



# Taste, olfactory, and food reward value processing in the brain



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## ABSTRACT

Complementary neuronal recordings in primates, and functional neuroimaging in humans, show that the primary taste cortex in the anterior insula provides separate and combined representations of the taste, temperature, and texture (including fat texture) of food in the mouth independently of hunger and thus of reward value and pleasantness. One synapse on, in a second tier of processing, in the orbitofrontal cortex, these sensory inputs are for some neurons combined by associative learning with olfactory and visual inputs, and these neurons encode food reward value on a continuous scale in that they only respond to food when hungry, and in that activations correlate linearly with subjective pleasantness. Cognitive factors, including word-level descriptions, and selective attention to affective value, modulate the representation of the reward value of taste and olfactory stimuli in the orbitofrontal cortex and a region to which it projects, the anterior cingulate cortex, a tertiary taste cortical area. The food reward representations formed in this way play an important role in the control of appetite, and food intake. Individual differences in these reward representations may contribute to obesity, and there are age-related differences in these value representations that shape the foods that people in different age groups find palatable. In a third tier of processing in medial prefrontal cortex area 10, decisions between stimuli of different reward value are taken, by attractor decision-making networks.

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## 1. Introduction

### 1.1. Aims

The aims of this paper are to describe how taste, olfactory, and food texture inputs are processed in the brain, how a representation of reward value is produced and is related to subjective pleasure, how cognition and selective attention influence this value-related processing, and how decisions are taken between stimuli with different reward value. The approach taken here is to consider together, side-by-side, the primate neuronal recording and the human functional magnetic resonance imaging (fMRI) evidence, to build a clear foundation for understanding taste and olfactory cortical processing and the underlying principles in primates including humans. This approach is important, for it appears that some of the underlying principles of taste and olfactory processing are different in rodents, as described below. The focus of this paper is on processing in the brain, with research on peripheral processing described elsewhere (Barretto et al., 2015; Buck and Bargmann, 2013; Chaudhari and Roper, 2010; Mombaerts, 2006; Mori and Sakano, 2011).

### 1.2. Food reward value and appetite

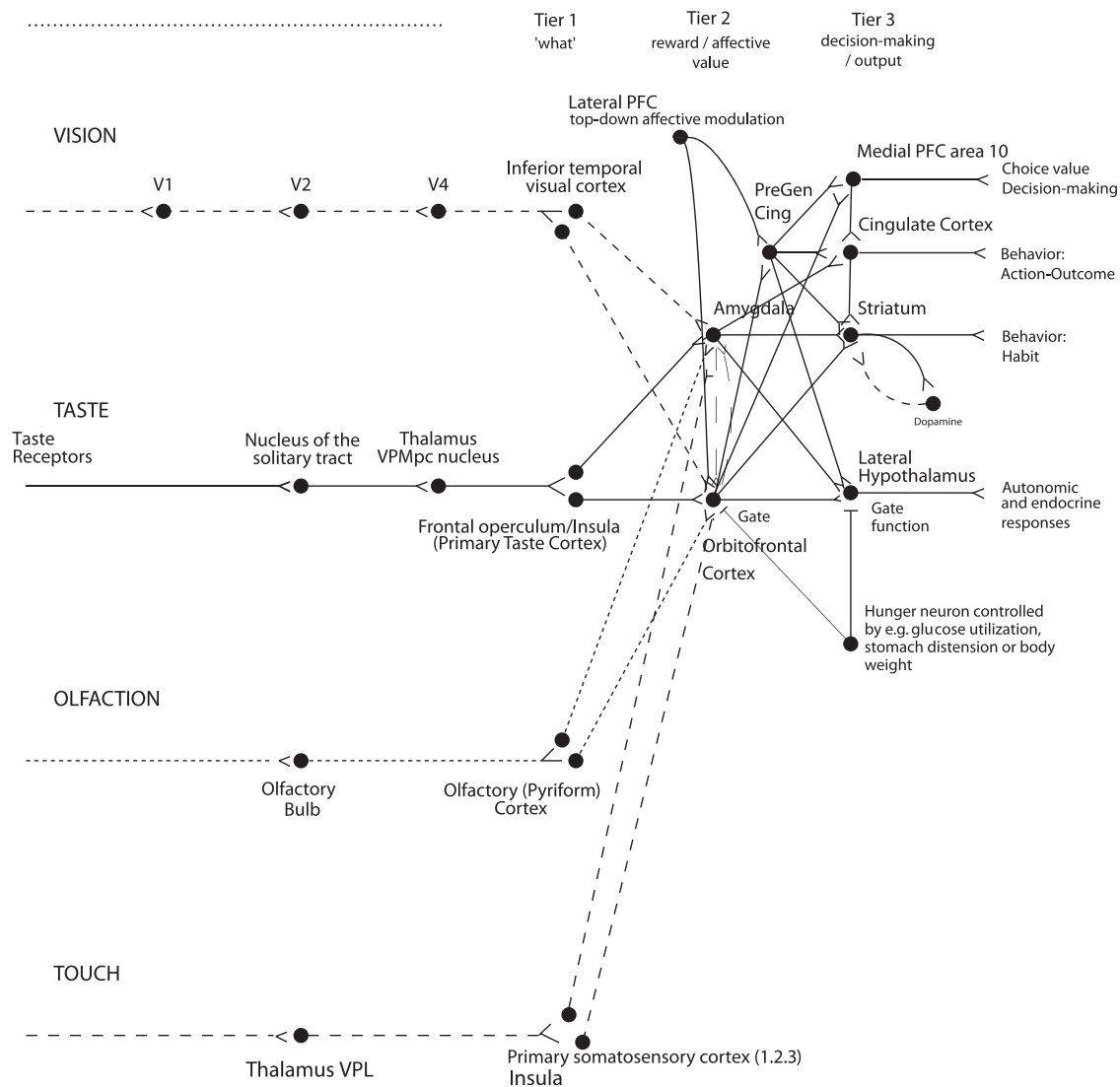
One reason why it is important to understand the brain systems for processing taste, olfactory, and oral texture inputs is that during cortical processing food reward value becomes, by the secondary taste and olfactory cortex in the orbitofrontal cortex, explicit in the representation, in that the reward value can be decoded simply from the firing rates of the neurons. This is important for understanding the control of food intake, in that the reward value of food (i.e. whether we will work for a food), measures our appetite for a food, and whether we will eat a food. Thus normally we want food (will work for it, and will eat it) when we like it. “We want because we like”: the goal value, the food reward value, makes us want it. For example, neurons in the orbitofrontal cortex and lateral hypothalamus described below respond to the reward value of a food when it is, for example, shown, and these neuronal responses predict whether that food will be eaten (Rolls, 1981, 2005b, 2014; Rolls et al., 1986, 1989). Similarly, in studies on sensory-specific satiety in humans based on these neurophysiological discoveries, the reported pleasantness in humans of a food is closely correlated with whether it will then be eaten, and even with how much is eaten (Rolls et al., 1981b, 1983b, 1984). (The situation when it has been suggested that wanting is not a result of liking (Berridge et al., 2009), is when behavior becomes a habit. A

habit is a stimulus-response type of behavior that is no longer under control of the goal, but is under the control of an overlearned conditioned stimulus involved in stimulus-response, habit, behavioral responses (Rolls, 2005b, 2014).) The concept here is that food reward is a goal that normally drives appetite and eating, and it is therefore important to understand the brain mechanisms involved in food reward, in order to understand the control of appetite and food intake. When the behavior is goal-directed, brain regions such as the cingulate cortex are likely to be engaged (see Fig. 1). However, it is a useful distinction to bear in mind that sometimes feeding can become an overlearned habit, and that then the brain systems likely to be engaged are likely to include the striatum and rest of the basal ganglia (see Fig. 1). The distinction between these two types of processing is that when humans operate from habit, they may less consciously evaluate the costs and benefits of a choice than when goal-directed behavior is engaged. Further discussion of these issues is provided elsewhere (Rolls, 2014).

### 1.3. Investigations in primates including humans

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

First, there are major anatomical differences in the neural processing of taste in rodents and primates (Rolls and Scott, 2003; Rolls, 2014; Scott and Small, 2009; Small and Scott, 2009). In rodents (and also in primates) taste information is conveyed by cranial nerves 7, 9 and 10 to the rostral part of the nucleus of the solitary tract (NTS) (Norgren and Leonard, 1971, 1973; Norgren, 1990) (see Fig. 1). However, although in primates the NTS projects to the taste thalamus and thus to the cortex (Fig. 1), in rodents the majority of NTS taste neurons responding to stimulation of the taste receptors of the anterior tongue project to the ipsilateral medial aspect of the pontine parabrachial nucleus (PbN), the rodent ‘pontine taste area’ (Cho et al., 2002; Small and Scott, 2009). The remainder project to adjacent regions of the medulla. From the PbN the rodent gustatory pathway bifurcates into two pathways: (1) a ventral ‘affective’ projection to the hypothalamus, central gray, ventral striatum, bed nucleus of the stria terminalis and amygdala; and (2) a dorsal ‘sensory’ pathway, which first synapses in the thalamus and then the agranular and dysgranular insular gustatory cortex (Norgren and Leonard, 1971; Norgren, 1974, 1976, 1990). These regions, in turn, project back to the PbN in rodents to sculpt the gustatory code and guide complex feeding



**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; 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, 2014). Tier 1: the column of brain regions including and below the inferior temporal visual cortex represents brain regions in which 'what' stimulus is present is made explicit in the neuronal representation, but not its reward or affective value which are represented in the next tier of brain regions (Tier 2), the orbitofrontal cortex and amygdala, and in the anterior cingulate cortex. In Tier 3 areas beyond these such as medial prefrontal cortex area 10, choices or decisions about reward value are taken (Rolls, 2008a, 2014; Rolls and Deco, 2010). Top-down control of affective response systems by cognition and by selective attention from the dorsolateral prefrontal cortex is also indicated. Medial PFC area 10, medial prefrontal cortex area 10; VPMpc, ventralposteromedial thalamic nucleus, the thalamic nucleus for taste.

behaviors (Di Lorenzo, 1990; Li et al., 2002; Lundy and Norgren, 2004; Norgren, 1976, 1990).

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

Second, a functional difference of rodent taste processing from that of primates is that physical and chemical signals of satiety

have been shown to reduce the taste responsiveness of neurons in the nucleus in the solitary tract, and the pontine taste area, of the rat, with decreases in the order of 30%, as follows (Rolls and Scott, 2003; Scott and Small, 2009). Gastric distension by air or with 0.3 M NaCl suppress taste responses in the rat NTS, with the greatest effect on glucose (Gleen and Erickson, 1976). Intravenous infusions of 0.5 g/kg glucose (Giza and Scott, 1983), 0.5 U/kg insulin (Giza and Scott, 1987b), and 40  $\mu$ g/kg glucagon (Giza et al., 1993), all cause reductions in taste responsiveness to glucose in the rat NTS. The intraduodenal infusion of lipids causes a decline in taste responsiveness in the rat PbN, with the bulk of the suppression borne by glucose-responding cells (Hajnal et al., 1999). The loss of signal that would otherwise be evoked by hedonically positive tastes implies that the reward value that sustains feeding is reduced at the brainstem level in rodents, making termination of a meal more likely (Giza et al., 1992). Further, if taste activity in NTS is affected by the rat's nutritional

state, then intensity judgments in rats should change with satiety. There is evidence that they do. Rats with conditioned aversions to 1.0 M glucose show decreasing acceptance of glucose solutions as their concentrations approach 1.0 M. This acceptance gradient can be compared between euglycemic rats and those made hyperglycemic through intravenous injections (Scott and Giza, 1987). Hyperglycemic rats showed greater acceptance at all concentrations from 0.6 to 2.0 M glucose, indicating that they perceived these stimuli to be less intense than did conditioned rats with no glucose load (Giza and Scott, 1987a). The implication is that in rodents, sensory (perceptual) and reward (hedonic) processing are not independent.

In contrast, in primates, the reward value of tastants is represented in the orbitofrontal cortex in that the responses of orbitofrontal cortex taste neurons are modulated by hunger in just the same way as is the reward value or palatability of a taste. In particular, it has been shown that orbitofrontal cortex taste neurons stop responding to the taste of a food with which a monkey is fed to satiety, and that this parallels the decline in the acceptability of the food (Critchley and Rolls, 1996c; Rolls et al., 1989). In contrast, the representation of taste in the primary taste cortex of non-human primates (Scott et al., 1986b; Yaxley et al., 1990) is not modulated by hunger (Rolls et al., 1988; Yaxley et al., 1988). Thus in the primary taste cortex of non-human primates (and at earlier stages of taste processing including the nucleus of the solitary tract (Yaxley et al., 1985)), the reward value of taste is not represented, and instead the identity of the taste is represented (Rolls, 2014). A perceptual correlate of this is that when humans feed to satiety, the intensity of the flavor changes very little, whereas the pleasantness of the flavor decreases to zero (Rolls et al., 1983c), showing that in humans perceptual representations of taste and olfaction are kept separate from hedonic representations. This is adaptive, in that we do not go blind to the sight, taste, and smell of food after eating it to satiety, and can therefore still learn about where food is located in the environment even when we are not hungry (Rolls, 2014). Moreover, and consistently, activations in the human insular primary taste cortex are related to the intensity and not to the pleasantness of taste (Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a) (see Fig. 15).

The importance of cortical processing of taste in primates, first for identity and intensity in the primary taste cortex, and then for reward value in the orbitofrontal cortex, is that both types of representation need to be interfaced to visual and other processing that requires cortical computation. For example, it may have adaptive value to be able to represent exactly what taste is present, and to link it by learning to the sight and location of the source of the taste, even when hunger is not present and reward is not being produced, so that the source of that taste can be found in future, when it may have reward value. In line with cortical processing to dominate the processing of taste in primates, there is no modulation of taste responsiveness at or before the primary taste cortex, and the pathways for taste are directly from the nucleus of the solitary tract in the brainstem to the taste thalamus and then to the taste cortex (Fig. 1) (Rolls, 2014).

The implication is that taste, and the closely related olfactory and visual processing that contribute to food reward, are much more difficult to understand in rodents than in primates, partly because there is less segregation of 'what' (identity and intensity) from hedonic processing in rodents in which they are confused, and partly because of the more serial hierarchical processing in primates, with a clear separation of perceptual processing (up to and including the primary taste and olfactory (pyriform) cortex) (Fig. 1), whereas in the rodent the system is more difficult to understand, because hedonics appear to be reflected from the first central taste relay, the nucleus of the solitary tract, onwards. Similar points may be made about taste aversion learning

(in which a taste is paired with sickness), in that the changes produced by this learning are reflected at the first central synapse in the nucleus of the solitary tract, though may depend on processing at higher levels (Scott, 2011), making the system complex to understand.

Third, the prefrontal cortex (and for that matter the temporal lobe visual cortical areas) have also undergone great development in primates, and one part of the prefrontal cortex, the orbitofrontal cortex, is very little developed in rodents, yet is one of the major brain areas involved in taste and olfactory processing, and emotion and motivation, in primates including humans. Indeed, it has been argued (on the basis of cytoarchitecture, connections, and functions) that the granular prefrontal cortex is a primate innovation, and the implication of the argument is that any areas that might be termed orbitofrontal cortex in rats (Schoenbaum et al., 2009) are homologous only to the agranular parts of the primate orbitofrontal cortex (shaded mid gray in Fig. 2), that is to areas 13a, 14c, and the agranular insular areas labeled Ia in Fig. 2 (Passingham and Wise, 2012). It follows from that argument that for most areas of the orbitofrontal and medial prefrontal cortex in humans and macaques (those shaded light gray in Fig. 2), special consideration must be given to research in macaques and humans. As shown in Fig. 2, there may be no cortical area in rodents that is homologous to most of the primate including human orbitofrontal cortex (Passingham and Wise, 2012; Preuss, 1995; Wise, 2008).

