Smell, Taste, Texture, and Temperature Multimodal Representations in the Brain, and Their Relevance to the Control of Appetite

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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, and to relate this to the brain mechanisms underlying emotion. Much of the fundamental evidence comes from studies in non-human primates, and this is being complemented by functional neuroimaging studies in humans.

Introduction

Studies of the brain mechanisms involved in smell and taste are revealing some of the brain processing relevant to understanding how the brain interprets different odors and tastes. Direct study of the brain activations produced by odor and taste may reveal effects that are not reported verbally. It has been shown that approximately 40% of neurons in the orbitofrontal cortex taste and olfactory areas provide a representation of odor that depends on the taste with which the odor has been associated previously, and that this representation is produced by a slowly acting learning mechanism. Other neurons in the orbitofrontal cortex respond to the odor and to sensory information about the texture of food in the mouth (including the mouth feel of fat) and some respond to the viscosity of what is in the mouth. The representation of odor thus moves beyond the domain of physicochemical properties of odors to a domain where the ingestion-related significance of the odor determines the representation provided by some neurons.

Another processing principle in the orbitofrontal cortex is that, in addition to unimodal representations of the taste, olfactory, somatosensory, and visual properties of sensory stimuli, some neurons combine inputs from these different modalities, and these combination-selective neurons provide an information-rich representation of a wide range of the sensory qualities of food. One key to understanding these combinatorial representations is learning how individual neurons come to respond to particular combinations of taste, olfactory, texture, and associated visual stimuli.

A third processing principle is that the orbitofrontal cortex represents the pleasantness of taste, olfactory, texture, and associated visual stimuli, as shown by experiments in which the activity decreases to zero as food is fed to satiety, a process that decreases the reward and affective value to zero.

Neuroimaging studies have shown that the human orbitofrontal cortex provides a representation of the pleasantness of odor. The activation produced by the odor of a food eaten to satiety decreases relative to another food-related odor 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. Activation in this area decreases to a food eaten to satiety, but not to a food that has not been eaten in the meal. With neuroimaging it is possible to show that pleasant and unpleasant odors activate different regions of the orbitofrontal cortex and cingulate cortex. It has also been shown that the combination of monosodium glutamate (MSG) and inosine monophosphate (IMP), which together produce an enhanced umami taste quality, result in supralinear activation of a part of the anterior orbitofrontal cortex, reflecting an effect of the combination of these two stimuli.

Studies of the brain activation produced by odors and tastes are thus revealing some of the principles of the representation of odor and taste in the brain, and also indicate that brain correlates of the acceptability and pleasantness of odors and tastes can be provided by neuroimaging. A broad perspective on brain processing

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involved in emotion is provided in a book entitled *The Brain and Emotion*.[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. In primates there is a direct projection from the rostral part of the nucleus of the solitary tract 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.[2,3] This emphasis on cortical processing of taste 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 analyzed representations from each modality are brought together in multi-modal regions is documented below. The multimodal convergence that enables single neurons to respond to different combinations of taste, olfactory, texture, temperature, and visual inputs to represent different flavors produced often by new combinations of sensory input is a theme of recent research.

