

REVIEW

Taste, olfactory and food texture reward processing in the brain and obesity

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Complementary neuronal recordings 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 the orbitofrontal cortex (OFC), these sensory inputs are for some neurons combined by learning with olfactory and visual inputs, and these neurons encode food reward in that they only respond to food when hungry, and in that activations correlate with subjective pleasantness. Cognitive factors, including word-level descriptions, and attention, modulate the representation of the reward value of food in the OFC. Further, there are individual differences in the representation of the reward value of food in the OFC. It is argued that overeating and obesity are related in many cases to an increased reward value of the sensory inputs produced by foods, and their modulation by cognition and attention, which overrides existing satiety signals. It is proposed that control of all rather than one or several of these factors that influence food reward and eating may be important in the prevention and treatment of overeating and obesity.

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Introduction

The aims of this paper 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 and attention modulate these affective representations, and how these affective representations have 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 neuro-imaging studies in humans. A broad perspective on brain processing involved in emotion and in hedonic aspects of the control of food intake is provided by Rolls in *Emotion Explained*.¹

Taste processing in the primate brain

Pathways

A diagram of the taste and related olfactory, somatosensory and visual pathways in primates is shown in Figure 1. The

multimodal convergence that enables single neurons to respond to different combinations of taste, olfactory, texture, temperature and visual inputs to represent different flavours produced often by new combinations of sensory input is a theme of recent research that will be described.

The primary taste cortex

Rolls *et al.*^{2–4} 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, and umami as exemplified by monosodium glutamate (MSG),^{5,6} but also other neurons that encode oral somatosensory stimuli including viscosity, fat texture, temperature and capsaicin.⁷ 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 such as the sight of food.⁷ 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.^{8,9}

The secondary taste cortex

A secondary cortical taste area in primates was discovered by Rolls *et al.*¹⁰ in the caudolateral orbitofrontal cortex (OFC), extending several millimetre in front of the primary taste cortex. Neurons in this region respond not only to each

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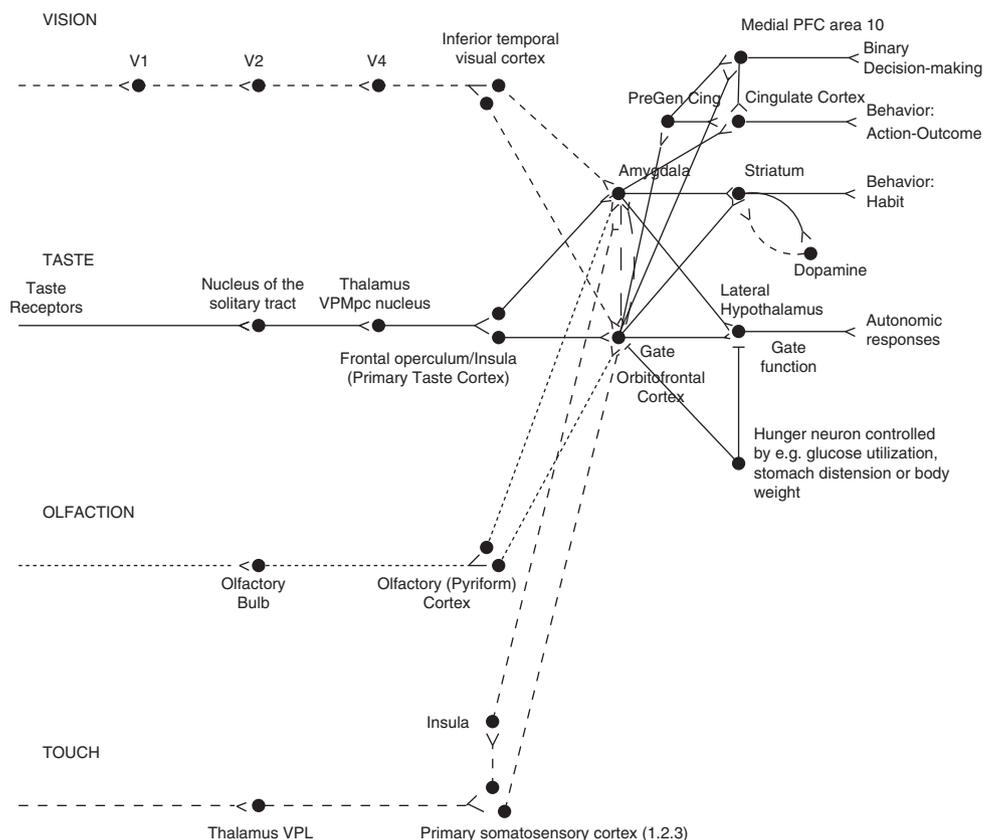


