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# Amygdala–frontal interactions and reward expectancy

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Recent evidence indicates that networks including the amygdala and prefrontal cortex provide a key interface between affect and cognition. Converging evidence from rodents, humans, and non-human primates indicates that interconnections between the basolateral complex of the amygdala and the orbitofrontal cortex are crucial to the formation and use of expectancies of reinforcers in the guidance of goal-directed behavior.

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## Abbreviations

**BLA** basolateral amygdala  
**CS** conditioned stimulus  
**fMRI** functional magnetic resonance imaging  
**OFC** orbitofrontal cortex

## Introduction

Traditionally, the amygdala has been assigned a crucial role in emotional learning [1,2], whereas the prefrontal cortex has been implicated in a variety of cognitive functions involving the strategic use of information in memory [3,4]. Recent recognition of the importance of emotion and the representation of value in memory and decision has led to the investigation of amygdala–prefrontal interactions in a number of experimental contexts. Evidence from studies of rodents, humans, and non-human primates indicates that interactions between the basolateral complex of the amygdala and the orbitofrontal cortex are crucial for generating and using reinforcer expectancies that guide goal-directed behavior. Here we focus on that evidence.

## Basolateral amygdala, orbitofrontal cortex and expectancy

The utility of learning and memory lies not in reminiscence about the past, but in allowing us to act in anticipation of future events. Expectancy is a key product of acquired knowledge and learning, which allows access to representations of future events, and the use of those

representations to guide behavior effectively, efficiently, and flexibly, on the basis of our current needs and values. From the straightforward anticipation of events based on everyday regularity (e.g. mealtimes) to the most complex calculations (e.g. weather forecasting), adaptive decision making requires the integration of information about the properties and likelihood of imminent events with information about our goals and current states. Recently, conventional associative learning paradigms have been adapted to allow systematic study of expectancy and action in a range of species, including humans.

Most modern views of associative learning acknowledge that both Pavlovian and instrumental conditioning procedures often establish associations between stimulus or response events and internal memorial representations of the reinforcer [5]. In this context, ‘expectancy’ refers to the associative activation of such reinforcer representations by the events that predict them, before the delivery of the reinforcer itself. Expectancy can serve many functions, including the control of conditioned behavior [5], the establishment of new learning [6], and the modulation of the efficacy of reinforcers [7]. In this review, we describe evidence from such associative learning experiments, which demonstrates the important involvement of basolateral amygdala (BLA) and orbitofrontal cortex (OFC) in the formation and use of expectancies of reinforcers.

## Reinforcer devaluation

One of the more frequently used methods to demonstrate expectancy in laboratory animals, which can also be used with human participants in experimental settings, is the reinforcer devaluation procedure [5]. In one rendition, animals learn an instrumental discrimination in which their actions yield different outcomes. If one action (pulling a chain) produces one food reinforcer (grain pellets) and another action (pressing a lever) produces a different food reinforcer (sucrose), the representation of the expected outcome can be isolated when the animal is tested after changing the value of one of the foods. After consumption of one food item (e.g. sucrose) to satiation, animals are given the opportunity to perform both actions in extinction (i.e. without delivery of either reinforcer). In this test, they show substantial reductions in the frequency of the action that predicts the devalued food, relative to the frequency of the other action.

Variants of reinforcer devaluation tasks use different methods of initial training, including instrumental and Pavlovian conditioning procedures, and of reinforcer devaluation, for example, satiation and taste aversion–learning. In an often-used example of reinforcer devaluation in

Pavlovian conditioning, rats are first presented with pairings of a conditioned stimulus of a light with a food reinforcer in a standard conditioning chamber. As a consequence of the formation of light–food associations, the rats learn to approach the food cup while the light is on. Next, in a devaluation phase conducted in the rats' home cages, the value of that same food is reduced by pairing it with a toxin, so that the rats form an aversion to the flavor of the food reinforcer and won't consume it. Finally, responding to the light alone is assessed in the conditioning chamber. If the learned food cup approach was mediated by a light-evoked expectancy of the food reinforcer, then rats will substantially reduce food cup approach during the light, relative to behavioral controls that did not experience intervening devaluation of the reinforcer.