The Secondary Taste Cortex. A secondary cortical taste area in primates was discovered in the caudolateral orbitofrontal cortex, extending several millimeters in front of the primary taste cortex.[4] 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. This specific tuning (especially when combined with olfactory inputs) helps to provide a basis for changes in the appetite for some but not other foods eaten during a meal.
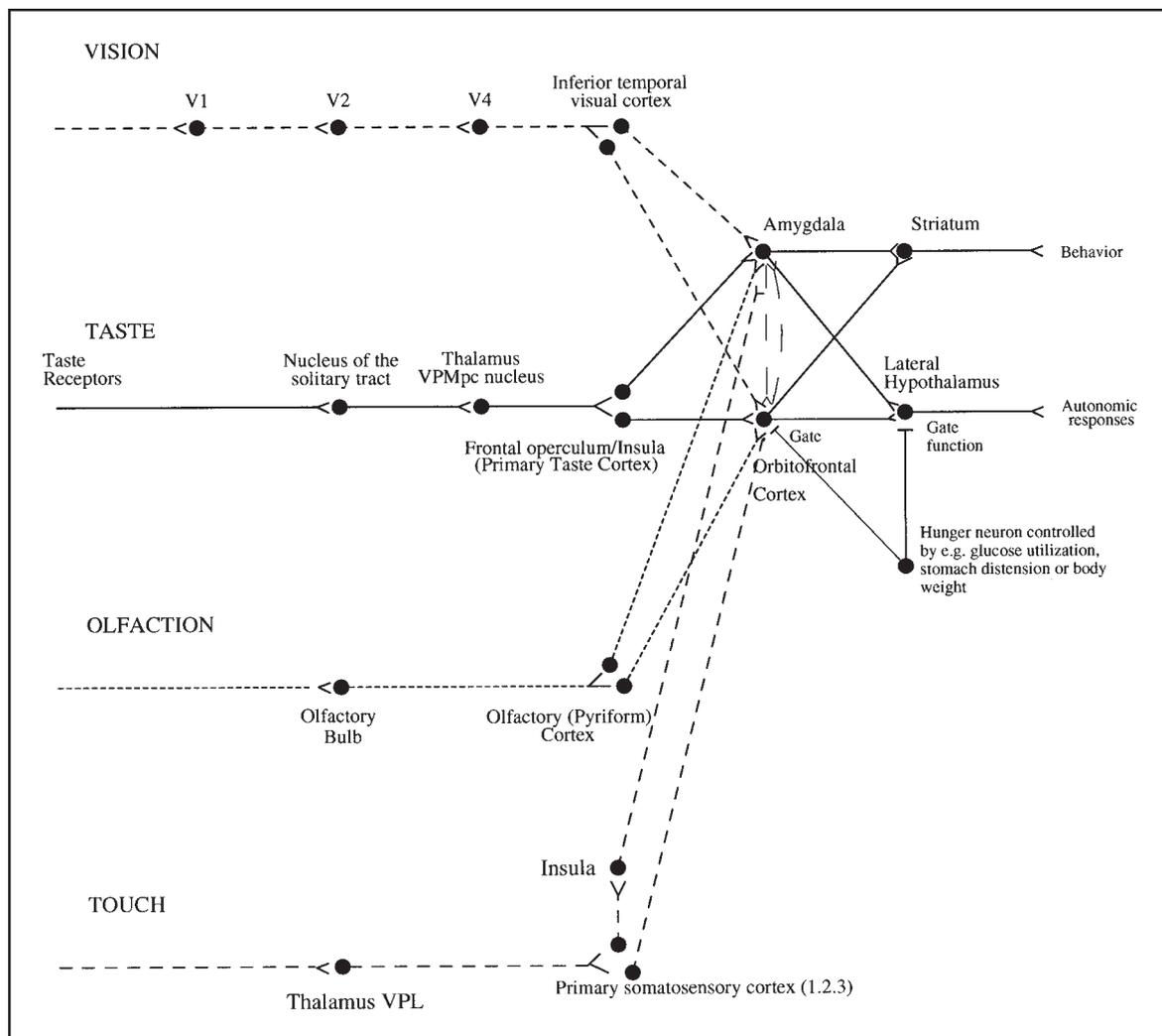

Figure 1. Schematic diagram of the taste and olfactory pathways in primates showing how they converge with each other and with visual pathways. The gate functions shown refer to the finding that the responses of taste neurons in the orbitofrontal cortex and the lateral hypothalamus are modulated by hunger.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

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[5]—but there are also many neurons that respond best to umami tastants such as glutamate (which is present in many natural foods such as tomatoes, mushrooms, and milk[6]) and IMP (which is present in meat and some fish such as tuna[7]). This evidence, together with the identification of a glutamate taste receptor,[8] leads to the view that there are five prototypical types of taste information channels, with umami contributing—often in combination with corresponding olfactory inputs[9]—to the flavor 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, for example, hunger, is one important way in which motivational behavior is controlled.[1] The subjective correlate of this modulation is that food tastes pleasant when we are 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 the early stages of the primate gustatory system. The responsiveness of taste neurons in the nucleus of the solitary tract[10] and in the primary taste cortex, the frontal opercular,[11] and the insular cortex,[12] 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 glucose decreased to zero while the monkey ate it to satiety, during the course of which the behavior turned from avid acceptance to active rejection.[13] 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 to the taste of the glucose but not to the taste of black currant juice decreased (see example in Figure 2). Conversely, in two experiments in which the monkey was fed to satiety with fruit juice, the responses of the neurons to fruit juice but not to glucose decreased.[13]

This evidence shows that the reduced acceptance of food that occurs when food is eaten to satiety, and the
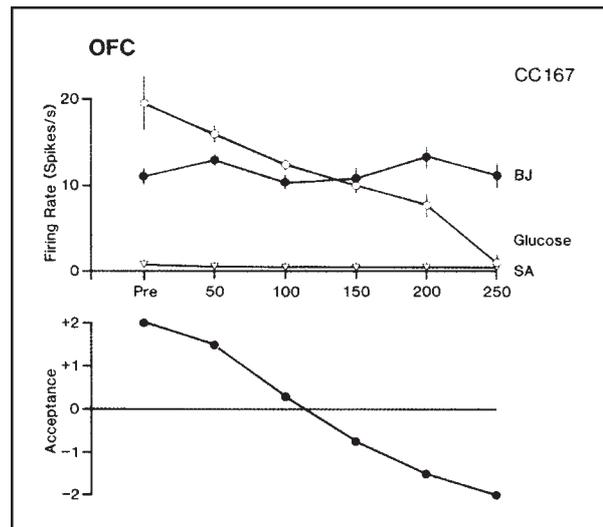
Figure 2. The effect of feeding to satiety with glucose solution on the responses of two neurons in the secondary taste cortex to the taste of glucose and of black currant juice (BJ). The spontaneous firing rate is also indicated (SA). Below the neuronal response data for each experiment, the behavioral measure of the acceptance or rejection of the solution on a scale from +2 to –2 (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 = Firing rate of the neuron before the satiety experiment started. The values shown are the mean firing rate and its standard error. (From Rolls et al.[13])

reduction in the pleasantness of its taste,[14-20] 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 with which they had been satiated tasted almost as intense as when they were hungry, though much less pleasant.[21] 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[22] 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.[1,23-28]

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

The Representation of Flavor: 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, for example, with olfactory inputs to form a representation of flavor (Figure 1). We found that in the orbitofrontal cortex taste areas, of 112 single neurons that responded to any of these modalities, many were unimodal (taste 34%, olfactory 13%, visual 21%), but were found in close proximity to each other.[29] 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., 1M glucose), and responded more in a visual discrimination task to the visual stimulus that signified sweet fruit juice than to that which signified saline, or responded to sweet taste and in an olfactory discrimination task to fruit odor.

