stress hormones are released into its bloodstream. These and other conditioned responses are expressed in essentially the same way in every rat, and also occur when a rat encounters its perennial archenemy, a cat, strongly suggesting that, as a result of fear conditioning, the sound activates the neural system that controls responses involved in dealing with predators and other natural dangers.

Fear conditioning is a variation on the procedure discovered by Ivan Pavlov around the turn of the century.[3] As everyone knows, the great Russian physiologist observed that his dogs salivated when a bell was rung if the sound of the bell had previously occurred while the dog had a juicy morsel of meat in its mouth. Pavlov proposed that the overlap in time of the meat in the mouth with the sound of the bell resulted in the creation of an association (a connection in the brain) between the two stimuli, such that the sound was able to substitute for the meat in the elicitation of salivation.

Pavlov abhorred psychological explanations of behavior and

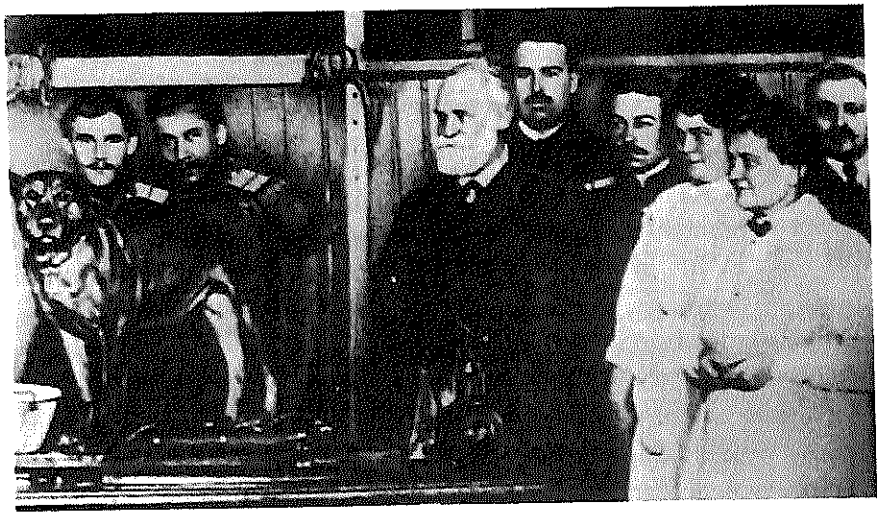

FIGURE 6-3
Pavlov and His Dog.

Photograph of I. P. Pavlov demonstrating classical conditioning to students and visitors at the Russian Army Medical Academy sometime around 1904. (Caption from figure on p. 177 of C. Blakemore and S. Greenfield [1987], *Mindwaves.* Oxford: Basil Blackwell.)

sought to account for the anticipatory salivation physiologically, without having to "resort to fantastic speculations as to the existence of any subjective state in the animal which may be conjectured on analogy with ourselves." He thus explicitly rejected the idea that salivation occurred because the hungry dogs began to think about the food when they heard the bell. In this way Pavlov, like William James (see Chapter 3), removed subjective emotional states from the chain of events leading to emotional behavior.

Pavlov called the meat an unconditioned stimulus (US), the bell a conditioned stimulus (CS), and the salivation elicited by the CS a conditioned response (CR). This terminology derives from the fact that the capacity of the bell to elicit salivation was conditional upon its relation to the meat, which elicited salivation naturally, which is to say, unconditionally. Applying these terms to the fear conditioning experiment described above, the tone was the CS, the shock was the US, and the behavioral and autonomic expressions were the CRs. And in the language used in the previous chapter to describe the stimuli that initiate emotional behaviors, a US is a *natural trigger* while a CS is a *learned trigger.*

Fear conditioning does not involve response learning. Although rats freeze when they are exposed to a tone after but not before conditioning, conditioning does not teach the rats how to freeze. Freezing is something that rats do naturally when they are exposed to danger. Laboratory-bred rats who have never seen a cat will freeze if they encounter one.[4] Freezing is a built-in response, an innate defense response, that can be activated by either *natural or learned triggers.*

Fear conditioning opens up channels of evolutionarily shaped responsivity to new environmental events, allowing novel stimuli that predict danger (like sounds made by an approaching predator or the place where a predator was seen) to gain control over tried-and-true ways of responding to danger. The danger predicted by these *learned trigger stimuli* can be real or imagined, concrete or abstract, allowing a great range of external (environmental) and internal (mental) conditions to serve as CSs.

Conditioned fear learning occurs quickly, and can occur after a single CS-US pairing. An animal in the wild does not have the opportunity for trial-and-error learning. Evolution has arranged things

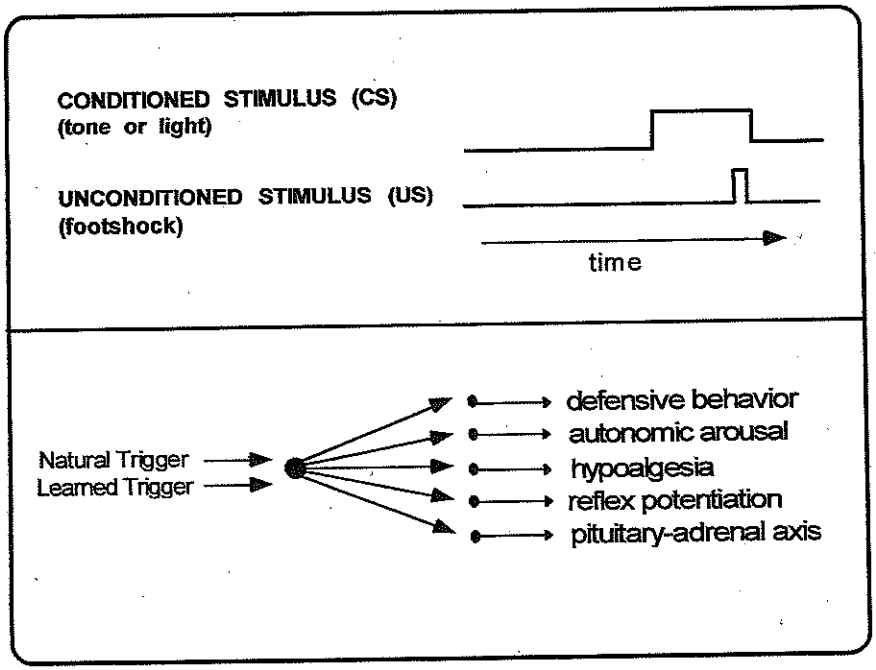

FIGURE 6-4
Fear Conditioning.

