c0005 # 5 From reward value to decision-making: neuronal and computational principles

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s0010 ## 5.1 Introduction

p0010 I start with some definitions [1]. A reward is anything for which an animal will work. AUQ2 A punisher is anything that an animal will work to escape or avoid, or that will suppress actions on which it is contingent. Rewards and punishers are instrumental reinforcing stimuli. Instrumental reinforcers are stimuli that, if their occurrence, termination, or omission is made contingent upon the making of an action, alter the probability of the future emission of that action [2–6]. Some stimuli are primary (unlearned) reinforcers (e.g., the taste of food if the animal is hungry, or pain); while others may become reinforcing by learning, because of their association with such primary reinforcers, thereby becoming "secondary reinforcers." This type of learning may thus be called "stimulus–reinforcer association," and occurs via an associative learning process between two stimuli, for a reinforcer is a stimulus. A positive reinforcer (such as food) increases the probability of emission of a response on which it is contingent; the process is termed *positive reinforcement*, and the outcome is a reward (such as food). A negative reinforcer (such as a painful stimulus) increases the probability of emission of a response that causes the negative reinforcer to be omitted (as in active avoidance) or terminated (as in escape), and the procedure is termed *negative reinforcement*. In contrast, *punishment* refers to procedures in which the probability of an action is decreased. Punishment thus describes procedures in which an action decreases in probability if it is followed by a painful stimulus, as in passive avoidance. Punishment can also be used to refer to a procedure involving the omission or termination of a reward ("extinction" and "time out," respectively), both of which decrease the probability of responses [1].

p0020 Part of the adaptive, evolutionary, value of primary rewards and punishers is that they are gene-specified goals for action, and a genome that specifies the goals to obtain (e.g., food when hungry) is much more efficient than one that attempts to specify responses to stimuli, for specifying a set of stimuli that are reinforcers is much simpler for the genome than specifying particular responses to each stimulus, and in addition allows flexibility of the action that is performed to obtain the goal [1,7]. Reinforcers are for these reasons extremely important in behavior, and their importance is underlined by the fact that emotions, acknowledged to be important by most people, can be defined as states elicited by rewards and punishers, that is, by instrumental reinforcers [1,2,8].

p0030 The focus is on humans and macaques, because there are many topological, cytoarchitectural, and probably connectional similarities between macaques and humans with respect to the orbitofrontal cortex and related structures important in reward processing (Fig. 5.1;

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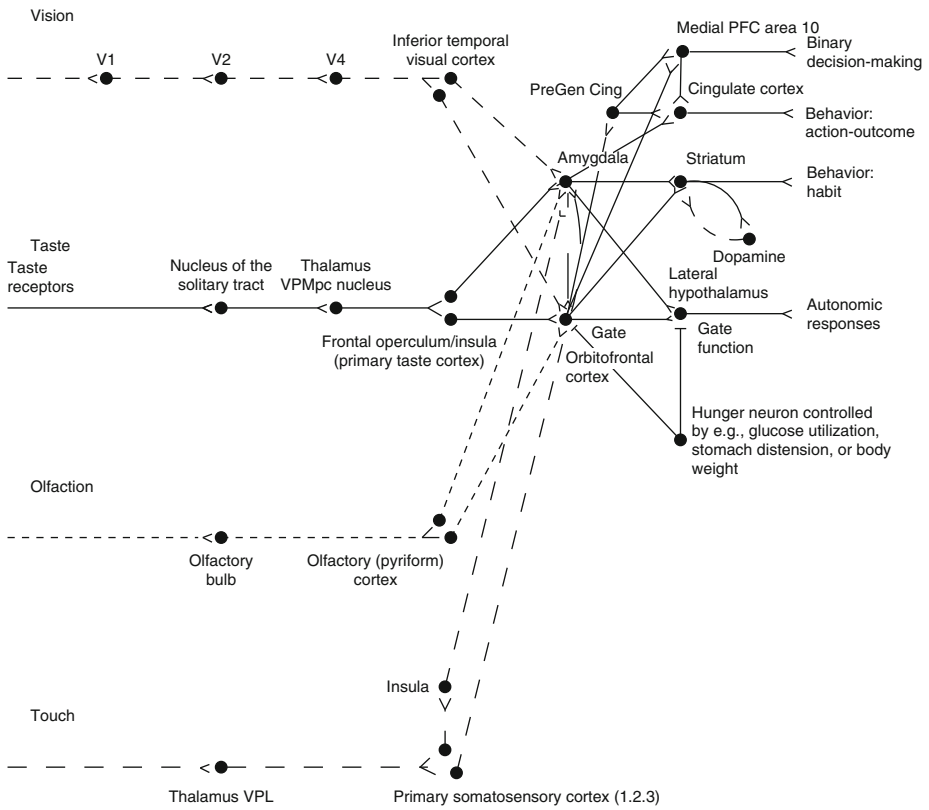
[9–14]). Moreover, the orbitofrontal cortex receives visual information in primates from the inferior temporal visual cortex, which is a highly developed area for primate vision enabling invariant visual object recognition [15–19], and which provides visual inputs used in the primate orbitofrontal cortex for one-trial object-reward association reversal learning, and for representing face expression and identity. 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 hypothalamus [20], and differences in where satiety influences taste-responsive neurons in primates and rodents [1,21]. The implication is that the reward pathways and reward processing for primary reinforcers, even as fundamental



f0010 **Figure 5.1** Schematic diagram showing some of the gustatory, olfactory, visual, and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex and the secondary olfactory cortex are within the orbitofrontal cortex (V1 – primary visual cortex; V4 – visual cortical area V4; PreGen Cing – pregenual cingulate cortex). "Gate" refers to the finding that inputs such as the taste, smell, and sight of food in some brain regions only produce effects when hunger is present [1]. The column of brain regions including and below the inferior temporal visual cortex represents brain regions in which what stimulus is present is made explicit in the neuronal representation, but not its reward or affective value, which are represented in the next tier of brain regions, the orbitofrontal cortex and amygdala, and in areas beyond these.

as taste, may be different in rodents and primates. For these reasons, and to understand reward processing, emotion, and decision-making in humans, the majority of the studies described here were performed with macaques or with humans. Although the nature of the representation of information is understood best at the levels of how individual neurons and populations of neurons respond, as these are the computing elements of the brain and the level at which information is exchanged between the computing elements which are the neurons [17], these data are complemented in what follows by functional neuroimaging studies in humans, and then by computational studies that indicate how populations of neurons achieve computations such as making a decision.

s0020 5.2 A connectional and functional framework

p0040 A connectional overview of the sensory pathways that lead into reward decoding systems in structures such as the orbitofrontal cortex and amygdala, and the structures to which they connect such as the ventral striatum, anterior cingulate cortex, and hypothalamus, is shown in Fig. 5.1, based on much anatomical and related work [1,9–11,13,14,17,22–25]. Conceptually, the orbitofrontal cortex and amygdala can be thought of as receiving from the ends of each modality-specific "what" cortical pathway. These areas are represented by the column in Fig. 5.1 with inferior temporal visual cortex, primary taste cortex in the anterior insula, pyriform olfactory cortex, and somatosensory cortex, and reward is not made explicit in the representation in these areas. By made explicit in the representation, I mean reflected in the firing rates (and can be decoded from the firing rates of the neurons by a process that could be implemented by a receiving neuron, dot product decoding) [17]. Some of the evidence for this is described below, and in more detail elsewhere [1,17,25].

p0050 Figure 5.1 helps to set a functional framework in which neuronal activity in the inferior temporal cortex, and the primary taste, olfactory, and somatosensory cortices provides a representation of what stimulus is present, and its intensity, and in which reward value is represented at the next stages of processing, the orbitofrontal cortex and the amygdala. Part of the utility of this functional architecture is that there is a representation of what stimulus is present, independent of its reward value, so that learning to associate that stimulus with its spatial position, to recognize and name it, and to learn about its properties can occur independently of its current affective value [1,17]. A simple example is that we can learn about the location of a food even if we are not hungry and it has no reward value. At the subjective level, we can report on the properties and intensity of stimuli independently of whether they are currently pleasant. A computational principle is thus that there are separate representations of what a stimulus is, together with its intensity and its affective value. Some computational reasons for this segregation into different areas are described later.

s0030 5.3 Taste reward

p0060 Taste can act as a primary reinforcer, and given that taste reward is represented in the orbitofrontal cortex, we now have the start for a fundamental understanding of the function of the orbitofrontal cortex in stimulus–reinforcer association learning [1,7,17,26]. The representation (shown by analyzing the responses of single neurons in macaques) of taste in the orbitofrontal cortex includes robust representations of the prototypical tastes sweet, salt, bitter, and sour [27], but also separate representations of the "taste" of water [27], and of protein or umami

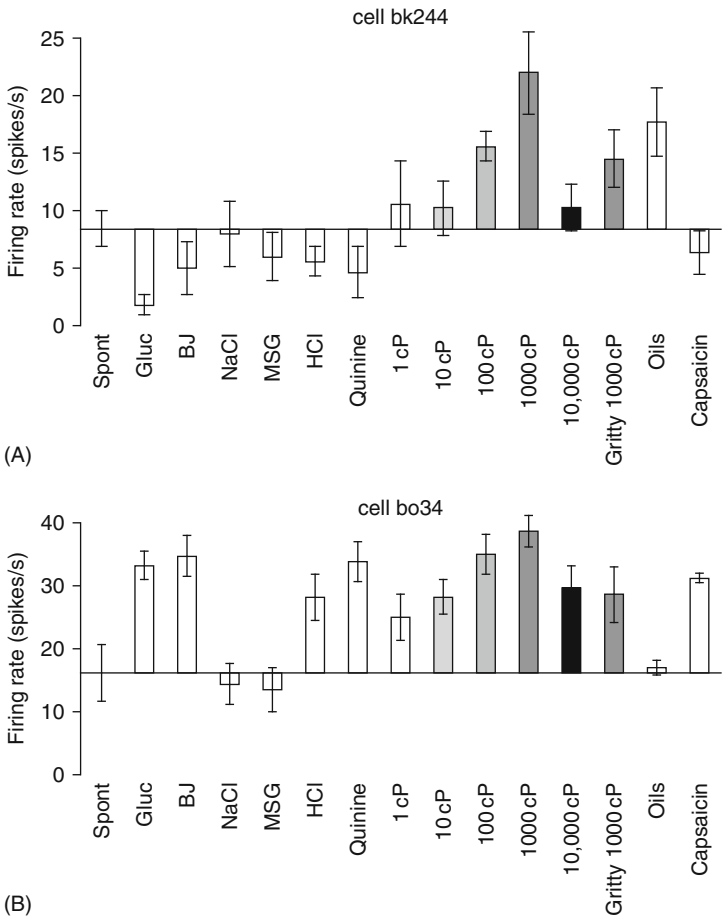
as exemplified by monosodium glutamate (MSG) [28,29] and inosine monophosphate [30,31]. An example of an orbitofrontal cortex neuron with different responses to different taste stimuli is shown in Fig. 5.2B. As will be described below, some neurons have taste-only responses, and others respond to a variety of oral somatosensory stimuli, including, for some neurons, viscosity [32], fat texture [33,34], and for other neurons, astringency as exemplified by tannic acid [35]. There are analogous data for distributed coding in rats of oral sensory including gustatory stimuli [36].

p0070 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 (as is the reward value or palatability of a taste). In particular, it has been shown that orbitofrontal cortex taste neurons gradually stop responding to the taste of a food as the monkey is fed to satiety [30,37]. The example shown in Fig. 5.3 is of a single neuron with taste, olfactory, and visual responses to food, and the neuronal responses elicited through all these sensory modalities showed a decrease. Moreover, this type of neuronal responsiveness shows that it is the preference for different stimuli that is represented by these neurons, in that the neuronal response decreases in parallel with the decrease in the acceptability or reward value of the food being eaten to satiety, but the neuronal responses remain high (or even sometimes become a little larger) to foods not eaten in the meal (see, e.g., Fig. 5.3), but which remain acceptable, with a high reward value. Sensory-specific satiety, the decrease in the reward value of a food eaten to satiety relative to other foods not eaten to satiety, is thus implemented in the orbitofrontal cortex. Further, in humans, feeding to satiety decreases the activation of the orbitofrontal cortex to the food eaten to satiety in a sensory-specific way [38], and activations in the human orbitofrontal cortex are correlated with the pleasantness of taste [39]. Additional evidence that the reward value of food is represented in the orbitofrontal cortex is that monkeys work for electrical stimulation of this brain region if they are hungry, but not if they are satiated [1,40]. Further, neurons in the orbitofrontal cortex are activated from many brain-stimulation reward sites [41,42].

p0080 The computational basis for sensory-specific satiety is that each neuron in the orbitofrontal cortex responds to different combinations of taste, odor, fat texture, viscosity, astringency, roughness, temperature, capsaicin, and visual inputs (see examples in Fig. 5.2), and by making it a property that these neurons show adaptation after several minutes of stimulation, the reward value can decrease to the particular combination of sensory inputs, but much less to others. *Reward-specific satiety* is probably a property of all rewards, and facilitates the selection of a variety of different rewards, which is adaptive [1,17].

p0090 An interesting property of sensory-specific satiety is that after eating one food to satiety, the neuronal responses and subjective pleasantness of other foods can increase a little (see example in Fig. 5.3, middle). This is probably part of a mechanism to facilitate behavioral switching between different positive reinforcers, and in the case of food, may facilitate eating a varied diet with the consequent beneficial nutritional implications, but may contribute to overeating and obesity if too much variety is available [1,43].