## 2. Taste, olfactory, and oral texture processing in the primate including human brain

### 2.1. Pathways

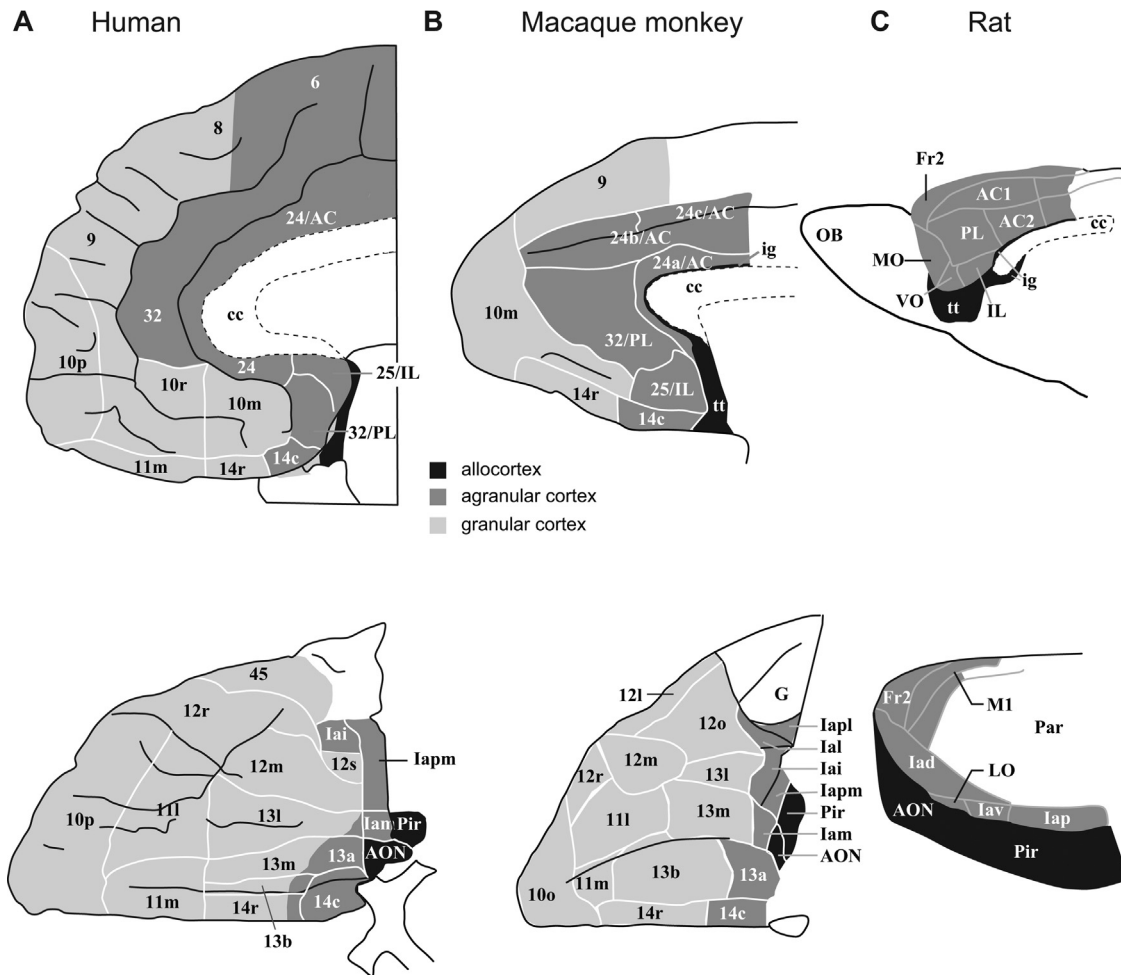
A diagram of the taste and related olfactory, somatosensory, and visual pathways in primates is shown in Fig. 1. The multimodal convergence that enables single neurons to respond to different combinations of taste, olfactory, texture, temperature, and visual inputs to represent different flavors produced often by new combinations of sensory input is a theme that will be addressed.

### 2.2. The insular primary taste cortex

#### 2.2.1. Neuronal responses to taste

Rolls, Scott, and colleagues have shown that the primary taste cortex in the primate anterior insula and adjoining frontal operculum contains not only taste neurons tuned to sweet, salt, bitter, sour (Plata-Salaman et al., 1992, 1993, 1995, 1996; Rolls and Scott, 2003; Scott et al., 1991, 1994, 1986b, 1998, 1999; Scott and Plata-Salaman, 1999; Smith-Swintosky et al., 1991; Yaxley et al., 1990), and umami as exemplified by monosodium glutamate (Baylis and Rolls, 1991; Rolls et al., 1996a), but also other neurons that encode oral somatosensory stimuli including viscosity, fat texture, temperature, and capsaicin (Verhagen et al., 2004). Some neurons in the primary taste cortex respond to particular combinations of taste and oral texture stimuli, but macaque insular taste cortex neurons do not respond to olfactory stimuli or visual stimuli such as the sight of food (Verhagen et al., 2004).

Neurons in the primary taste cortex do not represent the reward value of taste, that is the appetite for a food, in that their firing is not decreased to zero by feeding the taste to satiety (Rolls et al., 1988; Yaxley et al., 1988) (Fig. 3). This was confirmed in 17 separate experiments on neurons in the insular and frontal opercular primary taste cortex, using anatomical confirmation that these neurons were in the primary taste cortex by the use of X-ray localization and then histological reconstruction. The neurons showed no reduction in their firing to the taste (typically glucose) after it had been fed to satiety (Rolls et al., 1988; Yaxley et al., 1988).



**Fig. 2.** Comparison of the orbitofrontal (below) and medial prefrontal (above) cortical areas in humans, macaque monkeys, and rats. (A) Medial (top) and orbital (bottom) areas of the human frontal cortex (Öngür et al., 2003). (B) Medial (top) and orbital (bottom) areas of the macaque frontal cortex (Carmichael and Price, 1994). (C) Medial (top) and lateral (bottom) areas of rat frontal cortex (Palomero-Gallagher and Zilles, 2004). Rostral is to the left in all drawings. Top row: dorsal is up in all drawings. Bottom row: in (A) and (B), lateral is up; in (C), dorsal is up. Not to scale. *Abbreviations:* AC, anterior cingulate cortex; AON, anterior olfactory 'nucleus'; cc, corpus callosum; Fr2 second frontal area; G, gustatory cortex; Ia, agranular insular cortex; ig, induseum griseum; IL, infralimbic cortex; LO, lateral orbital cortex; MO, medial orbital cortex; OB, olfactory bulb; Pr, piriform (olfactory) cortex; PL, prelimbic cortex; tt, tenia tecta; VO, ventral orbital cortex; Subdivisions of areas are labeled caudal (c); inferior (i), lateral (l), medial (m); orbital (o), posterior or polar (p), rostral (r), or by arbitrary designation (a, b).  
 Reproduced with permission from Passingham and Wise (2012).

In macaques, neural processing peripheral to the primary taste cortex is consistent with this, with taste responses found in the rostral part of the nucleus of the solitary tract (Scott et al., 1986a) that are not influenced by feeding to satiety (Yaxley et al., 1985), and also taste-responsive neurons in the taste nucleus of the thalamus, VPMpc (Pritchard et al., 1989).

### 2.2.2. Neuronal responses to oral (food) texture and temperature

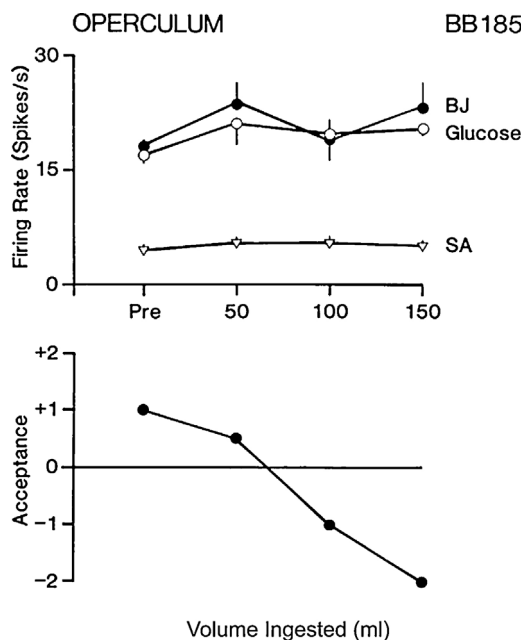
Fat texture, oral viscosity, and temperature, for some neurons in combination with taste, are represented in the macaque primary taste cortex in the rostral insula and adjoining frontal operculum (Verhagen et al., 2004). Example of these types of responsiveness is provided in the section on the orbitofrontal cortex. This provides a route for this information to reach the orbitofrontal cortex and amygdala. Of the orally responsive neurons, some (53%) represented the viscosity, tested using carboxymethyl-cellulose in the range 1–10,000 cP. Other neurons (8%) responded to fat in the mouth by encoding its texture (as shown by similar neuronal responses to non-fat oils), and 8% responded to gritty texture. Some neurons (35%) responded to the temperature of the liquid in the mouth. Some neurons responded to capsaicin, and others to fatty acids. Some neurons (56%) had taste responses. Some (50%) of

these neurons were unimodal, responding to one of these types of stimulus, and the others combined responsiveness to these types of stimulus, with 23% responding for example to both taste and temperature (Verhagen et al., 2004). None of these orally responsive neurons responded to odor or to the sight of food.

Some of these types of information may be transmitted to the insular taste cortex via the taste nerves and taste thalamus, for there is some evidence that some taste fibers in rodents may respond to trigeminal (somatosensory) stimuli (Simons, Duke University, personal communication, 2014).

### 2.2.3. Activations of the insular taste cortex in humans

In humans it has been shown in neuroimaging studies using functional magnetic resonance imaging (fMRI) that taste activates an area of the anterior insula/frontal operculum, which is probably the primary taste cortex (de Araujo et al., 2003b; O'Doherty et al., 2001b; Small et al., 1999; Small, 2010). This is illustrated in Fig. 4, which also illustrates activations to taste stimuli in the orbitofrontal cortex, which is probably the secondary taste cortex (de Araujo et al., 2003b; Francis et al., 1999; O'Doherty et al., 2001b; Rolls, 2005a, 2008b). Fig. 4 also illustrates activation of the anterior cingulate cortex to taste, with the pleasant taste of glucose



**Fig. 3.** No effect of feeding to satiety with glucose solution on the responses (firing rate  $\pm$  sem) of a neuron in the primary taste cortex in the insular/frontal opercular area to the taste of glucose (open circles) and of blackcurrant fruit juice (BJ). The spontaneous firing rate is also indicated (SA). Below the neuronal response data, the behavioral measure of the acceptance or rejection of the solution on a scale from +2 (strong acceptance) to  $-2$  (strong rejection) is shown. The solution used to feed to satiety was 20% glucose. The monkey was fed 50 ml of the solution at each stage of the experiment as indicated along the abscissa, until he was satiated as shown by whether he accepted or rejected the solution. Pre is the firing rate of the neuron before the satiety experiment started. (After Yaxley et al. (1988) and Rolls et al. (1988).)

activating the pregenual cingulate cortex, and the less pleasant taste of monosodium glutamate activating a more dorsal part of the anterior cingulate cortex (de Araujo et al., 2003a), consistent with the hedonic map found in this region (Grabenhorst and Rolls, 2011). We pioneered the use of a tasteless control with the same ionic constituents as saliva (de Araujo et al., 2003b; O'Doherty et al., 2001b), as water can activate some neurons in cortical taste areas (Rolls et al., 1990) and can activate the taste cortex (de Araujo et al., 2003b). Within individual subjects separate areas of the orbitofrontal cortex are activated by sweet (pleasant) and by salt (unpleasant, especially at higher concentrations (Rolls et al., 1983c)) tastes (O'Doherty et al., 2001b). The insular primary taste cortex is activated by oral temperature (Guest et al., 2007).

The primary taste cortex in the anterior insula of humans represents the identity and intensity of taste in that activations there are linearly correlated with the subjective intensity of the taste, and the orbitofrontal and anterior cingulate cortex represent the reward value of taste, in that activations there correlate with the subjective pleasantness of taste (Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a) (see Fig. 15); and in that activations in the orbitofrontal cortex decrease when humans are fed to with satiety, but were not found to in the insular taste cortex (Kringelbach et al., 2003).

In the insular cortex posterior to the taste cortex in the anterior insula, there is a somatosensory representation of oral texture (de Araujo and Rolls, 2004), which might be unpleasant.

One point of interest still is whether the human primary taste cortex contains a hedonic representation of taste, with taste responses to taste decreasing to zero after feeding to natural self-induced satiety. The evidence in macaques is quite clear. In the insular and frontal opercular taste cortex, neuronal responses to the taste fed to satiety do not decrease at all satiety (Rolls et al.,

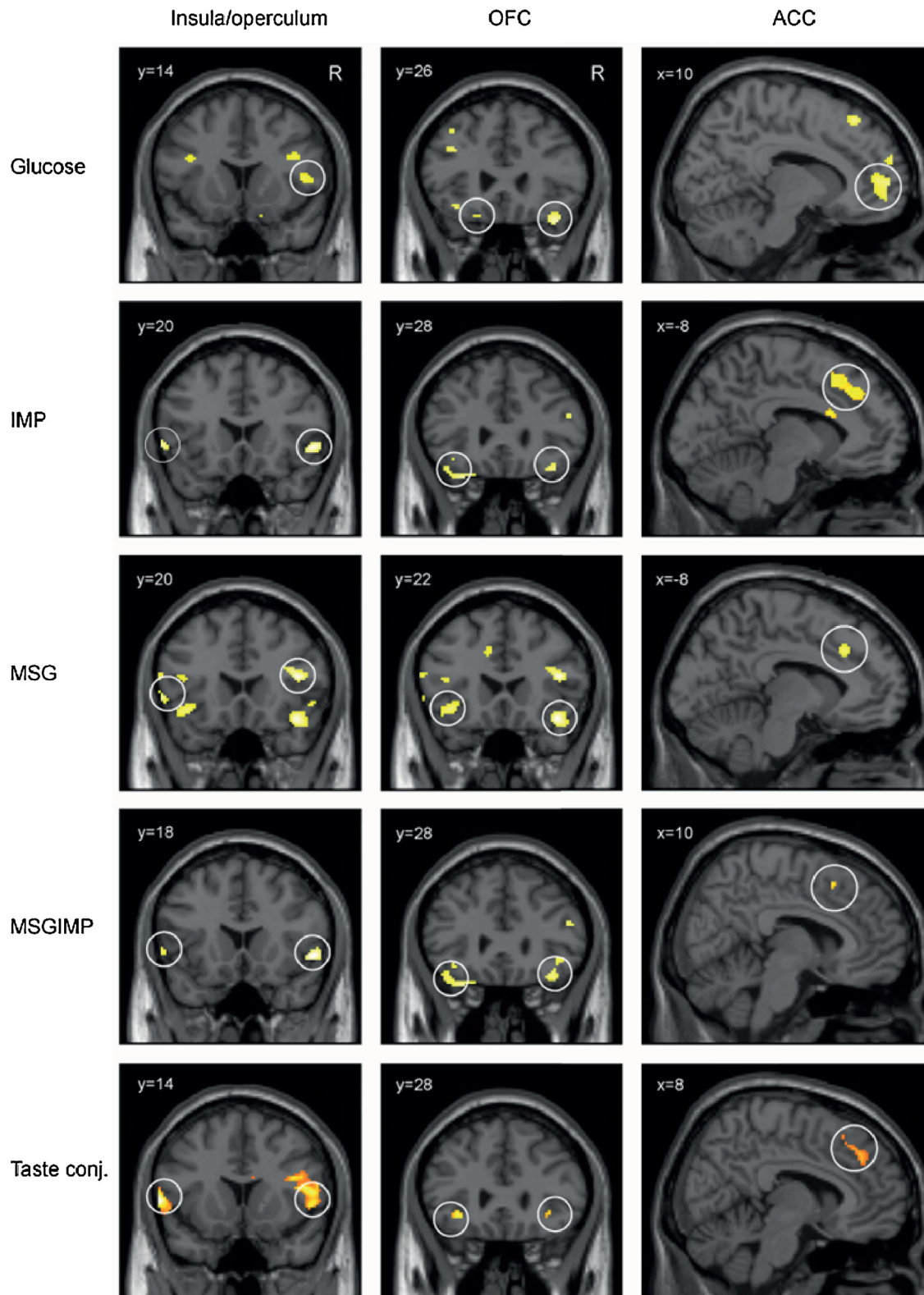
1988; Yaxley et al., 1988) (Fig. 3). In contrast, in the macaque orbitofrontal cortex, almost all neurons show a decrease to zero of the response to taste, that is, the neurons do not alter from their spontaneous firing rate after feeding to satiety (Critchley and Rolls, 1996c; Pritchard et al., 2008; Rolls et al., 1989) (Figs. 7 and 10). In the human orbitofrontal cortex, we found a large decrease in the BOLD signal to a food fed to satiety, but not in the insula (Kringelbach et al., 2003). Moreover, this was a sensory-specific decrease in the BOLD signal, a useful indication that this was a response related to real satiety, which is to a considerable extent sensory-specific, and not for every food. Further, we are looking for a brain region not just where there may be small changes, perhaps significant, to the response to a taste fed to satiety, but a region where the response decreases to zero, for this is what happens to the pleasantness of food after it is fed to satiety, with little effect on its intensity (Rolls et al., 1983c; Rolls and Grabenhorst, 2008; Rolls, 2014). Against this background, there are suggestions that the human insula taste cortex has decreased responses after feeding to satiety, and represents taste hedonics (de Araujo et al., 2012b; Small et al., 2001; Small, 2010; Sun et al., 2014). Let us evaluate these suggestions. First, taste stimuli were not used in these investigations. In one, chocolate was used (Small et al., 2001), and in another, milkshake (Sun et al., 2014), so that there were major somatosensory components. Second, in one study, the localization of the effects as due to the primary insular taste cortex rather than adjacent regions was poor, because PET was used (Small et al., 2001). In another study, in which milkshake was used (Sun et al., 2014), one site of insular activations appears to be in the visceral insula (see Section 2.2.4), in which changes related to satiety might be expected; and another appears to be in the mid insula, in which food including fat texture responses are found (de Araujo and Rolls, 2004), with frontal opercular and insular cortex anterior to the primary taste cortex reflecting a factor of oral including fat texture that relates to its unpleasantness (Grabenhorst et al., 2010b). (The primary taste cortex in humans is labeled G by Öngür et al. (2003), and has agranular insular areas anterior to it.) In this situation, a parsimonious view is that the stage in the human primate taste processing system where the activation tracks down to zero the pleasantness of food as it is fed to satiety is in the orbitofrontal cortex, not the primary insular taste cortex. In addition, the texture-related unpleasantness of some oral stimuli is represented in areas that are close to the insular taste cortex.