In fear conditioning an unconditioned stimulus (typically a brief, mild footshock) is delivered at the end of the conditioned stimulus (usually a tone or light). After a few pairings, the conditioned stimulus acquires the capacity to elicit a wide variety of bodily responses. Similar responses occur in the presence of natural dangers that are innately programmed into the brain. For example, in the presence of either a conditioned fear stimulus or a cat, rats will freeze and exhibit blood pressure and heart rate changes, alterations in pain responsivity, more sensitive reflexes, and elevation of stress hormones from the pituitary gland. Because rats do not require prior exposure to cats to exhibit these responses, the cat is a natural trigger *of defense responses for rats. And because the tone only elicits these responses after fear conditioning, it is a* learned trigger. *Similar patterns of defense responses occur in humans and other animals when exposed to fear triggers (natural and learned). Studies of nonhuman animals can thus illuminate important aspects of fear reactivity in humans.*

so that if you survive one encounter with a predator you can use your experience to help you survive in future situations. For example, if the last time a rabbit went to a certain watering hole it encountered a fox and barely escaped, it will probably either avoid that watering hole in the future or the next time it goes there it will approach the scene with trepidation, taking small cautious steps, searching the environment for any clue that might signal that a fox is near.[5] The watering hole and fox have been linked up in the rabbit's brain, and being near the watering hole puts the rabbit on the defensive.

Not only is fear conditioning quick, it is also very long lasting. In fact, there is little forgetting when it comes to conditioned fear. The passing of time is not enough to get rid of it.[6] Nevertheless, repeated exposure to the CS in the absence of the US can lead to "extinction." That is, the capacity of the CS to elicit the fear reaction is diminished by presentation of the CS over and over without the US. If our thirsty but fearful rabbit has only one watering hole to which it can go, and visits it day after day without again encountering a fox, it will eventually act as though it never met a fox there.

But extinction does not involve an elimination of the relation between the CS and US. Pavlov observed that a conditioned response could be completely extinguished on one day, and on the next day the CS was again effective in eliciting the response. He called this "spontaneous recovery."[7] Recovery of extinguished conditioned responses can also be induced. This has been nicely demonstrated in studies by Mark Bouton.[8] After rats received tone-shock pairings in one chamber, he put them in a new chamber and gave them the tone CS over and over until the conditioned fear responses were no longer elicited—the conditioned fear reaction was completely extinguished. He then showed that simply placing the animals back in the chamber where the CS and US were previously paired was enough to *renew* the conditioned fear response to the CS. Extinguished conditioned fear responses can also be *reinstated* by exposing the animals to the US or some other stressful event.[9] Spontaneous recovery, renewal, and reinstatement suggest that extinction does not eliminate the memory that the CS was once associated with danger but instead reduces the likelihood that the CS will elicit the fear response.

These findings in rats fit well with observations on humans with pathological fears (phobias).[10] As a result of psychotherapy, the fear

of the phobic stimulus can be kept under control for many years. Then, after some stress or trauma, the fear reaction can return in full force. Like extinction, therapy does not erase the memory that ties fear reactions to trigger stimuli. Both processes simply prevent the stimuli from unleashing the fear reaction. I'll have much more to say about this in Chapter 8.

The indelibility of learned fear has an upside and a downside. It is obviously very useful for our brain to be able to retain records of those stimuli and situations that have been associated with danger in the past. But these potent memories, which are typically formed in traumatic circumstances, can also find their way into everyday life, intruding into situations in which they are not especially useful, and such intrusions can be quite disruptive to normal mental functioning. We'll consider traumatic memory again in Chapters 7 and 8.

Although most of the research on the neural basis of conditioned fear has been conducted in animals, fear conditioning procedures can be used in identical ways in humans.[11] Numerous studies of humans have conditioned autonomic nervous system responses, such as changes in heart rate or in sweat gland activity (so-called galvanic skin responses), by pairing tones or other neutral stimuli with mild shocks. Because conditioned fear responses are not dependent on verbal behavior and conscious awareness, they have often been used to study unconscious (subliminal) emotional processing in humans, as described in Chapter 3.

When a human is presented with a consciously perceptible CS that predicts the imminent delivery of a painful stimulus, he or she typically feels fearful or anxious during the CS.[12] We might therefore be inclined to say that the CS elicits a state of fear that then causes the responses. In fact, a number of psychologists and neuroscientists who study fear conditioning assume that "fear" connects the CS to the CR.[13] However, like Pavlov and James, I find it neither necessary nor desirable to insert a conscious state of fear into the chain of events connecting trigger stimuli to fear responses. Here are my reasons why. First, fear conditioning procedures can be used to couple defensive responses to neutral stimuli in worms, flies, and snails, as well as in fish, frogs, lizards, pigeons, rats, cats, dogs, monkeys, and people.[14] I doubt that all of these animals consciously experience fear in the presence of a CS that predicts danger. This is admittedly a slippery slope to slide down, and one that I'm going to delay detailed discussion on until Chapter 9. But if for the time being we assume I'm correct that we don't need conscious fear to explain fear responses in some species, then we don't need it to explain fear responses in humans.[15] Second, even in humans, the one species in which we can study conscious processes with some confidence, fear conditioning can be achieved without conscious awareness of the CS or the relation between the CS and US.[16] The conscious fear that can come with fear conditioning in a human is not a cause of the fear responses; it is one consequence (and not an obligatory one) of activating the defense system in a brain that also has consciousness.

