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The Rules of Formation of the Olfactory Representations Found in the Orbitofrontal Cortex Olfactory Areas in Primates

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Approximately 35% of neurons in the orbitofrontal cortex taste and olfactory areas with olfactory responses provide a representation of odour that depends on the taste with which the odour has been associated previously. This representation is produced by a slowly acting learning mechanism that learns associations between odour and taste. Other neurons in the orbitofrontal cortex respond to both the odour and to the mouth feel of fat. The representation of odour thus moves for at least some neurons in the orbitofrontal cortex beyond the domain of physico-chemical properties of the odours to a domain where the ingestion-related significance of the odour determines the representation provided. Olfactory neurons in the primate orbitofrontal cortex decrease their responses to a food eaten to satiety, but remain responsive to other foods, thus contributing to a mechanism for olfactory sensory-specific satiety. It has been shown in neuroimaging studies that the human orbitofrontal cortex provides a representation of the pleasantness of odour, in that the activation produced by the odour of a food eaten to satiety decreases relative to another food-related odour not eaten in the meal. In the same general area there is a representation of the pleasantness of the smell, taste and texture of a whole food, in that activation in this area decreases to a food eaten to satiety, but not to a food that has not been eaten in the meal.

Introduction

The aims of this paper are to describe some of the rules of the cortical processing of smell in primates, and how the pleasantness or affective value of taste and smell are represented in the brain. Much of the fundamental evidence comes from studies in non-human primates, and this is being complemented by functional neuroimaging studies in humans. Because olfactory processing in the primate orbitofrontal cortex is closely linked to that for taste, a summary of the cortical representation of taste in the primate orbitofrontal cortex is provided first.

Taste processing in the primate brain

Pathways

A diagram of the taste and related olfactory pathways in primates is shown in Figure 1. Of particular interest is that in primates there is a direct projection from the rostral part of the nucleus of the solitary tract (NTS) to the taste thalamus, and thus to the primary taste cortex in the frontal operculum and adjoining insula, with no pontine taste area and associated subcortical projections as in rodents (Norgren, 1984; Pritchard *et al.*, 1986). This emphasis on cortical processing of taste in primates may be related to the great development of the cerebral cortex in primates, and the advantage of using extensive and similar cortical analysis of inputs from every sensory modality before the analysed representations from each modality are brought together in multimodal regions, as is documented below.

The secondary taste cortex

A secondary cortical taste area in primates was discovered by Rolls *et al.* (Rolls *et al.*, 1990) in the caudolateral orbitofrontal cortex, extending several millimetres in front of the primary taste cortex and receiving from it (Baylis *et al.*, 1994). One principle of taste processing is that by the secondary taste cortex, the tuning of neurons can become quite specific, with some neurons responding, for example, only to sweet taste (Rolls, 1995; Rolls and Scott, 2001) [see also (Scott *et al.*, 1986; Yaxley *et al.*, 1990)]. This specific tuning (especially when combined with olfactory inputs) helps to provide a basis for changes in appetite for some but not other foods eaten during a meal.

Five prototypical tastes, including umami

In the primary and secondary taste cortex, there are many neurons that respond best to each of the four classical prototypical tastes sweet, salt, bitter and sour (Rolls, 1997), but also there are many neurons that respond best to umami tastants such as glutamate (which is present in many natural foods such as tomatoes, mushrooms and milk) (Baylis and

