Neuron, Vol. 48, 175–187, October 20, 2005, Copyright ©2005 by Elsevier Inc. DOI 10.1016/j.neuron.2005.09.025

Contributions of the Amygdala to Emotion Processing: From Animal Models to Human Behavior

Review

Elizabeth A. Phelps[1,*] and Joseph E. LeDoux[2]
[1]Department of Psychology
New York University
4-6 Washington Place
New York, New York 10003
[2]Center for Neural Science
New York University
4-6 Washington Place
New York, New York 10003

Research on the neural systems underlying emotion in animal models over the past two decades has implicated the amygdala in fear and other emotional processes. This work stimulated interest in pursuing the brain mechanisms of emotion in humans. Here, we review research on the role of the amygdala in emotional processes in both animal models and humans. The review is not exhaustive, but it highlights five major research topics that illustrate parallel roles for the amygdala in humans and other animals, including implicit emotional learning and memory, emotional modulation of memory, emotional influences on attention and perception, emotion and social behavior, and emotion inhibition and regulation.

Introduction

Over the past two decades, the amygdala has gone from a being an obscure region of the brain to practically a household word (the phonetic ring of the word "amygdala" was the subject of a piece in the *New York Times* recently). Although known to be involved in emotion for some time (Weiskrantz, 1956), much of the recent scientific interest in the amygdala stems from its role in fear conditioning, a form of emotional learning in which a neutral stimulus comes to elicit defensive behavior and physiological responses after being associated with an aversive event (for review see LeDoux 1996, 2000; Maren, 2001; Davis and Whalen, 2001). This research, mostly conducted in rats, has not only identified the amygdala as a central structure in the circuitry underlying fear conditioning but has also implicated specific synaptic connections and molecular cascades in the amygdala in the acquisition and storage of memories of fear conditioning (see Rodrigues et al., 2004). Recent studies in humans have begun to search for parallels to the animal work (e.g., LaBar et al., 1995; Morris et al., 1998a, 1998b; Phelps et al., 2000; Adolphs et al., 2005). The results have complemented but also extended the basic findings from animals regarding the amygdala's role in emotional processing. In this review, we highlight what has been learned about the amygdala's involvement in emotion, focusing on several areas of research where the amygdala has been shown to play similar roles in humans and other animals.

Implicit Emotional Learning and Memory

It is now widely accepted that many brain systems are capable of learning and storing information (Squire and Kandel, 1999; Eichenbaum, 2002; Schacter, 1996). Some of these function explicitly and give rise to our conscious memories, while others function implicitly and store memories that are accessed and used automatically, or unconsciously. Emotion systems in the brain are generally viewed as belonging to the category of systems that form implicit memories (LeDoux, 1996). This does not imply that memories for emotional situations are only formed implicitly, as other systems, such as the explicit memory system of the medial temporal lobe, can form their own memories of emotional situations. It instead implies that the memories formed and stored by emotion systems are implicitly stored and accessed. This is in fact true of most systems that store information. These systems are perhaps not best thought of as memory systems. Instead, memory and its underlying neuronal plasticity are features that allow such systems to perform their function (emotional control, sensory processing, motor regulation, etc.) more effectively (LeDoux, 2002; Eichenbaum, 2002).

Much of the renewed enthusiasm for studies of emotion in neuroscience has come from studies of emotional learning and memory, especially studies of conditioned fear in rats and other mammals (LeDoux, 2000; Walker and Davis, 2002; Davis and Whalen, 2001; Fanselow and LeDoux, 1999; Kapp et al., 1992; Maren, 2001). In this procedure, the subject is exposed to an emotionally neutral conditioned stimulus (CS), such as a tone, that is paired with an aversive unconditioned stimulus (US), such as an electric shock. An association is formed between the CS and US, and later presentation of the CS alone elicits behavioral defense responses and associated autonomic and endocrine adjustments. The subject also typically forms an association between the US and the environmental context, thus often necessitating the testing of conditioning to the CS in a novel context.

Research on the neural system underlying fear responses conditioned by tone-shock pairings has implicated circuits into and through the amygdala as essential to the acquisition and storage of a memory of the conditioning experience and the expression of fear responses (Figure 1) (Kapp et al., 1992; Davis and Whalen, 2001; Fanselow and LeDoux, 1999; LeDoux, 2000; Maren, 2001; Medina et al., 2002; for an alternative view, see Cahill et al., 1999). The lateral nucleus (LA) is typically viewed as the sensory interface of the amygdala and as a key site of plasticity, while the central nucleus (CE) is viewed as the output region (but see Pare et al., 2004). LA receives inputs from both thalamic and cortical stations in the auditory system, and both are involved in CS transmission. LA projects to CE both directly and indirectly (Pitkänen et al., 1997). It is still unclear whether the direct connection from LA to CE is sufficient or whether a link through the basal nuclei and/or the intercalated cell masses might be involved, or even whether direct sensory connections to CE might play a role (see Pare et al., 2004). Other amygdala areas, though, do not seem to play an essential role in this simple form of conditioning (Amorapanth et al., 2000;

*Correspondence: liz.phelps@nyu.edu

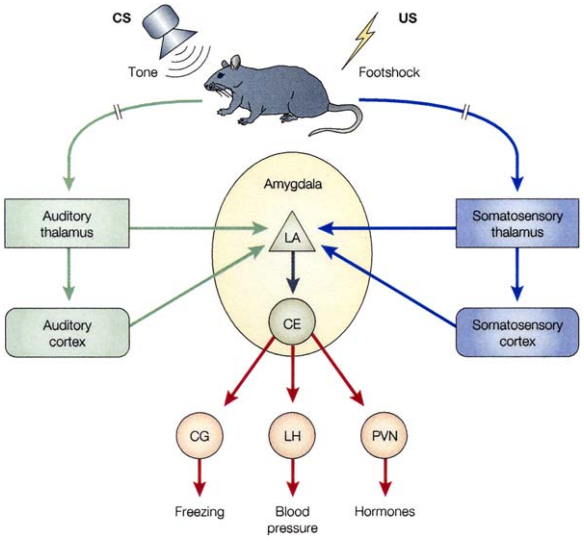

Figure 1. Neural Pathways underlying Fear Conditioning

Fear conditioning is a procedure in which an emotionally neutral conditioned stimulus (CS) is presented in association with an aversive unconditioned stimulus (US). In studies of rats, the CS has typically been an auditory tone and the US an electric footshock. The pathways mediating auditory fear conditioning in rats involve the convergence of the CS and US pathways onto single cells in the lateral nucleus of the amygdala (LA) from thalamic and cortical processing regions in the sensory systems that process the CS (auditory system) and US (somatosensory system). The LA then connects with the CE both directly and by way of other amygdala regions (not shown). Outputs of the CE then control the expression of fear responses, including freezing behavior and related autonomic nervous system (e.g., blood pressure and heart rate) and endocrine (pituitary-adrenal hormones) responses. Lesion and imaging studies, described in the text, have confirmed that the human amygdala is also involved in fear conditioning, but the involvement of subregions of the amygdala is still poorly understood in humans. CG, central gray; LH, lateral hypothalamus; PVN, paraventricular hypothalamus. From Medina et al. (2002).

Nader et al., 2001). For context conditioning, the inputs appear to enter the amygdala from the hippocampus (Maren, 2001; LeDoux, 2000). Connections likely to mediate this processing including the projections from the ventral CA1 and subiculum to the basal amygdala. As with tone conditioning, the CE is involved in controlling responses, but the input region involves synapses in the basal nucleus. The bed nucleus of the stria terminalis also seems to be involved in context conditioning (Sullivan et al., 2004; Walker et al., 2003b). While most fear conditioning studies to date have involved rodents, recent work in primates has confirmed the role of the central amygdala (Kalin et al., 2004).

Recent electrophysiological studies have identified two groups of cells in LA, one involved in initial learning and the other in memory storage (Repa et al., 2001; Medina et al., 2002; Radwanska et al., 2002). These cell types are in separate regions of the dorsal part of the LA, with each region containing about 12,000 neurons (unpublished data). This precise localization provides new clues about where to search for additional cellular and molecular events that occur during learning and memory.

Progress has also been made in elucidating the cellular and molecular mechanisms involved in fear conditioning (see Maren, 2001; Schafe et al., 2001; Blair et al., 2001; Rosenkranz and Grace, 2002; Sah et al., 2003; Rodrigues et al., 2004; Rosen, 2004; Fanselow and Poulos, 2005). While extensive discussion of these mechanisms is beyond the scope of this review, a brief summary is in order. This work has implicated NMDA receptors and voltage-gated calcium channels as sources of calcium entry during learning. The rise in calcium then triggers intracellular cascades that store the synaptic changes. Some of the intracellular processes involved include protein kinases (CamKII, PKA, PKC, MAPK), gene transcription factors (especially CREB), and RNA and protein synthesis. Protein synthesis has also been implicated in the maintenance of memory following retrieval, a process referred to as reconsolidation (see Nader et al., 2000).

Animal studies have shown that the amygdala receives sensory information via two routes: a rapid but crude input from the sensory thalamus and a slower but more veridical representation from the sensory cortex (LeDoux et al., 1984; LeDoux, 1994, 2002). Either the thalamic or cortical pathway can be used for simple sensory stimuli such as those typically used in animal-conditioning studies, but presumably more-complex stimuli would require cortical processing. However, even for complex stimuli it is possible that crude features of the stimulus might have emotional potency due to innate wiring. For example, through the thalamic pathway, the amygdala might be activated by features or fragments of stimuli. This could lead to inappropriate activation—for example, when walking through the woods, the amygdala might be activated by the curvature of a slender stick on the ground, as if it were a snake. Alternatively, through past learning certain stimulus features might acquire the ability to activate the amygdala unwittingly.

Current techniques for examining human brain function do not allow the exploration of neural systems with the same level of specificity as animal models. Nevertheless, studies exploring the role of the human amygdala in fear learning are consistent with these models. Fear conditioning in humans results in an increased blood-oxygen-level-dependent (BOLD) signal in the amygdala as assessed with functional magnetic resonance imaging (fMRI; Buchel et al., 1998; LaBar et al., 1998). The magnitude of this BOLD response is predictive of the strength of the conditioned response (LaBar et al., 1998, Phelps et al., 2004). In addition, a subliminally presented CS—one presented so quickly that subjects are unaware of its presentation—leads to coactivation between the amygdala and both the superior colliculus and pulvinar, which was not apparent for a CS presented supraliminally (Morris et al., 1998a). These structures are potential components of a subcortical pathway for emotional detection, supporting the animal results suggesting two pathways for conveying information to the amygdala (also see discussion below).

