to visual, taste and olfactory sensory inputs. The responses are shown before and after feeding to satiety with blackcurrant juice. The solid circles show the responses to blackcurrant juice. The olfactory 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).

taste is represented. 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., 1996a, 1989). The example shown in Fig. 4 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 relatively specific to the food eaten to satiety, and the responses of these neurons are thus very closely related to sensory-specific satiety. Moreover, this type of neuronal responsiveness shows that it is the relative preference for different stimuli that is represented by these neurons, in that the neuronal response decreases in parallel with the decrease in the acceptability or reward value of the food being eaten to satiety, but the neuronal responses remain high (or even sometimes become a little larger) to foods not eaten in the meal (see for example Fig. 4), which remain acceptable, with a high reward value. The responses of these orbitofrontal cortex neurons thus reflect the preferences of the macaque for different sensory stimuli (Critchley and Rolls, 1996a; Rolls et al., 1989), and some neurons encode relative preferences (Tremblay and Schultz, 1999). 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 primary taste cortex, the reward value of taste is not represented, and instead the identity and intensity of the taste are represented. 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., 1980b). Thus there is clear evidence that it is the reward value of taste that is represented in the orbitofrontal cortex (see further Rolls, 1999a, 2000e, 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).

The caudolateral part of the orbitofrontal cortex is secondary taste cortex, as defined anatomically (using horseradish peroxidase tracing from the site of the taste neurons) by major direct inputs from the primary taste cortex in the rostral insula and adjoining frontal operculum (Baylis et al., 1995). This region projects on to other regions in the orbitofrontal cortex (Baylis et al., 1995), and neurons with taste responses (in what can be considered as a tertiary gustatory cortical area) can be found in many regions of the orbitofrontal cortex (Rolls and Baylis, 1994; Rolls et al., 1996b, 1990). Although some taste neurons are found laterally in the orbitofrontal cortex (area 12 o) (Rolls and Baylis, 1994; Rolls et al., 1996b, 1990), others are found through the middle and even towards the medial part of the orbitofrontal cortex in areas 13 m and 13 l (see Fig. 1) (Critchley and Rolls, 1996a,c; Pritchard et al., 2005, 2007; Rolls and Baylis, 1994; Rolls et al., 1996a). Many but not all of these area 13 neurons decrease their responses to a taste with which the monkey is fed to satiety (Critchley and Rolls, 1996a,c; Pritchard et al., 2008; Rolls et al., 1996a). Sometimes neurons with flavor-related responses increase their activity a little to a flavor that has not been fed to satiety (see example in Fig. 4, Critchley and Rolls, 1996c), and correspondingly the subjective pleasantness rating may increase a little (Rolls et al., 1981b, 1982; Rolls and Rolls, 1997). (Pritchard et al., 2008 also observed increases to some stimuli as well as decreases after satiety, but there was apparently insufficient testing to allow statistics to be reported at the single neuron level.) This is probably part of a mechanism to facilitate behavioural switching between different positive reinforcers, and in the case of food, may facilitate eating a varied diet with the consequent beneficial nutritional implications, but may contribute to overeating and obesity if too much variety is available (Rolls, 2005, 2007e).

Functional neuroimaging studies have shown that the most medial part of the human orbitofrontal cortex is activated by taste, oral texture, and olfactory stimuli (de Araujo et al., 2003a; de

Araujo and Rolls, 2004; de Araujo et al., 2003c, 2005; Francis et al., 1999; Gottfried et al., 2006; McCabe and Rolls, 2007; O'Doherty et al., 2000; Rolls et al., 2003a; Rolls and McCabe, 2007; Small et al., 2001, 2005), and that the activations correlate with ratings of pleasantness (Kringelbach and Rolls, 2004; Rolls, 2005). This most medial part of the orbitofrontal cortex has been little explored in macaques, and a study has recently been performed by Rolls, Verhagen and Kadohisa (see Rolls, 2008d) to investigate how extensive the representation of taste is in the macaque orbitofrontal cortex, to help provide a foundation for understanding the functions of the medial orbitofrontal cortex in humans. Although there were few taste neurons more medial than 7 mm from the midline, there were taste neurons in the orbitofrontal cortex in regions more lateral than 7 mm from the midline, including areas 13 m and 13 l. This is consistent with previous findings in macaques that taste neurons have been shown to extend throughout area 13 in a region that is approximately 7–12 mm from the midline (Critchley and Rolls, 1996c; Rolls and Baylis, 1994; Rolls et al., 1996a), the area in which Pritchard et al. (2005) also found a population of taste neurons (see Fig. 1 with cytoarchitectonic areas indicated after Carmichael and Price, 1994; Öngür et al., 2003; Öngür and Price, 2000; Petrides and Pandya, 2001). 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 from area 13 m medially through area 12 o laterally, find similar proportions of taste neurons throughout this mediolateral extent (from 7 to 20 mm lateral) (Critchley and Rolls, 1996c; Kadohisa et al., 2004, 2005; Rolls and Baylis, 1994; Rolls et al., 1996a, 1989, 2003c, 1990; Verhagen et al., 2003). Moreover, even in area 13 m, 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, 1996c; Rolls et al., 1999); and olfactory properties (Critchley and Rolls, 1996a,b; Rolls et al., 1996c) which can become associated by learning with taste stimuli (Rolls et al., 1996b). Thus area 13 m contains taste, oral texture, and olfactory representations, some of these cells are multimodal in these modalities (Critchley and Rolls, 1996c; Rolls, 2008d; Rolls and Baylis, 1994; Rolls et al., 1996b), and many of these neurons have their responses to taste and/or olfactory stimuli modulated by hunger (Critchley and Rolls, 1996a; Pritchard et al., 2008; Rolls, 2008d).

Corresponding to the findings in non-human primate single neuron neurophysiology, in human functional neuroimaging experiments (e.g., with functional magnetic resonance imaging, fMRI), it has been shown that there is an orbitofrontal cortex area activated by sweet taste (Francis et al., 1999; Small et al., 2007; Small et al., 1999), and that there are at least partly separate areas activated by the aversive taste of saline (NaCl, 0.1 M) (O'Doherty et al., 2001b), by pleasant touch (Francis et al., 1999; Rolls et al., 2003b), and by pleasant vs. aversive olfactory stimuli (Francis et al., 1999; O'Doherty et al., 2000; Rolls, 2000e; Rolls et al., 2003a). Umami (protein) taste is not only represented by neurons in the primate orbitofrontal cortex (Baylis and Rolls, 1991; Rolls et al., 1996a), but also human fMRI studies show that umami taste is represented in the orbitofrontal cortex, with an anterior part responding supra-linearly to a combination of monosodium glutamate and inosine monophosphate (de Araujo et al., 2003a). 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 pleasantness of the taste of water in the mouth is represented in the orbitofrontal cortex (de Araujo et al., 2003b).

4.2. An olfactory representation in the orbitofrontal cortex

Takagi (1991) described single neurons in the macaque orbitofrontal cortex that were activated by odors. A ventral frontal region has been implicated in olfactory processing in humans (Jones-Gotman and Zatorre, 1988; Zatorre et al., 1992). Rolls and colleagues have analysed the rules by which orbitofrontal olfactory representations are formed and operate in primates. For 65% of neurons in the orbitofrontal olfactory areas, Critchley and Rolls (1996b) showed that the representation of the olfactory stimulus was independent of its association with taste reward (analysed in an olfactory discrimination task with taste reward). For the remaining 35% of the neurons, the odors to which a neuron responded were influenced by the taste (glucose or saline) with which the odor was associated. 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). (25% showed reversal; and 43% no longer discriminated after the reversal, so were conditional reward neurons analogous to that shown in Fig. 8 as also found in rats, Schoenbaum et al., 2007. The olfactory-to-taste reversal was quite slow, both neurophysiologically and behaviourally, often requiring 20–80 trials, consistent with the need for some stability of flavor representations. The relatively high proportion of olfactory neurons with modification of responsiveness by taste association in the set of neurons in this experiment was probably related to the fact that the neurons were pre-selected to show differential responses to the odors associated with different tastes in the olfactory discrimination task.) Thus the rule according to which the orbitofrontal olfactory representation was formed was for some neurons by association learning with taste.

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 Fig. 4). Thus for these neurons, the reward value of the odor is what is represented in the orbitofrontal cortex (cf. Rolls and Rolls, 1997). In that the neuronal responses decreased to the food with which the monkey is fed to satiety, and may even increase to a food with which the monkey has not been fed, it is the relative reward value of stimuli that is represented by these orbitofrontal cortex neurons (cf. Schultz et al., 2000), and this parallels the changes in the relative pleasantness of different foods after a food is eaten to satiety (Rolls et al., 1981a, 1981b; Rolls, 1997; see Rolls, 1999a, 2000e, 2005). We do not yet know whether this is the first stage of processing at which reward value is represented in the olfactory system in macaques (although in rodents the influence of reward association learning appears to be present in some neurons in the pyriform cortex—Schoenbaum and Eichenbaum, 1995). However, an 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).

Although individual neurons do not encode large amounts of information about which of 7–9 odors has been presented (Rolls et al., 1996c), we have shown that the information does increase linearly with the number of neurons in the sample. This ensemble encoding does result in useful amounts of information about which

odor has been presented being provided by orbitofrontal cortex olfactory neurons.

Corresponding to the findings in non-human primate single neuron neurophysiology, in human neuroimaging experiments it has been shown that there is an orbitofrontal cortex area activated by olfactory stimuli (Francis et al., 1999; Jones-Gotman and Zatorre, 1988; Zatorre et al., 1992). Moreover, the pleasantness or reward 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). Gottfried and Zald (2005) note that activations to odors in humans tend to be relatively anterior (y = 30–33 mm), but this is not discrepant from the orbitofrontal cortex areas in which olfactory neurons are recorded in macaques, which extend from area 13 forwards well into area 11, in regions that span at least 2 mm anterior to the sphenoid reference, to 12 mm anterior to the sphenoid reference (Critchley and Rolls, 1996a,b; Rolls and Baylis, 1994; Rolls et al., 1996b, 1996c).

In humans, the separate representations of pleasant and unpleasant odors appear to respond differently to hedonically complex odor mixtures that contain pleasant and unpleasant components. In brain areas such as the medial orbitofrontal cortex that represent pleasant odors, unpleasant components in the mixture were minimized and pleasant components were emphasized. In brain areas such as the mid-orbitofrontal cortex that represent unpleasant odors, unpleasant components were emphasized more (Grabenhorst et al., 2007). An implication is that the system may be able to represent simultaneously the pleasantness and unpleasantness of odor mixtures. Part of the interest of this is that interesting affective phenomena can arise with odor mixtures. For example, though musk and indole are unpleasant on their own, their presence in a complex mixture may not be unpleasant, and indeed may enhance the pleasantness (Grabenhorst et al., 2007). Moreover, the separate and simultaneous representations of the positive and negative hedonic value of a complex affective stimulus may be important for affective decision-making in the brain, in that separate representations of different affective components of the same sensory stimulus may provide the inputs for making a decision about whether to choose the stimulus or not.

4.3. Convergence of taste and olfactory inputs in the orbitofrontal cortex: the representation of flavor

In these further parts of 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. Fig. 5). It is probably here in the orbitofrontal cortex of primates including humans that these two modalities converge to produce the representation of flavor (de Araujo et al., 2003c; Rolls and Baylis, 1994), 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). Evidence will soon be described that indicates that these representations are built by olfactory-gustatory association learning, an example of stimulus-reinforcer association learning.