One of the key aspects of fear conditioning that makes it so valuable as a tool for studying the brain mechanisms of fear is that the fear responses come to be coupled to a specific stimulus. This offers

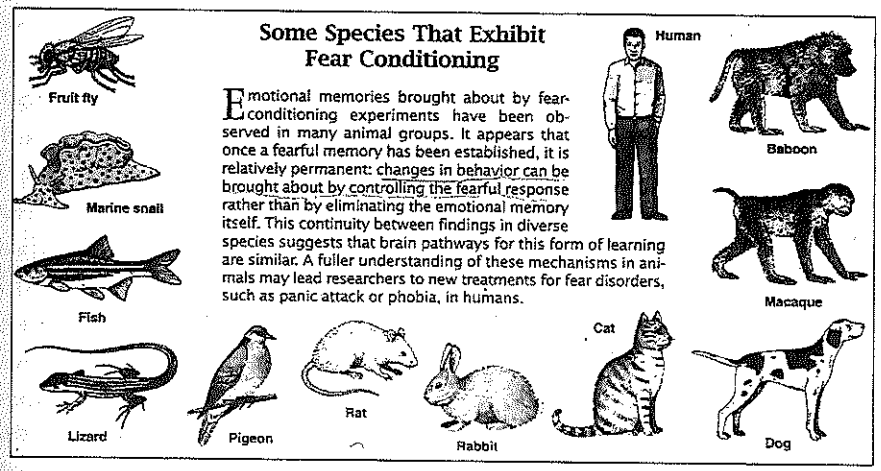

FIGURE 6-5
Animals Throughout the Phyla Can Be Fear Conditioned.

Fear conditioning is an evolutionarily old solution to the problem of acquiring and storing information about harmful or potentially harmful stimuli and situations. It has been studied in several invertebrate species, and in a variety of vertebrates. Within the vertebrates, the behavioral expression of fear conditioning and its neural basis appear very similar in all species that have been examined in detail. (From J.E. LeDoux, Emotion, memory and the brain. *Scientific American* [June, 1994], vol 270, p.39. © 1994 by Scientific American Inc., all rights reserved.)

several important advantages. First, once the stimulus is established as a learned trigger of fear, it will lead to the expression of fear responses each time it occurs. The expression of the fear response is thus under the control of the experimenter, which is very convenient. Second, we can begin to build the emotional processing circuit on the shoulders of the known organization of the sensory system engaged by the CS. Since the sensory systems are understood better than other aspects of the brain, we can use these as a launching pad, tracing the fear processing circuit forward from them. Third, the CS can be a very simple sensory stimulus that is processed with minimal brain power, allowing us to bypass much of the cognitive machinery in the study of fear. We can, in other words, study how the brain appraises the danger implied by a stimulus without getting too bogged down in how the stimulus itself is processed. While it is possible to use either a simple tone or a spoken sentence as a CS, it will be much more difficult to trace the pathways involved in fear conditioning to the sentence, since the processing of the sentence is a much more complex, and less well understood, brain operation.

Fear conditioning is thus an excellent experimental technique for studying the control of fear or defense responses by the brain. It can be applied up and down the phyla. The stimuli involved can be specified and controlled, and the sensory system that processes the CS can be used as the starting point for tracing the pathways through the brain. The learning takes place very quickly and lasts indefinitely. Fear conditioning can be used to study how the brain processes the conditioned fear stimulus and controls defense responses that are coupled to them. It can also be used to examine the mechanisms through which emotional memories are established, stored, and retrieved, and, in humans, the mechanisms underlying conscious fear.

Fear conditioning is not the only way to study fear behavior[17] and it may not be a valid model of all of the many phenomena that are referred to by the term "fear."[18] Nevertheless, it is a quite powerful and versatile model of fear behavior and has been very effectively used to trace brain pathways. Fear conditioning may not tell us everything we need to know about fear, but it has been an excellent way to get started.

Measure for Measure

Once the meaning of a stimulus has been modified by fear conditioning, the next occurrence of the stimulus unleashes a whole host of bodily responses that prepare the organism to deal with the impending danger about which the stimulus warns. Any of these can be used to measure the effects of conditioning.

For example, when a conditioned fear stimulus occurs, the subject will typically stop all movement—it will freeze.[19] Many predators respond to movement[20] and withholding movement is often the best thing to do when danger is near.[21] Freezing can also be thought of as preparatory to rapid escape when the coast clears, or to defensive fighting if escape is not possible. Since the muscle contractions that underlie freezing require metabolic energy, blood has to be sent to those muscles. Indeed, the autonomic nervous system is strongly activated by a conditioned fear stimulus, producing a variety of cardiovascular and other visceral responses that help support the freezing response. These also help the body prepare for the escape or fighting responses that are likely to follow.[22] Additionally, stress hormones are released into the bloodstream to further help the body cope with the threatening situation.[23] Reactivity to pain is also suppressed, which is useful since the conditioned stimulus often announces a situation in which the probability of bodily harm is high.[24] And reflexes (like eyeblink or startle responses) are potentiated, allowing quicker, more efficient reactions to stimuli that normally elicit protective movements.[25]

These various responses are part of the body's overall adaptive reaction to danger and each has been used to examine the brain systems involved in conditioned fear responses. For example, David Cohen[26] has studied the brain pathways of fear conditioning in pigeons using heart rate responses, and Bruce Kapp,[27] Neil Schneiderman and Phil McCabe[28] and Don Powell[29] have used heart rate responses in rabbits. Michael Fanselow[30] has used freezing and pain suppression in rats as measures, while Michael Davis[31] has exploited the potentiation of reflexes by a fear eliciting conditioned stimulus, also in rats. Orville Smith[32] has studied fear conditioning in baboons, measuring a variety of cardiovascular responses in conjunction with measures of movement inhibition. And in my research on the brain

mechanisms of fear conditioning, I've made simultaneous measurements of freezing and blood pressure responses in rats.[33]

The amazing fact is that it has not really mattered very much how conditioned fear has been measured, or what species has been studied, as all of the approaches have converged on a common set of brain structures and pathways that are important. Although there are some minor differences and controversies over some of the details, in broad outline there is remarkable consensus. This contrasts with studies of the neural basis of many other behaviors, where slight changes in the experimental procedure or the species can result in profound differences in the neural systems involved. Fear conditioning is so important that the brain does the job the same way no matter how we ask it to do it.