In addition, studies in patients with brain lesions are consistent with the animal models. Although the interpretation of lesion studies in humans can be problematic because these lesions almost always include damage to additional structures and often occur years before experimental testing, allowing the possibility for the development of compensatory mechanisms, these

studies can provide a hint into the critical function of structures in human brain. As expected from previous studies with other techniques, patients whose damage includes the amygdala fail to show physiological indications of conditioned fear. However, if the hippocampus in these patients is relatively intact, they are able to explicitly recollect and report the events of fear-conditioning procedures, such as the relation between the CS and US (Bechara et al., 1995; LaBar et al., 1995). In contrast, damage that includes the hippocampus bilaterally but spares the amygdala impairs the ability to consciously report the events of fear conditioning, although there is normal expression of conditioned fear as assessed through physiological measures (Bechara et al., 1995). This dissociation following amygdala or hippocampal damage between indirect physiological assessments of the conditioned fear response (amygdala dependent) and awareness of the aversive properties of the CS (hippocampal dependent) supports the conclusion that there are multiple systems for the encoding and expression of emotional learning.

We have emphasized the contribution of the amygdala in aversive emotional experiences because the neural basis of these has been elucidated most thoroughly in animal studies. However, some studies have explored positive emotions in animals (e.g., Holland and Gallagher, 1999; Rolls, 1999; Ono and Nishijo, 1992; Everitt et al., 1999; Baxter and Murray, 2002, Gallagher and Chiba, 1996) and humans (Anderson et al., 2003; Canli et al., 2002; Hamann et al., 1999; Johnsrude et al., 2000), suggesting that the amygdala's role in implicit learning and emotion processing is not limited to fear.

Emotional Modulation of Memory

In addition to undergoing plastic changes that constitute implicit memories, the amygdala contributes to the memory storage functions of other systems, including systems that function both implicitly and explicitly (for review, see McGaugh, 2000; Packard and Cahill, 2001). Studies of rats and other laboratory animals, for example, have shown that damage to the hippocampus prevents the formation of certain kinds of spatial memories (a rodent analog of explicit memory) while damage to the striatum prevents the formation of habit memories (an example of implicit memory) (see Martin and Morris, 2002; Eichenbaum, 2002; Packard and Cahill, 2001). These two kinds of memories can be enhanced by systemic treatment with drugs that mimic the effects of adrenal hormones, including both adrenergic hormones (epinephrine and norepinephrine) and steroid hormones (cortisol/corticosterone) (McGaugh, 2000, 2002, 2004; Packard and Cahill, 2001; Roozendaal, 2002). Infusion of these drugs into the lateral and basal regions of the amygdala has a similar effect. Moreover, blockade of β-adrenergic receptors in the amygdala interferes with the modulatory effects of systemically administered adrenergic drugs and steroid hormones, and modulatory effects are also induced by direct stimulation of β-adrenergic or glucocorticoid receptors in the amygdala (McGaugh, 2000, 2002, 2004; Roozendaal, 2002; Packard and Cahill, 2001).

The amygdala's modulation of hippocampal- or striatal-dependent memories comes about primarily by enhancing the consolidation of memory rather than initial encoding (McGaugh, 2000, 2004; Packard and Cahill, 2001), although the amygdala may also influence processing during memory encoding (see "Emotional Influences on Attention and Perception" below). This is indicated by the fact that posttraining manipulations of the amygdala, a time when encoding is presumably complete, alter later memory performance (Packard and Teather, 1998). The hormonal changes that influence consolidation are concomitants of emotional arousal and as noted are triggered, at least in situations of danger, by amygdala processing of the fear-arousing event (LeDoux, 1996). These neurohormonal changes persist after termination of the threat and continue to modulate memory storage during this time, helping to insure that stimuli and events that lead to an emotional reaction, and that are likely more important to survival, are not forgotten (McGaugh, 2000).

In spite of its ability to modulate spatial memories (hippocampal dependent) and habit memories (striatal dependent), the amygdala does not appear to be required to modulate memories of fear conditioning (amygdala dependent). Thus, posttraining manipulations that interfere with memory modulation in the hippocampus or striatum have no effect on the strength of conditioned fear (Wilensky et al., 1999; Lee et al., 2001).

In humans, both psychological and neuroscience research supports the conclusion that the storage of explicit memories is modulated with arousal and that this modulation depends on the amygdala. Early psychological research examining the effect of emotion on explicit memory found that arousal during encoding results in less forgetting over time (Berlyne and Carey, 1968; Kleinsmith and Kaplan, 1963), consistent with enhanced consolidation or storage. Damage to the amygdala results in similar forgetting curves for arousing and neutral stimuli (LaBar and Phelps, 1998) and impaired delayed memory for emotional stimuli (Adolphs et al., 2000; Cahill et al., 1995). More recently, a number of brain-imaging studies have reported activation of the amygdala during encoding that is predictive of later memory retention for emotional stimuli (Cahill et al., 1996; Canli et al., 2000; Hamann et al., 1999; Dolcos et al., 2004) (Figure 2). In addition, pharmacological blockade of β-adrenergic receptors impairs enhanced memory for emotional events in humans, suggesting that the amygdala's modulation

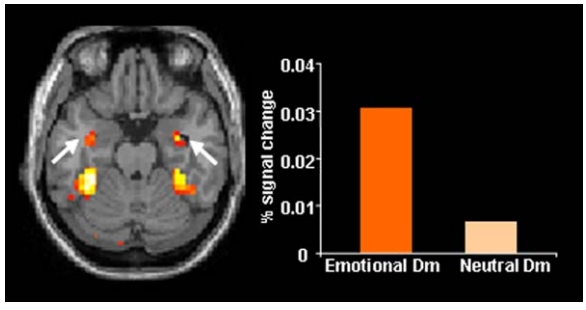

Figure 2. Amygdala Activation Predicts Memory for Emotional Items

Activation of the amygdala (arrows) during encoding predicts subsequent memory for emotional pictures (emotional Dm effect) but not for neutral pictures (neutral Dm effect). Adapted from Dolcos et al. (2004).

of consolidation is dependent on the neurohormonal changes that occur with arousal (Cahill et al., 1994).

These findings in humans indicate a role for arousal and the amygdala in the modulation of explicit or episodic memories, but they do not clearly demonstrate that this occurs through enhancing the consolidation stage of memory formation. Two recent studies induced an arousal response immediately after a stimulus was encountered using a pharmacological (Cahill and Alkire, 2003) or pain (Cahill et al., 2003) manipulation. These studies found that poststimulus arousal enhanced later memory. Interestingly, this effect only emerged for stimuli rated as emotional prior to the study (compared to similarly rated stimuli that were not followed by an arousal manipulation). There was no effect of poststimulus arousal on stimuli previously rated as neutral. These results suggest that the amygdala's modulation of memory consolidation in humans may favor stimuli that are predisposed to lead to an emotional reaction.

There is not yet direct evidence in humans demonstrating that the amygdala modulates striatal-dependent skill or habit learning. However, given the evidence that hippocampal-dependent memories are modulated by amygdala-dependent processes in humans, together with the fact that hippocampal-dependent and striatal-dependent learning is modulated by amygdala-dependent functions in rats, it seems likely that striatal-dependent memory in humans might also depend on amygdala modulation in emotional situations, but this remains to be determined.

Emotional Influences on Attention and Perception

In addition to modulating memory systems, the amygdala also alters processing in cortical systems involved in attention and perception and thereby potentially influences a range of downstream cognitive functions. Two lines of research support this view.

The Amygdala Influences Cortical Sensory Plasticity

In a pioneering series of studies beginning in the 1970s, Weinberger and colleagues demonstrated that fear conditioning, which depends on amygdala plasticity, alters the neural representation of an auditory CS in the auditory system (Weinberger, 1995; Edeline, 1999). Specifically, these researchers mapped the auditory-frequency-receptive fields of single cells in the auditory thalamus or auditory cortex. They then picked a frequency that was not the best frequency of the cell (the frequency that the cell responded strongest to) and used that as a CS. After several pairings with the US, they showed that the cell's frequency response had shifted such that the response to the CS frequency was selectively enhanced at the expense of other frequencies. Further, these changes persisted for weeks. Importantly, the changes were relatively small and only occurred if the CS frequency was within an octave of the cell's best frequency. In other words, emotional arousal does not completely rewire the auditory system but instead produces subtle shifts or biases that allow the system to become more attuned to important events and to then attend to these more strongly in the future. Plasticity is presumably restricted to the sensory system that is processing the CS. In contrast, plasticity in the amygdala occurs regardless of the CS modality. Modality-independent neural plasticity in the amygdala thus interacts with sensory-specific plasticity during fear conditioning.

That the amygdala actually influences plasticity in specific sensory-processing systems is suggested by three lines of evidence. First, during auditory fear conditioning, plasticity in the lateral amygdala appears to develop sooner (in fewer trials) than plasticity in the auditory cortex (Quirk et al., 1997). Second, damage to or inactivation of the amygdala prevents plasticity in the auditory system (Poremba and Gabriel, 2001; Maren et al., 2001). Third, the central nucleus of the amygdala, via connections to the basal forebrain cholinergic system, appears to be necessary for auditory cortex receptive field plasticity (Weinberger, 1995).

Due to limitations in techniques for examining the human brain, it is difficult to find conclusive evidence for lasting changes in the sensory representation of stimuli that have acquired an emotional significance through learning, as predicted by the findings from Weinberger and colleagues (Weinberger, 1995; Edeline, 1999). However, brain-imaging studies have demonstrated enhanced cortical responses to learned emotional stimuli. For instance, Dolan and colleagues (Morris et al., 2001a) conditioned subjects to fear a tone and found greater auditory cortex responses to this tone CS compared to a neutral tone. In addition, Anderson (2004) showed enhanced activation to arousing words in the lingual gyrus, a region thought to be important for the cortical representation of lexical items (Booth et al., 2002). In both of these studies, the amygdala also responded to these stimuli, consistent with the notion that the amygdala may support changes in the cortical representation of stimuli linked with emotion, though it is not possible to determine in such studies whether amygdala activity played a causal role in cortical activity.

