# Flavor: brain processing

8

*Edmund T. Rolls* [1,2,*]
[1]Oxford Centre for Computational Neuroscience, Oxford, United Kingdom; [2]University of Warwick, Department of Computer Science, Coventry, United Kingdom

## 8.1 Introduction

A schematic diagram of the taste and related olfactory, somatosensory, and visual pathways in the primate brain is shown in Fig. 8.1, with a view of their locations in the brain in Fig. 8.2. Neurophysiological studies in primates provide a foundation for understanding taste, olfactory, and flavor processing and neuroimaging in humans, for investigation of the tuning of individual neurons provide the fundamental information about how these stimuli are encoded in different brain areas using a sparsely distributed representation in which each neuron is tuned differently to other neurons (Kadohisa et al., 2005; Rolls, 2008a, 2015a, 2016a, 2021a; Rolls et al., 2010a; Rolls and Treves, 2011). Studies in nonhuman primates are especially relevant (Rolls, 2014a, 2015b, 2016b, 2021a), as the taste pathways in primates proceed via the thalamus to the taste cortex whereas in rodents there is a pontine taste area which has direct subcortical connections (Small and Scott, 2009; Rolls, 2016b, 2021a); effects of satiety are found peripherally in the nucleus of the solitary tract in rodents (Rolls and Scott, 2003; Scott and Small, 2009; Rolls, 2016b); and rodents do not have the major part of the primate including human orbitofrontal cortex, the granular part (Wise, 2008; Rolls, 2014a, 2019b, 2021a) (see Fig. 8.3). This makes the rodent a poor model of taste, olfactory, and flavor processing in the brains of humans and other primates (Rolls, 2016c, 2021a).

## 8.2 Flavor processing in the primate brain

### *8.2.1 Taste processing*

#### *8.2.1.1 Pathways*

A schematic diagram of the taste and related olfactory, somatosensory, and visual pathways in primates is shown in Figs. 8.1 and 8.2 shows where these pathways are on a primate brain. 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 the research that will be described.

* Author contact details: Email: Edmund.Rolls@oxcns.org; Url: https://www.oxcns.org.

**Flavor.** https://doi.org/10.1016/B978-0-323-89903-1.01003-3

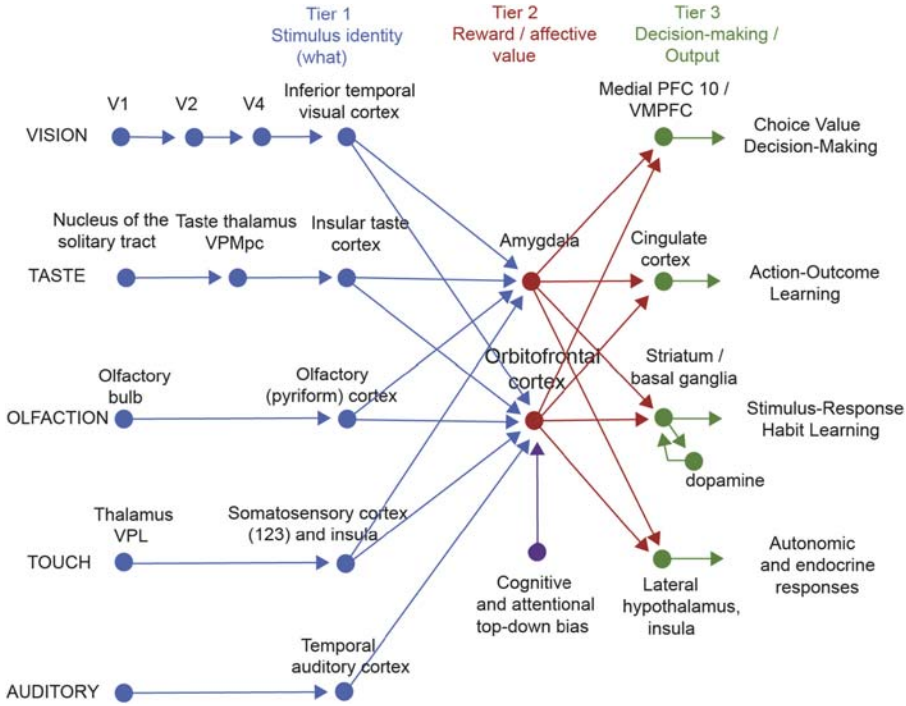


**Figure 8.1** Schematic diagram showing some of the gustatory, olfactory, visual, and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex and the secondary olfactory cortex are within the orbitofrontal cortex. V1 - primary visual cortex. V4 - visual cortical area V4. PreGen Cing – pregenual cingulate cortex. Tier 1: the column of brain regions including and below the inferior temporal visual cortex represents brain regions in which "what" stimulus is present is made explicit in the neuronal representation, but not its reward or affective value which are represented in the next tier of brain regions (Tier 2), the orbitofrontal cortex and amygdala, and in the anterior cingulate cortex. In Tier 3 areas beyond these such as medial prefrontal cortex area 10, choices or decisions about reward value are taken, with the mechanisms described elsewhere (Rolls and Deco, 2010; Rolls, 2014a, 2021a). Top-down control of affective response systems by cognition and by selective attention from the dorsolateral prefrontal cortex is also indicated. Medial PFC area 10 – medial prefrontal cortex area 10; VPMpc – ventralposteromedial thalamic nucleus.

### *8.2.1.2 The primary taste cortex*

Rolls (2016b) has 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 (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

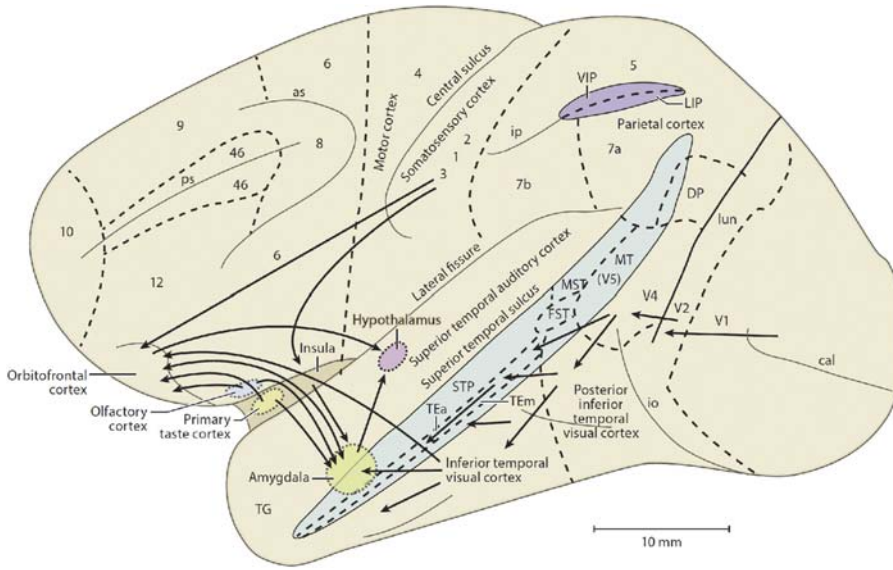


**Figure 8.2** Some of the pathways involved in processing food-related stimuli are shown in this lateral view of the primate brain (macaque). Connections from the primary taste and olfactory cortices to the orbitofrontal cortex and amygdala are shown. Connections are also shown in the "ventral visual system" from V1 to V2, V4, the inferior temporal visual cortex, etc., with some connections reaching the amygdala and orbitofrontal cortex. In addition, connections from the somatosensory cortical areas 1, 2, and 3 that reach the orbitofrontal cortex directly and via the insular cortex, and that reach the amygdala via the insular cortex, are shown. *AIT*, anterior inferior temporal cortex; *as*, arcuate sulcus; *cal*, calcarine sulcus; *cs*, central sulcus; *FST*, visual motion processing area; *io*, inferior occipital sulcus; *ip*, intraparietal sulcus (which has been opened to reveal some of the areas it contains); *lf*, lateral (or Sylvian) fissure; *LIP*, lateral intraparietal area; *lun*, lunate sulcus; *MST*, visual motion processing area; *MT*, visual motion processing area (also called V5); *PIT*, posterior inferior temporal cortex; *ps*, principal sulcus; *STP*, superior temporal plane; *sts*, superior temporal sulcus (which has been opened to reveal some of the areas it contains); *TA*, architectonic area including auditory association cortex; *TE*, architectonic area including high order visual association cortex, and some of its subareas TEa and TEm; *TEO*, architectonic area including posterior visual association cortex; *TG*, architectonic area in the temporal pole; *V1−V4*, visual areas V1−V4; *VIP*, ventral intraparietal area. The numerals refer to architectonic areas, and have the following approximate functional equivalence: 1, 2, 3, somatosensory cortex (posterior to the central sulcus); 4, motor cortex; 5, superior parietal lobule; 7a, inferior parietal lobule, visual part; 7b, inferior parietal lobule, somatosensory part; 6, lateral premotor cortex; 8, frontal eye field; 12, part of orbitofrontal cortex; 46, dorsolateral prefrontal cortex.

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 (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; Rolls, 2016b).

