Lights, Camembert, Action! The Role of Human Orbitofrontal Cortex in Encoding Stimuli, Rewards, and Choices

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ABSTRACT: This review outlines some of the main conclusions about the contributions of the orbitofrontal cortex to reward learning and decision making arising from functional neuroimaging studies in humans. It will be argued that human orbitofrontal cortex is involved in a number of distinct functions: signaling the affective value of stimuli as they are perceived, encoding expectations of future reward, and updating these expectations, either by making use of prediction error signals generated in the midbrain, or by using knowledge of the rules or structure of the decision problem. It will also be suggested that this region contributes to the decision making process itself, by encoding signals that inform an individual about what action to take next. Evidence for functional specialization within orbitofrontal cortex in terms of valence will also be evaluated, and the possible contributions of the orbitofrontal cortex in representing the values of actions as well as that of stimuli will be discussed. Finally, some of the outstanding questions for future neuroimaging research of orbitofrontal cortex function will be highlighted.

KEYWORDS: fMRI; neuroimaging; learning; conditioning; decision making

INTRODUCTION

It is well established that damage to human orbitofrontal cortex (OFC) and adjacent medial prefrontal cortex can result in impairments on tasks probing the ability to make decisions for reward under uncertainty, as well as to flexibly modulate action selection in the face of changing contingencies.[1–4] However, the precise nature of the computations being implemented by this region that

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Ann. N.Y. Acad. Sci. 1121: 254–272 (2007). © 2007 New York Academy of Sciences.
doi: 10.1196/annals.1401.036

give rise to such deficits are much less well understood. In this paper we review evidence about the functions of human OFC garnered from functional neuroimaging studies in humans.

Insight into the functions of the OFC can be derived from its anatomical location and connectivity. It is highly interconnected with sub-cortical structures involved in affective processing such as the amygdala and ventral striatum,[5] consistent with a role for OFC in reward and affect related processing. On the other hand, the OFC as a part of prefrontal cortex is also highly interconnected with other sectors within prefrontal cortex.[6] Therefore, it is plausible that OFC will in addition to its role in reward and affect, share functional commonalities with these other parts of prefrontal cortex. Here, it will be argued that as a key component of the reward system, OFC is involved in representing stimulus-reward value as well as in encoding representations of future expected reward, functions which it may share in common with the amygdala and ventral striatum. In addition, OFC receives signals pertaining to errors in reward prediction, that may underlie learning of reward predictions. Much like other parts of the prefrontal cortex,[7] OFC and adjacent ventral medial prefrontal cortex may also play a role in encoding abstract rules, in this case by incorporating knowledge of the structure pertaining to the rules of the decision problem, and in applying knowledge of such rules to guide reward expectations. Finally, in common with the prefrontal cortex as a whole, this region also plays an important role in the flexible control of behavior,[8] by generating decision signals that inform an individual about what action to take next.

REPRESENTATIONS OF STIMULUS VALUE

One of the most established findings regarding the OFC is that it is involved in coding for the reward value of a stimulus, shown initially in single-unit recording studies in monkeys whereby neurons in this region were found to respond to a particular taste or odor when an animal was hungry but decreased their firing rate once the animal was satiated and the corresponding food was no longer rewarding.[9,10] Imaging studies in humans have not only confirmed these findings for olfactory and gustatory stimuli[11–16] but have also shown that BOLD responses in OFC correlate with the reward value of stimuli in other sensory modalities, such as in the somatosensory, auditory, and visual domains.[15–17] It has also been shown that OFC responds to abstract rewards not tied to a particular sensory modality, such as money or social praise.[18–20] These findings suggest that human OFC is involved in flexibly encoding the reward value of a wide variety of stimuli in diverse modalities. There is also considerable evidence to suggest that OFC responds not only to rewards but also to punishers.[13,17,18,21]