Figure 1 Schematic diagram showing some of the gustatory, olfactory, visual and somatosensory pathways to the OFC, and some of the outputs of the OFC, in primates. The secondary taste cortex, and the secondary olfactory cortex, are within the OFC. ‘Gate’ refers to the finding that inputs such as the taste, smell and sight of food in some brain regions only produce effects when hunger is present.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, the OFC and amygdala, and in areas beyond these. Medial PFC area 10, medial prefrontal cortex area 10; VPMpc, ventralposteromedial thalamic nucleus; V1, primary visual cortex; V4, visual cortical area V4; PreGen Cing. pregenual cingulate cortex.

of the four classical prototypical tastes sweet, salt, bitter and sour,^{4,11} 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)⁵ and inosine monophosphate (which is present in meat and some fish such as tuna).⁶ This evidence, taken together with the identification of glutamate taste receptors,^{12,13} leads to the view that there are five prototypical types of taste information channels, with umami contributing, often in combination with corresponding olfactory inputs,^{14–16} to the flavour of protein. In addition, other neurons respond to water, and others to somatosensory stimuli including astringency as exemplified by tannic acid,¹⁷ and capsaicin.^{18,19} Taste responses are found in a large mediolateral extent of the OFC.^{17,20–22}

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 behaviour is controlled.^{1,23} 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,^{24,25} it has been shown that this is implemented in a region that projects to the hypothalamus, the orbitofrontal (secondary taste) cortex, for the taste, odour and sight of food.^{26,27}

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 flavour, and the effects of variety to increase food intake,^{28–39} are produced in the OFC, but not at earlier stages of processing in which the responses reflect factors such as the intensity of the taste, which is little affected by satiety.^{22,40} 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 the length of a course of a meal),

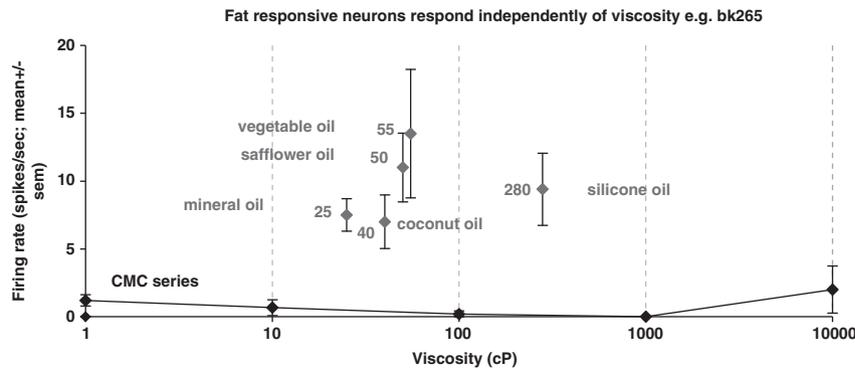


Figure 2 A neuron in the primate OFC responding to the texture of fat in the mouth independently of viscosity. The cell (bk265) increased its firing rate to a range of fats and oils (the viscosity of which is shown in centipoise). The information that reaches this type of neuron is independent of a viscosity 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.*⁴⁷).

it is likely that visceral and other satiety-related signals reach the OFC (as indicated in Figure 1) (from the nucleus of the solitary tract, through 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.¹

The representation of flavour: convergence of olfactory, taste and visual inputs in the OFC

Taste and olfactory pathways are brought together in the OFC in which flavour is formed by learned associations at the neuronal level between these inputs (see Figure 1).^{7,41–43} Visual inputs also become associated by learning in the OFC with the taste of food to represent the sight of food and contribute to flavour.^{44,45} The visual and olfactory as well as the taste inputs represent the reward value of the food, as shown by sensory-specific satiety effects.²⁷

The texture of food, including fat texture

Some OFC 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 1–10000 centiPoise), others independently encode the particulate quality of food in the mouth, produced quantitatively, for example, by adding 20–100 μm microspheres to methyl cellulose,¹⁸ and others encode the oral texture of fat^{46,47} as illustrated in Figure 2.

