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8. WHERE THE WILD THINGS ARE (pp. 225-266, 325-329).

"A phobia, like a psychoanalytic theory, is a story about where the wild things are." Adam Phillips, *On Kissing, Tickling, and Being Bored: Psychoanalytic Essays on the Unexamined Life*¹

In 1793, revolution was in the air in Paris. But the French Revolution about which we are concerned here took place, not in the streets, but in mental asylums. Philippe Pinel had the radical opinion that the mentally ill were not hopeless wild animals that should be incarcerated and tortured, but were people who should be treated with decency and respect. When the Revolution's prison commissioner heard of Pinel's plans to rehabilitate the insane, he asked, "Are you not yourself mad to free these beasts?" Pinel responded, "I am convinced that the *people* are not incurable if they can have air and liberty." Some of the "beasts" recovered under Pinel's guidance. One became his bodyguard.² By 1800 Pinel had become one of the most influential physicians in Paris and he was called upon by the Revolution's Society of Observers of Man to evaluate a truly wild beast, a boy around eleven years old, who, a few months earlier, had been captured in a small village in southern France. As recounted by Roger Shattuck, author of a fascinating book about the Wild Boy of Aveyron, the incident went like this:

Before dawn on January 9, 1800, a remarkable creature came out of the woods near the village of Saint-Sernin in southern France. No one expected him. No one recognized him. He was human in bodily form and walked erect. Everything else about him suggested an animal. He was naked except for the tatters of a shirt and showed no modesty, no awareness of himself as a human person related in any way to the people who had captured him. He could not speak and made only weird, meaningless cries.³

In spite of his prior successes, Pinel felt that rehabilitation was not possible in the case of the Wild Boy. According to Shattuck, Pinel seems not to have seriously pondered whether the boy's condition was due to "organic" or "functional" causes, a distinction that Pinel commonly made in other cases. Such an analysis might have led to a more informed decision about whether the boy was curable. If the problem was organic, say due to brain damage, then his wild state might indeed be untreatable. But if life's circumstances—the lack of nurturing care during his early childhood, the absence of social stimulation, his stressful, traumatic existence in a hostile environment—were the causes, some cure might have been possible. As Shattuck notes, we will never know the answer. So-called functional disorders are indeed more likely to be treatable than those related to organic causes. However, the distinction between organic and functional maladies needs to be made cautiously, and should in no way imply that some mental disorders are attacks on the brain and others on the mind. As Shakespeare said, the brain is the soul's dwelling place.⁴ Mental disorders, like mental order, reflect the workings of the brain.

Actually, Shakespeare's phrase was the soul's *frail* dwelling place, which speaks to the thinness of the line between mental health and illness. We all experience sadness and worry from time to time. But when these become excessive and inappropriate to the circumstances, we slide from normal to pathological emotions.

In this chapter we are going to be especially concerned with the pathological emotions called anxiety disorders. These are among the most common forms of mental illness.⁵ I will argue they involve the fear system of the brain, and that the progress we've made in understanding how the fear system normally works also helps us understand what goes wrong in anxiety disorders. I'll propose that anxiety disorders come about when the fear system breaks loose from the cortical controls that usually keep our primitive impulses—the wild things in us—at bay.

A Brief History of Mental Illness

The diagnosis of mental disorders has its roots in the work of Emil Kraepelin in the late nineteenth century. He distinguished schizophrenia from manic-depression by showing that these illnesses take different courses. Freud, Kraepelin's contemporary, was more concerned with neuroses than with psychotic conditions like schizophrenia and emphasized intra-psychic conflict and the resulting anxiety as the cause. According to psychiatrist Peter Kramer, by mid-century American psychiatrists had outdone Freud.⁶ They had adopted the spectrum model of mental illness, which assumed that all forms of psychopathology are secondary to anxiety.⁷ Neurosis was, in the typical Freudian view, the result of a partially successful defense against anxiety that was accompanied by symptom formation. But under the spectrum model even psychosis came to be viewed as the result of anxiety, such excess anxiety that the ego crumbled and regressed. Mental health and mental illness were distinguished by the degree of anxiety present, and the same treatment, the reduction of inner conflict via psychotherapy, was applicable to all ailments.

The tides have since shifted. Mental health professionals now have a dazzling array of diagnostic categories available to them. All one has to do to see how radically things have changed is to thumb through the diagnostic bible, the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM), first published in 1980, now in its fourth edition.⁸ There are a host of phobias, different kinds of panic attacks, a variety of mood and thought disorders, somatization disorders, antisocial personality conditions, numerous forms of substance abuse, and other conditions. In addition, there are overlaps, such as panic with agoraphobia (fear of open or crowded places), or manic-depression with cocaine dependence, and so on.

In spite of this diagnostic diversity, it is clear that some categories of mental illness occur more than others. The U.S. Public Health Service counts and classifies the prevalence of different forms of mental disorders.⁹ In 1994, about 51 million Americans eighteen years and older had some form of diagnosed mental illness, with about 11 million of those involving substance abuse. Of the remaining 40 million, more than half were accounted for by the category of anxiety disorders, and somewhat less than half by mood disorders (especially depression), with schizophrenia and assorted other conditions accounting for the rest.

The high proportion of mental disorders that involve anxiety does not vindicate the spectrum theory, for treating depression or schizophrenia as anxiety is probably not going to get you as far as treating them uniquely. However, it does emphasize the importance of understanding the nature of anxiety and its various manifestations. Fortunately, the understanding of the fear system that has been achieved can help us explain how anxiety disorders arise, and may also help us figure out how to treat them and possibly prevent their occurrence.

Fear and Loathing in Anxiety

Anxiety and fear are closely related. Both are reactions to harmful or potentially harmful situations. Anxiety is usually distinguished from fear by the lack of an external stimulus that elicits the reaction—anxiety comes from within us, fear from the outside world. The sight of a snake elicits fear, but the remembrance of some unpleasant experience with a snake or the anticipation that you may encounter a snake are conditions of anxiety. Anxiety has also been described as unresolved fear.¹⁰ Fear, according to this view, is related to the behavioral acts of escape and avoidance in threatening situations, and when these actions are thwarted, fear becomes anxiety.

Fear and anxiety are normal reactions to dangers (real or imagined) and are not themselves pathological conditions. When fear and anxiety are more recurrent and persistent than what is reasonable under the circumstances, and when they impede normal life, then a fear/anxiety disorder exists.¹¹

Conditions that reflect anxiety and its defences (conversion, repression, displacement)¹² were called neuroses by Freud. Today, the field of psychiatry is less devoutly Freudian than it once was and the term "neurosis" is de-emphasized in DSM to avoid the implication that symptoms of anxiety necessarily reflect Freudian defense mechanisms.¹³ Consequently, while DSM anxiety disorders include conditions that Freud called anxiety neuroses, more contemporary diagnoses appear as well.¹⁴ The full complement of DSM anxiety disorders are: panic, phobias, post-traumatic stress disorder, obsessive-compulsive disorder, and generalized anxiety.

The characteristic features of these disorders are intense feelings of anxiety and avoidance of situations that are likely to bring on these feelings.¹⁵ Phobias are fears of specific stimuli or situations that are in excess of the actual threat posed. Exposure to the phobic object or situation reliably elicits a profound state of anxiety. The person will go to great lengths to avoid the object or situation. Panic attacks involve discrete periods of intense anxiety and discomfort. The afflicted person often feels like he or she is suffocating. Unlike phobias, the attacks are often unpredictable and frequently not related to any particular external stimulus or situation. Sometimes panic is accompanied by agoraphobia. In severe cases, avoidance of such situations can lead to a sheltered existence. Post-traumatic stress disorder (PTSD) involves severe anxiety elicited by stimuli that were present during some extreme trauma or that are somehow related to stimuli that occurred during the trauma. It is common in war veterans but also occurs in victims of severe physical or sexual abuse or natural disasters. Situations or even thoughts that are likely to remind the person of the trauma are avoided. Obsessive-compulsive disorder involves intrusive, repetitive, and persistent thoughts and/or repetitive behaviors that are performed in a very precise way in response to obsessive thoughts. The compulsive behaviors are

meant to neutralize anxiety, but the behaviors are either not well connected to the situation or are excessive responses to the situation that they are intended to neutralize. Generalized anxiety, also known as free-floating anxiety, involves excessive worry about unrelated things for a long period of time.

DSM outlines symptoms and situational factors that allow skilled clinicians to distinguish the various anxiety disorders. However, Arne Öhman, a leader in the study of human fear and anxiety, has recently argued that, "when comparing the physiological responses seen in phobics exposed to their feared objects with those seen in PTSD patients exposed to relevant traumatic scenes for the disorder, and with physiological responses during panic attacks, one is much more struck by the similarities than by the differences."¹⁶ He goes on to argue that panic, phobic fear, and PTSD reflect the "activation of one and the same underlying anxiety response." This is essentially the case that I will make. However, I state the idea in terms of brain systems rather than symptoms: anxiety disorders reflect the operation of the fear system of the brain. Öhman leaves generalized anxiety out of his grouping because it involves a stable personality trait rather than discrete episodes of anxiety, a distinction that is often referred to as one between trait and state anxiety. However, generalized anxiety most likely involves the same underlying brain system (at least partly) as the other anxiety disorders.

Little Albert Meets Little Hans

Anxiety disorders can arise at any time, but most often appear in early adult life. Why does this happen? How does the brain go from a state in which it is not especially anxious to one in which it is pathologically worried or exhibiting neurotic behaviors that keep the worry in check;

Most theorists from Freud onward have assumed that clinically debilitating anxiety is the result of traumatic learning experiences that create unpleasant memories. Breuer and Freud,¹⁷ in the famous case of Anna O., for example, argued that "hysterics suffer mainly from reminiscences," or as Matthew Erdelyi puts it, "traumatic memories which they have expunged from consciousness."¹⁸

Since fear conditioning is the *sine qua non* of traumatic learning, it should come as no surprise that fear conditioning has been proposed to be involved in the genesis of pathogenic anxiety. Though long considered controversial and incomplete, as we will see, new findings have made it seem more likely, and even quite plausible, that fear conditioning contributes significantly to anxiety disorders.¹⁹

The conditioning theory of anxiety arose in the 1920s, a time when psychologists were beginning to explain most aspects of behavior in terms of learning experiences, and particularly in terms of Pavlov's conditioned reflexes.²⁰ John Watson, the father of behaviorism, claimed to have conditioned an animal phobia in an eleven-month-old boy, Little Albert, by making a loud clanging sound while the boy was happily playing with a rat.²¹ Thereafter, the boy avoided playing with the rat and cried when he was near it. To explain this finding, Watson proposed that certain stimuli (loud noises, painful stimuli, sudden loss of physical support) are innately capable of eliciting fear reactions. When these unconditioned stimuli occur, other stimuli that happen to be present acquire the capacity to elicit conditioned fear. According to Watson, neuroses arise as a result of these traumatic learning situations and then persist and influence behavior throughout life.²²

Watson's theory of anxiety, as well as his behaviorist view of psychology, was based on Pavlovian conditioned reflex learning. But by the 1930s, another form of learning, called instrumental conditioning, had come to be of equal importance to behaviorists.²³ In instrumental conditioning, an arbitrary response (like pressing a bar or making a turn in a maze) is learned if it is reinforced, which means it is either followed by the presentation of a reward or the omission of a punishment. The response is learned because it is reinforced, and thereafter is performed in order to get the reward or avoid the punishment. While Pavlovian conditioning involves the transfer of meaning from an emotionally arousing to a neutral stimulus, in instrumental conditioning the association is between an emotionally arousing stimulus and neutral response.

