The Orbitofrontal Cortex

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Summary

The orbitofrontal cortex is the key brain region involved in emotion in humans and other primates. The orbitofrontal cortex represents the reward or affective value of primary reinforcers including taste, touch, texture, and face expression. It learns to associate other stimuli with these to produce representations of the expected reward value for visual, auditory, and abstract stimuli, including monetary reward value. The orbitofrontal cortex thus plays a key role in emotion by representing the reward value of the goals for action. The learning process is stimulus–reinforcer association learning. Negative reward prediction error neurons are related to this affective learning. Activations in the orbitofrontal cortex correlate with the subjective emotional experience of affective stimuli, and damage to the orbitofrontal cortex impairs emotion-related learning, emotional behavior, and subjective affective state. Top-down attention to affect modulates orbitofrontal cortex representations, and attention to intensity modulates representations in earlier cortical areas that represent the physical properties of stimuli. Top-down word-level cognitive inputs can bias affective representations in the orbitofrontal cortex, providing a mechanism for cognition to influence emotion. Whereas the orbitofrontal cortex provides a representation of reward or affective value on a continuous scale, areas beyond the orbitofrontal cortex such as the ventromedial prefrontal cortex area 10 are involved in binary decision-making when a choice must be made. For this decision-making, the orbitofrontal cortex provides a representation of the value of each specific reward on the same scale, with no conversion to a common currency. Increased activity in a lateral orbitofrontal cortex non-reward region provides a new attractor-related approach to understanding and treating depression. Consistent with the theory, the lateral orbitofrontal cortex has increased functional connectivity and sensitivity to non-reward in depression, and the medial orbitofrontal cortex, involved in reward, has decreased functional connectivity and sensitivity to reward in depression.

Keywords: orbitofrontal cortex, emotion, reward value, ventromedial prefrontal cortex, depression, taste, smell, decision-making, hunger

Subjects: Cognitive Neuroscience

Introduction

The orbitofrontal cortex represents the reward and punishment value of stimuli. The orbitofrontal cortex is therefore fundamental to understanding the brain and emotion, for emotions are states elicited by rewarding or punishing stimuli (Rolls, 2023b, 2025). The orbitofrontal cortex is also fundamental to understanding the brain and motivation, for motivational states are states in which the individual will work to obtain the reward or goal (Rolls, 2023b, 2025). For example, hunger is the motivational state when the individual finds food rewarding and will work for that reward.

This article shows how the inputs to the orbitofrontal cortex enable many types of reward value to be represented in the orbitofrontal cortex; how the orbitofrontal cortex is involved in learning about rewards and altering behavior when no reward is obtained; and how the different outputs of the orbitofrontal cortex enable it to produce different types of emotional and motivational responses and emotional feelings. I also show how the effects of damage to the human orbitofrontal cortex can be understood in terms of these functions and how the orbitofrontal cortex is involved in key mental disorders including depression.

The focus here is on humans and macaques, because there are many topological, cytoarchitectural, and connectional similarities between humans and macaques with respect to the orbitofrontal cortex, and it is important to understand the human orbitofrontal cortex in health and disease (see Figure 1; Rolls, 2019a, 2019c, 2023a, 2023b). The rodent orbitofrontal cortex has many differences from the primate, including human orbitofrontal cortex, and is considered in the section "The rodent orbitofrontal cortex."

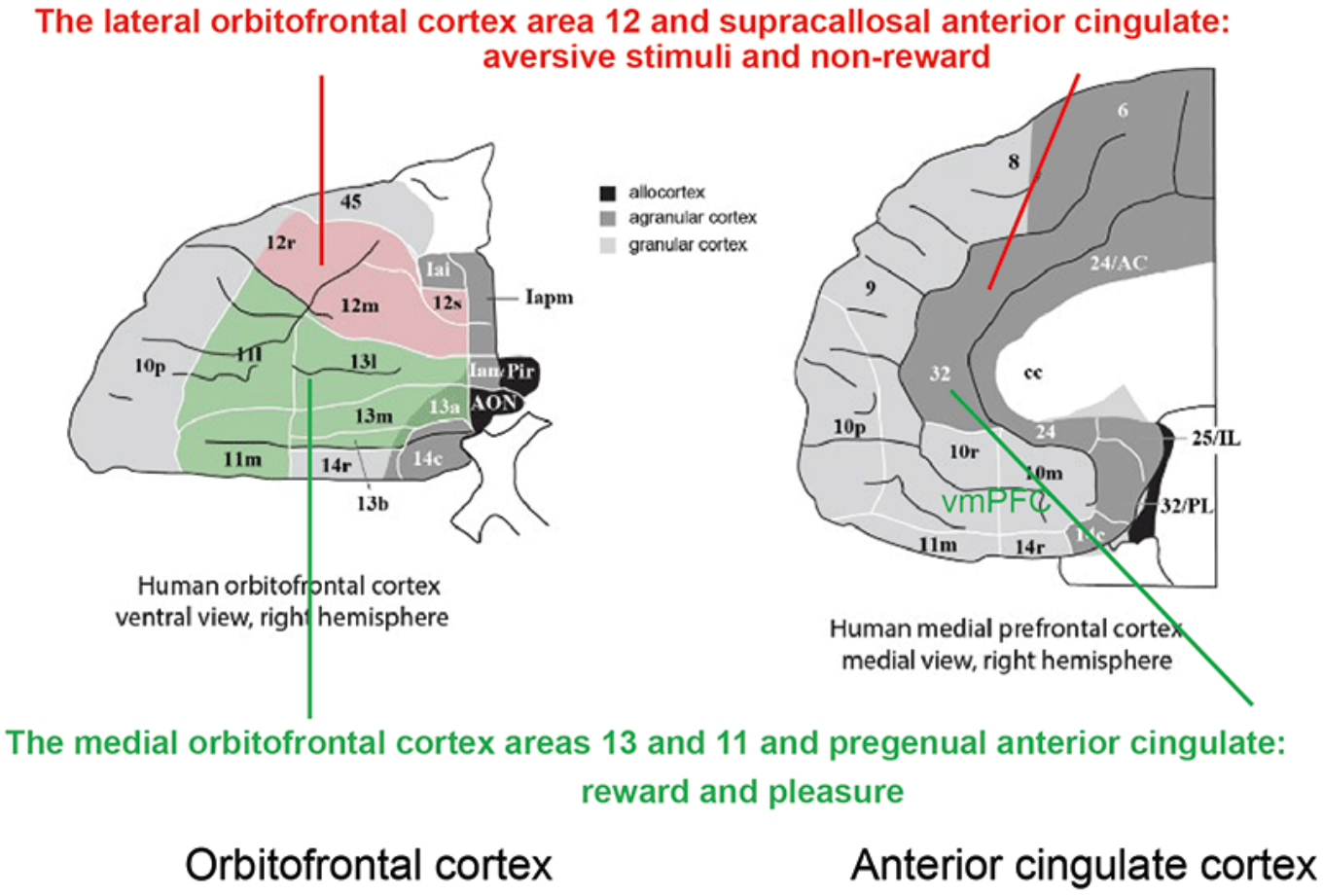

Figure 1. Maps of architectonic areas in the human orbitofrontal cortex (left, ventral view of the brain) and medial prefrontal cortex including anterior cingulate cortex (right, medial view of the brain). Left: The medial orbitofrontal cortex includes areas 13 and 11 (green). The lateral orbitofrontal cortex includes area 12 (red). (Area 12 is sometimes termed area 12/47 in humans. The figure shows two architectonic subdivisions of area 12.) Almost all of the human orbitofrontal cortex except area 13a is granular. Agranular cortex is shown in dark gray. The part of area 45 shown is the orbital part of the inferior frontal gyrus pars triangularis. Right: The anterior cingulate cortex includes the parts shown of areas 32, 25 (subgenual cingulate), and 24. The ventromedial prefrontal cortex includes

areas 14 (gyrus rectus) 10m and 10r. AON: anterior olfactory nucleus; Iai, Ial, Iam, Iapm: subdivisions of the agranular insular cortex. Modified after Öngür, Ferry, and Price (2003) to show the regions activated by reward versus aversive stimuli and non-reward (Rolls, 2014b, 2023a, 2023b).

Source: Modified from Rolls (2023a).

A Framework for Understanding the Orbitofrontal Cortex

A framework for understanding the primate including human orbitofrontal cortex is shown in Figure 2 and is built on evidence from neuronal recordings, the effects of brain damage, and functional magnetic resonance imaging (fMRI) in humans and macaques, some of which is summarized in this article (Rolls, 2014b, 2018, 2019a, 2019c, 2021b, 2023a, 2023b; Rolls, Cheng, & Feng, 2020). Part of the evidence for what is shown in Figure 2 comes from reward devaluation, in which when the reward value is changed, for example by feeding to satiety, neural responses to stimuli are little affected in Tier 1, but decrease to zero in Tier 2. Part of the evidence comes from the learning of associations between stimuli and reward value, which occurs mainly in Tier 2. Part of the evidence comes from the effects of brain damage on emotion, which occur primarily after damage to the orbitofrontal cortex and amygdala in Tier 2, and the cingulate cortex in Tier 3, in humans (Rolls, 2021d, 2023b).

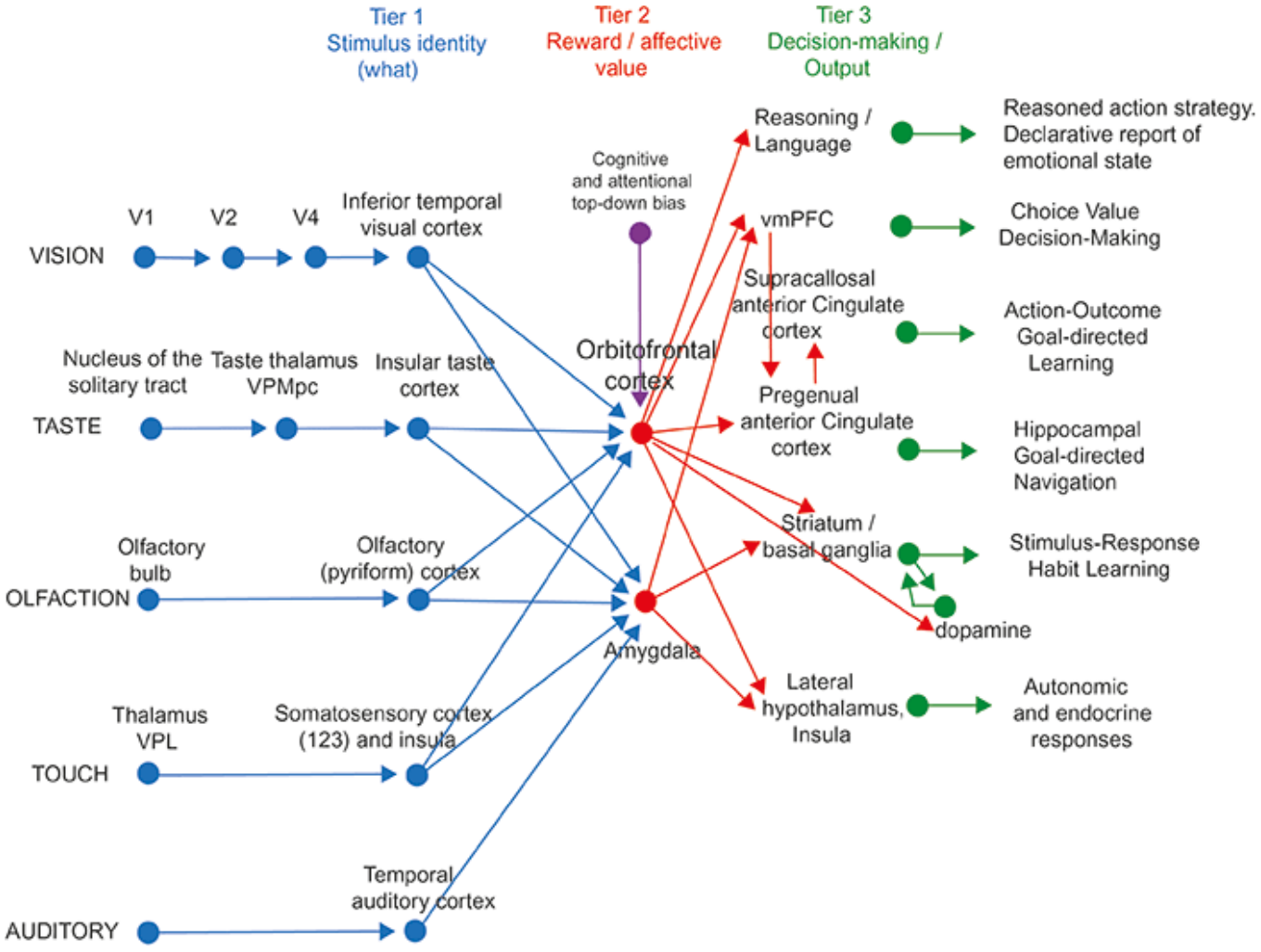

Figure 2. The systems-level organization of the brain for emotion in primates including humans. In Tier 1, representations are built of visual, taste, olfactory, and tactile stimuli that are independent of reward value and therefore of emotion. In Tier 2, reward value and emotion are represented. A pathway for top-down attentional and cognitive modulation of emotion is shown in purple. 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. 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. Auditory inputs also reach the amygdala. 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.

Source: Modified from Rolls (2023a).

Anatomy and Connections of the Orbitofrontal Cortex

Non-human Primates

Part of the background for understanding the orbitofrontal cortex is the anatomical connections of the orbitofrontal cortex summarized in Figure 2, with cytoarchitecture helping to define different orbitofrontal cortex regions in primates including humans (Figure 1; Barbas, 1995, 2007; Carmichael & Price, 1994, 1995; Henssen et al., 2016; Mackey & Petrides, 2010; Ongür & Price, 2000; Öngür et al., 2003; Pandya & Yeterian, 1996; Petrides & Pandya, 1995; Petrides et al., 2012; Price, 2006, 2007; Rolls, 2017b, 2019b, 2023a; Saleem et al., 2008, 2014).

Figure 2 shows that the orbitofrontal cortex can be thought of as receiving from the ends of each modality-specific cortical pathway that represents "what" stimulus is present, as summarized next.

Rolls et al. (1990) discovered a taste area with taste-responsive neurons in the lateral part of the macaque orbitofrontal cortex, and showed anatomically that this was the secondary taste cortex in that it receives a major projection from the primary taste cortex (Baylis et al., 1995). This region projects to more anterior areas of the orbitofrontal cortex (Baylis et al., 1995). Taste neurons are also found more medially (Critchley & Rolls, 1996c; Pritchard et al., 2005; Rolls, 2008a; Rolls & Baylis, 1994; Rolls, Critchley, Wakeman, et al., 1996).