Highways and Byways

Imagine being in a unfamiliar land. You are handed a piece of paper on which the locations of a starting point and a destination are indi-

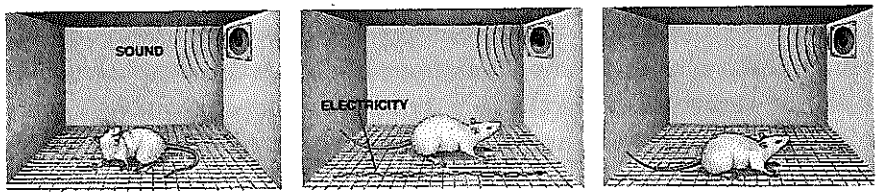

FIGURE 6-6
A Rat Undergoing Fear Conditioning.

The rat is first exposed to the sound alone. It orients toward the sound, but after several occurrences, the sound is ignored. Next, the sound and the brief, relatively mild shock occur together several times. Later, the sound, when presented alone, will elicit conditioned fear responses. The sound, by association with the shock, has become a learned trigger of fear responses. This is similar to what goes on in humans when they are exposed to dangers or trauma. The stimuli associated with the danger or trauma become learned triggers *that unleash emotional reactions in us. Studies of fear conditioning in rats can thus reveal important aspects of the way human emotional (fear) learning occurs.* (From J.E. LeDoux, Emotion, memory and the brain. *Scientific American* [June 1994], vol 270, p. 34. © 1994 by Scientific American Inc., all rights reserved.)

cated. There are lots of other points marked on the paper. There are also some lines between some of the points, indicating possible ways to get from one to another. But you are told that the lines between the points may or may not indicate real roads, and also that not all of the roads that exist between points are marked. Your job is to get in your car at the starting point and find the best way to the destination, and to make an accurate map along the way.

This is essentially the problem that we faced when we began to try to figure out how networks in the brain make it possible for a novel acoustic stimulus to come to elicit defensive responses as a result of fear conditioning. We knew the starting point (the ear and its connections into the brain) and the end point (the behavioral defense responses and their autonomic concomitants), but the points that linked the inputs and outputs in the brain were unclear. Many of the relevant connections in the brain had been demonstrated with older techniques that were prone to lead to false results—identifying nonexistent connections between two points or failing to find real ones.[34] Relatively little work on the neural basis of fear had used fear conditioning.[35] And while research on fear using techniques other than fear conditioning had suggested some ideas about which brain areas might be involved, it wasn't clear whether these were essential way stations, interesting detours, or just plain wrong turns.

Go with the Flow: Much of the earlier work on the emotional brain had started in the middle of the brain, not surprisingly, in the limbic system.[36] This work showed that lesions of limbic areas can interfere with some emotional behaviors, and that stimulation of limbic areas can elicit emotional responses. But these studies left unclear how the lesioned or stimulated area relates to the rest of the brain. Also, most of the earlier work used techniques that lacked a discrete eliciting stimulus and thus could not benefit from the advantages, described above, that a conditioned stimulus offers.

My approach was to let the natural flow of information through the brain be my guide.[37] In other words, I started at the beginning, at the point that the auditory-conditioned stimulus enters the brain, and tried to trace the pathways forward from this system toward the final destinations that control the conditioned fear responses. I thought that this strategy would be the best and most direct way of figuring out

the road map of fear. In retrospect, this strategy worked pretty well.

I began by asking a simple question: which parts of the auditory system are required for auditory fear conditioning (fear conditioning tasks in which an auditory stimulus serves the CS)?[38] The auditory system, like other sensory systems, is organized such that the cortical component is the highest level; it is the culmination of a sequence of information processing steps that start with the peripheral sensory receptors, in this case, receptors located in the ear. I reasoned that damaging the ear would be uninteresting, since a deaf animal is obviously not going to be able to learn anything about a sound. So, instead, I started by damaging the highest part of the auditory pathway. If auditory cortex lesions interfered with fear conditioning, I would be able to conclude that the auditory stimulus had to go all the way through the system in order for conditioning to occur, and that the next step in the pathway should be an output connection of the auditory cortex. If, however, auditory cortex lesions did not disrupt conditioning, I would have to make lesions in lower stations to find the highest level that the auditory stimulus has to reach in order for conditioning to take place.

Damage to the auditory cortex, in fact, turned out to have no effect at all on the conditioning of either the freezing or the blood pressure responses. I then lesioned the next lower station, the auditory thalamus, and these lesions completely prevented fear conditioning. So did lesions of the next lower auditory station in the midbrain. On the basis of these studies I concluded that the auditory stimulus has to rise through the auditory pathway from the ear to the thalamus, but does not have to go the full distance to the auditory cortex. This presented me with a paradox.

Traditionally, the sensory processing structures below the cortex are viewed as slaves to the cortical master. Their job is to get the information to the cortex, where all of the interesting things are done to the stimulus, like assembling neural bits and pieces of the input into the perceptions of the external world that we experience. According to neuroanatomy textbooks, the auditory cortex was the main if not the only target of the auditory thalamus. Where, then, was the auditory stimulus going after it left the thalamus in its journey toward emotional reactivity, if not to the cortex?

