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The functions of the orbitofrontal cortex

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Abstract

The orbitofrontal cortex contains the secondary taste cortex, in which the reward value of taste is represented. It also contains the secondary and tertiary olfactory cortical areas, in which information about the identity and also about the reward value of odours is represented. The orbitofrontal cortex also receives information about the sight of objects from the temporal lobe cortical visual areas, and neurons in it learn and reverse the visual stimulus to which they respond when the association of the visual stimulus with a primary reinforcing stimulus (such as taste) is reversed. This is an example of stimulus–reinforcement association learning, and is a type of stimulus–stimulus association learning. More generally, the stimulus might be a visual or olfactory stimulus, and the primary (unlearned) positive or negative reinforcer a taste or touch. A somatosensory input is revealed by neurons that respond to the texture of food in the mouth, including a population that responds to the mouth feel of fat. In complementary neuroimaging studies in humans, it is being found that areas of the orbitofrontal cortex are activated by pleasant touch, by painful touch, by taste, by smell, and by more abstract reinforcers such as winning or losing money. Damage to the orbitofrontal cortex can impair the learning and reversal of stimulus–reinforcement associations, and thus the correction of behavioural responses when there are no longer appropriate because previous reinforcement contingencies change. The information which reaches the orbitofrontal cortex for these functions includes information about faces, and damage to the orbitofrontal cortex can impair face (and voice) expression identification. This evidence thus shows that the orbitofrontal cortex is involved in decoding and representing some primary reinforcers such as taste and touch; in learning and reversing associations of visual and other stimuli to these primary reinforcers; and in controlling and correcting reward-related and punishment-related behavior, and thus in emotion. The approach described here is aimed at providing a fundamental understanding of how the orbitofrontal cortex actually functions, and thus in how it is involved in motivational behavior such as feeding and drinking, in emotional behavior, and in social behavior.

Keywords: Emotion; Orbitofrontal cortex; Reward reinforcement; Taste; Olfaction; Reversal learning; Face expression

1. Introduction

The prefrontal cortex is the cortex that receives projections from the mediodorsal nucleus of the thalamus (with which it is reciprocally connected) and is situated in front of the motor and premotor cortices (areas 4 and 6) in the frontal lobe. Based on the divisions of the mediodorsal nucleus, the prefrontal cortex may be divided into three main regions (Fuster, 1997). First, the magnocellular, medial, part of the mediodorsal nucleus projects to the orbital (ventral) surface of the prefrontal cortex (which includes areas 13 and 12). It is called the orbitofrontal cortex, and receives information from the ventral or object processing visual stream, and taste, olfactory, and somatosensory inputs. Second, the parvocellular, lateral, part of the mediodorsal nucleus projects to the dorsolateral prefrontal cortex. This part of the prefrontal cortex receives inputs from the parietal cortex, and is involved in tasks such as spatial short-term memory tasks (Fuster, 1997; see Rolls & Treves, 1998). Third, the pars paralamellaris (most lateral) part of the mediodorsal nucleus projects to the frontal eye fields (area 8) in the anterior bank of the arcuate sulcus.

The functions of the orbitofrontal cortex are considered here. This analysis provides a basis for investigations of how its functions develop in ontogeny. The

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cortex on the orbital surface of the frontal lobe includes area 13 caudally, and area 14 medially, and the cortex on the inferior convexity includes area 12 caudally and area 11 anteriorly (see Fig. 1 and Carmichael & Price, 1994; Öngür & Price, 2000; Petrides & Pandya, 1994; note that the names and numbers that refer to particular subregions are not uniform across species and investigators). This brain region is relatively poorly developed in rodents, but well developed in primates including humans. To understand the function of this brain region in humans, the majority of the studies described were therefore performed with macaques or with humans.

2. Connections

Rolls, Yaxley, and Sienkiewicz (1990) discovered a taste area in the lateral part of the orbitofrontal cortex, and showed that this was the secondary taste cortex in that it receives a major projection from the primary taste cortex (Baylis, Rolls, & Baylis, 1994). More medially, there is an olfactory area (Rolls & Baylis, 1994). Anatomically, there are direct connections from the primary olfactory cortex, pyriform cortex, to area 13a of the posterior orbitofrontal cortex, which in turn has onward projections to a middle part of the orbitofrontal cortex (area 11) (Barbas, 1993; Carmichael, Clugnet, & Price, 1994; Morecraft, Geula, & Mesulam, 1992; Price et al., 1991) (see Figs. 1 and 2). Visual inputs reach the orbitofrontal cortex directly from the inferior temporal cortex, the cortex in the superior temporal sulcus, and the temporal pole (see Barbas, 1988, 1993, 1995; Barbas & Pandya, 1989; Carmichael & Price, 1995; Morecraft et al., 1992; Seltzer & Pandya, 1989). There are corresponding auditory inputs (Barbas, 1988, 1993), and somatosensory inputs from somatosensory cortical areas 1, 2, and SII in the frontal and pericentral operculum, and from the insula (Barbas, 1988; Carmichael & Price, 1995). The caudal orbitofrontal cortex receives strong inputs from the amygdala (e.g., Price et al., 1991). The orbitofrontal cortex also receives inputs via the mediodorsal nucleus of the thalamus, pars magnocellularis,