Behaviorism and psychoanalysis were radically different approaches, but both sought to understand why we act the way we do. O. Hobart Mowrer, a leading behaviorist, saw value in both approaches and set out in the 1940s to translate Freud's theory of anxiety neurosis into the language of learning theory.²⁴ Using the principles of Pavlovian and instrumental conditioning, Mowrer hoped to solve what he called the "neurotic paradox": "a normal sensible man, or even a beast to the limits of his intelligence, will weigh and balance the consequences of his acts.... If the net effect is unfavorable, the action producing it will be inhibited, abandoned. In neurosis, however, one sees actions which have predominantly unfavorable consequences, yet they persist over a period of months, years, or a lifetime."²⁵

Anxiety, according to Mowrer, motivates us to deal with traumatic events in advance of their occurrence. And because anxiety reduction brings about relief or security, it is a powerful reinforcer of instrumental behaviors (arbitrary responses that are learned because they satisfy some need or accomplish some goal). Responses that reduce anxiety are thus learned and maintained.

Mowrer felt that anxiety is initially learned much like Watson had suggested—stimuli that are present during painful or traumatic stimulation acquire the capacity to elicit anxiety. Because anxiety is uncomfortable, when the stimuli that elicit it are present the anxious person will be motivated to change the circumstances, to remove himself from where the anxiety-causing stimuli are, and to avoid such situations in the future. The reduction in anxiety that these responses produce then reinforces the behaviors and perpetuate their performance. This is often useful, but sometimes it leads to neurotic symptoms.

Consider a real-life example. A man is mugged in an elevator. From that day on, he becomes afraid of riding in elevators. He avoids them as much as possible. He consults a therapist, who tries to reassure him that it is highly unlikely that he will be mugged again in an elevator, especially if he rides at busy times. But the reassurance is not helpful. The man must get to his office on the thirteenth floor. This makes him anxious. In spite of the inconvenience that it causes him, each day he takes the stairs. The reduction in anxiety that results from taking the stairs, according to Mowrer's theory, maintains the neurotic behavior of taking the stairs.

Mowrer, like existentialist philosophers, saw anxiety as an important part of human existence, as fundamental to what is special about humans, but also as a clue to our frailty:

By and large, behavior that reduces anxiety also operates to lessen the danger that it presages. An antelope that scents a panther is likely not only to feel less uneasy (anxious) if it moves out of the range of the odor of the panther but also likely to be in fact somewhat safer. A primitive village that is threatened by marauding men or beasts sleeps better after it has surrounded itself with a deep moat or a sturdy stockade. And a modern mother is made emotionally more comfortable after her child has been properly vaccinated against a dreaded disease. This capacity to be made uncomfortable by the mere prospect of traumatic experiences, in advance of their actual occurrence (or reoccurrence), and to be motivated thereby to take realistic precautions against them, is unquestionably a tremendously important and useful psychological mechanism, and the fact that the forward-looking, anxiety-arousing propensity of the human mind is more highly developed than it is in lower animals probably accounts for many of man's unique accomplishments. But it also accounts for some of his most conspicuous failures.²⁶

Mowrer paved the way for a behavioral interpretation of Freud, but this pursuit was most successfully implemented by another behavioral psychologist, Neal Miller.²⁷ Miller had been attempting to work out in detail how fear might serve as a drive, like hunger or sex, an internal signal that motivates one to act in a way that reduces the drive. Just as a hungry animal looks for food, a fearful one tries to get away from the stimuli that arouse fear. He trained rats to avoid being shocked by jumping over a hurdle that separated two compartments whenever a buzzer sounded.²⁸ The first phase involved fear conditioning: the buzzer came on and the rats were shocked. Then, through random actions, they learned that if they jumped over the hurdle during the buzzer, they could avoid getting shocked. Once the rat figured this out, it would jump every time it heard the buzzer, even if the shock was turned off. The shock was no longer present and was thus no longer the motivator. The avoidance response seemed, as Mowrer had suggested, to be maintained by the anticipation of shock, by the fear elicited by the warning signal. But to prove that fear was the motivator, Miller changed the rules on the rat. Previously, when the rat jumped over the hurdle, the buzzer went off, and turning the buzzer off seemed to be sufficient reinforcement to keep the rat jumping. But now the buzzer stayed on when the rat jumped and would only go off if the rat pressed a lever. And once this was learned Miller changed the game again, forcing the rat to learn still another response to turn the buzzer off. While the initial response was learned because it allowed the rat to avoid the shock, the subsequent ones were never associated with the shock. They were reinforced by the fact that they turned off the sound. According to Miller, the findings showed that fear is a drive, an internal energizer of behavior, and that behaviors that reduce fear are reinforced and thereby become habitual ways of acting (note, however, that "fear" is an internal bodily signal, like hunger, and does not necessarily refer to subjective, consciously experienced fear in this theory).

Miller felt that this new view of fear as a drive was the key to a truly scientific approach to psychoanalytic principles. Together with John Dollard, a trained analyst, Miller attempted to account for unconscious neurotic conflict and its expression as symptoms in terms of the principles of animal learning.²⁹ Just as a rat could learn any response that allowed it to escape from or avoid an

anxiety-provoking situation, humans learn all sorts of instrumental responses that allow them to escape or avoid anxiety and guilt caused by neurotic conflict.³⁰ As Dollard and Miller put it:

the symptoms of the neurotic are the most obvious aspects of his problem. These are what the patient is familiar with and feels he should be rid of. The phobias, inhibitions, avoidances, compulsions, rationalizations, and psychosomatic symptoms of the neurotic are experienced as a nuisance by him and by all who have to deal with him.... When a successful symptom occurs it is reinforced because it reduces neurotic misery. The symptom is thus learned as a habit.³¹

Conditioned fear theories of anxiety took a different turn in the early 1960s. In contrast to the tradition of Mowrer and Miller, who saw Freud as scientifically imprecise but on the right track, the new theorists had little patience with the psychoanalytic view of anxiety and its emphasis on unresolved and unconscious conflict. Joseph Wolpe was one of these. He reinterpreted Freud's famous phobic case, Little Hans,³² in terms of simple Pavlovian conditioning.³³ Hans, a five-year-old boy, became afraid of horses one day while witnessing a frightening event in which a horse fell down. Freud's view was that the horse phobia was an unresolved Oedipal conflict—Hans' fear of being castrated by his father for desiring his mother was displaced to horses. The trauma of witnessing the horse falling was the occasion that allowed the phobia to cover for the underlying conflict. But Wolpe saw it differently. Like all good conditioning theorists, he argued that a neutral stimulus, like a horse, that occurs in the presence of a trauma will acquire the capacity to elicit fear reactions, and that phobias are nothing more than fear (anxiety) that has been conditioned to some otherwise meaningless event. In making his case, Wolpe severely criticized Freud's selective use of information that confirmed his theory and his selective disregard for information that went against it. For example, Hans himself supposedly said that he "got the nonsense" when he saw the horse fall down, and his father, in support of this view, said the anxiety broke out immediately after the incident. Freud dismissed these surface explanations, but Wolpe took them at face value. For Wolpe, Little Hans was just like Little Albert. The conditioning theory had come full circle.

The distinction between Watson's and Wolpe's purely Pavlovian approach and Mowrer's and Miller's psychoanalytic translations is more than just one of the language used to describe how anxiety arises. It also impacts importantly on the issue of how anxiety should be treated. Freudians, and their behavioral protégés, saw the goal of therapy as the resolution of unconscious conflict. The other school, typified by Wolpe, had no use for unconscious explanations and saw neurotic symptoms as nothing more and nothing less than conditioned responses. In the words of Stanley Rachman and Hans Eysenck, two other leaders in this movement, "Get rid of the symptom . . . and you have eliminated the neurosis."³⁴

In spite of many important differences, there is a common theme that runs through psychoanalytic and the various conditioning theories—*anxiety is the result of traumatic learning experiences*. Since traumatic learning involves (at least in part) fear conditioning, it is possible that similar brain mechanisms contribute to pathogenic anxiety in humans and conditioned fear in animals. If so, findings from easily performed animal experiments could be used to understand how anxiety is

learned, unlearned, and controlled in humans. However, before we can accept this rather strong, and some would say controversial, conclusion, we need to consider some additional ideas about the relation of fear conditioning to anxiety disorders, and some additional facts about the organization and function of the fear system of the brain.

Ready to Fear

In the early 1970s, Martin Seligman, an experimental psychologist who had been studying conditioned fear in animals, pointed out some striking differences between human anxiety and laboratory conditioned fear.³⁵ Especially important to Seligman was the fact that avoidance conditioning extinguishes quickly if the animal is prevented from making the avoidance response and alternative solutions for escape or avoidance are not provided. Recall that Miller's rats kept jumping over the hurdle when the buzzer sounded even when the shock was turned off. They never had the chance to find out that the shock was off because they kept jumping. But Seligman's point is that if the hurdle is replaced with a wall, thus preventing the avoidance response, the rat soon learns that the buzzer is no longer followed by a shock and begins to ignore the buzzer. If the wall is now removed and the hurdle returned, jumping no longer occurs in response to the buzzer. Forcing the rat to see that the buzzer doesn't lead to danger extinguishes the fear and this leads to the extinction of the neurotic avoidance response. In contrast, telling an acrophobic that no one has ever accidentally fallen off the Empire State Building and that he will be just fine if he goes to the top, or forcing him to go up there to prove the point, does not help, and can even make the fear of heights worse rather than better. Human phobias seem more resistant to extinction, and more irrational, than conditioned fears in animals.

The key to this difference, in Seligman's view, is the fact that while laboratory experiments use arbitrary, meaningless stimuli (flashing lights or buzzers), phobias tend to involve specific classes of highly meaningful objects or situations (insects, snakes, heights). He argued that perhaps we are prepared by evolution to learn about certain things more easily than others, and that these biologically driven instances of learning are especially potent and long lasting. Phobias, in this light, reflect our evolutionary preparation to learn about danger and to retain the learned information especially strongly.

In a relatively stable environment, it is generally a good bet that the dangers a species faces will change slowly. As a result, having a ready-made means of rapidly learning about things that were dangerous to one's ancestors, and theirs, is in general useful. But since our environment is very different from the one in which early humans lived, our genetic preparation to learn about ancestral dangers can get us into trouble, as when it causes us to develop fears of things that are not particularly dangerous in our world.

With the notion of preparedness, Seligman injected a dose of biological realism into the plain vanilla conditioning theory that Watson and later behaviorists popularized. Ironically, the phenomenon of preparedness may have played a seminal role in Watson's conditioning of Little Albert. Several later studies failed to reproduce Watson's findings³⁶ and these results have often been used as ammunition against fear conditioning theories of anxiety. But Seligman notes that in choosing a furry animal as

the conditioned stimulus, Watson may have unwittingly used a prepared stimulus, and the failure of the later studies may well be because they used inanimate, meaningless stimuli.