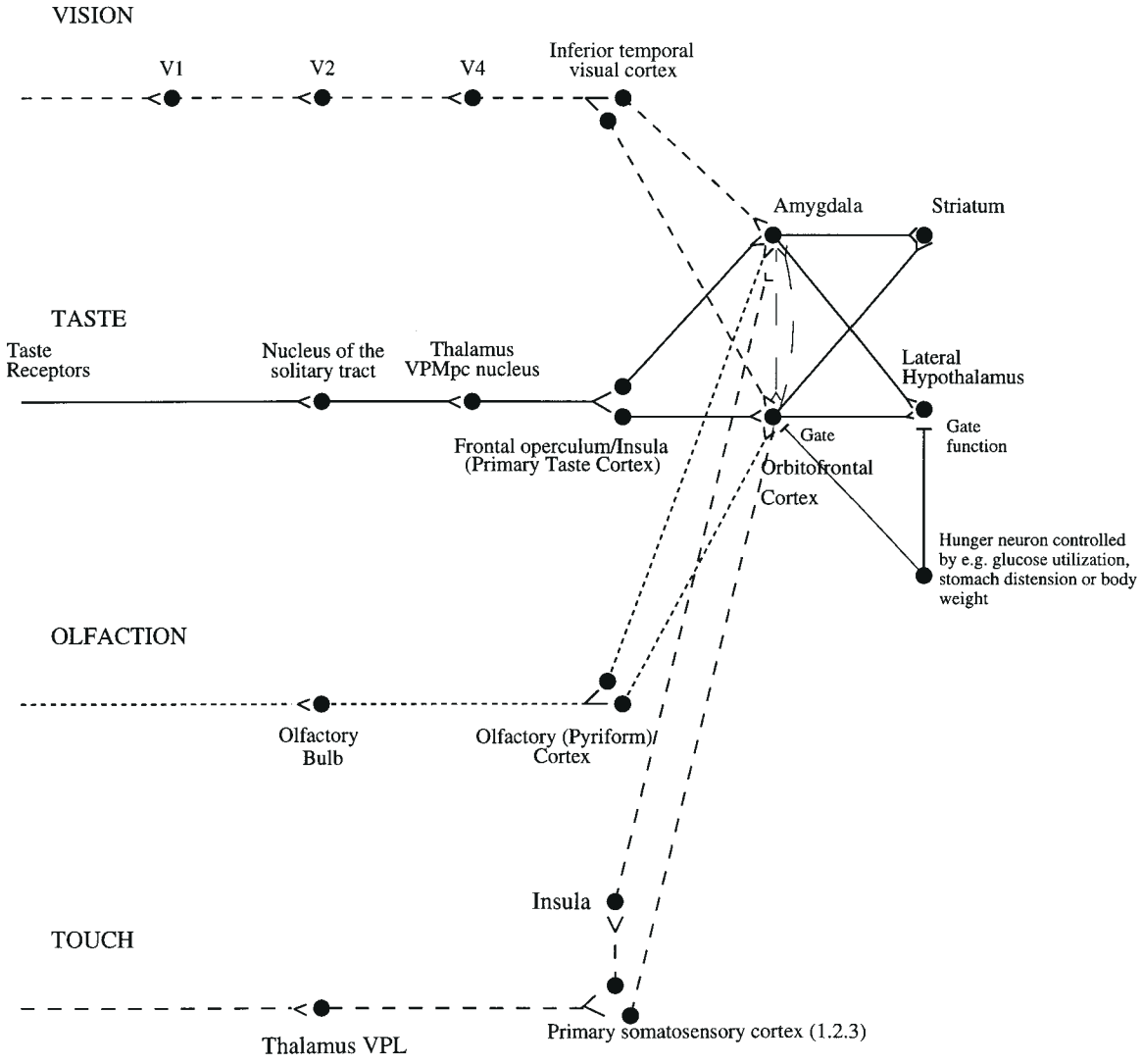

Figure 1 Schematic diagram of the taste and olfactory pathways in primates showing how they converge with each other and with visual pathways. The gate functions shown refer to the finding that the responses of taste neurons in the orbitofrontal cortex and the lateral hypothalamus are modulated by hunger. VPMpc, ventralposteromedial thalamic nucleus; V1, V2 and V4, visual cortical areas.

Rolls, 1991) and inosine monophosphate (which is present in many green vegetables) (Rolls *et al.*, 1996a). This evidence, taken together with the identification of the glutamate taste receptor (Chaudhari *et al.*, 2000), leads to the view that there are five prototypical types of taste information channels, with umami contributing, often in combination with corresponding olfactory inputs (Rolls *et al.*, 1998), to the flavour of protein.

The pleasantness of the taste of food

The modulation of the reward value of a sensory stimulus such as the taste of food by motivational state, e.g. hunger, is one important way in which motivational behaviour is controlled (Rolls, 1999a). The subjective correlate of this modulation is that food tastes pleasant when hungry and tastes hedonically neutral when it has been eaten to satiety. We have found that the modulation of taste-evoked signals by motivation is not a property found in early stages of the primate gustatory system. The responsiveness of taste neurons in the nucleus of the solitary tract (Yaxley *et al.*, 1985) and in the primary taste cortex [frontal opercular (Rolls *et al.*, 1988); insular (Yaxley *et al.*, 1988)] is not attenuated by feeding to satiety. In contrast, in the secondary taste cortex, in the caudolateral part of the orbitofrontal cortex, it has been shown that the responses of the neurons to the taste of the glucose decreased to zero while the monkey ate it to satiety, during the course of which the behaviour turned from avid acceptance to active rejection (Rolls *et al.*, 1989). This modulation of responsiveness of the gustatory responses of the orbitofrontal cortex neurons by satiety could not have been due to peripheral adaptation in the gustatory system or to altered efficacy of gustatory

stimulation after satiety was reached, because modulation of neuronal responsiveness by satiety was not seen at the earlier stages of the gustatory system, including the nucleus of the solitary tract, the frontal opercular taste cortex and the insular taste cortex.

Sensory-specific satiety

In the secondary taste cortex, it was also found that the decreases in the responsiveness of the neurons were relatively specific to the food with which the monkey had been fed to satiety. For example, in seven experiments in which the monkey was fed glucose solution, neuronal responsiveness decreased to the taste of the glucose but not to the taste of blackcurrant juice (see the example in Figure 2). Conversely, in two experiments in which the monkey was fed to satiety with fruit juice, the responses of the neurons decreased to fruit juice but not to glucose (Rolls *et al.*, 1989).

