Chapter 2

Taste, olfactory, oral texture and visual processing of food reward in the brain

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Flavor reflects taste, olfactory, and oral texture inputs, and can be influenced by the sight of food, and by cognitive descriptions and by attention. This contribution shows how flavor is built by the appropriate combinations of these different sensory inputs and modulatory processes in the primate including human brain. Complementary neuronal recordings, and functional neuroimaging in humans, show that the primary taste cortex in the anterior insula provides separate and combined representations of the taste, temperature, and texture (including fat texture) of food in the mouth independently of hunger and thus of reward value and pleasantness. A discovery that is highlighted is that fat in the mouth is encoded by the coefficient of sliding friction, and this has implications for the development of new foods with a pleasant mouth feel and optimized nutritional content. Once activated, in the orbitofrontal cortex, these sensory inputs are for some neurons combined by associative learning with olfactory and visual inputs, and these neurons encode food reward in that they only respond to food when hungry, and in that activations correlate with subjective pleasantness. Sensory-specific satiety is computed in the orbitofrontal cortex. Cognitive factors, including word-level descriptions, and selective attention to affective value, modulate the representation of the reward value of taste and olfactory stimuli in the orbitofrontal cortex and a region to which it projects, the anterior cingulate cortex, a tertiary taste cortical area. The food reward representations formed in this way play an important role in the control of appetite and food intake. Individual differences in these reward representations may contribute to obesity. Food reward systems are differently organised at the systems neuroscience level in rodents, and thus the neural systems and processes for food reward described here are very relevant to humans.

Introduction

A schematic diagram of the taste and related olfactory, somatosensory, and visual pathways in the primate (which includes humans throughout) brain is shown in Fig. 2.1, with a view of their locations in the brain in Fig. 2.2 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 sparse distributed representation in which each neuron is tuned differently to other neurons (Kadohisa et al., 2005; Rolls, 2015b, 2016a, 2023a; Rolls et al., 2010; Rolls & Treves, 2011). Studies in nonhuman primates are especially relevant (Rolls, 2014a, 2015, 2016b; Rolls, Deco, et al., 2023), for the taste pathways in primates proceed via the thalamus to the taste cortex, whereas in rodents there is a pontine taste area that has direct subcortical connections (Rolls, 2016a; 2016b; Rolls, Deco, et al., 2023; Small & Scott, 2009); effects of satiety are found peripherally in the nucleus of the solitary tract in rodents (Rolls, 2016b; Rolls & Scott, 2003; Scott & Small, 2009), and rodents do not have the major part of the primate including human orbitofrontal cortex, the granular part (Rolls, 2014, 2018; Rolls, Deco, et al., 2023; Wise, 2008) (see Fig. 2.3). This makes the rodent a poor model of taste, olfactory, and flavor processing in the brains of humans and other primates (see Chapter 19 of Rolls, 2023a; Rolls et al., 2023).