#### 2.2.4. An autonomic/visceral representation in the ventral insula

Parts of the insula can be activated by visual stimuli related to disgust, such as a face expression of disgust (Phillips et al., 2004), and this could reflect the fact that parts of the ventral anterior insula located probably mainly ventral to the taste cortex are part of the visceral efferent system involved in autonomic responses (Critchley, 2005; Rolls, 2014) (and may even overlap partly with the taste-responsive areas (Simmons et al., 2013)). (A disgust face expression is characterized by an open gaping mouth, consistent with rejection of an aversive oral stimulus from the mouth, such as a stimulus that might induce vomiting (Ekman, 1982; Ekman et al., 1983; Rolls, 2011c).) This viscer-autonomic part of the insula may not compute emotions, but may be activated as part of the efferent pathway by brain regions such as the orbitofrontal cortex when these brain regions produce autonomic responses to emotion-provoking including aversive stimuli (Rolls, 2014).

#### 2.3. The pyriform olfactory cortex

In humans, the pyriform (olfactory) cortex is activated by olfactory stimuli (Gottfried, 2010; Poellinger et al., 2001; Sobel et al., 2000; Zald and Pardo, 1997). Activations in the pyriform cortex are correlated with the intensity of odors and not their



**Fig. 4.** Activation of the human primary taste cortex in the insula/frontal operculum; the orbitofrontal cortex (OFC); and the anterior cingulate cortex (ACC) by taste. Coronal slices are shown. The stimuli used included glucose, two umami taste stimuli (monosodium glutamate (MSG) and inosine monophosphate (IMP)), and a mixture of the two umami stimuli. Taste conj. Refers to a conjunction analysis over all the taste stimuli. Reproduced from de Araujo et al. (2003a).

pleasantness (Rolls et al., 2003a). In addition, feeding to satiety has not been shown to reduce the activations of the pyriform cortex to odors though satiety does reduce activations of the orbitofrontal cortex to food-related odors (O'Doherty et al., 2000), and to flavors

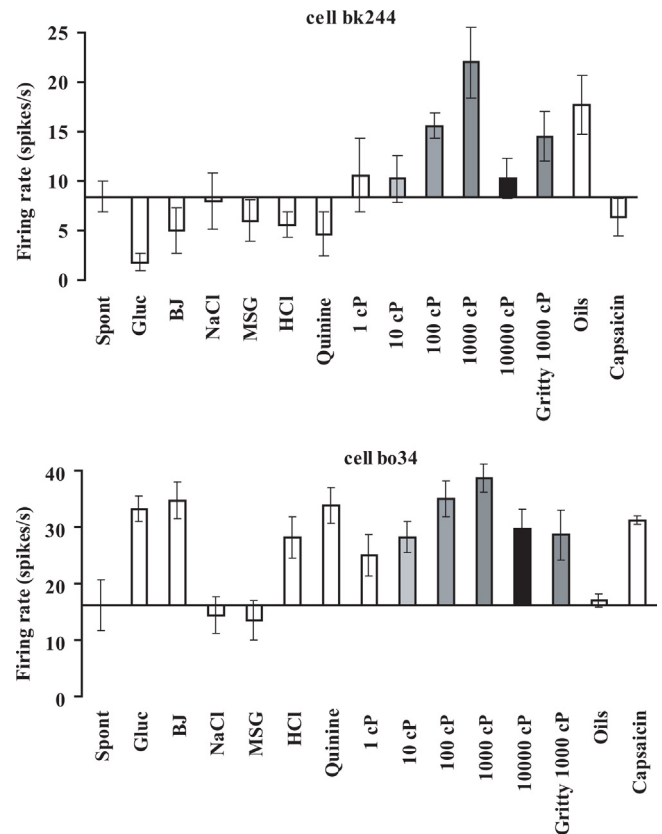
that include taste and olfactory components (Kringelbach et al., 2003). These findings provide evidence that the human pyriform cortex is involved in representing the intensity and identity of odors, but not their reward value or pleasantness.

## 2.4. The secondary taste and olfactory cortex in the orbitofrontal cortex, and the representation of reward value

### 2.4.1. Neuronal responses to taste

A secondary cortical taste area in primates was discovered by Rolls and colleagues (Rolls et al., 1989, 1990; Thorpe et al., 1983) in the orbitofrontal cortex, extending several mm in front of the primary taste cortex. This is defined as a secondary cortical taste area, for it receives direct inputs from the primary taste cortex, as shown by a combined neurophysiological and anatomical pathway tracing investigation (Baylis et al., 1995). Different neurons in this region respond not only to each of the four classical prototypical tastes sweet, salt, bitter and sour (Kadohisa et al., 2005a; Rolls et al., 1990, 2003b; Rolls, 1997; Verhagen et al., 2003), but also to umami tastants such as glutamate (which is present in many natural foods such as tomatoes, mushrooms and human milk) (Baylis and Rolls, 1991) and inosine monophosphate (which is present in meat and some fish such as tuna) (Rolls et al., 1996a). This evidence, taken together with the identification of glutamate taste receptors (Maruyama et al., 2006; Zhao et al., 2003), leads to the view that there are five prototypical types of taste information channels, with umami contributing, often in combination with corresponding olfactory inputs (McCabe and Rolls, 2007; Rolls et al., 1998; Rolls, 2009b), to the flavor of protein. In addition, other neurons respond to water (Rolls et al., 1990), and others to somatosensory stimuli including astringency as exemplified by tannic acid (Critchley and Rolls, 1996b), and capsaicin (Kadohisa et al., 2004; Rolls et al., 2003b).

Some of the coding principles are illustrated by the two neurons shown in Fig. 5. The two neurons each have their independent tuning to the set of stimuli. It is this independent tuning or coding that underlies the ability of the brain to represent the exact nature of a stimulus or event, and this applies to taste in addition to other sensory modalities (Rolls et al., 2010a; Rolls and Treves, 2011). The principles of coding that have been found mainly through research on vision (Rolls and Treves, 2011) appear to apply also to the encoding of taste and olfactory information in cortical areas (Rolls et al., 1996c, 2010a; Rolls and Treves, 2011). The principles include a sparse distributed representation, with each neuron having a large response to the best stimulus followed smaller responses to other stimuli which follow approximately an exponential distribution, implementing a distributed place code; independent tuning of different neurons to the set of stimuli so that the information increases approximately linearly with the number of neurons; most of the information is encoded by the number of spikes and not by temporal encoding within the spike train including oscillations, and not by stimulus-dependent cross-correlations between neurons; there may be a small amount of information in the latency of the neuronal response; and the information from a spike train becomes available rapidly, with much of what can be obtained from longer periods available within the first few spikes (Rolls, 2008a, 2016; Rolls and Treves, 2011). Some differences of taste and olfactory cortical encoding from coding in high-level vision is that the firing rates of neurons are lower, typically up to 30 instead of 100 spikes/s, with the need for rapid operation and information transmission in vision related to the multilayer cortical hierarchy and the sometimes more transient nature of visual stimuli; and that the information from multiple cells may asymptote more rapidly in taste as the number of neurons increases (Rolls et al., 2010a; Rolls and Treves, 2011), due in part to the lower dimensionality of the space, in that enormous numbers of very different objects need to be encoded independently of each other for vision, and there are fewer tastes. It is notable that in the orbitofrontal cortex, the proportion of neurons responding to any one stimulus type is quite low, with for example 5.7% of 2374 orbitofrontal cortex neurons having taste



**Fig. 5.** Taste and oral somatosensory inputs to orbitofrontal cortex neurons. Above: Firing rates (mean  $\pm$  sem) of viscosity-sensitive neuron bk244 which did not have taste responses, in that it did not respond differentially to the different taste stimuli. The firing rates are shown to the viscosity series (carboxymethylcellulose 1–10,000 centiPoise), to the gritty stimulus (1000 cP carboxymethylcellulose with Fillite microspheres), to the taste stimuli 1 M glucose (Gluc), 0.1 M NaCl, 0.1 M MSG, 0.01 M HCl and 0.001 M quinine HCl, and to fruit juice (BJ). Spont, spontaneous firing rate. Below: Firing rates (mean  $\pm$  sem) of viscosity-sensitive neuron bo34 which had responses to some taste stimuli and had no response to the oils (mineral oil, vegetable oil, safflower oil and coconut oil, which have viscosities that are all close to 50 cP). The neuron did not respond to the gritty stimulus in a way that was unexpected given the viscosity of the stimulus, was taste tuned, and did respond to capsaicin. (After Rolls et al. (2003b).)

responses (Rolls et al., 2010a). Part of the reason for this is that many different types of reward are represented in the orbitofrontal cortex (Grabenhorst and Rolls, 2011; Rolls and Grabenhorst, 2008; Rolls, 2014). However, even in the macaque primary taste cortex, only 5.5% of 1122 neurons responded to oral stimuli, and taste was 56% of the orally responsive neurons, with other neurons responding to oral texture and/or temperature (Verhagen et al., 2004). This relatively low proportion of neurons responding to stimuli in a cortical area is common in many cortical areas, and may be part of the way in which neurons remain unallocated to stimuli to provide potential for learning new representations (Rolls, 2016). It is also the case that there is some local self-organizing topography in cortical areas (Rolls, 2008a, 2016), and this may increase the estimate of the proportion of responsive neurons if one repeatedly samples from those patches. It is also relevant that in cortical areas such as the orbitofrontal cortex, stimuli, including olfactory stimuli, may be recoded from the space defined by the gene-specified olfactory receptors into a space that for many neurons reflects the lower dimensional space of hedonics, which for many olfactory stimuli is brought about by olfactory to taste association learning (Critchley and Rolls, 1996a; Rolls et al., 1996b; Rolls, 2016).

The encoding of information in the brain can of course not be captured by functional neuroimaging, because that takes an

average of the activity of tens of thousands of neurons (and activity may be what is measured by the fMRI BOLD signal (Rolls et al., 2010b)), whereas each neuron conveys information that is to a considerable extent independent of the information encoded by other neurons (Rolls et al., 2009, 2010a; Rolls and Treves, 2011).

Taste responses are found in a large mediolateral extent of the orbitofrontal cortex (Critchley and Rolls, 1996b; Pritchard et al., 2005; Rolls, 2008b; Rolls and Grabenhorst, 2008). Indeed, taste neurons have been shown to extend throughout area 13, including a region that is approximately 7–12 mm from the midline (Critchley and Rolls, 1996b; Rolls and Baylis, 1994; Rolls et al., 1996a; Rolls, 2008b), the exact area in which Pritchard et al. (2005) also found a population of taste neurons (see Fig. 3 with cytoarchitectonic areas indicated after Carmichael and Price, 1994; Öngür and Price, 2000; Öngür et al., 2003; Petrides and Pandya, 2001). We showed in our previous studies that these taste neurons extend from approximately 4 mm anterior to the clinoid process of the sphenoid bone to 12 mm anterior. (Pritchard et al. (2005) focussed their investigation on a region 5–9 mm anterior to the sphenoid.) Although Pritchard et al. (2005) commented that in their study there was a good proportion of taste neurons in this area, we, in comparing the proportions of taste neurons in different parts of the orbitofrontal cortex extending out laterally through area 12, find similar proportions of taste neurons throughout this mediolateral extent (from 7 mm to 20 mm lateral) (Critchley and Rolls, 1996b; Kadohisa et al., 2004, 2005a; Rolls et al., 1989, 1990, 1996a, 2003b; Rolls and Baylis, 1994; Rolls, 2008b; 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, 1996b; Rolls et al., 1999); and olfactory properties (Critchley and Rolls, 1996a, 1996c; 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, and some of these cells are multimodal in these modalities (Critchley and Rolls, 1996b; Rolls and Baylis, 1994; Rolls et al., 1996b). In a more recent investigation, we (Rolls, Verhagen, Gabbott and Kadohisa) measured the responses of 1753 neurons in rhesus macaques, and found taste neurons in the mid and medial orbitofrontal cortex region extending to within approximately 7 mm of the midline in area 13 m, but very few in the more medial areas 10, 14 and 25, as illustrated in Fig. 6 (Rolls, 2008b).

The majority of these orbitofrontal cortex neurons have their responses to taste and/or olfactory stimuli modulated by hunger (Critchley and Rolls, 1996c), as illustrated in Fig. 7, and described in more detail in Section 2.4.7.

#### 2.4.2. Activations of the orbitofrontal cortex in humans to taste stimuli

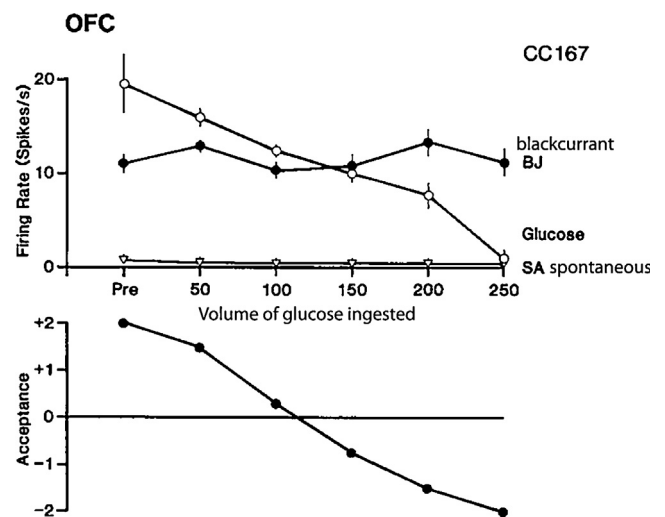
Different regions of the human orbitofrontal cortex can be activated by pleasant (sucrose or glucose) or by aversive (e.g. quinine or sodium chloride) taste stimuli (O'Doherty et al., 2001b; Zald et al., 1998, 2002).

Umami taste stimuli, of which an exemplar is monosodium glutamate (MSG) and which capture what is described as the taste of protein, activate the insular (primary), orbitofrontal (secondary), and anterior cingulate (tertiary (Rolls, 2008b)) taste cortical areas (de Araujo et al., 2003a) (see Fig. 4). When the nucleotide 0.005 M inosine 5'-monophosphate (IMP) was added to MSG (0.05 M), the BOLD (blood oxygenation-level dependent) signal in an anterior part of the orbitofrontal cortex showed supralinear additivity, and this may reflect the subjective enhancement of umami taste that has been described when IMP is added to MSG (Rolls, 2009b). (The supra-linear additivity refers to a greater activation to the combined stimulus MSG + IMP than to the sum of the activations to MSG and IMP presented separately. This evidence that the effect



**Fig. 6.** The reconstructed positions of the neurons in the primate medial orbitofrontal cortex with different types of response, with the cytoarchitectonic boundaries determined after Carmichael and Price (1994). The neurons within different planes at distances in mm anterior (A) to the sphenoid reference point are shown on the coronal sections.

Data from Rolls, Verhagen, Gabbott and Kadohisa, 2008, see Rolls (2008b).



**Fig. 7.** The effect of feeding to satiety with glucose solution on the responses (firing rate  $\pm$  sem) of a neuron in the orbitofrontal (secondary taste) cortex to the taste of glucose (open circles) and of blackcurrant juice (BJ). The spontaneous firing rate is also indicated (SA). Below the neuronal response data, the behavioral measure of the acceptance or rejection of the solution on a scale from +2 (strong acceptance) to -2 (strong rejection) is shown. The solution used to feed to satiety was 20% glucose. The monkey was fed 50 ml of the solution at each stage of the experiment as indicated along the abscissa, until he was satiated as shown by whether he accepted or rejected the solution. Pre is the firing rate of the neuron before the satiety experiment started. Reproduced from Rolls et al. (1989).

of the combination is greater than the sum of its parts indicates an interaction between the parts to form in this case an especially potent taste of umami, which is part of what can make a food taste delicious (Rolls, 2009b). Overall, these results illustrate that the responses of the brain can reflect inputs produced by particular combinations of sensory stimuli with supralinear activations, and that the combination of sensory stimuli may be especially represented in particular brain regions, and may help to make the food pleasant.

#### 2.4.3. Neuronal responses to odors in the primate orbitofrontal cortex

Some primate orbitofrontal cortex neurons respond well to olfactory stimuli (Critchley and Rolls, 1996a; Rolls et al., 1996b, 2010a). For many of these neurons, the response is related to tastes (Critchley and Rolls, 1996a) and can be learned by olfactory to taste association learning (Rolls et al., 1996b), providing evidence that the orbitofrontal cortex can remap odors from the olfactory gene-specified representation (Buck and Axel, 1991; Mombaerts, 2006) into a representation where the ‘meaning’ in terms of the association of the odor with other stimuli is paramount. Flavors are built by learning in the orbitofrontal cortex as combinations of taste and olfactory inputs, with oral texture also often being a component (Rolls et al., 1996b). The olfactory to taste association learning is though slow, taking 30–60 trials to reverse, so that flavor representations are somewhat stable (Rolls et al., 1996b). The representation of information by primate orbitofrontal cortex neurons (Rolls et al., 1996c) is approximately independent by different neurons, in that the information increases approximately linearly with the number of neurons (Rolls et al., 2010a).

