CHAPTER

4

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Taste, Olfactory and Food-texture Processing in the Brain and the Control of Appetite

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4.1 INTRODUCTION

p0010 The aims of this chapter are to describe the rules of the cortical processing of taste and smell, how the pleasantness or affective value of taste and smell are represented in the brain, how cognitive factors modulate these affective representations, and how these affective representations play an important role in the control of appetite, food intake and obesity. To make the results relevant to understanding the control of human food intake, complementary evidence is provided by neurophysiological studies in non-human primates, and by functional neuroimaging studies in humans. A broad perspective of the brain processing involved in emotion and in hedonic aspects of the control of food intake is provided by Rolls (2005a).

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4.2 TASTE-PROCESSING IN THE PRIMATE BRAIN

4.2.1 Pathways

A diagram of the taste and related olfactory, somatosensory and visual pathways in primates is shown in Figure 4.1. 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 by often new combinations of sensory inputs is a theme of recent research that will be described.

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4.2.2 The primary taste cortex

p0020 The primary taste cortex in the primate anterior insula and adjoining frontal operculum contains not only taste neurons tuned to sweet, salt, bitter, sour (Scott *et al.*, 1986; Yaxley *et al.*, 1990; Rolls and Scott, 2003) 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 do not respond to olfactory stimuli or visual stimuli (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).

4.2.3 The secondary taste cortex

A secondary cortical taste area in primates was discovered by Rolls, Yaxley and Sienkiewicz in the caudolateral orbitofrontal cortex, extending several millimeters in front of the primary taste cortex (Rolls *et al.*, 1990). Neurons in this region respond not only to each of the four classical prototypical tastes sweet, salt, bitter and sour (Rolls, 1997; Rolls and Scott, 2003); many also respond best to umami tastants such as glutamate (which is present in many natural foods, such as tomatoes, mushrooms and 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 (Zhao *et al.*, 2003; Maruyama *et al.*, 2006), 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; McCabe and Rolls, 2007; Rolls, 2009), to the flavor of protein. In addition, other neurons respond to water and some to somatosensory stimuli, including astringency as exemplified by tannic acid (Critchley and Rolls, 1996a), and capsaicin (Rolls *et al.*, 2003a; Kadohisa *et al.*, 2004). Taste responses are found in a large mediolateral extent of the orbitofrontal cortex (Pritchard *et al.*, 2005; Rolls, 2008; Rolls and Grabenhorst, 2008).

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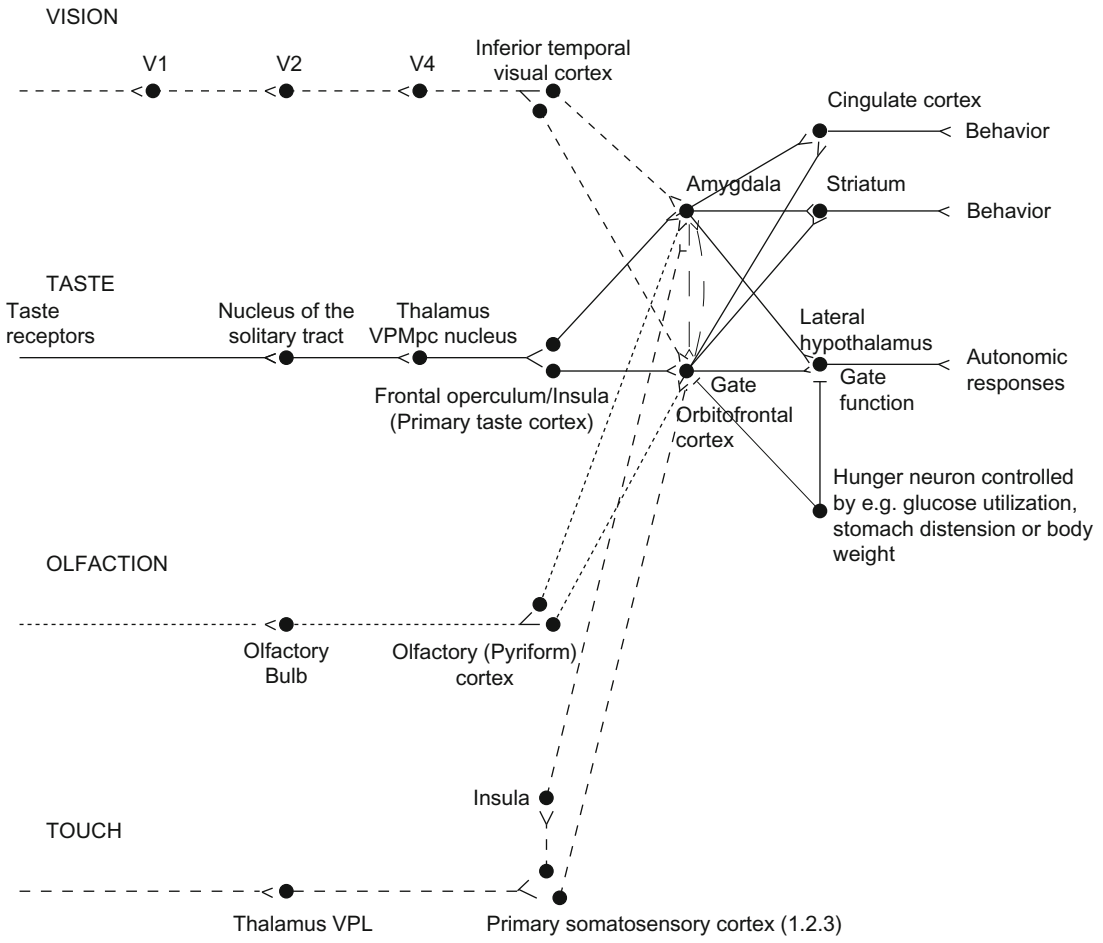