In normal rats, such devaluation effects have been observed repeatedly, using both Pavlovian and instrumental training procedures, and several taste aversion and satiation devaluation procedures. However, rats with excitotoxic lesions of BLA [8\*,9\*,10] or OFC [11] made before training failed to show a devaluation effect. That is, despite normal acquisition of conditioned responding in the training phase and normal reduction of food consumption in the devaluation phase, they failed to show reduced responding in testing. Likewise, monkeys with neurotoxic lesions of the amygdala [12] or lesions that disconnect the BLA from the OFC [13] fail to show devaluation effects in a procedure in which the incentive value of a food item was reduced by satiation on that food. Normal monkeys in those devaluation tests were less likely to select objects that had been previously paired with the devalued food, rather than some other food. At the same time, the lesioned monkeys were just as likely as controls to suppress consumption of the devalued food itself.

Similar involvement of the BLA and the OFC has also been reported in human brain imaging studies that used devaluation procedures. Previous positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies showed important roles for the BLA and the OFC in the representation of the incentive value of food-related stimuli. For example, in one such study, hunger was found to modulate amygdala activation by food stimuli but not by nonfood stimuli [14]. Likewise, OFC activation by presentation of foods was related to hunger [15] and pleasantness [16], and satiation by a food item reduced OFC activation by that specific food [17]. In a recent fMRI study using Pavlovian conditioning and selective satiation procedures [18\*\*], two visual conditioned stimuli (CSs) paired with two different food odors activated both the amygdala and the OFC in training. But after participants consumed one food to satiation, both the BLA and the OFC responded less to the devalued cues than to nondevalued cues for food items.

### Neural coding in discrimination learning

Tasks such as devaluation are used in behavioral studies to reveal the role of associatively activated representations of reinforcers. But it is assumed that these representations are active regardless of the invocation of special behavioral procedures to detect them. For example, when animals perform a discrimination by selecting between two actions that lead to different outcomes, the activation of representation of the outcome is used to guide behavior in addition to any stimulus–response associations. Recent studies of neural activity in rats, monkeys and humans in discrimination tasks provide another window through which to view learned expectancies in associative learning.

In go/no-go discriminations in which different odor cues predicted the delivery of sucrose or an aversive quinine solution [19–21], neurons in both the BLA and the OFC of rats responded selectively to the delivery of those reinforcers and, after learning, to the odor cues that predicted those reinforcers. Importantly, reinforcer-selective neurons also responded appropriately during a brief empty delay interval after correct and incorrect go responses were made as rats awaited the delivery of the sucrose or quinine reinforcer. Reversal of the reinforcer contingencies altered the coding properties of these cue- and response-activated neurons, demonstrating that their activity indeed reflected the value of the predicted outcomes. This anticipatory reinforcer-appropriate neural activity, observed in monkeys as well as in rats [22–25], has the requisite features for encoding learned expectancies of reinforcing events. Reinforcer-selective neurons that were activated by the odor cues could be said to represent stimulus–reinforcer expectancies, and reinforcer-selective neurons that were activated by responses in the delay intervals could be said to represent response–reinforcer expectancies.

### Basolateral amygdala and orbitofrontal cortex specializations in coding and function

Although basic aspects of encoding in the tasks just described were similar for BLA and OFC neurons in many respects, more subtle differences are notable. For example, although neurons in BLA coded odor–outcome relations early in training, OFC neurons did not code these relations until after a behavioral discrimination criterion had been met. Furthermore, when the reinforcement contingencies were reversed, expectancy-coding neurons in the BLA were more likely to reverse their reinforcer-selectivity than OFC neurons, which were more likely to simply lose their prior selectivity while previously non-selective neurons developed correlates in the reversal phase [20,21].

In addition to such differences in correlates observed when recording in each structure in the same task in the intact animal, further insights have come from companion