Many primate olfactory neurons encode the reward value of odor, not only in that their responses often reflect the taste primary reinforcer with which an odor is associated (Critchley and Rolls, 1996a; Rolls et al., 1996b), but also in that their activity is decreased in a sensory-specific satiety way by feeding a particular food to satiety (Critchley and Rolls, 1996c) (Section 2.4.7).

#### 2.4.4. Olfactory representations in the human orbitofrontal cortex

In humans, in addition to activation of the pyriform (olfactory) cortex (Poellinger et al., 2001; Sobel et al., 2000; Zald and Pardo, 1997), there is strong and consistent activation of the orbitofrontal cortex by olfactory stimuli (Francis et al., 1999; Rolls et al., 2003a; Zatorre et al., 1992). This region appears to represent the pleasantness of odor, as shown by a sensory-specific satiety experiment with banana vs vanilla odor (O’Doherty et al., 2000), and this has been confirmed by Gottfried et al. (personal communication, see Gottfried (2015)), who also showed that activations in the pyriform (primary olfactory) cortex were not decreased by odor devaluation by satiety. Further, pleasant odors tend to activate the medial, and unpleasant odors the more lateral, orbitofrontal cortex (Rolls et al., 2003a), adding to the evidence that it is a principle that there is a hedonic map in the orbitofrontal cortex, and also in the anterior cingulate cortex, which receives inputs from the orbitofrontal cortex (Grabenhorst and Rolls, 2011; Rolls and Grabenhorst, 2008). The primary olfactory (pyriform) cortex represents the identity and intensity of odor in that activations there correlate with the subjective intensity of the odor, and the orbitofrontal and anterior cingulate cortex represent the reward value of odor, in that activations there correlate with the subjective pleasantness (medially) or unpleasantness (laterally) of odor (Grabenhorst et al., 2007; Grabenhorst and Rolls, 2011; Rolls et al., 2003a, 2008a, 2009; Rolls and Grabenhorst, 2008).

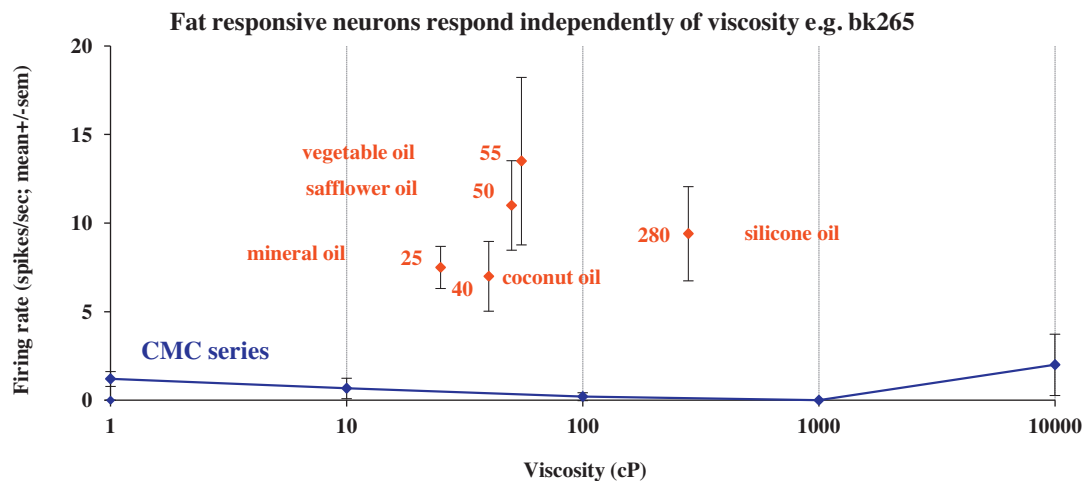
#### 2.4.5. The texture of food, including fat texture

2.4.5.1. *Viscosity, particulate quality, and astringency.* Some orbitofrontal cortex neurons have oral texture-related responses that

encode parametrically the viscosity of food in the mouth (shown using a methyl cellulose series in the range 1–10,000 centiPoise), and other neurons independently encode the particulate quality of food in the mouth, produced quantitatively for example by adding 20–100  $\mu\text{m}$  microspheres to methyl cellulose (Rolls et al., 2003b) (see Fig. 5). Somatosensory signals that transmit information about capsaicin (chilli) and astringency are also reflected in neuronal activity in these cortical areas (Critchley and Rolls, 1996b; Kadohisa et al., 2004, 2005a).

2.4.5.2. *Oral fat texture.* Texture in the mouth is an important indicator of whether *fat* is present in a food, which is important not only as a high value energy source, but also as a potential source of essential fatty acids. In the orbitofrontal cortex, Rolls et al. (1999) have found a population of neurons that responds when fat is in the mouth. The fat-related responses of these neurons are produced at least in part by the texture of the food rather than by chemical receptors sensitive to certain chemicals, in that such neurons typically respond not only to foods such as cream and milk containing fat, but also to paraffin oil (which is a pure hydrocarbon) and to silicone oil ((Si(CH<sub>3</sub>)<sub>2</sub>O)<sub>n</sub>). Moreover, the texture channels through which these fat-sensitive neurons are activated are separate from viscosity sensitive channels, in that the responses of these neurons cannot be predicted by the viscosity of the oral stimuli, as illustrated in Fig. 8 (Rolls, 2011a; Verhagen et al., 2003). The responses of these oral fat-encoding neurons are not related to free fatty acids such as linoleic or lauric acid (Kadohisa et al., 2005a; Rolls, 2011a; Verhagen et al., 2003), and the fat responsiveness of these primate orbitofrontal cortex neurons is therefore not related to fatty acid sensing (Gilbertson et al., 1997; Gilbertson, 1998), but instead to oral texture sensing (Rolls, 2011a, 2012c). (The hypothesis is that in rodents, with relatively high concentrations of lingual lipase, a fatty acid responsive ‘taste’ receptor might provide evidence about the presence of fat in the mouth (Gilbertson et al., 1997; Gilbertson, 1998). There is less lingual lipase in primates, and the neuronal responses to fat placed in the mouth in macaques are fast (Verhagen et al., 2003, 2004) so that the intervention of digestion by a salivary enzyme is unlikely to be the main mechanism that detects fat in the mouth. Moreover, oils that have the same texture as fat but that contain no fat, such as silicone and paraffin oil, activate the neurons in macaques that respond to fat in the mouth.) This has I believe very important implications for the development of foods with the mouth feel of fat, but low energy content (Rolls, 2011a, 2012c). A few neurons do have responses to linoleic and/or lauric acid, but these neurons do not respond to fat in the mouth, and may reflect the bad taste that rancid fats may have because of their free fatty acids (Rolls, 2011a; Verhagen et al., 2003). Some of the fat texture-related orbitofrontal cortex neurons do though have convergent inputs from the chemical senses, in that in addition to taste inputs, some of these neurons respond to the odor associated with a fat, such as the odor of cream (Rolls et al., 1999). Feeding to satiety with fat (e.g. cream) decreases the responses of these neurons to zero on the food eaten to satiety, but if the neuron receives a taste input from for example glucose taste, that is not decreased by feeding to satiety with cream (Rolls et al., 1999). Thus there is a representation of the macronutrient fat in this brain area, and the activation produced by fat is reduced by eating fat to satiety, that is by fat texture sensory-specific satiety. The mechanism of transduction and peripheral encoding of oral texture, for viscosity, fat texture, etc. is a topic of interest for future research.

2.4.5.3. *Oral temperature.* In addition, we have shown that some neurons in the insular cortex, orbitofrontal cortex, and amygdala reflect the temperature of substances in the mouth, and that this temperature information is represented independently of other



**Fig. 8.** A neuron in the primate orbitofrontal cortex responding to the texture of fat in the mouth independently of viscosity. The cell (bk265) increased its firing rate to a range of fats and oils (the viscosity of which is shown in centipoise). The information that reaches this type of neuron is independent of a viscosity sensing channel, in that the neuron did not respond to the methyl cellulose (CMC) viscosity series. The neuron responded to the texture rather than the chemical structure of the fat in that it also responded to silicone oil ( $\text{Si}(\text{CH}_3)_2\text{O}_n$ ) and paraffin (mineral) oil (hydrocarbon). Some of these neurons have taste inputs. (After Verhagen et al. (2003).)

sensory inputs by some neurons, and in combination with taste or texture by other neurons (Kadohisa et al., 2004, 2005a, 2005b; Verhagen et al., 2004). Somatosensory signals that transmit information about capsaicin (chilli) are also reflected in neuronal activity in these brain areas (Kadohisa et al., 2004, 2005a). Activations in the human orbitofrontal and insular taste cortex also reflect oral temperature (Guest et al., 2007).

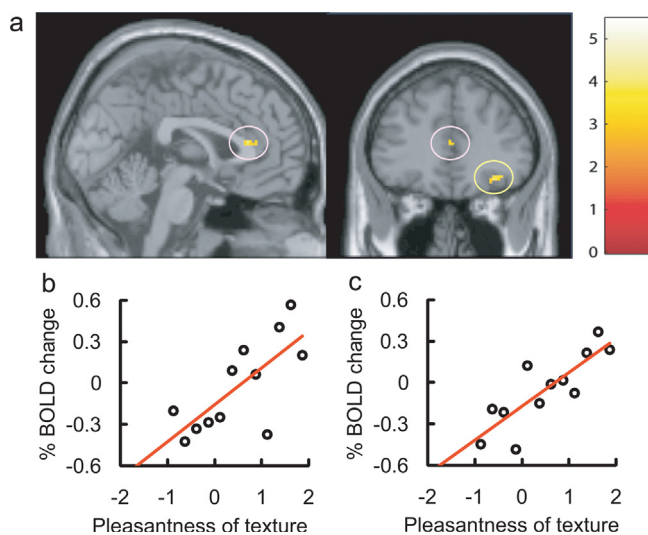
**2.4.5.4. Activations in humans.** The viscosity of food in the mouth is represented in the human primary taste cortex (in the anterior insula), and also in a mid-insular area that is not taste cortex, but which represents oral somatosensory stimuli (de Araujo and Rolls, 2004). Oral viscosity is also represented in the human orbitofrontal and perigenual cingulate cortices, and it is notable that the pregenual cingulate cortex, an area in which many pleasant stimuli are represented, is strongly activated by the texture of fat in the

mouth and also by oral sucrose (de Araujo and Rolls, 2004). We have shown that the pleasantness and reward value of fat texture is represented in the mid-orbitofrontal and anterior cingulate cortex, where activations are correlated with the subjective pleasantness of oral fat texture (Grabenhorst et al., 2010b; Rolls, 2009b, 2010c) (Fig. 9). This provides a foundation for future studies of whether activations in the fat reward system are heightened in people who tend to become obese (Rolls, 2012a). Interestingly, high fat stimuli with a pleasant flavor increase the coupling of activations between the orbitofrontal cortex and somatosensory cortex, suggesting a role for the somatosensory cortex in processing the sensory properties of food in the mouth (Grabenhorst and Rolls, 2014).

#### 2.4.6. Convergence of olfactory, taste and visual inputs in the orbitofrontal cortex

**2.4.6.1. Neuronal activity.** Taste and olfactory pathways are brought together in the orbitofrontal cortex where flavor is formed by learned associations at the neuronal level between these inputs (see Fig. 1) (Critchley and Rolls, 1996a; Rolls and Baylis, 1994; Rolls et al., 1996c). Visual inputs also become associated by learning in the orbitofrontal cortex with the taste of food to represent the sight of food and contribute to flavor (Rolls et al., 1996b; Thorpe et al., 1983). Olfactory-to-taste associative learning by these orbitofrontal cortex neurons may take 30–40 trials to reverse in an olfactory-to-taste discrimination task, and this slow learning may help to make a flavor stable (Rolls et al., 1996b). Olfactory neurons are found in a considerable anterior-posterior extent of the primate orbitofrontal cortex, extending far into areas 11 and 14 (Critchley and Rolls, 1996a, 1996c; Rolls and Baylis, 1994; Rolls et al., 1996b, 1996c), and are not restricted to a posterior region as some have thought (Gottfried and Zald, 2005).

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



**Fig. 9.** Brain regions in which the activations were correlated with the subjective pleasantness of fat texture: Mid-orbitofrontal cortex ( $[32\ 34\ -14]$ ,  $z = 3.38$ ,  $p = 0.013$ ) ((a) yellow circle, (c) showing the relation between the % change in the BOLD signal and the rating of the pleasantness of the texture) and anterior cingulate cortex ( $[2\ 30\ 14]$ ,  $z = 3.22$ ,  $p = 0.016$ ) ((a) pink circles, (b) showing the relation between the % change in the BOLD signal and the rating of the pleasantness of the texture). (After Grabenhorst et al. (2010b).)

2014). These visual-taste neurons thus respond to expected value (and in humans different orbitofrontal cortex neurons signal expected monetary value based on a visual offer (Rolls et al., 2008b)).

Different neurons in the orbitofrontal cortex respond when a visually signaled expected taste reward is not obtained, that is, to negative reward prediction error (Rolls and Grabenhorst, 2008; Rolls, 2014; Thorpe et al., 1983). There is evidence that dopamine neurons in the ventral tegmentum respond to positive reward prediction error (Schultz, 2007), and as such, they do not respond to taste reward (Rolls, 2014). The inputs to the dopamine neurons may originate from structures such as the orbitofrontal cortex, where expected value, reward outcome (e.g. taste), and negative reward prediction error are represented (Rolls, 2014).

**2.4.6.2. Taste-olfactory convergence shown by activations in humans.** Taste and olfactory conjunction analyses, and the measurement of superadditive effects that provide evidence for convergence and interactions in fMRI investigations, showed convergence for taste (sucrose) and odor (strawberry) in the orbitofrontal and anterior cingulate cortex, and activations in these regions were correlated with the pleasantness ratings given by the participants (de Araujo et al., 2003c; Small et al., 2004; Small and Prescott, 2005). These results provide evidence on the neural substrate for the convergence of taste and olfactory stimuli to produce flavor in humans, and where the pleasantness of flavor is represented in the human brain.

The first region where the effects of this olfactory-taste convergence are found is in an agranular part of what cytoarchitecturally is the insula (Ia) that is topologically found in the posterior orbitofrontal cortex, though it is anterior to the insular taste cortex, and posterior to the granular orbitofrontal cortex (see Fig. 2) (de Araujo et al., 2003c). We do not typically find olfactory activations in the anterior insular primary taste cortex. However, sometimes these are reported (Small, 2010; Veldhuizen et al., 2010). This might reflect the recall of a taste by an odor, using top-down backprojections which are implicated in memory recall (Rolls, 2008a), in this case from the multimodal orbitofrontal cortex. This is in contrast to feed-forward, bottom-up inputs, from the thalamus for a primary cortical area, or from a preceding cortical area in a cortical hierarchy (Rolls, 2008a, 2016). (A similar situation may apply to activation of olfactory cortical areas by taste stimuli, where the olfactory component of a flavor may be being recalled; and to the activation of primary taste or olfactory cortical areas by taste-related, by odor-related, or by flavor-related visual stimuli.) Another possible factor is that trigeminal (somatosensory) inputs do reach the insular taste cortex (de Araujo and Rolls, 2004; Kadohisa et al., 2004; Rolls et al., 2003b; Verhagen et al., 2003), and the activations there might reflect trigeminal inputs which are produced by many odors. Another possible factor is that if the olfactory stimuli produce any autonomic activity, this would be expected to be reflected in activations in the nearby viscer-autonomic part of the anterior insula.

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

O'Doherty et al. (2002) showed that visual stimuli associated with the taste of glucose activate the orbitofrontal cortex and some

connected areas, consistent with the primate neurophysiology. Simmons et al. (2005) found that showing pictures of foods, compared to pictures of places, can also activate the orbitofrontal cortex. Similarly, the orbitofrontal cortex and connected areas were also found to be activated after presentation of food stimuli to food-deprived subjects (Wang et al., 2004).

#### 2.4.7. Reward value in the orbitofrontal cortex

The visual and olfactory as well as the taste inputs represent the reward value of the food, as shown by sensory-specific satiety effects (Critchley and Rolls, 1996c) (see Fig. 7).

The modulation of the reward value of a sensory stimulus such as the taste of food by motivational state, for example hunger, is one important way in which motivational behavior is controlled (Rolls, 2005b, 2007, 2014). The subjective correlate of this modulation is that food tastes pleasant when hungry, and tastes hedonically neutral when it has been eaten to satiety. Following Edmund Rolls' discovery of sensory-specific satiety revealed by the selective reduction in the responses of lateral hypothalamic neurons to a food eaten to satiety (Rolls, 1981; Rolls et al., 1986), it has been shown that this is implemented by neurons in a region that projects to the hypothalamus, the orbitofrontal (secondary taste) cortex, for the taste, odor and sight of food (Critchley and Rolls, 1996c; Rolls et al., 1989) (Fig. 10).