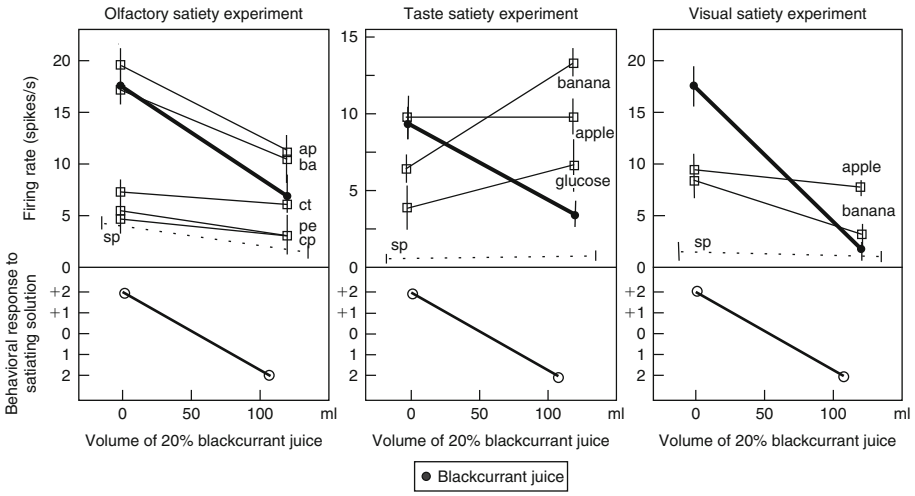
p0100 The caudolateral part of the orbitofrontal cortex is secondary taste cortex, as defined anatomically (using horseradish peroxidase tracing from the site of the taste neurons) by major direct inputs from the primary taste cortex in the rostral insula and adjoining frontal operculum [44]. This region projects onto other regions in the orbitofrontal cortex [44], and neurons with taste responses (in what can be considered as a tertiary gustatory cortical area) can be found in many regions of the orbitofrontal cortex [27,45,46]. Although some taste neurons are found laterally in the orbitofrontal cortex (area 12o) [27,45,46], others are found through the middle and even toward the medial part of the



f0020 **Figure 5.2** Oral somatosensory and taste inputs to orbitofrontal cortex neurons. (A) Firing rates (mean ± sem) of viscosity-sensitive neuron bk244, which did not have taste responses in that it did not respond differentially to the different taste stimuli. The firing rates are shown to the viscosity series, to the gritty stimulus (carboxymethylcellulose with Fillite microspheres), to the taste stimuli 1 M glucose (Gluc), 0.1 M NaCl, 0.1 M MSG, 0.01 M HCl, and 0.001 M QuinineHCl, and to fruit juice (BJ, blackcurrant juice; Spont, spontaneous firing rate). (B) Firing rates (mean ± sem) of viscosity-sensitive neuron bo34, which had no response to the oils (mineral oil, vegetable oil, safflower oil, and coconut oil, which have viscosities that are all close to 50 cP). The neuron did not respond to the gritty stimulus in a way that was unexpected given the viscosity of the stimulus, was taste tuned, and did respond to capsaicin. *Source*: After Rolls et al. (2003) [32].

orbitofrontal cortex in areas 13m and 13l [25,30,35,46–50]. Most but not all of these area 13 neurons decrease their responses to zero to a taste with which the monkey is fed to satiety [30,35,47,51].

p0110 The primate amygdala contains neurons activated by taste and also by oral texture and temperature [52–55], but satiety has inconsistent effects on neuronal responses to taste



f0030 **Figure 5.3** 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 AUQ1 spontaneous firing rate of the neuron is shown (sp). *Source*: After Critchley and Rolls, 1996.

and related stimuli, producing a mean suppression of 58% [56], indicating that reward is much less clearly represented here than in the orbitofrontal cortex (see above) and the hypothalamus [57], which receives inputs from the orbitofrontal cortex. The human amygdala is not specialized for taste stimuli that happen to be aversive, for pleasant stimuli such as the taste of glucose produce as much activation as salt [58].

p0120 The pregenual cingulate cortex also contains taste neurons, which respond to, for example, sweet taste if hunger is present and so represent reward value [50]. The pregenual cingulate cortex (which is clearly multimodal [59]) can be considered a tertiary taste cortical area, in that it receives inputs from the orbitofrontal cortex [50].

s0040 5.4 Olfactory reward

p0130 Although some odors (such as pheromones and perhaps some odors related to fruit/flowers or rotting/uncleanliness) are primary reinforcers; we learn about the reward value of most odors by association with a primary reinforcer such as taste [1].

p0140 A ventral frontal region has been implicated in olfactory processing in humans [60,61] and macaques [62]. For 35% of orbitofrontal cortex neurons with olfactory responses, Critchley and Rolls [63] showed that the odors to which a neuron responded were influenced by the taste (glucose or saline) with which the odor was associated. Thus the odor representation for 35% of orbitofrontal neurons appeared to be built by olfactory-to-taste association learning. This possibility was confirmed by reversing the taste with which an odor was associated in the reversal of an olfactory discrimination task. It was found

that 68% of the sample of neurons analyzed altered the way in which they responded to an odor when the taste reinforcement association of the odor was reversed [45] (25% showed reversal, and 43% no longer discriminated after the reversal, so were conditional reward neurons as also found in rats [64]). 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. Thus the rule according to which the orbitofrontal olfactory representation was formed was, for some neurons, by association learning with taste, a primary reinforcer.

p0150 To analyze the nature of the olfactory representation in the orbitofrontal cortex, Critchley and Rolls [47] measured the responses of olfactory neurons that responded to food while they fed the monkey to satiety. They found that the majority of orbitofrontal olfactory neurons decreased their responses to the odor of the food with which the monkey was fed to satiety (see example in Fig. 5.3). Thus, for these neurons, the reward value of the odor is what is represented in the orbitofrontal cortex. We do not yet know whether this is the first stage of processing at which reward value is represented in the olfactory system in macaques (although in rodents the influence of reward association learning appears to be present in some neurons in the pyriform cortex [65]). However, an fMRI investigation in humans showed that whereas in the orbitofrontal cortex the pleasantness versus unpleasantness of odors is represented, this was not the case in primary olfactory cortical areas, where instead the activations reflected the intensity of the odors [66]. Further evidence that the pleasantness or reward value of odor is represented in the orbitofrontal cortex is that feeding humans to satiety decreases the activation found to the odor of the food, and this effect is relatively specific to the food eaten in the meal [67–69].

s0050 5.5 Flavor reward

p0160 In the orbitofrontal cortex, not only are there unimodal taste and unimodal olfactory neurons, but also some single neurons respond to both gustatory and olfactory stimuli, often with correspondence between the two modalities [46]. It is probably here in the orbitofrontal cortex of primates, including humans, that these two modalities converge to produce the representation of flavor [46,70], for neurons in the macaque primary taste cortex in the insular/frontal opercular cortex do not respond to olfactory (or visual) stimuli [71]. As noted above, these neurons may be formed by olfactory–gustatory association learning, an example of stimulus–reinforcer association learning.

p0170 The importance of the combination of taste and smell for producing affectively pleasant and rewarding representations of sensory stimuli is exemplified by findings with umami, the delicious taste or flavor that is associated with combinations of components that include meat, fish, milk, tomatoes, and mushrooms, all of which are rich in umami-related substances such as glutamate or inosine 5′monophosphate. Umami taste is produced by glutamate acting on a fifth taste system [72–74]. Umami (protein) taste is not only represented by neurons in the primate orbitofrontal cortex [28,30], but also human fMRI studies show that umami taste is represented in the orbitofrontal cortex, with an anterior part responding supralinearly to a combination of MSG and inosine monophosphate [75]. Glutamate presented alone as a taste stimulus is not highly pleasant and does not act synergistically with other tastes (sweet, salt, bitter, and sour). However, when glutamate is given in combination with a consonant, savory odor (vegetable), the resulting flavor can be much more pleasant [76]. We showed, using functional brain imaging with fMRI, that this glutamate taste and savory odor combination produced much greater activation of the medial orbitofrontal

cortex and pregenual cingulate cortex than the sum of the activations by the taste and olfactory components presented separately [76]. Supralinear effects were much less (and significantly less) evident for sodium chloride and vegetable odor. Further, activations in these brain regions were correlated with the pleasantness and fullness of the flavor, and with the consonance of the taste and olfactory components. Supralinear effects of glutamate taste and savory odor were not found in the insular primary taste cortex. We suggested that umami can be thought of as a rich and delicious flavor that is produced by a combination of glutamate taste and a consonant savory odor. Glutamate is thus a flavor enhancer because of the way that it can combine supra-linearly with consonant odors in cortical areas where the taste and olfactory pathways converge far beyond the receptors [76].

p0180 A concept here is that combinations of sensory stimuli represented by neurons in the orbitofrontal cortex appear to contribute to the representation of the reward value of particular combinations of sensory stimuli, and these may involve nonlinear processing.

s0060 5.6 Oral texture and temperature reward

p0190 A 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 [33]. 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 [1,77]. Satiety produced by eating a fatty food, cream, can decrease the responses of orbitofrontal cortex neurons to the texture of fat in the mouth [33], showing that they represent oral texture reward.

p0200 Some orbitofrontal cortex neurons encode fat texture independently of viscosity (by a physical parameter that varies with the slickness of fat) [34]; other orbitofrontal cortex neurons encode the viscosity of the texture in the mouth (with some neurons tuned to viscosity, and others showing increasing or decrease firing rates as viscosity increases) [32]; other neurons have responses that indicate the presence of texture stimuli (such as grittiness and capsaicin) in the mouth independently of viscosity and slickness [32]. The ensemble (i.e., population, distributed) encoding of all these variables is illustrated by the different tuning to the set of stimuli of the two neurons shown in Fig. 5.2. An overlapping population of orbitofrontal cortex neurons represents the temperature of what is in the mouth [78].

p0210 These single-neuron recording studies thus provide clear evidence of the rich sensory representation of oral stimuli, and of their reward value, that is provided in the primate orbitofrontal cortex, and how this differs from what is represented in the primary taste cortex and in the amygdala [54]. In a complementary human functional neuroimaging study, it has been shown that activation of parts of the orbitofrontal cortex, primary taste cortex, and mid-insular somatosensory region posterior to the insular taste cortex have activations that are related to the viscosity of what is in the mouth, and that there is in addition a medial prefrontal/cingulate area where the mouth feel of fat is represented [79]. Also, in humans, there is a representation of the temperature of what is in the mouth [80]. The oral temperature stimuli (cooled and warmed, 5, 20, 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.

p0220 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 [71,78]. These combination-responsive neurons may provide the basis for particular combinations of temperature, taste, texture, and odor to be especially pleasant [1,81]; for sensory-specific satiety to apply to that combination, but not necessarily to the components; and more generally for learning and perception to apply to that combination and not necessarily to the components [17].

s0070 5.7 Somatosensory and temperature inputs to the orbitofrontal cortex, and affective value

p0230 In addition to these oral somatosensory inputs to the orbitofrontal cortex, there are also somatosensory inputs from other parts of the body, and indeed an 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 [67,82].

p0240 Non-glabrous skin, such as that on the forearm, contains C fiber tactile afferents that respond to light moving touch [83]. 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 [84].

p0250 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 [1]. Understanding the brain processing that underlies these prototypical reinforcers provides a direct approach to understanding the brain mechanisms of emotion. 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 [85]. 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.

p0260 A principle thus appears to be that processing related to the affective value and associated subjective emotional experience of thermal stimuli that are important for survival is performed in different brain areas than those where activations are related to sensory properties of the stimuli such as their intensity. This conclusion appears to be the case for processing in a number of sensory modalities, including taste [39,86] and olfaction [66,87,88], and the findings with such prototypical stimuli as warm and cold [85,89] provide strong support for this principle.

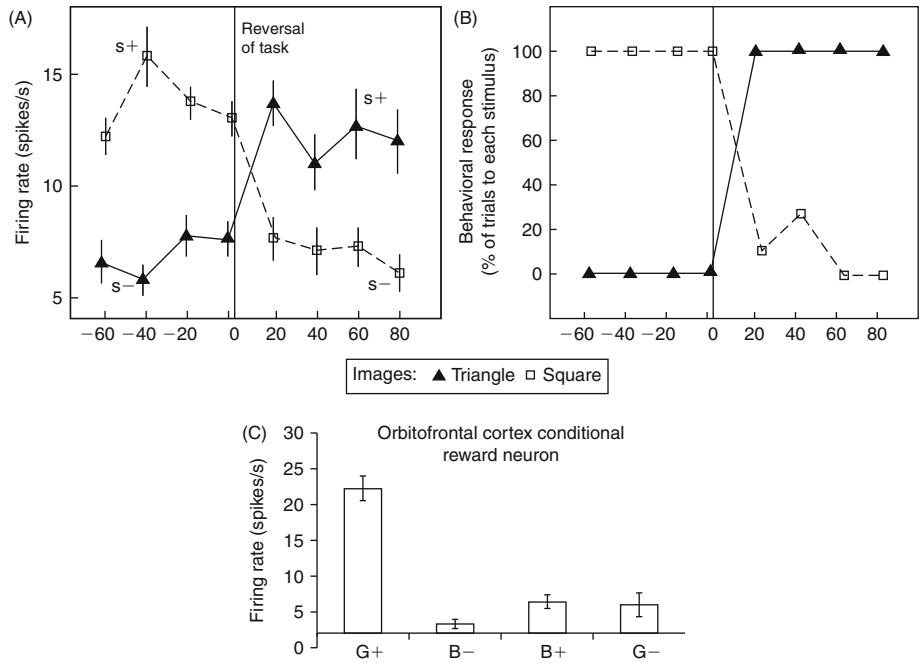
s0080 5.8 Visual inputs to the orbitofrontal cortex, and visual stimulus–reinforcement association learning and reversal

p0270 There is a major visual input to many neurons in the orbitofrontal cortex, and what is represented by these neurons is in many cases the reinforcement association of visual stimuli. The visual input is from the ventral, temporal lobe, visual stream concerned with