In addition, we have shown that some neurons in the OFC reflect the temperature of substances in the mouth, and that this temperature information is represented independently of other sensory inputs by some neurons, and in combination with taste or texture by other neurons.^{19,48}

Imaging studies in humans

Taste

In humans, it has been shown in neuroimaging studies using functional magnetic resonance imaging that taste activates an area of the anterior insula/frontal operculum, which is probably the primary taste cortex, and part of the OFC, which is probably the secondary taste cortex.^{49–51} Within individual subjects separate areas of the OFC are activated by sweet (pleasant) and by salt (unpleasant) tastes.⁵⁰ The primary taste cortex in the anterior insula of humans represents the identity and intensity of taste in that activations there correlate with the subjective intensity of the taste, and the orbitofrontal and ACC represents the reward value of taste, in that activations there correlate with the subjective pleasantness of taste.^{52,53}

We also found activation of the human amygdala by the taste of glucose.⁴⁹ Extending this study, O'Doherty *et al.*⁵⁰ 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 with rewarding stimuli. Zald *et al.*,⁵⁴ had shown earlier that the amygdala, as well as the OFC, respond to aversive (saline) taste stimuli.

Umami taste stimuli, of which an exemplar is MSG and which capture what is described as the taste of protein, activate the insular (primary), orbitofrontal (secondary) and anterior cingulate (tertiary²⁰) taste cortical areas.⁵⁵ When the nucleotide 0.005 M inosine 5'-monophosphate (IMP) was added to MSG (0.05 M), the blood oxygenation-level dependent signal in an anterior part of the OFC showed supralinear additivity, and this may reflect the subjective enhancement of umami taste that has been described when IMP is added to MSG.¹⁶ (The supralinear 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 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.¹⁶) 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.

Odour

In humans, in addition to activation of the pyriform (olfactory) cortex,^{56–58} there is strong and consistent activation of the OFC by olfactory stimuli,^{49,59} and this region seems to represent the pleasantness of odour, as shown by a sensory-specific satiety experiment with banana vs vanilla odour.⁶⁰ Further, pleasant odours tend to activate the medial, and unpleasant odours the more lateral, OFC,⁶¹ adding to the evidence that it is a principle that there is a hedonic map in the OFC, and also in the ACC, which receives inputs from the OFC.^{22,62} The primary olfactory (pyriform) cortex represents the identity and intensity of odour in that activations there correlate with the subjective intensity of the odour, and the orbitofrontal and ACC represents the reward value of odour, in that activations there correlate with the subjective pleasantness of odour.^{22,62,63}

Olfactory-taste convergence to represent flavour and the influence of satiety

Supradditive effects indicating convergence and interactions were found for taste (sucrose) and odour (strawberry) in the orbitofrontal and ACC, and activations in these regions were correlated with the pleasantness ratings given by the participants.^{64–66} These results provide evidence on the neural substrate for the convergence of taste and olfactory stimuli to produce flavour in humans, and where the pleasantness of flavour is represented in the human brain.

McCabe and Rolls¹⁵ have shown that the convergence of taste and olfactory information seems to be important for the delicious flavour of umami. They showed that when glutamate is given in combination with a consonant, savory, odour (vegetable), the resulting flavour can be much more pleasant than the glutamate taste or vegetable odour alone, and that this reflected activations in the pregenual cingulate cortex and medial OFC. 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.¹⁶

To assess how satiety influences the brain activations to a whole food that 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 OFC⁶⁷ but not in the primary taste cortex. This study provided evidence that the pleasantness of the flavour of food, and sensory-specific satiety, are represented in the OFC.

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.⁶⁸ Oral viscosity is also represented in the human orbitofrontal and perigenual cingulate cortices, and it is notable that the perigenual 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.⁶⁸ We have recently shown that the pleasantness and reward value of fat texture is represented in the mid-orbitofrontal and ACC, wherein activations are correlated with the subjective pleasantness of oral fat texture.^{16,69} This provides a foundation for studies of whether activations in the fat reward system are heightened in people who tend to become obese.