This evidence shows that the reduced acceptance of food which occurs when food is eaten to satiety, and the reduction in the pleasantness of its taste (Cabanac, 1971; Rolls and Rolls, 1977, 1982; Rolls *et al.*, 1981a,b, 1982, 1983), are not produced by a reduction in the responses of neurons in the nucleus of the solitary tract or frontal opercular or insular gustatory cortices to gustatory stimuli. Indeed, after feeding to satiety, humans reported that the taste of the food on which they had been satiated tasted almost as intense as when they were hungry, though much less pleasant (Rolls *et al.*, 1983). This comparison is consistent with the possibility that activity in the frontal opercular and insular taste cortices, as well as the nucleus of the solitary tract, does not reflect the pleasantness of the taste of a food but, rather, its sensory qualities independently of motivational state. On the other hand, the responses of the neurons in the caudolateral orbitofrontal cortex taste area and in the lateral hypothalamus (Rolls *et al.*, 1986) are modulated by satiety, and it is presumably in areas such as these that neuronal activity may be related to whether a food tastes pleasant, and to whether the food should be eaten [see further (Critchley and Rolls, 1996b; Rolls, 1996, 1999a, 2000b,c; Scott *et al.*, 1995)].

It is an important principle that the identity of a taste and its intensity are represented separately from its pleasantness. Thus it is possible to represent what a taste is, and to learn about it, even when we are not hungry.

The representation of flavour: convergence of olfactory and taste inputs

At some stage in taste processing, it is likely that taste representations are brought together with inputs from different modalities, e.g. with olfactory inputs to form a representation of flavour (see Figure 1). We found (Rolls and Baylis, 1994) that in the orbitofrontal cortex taste areas, many of 112 single neurons which responded to any of these modalities were unimodal (taste, 34%; olfactory, 13%; visual, 21%), but were found in close proximity to each other. Some single neurons showed convergence, responding, for example, to taste and visual inputs (13%), taste and olfactory inputs (13%), and olfactory and visual inputs (5%). Some of these multimodal single neurons had corresponding sensitivities in the two modalities, in that they responded best to sweet tastes (e.g. 1 M glucose), and responded more in a visual discrimination task to the visual stimulus which signified sweet fruit juice than to that which signified saline; or responded to sweet taste, and in an olfactory discrimination task to fruit odour. The different types of neurons (unimodal in different modalities and multimodal) were frequently found close to one another in tracks made into this region, consistent with the hypothesis that the multimodal representations are actually being formed from unimodal inputs to this region.

It thus appears to be in these orbitofrontal cortex areas that flavour representations are built, where flavour is taken to mean a representation which is evoked best by a combination of gustatory and olfactory input. This orbitofrontal region appears to be an important region for convergence, for there is only a low proportion of bimodal taste and

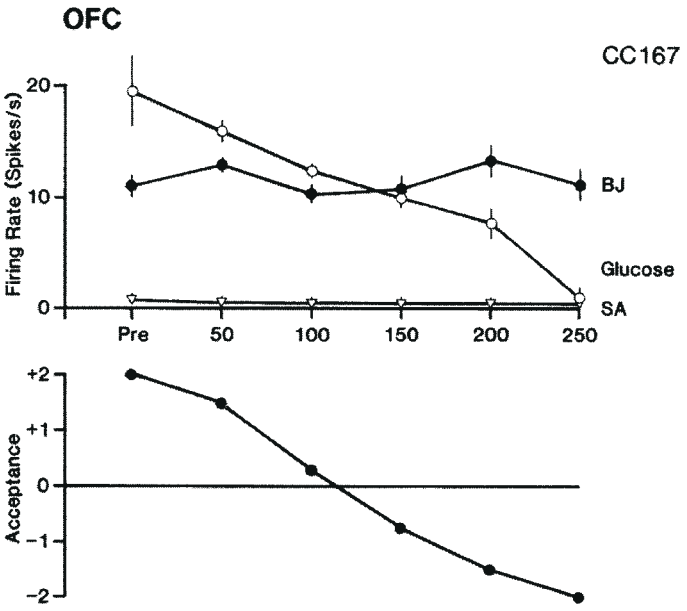

Figure 2 The effect of feeding to satiety with glucose solution on the responses of one neuron in the secondary taste cortex to the taste of glucose and of blackcurrant juice (BJ). The spontaneous firing rate is also indicated (SA). Below the neuronal response data, the behavioural measure of the acceptance or rejection of the solution on a scale from +2 to –2 (see text) 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, the firing rate of the neuron before the satiety experiment started. The values shown are the mean firing rate and its SE. From Rolls *et al.* (Rolls *et al.*, 1989).

olfactory neurons in the primary taste cortex (Rolls and Baylis, 1994; Rolls and Scott, 2001).