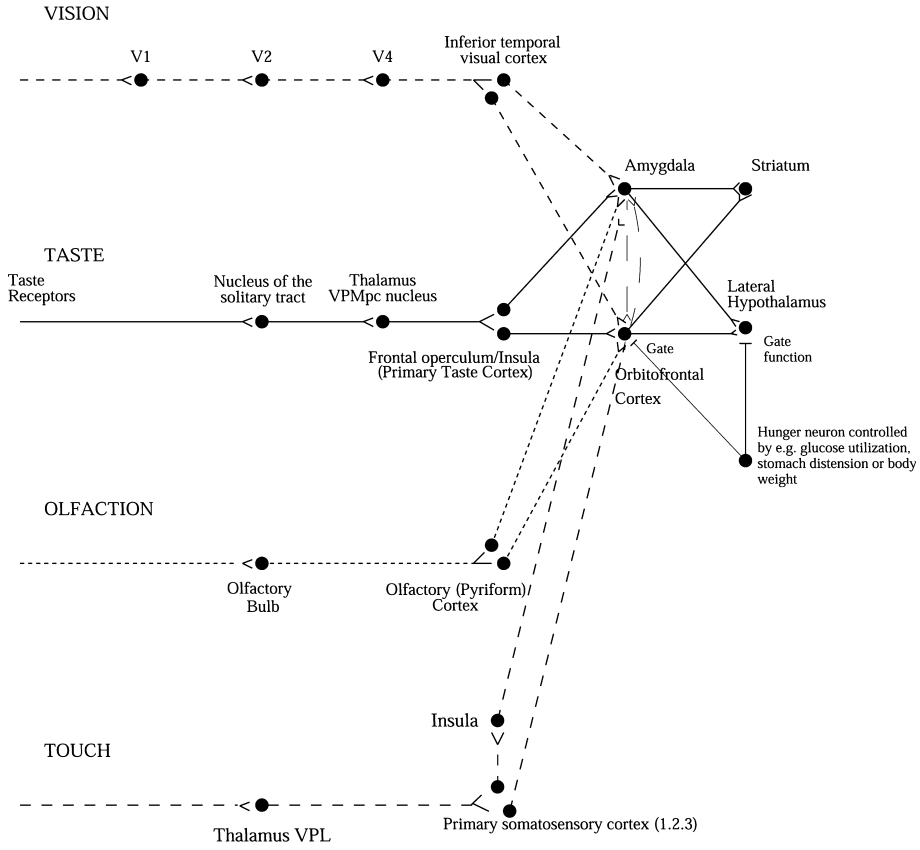

Fig. 1. Schematic diagram showing some of the gustatory, olfactory, visual and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex, and the secondary olfactory cortex, are within the orbitofrontal cortex. V1, primary visual cortex. V4, visual cortical area V4. Abbreviations: as, arcuate sulcus; cc, corpus callosum; cf, calcarine fissure; cgs, cingulate sulcus; cs, central sulcus; ls, lunate sulcus; ios, inferior occipital sulcus; mos, medial orbital sulcus; os, orbital sulcus; ots, occipito-temporal sulcus; ps, principal sulcus; rhs, rhinal sulcus; sts, superior temporal sulcus; lf, Lateral (or Sylvian) fissure (which has been opened to reveal the insula); A, amygdala; INS, insula; T, thalamus; TE (21), inferior temporal visual cortex; TA (22), superior temporal auditory association cortex; TF and TH, parahippocampal cortex; TG, temporal pole cortex; 12, 13, 11, orbitofrontal cortex; 35, perirhinal cortex; 51, olfactory (prepyriform and periamygdaloid) cortex (after Rolls, 1999).

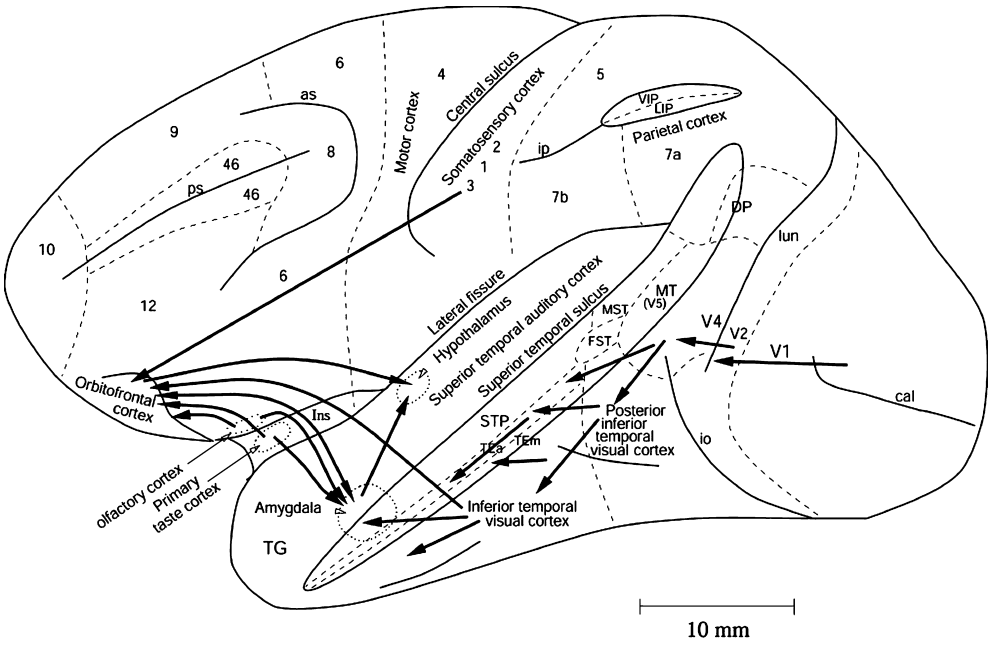

Fig. 2. Schematic diagram showing some of the gustatory, olfactory, visual, and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex, and the secondary olfactory cortex, are within the orbitofrontal cortex. V1—primary visual cortex, V4—visual cortical area V4 (after Rolls, 1999).

which itself receives afferents from temporal lobe structures such as the prepyriform (olfactory) cortex, amygdala, and inferior temporal cortex (see Öngür & Price, 2000). The orbitofrontal cortex projects back to temporal lobe areas such as the inferior temporal cortex. The orbitofrontal cortex has projections to the entorhinal cortex (or "gateway to the hippocampus"), and cingulate cortex (Insausti, Amaral, & Cowan, 1987). The orbitofrontal cortex also projects to the preoptic region and lateral hypothalamus, to the ventral tegmental area (Johnson, Rosvold, & Mishkin, 1968; Nauta, 1964), and to the head of the caudate nucleus (Kemp & Powell, 1970). Reviews of the cytoarchitecture and connections of the orbitofrontal cortex are provided by Petrides and Pandya (1994), Pandya and Yeterian (1996), Carmichael and Price (1994, 1995), Barbas (1995), and Öngür and Price (2000).

3. Effects of lesions of the orbitofrontal cortex

Macaques with lesions of the orbitofrontal cortex are impaired at tasks which involve learning about which stimuli are rewarding and which are not, and especially in 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 & Mishkin, 1970), in an object reversal task in that they respond to the object which was formerly rewarded with food, and in extinction in that they continue to respond to an object which is no longer rewarded (Butter, 1969; Jones & Mishkin, 1972). 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, area 13, produces the extinction deficit (Rosenkilde, 1979).

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, Bachevalier, & Mishkin, 1991; Mishkin & 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, Rainer, & Miller, 1997; Rosenkilde, Bauer, & Fuster, 1981; Wilson, O'Sclaidhe, & Goldman-Rakic, 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), and a medial part of the frontal cortex may also contribute to this function (Kowalska et al., 1991). 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) is different to the short-term memory system in the dorsolateral part of the prefrontal cortex, which is concerned with spatial short-term memories, consistent with its inputs from the

parietal cortex (see, e.g., Rolls & Deco, 2002; Rolls & Treves, 1998).

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, McDonald, & Snyder, 1969; Butter, Snyder, & McDonald, 1970; Butter & Snyder, 1972) or to display the normal preference ranking for different foods (Baylis & Gaffan, 1991). In humans, euphoria, irresponsibility, and lack of affect can follow frontal lobe damage (see Damasio, 1994; Kolb & Whishaw, 1996; Rolls, 1999), particularly orbitofrontal damage (Hornak, Rolls, & Wade, 1996; Hornak et al., 2003; Rolls, Hornak, Wade, & McGrath, 1994).

4. Neurophysiology of the orbitofrontal cortex

4.1. Taste

One of the recent discoveries that has helped us to understand the functions of the orbitofrontal cortex in behaviour is that it contains a major cortical representation of taste (see Rolls, 1989, 1995a, 1997a; Rolls & Scott, 2003; cf Fig. 2). Given that taste can act as a primary reinforcer, that is without learning as a reward or punishment, we now have the start for a fundamental understanding of the function of the orbitofrontal cortex in stimulus–reinforcement association learning. 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), of protein or umami as exemplified by monosodium glutamate (Baylis & Rolls, 1991; Rolls, 2000c) and inosine monophosphate (Rolls, Critchley, Browning, & Hernadi, 1998; Rolls, Critchley, Wakeman, & Mason, 1996b), and of astringency as exemplified by tannic acid (Critchley & Rolls, 1996c).