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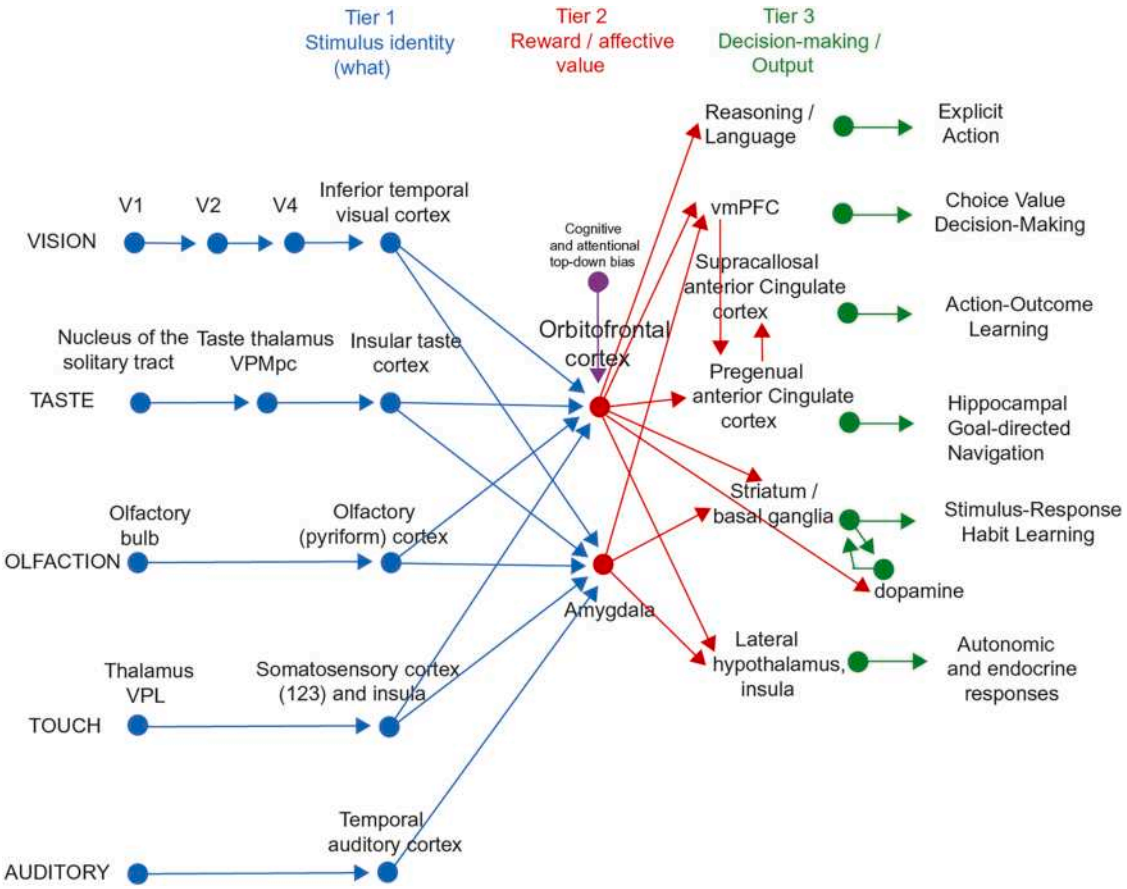

FIGURE 2.1 Schematic diagram showing some of the gustatory, olfactory, visual, and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates, including humans. The secondary taste cortex and the secondary olfactory cortex are within the orbitofrontal 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,actions are learned in the supracallosal (or dorsal) anterior cingulate cortex to obtain the reward values signaled by the orbitofrontal cortex and amygdala that are relayed in part via the pregenual anterior cingulate cortex and vmPFC. Decisions between stimuli of different reward value can be taken in the ventromedial prefrontal cortex, vmPFC (Rolls & Deco, 2010; Rolls, 2014; Rolls, Deco, et al., 2023). In Tier 3, orbitofrontal cortex inputs to the reasoning/language systems enable affective value to be incorporated and reported. In Tier 3, stimulus-response habits can also be produced using reinforcement learning. In Tier 3,autonomic responses can also be produced to emotion-provoking stimuli. Top-down control of affective response systems by cognition and by selective attention from the dorsolateral prefrontal cortex is also indicated in purple. V1,primary visual (striate) cortex; V2 and V4, further cortical visual areas; PFC,prefrontal cortex. The medial PFC area 10 is part of the ventromedial prefrontal cortex (vmPFC). VPL, ventro-postero-lateral nucleus of the thalamus, which conveys somatosensory information to the primary somatosensory cortex (areas 1, 2, and 3). VPMpc, ventro-postero-medial nucleus pars parvocellularis of the thalamus, which conveys taste information to the primary taste cortex.

Flavor processing in the primate brain

Taste processing

Pathways

A schematic diagram of the taste and related olfactory, somatosensory, and visual pathways in primates is shown in Fig. 2.1, and Fig. 2.2 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.