The sight of food

O'Doherty *et al.*⁷⁰ showed that visual stimuli associated with the taste of glucose activated the OFC and some connected areas, consistent with the primate neurophysiology. Simmons *et al.*⁷¹ found that showing pictures of foods, compared with pictures of locations, can also activate the OFC. Similarly, the OFC and connected areas were also found to be activated after presentation of food stimuli to food-deprived subjects.⁷²

Cognitive and selective attentional effects on representations of food

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 a functional magnetic resonance imaging investigation in which the delivery of a standard test odour (isovaleric acid combined with cheddar cheese flavour, presented orthonasally using an olfactometer) was paired with a descriptor word on a screen, which on different trials was 'Cheddar cheese' or 'Body odour'. Participants rated the affective value of the test odour as significantly more pleasant when labelled 'Cheddar Cheese' than when labelled 'Body odour', and these effects reflected activations in the medial OFC/rostral anterior cingulate cortex (ACC) that had correlations with the pleasantness ratings.⁷³ 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 processing, so that hedonic representations of odours are affected.⁷³ Similar cognitive effects and mechanisms have now been found for the taste and flavour of food, in which the cognitive word-level descriptor was, for example, 'rich delicious flavour' and activations to flavour were increased in the OFC and regions to which it projects including the pregenual cingulate cortex and ventral striatum, but were not influenced in the insular primary taste cortex in which activations reflected the intensity (concentration) of the stimuli⁵² (see Figure 3).

In addition, we have found that with taste, flavour and olfactory food-related stimuli, selective attention to pleasantness modulates representations in the OFC (see Figure 4), whereas selective attention to intensity modulates activations in areas such as the primary taste cortex.^{53,74} Thus, depending on the context in which tastes and odours are presented and whether affect is relevant, the brain responds to a taste and odour 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. This differential biasing of brain regions engaged in processing a sensory stimulus depending on whether the cognitive demand is for affect-related vs more sensory-related processing may be 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.^{53,74}

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. But after the reward evaluation, a decision has to be made regarding 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*,⁷⁵ and this has implications for whether a reward of a particular value will be selected.^{22,62,75-77} A tier of processing beyond the OFC, in medial prefrontal cortex area 10, becomes engaged when choices are made between odour stimuli