Preparedness theory quickly received strong support from studies by Susan Mineka.³⁷ It had long been thought that monkeys have an inherited fear of snakes, so that the first time a monkey saw a snake it would act afraid and protect itself. However, Mineka showed that laboratory-reared monkeys are in fact not afraid on the first exposure to a snake. Most of the earlier work had involved testing of the young monkeys in the presence of their mothers. If the young monkey is shown the snake when separated from its mother, it doesn't act afraid. It appears that the infant learns to be afraid of the snakes by seeing its mother acting afraid. The young monkeys did not learn about non-frightening things in this way, suggesting that there is something special about biologically relevant stimuli that makes them susceptible to rapid and potent observational learning. Humans learn many things by observing others in social situations and it has been proposed that anxiety, especially pathological anxiety, is sometimes or even often learned by social observation.³⁸

In recent years, preparedness theory has been championed by Öhman.³⁹ Öhman believes that evolution has equipped contemporary humans with a propensity to associate fear with situations that threatened the survival of our ancestors. To the extent that this propensity evolved, it must be based in our genes, and genetic variation must therefore exist. As a result, although humans are in general prepared to acquire fears of ancestral dangers easily, some individuals must be more prepared than others to acquire specific fears. These super-prepared humans are, he proposes, vulnerable to phobias. Öhman has subjected preparedness theory to stringent tests. He started with the assumption that snakes and insects are common objects of phobias and are likely to be prime examples of prepared stimuli, whereas flowers are not common phobic objects. He then used these fear-relevant (prepared) and fear-irrelevant stimuli in conditioning studies in humans. In support of preparedness theory, he found that conditioned fear (measured by autonomic nervous system responses) was more resistant to extinction with fear-relevant than with fear-irrelevant stimuli. Further, when modern fear-relevant stimuli (guns and knives) were used, no evidence for resistance to extinction was found, suggesting that evolution has not yet had enough time to build these dangers in. He also showed that phobics respond to a greater degree when they see stimuli relevant to their own phobia than when they see other fear-relevant stimuli—snake phobics gave bigger conditioned responses to snake pictures than to spider pictures and spider phobics did the reverse. This is consistent with his contention that phobics are super-prepared genetically to respond to the objects of their phobia. Finally, using special procedures to prevent conditioned stimuli from being consciously perceived, he was able to produce the prepared conditioning in the absence of awareness of the conditioned stimuli. This shows that phobias can be learned and expressed independently of consciousness, which may be related to their seemingly irrational nature.

Preparedness theory goes a long way toward dealing with some of the shortcomings of the traditional fear conditioning theories of anxiety, particularly the fact that in anxiety disorders fear doesn't extinguish easily and is especially irrational. Nevertheless, important aspects of phobias and other anxiety disorders remained unexplained. People become anxious about objects and situations that are not evolutionarily prepared—like fear of cars or elevators. Anxiety disorders can and often do exist in

the absence of a memory of a traumatic experience, suggesting that maybe traumatic conditioning is not so important. And sometimes a clear trauma precedes the onset of an anxiety disorder, but the trauma is unrelated to the disorder (for example, the death of one's mother preceding the development of a fear of heights)—this doesn't make sense if the anxiety was conditioned by the trauma. However, our understanding of the brain mechanisms of conditioned fear, together with new observations about the effects of stress on the brain, give us additional clues that help fill these gaps.

New Twists on Anxiety: Clues from the Brain

In further pursuing the nature of anxiety disorders, we'll draw upon the notion, developed in the previous chapter, of multiple memory systems. In particular, we'll examine some of the implications of the idea that during a traumatic learning situation, conscious memories are laid down by a system involving the hippocampus and related cortical areas, and unconscious memories established by fear conditioning mechanisms operating through an amygdala-based system. These two systems operate in parallel and store different kinds of information relevant to the experience. And when stimuli that were present during the initial trauma are later encountered, each system can potentially retrieve its memories. In the case of the amygdala system, retrieval results in expression of bodily responses that prepare for danger, and in the case of the hippocampal system, conscious remembrances occur. It is very helpful to keep the workings of the declarative system separate from other memory systems when considering how anxiety disorders might arise and be maintained. This point was made by Jake Jacobs and Lynn Nadel in a 1985 article that greatly influenced my thinking about the effects of stress on the fear system.⁴⁰

Stress-Induced Loss and Recovery of Traumatic Memories: The fact that some clinically anxious persons do not recall any particular traumatic event that might be the cause of their anxiety has been an especially sharp thorn in the side of conditioning theories. In contrast, the main competition, Freud's psychoanalytic theory, assumes that anxiety will only result when traumatic memories are dispatched to the unconscious corners of the mind. Not wanting to call upon anything so mysterious and scientifically unfounded as repression, conditioning theorists have struggled with instances where there is no memory of an instigating trauma. Either no trauma, and thus no conditioning, occurred, or the trauma occurred but is not remembered. Both possibilities leave conditioning theorists with something to explain.

A possible solution to this puzzle has emerged from recent work showing that stressful events can cause malfunctions in the hippocampus. This suggests that at least in some instances the failure to recall an instigating trauma may be due to a stress-induced breakdown in hippocampal memory function.⁴¹ In order to understand how and why this occurs, we need to explore the biological effects of stress.

When people or other animals are exposed to a stressful situation, the adrenal gland secretes a steroid hormone into the bloodstream.⁴² Adrenal steroids play an important role in helping the body mobilize its energy resources to deal with the stressful situation. As we saw in Chapter 6, the amygdala is critically involved in the control of the release of adrenal steroids. When the amygdala detects danger,

it sends messages to the hypothalamus, which in turn, sends messages to the pituitary gland, and the result is the release of a hormone called ACTH. ACTH flows through the blood to the adrenal gland to cause the release of steroid hormone. In addition to reaching target sites in the body, the steroid hormone flows through the blood into the brain, where it binds to receptors in the hippocampus, amygdala, prefrontal cortex, and other regions. Because the adrenal and pituitary secretions are reliably elicited by stressful events, they are called stress hormones.

It has been recognized for some time that the hippocampal steroid receptors are part of a control system that helps regulate how much adrenal steroid hormone is released.⁴³ When the hormone binds to receptors in the hippocampus, messages are sent to the hypothalamus to tell it to tell the pituitary and adrenal glands to slow down the release. In the face of stress, the amygdala keeps saying "release" and the hippocampus keeps saying "slow down." Through multiple cycles through these loops the concentration of the stress hormones in the blood is delicately matched to the demands of the stressful situation.

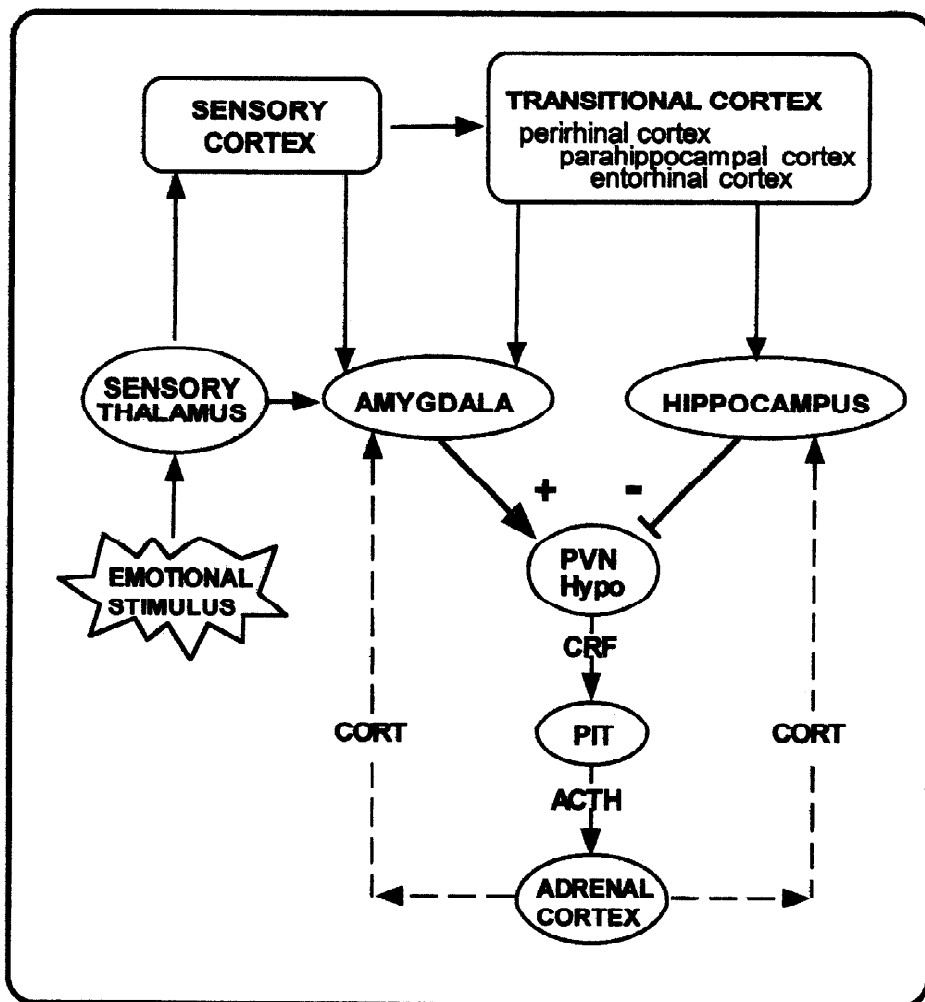


FIGURE 8-1 Stress Pathways.

Stimuli associated with danger activate the amygdala. By way of pathways from the amygdala to the paraventricular nucleus of the hypothalamus (PVN Hypo), corticotrophin-releasing factor (CRF) is sent to the pituitary gland, which, in turn, releases adrenocorticotrophic hormone (ACTH) into the

bloodstream. ACTH then acts on the adrenal cortex, causing it to release steroid hormones (CORT) into the bloodstream. CORT freely travels from the blood into the brain, where it binds to specialized receptors on neurons in regions of the hippocampus and amygdala, as well as other regions. Through the hippocampus, CORT inhibits the further release of CRF from the PVN. However, as long as the emotional stimulus is present, the amygdala will attempt to cause PVN to release CRF. The balance between the excitatory inputs (+) from the amygdala and the inhibitory inputs (-) from the hippocampus to PVN determines how much CRF, ACTH, and ultimately CORT will be released.

If stress persists too long, the hippocampus begins to falter in its ability to control the release of the stress hormones, and to perform its routine functions. Stressed rats are unable to learn and remember how to perform behavioral tasks that depend on the hippocampus.⁴⁴ For example, they fail to learn the location of the safe platform in the water maze task described in the last chapter. Stress also interferes with the ability to induce long-term potentiation in the hippocampus,⁴⁵ which probably explains why the memory failure occurs. Importantly, stress also impairs explicit conscious memory functions in humans.⁴⁶

Bruce McEwen, a leader in the study of the biology of stress, has shown that severe but temporary stress can result in a shriveling up of dendrites in the hippocampus.⁴⁷ Dendrites are the parts of neurons that receive incoming inputs and that are responsible, in large part, for the initial phases of long-term potentiation and memory formation.⁴⁸ McEwen has also shown that if the stress is discontinued these changes are reversible. However, with prolonged stress, irreversible changes take place. Cells in the hippocampus actually begin to degenerate. When this happens, the memory loss is permanent.