The nature of the representation of taste in the orbitofrontal cortex is that the reward value of the 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 stop responding to the taste of a food with which the monkey is fed to satiety (Rolls, Sienkiewicz, & Yaxley, 1989). In contrast, the representation of taste in the primary taste cortex (Scott, Yaxley, Sienkiewicz, & Rolls, 1986; Yaxley, Rolls, & Sienkiewicz, 1990) is not modulated by hunger (Rolls, Scott, Sienkiewicz, & Yaxley, 1988; Yaxley, Rolls, & Sienkiewicz, 1988). Thus in the primate primary taste cortex, the reward value of taste is not represented, and instead the identity of the taste is 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, Avrith, Phillips, & Rolls, 1979; Rolls, 1994c). Further, neurons in the orbitofrontal cortex are activated from many brain-stimulation reward sites (Mora, Avrith, & Rolls, 1980; Rolls, Burton, & Mora, 1980). Thus there is clear evidence that it is the reward value of taste that is represented in the orbitofrontal cortex (see further Rolls, 1999, 2000b).

The secondary taste cortex is in the caudolateral part of the orbitofrontal cortex, as defined anatomically (Baylis et al., 1994). This region projects on to other regions in the orbitofrontal cortex (Baylis et al., 1994), 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 (see Rolls & Baylis, 1994; Rolls et al., 1990, 1996b).

In human neuroimaging experiments (e.g., with functional magnetic resonance image, fMRI), it has been shown (corresponding to the findings in non-human primate single neuron neurophysiology) that there is an orbitofrontal cortex area activated by sweet taste (glucose, Francis et al., 1999; 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, Rolls, Francis, McGlone, & Bowtell, 2001b), by pleasant touch (Francis et al., 1999; Rolls et al., 2003a), and by pleasant vs aversive olfactory stimuli (Francis et al., 1999; O'Doherty et al., 2000; Rolls, Kringelbach, & De Araujo, 2003b).

4.2. Convergence of taste and olfactory inputs in the orbitofrontal cortex: The representation of flavour

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 & Baylis, 1994; cf. Fig. 2). It is probably here in the orbitofrontal cortex of primates that these two modalities converge to produce the representation of flavour (Rolls & Baylis, 1994). Evidence will soon be described that indicates that these representations are built by olfactory–gustatory association learning, an example of stimulus–reinforcement association learning.

4.3. An olfactory representation in the orbitofrontal cortex

Takagi, Tanabe and colleagues (see Takagi, 1991) described single neurons in the macaque orbitofrontal cortex that were activated by odours. A ventral frontal region has been implicated in olfactory processing in humans (Jones-Gotman & Zatorre, 1988; Zatorre, Jones-Gotman, Evans, & Meyer, 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 (1996a) 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 odours to which a neuron responded were influenced by the taste (glucose or saline) with which the odour was associated. Thus the odour 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 odour 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 odour when the taste reinforcement association of the odour was reversed (Rolls, Critchley, Mason, & Wakeman, 1996b). (Twenty-five percent showed reversal, and 43% no longer discriminated after the reversal. 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 flavour representations. The relatively high proportion of 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 preselected to show differential responses to the odours 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 (1996b) 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 odour of the food with which the monkey was fed to satiety. Thus for these neurons, the reward value of the odour is what is represented in the orbitofrontal cortex (cf. Rolls & 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 (as confirmed by Schultz and colleagues, see Schultz, Tremblay, & Hollerman, 2000), and this parallels the changes in the relative pleasantness of different foods after a food is eaten to satiety (Rolls, Rolls, Rowe, & Sweeney, 1981; Rolls, Rowe, & Rolls, 1982; Rolls et al., 1997a; see Rolls, 1999, 2000b). We do not yet know whether this is the first stage of processing at which reward value is represented in the olfactory system (although in rodents the influence of reward association learning appears to be present in some neurons in the pyriform cortex—Schoenbaum & Eichenbaum, 1995).

Although individual neurons do not encode large amounts of information about which of 7–9 odours has been presented, we have shown that the information does increase linearly with the number of neurons in the sample (Rolls, Critchley, & Treves, 1996c). This ensemble encoding does result in useful amounts of information about which odour has been presented being provided by orbitofrontal olfactory neurons.

In human neuroimaging experiments, it has been shown (corresponding to the findings in non-human primate single neuron neurophysiology) that there is an orbitofrontal cortex area activated by olfactory stimuli (Francis et al., 1999; Jones-Gotman & Zatorre, 1988; Zatorre et al., 1992). Moreover, the pleasantness or reward value of odour is represented in the orbitofrontal cortex, in that feeding the humans to satiety decreases the activation found to the odour of that food, and this effect is relatively specific to the food eaten in the meal (O'Doherty et al., 2000; cf. Morris & Dolan, 2001). 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 how unpleasant odors are subjectively (Rolls et al., 2003b).

4.4. Visual inputs to the orbitofrontal cortex, error detection neurons, visual stimulus–reinforcement association learning and reversal, and neurons with face-selective responses

We have been able to show that there is a major visual input to many neurons in the orbitofrontal cortex, and that what is represented by these neurons is in many cases the reinforcement association of visual stimuli. The visual input is from the ventral, temporal lobe, visual stream concerned with "what" object is being seen (see Rolls, 2000d; Rolls & Deco, 2002), in that orbitofrontal cortex visual neurons frequently respond differentially to objects or images depending on their reward association (Rolls et al., 1996b; Thorpe, Rolls, & Maddison, 1983). The primary reinforcer that has been used is taste. Many of these neurons show visual–taste reversal in one or a very few trials (see example in Fig. 3). (In a visual discrimination task, they will reverse the stimulus to which they respond, from, e.g., a triangle

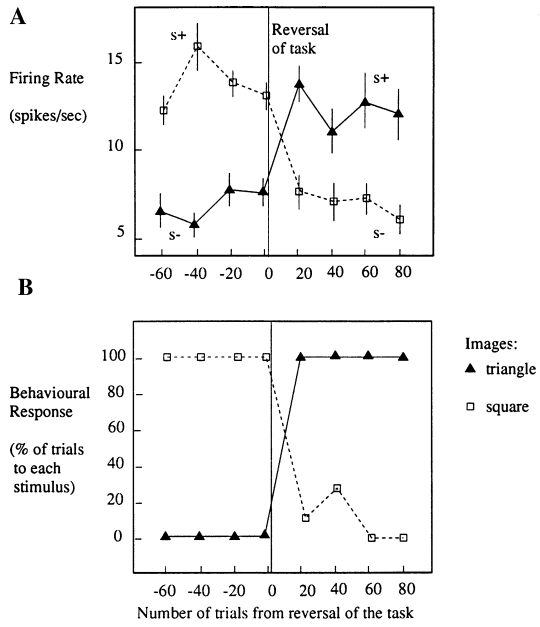

Fig. 3. Visual discrimination reversal of the responses of a single neuron in the macaque orbitofrontal cortex when the taste with which the two visual stimuli (a triangle and a square) were associated was reversed. Each point is the mean poststimulus firing rate measured in a 0.5 s period over approximately 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).

to a square, in one trial when the taste delivered for a behavioural response to that stimulus is reversed.) This reversal learning probably occurs in the orbitofrontal cortex, for it does not occur one synapse earlier in the visual inferior temporal cortex (Rolls, Judge, & Sanghera, 1977), and it is in the orbitofrontal cortex that there is convergence of visual and taste pathways onto the same neurons (Rolls & Baylis, 1994; Rolls et al., 1996b, 1996c; Thorpe et al., 1983). The probable mechanism for this learning is Hebbian modification of synapses conveying visual input onto taste-responsive neurons, implementing a pattern association network (Rolls, 1999; Rolls & Treves, 1998; Rolls & Deco, 2002). When the reinforcement association of a visual stimulus is reversed, other orbitofrontal cortex neurons stop responding, or stop responding differentially, to the visual discriminanda (Thorpe et al., 1983). For example, one neuron in the orbitofrontal cortex 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+. Similar conditional reward neurons were found for olfactory stimuli (Rolls et al., 1996b). Such conditional reward neurons convey information about the current reinforcement status of particular stimuli, and may reflect the fact that not every neuron which learns associations to primary reinforcers (such as taste) can sample the complete space of all possible conditioned (e.g., visual or olfactory) stimuli when acting as a pattern associator. Nevertheless such neurons can convey very useful information, for they indicate when one of the stimuli to which they are capable of responding (given their inputs) is currently associated with reward. Similar neurons are present for punishing primary reinforcers, such as the aversive taste of salt.