"what" object is being seen [15–19,90]. Using this object-related and transform invariant information, orbitofrontal cortex visual neurons frequently respond differentially to objects or images depending on their reward association [45,91]. The primary reinforcer that has been used is taste, and correlates of visual to taste association learning have been demonstrated in the human orbitofrontal cortex with fMRI [92]. Many of these neurons show visual–taste reversal in one or a very few trials (see example in Fig. 5.4A). (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 [91]. This reversal learning probably occurs in the orbitofrontal cortex, for it does not occur one synapse earlier in the visual inferior temporal cortex [93], and it is in the orbitofrontal cortex that there is convergence of visual and taste pathways onto the same single neurons [45,46,91].

p0280 The probable mechanism for this learning is an associative modification of synapses conveying visual input onto taste-responsive neurons, implementing a pattern association network [1,17,18,94] (see Section 5.16 and Fig. 5.6). When the reinforcement association of a visual stimulus is reversed, other "conditional reward" orbitofrontal cortex neurons stop responding, or stop responding differentially, to the visual discriminanda [91]. An example is a neuron in the orbitofrontal cortex that responded to a blue stimulus when it was rewarded (blue S+) and not to a green stimulus when it was associated with aversive saline (green S−). However, the neuron did not respond after reversal to the blue S− or to the green S+ (Fig. 5.4C). Similar conditional reward neurons are found not only for visual but also for olfactory stimuli [45]. Such conditional reward neurons convey information about the current reinforcement status of particular stimuli. They may be part of a system that can implement very rapid reversal, by being biased on by-rule neurons if that stimulus is currently associated with reward, and being biased off if that stimulus is currently not associated with reward [95], as described in Section 5.16. This theory provides an account of the utility of conditional reward neurons.

p0290 The visual and olfactory neurons in primates that respond to the sight or smell of stimuli that are primary reinforcers such as taste clearly signal an expectation of reward that is based on previous stimulus–reinforcement associations [45,91]. So do the conditional reward neurons [45,91]. Olfactory reward expectation and conditional reward neurons have also been found in rats in a region that may correspond to the orbitofrontal cortex, and some of these neurons can start to respond after a delay period as the expected taste becomes closer in time [96]. In primates the orbitofrontal cortex neurons that change their responses during olfactory to taste reversal learning do so sufficiently rapidly to play a role in the behavioral change [45], but in rodents it has been suggested that the amygdala may be more important in reflecting the changing association [64]. However, the situation is clear in the case of visual–taste association learning and reversal in primates, in which the orbitofrontal cortex neurons and the behavior can change in one trial [45,91], so that the changing responses of the orbitofrontal cortex neurons can contribute to the reversed behavior, a view supported by the impaired reversal learning produced in primates, including humans, by orbitofrontal cortex damage [97–99]. Indeed, in primates, visual-to-taste reversal is so rapid that after a punishment has been received to the negative discriminative stimulus (S−), the next time the previous S− is shown, the neurons respond to it as an S + , and the monkey responds [45,91]. This is a non-associative process that involves a rule change, 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 [95] that is described in Section 5.16.



f0040 **Figure 5.4** (A) 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 post-stimulus 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. (B) The behavioral response to the triangle and the square, indicating that the monkey reversed rapidly. (C) A conditional reward neuron recorded in the orbitofrontal cortex by Thorpe et al. [91] in a visual discrimination task which responded only to the green stimulus when it was associated with reward (G+), and not to the blue stimulus when it was associated with reward (B+), or to either stimulus when they were associated with a punisher, the taste of salt (G− and B−). *Source*: For B, after Rolls et al. (1996) [45].

p0300 With respect to the primate amygdala, the evidence is that any reversal of neurons in a visual discrimination reversal is relatively slow if it occurs taking tens of trials [52,100], and so in primates the amygdala appears to make a less important contribution than the orbitofrontal cortex. This is in line with the hypothesis that the orbitofrontal cortex, as a cortical area versus the subcortical amygdala, becomes relatively more important in primates, including humans, than in rodents [1]. This is based not only on the neurophysiology described here, but also on the relative development in primates including humans versus rodents of the orbitofrontal cortex versus amygdala, and the more severe effects of damage to the primate including human orbitofrontal cortex than amygdala on emotion and reward-related processing referred to elsewhere in this chapter. The computational basis for the hypothesis is that because of the well-developed recurrent collateral

excitatory connections of cortical areas, the orbitofrontal cortex can make especial contributions by its attractor dynamics when states must be remembered, as in rule-based reversal, and also in other operations where a short-term memory can facilitate reward-based processing, as described in Section 5.16. Indeed, attractor networks in cortical areas such as the orbitofrontal cortex and anterior cingulate cortex may contribute to the persistence of mood states, which is an adaptive function with respect to emotion in that, for example, after non-reward, the persistence of the state will keep behavior directed toward obtaining the goal. Cortical areas such as the orbitofrontal cortex may make a special contribution to the adaptive persistence of emotional states (which reflect rewards received) because of their attractor properties implemented by the local recurrent collaterals [1,17], as considered further in Section 5.16.

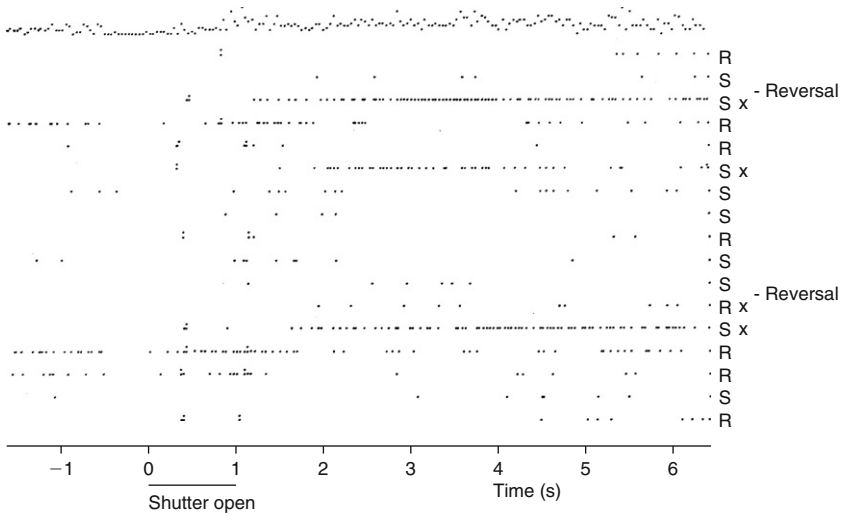
p0310 To analyze the nature of the visual representation of food-related stimuli in the orbitofrontal cortex, Critchley and Rolls [47] measured the responses of neurons that responded to the sight of food while they fed the monkey to satiety. They found that the majority of orbitofrontal visual food-related neurons decreased their responses to the sight of the food with which the monkey was fed to satiety (see example in Fig. 5.3). Thus, for these neurons, the reward value of the sight of food is what is represented in the orbitofrontal cortex. At a stage of visual processing one synapse earlier, in the inferior temporal visual cortex, neurons do not show visual discrimination reversal learning, nor are their responses modulated by feeding to satiety [93]. Thus, both of these functions are implemented for visual processing in the orbitofrontal cortex.

s0090 5.9 Reward prediction error neurons

p0320 In addition to these neurons that encode the reward association 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 [91] (Fig. 5.5), or when reward is no longer made available in a visual discrimination task, that is, in extinction [25,91]. These may be called "negative reward prediction error neurons." Different populations of such neurons respond to other types of non-reward, including the removal of a formerly approaching taste reward, and 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 [17,25,91]. 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 [1,17,95]. The finding that different orbitofrontal cortex neurons respond to different types of non-reward (or negative reward prediction error) [91] may provide part of the brain's mechanism that enables task or context-specific reversal to occur [17,25].

p0330 Evidence that there may be similar negative reward prediction 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 [101].

p0340 The orbitofrontal cortex negative reward prediction error neurons respond to a mismatch between the reward expected ("expected value") and the reward that is obtained ("reward outcome") [17]. Both signals are represented in the orbitofrontal cortex, in the



f0050 **Figure 5.5** Negative reward prediction error neuron: responses of an orbitofrontal cortex neuron that responded only when the monkey 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. Each single dot represents an action potential; each vertically arranged double dot represents a lick response. 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 x, which were the first 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. *Source*: After Thorpe et al. (1983) [91].

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, the taste (or texture or temperature). Similarly, in a probabilistic monetary reward task, activations in the human orbitofrontal and pregenual cingulate cortex are related to both expected value and to reward outcome (the magnitude of the reward actually obtained on each trial) [102]. The orbitofrontal cortex is the probable brain region for the computation of negative reward prediction error, because both 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 (see above).

p0350 It may be noted that the dopamine neurons in the midbrain may not be able to provide a good representation of negative reward prediction error, because their spontaneous firing rates are so low [103] that much further reduction would provide only a small signal. In any case, the dopamine neurons would not appear to be in a position to compute a negative reward prediction error, as they are not known to receive inputs that signal expected reward (expected value), and the actual reward (outcome) that is obtained, and indeed do not represent the reward obtained (reward outcome), in that they stop responding to a taste reward outcome if it is predictable [103,104]. Although dopamine neurons do appear to represent a positive reward prediction error signal (responding if a greater than expected

reward is obtained) [103,104], they do not appear to have the signals required to compute this, the expected reward, and the reward outcome obtained, so even this must be computed elsewhere. The orbitofrontal cortex does contain representations of these two signals, the expected reward value and the reward outcome, and has projections to the ventral striatum, which in turn projects to the region of the midbrain dopamine neurons, and so this is one possible pathway along which the firing of positive reward prediction error might be computed (see Fig. 5.1). Consistent with this, activations in parts of the human ventral striatum are related to positive reward prediction error (positive temporal difference error) [102,105]. Thus, the dopamine projections to the prefrontal cortex and other areas are not likely to convey information about reward to the prefrontal cortex, which instead is likely to be decoded by the neurons in the orbitofrontal cortex that represent primary reinforcers, and the orbitofrontal cortex neurons that learn associations of other stimuli to the primary reinforcers to represent expected value [17,45,91,102]. Although it has been suggested that the firing of dopamine neurons may reflect the earliest signal in a task that indicates reward and could be used as a positive reward prediction error signal during learning [104,106], it is likely, partly on the basis of the above evidence, though an interesting topic for future investigation, that any error information to which dopamine neurons fire originates from representations in the orbitofrontal cortex that encode expected value and reward outcome, and which connect to the ventral striatum [1,17,102].

p0360 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 [107], or when rewards are reduced [108] (and in similar imaging studies [109]). 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 behavioral responses or 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, when a reward prediction system needs to be corrected. Consistent with this, many studies provide evidence that errors made in many tasks activate the anterior/midcingulate cortex [110–113].

s0100 5.10 Social reinforcers such as face and voice expression

p0370 Another type of visual information represented in the orbitofrontal cortex is information about faces. There is a population of orbitofrontal cortex neurons that respond in many ways similarly to those in the temporal cortical visual areas [15–18,90,114–116]. The orbitofrontal face-responsive neurons, first observed by Thorpe et al. [91], then by Rolls et al. [117], tend to respond with longer latencies than temporal lobe neurons (140–200 ms typically, compared to 80–100 ms); they also convey information about which face is being seen, by having different responses to different faces; and they are typically rather harder to activate strongly than temporal cortical face-selective neurons, in that many of them respond much better to real faces than to two-dimensional images of faces on a video monitor (cf. [118]). Some of the orbitofrontal cortex face-selective neurons are responsive to face expression, gesture, or movement [117]. The findings are consistent with the likelihood that these neurons are activated via the inputs from the temporal cortical visual areas in which face-selective neurons are found (see Fig. 5.1).

p0380 The significance of these orbitofrontal cortex neurons is likely to be related to the fact that faces convey information that is important in social reinforcement in at least two ways that could be implemented by these neurons. The first is that some may encode face expression ([117]; cf. [119]), which can indicate reinforcement. The second way is that they encode information about which individual is present [117], which by stimulus–reinforcement association learning is important in evaluating and utilizing learned reinforcing inputs in social situations, for example, about the current reinforcement value as decoded by stimulus–reinforcement association to a particular individual.

p0390 This system has also been shown to be present in humans. For example, Kringelbach and Rolls [101] showed that activation of a part of the human orbitofrontal cortex occurs during a face discrimination reversal task. In the task, the faces of two different individuals are shown, and when the correct face is selected, the expression turns into a smile. (The expression turns to angry if the wrong face is selected.) After a period of correct performance, the contingencies reverse, and the other face must be selected to obtain a smile expression as a reinforcer. It was found that activation of a part of the orbitofrontal cortex occurred specifically in relation to the reversal, that is, when a formerly correct face was chosen, but an angry face expression was obtained. Thus in humans, there is a part of the orbitofrontal cortex that responds selectively in relation to face expression specifically when it indicates that behavior should change, and this activation is error-related [101] and occurs when the error neurons in the orbitofrontal cortex become active [91]. In addition, activations in the human orbitofrontal cortex are related to the attractiveness or beauty of a face [120].

p0400 Also prompted by the neuronal recording evidence of face and auditory neurons in the orbitofrontal cortex [117], it has further been shown that there are 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 [121]. The expression identification impairments could occur independently of perceptual impairments in facial recognition, voice discrimination, or environmental sound recognition. Poor performance on both expression tests was correlated with the degree of alteration of emotional experience reported by the patients. There was also a strong positive correlation between the degree of altered emotional experience and the severity of the behavioral problems (e.g., disinhibition) found in these patients [121]. 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 [121]. It has further been shown that 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 [122].

s0110 5.11 Top-down effects of cognition and attention on the reward value of affective stimuli

p0410 How does cognition influence affective 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?