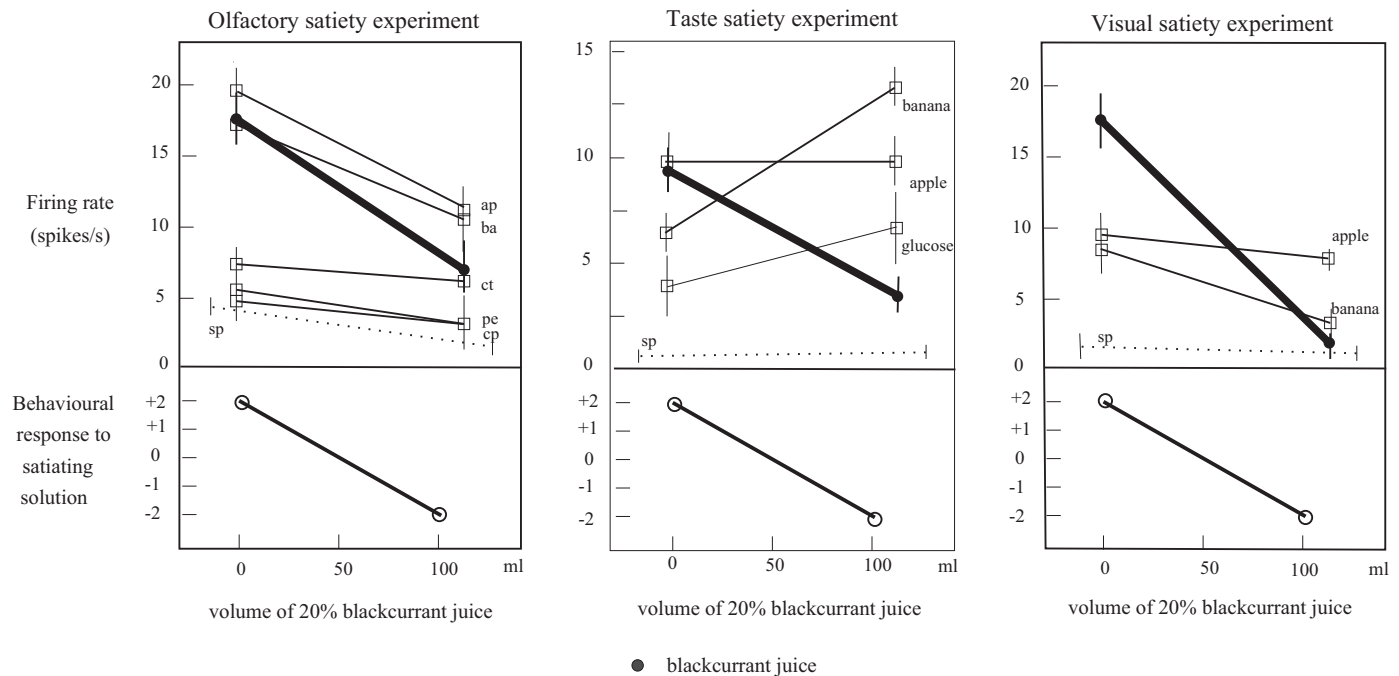
To assess how satiety influences the brain activations to a whole food which produces taste, olfactory, and texture stimulation, we measured brain activation by whole foods before and after the food is eaten to satiety. The foods eaten to satiety were either chocolate milk, or tomato juice. A decrease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

This evidence shows that the reduced acceptance of food that occurs when food is eaten to satiety, the reduction in the pleasantness of its taste and flavor, and the effects of variety to increase food intake (Cabanac, 1971; Hetherington, 2007; Rolls et al., 1981a, 1981b, 1982, 1983a, 1983b, 1984; Rolls and Hetherington, 1989; Rolls and Rolls, 1977, 1982, 1997), are produced in the primate orbitofrontal cortex, but not at earlier stages of processing including the insular-opercular primary taste cortex (Rolls et al., 1988; Yaxley et al., 1988) and the nucleus of the solitary tract (Yaxley et al., 1985), where the responses reflect factors such as the intensity of the taste, which is little affected by satiety (Rolls et al., 1983c; Rolls and Grabenhorst, 2008). In addition to providing an implementation of sensory-specific satiety (probably by adaptation of the synaptic afferents to orbitofrontal cortex neurons with a time course of the order of the length of a course of a meal), it is likely that visceral and other satiety-related signals reach the orbitofrontal cortex (as indicated in Fig. 1) (from the nucleus of the solitary tract, via thalamic and possibly hypothalamic nuclei) and there modulate the representation of food, resulting in an output that reflects the reward (or appetitive) value of each food (Rolls, 2014).

#### 2.4.8. The neuroeconomics of reward value in the orbitofrontal cortex

The reward value representations in the primate orbitofrontal cortex of taste, olfactory, and flavor stimuli are appropriate for economic decision-making in a number of ways, as follows.

One example is that the value of an offer (measured by whether it is chosen over another offer, and reflects the quality of the commodity or 'good' multiplied by the amount available), is reflected in the responses of orbitofrontal cortex neurons. In one experiment, one drop of grape juice was equal in reward value to 3 drops of peppermint tea, as measured by the monkey's choices



**Fig. 10.** Orbitofrontal cortex neuron with visual, olfactory and taste responses, showing the responses before and after feeding to satiety with blackcurrant juice. The solid circles show the responses to blackcurrant juice. The olfactory stimuli included apple (ap), banana (ba), citral (ct), phenylethanol (pe), and caprylic acid (cp). The spontaneous firing rate of the neuron is shown (sp). The taste panel is for the flavor of food in the mouth. The olfactory panel is for the application of olfactory stimuli presented in front of the nose on a cotton bud. The visual panel is for the sight of the stimuli shown just before they were provided orally. Below the neuronal response data for each experiment, the behavioral measure of the acceptance or rejection of the solution on a scale from +2 to -2 is shown. The values shown are the mean firing rate and its se. (After Critchley and Rolls (1996c).)

when different offers were made. (For example, if the choice was between 1 drop of grape juice and 2 drops of peppermint tea, then the grape juice was chosen.) The responses of some orbitofrontal cortex neurons reflect the reward value of these offers (Padoa-Schioppa and Assad, 2006). These neurons respond to the sight of the visual stimulus that shows what offer is available with a firing rate that reflects the 'economic' reward value of the offer (Padoa-Schioppa, 2011; Rolls, 2014). These neurons correspond to the visual reward neurons in the orbitofrontal cortex, the responses of which decrease to zero as the reward is devalued by feeding to satiety (Critchley and Rolls, 1996a, 1996c; Rolls et al., 1996b). Other neurons in the orbitofrontal cortex reflect the 'economic' value of the reward when it is delivered, in that their firing rate when the taste is delivered reflects the quality of the good and the amount delivered (Padoa-Schioppa and Assad, 2006; Padoa-Schioppa, 2011; Rolls, 2014). These neurons correspond to the taste and flavor reward neurons in the orbitofrontal cortex, the responses of which decrease to zero as the reward is devalued by feeding to satiety (Rolls et al., 1989).

In humans, activations in the orbitofrontal cortex reflect the 'subjective value' of foods (where 'subjective value' in economics refers strictly to what is chosen by a subject rather than to conscious subjective pleasantness (Rolls, 2014)), measured in a task in which the value is measured by choices between different foods and different amounts of money (Plassmann et al., 2007).

In the experiment of Padoa-Schioppa and Assad (2006), offers varied on two dimensions: juice type (commodity), and juice amount (quantity). The same method can be applied when offers vary on other dimensions, such as probability, cost, delay, etc. (Padoa-Schioppa, 2011; Rolls, 2014). Indeed, to be useful for economic choice, the encoding should be *domain general*, that is, the activity should represent the value of the good affected by all the relevant determinants (commodity, quantity, risk, cost, etc.) (Padoa-Schioppa, 2011; Rolls, 2014). There is evidence that this

applies to the value representations as influenced by some of these other dimensions for the orbitofrontal cortex and overlapping ventromedial prefrontal cortex (vmPFC). For example, the effects of risk, i.e. the probability of obtaining the good or reward, on subjective value have been shown to be reflected in the activations found in the human orbitofrontal cortex (Peters and Buchel, 2009; Rolls et al., 2008b). In addition, the delay of a reward decreases the value of the delayed reward and activations in the human vmPFC in a corresponding way (Kable and Glimcher, 2007), and consistent results have been found at the single neuron level in monkeys (Roesch and Olson, 2005). Further, the cost in terms of the effort involved in obtaining a reward also decreases the neuronal responses in the orbitofrontal cortex to a reward (Kennerley et al., 2009), providing evidence that subjective value representations in the orbitofrontal cortex do reflect the cost of the actions required to obtain the reward. This is an indication that what we have also termed the 'net value' of a reward, that is the value of the reward minus the cost/effort required to obtain it, needs to be represented, for this 'net value' input is what is required to the decision-making network (Grabenhorst and Rolls, 2011; Rolls, 2014). This is needed because the attractor decision-making network cannot relate separate inputs for the rewards and for the costs of several alternatives, for which cost was to be bound to each reward could not be implemented in the decision-making network.

A neuronal representation of value can be said to be 'abstract' (i.e., in the space of goods) not only if it is domain general (as just described), but also if the representation is *independent of the sensori-motor contingencies of choice*, indicating that the neurons do not just encode movements or stimulus-response habits (Padoa-Schioppa, 2011; Rolls, 2014). The relation of primate orbitofrontal cortex neuronal activity to the reward value of sensory stimuli including taste, olfactory, oral texture, and visual stimuli, and not to movements, for example of the mouth or arm, has been made clear since our earliest reports (Rolls et al., 1990; Rolls, 2005b;

Thorpe et al., 1983; Verhagen et al., 2003), and was confirmed by Padoa-Schioppa and Assad (2006), who found that less than 5% of orbitofrontal cortex neurons were significantly modulated by the spatial configuration of the offers on the monitor or by the direction of the eye movement response that was required. Similar independence of primate orbitofrontal cortex representations of value from the details of actions has also been reported by others (Kennerley and Wallis, 2009; Roesch and Olson, 2005).

It is of interest that insofar as a representation of value exists in rodents (Schoenbaum et al., 2009), it does not appear to meet the conditions for abstraction described above (Schoenbaum et al., 2009). For example, neurons in the rodent orbitofrontal cortex may be spatially selective and thus represent responses, i.e. movements (Feierstein et al., 2006; Roesch et al., 2006), and this means that it is not an equivalent of the primate orbitofrontal cortex. Further, experiments that manipulated two determinants of value found that different neuronal populations in the rat orbitofrontal cortex represent reward magnitude and time delay – a striking difference with primates (Roesch and Olson, 2005; Roesch et al., 2006). Differences in the anatomy and connections of the rat from the primate orbitofrontal cortex are apparent (e.g. with the rat having only agranular regions (Wise, 2008), see Fig. 2 and Section 1.3), and it is possible that an abstract representation of value may have emerged later in evolution in parallel with the expansion of the frontal lobe.

Consistent with these findings, damage to the orbitofrontal cortex does produce changes in emotion and the rewarding and punishing effects of stimuli. For example, rapid alterations in behavior when the reward value of stimuli is reversed are impaired (Berlin et al., 2004; Hornak et al., 2004; Rolls et al., 1994; Rolls, 2014), and the different values placed on different foods as measured by their choice become blunted (Baylis and Gaffan, 1991). In the gourmand syndrome, in which there is great interest in good cuisine, damage may be found in the right anterior temporal lobe (Regard and Landis, 1997) including the amygdala and temporal pole (Gallo et al., 2014). In contrast, lesions of the insula can impair taste detection and discrimination (Stevenson et al., 2013).

There is thus considerable evidence that the primate including human orbitofrontal cortex and adjoining ventromedial prefrontal cortex (vmPFC) provide an abstract representation of value. Important properties of the representation are that the subjective value, the value to the individual, is represented and not the actions required to obtain the reward or 'good'; and that the representation is domain general, that is reflects the value when it is altered in a number of ways including the magnitude of the good, risk, delay, and the cost/effort required to obtain the good. The single neuron data, including much that we have obtained (Rolls, 2014), indicates that the representation at the neuronal level is specific for each different type of reward or good, with a common scale of value, but no conversion into a common currency, as described in the next section.

#### 2.4.9. Representations in the orbitofrontal cortex of reward value on a common scale but not in a common currency

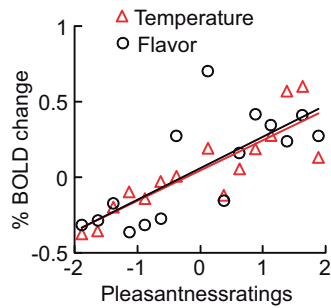
A classical view of economic decision theory (Bernoulli, 1738/1954) implies that decision-makers convert the value of different goods into a common scale of utility (Glimcher, 2011; Rolls, 2014). Some ecological (McFarland and Sibly, 1975), some psychological (Cabanac, 1992), and some neuroeconomic (Montague and Berns, 2002) approaches suggest that the values of different kinds of rewards are converted into a common currency. We have argued that different specific rewards must be represented on the same scale, but not converted into a common currency, as the specific goal selected (i.e. the particular reward selected) must be the output of the decision process and must be maintained active so

that the appropriate action for that particular goal can then be chosen (Grabenhorst et al., 2011; Rolls, 2005b, 2008a, 2014; Rolls and Grabenhorst, 2008). The key difference between the two concepts of common currency and common scaling lies in the specificity with which rewards are represented at the level of single neurons. While a common currency view may imply convergence of different types of rewards onto the same neurons (a process in which information about reward identity is lost), a common scaling view implies that different rewards are represented by different neurons (thereby retaining reward identity in information processing), with the activity of the different neurons scaled to be in the same value range.

The evidence from investigations of taste, olfactory, and flavor processing in the orbitofrontal cortex provides direct evidence that different rewards are encoded independently of each other by neurons using a sparse distributed representation. Single neurons in the orbitofrontal cortex encode different specific rewards (Grabenhorst et al., 2011; Rolls, 2005b, 2008a, 2014; Rolls and Grabenhorst, 2008). They do this by each neuron responding to different combinations of taste, olfactory, somatosensory, visual, and auditory stimuli, as illustrated in Fig. 5. Part of the adaptive utility of this reward-specific representation is that it provides for sensory-specific satiety as implemented by a decrease in the responsiveness of reward-specific neurons (Rolls, 2005b, 2008a, 2014). This is a fundamental property of every reward system that helps to ensure that a variety of different rewards is selected over time. Representations of both reward outcome and expected value are specific for the particular reward: not only do different neurons respond to different primary (unlearned) reinforcers, but different neurons also encode the conditioned stimuli for different outcomes, with different neurons responding for example to the sight or odor of stimuli based on the outcome that is expected (Rolls et al., 1996b; Thorpe et al., 1983). Moreover, the information encoded by different neurons about taste, olfaction, and flavor in the orbitofrontal cortex is approximately independent, that is, adds linearly (at least up to tens of neurons), as shown by information theoretic analyses of orbitofrontal cortex neuronal activity (Rolls et al., 1996c, 2010a; Rolls and Treves, 2011). This evidence from single neurons is important, for given the poor spatial resolution of fMRI (approximately 3 mm), it cannot provide very direct evidence on whether different rewards are represented independently. The neuronal recordings provide clear evidence that the reward value of different rewards is encoded by different subpopulations of neurons using a sparse distributed representation (Rolls et al., 1996c, 2010a; Rolls and Treves, 2011; Rolls, 2014).

To investigate whether these independently represented specific reward representations are on a common scale of reward value, we performed an fMRI study in which we were able to show that even fundamentally different primary rewards, taste in the mouth and warmth on the hand, produced activations in the human orbitofrontal cortex that were scaled to the same range as evaluated by reports made during the neuroimaging of the subjective pleasantness of the set of stimuli (Grabenhorst et al., 2010a) (Fig. 11). In this case, value was measured by human subjective ratings on the same scale of pleasantness. A different study found that the decision value for different categories of goods (food, non-food consumables, and monetary gambles) during purchasing decisions correlated with activations in the overlapping ventromedial prefrontal cortex (Chib et al., 2009). Further fMRI studies with similar indications are reviewed by Levy and Glimcher (2012).

With our current computational understanding of how decisions are made in attractor neural networks (Rolls, 2008a, 2014; Rolls and Deco, 2010; Wang, 2008) (see Section 4), it is important that different rewards are expressed on a similar scale for decision-making networks to operate correctly but retain



**Fig. 11.** A common scale for the subjective pleasure for different primary rewards. Neural activations in the orbitofrontal cortex correlate with the subjective pleasantness ratings for flavor stimuli in the mouth and somatosensory temperature stimuli delivered to the hand. The regression lines describing the relationship between neural activity (% BOLD signal change) and subjective pleasantness ratings were indistinguishable for both types of reward. Reprinted from Grabenhorst et al. (2010a), with permission from Elsevier.

information about the identity of the specific reward. The computational reason is that one type of reward (e.g. food reward) should not dominate all other types of reward and always win in the competition, as this would be maladaptive. Making different rewards approximately equally rewarding makes it likely that a range of different rewards will be selected over time (and depending on factors such as motivational state and sensory-specific satiety), which is adaptive and essential for survival (Rolls, 2014). The exact scaling for the inputs into a decision-making attractor network will be set by the number of inputs from each source, their firing rates, and the strengths of the synapses that introduce the different inputs into the decision-making network. In the decision process itself it is important to know which reward has won, and the mechanism is likely to involve competition between different rewards represented close together in the cerebral cortex, with one of the types of reward winning the competition, rather than convergence of different rewards onto the same neuron. A great advantage of this decision-making mechanism is that whichever attractor in the decision-making network wins, has the additional property that it represents and maintains active in an attractor short-term memory the specific reward that has won, and this allows behavior to be directed to perform actions to obtain that reward (Rolls, 2008a, 2014). The continuing firing of the specific reward decision attractor maintains active the goal for the action to direct the action until the action is completed. If the representation was in a common currency, the action system would have no evidence about the goal (e.g. food reward, monetary reward) that actions should be performed to acquire. Actions are typically different for different goals, such as the taste, smell, flavor, and sight of food vs other rewards.