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; Maruyama et al., 2006; Zhao et al., 2003). However, glutamate presented 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 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

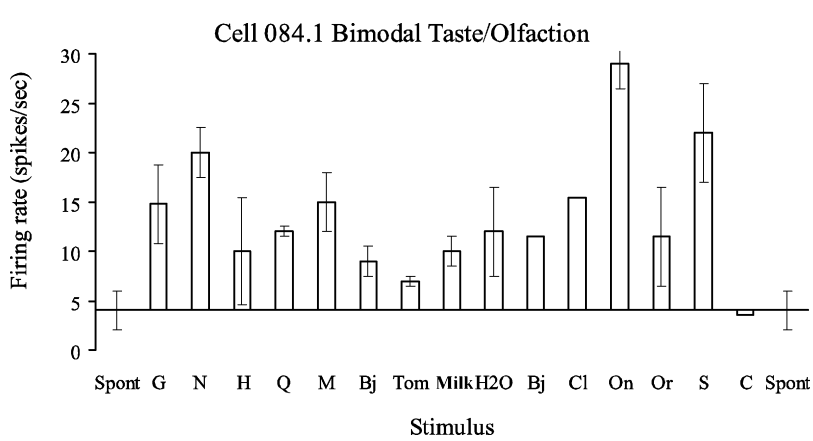

Fig. 5. The responses of a bimodal single neuron with taste and olfactory responses recorded in the caudolateral orbitofrontal cortex. G, 1 M glucose; N, 0.1 M NaCl; H, 0.01 M HCl; Q, 0.001 M quinine HCl; M, 0.1 M monosodium glutamate; Bj, 20% blackcurrant juice; Tom, tomato juice; B, banana odor; Cl, clove oil odor; On, onion odor; Or, orange odor; S, salmon odor; C, control no-odor presentation. The mean responses ± S.E.M. 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).

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).

4.4. Oral texture and temperature

Some neurons in the macaque orbitofrontal cortex respond to the texture of food in the mouth. Some neurons alter their responses when the texture of a food is modified by adding gelatine or methyl cellulose, or by partially liquefying a solid food such as apple (Critchley et al., 1993).

Another 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 ($Si(CH_3)_2O)_n$). 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, 2000e, 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).

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 cP), we have shown that some orbitofrontal cortex neurons encode fat texture independently of viscosity (by 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). The ensemble (i.e. population, distributed) encoding of all these variables is illustrated by the different tuning to the set of stimuli of the two neurons shown in Fig. 3.

An overlapping population of orbitofrontal cortex neurons represents the temperature of what is in the mouth (Kadohisa et al., 2004). These single neuron recording studies thus provide clear evidence on the rich sensory representation of oral stimuli, and of their reward value, that is provided in the primate orbitofrontal cortex, and how this differs from what is represented in the primary taste cortex and in the amygdala (Kadohisa et al., 2005). 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). Also, in humans, there is a representation of the temperature of what is in the mouth (Guest et al., 2007). The oral temperature stimuli (cooled and warmed, 5, 20 and 50 °C) activated the insular taste cortex (identified by glucose taste stimuli), a part of the somatosensory cortex, the orbitofrontal cortex, the anterior cingulate cortex, and the ventral striatum. Brain regions where activations correlated with the pleasantness ratings of the oral temperature stimuli included the orbitofrontal cortex and pregenual cingulate cortex. Part of the advantage of having a representation of oral temperature in these regions is that neurons can then encode combinations of taste, texture and oral temperature (Kadohisa et al., 2004; Verhagen et al., 2004). These combination-responsive neurons may provide the basis for particular combinations of temperature, taste, texture and odor to be especially pleasant (Rolls et al., 1980a; Rolls, 2005); for sensory-specific satiety to apply to that combination but not necessarily to the components; and more generally for learning and perception to apply to that combination and not necessarily to the components (Rolls, 2008e).

5. 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).

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).

Warm and cold stimuli have affective components such as feeling pleasant or unpleasant, and these components may have survival value, for approach to warmth and avoidance of cold may be reinforcers or goals for action built into us during evolution to direct our behaviour to stimuli that are appropriate for survival. Understanding the brain processing that underlies these prototypical reinforcers provides a direct approach to understanding the brain mechanisms of emotion. In an fMRI investigation in humans, it was found that the mid-orbitofrontal and pregenual cingulate cortex and 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) (see Fig. 6a–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 (see Fig. 6d–f).

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; Grabenhorst et al., 2007; Rolls et al., 2003a), and the finding with such prototypical stimuli as warm and cold (Rolls et al., 2008b) provides strong support for this principle.

6. Visual inputs to the orbitofrontal cortex, visual stimulus-reinforcement association learning and reversal, and negative reward prediction error neurons

We have been able to show that there is a major visual input to many neurons in the orbitofrontal cortex, and that what is

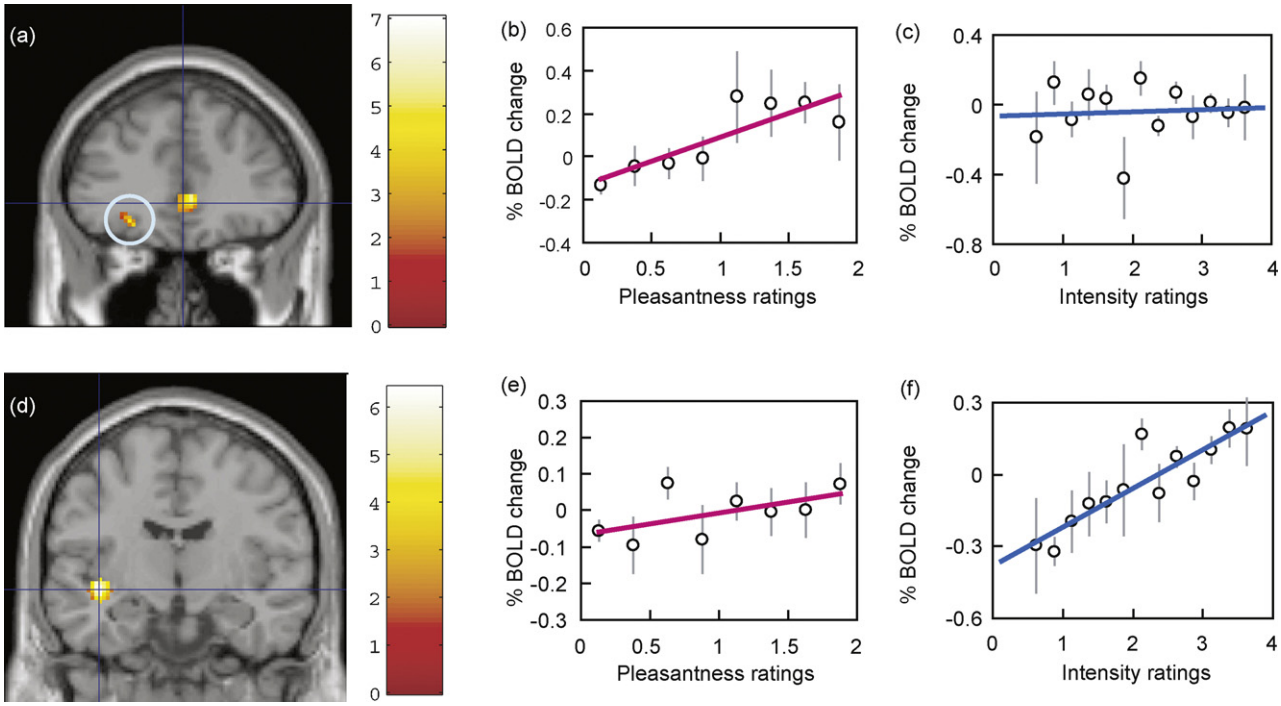

Fig. 6. Representation of the pleasantness but not intensity of thermal stimuli in the orbitofrontal cortex (top), and of the intensity but not the pleasantness in the mid-ventral (somatosensory) insular cortex (bottom). (a) SPM analysis showing a correlation in the mid-orbitofrontal cortex (blue circle) at [−26, 38, −10] between the BOLD signal and the pleasantness ratings of four 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 four 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., 2008b).

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, 2007c, 2008c,e; 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, 2008e; 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 (Rolls et al., 1996b; Thorpe et al., 1983). 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 (see example in Fig. 7). (In a visual discrimination task, they will reverse the stimulus to which they respond, from e.g., a triangle to a square, in one trial when the taste delivered for a behavioural 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 (Rolls and Baylis, 1994; Rolls et al., 1996b; Thorpe et al., 1983).

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, 2005, 2008e; Rolls and Deco, 2002; Rolls and Treves, 1998) (see below Section 13 and Fig. 13). When the reinforcement association of a visual stimulus is reversed, other 'conditional reward' orbitofrontal cortex neurons stop responding, or stop responding differentially, to the visual discriminanda (Thorpe et al., 1983). An example is a neuron in the orbitofrontal cortex that responded to a blue stimulus when it was rewarded (blue S+) and not to a green stimulus when it was associated with aversive saline (green S−). However, the neuron did not respond after reversal to the blue S− or to the green S+ (see Fig. 8). Similar conditional reward neurons are found not only for visual but also for olfactory stimuli (Rolls et al., 1996b). Such conditional reward neurons convey information about the current reinforcement status of particular stimuli. They may be part of a system that can implement very rapid reversal, by being biased on by rule neurons if that stimulus is currently associated with reward, and being biased off if that stimulus is currently not associated with reward (Deco and Rolls, 2005c), as described in Section 13. This theory provides an account of the utility of conditional reward neurons.