The rules underlying the formation of olfactory representations in the primate cortex

Critchley and Rolls (Critchley and Rolls, 1996a) showed that 35% of orbitofrontal cortex olfactory neurons categorized odours based on their taste association in an olfactory-to-taste discrimination task. This was the case in that 35% of the neurons either responded to all the odours associated with the taste of glucose but to none of the odours associated with the taste of aversive saline (0.1 M NaCl), or vice versa. Rolls *et al.* (Rolls *et al.*, 1996b) found that 68% of orbitofrontal cortex odour-responsive neurons modified their responses in some way following changes in the taste reward associations of the odorants during olfactory–taste discrimination learning and its reversal. (In an olfactory discrimination experiment, if a lick response to one odour, the S+, is made, a drop of glucose taste reward is obtained; if a lick response is made, incorrectly, to another odour, the S–, a drop of aversive saline is obtained. At some time in the experiment, the contingency between the odour and the taste is reversed, and when the 'meaning' of the two odours alters, so does the behaviour. It is of interest to investigate in which parts of the olfactory system the neurons show reversal, for where they do, it can be concluded that the neuronal response to the odour depends on the taste with which it is associated, and does not depend primarily on the physico-chemical structure of the odour.) Full reversal of the neuronal responses was seen in 25% of the neurons analysed. (In full reversal, the odour to which the neuron responded reversed when the taste with which it was associated reversed.) Extinction of the differential neuronal responses after task reversal was seen in 43% of these neurons. (These neurons simply stopped discriminating between the two odours after the reversal. This is termed conditional reversal.) These findings demonstrate directly a coding principle in primate olfaction whereby the responses of some orbitofrontal cortex olfactory neurons are modified by, and depend upon, the taste with which the odour is associated.

It was of interest, however, that this modification was less complete, and much slower, than the modifications found for orbitofrontal visual neurons during visual–taste reversal (Rolls *et al.*, 1996b). This relative inflexibility of olfactory responses is consistent with the need for some stability in odour–taste associations to facilitate the formation and perception of flavours. In addition, some orbitofrontal cortex olfactory neurons did not code in relation to the taste with which the odour was associated (Critchley and Rolls, 1996a), indicating that there is also a taste-independent representation of odour in this region.

The representation of the pleasantness of odour in the brain: olfactory and visual sensory-specific satiety, and their representation in the primate orbitofrontal cortex

It has also been possible to investigate whether the olfactory representation in the orbitofrontal cortex is affected by hunger, and thus whether the pleasantness of odour is represented in the orbitofrontal cortex. In satiety experiments, Critchley and Rolls (Critchley and Rolls, 1996b) showed that the responses of some olfactory neurons to a food odour are decreased during feeding to satiety with a food (e.g. fruit juice) containing that odour. In particular, seven of nine olfactory neurons that were responsive to the odours of foods, such as blackcurrant juice, were found to decrease their responses to the odour of the satiating food. The decrease was typically at least partly specific to the odour of the food that had been eaten to satiety, potentially providing part of the basis for sensory-specific satiety. It was also found for eight of nine neurons that had selective responses to the sight of food, that they demonstrated a sensory-specific reduction in their visual responses to foods following satiation. These findings show that the olfactory and visual representations of food, as well as the taste representation of food, in the primate orbitofrontal cortex are modulated by hunger. Usually a component related to sensory-specific satiety can be demonstrated.

These findings link at least part of the processing of olfactory and visual information in this brain region to the control of feeding-related behaviour. This is further evidence that part of the olfactory representation in this region is related to the hedonic value of the olfactory stimulus, and in particular that at this level of the olfactory system in primates, the pleasure elicited by the food odour is at least part of what is represented.

As a result of the neurophysiological and behavioural observations showing the specificity of satiety in the monkey (Rolls, 1999a), experiments were performed to determine whether satiety was specific to foods eaten in humans. It was found that the pleasantness of the taste of food eaten to satiety decreased more than for foods that had not been eaten (Rolls *et al.*, 1981a). One consequence of this is that if one food is eaten to satiety, appetite reduction for other foods is often incomplete, and this will lead to enhanced eating when a variety of foods is offered (Rolls *et al.*, 1981a,b, 1984). Because sensory factors such as similarity of colour, shape, flavour and texture are usually more important than metabolic equivalence in terms of protein, carbohydrate and fat content in influencing how foods interact in this type of satiety, it has been termed 'sensory-specific satiety' (Rolls and Rolls, 1977, 1982; Rolls *et al.*, 1981a,b, 1982; Rolls, 1990). It should be noted that this effect is distinct from alliesthesia, in that alliesthesia is a change in the pleasantness of sensory inputs produced by

internal signals (such as glucose in the gut) (Cabanac and Duclaux, 1970; Cabanac, 1971; Cabanac and Fantino, 1977), whereas sensory-specific satiety is a change in the pleasantness of sensory inputs which is accounted for at least partly by the external sensory stimulation received (such as the taste of a particular food), in that, as shown above, it is at least partly specific to the external sensory stimulation received.