In the mid-orbitofrontal cortex, there is an area with olfactory neurons (Rolls & Baylis, 1994) and, anatomically, there are direct connections from the primary olfactory cortex, pyriform cortex, to area 13a of the posterior orbitofrontal cortex, which in turn has onward projections to a middle part of the orbitofrontal cortex (area 13; Barbas, 1993; Carmichael et al., 1994; Morecraft et al., 1992; Price, 2007; Price et al., 1991).

Thorpe et al. (1983) found neurons with visual responses in the orbitofrontal cortex, and anatomically, visual inputs reach the orbitofrontal cortex directly from the inferior temporal cortex (Saleem et al., 2008; where object and face identity are represented, Rolls, 2007, 2016c), from the cortex in the superior temporal sulcus (Saleem et al., 2008; where face expression and gesture are represented, Hasselmo et al., 1989), and from the temporal pole (see Barbas, 1988, 1993, 1995; Barbas & Pandya, 1989; Carmichael & Price, 1995; Morecraft et al., 1992; Seltzer & Pandya, 1989). There are corresponding auditory inputs (Barbas, 1988, 1993; Romanski & Goldman-Rakic, 2001; Romanski et al., 1999; Rolls et al., 2006).

Some neurons in the orbitofrontal cortex respond to oral somatosensory stimuli such as the texture of food (Rolls, Verhagen, et al., 2003; Rolls et al., 1999), and anatomically there are inputs to the orbitofrontal cortex from somatosensory cortical areas 1, 2, and SII in the frontal and pericentral operculum, and from the insula (Barbas, 1988; Carmichael & Price, 1995). The caudal orbitofrontal cortex receives inputs from the amygdala (Price, 2006; Price et al., 1991). The orbitofrontal cortex also receives inputs via the mediodorsal nucleus of the thalamus, pars magnocellularis, which itself receives afferents from temporal lobe structures such as the pyriform (olfactory) cortex, amygdala, and inferior temporal cortex (see Ongür & Price, 2000). These connections provide some routes via which the responses of orbitofrontal cortex neurons can be produced. Within the orbitofrontal cortex, there are many intrinsic connections (Ongür & Price, 2000), and these may be part of what enables many orbitofrontal cortex neurons to have multimodal responses, as described below and elsewhere (Rolls, 2006, 2014b, 2016c).

Outputs of the orbitofrontal cortex connect by several different routes to output systems, as shown in Figure 2. The lowest levels in the hierarchy illustrated in Figure 2 are involved in reflexes, including, for example, reflex withdrawal of a limb to a nociceptive stimulus and autonomic responses.

The second level in the hierarchy can produce learned autonomic and some other behavioral responses to, for example, a previously neutral visual or auditory stimulus after it has been paired with a nociceptive stimulus or with a good taste stimulus. This route involves stimulus-reinforcer learning in the amygdala and orbitofrontal cortex. The orbitofrontal cortex projects to the insula as an output pathway and includes a projection to the viscero-autonomic cortex in the antero-ventral insula (Hassanpour et al., 2018; Quadt et al., 2022) that helps to account for why the insula is activated in some tasks in which the orbitofrontal cortex is involved (Rolls, 2016d, 2019b, 2023a). This antero-ventral part of the insula (Quadt et al., 2022) is just ventral to the primary taste cortex and has very strong connections in primates to (and probably from) the orbitofrontal cortex (Baylis et al., 1995).

A third level in the hierarchy shown in Figure 2 is the route from the orbitofrontal cortex and amygdala via the basal ganglia, including the ventral striatum to produce implicit stimulus-response habits. The responses are not under the control of the reward value of the stimulus, in that after devaluing the stimulus, the stimulus will still elicit the response for several trials. The orbitofrontal cortex does project reward-related information to the ventral striatum (Williams et al., 1993), and this provides a route, in part via the habenula (Lee & Hikosaka, 2022), for reward-related information to reach the dopamine neurons (Rolls, 2017b), which respond inter alia to positive

reward prediction error used in reinforcement learning (Bromberg-Martin et al., 2010; Schultz, 2016, 2017). As that system uses dopamine in reinforcement learning of stimulus-response habits, it is much less fast to learn than the orbitofrontal cortex (outcome) with anterior cingulate cortex (action) system for action-outcome, goal-based learning, and for emotion (Rolls, 2023a).

A fourth level in the hierarchy that is important in emotion is from especially the orbitofrontal cortex to the anterior cingulate cortex for goal-directed action. In this route to action, the evidence is that the orbitofrontal cortex encodes the value of stimuli (e.g., the reward value of the taste and sight of food), and the anterior cingulate cortex is the route to action and encodes the value of actions taking into account the cost of the action (Rolls, 2019a, 2023b; Rushworth et al., 2012). The emotional states implemented at this level may not necessarily be conscious.

A fifth level in the hierarchy shown in Figure 2 is from the orbitofrontal cortex (and much less the amygdala; Rolls et al., 2023a) via multiple-step reasoning systems involving syntax and language, which can be associated with explicit conscious states. A higher order syntactic thought system for correcting lower order thoughts is proposed to help correct this reasoning and to be associated with the explicit conscious states (Rolls, 2020). Connectivity from the lateral orbitofrontal cortex to language regions provides a route for emotional states to enter the reasoning system (Rolls, 2025; Rolls et al., 2023a).

In addition, the orbitofrontal cortex projects back to temporal lobe areas such as the amygdala (Barbas, 2007) and temporal cortex (Saleem et al., 2008, 2014), but these backprojections are not used in primates to make neurons in sensory/perceptual regions respond to reward but instead provide for top-down effects such as memory recall and attention (Rolls, 2016c, 2023a; section "Top-down effects of cognition and attention"). The orbitofrontal cortex also has connections to the entorhinal and perirhinal cortex (Barbas, 2007; Insausti et al., 1987; Saleem et al., 2008, 2014) providing a route for reward information to reach the hippocampus for memory and navigation (Rolls, 2022, 2023c; Rolls & Treves, 2024; Rolls & Xiang, 2005).

Each of these types of output have adaptive value in preparing individuals to deal physiologically and behaviorally with what may generally be described as emotion-provoking events (Rolls, 2023b, 2025).

Human Orbitofrontal Cortex Connectivity

Recent evidence on the connectivity of the orbitofrontal cortex in humans is shown in Figures 3 and 4, based on measurements of effective connectivity between 360 cortical regions and 24 subcortical regions measured in 171 humans from the Human Connectome Project and complemented with functional connectivity and diffusion tractography (Rolls et al., 2022b). Effective connectivity measures "causal" effects (in that they take into account time delays) in each direction between every pair of brain regions. The effective connectivities of the orbitofrontal cortex with other brain regions are summarized in Figures 3 and 4 (Rolls et al., 2022b, 2023a). The medial and lateral orbitofrontal cortex between them (and they have effective connectivity with each other) receive taste, somatosensory, olfactory, visual, and auditory inputs that are needed to build the reward and punishment value representations that are found in these regions but much less in the preceding

cortical areas that provide these inputs (Rolls, 2023a). Taste and somatosensory inputs provide information about primary reinforcers or outcome value, and the orbitofrontal cortex contains visual and olfactory neurons that can learn and reverse in one trial the associations with primary reinforcers and so represent expected value (Thorpe et al., 1983). This is consistent with the schematic diagram in Figure 2.

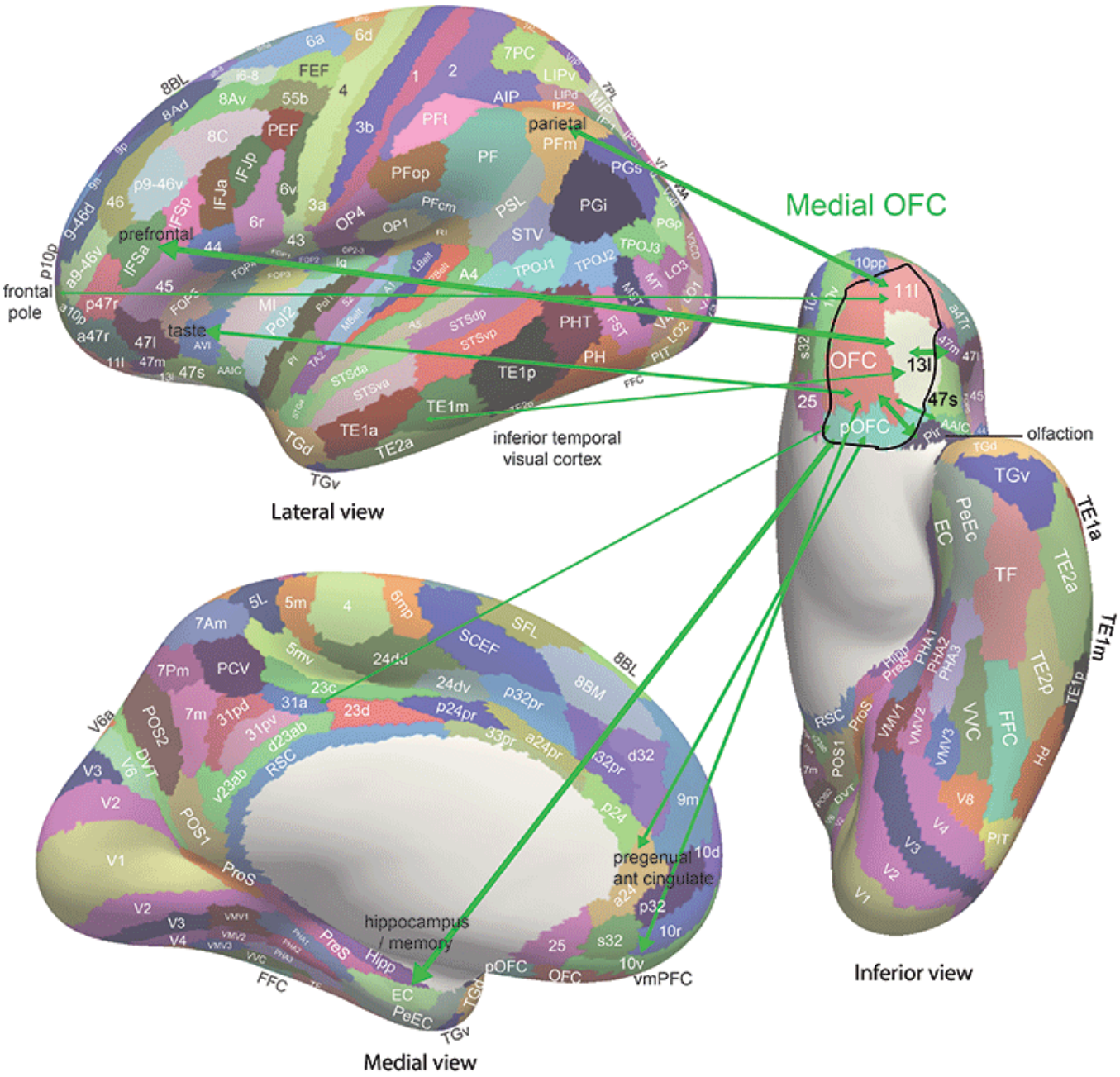

Figure 3. Summary of the effective connectivity of the human medial orbitofrontal cortex. The medial orbitofrontal cortex has taste, olfactory, and inferior temporal visual cortex inputs and connectivity with the hippocampus, pregenual anterior cingulate cortex, ventromedial prefrontal cortex (vmPFC), posterior cingulate cortex (e.g., 31), parietal cortex, inferior prefrontal cortex, and frontal pole. The main regions with which the medial

OFC has connectivity are indicated by names with the words in black font. The width of the arrows and the size of the arrow heads in each direction reflects the strength of the effective connectivity. The abbreviations are listed in Rolls et al. (2022b).

Source: Modified from Rolls (2023a).

In more detail (Figure 3; Rolls et al., 2022b, 2023a), parts of the medial orbitofrontal cortex (11l, 13l, OFC and pOFC, which are interconnected) have effective connectivity with the taste/olfactory/visceral anterior agranular insular complex (AAIC); the piriform (olfactory) cortex; the entorhinal cortex (EC); the inferior temporal visual cortex (TE1p, TE2a, TE2p); superior medial parietal 7Pm; inferior parietal PF which is somatosensory (Rolls et al., 2023b, 2023c); with parts of the posterior cingulate cortex (31pv, 7m, d23ab) related to memory (Rolls, Wirth, et al., 2023); with the pregenual anterior cingulate cortex (s32, a24, p24, p32, d32) and much less with the supracallosal anterior cingulate cortex (only 33pr); with ventromedial prefrontal 10r, 10d and 9m; with the frontal pole (10pp, p10p, a10p); with lateral orbitofrontal cortex (47m, 47s, a47r); and with dorsolateral prefrontal cortex (46 and a9-46v; Rolls et al., 2023b). Medial orbitofrontal cortex regions also have effective connectivity directed toward the caudate nucleus and nucleus accumbens (Rolls et al., 2022b).

Also with some detail, the lateral orbitofrontal cortex areas a47r, p47r and 47m share generally similar effective connectivities (Figure 4; Rolls et al., 2022b, 2023a) from the visual inferior temporal cortex (TE areas); from parts of the parietal cortex (PFm, which receives visual and auditory object-level information, and IP2, which is visuomotor; Rolls et al., 2023c); from the medial orbitofrontal cortex (11l, 13l, pOFC); from the inferior frontal gyrus regions, including IFJ, IFS and BA45; from the dorsolateral prefrontal cortex (8Av, 8BL, a9-46v and p9-46v) implicated in short-term memory (Rolls, 2023a; Rolls et al., 2023b); and from the frontal pole (a10p, p10p, 10pp; Rolls et al., 2022b, 2023a). In addition, 47m (which is relatively medial in this group) also has effective connectivity with the hippocampal system (Hipp, EC, perirhinal, and TF); with ventromedial prefrontal region 10r; and with the frontal pole (10d, and 9m; Rolls et al., 2024). The diffusion tractography provides, in addition, evidence for connections of these parts of the lateral orbitofrontal cortex with the anterior ventral insular region and the frontal opercular areas FOP4 and FOP5, which include the insular primary taste cortex (Rolls, 2015, 2016d; Rolls et al., 2022b, 2023a); with the AAIC, which may be visceral (Rolls, 2016d) and also has taste-olfactory convergence (de Araujo, Rolls, et al., 2003); with the middle insular region (MI), which is somatosensory (Rolls et al., 2023b); and with the piriform (olfactory) cortex.