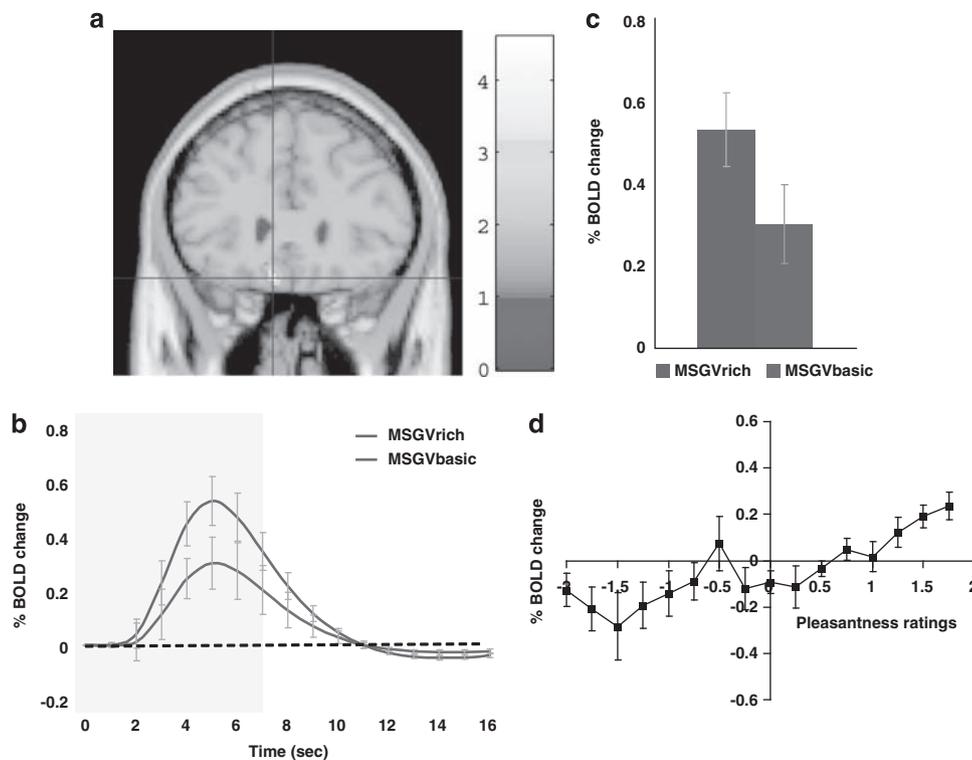


Figure 3 Cognitive modulation of flavour reward processing in the brain. (a) The medial OFC was more strongly activated when a flavour stimulus was labelled 'rich and delicious flavour' (MSGV rich and vegetable odour rich) than when it was labelled 'boiled vegetable water' (MSGVbasic) (-8 28 -20). (The flavour stimulus, MSGV, was the taste 0.1 M MSG + 0.005 M IMP combined with a consonant 0.4% vegetable odour.) (b) The timecourse of the blood oxygenation-level dependent (BOLD) signals for the two conditions. (c) The peak values of the BOLD signal (mean across subjects \pm s.e.m.) were significantly different ($t = 3.06$, $df = 11$, $P = 0.01$). (d) The BOLD signal in the medial OFC was correlated with the subjective pleasantness ratings of taste and flavour, as shown by the statistical parametric mapping analysis, and as illustrated (mean across subjects \pm s.e.m., $r = 0.86$, $P < 0.001$) (after Grabenhorst *et al.*⁵²).

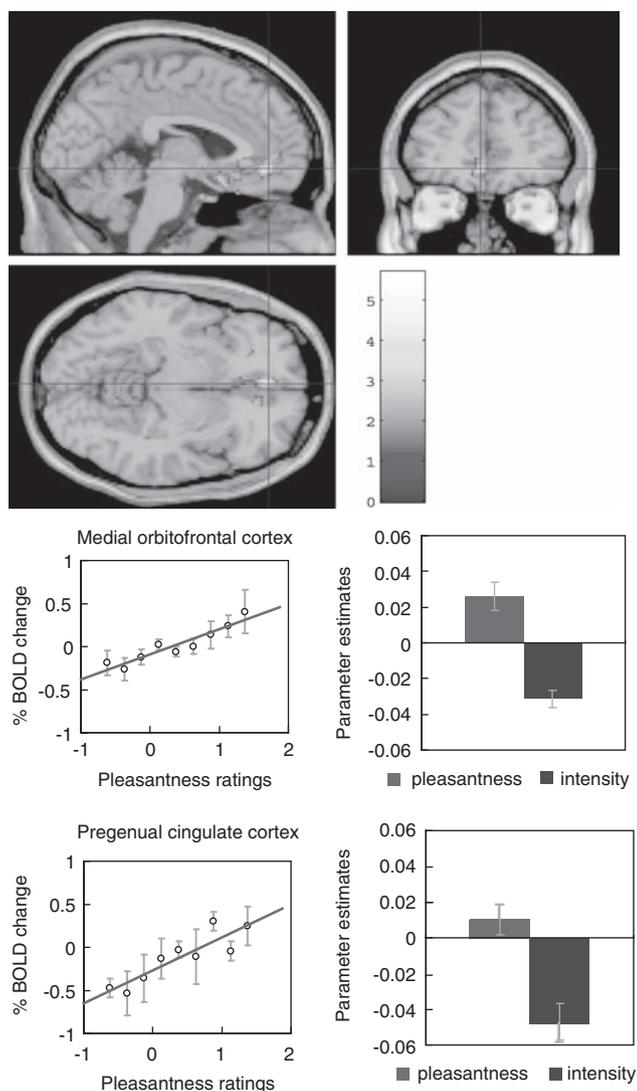


Figure 4 Effect of paying attention to the pleasantness vs the intensity of a taste stimulus. Top: a significant difference related to the taste period was found in the medial OFC at $(-6\ 14\ -20)$ $z = 3.81$ $P < 0.003$ (toward the back of the area of activation shown) and in the pregenual cingulate cortex at $(-4\ 46\ -8)$ $z = 2.90$ $P < 0.04$ (at the cursor). Middle: medial OFC. Right: the parameter estimates (mean \pm s.e.m. 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 OFC $t = 7.27$, $df = 11$, $P < 10^{-4}$. Left: the correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate ($r = 0.94$, $df = 8$, $P < 0.001$). 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 MSG, was identical on all trials (after Grabenhorst and Rolls.⁵³).