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 (Rolls et al., 1996b; Thorpe et al., 1983). So do the conditional reward neurons (Rolls et al., 1996b; Thorpe et al., 1983). Olfactory reward expectation and conditional reward neurons have also been found in rats in a region that may correspond to the orbitofrontal cortex, and some of these neurons can start to respond after a delay period as the expected taste becomes closer in time (Roesch and Schoenbaum, 2006). In primates the orbitofrontal cortex neurons that change their

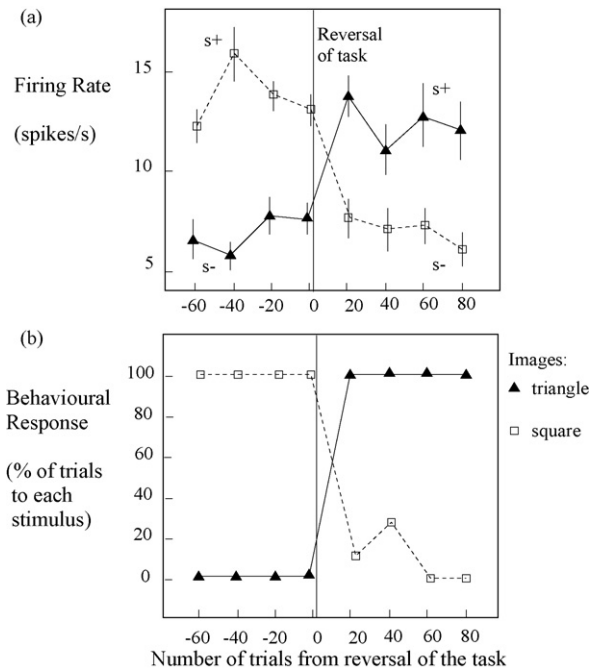

Fig. 7. Visual discrimination reversal of the responses of a single neuron in the macaque orbitofrontal cortex when the taste with which the two visual stimuli (a triangle and a square) were associated was reversed. Each point is the mean poststimulus firing rate measured in a 0.5 s period over approximately 10 trials to each of the stimuli. Before reversal, the neuron fired most to the square when it indicated (S+) that the monkey could lick to obtain a taste of glucose. After reversal, the neuron responded most to the triangle when it indicated that the monkey could lick to obtain glucose. The response was low to the stimuli when they indicated (S−) that if the monkey licked then aversive saline would be obtained. (B) shows the behavioural response to the triangle and the square, and indicates that the monkey reversed rapidly (after Rolls et al., 1996b).

responses during olfactory to taste reversal learning do so sufficiently rapidly to play a role in the behavioural change (Rolls et al., 1996b), but in rodents it has been suggested that the amygdala may be more important in reflecting the changing association (Schoenbaum et al., 2007). However, the situation is clear in the case of visual-taste association learning and reversal in primates, in which the orbitofrontal cortex neurons and the behaviour can change in one trial (Rolls et al., 1996b; Thorpe et al., 1983), so that the changing responses of the orbitofrontal cortex neurons can contribute to the reversed behaviour, a view of course supported by the impaired reversal learning produced in primates

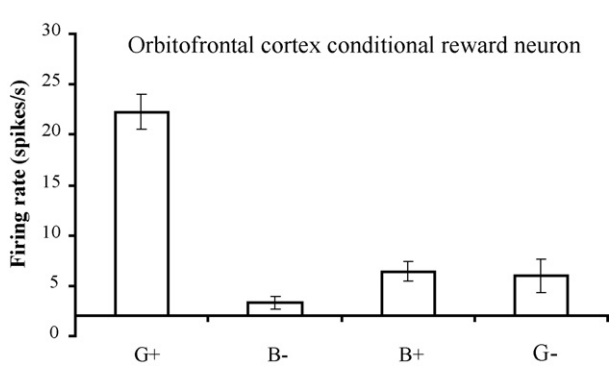

Fig. 8. A conditional reward neuron recorded in the orbitofrontal cortex by Thorpe et al. (1983) in a visual discrimination task which responded only to the Green stimulus when it was associated with reward (G+), and not to the Blue stimulus when it was associated with reward (B+), or to either stimuli when they were associated with a punisher, the taste of salt (G− and B−).

including humans by orbitofrontal cortex damage (e.g., Fellows and Farah, 2003; Hornak et al., 2004; Rolls et al., 1994). Indeed, in primates, visual-to-taste reversal is so rapid that after a punishment has been received to the negative discriminative stimulus (S−), the next time that the previous S− is shown, the neurons respond to it as an S+, and the monkey responds (Rolls et al., 1996b; Thorpe et al., 1983). This is a non-associative process that involves a rule change, and this is a special contribution that the primate orbitofrontal cortex makes to reversal learning, and for which a computational theory that utilizes the conditional reward and error neurons has been produced (Deco and Rolls, 2005c) that is described in Section 13 and Fig. 14. 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 (Paton et al., 2006; Sanghera et al., 1979), and so the amygdala appears to make a less important contribution than the orbitofrontal cortex. This is in line with the hypothesis that the orbitofrontal cortex, as a cortical area vs. the subcortical amygdala, becomes relatively more important in primates including humans than in rodents (Rolls, 2005). This is based not only on the neurophysiology described here, but also on the relative development in primates including humans vs. rodents of the orbitofrontal cortex vs. amygdala, and the more severe effects of damage to the primate including human orbitofrontal cortex than amygdala referred to elsewhere in this paper. The computational basis for the hypothesis is that because of the well-developed recurrent collateral excitatory connections of cortical areas, the orbitofrontal cortex can make especial contributions by its attractor dynamics when states must be remembered, as in rule-based reversal, and also in other operations where a short-term memory can facilitate reward-based processing, as described in Section 13. Indeed, attractor networks in cortical areas such as the orbitofrontal cortex and anterior cingulate cortex may contribute to the persistence of mood states, which is an adaptive function with respect to emotion in that for example after non-reward, the persistence of the state will keep behaviour directed towards obtaining the goal. Cortical areas such as the orbitofrontal cortex may make a special contribution to the adaptive persistence of emotional states because of their attractor properties implemented by the local recurrent collaterals (Rolls, 2005, 2008e), as considered further in Section 13.

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 Fig. 4). Thus for these neurons, the reward value of the sight of food is what is represented in the orbitofrontal cortex. In that the neuronal responses decreased to the food with which the monkey is fed to satiety, and may even increase to a food with which the monkey has not been fed, it is the relative reward value of stimuli that is represented by these orbitofrontal cortex neurons. At a stage of visual processing one synapse earlier, in the inferior temporal visual cortex, neurons do not show visual discrimination reversal learning, nor are their responses modulated by feeding to satiety (Rolls et al., 1977). Thus both these functions are implemented for visual processing in the orbitofrontal cortex.

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) (see Fig. 9 and Table 1, visual discrimination reversal), or when reward is no longer made

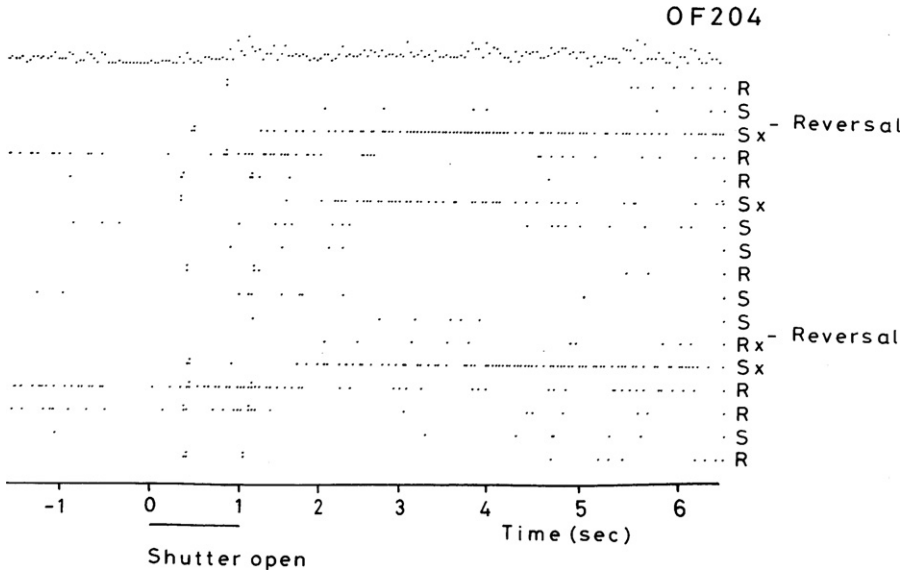

Fig. 9. Error neuron: responses of an orbitofrontal cortex neuron that responded only when the monkey licked to a visual stimulus during reversal, expecting to obtain fruit juice reward, but actually obtaining the taste of aversive saline because it was the first trial of reversal. Each single dot represents an action potential; each vertically arranged double dot represents a lick response. The visual stimulus was shown at time 0 for 1 s. The neuron did not respond on most reward (R) or saline (S) trials, but did respond on the trials marked x, which were the first trials after a reversal of the visual discrimination on which the monkey licked to obtain reward, but actually obtained saline because the task had been reversed (after Thorpe et al., 1983).

available in a visual discrimination task (Table 1, visual discrimination extinction). These may be called "negative reward prediction error neurons". Different populations of such neurons respond to other types of non-reward, including the removal of a formerly approaching taste reward (removal in Table 1), and the termination of a taste reward in the extinction of ad lib licking for juice (see Table 1), or the substitution of juice reward by aversive tasting saline during ad lib licking (Table 1, ad lib licking reversal) (Thorpe et al., 1983). The presence of these neurons is fully consistent with the hypothesis that they are part of the mechanism by which the orbitofrontal cortex enables very rapid reversal of behaviour by stimulus-reinforcement association relearning when the association of stimuli with reinforcers is altered or reversed (see Deco and Rolls, 2005c; Rolls, 1986b, 1990). The finding that different orbitofrontal cortex neurons respond to different types of non-reward (or negative reward prediction error) (Thorpe et al., 1983) may provide part of the brain's mechanism that enables task or context-specific reversal to occur.

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

Table 1
Different types of non-reward to which orbitofrontal cortex neurons respond

		D 90	D 127	D 153	D 154	D 195	D 204	D 262	F 466	B 24	B 7B	B 37B	B 57B	D 44A	D 48A	D 20	D 40	D 61	D 66
Visual discrimination	Reversal	1	0	1	0	0	1	1	0						0				
Visual discrimination	Extinction	1																	
Ad lib licking	Reversal	1	1		0	0	0		0	1									
Ad lib licking	Extinction	0	0		0	0	0		0	1									
Taste of saline		0		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Removal		0		0	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1
Visual arousal		1		1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0

Tasks (rows) (see text) in which individual neurons (columns) responded (1), did not respond (0), or were not tested (blank), after Thorpe et al. (1983).

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, the expected reward, and the reward outcome obtained, so even this 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 (see Fig. 2). 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., 2008e). 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 (Rolls, 2008e; Rolls et al., 1996b, 2008e; Thorpe et al., 1983). 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 use 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, 2008e).

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 behavioural 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 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 (Matsumoto et al., 2007; Rushworth and Behrens, 2008; Rushworth et al., 2004; Vogt, 2008).

7. Face-selective processing in the orbitofrontal cortex

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, 1992, 1996, 2000a, 2007c, 2008c,e; 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 (see Fig. 2). 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 utilising 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 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 behaviour 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 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 behaviour (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 behavioural 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 behavioural 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).

8. Top-down effects of cognition and attention on taste, olfactory, flavor, somatosensory, and visual processing: cognitive enhancement of the value of affective stimuli

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, or do cognitive influences descend down to influence the first regions that represent the affective value of stimuli?