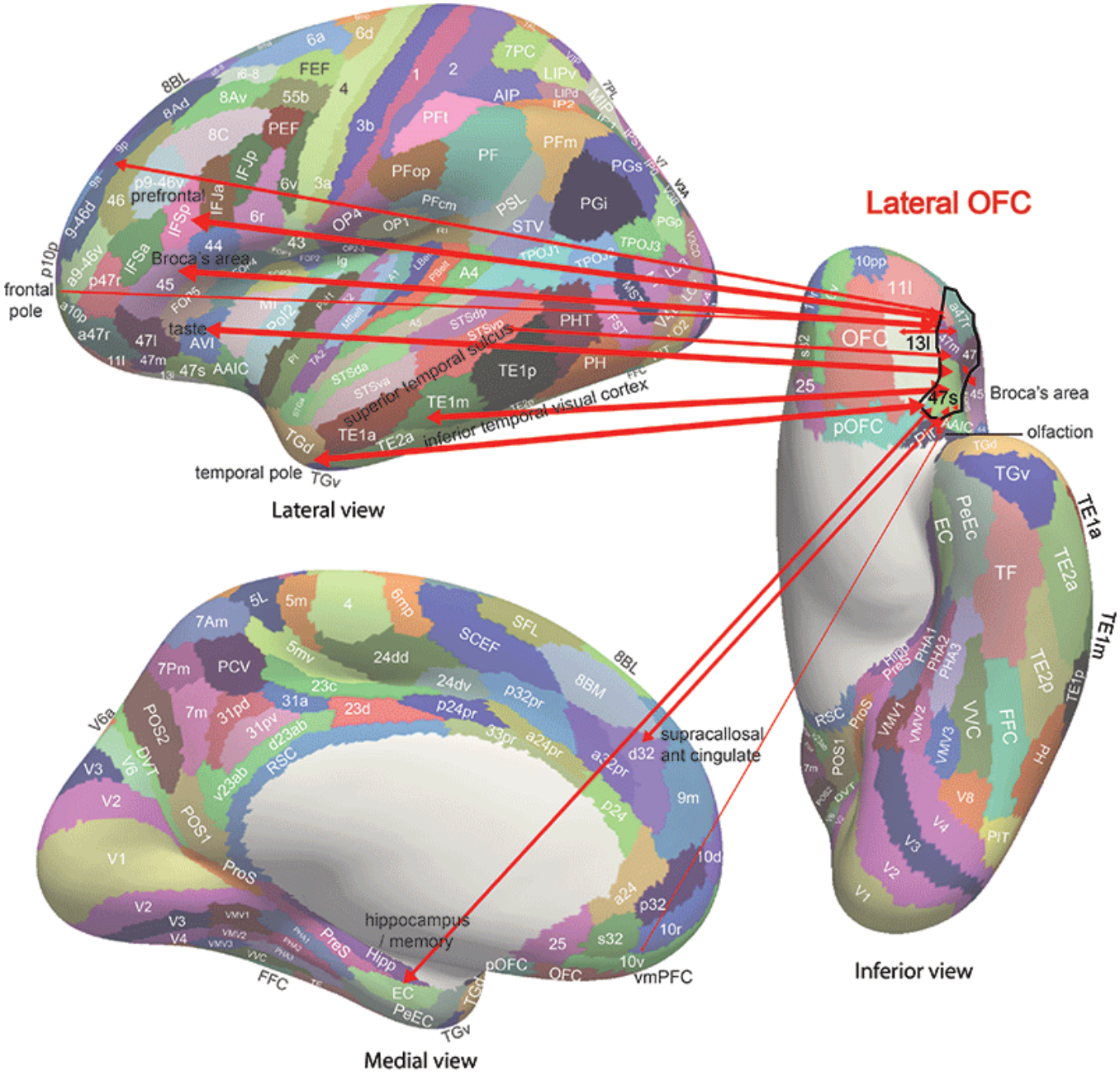

Figure 4. Summary of the effective connectivity of the human lateral orbitofrontal cortex. The lateral orbitofrontal cortex has taste, olfactory, and inferior temporal visual cortex inputs and connectivity with the hippocampus, supracallosal (dorsal) anterior cingulate cortex, inferior and dorsolateral prefrontal cortex, and frontal pole. However, the lateral OFC also has connectivity with language regions (the cortex in the superior temporal sulcus and Broca's area). The main regions with which the lateral OFC has connectivity are indicated by names with the words in black font. The width of the arrows and the size of the arrow heads in each direction reflects the strength of the effective connectivity. The abbreviations are listed in Rolls et al. (2022b).

Source: Modified from Rolls (2023a).

The human orbitofrontal cortex has connectivity to the hippocampal memory/navigation system that is both direct, and via the ventromedial prefrontal cortex (vmPFC) area 10 regions (10r, 10d, 10v and 9m), pregenual anterior cingulate cortex, and the memory-related parts of the posterior cingulate cortex (Figures 3 and 4; Rolls, 2022; Rolls et al., 2022b). It is proposed that this connectivity provides a key input about reward/punishment value for the hippocampal episodic memory system, adding to the "what," "where," and "when" information that are also key components of episodic memory (Rolls, 2022; Rolls et al., 2022b). Damage to the vmPFC/anterior cingulate cortex system is likely to contribute to episodic memory impairments by impairing a key component of episodic memory, the reward/punishment/emotional value component (Rolls, 2022; Rolls et al., 2022b). Moreover, the medial orbitofrontal cortex connects to the cholinergic nucleus basalis of Meynert and the pregenual cingulate to the septum, and damage to these cortical regions may contribute to memory impairments by disrupting cholinergic influences on the neocortex and hippocampus (Rolls, 2022; Rolls et al., 2022b). Navigation is generally towards goals, usually rewards, and it is proposed that this connectivity provides the goals for navigation to the hippocampal system to enable the hippocampus to be involved in navigation toward goals (Rolls, 2022, 2023c; Rolls et al., 2022b).

Two regions of the lateral orbitofrontal cortex, 47l and 47s, are especially connected with language systems in the temporal pole, cortex in the superior temporal sulcus (STS), and inferior frontal gyrus, including Broca's area 45 and 44 (Rolls et al., 2022a). This provides a route for subjective declarative reports to be made about the emotion-related pleasantness or unpleasantness of stimuli and events (Rolls, 2023a).

In the context that the anterior cingulate cortex is implicated in learning associations between actions and the rewards or punishers associated with the actions (Noonan et al., 2011; Rushworth et al., 2012; Rolls, 2019a, 2023a), the part of the human anterior cingulate cortex that is most likely to be involved in action-outcome learning is the supracallosal (or dorsal) anterior cingulate cortex (Rolls, 2019a). That part has effective connectivity with somato-motor areas involved in actions but also receives inputs from the medial orbitofrontal cortex and pregenual anterior cingulate cortex that, it is proposed, provide the reward/punishment "outcome" signals necessary for action-outcome learning (Rolls, 2023a; Rolls et al., 2022b).

Reward Value Representations in the Orbitofrontal Cortex

In this section, the representations of reward value found in the primate, including human, orbitofrontal cortex but not in the preceding cortical areas from which the orbitofrontal cortex receives it inputs, are described (Figure 2; Rolls, 2014a, 2014b, 2019b, 2019c, 2023a, 2023b).

Taste Reward Value: A Primary Reinforcer

One of the discoveries that have helped us to understand the functions of the orbitofrontal cortex in behavior is that it contains a major cortical representation of taste (see Kadohisa et al., 2005; Rolls, 2008a, 2014b, 2016b, 2023a; Rolls & Scott, 2003; Rolls et al., 1990). Given that taste can act as a primary reinforcer, that is without learning as a reward or punisher, we now have the start for a

fundamental understanding of the function of the orbitofrontal cortex in stimulus-reinforcer association learning (Rolls, 1999a, 2004, 2014b, 2016c, 2023a). This shows how one class of primary reinforcers reaches and is represented in the orbitofrontal cortex. A representation of primary reinforcers is essential for a system that is involved in learning associations between previously neutral stimuli and primary reinforcers, e.g., between the sight of an object and its taste (Rolls, 2014b, 2023a).

The representation (shown by analyzing the responses of single neurons in macaques) of taste in the primate orbitofrontal cortex includes robust representations of the prototypical tastes sweet, salt, bitter, and sour (Rolls et al., 1990) but also separate representations of the "taste" of water (Rolls et al., 1990) and of protein or umami as exemplified by monosodium glutamate (Baylis & Rolls, 1991; Rolls, 2000c) and inosine monophosphate (Rolls, Critchley, Wakeman, et al., 1996; Rolls et al., 1998).

The nature of the representation of taste in the orbitofrontal cortex is that for the majority of neurons, the reward value of the taste is represented. The evidence for this is that the responses of orbitofrontal taste neurons are modulated by hunger; that is, devaluation by feeding to satiety results in orbitofrontal cortex taste-related neurons no longer responding to the taste fed to satiety (Critchley & Rolls, 1996a; Rolls et al., 1989). The decrease is relatively specific to the food eaten to satiety. Figure 5 shows the response of a single macaque orbitofrontal cortex neuron with taste, olfactory, and visual responses to food when hungry, and a sensory-specific decrease in all three sensory modalities in responsiveness to the food eaten to satiety (Critchley & Rolls, 1996a; Rolls et al., 1989); and some neurons encode relative preferences (Tremblay & Schultz, 1999).

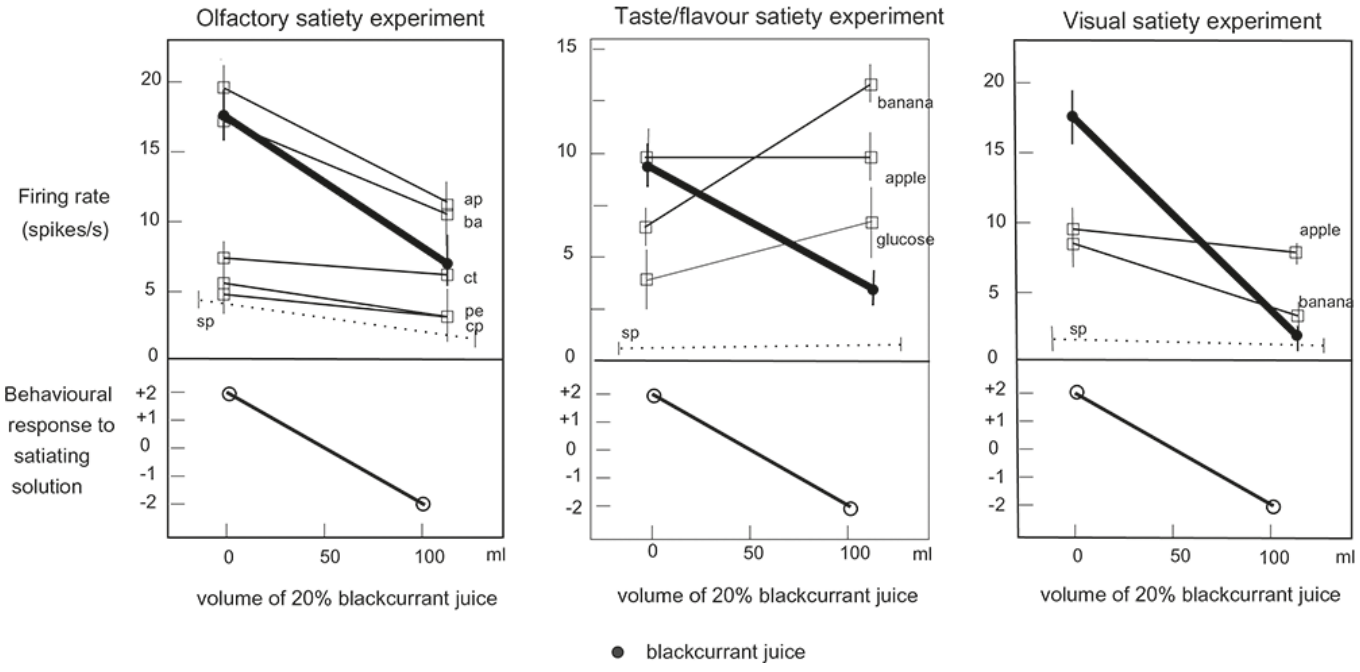

Figure 5. Multimodal orbitofrontal cortex neuron with sensory-specific satiety-related responses to visual, taste, and olfactory sensory inputs. The responses are shown before and after feeding to satiety with blackcurrant juice. The solid circles show the responses to blackcurrant juice. The olfactory stimuli included apple (ap), banana (ba), citral (ct), phenylethanol (pe), and caprylic acid (cp). The spontaneous firing rate of the neuron is shown (sp).

Source: After Critchley and Rolls (1996a).

In contrast, the representation of taste in the primary taste cortex (Scott et al., 1986; Yaxley et al., 1990) is not modulated by hunger (Rolls et al., 1988; Yaxley et al., 1988). Thus, in the primate primary taste cortex, the reward value of taste is not represented, and instead the identity and intensity of the taste are represented (Rolls, 2016d). Thus sensory-specific satiety is computed in the orbitofrontal cortex. The proposed mechanism is synaptic adaptation over the time course of a typical meal of the synapses from the primary taste cortex onto the olfactory neuron, for the same neuron remains easy to activate by a different food (Rolls et al., 2025). This can also be termed a reward-specific satiety effect (Pastor-Bernier et al., 2021; Rolls et al., 2025). The opposite effect, that initially making a reward available can increase its reward value (incentive motivation [Hebb, 1949] or "reward-specific motivation" [Rolls, 2026]) is proposed to be computed at the same synapses by a shorter term synaptic facilitation (Rolls et al., 2025).

Functional neuroimaging studies have shown that the most medial part of the human orbitofrontal cortex is activated by taste, oral texture, and olfactory stimuli (de Araujo & Rolls, 2004; de Araujo, Kringelbach, Rolls, & Hobden, 2003; de Araujo, Rolls, et al., 2003; de Araujo et al., 2005; Francis et al., 1999; Gottfried et al., 2006; McCabe & Rolls, 2007; O'Doherty et al., 2000; Rolls & McCabe, 2007; Rolls, Kringelbach, et al., 2003; Small et al., 2001, 2005) and that the activations correlate with ratings of subjective pleasantness (Kringelbach & Rolls, 2004; Rolls, 2014b). Some orbitofrontal cortex neurons respond to the taste of water in the mouth (Rolls et al., 1990), and their responses occur only when thirsty and not when satiated (Rolls et al., 1989); correspondingly, in humans, the pleasantness of the taste of water in the mouth is represented in the orbitofrontal cortex (de Araujo, Kringelbach, Rolls, & McGlone, 2003).

An Olfactory Representation in the Orbitofrontal Cortex

Rolls and colleagues have analyzed the rules by which orbitofrontal olfactory representations are formed and operate in primates. For 35% of the olfactory neurons, the odors to which a neuron responded were influenced by the taste (glucose or saline) with which the odor was associated (in an olfactory discrimination task with taste reward; Critchley & Rolls, 1996b). Thus the odor representation for 35% of orbitofrontal neurons appeared to be built by olfactory-to-taste association learning, and this was confirmed in that 68% of a sample of neurons analyzed reversed the odor to which they responded in an olfactory-taste reversal task (Rolls, Critchley, Mason, et al., 1996). The olfactory-to-taste reversal was quite slow, both neurophysiologically and behaviorally, often requiring 20–80 trials, consistent with the need for some stability of flavor representations. Orbitofrontal cortex olfactory neurons represent the reward value of the odors in that also devaluation by feeding to satiety decreased the responses of the majority of orbitofrontal cortex olfactory neurons to zero in a reward-specific way (see example in Figure 5; Critchley & Rolls, 1996a). Thus, for these neurons, the reward value of the odor is what is represented in the orbitofrontal cortex (Rolls et al., 1981, 1982; Rolls, 1997; cf. Rolls & Rolls, 1997; see Rolls, 1999a, 2000b, 2014b; Rolls et al., 2025).