p0420 An fMRI study to address these fundamental issues in brain design has shown that cognitive effects can reach down into the human orbitofrontal cortex and influence activations

produced by odors [123]. 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 [1,123].

p0430 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 influences in the brain, but also in relation to the topical issues of appetite control and obesity [43,124]. 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") [86]. 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 reward value of taste and flavor. This is an important way in which cognition influences the neural mechanisms that control reward and appetite.

p0440 When we see a person being touched, we may empathize the affective 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 [84]. 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 backprojections from the orbitofrontal cortex [84].

p0450 What may be a fundamental principle of how top-down attention can influence affective versus non-affective processing has recently 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 [39]. In an fMRI investigation, when subjects were instructed to remember and rate the pleasantness of a taste stimulus, 0.1 M MSG, activations were greater in the medial orbitofrontal and pregenual cingulate cortex than when subjects were instructed to remember and rate the intensity of the taste. When the subjects were instructed to remember and rate the intensity, activations were greater in the insular taste cortex. Thus, depending on the context in which tastes are presented and whether affect is relevant, the brain responds to a taste differently. 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 [39]. 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.

p0460 Indeed, 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 [125]. When the subjects were instructed to remember and rate the intensity, activations were greater in the inferior frontal gyrus. These top-down effects occurred not only during odor delivery, but started in a preparation period after the instruction before odor delivery, and continued after termination of the odor in a short-term memory period. These findings show that when attention is paid to affective value, the brain systems engaged to prepare for, represent, and remember a sensory stimulus are different from those engaged when attention is directed to the physical properties of a stimulus such as its intensity.

p0470 The principle thus appears to be that top-down attentional and cognitive effects on reward or affective value influence representations selectively in cortical areas that process the affective value and associated subjective emotional experience of taste [39,86] and olfactory [66,87,88] 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 [39,66,86–88]. This is computationally appropriate in top-down biased competition models of attention [17,18,126]. Indeed, the mechanisms that underlie these top-down attentional and cognitive effects include top-down biased competition of the bottom-up (sensory) effects, and are now starting to be elucidated computationally [17,18,127–129].

s0120 5.12 Emotion and reward

p0480 From earlier approaches [2,8,130], Rolls has developed the theory over a series of articles that emotions are states elicited by instrumental reinforcers [1,7,131–135]. Given that the evidence described above 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.

p0490 Further, the evidence described above 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 [97–99,136–138], and activation of different parts of the human orbitofrontal cortex by monetary gain versus loss [139], and other reinforcers [12].

p0500 The changes in emotion produced by damage to the orbitofrontal cortex are large, as the evidence described above and elsewhere shows [1,17,25]. 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 [140,141], decision-making with linked autonomic deficits [142,143], and autonomic conditioning [144], may not produce major changes in emotion that are readily apparent in everyday behavior [17,144,145].

p0510 Further evidence on the close relation between rewards (or, more generally, reinforcers, to include punishers) and emotion, including the subjective feelings of emotion, and the brain regions that implement this processing, such as the orbitofrontal cortex, pregenual cingulate cortex, and amygdala, is described elsewhere [1,17,25,146].

s0130 5.13 Individual differences in reward processing and emotion

p0520 Given that there are individual differences in emotion, can these individual differences be related to the functioning of brain systems involved in reward and affective behavior such as the orbitofrontal and pregenual cingulate cortex?

p0530 Some individuals, chocolate cravers, report that they crave chocolate more than non-cravers, and this is associated with increased liking of chocolate, increased wanting of chocolate, and eating chocolate more frequently than non-cravers (Rodriguez et al., 2007). In a test of whether these individual differences are reflected in the affective systems in the orbitofrontal cortex and pregenual cingulate cortex that are the subject of this chapter, Rolls and McCabe [147] used fMRI to measure the response to the flavor of chocolate, to the sight of chocolate, and to their combination, in chocolate cravers versus non-cravers. SPM analyses showed that the sight of chocolate produced more activation in chocolate cravers than in non-cravers in the medial orbitofrontal cortex and ventral striatum. For cravers versus non-cravers, a combination of a picture of chocolate with chocolate in the mouth produced a greater effect than the sum of the components (i.e., supralinearity) in the medial orbitofrontal cortex and pregenual cingulate cortex. Furthermore, the pleasantness ratings of the chocolate and chocolate-related stimuli had higher positive correlations with the fMRI BOLD signals in the pregenual cingulate cortex and medial orbitofrontal cortex in the cravers than in the non-cravers.

AUQ3 AUQ4 AUQ5

p0540 An implication is that individual differences in brain responses to very pleasant foods help to understand the mechanisms that drive the liking for specific foods by indicating that some brain systems (but not others such as the insular taste cortex) respond more to the rewarding aspects of some foods, and thus influence and indeed even predict the intake of those foods (which was much higher in chocolate cravers than non-cravers) [147].

p0550 Investigating another difference between individuals, Beaver et al. [148] showed that reward sensitivity in different individuals (as measured by a behavioral activation scale) is correlated with activations in the orbitofrontal cortex and ventral striatum to pictures of appetizing versus disgusting food.

p0560 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 [137,149,150]. 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 Behaviour Questionnaire, and had more BPD characteristics and anger, and less happiness, than control groups (either normals or patients with lesions outside the orbitofrontal cortex).

p0570 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 [151,152]. 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. 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.

p0580 AUQ6 The negative symptoms of schizophrenia include flattening of affect. As part of a dynamical attractor systems theory of schizophrenia, in which hypofunction of NMDA receptors [153] 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 [1,154,155].

p0590 Conversely, it has been proposed that hyperfunctionality of the glutamate system in obsessive compulsive disorder [156,157] 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 [158].

s0140 5.14 Beyond the representation of reward value to choice decision-making

p0600 In the neurophysiological studies described above, we have found that neuronal activity in the orbitofrontal cortex is related to the reward value of sensory stimuli, and how this changes when reward contingencies change, but is not related to the details of actions that are being performed, such as mouth or arm movements [1,17]. Wallis [159] and Padoa-Schioppa and Assad [160] have obtained evidence that supports this. An implication is that the orbitofrontal cortex represents the reward, affective (or, operationally, goal) value of a stimulus. Further, this value representation is on a continuous scale, as shown by the gradual decrease in orbitofrontal cortex neuronal responses to taste, olfactory, and visual rewarding stimuli during feeding to satiety [30,33,37,47]. Consistently, in humans the BOLD activations in different parts of the orbitofrontal cortex are continuously related to subjective pleasantness ratings of taste [39,86,161], olfactory [88], flavor [38,76,86,162], oral temperature [80], hand temperature [85], and face beauty [120] stimuli, and to monetary reward value [102,139], 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. It is, of course, essential to represent each reward separately, in order to make decisions about and between rewards, and separate representations (using distributed encoding [17]) of different rewards are present in the orbitofrontal cortex.

p0610 Approaches used in neuroeconomics help to define further the nature of the representation of reinforcers in the orbitofrontal cortex. When monkeys choose between different numbers of drops of two juices, one more preferred than the other, some neurons in the orbitofrontal cortex encode the offer value, some the choice value, and some the taste, but not the details of the motor response that is chosen [160]. Further, these neurons encode economic value, not relative preference, as shown by a study in which a particular reward was paired with other rewards. The fact that the neuronal responses are menu invariant suggests that transitivity, a fundamental trait of economic choice, may be rooted in the activity of individual neurons [163]. There is also evidence that relative reward value may be represented in the orbitofrontal cortex [164], and in what may provide a resolution of this, we are finding in a current study that some parts of the orbitofrontal cortex may represent the absolute pleasantness of stimuli and others the relative pleasantness of stimuli [165].

p0620 When a choice is made between stimuli with different reward probabilities, the choice made depends on the probability with which each reward will be obtained. In this probabilistic decision-making situation, we can define *expected value* as probability $\times$ reward magnitude) [166]. In an investigation of such a probabilistic choice decision task in which humans chose between two rewards, each available with different probabilities, it was found that the activation of the orbitofrontal cortex was related to expected value while the decision was being made, and also to the reward magnitude announced later on each trial [102]. Further evidence in a variety of tasks implicates a related and partly overlapping region of the ventromedial prefrontal cortex with expected value [105,167–169]. In contrast, the reward prediction errors or temporal difference errors as defined in reinforcement learning [104,170] are usually evident in the ventral striatum in imaging studies [102,105], though we should remember that negative reward prediction errors are represented by the error neurons in the primate orbitofrontal cortex [91] (see Section 5.9), and that the lateral orbitofrontal cortex is activated when a negative reward prediction error is generated in the reversal of a visual discrimination task [101].

p0630 Although it might be anticipated that the actual utility or "subjective utility" of an offer (a choice) to an individual approximately tracks the expected value, this is not exactly the case, with subjects typically undervaluing high rewards, and being over-sensitive to high punishments [171–177]. Subjects also typically have a subjective utility function that discounts rewards the further in the future they are delayed. Some parts of the ventromedial prefrontal cortex have activations that may follow the subjective utility of, for example, delayed rewards. In a study of this, it was found that activations in the ventromedial prefrontal cortex were correlated with the subjective utility of rewards delayed for different times, with the discount curve for each subject reconstructed from each subject's choices [178].

p0640 Clearly, a representation of reward magnitude, expected value, and even the subjective utility of a reward is an important input to a decision-making process, and the orbitofrontal cortex (with the ventromedial prefrontal area), appears to provide this information. When making a decision between two rewards, or whether to work for a reward that has an associated cost, it is important that the exact value of each reward is represented and enters the decision-making process. However, when a decision is reached, a system is needed that can make a binary choice, so that on one trial the decision might be reward 1, and on another trial reward 2, so that a particular action can be taken. For the evaluation, the neural activity

needs to represent a stimulus in a way that continuously and faithfully represents the affective or reward value of the stimulus, and this could be present independently of whether a binary choice decision is being made or not. On the other hand, when a binary (choice) decision must be reached, a neural system is needed that does not continuously represent the reward value of the stimulus, but which instead falls into a binary state, in which for example the high firing of some neurons represents one decision (i.e., choice), and the high firing of other neurons represents a different choice. Processes such as this transition from spontaneous firing to a binary state of firing of neurons (fast versus slow) are known to occur in some premotor and related areas such as the macaque ventral premotor cortex when decisions are taken, in this case about which vibrotactile stimulus to choose [179–181].

p0650 It has been proposed that there may be a similar binary system, perhaps in another brain region, that becomes engaged when choice decisions are between rewards, or about rewards with which there is an associated cost [17]. To investigate whether representing the affective value of a reward on a continuous scale may occur before and separately from making a binary (for example, yes–no) decision about whether to choose the reward, Grabenhorst et al. [182] used fMRI to measure activations produced by pleasant warm, unpleasant cold, and affectively complex combinations of these stimuli applied to the hand. On some trials the affective value was rated on a continuous scale, and on different trials a yes–no (binary choice) decision was made about whether the stimulus should be repeated in future. Activations that were continuously related to the pleasantness ratings and that were not influenced when a binary (choice) decision was made were found in the orbitofrontal and pregenual cingulate cortex, implicating these regions in the continuous representation of affective value, consistent with the evidence described above. In this study, decision-making, contrasted with just rating the affective stimuli, revealed activations in the medial prefrontal cortex area 10, implicating this area in choice decision-making [182].

p0660 Support for a contribution of medial prefrontal cortex area 10 to taking binary (choice) decisions comes from a fMRI study in which two odors were separated by a delay, with instructions on different trials to decide which odor was more pleasant, or more intense, or to rate the pleasantness and intensity of the second odor on a continuous scale without making a binary (choice) decision. Activations in the medial prefrontal cortex area 10, and in regions to which it projects, including the anterior cingulate cortex and insula, were higher when binary choice decisions were being made compared to making ratings on a continuous scale, further implicating these regions in choice decision-making [183].

p0670 Different brain systems were implicated in different types of choice decision-making [183]. Decision-making about the affective value of odors produced larger effects in the dorsal part of medial prefrontal cortex area 10 and the agranular insula, whereas decisions about intensity produced larger effects in the dorsolateral prefrontal cortex, ventral premotor cortex, and anterior insula.

p0680 Consistent with these findings, patients with medial prefrontal cortex lesions are impaired in a decision-making shopping task, as reflected for example by visits to previously visited locations [184–186]. In another imaging study, area 10 activation has been related to moral decision-making [187].

p0690 In the study with warm and cold stimuli, and mixtures of the two, when a (choice) decision was yes versus no, effects were found in the dorsal anterior cingulate cortex [182], an area implicated by many other studies in decision-making [188,189]. The anterior cingulate cortex has been implicated in action-outcome learning [190,191], and the study with warm and cold stimuli shows that the contribution of the anterior cingulate cortex is in the choice decision-making itself, and that its activation does not occur just in relation to the pleasantness or intensity of the stimuli [182].

p0700 The implications are that the orbitofrontal cortex, and the pregenual cingulate cortex to which it projects, are involved in making decisions primarily by representing reward value on a continuous scale. Although the orbitofrontal cortex can have activations in decision-making tasks [192–194], it is important to separate processes involved in representing reward value from those involved in reaching a choice decision, which are separate computational processes [17]. The evidence we describe indicates that another tier of processing beyond the affective value stages becomes engaged in relation to taking binary (choice) decisions, and these areas include the medial prefrontal cortex area 10. Having separable systems for these types of processing appears to be computationally appropriate, for at the same time that one brain system is entering a binary decision state, that on this trial the choice is probabilistically one or another, in a way that could be implemented by the settling of an attractor network into one of its two or more high firing rate attractor states, each representing a choice [17,195,196], another brain system (involving the orbitofrontal and pregenual cingulate cortex) can still be representing faithfully the reward or affective value of the stimuli on a continuous scale [25].