The Amygdala Facilitates Attention to Salient Stimuli

It has long been known that when salient stimuli appear they are more likely to enter into awareness (Cherry, 1953). An important goal of cognitive neuroscience is to understand how the brain allows unattended salient stimuli priority in awareness. One hypothesis is that after a salient stimulus is detected by the amygdala, projections from the amygdala to the cortex (Amaral et al., 2003) are able to facilitate attention and perception (Armony et al., 1997; Armony and LeDoux, 1999; Whalen et al., 1998).

Kapp and colleagues (B.S. Kapp et al., 1996, 1997, Soc. Neurosci., abstract) have shown that cells in CE respond to a CS and that fluctuations in the cortical EEG are correlated with changes in the spontaneous activity of CE cells. Both direct and indirect pathways are proposed for the amygdala's transitory modulation of cortical regions. First, there are reciprocal connections between amygdala nuclei and sensory cortex (Amaral et al., 2003), indicating a means by which the amygdala could influence sensory processes through direct projections. Second, the CE projects to the nucleus basalis of Meynert (NBM), which projects to widespread cortical areas, many of which are sensory-processing regions. Acetycholine, which is released in these cortical areas via the NBM, has been shown to facilitate neuronal responsivity (Chiba et al., 1995; Everitt and Robbins,

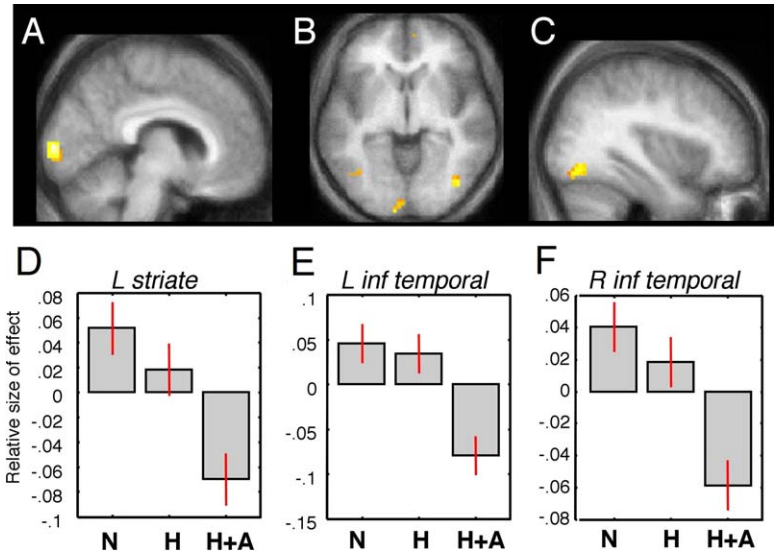

Figure 3. Activation of Visual Cortex to Fear Faces Is Diminished following Amygdala Damage

Statistical parametric maps of emotion × group interaction (A–C) across the whole brain, showing the main effect for fearful versus neutral faces between patient groups in (A) the left striate cortex, (B) left and right inferior temporal lobe, (C) and right inferior temporal lobe. Parameter estimates for the relative size of effect in this ANOVA (arbitrary units, mean centered) for peaks in (D) left striate cortex, (E) left inferior temporal lobe, and (F) right inferior temporal lobe, showing increased activation to fearful faces in both normal controls (N) and patients with damaged confined to the hippocampus (H), but not patients with both hippocampal and amygdala damage (H+A). Adapted from Vuilleumier et al. (2004).

1997; Weinberger et al., 1990; Edeline, 1999). The amygdala's transitory modulation of cortical regions might result in increased cortical attention and vigilance in situations of danger (Armony et al. 1997; Armony and LeDoux, 1999; Whalen, 1998; Davis and Whalen, 2001).

Evidence from a range of techniques in humans is consistent with a transitory-feedback model in which emotional stimuli, via the amygdala's influence on cortical sensory processing, can influence attention and perception. The first line of evidence in support of this model is brain-imaging studies demonstrating that amygdala activation to fear (versus neutral) faces does not depend on subjects' awareness of the presentation of the faces (Whalen et al., 1998), or whether or not the faces are the focus of attention (Vuilleumier et al., 2001, Anderson et al., 2003, Williams et al., 2004). These studies indicate that the amygdala responds to a fear stimulus automatically and prior to awareness. It is proposed that this quick amygdala response, early in stimulus processing, enables modulation of subsequent attention and perception (Whalen, 1998).

More direct evidence that the amygdala plays a critical role in the facilitation of attention and perception for emotional stimuli comes from studies examining patients with damage to the amygdala. These patients fail to show the normal facilitation of attention for emotional stimuli (Anderson and Phelps, 2001). Further support that this facilitation of attention occurs through feedback from the amygdala to sensory cortical regions is derived from fMRI studies reporting enhanced activation in the visual cortex for fear (versus neutral) faces that is correlated with the magnitude of amygdala activation (Morris et al., 1998a, 1998b). This enhanced activation in visual regions to fear faces is absent if the amygdala is damaged (see Figure 3; Vuilleumier et al., 2004). Although the visual-processing regions identified in these studies, such as extrastriate cortex (see Figure 3), are thought to support perceptual processes, not necessarily the allocation of attention (Corbetta and Shulman, 2002), there is increasing evidence that many standard attention effects can be explained by changes in perceptual abilities that occur with attention (Carrasco, 2004; Polonsky et al., 2000). A recent study found that even early perceptual functions (i.e., contrast sensitivity) are enhanced with fear face cues (Phelps et al., 2005), consistent with the amygdala's modulation of these primary visual regions (Vuilleumier et al., 2004).

These lesion and imaging studies in humans provide strong support for the idea that the amygdala modulates attention and perception via rapid feedback to sensory-processing regions. However, there is considerable debate concerning some of the neural pathways underlying this modulation. The amygdala's response to fear faces irrespective of awareness and attentional focus has led some to propose that the amygdala is detecting threat stimuli via a subcortical pathway that bypasses visual cortex (see the section on "Implicit Emotional Learning and Memory" for a description). In support of this argument, fMRI studies have reported a lack of activation in visual cortex when fear faces are processed without awareness (Pasley et al., 2004; Williams et al., 2004). In addition, Vuilleumier et al. (2003) took advantage of the fact that a visual subcortical pathway would be more sensitive to low-spatial-frequency information, whereas ventral visual cortex should respond preferentially to high-spatial-frequency information. They found that the amygdala, pulvinar, and superior colliculus (components of a proposed subcortical pathway) respond preferentially to low-spatial-frequency fear versus neutral faces, whereas the fusiform cortex responds preferentially to high-spatial-frequency fear versus neutral faces. Finally, two studies have reported amygdala activation to fear versus neutral faces in patients suffering from blindsight, whose visual cortices are damaged, resulting in an inability to identify stimuli (Morris et al., 2001b; Pegna et al., 2005). The amygdala's enhanced BOLD response to fear faces in the absence of awareness, high-spatial-frequency information, or an intact visual cortex is argued to support the existence of a subcortical pathway for the detection of threat stimuli by the amygdala.

However, a recent study by Pessoa et al. (2002) questions this conclusion. Using a demanding-attention task, they failed to observe amygdala activation in the

absence of attention. In this situation, the amygdala's response to fear faces is not automatic. Pessoa et al. (2002) argue that the presence of a subcortical pathway for the detection of threat by the amygdala should result in an obligatory response to a fear face, regardless of how demanding the attentional task. In other words, the amygdala's response should *never* be dependent on attention. In addition, there is not yet any anatomical evidence in primates verifying the existence of a subcortical pathway for the detection of visual information by the amygdala (Pessoa and Ungerleider, 2004). The research to date has been limited to rats using both auditory and visual stimuli (LeDoux et al., 1984, 1989; Romanski and LeDoux, 1992).

The finding that attention can modulate the amygdala's response to a fear face stimulus clearly demonstrates that activation of the amygdala can be dependent on attention in some circumstances. However, a limitation in interpreting the BOLD signal is that it is not an absolute response of neural function, but rather a relative response indicating the degree of difference between conditions (e.g., fear versus neutral faces). In such studies, it is only possible to demonstrate the abscence of a significant difference in BOLD signal rather than the abscence of an amygdala response. Of course, fMRI results used to argue in favor of a subcortical pathway by pointing to the lack of activation in visual regions in normal subjects suffer from the same limitation (Pasley et al., 2004; Williams et al., 2004). It is unclear whether fMRI, when used without other techniques, can provide sufficient evidence that a subcortical pathway for the detection of visual threat stimuli by the human amygdala does or does not exist.

Irrespective of whether the amygdala receives input about the emotional significance of a stimulus via a cortical or subcortical pathway, amygdala activation to fear faces meets most of the principles of automaticity—that is it is independent of attention and awareness, with certain limitations for highly demanding attention tasks. A combination of lesion and imaging studies has provided strong evidence that transitory feedback from the human amygdala to sensory cortical regions can facilitate attention and perception. The amygdala's influence on cortical sensory plasticity may also result in enhanced perception for stimuli that have acquired emotional properties through learning. By influencing attention and perception, the amygdala is altering the gateway of information processing. The amygdala enables preferential processing of stimuli that are emotional and potentially threatening, thus assuring that information of importance to the organism is more likely to influence behavior.

Emotion and Social Behavior

It has long been known that damage to the temporal lobes in monkeys results in a dramatic set of symptoms, including a reduction in the fear-arousing potency of predators (snakes and humans), changes in dietary habits (attempts to eat inedible objects), and unusual sexual behavior (engaging in homosexual behavior or attempting to copulate with members of other species) (Kluver and Bucy, 1937). In the 1950s, Weiskrantz (1956) proposed that many of the components of the so-called Kluver-Bucy syndrome were due to a dissociation of the sensory and affective properties of visual stimuli resulting from damage to amygdala. This was the origin of the idea that the amygdala plays a key role in emotional behavior. Much subsequent research in rats has elaborated on the importance of the amygdala in emotion (for review, see LeDoux, 2002; Davis and Whalen, 2001). In addition, a considerable body of research in monkeys has also further implicated the amygdala in emotion, including emotional responses to social stimuli (for review, see Ono and Nishijo, 1992; Aggleton and Mishkin, 1986; Rolls, 1999; Zola-Morgan et al., 1991; Meunier et al., 1999).