Correspondingly, in human neuroimaging experiments, the pleasantness or reward value of odor is represented in the orbitofrontal cortex, in that feeding the humans to satiety decreases the activation found to the odor of that food, and this effect is relatively specific to the food eaten in the meal (Howard et al., 2015; O'Doherty et al., 2000).

Importantly, the human medial orbitofrontal cortex has activation that is linearly related to the subjective pleasantness of a set of odors, and a more lateral area has activation that is related to the degree of subjective unpleasantness of odors (Rolls, Kringelbach, et al., 2003). In contrast, in primary olfactory cortical areas, the activations reflected the intensity of the odors (Rolls, Kringelbach, et al., 2003).

A combination of taste and odor produces flavor, and this combination is evident in the orbitofrontal cortex at the neuronal and neuroimaging levels (de Araujo, Rolls, et al., 2003; Rolls & Baylis, 1994). The combination is formed in the orbitofrontal in that neurons in the primary taste cortex in the insular/frontal opercular cortex do not respond to olfactory (or visual) stimuli (Verhagen et al., 2004). Moreover, we have argued that umami (the rich delicious flavor of protein) is pleasant because it is a combination of glutamate taste (itself not very pleasant) with a consonant savory odor (McCabe & Rolls, 2007).

Oral Including Fat Texture and Temperature

Some neurons in the macaque orbitofrontal cortex respond to the texture of food in the mouth. Some neurons alter their responses when the texture of a food is modified by adding gelatine or methyl cellulose or by partially liquefying a solid food such as apple (Critchley et al., 1993).

Another population of orbitofrontal neurons responds when a fatty food such as cream is in the mouth. These neurons can also be activated by pure fat such as glyceryl trioleate, and by non-fat substances with a fat-like texture such as paraffin oil (hydrocarbon) and silicone oil ($Si(CH_3)_2O)_n$). These neurons thus provide information by somatosensory pathways that a fatty food is in the mouth (Rolls et al., 1999). These inputs are perceived as pleasant when hungry because of the utility of ingestion of foods that are likely to contain essential fatty acids and to have a high calorific value (Rolls, 2000b, 2014b, 2016e). Satiety produced by eating a fatty food, cream, can decrease the responses of orbitofrontal cortex neurons to the texture of fat in the mouth, so it is the reward value of fat texture that is encoded by these neurons (Rolls et al., 1999). The oral representation in the orbitofrontal cortex of fat texture is encoded by the coefficient of sliding friction, which importantly opens the way to the development of new foods with the pleasant mouth feel of fat but with little or no fat content (Rolls, Mills, et al., 2018; Verhagen et al., 2003).

In humans, a medial prefrontal/cingulate cortex area is activated by the mouth feel of fat (de Araujo & Rolls, 2004); the pleasantness of fat texture in the mouth is correlated with activations in the midorbitofrontal and anterior cingulate cortex (Grabenhorst et al., 2010); and it has been confirmed that the coefficient of sliding friction (Rolls, Mills, et al., 2018) is involved in the representation in the orbitofrontal cortex of the pleasantness of fat texture in food (Khorisantono et al., 2023). In contrast, the somatosensory cortex is activated by fat texture, but here the ratings are not correlated with the pleasantness of the fat texture but with the rated fattiness, consistent with the hypothesis

that early cortical stages analyze the sensory properties of stimuli, and that the pleasantness and reward value are represented later in processing in the orbitofrontal cortex (Grabenhorst & Rolls, 2014).

A different population of orbitofrontal cortex neurons encodes oral viscosity (Rolls, Verhagen, et al., 2003), and an overlapping population of orbitofrontal cortex neurons represents the temperature of what is in the mouth (Kadohisa et al., 2004). Also, in humans, there is a representation of the temperature of what is in the mouth (Guest et al., 2007). The oral temperature stimuli (cool and warm, 5°C, 20°C, and 50°C) activated the insular taste cortex (identified by glucose taste stimuli), a part of the somatosensory cortex, the orbitofrontal cortex, the anterior cingulate cortex, and the ventral striatum. Brain regions where activations correlated with the pleasantness ratings of the oral temperature stimuli included the orbitofrontal cortex and pregenual cingulate cortex (Guest et al., 2007). Part of the advantage of having a representation of oral temperature in these regions is that neurons can then encode combinations of taste, texture, and oral temperature (Kadohisa et al., 2004; Rolls, 2014b, 2016c; Verhagen et al., 2004).

Somatosensory and Temperature Inputs to the Orbitofrontal Cortex, and Affective Value

In addition to these oral somatosensory inputs to the orbitofrontal cortex, there are also somatosensory inputs from other parts of the body, and indeed a functional magnetic resonance imaging (fMRI) investigation we have performed in humans indicates that pleasant and painful touch stimuli to the hand produce greater activation of the orbitofrontal cortex relative to the somatosensory cortex than do affectively neutral stimuli (Francis et al., 1999; Rolls, O'Doherty, et al., 2003).

Non-glabrous skin such as that on the forearm contains C fiber tactile afferents that respond to light moving touch (Olausson et al., 2002). The orbitofrontal cortex is implicated in some of the affectively pleasant aspects of touch that may be mediated through C fiber tactile afferents, in that it is activated more by light touch to the forearm than by light touch to the glabrous skin (palm) of the hand (McCabe et al., 2008; Rolls, 2010, 2016b).

Warm and cold stimuli have affective components such as feeling pleasant or unpleasant, and these components may have survival value, for approach to warmth and avoidance of cold may be reinforcers or goals for action built into us during evolution to direct our behavior to stimuli that are appropriate for survival. In an fMRI investigation in humans, it was found that the mid-orbitofrontal and pregenual cingulate cortex and the ventral striatum have activations that are correlated with the subjective pleasantness ratings made to warm (41°C) and cold (12°C) stimuli and combinations of warm and cold stimuli applied to the hand (Rolls, Grabenhorst, & Parris, 2008). Activations in the lateral and some more anterior parts of the orbitofrontal cortex were correlated with the unpleasantness of the stimuli. In contrast, activations in the somatosensory cortex and ventral posterior insula were correlated with the intensity but not the pleasantness of the thermal stimuli (Rolls, Grabenhorst, & Parris, 2008).

Visual Inputs and Expected Reward Value in the Orbitofrontal Cortex: Devaluation and Visual Stimulus-Reinforcement Association Learning and Reversal

We have been able to show that there is a major visual input to many neurons in the orbitofrontal cortex and that what is represented by these neurons is in many cases the reinforcement association of visual stimuli, that is, expected value. The visual input is from the ventral, temporal lobe, visual stream concerned with "what" object is being seen (see Rolls, 2000a, 2016c, 2023a, 2024b; Rolls & Deco, 2002). Many neurons in these temporal cortex visual areas have responses to objects or faces that are invariant with respect to size, position on the retina, and even view (Rolls, 2000a, 2012, 2021c, 2023a; Rolls & Deco, 2002), making these neurons ideal as an input to a system that may learn about the reinforcement association properties of objects and faces, in that after a single learning trial, the learning then generalizes correctly to other views, etc. (see Rolls, 2000a, 2023a; Rolls & Deco, 2002).

Using this object-related information, orbitofrontal cortex visual neurons frequently respond to objects or images based on their reward value (Rolls, Critchley, Mason, et al., 1996; Thorpe et al., 1983). Many of these neurons show visual-taste reversal in one or a very few trials (see example in Figure 6). (In a visual discrimination task, they will reverse the stimulus to which they respond, from, e.g., a triangle to a square, in one trial when the taste delivered for a behavioral response to that stimulus is reversed; Thorpe et al., 1983.) In principle, this could be implemented by associative modification of synapses conveying visual input onto taste-responsive neurons, implementing a pattern association network (Rolls, 2014b, 2023a). However, in primates, visual-to-taste reversal is so rapid that after a punishment has been received to the positive discriminative stimulus (S+), the next time that the previous S- is shown, the neurons respond to it as an S+, and the monkey chooses that stimulus (Rolls, Critchley, Mason, et al., 1996; Thorpe et al., 1983). This is a non-associative process that involves a rule change in a model-based system, and this is a special contribution that the primate orbitofrontal cortex makes to reversal learning, and for which a computational theory that utilizes the conditional reward and error neurons has been produced (Deco & Rolls, 2005c).

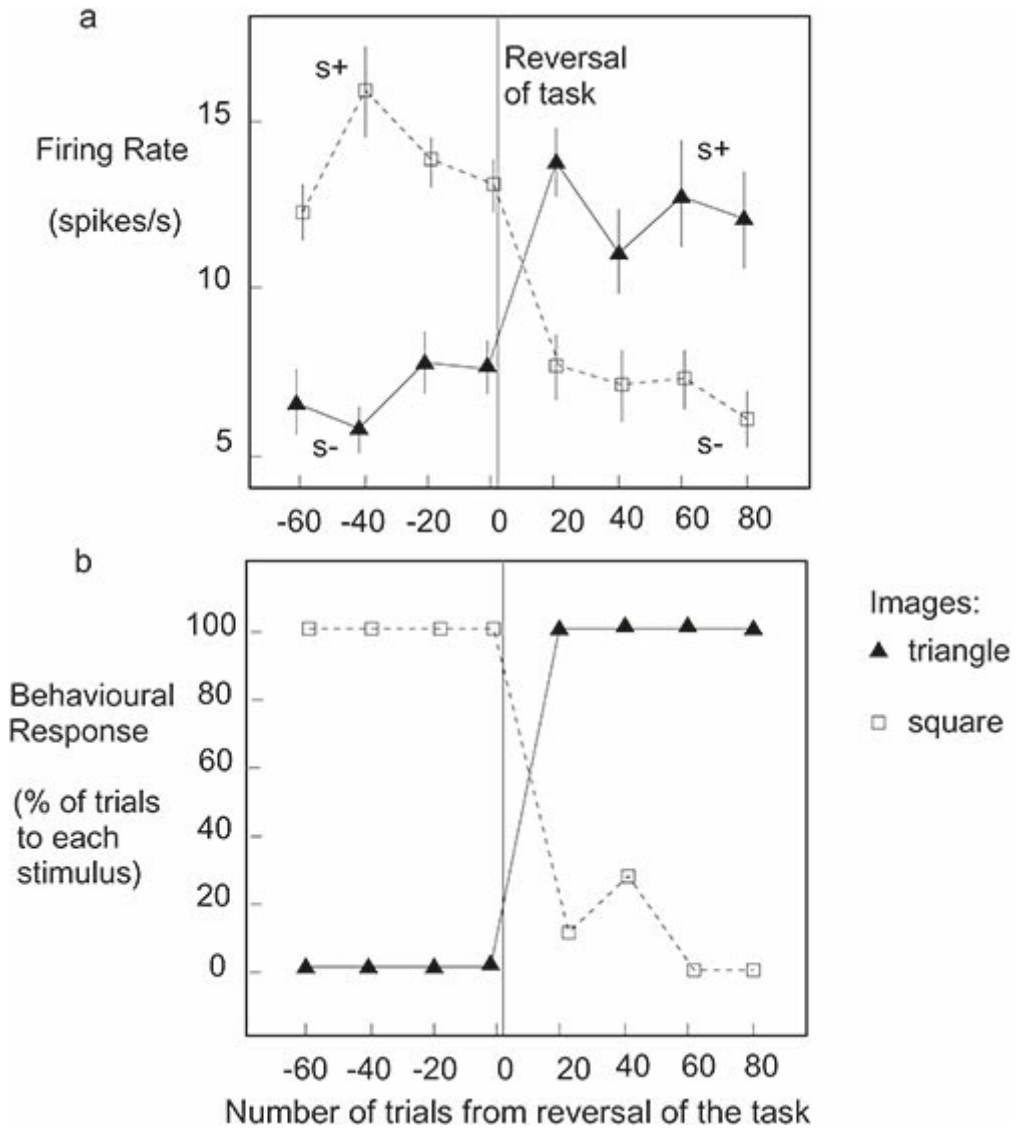

Figure 6. Visual discrimination reversal of the responses of a single neuron in the macaque orbitofrontal cortex when the taste with which the two visual stimuli (a triangle and a square) were associated was reversed. Each point is the mean poststimulus firing rate measured in a 0.5 s period over approximately 10 trials to each of the stimuli. Before reversal, the neuron fired most to the square when it indicated (S+) that the monkey could lick to obtain a taste of glucose. After reversal, the neuron responded most to the triangle when it indicated that the monkey could lick to obtain glucose. The response was low to the stimuli when they indicated (S−) that if the monkey licked, then aversive saline would be obtained. Panel B shows the behavioural response to the triangle and the square and indicates that the monkey reversed rapidly.

Source: After Rolls, Critchley, Mason, et al. (1996). Modified from Rolls (2023a).

A computational theory of how not receiving an expected reward reverses the rule neurons has also been developed (Rolls & Deco, 2016). This reversal learning probably does occur in the orbitofrontal cortex, for it does not occur one synapse earlier in the visual inferior temporal cortex (Rolls, Aggelopoulos, et al., 2003; Rolls et al., 1977), and it is in the orbitofrontal cortex that there is convergence of visual and taste pathways onto the same single neurons (Rolls & Baylis, 1994; Rolls, Critchley, Mason, et al., 1996; Thorpe et al., 1983).

The representation of expected value by primate orbitofrontal cortex is further shown by devaluation: feeding to satiety decreases the responses of orbitofrontal cortex to zero (Critchley & Rolls, 1996a). Moreover, this is a sensory-specific decrease (see example in Figure 5), and the orbitofrontal cortex is thus where reward-specific satiety or sensory-specific satiety is computed (Rolls et al., 2025).

Social Reinforcers are Represented in the Orbitofrontal Cortex

We extended these discoveries about visual expected value to social types of reward: we discovered orbitofrontal cortex visual neurons in macaques that respond to the sight of face expression or to face identity (Rolls et al., 2006), both of which are important in producing appropriate social behavior to another individual. This implicates the orbitofrontal cortex in social reward. This research was extended by the finding that some orbitofrontal cortex neurons are tuned to socially relevant categories of faces, such as juveniles (Barat et al., 2018). Socially relevant stimuli such as the sight of face expression and of change of face expression also activate the human orbitofrontal cortex (Kringelbach & Rolls, 2003, 2004).