The different types of neurons (unimodal in different modalities and multimodal) were frequently found close to one another in tracks made into this region, which is consistent with the hypothesis that the multimodal representations are actually being formed from unimodal inputs to this region. Therefore, it appears to be in these orbitofrontal cortex areas that flavor representations are built, where flavor is taken to mean a representation that is evoked best by a combination of gustatory and olfactory input. This orbitofrontal region does appear to be an important region for convergence, because there is only a low proportion of bimodal taste and olfactory neurons in the primary taste cortex.[29]

The Rules Underlying the Formation of Olfactory Representations in the Primate Cortex

Critchley and Rolls[23] showed that 35% of orbitofrontal cortex olfactory neurons categorized odors based on their taste association in an olfactory-to-taste discrimination task. Rolls et al.[7] found that 68% of orbitofrontal cortex odor-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 odor (the S+) was a drop of glucose, then a taste reward was obtained; if incorrectly a lick response was made to another odor (the S−) a drop of aversive saline was obtained. At some time in the experiment, the contingency between the odor and the taste was reversed, and when the "meaning" of the two odors altered, so did the behavior. It would be interesting to investigate in which parts of the olfactory system the neurons show reversal, because where they do, it can be concluded that the neuronal response to the odor depends on the taste with which it is associated, and does not depend primarily on the physicochemical structure of the odor. 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 odor is associated.[30-32]

This modification was less complete, and much slower, than the modifications found for orbitofrontal visual neurons during visual-taste reversal.[33] This relative inflexibility of olfactory responses is consistent with the need for some stability in odor-taste associations to facilitate the formation and perception of flavors. In addition, some orbitofrontal cortex olfactory neurons did not code in relation to the taste with which the odor was associated,[23] so there is also a taste-independent representation of odor in this region.

Representation of the Pleasantness of Odor 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 odor is represented in the orbitofrontal cortex. Satiety experiments[34] have shown that the responses of some olfactory neurons to a food odor are decreased during feeding to satiety with a food (e.g. fruit juice) containing that odor. In particular, seven of nine olfactory neurons that were responsive to the odors of foods, such as black currant juice, were found to decrease their responses to the odor of the satiating food. The decrease was typically at least partly specific to the odor 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, 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 behavior. 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 odor is at least part of what is represented.

As a result of the neurophysiological and behavioral observations showing the specificity of satiety in the monkey, 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.[15] 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.[15,16,35] Because sensory factors such as similarity of color, shape, flavor, 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."[15-19,36] 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),[14,37,38] whereas sensory-specific satiety is a change in the pleasantness of sensory inputs accounted for at least partly by the external sensory stimulation received (such as the taste of a particular food), and, as shown above, 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 odor of a food when it is eaten to satiety, one study[39] measured humans' responses to the smell of a food eaten to satiety. It was found that the pleasantness of the odor of a food, but much less significantly its intensity, was decreased when the subjects ate it to satiety. It was also found that the pleasantness of the smell of other foods (i.e. foods not eaten in the meal) showed much less 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 odor pleasantness ratings that could occur following meals. In an investigation of the mechanisms of this odor-specific sensory-specific satiety, this study[39] allowed humans to chew a food without swallowing for approximately as long as the food is normally in the mouth during eating. A sensory-specific satiety was demonstrated using this procedure, showing that the sensory-specific satiety does not depend on food reaching the stomach; therefore, at least part of the mechanism is likely to be produced by a change in processing in the olfactory pathways. The earliest stage of olfactory processing at which this modulation occurs is not yet known. It is unlikely to be in the receptors, because the change in pleasantness found was much more significant than the change in the intensity.[39]

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, 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.[40,41]

The Responses of Orbitofrontal Cortex Taste and Olfactory Neurons to the Sight, Texture, and Temperature of Food

Many of the neurons with visual responses in this region also show olfactory or taste responses,[29] reverse rapidly in visual discrimination reversal,[39,42] and only respond to the sight of food if hunger is present.[34] This part of the orbitofrontal cortex thus seems to implement a mechanism that can flexibly alter the responses to visual stimuli depending on the reinforcement (e.g. the taste) associated with the stimuli.[24,43] This enables prediction of the taste associated with ingestion of what is seen, and thus in the visual selection of foods,[1,26,44,45] and also provides a mechanism by which the sight of a food influences its flavor.