#### 2.4.10. Representations in the orbitofrontal cortex of non-reward: error neurons

If an expected taste reward is not obtained in a visual discrimination task, some primate orbitofrontal cortex neurons respond to the non-reward (Thorpe et al., 1983). Some of these neurons respond to receiving nothing (i.e. in extinction). Other error neurons respond to receiving the aversive taste of salt when glucose was expected, but salt was obtained. These are error neurons, for they do not respond to the taste of salt if salt is expected (Thorpe et al., 1983). These results have been confirmed (Ifuku et al., 2006), as has the presence of neurons in the orbitofrontal cortex that respond to expected value of in our case visual and olfactory stimuli (Critchley and Rolls, 1996c; Rolls et al., 1996b). The error neurons detect a mismatch of an expected

stimulus with the stimulus outcome, so are sensory–sensory error neurons (Rolls, 2014; Thorpe et al., 1983), and are different from the error neurons that respond when a response is in error that are found in the cingulate and medial prefrontal cortex (Matsumoto et al., 2007) which are implicated in action–outcome learning (Rolls, 2014).

In humans, consistently, the lateral parts of the orbitofrontal cortex are activated when an expected monetary reward is not obtained so that behavior must reverse (O'Doherty et al., 2001a), and when an expected face expression is not obtained so that behavior must reverse (Kringelbach and Rolls, 2003), with the expectation that different types of non-reward (as well as for other neurons reward) are represented by different populations of neurons, consistent with the neuronal evidence (Rolls, 2014; Thorpe et al., 1983).

#### 2.5. The amygdala

The amygdala is a structure in the temporal lobe with somewhat similar connections to the orbitofrontal cortex (see Fig. 1). The amygdala has been present in evolution for much longer than the primate orbitofrontal cortex, and appears to differ from the orbitofrontal cortex in that it cannot implement one-trial, rule-based, visual discrimination reversal when the taste or flavor associated with the visual stimulus is reversed (Rolls, 2014). The reason for this may be related to the advantage that cortical structures have with their well-developed local recurrent collateral connections in maintaining items in short-term memory, which serves in this case to maintain the rule of which visual stimulus is currently associated with reward (Rolls, 2014).

The primate amygdala contains neurons that respond to taste and oral texture (Kadohisa et al., 2005a, 2005b; Sanghera et al., 1979; Scott et al., 1993). Some neurons respond to visual stimuli associated with reinforcers such as taste, but do not reflect the reinforcing properties very specifically, do not rapidly learn and reverse visual-to-taste associations, and are much less affected by reward devaluation by feeding to satiety than are orbitofrontal cortex neurons (Kadohisa et al., 2005a, 2005b; Rolls, 2014; Sanghera et al., 1979; Wilson and Rolls, 2005; Yan and Scott, 1996). The primate orbitofrontal cortex appears to be much more closely involved in flexible (rapidly learned, and affected by reward devaluation) reward representations than is the primate amygdala (Rolls, 2014). In rodents, conditioning can influence amygdala taste-responsive neurons (Fontanini et al., 2009).

Fat texture, oral viscosity, and temperature, for some neurons in combination with taste, and also the sight and smell of food, are represented in the macaque amygdala (Kadohisa et al., 2005a, 2005b; Rolls, 2000; Rolls and Scott, 2003). Interestingly, the responses of these amygdala neurons do not correlate well with the preferences of the macaques for the oral stimuli (Kadohisa et al., 2005a), and feeding to satiety does not produce the large reduction in the responses of amygdala neurons to food (Rolls, 2000; Rolls and Scott, 2003; Yan and Scott, 1996) that is typical of orbitofrontal cortex neurons.

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

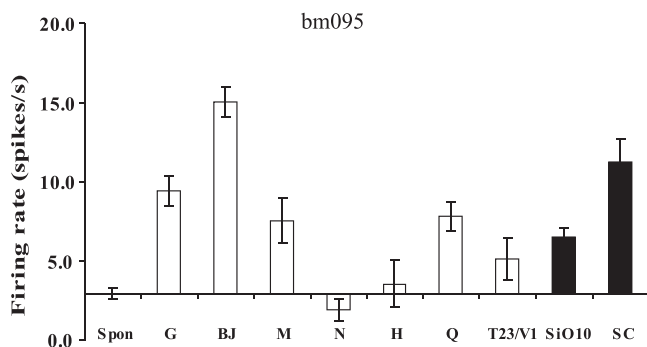
The roles of the amygdala vs the orbitofrontal cortex are compared and contrasted by Rolls (2014).

## 2.6. The anterior cingulate cortex: a tertiary taste cortical area

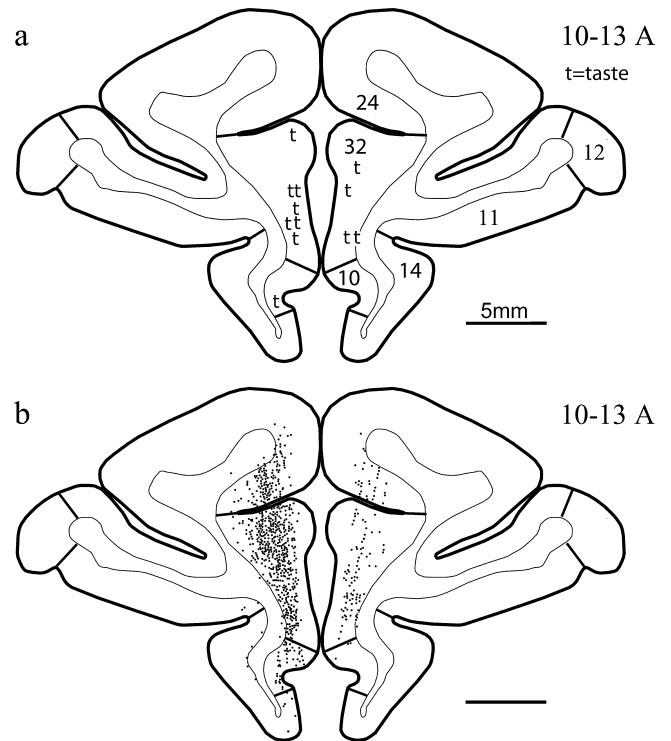
The orbitofrontal cortex, including the extensive areas where taste neurons noted above are found, projects to the pregenual cingulate cortex area 32 (Carmichael and Price, 1996) (see Figs. 1 and 2). In human imaging studies it has been shown that reward-related stimuli, such as the taste of sucrose and the texture of oral fat, activate the pregenual cingulate cortex (de Araujo and Rolls, 2004; Grabenhorst and Rolls, 2011; Rolls, 2005b, 2009a; Rolls and Grabenhorst, 2008). Examples of the cingulate cortical areas involved are illustrated in Fig. 4. However, little is known at the neuronal level of whether the responses of single neurons in the pregenual cingulate cortex are tuned to taste stimuli and respond differentially to different taste stimuli. We (Rolls, Gabbott, Verhagen and Kadohisa) therefore recorded from single neurons in the macaque pregenual cingulate cortex, in order to obtain evidence on these issues (see Rolls, 2008b).

The responses of a pregenual cingulate cortex neuron with taste responses are shown in Fig. 12. The neuron increased its firing rate primarily to glucose, fruit juice and cream, with some response to the oily texture of silicone oil, to monosodium glutamate, and to quinine. When the macaque was fed to satiety with glucose, the neuron showed a sensory-specific decrease in its response to the taste of glucose (Rolls, 2008b).

The data for the pregenual cingulate cortex and adjacent areas were obtained by Rolls, Gabbott, Verhagen and Kadohisa (Rolls, 2008b) in two rhesus macaques in recordings that extended from approximately 10 mm anterior with respect to the sphenoid reference to approximately 13 mm anterior, with the recording sites of the neurons shown in Fig. 13 (Rolls, 2008b). As shown, most of these neurons were in area 32, with one taste neuron in area 10. Although a small proportion of the neurons were classified as responding to taste, this proportion is not out of line with the proportion of taste neurons recorded with identical techniques in the same laboratory in the primary taste cortex in the macaque anterior insula and adjoining frontal opercular cortex. Of the 12 responsive neurons in the medial wall cortex, 11 had best responses to sweet stimuli (glucose and/or fruit juice) (as illustrated in Fig. 12), and one had best responses to quinine and NaCl. The spontaneous firing rates of neurons in the pregenual cingulate cortex were typically in the range 0–5 spikes/s, which increased significantly to 20–30 spikes/s when the neurons were responding selectively to specific taste stimuli.



**Fig. 12.** Responses of a pregenual cingulate cortex neuron (bm095) with differential responses to tastes and oral fat texture stimuli. The mean ( $\pm$ sem) firing rate responses to each stimulus calculated in a 5 s period over several trials are shown. The spontaneous (Spon) firing rate of 3 spikes/s is shown by the horizontal line, with the responses indicated relative to this line. The taste stimuli were 1 M glucose (G), blackcurrant fruit juice (BJ), 0.1 M NaCl (N), 0.1 M MSG (M), 0.01 M HCl (H) and 0.001 M quinine HCl (Q); water (T23/V1); single cream (SC); and silicone oil with a viscosity of 10 cP (SiO10). The neuron had significantly different responses to the different stimuli as shown by a one-way ANOVA [ $F(9, 46) = 17.7, p < 10^{-10}$ ]. Data from Rolls, Gabbott, Verhagen, and Kadohisa, see Rolls (2008b).



**Fig. 13.** (a) The reconstructed positions of the anterior cingulate neurons with taste (t) responses, together with the cytoarchitectonic boundaries determined by Carmichael and Price (1994). Most (11/12) of the taste neurons were in the pregenual cingulate cortex (area 32), as shown. The neurons are shown on a coronal section at 12 mm anterior (A) to the sphenoid reference point. The recording sites were reconstructed using X-radiographs made on every track and subsequent histology using the methods described by Rolls et al. (2003b). (b) The locations of all the 749 neurons recorded in the anterior cingulate region in this study are indicated to show the regions sampled.

Data from Rolls, Gabbott, Verhagen, and Kadohisa, see Rolls (2008b).

The presence of a neuronal representation of a primary (unlearned) reinforcer, taste, in the pregenual cingulate cortex is of importance for understanding the functions more generally of the anterior cingulate cortex in complex reward-related learning (Amiez et al., 2006), and in action selection using action-outcome learning (where the outcome refers to the reward) (Grabenhorst and Rolls, 2011; Rolls, 2014; Rushworth et al., 2011), for this evidence shows that primary rewards are represented in at least one part of the anterior cingulate cortex – the pregenual cingulate cortex area 32 (Rolls, 2008b, 2009a). The hypothesis is that with actions, behavioral responses, also represented in the cingulate cortex, this cortical area provides a brain region in which associations can be learned between actions and the rewards that are obtained when the actions are performed (Grabenhorst and Rolls, 2011; Rolls, 2014; Rushworth et al., 2011). Neurons responding to fruit juice used as a reinforcer in a saccade countermanding have been found in the dorsal part of the anterior cingulate sulcus area 24c (Ito et al., 2003), and the pregenual cingulate cortex provides a source of inputs to area 24 (Carmichael and Price, 1996). Indeed, establishing that the pregenual cingulate cortex contains a representation of a primary reinforcer, in this case a taste, is of importance more generally in relation to understanding the functions of the pregenual cingulate cortex in emotion (Grabenhorst and Rolls, 2011; Rolls and Grabenhorst, 2008; Rolls, 2009a), in that for example some disorders of emotion in humans produced by anterior cingulate damage include deficits in responding to what are probably other primary reinforcers, face and voice expression (Hornak et al., 2003; Rolls, 2005b, 2014).

## 2.7. Hypothalamus

The orbitofrontal cortex and amygdala project to the hypothalamus, which is implicated in the control of food intake (Rolls, 2014). The primate lateral hypothalamus contains taste-responsive neurons, which only respond to food when hunger is present, and indeed reflect sensory-specific satiety (Rolls, 1981; Rolls et al., 1986). The lateral hypothalamus also contains neurons that respond to the sight of food, and they also only respond to food when hunger is present, that is, when the food is rewarding (Burton et al., 1976; Mora et al., 1976; Rolls et al., 1976, 1979, 1986; Rolls, 1981, 2014). The traditional view of the hypothalamus is that it integrates many of the hormonal and nutritional signals that control appetite (Suzuki et al., 2010; Woods, 2013), but this neurophysiological evidence shows that the hypothalamus is also involved in the reward signals from taste, olfaction, and vision that need to be interfaced to hunger and satiety signals (Rolls, 2014).

## 2.8. Hippocampus

The primate hippocampus contains neurons that respond to the sight of locations in spatial scenes where flavor rewards are found, but not to the sight of objects associated with flavor reward (Rolls and Xiang, 2005), and this is part of the evidence for understanding the functions of the hippocampus in episodic memory, for example where one has seen a particular food (Kesner and Rolls, 2015; Rolls, 2008a, 2010b).

## 2.9. Striatum

The primate ventral striatum and adjoining part of the head of the caudate nucleus receive connections from the orbitofrontal cortex and amygdala (Haber and Knutson, 2009; Rolls, 2014). Consistent with this, some neurons in these striatal regions respond to the taste, flavor, and/or sight of food (Rolls et al., 1983d; Rolls and Williams, 1987; Rolls, 2014; Strait et al., 2015; Williams et al., 1993).

These taste and related inputs to the basal ganglia may be involved in stimulus-response habit formation, with the taste and other reinforcers helping to stamp in the connections between environmental stimuli and behavioral responses that co-occur just prior to receiving a reinforcer such as the taste, flavor, or sight of food (Rolls, 2014). Perhaps as part of this functionality, incentive stimuli such as the food can have effects on behavior that are mediated through the striatum (Everitt and Robbins, 2013; Smith and Robbins, 2013). The hypothesis that there is less D2 receptor binding in the dorsal striatum of the obese and that this system contributes to human obesity (Volkow et al., 2013) has been questioned (Cosgrove et al., 2015). There are smaller BOLD responses in the dorsal striatum to palatable food with increasing body mass index, with the reduced striatal response being interpreted as a consequence of the reduced incentive value of food in the overweight. There is in contrast a positive relation of D2/D3 receptor binding to body mass index, and this is not associated with the change in the BOLD response (Cosgrove et al., 2015).

The striatum receives a dopaminergic input that it has been suggested is a positive reward prediction error signal (Schultz, 2013), though there may be too much diversity in the activity of dopamine neurons for this to apply in a simple way (Bromberg-Martin et al., 2010; Rolls, 2014). Moreover, there is no evidence that the dopamine neurons encode a specific reward signal (for example for the taste of food vs the texture of fat) in the way that is required to account for the control of goal-directed rewarded behavior and that is present in the primate orbitofrontal cortex (Rolls, 2014). Moreover, the activity of ventral striatal neurons

appears to be more influenced by orbitofrontal cortex types of signal rather than by positive reward prediction error signals (Strait et al., 2015). The role of the striatum and of dopamine in the control of behavior is considered in more detail elsewhere (Rolls, 2014).