Economic Value Is Represented in the Orbitofrontal Cortex

Extending the analysis of reward value further, we made the discovery that an abstract type of reward, monetary reward, is represented in the human orbitofrontal cortex (O'Doherty et al., 2001). This discovery helped to seed interest in the orbitofrontal cortex and neuroeconomics, and enormous interest followed (Glimcher & Fehr, 2013; Padoa-Schioppa, 2007; Padoa-Schioppa & Assad, 2006, 2008; Padoa-Schioppa & Conen, 2017). One interesting advance is that we confirmed activation of the medial orbitofrontal cortex when winning points in a deterministic Go/NoGo task (like that used in macaques; Critchley & Rolls, 1996b; Rolls, Critchley, Mason, et al., 1996; Thorpe et al., 1983) and activation of the lateral orbitofrontal cortex when losing points (Rolls, Vatansever, et al., 2020). Another advance was the demonstration in a group of almost 2,000 adolescents that winning points in a monetary incentive delay task activates the medial orbitofrontal cortex and that losing points activates the lateral orbitofrontal cortex (Xie et al., 2021; Figure 7).

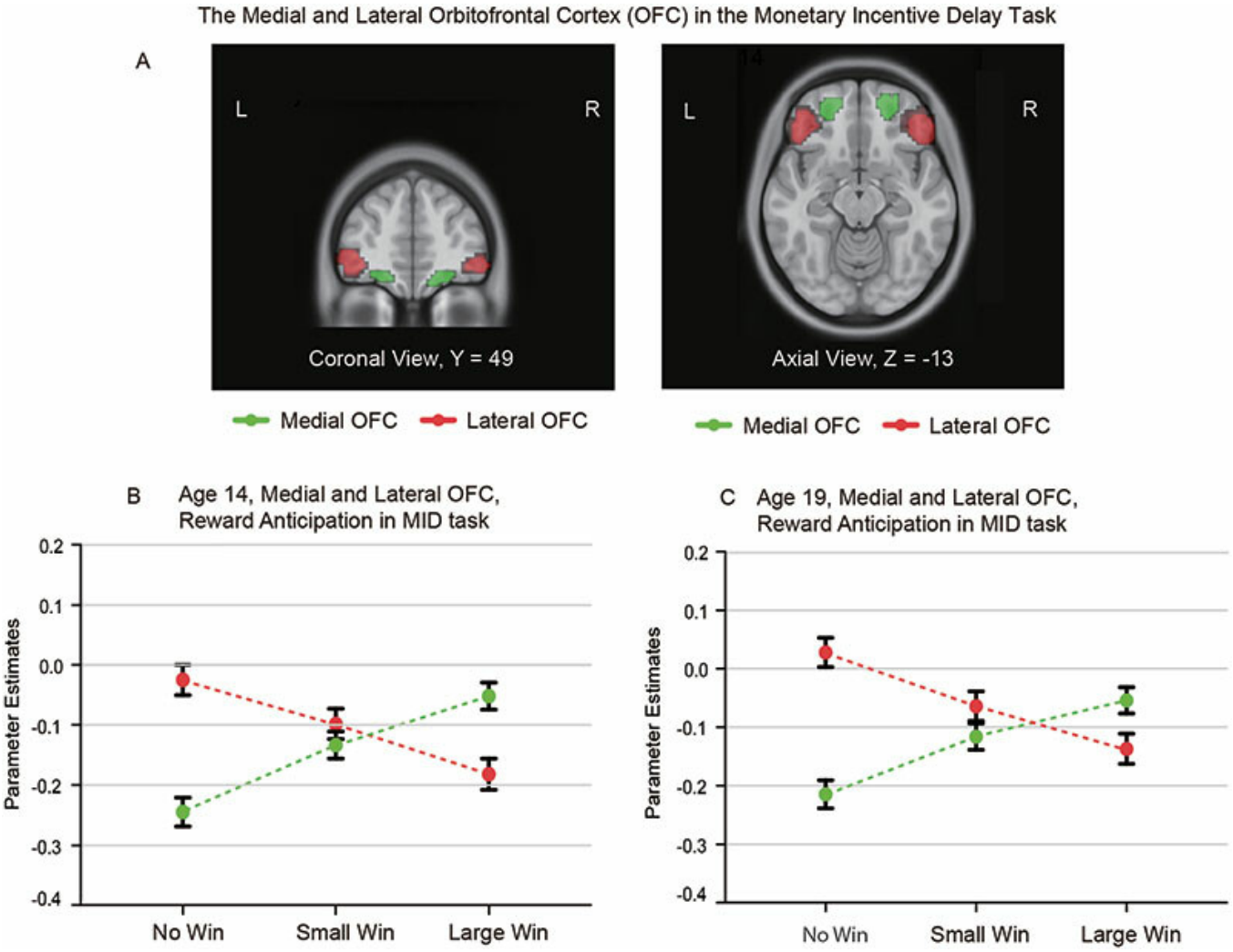

Figure 7. The lateral orbitofrontal cortex is activated by not winning and the medial orbitofrontal cortex by winning, in the monetary incentive delay task. The lateral orbitofrontal cortex region in which activations increased toward no reward (No Win) in the monetary incentive delay task are shown in red in 1,140 participants at age 19 and in 1,877 overlapping participants at age 14. The conditions were Large Win (10 points) to Small Win (2 points) to No Win (0 points; at 19; sweets were used at 14). The medial orbitofrontal cortex region in which activations increased with increasing reward from No Win to Small Win to High Win) is shown in green. The parameter estimates are shown from the activations for the participants (mean ± SEM) with the lateral orbitofrontal cortex in red and medial orbitofrontal cortex in green. The interaction term showing the sensitivity of the medial orbitofrontal cortex to reward and the lateral orbitofrontal cortex to non-reward was significant at $p = 10^{-50}$ at age 19 and $p < 10^{-72}$ at age 14.

Source: Modified from Xie et al. (2021) and Rolls (2023a).

Our neuroeconomic discoveries that reward value, including monetary reward value, are represented in the primate including human orbitofrontal cortex have been interestingly extended to the economic trade-off between the quality versus the amount of reward that is on offer and to the reward probability (Ballesta et al., 2020; Battista et al., 2025; Padoa-Schioppa, 2007; Padoa-Schioppa & Assad, 2006, 2008; Padoa-Schioppa & Conen, 2017).

Rewards are Represented Medially, and Punishers and Non-Reward Laterally, in the Human Orbitofrontal Cortex

Many types of reward and punisher are represented in the human orbitofrontal cortex. For example, monetary reward is represented in the medial orbitofrontal cortex and losing money in the lateral orbitofrontal cortex (O'Doherty et al., 2001). Beauty in a face is also represented in the medial orbitofrontal cortex (O'Doherty et al., 2003). In addition, it has been shown that amphetamine, a potent instrumental reinforcer, is self-administered to the orbitofrontal cortex by macaques (Phillips et al., 1981) and that in drug-naïve human participants, amphetamine activates the medial orbitofrontal cortex (Völlm et al., 2004). Many rewards are represented medially in the orbitofrontal cortex, in areas 13 and 11, and many punishers and non-rewards are represented laterally in area 47/12, as shown in Figure 8 (Grabenhorst & Rolls, 2011; Rolls, 2014b). These discoveries have been confirmed using economic rewards and punishers (Rolls, Vatansever, et al., 2020; Xie et al., 2021; Figures 7, 9 and 12).

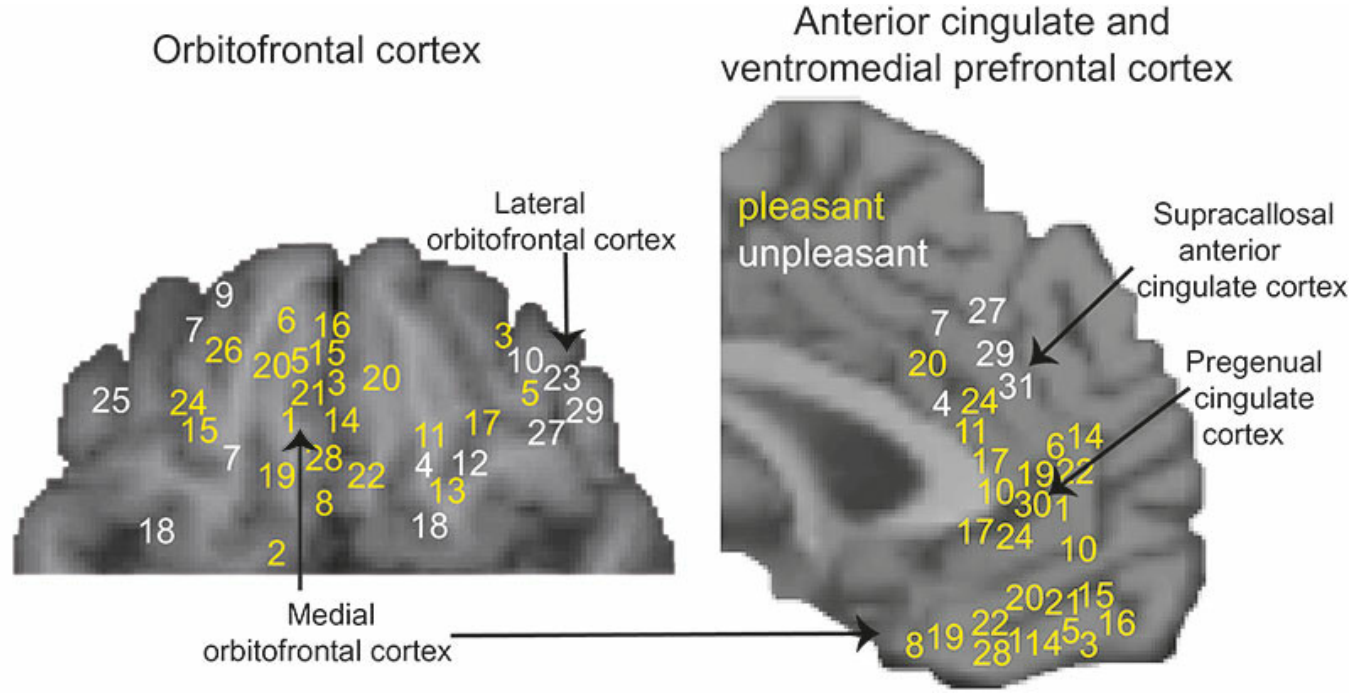

Figure 8. Rewards tend to be represented medially in the human orbitofrontal cortex and in the pregenual cingulate cortex and non-reward and punishment laterally in the orbitofrontal cortex and in the supracallosal anterior cingulate cortex. Maps of subjective pleasure in the human orbitofrontal cortex (ventral view) and anterior cingulate and ventromedial prefrontal cortex (sagittal view). Yellow: sites where activations correlate with subjective pleasantness. White: sites where activations correlate with subjective unpleasantness. The numbers refer to effects found in specific studies. Taste: 1, 2; odor: 3–10; flavor: 11–16; oral texture: 17, 18; chocolate: 19; water: 20; wine: 21; oral temperature: 22, 23; somatosensory temperature: 24, 25; the sight of touch: 26, 27; facial attractiveness: 28, 29; erotic pictures: 30; laser-induced pain: 31. Consistent laterality effects are not generally observed in these investigations.

Source: After Grabenhorst and Rolls (2011). Modified from Rolls (2023a).

Orbitofrontal Cortex Negative Reward Prediction Error Neurons

In addition to the neurons that encode the expected reward value of visual stimuli, other, "error," neurons in the orbitofrontal cortex detect non-reward, in that they respond, for example, when an expected reward is not obtained when a visual discrimination task is reversed (Thorpe et al., 1983; see Figure 9C), or when reward is no longer made available in a visual discrimination task. These neurons respond to a mismatch between the expected reward value (in this case, signaled by the visual stimulus) and the reward outcome (in this case, the taste). These neurons are thus termed "negative reward prediction error neurons" (Rolls, 2014b, 2016c, 2023a, 2026; Rolls & Grabenhorst, 2008). Consistent results were found in different tasks in a complementary study (10/140 non-reward neurons in the orbitofrontal cortex, or 7.1%; Rosenkilde et al., 1981).

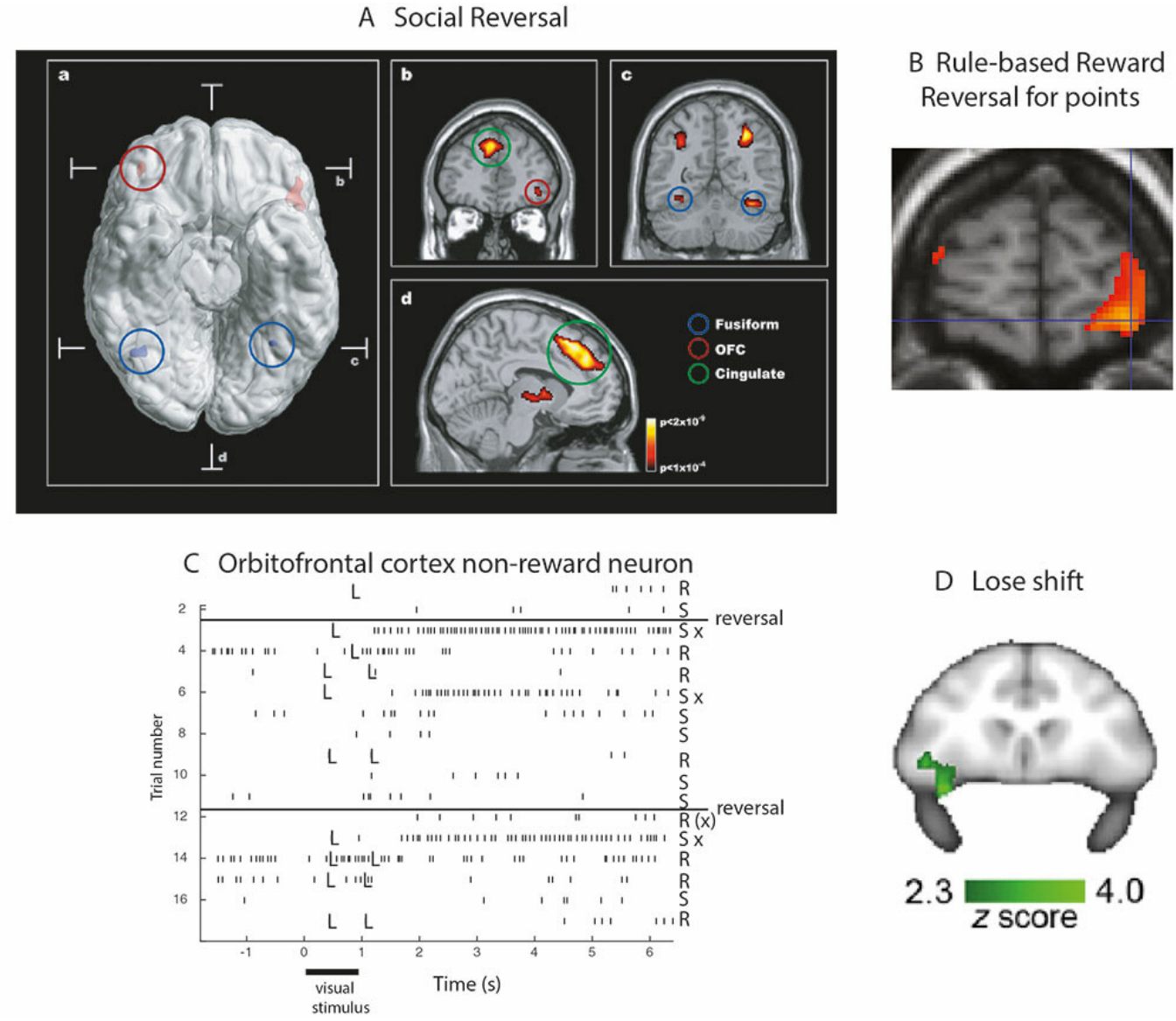

Figure 9. Evidence that the lateral orbitofrontal cortex is activated by non-reward. (A) Activation of the lateral orbitofrontal cortex in a visual discrimination reversal task on reversal trials, when a face was selected but the expected reward was not obtained, indicating that the subject should select the other face in future to obtain the