The primary taste cortex

Rolls and colleagues have shown (Rolls, 2016b) that the primary taste cortex in the primate anterior insula and adjoining frontal operculum contains not only taste

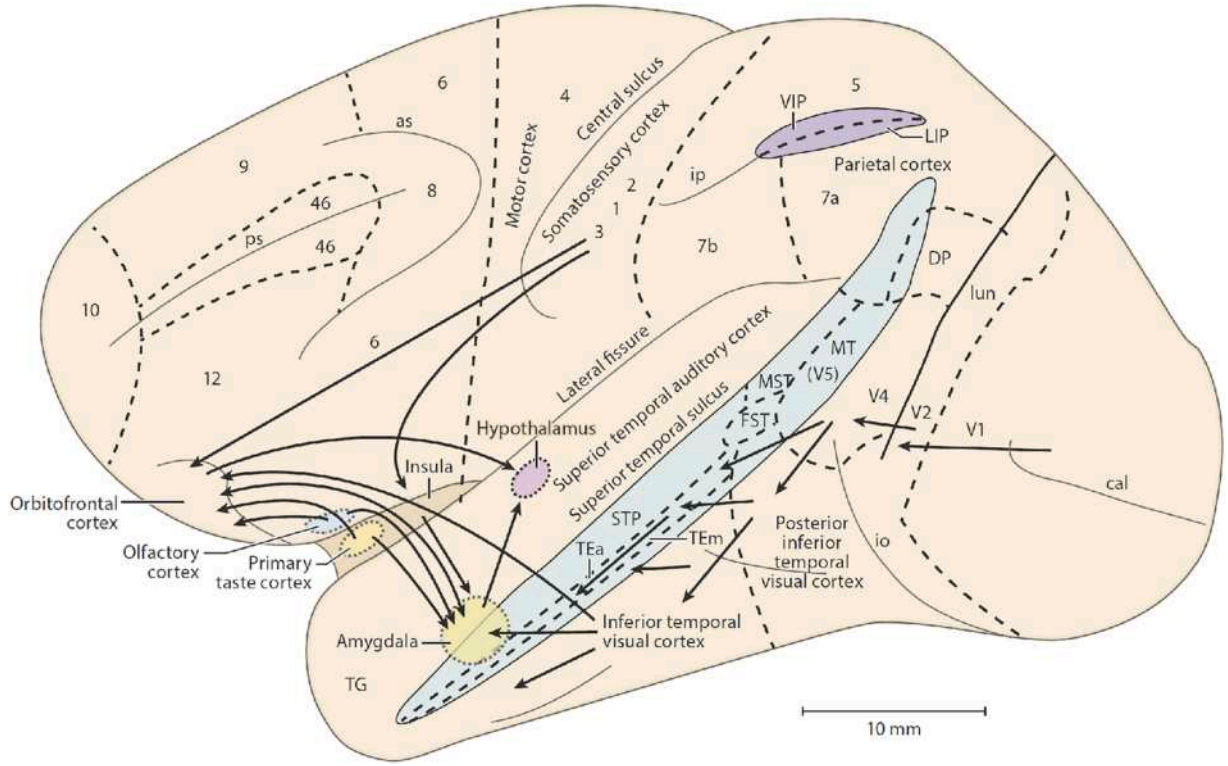

FIGURE 2.2 Some of the pathways involved in processing food-related stimuli are shown on this lateral view of the primate brain (macaque). Connections from the primary taste and olfactory cortices to the orbitofrontal cortex and amygdala are shown. Connections are also shown in the "ventral visual system" 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. as, arcuate sulcus; cal, calcarine sulcus; cs, central sulcus; lf, lateral (or Sylvian) fissure; lun, lunate sulcus; ps, principal sulcus; io, inferior occipital sulcus; ip, intraparietal sulcus (which has been opened to reveal some of the areas it contains); sts, superior temporal sulcus (which has been opened to reveal some of the areas it contains). AIT, anterior inferior temporal cortex; FST, visual motion processing area; LIP, lateral intraparietal area; MST, visual motion processing area; MT, visual motion processing area (also called V5); PIT, posterior inferior temporal cortex; STP, superior temporal plane; TA, architectonic area including auditory association cortex; TE, architectonic area including high order visual association cortex, and some of its subareas TEa and TEm; TG, architectonic area in the temporal pole; V1-V4, visual areas V1-V4; VIP, ventral intraparietal area; TEO, architectonic area including posterior visual association cortex. 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.