Regional Specialization within OFC: Rewards versus Punishers

This raises the question as to whether anatomically dissociable sub-regions within OFC are involved in responding to rewarding and punishing events respectively. Evidence in support of such a possibility was first provided by O'Doherty *et al.*,[21] who reported a medial versus lateral dissociation in OFC responses to rewards and punishers during performance of a task in which subjects could win or lose abstract monetary reward. Medial sectors of OFC were found to respond to monetary reward, and a part of lateral OFC was found to respond to monetary loss. Comparable results were obtained by Ursu and Carter[22] A similar dissociation was also found in an fMRI study of facial attractiveness in which both high and low attractiveness faces were presented to subjects while they performed an unrelated gender judgment task.[17] Faces high in attractiveness recruited medial OFC whereas low attractive faces recruited lateral OFC. Small and colleagues also reported a differential responses in medial and lateral OFC during the consumption of a chocolate meal to satiety.[23] Medial OFC responded during early stages of feeding, when the chocolate had high reward value, whereas enhanced lateral OFC activity was only evident when subjects were reaching satiety and the chocolate went from being pleasant to aversive. A number of imaging studies of olfaction have also reported a similar medial versus lateral dissociation, with medial OFC responding to pleasant odors and lateral to aversive odors.[11,12,15] More recently Kim and colleagues[24] reported that medial OFC was activated not only by receipt of a rewarding outcome but also by the successful avoidance of an aversive outcome, suggesting that successful avoidance in itself can act as an intrinsic reward (FIG. 1). On the other hand, more lateral areas of prefrontal cortex extending onto the orbital surface were found to respond both during receipt of an aversive outcome as well as following a failure to obtain reward.

While the above studies appear to support a medial vs lateral dissociation, a number of other studies have failed to report such a dissociation. For instance, Elliott and colleagues used a block fMRI design to measure neural responses to parametrically varied quantities of monetary gain and loss.[25] Significant activity was reported in both medial and lateral OFC to monetary gain and loss. Similarly, Breiter *et al.*[18] have also found that both medial and lateral regions of OFC responded equally to rewarding and punishing feedback. In a study of probabilistic reversal learning, monetary gains were associated with activity in both anterior medial and central OFC, whereas monetary loss recruited a part of posterior lateral OFC only if this was followed by a switch in behavioral strategy on the subsequent trial.[26] Furthermore, other studies have reported a role for the medial OFC in complex emotions such as regret which may contain both positive and negative affective components.[27] These discrepant findings suggest that the differential functions of medial and lateral OFC areas may be more complex than at first supposed. In order to understand

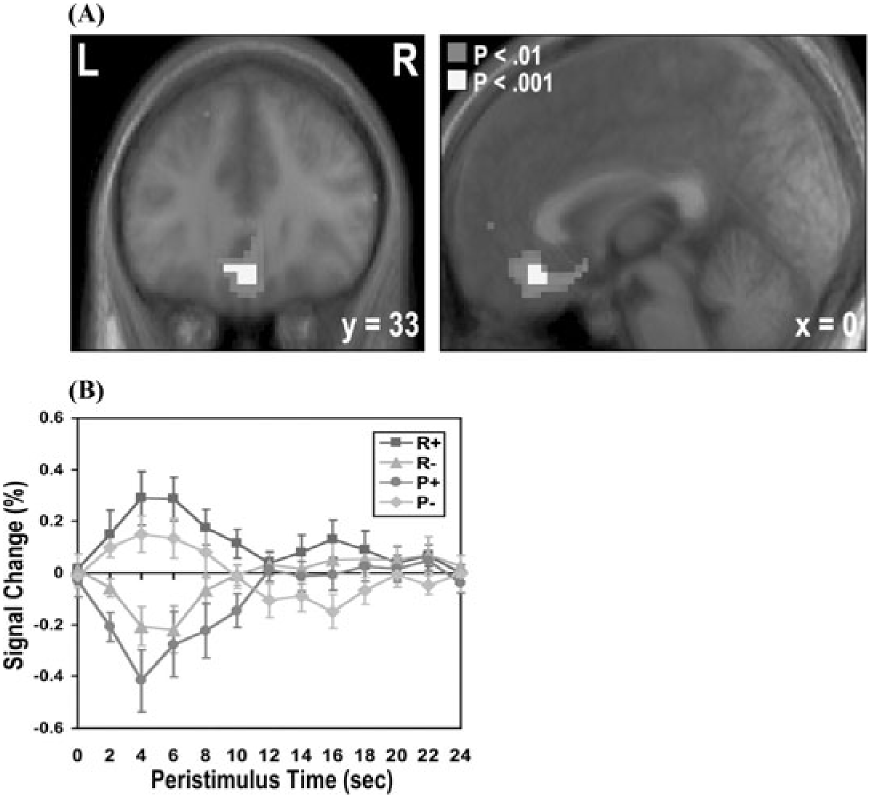

FIGURE 1. Responses to receipt of reward and successful avoidance of an aversive outcome in medial OFC. **(A)** Medial OFC showing a significant increase in activity after avoidance of an aversive outcome as well as after obtaining reward [$x = 0$, $y = 33$, $z = -18$, $Z = 3.48$, $P < 0.05$] (corrected for small volume using coordinates derived from a previous study). No other brain areas showed significant effects at $P < 0.001$, uncorrected. Voxels significant at $P < 0.001$ are shown in yellow. To illustrate the extent of the activation we also show voxels significant at $P < 0.01$ in red. **(B)** Time-course plots of peak voxels in the OFC for each of four different possible outcomes: receipt of reward (R+), avoidance of an aversive outcome (P−), missed reward (R−), and receipt of an aversive outcome (P+). The plots are arranged such that time 0 corresponds to the point of outcome delivery. These time courses are shown after adjusting for the effects of expected value and prediction error (i.e., removing those effects from the data). Data from Kim *et al.*[24] (In color in *Annals* online.)

the possible basis of such differences between studies it may be important to consider at least two factors.