f0010 **FIGURE 4.1** Schematic diagram of the taste and olfactory pathways in primates including humans showing how they converge with each other and with visual pathways.
Hunger modulates the responsiveness of the representations in the orbitofrontal cortex of the taste, smell, texture and sight of food (indicated by the gate function), and the orbitofrontal cortex is where the palatability and pleasantness of food is represented.
VPMpc, ventralposteromedial thalamic nucleus; V1, V2, V4, visual cortical areas.

4.2.4 The pleasantness of the taste of food, sensory-specific satiety, and the effects of variety on food intake

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, 2005a, 2007). The subjective correlate of this modulation is that food tastes pleasant when hungry, and tastes hedonically neutral when it has been eaten to satiety. The discovery of sensory-specific satiety was 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 in a region that projects to the hypothalamus, the orbitofrontal

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cortex (secondary taste), for the taste, odor, sight and texture of food (Rolls *et al.*, 1989; Critchley and Rolls, 1996b; Rolls *et al.*, 1999).

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; Rolls and Rolls, 1977, 1982, 1997; Rolls *et al.*, 1981a, 1981b, 1982, 1983a, 1983b, 1984; Rolls and Hetherington, 1989; Hetherington, 2007) are produced in the orbitofrontal cortex, but not at earlier stages of processing 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 habituation of the synaptic afferents to orbitofrontal neurons with a time-course of the order of length of a meal course), it is likely that visceral and other satiety-related signals reach the orbitofrontal cortex (as indicated in Figure 4.1) (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, 2005a).

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4.3 THE REPRESENTATION OF FLAVOR: CONVERGENCE OF OLFACTORY, TASTE AND VISUAL INPUTS IN THE ORBITOFRONTAL CORTEX

p0040 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 Figure 4.1) (Thorpe *et al.*, 1983; Rolls and Baylis, 1994; Critchley and Rolls, 1996c; Rolls, 1996; Rolls *et al.*, 1996b; Verhagen *et al.*, 2004). 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, 1996b).