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, 2007d,e). 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) (see Fig. 10). 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 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 moisturising 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 back projections 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 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 (Fig. 11a–c). When the subjects were instructed to remember and rate the intensity, activations were greater in the insular taste cortex (Fig. 11d–f). (Consistent with this role in representing what taste may be present independently of its affective value, trying to detect the presence of taste in a tasteless solution resulted in enhanced activity in the taste insula and overlying operculum but not the orbitofrontal cortex, Veldhuizen et al., 2007). For comparison, the orbitofrontal cortex responded preferentially during receipt of an unpredicted taste stimulus (Veldhuizen et al., 2007), and this could be related to emotional effects, or to novelty which as described in Section 11 is represented in the orbitofrontal cortex. 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

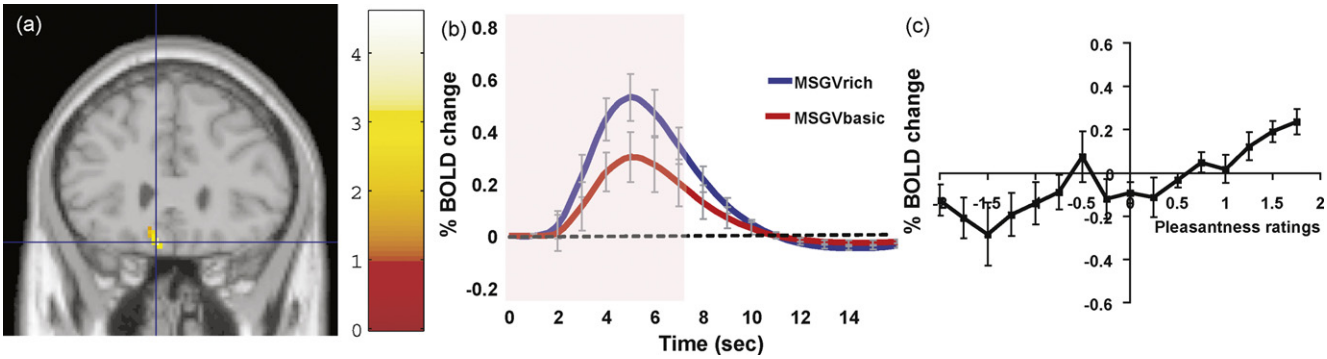

Fig. 10. Cognitive modulation of affective representations in the medial orbitofrontal cortex. (a) The medial orbitofrontal cortex was more strongly activated when the flavor stimulus was labelled 'rich and delicious flavor' (MSGVrich) than when it was labelled 'boiled vegetable water' (MSGVbasic) [−8, 28, −20]. (b) The timecourse of the BOLD signals for the two conditions. The means across subjects ± S.E.M. 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 ± S.E.M., $r = 0.86$, $p < 0.001$) (after Grabenhorst et al., 2008a).

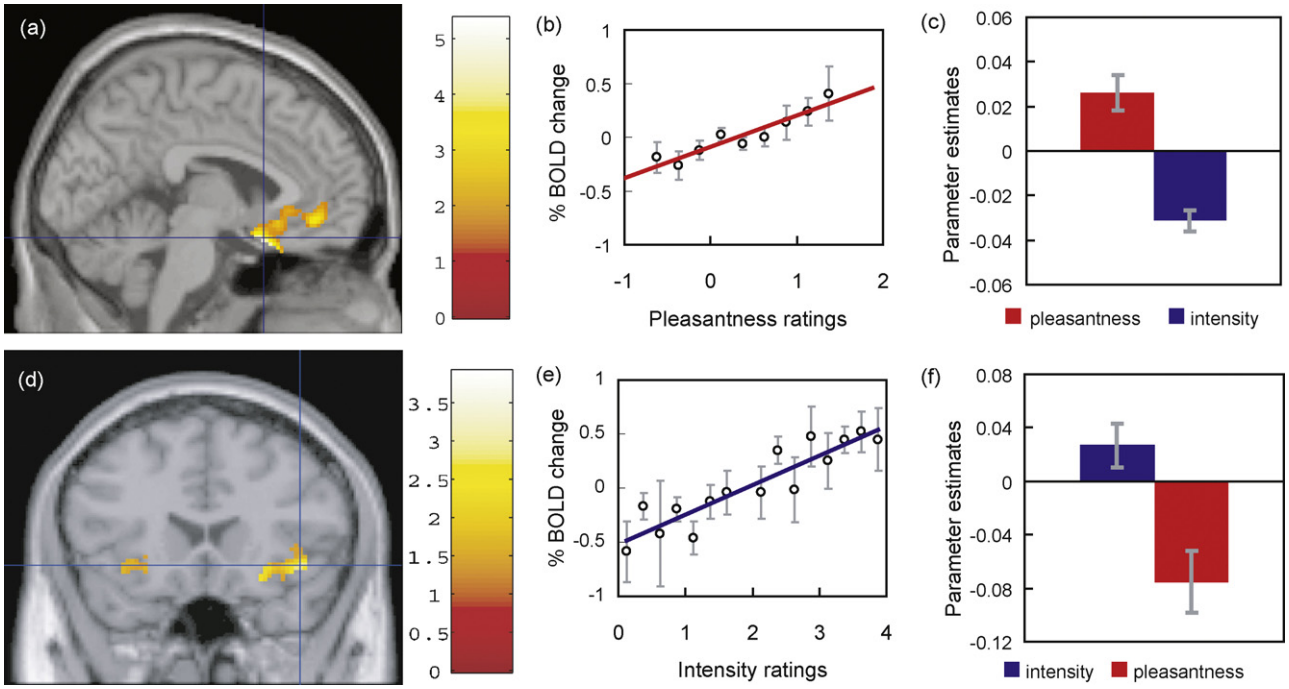

Fig. 11. Effects of attention to the pleasantness vs. the intensity of a taste stimulus (0.1 M monosodium glutamate, which was identical on all trials). Top: the contrast paying attention to pleasantness, paying attention to intensity. (a) A significant difference was found in the medial orbitofrontal 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 ± S.E.M. 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 ± S.E.M. 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).

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.

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; Grabenhorst et al., 2007; Rolls et al., 2003a) 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; Grabenhorst and Rolls, 2008; Grabenhorst et al., 2007, 2008a; Rolls et al., 2003a). This is computationally appropriate in top-down biased competition models of attention (Deco and Rolls, 2005a; Rolls, 2008e; Rolls and Deco, 2002). However, we note that in one study a cognitive label that increased the pleasantness of an odor did have some effect in primary olfactory areas such as the olfactory tubercle, though in that study the general principle was still evident, that odors independently of their pleasantness have strong effects on the primary olfactory areas, whereas pleasantness vs. unpleasantness are selectively (and separately) represented in areas such as the orbitofrontal cortex (de Araujo et al., 2005).

The mechanisms that underlie these top-down attentional and cognitive effects include top-down biased competition of the bottom-up (sensory) effects, and are now starting to be elucidated computationally (Deco and Rolls, 2005b; Desimone and Duncan, 1995; Rolls, 2008e, 2008f; Rolls and Deco, 2002).

9. Emotion and the orbitofrontal cortex

From earlier approaches (Gray, 1975; Millenson, 1967; Weiskrantz, 1968), Rolls has developed the theory over a series of stages that emotions are states elicited by instrumental reinforcers[1] (Rolls, 1986a,b, 1990, 1999a, 1999b, 2000c, 2005). Given that the evidence described above indicates that primary (unlearned) reinforcers, such as taste, touch, oral texture, are made explicit in the representations in the orbitofrontal cortex, there is a basis for understanding part of the role of the orbitofrontal cortex in emotion. (By made explicit, we mean that the firing rate of the neurons is related to what is being represented, Rolls, 2008e, for example the reward value of taste by a neuron that responds to sweet taste only when hunger is present and there is an appetite for the taste.)

Further, the evidence described above indicates that associations between previously neutral stimuli such as a visual stimulus with primary reinforcers are formed and rapidly reversed in the orbitofrontal cortex, and thus the orbitofrontal cortex is likely because of this to have important functions in emotions that are produced by these secondary (learned) reinforcers. For example, the ability to perform this learning very rapidly is probably very important in social situations in primates, in which reinforcing stimuli are continually being exchanged, and the reinforcement value of stimuli must be continually updated (relearned), based on the actual reinforcers received and given. This type of learning also allows the stimuli or events that give rise to emotions and are represented in the orbitofrontal cortex to be quite abstract and general, including for example working for 'points' or for monetary reward, as shown by visual discrimination reversal deficits in patients with orbitofrontal cortex lesions working for these rewards (Berlin et al., 2004; Fellows, 2007; Fellows and Farah, 2003, 2005; Hornak et al., 2004; Rolls et al., 1994), and activation of different parts of the human orbitofrontal cortex by monetary gain vs. loss (O'Doherty et al., 2001a), and other reinforcers (Kringelbach and Rolls, 2004).

The evidence from the effects of lesions to the orbitofrontal cortex indicates that there are close links between representing reinforcers, rapidly changing learned associations to reinforcers, and emotion including subjective emotional states. For example patients with damage to the orbitofrontal cortex may be impaired at decoding face and voice expression (which are social reinforcers) (Hornak et al., 1996, 2003; Rolls, 1999b), in reversing stimulus-reward associations (Berlin et al., 2004; Fellows, 2007; Fellows and Farah, 2003, 2005; Hornak et al., 2004; Rolls et al., 1994), and in emotional behaviour and subjective emotional states (Hornak et al., 2003; Rolls et al., 1994). To provide more detail, patients with discrete surgical lesions producing bilateral orbitofrontal cortex damage who were impaired at the visual discrimination reversal task had high scores on parts of a Social Behaviour Questionnaire in which the patients were rated on behaviours such as emotion recognition in others (e.g., their sad, angry, or disgusted mood); in interpersonal relationships (such as not caring what others think, and not being close to the family); emotional empathy (e.g., when others are happy, is not happy for them); interpersonal relationships (e.g., does not care what others think, and is not close to his family); public behaviour (is uncooperative); antisocial behaviour (is critical of and impatient with others); impulsivity (does things without thinking); and sociability (is not sociable, and has difficulty making or maintaining close relationships) (Hornak et al., 2003), all of which could reflect less behavioural sensitivity to different types of punishment and reward. Further, in a Subjective Emotional Change Questionnaire in which the patients reported on any changes in the intensity and/or frequency of their own experience of emotions, the bilateral orbitofrontal cortex lesion patients with deficits in the visual discrimination reversal task reported a number of changes, including changes in sadness, anger, fear and happiness (Hornak et al., 2003). Further evidence on these close links (Hornak et al., 1996; Rolls, 2008e; Rolls et al., 1994) provides further support for the theory that because the orbitofrontal cortex decodes and represents reinforcers, and updates the representations by rapid learning, it is an important brain region for emotion.

The changes in emotion produced by damage to the orbitofrontal cortex are large, as the evidence described above shows. The 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 produce major changes in emotion that are readily apparent in everyday behaviour (Phelps and LeDoux, 2005; Rolls, 2008e; Seymour and Dolan, 2008). A comparison of the roles of the amygdala and orbitofrontal cortex in emotion is provided elsewhere (Rolls, 2005).

To help clarify some of the fundamental ways in which emotion is linked to instrumental reinforcers, but not to all properties of stimuli that happen to be rewards or punishers, and as a guide to further research, it is useful to specify some important points about Rolls' theory of emotion (Rolls, 2005).

First, the theory specifies that it is instrumental reinforcers, which specify the goals for action, that produce emotions. The theory is set in an evolutionary, Darwinian context, for it holds that the specification by genes of a set of primary reinforcers (such as sweet taste when hungry, affiliative touch, pain, attachment, altruism) is an efficient way for genes to direct adaptive behaviour, and is much more efficient than specifying actions (such as climbing a tree when an apple is seen, reaching for the apple, and putting it in the mouth). By specifying the goals for action, the process allows the actual behaviour required to obtain the goal to be learned, providing great flexibility in the actions. The actual emotion that is produced by the reinforcer depends on the contingency (delivery of a reward or punisher; omission or termination of a reward or punisher); on the primary reinforcer; and on the particular secondary reinforcer (Rolls, 2005). The point made here is that it is by virtue of being a goal for action that instrumental reinforcers produce emotions. A stimulus that happens to be an instrumental reinforcer may be able to produce many other effects, and disrupting these other effects might not alter emotions. This is important when interpreting the effects of brain damage on emotion and reinforcers: it is only the goal-related aspect of the reinforcing stimulus that the theory holds is closely related to emotion (Rolls, 2005). An example comes from considering autonomic responses. An instrumental reinforcer such as sweet taste when hungry will produce autonomic responses such as salivation (and these can be classically conditioned). But the mechanisms and brain's circuitry for producing salivation, and more generally for classical (Pavlovian) conditioning (see Section 3 of Rolls, 2008e), may be quite different from the circuitry involved in specifying a stimulus as a goal for action, and performing action-outcome instrumental learning (where outcome refers to whether the reinforcer, the goal for action, is received). (This highlights how different Rolls' theory of emotion (Rolls, 2005) is to that of Damasio (1994), who argues that emotions are related to autonomic feedback, and his theory is not based on the concept of emotions as

[1] For the purposes of this paper, 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 (see further Rolls, 2005a).

being states elicited by instrumental reinforcers.) Evidence that autonomic effects are not required for emotions (Rolls, 2005) includes findings that patients with peripheral autonomic failure do not suffer from disrupted emotions (Heims et al., 2004).