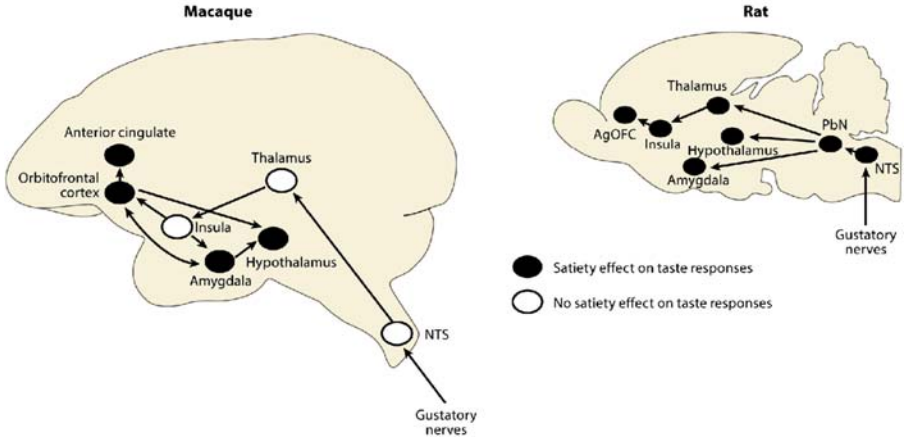


**Figure 8.3** Taste pathways in the macaque and rat. In the *macaque*, gustatory information reaches the nucleus of the solitary tract (NTS), which projects directly to the taste thalamus (ventral posteromedial nucleus, pars parvocellularis, VPMpc) which then projects to the taste cortex in the anterior insula (Insula). The insular taste cortex then projects to the orbitofrontal cortex and amygdala. The orbitofrontal cortex projects taste information to the anterior cingulate cortex. Both the orbitofrontal cortex and the amygdala project to the hypothalamus (and to the ventral striatum). In macaques, feeding to normal self-induced satiety does not decrease the responses of taste neurons in the NTS or taste insula (and by inference not VPMpc) (see text). In the *rat*, in contrast, the NTS projects to a pontine taste area, the parabrachial nucleus (PbN). The PbN then has projections directly to a number of subcortical structures, including the hypothalamus, amygdala, and ventral striatum, thus bypassing thalamo-cortical processing. The PbN in the rat also projects to the taste thalamus (VPMpc), which projects to the rat taste insula. The taste insula in the rat then projects to an agranular orbitofrontal cortex (AgOFC), which probably corresponds to the most posterior part of the primate OFC, which is agranular. (In primates, most of the orbitofrontal cortex is granular cortex, and the rat may have no equivalent to this (Wise, 2008; Small and Scott, 2009; Passingham and Wise, 2012; Rolls, 2019b, 2021a). In the rat, satiety signals such as gastric distension and satiety-related hormones decrease neuronal responses in the NTS (see text), and by inference therefore in the other brain areas with taste-related responses, as indicated in the figure.

### *8.2.1.3 The secondary taste cortex*

A secondary cortical taste area in primates was discovered by Rolls et al. (1990) in the orbitofrontal cortex, extending several millimeters in front of the primary taste cortex, which projects anatomically to the orbitofrontal cortex (Baylis et al., 1995). Different neurons in the orbitofrontal cortex respond not only to each of the four classical prototypical tastes sweet, salt, bitter, and sour (Rolls, 1997; Rolls and Scott, 2003), but also 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; Roper and Chaudhari, 2017), 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 and Baylis, 1994; Rolls et al., 1998; McCabe and Rolls, 2007; Rolls, 2009), to the flavor of protein. In addition, other neurons respond to water, and others to somatosensory stimuli including astringency as exemplified by tannic acid (Critchley and Rolls, 1996c), and capsaicin (Rolls et al., 2003b; Kadohisa et al., 2004). Taste responses are found in a large mediolateral extent of the orbitofrontal cortex (Critchley and Rolls, 1996c; Pritchard et al., 2005; Rolls, 2008a, 2015b; Rolls and Grabenhorst, 2008).

#### 8.2.1.4 *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 of the important ways by which motivational behavior is controlled (Rolls, 2014b, 2016c). The subjective correlate of this modulation is that food tastes pleasant when hungry, and tastes hedonically neutral when it has been eaten to satiety. Following Edmund Rolls' discovery of sensory-specific satiety revealed by the selective reduction in the responses of lateral hypothalamic neurons to a food eaten to satiety (Rolls, 1981; Rolls et al., 1986), it has been shown that this is implemented in a region that projects to the hypothalamus, the orbitofrontal (secondary taste) cortex, for the taste, odor, and sight of food (Rolls et al., 1989; Critchley and Rolls, 1996a; Rolls, 2015b).

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; Rolls, 2015b, 2019b). In addition to provide 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), it is likely that visceral and other satiety-related signals reach the orbitofrontal cortex (as indicated in Fig. 8.1) (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, 2014a, 2019b).

### 8.2.2 *The representation of flavor: convergence of olfactory, taste, and visual inputs in the orbitofrontal cortex*

Taste and olfactory pathways are brought together in the orbitofrontal cortex where flavor is formed by learned associations at the neuronal level between these inputs (see Fig. 8.1) (Rolls and Baylis, 1994; Critchley and Rolls, 1996b; Rolls et al., 1996b, 1996c; Verhagen et al., 2004; Rolls, 2011a, 2014a). Visual inputs also become

associated by learning in the orbitofrontal cortex with the taste of food to represent the sight of food and contribute to flavor (Thorpe et al., 1983; Rolls, 1996; Rolls et al., 1996b). 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, 1996a).

### 8.2.3 The texture of food, including fat texture

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) (see example in Fig. 8.4), and others independently encode the particulate quality of food in the mouth, produced quantitatively, for example, by adding 20−100 μm microspheres to methyl cellulose (Rolls et al., 2003b). Very interestingly, some neurons encode the oral texture of fat (Rolls et al., 1999; Verhagen et al., 2003; Rolls, 2011c, 2015b), and for a population of oral fat-sensitive neurons this is independent of texture, as illustrated in Fig. 8.5 (Rolls et al., 2018). The oral fat-sensitive neurons encode fat by the coefficient of sliding friction (Rolls et al., 2018; Rolls, 2020b). This discovery is very likely to be important in the design of foods in future, which can be designed to produce the pleasant mouth feel of fat with designed nutritional content (Rolls, 2020b). These oral fat-encoding neurons are separated from a small population that responds to free fatty acids, and which may be important instead in encoding "off" flavors of food (Rolls et al., 1999; Verhagen et al., 2003; Rolls, 2011c, 2015b, 2020b). Somatosensory signals that transmit information about capsaicin (chilli) and astringency are also reflected in neuronal activity in these cortical areas (Critchley and Rolls, 1996c; Kadohisa et al., 2004, 2005). Different neurons respond to different combinations of these food texture inputs and taste, with examples shown in Fig. 8.4.

In addition, we have shown 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 (Kadohisa et al., 2004, 2005).

## 8.3 Flavor processing in the human brain: functional neuroimaging

### 8.3.1 Taste

In humans it has been shown (Rolls, 2012b, 2014a, 2015a, 2015b) 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 (O'Doherty et al., 2001; de Araujo et al., 2003b; Small, 2010; Rolls, 2016b), 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., 2003b; Rolls, 2005b; Rolls, 2008a). We pioneered the use of a tasteless control with the same ionic constituents as saliva

