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Cognitive-emotional interactions

The amygdala, reward and emotion

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Recent research provides new insights into amygdala contributions to positive emotion and reward. Studies of neuronal activity in the monkey amygdala and of autonomic responses mediated by the monkey amygdala show that, contrary to a widely held view, the amygdala is just as important for processing positive reward and reinforcement as it is for negative. In addition, neuropsychological studies reveal that the amygdala is essential for only a fraction of what might be considered 'stimulus-reward processing', and that the neural substrates for emotion and reward are partially nonoverlapping. Finally, evidence suggests that two systems within the amygdala, operating in parallel, enable reward-predicting cues to influence behavior; one mediates a general, arousing effect of reward and the other links the sensory properties of reward to emotion.

Introduction

The amygdala is a unique part of the telencephalon. In primates, it appears almond shaped and lies in the anterior temporal lobe, toward its medial side (Figure 1a, b). Although sometimes treated as a single 'thing' [1], the amygdala contains an enormous diversity of nuclei and cell types (Figure 1a, c). It receives projections from most cortical fields [2–7], and usually returns them [8–11]. These anatomical facts, alone, illustrate the pivotal position of the amygdala in the telencephalon.

According to current thinking, the amygdala contributes to emotion, reward, motivation, learning, memory and attention. Yet the relationship among these cognitive processes, and the specific contribution of the amygdala to them, remains one of the central challenges in cognitive neuroscience. To complicate matters, 'reward' is not a unitary construct; rewards have sensory, affective and motivational properties, each of which is represented in the brain [12–14]. As an operational definition, 'reward' and 'reinforcement' are used interchangeably here to refer to something that an animal will work to obtain (if positive) or avoid (if negative). Reinforcement received after performance of an action also functions to increase the probability that the same action will be repeated, although this phenomenon will not be discussed further here. In addition, however, rewards might influence behavior through Pavlovian mechanisms that operate independently of actions. Because the content of emotion is inaccessible in nonhuman subjects, and is outside the scope of this article (but see Barrett *et al.* [15]), the term 'emotion' is used here for reactions to stimuli, including autonomic and skeletal motor ones. Finally, 'valence' is used to refer to the direction of value assignment (either positive or negative) as opposed to its absolute value or intensity, and 'affect' to refer collectively to the neural representations and processes related to emotion.

Three main themes are developed here. First, contrary to a widespread view, the amygdala has a major role in positive affect, not exclusively – or even mainly – in negative affect. Second, contrary to an influential model, recent evidence points to a distinction between emotion and reward and contradicts previous conclusions about the role of the amygdala in reward processing. Third, contrary to the tendency to consider the amygdala as a single 'thing', different parts of the amygdala mediate specific and general effects of reward on behavior.

Amygdala function in positive affect

The idea that the amygdala functions primarily in negative affect remains firmly entrenched, as evidenced by theories treating the amygdala as a 'protection device' that prevents animals from engaging in potentially harmful behaviors [16] or as a 'fear module' [17]. In part, this impression results from the dominance of fear conditioning as a model of emotional learning [18,19]. Neuroimaging studies, especially early ones, also viewed the amygdala as processing primarily negative emotions [20]. Yet numerous studies point to a role for the amygdala in processing positive affect.

Evidence from monkey amygdala

Neurophysiological studies in monkeys provide strong evidence for a role for the amygdala in positive affect. For example, Paton *et al.* [21] recorded from single neurons in the amygdala while visual stimuli acquired a positive or negative valence through Pavlovian conditioning. Their monkeys saw pictures that the experimenters paired with a liquid reward (positive reinforcement), an air puff directed at the face (negative reinforcement) or nothing (nonreinforced stimuli). The monkeys showed their learning by licking after positive pictures or blinking after negative ones. To determine whether neuronal activity reflected reinforcer valence, rather than stimulus features, pictures that initially signaled the agreeable liquid later signaled the aversive air puff, and vice versa. If amygdala activity reflected stimulus–valence pairings, then neuronal activity should change over trials to reflect