p0710 We may ask why, if the activations in the orbitofrontal cortex and the pregenual cingulate cortex are somewhat similar in their continuous representations of reward or affective value, are there these two different areas? A suggestion is that the orbitofrontal cortex is the region that computes the rewards, expected rewards, and so on, and updates these rapidly when the reinforcement contingencies change, based on its inputs about primary reinforcers from the primary taste cortex [44], the primary olfactory cortex [197], the somatosensory cortex [198], etc. The orbitofrontal cortex makes explicit in its representations the reward value, based on these inputs, and in a situation where reward value is not represented at the previous tier, but instead where the representation is about the physical properties of the stimuli, their intensity, and so on [39,82,85,86,88,199] (see Fig. 5.1). The orbitofrontal cortex computes the expected value of previously neutral stimuli, and updates these representations rapidly when the reinforcement contingencies change, as described in this review. Thus, the orbitofrontal cortex is the computer of reward magnitude and expected reward value. It can thus represent outcomes, and expected outcomes, but it does not represent actions such as motor responses or movements. It is suggested that the representations of outcomes, and expected outcomes, are projected from the orbitofrontal cortex to the pregenual cingulate cortex, as the cingulate cortex has longitudinal connections, which allows this outcome information to be linked to the information about actions that is represented in the midcingulate cortex, and that the outcome information derived from the orbitofrontal cortex can contribute to action-outcome learning implemented in the cingulate cortex [17,25,190,191]. Although the anterior cingulate cortex is activated in relation to autonomic function [200], its functions clearly extend much beyond this, as shown also, for example, by the emotional changes that follow damage to the anterior cingulate cortex and related areas in humans [122].

p0720 Why, then, are there also outputs from the orbitofrontal cortex to medial area 10 (directly [201] and via pregenual cingulate cortex [13,201])? We suggest, based on the choice decision-making studies described here [25,182,183], that when a binary decision must be made between two (or more) rewards, then area 10 becomes involved. If it is simply a case of linking an action to a reward (and thus deciding which response to perform), the mid-cingulate cortex may be engaged. But if a prior decision must be made, not about which action to take to obtain an outcome, but instead between different rewards or expected rewards, or whether or not to choose a reward, then the medial prefrontal cortex area 10 may be involved [182,183]. The implication here is that there are many decision systems in the brain, and that we must specify exactly what type of decision is being made when relating a brain area to decision-making [17,181]. Consistent

with this, in the odor decision-making study, when the decision between the first and second odor was not about which was more pleasant, but instead about which was more intense, the dorsolateral prefrontal cortex became engaged, rather than medial prefrontal cortex, area 10 [183].

s0150

5.15 Cortical networks that make choices between rewards: is there a common currency?

p0730 Attractor networks implemented by the recurrent collateral connections between cortical pyramidal cells provide a way to understand choice decision-making in the brain and its probabilistic nature [17,181,195,196]. Each set of neurons in the network that, if in the high firing rate state, represents one of the attractors corresponds to one of the decisions, and is biased on by the evidence for that decision, which might be the reward outcome expected if that decision is taken (i.e., the expected value). Because of the inhibitory interneurons, only one high firing rate attractor state can be active at any one time, so a choice is made on each trial. The state reached on a trial, that is, the decision taken, depends on the relative strength of the different expected rewards and on the noise within the network caused by the spiking of the neurons in the network. The network is essentially a short-term memory network, accumulating the evidence over short time periods (of, for example, 1 s) before finally falling into an attractor state in which one population of neurons only has won the competition on that trial, and is left with a high firing rate that represents the choice made.

p0740 In the application of this type of decision-making to rewards, the different inputs are the different rewards. One input might be an expected taste reward, another an expected monetary reward, another a social reward. Some authors have talked about a common currency for rewards [202–204]. What might this mean with this type of neuronal processing? In the neuronal decision mechanism described, the decision state is high firing activity of the representation of the particular reward that has won. This is excellent, because then action systems are provided with the information about the particular reward that is the goal of the action, and, of course, the actions selected will have to depend on the goal that has been selected. The fact that it is an attractor network that represents the reward selected is also very useful, for the short-term memory properties of the attractor network will keep the goal representation active while an action is being selected and performed. We can note that it would not be at all helpful to change the rewards into a common currency (such as points or dollars) as part of the selection process, as this would leave the selected goal just a number of points, or a number of dollars, which would not be useful to guide particular actions.

p0750 What is needed is that the different expected rewards that are the inputs to the decision networks must be on approximately the same scale. If food reward were to always be much stronger than other rewards, then the animal's genes would not survive, for it would never drink water, reproduce, etc. It has therefore been suggested that genes that specify rewards must be selected to ensure that the rewards they specify are approximately of the same maximum value, so that they will all be selected at some time [1]. There are, of course, factors that modulate the current value of each reward, such as hunger for food reward, thirst for water reward, etc. Important also in the modulation of the value of each reward is sensory-specific satiety, a property of it is suggested all reward types to help selection of different rewards AUQ7 which in general is adaptive. The opposite is also a useful principle, namely incentive motivation, the shorter term increase in the reward value of a particular reward after a particular

reward has been obtained (the salted nut phenomenon [205]), which has the adaptive utility of helping behavior to lock on to a goal for a useful and efficient amount of time, rather than continually switching between rewards [1]. Thus, we might speak of a common currency for different rewards in that each reward type must have a maximal value similar to other rewards as inputs that can drive the attractor decision-making network, so that each reward is selected at least sometimes. But there is no need to talk of a situation in which all specific rewards are converted into a common currency such as points. We can note that although the rewards that are specified as primary reinforcers by the genes should be specified to be approximately equipotent, learning mechanisms can adjust the reward value of what starts as a primary reinforcer, as when a taste is associated with sickness in taste aversion learning. As we shall see next, the costs associated with each reward can also be a factor.

p0760 Now in fMRI studies, it is frequently found that many different reward types (including taste, olfactory, flavor, texture, somatosensory, monetary, face expression, and social reputation rewards) activate rather similar brain areas, which often include the medial orbitofrontal cortex and pregenual cingulate cortex [1,25,59,204]. Does this provide evidence for a common reward representation of, for example, points? The evidence is that is does not, for all the single-neuron recording studies described above and elsewhere show that specific rewards are represented by each neuron, which often responds to a particular combination of sensory inputs. So why may all these different specific rewards be represented close together in, for example, the medial orbitofrontal cortex? The answer, I suggest, is that the implementation of decision-making between rewards by an attractor network means that all the different reinforcers have to be brought spatially close together to compete with each other in a single network. The spatial constraint is that cortical networks operate over a short range of a few mm (for very good computational reasons, described by Rolls [17]), and this is why in this case the different rewards, to compete within the same network using the short-range inhibitory interneurons, and to support each other using the short range cortical excitatory recurrent collaterals, need to be represented close together in the cerebral cortex [17].

p0770 I note that the decision-making need not be between two rewards, and in principle an attractor-based decision network can make a single choice between multiple inputs [17,181,196].

p0780 How are costs taken into account in this decision-making process between different rewards? I suggest that the costs incurred in obtaining each goal need to be subtracted from the reward value of each goal, before they enter the decision-making network. The reason for this is that the costs are different for each type of reward, and so it would not make sense to choose the best reward independently of the cost of obtaining that reward. And to choose the best reward independent of cost, and then to go through a process of evaluating the cost for the highest reward, then if that does not exceed some criterion moving to the second highest reward, would also be computationally very time consuming as well as difficult to implement. For these reasons, the cost specific to each reward should be subtracted from the expected value of that reward to produce a net value for that reward-cost pair before the decision-making network that makes the choice selection. It will be very interesting to discover whether there are such representations of net reward-cost value in the brain, and if they are the inputs to the choice decision-making networks.

p0790 What factors influence whether a network is likely to be involved in choice decision-making versus representing expected reward value (or expected net reward value) on a continuous scale? I propose that if there is a strong forward input to the pyramidal cells that drives them hard, the firing rates will tend to reflect on a continuous scale the magnitude of the forward input. If the recurrent collaterals are particularly efficacious in any

area, this will tend to make the cortical area more likely to produce "choices," that is, to end up with high firing rates for a winning population, with other cells inhibited. This may be a feature that, in terms of functional cortical architecture, may make some cortical areas more likely to represent inputs on a continuous scale, behaving perhaps linearly, whereas other areas may operate more nonlinearly, falling into an attractor state. Which is more likely may also be set dynamically, perhaps by acetylcholine and other modulators that may alter the relative efficacy of the recurrent collateral connections [25,206].

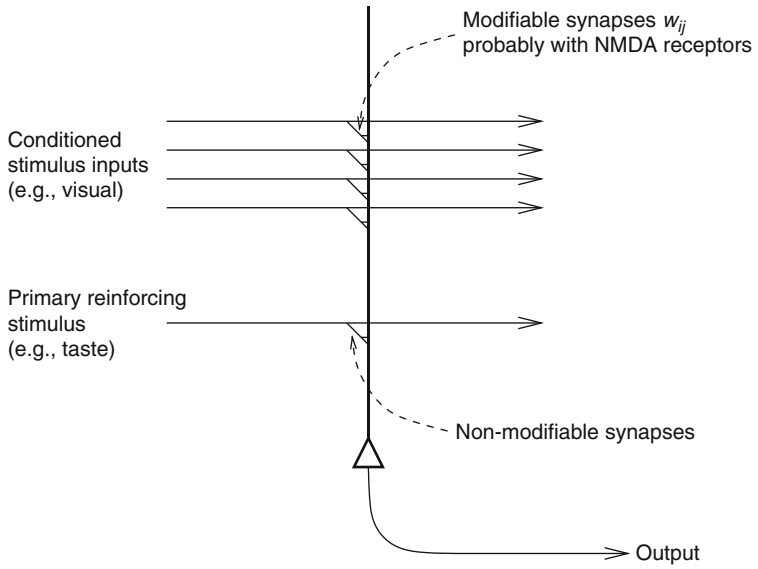
s0160

5.16 A computational basis for stimulus–reinforcer association learning and reversal in the orbitofrontal cortex involving conditional reward neurons and negative reward prediction error neurons

p0800 The neurophysiological, imaging, and lesion evidence described above suggests that one function implemented by the orbitofrontal cortex is rapid stimulus–reinforcement association learning and the correction of these associations when reinforcement contingencies in the environment change. How might this rapid stimulus–reinforcer association learning and reversal be implemented at the neuronal and neuronal network level? One mechanism could be implemented by Hebbian modification of synapses conveying visual input onto taste-responsive neurons, implementing a pattern association network [1,7,17,18,94,207]. Long-term potentiation would strengthen synapses from active conditioned stimulus neurons onto neurons responding to a primary reinforcer, such as a sweet taste, and homosynaptic long-term depression would weaken synapses from the same active visual inputs if the neuron was not responding because an aversive primary reinforcer (e.g., a taste of saline) was being presented (Fig. 5.6).

p0810 As described above, the conditional reward neurons in the orbitofrontal cortex convey information about the current reinforcement status of particular stimuli. In a new theory of how the orbitofrontal cortex implements rapid, one-trial, reversal, these neurons play a key part, for particular conditional reward neurons (responding to, e.g., "green is now rewarding"; see example in Fig. 5.4C) are biased on by a rule set of neurons if the association is being run direct, and are biased off if the association is being run reversed ("green is now not rewarding") [95]. One set of rule neurons in the short-term memory attractor network is active when the rule is direct, and a different set of neurons when the association is reversed. The state of the rule network is reversed when the error neurons fire in reversal, because the firing of the error neurons quenches the attractor by activating inhibitory neurons, and the opposite set of rule neurons emerge to activity after the quenching because of some adaptation in the synapses or neurons in the rule attractor that have just been active. The error-detection neurons themselves may be triggered by a mismatch between what was expected when the visual stimulus was shown and the primary reinforcer that was obtained, both of which are represented in the primate orbitofrontal cortex [91]. The whole system maps stimuli (such as green and blue) through a biased competition layer of conditional reward neurons in which the mapping is controlled by the biasing input from the rule neurons, to output neurons that fire if a stimulus is being shown that is currently associated with reward [95].

p0820 The model gives an account of the presence of conditional reward and error neurons in the orbitofrontal cortex, as well as neurons that respond to whichever visual stimulus is currently associated with reward, and neurons that signal whether a (e.g., taste) reward or punishment has just been obtained. The model also suggests that the orbitofrontal cortex



f0060 **Figure 5.6** Pattern association between a primary reinforcer, such as the taste of food, which activates neurons through non-modifiable synapses, and a potential secondary reinforcer, such as the sight of food, which has modifiable synapses onto the same neurons. The associative rule for the synaptic modification is that if there is both presynaptic and post-synaptic firing, then that synapse should increase in strength. Such a mechanism appears to be implemented in the amygdala and orbitofrontal cortex. (Homosynaptic) long-term depression (produced by presynaptic firing in the absence of strong postsynaptic firing) in the pattern associator could account for the response to the no-longer reinforced stimulus becoming weaker. For further details, see [1].

may be especially appropriate for this rapid reversal mechanism, because, in contrast to the amygdala, the orbitofrontal cortex as a cortical structure has a well-developed system of recurrent collateral synapses between the pyramidal cells, providing an appropriate basis for implementing a working memory to hold the current rule. The model also shows how when on a reversal trial a reward is not obtained to a previously rewarded stimulus, on the very next trial when the recently punished stimulus is shown, it is treated as a reward, and it is chosen. This type of behavior at the behavioral level is in fact illustrated in Fig. 5.5 (e.g., trials 4 and 14), and cannot be accounted for by a new association of the now to be rewarded stimulus with reward, for in its recent past it has been associated with saline. Thus, this type of one-trial rapid reversal cannot be accounted for by direct stimulus–reward association learning, and a rule-based system, such as the type implemented in the model, is needed. The model has been worked out in detail at the level of integrate-and-fire spiking neurons, and makes predictions about further types of neuron expected to be present in the orbitofrontal cortex [1,95].

p0830 In conclusion, some foundations for understanding reward processing and decision-making have been described. A fuller approach to understanding reward processing and emotion is provided by Rolls [1], a rigorous computational approach is provided by Rolls [17], and future directions are suggested by Rolls and Grabenhorst [25].

s0170 ## Acknowledgements

p0840 The author has worked on some of the experiments described here with I. Araujo, G.C. Baylis, L.L. Baylis, A. Bilderbeck, R. Bowtell, A.D. Browning, H.D. Critchley, S. Francis, F. Grabenhorst, M.E. Hasselmo, J. Hornak, M. Kadohisa, M. Kringelbach, C.M. Leonard, C. Margot, C. McCabe, F. McGlone, F. Mora, J. O'Doherty, B.A. Parris, D.I. Perrett, T.R. Scott, S.J. Thorpe, M.I. Velazco, J.V. Verhagen, E.A. Wakeman and F.A.W. Wilson, and their collaboration is sincerely acknowledged. Some of the research described was supported by the Medical Research Council, PG8513790 and PG9826105.