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. 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 gelatin or by puréeing a semi-solid food.[1,46]

It has been shown that some of these neurons with texture-related responses encode parametrically the viscosity of food in the mouth (using a methyl cellulose series in the range of 1–10,000 centipoise; Figure 3), and that 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.[47]

In addition, recent findings[48] have revealed that some neurons in the orbitofrontal cortex 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.

The Mouth Feel of Fat

Texture in the mouth is an important indicator of whether fat is present in a food, because fat is important not only as a high-value energy source, but also as a potential source of essential fatty acids. In the orbitofrontal cortex, there is a population of neurons that responds when fat is in the mouth.[49] A graphical representation of such a neuron is shown in Figure 4. The fat-related responses of these neurons are produced at least in part by the texture of the food rather than by receptors sensitive to certain chemicals. Such neurons typically respond not only to
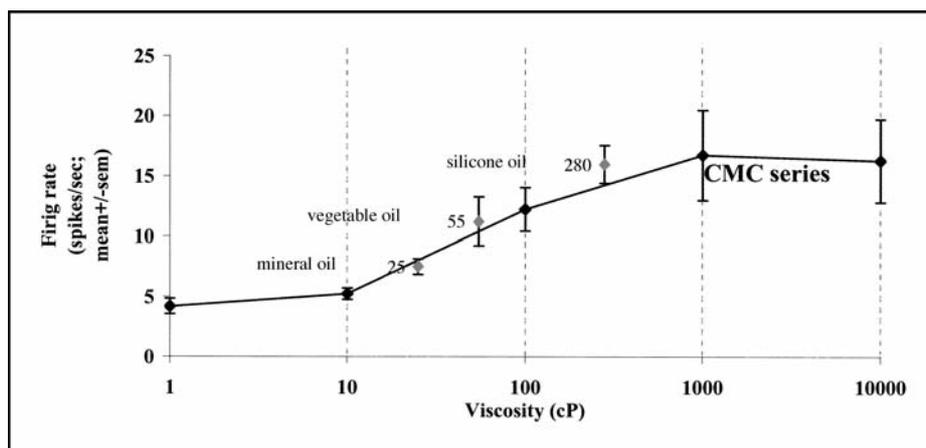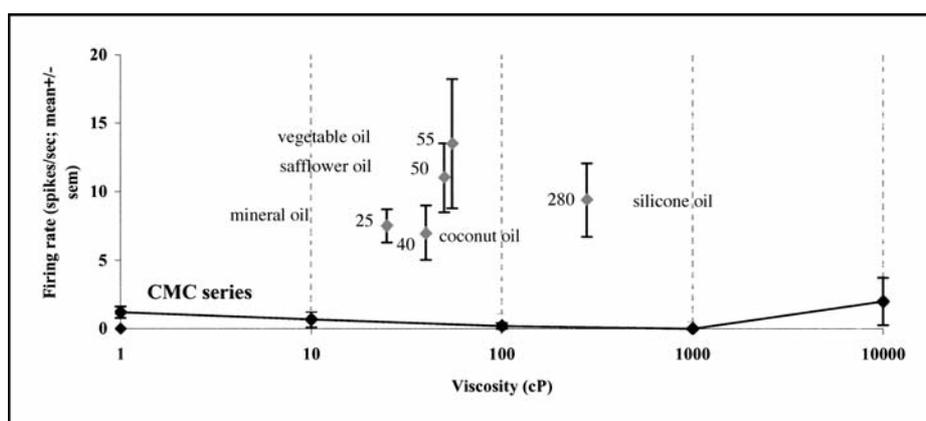
Figure 3. Graphical representation of a neuron in the primate orbitofrontal cortex responding to texture and in particular viscosity in the mouth. The cell (bk292c2) had a firing rate response that increased parametrically with the viscosity of methyl cellulose (CMC) in the mouth. The neuron encoded viscosity in that its response to fats and oils depended on their viscosity (in centipoise [cP]). Some of these neurons have taste inputs. The spontaneous firing rate of the neuron was approximately 5 spikes/s. (From Rolls et al., 2003.[47])

fat-containing foods such as cream and milk, but also to paraffin oil (which is a pure hydrocarbon) and to silicone oil, $Si(CH_3)_2O)_n$. Moreover, the texture channel through which these fat-sensitive neurons are activated are separate from viscosity-sensitive channels, in that the responses of these neurons cannot be predicted by the viscosity of the oral stimuli,[50] as illustrated in Figure 4. Some of the fat-related neurons do have convergent inputs from the chemical senses. In addition to taste inputs, some of these neurons respond to the odor associated with a fat, such as the odor of cream.[49] Feeding to satiety with fat (e.g., cream) decreases the responses of these neurons to zero on the food eaten to satiety, but if the neuron receives a taste input from, for example, glucose taste, that is not decreased by feeding to satiety

with cream. Therefore, 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. Studies using functional magnetic resonance imaging in humans have shown 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.[51-53] The orbitofrontal cortex taste area is distinct from areas activated by odors and by pleasant touch.[51] It has been shown that within individual subjects, separate areas of the orbitofrontal cortex are activated by sweet (pleasant)[52] and salt (unpleasant)[52] tastes. Francis et al.[48]