Research evolving from the Kluver-Bucy syndrome first emphasized the importance of the amygdala in social behavior (Rosvold et al., 1954; Kling and Brothers, 1992; Meunier et al., 1999; Meunier and Bachevalier, 2002). Amaral and colleagues (Amaral, 2003) have recently revisited this issue in both adult and infant monkeys and concluded that damage to the amygdala in adult animals, while reducing fear of toy snakes, fails to produce significant adverse alterations in social and affiliative behavior. In contrast, damage in infants alters later adult behavior in such a way that fear of a toy snake is intact, but fear in social situations is altered. This specific effect on social fear is consistent with studies that have emphasized the importance of amygdala alterations in autism (Bachevalier, 1994; Baron-Cohen et al., 2000; Kemper and Bauman, 1993).

Unlike the significant impairment in social responses observed in monkeys with early temporal lobe damage, especially involving the amygdala, humans with temporal lobe damage do not have social deficits that are readily apparent. The famous amnesic patient HM had his medial temporal lobe, including the amygdala, surgically removed in an effort to control epilepsy. However, even though HM had a lesion similar to the Kluver-Bucy lesion, his primary difficulty was explicit memory. His social behavior was reported as relatively normal (Milner et al., 1968). Case studies of patients with selective bilateral amygdala damage who are not amnesic also report relatively normal social behavior (Adolphs, 1999; Anderson and Phelps, 2002). These preserved social abilities may be related to intact components of the amygdala or to cognitive compensation for the loss of emotional functions. Specifically, patients with emotional impairments might use episodic or semantic memory of social information and responses, as well as habitual behavioral responses, to act normally in social and emotional situations. Indeed, such patients are aware of social norms and are able to correctly interpret appropriate social reactions from verbal descriptions (Adolphs et al., 1995). They also show normal facial expressions of emotion (Anderson and Phelps, 2000) and rate their daily emotional states as similar to control subjects (Anderson and Phelps, 2002). It may be that this intact explicit representation and understanding of social responding and the normal subjective sense of emotion is sufficient to guide social behavior in most circumstances, especially if the person went though development with an intact amygdala and only developed amygdala pathology later in life. In this regard, it is important to note that for most reported cases of patients with selective bilateral amygdala lesions, it is unclear when, during development, the damage

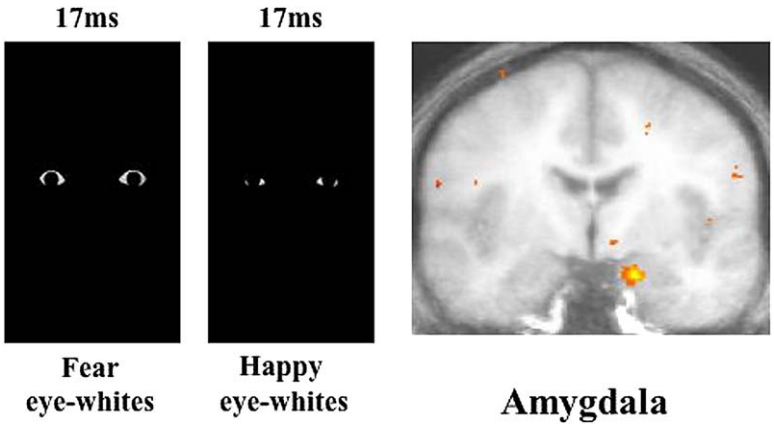

Figure 4. Activation of the Amygdala to Subliminal Presentation of Fearful versus Happy Eyes

Presenting the whites of fear (far left) versus happy (middle) eyes for only 17 ms, which is too quick for subjects to consciously detect the stimuli (subliminal presentation), results in a differential BOLD-signal response in the amygdala (far right). Adapted from Whalen et al. (2004).

occurred (Adolphs et al., 1995; Cahill et al., 1995; Phelps et al., 1998). It is possible that they learned, with their amygdala intact, how to behave in social situations. Such individuals may be especially capable of cognitively compensating for the absence of the amygdala later in life.

Even though patients with amygdala damage do not have markedly impaired social behavior, they do have deficits in social responses in some circumstances. In spite of their ability to generate normal facial expressions of emotion, they do not always interpret facial expression in others correctly. This impairment is most apparent for fear expressions. Damage to the amygdala results in an impairment in interpreting the intensity of fear expressions in others (Adolphs et al., 1999). Recent studies suggest that the amygdala primarily responds to the eyes in fear faces (see Figure 4; Whalen et al., 2004), and amygdala lesions result in a deficit in appropriately focusing on the eyes when interpreting facial expression (Adolphs et al., 2005). This impairment in decoding facial expressions also leads these patients to rate some faces as more trustworthy and approachable than normal controls (Adolphs et al., 1998). The deficit in responding to facial expressions is subtle, but nonetheless reliable and potentially important. Further, it is consistent with the results of the primate mentioned studies above suggesting a role for the amygdala in social emotions (Amaral, 2003).

Another deficit in social responding observed following amygdala damage is the ability to read social interpretations into ambiguous circumstances. The tendency to anthropomorphize, that is, to apply human traits to nonhuman forms, occurs naturally without effort. For example, a classic video by Heider and Simmel (Heider and Simmel, 1944) shows triangles and a circle moving around a box. Although these are simple geometric shapes, the nature of the movements result in most people describing the shapes as characters engaging in a social interaction. Patients with amygdala damage, however, fail to read any social intent and simply describe the movement of the shapes when responding to this video (Heberlein and Adolphs, 2004). It is suggested that this deficit in anthropomorphizing may be indicative of the kind of implicit social signals that depend on the amygdala for normal interpretation.

The impairments in social responses following amygdala damage in humans are robust, but limited. In contrast, brain-imaging studies in normal subjects have reported amygdala activation to a range of social stimuli, from bodily movements indicating fear (de Gelder et al., 2004), to race group information (Phelps et al., 2000), to pictures of individuals who have previously acted unstrustworthy (Singer et al., 2004). These imaging studies suggest that the amygdala responds to a wide range of social cues and indicate that the subtle deficits observed following amygdala lesions may reflect compensatory mechanisms and may not be indicative of the extent of the amygdala's involvement in normal social behavior. Across species, there is evidence that the amygdala is an important component of the network of neural systems that produce adaptive social interactions.

Inhibition and Regulation of Emotion

Until recently, researchers investigating the neural systems of emotion have primarily focused on understanding how stimuli acquire an emotional significance or how an emotional response might alter perception or cognition. However, there is a growing interest in translating this research on the neural systems of emotion to the treatment of emotional disorders. Although understanding how emotional significance is learned and expressed is important in this endeavor, it is equally important to discover how learned emotional responses might be diminished or controlled. There has been recent progress uncovering the neural mechanisms underlying the alteration of emotional responses. Below we will discuss research on extinction, reconsolidation, and emotion regulation. Each of these involves the amygdala, as well as other brain regions.

Extinction of Emotional Learning

One technique for altering learned emotional responses, especially those established as Pavlovian associations, is experimental extinction (Myers and Davis, 2002; Morgan et al., 1993; Bouton, 2002; Sotres-Bayon et al., 2004). With this procedure, a CS previously linked to aversive US is presented alone for a number of trials until the subject learns that the CS no longer predicts the US. Although conditioned emotional responses (CRs) are diminished with extinction, the responses are inhibited rather than eliminated. Thus, after complete extinction a number of situations can result in the reexpression of previously extinguished CRs, such as the passage of time (spontaneous recovery), exposure to the US

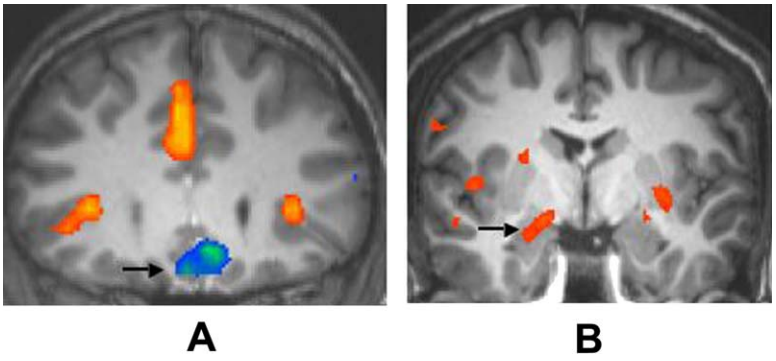

Figure 5. Regions of Activation during Extinction of Conditioned Fear in Humans

(A) Activation of the vmPFC (arrow), indicating a decrease in BOLD signal to the CS+ (relative to a CS−) during acquisition. This vmPFC BOLD response increased as extinction training progressed, and the magnitude of this increase predicted the retention of extinction learning. (B) Amygdala activation (arrow) to the CS+ during acquisition versus early extinction, indicating that extinction training results in a reduction in BOLD signal to the CS+. This change in the amygdala response during extinction training predicted early extinction success. Adapted from Phelps et al. (2004).

(reinstatement), or exposure to the original learning context (renewal) (for a review, see Bouton, 2002). The reappearance of extinguished CRs demonstrates that the learned response was stored and that its expression was inhibited by extinction learning. Animal research on extinction has implicated the amygdala and medial prefrontal cortex (mPFC). We start with the mPFC because it was implicated in fear extinction first.

Damage to mPFC, especially the ventral-most portion of this region (vmPFC), significantly alters the ability of rats to undergo extinction learning (Morgan et al., 1993, 2003; Morgan and LeDoux, 1995; Quirk et al., 2000; Quirk and Gehlert 2003; Garcia, 2002). Furthermore, neural activity increases in the mPFC as extinction is learned (Milad and Quirk, 2002; Rosenkranz et al., 2003), and electrical sitmulation of mPFC can facilitate extinction learning (Milad et al., 2004). It appears that vmPFC may be particularly involved in the memory or retention of extinction (Quirk and Gehlert, 2003).

Because the amygdala is needed to express fear responses, most work on the role of the amygdala in extinction has used pharmacological manipulations rather than lesions. Particularly important have been studies by Davis and colleagues (Myers and Davis, 2002; Walker and Davis, 2002; Walker et al., 2002). They have shown that blockade of NMDA receptors in the amygdala disrupts extinction and that facilitation of NMDA receptor function with d-cycloserine enhances extinction (Walker and Davis, 2002; Walker et al., 2002). This work has important implications for the treatment of fear disorders (Davis and Myers, 2002). It has recently been reported that the administration of d-cycloserine to humans prior to exposure therapy for the treatment of phobia enhances the treatment response (Ressler et al., 2004).