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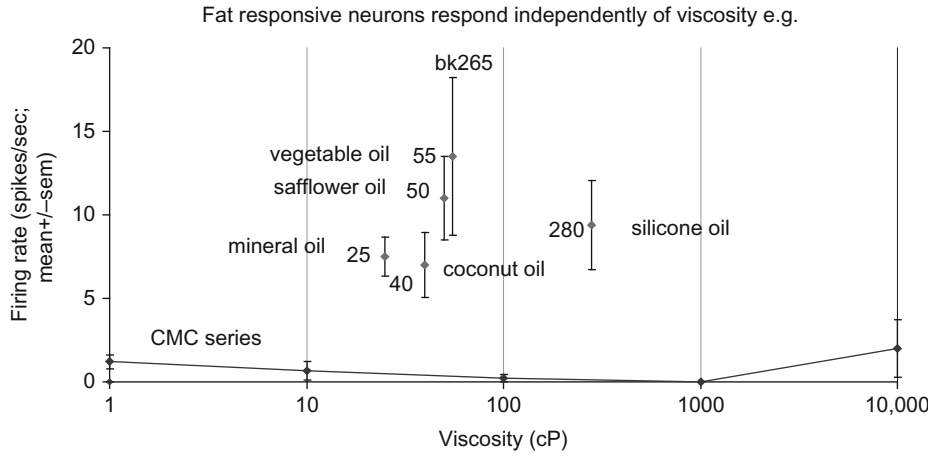
4.4 THE TEXTURE OF FOOD, INCLUDING FAT TEXTURE

p0045 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). Others independently encode the particulate quality of food in the mouth, produced quantitatively, for example, by adding 20- to 100-μm microspheres to methyl cellulose (Rolls *et al.*, 2003a). Others, finally, encode the oral texture of fat (Rolls *et al.*, 1999; Verhagen *et al.*, 2003), as illustrated in Figure 4.2. In addition, some neurons in the orbitofrontal cortex reflect the temperature of substances in the mouth (Kadohisa *et al.*, 2004, 2005). This temperature information is represented independently of other sensory inputs by some neurons, and in combination with taste or texture by other neurons.

4.5 IMAGING STUDIES IN HUMANS

4.5.1 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/frontal operculum, which is probably the primary taste cortex, and part of the orbitofrontal cortex, which is probably the secondary taste cortex (Francis *et al.*, 1999; O'Doherty *et al.*, 2001; de Araujo *et al.*, 2003a). Within individual subjects, separate areas of the orbitofrontal cortex are activated by sweet (pleasant) and by salt (unpleasant) tastes (O'Doherty *et al.*, 2001).



f0015 **FIGURE 4.2** 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 (Si(CH3)2O)n) and paraffin (mineral) oil (hydrocarbon). Some of these neurons have taste inputs.
Source: Adapted from Verhagen and colleagues (2003).

p0055 We also found activation of the human amygdala by the taste of glucose (Francis *et al.*, 1999). Extending this study, O'Doherty and colleagues (2001) showed that the human amygdala was as much activated by the affectively pleasant taste of glucose as by the affectively negative taste of salt, and thus provided evidence that the human amygdala is not especially involved in processing aversive as compared to rewarding stimuli. Zald and colleagues (1998) had shown earlier that the amygdala, as well as the orbitofrontal cortex, responds to aversive (saline) taste stimuli.

p0060 Umami taste stimuli activate the insular (primary), orbitofrontal (secondary) and anterior cingulate (tertiary; Rolls, 2008) taste cortical areas (de Araujo *et al.*, 2003b). 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. This may reflect the subjective enhancement of umami taste that has been described when IMP is added to MSG (Rolls, 2009). Overall, these results illustrate that the responses of the brain can reflect inputs produced by particular combinations of sensory stimuli with supralinear activations. The combination of sensory stimuli may be especially represented in particular brain regions, and may help to make the food pleasant.

4.5.2 Odor s0060

p0065 In humans, in addition to activation of the pyriform (olfactory) cortex (Zald and Pardo, 1997; Sobel *et al.*, 2000; Poellinger *et al.*, 2001), there is strong and consistent activation of the orbitofrontal cortex by olfactory stimuli (Zatorre *et al.*, 1992; Francis *et al.*, 1999). This region appears to represent the pleasantness of odor, as shown by a sensory-specific satiety experiment with banana versus vanilla odor (O'Doherty *et al.*, 2000). Further, pleasant odors tend to activate the medial, and unpleasant odors the more lateral, orbitofrontal cortex (Rolls *et al.*, 2003b), adding to the evidence that there is a hedonic map in the

s0070 p0085 orbitofrontal cortex and in the anterior cingulate cortex, which receives inputs from the orbitofrontal cortex (Rolls and Grabenhorst, 2008).