reward. (a) A ventral view of the human brain with indication of the location of the two coronal slices (b,c) and the transverse slice (d). The activations with the red circle in the lateral orbitofrontal cortex (OFC, peaks at [42 42 -8] and [-46 30 -8]) show the activation on reversal trials compared to the nonreversal trials. For comparison, the activations with the blue circle show the fusiform face area produced just by face expressions, not by reversal, which are also indicated in the coronal slice in c. (b) A coronal slice showing the activation in the right orbitofrontal cortex on reversal trials. Activation is also shown in the supracallosal anterior cingulate region (cingulate, green circle) that is also known to be activated by many punishing, unpleasant, stimuli (see Grabenhorst & Rolls, 2011). (B) Activations in the human right lateral orbitofrontal cortex on the reversal trials of a Go/NoGo visual discrimination reversal task in humans. This was a deterministic task in which points could be won or lost and the reversal was rule-based in one trial, analogous to the task in which non-reward neurons were discovered in macaques. (C) Non-reward error-related neurons maintain their firing after non-reward is obtained. Responses of an orbitofrontal cortex neuron that responded only when the macaque licked to a visual stimulus during reversal, expecting to obtain fruit juice reward but actually obtaining the taste of aversive saline because it was the first trial of reversal (trials 3, 6, and 13). Each vertical line represents an action potential; each L indicates a lick response in the Go/NoGo visual discrimination task. The visual stimulus was shown at time 0 for 1 s. The neuron did not respond on most reward (R) or saline (S) trials but did respond on the trials marked S x, which were the first or second trials after a reversal of the visual discrimination on which the monkey licked to obtain reward but actually obtained saline because the task had been reversed. The two times at which the reward contingencies were reversed are indicated. After responding to non-reward, when the expected reward was not obtained, the neuron fired for many seconds and was sometimes still firing at the start of the next trial. It is notable that after an expected reward was not obtained due to a reversal contingency being applied, on the very next trial the macaque selected the previously non-rewarded stimulus. This shows that rapid reversal can be performed by a nonassociative process, and must be rule-based. (D) Bold signal in the macaque lateral orbitofrontal related to win-stay/lose-shift performance, that is, to reward reversal performance on the lose-shift trials shown.

Source: (A) From Kringelbach and Rolls (2003), Copyright, 2003, with permission from Elsevier; (B) after Rolls, Vatansever, et al. (2020); (C) after Thorpe et al. (1983); (D) after Chau et al. (2015). Modified from Rolls (2023a).

Both signals needed for the computation of negative reward prediction error are represented in the orbitofrontal cortex, in the form of, for example, neurons that respond to the sight of a learned reinforcer, such as the sight of a stimulus paired with taste, and neurons that respond to the primary reinforcer (or outcome), the taste (or texture or temperature). The orbitofrontal cortex is the probable brain region for this computation because both of the signals required to compute negative reward prediction error are present in the orbitofrontal cortex, as are the negative reward prediction error neurons, and lesions of the orbitofrontal cortex impair tasks such as visual discrimination reversal, in which this type of negative reward prediction error is needed (Rolls, 2023a). Different populations of such neurons respond to other types of non-reward, including the removal of a formerly approaching taste reward, the termination of a taste reward in the extinction of ad lib licking for juice, or the substitution of juice reward by aversive tasting saline during ad lib licking (Rolls & Grabenhorst, 2008; Thorpe et al., 1983). The presence of these neurons is fully consistent with the hypothesis that they are part of the mechanism by which the orbitofrontal cortex enables very rapid reversal of behavior by stimulus–reinforcement association relearning when the association of stimuli with reinforcers is altered or reversed (Deco & Rolls, 2005c; Rolls &

Deco, 2016). The finding that different orbitofrontal cortex neurons respond to different types of non-reward (or negative reward prediction error; Thorpe et al., 1983) may provide part of the brain's mechanism that enables task- or context-specific reversal to occur.

Evidence that there may be similar error neurons in the human orbitofrontal cortex is that in a model of social learning, orbitofrontal cortex activation occurred in a visual discrimination reversal task at the time when the face of one person no longer was associated with a smile but became associated with an angry expression, indicating on such error trials that reversal of choice to the other individual's face should occur (Kringelbach & Rolls, 2003; Figure 9A). Further evidence supporting this is that the lateral orbitofrontal cortex is activated when money is not received in a monetary reward task (O'Doherty et al., 2001; Xie et al., 2021; see Figure 7), and in a rule-based deterministic one-trial reward reversal task for points as illustrated in Figure 9B (Rolls, Vatansever, et al., 2020).

Consistent with this evidence for humans, functional neuroimaging in macaques reveals that the macaque lateral orbitofrontal cortex is activated by non-reward during a reversal task (Chau et al., 2015; Figure 9D).

In responding when the reward obtained is less than that expected, the orbitofrontal cortex negative reward prediction error neurons are working in a domain that is related to the sensory inputs being received (expected reward and reward obtained). There are also error neurons in the anterior cingulate cortex that respond when errors are made (Niki & Watanabe, 1979) or when rewards are reduced (Shima & Tanji, 1998; see Rolls, 2019a). Some of these neurons may be influenced by the projections from the orbitofrontal cortex and reflect a mismatch between the reward expected and the reward that is obtained. However, some error neurons in the anterior cingulate cortex may reflect errors that arise when particular actions are in error, and this type of error may be important in helping an action system to correct itself, rather than, as in the orbitofrontal cortex, a reward prediction system needing to be corrected. Consistent with this, many studies provide evidence that errors made in many tasks activate the anterior/midcingulate cortex, whereas tasks with response conflict activate the superior frontal gyrus (Matsumoto et al., 2007; Rolls, 2019a; Rushworth & Behrens, 2008; Rushworth et al., 2004; Vogt, 2009).

A Representation of Novel Visual Stimuli in the Orbitofrontal Cortex.

A population of neurons has been discovered in the primate orbitofrontal cortex that responds to novel but not familiar visual stimuli and takes typically a few trials to habituate (Rolls et al., 2005). The memories of these neurons last for at least 24 h. Exactly what role these neurons have in memory is not yet known, but there are connections from the area in which these neurons are recorded to the temporal lobe, and activations in a corresponding orbitofrontal cortex area in humans are found when new visual stimuli must be encoded in memory (Frey & Petrides, 2002, 2003; Petrides, 2007).

Top-Down Effects of Cognition and Attention on Taste, Olfactory, Flavor, Somatosensory, and Visual Processing: Cognitive Enhancement of the Value of Affective Stimuli

How does cognition influence affective/reward value? How does cognition influence the way that we feel emotionally? Do cognition and emotion interact in regions that are high in the brain's hierarchy of processing, or do cognitive influences descend down to influence the first regions that represent the affective value of stimuli, such as the orbitofrontal cortex?

A functional magnetic resonance imaging (fMRI) study to address these fundamental issues in human brain design has shown that cognitive effects can reach down into the orbitofrontal cortex and influence activations produced by odors (de Araujo et al., 2005). In this study, a standard test odor, isovaleric acid with a small amount of cheese flavor, was delivered through an olfactometer. (The odor alone, like the odor of brie, might have been interpreted as pleasant, or perhaps as unpleasant.) On some trials, the test odor was accompanied with the visually presented word label "cheddar cheese", and on other trials with the word label "body odor." It was found that the activation in the medial orbitofrontal cortex to the standard test odor was much greater when the word label was "cheddar cheese" than when it was "body odor." (Controls with clean air were run to show that the effect could not be accounted for by the word label alone.) Moreover, the word labels influenced the subjective pleasantness ratings to the test odor, and the changing pleasantness ratings were correlated with the activations in the human medial orbitofrontal cortex. Part of the interest and importance of this finding is that it shows that cognitive influences, originating here purely at the word level, can reach down and modulate activations in the first stage of cortical processing that represents the affective value of sensory stimuli, the orbitofrontal cortex (de Araujo et al., 2005; Rolls, 2014b, 2023a).

Also important is how cognition influences the affective brain representations of the taste and flavor of a food. This is important not only for understanding top-down attentional and memory recall influences in the brain but also in relation to the issues of appetite control and obesity (Rolls, 2016e). In an fMRI study, it was shown that activations related to the affective value of umami taste and flavor (as shown by correlations with pleasantness ratings) in the orbitofrontal cortex were modulated by word-level descriptors (e.g., "rich and delicious flavor"; Grabenhorst, Rolls, & Bilderbeck, 2008; see Figure 10). Affect-related activations to taste were modulated in a region that receives from the orbitofrontal cortex, the pregenual cingulate cortex, and to taste and flavor in another region that receives from the orbitofrontal cortex, the ventral striatum. Affect-related cognitive modulations were not found in the insular taste cortex, where the intensity but not the pleasantness of the taste was represented. Thus, the top-down language-level cognitive effects reach far down into the earliest cortical areas that represent the appetitive value of taste and flavor. This is an important way in which cognition influences the neural mechanisms that control appetite (Grabenhorst, Rolls, & Bilderbeck, 2008).

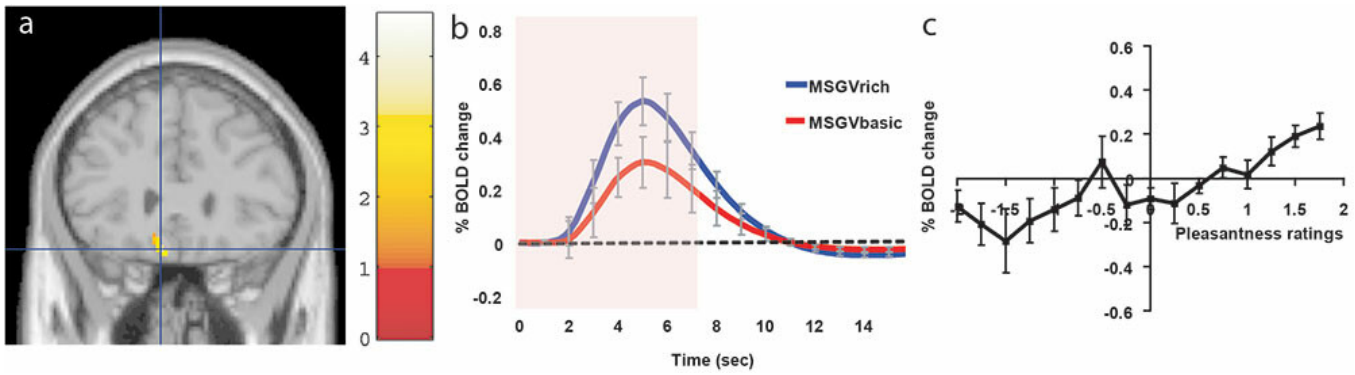

Figure 10. Cognitive modulation of affective representations in the medial orbitofrontal cortex. (A) The medial orbitofrontal cortex was more strongly activated when the flavor stimulus was labeled "rich and delicious flavor" (MSGVrich) than when it was labeled "boiled vegetable water" (MSGVbasic; [-8 28 -20]). (B) The timecourse of the BOLD signals for the two conditions. The means across subjects ± SEM are shown. (C) The BOLD signal in the medial orbitofrontal cortex was correlated with the subjective pleasantness ratings of taste and flavor (mean across subjects ± SEM, $r = 0.86$, $p < 0.001$).

Source: After Grabenhorst, Rolls, and Bilderbeck (2008). Modified from Rolls (2023a).

When we see a person being touched, we may empathize the feelings being produced by the touch. Interestingly, cognitive modulation of this effect can be produced. When subjects were informed by word labels that a cream seen being rubbed onto the forearm was a "Rich moisturizing cream" versus "Basic cream," these cognitive labels influenced activations in the orbitofrontal/pregenual cingulate cortex and ventral striatum to the sight of touch and their correlations with the pleasantness ratings (McCabe et al., 2008). Some evidence for top-down cognitive modulation of the effects produced by the subject being rubbed with the cream was found in brain regions such as the orbitofrontal and pregenual cingulate cortex and ventral striatum, but some effects were found in other brain regions, perhaps reflecting back projections from the orbitofrontal cortex (McCabe et al., 2008).

What may be a fundamental principle of how top-down attention can influence affective versus non-affective processing has been discovered. For an identical taste stimulus, paying attention to pleasantness activated some brain systems, and paying attention to intensity, which reflected the physical and not the affective properties of the stimulus, activated other brain systems (Grabenhorst & Rolls, 2008). In an fMRI investigation, when participants were instructed to remember and rate the pleasantness of a taste stimulus, 0.1 M monosodium glutamate, activations were greater in the medial orbitofrontal and pregenual anterior cingulate cortex than when subjects were instructed to remember and rate the intensity of the taste (Figure 11a–c). When the participants were instructed to remember and rate the intensity, activations were greater in the insular taste cortex (Figure 11d–f). Thus, depending on the context in which tastes are presented and whether affect is relevant, the brain responds to a taste differently.