In addition to these neurons that encode the reward association of visual stimuli, other 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) (Table 1, Visual Discrimination Reversal), or when reward is no longer made available in a visual discrimination task (Table 1, Visual Discrimination Extinction). 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 for aversive tasting saline during ad lib licking (Table 1, Ad Lib Licking Reversal) (Thorpe et al., 1983) (see Table 1). 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 Rolls, 1986a, 1990). The finding that different orbitofrontal cortex neurons respond to different types of non-reward (Thorpe et al., 1983), may provide part of the brain's mechanism that enables task or context-specific reversal to occur.

Another type of information represented in the orbitofrontal cortex is information about faces. There is a population of orbitofrontal neurons which respond in many ways similar to those in the temporal cortical visual areas (see Rolls, 1984a, 1992a, 1994a, 1995b, 1996, 1997b, 2000d; Rolls & Deco, 2002; Wallis & Rolls, 1997 for a description of their properties). The orbitofrontal face-responsive neurons, first observed by Thorpe et al. (1983), then by Rolls, Critchley, and Browning (2002 in preparation, see Booth, Rolls, Critchley, Browning, & Hernadi, 1998) 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

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	1	0	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).

than to two-dimensional images of faces on a video monitor (cf. Rolls & Baylis, 1986). Some of the orbitofrontal cortex face-selective neurons are responsive to face gesture or movement. 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 (cf. Hasselmo, Rolls, & Baylis, 1989), which can indicate reinforcement. The second way is that they encode information about which individual is present, which by stimulus–reinforcement association learning is important in evaluating and utilizing learned reinforcing inputs in social situations, e.g., about the current reinforcement value as decoded by stimulus–reinforcement association of a particular individual.

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

4.5. Somatosensory inputs to the orbitofrontal cortex

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, Rolls, & Wakeman, 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,

Critchley, Browning, Hernadi, & Lenard, 1999a). These inputs are perceived as pleasant when hungry, because of the utility of ingestion of foods which are likely to contain essential fatty acids and to have a high calorific value (Rolls, 1999, 2000b). We have recently 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, Rolls, & Kadohisa, 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, Verhagen, & Kadohisa, 2003c); and that other neurons have responses that indicate the presence of stimuli in the mouth independently of viscosity and slickness (Rolls et al., 2003b). 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.

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., 1997a, 2003a; see below).

5. A neurophysiological basis for stimulus–reinforcement learning and reversal in the orbitofrontal cortex

The neurophysiological, imaging, and lesion evidence described 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. To implement this, the orbitofrontal cortex has the necessary representation of primary reinforcers, including taste and somatosensory stimuli. It also receives information about objects, e.g., visual view-invariant information (Booth & Rolls, 1998; Rolls, 2000d), and can associate this at the neuronal level with primary reinforcers such as taste, and reverse these associations very rapidly (Rolls et al., 1996b; Thorpe et al., 1983). Another type of stimulus which can be conditioned in this way in the orbitofrontal cortex is olfactory, although here the learning is slower. It is likely that auditory stimuli can be associated with primary reinforcers in the orbitofrontal cortex, though there is less direct evidence of this yet. The orbitofrontal cortex also has neurons which detect non-reward, which are likely to be used in behavioural extinction and reversal (Thorpe et al., 1983). They may do this not only by helping to reset the reinforcement association of neurons in the orbitofrontal cortex, but also by sending a signal to the striatum which could be routed by the striatum to produce appropriate behaviours for non-reward (Rolls, 1994b; Rolls & Johnstone, 1992; Williams, Rolls, Leonard, & Stern, 1993). Indeed, it is via this route, the striatal, that the orbitofrontal cortex may directly influence behaviour when the orbitofrontal cortex is decoding reinforcement contingencies in the environment, and is altering behaviour in response to altering reinforcement contingencies (see Rolls, 1999). Some of the evidence for this is that neurons that reflect these orbitofrontal neuronal responses are found in the ventral part of the head of the caudate nucleus and the ventral striatum, which receive input from the orbitofrontal cortex (Rolls, Thorpe, & Maddison, 1983a; Williams et al., 1993); and lesions of the ventral part of the head of the caudate nucleus impair visual discrimination reversal (Divac, Rosvold, & Szwarcbart, 1967).

Decoding the reinforcement value of stimuli, which involves for previously neutral (e.g., visual) stimuli learning their association with a primary reinforcer, often rapidly, and which may involve not only rapid learning but also rapid relearning and alteration of responses when reinforcement contingencies change, is then a function proposed for the orbitofrontal cortex. This way of producing behavioural responses would be important in for example motivational and emotional behaviour. It would be important for example in motivational behaviour such as feeding and drinking by enabling primates to learn rapidly about the food reinforcement to be expected from visual stimuli (see Rolls, 1994c, 1999). This is important, for primates frequently eat more than 100 varieties of food; vision by visual–taste association learning can be used to identify when foods are ripe; and during the course of a meal, the pleasantness of the sight of a food eaten in the meal decreases in a sensory-specific way (Rolls, Rolls, & Rowe, 1983b), a function that is probably implemented by the sensory-specific satiety-related responses of orbitofrontal visual neurons (Critchley & Rolls, 1996b).

With respect to emotional behaviour, decoding and rapidly readjusting the reinforcement value of visual signals is likely to be crucial, for emotions can be described as responses elicited by reinforcing signals[1]

[1] For the purposes of this paper, a positive reinforcer or reward can be defined as a stimulus which the animal will work to obtain, and a negative reinforcer or punishment as a stimulus that an animal will work to avoid or escape (see further Rolls, 1990, 1999).

(Rolls, 1986a, 1986b, 1990, 1995b, 1999, 2000a). 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. Although the functions of the orbitofrontal cortex in implementing the operation of reinforcers such as taste, smell, tactile, and visual stimuli including faces are most understood, in humans the rewards processed in the orbitofrontal cortex include quite general rewards such as working for "points," as will be described shortly.

Although the amygdala is concerned with some of the same functions as the orbitofrontal cortex, and receives similar inputs (see Fig. 2), there is evidence that it may function less effectively in the very rapid learning and reversal of stimulus–reinforcement associations, as indicated by the greater difficulty in obtaining reversal from amygdala neurons (see, e.g., Rolls, 1992b, 2000e, 2000f), and by the greater effect of orbitofrontal lesions in leading to continuing choice of no longer rewarded stimuli (Jones & Mishkin, 1972). In primates, the necessity for very rapid stimulus–reinforcement re-evaluation, and the development of powerful cortical learning systems, may result in the orbitofrontal cortex effectively taking over this aspect of amygdala functions (see Rolls, 1992b, 1999).