neurons tuned to sweet, salt, bitter, sour (Rolls & Scott, 2003; Scott et al., 1986; Yaxley et al., 1990), and umami as exemplified by monosodium glutamate (Baylis & Rolls, 1991; Rolls, Critchley, Wakeman, et al., 1996), but also other neurons that encode oral somatosensory stimuli including viscosity, fat texture, temperature, and capsaicin (Verhagen et al., 2004). Some neurons in the primary taste cortex respond to particular combinations of taste and oral texture stimuli, but do not respond to olfactory stimuli or visual stimuli 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; Rolls, 2016b; Yaxley et al., 1988).

The secondary taste cortex

A secondary cortical taste area in primates was discovered by Rolls et al. (1990) in the orbitofrontal cortex, extending several mm 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 & Scott, 2003), but also to umami tastants such as glutamate (which is present in many natural foods such as tomatoes, mushrooms and milk) (Baylis & Rolls, 1991) and inosine monophosphate (which is present in meat and some fish such as tuna) (Rolls, Critchley, Wakeman, et al., 1996). This evidence, taken together with the identification of glutamate taste receptors (Roper & Chaudhari, 2017; Zhao

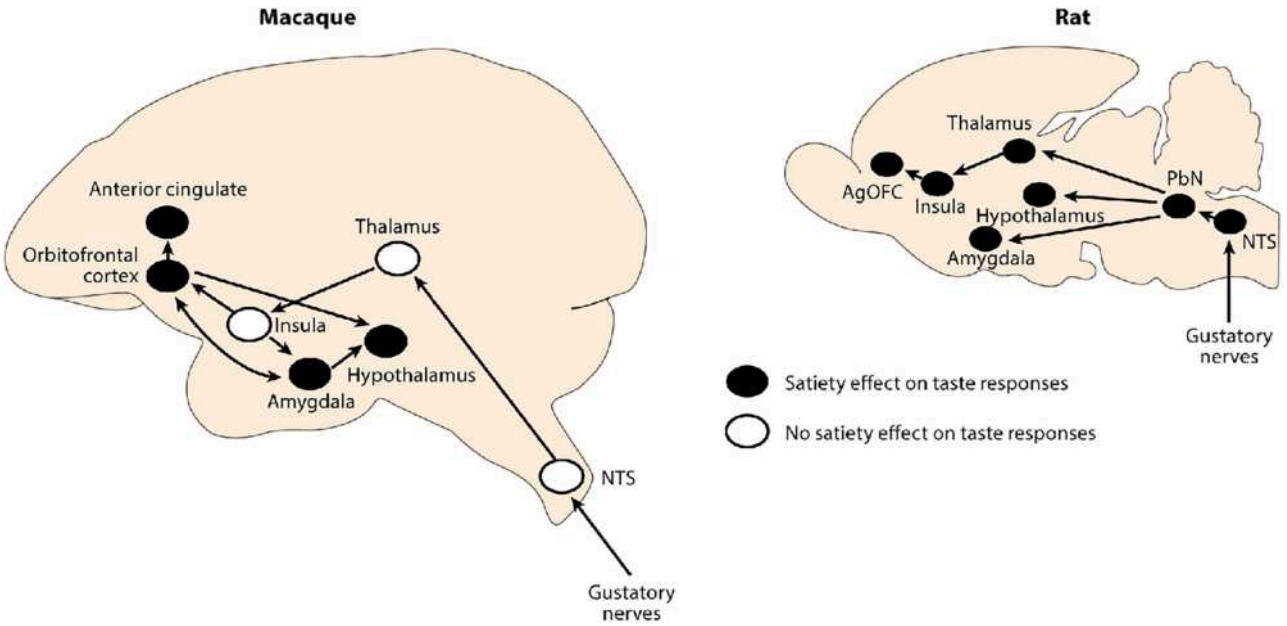

FIGURE 2.3 Taste pathways in the primate (macaque, but similarly in humans) and a rodent, the rat. In the *macaque*, gustatory information reaches the nucleus of the solitary tract (NTS), which projects directly to the taste thalamus (ventral posteromedial nucleus, pars parvocellularis, VPMpc), which 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 thalamocortical 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 (Passingham, 2021; Passingham & Wise, 2012; Rolls, Deco, et al., 2023). 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.