4.5.3 Olfactory–taste convergence to represent flavor and the influence of satiety

Supra-additive effects indicating convergence and interactions were found for taste (sucrose) and odor (strawberry) in the orbitofrontal and anterior cingulate cortex. 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 on where the pleasantness of flavor is represented in the human brain.

McCabe and Rolls (2007) have shown that the convergence of taste and olfactory information appears to be important for the pleasantness 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. This reflected activations in the pregenual cingulate cortex and medial orbitofrontal cortex. Certain sensory combinations, therefore, can produce very pleasant food stimuli, which may be important in driving food intake.

p0080 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 (de Araujo *et al.*, 2003b). 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 pleasantness of the flavor of food and sensory-specific satiety are represented in the orbitofrontal cortex.

4.5.4 Oral viscosity and fat texture

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). s0065 Oral viscosity is also represented in the human orbitofrontal and perigenual cingulate cortices. It p0070 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 by oral sucrose (de Araujo and Rolls, 2004). The pleasantness of fat texture may be represented in the orbitofrontal and anterior cingulate cortex, for activations in these regions are correlated with the subjective pleasantness of fat (Grabenhorst *et al.*, 2009).

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4.5.5 The sight of food

p0075 p0090 O'Doherty and colleagues (2002) showed that visual stimuli associated with the taste of glucose activated the orbitofrontal cortex and some connected areas, consistent with the primate neurophysiology. Simmons, Martin and Barsalou found that showing pictures of foods, compared to pictures of locations, can also activate the orbitofrontal cortex (Simmons *et al.*, 2005). 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).

4.6 COGNITIVE EFFECTS ON REPRESENTATIONS OF FOOD

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p0095 To what extent does cognition influence the hedonics of food-related stimuli, and how far down into the sensory system does 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 flavor, 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". 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) (see Figure 4.3).

The implication is that cognitive factors can have profound effects on our responses to the hedonic and sensory properties of food: these effects are manifest quite far down into sensory processing, so that hedonic representations of odors are affected (de Araujos *et al.*, 2005). Similar cognitive effects and mechanisms have now been found for the taste and flavor of food (Grabenhorst *et al.*, 2008). In addition, it has been found that with taste, flavor and olfactory food-related stimuli, attention to pleasantness modulates representations in the orbitofrontal cortex, whereas attention to intensity modulates activations in areas such as the primary taste cortex (Grabenhorst and Rolls, 2008; Rolls *et al.*, 2008).

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4.7 SYNTHESIS

p0105 These investigations show that representations of the reward/hedonic value and pleasantness of sensory, including food-related, stimuli in the brain are formed separately from representations of what the stimuli are. The pleasantness/reward value is represented in areas such as the orbitofrontal cortex and pregenual cingulate cortex. It is here that satiety signals modulate the representations of food to make them implement reward so that they only occur when hunger is present. The satiety signals that help in this modulation may reach the orbitofrontal cortex from the hypothalamus. 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 (Rolls, 2007; 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. Below is developed a hypothesis that obesity is associated with overstimulation of these reward systems by very rewarding combinations of taste, odor, texture, visual and cognitive inputs.