research using experimental manipulation of one structure while recording in the other [26<sup>••</sup>,27<sup>••</sup>]. This research shows that interactions between BLA and OFC play an important part in the development of expectancy coding, and reveals additional differences between BLA and OFC function in odor discrimination tasks. Rats with lesions in BLA or OFC (placed ipsilateral to the recording site) showed several differences in neural coding in the other region compared to that of rats with sham lesions. For example, although BLA lesions had little effect on the proportion of OFC neurons that reversed their selectivity after a reversal of reinforcement contingencies, OFC lesions substantially reduced the proportion of BLA neurons that showed such reversal, consistent with the frequent observation that the OFC is crucial for reversal learning [28–31]. Furthermore, the proportion of OFC neurons that came to code stimulus-reinforcer expectancies, that is, which showed reinforcer-specific activity in the presence of the odor cues, was lower in rats with BLA lesions than in intact rats. By contrast, OFC lesions had little effect on the proportion of such stimulus-reinforcer expectancy neurons in BLA. The two lesions had opposite effects on neurons that coded response-reinforcer expectancies; although BLA lesions had no effect on the proportion of reinforcer-selective OFC neurons that responded in the delay interval between responding and reinforcer delivery, rats with OFC lesions showed fewer such response-reinforcer expectancy neurons in BLA than controls. Thus, exchange of information between BLA and OFC is necessary for normal coding in each region: BLA is crucial to the representation of stimulus-reinforcer expectancies in OFC, and OFC is needed for the representation of response-reinforcer expectancies in BLA.

These last observations are at least superficially comparable to the view, generated from recent lesion studies in devaluation tasks, that BLA is especially important for the formation of cue-reinforcer expectancies, and OFC for generating responses on the basis of those expectancies [32<sup>••</sup>]. That view is supported by results obtained when lesions are made at different phases in devaluation protocols. In contrast to the detrimental effect of BLA damage before all phases of such experiments, when rats were given their initial light-food training before surgery BLA lesions had no effect on subsequent sensitivity of conditioned responding to devaluation. This result suggests that the BLA is crucial for processes by which initially neutral events (CSs) gain associative access to the incentive value of reinforcers, but not to the use of those expectancies in guiding behavior. By contrast, OFC lesions made either after initial training [32<sup>••</sup>] or after the devaluation phase [33] eliminated the devaluation effect, just as lesions made before all training. Thus, unlike the BLA, the OFC is crucial to the use of expectancy information to guide behavior. Similar conclusions can be derived

from recent human imaging studies [34<sup>•</sup>,35<sup>••</sup>,36<sup>••</sup>]. In one study [34<sup>•</sup>], amygdala activation was related to presentation of visual signals for pleasant odors early in training, but this response habituated over training, whereas medial OFC activity associated with those visual cues was maintained. Another study [35<sup>••</sup>] found activation of some subregions of OFC by words that signified high-incentive menu items only when participants had to choose among them, but activation of amygdala and other OFC subregions by these words regardless of whether or not a choice response was required.

These observations might also help to account for reported effects of BLA and OFC ablations on reversal learning. Although the effects of BLA lesions on reversal learning are mixed [31,37], damage to the OFC has been found to impair reversal learning broadly across species and tasks [28,30,31,38–40]. Recent behavioral data suggest that outcome expectancies are not lost in reversal learning, and successful reversal learning instead reflects the acquisition of some competing response or inhibitory state [41]. If the OFC is crucial for guiding action on the basis of outcome expectancies, then the activation of competing expectancies (mediated by BLA encoding that survives OFC lesions) throughout reversal training, leading to impaired reversal performance, might be especially evident in subjects with OFC damage. Consistent with this claim, animals with OFC damage show persistent deficits in successive reversals, even when returned to their original discrimination tasks [31]. By contrast, no such competing expectancies would be formed by animals with BLA damage. These animals would be unimpaired in reversal learning if another equally effective learning strategy, for example one based on simple stimulus-response learning, was available to them. Variability in the effectiveness of BLA lesions on reversal performance might reflect variation in the effectiveness of these alternative strategies.

#### **Content of expectancies in basolateral amygdala and orbitofrontal cortex**

The experiments with rats and monkeys cited in the previous section demonstrated neural coding of both aversive and appetitive events, and expectancies for those events. Recent human imaging studies have also shown such differential coding in OFC, for both stimuli with intrinsic positive or negative value (pleasant/unpleasant odors or tastes, [34<sup>•</sup>,42,43<sup>•</sup>,44–46]; but see [47]) and more abstract events (monetary gains and losses, [48,49<sup>•</sup>]). Medial regions of the OFC responded more to positive events and lateral OFC responded more to negative events. Most relevant to this review, this value-dependent regional OFC activation was observed to come under the associative control by predictive visual CSs paired with affectively significant stimuli odors and tastes [34<sup>•</sup>,50]. By contrast, in these same studies there was little evidence for coding of stimulus value in the amygdala;

instead, amygdala activation was found to vary with stimulus intensity, a variable which did not affect OFC activation (but see [35<sup>••</sup>]). However, region-of-interest analyses like these can only reveal coding differences that are spatially segregated; notably, in rat and monkey, individual neurons that selectively respond to appetitive and aversive stimuli appear intermixed. Thus, the claim that the human amygdala fails to encode stimulus value could be premature [42,43<sup>•</sup>,44].