et al., 2003), leads to the view that there are five prototypical types of taste information channels, with umami contributing, often in combination with corresponding olfactory inputs (McCabe & Rolls, 2007; Rolls & Baylis, 1994; Rolls et al., 1998; 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 & Rolls, 1996a, 1996b, 1996c; Rolls, 1996), and capsaicin (Kadohisa et al., 2004; Rolls, Verhagen, & Kadohisa, 2003). Taste responses are found in a large mediolateral extent of the orbitofrontal cortex (Critchley and Rolls, 1996a, 1996b, 1996c; Rolls, 1996, 2015).

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

The modulation of the reward value of a sensory stimulus such as the taste of food by motivational state, for example, hunger, is one important way in which motivational behavior is controlled (Rolls, 2014, 2016c; Rolls, Feng, et al., 2023). 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 et al., 1986; Rolls, 1981), 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 (Critchley & Rolls, 1996a, 1996b, Rolls et al., 1989, Rolls, 1996, 2015).

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 (Rolls, 1997; Rolls et al., 1981a, 1981b, 1982, 1983a, 1983b, 1984, Rolls & Rolls, 1977, 1982), 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., 1983; Rolls, 2015, 2019b). In addition to providing an implementation of sensory-specific satiety (probably by habituation of the synaptic afferents to orbitofrontal neurons with a time course of the order of the length of a course of a meal), it is

likely that visceral and other satiety-related signals reach the orbitofrontal cortex (as indicated in Fig. 2.1) (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; Rolls, Feng, et al., 2023).

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. 2.1) (Critchley & Rolls, 1996a, 1996b, Rolls & Baylis, 1994, Rolls, 1996, 2011a, 2014, Rolls, Critchley, Mason, et al., 1996, Rolls, Critchley, Treves, et al., 1996, Verhagen et al., 2004). 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 (Rolls, 1996; Rolls, Critchley, Mason, et al., 1996; Thorpe et al., 1983). 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, 1996b, 1996c; Rolls, 1996).

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), 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, Verhagen, & Kadohisa, 2003). Very interestingly, some neurons encode the oral texture of fat (Rolls et al., 1999; Rolls, 2011b, 2015; Verhagen et al., 2003), and for a population of oral fat-sensitive neurons, this is independent of texture (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 the 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 separate 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; Rolls, 2011b, 2015, 2020b; Verhagen et al., 2003). Somatosensory signals that transmit information about capsaicin (chili) and astringency are also reflected in neuronal activity in these cortical areas (Critchley and Rolls, 1996a, 1996b, 1996c; Kadohisa et al., 2004, 2005; Rolls, 1996). Different neurons respond to different combinations of these food texture inputs and taste.

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).

Flavor processing in the human brain: functional neuroimaging

Taste

In humans it has been shown (Rolls, 2012b, 2014a, 2015a, 2015b; Rolls, Deco, et al., 2023; Rolls, Feng, et al., 2023) 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 (De Araujo, Rolls, et al., 2003; O'Doherty et al., 2001; Rolls, 2016b; Small, 2010), and part of the orbitofrontal cortex, which is probably the secondary taste cortex (De Araujo, Rolls, et al., 2003; Francis et al., 1999; O'Doherty et al., 2001; 2001; Rolls, 2005). We pioneered the use of a tasteless control with the same ionic constituents as saliva (De Araujo, Rolls, et al., 2003; O'Doherty et al., 2001), as water can activate some neurons in cortical taste areas (Rolls et al., 1990) and can activate the taste cortex (de Araujo, Kringelbach, Rolls et al., 2003). Within individual subjects, separate areas of the orbitofrontal cortex are activated by sweet (pleasant) and by 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 & Rolls, 2008; Grabenhorst, Rolls & Bilderbeck, 2008; Rolls, 2015b, 2016b) (Fig. 2.2).