The effects of stress on the hippocampus were first discovered by Robert Sapolsky, who had been studying the effects of social stress on the behavior of monkeys.⁴⁹ The monkeys had lived in a colony as social subordinates to a dominant male. Over several years, some died. Upon autopsy, they were found to have stomach ulcers, consistent with their having lived under stress. Most dramatically, though, it was discovered that marked degeneration of the hippocampus had occurred. There was little sign of damage to any other part of the brain. This basic finding has now been confirmed in a number of situations. For example, the hippocampus is degenerated in mice living under social stress.⁵⁰ Recent studies have shown that the human hippocampus too is vulnerable to stress.⁵¹ In survivors of trauma, like victims of repeated childhood abuse or Vietnam veterans with post-traumatic stress disorder, the hippocampus is shrunken. These same persons exhibit significant deficits in memory ability, without any loss in IQ or other cognitive functions. Stressful life events can alter the human hippocampus and its memory functions.

It seems clear that adrenal steroids account for these physical changes in the hippocampus and in the memory problems that result.⁵² For example, there is a condition called Cushing's disease in which tumors develop in the adrenal gland and excess steroid hormone is secreted. These persons have long been known to have memory problems. Recent studies have also shown that the hippocampus is shrunken in this disease. Also, if rats or humans are injected with high levels of steroids, mimicking the effects of severe stress, hippocampal cell death and memory problems result. And if rats are given

drugs that block the effects of steroids, they are made immune to the effects of stress on the hippocampus and on memory.

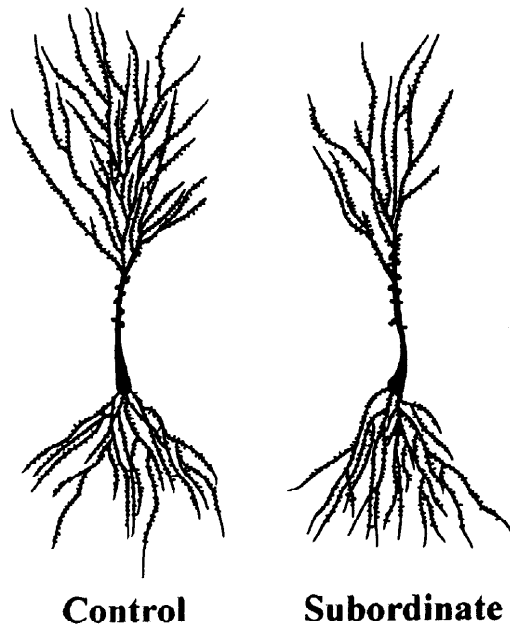


FIGURE 8-2 Dendrites Shrivelled by Social Stress.

Neurons are shown from unstressed (control) and stressed (subordinate) tree shrews, a mammalian species related to early primate evolution. The stress in this experiment involved exposing subordinate males to a dominant male. Repeated social stress of this type reduced the branching and length of dendrites. Compare the top half of the cell from the unstressed control and from the stressed subordinate. (Reprinted from A.M. Magarinos, B.S. McEwen, G. Flugge, and E. Fuchs [1996], Chronic psychosocial stress causes apical dendritic atrophy of hippocampal CA3 pyramidal neurons in subordinate tree shrews. *Journal of Neuroscience* 16 (3534-40).)

There's one more relationship between stress and memory that's worth pointing out. One of the consequences of excess life stress is depression, and depressed persons sometimes have poor memory. It is quite possible that the memory disturbances that occur in depression are closely tied up with the effects of stress on the hippocampus.

Sometimes stress helps in the formation of explicit memories, making them stronger (recall the flashbulb hypothesis), but it can also devastate explicit memory. We now have a plausible explanation for this paradox. Memory is likely to be enhanced by mild stress, due to the facilitatory effects of adrenaline (Chapter 7), but may be interfered with if the stress is sufficiently intense and prolonged to raise the level of adrenal steroids to the point where the hippocampus is adversely affected.

Most of the evidence for adverse effects of stress on memory has come from rather severe conditions in which the stress continued for days. A key issue is whether a single, unrepeated traumatic experience, such as being mugged or raped, can raise steroid levels sufficiently to adversely affect the hippocampus and produce a loss of memory for the incident. Although there are no definitive answers yet, recent studies have shown that a brief period of stress can disrupt spatial memory in rats and

interfere with the induction of long-term potentiation in the hippocampus.⁵³ And both of these effects are prevented if the adrenal gland is removed, implicating adrenal steroids.

Now comes the tricky part. Let's assume that it is indeed possible for a temporary period of trauma to lead to an amnesia for the experience. Can one then later recover a memory of these events? Although we can identify in a general sense the kinds of conditions under which recovery is possible or impossible, we can't say whether it occurred in a particular instance. For example, if the hippocampus was completely shut down by the stress to the point where it had no capacity to form a memory during the event,⁵⁴ then it will be impossible through any means to dredge up a conscious memory of the event. If no such memory was formed, then no such memory can be retrieved or recovered. On the other hand, if the hippocampus was only partially affected by the trauma, it may have participated in the formation of a weak and fragmented memory. In such a situation, it may be possible to mentally reconstruct aspects of the experience. Such memories will by necessity involve "filling in the blanks," and the accuracy of the memory will be a function of how much filling in was done and how critical the filled-in parts were to the essence of the memory.

Explicit, conscious memories, as I emphasized in the last chapter, are reconstructions that blend information stored in long-term memory with one's current frame of mind. Even memories that are formed with a perfectly well-functioning hippocampus are easily distorted by experiences that occur between the formation of the memory and its retrieval. This has been demonstrated in numerous experiments by Elizabeth Loftus and her colleagues.⁵⁵ Particularly important are their studies showing how easy it is to induce a false memory by controlling events that happen after the memory is established, or to create from scratch a memory of an experience that never happened. The subjects in these studies fully believe their memories, but because they have occurred in controlled laboratory experiments it is possible to show that the memory is fabricated. At the same time, there are also carefully controlled laboratory studies showing that information that was initially processed consciously and stored, but later forgotten, can be brought back, a phenomenon called hypermesia that we looked at in Chapter 3.⁵⁶

The only thing that is clear about memory recovery in real life is that there is no way for outsiders to definitely determine whether a particular memory is real or fabricated in the absence of solid corroborating evidence (fabrication does not imply that the person is lying, only that the memory is false). There are surely victims of horrible incidents who have lost their memory of the event, and there may be some who can later piece together a memory of what happened. However, distinguishing between fabricated and real memories simply on the basis of self-knowledge can be tricky. Salvador Dali once said, "The difference between false memories and true ones is the same as for jewels: it is always the false ones that look the most real, the most brilliant."⁵⁷ Whether he was right might be debated, but as we saw earlier (Chapters 2 and 3), introspective knowledge of thought processes provides a highly inaccurate window into the mind, even in mundane (nontraumatic) situations. Things are likely to be even worse when confusion abounds, as it must during and following trauma. The waters of memory recovery are treacherous and should be walked through very carefully.

As far as is known, stress does not interfere with the workings of the amygdala, and, as we'll see below, stress may even enhance amygdala functions. It is thus completely possible that one might have

poor conscious memory of a traumatic experience, but at the same time form very powerful implicit, unconscious emotional memories through amygdala-mediated fear conditioning. And because of other effects of stress to be described below, these potent unconscious fears can become very resistant to extinction. They can, in other words, become unconscious sources of intense anxiety that potentially exert their opaque and perverse influences throughout life. However, there is no way for these powerful implicit memories to then be converted into explicit memories. Again, if a conscious memory wasn't formed, it can't be recovered.

That Freud was correct in his belief that aspects of traumatic experiences are sometimes stored in memory systems that are not directly accessible from consciousness seems clear. Less certain is whether repression (in the Freudian sense) is involved. The failure to remember traumatic events may sometimes be due to a stress-induced shutdown of the hippocampus, although this remains to be proven. In light of this, though, there is nothing particularly devastating to the conditioning theory of anxiety about the fact that the traumatic origin of the anxiety is not always remembered. Of course, repression of unpleasant experience may well be a real phenomenon, one that we still don't understand scientifically. And some anxiety disorders may develop without an initial trauma. Nevertheless, we at least have a possible mechanism that might account for some aspects of these disorders in easily understood biological terms.

Amplification of Emotional Memory by Irrelevant Stressors: There is a flip side to the debilitating effects of intense stress on explicit conscious memory of trauma. The same amount of stress that can lead to an amnesia for a trauma may amplify implicit or unconscious memories that are formed during the traumatic event.

For example, recent studies have shown that if rats are given injections of adrenal steroids at levels that mimic very severe stress, there is a dramatic decrease in the amount of a certain chemical, called corticotropin-releasing factor (CRF), in the part of the hypothalamus that controls the release of the stress hormone, ACTH, from the pituitary gland.⁵⁸ CRF is in fact the neurotransmitter that stimulates ACTH release. The decrease in CRF in this pathway reflects the negative feedback control over stress hormones by the hippocampus—once the blood level of adrenal steroids reaches a certain level, the hippocampus tells the hypothalamus to slow down the secretions. And when the steroid level reaches a critical point, the hippocampal circuits begin to falter. In stark contrast, there is a dramatic increase in CRF in the central nucleus of the amygdala under the same conditions—as blood levels of steroids increase, the amygdala may keep getting more and more active. The bottom line is that the effects of stress on the amygdala seem very different from the effects on the hippocampal-hypothalamic circuit. On the basis of these observations, Keith Corodimas, Jay Schulkin, and I predicted that during intense stress the learning and memory processes mediated by the amygdala might be facilitated and we examined the effects of stress hormone overload on conditioned fear behavior.⁵⁹ In line with the prediction, we found that the strength of learned fear was increased in the steroid-treated rats relative to other rats that didn't have the steroids. Although this result is somewhat preliminary, studies using other forms of Pavlovian conditioning have also found that stress enhances conditioned responses.⁶⁰

If indeed the hippocampus is impaired and the amygdala facilitated by stress, it would suggest the possibility that stress shifts us into a mode of operation in which we react to danger rather than think about it. It's not clear whether this is a specific adaptation or whether we're just lucky that when the higher functions break down our fall-back position is one in which we can let evolution do the thinking for us.

The finding that stress hormones can amplify conditioned fear responses has an important implication for our understanding of anxiety disorders, and in particular for understanding why these sometimes seem to occur or get worse after unrelated stressful events.⁶¹ During stress, weak conditioned fear responses may become stronger. The responses could be weak either because they were weakly conditioned, or because they were previously extinguished or were otherwise treated into remission. Either way, their strength might be increased by stress. For example, a snake phobic might be in remission for years but upon the death of his spouse the phobia returns. Alternatively, a mild fear of heights, one that causes few problems in everyday life, might be converted into a pathological fear under the amplifying influences of stress. The stress is unrelated to the disorder that develops and is instead a condition that lowers the threshold for an anxiety disorder, making the individual vulnerable to anxiety, but not dictating the nature of the disorder that will emerge. The latter is probably determined by the kinds of fears and other vulnerabilities that the person has lurking inside.