based on their pleasantness.^{78–81} The choices are made by a local 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 with high firing rates, which competes through inhibitory interneurons with other possible attractors formed by other groups of excitatory neurons.^{76,82} 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.^{75,76,83} 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.^{75,81} 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.^{22,62,76} The reasoning or rational system with its long-term goals (introducing evidence such as 'scientific studies have shown that fish oils rich in omega 3 may reduce the probability of Alzheimer's disease') then competes with the rewards such as the pleasant flavour of food (which are gene specified,¹ although subject to conditioned effects^{1,84}) in a further decision process, which may itself be subject to noise.^{1,75,76} This can be described as a choice between the selfish phenotype (standing for phenotype) and the selfish gene.⁷⁷ In this context, the findings described in this paper that the cognitive system can have a top-down influence on the food reward system are important advances in our understanding of how these decisions are reached.

Synthesis

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. The pleasantness/reward value is represented in areas such as the OFC and pregenual cingulate cortex, and it is here that satiety signals modulate the representations of food to make them implement reward in that they only occur when hunger is present. The satiety signals that help in this modulation may reach the OFC from the hypothalamus, and in turn, the OFC projects to the hypothalamus in which neurons are found that respond to the sight, smell and taste of food if hunger is present.^{22,23} We have observed above some of the principles that help to make the food pleasant, including particular combinations of taste, olfactory, texture, visual, and cognitive inputs.

I develop a hypothesis below (in the section 'Brain processing of the sensory properties and pleasantness of

food') that obesity is associated with overstimulation of these reward systems by very rewarding combinations of taste, odour, texture, visual and cognitive inputs.

Implications for understanding, preventing and treating obesity

Understanding the mechanisms that control appetite are becoming an increasingly important issue, given the increasing incidence of obesity (a threefold increase in the United Kingdom since 1980 to a figure of 20% defined by a body mass index $>30\text{ kg m}^{-2}$) and the realization that it is associated with major health risks (with 1000 deaths each week in the United Kingdom 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 hypertension, cardiovascular disease, hypercholesterolaemia and gall bladder disease; and in addition obesity is associated with some deficits in reproductive function (for example, ovulatory failure), and with an excess mortality from certain types of cancer.^{85–88}

There are many factors that can cause or contribute to obesity in humans^{89–91} that are analyzed with approaches within or related to neuroscience and psychology.^{1,23,92,93} Rapid progress is being made in understanding many of these factors at present with the aim of leading to better ways to minimize and treat obesity. These factors include the following:

Genetic factors

These are of some importance, with some of the variance in weight and resting metabolic rate in a population of humans attributable to inheritance.^{90,91} However, the 'obesity epidemic' that has occurred since 1990 cannot be attributed to genetic changes, for which the time scale is far too short, but instead to factors such as the increased palatability, variety and availability of food (as well as less exercise) which are some of the crucial drivers of food intake and the amount of food that is eaten^{1,23,92,93} and that are described below.

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% of obese people having deficient (MC4) receptors for melanocyte-stimulating hormone.^{90,91} Cases of obesity that can be related to changes in the leptin hormone satiety system are very rare.⁹¹ Further, obese people generally have high levels of leptin, so leptin production is not the problem, and instead leptin resistance (that is, insensitivity) may be somewhat related to obesity, with the resistance perhaps related in part to smaller effects of leptin

on arcuate nucleus neuropeptide Y/agouti-related peptide neurons.⁹⁴ However, although there are similarities in fatness within families, these are as strong between spouses as they are between parents and children, so that these similarities cannot be attributed to genetic influences, but presumably reflect the effect of family attitudes to food and weight.

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 1 and 5. The concept is that convergence of sensory inputs produced by the taste, smell, texture and sight of food occurs in the OFC to build a representation of food flavour. The OFC is where the pleasantness and palatability of food are represented, as shown by the discoveries that these representations of food are only activated if hunger is present, and correlate with the subjective pleasantness of the food flavour.^{1,22,23,62,92,93} The OFC 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 behaviour.