First, some of the studies that have failed to report functional dissociations within OFC are complex gambling or decision making tasks in which a number of distinct processes are engaged besides coding outcome value, such as anticipation or expectation of reward, selection of appropriate behavioral responses, detecting change in contingencies, and/or implementing changes in behavioral strategy. Thus, the degree to which these different processes are engaged in a given task, and the extent to which these different processes are disambiguated from each other in the experimental design and analysis, could contribute to discrepancies in reported results between studies. In support of the this possibility, in the Kim *et al.*[24] study, it was found that both medial and central parts of OFC were engaged during expectation of reward, whereas only medial OFC was engaged following receipt of a rewarding outcome and avoidance of an aversive one. These findings suggest that a clear dissociation between responses may only be present in relation to the receipt but not the expectation of reward. However, a recent study found a medial versus lateral dissociation within OFC during *both* anticipation and receipt, such that medial OFC was more active when subjects were anticipating, receiving and evaluating monetary gains, and lateral OFC was more engaged under situations where subjects were anticipating, obtaining or evaluating monetary losses.[28]

The second factor likely to play a role in accounting for differences between studies is that monetary loss may differ from other more biologically relevant punishers in that the behavioral significance of a loss to an individual likely depends strongly on the context in which that outcome is presented. Contextual effects on decision making have long been demonstrated in the behavioral economics literature, such that for instance subjects respond differently to outcomes framed in a loss context than they do to the same outcomes framed in a gain context.[29] In most human imaging studies where feedback is obtained on a trial by trial basis, neural responses to monetary loss may depend on the degree to which those losses signal to the subjects that a change in their current behavior is warranted. In the case of more natural or primary reinforcers, such as pain or unpleasant taste, obtaining such an outcome may naturally lead to a change in behavior in order to avoid the outcome in the future. However, in some gambling or decision-making tasks, a monetary loss does not automatically signal that behavior should be altered. For example in the case of probabilistic reversal learning, the nature of the probabilistic contingencies imply that sometimes one receives a monetary loss for choosing the correct stimulus and sometimes a reward is obtained even when choosing the incorrect stimulus. This introduces an ambiguity into the meaning of a rewarding or punishing outcome. It is no longer the case that the reward or punisher itself is a straightforward cue as to what behavioral strategy should be adopted because a punishing outcome can occur following choice of the correct stimulus as well as following choice of the incorrect stimulus. This is the case in many other types of decision-making tasks besides reversal, such as in gambling tasks where it is advantageous to sustain monetary loss in the short term in order to gain monetarily in the long run. Thus, the context in which rewarding or punishing stimuli are presented, particularly monetary outcomes, may need to be taken into account when interpreting the degree to which different tasks result in varying recruitment of appetitive and aversive motivational systems.

RESPONSES RELATED TO PREDICTIONS OF FUTURE REWARD

It is known from single-unit neurophysiology studies that neurons in OFC are involved not only in responding to the receipt of rewarding and punishing outcomes, but also respond in anticipation of the receipt of such outcomes in the future.[40,41,58] Consistent with these findings from animal studies, human neuroimaging studies have implicated OFC alongside other structures, such as amygdala and ventral striatum, in predicting future rewards. An example is a study by O'Doherty and colleagues,[30] where arbitrary fractal stimuli were presented and followed, after a variable interval, by either a pleasant taste (glucose), an affectively neutral taste (control tasteless solution), or by an aversive taste (saline). Significant effects were found in anterior OFC during anticipation, as well as receipt of, reward. These results have subsequently been confirmed in other paradigms, using different types of reward. For instance, in one study neural responses to cues associated with subsequent delivery of either a pleasant or aversive odor where each cue was followed on 50% of occasions by a specific odor.[31] Significant orbitofrontal responses (in anterior central OFC) were found to the predictive cues associated with the pleasant and aversive odors. These findings also implicate OFC in maintaining predictions for negatively as well as positively valenced stimuli.