References

[1] E.T. Rolls, Emotion Explained, Oxford University Press, Oxford, 2005.
[2] J.A. Gray, Elements of a Two-Process Theory of Learning, Academic Press, London, 1975.
[3] A. Dickinson, Contemporary Animal Learning Theory, Cambridge University Press, Cambridge, 1980.
[4] N.J. Mackintosh, Conditioning and Associative Learning, Oxford University Press, Oxford, 1983.
[5] J.E. Mazur, Learning and Behavior, fourth ed., Prentice Hall, Upper Saddle River, NJ, 1998.
[6] D.A. Lieberman, Learning, Wadsworth, Belmont, CA, 2000.
[7] E.T. Rolls, The Brain and Emotion, Oxford University Press, Oxford, 1999.
[8] L. Weiskrantz, Emotion, in: L. Weiskrantz (Ed.), Analysis of Behavioural Change, Harper and Row, New York and London, 1968, pp. 50–90.
[9] S.T. Carmichael, J.L. Price, Architectonic subdivision of the orbital and medial prefrontal cortex in the macaque monkey, J. Comp. Neurol. 346 (1994) 366–402.
[10] M. Petrides, D.N. Pandya, Comparative architectonic analysis of the human and macaque frontal cortex, in: F. Boller, J. Grafman (Eds.), Handbook of Neuropsychology, Elsevier Science, Amsterdam, 1995, pp. 17–58.
[11] D. Öngür, J.L. Price, The organisation of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans, Cereb. Cortex 10 (2000) 206–219.
[12] M.L. Kringelbach, E.T. Rolls, The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology, Prog. Neurobiol. 72 (2004) 341–372.
[13] J.L. Price, Connections of orbital cortex, in: D.H. Zald, S.L. Rauch (Eds.), The Orbitofrontal Cortex, Oxford University Press, Oxford, 2006, pp. 39–55.
[14] J.L. Price, Definition of the orbital cortex in relation to specific connections with limbic and visceral structures and other cortical regions, Ann. NY Acad. Sci. 1121 (2007) 54–71.
[15] E.T. Rolls, Functions of the primate temporal lobe cortical visual areas in invariant visual object and face recognition, Neuron 27 (2000) 205–218.
[16] E.T. Rolls, The representation of information about faces in the temporal and frontal lobes, Neuropsychologia 45 (2007) 125–143.
[17] E.T. Rolls, Memory, Attention, and Decision-making: A Unifying Computational Neuroscience Approach, Oxford University Press, Oxford, 2008.
[18] E.T. Rolls, G. Deco, Computational Neuroscience of Vision, Oxford University Press, Oxford, 2002.
[19] E.T. Rolls, S.M. Stringer, Invariant visual object recognition: a model, with lighting invariance, J. Physiol. Paris 100 (2006) 43–62.
[20] R. Norgren, Central neural mechanisms of taste, in: I. Darien-Smith (Ed.), Handbook of Physiology – The Nervous System III, Sensory Processes 1, American Physiological Society, Washington, DC, 1984, pp. 1087–1128.

[21] E.T. Rolls, T.R. Scott, Central taste anatomy and neurophysiology, in: R.L. Doty (Ed.), Handbook of Olfaction and Gustation, second ed., Dekker, New York, 2003, pp. 679–705.
[22] S.T. Carmichael, J.L. Price, Sensory and premotor connections of the orbital and medial prefrontal cortex of macaque monkeys, J. Comp. Neurol. 363 (1995) 642–664.
[23] H. Barbas, Anatomic basis of cognitive-emotional interactions in the primate prefrontal cortex, Neurosci. Biobehav. Rev. 19 (1995) 499–510.
[24] D.N. Pandya, E.H. Yeterian, Comparison of prefrontal architecture and connections, Philos. Trans. R. Soc. Lond. B Biol. Sci. 351 (1996) 1423–1431.
[25] E.T. Rolls, F. Grabenhorst, The orbitofrontal cortex and beyond: from affect to decision-making, Prog. Neurobiol. (2008), (in press).
AUQ8
[26] E.T. Rolls, The functions of the orbitofrontal cortex, Brain Cogn. 55 (2004) 11–29.
[27] E.T. Rolls, S. Yaxley, Z.J. Sienkiewicz, Gustatory responses of single neurons in the caudolateral orbitofrontal cortex of the macaque monkey, J. Neurophysiol. 64 (1990) 1055–1066.
[28] L.L. Baylis, E.T. Rolls, Responses of neurons in the primate taste cortex to glutamate, Physiol. Behav. 49 (1991) 973–979.
[29] E.T. Rolls, The representation of umami taste in the taste cortex, J. Nutr. 130 (2000) S960–S965.
[30] E.T. Rolls, H. Critchley, E.A. Wakeman, R. Mason, Responses of neurons in the primate taste cortex to the glutamate ion and to inosine 5′-monophosphate, Physiol. Behav. 59 (1996) 991–1000.
[31] E.T. Rolls, H.D. Critchley, A. Browning, I. Hernadi, The neurophysiology of taste and olfaction in primates, and umami flavor, Ann. NY Acad. Sci. 855 (1998) 426–437.
[32] E.T. Rolls, J.V. Verhagen, M. Kadohisa, Representations of the texture of food in the primate orbitofrontal cortex: neurons responding to viscosity, grittiness and capsaicin, J. Neurophysiol. 90 (2003) 3711–3724.
[33] E.T. Rolls, H.D. Critchley, A.S. Browning, A. Hernadi, L. Lenard, Responses to the sensory properties of fat of neurons in the primate orbitofrontal cortex, J. Neurosci. 19 (1999) 1532–1540.
[34] J.V. Verhagen, E.T. Rolls, M. Kadohisa, Neurons in the primate orbitofrontal cortex respond to fat texture independently of viscosity, J. Neurophysiol. 90 (2003) 1514–1525.
[35] H.D. Critchley, E.T. Rolls, Responses of primate taste cortex neurons to the astringent tastant tannic acid, Chem. Senses 21 (1996) 135–145.
[36] S.A. Simon, I.E. de Araujo, R. Gutierrez, M.A. Nicolelis, The neural mechanisms of gustation: a distributed processing code, Nat. Rev. Neurosci. 7 (2006) 890–901.
[37] E.T. Rolls, Z.J. Sienkiewicz, S. Yaxley, Hunger modulates the responses to gustatory stimuli of single neurons in the caudolateral orbitofrontal cortex of the macaque monkey, Eur. J. Neurosci. 1 (1989) 53–60.
[38] M.L. Kringelbach, J. O'Doherty, E.T. Rolls, C. Andrews, Activation of the human orbitofrontal cortex to a liquid food stimulus is correlated with its subjective pleasantness, Cereb. Cortex 13 (2003) 1064–1071.
[39] F. Grabenhorst, E.T. Rolls, Selective attention to affective value alters how the brain processes taste stimuli, Eur. J. Neurosci. 27 (2008) 723–729.
[40] F. Mora, D.B. Avrith, A.G. Phillips, E.T. Rolls, Effects of satiety on self-stimulation of the orbitofrontal cortex in the monkey, Neurosci. Lett. 13 (1979) 141–145.
[41] F. Mora, D.B. Avrith, E.T. Rolls, An electrophysiological and behavioural study of self-stimulation in the orbitofrontal cortex of the rhesus monkey, Brain Res. Bull. 5 (1980) 111–115.
[42] E.T. Rolls, M.J. Burton, F. Mora, Neurophysiological analysis of brain-stimulation reward in the monkey, Brain Res. 194 (1980) 339–357.
[43] E.T. Rolls, Understanding the mechanisms of food intake and obesity, Obes. Rev. 8 (2007) 67–72.
[44] L.L. Baylis, E.T. Rolls, G.C. Baylis, Afferent connections of the orbitofrontal cortex taste area of the primate, Neuroscience 64 (1995) 801–812.

[45] E.T. Rolls, H.D. Critchley, R. Mason, E.A. Wakeman, Orbitofrontal cortex neurons: role in olfactory and visual association learning, J. Neurophysiol. 75 (1996) 1970–1981.
[46] E.T. Rolls, L.L. Baylis, Gustatory, olfactory, and visual convergence within the primate orbitofrontal cortex, J. Neurosci. 14 (1994) 5437–5452.
[47] H.D. Critchley, E.T. Rolls, Hunger and satiety modify the responses of olfactory and visual neurons in the primate orbitofrontal cortex, J. Neurophysiol. 75 (1996) 1673–1686.
[48] T.C. Pritchard, E.M. Edwards, C.A. Smith, K.G. Hilgert, A.M. Gavlick, T.D. Maryniak, G.J. Schwartz, T.R. Scott, Gustatory neural responses in the medial orbitofrontal cortex of the old world monkey, J. Neurosci. 25 (2005) 6047–6056.
[49] T.C. Pritchard, G.J. Schwartz, T.R. Scott, Taste in the medial orbitofrontal cortex of the macaque, Ann. NY Acad. Sci. 1121 (2007) 121–135.
[50] E.T. Rolls, Functions of the orbitofrontal and pregenual cingulate cortex in taste, olfaction, appetite and emotion, Acta Physiol. Hung. 95 (2008) 131–164.
[51] T.C. Pritchard, E.N. Nedderman, E.M. Edwards, A.C. Petticoffer, G.J. Schwartz, T.R. Scott, Satiety-responsive neurons in the medial orbitofrontal cortex of the macaque, Behav. Neurosci. 122 (2008) 174–182.
[52] M.K. Sanghera, E.T. Rolls, A. Roper-Hall, Visual responses of neurons in the dorsolateral amygdala of the alert monkey, Exp. Neurol. 63 (1979) 610–626.
[53] T.R. Scott, Z. Karadi, Y. Oomura, H. Nishino, C.R. Plata-Salaman, L. Lenard, B.K. Giza, S. Ao, Gustatory neural coding in the amygdala of the alert monkey, J. Neurophysiol. 69 (1993) 1810–1820.
[54] M. Kadohisa, E.T. Rolls, J.V. Verhagen, Neuronal representations of stimuli in the mouth: the primate insular taste cortex, orbitofrontal cortex, and amygdala, Chem. Senses 30 (2005) 401–419.
[55] M. Kadohisa, E.T. Rolls, J.V. Verhagen, The primate amygdala: neuronal representations of the viscosity, fat texture, temperature, grittiness and taste of foods, Neuroscience 132 (2005) 33–48.
[56] J. Yan, T.R. Scott, The effect of satiety on responses of gustatory neurons in the amygdala of alert cynomolgus macaques, Brain Res. 740 (1996) 193–200.
[57] M.J. Burton, E.T. Rolls, F. Mora, Effects of hunger on the responses of neurones in the lateral hypothalamus to the sight and taste of food, Exp. Neurol. 51 (1976) 668–677.
[58] J. O'Doherty, E.T. Rolls, S. Francis, R. Bowtell, F. McGlone, The representation of pleasant and aversive taste in the human brain, J. Neurophysiol. 85 (2001) 1315–1321.
[59] E.T. Rolls, The anterior and midcingulate cortices and reward, in: B.A. Vogt (Ed.), Cingulate Neurobiology & Disease, Oxford University Press, Oxford, 2008.
[60] M. Jones-Gotman, R.J. Zatorre, Olfactory identification in patients with focal cerebral excision, Neuropsychologia 26 (1988) 387–400.
[61] R.J. Zatorre, M. Jones-Gotman, A.C. Evans, E. Meyer, Functional localization of human olfactory cortex, Nature 360 (1992) 339–340.
[62] S.F. Takagi, Olfactory frontal cortex and multiple olfactory processing in primates, in: A. Peters, E.G. Jones (Eds.), Cerebral Cortex, Plenum Press, New York, 1991, pp. 133–152.
[63] H.D. Critchley, E.T. Rolls, Olfactory neuronal responses in the primate orbitofrontal cortex: analysis in an olfactory discrimination task, J. Neurophysiol. 75 (1996) 1659–1672.
[64] G. Schoenbaum, M.P. Saddoris, T.A. Stalnaker, Reconciling the roles of orbitofrontal cortex in reversal learning and the encoding of outcome expectancies, Ann. NY Acad. Sci. 1121 (2007) 320–335.
[65] G. Schoenbaum, H. Eichenbaum, Information encoding in the rodent prefrontal cortex .1. Single-neuron activity in orbitofrontal cortex compared with that in pyriform cortex, J. Neurophysiol. 74 (1995) 733–750.
[66] E.T. Rolls, M.L. Kringelbach, I.E.T. de Araujo, Different representations of pleasant and unpleasant odors in the human brain, Eur. J. Neurosci. 18 (2003) 695–703.