In all of the work reviewed here, the expectancies involved were of motivationally significant events, with substantial reinforcement or incentive value. Although it is well known that animals can also form associations between relatively neutral events, there has been little investigation of amygdala or OFC involvement in learned expectancies for such events. However, consistent with the view that the BLA is primarily concerned with representation of emotional/incentive value, the acquisition and use of expectancies of relatively neutral events was unaffected by BLA lesions in two recent studies [37,51].

Given the frequent claim from both human [34<sup>•</sup>,42,43<sup>•</sup>, 44–46] and animal [23,25,52] research that the OFC does not represent sensory features of events independent of their incentive properties, the OFC's role might be similarly confined to orchestrating behavior on the basis of expectancies of emotionally significant events. Recent human imaging studies support this claim [53]. On the other hand, the anatomical relations among the OFC and sensory regions (discussed later) are consistent with an important role for the OFC's use of information from a variety of senses to guide behavior.

#### **Orbitofrontal cortex, expectancy and surprise**

A key notion common to many contemporary theories of associative learning is that the ability of events to enter into associations depends not only on their intrinsic properties (such as salience or incentive value) but also on how well the occurrence of those events is predicted. For example, in the Rescorla-Wagner model [7], the amount of learning that occurs on a conditioning trial is a function of the discrepancy between the intrinsic value of the reinforcer and the extent to which that value is expected on the basis of the cues present on that trial. Other theorists have argued that this discrepancy can also determine the allocation of attention to the cues themselves [54,55]. Neural correlates of this 'prediction error' have been observed in a variety of brain regions (reviewed in [56]), including the OFC [55,57–61]. In these studies, OFC activation by reinforcers was greater when those events were presented under conditions of uncertainty than when they were well-predicted by context or explicit cues. The relation among error detection in OFC, attention, reinforcement and functions of expectancy reviewed here deserves further investigation.

#### **Anatomy and function of the amygdala and prefrontal cortex**

The research we have surveyed provides functional support for evolving neuroanatomical conceptualizations of both the amygdala and the prefrontal cortex. On embryological, neurochemical, connective, and functional grounds, many anatomists have argued that the classical amygdala complex forms neither a functionally nor a structurally coherent entity, and that each of its several major cell groups is better described in relation to different adjacent brain systems [62,63]. Arguments for the concept of the 'extended amygdala' were based on such considerations [63]. On somewhat different grounds, Swanson and Petrovich [62] suggested that the amygdala comprises components of four functional systems. Notably, in the context of the research reviewed here, they characterized the lateral and basolateral amygdala as an extension of the deep regions of frontal and temporal cortex. Consistent with this view, the data on BLA and OFC have revealed links between functions of this circuit, which are not shared with other amygdalar regions. Note, for example, that the lesions of central nucleus of the amygdala entirely spare devaluation performance [10].

Likewise, prefrontal cortex is now widely described as comprising multiple, dissociable systems. Some investigators have distinguished between a ventral processing stream, conveying emotional arousal information from the amygdala to ventral prefrontal cortex, and a dorsal stream that relays attentional information from posterior parietal cortex to dorsal prefrontal cortex [64]. Similarly, three major anatomical divisions, medial, dorsolateral, and orbitofrontal regions are usually defined [4<sup>•</sup>,38,65<sup>•</sup>]. Homologies of these anatomical regions across primates and rodents have been identified; crucially, a homolog of primate orbitofrontal cortex (OFC) in rats shares patterns of connections with many other brain regions, including its innervation from medio-dorsal thalamus (which traditionally defined cortical boundaries). Most importantly, the comparability of OFC function across rodent, human, and non-human primate studies reviewed here adds strong support for homology.