The Content of Predictive Representations in OFC

The finding that predictive reward representations are present in OFC leaves open the question as to the content of these representations. In order to appreciate the importance of this question it is useful to consider the ultimate function of predictive representations. Predictions enable behavior to be organized prospectively so that an organism is prepared in advance for the occurrence of an affectively significant event. Many such responses can be considered to be reflexive, in they are automatically elicited by a conditioned stimulus (CS). The paradigmatic example of this is the conditioned salivatory response that Pavlov observed in his food conditioned dogs.[32] In this example as in others, the conditioned responses are identical to those elicited by the unconditioned stimulus (UCS). For example, Pavlov's dogs salivate to the food itself and then also come to salivate to the CS after learning. A central question in learning theory concerns the nature of the CS encoding. Pavlov proposed that a CS constitutes a 'stimulus substitute' for the UCS in that it elicits the same response that occurs following presentation of the UCS (see also Ref. 33). Stimulus substitution could be a very useful mechanism for enabling the animal to know *what* is predicted. However, not all conditioned responses are identical to those elicited by the UCS. For example, a CS for food reward can involve approach and orientation responses distinct from those produced by the UCS itself.[34–36] Consequently stimulus substitution may not be the only mechanism by which a CS acquires predictive value. Indeed it would be extremely useful for the animal to have a predictive mechanism that signals an impending behaviorally significant event without eliciting a representation of the event itself. In effect this would enable an animal to distinguish cues that predict a stimulus from the actual UCS itself. In many instances different behavioral responses are appropriate when anticipating a rewarding or punishing event than when experiencing it. If stimulus substitution were to be the only mechanism in place then a CS would be indistinguishable from the UCS from the point of view of the animal. Thus, a light cue predicting food would be treated as if it were the food itself and the animal would attempt to consume it. Intriguingly this type of behavior has been observed in some instances.[33] However, given that in many cases, animals (including humans) can distinguish a predictive cue from the UCS itself, as indicated by distinct behavioral responses in these two cases, it seems likely from that there are at least two distinct associative mechanisms in the brain, one based on stimulus substitution and the other uniquely signalling prediction.

With regard to the OFC there is some preliminary evidence to suggest that this region may be involved in maintaining both CS-specific and stimulus-substitution related predictions. Galvan *et al.*,[37] reported a region of lateral OFC that responded in anticipation of future rewards, but where responses did not occur initially following presentation of the reward, suggesting a CS-specific encoding in this area. In the Kim *et al.* study discussed previously,[24] a region of central OFC was found to respond during anticipation of reward but not during its receipt, again consistent with a CS-specific representation, whereas a region of medial OFC was found to respond both during expectation of reward and receipt of reward, suggestive of predictive responses based on stimulus-substitution. Moreover, Rolls *et al.*,[38] also reported activation in medial OFC during both anticipation and receipt of reward.

Another related question is to what feature of the UCS or reward stimulus does the prediction pertain? One form of predictive coding could be to simply elicit a representation of the sensory properties of the reward stimulus (e.g., its specific taste or flavor), without encoding its underlying hedonic value. Alternatively, such a representation could link directly to the underlying value of the reward stimulus. One way to discriminate between such possibilities is to change the value of the associated reward after the CS-reward association has been established and determine whether the associated CS representation changes as a function of devaluation or remains unchanged. If the CS representation were to access the underlying reward value of the UCS, the former result should be found, whereas if the CS accesses only the stimulus properties of the reward then the latter effect should be observed. To address this question, Gottfried and colleagues[39] performed a study in which predictive cues were associated with one of two food-related odors, and subjects were scanned while being presented with such cues before and after feeding to satiety on one of the corresponding foods, thereby selectively devaluing the odor of the food eaten. Predictive responses in anterior central OFC were found to track the specific value of the corresponding odors, indicating that the reward value and not the sensory properties of a stimulus is coded in this region.

Yet another distinction concerning the nature of predictive representations is whether such responses occur directly following presentation of a cue stimulus or whether such responses occur later in a trial in anticipation of the impending receipt of the subsequent outcome. Although some imaging studies have attempted to distinguish between these two possibilities, supporting a role for OFC in the latter,[37] limitations in the temporal resolution of fMRI has so far precluded definitive conclusions about the temporal characteristics of predictive representations in human OFC. However, as both types of predictive representations have been found to be present in OFC in single-unit recording studies in both rats and non-human primates,[40,41] it is reasonable to presume that both types of predictive signal will also be found in human OFC.

Stimulus or Action Values in Human OFC?