Figure 4. Graphical representation of 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 [cP]). The information that reaches this type of neuron is independent of a viscosity-sensing channel, as 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, because it also responded to silicone oil and paraffin (mineral) oil (hydrocarbon). Some of these neurons have taste inputs. (From Rolls et al., 2003.[47])

also found activation of the human amygdala by the taste of glucose. Extending this study,[52] the same investigators 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 compared with rewarding stimuli. Another study has recently shown that umami taste stimuli, for example, MSG, which capture what is described as the taste of protein, activate cortical regions of the human taste system similar to those activated by a prototypical taste stimulus, glucose.[54] A part of the rostral anterior cingulate cortex was also activated. When the nucleotide 0.005 M IMP was added to MSG (0.05 M), the BOLD (blood oxygenation-level dependent) signal in an anterior part of the orbitofrontal cortex showed supralinear additivity, and this may reflect the subjective enhancement of umami taste that has been described when IMP is added to MSG. The supralinear additivity in the BOLD signal is further demonstrated by the time courses for each of the umami taste stimuli in this significant cluster of voxels in the orbitofrontal cortex, as shown in Figure 5 (the time courses across all 10 subjects are shown with respect to the tasteless solution). In these voxels there is a greater activation by MSG-IMP than by either alone. For comparison, Figure 6 shows the time courses for the largest peak in the main effects comparison for umami taste for the insular/operculum primary taste cortex region, and it is evident that the MSG-IMP response was not especially prominent in the insular/opercular taste cortex. 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.

Odor. In humans, in addition to activation of the pyriform (olfactory) cortex,[55-57] there is strong and consistent activation of the orbitofrontal cortex by olfactory stimuli.[51,58] In a study investigating where the pleasantness of olfactory stimuli might be represented in humans, O'Doherty et al.[59] showed that the activation of an area of the orbitofrontal cortex to banana odor was decreased (relative to a control vanilla odor) after bananas were eaten to satiety. Therefore, 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 odor is represented.

We have also measured brain activation by whole foods before and after the food is eaten to satiety.[54] The aim 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 odor, taste, and texture of food are represented. 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[60] but not in the primary taste cortex. This study provided evidence that the pleasantness of the flavor of food is represented in the orbitofrontal cortex.

An important issue is whether there are separate regions of the brain discriminable with functional MRI that represent pleasant and unpleasant odors. To investigate this, we measured the brain activations produced
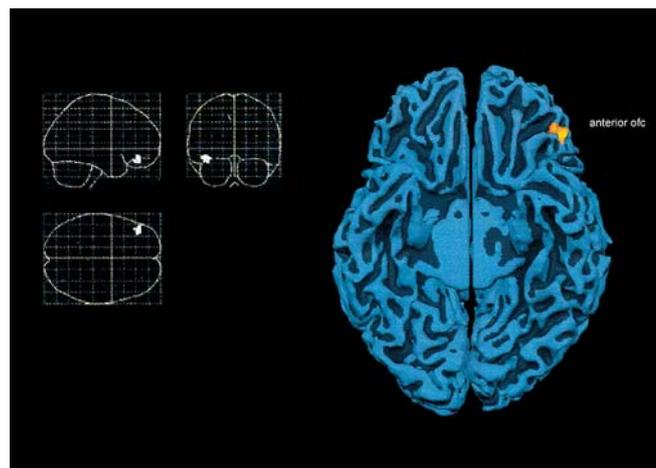
Figure 5. Results of an SPM analysis to show brain regions where significantly larger activations were found to the taste stimulus that was a combination of MSG (0.05 M) and IMP (0.005 M) than to the sum of the activations produced by the same stimuli delivered separately. The statistical analysis revealed a region of the orbitofrontal cortex ($-44,34,-18$; z = 3.49, $p < 0.05$ corrected for multiple comparisons with S.V.C). Left, Unmasked results in a glass brain. Right, Activation in the anterior orbitofrontal cortex (ofc) is shown rendered on the ventral surface of human cortical areas with the cerebellum removed. (From de Araujo et al., 2003.[54])
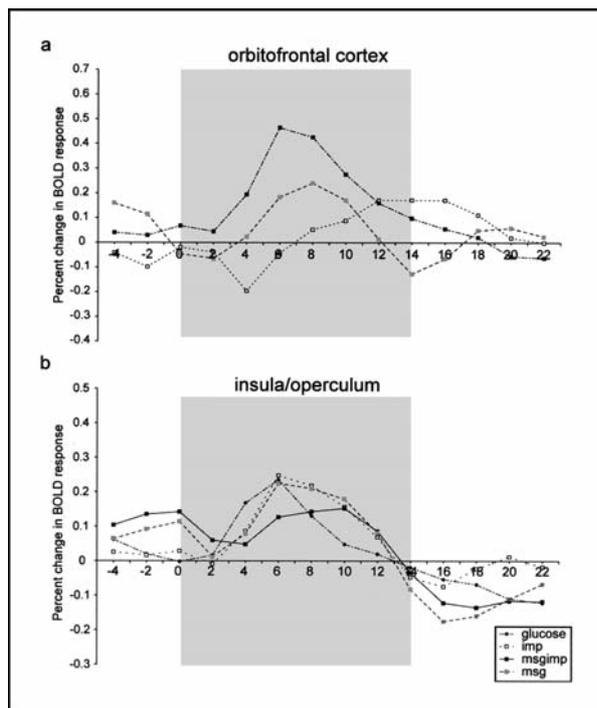
Figure 6. Time courses of cortical activation to taste. a, Time course (averaged across all 10 subjects) within the significant cluster of 30 activated voxels in the orbitofrontal cortex in the group analysis from the supra-additivity contrast showing the percent change in BOLD signal for MSGIMP, MSG, and IMP compared with the tasteless control. The peak voxel of the cluster was at x,y,z = −44,34,−18; with z = 3.49. b, Time course (averaged across all 10 subjects) within the significant cluster of voxels in the insular/opercular taste cortex (from the main effects of taste contrast shown in Figure 2, group effect across all 10 subjects, $p < 0.05$, corrected for multiple comparisons) averaged over a group of 53 voxels in the primary gustatory cortex (x,y,z = 52,12,10; z = 5.48). The percent changes in the BOLD signal for glucose, MSG, IMP, and MSGIMP compared with the tasteless control are shown. (From de Araujo et al., 2003.[54])