To investigate whether the sensory-specific reduction in the responsiveness of the orbitofrontal olfactory neurons might be related to a sensory-specific reduction in the pleasure produced by the odour of a food when it is eaten to satiety, Rolls and Rolls (Rolls and Rolls, 1997) measured humans' responses to the smell of a food which was eaten to satiety. It was found that the pleasantness of the odour of a food, but much less significantly its intensity, was decreased when the subjects ate it to satiety (see Figure 3). It was also found that the pleasantness of the smell of other foods (i.e. foods not eaten in the meal) showed a much smaller decrease. This finding has clear implications for the control of food intake; for ways to keep foods presented in a meal appetitive; and for effects on odour pleasantness ratings that could occur following meals.

In an investigation of the mechanisms of this odour-specific sensory-specific satiety, Rolls and Rolls (Rolls and Rolls, 1997) allowed humans to chew a food without swallowing, for approximately as long as the food is normally in the mouth during eating. They demonstrated some sensory-specific satiety with this procedure, showing that the sensory-specific satiety does not depend on food reaching the stomach. They were also able to demonstrate some sensory-specific satiety produced by smelling the food for approximately as long as the food is normally in the mouth during eating. Thus at least part of the mechanism is likely to be produced by a change in processing in the olfactory pathways. It is not yet known which is the earliest stage of olfactory processing at which this modulation occurs. It is unlikely to be in the receptors, because the change in pleasantness found was much more significant than the change in the intensity (Rolls and Rolls, 1997).

The enhanced eating when a variety of foods is available, as a result of the operation of sensory-specific satiety, may have been advantageous in evolution in ensuring that different foods with important different nutrients were consumed, but today in humans, when a wide variety of foods is readily available, it may be a factor that can lead to overeating and obesity. In a test of this in the rat, it has been found that variety itself can lead to obesity (Rolls *et al.*, 1983; Rolls and Hetherington, 1989).

The responses of orbitofrontal cortex taste and olfactory neurons to the sight and texture of food

Many of the neurons with visual responses in this region also show olfactory or taste responses (Rolls and Baylis, 1994), reverse rapidly in visual discrimination reversal (Rolls *et al.*, 1996b) and only respond to the sight of food if hunger is present (Critchley and Rolls, 1996b). This part of the

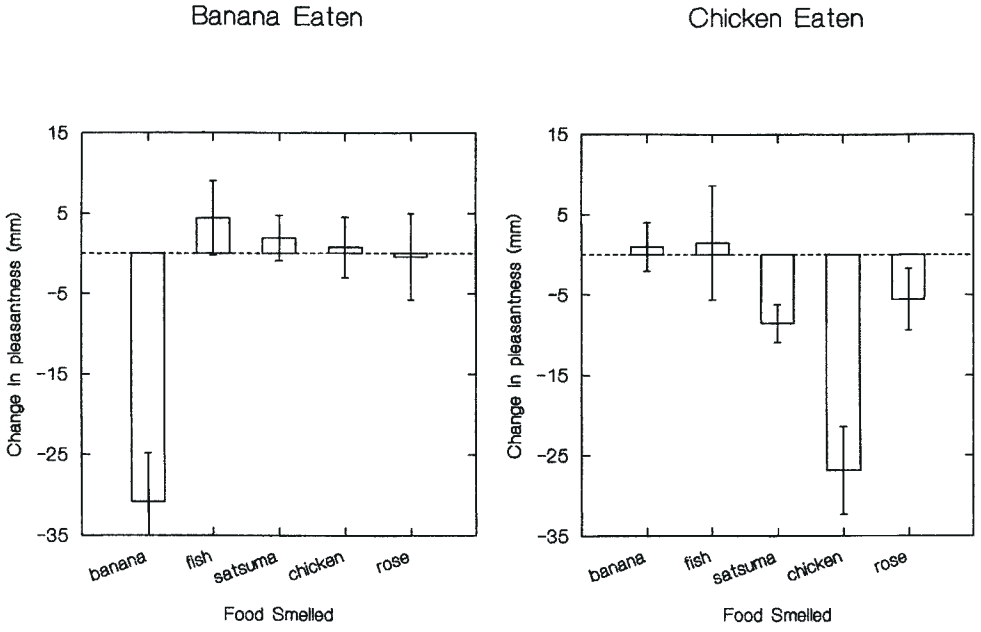

Figure 3 Olfactory sensory-specific satiety in humans. The pleasantness of the smell of a food became less when the humans ate that food (banana or chicken) to satiety. A similar reduction was not found for other foods not eaten in the meal. The changes in pleasantness were measured on a 100 mm visual analogue rating scale. The number of subjects was 12, and the results (as shown by the interaction term in a two-way within-subjects analysis of variance) were very significant ($P < 0.001$). From Rolls and Rolls (Rolls and Rolls, 1997).

orbitofrontal cortex thus seems to implement a mechanism which can flexibly alter the responses to visual stimuli depending on the reinforcement (e.g. the taste) associated with the visual stimulus (Thorpe *et al.*, 1983; Rolls, 1996). This enables prediction of the taste associated with ingestion of what is seen, and thus in the visual selection of foods (Rolls, 1993, 1994, 1999a, 2000c). It also provides a mechanism for the sight of a food to influence its flavour.