6. The human orbitofrontal cortex

6.1. Neuropsychology

It is of interest that a number of the symptoms of frontal lobe damage in humans appear to be related to this type of function, of altering behaviour when stimulus–reinforcement associations alter, as described next. Thus, humans with frontal lobe damage can show impairments in a number of tasks in which an alteration of behavioural strategy is required in response to a change in environmental reinforcement contingencies (see Goodglass & Kaplan, 1979; Jouandet & Gazzaniga, 1979; Kolb & Whishaw, 1996). For example, Milner (1963) showed that in the Wisconsin Card Sorting Task (in which cards are to be sorted according to the colour, shape, or number of items on each card depending on whether the examiner says "right" or "wrong" to each placement), frontal patients either had difficulty in determining the first sorting principle, or in shifting to a second principle when required to. Also, in stylus mazes, frontal patients have difficulty in changing direction when a sound indicates that the correct path has been left (see Milner, 1982). It is of interest that, in both types of test, frontal patients may be able to verbalize the correct rules, yet may be unable to correct their behavioral sets or strategies appropriately. Some of the personality changes that can follow frontal lobe damage may be related to a similar type of dysfunction. For example, the euphoria, irresponsibility, lack of affect, and lack of concern for the present or future which can follow frontal lobe damage (see Damasio, 1994; Hecaen & Albert, 1978) may also be related to a dysfunction in altering behaviour appropriately in response to a change in reinforcement contingencies. Indeed, in so far as the orbitofrontal cortex is involved in the disconnection of stimulus–reinforcer associations, and such associations are important in learned emotional responses (see above), then it follows that the orbitofrontal cortex is involved in emotional responses by correcting stimulus–reinforcer associations when they become inappropriate.

These hypotheses, and the role in particular of the orbitofrontal cortex in human behaviour, have been investigated in recent studies in humans with damage to the ventral parts of the frontal lobe. (The description ventral is given to indicate that there was pathology in the orbitofrontal or related parts of the frontal lobe, and not in the more dorso-lateral parts of the frontal lobe.) A task that was directed at assessing the rapid alteration of stimulus–reinforcement associations was used, because the findings above indicate that the orbitofrontal cortex is involved in this type of learning. This was used instead of the Wisconsin Card Sorting Task, which requires patients to shift from category (or dimension) to category, e.g., from colour to shape. The task used was visual discrimination reversal, in which patients could learn to obtain points by touching one stimulus when it appeared on a video monitor, but had to withhold a response when a different visual stimulus appeared, otherwise a point was lost. After the subjects had acquired the visual discrimination, the reinforcement contingencies unexpectedly reversed. The patients with ventral frontal lesions made more errors in the reversal task (or in a similar extinction task in which the reward was no longer given), and completed fewer reversals, than control patients with damage elsewhere in the frontal lobes or in other brain regions (Rolls et al., 1994; see Table 2). The impairment correlated highly with the socially inappropriate or disinhibited behaviour of the patients (assessed in a Behaviour Questionnaire) (see Table 2), and also with their subjective evaluation of the changes in their emotional state since the brain damage (see Table 2 and Rolls et al., 1994). The patients were not impaired at other types of memory task, such as paired associate learning. The continued choice of the no longer rewarded stimulus in the reversal of the visual discrimination task is interpreted as a failure to reverse stimulus–reinforcer, that is sensory–sensory, associations, and not as motor response perseveration which may follow much more dorsal damage to the frontal lobes. This has been confirmed in a new reversal task in which one of two simultaneously shown stimuli in

Table 2
Vocal and face expression identification in patients with damage to the ventral parts of the frontal lobes and in control patients

	Behavior quest	Subjective emotional change	Face expression % Corr (*SD*)	Vocal expression % Corr (*SD*)	Number of Reversals	Last error reversal	Last error extinction
Ventral frontal case No.							
1	6.0	—	29 (−6.5)**	42 (−3.7)**	0 (76%)	38F	—
2	4.0	2.0	84 (−0.4)	30 (−4.8)**	0 (83%)	50F	30F (93%)
3	6.0	7.5	60 (−3.1)**	36 (−4.9)**	0 (75%)	20F	—
4	7.5	4.5	60 (−3.0)**	54 (−2.5)**	0 (67%)	30F	—
5	8.5	7.0	58 (−3.2)**	39 (−4.0)**	—	—	34F
6	5.0	1.5	75 (−1.3)	67 (−1.3)	0 (54%)	51F	53F (38%)
7	6.0	5.0	67 (−2.3)**	58 (−2.1)**	2	4	30F (86%)
8	7.0	2.5	54 (−3.7)**	—	0 (100%)	50F	48F (93%)
9	4.0	1.5	83 (−0.4)	81 (+0.1)	2	5	36 (45%)
10	5.0	4.0	67 (−2.2)**	60 (−1.9)*	1	23	9
11	4.5	6.5	40 (−5.3)**	53 (−2.6)**			
12	3.0		38 (−5.6)**	43 (−3.5)**			
Medians	5.5	4.3	60	53	0	30	34
Non-ventral case No.							
1	0.0	0.5	79 (−0.9)		2 (14%)	4	21 (43%)
2	2.5	1.0	83 (−0.4)		2 (46%)	11	12 (36%)
3	0.5	0.0	83 (−0.4)	61 (−1.8)*	2 (25%)	7	4 (7%)
4	0.0	2.0	75 (−1.4)	61 (−1.8)*	2 (8%)	4	3 (7%)
5	0.0	1.5	71 (−1.8)*	67 (−1.2)	1	14	13 (21%)
6	2.0	1.0	92 (+0.6)	75 (−0.5)	2 (42%)	13	100 (0%)
7	2.5	1.0	75 (−1.4)	61 (−1.8)*			
8	0.0	2.5	96 (+0.1)	78 (−0.2)			
9	0.5	1.0	67 (−2.3)**				
10	1.0	1.5	79 (−0.9)	72 (−0.7)			
11	0.5	1.0	83 (−0.4)	61 (−1.8)*			
12							4 (7%)
13					2 (8%)	4	4 (7%)
Medians	0.5	1.0	79	64	2	7	4

Also shown are the number of reversals completed in 30 trials, and the number of the last trial on which an error occurred during Reversal or Extinction. Data from Rolls et al. (1994) and Hornak et al. (1996).

Key: Behavior Quest: Behavior Questionnaire.

SD, number of standard deviations above (+) or below (−) the means for normal subjects.

*Scores which fall below the 5th centile of the normal distribution, i.e., $SD < -1.64$ (impaired).

**Scores which fall below the 1st centile of the normal distribution, i.e., $SD < -1.96$ (severely impaired).

The median values for reversal and extinction are for a larger group.

F, failed to reach criterion in reversal or extinction.