Reinforcing stimuli may produce many other effects (Rolls, 2005, 2008e), including informational in which they may not be acting as a goal for an action (Murray and Izquierdo, 2007), Pavlovian Instrumental Transfer in which a classically conditioned stimulus may enhance instrumental behaviour (Cardinal et al., 2002), incentive effects in which reward devaluation outside the instrumental task may not immediately influence the goal value with respect to instrumental actions (Balleine and Dickinson, 1998), etc. (Cardinal et al., 2002), and these will only be related to emotion in so far as they influence the goal-related aspects of the stimulus for instrumental behaviour. In summary, we would expect a close link between the goal-related aspects of the reinforcing stimulus and emotion, but not necessarily between other effects produced by stimuli that happen to be instrumental reinforcers, or produce classically conditioned effects (see Section 3 of Rolls, 2005, 2008e). It is important to appreciate this when assessing whether there are in fact any dissociations between brain mechanisms involved in emotion and brain mechanisms that are involved in instrumental learning where the stimulus acts as a goal for action as in action-outcome learning (cf. Murray and Izquierdo, 2007). In so far as classical (Pavlovian) conditioning can influence instrumental actions, for example in some of the ways described above, then this type of learning can play a role in emotion, and indeed the amygdala has been implicated in some of these classically conditioned effects on emotion (Cardinal et al., 2002; Rolls, 2005; Seymour and Dolan, 2008). Further, in so far as stimulus-reinforcer association learning (also known as stimulus-outcome learning, where the outcome is the reinforcer) is essential for defining the goals for action when the stimulus is associated by learning with a reinforcer, then this is very important in emotion, and neurons in the orbitofrontal cortex learn this type of association, and can reverse it rapidly, and this is a fundamental role that the orbitofrontal cortex plays in emotion. The use of these goals identified by associative learning for association with action to implement action-outcome learning is a process that we identify in this review as taking place beyond the orbitofrontal cortex, in structures to which it projects such as the anterior cingulate cortex.

To make the point in everyday language, Rolls' theory (2005) holds that emotions are states elicited by goals (which are reinforcers). Does not this resonate with common understanding of emotions? Do we not have emotions when we attain our goals; and if we do not?

We may note that it is not an improvement to the theory to hold that the goal for which the animal or human works is the emotional state, for this does not provide an answer, but immediately leads to the questions: What is it that accounts for these emotional states? Why and how are emotions related to goals for action? How are emotional states selected for in evolution so that they are produced by something in the environment? That approach would not provide an explanation, but would just raise questions. It is much clearer to hold that instrumental reinforcers are selected in evolution to be the goals for action because they are a way for genes to specify useful goals in terms of survival value; and then to note that the states elicited by these instrumental reinforcers are emotional states (Rolls, 2005). Unless exceptions are found to this rule (that instrumental reinforcers in their goal-related effects produce emotional states, and that emotional states are produced by instrumental reinforcers in their goal-related effects), then this seems a powerful account of emotions (Rolls, 2005).

Second, action-outcome learning, not habit learning, even though the latter is instrumental, is what the theory holds is related to emotion (Rolls, 2005). If a rewarded behaviour is performed for a large number of trials, it becomes a habit and may be implemented by stimulus-response associations that are formed in brain regions such as the basal ganglia (Rolls, 2005). After such overlearning, the behaviour may be performed rather automatically and calmly, without much emotion, as in a well-learned active avoidance task. It is therefore argued that instrumental behaviour when performed in this automated way by a 'habit' system does not require the type of processing that is related to emotion. On the other hand, while the instrumental behaviour is being learned, associations are being formed between actions and outcomes, and the outcomes are being tested to see whether they meet the goals. Thus in action-outcome learning the goals are being explicitly processed and are instrumental reinforcers, and are being met or not, and it is in these conditions of goal-related events that the theory holds that emotions arise (Rolls, 2005).

Third, the instrumental reinforcer and the emotion correspond. If a food reward is not given, the emotional state will be different from when a social reinforcer is not given, or when a monetary reward is not given (Rolls, 2005). As there is some dissociation between brain systems involved in processing different instrumental reinforcers, the prediction is that a particular emotion will only be impaired if the relevant brain system involved in representing the goals or instrumental reinforcers involved in that particular emotion are impaired. It would of course be necessary to test cases where this correspondence of instrumental reinforcer and the emotion being measured applies in order to test whether instrumental reinforcers are linked to emotional states. It would be important to consider this when assessing the effects of lesions on emotion (cf. Murray and Izquierdo, 2007).

10. Individual differences in emotion, and the orbitofrontal cortex

Given that there are individual differences in emotion, can these individual differences be related to the functioning of brain systems involved in affective behaviour such as the orbitofrontal and pregenual cingulate cortex?

Some individuals, chocolate cravers, report that they crave chocolate more than non-cravers, and this is associated with increased liking of chocolate, increased wanting of chocolate, and eating chocolate more frequently than non-cravers (Rodriguez et al., 2007). In a test of whether these individual differences are reflected in the affective systems in the orbitofrontal cortex and pregenual cingulate cortex that are the subject of this paper, Rolls and McCabe (2007) used fMRI to measure the response to the flavor of chocolate, to the sight of chocolate, and to their combination, in chocolate cravers vs. non-cravers. SPM analyses showed that the sight of chocolate produced more activation in chocolate cravers than non-cravers in the medial orbitofrontal cortex and ventral striatum. For cravers vs. non-cravers, a combination of a picture of chocolate with chocolate in the mouth produced a greater effect than the sum of the components (i.e. supra-linearity) in the medial orbitofrontal cortex and pregenual cingulate cortex. Furthermore, the pleasantness ratings of the chocolate and chocolate-related stimuli had higher positive correlations with the fMRI BOLD signals in the pregenual cingulate cortex and medial orbitofrontal cortex in the cravers than in the non-cravers. Thus there were differences between cravers and non-cravers in their responses to the sensory components of a craved food in the orbitofrontal cortex, pregenual cingulate cortex, and ventral striatum, and in some of these regions the differences are related to the subjective pleasantness of the craved foods. An implication is that individual differences in brain responses to very

pleasant foods help to understand the mechanisms that drive the liking for specific foods by indicating that some brain systems (but not others such as the insular taste cortex) respond more to the rewarding aspects of some foods, and thus influence and indeed even predict the intake of those foods (which was much higher in chocolate cravers than non-cravers) (Rolls and McCabe, 2007).

Investigating another difference between individuals, Beaver et al. (2006) showed that reward sensitivity in different individuals (as measured by a behavioural activation scale) is correlated with activations in the orbitofrontal cortex and ventral striatum to pictures of appetizing vs. disgusting food.

When cognitive labels (such as "Rich delicious flavor") modulate humans' ratings of the pleasantness of flavor, it is possible that some individuals are more affected by this suggestion than others. We investigated this in relation to the study by Grabenhorst et al. (2008a) on cognitive effects on flavor by measuring the suggestibility of the subjects using parts of the SHSS (Stanford Hypnotic) Suggestibility Scale (Weitzenhoffer and Hilgard, 1962). It was found that one of the most reliable measures in this scale, the moving hands apart test in which subjects are told that there is a force pushing the hands apart, was correlated with the magnitude of the effect of the cognitive label "Rich delicious flavor" on the pleasantness rating of a standard flavor ($r = 0.71$, df = 9, $p = 0.023$) in the subjects used in this study. An implication is that an underlying personality variable related to suggestibility is also related to cognitive effects on affective ratings (and thus emotion), with the brain region showing a large modulation of its BOLD response by the cognitive labels to these stimuli being the medial orbitofrontal cortex and pregenual cingulate cortex (Grabenhorst et al., 2008a).

It is also becoming possible to relate the functions of the orbitofrontal cortex to some psychiatric symptoms that may reflect changes in behavioural responses to reinforcers, which may be different in different individuals. We compared the symptoms of patients with a personality disorder syndrome, Borderline Personality Disorder (BPD), with those of patients with lesions of the orbitofrontal cortex (Berlin and Rolls, 2004; Berlin et al., 2004, 2005). The symptoms of the self-harming BPD patients include high impulsivity, affective instability, and emotionality; and low extroversion. It was found that orbitofrontal cortex and BPD patients performed similarly in that they were more impulsive, reported more inappropriate behaviours in the Frontal Behaviour Questionnaire, and had more BPD characteristics, and anger, and less happiness, than control groups (either normals or patients with lesions outside the orbitofrontal cortex).

Both the orbitofrontal and BPD groups also had a faster perception of time (i.e. they underproduced time) than normal controls (Berlin and Rolls, 2004; Berlin et al., 2004, 2005). This may be one factor underlying their increased impulsiveness, in that they feel that sufficient time has elapsed to initiate action. This interesting hypothesis and finding deserve further exploration. It was of interest that the BPD group, as well as the orbitofrontal group, scored highly on a Frontal Behaviour Questionnaire which assessed inappropriate behaviours typical of orbitofrontal cortex patients including disinhibition, social inappropriateness, perseveration, and uncooperativeness. Both groups were also less open to experience (i.e. less open-minded), a personality characteristic. On the other hand, other aspects of BPD do not appear to be related to orbitofrontal cortex functions, including the more neurotic and more emotional personality characteristics of the BPD patients together with their lower extroversion and conscientious (Berlin and Rolls, 2004; Berlin et al., 2004, 2005).

Another case in which it is possible to relate psychiatric types of symptom to the functions of the orbitofrontal cortex in processing reinforcers is frontotemporal dementia, which is a progressive neurodegenerative disorder attacking the frontal lobes and producing major and pervasive behavioural changes in personality and social conduct some of which resemble those produced by orbitofrontal lesions (Rahman et al., 1999; Viskontas et al., 2007). Patients appear either socially disinhibited with facetiousness and inappropriate jocularity, or apathetic and withdrawn. The dementia is accompanied by gradual withdrawal from all social interactions. These behaviours could reflect impaired processing of reinforcers. (In addition, many patients show mental rigidity and inability to appreciate irony or other subtle aspects of language. They tend to engage in ritualistic and stereotypical behaviour, and their planning skills are invariably impaired. Memory is usually intact but patients have difficulties with working memory and concentration.) Interestingly, given the anatomy and physiology of the orbitofrontal cortex, frontotemporal dementia causes profound changes in eating habits, with escalating desire for sweet food coupled with reduced satiety, which is often followed by enormous weight gain.