Much like research on the acquisition of fear conditioning, brain-imaging evidence in humans indicates that the neural mechanisms of fear extinction are preserved across species (LaBar et al., 1998; Knight et al., 2004; Phelps et al. 2004). A recent study (Phelps et al., 2004) found that amygdala activation was correlated with the expression of the CR during both acquisition and early extinction, suggesting that the amygdala is involved in initial extinction learning. After a day, however, activity in the subgenual anterior cingulate—a region hypothesized to be homologous to infralimibic cortex in rats and monkeys (Kim et al., 2003)—was predictive of the retention of extinction and the expression of the CR, consistent with a role for this region in the recall of extinction learning (see Figure 5). Although it is not possible to determine a critical functional role from brain-imaging data, these results are largely consistent with research from nonhuman animals on the mechanisms of extinction learning.

Reconsolidation of Emotional Learning

A second mechanism by which learned emotional responses could be altered is through disrupting reconsolidition. It is well established that in order for short-term memory (STM) to persist as long-term memory (LTM), the neurons storing the memory have to synthesize new proteins (Davis and Squire, 1984; Bailey et al., 1996). Thus, STM is labile and subject to disruption until it is converted to LTM by protein synthesis and consolidated. However, there is also evidence that consolidated LTM becomes labile and subject to disruption after retrieval (Sara, 2000; Nader et al., 2000). The latter is said to show that memory is reconsolidated following retrieval (Sara, 2000; Nader et al., 2000). For example, in a fear-conditioning paradigm, disruption of protein synthesis in the lateral amygdala immediately after training (Schafe and LeDoux, 2000) or immediately after retrieval of the CS (Nader et al., 2000) has no effect on the CR for several hours but then prevents the expression of the CR the next day. The impairment observed in the later expression of the CR when protein synthesis in the amygdala is disrupted immediately after retrieval of the CS indicates that previously learned emotional responses can be disrupted after memory reactivation. Reconsolidation of memory has now been shown in a variety of species and for a variety of training conditions exploring both hippocampal- and amygdala-dependent learned-fear responses (Sara, 2000; Nader et al., 2000; Debiec et al., 2002; Dudai 2002; Eisenberg et al., 2003; Milekic and Alberini, 2002).

Blockade of reconsolidation has been proposed as a possible treatment for PTSD and other conditions in humans involving intrusive memories (Nader et al., 2000; Debiec and LeDoux, 2004). There is some evidence for reconsolidaiton in humans (Sara, 2000; Walker et al., 2003a), but more work on human subjects is needed.

While there are many questions regarding the mechanisms underlying postretrieval memory vulnerabiltiy and whether the phenomenon involves storage deficits, retrieval deficits, or extinction (Sara, 2000; Nader et al., 2000; Debiec et al., 2002; Dudai 2002; Eisenberg et al., 2003; Milekic and Alberini, 2002; Lattal et al., 2004; Riccio et al., 2002), the fact is that manipulations of the

brain after retrieval with drugs or behaviorally with interference tasks (Anderson et al., 2004) can affect memory performance. These dramatic effects on memory need to be more thoroughly incorporated into psychological and biological models of memory in the future.

Emotional Regulation and Coping

In complex social and emotional environments, it is often important to be able to control our emotional reactions in order to behave in adaptive or appropriate ways. The ability to regulate and cope with emotion is a fundamental skill for normal social interaction. It is also an important component of mental health. A characteristic difficulty in many psychological disorders, such as depression or anxiety, is the maladaptive cognitive interpretation of situations or events. A component of treatment for these disorders is to teach active coping skills, consciously applied strategies that help assure adaptive interpretations or reactions to emotional stimuli. In humans, a significant portion of our emotional life is generated by our thoughts, interpretations, and imagination. The habits and skills we develop to guide these internally generated emotional events are critical. Recent research on the neural systems of emotion regulation explores the mechanisms underlying the ability to use cognitive and active coping strategies to alter emotional reactions.

In animals, emotion regulation (coping) can be studied by examining the manner in which fear-arousing stimuli are dealt with. Although rats initially freeze to a CS associated with shock, they can, with training, learn to actively control their exposure to the CS and thus reduce its aversive consequences (Amorapanth et al., 2000). For example, rats can learn to cross to the other side of a chamber to terminate or prevent the occurrence of a fear-arousing CS. Damage to the central nucleus of the amygdala prevents freezing to the CS (a passive form of coping) but does not interfere with the ability to learn responses that terminate or prevent the CS (active coping). In contrast, damage to the basal amygdala has no effect on freezing but prevents learning of the active coping response. Damage to the lateral nucleus prevents both forms of learning. This suggests that the lateral nucleus is essential for processing the CS and that passive and active coping responses elicited by the CS involve different outputs of the lateral nucleus within the amygdala. These findings are relevant to understanding the benefits of active coping strategies in anxiety disorders (LeDoux and Gorman, 2001). For related studies involving both appetitive and aversive conditioning, see Killcross et al. (1997) and Everitt et al. (1999).

In humans, emotion regulation using cognitive control has been examined in several ways. For example, reappraisal involves reinterpreting an emotional stimulus in such a way that the emotional reaction is altered. If shown a scene of women crying outside a church, subjects might interpret it as representing a funeral and the women as expressing grief. However, an attempt to reappraise this ambiguous scene might lead to another interpretation in which subjects imagine the women are crying in joy at the end of a wedding. Successful reappraisal of emotional scenes alters physiological arousal responses, as well as ratings of emotional reactions (Gross, 2002). Two recent fMRI studies found that this type of reappraisal of emotional scenes also leads to a decrease in amygdala activation (Ochsner et al., 2002; Schaefer et al., 2002). This cognitive modulation of the amygdala may be linked to regions in the prefrontal cortex (PFC) thought to be important for the online processing of information, or working memory. The study by Ochsner and colleagues (Ochsner et al., 2002) found that the activation in the left middle frontal gyrus increased during successful reappraisal and was negatively correlated with the amygdala response. Although there are not direct projections between the amygdala and this lateral PFC region, this region does project to more-directly connected medial PFC regions (Barbas, 2000), which may be part of a circuit that helps regulate the amygdala.

Fears acquired through conditioning can also be diminished using emotion-regulation strategies (Delgado et al., 2004). A recent study examined the ability to reinterpret the meaning of a CS paired with a shock, by using the CS (a colored square) as a cue to imagine a soothing scene. When the CS prompted the imagination of a soothing scene, subjects showed less of an arousal response and diminished amygdala activation. Similar to the reappraisal study by Ochsner et al. (2002), a region of the left middle frontal gyrus showed increased activation during the reinterpretation of the CS. Interestingly, the vmPFC region that has previously been linked to extinction learning in humans (Phelps et al., 2004) also showed a similar pattern of response when conditioned fear was diminished with a cognitive strategy, suggesting that overlapping neural mechanisms for amygdala inhibition/regulation may support both cognitive emotion-regulation strategies and extinction learning.

Cognitive interpretation of a stimulus can also enhance amygdala activation and the expression of negative affect or fear. Fears to previously neutral stimuli that have been acquired symbolically, through verbal instruction, result in physiological expression and amygdala activation that is similar to that observed in fear conditioning (Phelps, et al., 2001). Damage to the left amygdala impairs the physiological expression of these instructed, abstract fears (Funayama et al., 2001). In addition, reappraising the meaning of an ambiguous scene so that it is more fearful results in enhanced amygdala activation (Ochsner et al., 2004). In everyday human life, many of our fears are imagined and anticipated, but never actually experienced. These results suggest that the expression of fears that are represented abstractly, and based on imagination and interpretation, rely on similar neural systems as fears learned directly though fear conditioning.

Understanding the mechanisms mediating the alteration of emotional responses will be critical as we attempt to apply research on the neuroscience of emotion to the treatment of emotional disorders. By inhibiting, disrupting, or regulating emotional responses we may be able to change maladaptive emotional reactions. Reconsolidation, extinction, and emotion regulation are three important tools in the translation of basic neuroscience to clinical practice.

Conclusion

Animal models of amygdala function have provided a foundation on which to explore the representation of emotion in the human brain. In this review, we highlight

the evidence for similarities in amygdala function across species, focusing on five topics of investigation. Studies on the neural systems of implicit emotional learning, emotion and memory, emotion's influence on attention and perception, social responding, and emotion inhibition and regulation indicate an important role for the amygdala. Although studies in humans cannot explore the neural systems of behavior with the same level of specificity as research in nonhuman animals, identifying links in the neural representation of behavior across species results in a greater understanding of both the behavioral influence and neural representation of emotion in humans.

Acknowledgments

This research was supported by the National Institutes of Health MH62104 and the James S. McDonnell Foundation to E.A.P.; and MH38774, MH46516, MH067048, and MH58911 to J.E.L.

References

Adolphs, R. (1999). Social cognition and the human brain. Trends Cogn. Sci. *3*, 469–479.

Adolphs, R., Tranel, D., Damasio, H., and Damasio, A.R. (1995). Fear and the human amygdala. J. Neurosci. *15*, 5879–5891.

Adolphs, R., Tranel, D., and Damasio, A.R. (1998). The human amygdala in social judgment. Nature *393*, 470–474.

Adolphs, R., Tranel, D., Hamann, S., Young, A.W., Calder, A.J., Phelps, E.A., Anderson, A., Lee, G.P., and Damasio, A.R. (1999). Recognition of facial emotion in nine individuals with bilateral amygdala damage. Neuropsychologia *37*, 1111–1117.

Adolphs, R., Tranel, D., and Denburg, N. (2000). Impaired emotional declarative memory following unilateral amygdala damage. Learn. Mem. *7*, 180–186.

Adolphs, R., Gosselin, F., Buchanan, T.W., Tranel, D., Schyns, P., and Damasio, A.R. (2005). A mechanism for impaired fear recognition after amygdala damage. Nature *433*, 68–72.

Aggleton, J.P., and Mishkin, M. (1986). The amygdala: sensory gateway to the emotions. In Emotion: Theory, Research and Experience, *Volume 3*, R. Plutchik, and H. Kellerman, eds. (Orlando: Academic Press), pp. 281–299.

Amaral, D.G. (2003). The amygdala, social behavior, and danger detection. Ann. N Y Acad. Sci. *1000*, 337–347.

Amaral, D.G., Behniea, H., and Kelly, J.L. (2003). Topographic organization of projections from the amygdala to the visual cortex in the macaque monkey. Neuroscience *118*, 1099–1120.

Amorapanth, P., LeDoux, J.E., and Nader, K. (2000). Different lateral amygdala outputs mediate reactions and actions elicited by a fear-arousing stimulus. Nat. Neurosci. *3*, 74–79.