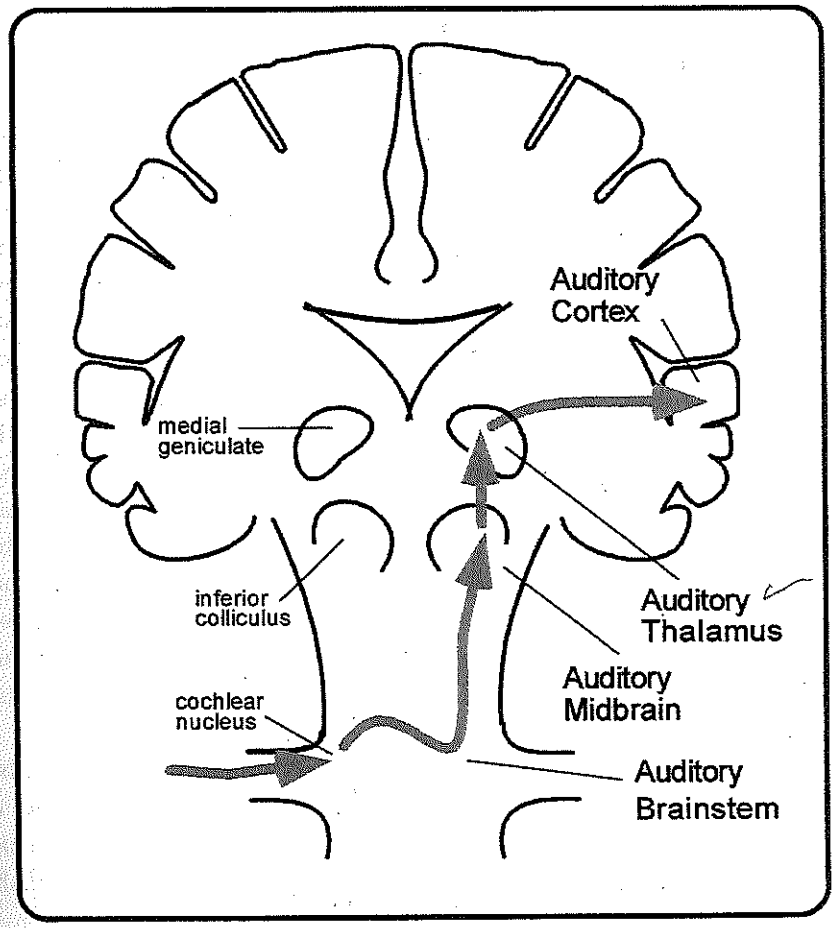

FIGURE 6-7
Auditory Processing Pathways.

This is a highly simplified depiction of auditory pathways in the human brain. A similar organization plan holds for other vertebrate species. Acoustic signals in the environment are picked up by special receptors in the ear (not shown) and transmitted into the brain by way of the auditory nerve (arrow at bottom left), which terminates in the auditory brainstem nuclei (cochlear nucleus and related regions). Axons from these regions then mostly cross over to the other side of the brain and ascend to the inferior colliculus of the midbrain. Inferior collicular axons then travel to the auditory thalamic relay nucleus, the medial geniculate body, which provides the major inputs to the auditory cortex. The auditory cortex is composed of a number of regions and subregions (not shown).

Through the Looking Glass: In order to get some reasonable ideas about where the signal might go to after the auditory thalamus, I took advantage of techniques for tracing pathways in the brain. To use these, you have to inject a small amount of a tracer substance in the brain area you are interested in. Tracers are chemicals that are absorbed by the cell bodies of neurons located in the injected area and shipped down the axon to the nerve terminals. Neurons are constantly moving molecules around inside them—many important things, like neurotransmitters, are manufactured in the cell body and then transported down the axon to the terminal region where they are used in communication across synapses. After the tracer enters the cell body, it can ride piggyback on these mobile substances until it reaches the terminal region of the axon, where it is deposited. The fate of the tracer can then be visualized by chemical reactions that "stain" those parts of the brain that contain the transported substance. These techniques make it possible to figure out where the neurons in one area send their fibers. Since information can only get from one area of the brain to another by way of fibers, knowing the fiber connections of an area tells us where information processed in an area is sent next.

So we injected a tracer into the auditory thalamus.[39] The substance injected sounds more like an ingredient of an exotic salad in a macrobiotic café than the chemical basis of a sophisticated neuroscience technique: wheat germ agglutinin conjugated horseradish peroxidase, or just WGA-HRP for short. The next day the brain was removed and sectioned, and the sections were stained by reacting them with a special chemical potion. We put the stained sections on slides and then looked at them with a microscope set up for dark-field optics, which involves shining indirect light onto the slide—this makes it easier to see the tracer reaction in the sections.

I'll never forget the first time I looked at WGA-HRP with dark-field optics. Bright orange particles formed streams and speckles against a dark blue-gray background. It was like looking into a strange world of inner space. It was incredibly beautiful and I stayed glued to the microscope for hours.

Once I got past the sheer beauty of the staining, I turned to the task at hand, which was to find out where, if anywhere, the auditory thalamus projected to besides the auditory cortex. I found four sub-

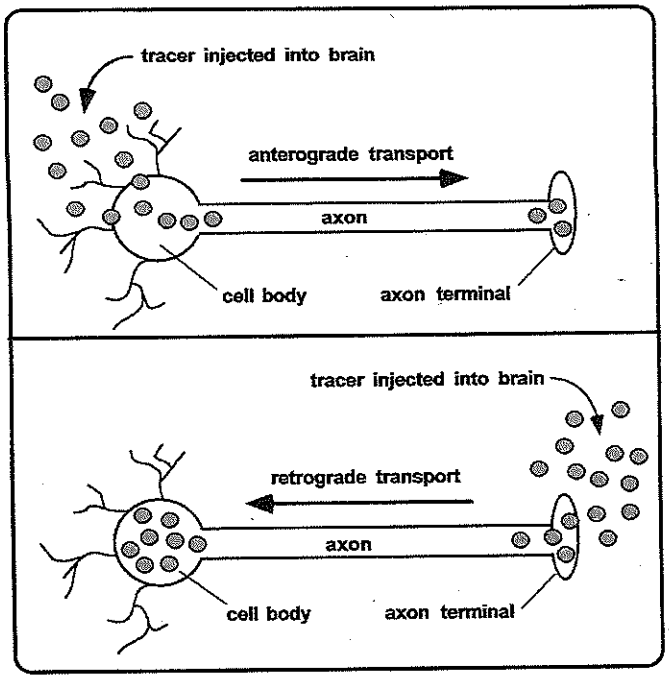

FIGURE 6-8
Tracing Pathways in the Brain with Axonal Transport.

In order to figure out whether neurons in two different brain regions are interconnected, tracers are injected into one of the regions. The tracer is then picked up by neurons that are bathed by the injection. Once the tracer is inside the neuron, it is transported through the axon. Some tracers are picked up by cell bodies and transported to axon terminals (anterograde transport), whereas other tracers are picked up by terminals and transported to cell bodies (retrograde transport).

cortical regions that contained heavy sprinkling with the tiny orange dots, suggesting that these regions receive projections from the auditory thalamus. This was surprising, given the well-received view that sensory areas of the thalamus project mainly, if not exclusively, to the cortex.