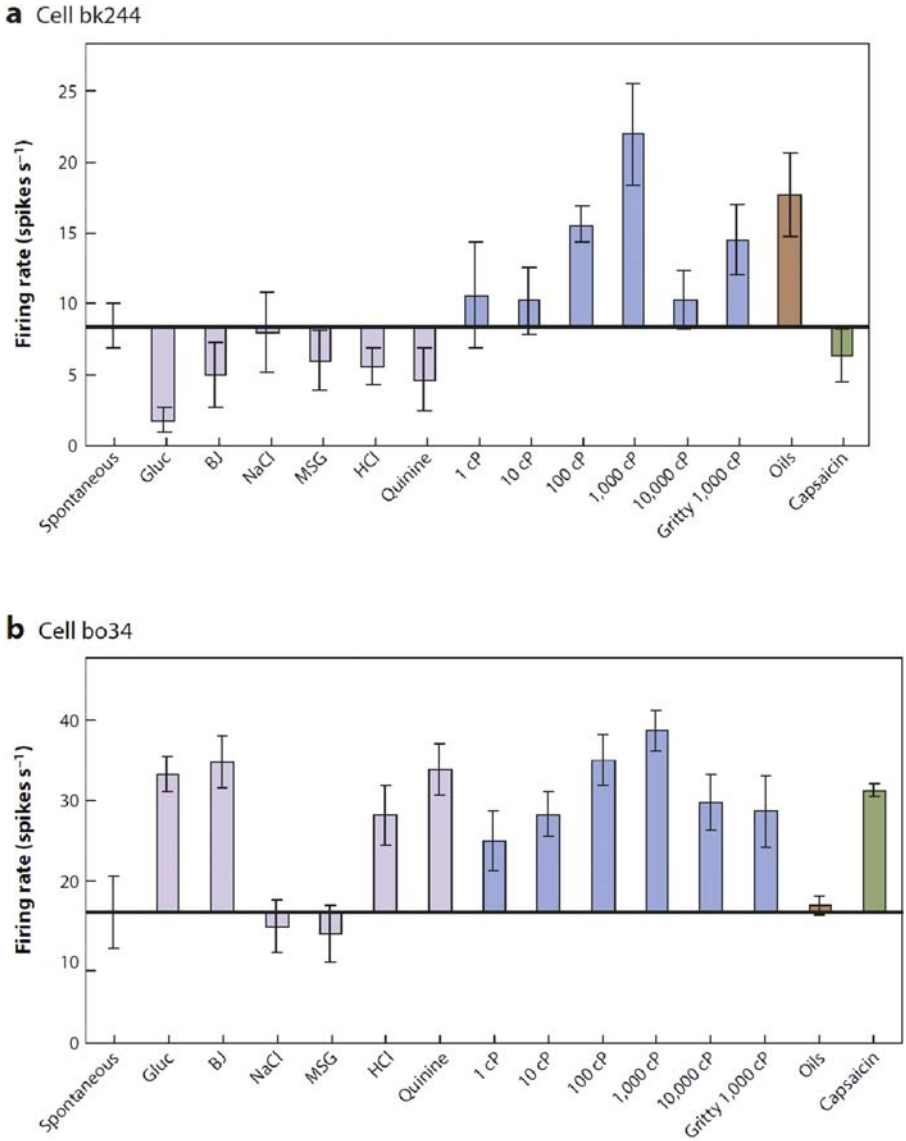


**Figure 8.4** Above. Firing rates (mean ± s.e.m.) of macaque orbitofrontal cortex viscosity-sensitive neuron bk244 which did not have taste responses. The firing rates are shown to the viscosity series (carboxymethylcellulose in the range 1−10,000 centiPoise), to the gritty stimulus (carboxymethylcellulose with Fillite microspheres), to the taste stimuli 1M glucose (Gluc), 0.1M NaCl, 0.1M MSG, 0.01M HCl and 0.001M QuinineHCl, and to fruit juice (BJ). Spont = spontaneous firing rate. Below. Firing rates (mean ± s.e.m.) of viscosity-sensitive neuron bo34 which had no response to the oils (mineral oil, vegetable oil, safflower oil, and coconut oil, which have viscosities which are all close to 50 cP). The neuron did not respond to the gritty stimulus in a way that was

(O'Doherty et al., 2001; de Araujo et al., 2003b), as water can activate some neurons in cortical taste areas (Rolls et al., 1990) and can activate the taste cortex (de Araujo et al., 2003b). Within individual subjects separate areas of the orbitofrontal cortex are activated by sweet (pleasant) and salt (unpleasant) tastes (O'Doherty et al., 2001).

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 anterior cingulate cortex represents the reward value of taste, in that activations there correlate with the subjective pleasantness of taste (Grabenhorst and Rolls, 2008; Grabenhorst et al., 2008a; Rolls, 2015b, 2016b) (Fig. 8.6).

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

Umami taste stimuli, of which an exemplar is monosodium glutamate (MSG) and which capture what is described as the taste of protein, activate the insular (primary), orbitofrontal (secondary), and anterior cingulate (tertiary; Rolls, 2008a) taste cortical areas (de Araujo et al., 2003a). When the nucleotide 0.005M inosine 5'-monophosphate (IMP) was added to MSG (0.05M), the blood oxygenation-level dependent (BOLD) signal in an anterior part of the orbitofrontal cortex showed supralinear additivity, and this may reflect the subjective enhancement of umami taste that has been described when IMP is added to MSG (Rolls, 2009). 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 (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, and that the combination of sensory stimuli may be especially represented in particular brain regions, and may help to make the food pleasant.

### 8.3.2 Odor

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

unexpected given the viscosity of the stimulus, was taste tuned, and did respond to capsaicin. Other neurons respond to fats and other oils independently of viscosity (see text Rolls et al., 1999; Verhagen et al., 2003; Rolls et al., 2018; Rolls, 2020b).
After Rolls, E.T., Verhagen, J.V. & Kadohisa, M., 2003b. Representations of the texture of food in the primate orbitofrontal cortex: neurons responding to viscosity, grittiness and capsaicin. J. Neurophysiol. 90, 3711−3724.

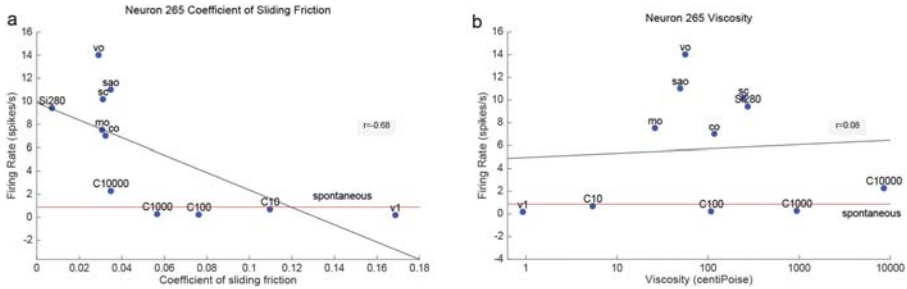


**Figure 8.5** An orbitofrontal cortex neuron with responses nonlinearly correlated with decreases in the coefficient of sliding friction (A). The neuron responds almost not at all until the coefficient of sliding friction falls below 0.04. The neuron is thus very selective for fat texture, because of its nonlinear response in relation to the coefficient of sliding friction. The linear regression line has a correlation of $r = -0.68$ ($P = .02$). (B): There is a much weaker relation to viscosity ($r = 0.08$, $P = .82$), with the oils producing a larger response than predicted linearly. Further, a regression line through the nonoil stimuli would have a lower slope. C10−C10000: carboxymethyl cellulose with the nominal viscosity of 10, 100, 1000, and 10,000 cP v1: water (1 cP). co: coconut oil; mo: mineral oil; sao: safflower oil; vo: vegetable oil; sc: single cream. Si280: silicone oil with a nominal viscosity of 280 cP. Li: linoleic acid; La; lauric acid. The *horizontal red line* indicates the spontaneous firing rate. The Pearson correlation between the firing rate of each neuron and (A) the coefficient of sliding friction, and (B) the viscosity, was calculated to show to what extent the firing of a neuron reflected one or other of these measures. Linear regression lines are shown in the figure for how the firing rates were related to the coefficient of sliding friction, or to the log of the viscosity.
After Rolls, E.T., Mills, T., Norton, A., et al. 2018. Neuronal encoding of fat using the coefficient of sliding friction in the cerebral cortex and amygdala. Cereb Cortex 28, 4080−4089.

of the orbitofrontal cortex by olfactory stimuli (Zatorre et al., 1992; Francis et al., 1999; Rolls et al., 2003a). 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), and this has been confirmed by Gottfried et al. (personal communication, see Gottfried (2015)), who also showed that activations in the pyriform (primary olfactory) cortex were not decreased by odor devaluation by satiety. Further, pleasant odors tend to activate the medial, and unpleasant odors the more lateral, orbitofrontal cortex (Rolls et al., 2003a), adding to the evidence that it is a principle that there is a hedonic map in the orbitofrontal cortex, and also in the anterior cingulate cortex, which receives inputs from the orbitofrontal cortex (Rolls and Grabenhorst, 2008; Grabenhorst and Rolls, 2011). The primary olfactory (pyriform) cortex represents the identity and intensity of odor in that activations there correlate with the subjective intensity of the odor, and the orbitofrontal and anterior cingulate cortex represent the reward value of odor, in that activations there correlate with the subjective pleasantness (medially) or unpleasantness (laterally) of odor (Rolls et al., 2003a, 2008, 2009; Grabenhorst et al., 2007; Rolls and Grabenhorst, 2008; Grabenhorst and Rolls, 2011; Rolls, 2019b, 2021a). Indeed, the reward-related medial orbitofrontal cortex/ventromedial prefrontal cortex connects preferentially with the reward-related pregenual anterior cingulate cortex;