## 3. Further imaging studies on reward value representations in humans

### 3.1. Top-down cognitive effects on taste, olfactory, and flavor processing

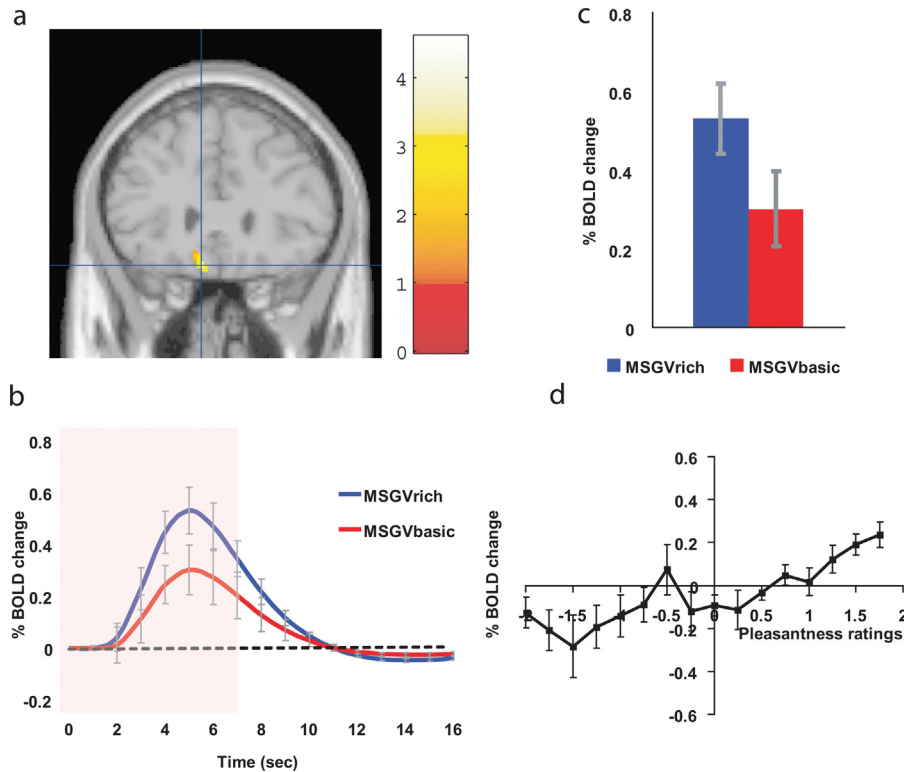
To what extent does cognition influence the hedonics of food-related stimuli, and how far down into the sensory system does the cognitive influence reach? To address this, we performed an fMRI investigation in which the delivery of a standard test odor (isovaleric acid combined with cheddar cheese odor, presented orthonasally using an olfactometer) was paired with a descriptor word on a screen, which on different trials was “Cheddar cheese” or “Body odor”. Participants rated the affective value of the test odor as significantly more pleasant when labeled “Cheddar Cheese” than when labeled “Body odor”, and these effects reflected activations in the medial orbitofrontal cortex (OFC)/rostral anterior cingulate cortex (ACC) that had correlations with the pleasantness ratings (de Araujo et al., 2005). The implication is that cognitive factors can have profound effects on our responses to the hedonic and sensory properties of food, in that these effects are manifest quite far down into sensory and hedonic processing (in the orbitofrontal cortex, see Fig. 1), so that hedonic representations of odors are affected (de Araujo et al., 2005).

Similar cognitive effects and mechanisms have now been found for the taste and flavor of food, where the cognitive word level descriptor was for example ‘rich delicious flavor’ and activations to flavor were increased in the orbitofrontal cortex and regions to which it projects including the pregenual cingulate cortex and ventral striatum, but were not influenced in the insular primary taste cortex where activations reflected the intensity (concentration) of the stimuli (Grabenhorst et al., 2008a) (see Fig. 14). Cognitive factors can also influence the release of the hunger-related hormone ghrelin (Crum et al., 2011: #6434). If self control of reward-related processing is required, the dorsolateral prefrontal cortex may be involved in the attentional and related aspects of the processing (Hare et al., 2009: #4292) (Rolls, 2014).

### 3.2. Effects of top-down selective attention to affective value vs intensity on representations of taste, olfactory, and flavor processing

We have found that with taste, flavor, and olfactory food-related stimuli, selective attention to pleasantness modulates representations in the orbitofrontal cortex (see Fig. 15), whereas selective attention to intensity modulates activations in areas such as the primary taste cortex (Grabenhorst and Rolls, 2008; Rolls et al., 2008a). Thus, depending on the context in which tastes and odors are presented and whether affect is relevant, the brain responds to a taste, odor or flavor differently. These findings show that when attention is paid to affective value, the brain systems engaged to represent the stimulus are different from those engaged when attention is directed to the physical properties of a stimulus such as its intensity.

The source of the top-down modulation by attention of the orbitofrontal cortex appears to be the lateral prefrontal cortex, as shown by PPI (psychophysiological interaction) analyses (Grabenhorst and Rolls, 2010), and by Granger causality analyses (Ge et al., 2012; Luo et al., 2013). The mechanism probably involves a weak top-down biased competition effect on the taste and olfactory processing (Deco and Rolls, 2005a; Desimone and



**Fig. 14.** Cognitive modulation of flavor reward processing in the brain. (a) The medial orbitofrontal cortex was more strongly activated when a flavor stimulus was labeled 'rich and delicious flavor' (MSGVrich) than when it was labeled 'boiled vegetable water' (MSGVbasic) ( $[-8\ 28\ -20]$ ). (The flavor stimulus, MSGV, was the taste 0.1 M MSG + 0.005 M inosine 5' monophosphate combined with a consonant 0.4% vegetable odor.) (b) The timecourse of the BOLD signals for the two conditions. (c) The peak values of the BOLD signal (mean across subjects  $\pm$  sem) were significantly different ( $t = 3.06$ ,  $df = 11$ ,  $p = 0.01$ ). (d) The BOLD signal in the medial orbitofrontal cortex was correlated with the subjective pleasantness ratings of taste and flavor, as shown by the SPM analysis, and as illustrated (mean across subjects  $\pm$  sem,  $r = 0.86$ ,  $p < 0.001$ ). (After Grabenhorst et al. (2008a)).

Duncan, 1995; Rolls, 2008a, 2013). Because whole streams of cortical processing are influenced (orbitofrontal and cingulate cortex, and even their coupling to the primary taste cortex, by pleasantness-related processing; and insular taste cortex and the mid-insula by intensity-related processing (Grabenhorst and Rolls, 2010; Luo et al., 2013)), the process has been described as a biased activation model of attention (Grabenhorst and Rolls, 2010; Rolls, 2013), which is illustrated in Fig. 16.

This differential biasing by prefrontal cortex attentional mechanisms (Ge et al., 2012; Grabenhorst and Rolls, 2010) of brain regions engaged in processing a sensory stimulus depending on whether the cognitive demand is for affect-related vs more sensory-related processing may be an important aspect of cognition and attention which have implications for how strongly the reward system is driven by food, and thus for eating and the control of appetite (Grabenhorst and Rolls, 2008, 2011; Rolls et al., 2008a; Rolls, 2012a). The top-down modulations of processing have many implications for investigations of taste, olfactory, and other sensory processing, and for the development of new food and perfumery products.

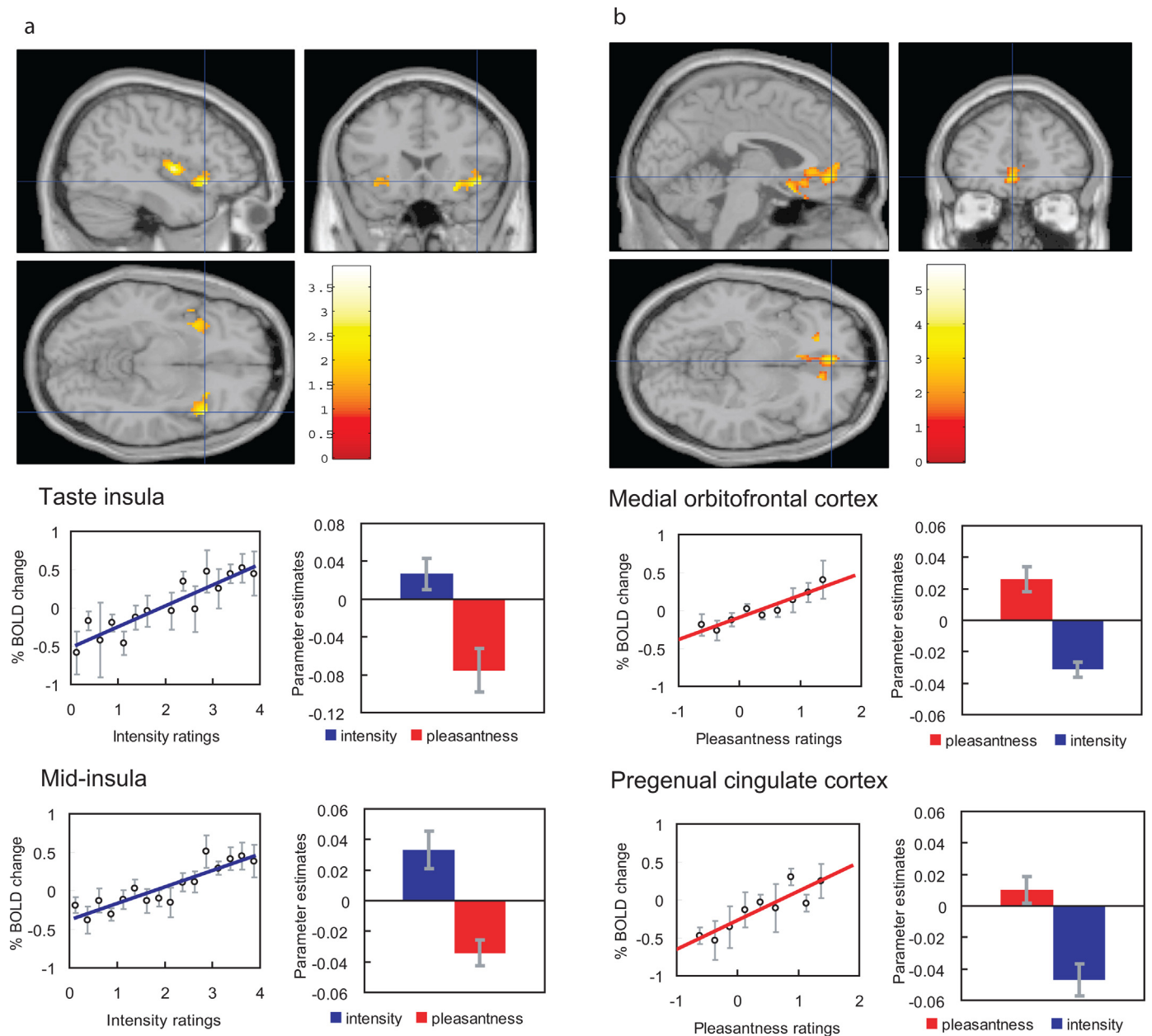
### 3.3. Individual differences

An important hypothesis is that different humans may have reward systems that differ in how strongly their reward systems are activated, driven by the sensory and cognitive factors that make taste, olfactory, and flavor stimuli attractive. In a test of this, we showed that activations to the sight and flavor of chocolate in the orbitofrontal and pregenual cingulate cortex were much higher in chocolate cravers than non-cravers (Rolls and McCabe, 2007), though there were no differences at the level of the insular taste

cortex. This provides evidence that differences in specific reward systems, and not necessarily in earlier sensory processing, can lead to individual differences in behavior to taste, olfactory, and flavor stimuli. This is consistent with the hypothesis that part of the way in which evolution results in effective specific reward systems is by utilizing natural variation in these reward systems, and selecting for reward systems that lead to reproductive success (Rolls, 2014). This concept that individual differences in responsiveness to food reward are reflected in brain activations in regions related to the control food intake (Beaver et al., 2006; Rolls and McCabe, 2007) may provide a way for understanding and helping to control food intake and obesity (Rolls, 2012a, 2014).

### 3.4. Effects of aging

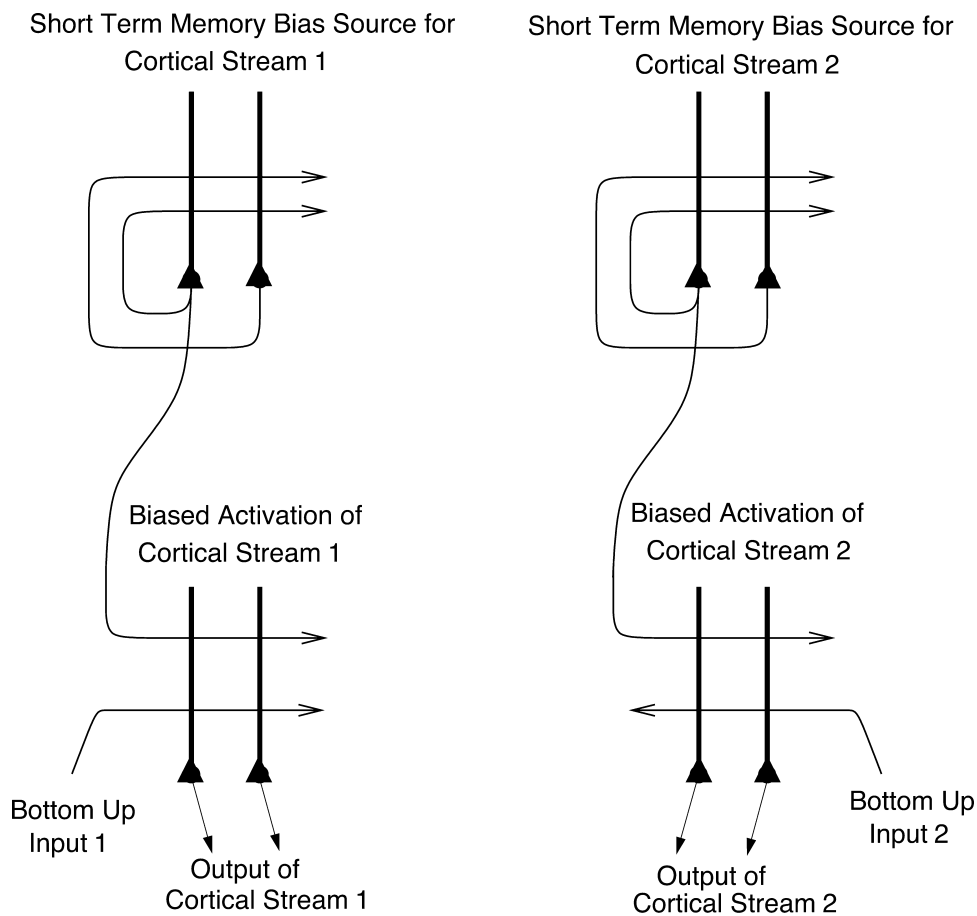
There are age-related differences in the acceptability of different foods. For example children may not take readily to a wide range of vegetables, yet find sweet foods palatable (Birch, 1999; Hetherington et al., 2011). Adults may find a wide range of foods pleasant. As people age, smell and even taste may become less sensitive (Jacobson et al., 2010; Murphy, 1993; Murphy et al., 2002; Stevens et al., 1995), and this may contribute to the changes in eating that can occur in aging (Green et al., 2011; Murphy, 1989; Rolls, 1999). In order to examine the neural mechanisms underlying these age-related differences in the acceptability of different flavors and foods, we performed an fMRI study (Rolls et al., 2015) with three different age groups (21, 41 and 61 years) and used foods, that is stimuli that include different taste, olfactory, and texture components, rather than pure tastes (such as sweet or bitter) which have been used in some previous studies (Green et al., 2013; Jacobson et al., 2010), because we are



**Fig. 15.** Effect of paying attention to the pleasantness vs the intensity of a taste stimulus, monosodium glutamate. (a) Top: A significant difference related to the taste period was found in the taste insula at  $[42\ 18\ -14]$ ,  $z = 2.42$ ,  $p < 0.05$  (indicated by the cursor) and in the mid insula at  $[40\ -2\ 4]$ ,  $z = 3.03$ ,  $p < 0.025$ . Middle: Taste Insula. Right: The parameter estimates (mean  $\pm$  sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the taste insula  $t = 4.5$ ,  $df = 10$ ,  $p = 0.001$ . Left: The correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate ( $r = 0.91$ ,  $df = 14$ ,  $p \ll 0.001$ ). Bottom: Mid Insula. Right: The parameter estimates (mean  $\pm$  sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the mid insula  $t = 5.02$ ,  $df = 10$ ,  $p = 0.001$ . Left: The correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate ( $r = 0.89$ ,  $df = 15$ ,  $p \ll 0.001$ ). The taste stimulus, monosodium glutamate, was identical on all trials. (b) Top: A significant difference related to the taste period was found in the medial orbitofrontal cortex at  $[-6\ 14\ -20]$ ,  $z = 3.81$ ,  $p < 0.003$  (toward the back of the area of activation shown) and in the pregenual cingulate cortex at  $[-4\ 46\ -8]$ ,  $z = 2.90$ ,  $p < 0.04$  (at the cursor). Middle: Medial orbitofrontal cortex. Right: The parameter estimates (mean  $\pm$  sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the orbitofrontal cortex  $t = 7.27$ ,  $df = 11$ ,  $p < 10^{-4}$ . Left: The correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate ( $r = 0.94$ ,  $df = 8$ ,  $p \ll 0.001$ ). Bottom: Pregenual cingulate cortex. Conventions as above. Right: The parameter estimates were significantly different for the pregenual cingulate cortex  $t = 8.70$ ,  $df = 11$ ,  $p < 10^{-5}$ . Left: The correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate ( $r = 0.89$ ,  $df = 8$ ,  $p = 0.001$ ). The taste stimulus, 0.1 M monosodium glutamate, was identical on all trials. (After Grabenhorst and Rolls (2008)).

interested in responses to real, ecologically valid, foods. We used orange juice, orange soda (Fanta), and vegetable juice with a large tomato component (V8). Orange juice and orange soda were found to be liked by all age groups, while vegetable juice was disliked by the Young, but liked by the Elderly. In the insular primary taste cortex, the activations to these stimuli were similar in the 3 age groups, indicating that the differences in liking for these stimuli

between the 3 groups were not represented in this first stage of cortical taste processing. In the agranular insula where flavor is represented, the activations to the stimuli were similar in the Elderly, but in the Young the activations were larger to the vegetable juice than to the orange drinks; and the activations here were correlated with the unpleasantness of the stimuli in the Young group. In the anterior midcingulate cortex, investigated as a



**Fig. 16.** Biased activation mechanism for top-down selective attention. The short-term memory systems that provide the source of the top-down activations may be separate (as shown), or could be a single network with different attractor states for the different selective attention conditions. The top-down short-term memory systems hold what is being paid attention to active by continuing firing in an attractor state, and bias separately either cortical processing system 1, or cortical processing system 2. This weak top-down bias interacts with the bottom up input to the cortical stream and produces an increase of activity that can be supralinear (Deco and Rolls, 2005a; Rolls, 2008a). Thus the selective activation of separate cortical processing streams can occur. In the example, stream 1 might process the affective value of a stimulus, and stream 2 might process the intensity and physical properties of the stimulus. The outputs of these separate processing streams then must enter a competition system, which could be for example a cortical attractor decision-making network that makes choices between the two streams, with the choice biased by the activations in the separate streams.

site where the activations were correlated with the unpleasantness of the stimuli, there was again a greater activation to the vegetable than to the orange stimuli in the Young but not in the Elderly. In the amygdala (and orbitofrontal cortex), investigated as sites where the activations were correlated with the pleasantness of the stimuli, there was a smaller activation to the vegetable than to the orange stimuli in the Young but not in the Elderly. The Middle group was intermediate with respect to the separation of their activations to the stimuli in the brain areas that represent the pleasantness or unpleasantness of flavors. Thus age differences in the activations to different flavors can in some brain areas where olfactory, taste, and flavor stimuli are represented in terms of their hedonic value, be related to, and probably cause, the differences in pleasantness of foods as they differ for people of different ages (Rolls et al., 2015).