It seemed likely that one of the four labeled regions might be the crucial next step in the fear conditioning pathway—the place where the stimulus goes after the thalamus. So, I designed a lesion study that would interrupt the flow of information from the auditory thalamus to each of these regions.[40] Three of the lesions had absolutely no

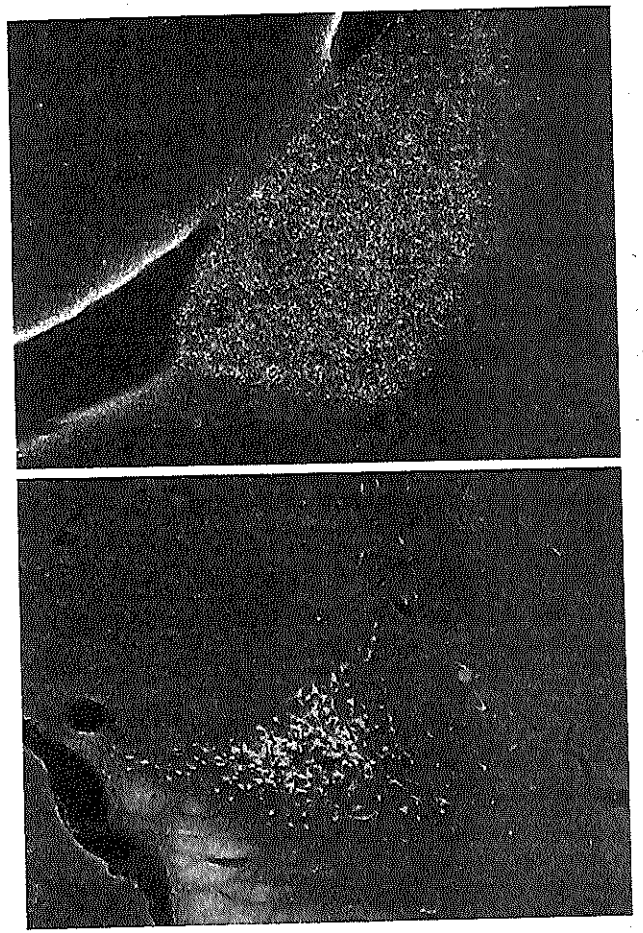

FIGURE 6-9
Examples of Anterograde and Retrograde Transport in the Thalamo-Amygdala Pathway.

The top photograph shows anterograde labeling of terminals in the lateral amygdala after an injection of a tracer in the auditory thalamus. These terminals in the lateral amygdala thus originate from cell bodies in the auditory thalamus. Note the fine, punctate nature of anterograde terminal labeling. The bottom photograph shows cell bodies in the auditory thalamus that were retrogradely labeled by an injection of a tracer in the lateral nucleus of the amygdala. The labeled cells are the bright white structures that cluster together in a triangular region. The cells in the auditory thalamus thus send their axons to the lateral amygdala. Note the large size of the labeled cell bodies, as compared to the terminals above. The two images are black-and-white photographs of dark-field illuminated brain sections taken through a microscope.

effect. But disconnection of auditory thalamus from the fourth area—the amygdala—prevented conditioning from taking place.

Almond Joy: The amygdala is a small region in the forebrain, named by the early anatomists for its almond shape (amygdala is the Latin word for almond). It was one of the areas of the limbic system and had long been thought of as being important for various forms of emotional behavior—earlier studies of the Klüver-Bucy syndrome had pointed to it (see Chapter 4), as had electrical stimulation studies (see below).

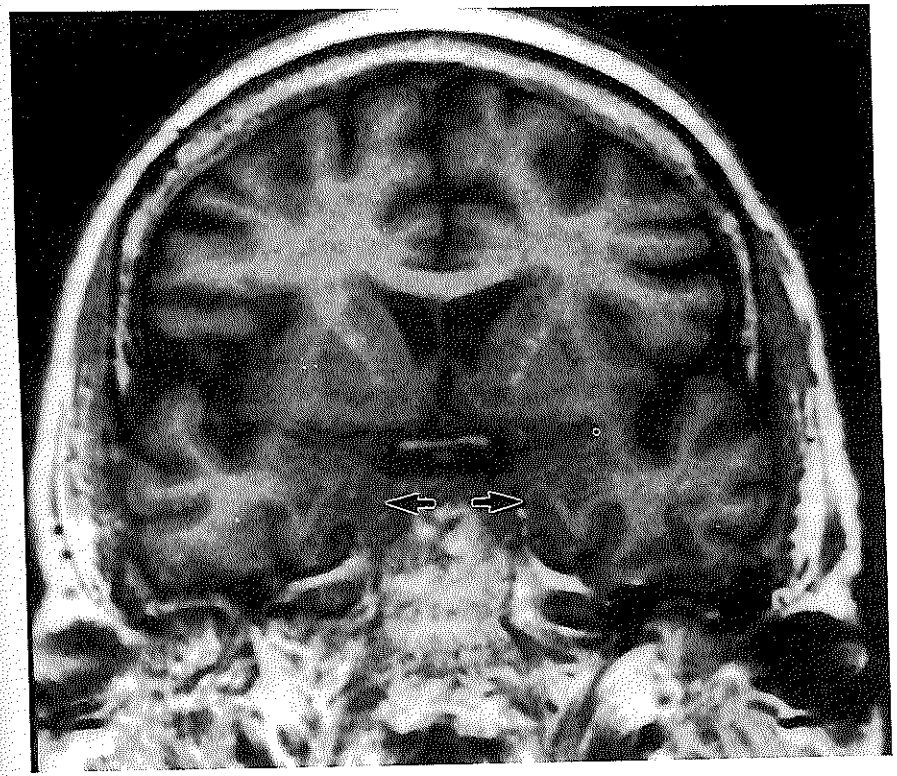

FIGURE 6-10
Magnetic Resonance Imaging Scan Showing the Location of the Amygdala in the Human Brain.

The amygdala on each side of the brain is indicated by the arrows. (Image provided by E. A. Phelps of Yale University.)

The discovery of a pathway that could transmit information directly to the amygdala from the thalamus suggested how a conditioned fear stimulus could elicit fear responses without the aid of the cortex. The direct thalamic input to the amygdala simply allowed the cortex to be bypassed. The brain is indeed a complex mesh of connections, but anatomical findings were taking us on a delightful journey of discovery through this neuronal maze.