The fundamental concept this leads to regarding some of the major causes of obesity is that, over the last 30 years, sensory stimulation produced by the taste, smell, texture and appearance of food, as well as its availability, have increased dramatically, yet the satiety signals produced by stomach distension, satiety hormones, and so on,⁹⁵ have remained essentially unchanged, so that the effect on the brain's control system for appetite (shown in Figures 1 and 5) is to lead to a net average increase in the reward value and palatability of food, which overrides the satiety signals, and contributes to the tendency to be overstimulated by food and to overeat.

In this scenario, 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. Advances in understanding the receptors that encode the taste and olfactory properties of food,^{12,96} and the processing in the brain of these properties,^{1,93,97} 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 especially 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 flavour of chocolate in

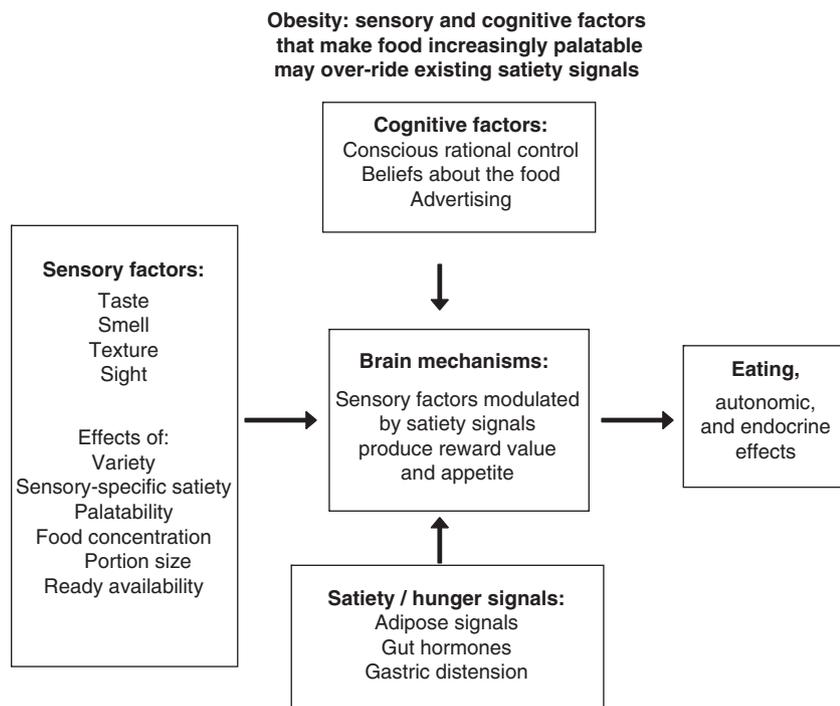


Figure 5 Schematic diagram to show how sensory factors interact in the OFC with satiety signals to produce the hedonic, rewarding value of food, which leads to appetite and eating. Cognitive and attentional factors directly modulate the reward system in the brain.

the orbitofrontal and pregenual cingulate cortex were much higher in chocolate cravers than non-cravers.⁹⁸ This concept that individual differences in responsiveness to food reward are reflected in brain activations in regions related to the control food intake^{98,99} may provide a way for understanding and helping to control food intake.

Food palatability

A factor in obesity (as shown under section 'Brain processing of the sensory properties and pleasantness of food') 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. 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.^{1,93,97} 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, so that extra food is eaten in a meal (see Figure 5).

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

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,^{1,93,97} as shown above. It is an

important factor influencing how much of each food is eaten in a meal, and 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 very wide range of food flavours, textures and appearances, and that such foods are readily available, this variety effect may be a factor in promoting excess food intake.

Fixed meal times and the availability of food

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, and food may be eaten at a meal-time even if hunger is not present.¹ 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.

Food saliency and portion size

Making food salient, for example, by placing it on display, may increase food selection particularly in the

obese,^{100,101} and portion size is a factor, with more being eaten if a large portion of food is presented,¹⁰² although whether this is a factor that can lead to obesity and not just alter meal size is not yet clear. 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 may contribute to obesity.