The orbitofrontal cortex of primates is also important as an area of convergence for somatosensory inputs, related, for example, to the texture of food, including fat in the mouth. We have shown, for example, in recent recordings that single neurons influenced by taste in this region can in some cases have their responses modulated by the texture of the food. This was shown in experiments in which the texture of food was manipulated by the addition of methyl cellulose or gelatine, or by puréeing a semi-solid food (Rolls, 1997, 1999a) (E.T. Rolls and H.D. Critchley, in preparation).

The mouth feel of fat

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.* (Rolls *et al.*, 1999) found a population of neurons that responds when fat is in the mouth. An example of such a neuron is shown in Figure 4. The neuron illustrates that information about fat as well as about taste can converge onto the same neuron in this region. The neuron responded to taste in that its firing rate was significantly different within the group of tastants sweet, salt, bitter and sour. However, its response to fat in the mouth was larger. 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 that contain fat, such as cream and milk, but also to paraffin oil (which is a pure hydrocarbon) and to silicone oil $[Si(CH_3)_2O)_n]$. Some fat-related neurons have convergent inputs from the chemical senses, in that in addition to taste inputs, they respond to the odour associated with a fat, such as the odour of cream (Rolls *et al.*, 1999). Feeding to satiety with fat (e.g. cream) decreases the responses of these neurons to zero on the food eaten to satiety, but if the neuron receives a taste input from, for example, glucose, its reponse is not decreased by feeding to satiety with cream. 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.

Imaging studies in humans

Taste

In humans it has been shown in neuroimaging studies using functional magnetic resonance imaging (fMRI) that taste activates an area of the anterior insula, which is probably

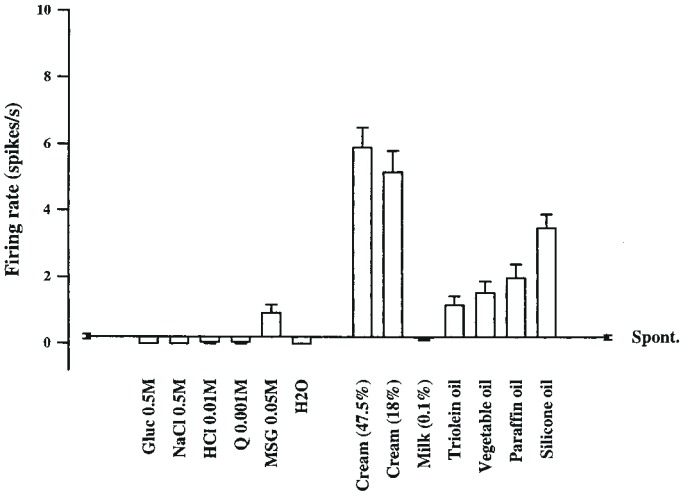

Figure 4 A neuron in the primate orbitofrontal cortex responding to the texture of fat in the mouth. The cell (Be047) increased its firing rate to cream (double and single cream), and responded to texture rather than the chemical structure of the fat in that it also responded to 0.5 ml of silicone oil (SiO_2) or paraffin oil (hydrocarbon). The cell has a taste input too, in that it had a consistent but small response to umami taste (monosodium glutamate, MSG). Gluc, glucose; NaCl, salt; HCl, sour; Q, quinine, bitter. The spontaneous firing rate of the cell is also shown. From Rolls *et al.* (Rolls *et al.*, 1999).

the primary taste cortex, and part of the orbitofrontal cortex, which is probably the secondary taste cortex (Francis *et al.*, 1999; Small *et al.*, 1999). The orbitofrontal cortex taste area is distinct from areas activated by odours and by pleasant touch (Francis *et al.*, 1999). It has been shown that, within individual subjects, partly overlapping but also partly separate areas of the orbitofrontal cortex are activated by sweet (pleasant) and by salt (unpleasant) tastes (O'Doherty *et al.*, 2001a). Francis *et al.* (Francis *et al.*, 1999) also found activation of the human amygdala by the taste of glucose. Extending this study, O'Doherty *et al.* (O'Doherty *et al.*, 2001a) 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 this provided evidence that the human amygdala is involved in processing rewarding as well as aversive stimuli.

Odour

In humans, there is strong and consistent activation of the right orbitofrontal cortex by olfactory stimuli (Zatorre *et al.*, 1992; Francis *et al.*, 1999). In an investigation of where the pleasantness of olfactory stimuli might be represented in humans, O'Doherty *et al.* (O'Doherty *et al.*, 2000) showed that the activation of an area of the orbitofrontal cortex to banana odour was decreased (relative to a control vanilla odour) after bananas were eaten to satiety (see Figure 5). Thus, activity in a part of the human orbitofrontal cortex olfactory area is related to sensory-specific satiety, and this is one brain region where the pleasantness of odour is represented.