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.

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) taste cortical areas (de Araujo, Kringelbach,

Rolls, Hobden, 2003). When the nucleotide 0.005 M inosine 5'-monophosphate (IMP) was added to MSG (0.05 M), the BOLD (blood oxygenation-level dependent) signal in an anterior part of the orbitofrontal cortex showed supralinear additivity, 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 of 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.

Odor

In humans, in addition to activation of the pyriform (olfactory) cortex (Rolls et al., 2008; Sobel et al., 2000; Zald & Pardo, 1997), there is strong and consistent activation of the orbitofrontal cortex by olfactory stimuli (Francis et al., 1999; Rolls, Kringelbach & De Araujo, 2003; Zatorre et al., 1992). This region appears to represent the pleasantness of odor, as shown by a sensory-specific satiety experiment with banana vs vanilla odor (O'Doherty et al., 2000). Further, pleasant odors tend to activate the medial, and unpleasant odors the more lateral, orbitofrontal cortex (Rolls, Kringelbach & De Araujo, 2003), 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 (Grabenhorst & 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 represents the reward value of odor, in that activations there correlate with the subjective pleasantness (medially) or unpleasantness (laterally) of odor (Grabenhorst & Rolls, 2011; Grabenhorst et al., 2007; Rolls et al., 2003, 2008, 2009; Rolls, 2018; Rolls, Deco, et al., 2023). Indeed, the reward-related medial orbitofrontal cortex/ventromedial prefrontal cortex connects preferentially with the reward-related pregenual anterior cingulate cortex, and the punishment/non-reward-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, 2023). 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; Rolls, Deco, et al., 2023; Rolls, Feng, et al., 2023).

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

Taste and olfactory conjunction analyses, and the measurement of supradditive 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, Rolls, et al., 2003; Small & Prescott, 2005; Small et al., 2004). 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, although it is anterior to the insular taste cortex, and posterior to the granular orbitofrontal cortex (see Fig. 2.4) (De Araujo, Rolls, et al., 2003).

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 that produces taste, olfactory, and texture stimulation, we measured brain activation by whole foods before and after the food is eaten to satiety. The foods eaten to satiety were either chocolate milk or tomato juice. A decrease in activation by the food eaten to satiety relative to the other food was found in the 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; Rolls, Deco, et al., 2023; Rolls, Feng, et al., 2023), are represented in the orbitofrontal cortex.