by three pleasant and three unpleasant odors. The pleasant odors chosen were linalyl acetate (floral, sweet), geranyl acetate (floral), and alpha-ionone (woody, slightly food-related). Chiral substances were used as racemates. The unpleasant odors chosen were hexanoic acid, octanol, and isovaleric acid, which were found to activate dissociable parts of the human brain.[61] Pleasant but not unpleasant odors were found to activate a medial region of the rostral orbitofrontal cortex (Figures 7 and 8). Further, there was a correlation between the subjective pleasantness ratings of the six odors given during the investigation with activation of a medial region of the rostral orbitofrontal cortex (Figure 9). In contrast, a correlation between the subjective unpleasantness ratings of the six odors was found in regions of the left and more lateral orbitofrontal cortex. Activation was also found in
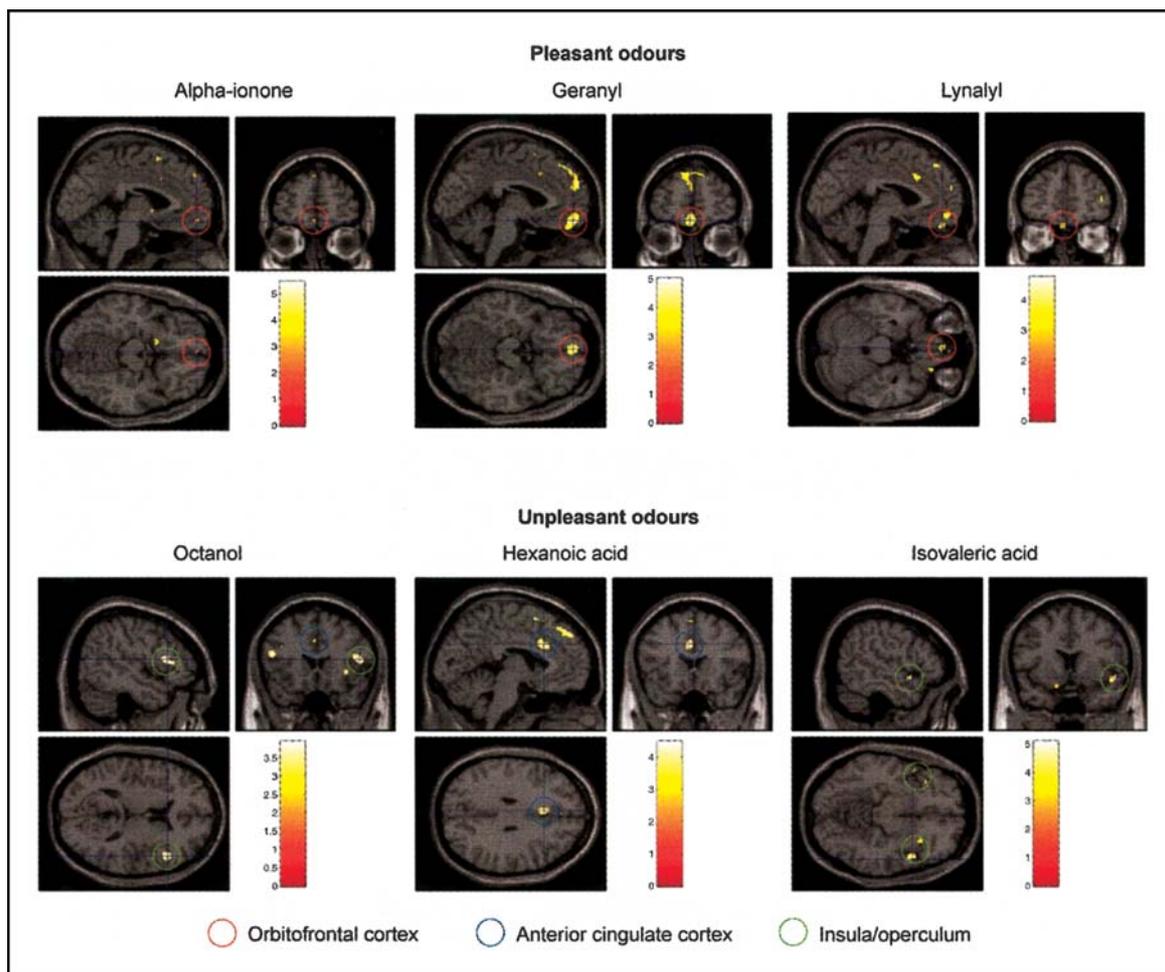
the anterior cingulate cortex, with a middle part of the anterior cingulate activated by both pleasant and unpleasant odors, and a more anterior part of the anterior cingulate cortex showing a correlation with the subjective pleasantness ratings of the odors.