The vast majority of studies of reward prediction in both the animal neurophysiology and the human imaging literature have implicated OFC in stimulus bound predictions of future reward. That is, activity in OFC has been found to occur in response to the presentation of a cue (such as an odor or visual stimulus) that signals a future reward, or in the interval before a reward is delivered following presentation of such a cue. Although stimulus bound predictions provide information about whether a reward may be expected to occur, such predictions provide no information about what actions need to be performed in order to obtain it. For this, it is necessary to learn associations between stimuli, actions and outcomes, so that in a given context an animal can learn to perform a specific response in order to obtain reward. Evidence from animal learning studies suggests the process of action selection for reward may be implemented via two distinct learning processes, a goal-directed component which involves learning of associations between actions and the incentive value of outcomes (action-outcome or stimulus-action-outcome learning), and a habit learning component which involves learning associations between stimuli (or context) and actions (stimulus-response learning).[42] Substantial neurobiological evidence supports the existence of distinct goal-directed and habit learning systems in rats, implicating a part of the prefrontal cortex (prelimbic cortex) and dorsomedial striatum in the former and the dorsolateral striatum in the latter.[43–47] The finding that a part of rat prefrontal cortex contributes to action-outcome learning raises the question of whether there exists a homologous region of the primate brain performing a similar function.

To address this, Valentin and colleagues[48] scanned human subjects with fMRI while they learned to choose instrumental actions that were associated with the subsequent delivery of different food rewards (tomato juice, chocolate milk, and orange juice). Following training, one of these foods was devalued by feeding the subject to satiety on that food. The subjects were then scanned again, while being re-exposed to the instrumental choice procedure (in extinction). By testing for regions of the brain showing a change in activity during selection of the devalued action compared to that elicited during selection of the valued action from pre to post satiety, it was possible to test for regions showing sensitivity to the learned action-outcome associations. The regions found to show such a response profile were medial and central OFC (FIG. 2). These findings suggest that action-outcome information is present in OFC alongside stimulus–outcome representations, indicative of a role for OFC in encoding expectations of reward tied to specific actions above and beyond its role in encoding stimulus bound predictions. A number of recent single-unit neurophysiology studies in rats have also found evidence of response selectivity in OFC neurons, consistent with the findings of the Valentin *et al.*[48] study. However, in contradiction of the above findings, it has also been recently shown that lesions of OFC in rats do not produce impairments at goal-directed learning in contrast to the effects of lesions of the prelimbic area that do produce robust deficits in this capacity.[67]

The source of such discrepancies between studies remains to be determined, but one intriguing possibility is that rat and human OFC may not be entirely homologous in their entirety. It is interesting to note that in the previous stimulus-based devaluation study by Gottfried *et al.*,[39] modulatory effects of reinforcer devaluation were found in central, but not medial OFC areas, whereas in the Valentin *et al.*[48] study, evidence was found of instrumental devaluation effects in both central and medial areas. This raises the possibility that the medial OFC may be more involved in the goal-directed component of instrumental conditioning whereas central OFC may be more involved in pavlovian stimulus–outcome learning (as this area was found in both the Valentin *et al.*[48] study and in the previous pavlovian devaluation study). This speculation is consistent with the known anatomical connectivity of these areas in which central areas of OFC (Brodmann areas 11 and 13) receive input primarily from sensory areas, consistent with a role for these areas in stimulus–stimulus learning, whereas the medial OFC (areas 14 and 25) receives input primarily from structures on the adjacent medial wall of prefrontal cortex, such as cingulate cortex, an area often implicated in response selection and/or reward-based action choice.[49] It is also notable that although the majority of single-unit studies in monkeys have reported stimulus-related activity and not response-related selectivity in the OFC (e.g., Refs. 41, 50, 51) these studies have typically recorded from more lateral and central areas of the OFC (Brodmann areas 12/47 and 13, respectively), and not from more medial areas. It is therefore plausible that the more medial sectors of the OFC in humans correspond to regions considered part of medial prefrontal cortex in rats that have been more conclusively linked to goal-directed learning in the rat lesion studies.[44,45]