Brain Malfunctions Can Make Unprepared Learning Resistant to Extinction: Neurotic fears are notoriously difficult to shake. This is the bane of a therapist's professional existence, but also his or her bread and butter. While preparedness provides one way out of this dilemma, there is another. Fear responses conditioned to arbitrary tones or lights in rats can be made highly resistant to extinction if certain cortical areas that project to the amygdala are damaged. This suggests that these areas of the cortex may be malfunctioning in some cases of pathogenic anxiety, allowing ordinary stimuli to be conditioned by the amygdala in a way that resists extinction.

Several years ago we were examining the effects of damage to visual areas of the cortex on the ability of rats to be conditioned to visual stimuli.⁶² The lesioned rats learned just fine, supporting our contention that there are subcortical pathways that take sensory information to the amygdala during conditioning. But when we tried to extinguish the fear responses in these animals, something unusual happened. We couldn't do it. Normal rats, after several days of seeing the light without the shock, stopped acting afraid in the presence of the light. But the rats with lesions of the visual cortex were like Energizer batteries—they just kept going and going and going.

We never thought that the visual cortex was the seat of extinction. Instead, we proposed that the visual cortex might be a necessary link between the visual world and other higher order cortical areas that are necessary for extinction. One area that seemed like a possible regulator of extinction was the medial prefrontal cortex. This area receives signals from the sensory regions of the cortex and from the amygdala, and sends connections back to the amygdala, as well as to many of the areas to which the amygdala projects.⁶³ The medial prefrontal cortex is thus nicely situated to be able to regulate the outputs of the amygdala on the basis of events in the outside world as well as on the basis of the amygdala's interpretation of those events. When Maria Morgan made lesions of this region, rats

continued to act fearful in the presence of a conditioned fear stimulus long after rats without lesions of this area had stopped acting afraid.⁶⁴

The amygdala of the cortically lesioned rat, like the neurotic human, stubbornly expresses its fear memories in the face of information showing that the stimulus is no longer associated with danger. Extinction appears to involve the cortical regulation over the amygdala, and even unprepared conditioned fear can be resistant to extinction when the amygdala is freed from these cortical controls. One of the hallmarks of frontal lobe damage in humans is perseveration, the inability to stop doing something once it is no longer appropriate.⁶⁵ For example, when frontal lobe patients are performing a task in which a rule must be followed, they have great difficulty in changing their behavior when the rule is switched. In a standard version of this test, the patient is given a stack of cards, each with one or more colored symbols on it. The patient's job is to figure out, on the basis of feedback about whether each response is correct, which kind of cue (color, shape, or number) is the current solution. Once they get going on a principle (like shape) they can do the task fine. But if all of a sudden the principle shifts (say, to color), they keep following the old rule. Sometimes they even know what they should do, but can't make their behavior match their knowledge. They are rigid and inflexible, and perseverate in their ways, even when it is obvious that the behavior is not appropriate to the situation. This seems to characterize their behavior in real life as well.

Although perseveration is usually thought of as a cognitive or thought disorder, it seems that our findings about fear extinction in rats with prefrontal lesions might reflect the same kind of difficulty, but in the domain of emotion. In fact, we used the expression "emotional perseveration" to describe the failure of our rats to extinguish conditioned fear responses.⁶⁶ While cognitive perseveration is produced by damage to the lateral areas of the prefrontal cortex, emotional perseveration resulted from damage to a small part of the medial prefrontal region.⁶⁷ The lateral and medial prefrontal areas may perform the same operation, adapting behavior to changing conditions, with the involvement in cognitive or emotional functions determined by the areas with which the prefrontal region works in conjunction. The medial cortex, in other words, engages in response switching behavior because it is part of the prefrontal cortex, and it engages in response switching guided by emotional information because it is connected with the amygdala. Edmund Rolls has proposed a similar role for the medial prefrontal cortex in emotion on the basis of studies in which he has recorded from neurons in this region while monkeys performed tasks where the reinforcer (reward or punishment) associated with certain responses changed frequently.⁶⁸ Other ideas about the contribution of prefrontal cortex to emotion have been proposed as well, and the work of Antonio Damasio is particularly notable.⁶⁹ Some of these ideas will be considered in the next chapter on emotional consciousness.

The prefrontal cortex, like the hippocampus, may be altered by stress. Recent research has shown that the prefrontal cortex, like the hippocampus, offers a counterforce that keeps too much of the stress hormones from being released.⁷⁰ Since prolonged stress results in a breakdown in this negative feedback control function, it may be the case that both the prefrontal cortex and hippocampus are adversely affected. A stress-induced shutdown of the prefrontal cortex might release the brakes on the amygdala, making new learning stronger and more resistant to extinction, and possibly allowing previously extinguished conditioned fears to be expressed anew.

Just because clinical fear is difficult to extinguish does not mean that it involves a different brain system from the one that mediates extinguishable conditioned fears in animals. Differences in the ease of extinction of conditioned fear in laboratory experiments and in anxious persons are more likely to reflect differences in the way the fear system works in normal and anxious brains rather than differences in the system used by the brain to learn conditioned fear and clinical anxiety. This doesn't mean that anxious persons, like our rats, are walking around with holes in their prefrontal cortex. There are many subtle ways in which disruptions in electrical and chemical functions can adversely affect a brain region, with lesions being just an extreme example of this.

Gone but Not Forgotten—The Indelibility of Emotional Memory: Our finding that when the medial prefrontal cortex is damaged routine fear conditioning becomes resistant to extinction has another important implication. It also suggests that extinction prevents the expression of conditioned fear responses but does not erase the implicit memories that underlie these responses.⁷¹ Extinction, in other words, involves the cortical control over the amygdala's output rather than a wiping clean of the amygdala's memory slate.

The idea that extinction does not involve the erasure of emotional memories but instead prevents their expression is consistent with a number of findings about conditioned responses.⁷² Pavlov, for example, found that extinguished responses would, with simply the passage of time, spontaneously recover. It is also known that if a rat is conditioned by pairing a tone and shock in one box, and the fear response elicited by the tone is completely extinguished in another box, the conditioned response elicited by the tone will be renewed if the rat is returned to the original training box. An extinguished response can also be reinstated by giving the rat an exposure to the US or, importantly, to other forms of stressful stimulation. Stress, in other words, can bring back extinguished, or perhaps weakly established but unextinguished, conditioned responses.⁷³ Each of these examples, like our lesion study, demonstrates that emotional memories are not erased by extinction but are simply held in check. Extinguished memories, like Lazarus, can be called back to life.

I recently had a scientific "ah ha" experience, one of those rare, wonderful moments when a new set of findings from the lab suddenly makes you see something puzzling in a new, crystal clear way. The studies involved recordings of electrical activity of the amygdala before and after fear conditioning by Greg Quirk, Chris Repa, and me.⁷⁴ We found dramatic increases in electrical responses elicited by the tone CS after conditioning, and these increases were reversed by extinction. However, because we were recording from multiple individual neurons at the same time, we were also able to look at the activity relationships between the cells. Conditioning increased the functional interactions between neurons so that the likelihood that two cells would fire at the same time dramatically increased. These interactions were seen both in the response to the stimulus and in the spontaneous firing of the cells when nothing in particular was going on. What was most interesting was that in some of the cells, these functional interactions were not reversed by extinction. Conditioning appears to have created what Donald Hebb called "cell assemblies,"⁷⁵ and some of these seemed to be resistant to extinction. Although the tone was no longer causing the cells to fire (they had extinguished), the functional interactions between the cells, as seen in their spontaneous firings, remained. It is as if these functional

couplings are holding the memory even at a time when the external triggers of the memory (for example, phobic stimuli) are no longer effective in activating the memory and its associated behaviors (for example, phobic responses). Although highly speculative at this point, the observations suggest clues as to how memories can live in the brain at a time when they are not accessible by external stimuli (Figure 8-3). All that it would take to reactivate those memories would be a change in the strength of the input to the cell assembly. This may be something that stress can accomplish. Unconscious fear memories established through the amygdala appear to be indelibly burned into the brain. They are probably with us for life. This is often very useful, especially in a stable, unchanging world, since we don't want to have to learn about the same kinds of dangers over and over again. But the downside is that sometimes the things that are imprinted in the amygdala's circuits are maladaptive. In these instances, we pay dearly for the incredible efficiencies of the fear system.

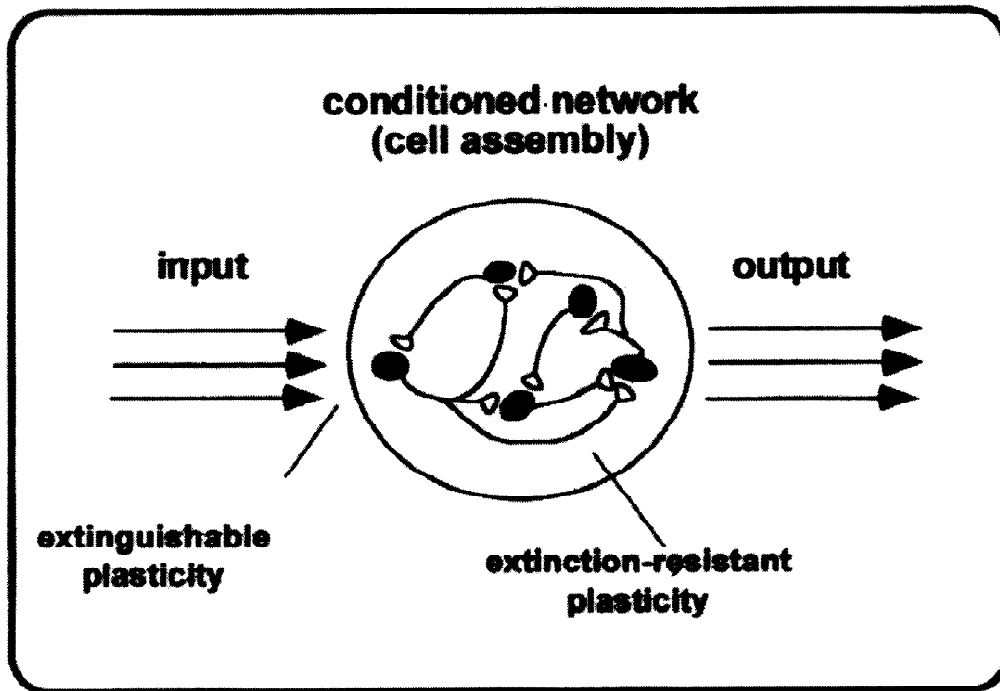
Psychiatrist Roger Pitman has astutely noted that findings from studies of fear conditioning in rats have important implications for how anxiety is treated.⁷⁶ The classic treatment, based on Mowrer's and Miller's theory, was to force the patient to be exposed to the anxiety-causing stimuli without allowing any avoidance or escape behavior and thereby try to extinguish the anxiety that the stimuli elicit. But in light of the indelibility of the amygdala's hold on traumatic memories, he suggests a bleaker, though perhaps more realistic, assessment. We may not be able to get rid of the implicit memories that underlie anxiety disorders. If this is the case, the best we can hope for is to exercise control over them.

The Fear System and Specific Anxiety Disorders

Until fairly recently, the various anxiety disorders were not distinguished and were not treated differently.⁷⁷ Panic and PTSD, for example, did not appear in the DSM until 1980. And although phobias have long been associated with neuroses, they were typically thought of as neurotic symptoms rather than a particular kind of anxiety disorder. With the emergence of clear diagnostic distinctions between different anxiety disorders, disorder-specific fear conditioning theories have been proposed. Below, I'll attempt to buttress disorder-specific theories of phobias, PTSD, and panic with findings about the brain mechanisms of fear conditioning.⁷⁸

FIGURE 8-3 Creation of Extinction-Resistant Learning in the Brain.