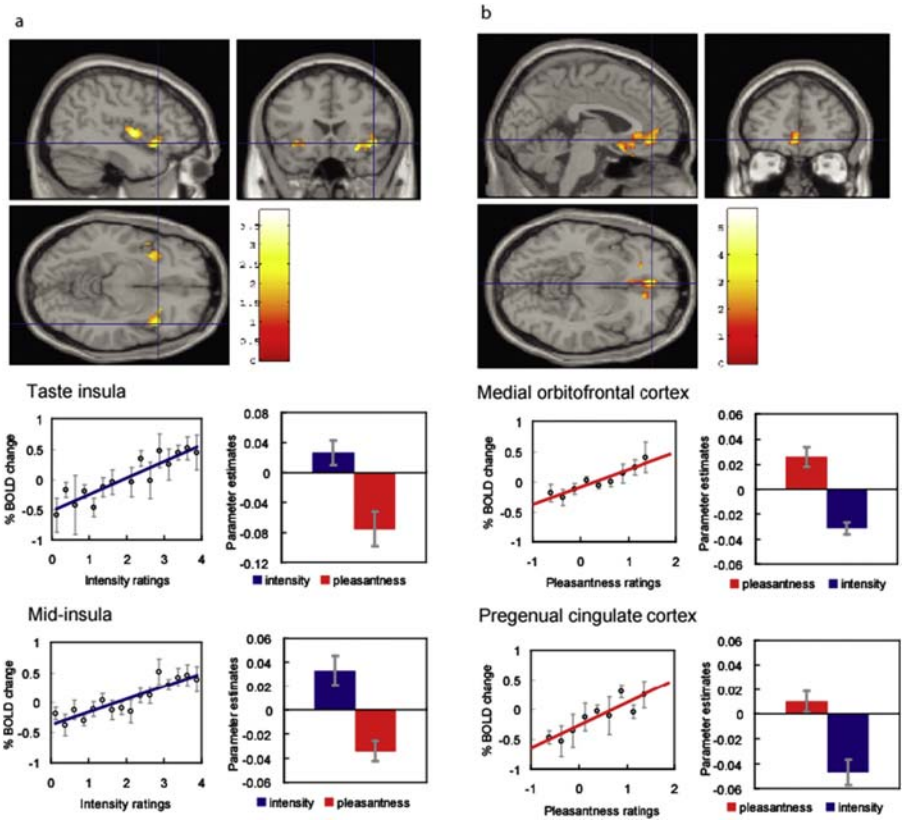


**Figure 8.6** Effect of paying attention to the pleasantness versus the intensity of a taste stimulus. (A) Top: A significant difference related to the taste period was found in the taste insula at [42 18 −14] $z = 2.42$ $P < .05$ (indicated by the cursor) and in the mid-insula at [40 −2 4] $z = 3.03$ $P < .025$. Middle: Taste Insula. Right: The parameter estimates (mean ± sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the taste insula $t = 4.5$, df = 10, $P = .001$. Left: The correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate ($r = 0.91$, df = 14, $P << .001$). Bottom: Mid-Insula. Right: The parameter estimates (mean ± sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the mid-insula $t = 5.02$, df = 10, $P = .001$. Left: The correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate ($r = 0.89$, df = 15, $P << .001$). The taste stimulus, monosodium glutamate, was identical on all trials. (B) Top: A significant difference related to the taste period was found in the medial orbitofrontal cortex at [−6 14 −20] $z = 3.81$ $P < .003$ (toward the back of the area of activation shown) and in the pregenual cingulate cortex at [−4 46 −8] $z = 2.90$ $P < .04$ (at the cursor). Middle: Medial orbitofrontal cortex. Right: The parameter estimates (mean ± sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the orbitofrontal cortex $t = 7.27$, df = 11, $P < 10^{-4}$. Left: The

and the punishment/nonreward-related lateral orbitofrontal cortex connects preferentially with the punishment/nonreward-related supracallosal anterior cingulate cortex (Du et al., 2020; Hsu et al., 2020; Rolls et al., 2020; Rolls et al., 2022). The concept is that the orbitofrontal cortex encodes the reward value of the stimuli, and the anterior cingulate cortex uses these inputs to reinforce actions that are being made and signaled to the posterior cingulate cortex from the parietal cortex (Rolls, 2019a).

### 8.3.3 Olfactory-taste convergence to represent flavor, and the influence of satiety on flavor representations

Taste and olfactory conjunction analyses, and the measurement of supraadditive effects indicating convergence and interactions, showed convergence for taste (sucrose) and odor (strawberry) in the orbitofrontal and anterior cingulate cortex, and activations in these regions were correlated with the pleasantness ratings given by the participants (de Araujo et al., 2003c; Small et al., 2004; Small and Prescott, 2005). These results provide evidence on the neural substrate for the convergence of taste and olfactory stimuli to produce flavor in humans, and on where the pleasantness of flavor is represented in the human brain. The first region where the effects of this convergence are found is in an agranular part of what cytoarchitecturally is the insula (Ia) that is topologically found in the posterior orbitofrontal cortex, though it is anterior to the insular taste cortex, and posterior to the granular orbitofrontal cortex (see Fig. 8.6) (de Araujo et al., 2003c).

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

To assess how satiety influences the brain activations to a whole food which produces taste, olfactory, and texture stimulation, we measured brain activation by whole foods before and after the food is eaten to satiety. The foods eaten to satiety were either chocolate milk or tomato juice. A decrease in activation by the food eaten to satiety

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, $P = .001$). The taste stimulus, 0.1M monosodium glutamate, was identical on all trials. After Grabenhorst, F. & Rolls, E.T. 2008. Selective attention to affective value alters how the brain processes taste stimuli. Eur. J. Neurosci. 27, 723−729.

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 which is an important component of appetite and the control of food intake (Rolls, 2014a, 2016c) are represented in the orbitofrontal cortex.

### 8.3.4 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). 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 (de Araujo and Rolls, 2004). We have shown that the pleasantness and reward value of fat texture is represented in the mid-orbitofrontal and anterior cingulate cortex, where activations are correlated with the subjective pleasantness of oral fat texture (Rolls, 2009, 2010b; Grabenhorst et al., 2010) (Fig. 8.7). This provides a foundation for studies of whether activations in the fat reward system are heightened in people who tend to become obese (Rolls, 2012b). Interestingly, high fat stimuli with a pleasant flavor increase the coupling of activations between the orbitofrontal cortex and somatosensory cortex, suggesting a role for the somatosensory cortex in processing the sensory properties of food in the mouth (Grabenhorst and Rolls, 2014).

### 8.3.5 The sight of food

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

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

To what extent does cognition influence the hedonics of food-related stimuli, and how far down into the sensory system does the cognitive influence reach? To address this, we performed an fMRI investigation in which the delivery of a standard test odor (isovaleric acid combined with cheddar cheese odor, presented orthonasally using an olfactometer) was paired with a descriptor word on a screen, which on different trials was "Cheddar cheese" or "Body odor." Participants rated the affective value of the test odor as significantly more pleasant when labeled "Cheddar Cheese" than when labeled "Body odor," and these effects reflected activations in the medial orbitofrontal cortex

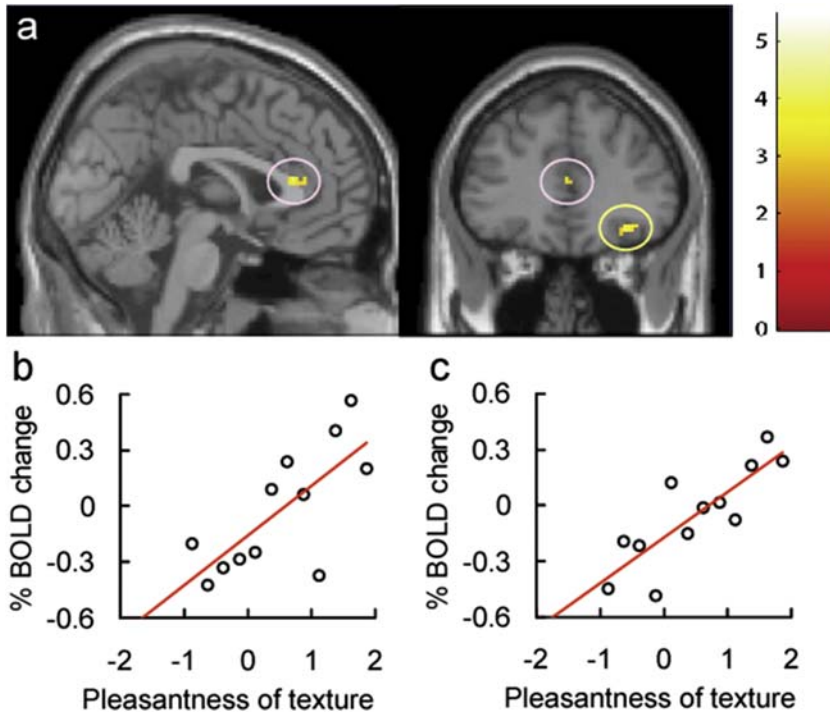


**Figure 8.7** Brain regions in which the activations were correlated with the subjective pleasantness of fat texture: Mid-orbitofrontal cortex ([32 34 −14] $z = 3.38$ $P = .013$) (A) yellow circle, (C) showing the relation between the % change in the BOLD signal and the rating of the pleasantness of the texture) and anterior cingulate cortex ([2 30 14] $z = 3.22$ $P = .016$) (A, pink circles, and B).
After Grabenhorst, F. & Rolls, E.T. 2010. Attentional modulation of affective vs sensory processing: functional connectivity and a top-down biased activation theory of selective attention. J. Neurophysiol. 104, 1649−1660; Grabenhorst, F., Rolls, E.T., Parris, B.A., et al. 2010. How the brain represents the reward value of fat in the mouth. Cereb Cortex 20, 1082−1091.