Anderson, A.K. (2004). Pay attention! Psychological and neural explorations of emotion and attention. 16th Annual Meeting of the American Psychological Society, Chicago.

Anderson, A.K., and Phelps, E.A. (2000). Expression without recognition: contributions of the human amygdala to emotional communication. Psychol. Sci. *11*, 106–111.

Anderson, A.K., and Phelps, E.A. (2001). Lesions of the human amygdala impair enhanced perception of emotionally salient events. Nature *411*, 305–309.

Anderson, A.K., and Phelps, E.A. (2002). Is the human amygdala critical for the subjective experience of emotion? Evidence of intact dispositional affect in patients with amygdala lesions. J. Cogn. Neurosci. *14*, 709–720.

Anderson, A.K., Christoff, K., Panitz, D., De Rosa, E., and Gabrieli, J.D. (2003). Neural correlates of the automatic processing of threat facial signals. J. Neurosci. *23*, 5627–5633.

Anderson, M.C., Ochsner, K.N., Kuhl, B., Cooper, J., Robertson, E., Gabrieli, S.W., Glover, G.H., and Gabrieli, J.D. (2004). Neural systems underlying the suppression of unwanted memories. Science *303*, 232–235.

Armony, J.L., and LeDoux, J.E. (1999). How danger is encoded: Towards a systems, cellular, and computational understanding of cognitive-emotional interactions in fear circuits. In The Cognitive Neurosciences, M.S. Gazzaniga, ed. (Cambridge: MIT Press).

Armony, J.L., Servan-Schreiber, D., Cohen, J.D., and LeDoux, J.E. (1997). Computational modeling of emotion: Explorations through the anatomy and physiology of fear conditioning. Trends Cogn. Sci. *1*, 28–34.

Bachevalier, J. (1994). Medial temporal lobe structures and autism: A review of clinical and experimental findings. Neuropsychologia *32*, 627–648.

Bailey, C.H., Bartsch, D., and Kandel, E.R. (1996). Toward a molecular definition of long-term memory storage. Proc. Natl. Acad. Sci. USA *93*, 13445–13452.

Barbas, H. (2000). Connections underlying the synthesis of cognition, memory, and emotion in primate prefrontal cortices. Brain Res. Bull. *52*, 319–330.

Baron-Cohen, S., Ring, H.A., Bullmore, E.T., Wheelwright, S., Ashwin, C., and Williams, S.C. (2000). The amygdala theory of autism. Neurosci. Biobehav. Rev. *24*, 355–364.

Baxter, M.G., and Murray, E.A. (2002). The amygdala and reward. Nat. Rev. Neurosci. *3*, 563–573.

Bechara, A., Tranel, D., Damasio, H., Adolphs, R., Rockland, C., and Damasio, A.R. (1995). Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. Science *269*, 1115–1118.

Berlyne, D.E., and Carey, S.T. (1968). Incidental learning and the timing of arousal. Psychon. Sci. *13*, 103–104.

Blair, H.T., Schafe, G.E., Bauer, E.P., Rodrigues, S.M., and LeDoux, J.E. (2001). Synaptic plasticity in the lateral amygdala: a cellular hypothesis of fear conditioning. Learn. Mem. *8*, 229–242.

Booth, J.R., Burman, D.D., Meyer, J.R., Gitelman, D.R., Parrish, T.B., and Mesulam, M.M. (2002). Modality independence of word comprehension. Hum. Brain Mapp. *16*, 251–261.

Bouton, M.E. (2002). Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. Biol. Psychiatry *52*, 976–986.

Buchel, C., Morris, J., Dolan, R.J., and Friston, K.J. (1998). Brain systems mediating aversive conditioning: an event-related fMRI study. Neuron *20*, 947–957.

Cahill, L., and Alkire, M.T. (2003). Epinephrine enhancement of human memory consolidation: interaction with arousal at encoding. Neurobiol. Learn. Mem. *79*, 194–198.

Cahill, L., Prins, B., Weber, M., and McGaugh, J.L. (1994). Beta-adrenergic activation and memory for emotional events. Nature *371*, 702–704.

Cahill, L., Babinsky, R., Markowitsch, H.J., and McGaugh, J.L. (1995). The amygdala and emotional memory. Nature *377*, 295–296.

Cahill, L., Haier, R.J., Fallon, J., Alkire, M.T., Tang, C., Keator, D., Wu, J., and McGaugh, J.L. (1996). Amygdala activity at encoding correlated with long-term, free recall of emotional information. Proc. Natl. Acad. Sci. USA *93*, 8016–8021.

Cahill, L., Weinberger, N.M., Roozendaal, B., and McGaugh, J.L. (1999). Is the amygdala a locus of "conditioned fear"? Some questions and caveats. Neuron *23*, 227–228.

Cahill, L., Gorski, L., and Le, K. (2003). Enhanced human memory consolidation with post-learning stress: interaction with the degree of arousal at encoding. Learn. Mem. *10*, 270–274.

Canli, T., Zhao, Z., Brewer, J., Gabrieli, J.D., and Cahill, L. (2000). Event-related activation in the human amygdala associates with later memory for individual emotional experience. J. Neurosci. *20*, RC99.

Canli, T., Sivers, H., Whitfield, S.L., Gotlib, I.H., and Gabrieli, J.D. (2002). Amygdala response to happy faces as a function of extraversion. Science *296*, 2191.

Carrasco, M. (2004). Covert transient attention increases contrast sensitivity and spatial resolution: Support for signal enhancement. In Neurobiology of Attention, L. Itti, G. Rees, and J. Tsotsos, eds. (San Diego: Elsevier).

Cherry, E.C. (1953). Some experiments on the recognition of speech, with one and two ears. J. Acoust. Soc. Am. *25*, 975–979.

Chiba, A.A., Bucci, D.J., Holland, P.C., and Gallagher, M. (1995). Basal forebrain cholinergic lesions disrupt increments but not decrements in conditioned stimulus processing. J. Neurosci. *15*, 7315–7322.

Corbetta, M., and Shulman, G.L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nat. Rev. Neurosci. *3*, 201–215.

Davis, H.P., and Squire, L.R. (1984). Protein synthesis and memory: a review. Psychol. Bull. *96*, 518–559.

Davis, M., and Whalen, P.J. (2001). The amygdala: vigilance and emotion. Mol. Psychiatry *6*, 13–34.

Davis, M., and Myers, K.M. (2002). The role of glutamate and gamma-aminobutyric acid in fear extinction: clinical implications for exposure therapy. Biol. Psychiatry *52*, 998–1007.

de Gelder, B., Snyder, J., Greve, D., Gerard, G., and Hadjikhani, N. (2004). Fear fosters flight: a mechanism for fear contagion when perceiving emotion expressed by a whole body. Proc. Natl. Acad. Sci. USA *101*, 16701–16706.

Debiec, J., and LeDoux, J.E. (2004). Disruption of reconsolidation but not consolidation of auditory fear conditioning by noradrenergic blockade in the amygdala. Neuroscience *129*, 267–272.

Debiec, J., LeDoux, J.E., and Nader, K. (2002). Cellular and systems reconsolidation in the hippocampus. Neuron *36*, 527–538.

Delgado, M.R., Trujillo, J.L., Holmes, B., Nearing, K.I., LeDoux, J.E., and Phelps, E.A. (2004). Emotion regulation of conditioned fear: The contributions of reappraisal. 11th Annual Meeting of the Cognitive Neuroscience Society, San Francisco.

Dolcos, F., LaBar, K.S., and Cabeza, R. (2004). Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. Neuron *42*, 855–863.

Dudai, Y. (2002). Molecular bases of long-term memories: a question of persistence. Curr. Opin. Neurobiol. *12*, 211–216.

Edeline, J.M. (1999). Learning-induced physiological plasticity in the thalamo-cortical sensory systems: a critical evaluation of receptive field plasticity, map changes and their potential mechanisms. Prog. Neurobiol. *57*, 165–224.

Eichenbaum, H. (2002). The Cognitive Neuroscience of Memory (New York: Oxford University Press).

Eisenberg, M., Kobilo, T., Berman, D.E., and Dudai, Y. (2003). Stability of retrieved memory: inverse correlation with trace dominance. Science *301*, 1102–1104.

Everitt, B.J., and Robbins, T.W. (1997). Central cholinergic systems and cognition. Annu. Rev. Psychol. *48*, 649–684.

Everitt, B.J., Parkinson, J.A., Olmstead, M.C., Arroyo, M., Robledo, P., and Robbins, T.W. (1999). Associative processes in addiction and reward. The role of amygdala-ventral striatal subsystems. Ann. N Y Acad. Sci. *877*, 412–438.

Fanselow, M.S., and LeDoux, J.E. (1999). Why we think plasticity underlying Pavlovian fear conditioning occurs in the basolateral amygdala. Neuron *23*, 229–232.

Fanselow, M.S., and Poulos, A.M. (2005). The neuroscience of mammalian associative learning. Annu. Rev. Psychol. *56*, 207–234.

Funayama, E.S., Grillon, C., Davis, M., and Phelps, E.A. (2001). A double dissociation in the affective modulation of startle in humans: effects of unilateral temporal lobectomy. J. Cogn. Neurosci. *13*, 721–729.

Gallagher, M., and Chiba, A.A. (1996). The amygdala and emotion. Curr. Opin. Neurobiol. *6*, 221–227.

Garcia, R. (2002). Stress, synaptic plasticity, and psychopathology. Rev. Neurosci. *13*, 195–208.

Gross, J.J. (2002). Emotion regulation: affective, cognitive, and social consequences. Psychophysiology *39*, 281–291.

Hamann, S.B., Ely, T.D., Grafton, S.T., and Kilts, C.D. (1999). Amygdala activity related to enhanced memory for pleasant and aversive stimuli. Nat. Neurosci. *2*, 289–293.

Heberlein, A.S., and Adolphs, R. (2004). Impaired spontaneous anthropomorphizing despite intact perception and social knowledge. Proc. Natl. Acad. Sci. USA *101*, 7487–7491.

Heider, F., and Simmel, M. (1944). An experimental study of apparent behavior. Am. J. Psychol. *57*, 243–259.

Holland, P.C., and Gallagher, M. (1999). Amygdala circuitry in attentional and representational processes. Trends Cogn. Sci. *3*, 65–73.

Johnsrude, I.S., Owen, A.M., White, N.M., Zhao, W.V., and Bohbot, V. (2000). Impaired preference conditioning after anterior temporal lobe resection in humans. J. Neurosci. *20*, 2649–2656.