The negative symptoms of schizophrenia include flattening of affect. As part of a dynamical attractor systems theory of schizophrenia in which hypofunction of NMDA receptors (Coyle et al., 2003) contributes to the cognitive symptoms such as attentional, working memory, and dysexecutive impairments by reducing the depth of the basins of attraction of the prefrontal cortex networks involved in these functions, it has been proposed that the flattening of affect is produced by the same reduced NMDA receptor function, which decreases the neuronal firing rates, and in the orbitofrontal cortex and related areas would lead to decreased affect (Loh et al., 2007; Rolls, 2005; Rolls et al., 2008d). Conversely, it has been proposed that hyperfunctionality of the glutamate system in obsessive compulsive disorder (Chakrabarty et al., 2005; Pittenger et al., 2006) would contribute to overstability in prefrontal and related networks that would contribute to the perseverative/obsessional symptoms, and that the concomitant increased firing rates of neurons in the orbitofrontal cortex and related areas contributes to the increased emotionality that may be present in obsessive-compulsive disorder (Rolls et al., 2008c).

11. A representation of novel visual stimuli in the orbitofrontal cortex

A population of neurons has been discovered in the 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 of these neurons last for at least 24 h. 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).

12. Beyond the orbitofrontal cortex to choice decision-making

In the neurophysiological studies described above, 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, 2008e). 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 (Critchley and Rolls, 1996a; Rolls et al., 1996a, 1999, 1989). 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 (Grabenhorst et al., 2008a; Kringelbach et al., 2003; McCabe and Rolls, 2007; 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., 2001a), 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, 2008e) of different rewards are present in the orbitofrontal cortex.

Approaches used in neuroeconomics help to define further the nature of the representation of reinforcers in the orbitofrontal cortex. When monkeys choose between different numbers of drops of two juices, one more preferred than the other, some neurons in the orbitofrontal cortex encode the offer value, some the choice value, and some the taste, but not the details of the motor response that is chosen (Padoa-Schioppa and Assad, 2006). Further, these neurons encode economic value, not relative preference, as shown by a study in which a particular reward was paired with other rewards. The fact that the neuronal responses are menu invariant suggests that transitivity, a fundamental trait of economic choice, may be rooted in the activity of individual neurons (Padoa-Schioppa and Assad, 2008). There is also evidence that relative reward value may be represented in the orbitofrontal cortex (Tremblay and Schultz, 1999), and in what may provide a resolution of this, we are finding in a current study that some parts of the orbitofrontal cortex may represent the absolute pleasantness of stimuli and others the relative pleasantness of stimuli (Grabenhorst and Rolls, in preparation).

When a choice is made between stimuli with different reward values, the choice made depends on the probability with which each reward will be obtained. In this probabilistic decision-making situation, we can define *expected value* as probability × reward magnitude) (Glimcher, 2004). In an investigation of such a probabilistic choice decision task in which humans chose between two rewards each available with different probabilities, it was found that the activation of the orbitofrontal cortex was related to expected value while the decision was being made, and also to the reward magnitude announced later on each trial (Rolls et al., 2008e). Further evidence in a variety of tasks implicates a related and partly overlapping region of the ventromedial prefrontal cortex with expected value (Daw et al., 2006; Hare et al., 2008; Kim et al., 2006; Tanaka et al., 2004). In contrast, the reward prediction errors or temporal difference errors as defined in reinforcement learning (Schultz, 2006; Sutton and Barto, 1998) are usually evident in the ventral striatum in imaging studies (Hare et al., 2008; Rolls et al., 2008e), though we should remember that negative reward prediction errors are represented by the error neurons in the primate orbitofrontal cortex (Thorpe et al., 1983) (see Section 6), and that the lateral orbitofrontal cortex is activated when a negative reward prediction error is generated in the reversal of a visual discrimination task (Kringelbach and Rolls, 2003).

Although it might be anticipated that the actual utility or 'subjective utility' of an offer (a choice) to an individual approximately tracks the expected value, this is not exactly the case, with subjects typically undervaluing high rewards, and being over-sensitive to high punishments (Bernoulli, 1738/1954; Gintis, 2000; Kahneman and Tversky, 1979, 1984; Rangel et al., 2008; Tversky and Kahneman, 1986; von Neumann and Morgenstern, 1944). Subjects also typically have a subjective utility function that discounts rewards the further in the future they are delayed. Some parts of the ventromedial prefrontal cortex have activations that may follow the subjective utility, of for example delayed rewards. In a study of this, it was found that activations in the ventromedial prefrontal cortex were correlated with the subjective utility of rewards delayed for different times, with the discount curve for each subject reconstructed from each subject's choices (Kable and Glimcher, 2007). Moreover, the activations in the ventromedial prefrontal cortex fitted the curves for each participant well, even though there were large individual differences in the reward discounting function, with some participants being impulsive and placing much more value on rewards available immediately, and other 'patient' participants showing very little discounting of rewards available a long time in the future. Thus activations in the ventromedial prefrontal cortex may continuously track even the subjective utility of available rewards. In further studies, it has been shown that counterfactual effects are manifested in the human orbitofrontal cortex during expectation of outcomes, such that the anticipated affective impact of outcomes is modulated by the nature of the various possible alternative outcomes (Ursu and Carter, 2005); and that activity in the orbitofrontal cortex correlated with the degree of regret, measured in a gambling task in which the outcome of the unchosen gamble would have been greater than the outcome that was obtained by the choice made (Coricelli et al., 2005).

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. 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 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 (de Lafuente and Romo, 2006; Romo et al., 2004). It has been proposed that there may be a similar binary system, perhaps in another brain region, that becomes engaged when choice decisions are between rewards, or about rewards with which there is an associated cost (Rolls, 2008e). This proposal has been investigated as follows.

To investigate whether representing the affective 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. 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 (Anderson et al., 2003; Grabenhorst et al., 2007; Rolls et al., 1996b, 2003a), taste (Grabenhorst et al., 2008a; Rolls et al., 1989; Small et al., 2003), somatosensory (Rolls et al., 2003b), temperature (Guest et al., 2007), visual (O'Doherty et al., 2003), monetary (Knutson et al., 2007; O'Doherty et al., 2001a), 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, 2005, 2008a). 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) (see Fig. 12).

Support for a contribution of medial prefrontal cortex 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., in preparation).

Different brain systems were implicated in different types of choice decision-making (Rolls et al., in preparation). Decision-making about the affective value of odors produced larger effects in the dorsal part of medial prefrontal cortex area 10 and the agranular insula, whereas decisions about intensity produced larger effects in the dorsolateral prefrontal cortex, ventral premotor cortex, and anterior insula. For comparison, the mid-orbitofrontal cortex had activations related to the subjective pleasantness ratings, providing a continuous representation of affective value, but not showing effects that were related to taking choices about the odors.

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

In the study with warm and cold stimuli, and mixtures of them, when a (choice) decision was yes vs. no, effects were found in the dorsal anterior cingulate cortex (Grabenhorst et al., 2008b), an area implicated by many other studies in decision-making (Behrens et al., 2007; Marsh et al., 2007). The anterior cingulate cortex has been implicated in action-outcome learning (Rushworth et al., 2007a; Rushworth et al., 2007b), and the study with warm and cold stimuli shows that the contribution of the anterior cingulate cortex is in the choice decision-making itself, and that its activation does not occur just in relation to the pleasantness or intensity of the stimuli (Grabenhorst et al., 2008b).

The implications are that the orbitofrontal cortex, and the pregenual cingulate cortex to which it projects, are involved in making decisions primarily by representing reward value on a continuous scale. Although the orbitofrontal cortex can have activations in decision-making tasks (Arana et al., 2003; Kim et al., 2007; Moll et al., 2006), it is important to separate processes involved in representing reward value from those involved in reaching a binary (choice) decision, which are separate computational processes (Rolls, 2008e). 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. Having separable systems 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 (Deco and Rolls, 2006; Rolls, 2008e; Wang, 2002), 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.

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 we 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.,

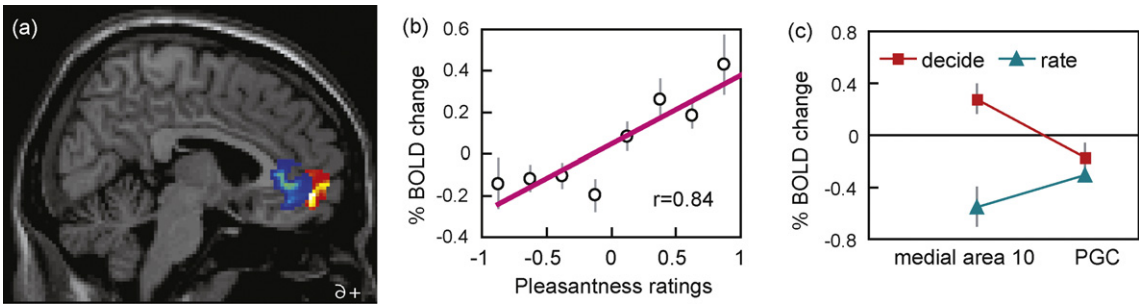

Fig. 12. Pregenual cingulate cortex vs. medial area 10 in decision-making. (a) A contrast of all trials on which decisions were made vs. all trials on which ratings were made between thermal stimuli showed a significant effect in the medial prefrontal cortex area 10, as indicated in red [6, 54, −8]. 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) Shows that 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 ± S.E.M.) 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).

1995), the primary olfactory cortex (Carmichael 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 (Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a; Grabenhorst et al., 2007; Rolls et al., 2008b, 2003b; Small et al., 2003) (see Fig. 2). 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 mid-cingulate cortex, and that the outcome information derived from the orbitofrontal cortex can contribute to action-outcome learning implemented in the cingulate cortex (Rolls, 2008e; Rushworth et al., 2007a,b). 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).

Why then are there also outputs from the orbitofrontal cortex to medial area 10 (directly Carmichael and Price, 1996 and via pregenual cingulate cortex Carmichael and Price, 1996; Price, 2006)? We suggest, based on the choice decision-making studies described here (Grabenhorst et al., 2008b; Rolls et al., in preparation), that when a binary decision must be made between two (or more) rewards, then area 10 becomes involved. If it is simply a case of linking an action to a reward (and thus deciding which response to perform), the mid-cingulate cortex may be engaged. But if a prior decision must be made, not about which action to make to obtain an outcome, but instead between different rewards or expected rewards, or whether or not to choose a reward, then the medial prefrontal cortex area 10 may be involved (Grabenhorst et al., 2008b; Rolls et al., in preparation). The implication here is that there are many decision systems in the brain, and that we must specify exactly what type of decision is being made when relating a brain area to decision-making. Consistent with this, in the odor decision-making study, when the decision between the first and second odor was not about which was more pleasant, but instead about which was more intense, the dorsolateral prefrontal cortex became engaged, rather than medial prefrontal cortex, area 10 (Rolls et al., in preparation).