(OFC)/rostral anterior cingulate cortex (ACC) that had correlations with the pleasantness ratings (de Araujo et al., 2005). The implication is that cognitive factors can have profound effects on our responses to the hedonic and sensory properties of food, in that these effects are manifest quite far down into sensory and hedonic processing (in the orbitofrontal cortex, see Fig. 8.1), so that hedonic representations of odors are affected (de Araujo et al., 2005).

Similar cognitive effects and mechanisms have now been found for the taste and flavor of food, where the cognitive word-level descriptor was, for example, "rich delicious flavor" and activations to flavor were increased in the orbitofrontal cortex and regions to which it projects including the pregenual cingulate cortex and ventral striatum, but were not influenced in the insular primary taste cortex where activations reflected the intensity (concentration) of the stimuli (Grabenhorst et al., 2008a) (see Fig. 8.8).

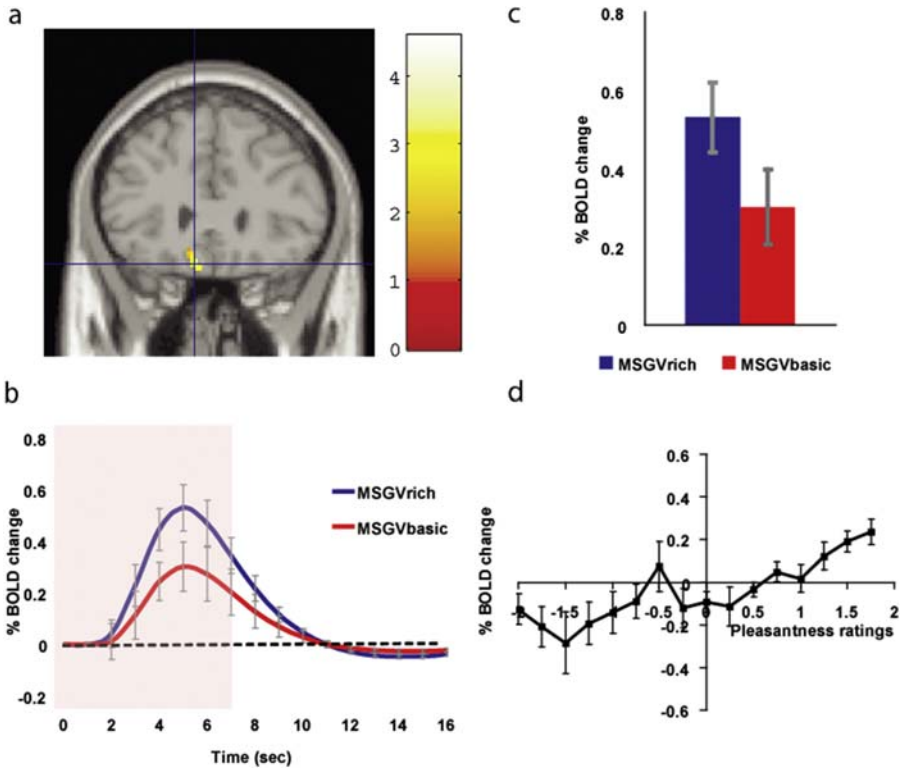


**Figure 8.8** Cognitive modulation of flavor reward processing in the brain. (A) The medial orbitofrontal cortex was more strongly activated when a flavor stimulus was labeled "rich and delicious flavor" (MSGVrich) than when it was labeled "boiled vegetable water" (MSGVbasic) ([−8 28 −20]). (The flavor stimulus, MSGV, was the taste 0.1M MSG + 0.005M inosine 5'monophosphate combined with a consonant 0.4% vegetable odor). (B) The timecourse of the BOLD signals for the two conditions. (C) The peak values of the BOLD signal (mean across subjects ± sem) were significantly different ($t = 3.06$, df = 11, $P = .01$). (D) The BOLD signal in the medial orbitofrontal cortex was correlated with the subjective pleasantness ratings of taste and flavor, as shown by the SPM analysis, and as illustrated (mean across subjects ±sem, $r = 0.86$, $P < .001$).
After Grabenhorst, F., Rolls, E.T. & Bilderbeck, A. 2008a. How cognition modulates affective responses to taste and flavor: top down influences on the orbitofrontal and pregenual cingulate cortices. Cereb Cortex 18, 1549−1559.

### 8.3.7 *Effects of selective attention to affective value versus intensity on representations of taste, olfactory, and flavor processing*

We have found that with taste, flavor, and olfactory food-related stimuli, selective attention to pleasantness modulates representations in the orbitofrontal cortex (see Fig. 8.6), whereas selective attention to intensity modulates activations in areas such

as the primary taste cortex (Grabenhorst and Rolls, 2008; Rolls et al., 2008). Thus, depending on the context in which tastes and odors are presented and whether affect is relevant, the brain responds to a taste, odor or flavor differently. These findings show that when attention is paid to affective value, the brain systems engaged to represent the stimulus are different from those engaged when attention is directed to the physical properties of a stimulus such as its intensity.

The source of the top-down modulation by attention of the orbitofrontal cortex appears to be the lateral prefrontal cortex, as shown by PPI (psychophysiological interaction) analyses (Grabenhorst and Rolls, 2010) and Granger causality analyses (Ge et al., 2012; Luo et al., 2013). The mechanism probably involves a weak top-down biased competition effect on the taste and olfactory processing (Desimone and Duncan, 1995; Deco and Rolls, 2005; Rolls, 2008b). Because whole streams of cortical processing are influenced (orbitofrontal and cingulate cortex, and even their coupling to the primary taste cortex, by pleasantness-related processing; and insular taste cortex and the mid-insula by intensity-related processing (Grabenhorst and Rolls, 2010; Luo et al., 2013)), the process has been described as a biased activation model of attention (Grabenhorst and Rolls, 2010; Rolls, 2013).

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

### 8.3.8 Individual differences in flavor processing in the brain

There are some fascinating differences in the brain systems that respond to food flavor in different individual humans.

There are age-related differences in the acceptability of foods and beverages (Birch, 1999; Hetherington et al., 2011). To examine the neural foundations underlying these age-related differences in the acceptability of different flavors and foods, an fMRI study was performed to investigate brain and hedonic responses to orange juice, orange soda, and vegetable juice in three different age groups: Young (22), Middle (40), and Elderly (60 years) (Rolls et al., 2015). Orange juice and orange soda were found to be liked by all age groups, while vegetable juice was disliked by the Young, but liked by the Elderly. In the insular primary taste cortex, the activations to these stimuli were similar in the three age groups, indicating that the differences in liking for these stimuli between the three groups were not represented in this first stage of cortical taste processing. In the agranular insula (anterior to the insular primary taste cortex) where flavor is represented, the activations to the stimuli were similar in the Elderly, but in the Young the activations were larger to the vegetable juice than to the orange drinks; and the activations here were correlated with the unpleasantness

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

In another example, it has been shown that there are larger responses in regions such as the orbitofrontal cortex and anterior cingulate cortex to the sight or taste of chocolate in chocolate cravers (Rolls and McCabe, 2007).

In another investigation, resting state functional connectivity was measured to investigate whether even when food is not being presented, there are individual, different, regions in the brain that relate to the liking for food and then perhaps as a consequence of that to obesity (Rolls et al., 2021). In 37,286 humans from the UK Biobank, resting state functional connectivities of the orbitofrontal cortex, especially with the anterior cingulate cortex were positively correlated with the liking for sweet foods (FDR $p < .05$). They were also positively correlated with the body mass index (BMI) (FDR $p < .05$). Moreover, in a sample of 502,492 people, the "liking for sweet foods" was correlated with their BMI ($r = 0.06$, $p < 10^{-125}$). In a cross-validation with 545 participants from the Human Connectome Project, higher functional connectivity involving the orbitofrontal cortex relative to other brain areas was associated with high BMI (>=30) compared to a mid-BMI group (22−25; $p = 6 \times 10^{-5}$); and low orbitofrontal cortex functional connectivity was associated with low BMI (<=20.5; $p < .024$). It is proposed that high BMI relates to increased efficacy of orbitofrontal cortex food reward systems, and low BMI to decreased efficacy (Rolls et al., 2021). This was found with no stimulation by food, so there is an underlying individual difference in brain connectivity that is related to food reward and BMI (Rolls, 2021b; Rolls et al., 2021).

Individual differences in the reward value of different types of stimuli may be a key way in which evolution by natural selection based on individual variation operates (Rolls, 2014a).

## 8.4 Beyond the reward value of flavor to decision-making

Representations of the reward value of food, and their subjective correlate, the pleasantness of food, are fundamental in determining appetite and processes such as economic decision-making (Rolls, 2005a, 2014a, 2021a; Padoa-Schioppa, 2011; Padoa-Schioppa and Cai, 2011). But after the reward evaluation, a decision has to be made about whether to seek for and consume the reward. We are now starting to understand how the brain

takes decisions as described in *The Noisy Brain* (Rolls and Deco, 2010), *Emotion and Decision-Making Explained* (Rolls, 2014a), and *Brain Computations: What and How* (Rolls, 2021a), and this has implications for whether a reward of a particular value will be selected (Rolls, 2008b, 2011b, 2014a, 2021a; Rolls and Grabenhorst, 2008; Rolls and Deco, 2010; Grabenhorst and Rolls, 2011; Deco et al., 2013).