[67] S. Francis, E.T. Rolls, R. Bowtell, F. McGlone, J. O'Doherty, A. Browning, S. Clare, E. Smith, The representation of pleasant touch in the brain and its relationship with taste and olfactory areas, Neuroreport 10 (1999) 453–459.
[68] J. O'Doherty, E.T. Rolls, S. Francis, R. Bowtell, F. McGlone, G. Kobal, B. Renner, G. Ahne, Sensory-specific satiety related olfactory activation of the human orbitofrontal cortex, Neuroreport 11 (2000) 893–897.
[69] J.S. Morris, R.J. Dolan, Involvement of human amygdala and orbitofrontal cortex in hunger-enhanced memory for food stimuli, J. Neurosci. 21 (2001) 5304–5310.
[70] I.E.T. de Araujo, E.T. Rolls, M.L. Kringelbach, F. McGlone, N. Phillips, Taste-olfactory convergence, and the representation of the pleasantness of flavour, in the human brain, Eur. J. Neurosci. 18 (2003) 2374–2390.
[71] J.V. Verhagen, M. Kadohisa, E.T. Rolls, The primate insular/opercular taste cortex: neuronal representations of the viscosity, fat texture, grittiness, temperature and taste of foods, J. Neurophysiol. 92 (2004) 1685–1699.
[72] N. Chaudhari, A.M. Landin, S.D. Roper, A metabotropic glutamate receptor variant functions as a taste receptor, Nat. Neurosci. 3 (2000) 113–119.
[73] G.Q. Zhao, Y. Zhang, M.A. Hoon, J. Chandrashekar, I. Erlenbach, N.J. Ryba, C.S. Zuker, The receptors for mammalian sweet and umami taste, Cell 115 (2003) 255–266.
[74] Y. Maruyama, E. Pereira, R.F. Margolskee, N. Chaudhari, S.D. Roper, Umami responses in mouse taste cells indicate more than one receptor, J. Neurosci. 26 (2006) 2227–2234.
[75] I.E.T. de Araujo, M.L. Kringelbach, E.T. Rolls, P. Hobden, The representation of umami taste in the human brain, J. Neurophysiol. 90 (2003) 313–319.
[76] C. McCabe, E.T. Rolls, Umami: a delicious flavor formed by convergence of taste and olfactory pathways in the human brain, Eur. J. Neurosci. 25 (2007) 1855–1864.
[77] E.T. Rolls, Taste, olfactory, visual and somatosensory representations of the sensory properties of foods in the brain, and their relation to the control of food intake, in: H-R. Berthoud, R.J. Seeley (Eds.), Neural and Metabolic Control of Macronutrient Intake, CRC Press, Boca-Raton, FL, 2000, pp. 247–262.
[78] M. Kadohisa, E.T. Rolls, J.V. Verhagen, Orbitofrontal cortex neuronal representation of temperature and capsaicin in the mouth, Neuroscience 127 (2004) 207–221.
[79] I.E.T. de Araujo, E.T. Rolls, The representation in the human brain of food texture and oral fat, J. Neurosci. 24 (2004) 3086–3093.
[80] S. Guest, F. Grabenhorst, G. Essick, Y. Chen, M. Young, F. McGlone, I. de Araujo, E.T. Rolls, Human cortical representation of oral temperature, Physiol. Behav. 92 (2007) 975–984.
[81] B.J. Rolls, R.J. Wood, E.T. Rolls, Thirst: the initiation, maintenance, and termination of drinking, Prog. Psychobiol. Physiol. Psychol. 9 (1980) 263–321.
[82] E.T. Rolls, J. O'Doherty, M.L. Kringelbach, S. Francis, R. Bowtell, F. McGlone, Representations of pleasant and painful touch in the human orbitofrontal and cingulate cortices, Cereb. Cortex 13 (2003) 308–317.
[83] H. Olausson, Y. Lamarre, H. Backlund, C. Morin, B.G. Wallin, G. Starck, S. Ekholm, I. Strigo, K. Worsley, A.B. Vallbo, M.C. Bushnell, Unmyelinated tactile afferents signal touch and project to insular cortex, Nat. Neurosci. 5 (2002) 900–904.
[84] C. McCabe, E.T. Rolls, A. Bilderbeck, F. McGlone, Cognitive influences on the affective representation of touch and the sight of touch in the human brain, Soc. Cogn. Affect. Neurosci. 3 (2008) 97–108.
[85] E.T. Rolls, F. Grabenhorst, B.A. Parris, Warm pleasant feelings in the brain, Neuroimage 41 (2008) 1504–1513.
[86] F. Grabenhorst, E.T. Rolls, A. Bilderbeck, How cognition modulates affective responses to taste and flavor: top down influences on the orbitofrontal and pregenual cingulate cortices, Cereb. Cortex 18 (2008) 1549–1559.

[87] A.K. Anderson, K. Christoff, I. Stappen, D. Panitz, D.G. Ghahremani, G. Glover, J.D. Gabrieli, N. Sobel, Dissociated neural representations of intensity and valence in human olfaction, Nat. Neurosci. 6 (2003) 196–202.
[88] F. Grabenhorst, E.T. Rolls, C. Margot, M.A. da Silva, M.I.A.P. Velazco, How pleasant and unpleasant stimuli combine in different brain regions: odor mixtures, J. Neurosci. 27 (2007) 13532–13540.
[89] E.T. Rolls, The affective and cognitive processing of touch, oral texture, and temperature in the brain, Neurosci. Biobehav. Rev. (2008), (in press).
AUQ9
[90] E.T. Rolls, Face processing in different brain areas, and critical band masking, J. Neuropsychol. 2 (2008) 325–360.
[91] S.J. Thorpe, E.T. Rolls, S. Maddison, Neuronal activity in the orbitofrontal cortex of the behaving monkey, Exp. Brain Res. 49 (1983) 93–115.
[92] J.P. O'Doherty, R. Deichmann, H.D. Critchley, R.J. Dolan, Neural responses during anticipation of a primary taste reward, Neuron 33 (2002) 815–826.
[93] E.T. Rolls, S.J. Judge, M. Sanghera, Activity of neurones in the inferotemporal cortex of the alert monkey, Brain Res. 130 (1977) 229–238.
[94] E.T. Rolls, A. Treves, Neural Networks and Brain Function, Oxford University Press, Oxford, 1998.
[95] G. Deco, E.T. Rolls, Synaptic and spiking dynamics underlying reward reversal in orbitofrontal cortex, Cereb. Cortex 15 (2005) 15–30.
[96] M. Roesch, G. Schoenbaum, From associations to expectancies: orbitofrontal cortex as gateway between the limbic system and representational memory, in: D.H. Zald, S.L. Rauch (Eds.), The Orbitofrontal Cortex, Oxford University Press, Oxford, 2006, pp. 199–236.
[97] E.T. Rolls, J. Hornak, D. Wade, J. McGrath, Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage, J. Neurol. Neurosurg. Psychiatry 57 (1994) 1518–1524.
[98] L.K. Fellows, M.J. Farah, Ventromedial frontal cortex mediates affective shifting in humans: evidence from a reversal learning paradigm, Brain 126 (2003) 1830–1837.
[99] J. Hornak, J. O'Doherty, J. Bramham, E.T. Rolls, R.G. Morris, P.R. Bullock, C.E. Polkey, Reward-related reversal learning after surgical excisions in orbitofrontal and dorsolateral prefrontal cortex in humans, J. Cogn. Neurosci. 16 (2004) 463–478.
[100] J.J. Paton, M.A. Belova, S.E. Morrison, C.D. Salzman, The primate amygdala represents the positive and negative value of visual stimuli during learning, Nature 439 (2006) 865–870.
[101] M.L. Kringelbach, E.T. Rolls, Neural correlates of rapid reversal learning in a simple model of human social interaction, Neuroimage 20 (2003) 1371–1383.
[102] E.T. Rolls, C. McCabe, J. Redoute, Expected value, reward outcome, and temporal difference error representations in a probabilistic decision task, Cereb. Cortex 18 (2008) 652–663.
[103] W. Schultz, Neural coding of basic reward terms of animal learning theory, game theory, microeconomics and behavioural ecology, Curr. Opin. Neurobiol. 14 (2004) 139–147.
[104] W. Schultz, Behavioral theories and the neurophysiology of reward, Annu. Rev. Psychol. 57 (2006) 87–115.
[105] T.A. Hare, J. O'Doherty, C.F. Camerer, W. Schultz, A. Rangel, Dissociating the role of the orbitofrontal cortex and the striatum in the computation of goal values and prediction errors, J. Neurosci. 28 (2008) 5623–5630.
[106] W. Schultz, L. Tremblay, J.R. Hollerman, Reward processing in primate orbitofrontal cortex and basal ganglia, Cereb. Cortex 10 (2000) 272–284.
[107] H. Niki, M. Watanabe, Prefrontal and cingulate unit activity during timing behavior in the monkey, Brain Res. 171 (1979) 213–224.
[108] K. Shima, J. Tanji, Role for cingulate motor area cells in voluntary movement selection based on reward, Science 282 (1998) 1335–1338.

[109] G. Bush, B.A. Vogt, J. Holmes, A.M. Dale, D. Greve, M.A. Jenike, B.R. Rosen, Dorsal anterior cingulate cortex: a role in reward-based decision making, Proc. Natl. Acad. Sci. USA 99 (2002) 523–528.
[110] M.F. Rushworth, M.E. Walton, S.W. Kennerley, D.M. Bannerman, Action sets and decisions in the medial frontal cortex, Trends Cogn. Sci. 8 (2004) 410–417.
[111] M. Matsumoto, K. Matsumoto, H. Abe, K. Tanaka, Medial prefrontal selectivity signalling prediction errors of action values, Nat. Neurosci. 10 (2007) 647–656.
[112] M.F. Rushworth, T.E. Behrens, Choice, uncertainty and value in prefrontal and cingulate cortex, Nat. Neurosci. 11 (2008) 389–397.
[113] B.A. Vogt (Ed.), Cingulate Neurobiology & Disease, Oxford University Press, Oxford, 2008.
[114] E.T. Rolls, Neurons in the cortex of the temporal lobe and in the amygdala of the monkey with responses selective for faces, Hum. Neurobiol. 3 (1984) 209–222.
[115] E.T. Rolls, Neurophysiological mechanisms underlying face processing within and beyond the temporal cortical visual areas, Philos. Trans. R. Soc. Lond. B Biol. Sci. 335 (1992) 11–21.
[116] E.T. Rolls, The orbitofrontal cortex, Philos. Trans. R. Soc. Lond. B Biol. Sci. 351 (1996) 1433–1444.
[117] E.T. Rolls, H.D. Critchley, A.S. Browning, K. Inoue, Face-selective and auditory neurons in the primate orbitofrontal cortex, Exp. Brain Res. 170 (2006) 74–87.
[118] E.T. Rolls, G.C. Baylis, Size and contrast have only small effects on the responses to faces of neurons in the cortex of the superior temporal sulcus of the monkey, Exp. Brain Res. 65 (1986) 38–48.
[119] M.E. Hasselmo, E.T. Rolls, G.C. Baylis, The role of expression and identity in the face-selective responses of neurons in the temporal visual cortex of the monkey, Behav. Brain Res. 32 (1989) 203–218.
[120] J. O'Doherty, J. Winston, H. Critchley, D. Perrett, D.M. Burt, R.J. Dolan, Beauty in a smile: the role of medial orbitofrontal cortex in facial attractiveness, Neuropsychologia 41 (2003) 147–155.
[121] J. Hornak, E.T. Rolls, D. Wade, Face and voice expression identification in patients with emotional and behavioural changes following ventral frontal lobe damage, Neuropsychologia 34 (1996) 247–261.
[122] J. Hornak, J. Bramham, E.T. Rolls, R.G. Morris, J. O'Doherty, P.R. Bullock, C.E. Polkey, Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices, Brain 126 (2003) 1691–1712.
[123] I.E.T. de Araujo, E.T. Rolls, M.I. Velazco, C. Margot, I. Cayeux, Cognitive modulation of olfactory processing, Neuron 46 (2005) 671–679.
[124] E.T. Rolls, Sensory processing in the brain related to the control of food intake, Proc. Nutr. Soc. 66 (2007) 96–112.
[125] E.T. Rolls, F. Grabenhorst, C. Margot, M.A.A.P. da Silva, M.I. Velazco, Selective attention to affective value alters how the brain processes olfactory stimuli, J. Cogn. Neurosci. 20 (2008) 1815–1826.
[126] G. Deco, E.T. Rolls, Attention, short-term memory, and action selection: a unifying theory, Prog. Neurobiol. 76 (2005) 236–256.
[127] R. Desimone, J. Duncan, Neural mechanisms of selective visual attention, Annu. Rev. Neurosci. 18 (1995) 193–222.
[128] G. Deco, E.T. Rolls, Neurodynamics of biased competition and co-operation for attention: a model with spiking neurons, J. Neurophysiol. 94 (2005) 295–313.
[129] E.T. Rolls, Top-down control of visual perception: attention in natural vision, Perception 37 (2008) 333–354.
[130] J.R. Millenson, Principles of Behavioral Analysis, MacMillan, New York, 1967.