The % columns refer for reversal and extinction to the percentage of errors of commission, that is responses made to the stimulus that was before reversal or extinction the reward-related stimulus (old S+).

random screen positions must be selected on every trial, so that response preseveration is not a factor. It has been found that patients with circumscribed surgical lesions confined to the orbitofrontal cortex are impaired at this new reversal task (Hornak et al., 2004). In addition, I note that one of the types of evidence which bears very directly on this comes from the responses of orbitofrontal cortex neurons. The evidence comes from the neurons which respond in relation to a sensory stimulus such as a visual stimulus when it is paired with another sensory stimulus to which the neuron responds such as a taste stimulus. The taste stimulus is a primary reinforcer. These neurons do not respond to motor responses, and could not be involved in stimulus to motor response association learning. Bechara and colleagues also have findings which are consistent with these in patients with frontal lobe damage when they perform a gambling task (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Tranel, Damasio, & Damasio, 1996; Bechara, Damasio, Tranel, & Damasio, 1997; see also Damasio, 1994). The patients could choose cards from several decks. The patients with frontal damage were more likely to choose cards from a deck which did give rewards with a reasonable probability, but also had occasional very heavy penalties resulting in lower net gains than choices from the other deck. In this sense, the patients were not affected by the negative consequences of their actions: they did not switch from the deck of cards which was providing significant rewards even when large punishments were incurred. In a further recent study it was shown that the type of impulsiveness found in borderline personality disorder patients in

which choices are made more rapidly than normal (in a matching familiar figures task) is also produced by orbitofrontal cortex lesions (Berlin, Rolls, & Kischka, 2004a; Berlin, Rolls, & Iversen, 2004b; Berlin & Rolls, 2004).

It is of interest that in the reversal and extinction tasks the patients can often verbalize the correct response, yet commit the incorrect action (Rolls et al., 1994). This is consistent with the hypothesis that the orbitofrontal cortex is normally involved in executing behaviour when the behaviour is performed by evaluating the reinforcement associations of environmental stimuli (see below and Rolls, 1999, Chap. 9). The orbitofrontal cortex appears to be involved in this in both humans and non-human primates, when the learning must be performed rapidly, for example in acquisition, and during reversal.

An idea of how such stimulus–reinforcer learning may play an important role in normal human behaviour, and may be related to the behavioural changes seen clinically in these patients with ventral frontal lobe damage, can be provided by summarizing the behavioural ratings given by the carers of these patients. The patients were rated high in the Behaviour Questionnaire on at least some of the following: disinhibited or socially inappropriate behaviour; misinterpretation of other people's moods; impulsiveness; unconcern or underestimation of the seriousness of their condition; and lack of initiative (Rolls et al., 1994). Such behavioural changes correlated with the stimulus–reinforcer reversal and extinction learning impairment (Rolls et al., 1994). The suggestion thus is that the insensitivity to reinforcement changes in the learning task may be at least part of what produces the changes in behaviour found in these patients with ventral frontal lobe damage. The more general impact on the behaviour of these patients is that their irresponsibility tended to affect their everyday lives. For example, if such patients had received their brain damage in a road traffic accident, and compensation had been awarded, the patients often tended to spend their money without appropriate concern for the future, sometimes for example buying a very expensive car. Such patients often find it difficult to invest in relationships too, and are sometimes described by their family as having changed personalities, in that they care less about a wide range of factors than before the brain damage. The suggestion that follows from this and from impairments of patients with circumscribed surgical lesions of the orbitofrontal cortex on a similar behaviour questionnaire (Hornak et al., 2003) is that the orbitofrontal cortex may normally be involved in much social behaviour, and the ability to respond rapidly and appropriately to social reinforcers is of course an important aspect of primate (including human) social behaviour (see further Kringelbach & Rolls, 2003).

To investigate the possible significance of face-related inputs to orbitofrontal visual neurons described above, we also tested the responses of these patients to faces. We included tests of face (and also voice) expression decoding, because these are ways in which the reinforcing quality of individuals is often indicated. Impairments in the identification of facial and vocal emotional expression were demonstrated in a group of patients with ventral frontal lobe damage who had socially inappropriate behaviour (Hornak et al., 1996; see Tables 2–4). The expression identification impairments could occur independently of perceptual impairments in facial recognition, voice discrimination, or environmental sound recognition. The face and voice expression problems did not necessarily occur together in the same patients, providing an indication of separate processing. The impairment was found on most expressions apart from happy (which as the only positive face expression was relatively easily discriminable from the others), with sad, angry, frightened, and disgusted showing lower identification than surprised and neutral (see Table 3). 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

Table 3
Facial expression identification

	Sad	Angry	Frightened	Disgusted	Surprised	Happy	Neutral
Normal subjects, $N = 11$	68.6	94.7	77.6	81.8	92.0	100.0	93.9
Frontal patients, $N = 9$	22.6	39.3	31.9	48.1	66.2	94.0	65.7

Group mean percent correct on each emotion in normal subjects and in impaired ventral frontal patients (data from Hornak et al. (1996)).

Table 4
Vocal expression identification

	Sad	Angry	Frightened	Disgusted	Puzzled	Contented
Normal subjects, $N = 10$	80.8	66.1	88.1	95.0	78.9	68.9
Frontal patients, $N = 7$	14.7	25.0	52.8	80.9	42.8	33.3

Group mean percent correct on each emotion in normal subjects and in impaired ventral frontal patients. Data from Hornak et al. (1996).

emotional experience and the severity of the behavioural problems (e.g., disinhibition) found in these patients (see Hornak et al., 1996 and Table 2). 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 (see Hornak et al., 1996 and Table 2). In current studies, these investigations are being extended, and it is being found that patients with face expression decoding problems do not necessarily have impairments at visual discrimination reversal, and vice versa (Hornak et al., 2003). This is consistent with some topography in the orbitofrontal cortex (see, e.g., Rolls & Baylis, 1994).

Studies are now being performed to obtain precise evidence of the precise areas of brain damage that give rise to these deficits in humans. The studies are being performed with patients with discrete surgical lesions of the orbitofrontal cortex (performed for example to remove tumors). These studies are valuable in the context that closed head injuries may, although producing demonstrable damage to the orbitofrontal cortex in structural MRI scans, also produce some damage elsewhere. It is being found (Hornak et al., 2003, 2004) that bilateral surgically circumscribed lesions (but not usually unilateral) lesions of the human orbitofrontal cortex produce deficits in a probabilistic version of a visual discrimination reversal task with monetary reward (described by O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001a).

6.2. Neuroimaging

To elucidate the role of the human orbitofrontal cortex in emotion further, Rolls, Francis et al. (1997a; Francis et al., 1999) performed an investigation to determine where the pleasant affective component of touch is represented in the brain. Touch is a primary reinforcer that can produce pleasure. They found with fMRI that a weak but very pleasant touch of the hand with velvet produced much stronger activation of the orbitofrontal cortex than a more intense but affectively neutral touch of the hand with wood. In contrast, the affectively neutral but more intense touch produced more activation of the primary somatosensory cortex than the pleasant stimuli. These findings indicate that part of the orbitofrontal cortex is concerned with representing the positively affective aspects of somatosensory stimuli. The significance of this finding is that a primary reinforcer that can produce affectively positive emotional responses is represented in the human orbitofrontal cortex. This provides one of the bases for the human orbitofrontal cortex to be involved in the stimulus–reinforcement association learning that provides the basis for emotional learning. In more recent studies, we (Rolls et al., 2003a) are finding that there is also a representation of the affectively negative aspects of touch, including pain, in the human orbitofrontal cortex. This is consistent with the reports that humans with damage to the ventral part of the frontal lobe may report that they know that a stimulus is pain-producing, but that the pain does not feel very bad to them (see Freeman & Watts, 1950; Melzack & Wall, 1996; Valenstein, 1974). It will be of interest to determine whether the regions of the human orbitofrontal cortex that represent pleasant touch and pain are close topologically or overlap. Even if fMRI studies show that the areas overlap, it would nevertheless be the case that different populations of neurons would be being activated, for this is what recordings from single cells in monkeys indicate about positively vs negatively affective taste, olfactory and visual stimuli (see above).