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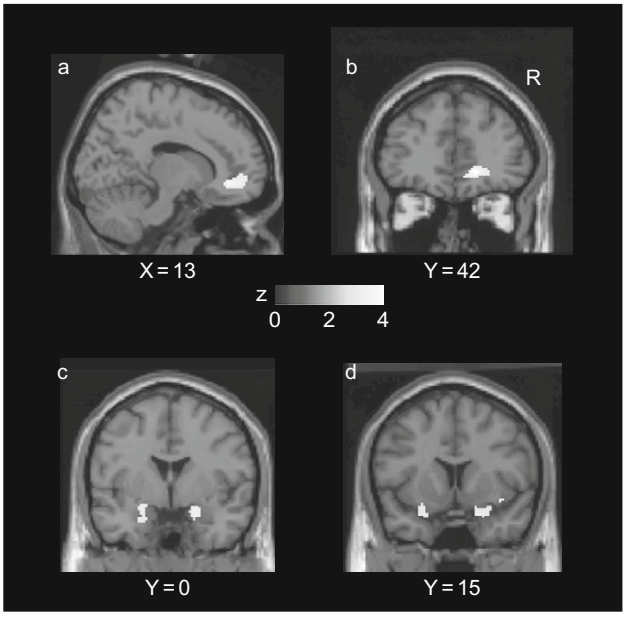
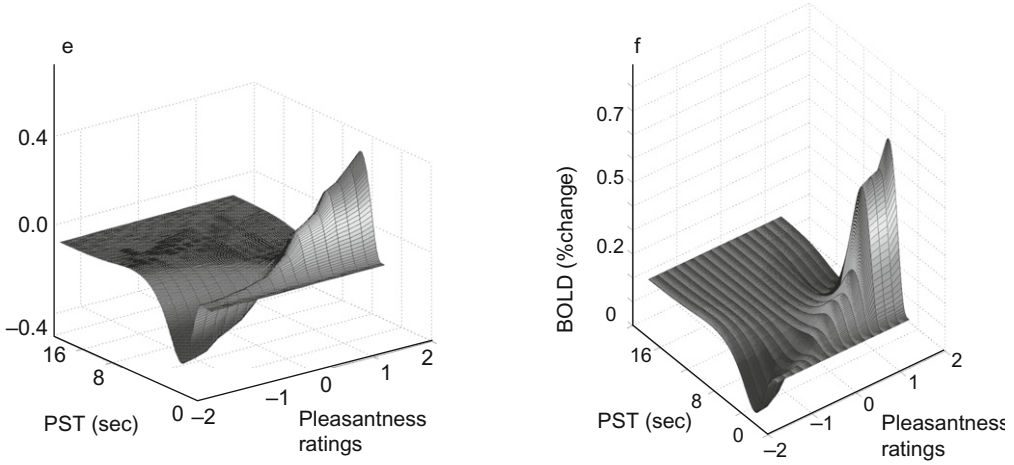
4.8 IMPLICATIONS FOR UNDERSTANDING, PREVENTING AND TREATING OBESITY

p0110 Understanding the mechanisms that control appetite is becoming an increasingly important issue, given the growing incidence of obesity (a three-fold increase in the UK since 1980 to a figure of 20 percent, as defined by a BMI >30) and its association with major health risks (with 1000 deaths each week in the UK attributable to obesity). It is important to understand and thereby be able to minimize and treat obesity, because many diseases are associated with a body weight that is much above normal. These diseases include diabetes, hypertension, cardiovascular disease, hypercholesterolaemia and gall bladder disease; in addition, obesity is associated with some deficits in reproductive function (e.g., ovulatory failure) and an excess mortality from certain types of cancer (Garrow, 1988; Barsh and Schwartz, 2002; Cummings and Schwartz, 2003; Schwartz and Porte, 2005). There are many factors that can cause or contribute to obesity in humans (Brownell and Fairburn, 1995; Morton *et al.*, 2006; O'Rahilly and Farooqi, 2006) that are investigated with approaches within or related to neuroscience and psychology (Rolls, 2005a, 2005b, 2006, 2007). Rapid progress is being made in understanding these, with the aim of leading to better





f0020 **FIGURE 4.3** Cognitive influences on olfactory representations in the human brain.
Group (random) effects analysis showing the brain regions where the BOLD signal was correlated with pleasantness ratings given to the test odor. The pleasantness ratings were being modulated by the word labels. (a) Activations in the rostral anterior cingulate cortex, in the region adjoining the medial OFC, shown in a sagittal slice. (b) The same activation shown coronally. (c) Bilateral activations in the amygdala. (d) These activations extended anteriorly to the primary olfactory cortex. The image was thresheld at $P < 0.0001$ uncorrected in order to show the extent of the activation. (e) Parametric plots of the data averaged across all subjects showing that the percentage BOLD change (fitted) correlates with the pleasantness ratings in the region shown in (a) and (b). The parametric plots were very similar for the primary olfactory region shown in D. PST, post-stimulus time(s). (f) Parametric plots for the amygdala region shown in (c).