The generality of these findings across rodent and primate species might reflect specific anatomical features of the network that includes the BLA and the OFC, especially in the context of representation and association (see [4<sup>•</sup>,38,65<sup>•</sup>] for reviews). First, BLA and OFC each receive highly-processed sensory information from several higher-level sensory cortical areas. Second, in the BLA, these sensory projections overlap with projections from the OFC, and in the OFC, they overlap with projections from the BLA. Most crucially, the OFC and the BLA are linked directly by strong bidirectional connections, and indirectly through thalamic connections [66], providing significant substrates for information exchange between



these two regions. Finally, this network has strong connections with several brain regions that are also implicated in reward processing (e.g. the striatum [57,67]) and decision (e.g. dorsolateral prefrontal cortex, [68]).

### Conclusions and additional reflections

We have reviewed studies of amygdala–prefrontal involvement in reinforcer expectancies conducted across a range of species. Although most of this research relied on a few simple behavioral discrimination and reinforcer devaluation tasks to assess expectancy, the behavioral literature is rich with converging operations and tasks that can be used to define that construct. To date, the role of the BLA and the OFC in these tasks has not been explored in much depth. However, it is notable that BLA lesions have also been found to impair performance in two of these procedures, the differential-outcome-expectancy task and reinforcer-specific Pavlovian-instrumental transfer [51].

Although the current review has concentrated on a single aspect of OFC function, it is notable that it informs more general considerations of prefrontal function. Recent accounts of orbitofrontal function fall in three broad categories, those that emphasize the OFC's role in representing the affective value of goals and other events [11,69,70\*,71], those that stress its role in response selection [35\*\*,72], and those that emphasize its role in response inhibition [40,72]. The research surveyed here supports each of these broad claims, indicating that interaction between amygdala and OFC is important for establishing expectancies of the incentive value of upcoming events in both regions, and that OFC, to a greater extent than amygdala, is crucial to the guidance of action based on those expectancies, especially for the case of suppressing responses based on competing, but less desirable expected consequences. Because selection among responses might involve estimates of expected value of the consequences of each response, response selection might frequently be intertwined with expectancy.

The body of research reviewed here has several salutary aspects that are worth special note. First, it broadens our view of the role of the amygdala in affect and emotion. Although much of the classic literature stresses the role of the amygdala in negative affect (e.g. fear, anxiety and disgust) and defensive learning, it is striking that most of the studies reviewed here used appetitive, food-reinforced learning tasks, supporting the view that the amygdala is at least as importantly involved in positive affect and appetitive learning [73,74].

Second, the linkage of amygdala and prefrontal function and structure further encourages the experimental and theoretical integration of emotional and cognitive processes and shows that the use of comparable tasks and

hypotheses across rodent, human, and nonhuman primate models can provide a fairly unified approach to these issues. Each of these experimental preparations promises different contributions to the interdisciplinary study of cognition, affect, and behavior, but linked to a common theoretical perspective and a well-defined empirical approach.

Finally, this research might eventually provide a better foundation for understanding human psychopathology involving the amygdala and OFC. Patients with damage to either amygdala or OFC show a range of abnormalities of cognition, affect, and behavior [38,75–78]. In many instances, when exposed to training procedures like those reviewed here, such patients show deficits comparable to those observed in animal lesion studies, albeit with more damage that is less well-defined. Likewise, neurologically intact individuals, diagnosed with certain disorders of emotion and decision, have been observed to display similar behavioral deficits, as well as atypical neural activity in the brain systems reviewed herein [29,79]. Irregularities in the formation of accurate representations of the expected value of the consequences of both environmental events and our own actions, and the use of those representations in selecting appropriate and adaptive responses could underlie a range of disorders of decision-making, emotional function, social behavior, and personality in general.

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- of special interest
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The authors present a brief review of recent evidence, primarily from studies with rats and monkeys, for an important role of the amygdala in processing of positive rewards. The authors contrast amygdala-independent and amygdala-dependent reward processing, emphasizing the role of amygdala in the formation of stimulus value associations in learning about the positive consequences of events.

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text), rats with BLA lesions made after light–food training but before food devaluation were unimpaired. By contrast, responding of rats with OFC lesions made after light–food pairings was not sensitive to subsequent food devaluation. The authors suggested that BLA is crucial for forming representations linking cues to the incentive properties of outcomes but not for the use of the those representations to guide behavior, which is instead dependent on OFC function.

33. Pickens CP, Saddoris MP, Gallagher M, Holland PC: **Orbitofrontal lesions impair use of cue–outcome associations in a devaluation task [abstract]**. *Soc Neurosci* 2003: 89.13.