A tier of processing beyond the orbitofrontal cortex, in the medial prefrontal cortex area 10, becomes engaged when choices are made between odor stimuli based on their pleasantness (Grabenhorst et al., 2008b; Rolls et al., 2010b, 2010c, 2010d) (tier 3 in Fig. 8.1). 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 (Rolls, 2010a, 2021a). 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 nonlinear system is that one attractor wins, and this implements a mechanism for decision-making with one winner (Rolls, 2008b, 2014a, 2016a, 2021a; Wang, 2008; Rolls and Deco, 2010; Deco et al., 2013). The decisions are probabilistic as they reflect the noise in the competitive nonlinear decision-making process that is introduced by the random spiking times of neurons for a given mean rate that reflects a Poisson process (Rolls and Deco, 2010; Rolls et al., 2010c; Rolls, 2021a). 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 (Rolls, 2008b, 2014a, 2021a; Rolls and Grabenhorst, 2008; Grabenhorst and Rolls, 2011). 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 flavor of food (which are partly gene-specified (Rolls, 2005a, 2014a), though subject to conditioned effects (Booth, 1985; Rolls, 2014a, 2021b)) in a further decision process which may itself be subject to noise (Rolls, 2008b, 2014a, 2021a; Rolls and Deco, 2010). This can be described as a choice between the selfish phene (standing for phenotype) and the selfish gene (Rolls, 2011b, 2012a, 2014a, 2020a, 2021a). In this context, the findings described here that the cognitive system can have a top-down influence on the reward system including the flavor reward system are important advances in our understanding of how these decisions are reached.

## 8.5 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 orbitofrontal cortex and pregenual cingulate cortex, and it is here that hunger/satiety signals modulate the representations of food to make them implement reward. The satiety signals that help in this modulation may reach the orbitofrontal cortex from the hypothalamus, and in turn, the orbitofrontal cortex projects to the hypothalamus where neurons are found that respond to the sight, smell, and taste of food if hunger is present (Rolls and Grabenhorst, 2008; Rolls, 2014a). 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.

A hypothesis is developed elsewhere that obesity is associated in part with overstimulation of these reward systems by very rewarding combinations of taste, odor, texture, visual, and cognitive inputs that together produce the flavor of food (Rolls, 2005a, 2011d, 2012b, 2014a, 2015b, 2016c, 2021b).

## Acknowledgments

This research was supported by the UK Medical Research Council. The participation of many colleagues in the studies cited is sincerely acknowledged. They include Ivan de Araujo, Gordon Baylis, Leslie Baylis, Wei Cheng, Hugo Critchley, Ruiqing Feng, Paul Gabbott, Fabian Grabenhorst, Chu-Chung Huang, Mikiko Kadohisa, Michel Kellerhals, Morten Kringelbach, Christian Margot, Francis McGlone, Ciara McCabe, Thomas Mills, Ian Norton, John O'Doherty, Barbara Rolls, Juliet Rolls, Thomas Scott, Zenon Sienkiewicz, Simon Thorpe, Maria Ines Velazco, Justus Verhagen, and Simon Yaxley.

## References

Baylis, L.L., Rolls, E.T., 1991. Responses of neurons in the primate taste cortex to glutamate. Physiol. Behav. 49, 973–979.

Baylis, L.L., Rolls, E.T., Baylis, G.C., 1995. Afferent connections of the orbitofrontal cortex taste area of the primate. Neuroscience 64, 801–812.

Birch, L.L., 1999. Development of food preferences. Annu. Rev. Nutr. 19, 41–62.

Booth, D.A., 1985. Food-conditioned eating preferences and aversions with interoceptive elements: learned appetites and satieties. Ann. New York Acad. Sci. 443, 22–37.

Cabanac, M., 1971. Physiological role of pleasure. Science 173, 1103–1107.

Critchley, H.D., Rolls, E.T., 1996a. Hunger and satiety modify the responses of olfactory and visual neurons in the primate orbitofrontal cortex. J. Neurophysiol. 75, 1673–1686.

Critchley, H.D., Rolls, E.T., 1996b. Olfactory neuronal responses in the primate orbitofrontal cortex: analysis in an olfactory discrimination task. J. Neurophysiol. 75, 1659–1672.

Critchley, H.D., Rolls, E.T., 1996c. Responses of primate taste cortex neurons to the astringent tastant tannic acid. Chem. Sens. 21, 135–145.

de Araujo, I.E.T., Kringelbach, M.L., Rolls, E.T., et al., 2003a. The representation of umami taste in the human brain. J. Neurophysiol. 90, 313–319.

de Araujo, I.E.T., Kringelbach, M.L., Rolls, E.T., et al., 2003b. Human cortical responses to water in the mouth, and the effects of thirst. J. Neurophysiol. 90, 1865−1876.
de Araujo, I.E.T., Rolls, E.T., 2004. The representation in the human brain of food texture and oral fat. J. Neurosci. 24, 3086−3093.
de Araujo, I.E.T., Rolls, E.T., Kringelbach, M.L., et al., 2003c. Taste-olfactory convergence, and the representation of the pleasantness of flavour, in the human brain. Eur. J. Neurosci. 18, 2059−2068.
de Araujo, I.E.T., Rolls, E.T., Velazco, M.I., et al., 2005. Cognitive modulation of olfactory processing. Neuron 46, 671−679.
Deco, G., Rolls, E.T., 2005. Neurodynamics of biased competition and co-operation for attention: a model with spiking neurons. J. Neurophysiol. 94, 295−313.
Deco, G., Rolls, E.T., Albantakis, L., et al., 2013. Brain mechanisms for perceptual and reward-related decision-making. Prog. Neurobiol. 103, 194−213.
Desimone, R., Duncan, J., 1995. Neural mechanisms of selective visual attention. Annu. Rev. Neurosci. 18, 193−222.
Du, J., Rolls, E.T., Cheng, W., et al., 2020. Functional connectivity of the orbitofrontal cortex, anterior cingulate cortex, and inferior frontal gyrus in humans. Cortex 123, 185−199.
Francis, S., Rolls, E.T., Bowtell, R., et al., 1999. The representation of pleasant touch in the brain and its relationship with taste and olfactory areas. NeuroReport 10, 453−459.
Ge, T., Feng, J., Grabenhorst, F., et al., 2012. Componential Granger causality, and its application to identifying the source and mechanisms of the top-down biased activation that controls attention to affective vs sensory processing. Neuroimage 59, 1846−1858.
Gottfried, J.A., 2015. Structural and functional imaging of the human olfactory system. In: Doty, R.L. (Ed.), Handbook of Olfaction and Gustation, third ed. Wiley Liss, New York.
Grabenhorst, F., Rolls, E.T., 2008. Selective attention to affective value alters how the brain processes taste stimuli. Eur. J. Neurosci. 27, 723−729.
Grabenhorst, F., Rolls, E.T., 2010. Attentional modulation of affective vs sensory processing: functional connectivity and a top-down biased activation theory of selective attention. J. Neurophysiol. 104, 1649−1660.
Grabenhorst, F., Rolls, E.T., 2011. Value, pleasure, and choice in the ventral prefrontal cortex. Trend. Cognit. Sci. 15, 56−67.
Grabenhorst, F., Rolls, E.T., 2014. The representation of oral fat texture in the human somatosensory cortex. Hum. Brain Mapp. 35, 2521−2530.
Grabenhorst, F., Rolls, E.T., Bilderbeck, A., 2008a. How cognition modulates affective responses to taste and flavor: top down influences on the orbitofrontal and pregenual cingulate cortices. Cereb. Cort. 18, 1549−1559.
Grabenhorst, F., Rolls, E.T., Margot, C., et al., 2007. How pleasant and unpleasant stimuli combine in different brain regions: odor mixtures. J. Neurosci. 27, 13532−13540.
Grabenhorst, F., Rolls, E.T., Parris, B.A., 2008b. From affective value to decision-making in the prefrontal cortex. Eur. J. Neurosci. 28, 1930−1939.
Grabenhorst, F., Rolls, E.T., Parris, B.A., et al., 2010. How the brain represents the reward value of fat in the mouth. Cereb. Cort. 20, 1082−1091.
Hetherington, M.M., 2007. Cues to overeat: psychological factors influencing overconsumption. Proc. Nutr. Soc. 66, 113−123.
Hetherington, M.M., Cecil, J.E., Jackson, D.M., et al., 2011. Feeding infants and young children. From guidelines to practice. Appetite 57, 791−795.
Hsu, C.-C.H., Rolls, E.T., Huang, C.-C., et al., 2020. Connections of the human orbitofrontal cortex and inferior frontal gyrus. Cereb Cort. 30, 5830−5843.

Kadohisa, M., Rolls, E.T., Verhagen, J.V., 2004. Orbitofrontal cortex neuronal representation of temperature and capsaicin in the mouth. Neuroscience 127, 207−221.

Kadohisa, M., Rolls, E.T., Verhagen, J.V., 2005. Neuronal representations of stimuli in the mouth: the primate insular taste cortex, orbitofrontal cortex, and amygdala. Chem. Sens. 30, 401−419.