This approach is further consistent with our computational approach to choice decision-making, which allows attractor networks implemented by the recurrent collateral connections between cortical pyramidal cells, to contribute in many different brain areas to different types of decision-making depending on what is represented in a brain area. For example, this process implemented in cortical visual areas provides an account of the mechanisms of binocular rivalry, and in the ventral premotor cortex for decisions between different vibrotactile frequencies (Deco and Rolls, 2006; Deco et al., 2008; Rolls, 2008e). An important computational concept here then is that choices may be made in the brain by attractor networks in which each attractor state, consisting of a set of neurons firing with high rates, represents one of the choices. Biasing inputs to each set of neurons allow competition between the different sets of neurons via the inhibitory neurons, and the positive feedback implemented by the recurrent collateral excitatory connections encourages one population to increase from low or intermediate firing rates to a high firing rate. This population that wins the competition suppresses the other populations via the inhibitory neurons, so that we end up with a binary outcome that represents the choice made (Deco and Rolls, 2006; Rolls, 2008e; Wang, 2002). Given that this architecture, local excitatory recurrent collateral connections between the pyramidal cells, and inhibitory interneurons that implement feedback inhibition, is prototypical of the cerebral cortex, then this type of "choice" process could take place in many different cortical areas, making choices locally between whatever is represented in an area (Deco et al., 2008; Rolls, 2008e).

We now propose that if there is a strong forward input to the pyramidal cells that drives them hard, the firing rates will tend to reflect on a continuous scale the magnitude of the forward input. If the recurrent collaterals are particularly efficacious in any area, this will tend to make the cortical area more likely to produce "choices", that is to end up with high firing rates for a winning population, with other cells inhibited. This may be a feature that in terms of functional cortical architecture may make some cortical areas more likely to represent inputs on a continuous scale, behaving perhaps linearly, whereas other areas may operate more non-linearly, falling into an attractor state. Which is more likely may also be set dynamically, perhaps by acetylcholine and other modulators that may alter the relative efficacy of the recurrent collateral connections (Giocomo and Hasselmo, 2007). Given that high acetylcholine tends to reduce the relative magnitude of the recurrent collateral synaptic effects, it could be that high acetylcholine would tend to make the system less likely to fall into a binary choice state representing a choice decision, whereas low acetylcholine would tend to facilitate attractor states representing a choice decision. Acetylcholine tends to be high during arousal, alertness, and attention, and although this is a speculation, one wonders whether this makes coming to a definite decision harder during arousal when all the evidence may be being continually weighed, whereas decision-making produced by falling into an attractor state may occur more easily during low arousal. (We do not suggest this, but someone might suggest that this could be a factor in what happens when people state that they are going to sleep on it.)

13. A computational basis for stimulus-reinforcer association learning and reversal in the orbitofrontal cortex involving conditional reward neurons and negative reward prediction error neurons

The neurophysiological, imaging, and lesion evidence described above suggests that one function implemented by the orbitofrontal cortex is rapid stimulus-reinforcement association learning and the correction of these associations when reinforcement contingencies in the environment change. In addition, it has been shown that amphetamine, a potent instrumental reinforcer, is self-administered to the orbitofrontal cortex by macaques (Phillips et al., 1981), and that in drug naïve human participants amphetamine activates the orbitofrontal cortex (Völlm et al., 2004). How might this rapid stimulus-reinforcer association learning and reversal be implemented at the neuronal and neuronal network level? One mechanism could be implemented by Hebbian modification of synapses conveying visual input onto taste-responsive neurons, implementing a pattern association network (Rolls, 1999a, 2000b, 2005, 2008e; Rolls and Deco, 2002; Rolls and Treves, 1998). Long-term potentiation would strengthen synapses from active conditioned stimulus neurons onto neurons

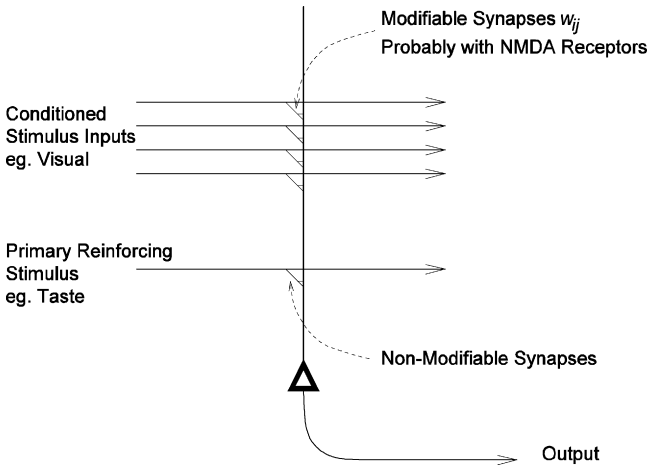

Fig. 13. Pattern association between a primary reinforcer, such as the taste of food, which activates neurons through non-modifiable synapses, and a potential secondary reinforcer, such as the sight of food, which has modifiable synapses on to the same neurons. The associative rule for the synaptic modification is that if there is both presynaptic and post-synaptic firing, then that synapse should increase in strength. Such a mechanism appears to be implemented in the amygdala and orbitofrontal cortex. (Homosynaptic) long-term depression (produced by presynaptic firing in the absence of strong postsynaptic firing) in the pattern associator could account for the response to the no-longer reinforced stimulus becoming weaker. For further details, see Rolls (2005).

responding to a primary reinforcer such as a sweet taste, and homosynaptic long-term depression would weaken synapses from the same active visual inputs if the neuron was not responding because an aversive primary reinforcer (e.g., a taste of saline) was being presented (see Fig. 13).

As noted above, the conditional reward neurons in the orbitofrontal cortex convey information about the current reinforcement status of particular stimuli. In a new theory of how the orbitofrontal cortex implements rapid, one-trial, reversal, these neurons play a key part, for particular conditional reward neurons (responding to for example 'green is now rewarding', see example in Fig. 8) are biased on by a rule set of neurons if the association is being run direct, and are biased off if the association is being run reversed ('green is now not rewarding') (Deco and Rolls, 2005c). A diagram of the neural architecture of the network model is shown in Fig. 14. One set of rule neurons in the short-term memory attractor network is active when the rule is direct, and a different set of neurons when the association is reversed. The state of the rule network is reversed when the error neurons fire in reversal, because the firing of the error neurons quenches the attractor by activating inhibitory neurons, and the opposite set of rule neurons emerge to activity after the quenching because of some adaptation in the synapses or neurons in the rule attractor that have just been active. The error-detection neurons themselves may be triggered by a mismatch between what was expected when the visual stimulus was shown, and the primary reinforcer that

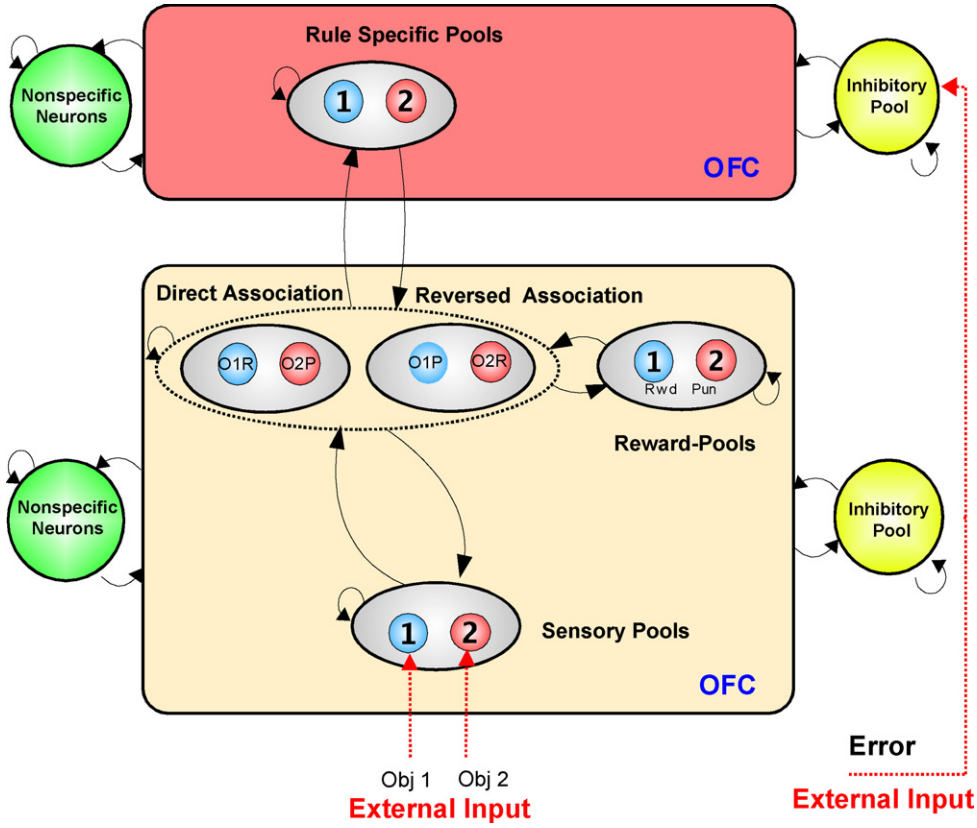

Fig. 14. Cortical architecture of a reward reversal model implemented at the level of integrate-and-fire neurons so that the spiking activity of neurons in the model can be implemented and compared to real neuronal recordings. There is a rule module (top) and a sensory – intermediate neuron – reward module (below). Neurons within each module are fully connected, and form attractor states. The sensory – intermediate neuron – reward module consists of three hierarchically organized levels of attractor network, with stronger synaptic connections in the forward than the back projection direction. The intermediate level of the sensory – intermediate neuron – reward module contains conditional reward neurons (as recorded in the orbitofrontal cortex) that respond to combinations of an object and its association with reward or punishment, e.g., object 1-reward (O1R, in the direct association set of pools), and object 1-punishment (O1P in the reversed association set of pools). The rule module acts as a biasing input to bias the competition between the object – reward combination neurons at the intermediate level of the sensory – intermediate neuron—reward module. OFC, orbitofrontal cortex (after Deco and Rolls, 2005c).

was obtained, both of which are represented in the primate orbitofrontal cortex (Thorpe et al., 1983). The whole system maps stimuli (such as green and blue) through a biased competition layer of conditional reward neurons in which the mapping is controlled by the biasing input from the rule neurons, to output neurons that fire if a stimulus is being shown that is currently associated with reward (Deco and Rolls, 2005c). The model gives an account of the presence of conditional reward and error neurons in the orbitofrontal cortex, as well as neurons that respond to whichever visual stimulus is currently associated with reward, and neurons that signal whether a (for example taste) reward or punishment has just been obtained. The model also suggests that the orbitofrontal cortex may be especially appropriate for this rapid reversal mechanism, because, in contrast to the amygdala, the orbitofrontal cortex as a cortical structure has a well-developed system of recurrent collateral synapses between the pyramidal cells, which provide an appropriate basis for implementing a working memory to hold the current rule. The model also shows how when on a reversal trial a reward is not obtained to a previously rewarded stimulus, on the very next trial when the recently punished stimulus is shown, it is treated as a reward, and it is chosen. This type of behaviour at the behavioural level is in fact illustrated in Fig. 9 (e.g., trials 4 and 14), and cannot be accounted for by a new association of the now to be rewarded stimulus with reward, for in its recent past it has been associated with saline. Thus this type of one-trial rapid reversal cannot be accounted for by direct stimulus-reward association learning, and a rule-based system, such as the type implemented in the model, is needed. The model has been worked out in detail at the level of integrate-and-fire spiking neurons, and makes predictions about further types of neuron expected to be present in the orbitofrontal cortex (Deco and Rolls, 2005c; Rolls, 2005).