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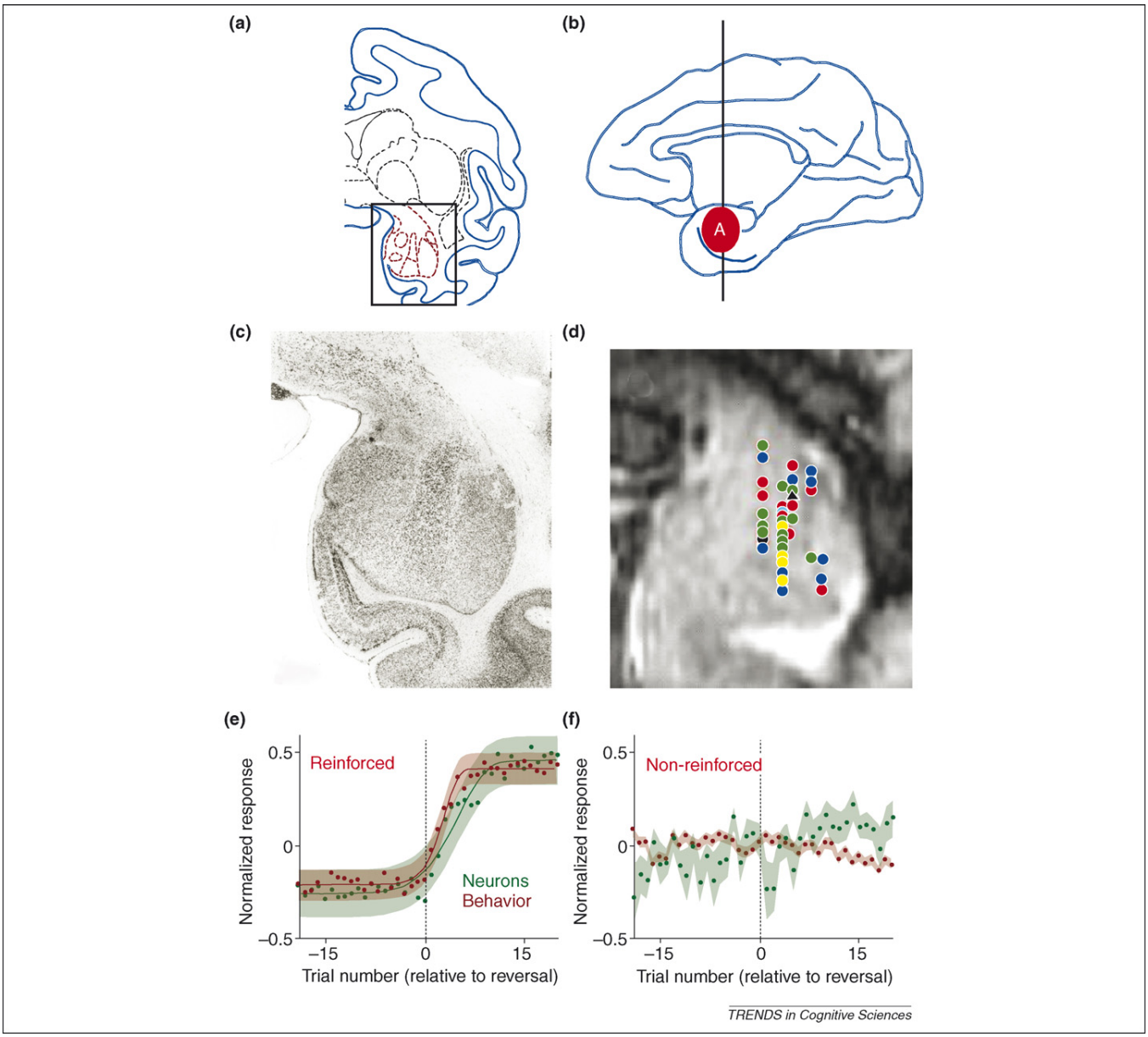

Figure 1. Primate amygdala: positive and negative reinforcement. **(a)** Line drawing of a coronal section through the right hemisphere of a rhesus monkey brain. The section is located at roughly the middle of the amygdala in its anterior–posterior dimension. The rectangle is drawn around the amygdala and neighboring structures. **(b)** Medial aspect of the right hemisphere of a rhesus monkey brain. The line corresponds to the level of the section shown in (a). **(c)** Photomicrograph of a Nissl-stained coronal section matching the location of the rectangle shown in (a). Due to differences in cell sizes, cell packing density and staining properties, some of the nuclear boundaries of the amygdala are clearly visible. **(d)** Recording sites (filled circles) of amygdala neurons with activity that reflected positive value or negative value independent of image identity and independent of upcoming motor responses. The analysis considered neuronal activity during picture presentation and the ensuing unfilled interval, before the delivery of the liquid reward or air puff. Hence, the neuronal activity is predicting the valence of the expected reinforcer. Because recording sites are collapsed across 2 mm in the anterior–posterior dimension, some circles represent multiple cells. Green circles show locations of cells that signaled positive reinforcement, red circles show locations of cells that signaled negative reinforcement, and blue circles show locations of cells that predicted neither type of reinforcement. Yellow filled circles and black triangle show locations of multiple cells, some signaling positive reinforcement and some negative reinforcement. **(e)** Average activity of amygdala neurons that are active in relation to a positive or negative picture (green) and behavioral responses (gray) plotted as a function of trials from reversal (0). Shaded regions show 95% prediction intervals for best fit functions. On average, neurons begin to change their activity within a few trials of a change in picture value (i.e. a reversal), and across the population, the rate of change after a reversal is indistinguishable from the rate of changes in responses (i.e. learning). Thus, in principle, decisions to lick or blink could be based on the representation of picture value provided by the amygdala. **(f)** Same analysis as in (e) applied to neurons active in relation to nonreinforced pictures. (d), (e) and (f) modified, with permission, from Ref. [21].

the new pairings. Paton *et al.* observed exactly that (Figure 1d). Furthermore, after reinforcer reassignment, licking and blinking responses to the reinforced stimuli correlated closely with neural activity (Figure 1e, f), suggesting that the changes in associative encoding in amygdala neurons might be responsible for the learning. Importantly, one population of neurons encoded positive valence and a largely separate group of cells encoded negative valence. There was no obvious spatial segregation of these populations, and most were in the basolateral portion of the amygdala (BLA; Figure 1d). Although other physiological studies have also shown amygdala activity reflecting aspects of positive reinforcement [22,23], earlier studies failed to observe neurons similar to those recorded by Paton *et al.* [24,25]. This apparent discrepancy probably resulted from the use of a single, overlearned pair of

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stimuli, leading to a situation in which one trial can trigger a switch between two well-learned states, rendering learning unnecessary. Regardless, the recent results make it clear that the amygdala has signals related to positive, as well as negative, reinforcement. In addition to providing a foundation for representing expected reinforcement outcomes, such signals might also influence perception and memory (Box 1).