Source: Adapted from DeAraujo *et al.*, 2005.

ways to minimize and treat obesity. These factors include the following:

4.8.1 Brain processing of the sensory properties and pleasantness of food

The way in which the sensory factors produced by the taste, smell, texture and sight of food interact in the brain with satiety signals (such as gastric distension and satiety-related hormones) to determine the pleasantness and palatability of food, and therefore whether and how much food will be eaten, is described above and shown in Figures 4.1 and 4.4. The concept is that convergence of sensory inputs occurs in the orbitofrontal cortex and builds a representation of food flavor. The orbitofrontal cortex is where the pleasantness and palatability of food are represented, as demonstrated by the discoveries that these representations of food are only activated if hunger is present, and correlate with the subjective pleasantness of the food flavor (Rolls, 2005a, 2005b, 2006, 2007; Rolls and Grabenhorst, 2008) The orbitofrontal cortex representation of whether food is pleasant (given any satiety signals present) then drives brain areas such as the striatum and cingulate cortex that then lead to eating behavior.

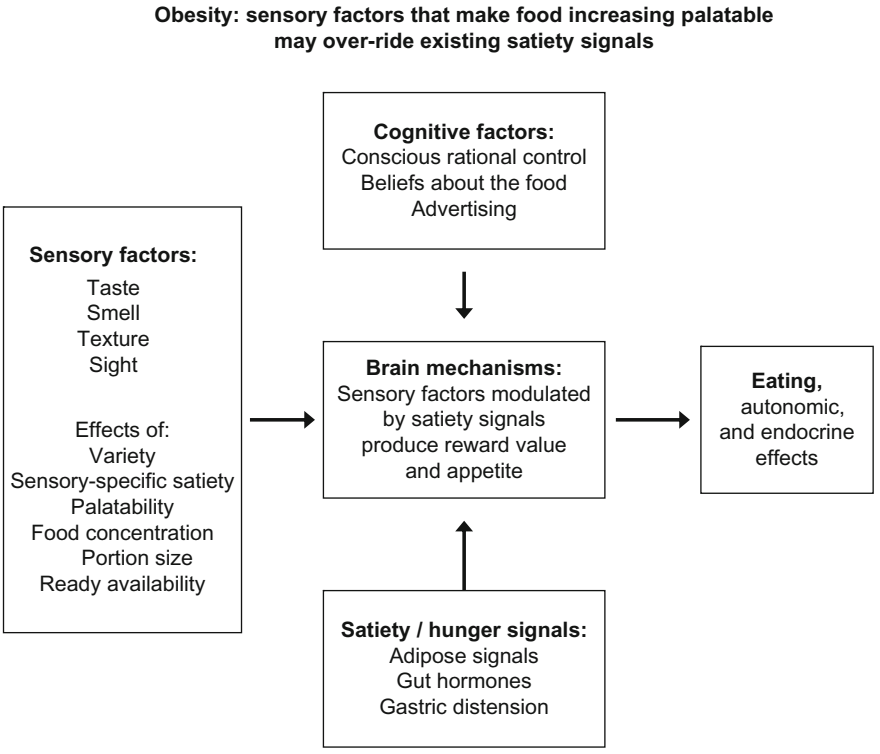
In the context of the obesity crisis, the past 30 years have seen a dramatic increase of the sensory stimulation produced by the taste, smell, texture and appearance of food, as well as its availability. Conversely, the satiety signals produced by stomach distension, satiety hormones, etc., have remained essentially unchanged. The effect on the brain's control system for appetite (shown in Figures 4.1 and 4.4) is to lead to a net average increase in the reward value and palatability of food which overrides the satiety signals, contributes to the tendency to be over-stimulated by food, and therefore leads to overeating.

In this scenario, it is important to better understand the rules used by the brain to produce the representation of the pleasantness of food and how the system is modulated by eating and satiety. This understanding, and how the sensory factors can be designed and controlled so as not to override satiety signals, are important research areas in the understanding, prevention and treatment of obesity. Advances in understanding the receptors that encode the taste and olfactory properties of food (Buck, 2000; Zhao *et al.*, 2003), and the processing in the brain of these properties (Rolls, 2004, 2005a, 2005b), are also important in providing the potential to produce highly palatable food that is at the same time nutritious and healthy.

An important aspect of this hypothesis is that different humans may have reward systems that are strongly driven by the sensory and cognitive factors that make food highly palatable. In a test of this, we showed that activation to the sight and flavor of chocolate in the orbitofrontal and pregenual cingulate cortex was much higher in chocolate cravers and non-cravers (Rolls and McCabe, 2007). The 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; Lowe *et al.*, 2009; Van den Eynde and Treasure, 2009) may provide a way for understanding and helping to control food intake.