#### 4. Beyond reward value to decision-making

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

*Emotion and Decision-Making Explained* (Rolls, 2014), and this has implications for whether a reward of a particular value will be selected (Deco et al., 2013; Grabenhorst and Rolls, 2011; Rolls, 2008a; Rolls and Grabenhorst, 2008; Rolls and Deco, 2010; Rolls, 2011b, 2014).

A tier of processing beyond the orbitofrontal cortex, in the medial prefrontal cortex area 10, becomes engaged when choices are made between odor stimuli based on their pleasantness (Grabenhorst et al., 2008b; Rolls et al., 2010b, 2010c, 2010d) (tier 3 in Fig. 1). For example, activations in this area are larger when humans make a decision about which of two odors they prefer, compared to only rating the odors on a continuous scale of reward value (Grabenhorst et al., 2008b).

The decision-making mechanism that is proposed to be implemented in a number of brain areas for different types of decision is an attractor network in which the winning attractor represents the decision, with each possible attractor representing a different choice, and each attractor receiving inputs that reflect the evidence for that choice. [The attractor network is formed in a part of the cerebral cortex by strengthening of the recurrent collateral excitatory synapses between nearby pyramidal cells. One group of neurons with strengthened synapses between its members can form a stable attractor state with high firing rates, which competes through inhibitory interneurons with other possible attractors formed by other groups of excitatory neurons (Rolls, 2008a, 2010a). The word attractor refers to the fact that inexact inputs are

attracted to one of the states of high firing that are specified by the synaptic connections between the different groups of neurons. The result in this non-linear system is that one attractor wins, and this implements a mechanism for decision-making with one winner (Deco et al., 2013; Rolls, 2008a; Rolls and Deco, 2010; Rolls, 2014; Wang, 2002, 2008) (see Fig. 17.) The decisions are probabilistic as they reflect the noise in the competitive non-linear decision-making process that is introduced by the random spiking times of neurons for a given mean rate that reflect a Poisson process (Rolls and Deco, 2010; Rolls et al., 2010c). The costs of each reward need to be subtracted from the value of each reward to produce a net reward value for each available reward before the decision is taken (Grabenhorst and Rolls, 2011; Rolls, 2008a; Rolls and Grabenhorst, 2008).

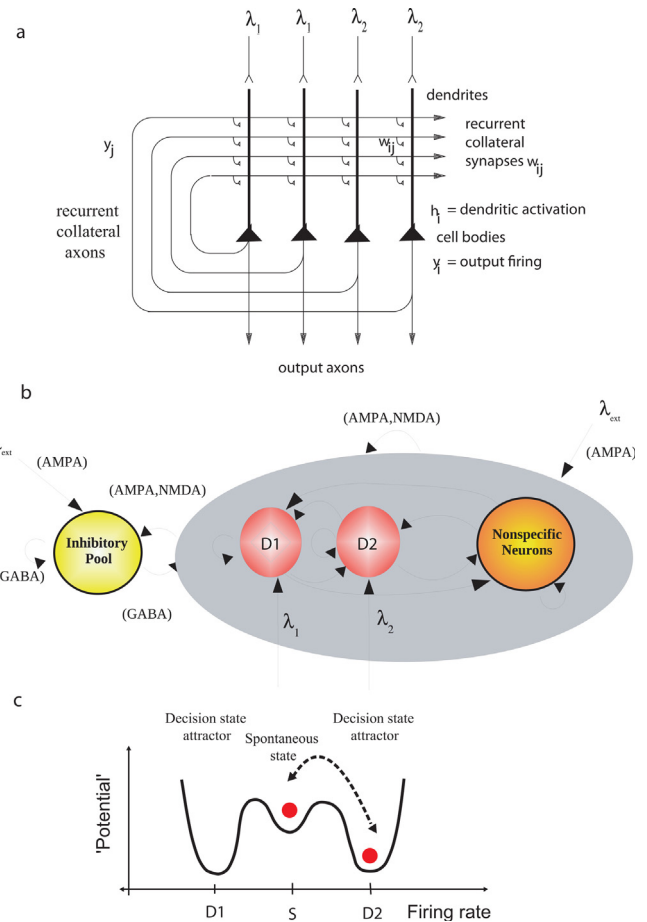
Integrate-and fire neuronal network models (in which the neuronal and synaptic dynamics of each of a large population of neurons is modeled) building on a foundation in theoretical physics make the prediction that such a network would produce somewhat higher firing rates and hence BOLD signals in the winning attractor for easy than for difficult choices, that is when the difference between the two reward values between which a choice was being made is large (Rolls et al., 2010b). The prediction arises because the firing rate of the decision variables adds to the attractor decision state promoted by the internal recurrent collateral synaptic connections. This prediction was confirmed for medial prefrontal cortex area 10 when choices were being made about which of two successively presented odors was more pleasant (Rolls et al., 2010b) (Fig. 18). The prediction from the integrate-and-fire simulation was that the BOLD signal would increase linearly with the difference in the pleasantness of the stimuli, and this prediction was confirmed. Moreover, this signature of decision-making was not found more posteriorly, in the orbitofrontal cortex and pregenual cingulate cortex (Fig. 18), where value is represented on a continuous scale, providing the appropriate inputs to the decision-making regions more anteriorly in the medial prefrontal cortex area 10.

A second prediction from the model was that conversely, on trials on which the subject made an error, the firing rates, and hence the BOLD signal, should decrease as the difference between the two odors became greater. This prediction was confirmed for medial prefrontal cortex area 10 when choices were being made about which of two successively presented odors was more pleasant (Rolls et al., 2010c).

Thus there are now clear models about how the brain uses value representations as the inputs to a third tier (see Fig. 1) of processing in which reward-related decisions are made, including decisions about the pleasantness of olfactory stimuli.

## 5. Relevance to the control of food intake

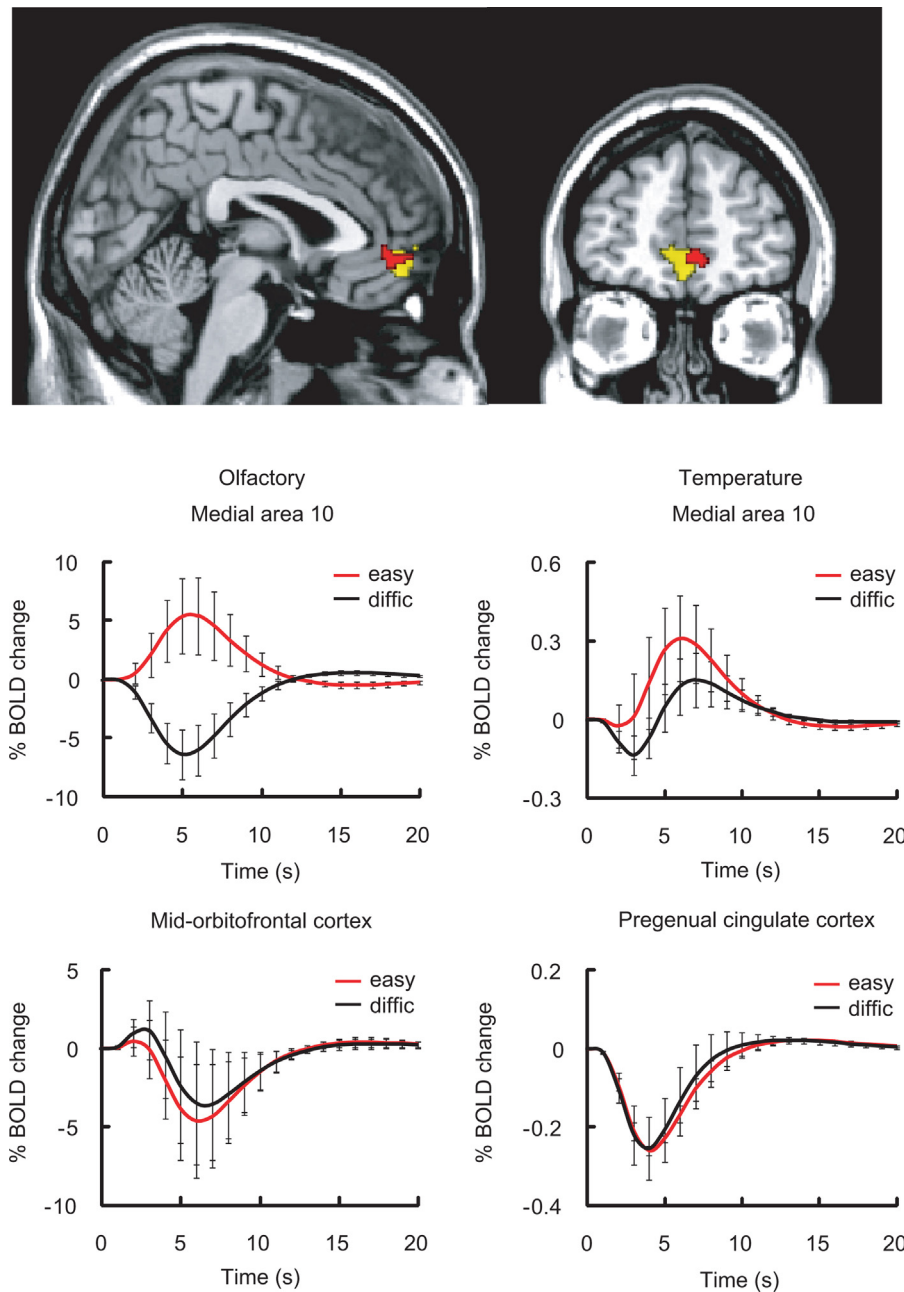
These investigations show that a principle of brain function is that representations of the reward/hedonic value and pleasantness of sensory including food-related stimuli are formed separately from representations of what the stimuli are and their intensity. The pleasantness/reward value is represented in areas such as the orbitofrontal cortex and pregenual cingulate cortex, and it is here that hunger/satiety signals modulate the representations of food to lead to a representation of reward value. The satiety signals that help in this modulation may reach the orbitofrontal cortex from the hypothalamus, and in turn, the orbitofrontal cortex projects to the hypothalamus where neurons are found that respond to the sight, smell, and taste of food if hunger is present (Burton et al., 1976; Rolls et al., 1976; Rolls, 1981, 2014; Rolls and Grabenhorst, 2008). We have seen above some of the principles that help to make the food pleasant, including particular combinations of taste, olfactory, texture, visual, and cognitive inputs.



**Fig. 17.** (a) Attractor or autoassociation single network architecture for decision-making. The evidence for decision 1 is applied via the  $\lambda_1$  inputs, and for decision 2 via the  $\lambda_2$  inputs. The synaptic weights  $w_{ij}$  have been associatively modified during training in the presence of  $\lambda_1$  and at a different time of  $\lambda_2$ . When  $\lambda_1$  and  $\lambda_2$  are applied, each attractor competes through the inhibitory interneurons (not shown), until one wins the competition, and the network falls into one of the high firing rate attractors that represents the decision. The noise in the network caused by the random (Poisson) spiking times of the neurons for a given mean rate means that on some trials, for given inputs, the neurons in the decision 1 (D1) attractor are more likely to win, and on other trials the neurons in the decision 2 (D2) attractor are more likely to win. This makes the decision-making probabilistic, for the noise influences when the system will jump out of the spontaneous firing stable (low energy) state, and whether it jumps into the high firing state for decision 1 (D1) or decision 2 (D2). (b) The architecture of the integrate-and-fire network used to model decision-making. The excitatory transmission is mediated by the release of glutamate acting on AMPA and NMDA receptors. The inhibitory transmission is mediated by gamma-aminobutyric acid (GABA) acting on GABA receptors. (After Rolls et al. (2010b)).

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

The overall understanding for this processing in primates including humans is that the identity and intensity of taste and olfactory stimuli is computed first and is represented in a first tier of cortical processing, the taste insula and pyriform cortex, independent of hedonic representations as they are influenced by for example hunger. Consistent with this, in humans ratings of the intensity of taste and olfactory stimuli depend on the concentration of the stimulus, and not on whether hunger is present (Rolls et al., 1983c). On the other hand, the pleasantness of taste, olfactory, and flavor stimuli is represented in a second tier of processing in the orbitofrontal cortex and pregenual cingulate cortex (Fig. 2). Consistent with this, the pleasantness of these



**Fig. 18.** Decision-making between the pleasantness of two successively presented olfactory stimuli. Top: Medial prefrontal cortex area 10 activated on easy vs difficult trials in the olfactory pleasantness decision task (yellow) (and in a thermal pleasantness decision task (red)). Middle: experimental data showing the BOLD signal in medial area 10 on easy and difficult trials of the olfactory affective decision task (left) and the thermal affective decision task (right). This medial prefrontal cortex area 10 was a region identified by other criteria as being involved in choice decision-making. Bottom: The BOLD signal for the same easy and difficult trials, but in parts of the pregenual cingulate and mid-orbitofrontal cortex implicated by other criteria in representing the subjective reward value of the stimuli on a continuous scale, but not in making choice decisions between the stimuli, or about whether to choose the stimulus in future. Reprinted from [Rolls et al. \(2010b\)](#), with permission from Elsevier.

stimuli is influenced by hunger, but rather little by concentration ([Rolls et al., 1983c](#)). In humans, we do not become blind to the sight of food, nor ageusic or anosmic, when we have fed to satiety, and the food is no longer rewarding. Indeed, when partial sensory-specific satiety is produced for the odor of food by chewing it or even just smelling it for the duration of a meal, there is a reduction in the pleasantness of the odor, but not of its intensity ([Rolls and Rolls, 1997](#)). This is an important design principle of the primate including human brain, that sensory and perceptual processing are kept separate and independent from reward value processing. The implication is that in primates including humans motivational

states, such as hunger, do not cause peripheral modulation of taste and olfactory processing.

As described in Section 1, the separation of sensory and hedonic processing in rodents may be much less distinct, and the situation in the rat taste system was summarized. For the olfactory system, quite early evidence suggested that in rats centrifugal fibers reduce olfactory bulb responses to the odor of food when hunger is reduced ([Pager et al., 1972](#)). More recently, evidence has been described that in mice diet-induced obesity produced by a hyperlipidemic diet causes loss of olfactory sensory neurons in the olfactory epithelium, and reduces olfactory discrimination

(Thiebaud et al., 2014), and there is further evidence in rodents for peripheral changes in the olfactory system related to metabolic status (Palouzier-Paulignan et al., 2012). Given the separation of sensory from hedonic processing in primates including humans at least during normal appetite control, it remains to be shown whether these findings in rodents are relevant to human appetite control and obesity.

Another interesting design principle of primate including human olfaction is that the olfactory representation can be mapped beyond olfactory receptor defined space by association learning with tastes, as described in this paper. This raises the issue of whether tastes, and some odors, have genetically defined hedonic value. The first time that rat pups taste salt when they are salt-deprived, they ingest it, providing evidence that the hedonics for taste have an innate component (Liedtke, 2014). Indeed, it is likely that sweet taste and the texture of fat are innately linked to reward value because they are indicators of energy in a food, and that bitter taste is innately aversive because it is a marker of many poisons (Rolls, 2014). Some odors such as the smell of flowers may be innately rewarding because they are indicators of fruit later in the season; and some perhaps especially trigeminal odors may be innately unpleasant because they are markers of danger, such as the smell of rotting food. However, these innate gene-specified values for some taste and olfactory stimuli can be modified by learning. For example, if a flavor is associated with the post-ingestive consequences produced by a high energy food, the preference for the food will be altered in what are termed learned appetites and satieties (Booth, 1985). These effects have been extensively studied in rodents (Ackroff and Sclafani, 2014; de Araujo et al., 2012a, 2013; Sclafani, 2013).

In conclusion, in this paper some of the rules of the cortical processing of taste, olfactory, and flavor stimuli in primates including humans have been described. The discoveries provide an important foundation for understanding the brain mechanisms underlying the control of food intake, emotion, and decision-making.

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