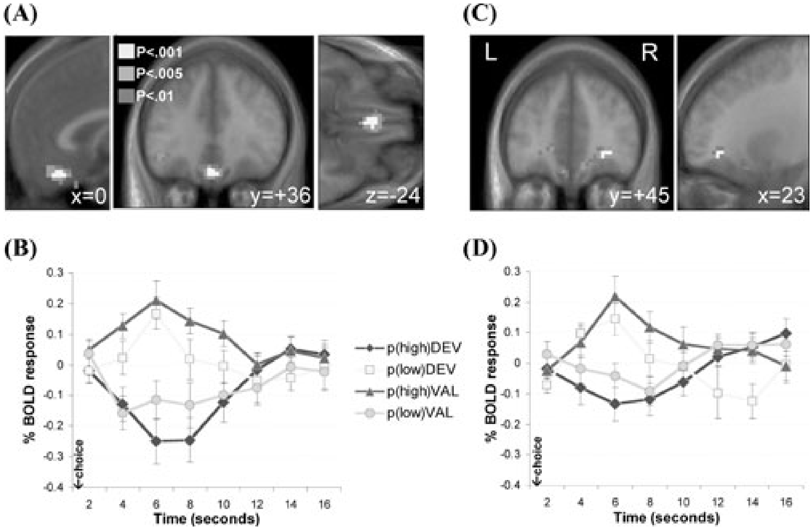

FIGURE 2. Regions of OFC exhibiting response properties consistent with action-outcome learning. Neural activity during action selection for reward in OFC showing a change in response properties as a function of the value of the outcome with each action. Choice of an action leading to a high probability of obtaining an outcome that had been devalued (p(high)DEV) led to a decrease in activity in these areas whereas choice of an action leading to a high probability of obtaining an outcome that was still valued by led to an increase in activity in the same areas. Devaluation was accomplished by means of feeding the subject to satiety on that outcome prior to the test period. **(A)** A region of medial OFC showing a significant modulation in its activity during instrumental action selection as a function of the value of the associated outcome [medial OFC; −3, 36, −24 mm, Z = 3.29, $P < 0.001$]. **(B)** Time-course plots derived from the peak voxel (from each individual subject) in the medial OFC during trials in which subjects chose each one of the four different actions (choice of the high vs low probability action in either the Valued or Devalued conditions). (**C**) A region of right central OFC also showing a significant interaction effect [24, 45, −6 mm, Z = 3.19, $P < 0.001$]. (**D**) Time-course plots from the peak voxel (from each individual subject) in the right central OFC. Data from Valentin *et al.*[48] Copyright 2007 The Society for Neuroscience.

PREDICTION ERROR SIGNAL INPUTS TO OFC

How does the OFC and indeed other brain regions acquire predictive value representations be they stimulus or action bound? Some contemporary models of animal learning consider that learning occurs via a prediction error which signals discrepancies between expected and actual reward (or punishment).[52] In one extension of this theory—temporal difference learning, predictions are formed about the expected future reward in a trial, and a prediction error reports differences in successive predictions of future reward.[53] Single-unit studies in non-human primates implicate phasic activity within dopaminergic neurons as a possible neural substrate of this signal.[54,55] Over the course of learning, the signal shifts its responses from the reward to the CS, unexpected omission of reward results in a decrease in activity from baseline (a negative prediction error), whereas unexpected presentation of reward results in an increase in activity (positive prediction error). Human neuroimaging studies of classical conditioning for reward report prediction error signals in prominent target areas of dopamine neurons, including the OFC.[56,57] Dopamine neurons could facilitate learning of value predictions in these areas by gating plastic changes between sensory, action, and reward representations. The finding that prediction error related responses are present in OFC and throughout the reward network, is consistent with the possibility that this mechanism is used to mediate flexible learning and updating of reward associations, a function often ascribed to the OFC.[58]

RESPONSES RELATED TO ABSTRACT RULES IN A DECISION PROBLEM

Theories of learning based on prediction errors provide an account of how expected reward representations in OFC can be updated on an incremental basis through experience. However, in at least some situations an error correcting learning mechanism may not be the only means by which reward expectations can be modulated. Many types of decision problems, may have abstract rules or structure, that impact on the rewards available following choice of a particular action or set of actions. An example of such structure is in probabilistic reversal learning whereby an anti-correlation exists between the rewards available following choice of either action such that when one action yields a high probability of reward, the other action offers a low probability of reward. Thus at any one time, when one action is a good prospect the other is a bad prospect. Knowledge of such rules would confer considerable advantage to an individual attempting to solve such a problem and maximize reward. In a recent study, Hampton *et al.*[59] showed that during performance of a reversal-learning task, responses related to expected reward in medial OFC and adjacent medial prefrontal cortex did indeed incorporate knowledge of the abstract structure of this task, by reflecting the anti-correlation in the rewards that could be obtained from choice of either action. Thus, expected reward representations in OFC are updated not only via prediction errors but also according to knowledge of the abstract structure in a given decision problem. For a more detailed discussion of this particular feature of OFC function see O'Doherty *et al.*[60]

DECISION SIGNALS IN OFC

Lesion studies of orbital and ventral medial prefrontal cortex suggest that OFC is necessary for adaptive decision making.[1–4] However, the precise functional contribution of OFC to the decision-making process is not immediately clear on the basis of those lesion studies. Impairments in such patients could be due to an inability to maintain representations of predicted reward that are used to guide decision making processes elsewhere. Alternatively, OFC could play a role in the actual decision-making process itself, that is, in the actual comparison process between the expected values of different actions and in the selection of a specific action.