I wasn't really looking for the amygdala in my work. The dissection of the brain's pathways just took me there. But my studies, when they first started coming out, fit nicely with a set of findings that Bruce Kapp had obtained concerning a subregion of the amygdala—the central nucleus. Noting that the central nucleus has connections with the brain stem areas involved in the control of heart rate and other autonomic nervous system responses, he proposed that this region might be a link in the neural system through which the autonomic responses elicited by a conditioned fear stimulus are expressed. And when he lesioned the central nucleus in the rabbit, his hypothesis was confirmed—the lesions dramatically interfered with the conditioning of heart rate responses to a tone paired with shock.[41]

Kapp went on to show that stimulation of the central amygdala produced heart rate and other autonomic responses, strengthening his idea that the central nucleus was an important forebrain link in the control of autonomic responses by the brain stem. However, he also found that stimulation of the central nucleus elicited freezing responses, suggesting that the central amygdala might not just be involved in the control of autonomic responses, but might be part of a general-purpose defense response control network.

Indeed, subsequent research by several laboratories has shown that lesions of the central nucleus interfere with essentially every measure of conditioned fear, including freezing behavior, autonomic responses, suppression of pain, stress hormone release, and reflex potentiation.[42] It was also found that each of these responses are mediated by different outputs of the central nucleus.[43] For example, I demonstrated that lesions of different projections of the central nucleus separately interfered with freezing and blood pressure conditioned responses—lesions of one of the projections (the periaqueductal gray) interfered with freezing but not blood pressure responses, whereas lesions of another (the lateral hypothalamus) interfered with the blood pressure but not the freezing response.[44] And while lesions of a third projection (the bed nucleus of the stria terminalis) had no effect on either of these responses, other scientists later showed that lesions of this region interfere with the elicitation of stress hormones by the CS.[45]

Journey to the Center of the Amygdala: The studies of the central amygdala and its outputs seemed to clear up how the responses get expressed, but some mysteries still remained about how the stimulus reaches the central nucleus in its quest to gain control over the responses. Again using the WGA-HRP tracing techniques, I examined whether the auditory stimulus might be sent to the central amygdala directly from the auditory thalamus.[46]

I injected the tracer WGA-HRP into the central nucleus. This time, though, I was tracing connections in the reverse direction, from the area of termination of a pathway back to the cell bodies that give rise to it—the tracer does its piggyback ride in this direction as well. When I examined the sections under the microscope, I found bright orange cells containing the tracer in thalamic areas adjacent to the auditory thalamus but not the auditory thalamus itself. As a result, it seemed unlikely that an auditory stimulus is sent directly to the central nucleus in the process of controlling fear responses.

But when I made injections in another amygdala subregion, the lateral nucleus, there were orange cell bodies in the auditory thalamus.[47] And when I aimed injections for the region of the auditory thalamus that contained these labeled cells, I found the fine orange speckles characteristic of terminals in the lateral nucleus (see Figure 6-9). It seemed that the auditory stimulus might travel from the thalamus to the lateral nucleus of the amygdala. To test this hypothesis, I made lesions of the lateral nucleus. Like central amygdala lesions, these interfered with fear conditioning.[48]

On the basis of these lesion studies, together with the results of anatomical tracing experiments, the lateral nucleus came to be thought of as the region of the amygdala that receives the CS inputs in fear conditioning and the central nucleus as the interface with response control systems. The inputs and outputs had been mapped.

Still, an important set of linkages remained uncharted. If the CS inputs enter the amygdala by way of the lateral nucleus and the CR

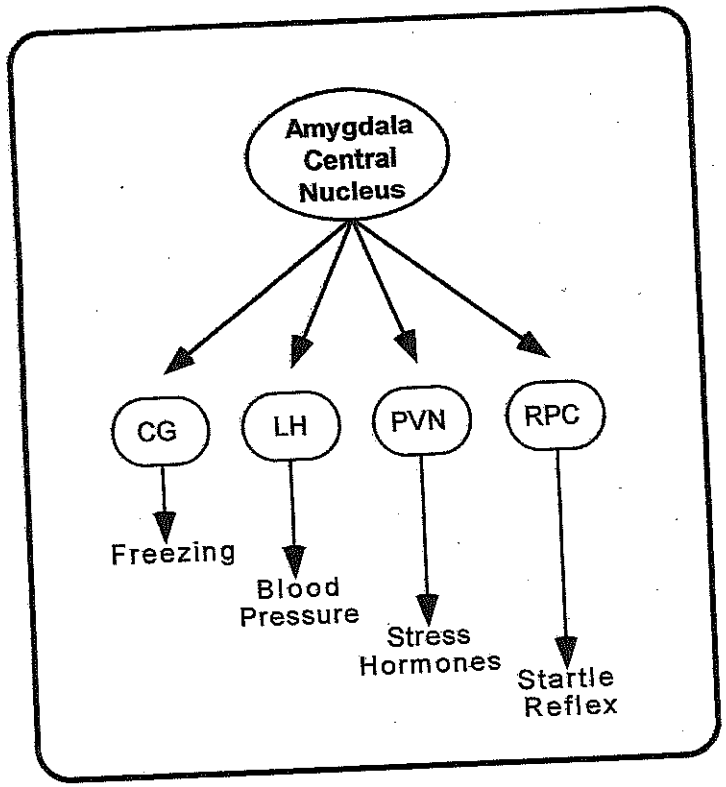

FIGURE 6-11
Different Outputs of the Amygdala Control Different Conditioned Fear Responses.

In the presence of danger or stimuli that warn of danger, behavioral, autonomic, and endocrine responses are expressed, and reflexes are modulated. Each of these responses is controlled by a different set of outputs from the central nucleus of the amygdala. Lesions of the central nucleus block the expression of all these responses, whereas lesions of the output pathways block only individual responses. Selected examples of central amygdala outputs are shown. Abbreviations: CG, central gray; LH, lateral hypothalamus; PVN, paraventricular hypothalamus (which receives inputs from the central amygdala directly and by way of the bed nucleus of the stria terminalis); RPC, reticulopontis caudalis.

outputs leave through the central nucleus, how does information received by the lateral nucleus reach the central nucleus? Although this question has not yet been answered completely, anatomical findings have provided us with some clues.[49] The lateral nucleus has some direct projections to the central nucleus, and also can influence the central nucleus by way of projections to two other amygdala nuclei (the basal and accessory basal), each of which gives rise to strong projections to the central nucleus. There are thus several ways for information entering the lateral nucleus to reach the central nucleus, but exactly which is most crucial is not yet known.