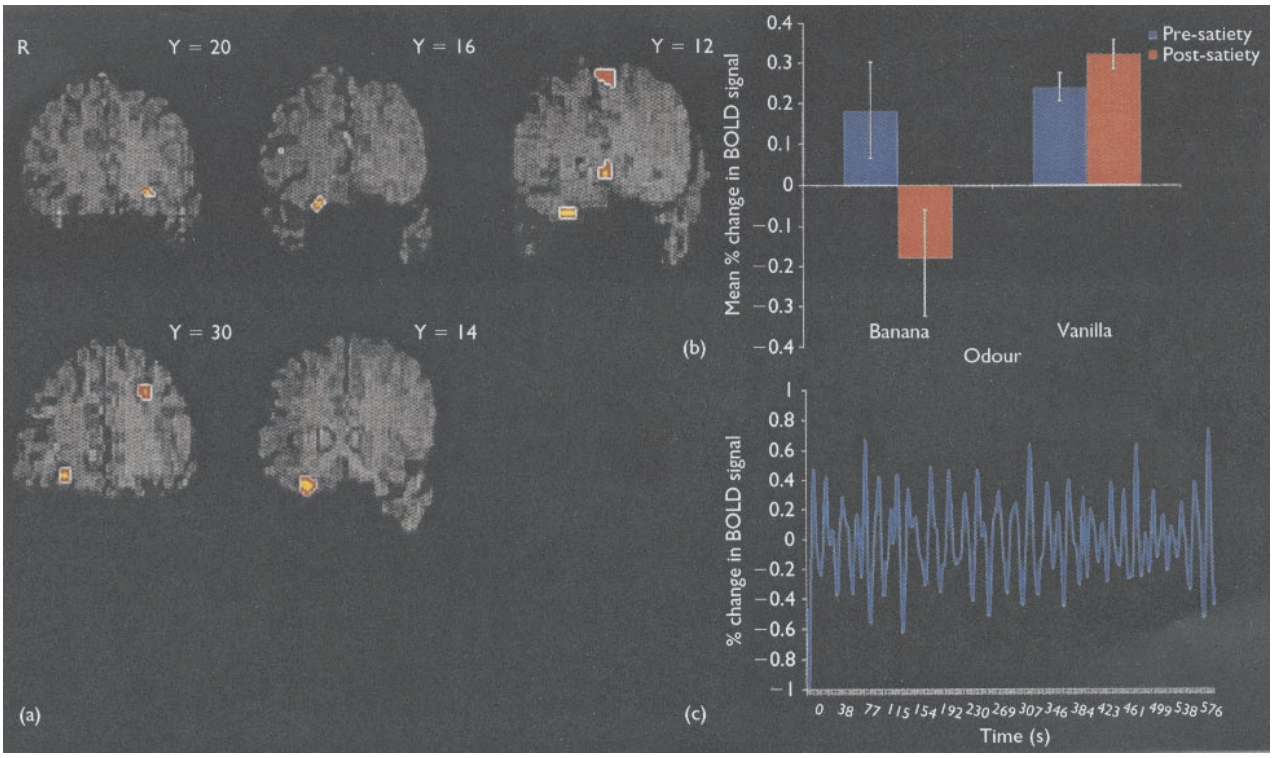

Figure 5 **(a)** Regions of the orbitofrontal cortex in which the BOLD-measure activation was related to sensory-specific satiety. Coronal sections at the anterior (y) levels shown through the orbitofrontal cortex are shown for each subject. The activations that were significant ($P < 0.05$ corrected) in the SPM olfactory sensory-specific satiety contrast (see text) are shown in colour. **(b)** Mean percentage change in the BOLD signal across subjects of significantly activated clusters in the orbitofrontal cortex for each condition. **(c)** Time course of activation produced in one subject in the banana pre-satiety condition. From O'Doherty *et al.* (O'Doherty *et al.*, 2000).

In the next study in this series, we measured brain activation by whole foods before and after the food was eaten to satiety. The idea was to show, using a food that has olfactory, taste and texture components, the extent of the region that shows decreases when the food becomes less pleasant, in order to identify the different brain areas where the pleasantness of the odour, taste and texture of food are represented. The foods eaten to satiety were either chocolate milk or tomato purée. A decrease in activation by the food eaten to satiety relative to the other food was shown in the orbitofrontal cortex.

It is of interest that in humans there is an area of the far anterior insula that is activated by olfactory stimuli (Francis *et al.*, 1999; O'Doherty *et al.*, 2000). It is not clear whether this area is separate from the part of the insula activated by taste. This human anterior insular olfactory area may thus correspond to what in macaques is the caudal transitional area of the orbitofrontal cortex where it adjoins the insula, area Ofdg, where part of the secondary taste cortex is located (Baylis *et al.*, 1994).