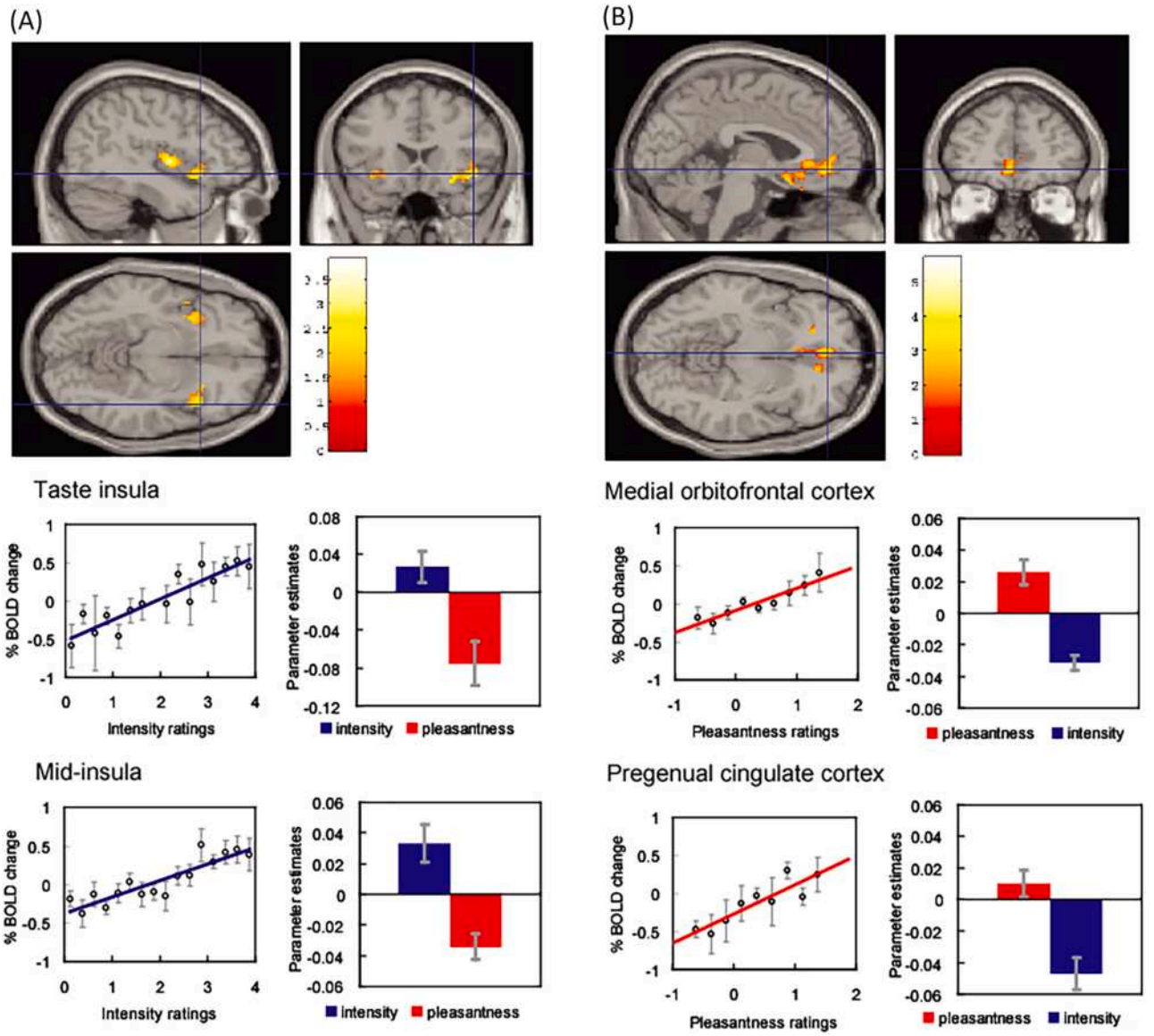

FIGURE 2.4 Effect of paying attention to the pleasantness vs the intensity of a taste stimulus. (A) Top: A significant difference related to the taste period was found in the taste insula at [42 18 -14] z=2.42, P < 0.05 (indicated by the cursor) and in the mid-insula at [40 -2 4] z=3.03, $P < 0.025$. 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, $P = 0.001$. Left: The correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate (r=0.91, df=14, $P < < 0.001$). 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, $P = 0.001$. Left: The correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate (r=0.89, df=15, $P < < 0.001$). 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, $P < 0.003$ (toward the back of the area of activation shown) and in the pregenual cingulate cortex at [-4 46 -8] z=2.90, $P < 0.04$ (at the cursor). Middle: Medial 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 correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate (r=0.94, df=8, $P < < 0.001$). Bottom: Pregenual cingulate cortex. Conventions as above. Right: The parameter estimates were significantly different for the pregenual cingulate cortex t=8.70, df=11, $P < 10^{-5}$. Left: The correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate (r=0.89, df=8, P=0.001). The taste stimulus, 0.1 M monosodium glutamate, was identical on all trials (after Grabenhorst & Rolls, 2008).

After Grabenhorst and Rolls (2008).

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 & Rolls, 2004). Oral viscosity is also represented in the human orbitofrontal and pregenual anterior cingulate cortices, and it is notable that the pregenual anterior 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 & 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 (Grabenhorst et al., 2010; Rolls et al., 2010a; Rolls, 2009). 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 & Rolls, 2014).