As we have seen, there is now considerable evidence to implicate OFC in maintaining predictions of future reward, consistent with the first possibility. However, a study by O'Doherty and colleagues,[26] also provides evidence to support the second possibility—a role for OFC in the actual decision-making process itself. This study involved reversal learning, a task described previously, in which subjects must choose between two different actions that yield rewards and punishers with different probabilities. One action is advantageous in that choice of that action has a high probability of reward (70%) and a low probability of punisher (30%), whereas the other action is disadvantageous in that choice of that action yields reward with a low probability (30%) and punisher with high probability (70%). Occasionally, the contingencies reverse such that subjects must work out on a trial by trial basis if contingencies have changed and switch their choice of action in order to perform adaptively. The design of the study enabled responses to rewards and punishers to be dissociated from signals related to behavioral choice. In this task subjects can make one of two decisions: maintain responding to the current stimulus or switch their choice of stimulus. In order to separate out this decision process from rewarding and punishing feedback, trials in which a punisher is obtained and followed by a switch in stimulus choice (punish_switch) were evaluated separately from trials in which a punisher is obtained and subjects maintain responding to the current stimulus (punish_noswitch). Regions involved in behavioral choice (stay versus switch) were identified by comparing punish_switch trials to reward (no_switch) and/or punish (no_switch) trials. A region of medial and anterior central OFC was found to respond on trials in which the subject maintained responding on the subsequent trial (irrespective of whether the outcome was a reward or a punisher) (see FIG. 3). A different region of posterior lateral OFC (contiguous with anterior insula) was found to respond following a punisher on trials in which subjects switched their choice of stimulus on the subsequent trial, but not otherwise. These findings suggest that OFC is involved in behavioral choice and that different sectors of OFC signal the appropriateness of different behavioral strategies—some regions signal that on-going behavior should be maintained, whereas other regions signal that behavior should be changed. These findings suggest that OFC may be involved in actively computing the decision about what action to take next, or at least in reporting the consequences of that decision. It should be noted that while OFC may contribute to this process it is certainly not the only region containing signals relevant to decision making. For example, by using a

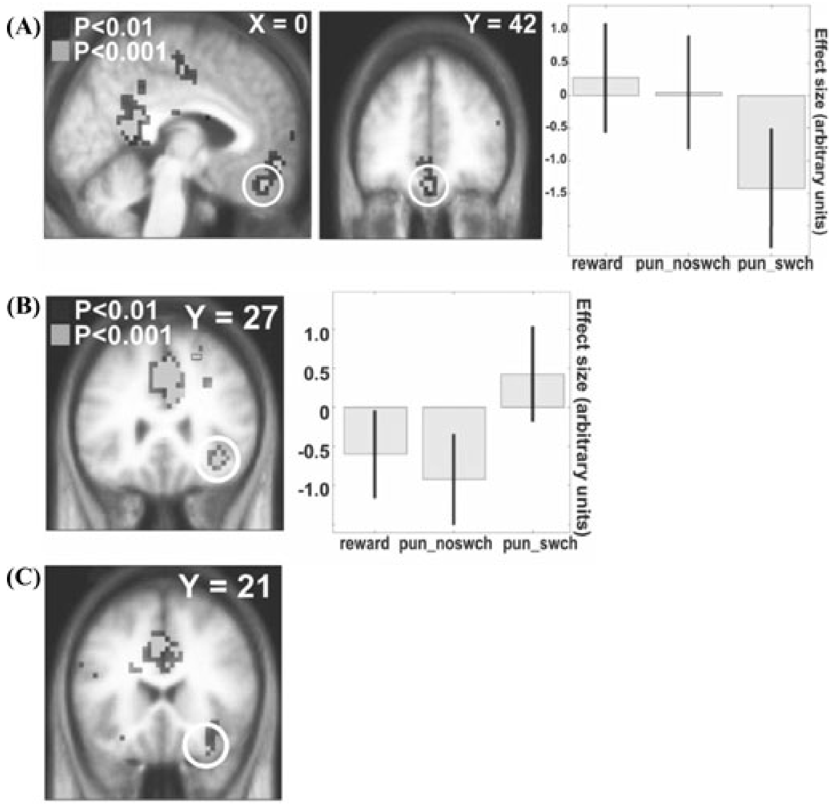

FIGURE 3. Decision signals in OFC and adjacent ventral prefrontal cortex. **(A)** Sagittal and axial slices through a region of medial OFC that is involved in signaling that a behavioral response should be maintained.The plot of parameter estimates (*right of figure*) indicates that this region does not respond to rewards or punishments per se, but shows greater responses on rewarding and punishing trials if the subject does not switch their behavior compared to punishing trials followed by a switch in behavior (pun_swch). **(B)** Region of anterior insula extending into posterior lateral OFC that shows enhanced responses following a punishment if on the subsequent trial the subject switches their choice of stimulus (pun_swch) compared to rewarding or punishing trials were no such switch of behavior occurs. **(C)** Region of posterior lateral OFC that shows enhanced responses on punished trials following a switch in behavior compared to punished trials followed by no switch in behavior. Data from O'Doherty *et al.*[26] Copyright 2003 Society for Neuroscience.