Kalin, N.H., Shelton, S.E., and Davidson, R.J. (2004). The role of the central nucleus of the amygdala in mediating fear and anxiety in the primate. J. Neurosci. *24*, 5506–5515.

Kapp, B.S., Whalen, P.J., Supple, W.F., and Pascoe, J.P. (1992). Amygdaloid contributions to conditioned arousal and sensory information processing. In The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction, J.P. Aggleton, ed. (New York: Wiley-Liss), pp. 229–254.

Kemper, T.L., and Bauman, M.L. (1993). The contribution of neuropathologic studies to the understanding of autism. Neurol. Clin. *11*, 175–187.

Killcross, S., Robbins, T.W., and Everitt, B.J. (1997). Different types of fear-conditioned behaviour mediated by separate nuclei within amygdala. Nature *388*, 377–380.

Kim, H., Somerville, L.H., Johnstone, T., Alexander, A.L., and Whalen, P.J. (2003). Inverse amygdala and medial prefrontal cortex responses to surprised faces. Neuroreport *14*, 2317–2322.

Kleinsmith, L.J., and Kaplan, S. (1963). Paired-associate learning as a function of arousal and interpolated interval. J. Exp. Psychol. *65*, 190–193.

Kling, A.S., and Brothers, L.A. (1992). The amygdala and social behavior. In The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction, J.P. Aggleton, ed. (New York: Wiley-Liss, Inc), pp. 353–377.

Kluver, H., and Bucy, P.C. (1937). "Psychic blindness" and other symptoms following bilateral temporal lobectomy in rhesus monkeys. Am. J. Physiol. *119*, 352–353.

Knight, D.C., Smith, C.N., Cheng, D.T., Stein, E.A., and Helmstetter, F.J. (2004). Amygdala and hippocampal activity during acquisition and extinction of human fear conditioning. Cogn. Affect. Behav. Neurosci. *4*, 317–325.

LaBar, K.S., and Phelps, E.A. (1998). Arousal-mediated memory consolidation: role of the medial temproal lobe in humans. Psychol. Sci. *9*, 490–493.

LaBar, K.S., LeDoux, J.E., Spencer, D.D., and Phelps, E.A. (1995). Impaired fear conditioning following unilateral temporal lobectomy in humans. J. Neurosci. *15*, 6846–6855.

LaBar, K.S., Gatenby, J.C., Gore, J.C., LeDoux, J.E., and Phelps, E.A. (1998). Human amygdala activation during conditioned fear acquisition and extinction: a mixed-trial fMRI study. Neuron *20*, 937–945.

Lattal, K.M., Honarvar, S., and Abel, T. (2004). Effects of post-session injections of anisomycin on the extinction of a spatial preference and on the acquisition of a spatial reversal preference. Behav. Brain Res. *153*, 327–339.

LeDoux, J.E. (1994). Emotion, memory and the brain. Sci. Am. *270*, 50–57.

LeDoux, J.E. (1996). The Emotional Brain (New York: Simon and Schuster).

LeDoux, J.E. (2000). Emotion circuits in the brain. Annu. Rev. Neurosci. *23*, 155–184.

LeDoux, J.E. (2002). Synaptic Self: How Our Brains Become Who We Are (New York: Viking).

LeDoux, J.E., and Gorman, J.M. (2001). A call to action: overcoming anxiety through active coping. Am. J. Psychiatry *158*, 1953–1955.

LeDoux, J.E., Sakaguchi, A., and Reis, D.J. (1984). Subcortical efferent projections of the medial geniculate nucleus mediate emotional responses conditioned to acoustic stimuli. J. Neurosci. *4*, 683–698.

LeDoux, J.E., Romanski, L.M., and Xagoraris, A.E. (1989). Indelibility of subcortical emotional memories. J. Cogn. Neurosci. *1*, 238–243.

Lee, H.J., Choi, J.S., Brown, T.H., and Kim, J.J. (2001). Amygdalar nmda receptors are critical for the expression of multiple conditioned fear responses. J. Neurosci. *21*, 4116–4124.

Maren, S. (2001). Neurobiology of Pavlovian fear conditioning. Annu. Rev. Neurosci. *24*, 897–931.

Maren, S., Yap, S.A., and Goosens, K.A. (2001). The amygdala is essential for the development of neuronal plasticity in the medial geniculate nucleus during auditory fear conditioning in rats. J. Neurosci. *21*, RC135.

Martin, S.J., and Morris, R.G. (2002). New life in an old idea: the synaptic plasticity and memory hypothesis revisited. Hippocampus *12*, 609–636.

McGaugh, J.L. (2000). Memory—a century of consolidation. Science *287*, 248–251.

McGaugh, J.L. (2002). Memory consolidation and the amygdala: a systems perspective. Trends Neurosci. *25*, 456.

McGaugh, J.L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. Annu. Rev. Neurosci. *27*, 1–28.

Medina, J.F., Christopher Repa, J., Mauk, M.D., and LeDoux, J.E. (2002). Parallels between cerebellum- and amygdala-dependent conditioning. Nat. Rev. Neurosci. *3*, 122–131.

Meunier, M., and Bachevalier, J. (2002). Comparison of emotional responses in monkeys with rhinal cortex or amygdala lesions. Emotion *2*, 147–161.

Meunier, M., Bachevalier, J., Murray, E.A., Malkova, L., and Mishkin, M. (1999). Effects of aspiration versus neurotoxic lesions of the amygdala on emotional responses in monkeys. Eur. J. Neurosci. *11*, 4403–4418.

Milad, M.R., and Quirk, G.J. (2002). Neurons in medial prefrontal cortex signal memory for fear extinction. Nature *420*, 70–74.

Milad, M.R., Vidal-Gonzalez, I., and Quirk, G.J. (2004). Electrical stimulation of medial prefrontal cortex reduces conditioned fear in a temporally specific manner. Behav. Neurosci. *118*, 389–394.

Milekic, M.H., and Alberini, C.M. (2002). Temporally graded requirement for protein synthesis following memory reactivation. Neuron *36*, 521–525.

Milner, B., Corkin, S., and Teuber, H.L. (1968). Further analysis of the hippocampal amnesic syndrome: 14-year follow-up study of H.M. Neuropsychologia *6*, 216–234.

Morgan, M.A., and LeDoux, J.E. (1995). Differential contribution of dorsal and ventral medial prefrontal cortex to the acquisition and extinction of conditioned fear in rats. Behav. Neurosci. *109*, 681–688.

Morgan, M.A., Romanski, L.M., and LeDoux, J.E. (1993). Extinction of emotional learning: contribution of medial prefrontal cortex. Neurosci. Lett. *163*, 109–113.

Morgan, M.A., Schulkin, J., and LeDoux, J.E. (2003). Ventral medial prefrontal cortex and emotional perseveration: the memory for prior extinction training. Behav. Brain Res. *146*, 121–130.

Morris, J.S., Friston, K.J., Buchel, C., Frith, C.D., Young, A.W., Calder, A.J., and Dolan, R.J. (1998a). A neuromodulatory role for the human amygdala in processing emotional facial expressions. Brain *121*, 47–57.

Morris, J.S., Ohman, A., and Dolan, R.J. (1998b). Conscious and unconscious emotional learning in the human amygdala. Nature *393*, 467–470.

Morris, J.S., Buchel, C., and Dolan, R.J. (2001a). Parallel neural responses in amygdala subregions and sensory cortex during implicit fear conditioning. Neuroimage *13*, 1044–1052.

Morris, J.S., DeGelder, B., Weiskrantz, L., and Dolan, R.J. (2001b). Differential extrageniculostriate and amygdala responses to presentation of emotional faces in a cortically blind field. Brain *124*, 1241–1252.

Myers, K.M., and Davis, M. (2002). Behavioral and neural analysis of extinction. Neuron *36*, 567–584.

Nader, K., Schafe, G.E., and Le Doux, J.E. (2000). Fear memories require protein synthesis in the amygdala for reconsolidation after retrieval. Nature *406*, 722–726.

Nader, K., Majidishad, P., Amorapanth, P., and LeDoux, J.E. (2001). Damage to the lateral and central, but not other, amygdaloid nuclei prevents the acquisition of auditory fear conditioning. Learn. Mem. *8*, 156–163.

Ochsner, K.N., Bunge, S.A., Gross, J.J., and Gabrieli, J.D. (2002). Rethinking feelings: an FMRI study of the cognitive regulation of emotion. J. Cogn. Neurosci. *14*, 1215–1229.

Ochsner, K.N., Ray, R.D., Cooper, J.C., Robertson, E.R., Chopra, S., Gabrieli, J.D., and Gross, J.J. (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. Neuroimage *23*, 483–499.

Ono, T., and Nishijo, H. (1992). Neurophysiological basis of the Kluver-Bucy syndrome: responses of monkey amygdaloid neurons to biologically significant objects. In The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction, J.P. Aggleton, ed. (New York: Wiley-Liss, Inc), pp. 167–190.

Packard, M.G., and Teather, L.A. (1998). Amygdala modulation of multiple memory systems: hippocampus and caudate-putamen. Neurobiol. Learn. Mem. *69*, 163–203.

Packard, M.G., and Cahill, L. (2001). Affective modulation of multiple memory systems. Curr. Opin. Neurobiol. *11*, 752–756.

Pare, D., Quirk, G.J., and Ledoux, J.E. (2004). New vistas on amygdala networks in conditioned fear. J. Neurophysiol. *92*, 1–9.

Pasley, B.N., Mayes, L.C., and Schultz, R.T. (2004). Subcortical discrimination of unperceived objects during binocular rivalry. Neuron *42*, 163–172.

Pegna, A.J., Khateb, A., Lazeyras, F., and Seghier, M.L. (2005). Discriminating emotional faces without primary visual cortices involves the right amygdala. Nat. Neurosci. *8*, 24–25.

Pessoa, L., and Ungerleider, L.G. (2004). Neuroimaging studies of attention and the processing of emotion-laden stimuli. Prog. Brain Res. *144*, 171–182.

Pessoa, L., McKenna, M., Gutierrez, E., and Ungerleider, L.G. (2002). Neural processing of emotional faces requires attention. Proc. Natl. Acad. Sci. USA *99*, 11458–11463.

Phelps, E.A., LaBar, K.S., Anderson, A., O'Connor, K.J., Fulbright, R.K., and Spencer, D.D. (1998). Specifying the contributions of the human amygdala to emotional memory: A Case Study. Neurocase *4*, 527–540.