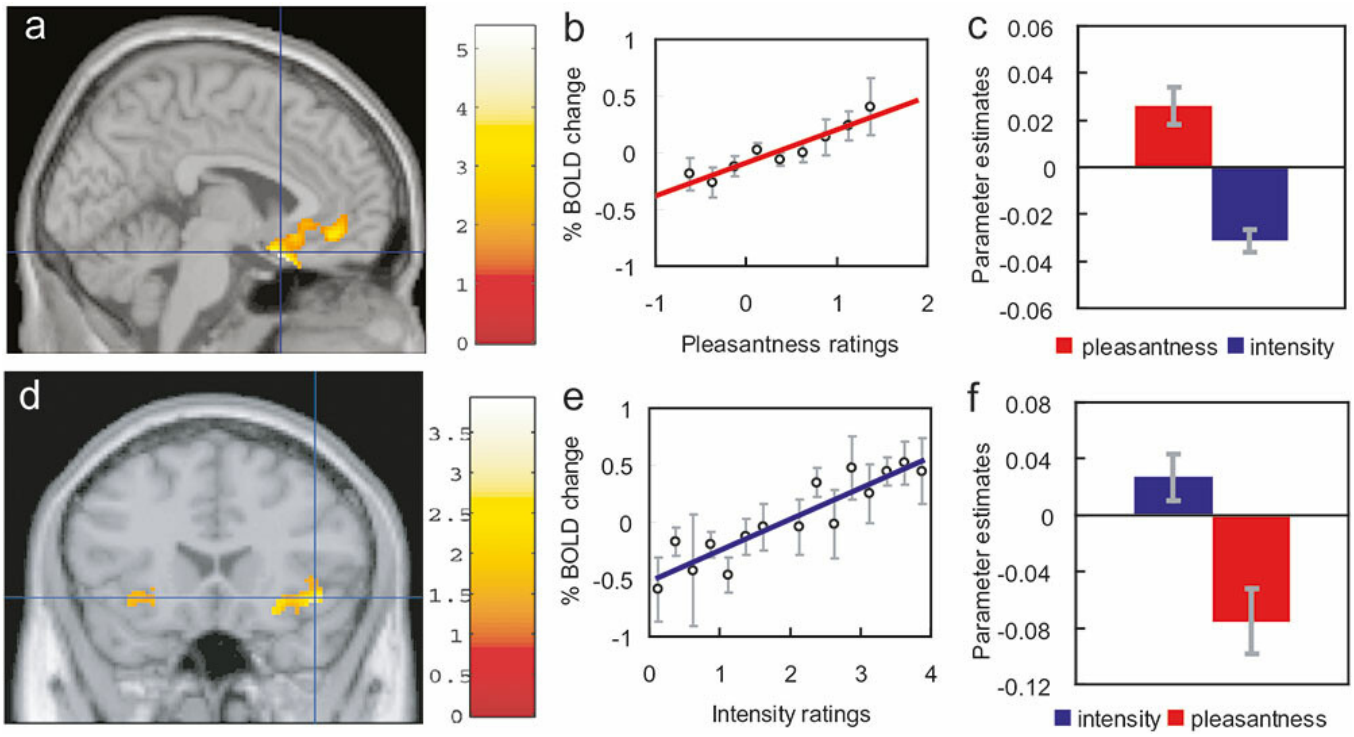

Figure 11. Effects of attention to the pleasantness versus the intensity of a taste stimulus (0.1 M monosodium glutamate, which was identical on all trials). Top: The contrast paying attention to pleasantness—paying attention to intensity. (a) A significant difference was found in the medial orbitofrontal cortex at [-6 14 -20] (at the cursor) which extended forward into the pregenual cingulate cortex (at [-4 46 -8]). (b) The activations (% BOLD change) were correlated with the subjective pleasantness ratings in the medial orbitofrontal cortex. ($r = 0.94$, df = 8, $p << 0.001$). (c) The parameter estimates (mean ± SEM across subjects) for the medial orbitofrontal cortex activations for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different ($p < 10^{-4}$). Bottom: The contrast paying attention to intensity—paying attention to pleasantness. (d) A significant difference was found in the taste insula at [42 18 -14] (indicated by the cursor). (e) The activations (% BOLD change) were correlated with the subjective intensity ratings in the taste insula medial orbitofrontal cortex. (r = 0.89, df = 15, $p << 0.001$). (f) The parameter estimates (mean ± SEM across subjects) for the taste insula for the conditions of paying attention to intensity or to pleasantness. The parameter estimates were significantly different ($p < 0.001$).

Source: After Grabenhorst and Rolls (2008). Modified from Rolls (2023a).

These findings show that when attention is paid to affective value, the brain systems engaged to represent the sensory stimulus of taste are different from those engaged when attention is directed to the physical properties of a stimulus, such as its intensity. This differential biasing of brain regions engaged in processing a sensory stimulus depending on whether the attentional demand is for affect-related versus more sensory-related processing may be an important aspect of cognition and attention. This has many implications for understanding attentional effects to affective value not only on taste but also on other sensory stimuli.

The concept has been validated in the olfactory system, too. In an fMRI investigation, when subjects were instructed to remember and rate the pleasantness of a jasmine odor, activations were greater in the medial orbitofrontal and pregenual cingulate cortex than when subjects were instructed to remember and rate the intensity of the odor (Rolls, Grabenhorst, Margot, et al., 2008).

The principle, thus, is that top-down attentional and cognitive effects on affective value influence representations selectively in cortical areas that process the affective value and associated subjective emotional experience of taste (Grabenhorst & Rolls, 2008; Grabenhorst, Rolls, & Bilderbeck, 2008) and olfactory (Anderson et al., 2003; Grabenhorst et al., 2007; Rolls, Kringelbach, et al., 2003) stimuli in brain regions such as the orbitofrontal cortex; whereas top-down attentional and cognitive effects on intensity influence representations in brain areas that process the intensity and identity of the stimulus such as the primary taste and olfactory cortical areas (Anderson et al., 2003; Grabenhorst & Rolls, 2008; Grabenhorst, Rolls, & Bilderbeck, 2008; Grabenhorst et al., 2007; Rolls, Kringelbach, et al., 2003).

The mechanisms that underlie these top-down attentional and cognitive effects include top-down biased competition, and biased activation of the bottom-up (sensory) effects, and are now starting to be elucidated computationally (Desimone & Duncan, 1995; Deco & Rolls, 2005a, 2005b; Rolls, 2008b, 2013, 2014b, 2016c, 2023a; Rolls & Deco, 2002).

Effects of Damage to and Dysfunction of the Human Orbitofrontal Cortex

In humans, euphoria, irresponsibility, lack of affect, and impulsiveness can follow frontal lobe damage (Damasio, 1994; Kolb & Whishaw, 2021; Rolls, 1999a), particularly orbitofrontal cortex damage (Berlin et al., 2004, 2005; Hornak et al., 1996, 2003; Rolls, 1999a, 2014b, 2019b; Rolls et al., 1994). These emotional changes may be related, at least in part, to a failure to rapidly update the reinforcement associations of stimuli when the contingencies are changed as in a visual discrimination reversal task (Fellows & Farah, 2003; Hornak et al., 2004; Rolls, 1999b, 2014b, 2019b; Rolls et al., 1994). Similar mechanisms may contribute, at least in part, to the poor performance of humans with ventromedial prefrontal cortex damage on the Iowa Gambling Task (Bechara et al., 2000; Maia & McClelland, 2004).

The evidence from the effects of lesions to the orbitofrontal cortex indicates that there are close links between representing reinforcers, rapidly changing learned associations to reinforcers, and emotion including subjective emotional states. For example, patients with damage to the orbitofrontal cortex may be impaired at decoding face and voice expression (which are social reinforcers; Hornak et al., 1996, 2003; Rolls, 1999b), in reversing stimulus-reward associations (Berlin et al., 2004; Fellows, 2007; Fellows & Farah, 2003, 2005; Hornak et al., 2004; Rolls et al., 1994), and in emotional behavior and subjective emotional states (Hornak et al., 2003; Rolls et al., 1994).

To provide more detail, patients with discrete surgical lesions producing bilateral orbitofrontal cortex damage who were impaired at the visual discrimination reversal task had high scores on parts of a Social Behavior Questionnaire in which the patients were rated on behaviors such as

emotion recognition in others (e.g., their sad, angry, or disgusted mood); in interpersonal relationships (such as not caring what others think and not being close to the family); emotional empathy (e.g., when others are happy, is not happy for them); interpersonal relationships (e.g., does not care what others think and is not close to their family); public behavior (is uncooperative); antisocial behavior (is critical of and impatient with others); impulsivity (does things without thinking); and sociability (is not sociable, and has difficulty making or maintaining close relationships; Hornak et al., 2003), all of which could reflect less behavioral sensitivity to different types of punishment and reward. Further, in a Subjective Emotional Change Questionnaire in which the patients reported on any changes in the intensity and/or frequency of their own experience of emotions, the bilateral orbitofrontal cortex lesion patients with deficits in the visual discrimination reversal task reported a number of changes, including changes in sadness, anger, fear and happiness (Hornak et al., 2003). Further evidence on these close links (Hornak et al., 1996; Rolls, 2016c, 2019b; Rolls et al., 1994) provides further support for the theory that because the orbitofrontal cortex decodes and represents reinforcers and updates the representations by rapid learning, it is an important brain region for emotion.

The impairments in the identification of facial and vocal emotional expression in a group of patients with ventral frontal lobe damage who had socially inappropriate behavior could occur independently of perceptual impairments in facial recognition, voice discrimination, or environmental sound recognition (Hornak et al., 1996). Poor performance on both expression tests was correlated with the degree of alteration of emotional experience reported by the patients. A comparison group of patients with brain damage outside the ventral frontal lobe region, without these behavioral problems, was unimpaired on the face expression identification test; was significantly less impaired at vocal expression identification; and reported little subjective emotional change (Hornak et al., 1996). Further, patients with discrete surgical lesions of restricted parts of the orbitofrontal cortex may have face and/or voice expression identification impairments, and these are likely to contribute to their difficulties in social situations (Hornak et al., 2003).

The changes in emotion produced by damage to the orbitofrontal cortex are large, as the evidence shows. The importance of the orbitofrontal cortex in emotion in humans is emphasized by a comparison with the effects of bilateral amygdala damage in humans, which although producing demonstrable deficits in face processing (Adolphs et al., 2005; Spezio et al., 2007), decision-making with linked autonomic deficits (Bechara et al., 1999; Brand et al., 2007), and autonomic conditioning (Phelps & LeDoux, 2005), may not produce major changes in emotion that are readily apparent in everyday behavior and reported emotion (LeDoux & Pine, 2016; LeDoux et al., 2018; Phelps & LeDoux, 2005; Rolls, 2023b, 2026; Seymour & Dolan, 2008). A difference is that the orbitofrontal cortex has connectivity to language areas that is likely to be involved in declarative reports about emotional states, and the amygdala has much less (Rolls et al., 2023a). Comparisons of the roles of the amygdala and orbitofrontal cortex in emotion are provided elsewhere (Rolls, 2014b, 2023b, 2026).

It is also becoming possible to relate the functions of the orbitofrontal cortex to some psychiatric symptoms that may reflect changes in behavioral responses to reinforcers, which may be different in different individuals. We compared the symptoms of patients with a personality disorder syndrome, Borderline Personality Disorder (BPD), with those of patients with lesions of the

orbitofrontal cortex (Berlin & Rolls, 2004; Berlin et al., 2004, 2005). The symptoms of the self-harming BPD patients include high impulsivity, affective instability, and emotionality, as well as low extroversion. It was found that orbitofrontal cortex and BPD patients performed similarly in that they were more impulsive, reported more inappropriate behaviors in the Frontal Behavior Questionnaire, and had more BPD characteristics and anger and less happiness than control groups (either normals, or patients with lesions outside the orbitofrontal cortex).

Both the orbitofrontal and BPD groups also had a faster perception of time (i.e., they underproduced time) than normal controls (Berlin & Rolls, 2004; Berlin et al., 2004, 2005). This may be one factor underlying their increased impulsiveness, in that they feel that sufficient time has elapsed to initiate action. This interesting hypothesis and finding deserve further exploration. It was of interest that the BPD group, as well as the orbitofrontal group, scored highly on a Frontal Behavior Questionnaire which assessed inappropriate behaviors typical of orbitofrontal cortex patients including disinhibition, social inappropriateness, perseveration, and uncooperativeness. Both groups were also less open to experience (i.e., less open-minded), a personality characteristic. On the other hand, other aspects of BPD do not appear to be related to orbitofrontal cortex functions, including the more neurotic and more emotional personality characteristics of the BPD patients together with their lower extroversion and conscientious (Berlin & Rolls, 2004; Berlin et al., 2004, 2005).

Another case in which it is possible to relate psychiatric types of symptom to the functions of the orbitofrontal cortex in processing reinforcers is frontotemporal dementia, which is a progressive neurodegenerative disorder attacking the frontal lobes and producing major and pervasive behavioral changes in personality and social conduct, some of which resemble those produced by orbitofrontal lesions (Hodges & Piguet, 2018). Patients appear either socially disinhibited, with facetiousness and inappropriate jocularity, or apathetic and withdrawn. The dementia is accompanied by gradual withdrawal from all social interactions. These behaviors could reflect impaired processing of reinforcers. (In addition, many patients show mental rigidity and inability to appreciate irony or other subtle aspects of language. They tend to engage in ritualistic and stereotypical behavior, and their planning skills are invariably impaired. Memory is usually intact, but patients have difficulties with working memory and concentration.) Interestingly, given the anatomy and physiology of the orbitofrontal cortex, frontotemporal dementia causes profound changes in eating habits, with escalating desire for sweet food coupled with reduced satiety, which is often followed by enormous weight gain. Moreover, emotional apathy in dementia is associated with impaired social reward learning (Wong et al., 2023).

The negative symptoms of schizophrenia include flattening of affect. As part of a dynamical attractor systems theory of schizophrenia in which hypofunction of N-methyl-d-aspartate (NMDA) receptors (Coyle et al., 2020) contributes to the cognitive symptoms such as attentional, working memory, and dysexecutive impairments by reducing the depth of the basins of attraction of the prefrontal cortex networks involved in these functions, it has been proposed that the flattening of affect is produced by the same reduced NMDA receptor function, which decreases the neuronal firing rates, and in the orbitofrontal cortex and related areas would lead to decreased affect (Loh et al., 2007; Rolls, 2014b, 2021a; Rolls, Loh, Deco, & Winterer, 2008).

Conversely, it has been proposed that hyperfunctionality of the glutamate system in obsessive-compulsive disorder (Chakrabarty et al., 2005; Pittenger et al., 2006) would contribute to overstability in prefrontal and related networks that would contribute to the perseverative/obsessional symptoms and that the concomitant increased firing rates of neurons in the orbitofrontal cortex and related areas contributes to the increased emotionality that may be present in obsessive-compulsive disorder (Rolls, 2024a; Rolls, Loh, & Deco, 2008).

Consistent with the evidence and discoveries described here, posterior orbitofrontal cortex (area 13) lesions in macaques impair the effects of satiation on reward value, whereas anterior orbitofrontal cortex (area 11) lesions impair choice decision-making (Murray et al., 2015). Further, macaques with lateral orbitofrontal cortex lesions (termed ventrolateral prefrontal lesions) were impaired at updating choices in response to changes in reward availability (as manipulated by the probability of obtaining food; Murray & Rudebeck, 2018; Rudebeck et al., 2017). Earlier work had shown that monkeys with lateral orbitofrontal/inferior prefrontal convexity damage are impaired on Go/NoGo task performance, in that they Go on the NoGo trials (Iversen & Mishkin, 1970), and in an object reversal task, in that they respond to the object which was formerly rewarded with food (Iversen & Mishkin, 1970). Similar effects were found in another study when the lesions included the lateral orbitofrontal cortex (Jones & Mishkin, 1972). I interpret this as a failure to respond to non-reward, given the activations found in humans in this region in reward reversal tasks (Kringelbach & Rolls, 2003; Rolls, Vatansever, et al., 2020; Figure 9b; confirmed in monkeys; Chau et al., 2015) and when losing or not winning money or points (O'Doherty et al., 2001; Xie et al., 2021; Figures 7 and 12).