These results provide evidence that there is a hedonic map of the sense of smell in brain regions such as the orbitofrontal cortex and cingulate cortex. It will be of interest in future studies to extend the range of odors to include perfumes and flavors to determine how they map onto the areas just described. It will also be interesting to investigate where flavors formed by a combination of olfactory and taste input are represented, and how cognitive factors affect the brain activations produced by odors.

The topological representation of the hedonic properties of sensory stimuli such as smell in the orbitofrontal cortex can be understood with some of the fundamental principles of computational neuroscience,[62,63] as follows. Given the evidence described above that the reward-related or affective properties of sensory stimuli, rather than, for example, the intensity of the stimuli, is represented in the orbitofrontal cortex, a topological map of the hedonic value of stimuli is produced in which neurons that have similar hedonic value are placed close together. This self-organizing map results from processes that occur in competitive networks, the building blocks of sensory systems, in which the neurons are coupled by short-range (~1 mm) excitation (implemented by the recurrent excitatory connections between cortical pyramidal cells) and longer-range inhibition (implemented by inhibitory interneurons).[62,63] Such self-organizing maps are a useful feature for brain connectivity, because they help to minimize the length of the connections between neurons that need to exchange information to perform their computations. It is for this reason, it is hypothesized, that neurons with similar hedonic value are placed close together. In the case of olfactory stimuli, this results in an activation region for pleasant olfactory stimuli (in the medial orbitofrontal cortex), and a separate activation region for unpleasant olfactory stimuli (more laterally in the orbitofrontal cortex). Of course, part of the support for such a map (i.e. a factor that helps different types of stimuli to be separated in the map) may arise because unpleasant olfactory stimuli may be more generally associated with other sensory inputs such as trigeminal inputs. Understanding this principle may be very valuable in helping to interpret the results of neuroimaging experiments.

Olfactory-Taste Convergence to Represent Flavor. To investigate where in the human brain interactions between taste and odor stimuli may be realized to implement flavor, we performed an event-related functional MRI study with sucrose and MSG taste and strawberry

Figure 7. Activations produced by individual pleasant and unpleasant odors. The figure shows group activations for each individual odor across 11 subjects with representative sagittal, axial, and coronal slices. The activations were thresholded at $p < 0.001$ to show the extent of the activations. The scale shows the t value. (From Rolls et al., 2003.[61])

and methional (chicken) odors delivered unimodally or in different combinations.[64] The brain regions that were activated by both taste and smell included parts of the caudal orbitofrontal cortex, amygdala, insular cortex, and adjoining areas, and the anterior cingulate cortex. It was shown that a small part of the anterior (putatively agranular) insula responds to unimodal taste and to unimodal olfactory stimuli, and that a part of the anterior frontal operculum is a unimodal taste area (putatively the primary taste cortex) not activated by olfactory stimuli. Activations to combined olfactory and taste stimuli where there was little or no activation to either alone (providing positive evidence for interactions between the olfactory and taste inputs) were found in a lateral anterior part of the orbitofrontal cortex. Correlations with consonance ratings for smell and taste combinations, and for their pleasantness, were found in a medial anterior part of the orbitofrontal cortex. These results provide evidence on the neural substrate for the convergence of taste and olfactory stimuli to produce flavor in humans and where

the pleasantness of flavor is represented in the human brain. It has also been shown that oral texture inputs converge into some of these systems in humans, activation of the insular primary taste cortex and the orbitofrontal cortex is related to the viscosity of texture in the mouth, and that fat texture activates the orbitofrontal cortex and perigenual cingulate cortex.[65]