[131] E.T. Rolls, A theory of emotion, and its application to understanding the neural basis of emotion, in: Y. Oomura (Ed.), Emotions. Neural and Chemical Control, Karger, Basel, 1986, pp. 325–344.
[132] E.T. Rolls, Neural systems involved in emotion in primates, in: R. Plutchik, H. Kellerman (Eds.), Emotion: theory, research, and experience, Vol. 3. Biological foundations of emotion, Academic Press, New York, 1986, pp. 125–143.
[133] E.T. Rolls, A theory of emotion, and its application to understanding the neural basis of emotion, Cogn. Emotion 4 (1990) 161–190.
[134] E.T. Rolls, The functions of the orbitofrontal cortex, Neurocase 5 (1999) 301–312.
[135] E.T. Rolls, Précis of The brain and emotion, Behav. Brain Sci. 23 (2000) 177–233.
[136] L.K. Fellows, M.J. Farah, Different underlying impairments in decision-making following ventromedial and dorsolateral frontal lobe damage in humans, Cereb. Cortex 15 (2005) 58–63.
[137] H. Berlin, E.T. Rolls, U. Kischka, Impulsivity, time perception, emotion, and reinforcement sensitivity in patients with orbitofrontal cortex lesions, Brain 127 (2004) 1108–1126.
[138] L.K. Fellows, The role of orbitofrontal cortex in decision making: a component process account, Ann. NY Acad. Sci. 1121 (2007) 421–430.
[139] J. O'Doherty, M.L. Kringelbach, E.T. Rolls, J. Hornak, C. Andrews, Abstract reward and punishment representations in the human orbitofrontal cortex, Nat. Neurosci. 4 (2001) 95–102.
[140] R. Adolphs, F. Gosselin, T.W. Buchanan, D. Tranel, P. Schyns, A.R. Damasio, A mechanism for impaired fear recognition after amygdala damage, Nature 433 (2005) 68–72.
[141] M.L. Spezio, P.Y. Huang, F. Castelli, R. Adolphs, Amygdala damage impairs eye contact during conversations with real people, J. Neurosci. 27 (2007) 3994–3997.
[142] A. Bechara, H. Damasio, A.R. Damasio, G.P. Lee, Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making, J. Neurosci. 19 (1999) 5473–5481.
[143] M. Brand, F. Grabenhorst, K. Starcke, M.M. Vandekerckhove, H.J. Markowitsch, Role of the amygdala in decisions under ambiguity and decisions under risk: evidence from patients with Urbach-Wiethe disease, Neuropsychologia 45 (2007) 1305–1317.
[144] E.A. Phelps, J.E. LeDoux, Contributions of the amygdala to emotion processing: from animal models to human behavior, Neuron 48 (2005) 175–187.
[145] B. Seymour, R. Dolan, Emotion, decision making, and the amygdala, Neuron 58 (2008) 662–671.
[146] E.T. Rolls, Emotion, higher order syntactic thoughts, and consciousness, in: L. Weiskrantz, M.K. Davies (Eds.), Frontiers of Consciousness, Oxford University Press, Oxford, 2008, pp. 131–167.
[147] E.T. Rolls, C. McCabe, Enhanced affective brain representations of chocolate in cravers vs non-cravers, Eur. J. Neurosci. 26 (2007) 1067–1076.
[148] J.D. Beaver, A.D. Lawrence, Jv. Ditzhuijzen, M.H. Davis, A. Woods, A.J. Calder, Individual differences in reward drive predict neural responses to images of food, J. Neurosci. 26 (2006) 5160–5166.
[149] H. Berlin, E.T. Rolls, Time perception, impulsivity, emotionality, and personality in self-harming borderline personality disorder patients, J. Pers. Disord. 18 (2004) 358–378.
[150] H. Berlin, E.T. Rolls, S.D. Iversen, Borderline personality disorder, impulsivity and the orbitofrontal cortex, Am. J. Psychiatry 162 (2005) 2360–2373.
[151] S. Rahman, B.J. Sahakian, J.R. Hodges, R.D. Rogers, T.W. Robbins, Specific cognitive deficits in mild frontal variant frontotemporal dementia, Brain 122 (1999) 1469–1493.
[152] I.V. Viskontas, K.L. Possin, B.L. Miller, Symptoms of frontotemporal dementia provide insights into orbitofrontal cortex function and social behavior, Ann. NY Acad. Sci. 1121 (2007) 528–545.
[153] J.T. Coyle, G. Tsai, D. Goff, Converging evidence of NMDA receptor hypofunction in the pathophysiology of schizophrenia, Ann. NY Acad. Sci. 1003 (2003) 318–327.
[154] M. Loh, E.T. Rolls, G. Deco, A dynamical systems hypothesis of schizophrenia, PLoS Comput. Biol. 3 (2007) e228. doi:210.1371/journal.pcbi.0030228.

[155] E.T. Rolls, M. Loh, G. Deco, G. Winterer, Computational models of schizophrenia and dopamine modulation in the prefrontal cortex, Nat. Rev. Neurosci. 9 (2008) 696–709.
[156] K. Chakrabarty, S. Bhattacharyya, R. Christopher, S. Khanna, Glutamatergic dysfunction in OCD, Neuropsychopharmacology 30 (2005) 1735–1740.
[157] C. Pittenger, J.H. Krystal, V. Coric, Glutamate-modulating drugs as novel pharmacotherapeutic agents in the treatment of obsessive-compulsive disorder, NeuroRx 3 (2006) 69–81.
[158] E.T. Rolls, M. Loh, G. Deco, An attractor hypothesis of obsessive-compulsive disorder, Eur. J. Neurosci. 28 (2008) 782–793.
[159] J.D. Wallis, Neuronal mechanisms in prefrontal cortex underlying adaptive choice behavior, Ann. NY Acad. Sci. 1121 (2007) 447–460.
[160] C. Padoa-Schioppa, J.A. Assad, Neurons in the orbitofrontal cortex encode economic value, Nature 441 (2006) 223–226.
[161] I.E.T. de Araujo, M.L. Kringelbach, E.T. Rolls, F. McGlone, Human cortical responses to water in the mouth, and the effects of thirst, J. Neurophysiol. 90 (2003) 1865–1876.
[162] H. Plassmann, J. O'Doherty, B. Shiv, A. Rangel, Marketing actions can modulate neural representations of experienced pleasantness, Proc. Natl. Acad. Sci. USA 105 (2008) 1050–1054.
[163] C. Padoa-Schioppa, J.A. Assad, The representation of economic value in the orbitofrontal cortex is invariant for changes of menu, Nat. Neurosci. 11 (2008) 95–102.
[164] L. Tremblay, W. Schultz, Relative reward preference in primate orbitofrontal cortex, Nature 398 (1999) 704–708.
[165] F. Grabenhorst, E.T. Rolls, Different representations of relative and absolute value in the human brain, (2009) (in press).
[166] P. Glimcher, Decisions, Uncertainty, and the Brain, MIT Press, Cambridge, MA, 2004.
[167] S.C. Tanaka, K. Doya, G. Okada, K. Ueda, Y. Okamoto, S. Yamawaki, Prediction of immediate and future rewards differentially recruits cortico-basal ganglia loops, Nat. Neurosci. 7 (2004) 887–893.
[168] N.D. Daw, J.P. O'Doherty, P. Dayan, B. Seymour, R.J. Dolan, Cortical substrates for exploratory decisions in humans, Nature 441 (2006) 876–879.
[169] H. Kim, S. Shimojo, J.P. O'Doherty, Is avoiding an aversive outcome rewarding? Neural substrates of avoidance learning in the human brain, PLoS Biol. 4 (2006) e233.
[170] R.S. Sutton, A.G. Barto, Reinforcement Learning, MIT Press, Cambridge, MA, 1998.
[171] J. Bernoulli, Exposition of a new theory on the measurement of risk, Econometrica 22 (1738/1954) 23–36.
[172] J. von Neumann, O. Morgenstern, The Theory of Games and Economic Behavior, Princeton University Press, Princeton, NJ, 1944.
[173] D. Kahneman, A. Tversky, Prospect theory: an analysis of decision under risk, Econometrica 47 (1979) 263–292.
[174] D. Kahneman, A. Tversky, Choices, values, and frames, Am. Psychol. 4 (1984) 341–350.
[175] A. Tversky, D. Kahneman, Rational choice and the framing of decisions, J. Bus. 59 (1986) 251–278.
[176] H. Gintis, Game Theory Evolving, Princeton University Press, Princeton, NJ, 2000.
[177] A. Rangel, C. Camerer, P.R. Montague, A framework for studying the neurobiology of value-based decision making, Nat. Rev. Neurosci. 9 (2008) 545–556.
[178] J.W. Kable, P.W. Glimcher, The neural correlates of subjective value during intertemporal choice, Nat. Neurosci. 10 (2007) 1625–1633.
[179] R. Romo, A. Hernandez, A. Zainos, Neuronal correlates of a perceptual decision in ventral premotor cortex, Neuron 41 (2004) 165–173.
[180] V. de Lafuente, R. Romo, Neural correlate of subjective sensory experience gradually builds up across cortical areas, Proc. Natl. Acad. Sci. USA 103 (2006) 14266–14271.

AUQ10

[181] G. Deco, E.T. Rolls, R. Romo, Stochastic dynamics as a principle of brain function, (2008) (in press).
AUQ11
[182] F. Grabenhorst, E.T. Rolls, B.A. Parris, From affective value to decision-making in the prefrontal cortex, Eur. J. Neurosci. 28 (2008) 1930–1939.
[183] E.T. Rolls, F. Grabenhorst, B.A. Parris, Neural systems underlying decisions about affective odors, (2008), (in press).
AUQ12
[184] T. Shallice, P.W. Burgess, Deficits in strategy application following frontal lobe damage in man, Brain 114 (Pt 2) (1991) 727–741.
[185] P.W. Burgess, Strategy application disorder: the role of the frontal lobes in human multitasking, Psychol. Res. 63 (2000) 279–288.
[186] P.W. Burgess, I. Dumontheil, S.J. Gilbert, The gateway hypothesis of rostral prefrontal cortex (area 10) function, Trends Cogn. Sci. 11 (2007) 290–298.
[187] H.R. Heekeren, I. Wartenburger, H. Schmidt, K. Prehn, H.P. Schwintowski, A. Villringer, Influence of bodily harm on neural correlates of semantic and moral decision-making, Neuroimage 24 (2005) 887–897.
[188] T.E. Behrens, M.W. Woolrich, M.E. Walton, M.F. Rushworth, Learning the value of information in an uncertain world, Nat. Neurosci. 10 (2007) 1214–1221.
[189] A.A. Marsh, K.S. Blair, M. Vythilingam, S. Busis, R.J. Blair, Response options and expectations of reward in decision-making: the differential roles of dorsal and rostral anterior cingulate cortex, Neuroimage 35 (2007) 979–988.
[190] M.F. Rushworth, T.E. Behrens, P.H. Rudebeck, M.E. Walton, Contrasting roles for cingulate and orbitofrontal cortex in decisions and social behaviour, Trends Cogn. Sci. 11 (2007) 168–176.
[191] M.F. Rushworth, M.J. Buckley, T.E. Behrens, M.E. Walton, D.M. Bannerman, Functional organization of the medial frontal cortex, Curr. Opin. Neurobiol. 17 (2007) 220–227.
[192] F.S. Arana, J.A. Parkinson, E. Hinton, A.J. Holland, A.M. Owen, A.C. Roberts, Dissociable contributions of the human amygdala and orbitofrontal cortex to incentive motivation and goal selection, J. Neurosci. 23 (2003) 9632–9638.
[193] J. Moll, F. Krueger, R. Zahn, M. Pardini, R. de Oliveira-Souza, J. Grafman, Human fronto-mesolimbic networks guide decisions about charitable donation, Proc. Natl. Acad. Sci. USA 103 (2006) 15623–15628.
[194] H. Kim, R. Adolphs, J.P. O'Doherty, S. Shimojo, Temporal isolation of neural processes underlying face preference decisions, Proc. Natl. Acad. Sci. USA 104 (2007) 18253–18258.
[195] X.J. Wang, Probabilistic decision making by slow reverberation in cortical circuits, Neuron 36 (2002) 955–968.
[196] G. Deco, E.T. Rolls, Decision-making and Weber's Law: a neurophysiological model, Eur. J. Neurosci. 24 (2006) 901–916.
[197] S.T. Carmichael, M-C. Clugnet, J.L. Price, Central olfactory connections in the macaque monkey, J. Comp. Neurol. 346 (1994) 403–434.
[198] R.J. Morecraft, C. Geula, M-M. Mesulam, Cytoarchitecture and neural afferents of orbitofrontal cortex in the brain of the monkey, J. Comp. Neurol. 232 (1992) 341–358.
[199] D.M. Small, M.D. Gregory, Y.E. Mak, D. Gitelman, M.M. Mesulam, T. Parrish, Dissociation of neural representation of intensity and affective valuation in human gustation, Neuron 39 (2003) 701–711.
[200] H.D. Critchley, S. Wiens, P. Rotshtein, A. Ohman, R.J. Dolan, Neural systems supporting interoceptive awareness, Nat. Neurosci. 7 (2004) 189–195.
[201] S.T. Carmichael, J.L. Price, Connectional networks within the orbital and medial prefrontal cortex of macaque monkeys, J. Comp. Neurol. 371 (1996) 179–207.
[202] D.J. McFarland, Problems of Animal Behaviour, Longman, Harlow, 1989.

[203] P.R. Montague, G.S. Berns, Neural economics and the biological substrates of valuation, Neuron 36 (2002) 265–284.
[204] K. Izuma, D.N. Saito, N. Sadato, Processing of social and monetary rewards in the human striatum, Neuron 58 (2008) 284–294.
[205] D.O. Hebb, The Organization of Behavior: A Neuropsychological Theory, Wiley, New York, 1949.
[206] L.M. Giocomo, M.E. Hasselmo, Neuromodulation by glutamate and acetylcholine can change circuit dynamics by regulating the relative influence of afferent input and excitatory feedback, Mol. Neurobiol. 36 (2007) 184–200.
[207] E.T. Rolls, Memory systems in the brain, Annu. Rev. Psychol. 51 (2000) 599–630.

Author Query

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{AUQ7} Wording of the passage "Important also in the modulation of the value ... which in general is adaptive" is somewhat obscure. Please clarify.
{AUQ8} Please update reference 25 (i.e., Rolls and Grabenhorst, 2008) with volume and page numbers.
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