The primary olfactory cortex does not always show strong evidence for activation in fMRI neuroimaging studies. Part of the reason for this may be that this area is particularly likely to show adaptation (Sobel *et al.*, 2000).

Conclusions

The primate orbitofrontal cortex is an important site for the convergence of representations of the taste, smell, sight and mouth feel of food, and this convergence allows the sensory properties of each food to be represented and defined in detail. The primate orbitofrontal cortex is also the region where a short-term, sensory-specific control of appetite and eating is implemented. Moreover, it is likely that visceral and other satiety-related signals reach the orbitofrontal cortex and there modulate the representation of food, resulting in an output that reflects the reward (or appetitive) value of each food (Rolls, 1999a). Part of the evidence that the reward value and pleasantness of food in humans is repre- sented in the orbitofrontal cortex is that macaques will work to obtain electrical stimulation of this brain region if they are hungry, but much less if they are satiated (Rolls, 1999a). Further, monkeys or humans with damage to this brain region show altered, often less selective, food preferences (Baylis and Gaffan, 1991; Rolls, 1999b). The orbitofrontal cortex contains representations not only of taste and ol- factory stimuli, but also of other types of rewarding and punishing stimuli, including pleasant touch, and all these inputs, together with the functions of the

cortex in stimulus–reward and stimulus–punishment association learning, provide a basis for understanding its functions in emotional and motivational behaviour (Rolls, 1999a, 2000a–e; O'Doherty *et al.*, 2001b).

The learning and reversal of associations between olfactory and taste stimuli that occurs in the orbitofrontal cortex could be implemented by Hebbian modification of synapses conveying olfactory input onto taste-responsive neurons, implementing a pattern association network (Rolls and Treves, 1998; Rolls, 1999a, 2000f). Long-term potentiation would strengthen synapses from active conditioned stimulus neurons onto neurons responding to a primary reinforcer such as a sweet taste, and homosynaptic long-term depression would weaken synapses from the same active visual inputs if the neuron were not responding because an aversive primary reinforcer (e.g. a taste of saline) was being presented (see Figure 6). As described above, there are some conditional reward neurons in the orbitofrontal cortex that convey information about the current reinforcement status of particular stimuli. This situation may reflect the fact that not every neuron which learns associations to primary reinforcers (such as taste) can sample the complete space of all possible conditioned (e.g. visual or olfactory) stimuli when acting as a pattern associator. Nevertheless, such neurons can convey very useful information, for they indicate when one of the stimuli to which they are capable of responding (given their inputs) is currently associated with a primary reward, such as taste. Similar neurons are present for primary punishing reinforcers, such as the aversive taste of salt.

The neural basis of sensory-specific satiety may be that in a part of the brain in which the pleasantness of the taste or odour of a food is represented (such as the orbitofrontal cortex), it is a property of the neurons that they habituate to several minutes of stimulation such as would be produced by eating that food in a meal. The neuronal habituation must be a central phenomenon, in that the intensity of a food is not reduced greatly by eating it to satiety, and, indeed, we can taste, smell and see foods after we have eaten them to satiety. The decrease in neuronal responses must therefore be primarily for those neurons that represent the pleasantness of the flavour of the food. In the case of taste, it is known in primates that taste neurons in the primary taste cortex still respond after eating the food to satiety, and it is orbitofrontal cortex neurons that reflect sensory-specific satiety. In the case of olfaction, the evidence described above shows that this is represented in the orbitofrontal cortex olfactory areas, but it is not yet clear whether this is the first stage in olfactory processing in primates where olfactory sensory-specific satiety is represented.

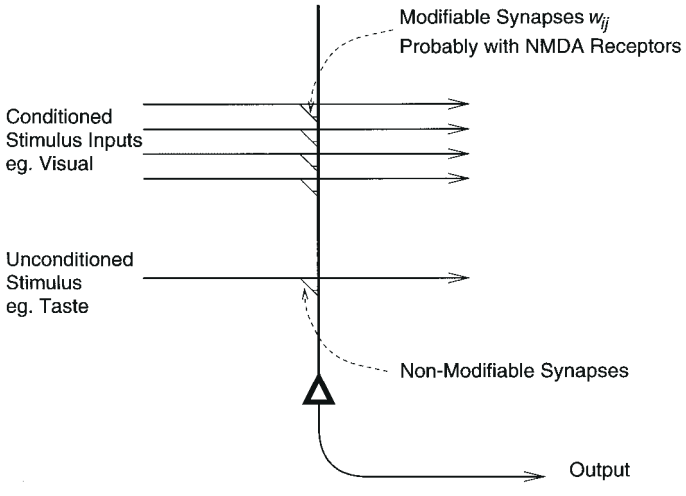

Figure 6 A pattern association network that could underlie the learning and reversal of stimulus-reinforcement association learning in the orbitofrontal cortex (see text). The conditioned stimuli can include olfactory stimuli.

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