Additional evidence for amygdala contributions to positive affect comes from studying emotional reactions in marmoset monkeys. Monkeys studied by Braesicke *et al.* [26] viewed high- or low-incentive food through a transparent barrier for 20 seconds, and later had access to the food for five minutes; the 20-second and five-minute periods constituted the anticipatory and consummatory periods, respectively. During the anticipatory period, the visual properties of the food served as a conditioned stimulus (CS), which predicted its subsequent availability. With repeated experience, the monkeys developed emotional responses to the high-incentive but not low-incentive food during the anticipatory period. The sight of the high-incentive food induced looking and scratching at the barrier, and also increases in blood pressure and heart rate. The cardiovascular responses also occurred during the consummatory period, again for the high- but not low-incentive food. Monkeys with selective bilateral amygdala removals lacked the CS-induced cardiovascular responses during the anticipatory period but they continued to show both skeletomotor responses during the anticipatory period as well as cardiovascular responses during the consummatory period. Presumably, the conditioned autonomic responses during the anticipatory period reflected increases in arousal that accompanied the sight of the high-incentive food, which provides further evidence that the amygdala contributes to positive affect.

Studies of reinforcer devaluation also demonstrate the role of the amygdala in positive affect. As reviewed previously [27], amygdala lesions cause dramatic deficits in the ability of monkeys to choose an object based on the current value of a food reward associated with that object. Unlike intact monkeys, which avoid an object associated with a food recently consumed to satiety, monkeys with amygdala lesions choose an object associated with a more preferred food, whether devalued by selective satiation or maintaining a high value. Recent studies have clarified the role of the amygdala in this task. Experiments using reversible inactivations [28] have shown that the role of the amygdala is limited to updating the monkeys' estimation of the current biological value of the food. Once the updating function has been accomplished, the amygdala is no longer necessary for choosing objects based on current food value. Accordingly, representations of expected food value must be stored outside the amygdala, a point taken up later.

Box 1. Influence of amygdala activity on sensory processing

One recent study focused on the relationship between the activity of amygdala neurons and those in anatomically related cortical fields in cats. Specifically, Paz *et al.* [68] investigated whether the activity of neurons in the BLA influenced the activity of neurons in the perirhinal and entorhinal cortex. They recorded from trios of perirhinal, entorhinal and BLA neurons and used a method of spike-triggered joint histograms in which the amygdala activity acted as a reference to study correlated perirhinal and entorhinal cortex activity (collectively, 'rhinal' cortex activity). Under most conditions, despite the strong reciprocal connections between the perirhinal and entorhinal cortex, there is surprisingly little correlated neuronal firing in the perirhinal and entorhinal cortex. If, however, analysis is restricted to rhinal cortex activity that occurs in close temporal proximity to amygdala cell firing, then a much greater proportion of rhinal neurons shows correlated activity. These data suggest that when BLA neurons discharge, impulse transmission between the perirhinal and entorhinal cortex is facilitated. Interestingly, Paz *et al.* found that the proportion of rhinal cortex neurons showing significantly correlated firing increased markedly after amygdala neuron firing triggered by the delivery of unexpected rewards. The timing was such that this occurred shortly after the amygdala cell firing, suggesting that the amygdala activity was a causal factor. Although these joint correlations could stem from common, third-party inputs to both the perirhinal and entorhinal fields, it seems likely that it is the amygdala that serves to enhance sensory processing in the rhinal cortex. Because the rhinal cortex serves as a gateway for sensory information to reach the hippocampus, the increased rhinal cortex transmission could lead to enhanced processing and storage of emotional memories, as Paz and his colleagues propose. This idea is consistent with the identified role for the amygdala in facilitating hippocampal-dependent information storage [69]. Alternatively, because neurons in the perirhinal cortex have reciprocal connections with higher-order modality-specific neocortical sensory processing areas [70], it could represent a general mechanism whereby surprising and/or salient events lead to enhanced sensory processing. For example, in humans, the amygdala is implicated in the enhanced sensory processing of angry and fearful faces in the inferior temporal visual cortex [71] and in the enhanced processing of emotionally laden words [72].

Evidence from rat amygdala

Studies of Pavlovian approach behavior in rats also inform the role of the amygdala in positive affect. Rats are exposed – on separate occasions – to two different stimuli, and food is provided in association with only one of them. Later, both stimuli appear simultaneously but no food shows up. Although the animals do not need to do or learn anything, they nevertheless spend more time near the stimulus associated with the food. This Pavlovian approach behavior reflects a tendency to associate physically with stimuli of positive affective valence. In some experimental settings, rats with lesions of the central nucleus of the amygdala (CeA) fail to show approach behavior [29]; in others, damage to portions of the BLA, which consists of the lateral, basal and accessory basal nuclei, lead to this impairment [30]. The final section takes up differences in function of the CeA and BLA; both regions mediate positive affect.