It is also of interest that nearby, but not overlapping, parts of the human orbitofrontal cortex are activated by taste stimuli (such as glucose, umami, and water) (De Araujo, Kringelbach, Rolls, & Hobden, 2003a; De Araujo, Kringelbach, Rolls, & McGlone, 2003b; O'Doherty et al., 2001b; Small et al., 1999), and that it has recently been shown that it is the pleasantness of olfactory stimuli that is represented in the human orbitofrontal cortex, in that orbitofrontal cortex activation decreases to an odor that has been eaten to satiety so that it no longer is rewarding and smells pleasant (O'Doherty et al., 2000; see also Kringelbach et al., 2003). Further, a discrete region of the human medial orbitofrontal cortex has been shown to be activated by subjectively pleasant odors (Rolls et al., 2003b) and by flavor (De Araujo, Rolls, Kringelbach, McGlone, & Phillips, 2003c). Thus many hedonically effective stimuli activate the human orbitofrontal cortex.

In a task designed to show whether the human orbitofrontal cortex is involved in more abstract types of reward and punishment, O'Doherty et al. (2001a) found that the medial orbitofrontal cortex showed activation that was correlated with the amount of money just received in a probabilistic visual association task, and that the lateral orbitofrontal cortex showed activation that was correlated with the amount of money just lost. This study shows that the magnitudes of quite abstract rewards and punishers are represented in the orbitofrontal cortex.

These human neuroimaging studies on the orbitofrontal cortex are thus providing confirmation that the theory of emotion and how it is relevant to understanding orbitofrontal cortex function (Rolls, 1999, 2000a) does apply also to humans, in that representations of many types of reward and punisher are being found in the human orbitofrontal cortex (Kringelbach & Rolls, 2004). This evidence helps us to understand behavioral changes after orbitofrontal cortex damage in humans as related to alterations in processing and learning associations to rewards and punishers which

are normally important in emotional and social behavior. The aim here is to understand the functions of the human orbitofrontal cortex in terms of the operations it performs, and with the help of the precise neurophysiological evidence available from studies in non-human primates.

7. Neuronal network computations in the prefrontal cortex

7.1. Stimulus–reinforcement association and reversal

This reversal learning that occurs in the orbitofrontal cortex could be implemented by Hebbian modification of synapses conveying visual input onto taste-responsive neurons, implementing a pattern association network (Rolls, 1999, 2000f; Rolls & Treves, 1998; Rolls & Deco, 2002). Long-term potentiation would strengthen synapses from active conditional stimulus neurons onto neurons 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. 4). As noted above, the conditional reward neurons in the orbitofrontal cortex convey information about the current reinforcement status of particular stimuli, and may reflect the fact that not every neuron which learns associations to primary reinforcers (such as taste) can sample the complete space of all possible conditioned (e.g., visual or olfactory) stimuli when acting as a pattern associator. Nevertheless such neurons can convey very useful information, for they indicate when one of the stimuli to which they are capable of responding (given their inputs) is currently associated with reward (Thorpe et al., 1983). Similar neurons are present for punishing primary reinforcers, such as the aversive taste of salt. It has recently been proposed that the very rapid, one-trial, reversal that is a property of visual orbitofrontal cortex neurons, may require a short term memory attractor network to retain the current rule (e.g., stimulus A is currently rewarded), and that a small degree of synaptic adaptation in this rule network would provide for the alternative rule state to emerge after the attractor is quenched by a non-reward signal (Deco & Rolls, 2004).

The error-detection neurons that respond during frustrative non-reward may be triggered by a mismatch between what was expected when the visual stimulus was shown, and the primary reinforcer that was obtained, both of which are represented in the primate orbitofrontal cortex (Thorpe et al., 1983).

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. 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 an error signal during learning (see Schultz et al., 2000), there is evidence that instead dopamine release is more closely related to whether active initiation of behaviour is required, whether this is to

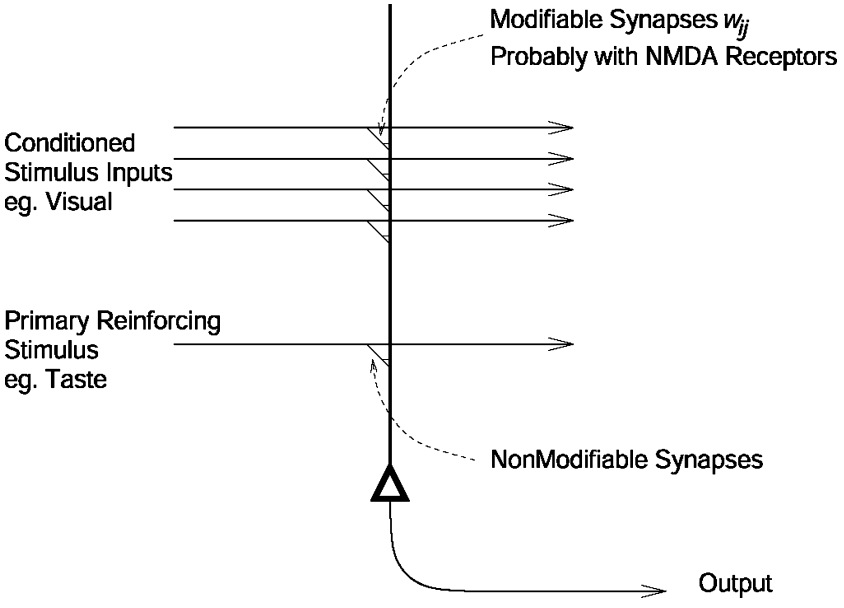

Fig. 4. A pattern association network that could underlie the learning and reversal of stimulus–reinforcement association learning in the orbitofrontal cortex (see text) (after Rolls, 1999).

obtain rewards or escape from or avoid punishers (see Rolls, 1999, 2000a).

7.2. Prefrontal cortex neuronal networks for working memory

In a sense, the orbitofrontal cortex by its rapid stimulus–reinforcer association learning remembers the recent reward association of stimuli, and implements this by synaptic plasticity, so that no ongoing neuronal firing is needed to implement stimulus–reinforcer association memory. In contrast, the inferior convexity prefrontal cortex, and the dorsolateral prefrontal cortex, implement a short-term memory for stimuli that is maintained by the active continuing firing of neurons. I now consider how this latter form of memory appears to be implemented in the prefrontal cortex.