Kringelbach, M.L., O'Doherty, J., Rolls, E.T., et al., 2003. Activation of the human orbitofrontal cortex to a liquid food stimulus is correlated with its subjective pleasantness. Cereb Cort. 13, 1064−1071.

Luo, Q., Ge, T., Grabenhorst, F., et al., 2013. Attention-dependent modulation of cortical taste circuits revealed by Granger causality with signal-dependent noise. PLoS Comput. Biol. 9, e1003265.

Maruyama, Y., Pereira, E., Margolskee, R.F., et al., 2006. Umami responses in mouse taste cells indicate more than one receptor. J. Neurosci. 26, 2227−2234.

McCabe, C., Rolls, E.T., 2007. Umami: a delicious flavor formed by convergence of taste and olfactory pathways in the human brain. Eur. J. Neurosci. 25, 1855−1864.

O'Doherty, J., Rolls, E.T., Francis, S., et al., 2001. Representation of pleasant and aversive taste in the human brain. J. Neurophysiol. 85, 1315−1321.

O'Doherty, J., Rolls, E.T., Francis, S., et al., 2000. Sensory-specific satiety related olfactory activation of the human orbitofrontal cortex. NeuroReport 11, 893−897.

O'Doherty, J.P., Deichmann, R., Critchley, H.D., et al., 2002. Neural responses during anticipation of a primary taste reward. Neuron 33, 815−826.

Padoa-Schioppa, C., 2011. Neurobiology of economic choice: a good-based model. Annu. Rev. Neurosci. 34, 333−359.

Padoa-Schioppa, C., Cai, X., 2011. The orbitofrontal cortex and the computation of subjective value: consolidated concepts and new perspectives. Ann.. N. Y. Acad. Sci. 1239, 130−137.

Passingham, R.E.P., Wise, S.P., 2012. The Neurobiology of the Prefrontal Cortex. Oxford University Press, Oxford.

Poellinger, A., Thomas, R., Lio, P., et al., 2001. Activation and habituation in olfaction- an fMRI study. Neuroimage 13, 547−560.

Pritchard, T.C., Edwards, E.M., Smith, C.A., et al., 2005. Gustatory neural responses in the medial orbitofrontal cortex of the old world monkey. J. Neurosci. 25, 6047−6056.

Rolls, B.J., Hetherington, M., 1989. The role of variety in eating and body weight regulation. In: Shepherd, R. (Ed.), Handbook of the Psychophysiology of Human Eating. Wiley, Chichester.

Rolls, B.J., Rolls, E.T., Rowe, E.A., 1983a. Body fat control and obesity. Behav. Brain Sci. 4, 744−745.

Rolls, B.J., Rolls, E.T., Rowe, E.A., et al., 1981a. Sensory specific satiety in man. Physiol. Behav. 27, 137−142.

Rolls, B.J., Rowe, E.A., Rolls, E.T., 1982. How sensory properties of foods affect human feeding behavior. Physiol. Behav. 29, 409−417.

Rolls, B.J., Rowe, E.A., Rolls, E.T., et al., 1981b. Variety in a meal enhances food intake in man. Physiol. Behav. 26, 215−221.

Rolls, B.J., Van Duijenvoorde, P.M., Rowe, E.A., 1983b. Variety in the diet enhances intake in a meal and contributes to the development of obesity in the rat. Physiol. Behav. 31, 21−27.

Rolls, B.J., Van Duijvenvoorde, P.M., Rolls, E.T., 1984. Pleasantness changes and food intake in a varied four-course meal. Appetite 5, 337−348.

Rolls, E.T., 1981. Central nervous mechanisms related to feeding and appetite. Br. Med. Bull. 37, 131−134.

Rolls, E.T., 1996. The orbitofrontal cortex. Philosoph. Trans. Royal Soc. Lond. B 351, 1433−1444.
Rolls, E.T., 1997. Taste and olfactory processing in the brain and its relation to the control of eating. Crit. Rev. Neurobiol. 11, 263−287.
Rolls, E.T., 2005a. Emotion Explained. Oxford University Press, Oxford.
Rolls, E.T., 2005b. Taste, olfactory, and food texture processing in the brain, and the control of food intake. Physiol. Behav. 85, 45−56.
Rolls, E.T., 2008a. Functions of the orbitofrontal and pregenual cingulate cortex in taste, olfaction, appetite and emotion. Acta. Physiol. Hung. 95, 131−164.
Rolls, E.T., 2008b. Memory, Attention, and Decision-Making: A Unifying Computational Neuroscience Approach. Oxford University Press, Oxford.
Rolls, E.T., 2009. Functional neuroimaging of umami taste: what makes umami pleasant. Am. J. Clin. Nutr. 90, 803S−814S.
Rolls, E.T., 2010a. Attractor networks. WIREs Cognit. Sci. 1, 119−134.
Rolls, E.T., 2010b. Neural representation of fat texture in the mouth. In: Montmayeur, J.-P., Coutre, L.J. (Eds.), Fat Detection: Taste, Texture, and Postingestive Effects. CRC Press, Boca Raton, FL.
Rolls, E.T., 2011a. Chemosensory learning in the cortex. Front. Syst. Neurosci. 78 (71−13).
Rolls, E.T., 2011b. Consciousness, decision-making, and neural computation. In: Cutsuridis, V., Hussain, A., Taylor, J.G. (Eds.), Perception-Action Cycle: Models, Algorithms and Systems. Springer, Berlin.
Rolls, E.T., 2011c. The neural representation of oral texture including fat texture. J. Text. Stud. 42, 137−156.
Rolls, E.T., 2011d. Taste, olfactory, and food texture reward processing in the brain and obesity. Int. J. Obes. 35, 550−561.
Rolls, E.T., 2012a. Neuroculture. On the Implications of Brain Science. Oxford University Press, Oxford.
Rolls, E.T., 2012b. Taste, olfactory, and food texture reward processing in the brain and the control of appetite. Proc. Nutr. Soc. 71, 488−501.
Rolls, E.T., 2013. A biased activation theory of the cognitive and attentional modulation of emotion. Front. Hum. Neurosci. 7, 74.
Rolls, E.T., 2014a. Emotion and Decision-Making Explained. Oxford University Press, Oxford.
Rolls, E.T., 2014b. Emotion and decision-making explained: Précis. Cortex 59, 185−193.
Rolls, E.T., 2015a. Neural integration of taste, smell, oral texture, and visual modalities. In: Doty, R.L. (Ed.), Handbook of Olfaction and Gustation, third ed. Wiley, New York.
Rolls, E.T., 2015b. Taste, olfactory, and food reward value processing in the brain. Prog. Neurobiol. 127-128, 64−90.
Rolls, E.T., 2016a. Cerebral Cortex: Principles of Operation. Oxford University Press, Oxford.
Rolls, E.T., 2016b. Functions of the anterior insula in taste, autonomic, and related functions. Brain Cognit. 110, 4−19.
Rolls, E.T., 2016c. Reward systems in the brain and nutrition. Annu. Rev. Nutr. 36, 435−470.
Rolls, E.T., 2019a. The cingulate cortex and limbic systems for emotion, action, and memory. Brain Struct. Funct. 224, 3001−3018.
Rolls, E.T., 2019b. The Orbitofrontal Cortex. Oxford University Press, Oxford.
Rolls, E.T., 2020a. Neural computations underlying phenomenal consciousness: a Higher Order Syntactic Thought theory. Front. Psychol. Conscious Res. 11, 655.
Rolls, E.T., 2020b. The texture and taste of food in the brain. J. Text. Stud. 51, 23−44.
Rolls, E.T., 2021a. Brain Computations: What and How. Oxford University Press, Oxford.