Although the neurophysiological work discussed so far was carried out in nonhuman primates, Schoenbaum *et al.* [31,32] also reported that neuronal activity in the rat BLA reflects stimulus–reinforcer associations, including positive ones. In their study, one odor instructed a 'go' response (entering a fluid port to obtain sucrose) and a different odor instructed a 'no-go' response. If rats entered the fluid port on a no-go trial, they received quinine, an aversive fluid, rather than sucrose, a positive one. As rats learned the task, the activity of many BLA neurons came to reflect either sucrose or quinine, independent of the odor. This activity changed in parallel to learning, similarly to the result shown in Figure 1e, for monkeys. Taken together, the data in rats and monkeys provide strong

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support for the idea that the BLA is involved in encoding the predictive relationship between stimuli and primary reinforcers such as food and fluids, and that it encodes positive valences as often as negative ones.

Evidence from human amygdala

Functional imaging studies in humans have likewise provided evidence supporting the role of the amygdala in positive affect. Somerville *et al.* [33] presented subjects with pictures of unfamiliar faces. Across sessions, the subjects learned common first names for each face, and some additional information that was positive, negative or neutral. For example, the experimenters told subjects that 'Emily helps the homeless' or that 'Bob is a deadbeat dad'. Somerville *et al.* found that the right amygdala was selectively sensitive to faces that had been associated with emotional descriptions – either positive or negative – compared with those with faces that had been associated with neutral information. Sometimes, the same subjects could not report the information associated with the faces. Somerville *et al.* suggested that the amygdala generates a nonspecific arousal signal but their results are equally compatible with the idea that the amygdala encodes stimulus–valence associations that are sometimes inaccessible to conscious awareness.

In support of the latter idea, Johnsrude *et al.* [34] presented human subjects with two-dimensional abstract images, each paired with a high, medium or low probability of food reward. They found that subjects expressed a preference for images paired with a high reward probability, although they remained unaware of the relationship between the images and food probability. Patients with anterior temporal lobe resections that included the amygdala, however, failed to display such preferences. Taken together with the neuroimaging results of Somerville *et al.* [33], this result supports the idea that the amygdala mediates an association between sensory inputs and their affective valence, that people can remain unaware of these associations yet behave on the basis of them, and that the role of the amygdala for positive emotions is at least as important is its role for negative ones.

Amygdala function in emotion versus reward

In an influential two-dimensional model of emotion, developed by Rolls [35], emotions are seen as by-products of positive and negative reinforcement. One dimension comes from administration of negative reinforcement to administration of positive reinforcement, which corresponds to emotions ranging from fear to pleasure, respectively. The second dimension comes from termination or omission of positive or negative reinforcers, with emotions ranging from rage to relief, respectively. This model emerged, in part, from neuropsychological studies in the 1960s and 1970s which seemed to indicate that the same neural structures mediated reward processing and emotion (Box 2). Recent work has overturned these neuropsychological results and led to a reevaluation of the model.

Stimulus–reward association

Reward processing is often assessed with tests of stimulus–reward association, which measure the ability to link neutral stimuli with reinforcers such as foods, fluids or certain drugs. Historically, tasks such as object-reversal learning and 'win-stay, lose-shift' have been used to assess reward processing in monkeys. Both tasks require the subject to choose objects according to the presence or absence of a food reward. In object-reversal learning, animals must rapidly make and break stimulus–reward associations. After a reversal, a stimulus that was initially associated with a reward no longer is, and a different stimulus previously associated with no reward, now is. In win-stay, lose-shift, after a single acquisition trial in which one of two stimuli is associated with a reward, animals must return to the stimulus associated with a reward and avoid the other one. Profound impairments on these tasks were reported to follow 'amygdala' lesions in monkeys [36–40], and these findings were widely interpreted as supporting a role for the amygdala in forming stimulus–reward associations. Because amygdala damage was also linked to changes in emotional behavior [41], the results pointed to a role for the amygdala in both reward processing and emotion.

Unfortunately, the older studies cited above, which formed the basis of the two-dimensional model described

Box 2. Common brain systems for emotion and reward?