Recent studies have recorded neural activity in the amygdala during conditioning and extinction. After conditioning, the response of individual cells to the conditioned stimulus is increased (the same input produces a bigger output). In addition, individual cells develop stronger interconnections so that when one fires the others also fire. These interconnected neurons are called a cell assembly. While the response of individual cells to the conditioned stimulus diminishes during extinction, in some cases the conditioned interconnections persist. These cell assemblies within the amygdala, or between the amygdala and cortical areas, may constitute an important aspect of the long-term, extinction-resistant, implicit memory created by fear conditioning.



Phobic Fears: Contemporary ideas about phobias continue to be centered around the notion of preparedness. Normally, the strength of conditioning is determined mainly (though not exclusively) by how traumatic the unconditioned stimulus is. But in prepared fear conditioning, the CS also contributes some of the emotional impact. As a result, given two conditioned stimuli, one biologically prepared to be conditioned to danger and the other not, the same unconditioned stimulus should support the establishment of a stronger conditioned response for the prepared stimulus. How might that work in the brain?

Perhaps neurons in the amygdala that process prepared stimuli have some prewired but normally impotent connections to other cells that control emotional responses. The trauma might only have to mildly massage these pathways rather than create from scratch novel synaptic assemblages between the input and output neurons of the amygdala. In this way, the same amount of trauma might buy more conditioning when prepared stimuli are involved.

Although there are no studies that have examined the role of the amygdala in prepared fear conditioning, evidence has been obtained indicating that the amygdala is particularly responsive to stimuli that serve as species-specific emotional signals, with stimuli that support prepared learning being a prime example of these. For instance, when rats are exposed to a cat, they give off calls, sounds that warn other rats to stay clear of where the sounds are coming from.⁷⁹ These sounds, it turns out, are in the ultrasonic range (the range beyond human hearing). Since cats can't hear in this range, the calls are like secret encrypted messages that pass undetected through enemy lines. In recent experiments, Fabio Bordi and I found some neurons in the rat amygdala that responded especially briskly to ultrasounds similar to the warning calls.⁸⁰ The rat amygdala may be evolutionarily prepared to respond to these sounds and to learn about them. In fact, the amygdala of all creatures may be prepared to respond to species-relevant cues.⁸¹ For example, faces are important emotional signals in

the lives of primates, and neurons in the monkey amygdala respond briskly to the sight of monkey faces.⁸²

As we saw in Chapter 6, information about external stimuli reaches the amygdala from two pathways, one subcortical, the other cortical. The subcortical pathway is shorter and faster but imprecise, and the cortical pathway has the opposite attributes. And as we saw in Chapter 7, learning and memory appear to involve the potentiation of synaptic transmission in these pathways. In the normal brain the potentiation probably occurs in both pathways, which work together in the conditioning and expression of fear responses to external stimuli. But suppose, because of genetic predisposition or past experiences, phobic learning were to involve the subcortical pathway to a greater extent than the cortical pathway, especially for prepared stimuli. This might explain why phobias generalize broadly—as Öhman has pointed out, phobics can sometimes lose track of what they are afraid of when fear generalizes.⁸³ The subcortical pathway, not being very capable of making fine distinctions, may produce learning that more freely spreads to other stimuli. And this pathway, being subcortical, would also presumably be particularly difficult to gain conscious, cortical control over. Interestingly, the high-frequency sounds that turned on amygdala cells so effectively did so through the quick and dirty subcortical pathways.

Although amygdala-mediated fear conditioning is a form of implicit learning (regardless of the input pathways involved), phobics are consciously afraid of their phobic stimuli. This means that they also have an explicit conscious memory, formed through their temporal lobe memory system, that reminds them that they are afraid of snakes, heights, or whatever. This memory might be established during the initial traumatic learning situation, but some phobics do not recall such a learning experience, possibly because of a stress-induced memory loss. In such instances, the conscious memory of being phobically afraid could be established in later experiences with the phobic object. When the object is encountered, the amygdala will unconsciously detect the stimulus and produce the bodily expression of fear. Upon becoming aware of this bodily response, the person attributes (à la Schachter and Singer) the arousal to the most likely object and forms the memory that they are afraid of objects of that type. In the case of standard phobic objects (snakes, spiders, heights), these phobic attributions are probably facilitated by the fact that the person knows that people are often afraid of these things. Once this explicit memory is created, its retrieval into consciousness becomes a potent stimulus that is itself capable of activating the amygdala and producing anxiety by way of connections from cortical areas (including the hippocampus) to the amygdala. Even if one does not have a conscious memory of the initial learning, there is likely to be an awareness of the phobic condition stored in explicit memory.

Not everyone exposed to a traumatic event develops a phobia. Some people's brains, because of their genetic makeup or past experiences, must be predisposed to react to traumatic learning experiences in this particular way. In these people, the amygdala may be supersensitive to some class of prepared stimuli or the amygdala may have other alterations that make fear conditioning especially potent. On the other hand, as we've seen, changes in the frontal lobe may predispose some people to develop fears that resist extinction, even when unprepared stimuli are involved.

Traumatic Stress: PTSD was once known as shell shock, battle fatigue, or war neurosis, because it was most commonly diagnosed in war veterans.⁸⁴ Although it occurs in victims of many kinds of trauma, the following quotation from a Vietnam veteran illustrates the phenomenon:

I can't get the memories out of my mind! The images come flooding back in vivid detail, triggered by the most inconsequential things, like a door slamming or the smell of stir-fried pork. Last night I went to bed, was having a good sleep for a change. Then . . . there was a bolt of crackling thunder. I awoke instantly, frozen in fear. I am right back in Vietnam.... My hands are freezing, yet sweat pours from my entire body. I feel each hair on the back of my neck standing on end. I can't catch my breath and my heart is pounding.... The next clap of thunder makes me jump so much that I fall to the floor. ⁸⁵

The similarity between disorders of this type and laboratory-conditioned fear has not escaped the notice of psychiatrists. Conditioned fear was in fact proposed as the explanation of war neuroses in veterans of World War I.⁸⁶ Two of the most noted contemporary psychiatrists who study PTSD are Dennis Charney of Yale and Roger Pitman of Harvard, both of whom champion the notion that fear conditioning is involved in the disorder.⁸⁷

The difference between a fear conditioning theory of phobia and PTSD is one of where the conditioning process gets its strength. In the case of prepared phobic learning, the conditioned stimulus makes the learning especially strong. The unconditioned stimulus is typically unpleasant and may even be painful, but is not necessarily extraordinary. However, in the case of PTSD, the conditioned stimulus events are less notable than the unconditioned stimulus. PTSD, in fact, is defined in DMS-III-R as involving a trauma that is far outside the realm of experiences in ordinary life.

Once we assume that the trauma in PTSD is an extraordinary event, an especially potent US, a fairly standard view of the way the amygdala mediates conditioned fear provides a plausible account of this disorder. Admittedly, we don't know exactly what combination of factors come together to make up the horrendous US at the neuronal level, but we can easily imagine that such a neural condition exists, one that bombards the amygdala with electrical and chemical signals that are particularly potent as reinforcers of Pavlovian conditioning. These powerful reinforcing stimuli are then linked synaptically with the sounds, sights, and smells of the battle, which also reach the amygdala. Later, the occurrence of these same conditioned stimuli, or stimuli related to them, elicit profound fear responses by reactivating these powerfully potentiated amygdala circuits.

Conditioned stimuli activate the amygdala unconsciously, but at the same time reach the temporal lobe memory system and can lead to the recall of the initial trauma or to the recall of recent episodes in which the initial trauma is relieved. These conscious memories, together with the awareness of now being in a state of strong emotional arousal (due to the unconscious activation of fear responses through the amygdala), then gives rise to conscious anxiety and worry. These cognitions about the emotional arousal, in turn, flow from the neocortex and hippocampus to further arouse the amygdala. And the bodily expression of the amygdala's responses keeps the cortex aware that emotional arousal

is ongoing, and further facilitates the anxious thoughts and memories. The brain enters into a vicious cycle of emotional and cognitive excitement and, like a runaway train, just keeps picking up speed. It is possible that in PTSD, as proposed for phobic learning, the direct projections to the amygdala from subcortical sensory processing regions are involved. If this were so, it would explain why the attacks are so impulsive and uncontrollable, and tend to generalize so readily (from gunshots to lightning to slamming doors). As we've seen, the subcortical pathways are quick and dirty transmission routes. They turn the amygdala on and start emotional reactions before the cortex has a chance to figure out what it is that is being reacted to. And since these pathways are not very capable of distinguishing between stimuli, generalization readily occurs (a slamming door may indeed not sound very different from a gunshot to this circuit). Perhaps trauma, for some reasons (genetic or experiential) in some persons, biases the brain in such a way that the thalamic pathways to the amygdala predominate over the cortical ones, allowing these low-level processing networks to take the lead in the learning and storage of information. Later exposure to stimuli that even remotely resemble those occurring during the trauma would then pass, like greased lightning, over the potentiated pathways to the amygdala, unleashing the fear reaction. Quite possibly, it is harder for one to gain conscious willful control over these subcortical pathways. At the same time, because conscious memories are formed during anxiety attacks, the bodily sensations associated with those attacks, when recognized consciously, become potent elicitors or at least facilitators of anxiety. Next, we'll see just how bodily sensations can drive anxiety in panic disorders, which often occur in conjunction with PTSD.

Panic: Panic attacks are the most commonly diagnosed anxiety disorder.⁸⁸ They are similar to phobic and PTSD reactions in the sense that the patient suffers from strong emotional arousal, including intense activation of the sympathetic nervous system. However, while phobic and PTSD responses occur in the presence of external stimuli, panic attack appears to be more related to internal stimuli.⁸⁹ And because panic involves internal events, it is especially difficult for the person to avoid the stimuli that bring it on. Panic patients thus differ in this respect from patients with PTSD and phobia, who engage in extensive avoidance behavior.⁹⁰

A panic attack can be induced by having the patient hyperventilate or inhale a gaseous mixture rich in carbon dioxide, or giving the patient an intravenous injection of sodium lactate.⁹¹ These procedures give rise to internal signals (bodily sensations) similar to those that are typically present during a naturally occurring attack. Panic can also be induced by the provision of false feedback about the rate at which the heart is beating, making the patient believe that heightened bodily arousal is occurring when it is not.⁹² The belief that panic is occurring may be an important link in the chain of events that tie together the occurrence of bodily sensations and full-blown panic.

There are a number of theories of why panic occurs, including biological explanations (e.g., supersensitivity to carbon dioxide) and psychological ones (e.g., a history of childhood separation anxiety).⁹³ I will make no attempt to review or evaluate the various theories here. My aim instead is to discuss one theory, the conditioning theory, and to consider how it might be implemented in the brains of panic patients.