Energy density of food

Although gastric emptying rate is slower for high energy density foods, this does not fully compensate for the energy density of the food.^{103,104} The implication is that eating energy dense foods (for example, high fat foods) may not allow gastric distension to contribute sufficiently to satiety. As a result of this, the energy density of foods may be an important factor that influences how much energy is consumed in a meal.¹⁰² Indeed, it is notable that obese people tend to eat foods with high energy density, and to visit restaurants with high energy density (for example, high fat) foods. It is also a matter of clinical experience that gastric emptying is faster in obese than in thin individuals, so that gastric distension may have a less effective role in contributing to satiety in the obese. It is also important to remember that the flavour of a food can be conditioned to its energy density, leading over a few days to more eating of low than high energy dense foods, in the phenomenon known as conditioned satiety.^{1,84}

Eating rate

A factor related to the effects described in the previous section is eating rate, which is typically fast in the obese, and may provide insufficient time for the full effect of satiety signals as food reaches the intestine to operate.

Stress

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

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.^{105–108} The binge eating is associated with the release of dopamine. This model brings binge eating close to an addictive process, at least in this model, in that after the 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 including teeth chattering. In withdrawal, the animals are also hypersensitive to the effects of amphetamine. Another rat model is being used to analyze the binge eating of fat, and whether the reinforcing cues associated with this can be reduced by the γ -amino butyric acid B receptor agonist baclofen.¹⁰⁹

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 or the presence of high room temperatures, may tend to limit energy output, and thus contribute to obesity. It should be noted although 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 humans⁸⁵ (at least at their obese body weights: it might be interesting to analyze this further).

Cognitive factors and attention

As shown above, cognitive factors, such as preconceptions regarding the nature of a particular food or odour, can reach down into the olfactory and taste system in the OFC, which controls the palatability of food to influence how pleasant an olfactory, taste or flavour stimulus is.^{52,73} This has implications for further ways in which food intake can be controlled by cognitive factors, and this needs further investigation. For example, the cognitive factors that have been analyzed in these studies are descriptors of the reward value of the food, such as 'rich and delicious'. But it could be that cognitive descriptions of the consequences of eating a particular food, such as 'this food tends to increase body weight', 'this food tends to alter your body shape toward fatness', 'this food tends to make you less attractive', 'this food will reduce the risk of a particular disease', and so on, could also modulate the reward value of the food as it is represented in the OFC. If so, these further types of cognitive modulation could be emphasized in the prevention and treatment of obesity.

Further, attention to the affective properties of food modulates processing of the reward value of food in the OFC,^{53,74} and this again suggests that how attention is directed may be important in the extent to which food overstimulates food intake. Not drawing attention to the reward properties of food, or drawing attention to other properties such as its nutritional value and energy content, could reduce the activation of the brain's reward system by the food, and could be another useful way to help prevent and treat obesity.

The neuroscience and psychology of compliance with information regarding 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. In this respect, the individual differences in the brain's response to the reward value of a food, found, for example, in our study with chocolate cravers and non-cravers,⁹⁸ is one type of factor that may influence whether an individual can comply. But there are individual differences in other factors that may influence compliance, such as impulsiveness, and the OFC is implicated in this.^{110–112} It is important to better understand possible individual differences in the ability for an individual to stop, and be influenced by the reasoning system with its long-term interests in comparison with the immediate rewards specified by genes.^{1,76,77} It could also be that substances such as alcohol shift this balance, making an individual temporarily or possibly in the long term more impulsive and less under control of the reasoning executive system,¹¹³ and therefore more likely to eat, and to eat unhealthily. These effects of alcohol on impulsiveness may be complemented by hormonal processes.¹¹⁴ Understanding these processes, and enabling individuals to benefit from this understanding, may also be useful in the prevention and treatment of obesity.

Overall, I suggest that understanding of all the above processes, and their use in combination rather than purely individually, may provide new avenues to the control of overeating and body weight. I have outlined in this paper a number of factors that may tend to promote overeating and obesity in our modern society, for example, by increasing the effect of reward signals on the brain's appetite control system, or by making it difficult for individuals to resist the increased hedonic value of food. It is possible that any one of these, or a few in combination, could produce overeating and obesity. In these circumstances, to prevent and treat obesity it is unlikely to be sufficient to reduce and focus on or test just one or a few of these factors. As there are many factors, there may always be others that apply and that tend to promote overeating and obesity. The conclusion I therefore reach is that to prevent and treat obesity, it may be important to address all of the above factors together, given that any one, or a few, could tend to lead to overeating and obesity. The science I have described suggests that taking this overall approach, minimizing the effect of all these factors, could be an important aim for future research and strategy.

Conflict of interest

The author declares no conflict of interest.

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