Emotion and the Orbitofrontal Cortex

From earlier approaches (Gray, 1975; Millenson, 1967; Weiskrantz, 1968), Rolls has developed the theory that emotions are states elicited by instrumental reinforcers (Rolls, 1990, 2014b, 2023b, 2025).[1] Given that the evidence described in section 4 indicates that primary (unlearned) reinforcers, such as taste, touch, and oral texture, are made explicit in the representations in the orbitofrontal cortex, there is a basis for understanding part of the role of the orbitofrontal cortex in emotion. Further, the evidence described in section 4 indicates that associations between previously neutral stimuli such as a visual stimulus with primary reinforcers are formed and rapidly reversed in the orbitofrontal cortex, and thus the orbitofrontal cortex is likely because of this to have important functions in emotions that are produced by these secondary (learned) reinforcers. For example, the ability to perform this learning very rapidly is probably very important in social situations in primates, in which reinforcing stimuli are continually being exchanged, and the reinforcement value of stimuli must be continually updated (relearned), based on the actual reinforcers received and given. This type of learning also allows the stimuli or events that give rise to emotions and are represented in the orbitofrontal cortex to be quite abstract and general, including, for example, working for "points" or for monetary reward, as shown by visual discrimination reversal deficits in patients with orbitofrontal cortex lesions working for these rewards (Berlin et al., 2004; Fellows, 2007; Fellows & Farah, 2003, 2005; Hornak et al., 2004; Rolls et

al., 1994), and activation of different parts of the human orbitofrontal cortex by monetary gain versus loss (O'Doherty et al., 2001; Rolls, Vatansever, et al., 2020; Xie et al., 2021), and other reinforcers (Rolls, 2018, 2019b).

Rolls theory of emotion, that emotions are states elicited by instrumental reinforcers, has been extended to show how motivational states are states in which individuals perform actions to obtain reinforcers and shows how the orbitofrontal cortex is a key brain region in motivation as well as in emotion (Rolls, 2023b, 2025).

Individual Differences in Emotion, and the Orbitofrontal Cortex

Given that there are individual differences in emotion, can these individual differences be related to the functioning of brain systems involved in affective behavior such as the orbitofrontal cortex? In a test of this, we showed that in chocolate cravers, the pleasantness ratings of the chocolate had higher positive correlations with the fMRI BOLD (blood oxygenation-level dependent) signals in the pregenual cingulate cortex and medial orbitofrontal cortex in than in the non-cravers. It is proposed that many differences in personality can be related to differences in the sensitivity to different rewards, non-rewards, and punishers that are decoded in the orbitofrontal cortex (Rolls, 2014b, 2019b, 2023b).

Beyond the Orbitofrontal Cortex to Choice Decision-making

In humans the blood oxygenation-level dependent (BOLD) activations in different parts of the orbitofrontal cortex are continuously, indeed typically linearly, related to subjective pleasantness ratings of taste (de Araujo, Kringelbach, Rolls, & McGlone, 2003; Grabenhorst & Rolls, 2008; Grabenhorst, Rolls, & Bilderbeck, 2008), olfactory (Grabenhorst et al., 2007), flavor (Grabenhorst, Rolls, & Bilderbeck, 2008; Kringelbach et al., 2003; McCabe & Rolls, 2007; Plassmann et al., 2008), oral temperature (Guest et al., 2007), hand temperature (Rolls, Grabenhorst, & Parris, 2008), and face beauty (O'Doherty et al., 2003) stimuli, and to monetary reward value (O'Doherty et al., 2001), as shown by correlation analyses. An implication of these findings is that the orbitofrontal cortex may contribute to decision-making by representing on a continuous scale the value of each reward, with, as shown by the single neuron neurophysiology, different subsets of neurons for each different particular reward. However, when making a binary, for example yes-no, decision about whether to choose a thermal reward, Grabenhorst, Rolls, and Parris (2008) found activations in the ventromedial prefrontal cortex area 10, implicating this area in choice decision making, and similar effects were found for odors (Rolls et al., 2010).

To further explore how choice decision-making is implemented in the brain, we have utilized an attractor network model of decision-making with spiking neurons in which the representations of each choice are by a subpopulation of neurons, and the attractor network settles into one of its two or more high firing rate attractor states each representing a choice (Deco & Rolls, 2006; Deco et al., 2013; Rolls, 2016c, 2023a; Rolls & Deco, 2010; Wang, 2002). We showed that the model predicts that the BOLD signal becomes larger with the easiness of the decision (i.e., the difference between the

two decision variables) on correct trials, and showed that this signature is found anterior to the orbitofrontal cortex, in medial prefrontal cortex area 10 (often termed the ventromedial prefrontal cortex) during choice of pleasantness for both olfactory and thermal stimuli (warmth to the hand; Rolls et al., 2010a). The model also predicts that the BOLD signal become smaller with the easiness of the decision on error trials, and we showed that this signature is also found in ventromedial prefrontal cortex area 10 in the same pleasantness choice tasks (Rolls et al., 2010b).

These computational investigations of how the brain takes decisions about reward value are presented in detail elsewhere (Rolls, 2019b, 2023a; Rolls et al., 2010a, 2010b).

The Orbitofrontal Cortex and Depression

Given the key functions of the orbitofrontal cortex in emotion, including representations of reward in the medial orbitofrontal cortex, and non-reward (which can lead to depression) in the lateral orbitofrontal cortex (Rolls, 2019b, 2023a, 2023b), I proposed a theory of depression in which the lateral orbitofrontal cortex is more sensitive to non-reward in depression, and the medial orbitofrontal cortex is less sensitive to reward, leading to the anhedonia of depression (Rolls, 2016a). We performed a large series of investigations in which we found that, consistent with the hypothesis, the lateral orbitofrontal cortex has increased functional connectivity in depression, and the medial orbitofrontal cortex has reduced functional connectivity in depression (Cheng, Rolls, Qiu, Xie, Lyu, et al., 2018; Cheng, Rolls, Qiu, Xie, Wei, et al., 2018; Cheng, Rolls, Qiu, Yang, et al., 2018; Cheng et al., 2016; Rolls, 2018, 2019c; Rolls, Cheng, Du, et al., 2020; Rolls, Cheng, & Feng, 2020; Rolls, Cheng, et al., 2018; Rolls et al., 2019; Zhang et al., 2024). Importantly, treatment with modern antidepressants restores the increased functional connectivity of the lateral orbitofrontal toward normal, but does not treat the reduced functional connectivity of the medial orbitofrontal cortex, suggesting the latter as a key aim for future treatments (Rolls, 2018; Rolls, Cheng, & Feng, 2020; Zhang et al., 2024).

We were able to extend the theory by testing activations in different parts of the orbitofrontal cortex in a monetary reward task in which activations related to reward (Winning) and non-reward (Not Winning) could be measured. In 1,140 adolescents at age 19 and 1,877 at age 14 in the monetary incentive delay task, we found that the medial orbitofrontal cortex had graded increases in activation as the reward (Win) value increased (Xie et al., 2021). The lateral orbitofrontal cortex had graded increases of activation as the reward value dropped to zero (the No-Win condition; Figure 12). In a subgroup with a high score on the Adolescent Depression Rating Scale at age 19 and 14, the medial orbitofrontal cortex activations had reduced sensitivity to the different reward conditions; and the lateral orbitofrontal cortex activation showed high activation to the No-Win (i.e., Non-reward) condition (Xie et al., 2021; Figure 12). These findings provide support for the hypothesis that those with symptoms of depression have increased sensitivity to non-reward in the lateral orbitofrontal cortex and decreased sensitivity for differences in reward of the medial orbitofrontal cortex. Moreover, these differences are evident at an age as early as 14 years old (Xie et al., 2021). This increase in non-reward sensitivity of the lateral orbitofrontal cortex in depression and decreased reward sensitivity of the medial orbitofrontal cortex may act together with the altered

functional connectivity of these regions to make some individuals susceptible to depression, and this theory has implications for treatment (Rolls, 2016a, 2018, 2019c; Rolls, Cheng, & Feng, 2020; Zhang et al., 2024).

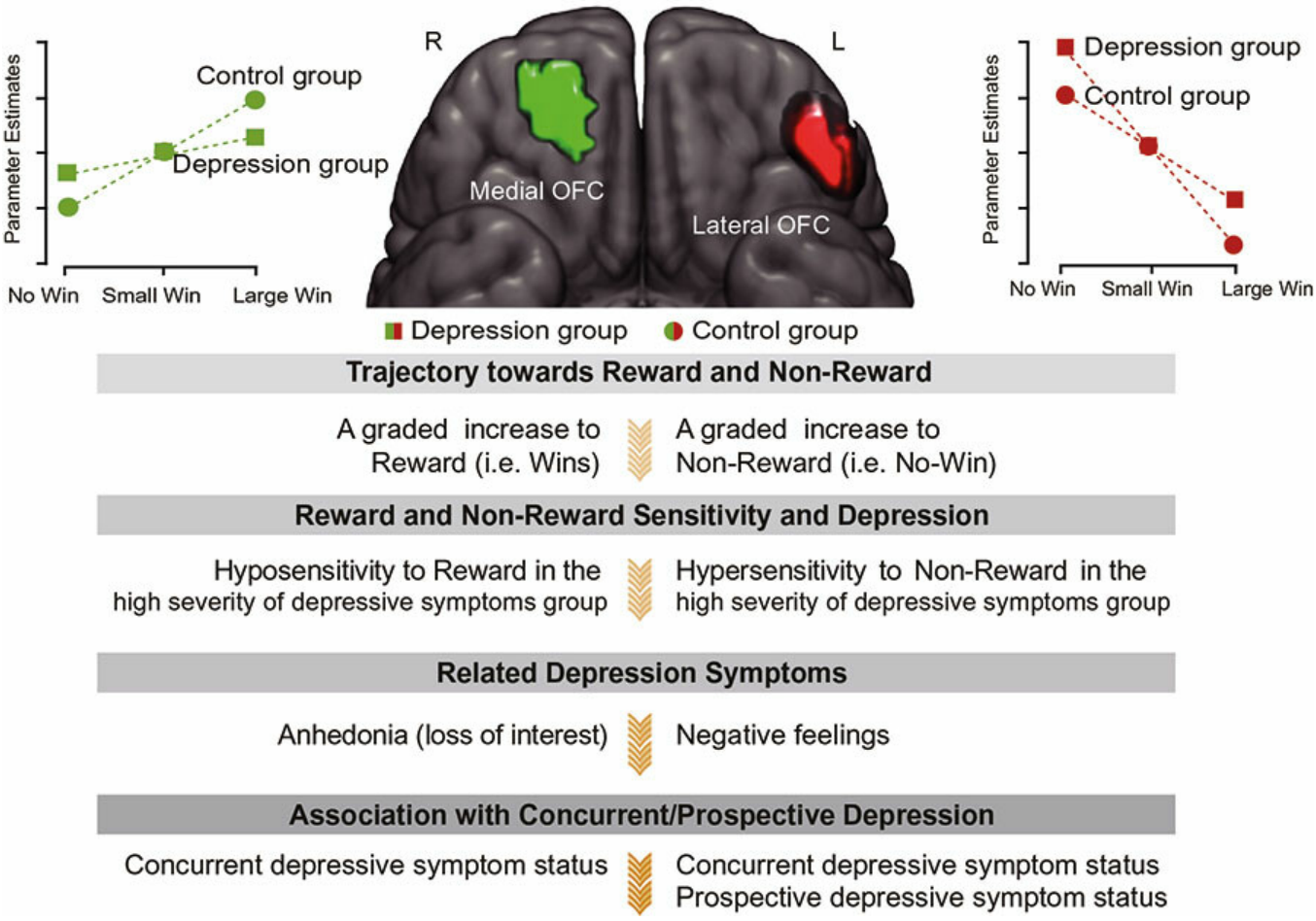

Figure 12. Reduced sensitivity to reward of the medial orbitofrontal cortex, and increased sensitivity of the lateral orbitofrontal cortex to non-reward (No Win) in individuals with high scores on the Adolescent Depression Rating Scale (squares) compared to a control group (circles) in the Monetary Incentive Delay task. The summary is based on findings in 1,140 adolescents at age 19 and 1,877 at age 14. L, left; R, right.

Source: After Xie et al. (2021). Modified from Rolls (2023a).

The Rodent Orbitofrontal Cortex

The orbitofrontal cortex is much less well developed in rodents than in primates, including humans, with rodents having only an agranular orbitofrontal cortex that corresponds to a small posterior part of the primate orbitofrontal cortex (Rolls, 2014b; Passingham, 2021; Wise, 2008). A major difference between the primate and rodent orbitofrontal cortex is that the primate including human orbitofrontal cortex receives visual information from the inferior temporal visual cortex, which is a highly developed area for primate vision enabling invariant visual object and face recognition (Rolls, 2000a, 2007, 2011, 2012, 2016c, 2023a, 2026; Rolls & Deco, 2002) and which provides visual inputs

used in the primate orbitofrontal cortex for one-trial object-reward association reversal learning and for representing face expression and identity. Moreover, the specialization of the primate visual system for processing what is at the fovea makes the information that it passes on to receiving structures quite different from that in rodents (Rolls, 2023a; Rolls & Wirth, 2018; Rolls, 2023c). Further, even the taste system of primates and rodents may be different, with obligatory processing from the nucleus of the solitary tract via the thalamus to the cortex in primates but a subcortical pathway in rodents via a pontine taste area to the amygdala and differences in where satiety influences taste responsive neurons in primates and rodents (Norgren, 1984; Rolls, 2014b, 2015, 2016d, 2016e, 2017a, 2023a; Rolls & Scott, 2003). That is why the rodent orbitofrontal cortex is left for consideration elsewhere (Izquierdo, 2017; Barreiros et al., 2021; Rolls, 2019b, 2023a; Sharpe et al., 2015; Wilson et al., 2014).

In conclusion, the functions of the primate, including human orbitofrontal cortex, have been described here and elsewhere (Rolls, 2018, 2019b, 2023b), and the rodent orbitofrontal cortex appears to have many differences (Passingham, 2021; Rolls, 2019b, 2023a).

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Notes

1. For the purposes of this article, a positive reinforcer or reward can be defined as a stimulus that the animal will work to obtain, and a punisher can be defined as a stimulus that will reduce the probability of an action on which it is contingent or that an animal will work to avoid or escape (see further Rolls, 2014b).