4.8.2 Genetic factors

Genetic factors are of some importance, with some of the variance in weight and resting metabolic rate in a population of humans attributable to inheritance (Morton *et al.*, 2006; O'Rahilly and Farooqi, 2006, 2008). However the "obesity epidemic" that has occurred since the 1990s cannot be solely attributed to genetic changes, for which the timescale is far too short. Factors such as the increased palatability, variety and availability of food (as well as less exercise), crucial drivers of food intake, and the amount of food that is eaten (Rolls, 2005a, 2005b, 2006, 2007) are



f0025 **FIGURE 4.4** Obesity: sensory factors that make food increasingly palatable may over-ride existing satiety signals. Schematic diagram to show how sensory factors interact in the orbitofrontal cortex with satiety signals to produce the hedonic, rewarding value of food, which leads to appetite and eating. Cognitive factors directly modulate this system in the brain.

more likely to be responsible for the upsurge in the incident of obesity.

4.8.3 Endocrine factors and their interaction with brain systems

A small proportion of cases of obesity can be related to gene-related dysfunctions of the peptide systems in the hypothalamus, with, for example, 4 percent of obese people having deficient (MC4) receptors for melanocyte stimulating hormone (Morton *et al.*, 2006; O'Rahilly and Farooqi, 2006). Cases of obesity that can be related to changes in the leptin hormone satiety system are very rare (O'Rahilly and Farooqi, 2006; Farooqi and O'Rahilly, 2009). Further, obese people generally have high levels of leptin, so leptin production is not the problem. Instead, leptin resistance (i.e., insensitivity) may be somewhat related to obesity, with the resistance perhaps related in part to smaller effects of leptin on arcuate nucleus NPY/AGRP neurons (Munzberg and Myers, 2005). s0105 p0140

4.8.4 Food palatability s0110

A factor in obesity is food palatability, which, with modern methods of food production, can now be greater than would have been the case during the evolution of our feeding control systems. p0145

These brain systems evolved so that internal signals from, for example, gastric distension and glucose utilization could act to decrease the pleasantness of the sensory sensations produced by feeding sufficiently by the end of a meal to stop further eating (Rolls, 2004, 2005a, 2005b).

s0125 p0160 However, the greater palatability of modern food may mean that this balance is altered, so that there is a tendency for the greater palatability of food to be insufficiently decreased by a standard amount of food eaten (see Figure 4.4).

4.8.5 Sensory-specific satiety and the effects of variety on food intake

p0150 Sensory-specific satiety is the decrease in the appetite for a particular food as it is eaten in a meal, without a decrease in the appetite for different foods (Rolls, 2004, 2005a, 2005b), as shown above. It is an important factor influencing how much of each food is eaten in a meal. Its evolutionary significance may be to encourage eating of a range of different foods, and thus obtaining a range of nutrients. As a result of sensory-specific satiety, if a wide variety of foods is available, overeating in a meal can occur. Given that it is now possible to make available a wide range of food flavors, textures and appearances, and that such foods are readily available, this variety effect may be a factor in promoting excess food intake.

s0120 4.8.6 Fixed meal-times and the availability of food

p0155 Another factor that could contribute to obesity is fixed meal-times, in that the normal control of food intake by alterations in inter-meal interval is not readily available in humans. Therefore, food may be eaten at a meal-time even if hunger is not present (Rolls, 2005a). Even more than this, because of the high and easy availability of food (in the home and workplace) and stimulation by advertising, there is a tendency to start eating again when satiety signals after a previous meal have decreased only a little, and the consequence is that the system again becomes overloaded.