Rolls, E.T., 2021b. The orbitofrontal cortex, food reward, body weight, and obesity. Soc. Cognit., Affect. Neurosci. https://doi.org/10.1093/scan/nsab1044.
Rolls, E.T., Baylis, L.L., 1994. Gustatory, olfactory, and visual convergence within the primate orbitofrontal cortex. J. Neurosci. 14, 5437–5452.
Rolls, E.T., Cheng, W., Feng, J., 2020. The orbitofrontal cortex: reward, emotion, and depression. Brain Commun. 2, fcaa196.
Rolls, E.T., Critchley, H., Wakeman, E.A., et al., 1996a. Responses of neurons in the primate taste cortex to the glutamate ion and to inosine 5'-monophosphate. Physiol. Behav. 59, 991–1000.
Rolls, E.T., Critchley, H.D., Browning, A., et al., 1998. The neurophysiology of taste and olfaction in primates, and umami flavor. Ann. New York Acad. Sci. 855, 426–437.
Rolls, E.T., Critchley, H.D., Browning, A.S., et al., 1999. Responses to the sensory properties of fat of neurons in the primate orbitofrontal cortex. J. Neurosci. 19, 1532–1540.
Rolls, E.T., Critchley, H.D., Mason, R., et al., 1996b. Orbitofrontal cortex neurons: role in olfactory and visual association learning. J. Neurophysiol. 75, 1970–1981.
Rolls, E.T., Critchley, H.D., Treves, A., 1996c. The representation of olfactory information in the primate orbitofrontal cortex. J. Neurophysiol. 75, 1982–1996.
Rolls, E.T., Critchley, H.D., Verhagen, J.V., et al., 2010a. The representation of information about taste and odor in the orbitofrontal cortex. Chemosens. Percept. 3, 16–33.
Rolls, E.T., Deco, G., 2010. The Noisy Brain: Stochastic Dynamics as a Principle of Brain Function. Oxford University Press, Oxford.
Rolls, E.T., Deco, G., Huang, C-C., Feng, J., 2022. The human orbitofrontal cortex, vmPFC, and anterior cingulate cortex effective connectome: emotion, memory, and action. Cereb. Cortex. https://doi.org/10.1093/cercor/bhac070.
Rolls, E.T., Feng, R., Cheng, W., et al., 2021. Orbitofrontal cortex connectivity is associated with food reward and body weight. Soc. Cognit., Affect. Neurosci. https://doi.org/10.1093/scan/nsab083.
Rolls, E.T., Grabenhorst, F., 2008. The orbitofrontal cortex and beyond: from affect to decision-making. Prog. Neurobiol. 86, 216–244.
Rolls, E.T., Grabenhorst, F., Deco, G., 2010b. Choice, difficulty, and confidence in the brain. Neuroimage 53, 694–706.
Rolls, E.T., Grabenhorst, F., Deco, G., 2010c. Decision-making, errors, and confidence in the brain. J. Neurophysiol. 104, 2359–2374.
Rolls, E.T., Grabenhorst, F., Franco, L., 2009. Prediction of subjective affective state from brain activations. J. Neurophysiol. 101, 1294–1308.
Rolls, E.T., Grabenhorst, F., Margot, C., et al., 2008. Selective attention to affective value alters how the brain processes olfactory stimuli. J. Cognit. Neurosci. 20, 1815–1826.
Rolls, E.T., Grabenhorst, F., Parris, B.A., 2010d. Neural systems underlying decisions about affective odors. J. Cognit. Neurosci. 22, 1069–1082.
Rolls, E.T., Kellerhals, M.B., Nichols, T.E., 2015. Age differences in the brain mechanisms of good taste. Neuroimage 113, 298–309.
Rolls, E.T., Kringelbach, M.L., de Araujo, I.E.T., 2003a. Different representations of pleasant and unpleasant odors in the human brain. Eur. J. Neurosci. 18, 695–703.
Rolls, E.T., McCabe, C., 2007. Enhanced affective brain representations of chocolate in cravers vs non-cravers. Eur. J. Neurosci. 26, 1067–1076.
Rolls, E.T., Mills, T., Norton, A., et al., 2018. Neuronal encoding of fat using the coefficient of sliding friction in the cerebral cortex and amygdala. Cereb. Cort. 28, 4080–4089.

Rolls, E.T., Murzi, E., Yaxley, S., et al., 1986. Sensory-specific satiety: food-specific reduction in responsiveness of ventral forebrain neurons after feeding in the monkey. Brain Res. 368, 79–86.

Rolls, E.T., Rolls, B.J., 1977. Activity of neurones in sensory, hypothalamic and motor areas during feeding in the monkey. In: Katsuki, Y., Sato, M., Takagi, S., et al. (Eds.), Food Intake and Chemical Senses. University of Tokyo Press, Tokyo.

Rolls, E.T., Rolls, B.J., 1982. Brain mechanisms involved in feeding. In: Barker, L.M. (Ed.), Psychobiology of Human Food Selection. AVI Publishing Company, Westport, Connecticut.

Rolls, E.T., Rolls, B.J., Rowe, E.A., 1983c. Sensory-specific and motivation-specific satiety for the sight and taste of food and water in man. Physiol. Behav. 30, 185–192.

Rolls, E.T., Rolls, J.H., 1997. Olfactory sensory-specific satiety in humans. Physiol. Behav. 61, 461–473.

Rolls, E.T., Scott, T.R., 2003. Central taste anatomy and neurophysiology. In: Doty, R.L. (Ed.), Handbook of Olfaction and Gustation, second ed. Dekker, New York.

Rolls, E.T., Scott, T.R., Sienkiewicz, Z.J., et al., 1988. The responsiveness of neurones in the frontal opercular gustatory cortex of the macaque monkey is independent of hunger. J. Physiol. 397, 1–12.

Rolls, E.T., Sienkiewicz, Z.J., Yaxley, S., 1989. Hunger modulates the responses to gustatory stimuli of single neurons in the caudolateral orbitofrontal cortex of the macaque monkey. Eur. J. Neurosci. 1, 53–60.

Rolls, E.T., Treves, A., 2011. The neuronal encoding of information in the brain. Prog. Neurobiol. 95, 448–490.

Rolls, E.T., Verhagen, J.V., Kadohisa, M., 2003b. Representations of the texture of food in the primate orbitofrontal cortex: neurons responding to viscosity, grittiness and capsaicin. J. Neurophysiol. 90, 3711–3724.

Rolls, E.T., Yaxley, S., Sienkiewicz, Z.J., 1990. Gustatory responses of single neurons in the caudolateral orbitofrontal cortex of the macaque monkey. J. Neurophysiol. 64, 1055–1066.

Roper, S.D., Chaudhari, N., 2017. Taste buds: cells, signals and synapses. Nat. Rev. Neurosci. 18, 485–497.

Scott, T.R., Small, D.M., 2009. The role of the parabrachial nucleus in taste processing and feeding. Ann. N. Y. Acad. Sci. 1170, 372–377.

Scott, T.R., Yaxley, S., Sienkiewicz, Z.J., et al., 1986. Gustatory responses in the frontal opercular cortex of the alert cynomolgus monkey. J. Neurophysiol. 56, 876–890.

Simmons, W.K., Martin, A., Barsalou, L.W., 2005. Pictures of appetizing foods activate gustatory cortices for taste and reward. Cereb Cort. 15, 1602–1608.

Small, D.M., 2010. Taste representation in the human insula. Brain Struct. Funct. 214, 551–561.

Small, D.M., Prescott, J., 2005. Odor/taste integration and the perception of flavor. Exp. Brain Res. 166, 345–357.

Small, D.M., Scott, T.R., 2009. Symposium overview: what happens to the pontine processing? Repercussions of interspecies differences in pontine taste representation for tasting and feeding. Ann. N. Y. Acad. Sci. 1170, 343–346.

Small, D.M., Voss, J., Mak, Y.E., et al., 2004. Experience-dependent neural integration of taste and smell in the human brain. J. Neurophysiol. 92, 1892–1903.

Sobel, N., Prabkakaran, V., Zhao, Z., et al., 2000. Time course of odorant-induced activation in the human primary olfactory cortex. J. Neurophysiol. 83, 537–551.

Thorpe, S.J., Rolls, E.T., Maddison, S., 1983. Neuronal activity in the orbitofrontal cortex of the behaving monkey. Exp. Brain Res. 49, 93–115.

Verhagen, J.V., Kadohisa, M., Rolls, E.T., 2004. The primate insular/opercular taste cortex: neuronal representations of the viscosity, fat texture, grittiness, temperature and taste of foods. J. Neurophysiol. 92, 1685−1699.

Verhagen, J.V., Rolls, E.T., Kadohisa, M., 2003. Neurons in the primate orbitofrontal cortex respond to fat texture independently of viscosity. J. Neurophysiol. 90, 1514−1525.

Wang, G.J., Volkow, N.D., Telang, F., et al., 2004. Exposure to appetitive food stimuli markedly activates the human brain. Neuroimage 21, 1790−1797.

Wang, X.J., 2008. Decision making in recurrent neuronal circuits. Neuron 60, 215−234.

Wise, S.P., 2008. Forward frontal fields: phylogeny and fundamental function. Trends Neurosci. 31, 599−608.

Yaxley, S., Rolls, E.T., Sienkiewicz, Z.J., 1988. The responsiveness of neurons in the insular gustatory cortex of the macaque monkey is independent of hunger. Physiol. Behav. 42, 223−229.

Yaxley, S., Rolls, E.T., Sienkiewicz, Z.J., 1990. Gustatory responses of single neurons in the insula of the macaque monkey. J. Neurophysiol. 63, 689−700.

Zald, D.H., Hagen, M.C., Pardo, J.V., 2002. Neural correlates of tasting concentrated quinine and sugar solutions. J. Neurophysiol. 87, 1068−1075.

Zald, D.H., Lee, J.T., Fluegel, K.W., et al., 1998. Aversive gustatory stimulation activates limbic circuits in humans. Brain 121, 1143−1154.

Zald, D.H., Pardo, J.V., 1997. Emotion, olfaction, and the human amygdala: amygdala activation during aversive olfactory stimulation. Proc. Nat. Acad. Sci. U. S. A. 94, 4119−4124.

Zatorre, R.J., Jones-Gotman, M., Evans, A.C., et al., 1992. Functional localization of human olfactory cortex. Nature 360, 339−340.

Zhao, G.Q., Zhang, Y., Hoon, M.A., et al., 2003. The receptors for mammalian sweet and umami taste. Cell 115, 255−266.