34. Gottfried JA, O'Doherty J, Dolan RJ: **Appetitive and aversive olfactory learning in humans studied using event-related functional magnetic resonance imaging**. *J Neurosci* 2002, **15**:10829–10837.

In this event-related fMRI study, pictures of faces were paired or unpaired with pleasant, neutral, or unpleasant odors in classical conditioning procedures. Activity of medial and lateral OFC was associated with presentations of faces that signaled pleasant and unpleasant odors, respectively. Amygdala activity was initially related to presentations of signals for pleasant odors, but that response habituated over testing. Activity of the nucleus accumbens increased with presentations of signals for pleasant odors but decreased with signals for unpleasant odors.

35. Arana FS, Parkinson JA, Hinton E, Holland AJ, Owen AM, Roberts AC: **Dissociable contributions of the human amygdala and orbitofrontal cortex to incentive motivation and goal selection**. *J Neurosci* 2003, **29**:9632–9638.

In this study, food-sated participants were shown restaurant menus that varied in incentive value, based on a prior survey of their food preferences. On half of the trials, the participants were asked to choose from the menus. PET analysis of regional cerebral blood flow showed activation of the amygdala by high-incentive menus, regardless of whether a choice had to be made; that activation was proportional to participants' subjective ratings of menu incentive value. Medial OFC responded to high-incentive menus and on any trials that required a choice response; activation on choice trials was proportional to participants' subjective ratings of choice difficulty. Finally, lateral OFC responded when participants had to choose among similarly desirable alternatives. The authors suggest that amygdala and OFC have specialized roles within a system that underlies the selection of goals based on expectancies of their incentive values. Whereas the amygdala provides magnitude estimates, the OFC “integrate(s) diverse aspects of goal information including value, sensory, experiential and semantic components to guide prospective (expectancy-based) behavior”.

36. O'Doherty J, Critchley H, Deichmann R, Dolan RJ: **Dissociating valence of outcome from behavioral control in human orbital and ventral prefrontal cortices**. *J Neurosci* 2003, **23**:7931–7939.

The authors present an fMRI study of normal participants in a two-choice visual discrimination reversal task. In a ‘choice’ condition, responses to one visual cue yielded a monetary gain 70% of the time and a monetary loss 30% of the time; responses to the other stimulus had the opposite consequences. After a discrimination criterion was met, the discrimination contingencies were reversed. In a response independent condition, participants could not choose their responses, rather reinforcement was determined by the performance of another ‘yoked’ subject. Outcome-dependent activation of central/medial OFC was found in both choice and response-independent conditions, but was greater in the choice condition. Amygdala and striatal activation to reward versus punishment occurred without regard to choice condition. Finally, enhanced responding of medial and left lateral OFC was observed after both reinforced (correct) and punished (incorrect) trials that were not followed by a change in response on the next trial, relative to the neural response on punished trials that were followed by a subsequent correct response. Thus, this signal reflected a continuing behavioral strategy of response maintenance or persistence rather than the trial outcome alone. The authors conclude that some prefrontal regions “represent valence irrespective of behavioral choice, other regions are sensitive to response maintenance, and other regions are involved in detecting a change in response contingencies”.

37. Setlow B, Gallagher M, Holland PC: **The basolateral complex of the amygdala is necessary for acquisition but not expression of CS motivational value in appetitive Pavlovian conditioning**. *Eur J Neurosci* 2002, **15**:1841–1853.

38. Schoenbaum G, Setlow B, Gallagher M: **Orbitofrontal cortex: modeling prefrontal function in rats**. In *The Neuropsychology of Memory*. Edited by Squire L, Schachter D. New York: Guilford Press, 2002:463–477.

39. Bechara A, Damasio AR, Damasio H, Anderson SW: **Insensitivity to future consequences following damage to human prefrontal cortex**. *Cognition* 1994, **50**:7–15.

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Using fMRI imaging techniques, the authors found that amygdala activation was associated with the intensity but not valence (subjective pleasantness) of taste stimuli, whereas OFC activation was related to the valence of those stimuli, independent of their intensity.

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In this event-related fMRI study, participants were exposed to a visual reversal task in which correct choices led to higher probability of monetary gain and incorrect choices led to cue to monetary losses. Monetary gains were associated with activation of the lateral OFC and suppression of activity of the medial OFC, and losses were associated with the opposite activation patterns in these two regions. Furthermore, the magnitude of activation of these regions was related to the magnitudes of the gains and losses.

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