The effects of (nonselective) amygdala lesions have, historically, closely resembled those of OFC lesions. This has given rise to the view that there is a single neural system underlying both emotion and reward processing [35,38,40,73]. For example, bilateral damage to either the amygdala or OFC disrupts both emotional responses [43,50,74,75] and reinforcer-devaluation effects [76,77]. In addition, both structures were thought to be necessary for stimulus–reward association, as measured by object-reversal learning and instrumental extinction [37,78–80]. If the neural bases of emotion processing and reward processing are one and the same, brain damage that yields an impairment in one domain should also produce impairment in the other; dissociations between the neural bases of emotion and reward should not be possible. Recent work, however, reveals such dissociations. In one case, rhesus monkeys with selective amygdala lesions that exhibited markedly reduced emotional reactions to a fake snake [50] showed no impairment on a classic test of stimulus–reward association, object-reversal learning [44]. Thus, selective amygdala lesions, which have a clear effect on emotional processing, have no effect on the type of reward processing required by object-reversal learning (Figure 2). Even more striking, when given a test of extinction, monkeys with selective amygdala lesions, rather than being impaired in reward processing, were facilitated [81]. In another study, carried out by Rudebeck *et al.* [82], rhesus monkeys with lesions of either the anterior cingulate gyrus or the banks of the anterior cingulate sulcus were tested for their emotional responses to two different types of stimuli: social stimuli (e.g. a video clip of the face of a dominant male monkey or video of female monkey perineum) and a fake snake. The same groups were tested for their ability to form stimulus–reward associations using the object-reversal learning task. Monkeys with lesions of the anterior cingulate gyrus showed a selective deficit in their emotional reactions to social stimuli, whereas monkeys with anterior cingulate sulcus lesions showed a selective deficit in their emotional reactions to fake snakes. As was the case for monkeys with selective amygdala lesions, however, neither group was impaired in object-reversal learning. These data reveal that several brain regions, including the amygdala, OFC and anterior cingulate cortex, are involved in responding appropriately to emotion-provoking cues, and, furthermore, that the regions mediating emotional reactions (if not emotions, *per se*) are not the same as those for stimulus–reward processing, at least not as traditionally evaluated.

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earlier, used aspirative or radiofrequency methods to remove the amygdala. In addition to removing the neurons that comprise the amygdala, these methods damage projection fibers passing near and through the amygdala. Findings based on more selective lesions of the amygdala, made with fiber-sparing excitotoxins, have overturned the earlier findings and conclusion [42]. Specifically, although nonselective, aspirative lesions of the amygdala severely disrupt the performance of both tasks [37–39], the more selective, excitotoxic lesions lead to only a mild, transient impairment on win-stay, lose-shift [43] and have no effect on object-reversal learning [44] (Figure 2c, d). Thus, the two tasks that historically have linked the amygdala with stimulus–reward association in monkeys – the win-stay, lose-shift task and the object-reversal learning task – do not depend on the amygdala.

So how could the monkeys perform these tasks without an amygdala? One plausible explanation is that monkeys quickly learn a visually based performance rule [44] and treat the positive reinforcement much as they would any other sensory signal. According to this idea, the occurrence (or nonoccurrence) of food guides the selection of a performance rule, and this function is independent of the amygdala. Once a performance rule has been learned, the role of food in such tasks is largely limited to its informational value, as opposed to its reinforcing or emotional value, and this informational processing does not depend on the amygdala. The false-positive results from 'amygdala' lesions that caused inadvertent damage to other structures [36–40] implicate the inferior temporal cortex and its connections with the medial thalamus or prefrontal cortex as the likely source of the impairments because their axonal course takes them close to the amygdala [45].

Does this analysis mean that the amygdala has no role in stimulus–reward association? Not really. It means that, despite their intent, neuropsychologists in the 1970s and 1980s tested neither primate amygdala function nor stimulus–reward association, at least not in any sense relevant to affective information processing. The simple view that the amygdala has a major role in associating stimuli with rewards cannot stand up to critical scrutiny.