One common view is that artificial panic induction procedures lead to bodily sensations that then serve as conditioned stimuli.⁹⁴ Having experienced panic before, the patient learns the warning signs. When these internal signals occur (even when artificially induced) the patient feels that panic is starting.⁹⁵ This cognitive appraisal of bodily sensations then drives the system into panic. Induced panic, and presumably natural panic, by this way of thinking, is a conditioned response to internal stimuli that occurred during past panic attacks. It has even been argued that these internal sensations might be prepared stimuli, thus further linking panic and phobia and their underlying mechanism.⁹⁶ Support for the preparedness of such internal stimuli comes from Donald Klein's theory that panic represents the activation of an evolutionarily old suffocation alarm system.⁹⁷

The most complete conditioning theory of panic has been developed by Wolpe.⁹⁸ He has argued that the first panic attack is the result of experiencing the consequences of hyperventilation, which increases the carbon dioxide in the lungs and blood and results in a variety of unpleasant bodily sensations (dizziness, racing heart, the feeling of suffocation). The hyperventilation can arise for a variety of reasons. Certain drugs like cocaine, amphetamine, or LSD, or exposure to toxic chemicals in the workplace, can be the cause. However, according to Wolpe, most often panic occurs in persons who are particularly anxious and worried and who have been under a lot of stress. One study cited by Wolpe found that severe marital conflict occurred during the year before the first panic attack in 84 percent of the patients surveyed, emphasizing again that cognitive factors can lift anxiety over the threshold.

According to Wolpe, the cause of the first panic is not important. It can be organic or psychological. Regardless, once panic occurs, the stimuli that happen to be present at the time will become conditioned fear stimuli. But unlike typical fear conditioning situations, the critical stimuli are internal rather than external. For example, an elevation of blood pressure that occurs in response to hyperventilation might become a conditioned fear stimulus. If blood pressure happens to increase for some other reason, such as talking to a superior or being in some other socially tense situation, the noxious sensations previously elicited by hyperventilation, having been conditioned to increases in blood pressure levels, are now brought on. These sensations are then noticed and interpreted as indicative of the onset of a panic attack. In contrast, the CS (elevation of blood pressure) is not easily noticed (high blood pressure is in fact sometimes called the "silent killer"), and the panic appears to be spontaneous. External stimuli can also become conditioned panic stimuli. If the first panic occurred in a car, then being in cars may make it more likely that panic will occur there. Nevertheless, in Wolpe's model, the internal stimuli play the leading role.

Let's now consider the sequence of events by which the amygdala might participate in conditioned panic. There are neurons in the lower brain stem that are very sensitive to changes in blood level of carbon dioxide.⁹⁹ The amygdala, it turns out, receives inputs from the neurons in this region.¹⁰⁰ The amygdala also receives information about the status of the internal organs—the rate at which the heart is beating, the level of blood pressure, and other vital statistics from the inner core of the body.¹⁰¹ By integrating these internal signals about the state of bodily organs (the conditioned stimuli) with information about the level of carbon dioxide in the blood (the unconditioned stimulus), the amygdala could form synaptic linkages between the co-occurring events, allowing the internal signals to

substitute for the carbon dioxide effects in producing a profound activation of the sympathetic nervous system through the outputs of the amygdala. Once the sympathetic nervous system is activated in this way, the person becomes aware of the bodily arousal and is reminded, through explicit memory, that the symptoms being experienced tend to occur in panic attacks, suggesting that one might be starting. These conscious memories and thoughts about the possibility of panic might, then, by way of projections to the amygdala from the hippocampus and neocortex, lead to further and continued activation of the sympathetic nervous system, and to the build-up of a full-blown panic attack. Alternatively, in the case of false feedback about the status of heart rate or other bodily functions, the chain of events probably starts with cortical cognitions (for example, the belief that the heart is beating fast), which then serve as retrieval cues for explicit memories of past experiences in which fast heart beating occurred (past panic attacks). These conscious thoughts and explicit memories, again by way of connections from neocortical areas and the hippocampus to the amygdala, then trigger the amygdala and its sympathetic outflow as before.

These neuro-scenarios, of course, are hypothetical, as there has not been any research on the role of the amygdala in panic. However, while the contribution of these circuits to human panic disorder is hypothetical, the circuits and their functions are real and it is quite conceivable that they might contribute to panic in the way described.

Bad Habits and Anxious Thoughts

The avoidance responses that so typify anxiety disorders fall somewhere between what I described earlier as innate emotional reactions and voluntary emotional actions. Avoidance responses are instrumental responses that are learned because they are reinforced. They are then performed habitually, which is to say automatically, when the appropriate stimuli occur. But unlike innate responses, avoidance responses are more or less arbitrarily related to danger. Innate emotional reactions occur when the amygdala is turned on (by innate or learned triggers) because the response is hardwired to the amygdala. In contrast, for avoidance, the brain has learned some response that can be performed in the presence of a learned trigger that short-circuits the innate response. For example, initially rats freeze when they hear a sound that predicts a shock. With time, they may learn to jump up at just the right moment during the sound to avoid the shock, or to jump over a barrier during the sound, or to turn a wheel to inactivate the shock. These responses, once learned, prevent emotional arousal. They are performed automatically, without conscious decision. They become habits, ways of automatically responding to stimuli that routinely warn of danger. Like conditioned fear responses, they are performed automatically, but they are learned rather than innate responses.

Emotional habits can be very useful. If you find out that going to a certain water hole is likely to put you face to face with a bloodthirsty predator, then the best thing to do is to avoid going there. But if you stop going to water holes because you become anxious whenever you begin to look for water, or you start drinking less water than you need to maintain your health whenever you do get around to drinking, then your avoidance response has become detrimental to routine life. You have an anxiety disorder.

The automatic nature of emotional habits can be extremely useful, allowing you to avoid routine dangers without having to give them much thought. However, when emotional habits become anxiety disorders, then the rigid unextinguishable learning that typifies avoidance behavior becomes a liability. Many of the leading drugs for treating anxiety have been developed because of their efficiency in reducing avoidance behavior in animals. For example, if a rat is shocked when it steps off a platform in a test chamber, it will remain on the platform when it is placed in the chamber the next day. However, if the rat gets a shot of Valium just before being placed on the platform on the second day, it will be much more likely to step off the platform to figure out if the danger still exists. In other words, the rat is less fearful, less anxious, about the situation when it receives the drug.

As Mowrer and Miller proposed, avoidance learning is usually thought of as taking place in two stages. First, fear conditioning occurs. Then, a response is learned because it supposedly reduces the learned fear. We know that the amygdala is required for the fear conditioning part, but the brain mechanisms involved in the instrumental avoidance response are less clearly understood. It seems that structures like the basal ganglia, frontal cortex, and hippocampus may be involved.¹⁰² There is controversy as to just where in the brain drugs like Valium have their anxiety-reducing effects.¹⁰³ In fact, however, they probably act in a number of places.

Let's consider how a drug like Valium might work in the amygdala. Valium belongs to the class of drugs known as benzodiazepines. These drugs have natural receptors in the brain. When you take Valium, it binds to the benzodiazepine receptors all over the brain. These receptors do a very specific thing. They facilitate the effects of the inhibitory neurotransmitter, GABA. So you basically increase inhibition in a variety of brain areas. In some brain regions, this will not have any consequence for anxiety because that region is not involved in that function. Basically, if a brain region is involved in anxiety, whatever it does during anxiety-provoking situations, it will probably do less of it in the presence of Valium. For example, the lateral nucleus is the sensory-input region of the amygdala. The increase of inhibition in this region will raise the threshold for anxiety. Stimuli that would normally elicit fearful responses through the amygdala no longer do so (see Figure 8-4). Jeffrey Gray has proposed that the anti-anxiety drugs work through the hippocampus (albeit indirectly).¹⁰⁴ This may be true as well, reducing the ability of explicit memories to make us anxious and afraid.

The brain circuits of avoidance are far less clear than the circuits of fear conditioning. Avoidance is more complex: it involves fear conditioning plus instrumental learning. Also, there are many ways in which avoidance conditioning studies can be performed and a great variety of responses can be conditioned this way. Avoidance responses are arbitrary. Anything that reduces the exposure to fear-eliciting events can be an avoidance response. These factors make the brain systems of avoidance more difficult to track down. However, now that we have a good handle on the brain mechanisms involved in the first phase of avoidance learning (the fear conditioning phase), we can more wisely approach the second phase.

Psychotherapy: Just Another Way to Rewire the Brain

Freud's psychoanalytic theory and the various conditioning theories all assume that anxiety is the result of traumatic learning experiences that foster the establishment of anxiety-producing long-term

memories. In this sense, psychoanalytic and conditioning theories have drawn similar conclusions about the origins of anxiety. However, the two kinds of theories lead to different therapeutic approaches. Psychoanalysis seeks to help make the patient conscious of the origins of inner conflict, whereas behavior therapy, the name given to therapies inspired by conditioning theories, tries to rid the person of the symptoms of anxiety, often through various forms of extinction therapy. There is a good deal of debate about the best treatment strategy: psychoanalysis, behavioral therapy, or most recently cognitive therapy.¹⁰⁵ However, extinction therapies, either alone or in combination with other approaches, are commonly recommended for many anxiety disorders.¹⁰⁶

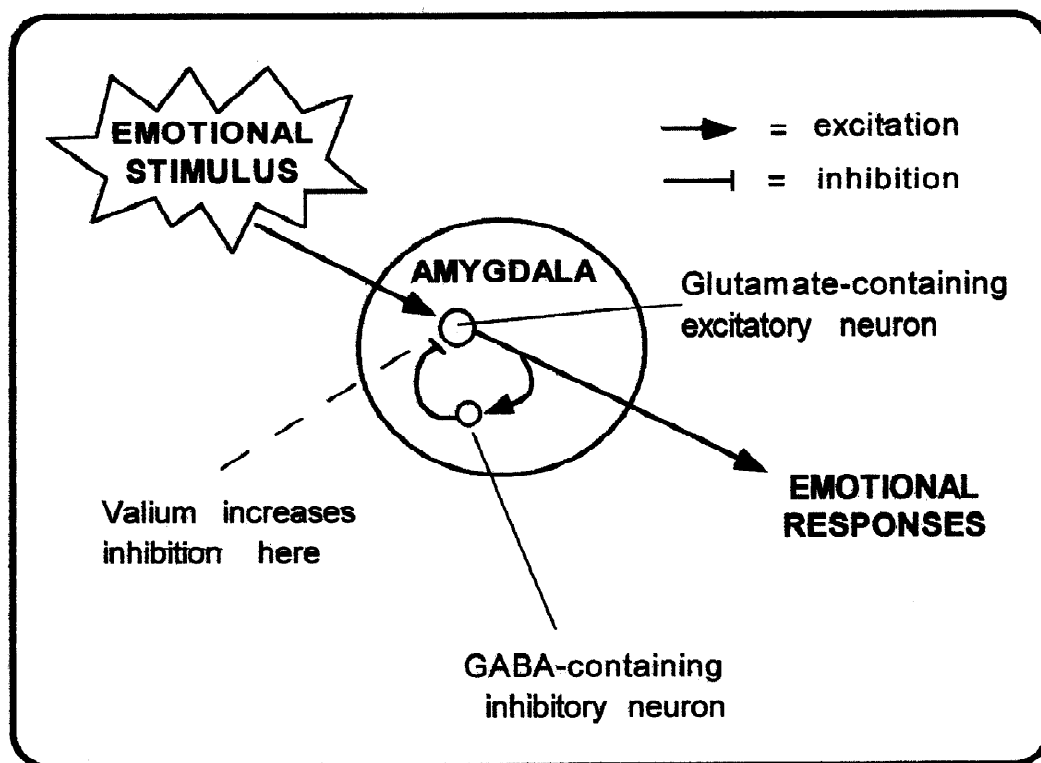


FIGURE 8-4 One Way Valium Might Reduce Fear and Anxiety.