14. Conclusions and future directions

14.1. Representations of affective value vs. intensity and identity

An important principle that emerges from research on the brain mechanisms of emotion is that there is a specialized system that provides representations of the reward or reinforcing value of stimuli, and that this is separate from brain systems that represent the physical properties of a stimulus such as its identity (e.g., that it is sweet, independently of hunger and whether we want it and it is currently rewarding; what object we are looking at, independently of whether we want it and it is currently rewarding, etc.). This was originally made clear by single neuron findings on taste, which showed that neurons in the primary taste cortex represent which stimulus is present (sweet, salt, bitter, sour, umami) independently of whether hunger is present (Rolls et al., 1988; Scott et al., 1986; Yaxley et al., 1988, 1990); and that neurons in the orbitofrontal cortex respond to for example sweet taste only when hunger is present and the taste is rewarding (Rolls et al., 1989, 1990). In fact, we were led to the orbitofrontal cortex as a possible brain region that represents the rewarding properties of stimuli by findings with brain-stimulation reward (Phillips et al., 1981; Rolls, 2005; Rolls et al., 1980b). The evidence from taste was followed by analogous findings in vision, that neurons in the primate inferior temporal visual cortex do not alter their responses depending on whether the visual stimulus is associated during learning with a reward vs. a punisher, or depending on whether hunger is present for that object (Rolls et al., 1977); whereas visual neurons in the orbitofrontal cortex do reverse their responses in as little as one trial during visual to taste association learning (Rolls et al., 1996b; Thorpe et al., 1983), and gradually stop responding to the visual stimulus as satiety for the food being seen is reached (Critchley and Rolls, 1996a). Correspondingly, in humans satiety to a particular flavor decreases flavor-related activations in the orbitofrontal cortex, but not in the primary taste cortex in the taste insula (Kringelbach et al., 2003). Further, in the orbitofrontal cortex activations are correlated with the pleasantness of olfactory stimuli, but in the pyriform cortex (a primary olfactory cortical area) with intensity (Grabenhorst et al., 2007). In addition, in humans it has been possible to show that activations in the orbitofrontal cortex correlate with the pleasantness of thermal stimuli, and in the insular somatosensory cortex with their intensity (Rolls et al., 2008b). Further, with somatosensory stimuli applied to the hand, activations in the orbitofrontal cortex reflected the affective value, and in the somatosensory cortex the intensity (Rolls et al., 2003b).

The separation of affective processing from processing about the identity and intensity of stimuli is highly adaptive, and a fundamental principle of brain design revealed by these investigations, for it enables us to see and learn about stimuli independently of whether we currently want them and find them rewarding. This enables goal-directed, emotional and motivational, behaviour to be separated from other types of learning that are independent of the current emotional and motivational value of stimuli (Rolls, 2008e).

14.2. Attention to affective value vs. intensity

In recent findings, these concepts have been extended to the effects of attention. For example, when subjects are instructed to pay attention to the pleasantness of taste stimuli (monosodium glutamate), activations were larger in the orbitofrontal and pregenual cingulate cortex; and when paying attention to intensity, activations were larger in the taste insula (see Fig. 11) (Grabenhorst and Rolls, 2008). Further, when subjects are instructed to pay attention to the pleasantness of olfactory stimuli, activations were larger in brain areas such as the orbitofrontal and pregenual cingulate cortex and hypothalamus; and when paying attention to intensity, activations were larger in brain areas such as the pyriform cortex and inferior frontal gyrus (Rolls et al., 2008a). These interesting effects are related to the fact that the processing of affective value and intensity are separable processes, and indicate that the exact way in which we respond to stimuli depends on whether we are engaged in processing their affective value or their physical properties. This has important implications for sensory testing, as well as for emotional responsiveness more generally.

14.3. Cognitive modulation of affective value

It has also been possible to extend these concepts to the cognitive modulation of the affective and reward value of stimuli and emotion-related states. For example, it has been shown that highly cognitive, word-level, descriptions of olfactory (de Araujo et al., 2005), taste (Grabenhorst et al., 2008a), flavor (Grabenhorst et al., 2008a; Plassmann et al., 2008), and somatosensory stimuli (McCabe et al., 2008) can alter activations produced by these stimuli in brain areas that represent the pleasantness of these stimuli such as the orbitofrontal and pregenual cingulate cortex, and in a region to which these project, the ventral striatum. The implication of these findings is again fascinating, for it shows that cognition can descend into the first stage of processing at which affective value is made explicit in the representation, to alter the representations that are related to affective value in these areas.

14.4. Identity, affective, and decision-making tiers of processing

Fig. 2 is designed to draw out these issues in terms of processing hierarchies. The level of the tiered structure that forms a column

including inferior temporal visual cortex, primary taste cortex, pyriform cortex, and somatosensory cortex is the level at which intensity, physical properties, and the identity of stimuli are represented, and in an affect-neutral way. The next tier of processing, including the orbitofrontal cortex, amygdala, and pregenual cingulate cortex, represents the reward/reinforcing value of stimuli and their corresponding subjective affective value. The next tier of processing provides a stage at which responses are organised to the stimuli, including autonomic responses via the lateral hypothalamus (and visceral insula not shown in Fig. 2); habit responses by brain regions that include the basal ganglia; and action-outcome learning to enable the goals represented at the second tier to be obtained.

Some of the research described here also indicates that the continuous representation of affective value in brain areas such as the orbitofrontal and pregenual cingulate cortex is followed by processing in brain regions such as the medial prefrontal cortex area 10, and probably the cingulate cortex, at which the processing is related to binary decision-making, which is computationally different. Indeed, even at the time that we take a binary decision to choose on a particular trial one of two affectively somewhat similar stimuli, we can at the same time represent the exact affective value of the stimuli, and indeed these representations are an essential input to a decision-making process. However, these two processes are different, can co-exist in the brain, require different types of computation, and perhaps for these reasons are represented in different cortical areas (see Fig. 2). There is an indication that different types of binary decision engage different areas, with medial prefrontal cortex area 10 activated when taking decisions about the pleasantness of olfactory or thermal stimuli (Grabenhorst et al., 2008b; Rolls et al., in preparation), with the dorsolateral prefrontal activations related to decisions about which of two olfactory stimuli was more intense (Rolls et al., in preparation), and ventral premotor cortex activity related to which of two vibrotactile stimuli had the higher frequency (Deco et al., 2008; Romo et al., 2004).

14.5. Affective value, consciousness, and the affective tier

The reward value of stimuli, operationally defined, is represented in the orbitofrontal cortex. But it is a feature of our human functional neuroimaging studies that the subjective, conscious, ratings of pleasantness are correlated with activations in the orbitofrontal cortex. Rolls has argued that there are dual routes to action, and that one, concerned with simple reinforcers such as taste, can in some cases be implemented implicitly, that is unconsciously (Rolls, 1999a, 2004b, 2005, 2007a, 2007b, 2008b). The conjecture is that the conscious route is needed for rational (i.e. reasoning) thought about plans that may have multiple steps, and that the processing in this system happens to feel like something. Why then might activations of simple reinforcers such as taste or warmth have their subjective affective value represented at all? The suggestion that is made is that reasoning may have to occur about the advantages of different rewards (e.g., deferring an immediate taste reward for a longer term financial reward), and that the simple rewards, such as taste or warmth, become conscious by virtue of entering this reasoning processing system (Rolls, 1999a, 2004b, 2005, 2007a, 2007b, 2008b). (If the limited capacity reasoning system is not engaged in reasoning about something else, then simple rewards may, while it is monitoring events in the world, enter it and become conscious.) In any case, the activations in the orbitofrontal cortex are clearly closely related to the subjectively experienced affective value, and may thus provide inputs to the reasoning system. In an analogous way, the activity in the first tier of processing, at which intensity and identity are represented, is closely correlated with the subjective intensity of the stimuli, showing how the properties of what is represented in conscious experience reflects processing in different cortical areas. We have seen in this paper that processing in two particular brain areas, the orbitofrontal and pregenual cingulate cortex, is closely related to experienced affective value.

14.6. Specific reward representations in a common currency

The representations in the orbitofrontal cortex provide evidence about the exact nature of each reward, as shown most clearly by the single neuron recording studies. These show that different and overlapping populations of neurons provide representations of combinations of the taste, texture, odor, temperature and visual appearance of stimuli (e.g., Fig. 3). Other orbitofrontal cortex neurons provide representations of which expression is present on a face, and of face identity (Rolls et al., 2006). Thus it is not general reward or affect that is represented. The computational reason for this is that to guide behaviour adaptively and correctly, each reinforcer must be represented separately. When we are hungry, we should eat food; when thirsty, we should drink water; etc. Moreover, social behaviour to an individual may require representations not only of face expression, but also of face identity, and both are involved in typical social behaviour.

All these different rewards have to be in a common currency, that is, one type of reward (e.g., food reward) should not dominate all other types of reward, for this would be maladaptive. Making different rewards approximately equally rewarding makes it likely that a range of different rewards will be chosen over time (and depending on factors such as need state in some cases), which is adaptive and essential for survival (Rolls, 2005).

There are special mechanisms that help this common currency to operate gracefully. One is sensory-specific satiety, the decrease in the reward value of a stimulus that typically occurs over several minutes. This is an elegant way of ensuring that different rewards are selected at different times, and helps to keep the rewards competing evenly in a common currency.

14.7. Decisions between the rewards in the common currency

We may then ask how the highest reward in this common currency becomes selected as the current goal for action. What we propose is that this involves a mechanism like binary (choice) decision-making, in which the inputs are representations of the different rewards that are available. We propose that an attractor network that can represent a decision (Deco and Rolls, 2006) for each reward as a different subset of neurons firing is biased by each of the currently available rewards, and falls into an attractor in which one reward, that with the highest value in the common currency, wins (Rolls, 2008e). This may take place in the medial prefrontal cortex area 10, and this competitive process helps, probabilistically because of the spiking noise (Deco and Rolls, 2006), to select a goal for the current trial or short time period. The implementation of this by an attractor network means that all the different reinforcers have to be brought together to compete with each other in a single network, and this is an account we give for why so many different rewards are represented in the same set of cortical areas, the medial orbitofrontal cortex, and, particularly for the choice decision-making, regions to which this projects such as the medial prefrontal cortex area 10. Cortical networks operate over a short range of a few mm, and this is why in this case the different rewards, to compete within the same network, need to be represented close together in the cerebral cortex (Rolls, 2008e). Of course, the decision-making need not be between two rewards, and in principle an attractor-based decision network can make a

single choice from multiple inputs (Deco and Rolls, 2006; Deco et al., 2008). In addition, the costs incurred in obtaining each goal need to be subtracted from the reward value of each goal, probably before they enter the decision-making network, and the exact implementation of this will be exciting to discover.

In this choice decision-making system between different specific rewards, the attractor that wins represents the choice of a specific reward. This is appropriate, so that the behaviour can be directed towards obtaining that particular reward, which will be the goal for an action. The winner is not a general reward, and a general reward as the output would not be useful to direct behaviour towards an appropriate goal, such as food for a hungry person, or water for a thirsty person. The common-ness between rewards in this system is just that the different specific rewards must have approximately equally potency at their maximal value, to ensure that different rewards are chosen sometimes, and that behaviour is not always directed towards a few super-potent specific rewards. We refer to this as the common currency of rewards, that they can compete on an approximately equal basis (set by evolution, and as a function of hunger, sensory-specific satiety, etc.), to produce in the end optimal fitness (of the genes that specify the rewards) (Rolls, 2005).

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 behavioural responses, as part of a system involved in more than just affective value, including interfacing stimuli to responses (Rolls, 2005, 2008e).

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