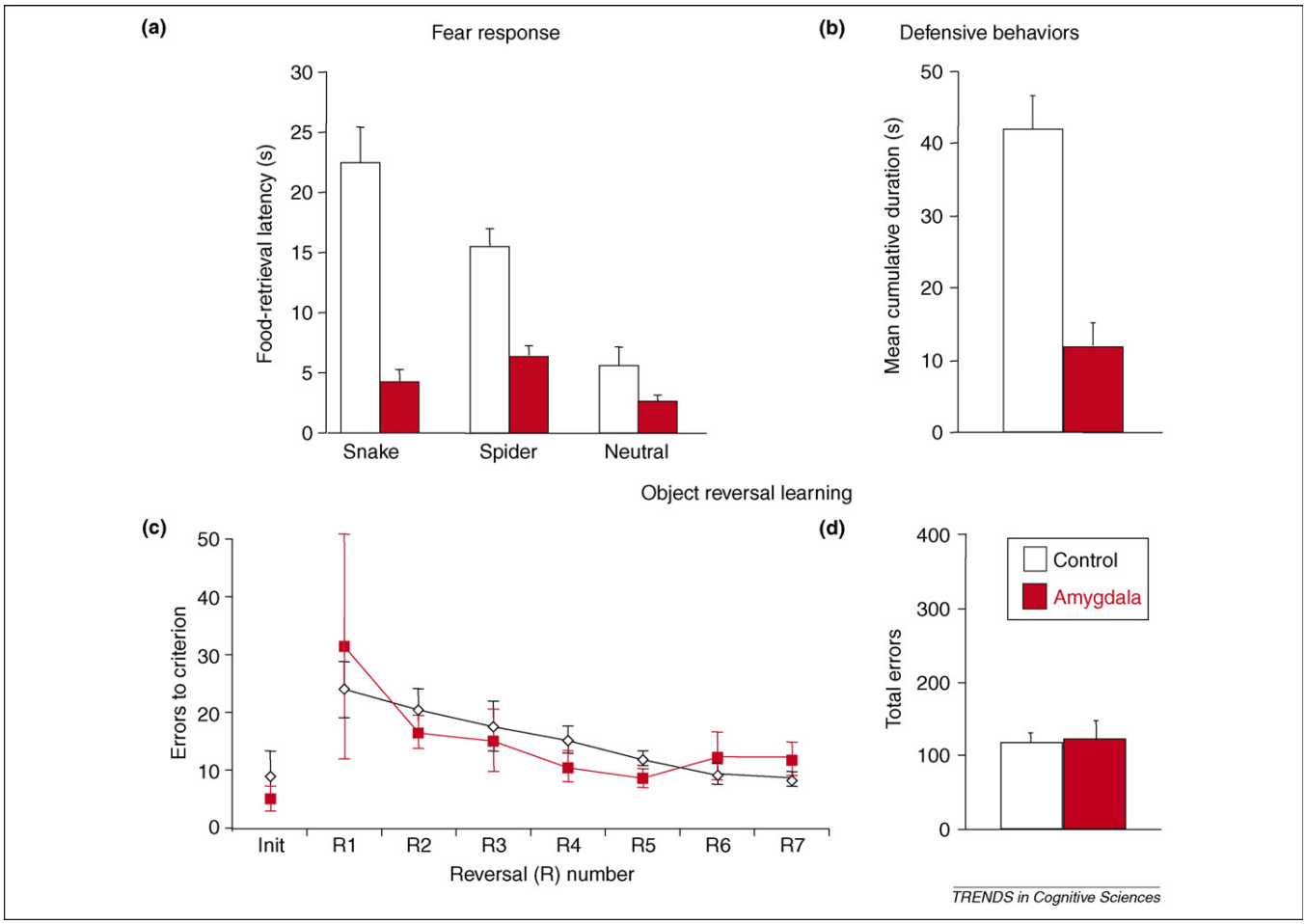

Figure 2. Amygdala, reward processing and emotion. **(a)** Food-retrieval latencies of rhesus monkeys when confronted with a rubber snake, a rubber spider or neutral objects. On each trial, a single object was placed within a Plexiglas box; monkeys could retrieve a food reward located on top of the box only by reaching over the object. When confronted with the snake, control monkeys often failed to take the food within the 30-second trial limit, in which case they were assigned a score of 30 seconds. Monkeys with amygdala lesions reached for the food significantly faster than unoperated controls on trials with the snake and spider but not on trials with neutral objects. **(b)** Relative to unoperated controls, monkeys with amygdala lesions exhibited significantly less defensive behavior (moving away, freezing, head aversion, piloerection etc.) when confronted with a rubber snake. Duration of defensive behavior can exceed the trial length because the duration of several different behaviors is summed. **(c)** Monkeys with selective amygdala lesions learn a visual object discrimination problem (Initial learning, Init) and subsequent object reversals (R1–R7) as quickly as unoperated controls. **(d)** Same data as in (c) collapsed across reversals. There is no difference between the two groups in their ability to perform object reversals. Modified, with permission, from Refs [44,50].

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As reviewed elsewhere [27], there are many tasks conducted with food reward, some of them taxing, for which the amygdala is not essential. In addition, as we have just seen, the amygdala has no part in many tasks that would, at first glance, seem to require the association of stimuli with food rewards. As discussed earlier, however, the amygdala is essential for linking objects with the current value of food rewards. To the extent that an affective tag from the amygdala provides this value signal [46,47], the amygdala contributes to stimulus–reward association.

Emotional responses

Another approach to addressing affect in monkeys relies on inferring emotional states from actions. For example, it is widely accepted that defensive behaviors represent the expression of fear in an animal. Nonhuman primates express defensive responses through vocalizations, piloerection, freezing, fleeing, or hostility and aggression, among other behaviors.

To examine the neural substrates of emotion in monkeys, we used a method adapted from Mineka *et al.* [48] to assess behavioral reactions to emotionally provocative stimuli. Monkeys saw objects located inside a clear Plexiglas box. These consisted of a rubber snake, a rubber spider and neutral objects, presented one at a time. In addition, a food reward was placed on top of the far edge of the box. On each trial, the monkeys could reach for and procure the food, which was always located at the edge of the box farthest from the monkey. Thus, this method pits approach responses elicited by food against defensive responses caused by the snake.

As expected, intact monkeys showed robust emotional reactions to a fake snake. Although they quickly reached for the food reward on trials with neutral objects, they hesitated or failed to reach altogether on trials with the snake. The facial expressions and movements made in the presence of the snake were mainly defensive, including moving to the back of the cage, eye and head aversion, freezing and piloerection. Their behavior matched closely that described in previous reports, which observers interpreted as orienting responses, wariness and fear [48,49]. Amygdala lesions have a profound effect on these behaviors. In the presence of the snake, monkeys with selective amygdala lesions show much shorter food-retrieval latencies (Figure 2a) and fewer defensive responses (Figure 2b) compared with controls. In short, they show little or no emotional reaction to the fake snake. Importantly, in the same monkeys, selective amygdala lesions had no effect on object-reversal learning but yielded a dramatic reduction in emotional responses [44,50]. These findings point to a distinction between reward processing and emotional reactions, with the amygdala having a crucial role in the latter and only a conditional role in the former.

Amygdala function in specific and general affect

The discussion to this point has focused on two dichotomies: one involving positive versus negative affect, the other involving reward processing versus emotional reactions. This section deals with a third dichotomy: specific versus general affect.