Phelps, E.A., O'Connor, K.J., Cunningham, W.A., Funayama, E.S., Gatenby, J.C., Gore, J.C., and Banaji, M.R. (2000). Performance on indirect measures of race evaluation predicts amygdala activation. J. Cogn. Neurosci. *12*, 729–738.

Phelps, E.A., O'Connor, K.J., Gatenby, J.C., Gore, J.C., Grillon, C., and Davis, M. (2001). Activation of the left amygdala to a cognitive representation of fear. Nat. Neurosci. *4*, 437–441.

Phelps, E.A., Delgado, M.R., Nearing, K.I., and LeDoux, J.E. (2004). Extinction learning in humans: role of the amygdala and vmPFC. Neuron *43*, 897–905.

Phelps, E.A., Ling, S., and Carrasco, M. (2005). Emotion facilitates perception and potentiates the perceptual benefit of attention. Psychol. Sci., in press.

Pitkänen, A., Savander, V., and LeDoux, J.E. (1997). Organization of intra-amygdaloid circuitries in the rat: an emerging framework for understanding functions of the amygdala. Trends Neurosci. *20*, 517–523.

Polonsky, A., Blake, R., Braun, J., and Heeger, D.J. (2000). Neuronal activity in human primary visual cortex correlates with perception during binocular rivalry. Nat. Neurosci. *3*, 1153–1159.

Poremba, A., and Gabriel, M. (2001). Amygdalar efferents initiate auditory thalamic discriminative training-induced neuronal activity. J. Neurosci. *21*, 270–278.

Quirk, G.J., and Gehlert, D.R. (2003). Inhibition of the amygdala: key to pathological states? Ann. N Y Acad. Sci. *985*, 263–272.

Quirk, G.J., Armony, J.L., and LeDoux, J.E. (1997). Fear conditioning enhances different temporal components of tone-evoked spike trains in auditory cortex and lateral amygdala. Neuron *19*, 613–624.

Quirk, G.J., Russo, G.K., Barron, J.L., and Lebron, K. (2000). The role of ventromedial prefrontal cortex in the recovery of extinguished fear. J. Neurosci. *20*, 6225–6231.

Radwanska, K., Nikolaev, E., Knapska, E., and Kaczmarek, L. (2002). Differential response of two subdivisions of lateral amygdala to aversive conditioning as revealed by c-Fos and P-ERK mapping. Neuroreport *13*, 2241–2246.

Repa, J.C., Muller, J., Apergis, J., Desrochers, T.M., Zhou, Y., and LeDoux, J.E. (2001). Two different lateral amygdala cell populations contribute to the initiation and storage of memory. Nat. Neurosci. *4*, 724–731.

Ressler, K.J., Rothbaum, B.O., Tannenbaum, L., Anderson, P., Graap, K., Zimand, E., Hodges, L., and Davis, M. (2004). Cognitive enhancers as adjuncts to psychotherapy: use of D-cycloserine in phobic individuals to facilitate extinction of fear. Arch. Gen. Psychiatry *61*, 1136–1144.

Riccio, D.C., Moody, E.W., and Millin, P.M. (2002). Reconsolidation reconsidered. Integr. Physiol. Behav. Sci. *37*, 245–253.

Rodrigues, S.M., Schafe, G.E., and LeDoux, J.E. (2004). Molecular mechanisms underlying emotional learning and memory in the lateral amygdala. Neuron *44*, 75–91.

Rolls, E.T. (1999). The Brain and Emotion (Oxford: Oxford University Press).

Romanski, L.M., and LeDoux, J.E. (1992). Equipotentiality of thalamo-amygdala and thalamo-cortico-amygdala circuits in auditory fear conditioning. J. Neurosci. *12*, 4501–4509.

Roozendaal, B. (2002). Stress and memory: opposing effects of glucocorticoids on memory consolidation and memory retrieval. Neurobiol. Learn. Mem. *78*, 578–595.

Rosen, J.B. (2004). The neurobiology of conditioned and unconditioned fear: a neurobehavioral system analysis of the amygdala. Behav. Cogn. Neurosci. Rev. *3*, 23–41.

Rosenkranz, J.A., and Grace, A.A. (2002). Dopamine-mediated modulation of odour-evoked amygdala potentials during pavlovian conditioning. Nature *417*, 282–287.

Rosenkranz, J.A., Moore, H., and Grace, A.A. (2003). The prefrontal cortex regulates lateral amygdala neuronal plasticity and responses to previously conditioned stimuli. J. Neurosci. *23*, 11054–11064.

Rosvold, H.E., Mirsky, A.F., and Pribram, K.H. (1954). Influence of amygdalectomy on social behavior in monkeys. J. Comp. Physiol. Psychol. *47*, 173–178.

Sah, P., Faber, E.S., Lopez De Armentia, M., and Power, J. (2003). The amygdaloid complex: anatomy and physiology. Physiol. Rev. *83*, 803–834.

Sara, S.J. (2000). Retrieval and reconsolidation: toward a neurobiology of remembering. Learn. Mem. *7*, 73–84.

Schacter, D.L. (1996). Memory distortion: How minds, brains, and societies reconstruct the past. Nature *380*, 214.

Schaefer, S.M., Jackson, D.C., Davidson, R.J., Aguirre, G.K., Kimberg, D.Y., and Thompson-Schill, S.L. (2002). Modulation of amygdalar activity by the conscious regulation of negative emotion. J. Cogn. Neurosci. *14*, 913–921.

Schafe, G.E., and LeDoux, J.E. (2000). Memory consolidation of auditory Pavlovian fear conditioning requires protein synthesis and protein Kinase A in the amygdala. J. Neurosci. *20*, RC96.

Schafe, G.E., Nader, K., Blair, H.T., and LeDoux, J.E. (2001). Memory consolidation of Pavlovian fear conditioning: a cellular and molecular perspective. Trends Neurosci. *24*, 540–546.

Singer, T., Kiebel, S.J., Winston, J.S., Dolan, R.J., and Frith, C.D. (2004). Brain responses to the acquired moral status of faces. Neuron *41*, 653–662.

Sotres-Bayon, F., Bush, D.E., and LeDoux, J.E. (2004). Emotional perseveration: an update on prefrontal-amygdala interactions in fear extinction. Learn. Mem. *11*, 525–535.

Squire, L.R., and Kandel, E.R. (1999). Memory: From Mind to Molecules (New York: Scientific American Library).

Sullivan, G.M., Apergis, J., Bush, D.E., Johnson, L.R., Hou, M., and Ledoux, J.E. (2004). Lesions in the bed nucleus of the stria terminalis disrupt corticosterone and freezing responses elicited by a contextual but not by a specific cue-conditioned fear stimulus. Neuroscience *128*, 7–14.

Vuilleumier, P., Armony, J.L., Driver, J., and Dolan, R.J. (2001). Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. Neuron *30*, 829–841.

Vuilleumier, P., Armony, J.L., Driver, J., and Dolan, R.J. (2003). Distinct spatial frequency sensitivities for processing faces and emotional expressions. Nat. Neurosci. *6*, 624–631.

Vuilleumier, P., Richardson, M.P., Armony, J.L., Driver, J., and Dolan, R.J. (2004). Distant influences of amygdala lesion on visual cortical activation during emotional face processing. Nat. Neurosci. *7*, 1271–1278.

Walker, D.L., and Davis, M. (2002). The role of amygdala glutamate receptors in fear learning, fear-potentiated startle, and extinction. Pharmacol. Biochem. Behav. *71*, 379–392.

Walker, D.L., Ressler, K.J., Lu, K.T., and Davis, M. (2002). Facilitation of conditioned fear extinction by systemic administration or intra-amygdala infusions of D-cycloserine as assessed with fear-potentiated startle in rats. J. Neurosci. *22*, 2343–2351.

Walker, M.P., Brakefield, T., Hobson, J.A., and Stickgold, R. (2003a). Dissociable stages of human memory consolidation and reconsolidation. Nature *425*, 616–620.

Walker, D.L., Toufexis, D.J., and Davis, M. (2003b). Role of the bed nucleus of the stria terminalis versus the amygdala in fear, stress, and anxiety. Eur. J. Pharmacol. *463*, 199–216.

Weinberger, N.M. (1995). Retuning the brain by fear conditioning. In The Cognitive Neurosciences, M.S. Gazzaniga, ed. (Cambridge, MA: The MIT Press), pp. 1071–1090.

Weinberger, N., Ashe, J., Metherate, R., McKenna, T., Diamond, D., Bakin, J., Lennartz, R., and Cassady, J. (1990). Neural adaptive information processing: A preliminary model of receptive-field plasticity in auditory cortex during Pavlovian conditioning. In Learning and Computational Neuroscience: Foundations of Adaptive Networks, M. Gabriel, and J. Moore, eds. (Cambridge, MA: The MIT Press), pp. 91–138.

Weiskrantz, L. (1956). Behavioral changes associated with ablation of the amygdaloid complex in monkeys. J. Comp. Physiol. Psychol. *49*, 381–391.

Whalen, P.J. (1998). Fear, vigilance, and ambiguity: initial neuroimaging studies of the human amygdala. Curr. Dir. Psychol. Sci. *7*, 177–188.

Whalen, P.J., Rauch, S.L., Etcoff, N.L., McInerney, S.C., Lee, M.B., and Jenike, M.A. (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. J. Neurosci. *18*, 411–418.

Whalen, P.J., Kagan, J., Cook, R.G., Davis, F.C., Kim, H., Polis, S., McLaren, D.G., Somerville, L.H., McLean, A.A., Maxwell, J.S., and Johnstone, T. (2004). Human amygdala responsivity to masked fearful eye whites. Science *306*, 2061.

Wilensky, A.E., Schafe, G.E., and LeDoux, J.E. (1999). Functional inactivation of the amygdala before but not after auditory fear conditioning prevents memory formation. J. Neurosci. *19*, RC48.

Williams, M.A., Morris, A.P., McGlone, F., Abbott, D.F., and Mattingley, J.B. (2004). Amygdala responses to fearful and happy facial expressions under conditions of binocular suppression. J. Neurosci. *24*, 2898–2904.

Zola-Morgan, S., Squire, L.R., Alvarez-Royo, P., and Clower, R.P. (1991). Independence of Memory Functions and Emotional Behavior: Separate Contributions of the Hippocampal Formation and the Amygdala. Hippocampus *1*, 207–220.