A common way that the brain uses to implement a short-term memory is to maintain the firing of neurons during a short memory period after the end of a stimulus (see Rolls, 2000d; Rolls & Treves, 1998). In the inferior temporal cortex this firing may be maintained for a few hundred milliseconds even when the monkey is not performing a memory task (Rolls & Tovee, 1994; Rolls et al., 1994; Rolls, Tovee, & Panzeri, 1999b; cf. Desimone, 1996). In more ventral temporal cortical areas such as the entorhinal cortex the firing may be maintained for longer periods in delayed match to sample tasks (Suzuki, Miller, & Desimone, 1997), and in the prefrontal cortex for even tens of seconds (see Fuster, 1997). In the dorsolateral and inferior convexity prefrontal cortex the firing of the neurons may be related to the memory of spatial responses or objects (Goldman-Rakic, 1996, Wilson et al., 1993) or both (Rao et al., 1997), and in the principal sulcus/frontal eye field/arcuate sulcus region to the memory of places for eye movements (Funahashi, Bruce, & Goldman-Rakic, 1989). The firing may be maintained by the operation of associatively modified recurrent collateral connections between nearby pyramidal cells producing attractor states in autoassociative networks (Amit, 1995; Rolls & Treves, 1998). For the short-term memory to be maintained during periods in which new stimuli are to be perceived, there *must* be separate networks for the perceptual and short-term memory functions, and indeed two coupled networks, one in the inferior temporal visual cortex for perceptual functions, and another in the prefrontal cortex for maintaining the short-term memory during intervening stimuli, provides a precise model of the interaction of perceptual and short-term memory systems (Renart, Parga, & Rolls, 2000; Rolls & Deco, 2002). In particular, it is shown how a prefrontal cortex attractor (autoassociation) network could be triggered by a sample visual stimulus represented in the inferior temporal visual cortex in a delayed match to sample task, and could keep this attractor active during a memory interval in which intervening stimuli are shown. Then when the sample stimulus reappears in the task as a match stimulus, the inferior temporal cortex module showed a large response to the match stimulus, because it is activated both by the incoming match stimulus, and by the consistent backprojected memory of the sample stimulus still being represented in the prefrontal cortex memory module (see Fig. 5).

This computational model makes it clear that in order for ongoing perception to occur unhindered implemented by posterior cortex (parietal and temporal lobe) networks, there must be a separate set of modules that is capable of maintaining a representation over intervening stimuli (Rolls & Deco, 2002). This approach emphasizes that in order to provide a good brain lesion test of prefrontal cortex short-term memory functions, the task

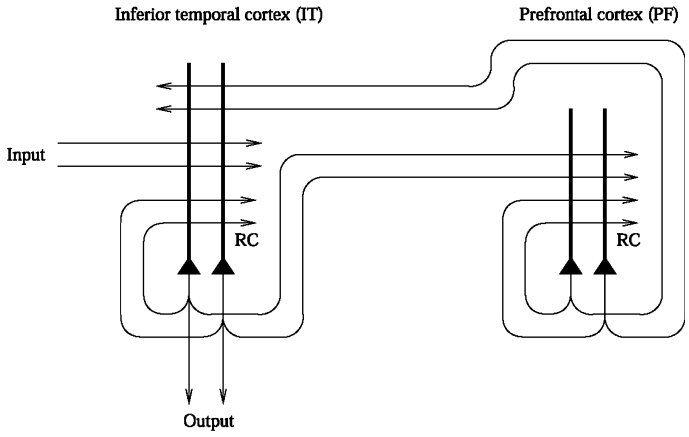

Fig. 5. A short-term memory autoassociation network in the prefrontal cortex could hold active a working memory representation by maintaining its firing in an attractor state. The prefrontal module would be loaded with the to-be-remembered stimulus by the posterior module (in the temporal or parietal cortex) in which the incoming stimuli are represented. Backprojections from the prefrontal short-term memory module to the posterior module would enable the working memory to be unloaded, to for example influence on-going perception (see text) (after Rolls & Deco, 2002).

set should require a short-term memory for stimuli over an interval in which other stimuli are being processed, because otherwise the posterior cortex perceptual modules could implement the short-term memory function by their own recurrent collateral connections. This approach also emphasizes that there are many at least partially independent modules for short-term memory functions in the prefrontal cortex (e.g., several modules for delayed saccades in the frontal eye fields; one or more for delayed spatial (body) responses in the dorsolateral prefrontal cortex; one or more for remembering visual stimuli in the more ventral prefrontal cortex; and at least one in the left prefrontal cortex used for remembering the words produced in a verbal fluency task—see Rolls & Treves, 1998, Chap. 10). This computational approach thus provides a clear understanding for why a separate (prefrontal) mechanism is needed for working memory functions (Rolls & Deco, 2002). It may also be commented that if a prefrontal cortex module is to control behaviour in a working memory task, then it must be capable of assuming some type of executive control. There may be no need to have a single central executive additional to the control that must be capable of being exerted by every short-term memory module (see Deco & Rolls, 2003).

To set up a new short-term memory attractor, synaptic modification is needed to form the new stable attractor. Once the attractor is set up, it may be used repeatedly when triggered by an appropriate cue to hold the short-term memory state active by continued neuronal firing even without any further synaptic modification (see Kesner & Rolls, 2001). Thus agents that impair the long-term potentiation of synapses (LTP) may impair the formation of new short-term memory states, but not the use of previously learned short-term memory states (see Kesner & Rolls, 2001).

8. Conclusions and summary

The orbitofrontal cortex contains the secondary taste cortex, in which the reward value of taste is represented. It also contains the secondary and tertiary olfactory cortical areas, in which information about the identity and also about the reward value of odours is represented. The orbitofrontal cortex also receives information about the sight of objects from the temporal lobe cortical visual areas, and neurons in it learn and reverse the visual stimulus to which they respond when the association of the visual stimulus with a primary reinforcing stimulus (such as taste) is reversed. This is an example of stimulus–reinforcement association learning, and is a type of stimulus–stimulus association learning. More generally, the stimulus might be a visual or olfactory stimulus, and the primary (unlearned) positive or negative reinforcer a taste or touch. A somatosensory input is revealed by neurons that respond to the texture of food in the mouth, including a population that responds to the mouth feel of fat. In complementary neuroimaging studies in humans, it is being found that areas of the orbitofrontal cortex are activated by pleasant touch, by painful touch, by taste, by smell, and by more abstract reinforcers such as winning or losing money. Damage to the orbitofrontal cortex can impair the learning and reversal of stimulus–reinforcement associations, and thus the correction of behavioural responses when these are no longer appropriate because previous reinforcement contingencies change. The information which reaches the orbitofrontal cortex for these functions includes information about faces, and damage to the orbitofrontal cortex can impair face (and voice) expression identification. This evidence thus shows that the orbitofrontal cortex is involved in decoding and representing some primary reinforcers such as taste and touch; in learning and reversing associations of visual and other stimuli to these primary reinforcers; and in controlling and correcting reward-related and punishment-related behaviour, and thus in emotion. The approach described here is aimed at providing a fundamental understanding of how the orbitofrontal cortex actually functions, and thus in how it is involved in motivational behavior such as feeding and drinking, in emotional behavior, and in social behavior.

A special role of the orbitofrontal cortex in behavior may arise from the fact that it receives outputs from the ends of a number of sensory systems that define "what" stimuli are being presented (as contrasted for example with "where" stimuli are in space). The inputs it receives include taste and somatosensory stimuli, which are prototypical primary reinforcers. This helps to give the orbitofrontal cortex a special role in behaviors produced by rewards and punishers, which happen to encompass in particular emotional and motivational behavior. The particular role that the orbitofrontal cortex implements for these functions is that it decodes the reward (and punishment) value of these primary reinforcers, and also implements a learning mechanism to enable sensory representations of objects (in, e.g., the visual and olfactory sensory modalities) to be associated with these primary reinforcers. Indeed, the orbitofrontal cortex appears to play a special role in such learning, because it can rapidly reverse such stimulus–reinforcement associations. It may be able to perform this reversal more efficiently and rapidly than the amygdala because, as a neocortical structure, its learning mechanisms include rapid and powerful long-term associative synaptic depression (LTD), occurring for example if a visual stimulus represented presynaptically is no longer associated with firing of a post-synaptic neuron responsive to a reward such as sweet taste (see Rolls & Deco, 2002).

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