Recent research in rats suggests contrasting roles for the BLA and the CeA in affective processing. Several studies have demonstrated a role for CeA in positive affect. Its role in Pavlovian approach behavior, for example, has been described earlier. Another experimental procedure employed in exploring the neural bases of positive effect is known as Pavlovian-instrumental transfer (PIT), described below. Blundell *et al.* [47] and Corbit and Balleine [51] have clarified the role of the amygdala in PIT, showing that BLA and CeA operate in parallel to mediate distinct aspects of affect. Whereas BLA is essential for linking a stimulus with specific sensory features of food (e.g. taste) that have affective properties based on nutritive value, CeA is essential for linking a stimulus with general affective properties of food (e.g. positive emotion or arousal). This dissociation was demonstrated in an experiment in which rats learned, first, that two different food rewards (F1 and F2) could be earned by distinct lever presses. For example, a left lever press would produce F1 and a right lever press would produce F2. In a second phase of training, three different sounds (S1–3) were paired with three different foods (F1–3) through experimenter-generated paired presentation of S1 with F1, S2 with F2 and S3 with F3. In test conditions in which no food was provided, Corbit and Balleine found that presentation of S1 increased responding only on the lever that produced F1, whereas presentation of S2 increased responding only on the lever that produced F2. These influences are specific to a given food. By contrast, presentation of S3, which was not paired with any action, increased the performance of both actions. Thus, S3 seemed to have a general influence on behavior.

BLA lesions disrupted reinforcer-specific affect but left the general affect untouched. Conversely, lesions of the CeA disrupted general affect but not specific affect [48,49]. These findings clarify the relationship between sensory cues and their affective significance. General affective processing brings animals physically closer to a 'positive' object, such as one associated with food, and can influence the performance of learned actions by providing increased arousal. It remains to be seen whether all CeA-dependent functions that operate independently of the identity of the reinforcer, such as conditioned orienting and conditioned suppression [52], can be classified as being due to general affective processing. Specific affective processing promotes behaviors that aid in procuring and consuming a particular type of reward, and can influence not only the performance of learned actions, as described earlier, but also can enhance feeding in sated rats [53]. Although the specific and general roles for the amygdala are most well studied for positive affect in appetitive settings, it seems likely that the same idea applies to negative affect [54].

Because the BLA is essential for two different phenomena reviewed here – responding appropriately after changes in reinforcer value (mentioned earlier) and reinforcer-specific PIT – the question arises whether there is a common mechanism underlying the two. For example, perhaps the representation of expected food value mediates both reinforcer-devaluation effects and reinforcer-specific PIT. Although this idea is appealing, the evidence argues against it; devaluation and transfer effects seem to be mediated by different aspects of learned associations [55].

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Amygdala function: passions and prejudices

The function of the amygdala is more general than often thought: it contributes to both positive and negative affect, not just – or even mainly – to negative affect. Its function is also more specific than some current theories suggest: it makes an essential contribution to emotional responses, such as reactions to a fake snake or to the sight of food, yet has little or no role in the reward processing that underlies tasks such as object-reversal learning and win-stay, lose-shift. These findings also show that reward and emotion are not identical. Although the amygdala is essential for processing emotional aspects of reward, including its valence (positive or negative) and its relative value (e.g. good versus superb), many other aspects of reward processing are effected outside the amygdala. In addition, the amygdala is less homogeneous than commonly recognized: within the amygdala, the central amygdala mediates a general affective reaction that promotes the appropriate skeletomotor and autonomic response to a particular opportunity or threat, whereas the BLA mediates a more specific affective reaction, one linked to the sensory properties of the reinforcer.

As indicated earlier, the amygdala, particularly its basolateral portion, is reciprocally connected to many parts of the neocortex, including the orbital frontal cortex (OFC) and sensory areas. Figure 3 shows a model of amygdala function in the context of its connections with sensory areas such as the inferior temporal and perirhinal cortex (IT/PRh) and with the OFC, which is thought to be important for response selection. Some amygdala functions are carried out in concert with the OFC [56,57], such as updating the values of expected outcomes. Once the amygdala completes its updating function, the OFC stores the values of expected reward outcomes [58]. Thus, interactions between the amygdala and OFC enable animals to choose advantageously in the face of multiple competing cues, based on the current value of associated outcomes. The 'direction' of the updating – from amygdala to OFC – is supported by lesion studies in rats demonstrating that the amygdala is necessary only temporarily for acquiring stimulus–food associations, whereas the OFC is essential at all times tested [59], and by physiological studies in rats showing that OFC neurons fail to code value in a normal fashion in the absence of the amygdala [60]. This amygdala–OFC mechanism enables animals to maximize positive outcomes (e.g. high-value foods or desirable sexual partners) and to minimize negative ones (e.g. distasteful foods or pain). Because the choices of animals are guided by the value of the outcome, the amygdala–OFC network is thought to contribute to goal-directed behavior and decision making. Amygdala interactions with portions of medial frontal cortex might have an analogous role for associating actions – as opposed to cues – with current biological value [61,62]. At the same time, it should be acknowledged that the OFC influences neuronal activity and associative encoding in the amygdala [63]. It would be valuable to determine whether similar amygdala–OFC interactions are evident in nonhuman primates and, if so, whether they apply to caudal, agranular portions of the OFC common to all mammals, and also to the dysgranular and granular OFC regions specific to primates [64].