Emotion. The brain areas where the pleasantness or affective value of smell and taste are represented are closely related to the brain areas involved in emotion. Emotions can usefully be defined as states elicited by rewards and punishers,[1] and olfactory and taste stimuli can be seen as some of the classes of stimuli that can produce emotional states. Part of the importance of the orbitofrontal cortex in emotion is that it represents some primary (or unlearned) rewards and punishers, such as taste and pleasant touch,[51,66] and also learns the association between previously neutral stimuli and primary reinforcers. This type of learning is called stimulus-reinforcement association learning, and is fundamental in
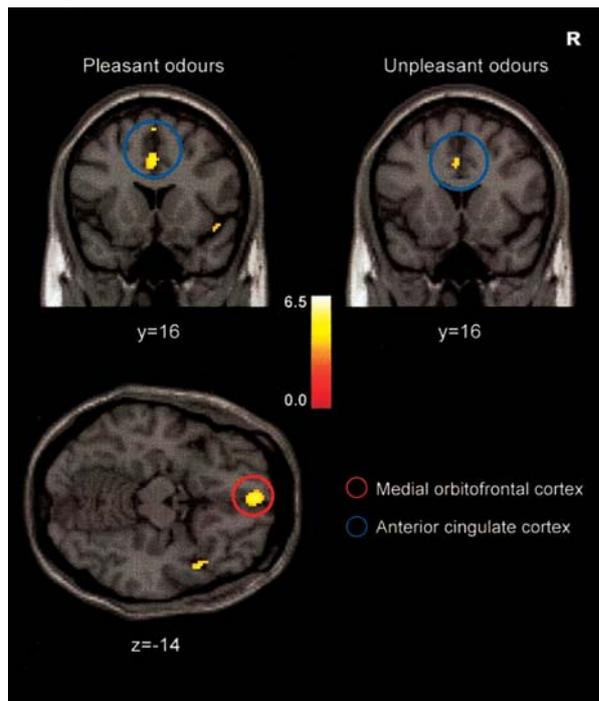
Figure 8. Group conjunction results for pleasant and unpleasant odor activations. On the top left is shown the activation to pleasant odors in the anterior cingulate cortex (x,y,z = 2,20,32; z = 4.06; $p < 0.05$, S.V.C.) (coronal slice), and on the bottom left is shown the activation to pleasant odors in the medio-rostral region of the orbitofrontal cortex (x,y,z = 0,52,–14; z = 4.51) (horizontal slice). On the right is shown the activation to unpleasant odors in the anterior cingulate cortex (x,y,z = –2,16,36; z = 4.27; $p < 0.05$, S.V.C.). The activations were thresholded at $p < 0.0001$ to show the extent of the activations. (From Rolls et al., 2003.[61])

learned emotional states. In addition to reinforcers such as taste, odor, and touch, quite abstract emotion-producing stimuli are represented in other parts of the orbitofrontal cortex. For example, the medial orbitofrontal cortex is activated in humans according to how much money is won in a probabilistic reward/punishment task, and the lateral orbitofrontal cortex is activated according to how much money is lost in the same task.[67]

We are starting to understand not only where the affective value of smell and taste is represented in the brain, but also how these representations fit into a wider picture of the brain processes underlying emotion.

Conclusion

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 (includ-

ing human) 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. The orbitofrontal cortex contains not only representations of taste and olfactory stimuli, but also of other types of rewarding and punishing stimuli, including the texture and temperature of food and pleasant touch. All of these inputs, together with the functions of the orbitofrontal cortex in stimulus-reward and stimulus-punishment association learning, provide a basis for understanding its functions in emotional and motivational behavior.[1,25,26,68,69] Moreover, the orbitofrontal cortex shows responses that reflect combinations of sensory inputs and help us to understand the ways in which sensory inputs are combined, sometimes nonlinearly, to produce complex representations reflecting combinations of particular sensory inputs.
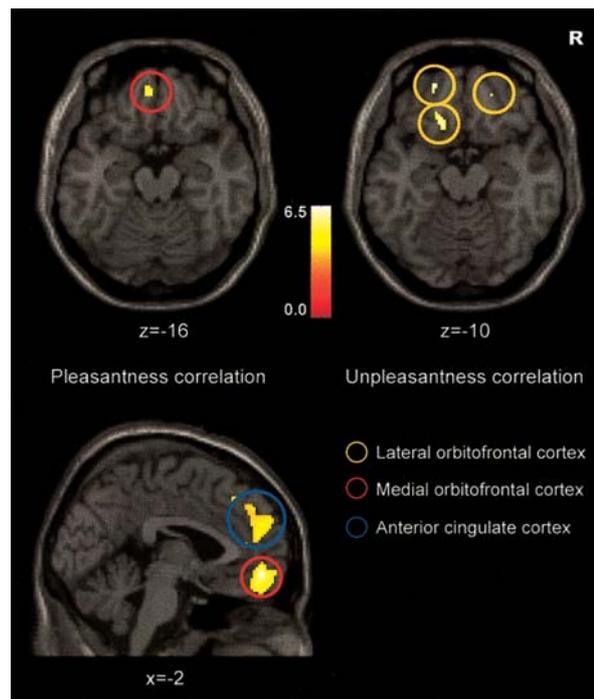
Figure 9. Random effects group correlation analysis of the BOLD signal with the subjective pleasantness ratings. On the left is shown the region of the medio-rostral orbitofrontal (peak at x,y,z = –2,52,–10; z = 4.28) correlating positively with pleasantness ratings, as well as the region of the anterior cingulate cortex on the bottom left. On the right is shown the regions of the left more lateral orbitofrontal cortex (peaks at x,y,z = –20,54,–14; z = 4.26 and –16,28,–18; z = 4.08) correlating negatively with pleasantness ratings. The activations were thresholded at $p < 0.0001$ to show the extent of the activations. (From Rolls et al., 2003.[61])

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