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).

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 (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. 2.1), 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, Rolls & Bilderbeck, 2008).

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. 2.2), whereas selective attention to intensity modulates activations in areas such as the primary taste cortex (Grabenhorst & 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 & Rolls, 2010), and by 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 (Deco & Rolls, 2005; Desimone & Duncan, 1995; Rolls, Deco, et al., 2023). 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 & Rolls, 2010; Luo et al., 2013), the process has been described as a biased activation model of attention (Grabenhorst & Rolls, 2010; Rolls, 2013).

This differential biasing by prefrontal cortex attentional mechanisms (Ge et al., 2012; Grabenhorst & Rolls, 2010) of brain regions engaged in processing a sensory stimulus

depending on whether the cognitive demand is for affect-related vs more sensory-related processing may be an important aspect of cognition and attention which have implications for how strongly the reward system is driven by food, and thus for eating and the control of appetite (Grabenhorst & 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.

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 midcingulate 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 & McCabe, 2007).

In another investigation, resting state functional connectivity was measured to investigate whether, even when food is not being presented, there are individual differences in the brain that relate to the liking for food and then perhaps as a consequence of that to obesity (Rolls, Deco, et al., 2023). 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 $p < 0.05$). They were also positively correlated with the body mass index (BMI) (FDR $P < 0.05$). 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; $P < 0.024$)). It is proposed that high BMI relates to increased efficacy of orbitofrontal cortex food reward systems, and low BMI to decreased efficacy (Rolls, Deco, et al., 2023). This was found with no stimulation by food, so it may be an underlying individual difference in brain connectivity that is related to food reward and BMI (Rolls, Deco, et al., 2023; Rolls, Feng, et al., 2023).

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, 2018; Rolls, Feng, et al., 2023).

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 (Padoa-Schioppa and Cai, 2011; Padoa-Schioppa, 2011; Rolls, 2005, 2014; Rolls, Deco, et al., 2023). But after the reward evaluation, a decision has to be made about whether to seek and consume the reward. We are now starting to understand how the brain takes decisions as described in *The Noisy Brain* (Rolls & Deco, 2010), *Emotion and Decision-Making Explained* (Rolls, 2014a), and *Brain Computations and Connectivity* (Rolls, Deco, et al., 2023), and this has implications for whether a reward of a particular value will be selected (Deco et al., 2013; Grabenhorst & Rolls, 2011; Rolls & Deco, 2010; Rolls, 2014; Rolls, Deco, et al., 2023).

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, Rolls, & Parris, 2008; Rolls et al., 2010a, 2010b, 2010c) (tier 3 in Fig. 2.1). 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 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 et al., 2010; Rolls, Deco, et al., 2023). The word attractor refers to the fact that inexact inputs are attracted to one of the states of high firing that are specified by the synaptic connections between the different groups of neurons. The result in this non-linear system is that one attractor wins, and this implements a mechanism for decision-making with one winner (Deco et al., 2013; Rolls & Deco, 2010; Rolls, 2014; Rolls, 2016a; Rolls, Deco, et al., 2023; Wang, 2008). 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 & Deco, 2010; Rolls et al., 2010; Rolls, Deco, et al., 2023). 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 (Grabenhorst & Rolls, 2011; Rolls, 2014; Rolls, Deco, et al., 2023). 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, 2014; Rolls, Deco, et al., 2023; Rolls, Feng, et al., 2023) in a further decision process which may itself be subject to noise (Rolls & Deco, 2010; Rolls, 2014; Rolls, Deco, et al., 2023; Rolls, Feng, et al., 2023). This can be described as a choice between the selfish phene (standing for phenotype) and the selfish gene (Rolls, 2012a, 2014a, 2020a; Rolls, Deco, et al., 2023). 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.

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 anterior 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, 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, 2011c, 2012b, 2014a, 2015, 2016c; Rolls, Deco, et al., 2023; Rolls, Feng, et al., 2023).

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