Recent evidence suggests that IT/PRh interaction with the frontal cortex is necessary for implementation of visually guided rules [65,66]. Interestingly, although object-reversal learning does not require an intact amygdala, it does depend on both the OFC and the 'rhinal cortex' – that is, the perirhinal and entorhinal cortex [67]. Thus, as suggested in Figure 3, it is possible that object-reversal learning, together with other visually guided rules, depends on IT/PRh–OFC mechanisms. The two routes to the OFC could subserve reward-based decisions generally, with the IT/PRh–OFC route processing visual information (including the visual, 'informational' aspect of foods and other rewards) and the amygdala–OFC route processing

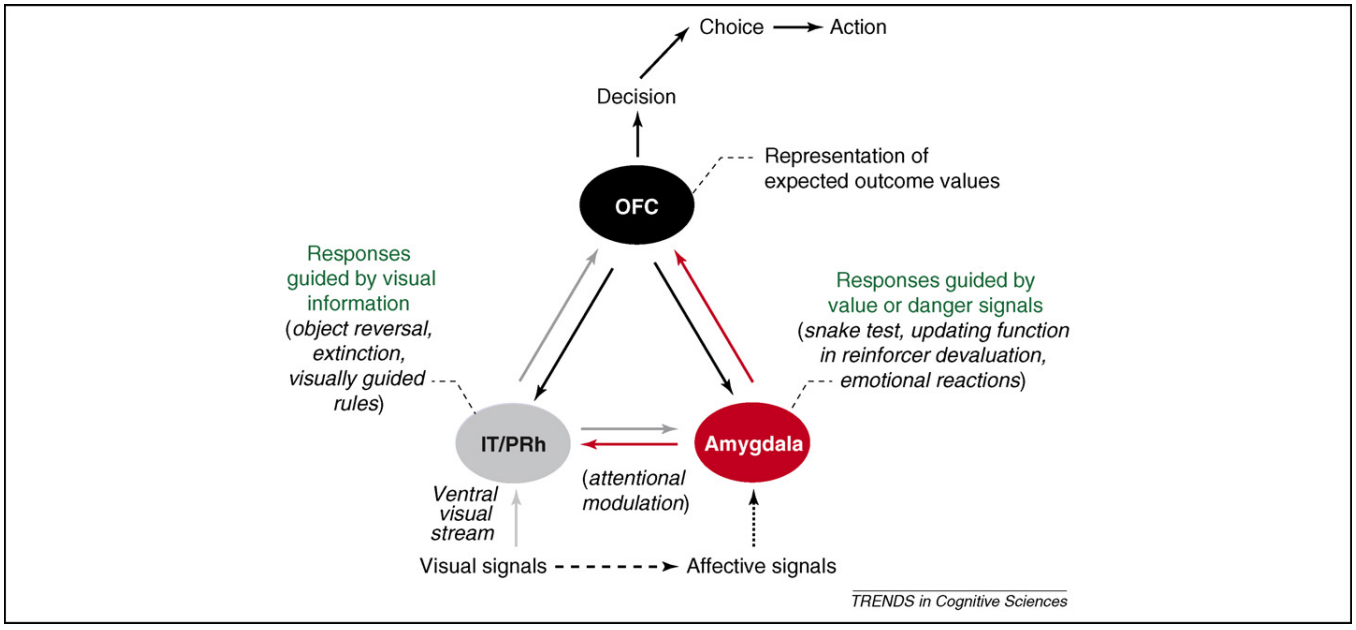

Figure 3. Schematic diagram of the interactions of the amygdala, IT/PRh and OFC in selected affective processes. The model suggests that both the amygdala and IT/PRh interact with the OFC to guide decisions. In addition, each structure interacts with each of the others. For example, the amygdala can modulate activity in the IT/PRh to enhance sensory processing of biologically significant stimuli and events.

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affective information. The amygdala interacts not only with OFC to promote adaptive choices, but also interacts with sensory areas, directly or indirectly, to influence perception and memory (Box 1).

One of the most important aspects of amygdala function, and one of the least well understood, is the extent to which it covertly influences daily life activities and experiences. As discussed earlier for human subjects, Pavlovian processes can lead to subconscious, amygdala-dependent preferences and biases for (and probably against) stimuli. Physiological studies in rats indicate that the amygdala is important for establishing links between cues and values of expected outcomes. The work in marmosets shows that the amygdala has a special role in anticipatory autonomic and neuroendocrine responses, as opposed to those that occur during the anticipated event. Taken together, these studies suggest that the amygdala mediates not only unconscious biases and preferences about objects, but also similar feelings about abstractions, such as ideas, concepts and beliefs, and also dreads, hopes and dreams. The amygdala is not only essential for establishing these affective associations, but also has an important role in registering changes from the *status quo*. Finally, the distinction between an amygdala-independent route for visually guided rules and an amygdala-dependent route for affective information brings to mind the age-old struggle between rational and emotional decision making. Although affective signals can coincide with and support rational decisions, they often produce conflicts, as in moral dilemmas. The amygdala ensures – for better and worse – that affective signals enter into the decision-making process.

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