classifier based approach, Hampton and O'Doherty[61] showed that information contained in three regions outside OFC: medial prefrontal cortex, ventral striatum, and anterior cingulate cortex were the most significant predictors of a subjects' subsequent decision out of all the regions studied (including OFC).

OUTSTANDING ISSUES

Considerable progress has been made in uncovering the functional contributions of human OFC since human neuroimaging became a mainstream tool for probing the functions of this brain area over 15 years ago. Yet, many outstanding questions remain. One such question is whether OFC contains a representation of common reward value. In order to make decisions between diverse types of reward it is reasonable to assume that somewhere in the brain a common currency for reward might be computed, such that the value of different rewards are encoded in the same relative scale.[62] Given the OFC's general role in encoding stimulus-reward value, this region would seem to be a strong candidate for encoding such a common currency. One possible mechanism by which such a common currency could be implemented at the neural level, is for information about the reward value of different types of reward to converge into the same brain region such that spatially overlapping neural representations would exist for the value of different rewards. As yet there is little evidence to either confirm or reject the possibility that OFC may play a role in encoding a common currency for reward, clearly an important direction for future research.

The precise nature of the functional anatomical specialization within OFC is also an unresolved issue. The OFC and adjacent medial prefrontal cortex is a vast area of cortex with over 22 different cytoarchitectonic sub-regions,[63] and therefore some degree of functional specialization within these areas is almost certainly going to be present. Here we have considered two possible sources for functional specialization: valence, or whether an outcome is rewarding or punishing; and the nature of the predictive associations being learned—whether they are stimulus or action bound. Another source of functional specialization not discussed in detail here is the nature of the reward itself, that is the sensory modality of the reward—whether it is conveyed in an auditory, visual, gustatory, olfactory, or somatosensory domain, and the associative history of that reward—whether it is a primary or secondary reinforcer. Future studies will be needed to evaluate these and other possibilities. It is likely that simple medial versus lateral or anterior-posterior dichotomies will provide an incomplete picture of the nature of the true functional heterogeneity in this area. Yet another issue for on-going research is the need to determine the differential contribution of OFC to reward-related learning and decision making compared to other interconnected brain regions, such as the amygdala, ventral striatum, and other sectors of prefrontal cortex, including the anterior cingulate cortex. Future studies will need to focus not only on the functions of each of these individual areas, but also on the nature of the interactions between them, mirroring recent progress being made along these lines in the animal literature.[40,64–66]

CONCLUSIONS

The OFC is both an integral part of the reward network and a part of prefrontal cortex. As a consequence, it simultaneously shares many functional commonalities with other parts of the reward system, and with other parts of prefrontal cortex. In this paper we have reviewed evidence primarily from functional neuroimaging studies in humans to suggest that OFC is involved in implementing at least five distinct functions, each of which are important for adaptive decision making. First of all, OFC encodes the value of stimuli as they are perceived. Such a basic valuation mechanism is necessary for the initial selection of goals, as stimuli perceived as having high reward value may be selected as items to be obtained in future, whereas stimuli perceived as having low or aversive significance may be selected as items to be avoided in future. Second, OFC is involved in maintaining representations of expected reward, both stimulus bound and action bound, computations that are necessary for providing information about the consequences that follow from taking particular courses of action or when choosing particular stimuli. Third, this region receives prediction error signals likely originating from dopamine neurons, an afferent signal that may underlie learning of reward predictions. Fourth, in addition to updating of expected value on the basis of prediction errors, OFC is also involved in using knowledge of the abstract structure of a decision problem to guide predictions of future reward. Finally, this region may also play a role in actually computing the decision itself, or at the very least in representing the consequences of that decision.

ACKNOWLEDGEMENTS

J.P.O. is supported by a Searle Scholarship, and by grants from the National Science Foundation, National Institute of Mental Health, and the Gordon and Betty Moore Foundation. The author would like to thank Peter Bossaerts, Alan Hampton, Hackjin Kim, Shin Shimojo, and Vivian Valentin at Caltech and Hugo Critchley, Peter Dayan, Ray Dolan, Jay Gottfried, Ben Seymour, and Joel Winston at UCL for their collaboration on many of the studies described here.

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