4.8.7 Food saliency and portion size

Making food salient, for example by placing it on display, may increase food selection, particularly in the obese (Schachter, 1971; Rodin, 1976). Portion size is a factor, since more is eaten if a large portion of food is presented (Kral and Rolls, 2004). Whether it can lead to obesity has not yet been demonstrated. The driving effects of visual and other stimuli (including the effects of advertising) on the brain systems that are activated by food reward may be different in different individuals, and contribute to obesity. s0115

4.8.8 Energy density of food s0130

p0165 Although the gastric emptying rate is slower for high energy-density foods, this does not fully compensate for the energy density of the food (Hunt and Stubbs, 1975; Hunt, 1980). The implication is that eating energy-dense foods (e.g., high-fat foods) may not allow gastric distension to contribute sufficiently to satiety. Because of this, the energy density of foods may be an important factor that influences how much energy is consumed in a meal. Indeed, it is thought that obese people tend to eat foods with high energy-density, and to visit restaurants with high-energy density (e.g., high-fat) foods. It is also a matter of clinical experience that gastric emptying is faster in obese than in normal-weight individuals, meaning that gastric distension may play a less effective role in contributing to satiety in the obese.

4.8.9 Eating rate s0135

p0170 A factor related to the effects described above is the eating rate, which is typically fast in the

obese (Otsuka *et al.*, 2006) and may provide insufficient time for the full effect of satiety signals as food reaches the intestine to operate.

4.8.10 Stress

Another potential factor in obesity is stress, which can induce eating and contribute to obesity. In a rat model of this, mild stress in the presence of food can lead to overeating and obesity (Torres and Nowson, 2007). This overeating is reduced by anti-anxiety drugs.

4.8.11 Food craving

Binge-eating has some parallels to addiction. In one rodent model of binge-eating, access to sucrose for several hours each day can lead to binge-like consumption of the sucrose over a period of days (Colantuoni *et al.*, 2002; Avena and Hoebel, 2003a, 2003b; Spangler *et al.*, 2004). The binge-eating is associated with the release of dopamine. In this model, binge-eating resembles an addictive process, in that after binge-eating has become a habit, sucrose withdrawal decreases dopamine release in the ventral striatum (a part of the brain involved in addiction to drugs such as amphetamine), altered binding of dopamine to its receptors in the ventral striatum is produced, and signs of withdrawal from an addiction occur. In withdrawal, the animals are also hypersensitive to the effects of amphetamine. Another rat model is being used to investigate the binge-eating of fat, and whether the reinforcing cues associated with it can be reduced by the GABA-B receptor agonist baclofen (Corwin and Buda-Levin, 2004).

4.8.12 Energy output

If energy intake is greater than energy output, body weight increases. Energy output is thus an important factor in the equation. A lack of exercise tends to limit energy output, and thus contributes to obesity. It should be noted, though, that obese people do not generally suffer from a very low metabolic rate: in fact, as a population, in line with their elevated body weight, obese people have higher metabolic rates than normal-weight humans (Garrow, 1988).

4.8.13 Cognitive factors

As shown above, cognitive factors, such as preconceptions about the nature of a particular food or odor, can reach down into the olfactory system in the orbitofrontal cortex which controls the palatability of food to influence how pleasant an olfactory stimulus is (de Araujo *et al.*, 2005). This has implications for further ways in which food intake can be controlled, and needs more investigation.

4.8.14 The psychology of compliance with information about risk factors for obesity

It is important to develop better ways to provide information that will be effective in the long term in decreasing food intake while maintaining a healthy diet, and in promoting an increase in energy expenditure by, for example, encouraging exercise.

4.9 CONCLUDING REMARKS

Recent advances are showing how the reward value of food is represented in the brain as a combination of taste, oral texture, olfactory and visual attributes of food; and how this reward representation which drives appetite and food intake is modulated by internal satiety signals, by sensory-specific satiety, by cognition and by attention.

In this context, it is argued that the factors that contribute to driving people towards obesity include the greater stimulation in the past 30 years of the brain by sensory stimuli that make food palatable and pleasant, relative to internal satiety signals, which have remained unchanged in this short time. In this situation, it is important to understand much better the rules used by the brain to produce the representation of the pleasantness of food, and how the system is modulated by eating and satiety. This understanding, and how the sensory factors can be designed and controlled so as not to override satiety signals, are important research areas in the understanding, prevention and treatment of obesity.

p0210 In this context, it may be important to better understand individual differences in the sensitivity of this food reward system.

p0215 The factors that contribute to overstimulating the brain's food reward systems relative to satiety signals include food palatability and appearance, sensory-specific satiety, food variety, food availability, the effects of visual stimulation and advertising, the energy density and nutritional content of food, portion size, and cognitive states. All these factors may need to be taken into account in the prevention of obesity.

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