Valium and some other anti-anxiety drugs act by increasing the ability of inhibitory neurons to prevent excitatory transmission. When we are under the influence of Valium, external emotional stimuli (as well as thoughts) are less capable of producing emotional responses, in part (perhaps) because of an action on GABA inhibitory neurons in the amygdala.

The prototypical extinction therapy pioneered by Wolpe starts off with relaxation training.¹⁰⁷ Once the patient learns to feel comfortable in the therapeutic setting, he or she is asked to produce emotional images, starting with less frightening images and working toward more frightening ones. This is called systematic desensitization. The desensitization can then move from images to real objects and situations that cause anxiety, again starting with the least and moving toward the more frightening. Erdelyi interpreted systematic desensitization in the language of conditioning: present the CS in degrees until the conditioned emotional responses drop out.¹⁰⁸ The CS comes to be associated with a new US, safety, and the new conditioned response is no response. Erdelyi suggests that the standard

techniques of psychoanalytic cathartic therapy (hypnotic induction, lying on a couch, trust in the therapist, image production) may accomplish the same thing as Wolpian therapy: extinction of the learned emotional reaction.

Figuring out the brain mechanisms of extinction is obviously going to be an important part of understanding how therapy works. As we've seen, extinction appears to involve interactions between the medial prefrontal cortex and the amygdala. And work by Michael Davis has shown that extinction occurs through the same kind of synaptic mechanism that conditioning does: NMDA-dependent synaptic plasticity in the amygdala.¹⁰⁹ When NMDA receptors are blocked, it may be that the amygdala can't learn what the prefrontal cortex is trying to teach it—to inhibit a particular emotional memory.

These observations give us a different kind of understanding of therapy. Therapy is just another way of creating synaptic potentiation in brain pathways that control the amygdala. The amygdala's emotional memories, as we've seen, are indelibly burned into its circuits. The best we can hope to do is to regulate their expression. And the way we do this is by getting the cortex to control the amygdala. Behavior (extinction) therapy and psychoanalysis have the same goal—help the person with their problem. In both cases, the effects may be achieved by helping the cortex gain control over the amygdala. However, the neural roads taken may be different. Extinction therapy may take place through a form of implicit learning involving the prefrontal-amygdala circuit, whereas psychoanalysis, with emphasis on conscious insight and conscious appraisals, may involve the control of the amygdala by explicit knowledge through the temporal lobe memory system and other cortical areas involved in conscious awareness (see Chapter 9). Interestingly, it is well known that the connections from the cortical areas to the amygdala are far weaker than the connections from the amygdala to the cortex.¹¹⁰ This may explain why it is so easy for emotional information to invade our conscious thoughts, but so hard for us to gain conscious control over our emotions. Psychoanalysis may be such a prolonged process because of this asymmetry in connections between the cortex and amygdala.

(No) Thanks for the Memories

The ability to rapidly form memories of stimuli associated with danger, to hold on to them for long periods of time (perhaps eternally), and use them automatically when similar situations occur in the future is one of the brain's most powerful and efficient learning and memory functions. But this incredible luxury is costly. We sometimes, perhaps all too often, develop fears and anxieties about things that we would just as well not have. What is so useful about being afraid of heights or elevators or certain foods or means of travel? While there are risks associated with each of these things, the chances of them causing harm are usually relatively small. We have more fears than we need, and it seems that our utterly efficient fear conditioning system, combined with an extremely powerful ability to think about our fears and an inability to control them, is probably at fault. As we'll see in the next chapter, though, there is some hope that the future evolution of the human brain will take care of this imbalance.

1. Phillips (1993).
2. Wilson (1968).
3. Shattuck (1980).
4. Shakespeare, quoted in Grey Walter (1953).
5. Manderscheid and Sonnenschein (1994).
6. This paragraph is based on Kramer (1993).
7. Klein (1981).
8. *Diagnostic and statistical manual of mental disorders* (1994).
9. Manderscheid and Sonnenschein (1994).
10. Öhman (1992); Epstein (1972).
11. Öhman (1992); Lader and Marks (1973).
12. Zuckerman (1991).
13. Ibid.
- 14 Freud included dysthymia and somatoform disorders under anxiety, DSM IV includes dysthymia with depressive illness under mood disorders and has a separate classification for somatoform disorders
15. The following brief descriptions of anxiety disorders are taken from the longer DSM IV descriptions.
16. Öhman (1992).
17. Breuer and Freud, quoted in Erdelyi (1985).
18. Erdelyi (1985).
19. It's not necessary for a fear conditioning interpretation of anxiety to be correct in order to make the point I want to make here—that anxiety disorders reflect the operation of the fear system of the brain. However, since the most thorough understanding of the fear system has come from studies of fear conditioning, my job is made much easier if I can piggyback on fear conditioning explanations of anxiety. As the following discussion will, I hope, show, the conditioning theory is in fact plausible
20. This history is summarized in Chapter 2.
21. Watson and Rayner (1920).
22. Watson's position is summarized by Eysenck (1979).
23. Thorndike (1913); Skinner (1938); Hull (1943); Tolman (1932).
24. Mowrer (1939).
25. Ibid.
26. Ibid.
27. N.E. Miller (1948).
28. This experiment was described by Hall and Lindzey (1957).
29. Dollard and Miller (1950).
30. This point was made by Hall and Lindzey (1957).
31. Dollard and Miller (1950).
32. Freud (1909).

33. Wolpe and Rachman (1960).
34. Eysenck and Rachman (1965).
35. Seligman (1971).
36. Reviewed by Seligman (1971).
37. Mineka et al (1984).
38. Bandura (1969).
39. Öhman (1992).
40. Jacobs and Nadel (1985).
41. Ibid.
42. For a summary of the adrenal steroid response to stress, see: J. A. Gray (1987); McEwen and Sapolsky (1995).
43. Jacobson and Sapolsky (1991).
44. Diamond and Rose (1994); Diamond and Rose (1993); Diamond et al (1994); Luine (1994).
45. Shors et al (1990); Pavlides, Watanabe, and McEwen (1993); Diamond et al (1994); Diamond and Rose (1994).
46. McNally et al (1995); Bremner et al (1993); Newcomer et al (1994); Wolkowitz, Reuss, and Weingartner (1990); McEwen and Sapolsky (1995).
47. McEwen (1992).
48. Bekkers and Stevens (1989); Coss and Perkel (1985); Koch, Zador, and Brown (1992).
49. Sapolsky (1990); Uno et al (1989).
50. McKittrick et al (1995); Blanchard et al (1995).
51. Bremner et al (1995).
52. McEwen and Sapolsky (1995).
53. Diamond and Rose (1994); Diamond et al (1993); Diamond et al (1994); Luine (1994).
54. It is important to point out that damage to the hippocampus can result in a retrograde amnesia as well as an anterograde one. This is important since it takes time for the steroids to build up and have their effect. So even though the hippocampus may participate in the initial phases of memory formation while the trauma is just beginning, and it may take a while for the steroids to build up. Once the hippocampus is interfered with, the effects can act to prevent the solidification of the memories that happened at the beginning of the trauma as well.
55. Loftus and Hoffman (1989); Loftus et al (1989); Loftus (1993).
56. Erdelyi (1984).
57. Dali (1948).
58. Makino, Gold, and Schulkin (1994); Swanson and Simmons (1989).
59. Corodimas et al (1994).
60. Servatius and Shors (1994).
61. Jacobs and Nadel (1985).
62. LeDoux, Romanski, and Xagoraris (1989).
63. Amaral et al (1992).
64. Morgan, Romanski, and LeDoux (1993).

65. Luria (1966); Fuster (1989); Nauta (1971); Damasio (1994); Stuss (1991); Petrides (1994); Stuss (1991); Shimamura (1995); Milner (1964).
66. Morgan, Romanski, and LeDoux (1993).
67. Morgan and LeDoux (1995).
68. Thorpe, Rolls, and Maddison (1983); Rolls (1985); Rolls (1992b)
69. Damasio (1994); Stuss (1991); Luria (1966); Fuster (1989); Nauta (1971).
70. Diorio, Viau, and Meaney (1993).
71. LeDoux, Romanski, and Xagoraris (1989).
72. Bouton and Peck (1989); Bouton and Swartzentruber (1991); Buton (1994).
73. Jacobs and Nadel (1985).
74. Quirk, Repa, and LeDoux (1995).
75. Hebb (1949).
76. Shalev, Rogel-Fuchs, and Pitman (1992).
77. Kramer (1993).
78. I will have relatively little to say about generalized anxiety and obsessive compulsive disorder. For a theory of general anxiety, see J.A. Gray (1982). And for a critique of his theory, especially of the fact that the theory does not include a major role for the amygdala in anxiety, see LeDoux (1993). For the record, though, it should be noted that Neil McNaughton and Gray are currently working on a revision of *The Neuropsychology of Anxiety*, based on the large body of work that has emerged since 1982, which will give the amygdala a more prominent role.
79. Blanchard et al (1991).
80. Bordi and LeDoux (1992).
81. Of course, genetic preparation to respond to certain stimuli and past learning about stimuli that are important to the species probably both contribute.
82. Rolls (1992a); Allman and Brothers (1994).
83. Öhman (1992).
84. Charney et al (1993); Kolb (1987).
85. Charney et al (1993).
86. Kolb (1987).
87. Charney et al (1993); Shalev, Rogel-Fuchs, and Pitman (1992).
88. *Diagnostic and statistical manual of mental disorders* (1987).
89. *Diagnostic and statistical manual of mental disorders* (1987); Öhman (1992).
90. *Diagnostic and statistical manual of mental disorders* (1987).
91. Margraf, Ehlers, and Roth (1986b); Margraf, Ehlers, and Roth (1986a); Klein (1993).
92. Ehlers and Margraf (1987).
93. Ackerman and Sachar (1974); Margraf, Ehlers, and Roth (1986b); Wolpe (1988).
94. Ackerman and Sachar (1974); Margraf, Ehlers, and Roth (1986b); Wolpe (1988).
95. Margraf, Ehlers, and Roth (1986a).
96. Ibid.
97. Klein (1993).

98. Wolpe (1988).
99. Benarroch et al (1986); Ruggiero et al (1991).
100. Ruggiero et al (1991).
101. Cechetto and Calaresu (1984).
102. J. A. Gray (1982); J.A. Gray (1987); Sarter and Markowitsch (1985); LeDoux (1993); Isaacson (1982).
103. J. A. Gray (1982); Nagy, Zambo, and Decsi (1979).
104. J. A. Gray (1982).
105. Cognitive therapy attempts to eliminate pathological emotions by changing appraisals and thoughts. Some representative cognitive approaches to phobias and other anxiety disorders are: Lang (1979); Lang (1993); Koa and Kozak (1986); Beck and Emery (1985).
106. Reid (1989).
107. Summarized by Erdelyi (1985).
108. Erdelyi (1985).
109. Falls, Miserendino, and Davis (1992).
110. Amaral et al (1992).