The amygdala is composed of about a dozen or so subregions, and not all or even most are involved in fear conditioning. Only lesions that damage amygdala regions that are part of the fear conditioning circuitry should be expected to disrupt fear conditioning. The lateral and central nuclei are, without doubt, crucially involved, but the role of other amygdala regions is still under study.

The Low and the High Road: The fact that emotional learning can be mediated by pathways that bypass the neocortex is intriguing, for it suggests that emotional responses can occur without the involvement of the higher processing systems of the brain, systems believed to be involved in thinking, reasoning, and consciousness. But before we pursue this notion, we need to further consider the role of the auditory cortex in fear conditioning.

In the experiments described so far, a simple sound was paired with a shock. The auditory cortex is clearly not needed for this. But suppose the situation is somewhat more complex. Instead of just one tone paired with a shock, suppose the animal gets two similar tones, one paired with the shock and the other not, and has to learn to distinguish between them. Would the auditory cortex then be required? Neil Schneidermann, Phil McCabe, and their colleagues looked at this question in a study of heart rate conditioning in rabbits.[50] With enough training, the rabbits eventually only expressed heart rate responses to the sound that had been associated with the shock. And when the auditory cortex was lesioned, this capacity was lost. Interestingly, the auditory cortex lesions did not interfere with conditioning by blocking responses to the stimulus paired with the shock. Instead, the cortically lesioned animals responded to both stimuli as if they had each been paired with the shock.

These findings make sense given what we know about the neurons in the thalamus that project to the amygdala as opposed to those that provide the major inputs to the auditory cortex.[51] If you put an

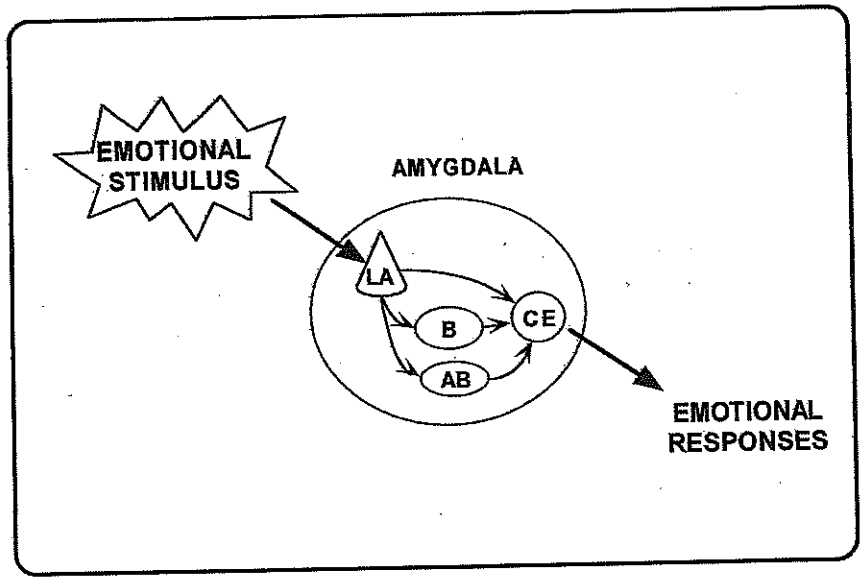

FIGURE 6-12
Organization of Information-Processing Pathways in the Amygdala.

The lateral nucleus (LA) is the gateway into the amygdala. Stimuli from the outside world are transmitted to LA, which then processes the stimuli and distributes the results to other regions of the amygdala, including the basal (B), accessory basal (AB), and central nuclei (CE). The central nucleus is then the main connection with areas that control emotional responses. As shown in figure 6-11, different outputs of the central nucleus regulate the expression of different responses.

electrode in the brain, you can record the electrical activity of individual neurons in response to auditory stimulation. Neurons in the area of the thalamus that projects to the primary auditory cortex are narrowly tuned—they are very particular about what they will respond to. But cells in the thalamic areas that project to the amygdala are less picky—they respond to a much wider range of stimuli and are said to be broadly tuned. The Beatles and Rolling Stones (or, if you like, Oasis and the Cranberries) will sound the same to the amygdala by way of the thalamic projections but quite different by way of the cortical projections. So when two similar stimuli are used in a conditioning study, the thalamus will send the amygdala essentially the

same information, regardless of which stimulus it is processing, but when the cortex processes the different stimuli it will send the amygdala different signals. If the cortex is damaged, the animal has only the direct thalamic pathway and thus the amygdala treats the two stimuli the same—both elicit conditioned fear.

The Quick and the Dead: Why should the brain be organized this way? Why should it have the lowly thalamic road when it also has the high cortical road?

Our only source of information about the brains of animals from long ago is the brains of their living descendants. Studies of living fish, amphibians, and reptiles suggest that sensory projections to rudimentary cortical areas were probably relatively weak compared to projections to subcortical regions in primordial animals.[52] In contemporary mammals, the thalamic projections to cortical pathways are far more elaborate and important channels of information processing. As a result, it is possible that in mammals the direct thalamic pathway to the amygdala is simply an evolutionary relic, the brain's version of an appendix. But I don't think this is the case. There's been ample time for the direct thalamo-amygdala pathways to have atrophied if they were not useful. But they have not. The fact that they have existed for millions and millions of years side by side with thalamocortical pathways suggests that they still serve some useful function. But what could that function be?

Although the thalamic system cannot make fine distinctions, it has an important advantage over the cortical input pathway to the amygdala. That advantage is time. In a rat it takes about twelve milliseconds (twelve one-thousandths of a second) for an acoustic stimulus to reach the amygdala through the thalamic pathway, and almost twice as long through the cortical pathway. The thalamic pathway is thus faster. It cannot tell the amygdala exactly what is there, but can provide a fast signal that warns that something dangerous may be there. It is a quick and dirty processing system.

Imagine walking in the woods. A crackling sound occurs. It goes straight to the amygdala through the thalamic pathway. The sound also goes from the thalamus to the cortex, which recognizes the sound to be a dry twig that snapped under the weight of your boot, or that of a rattlesnake shaking its tail. But by the time the cortex has

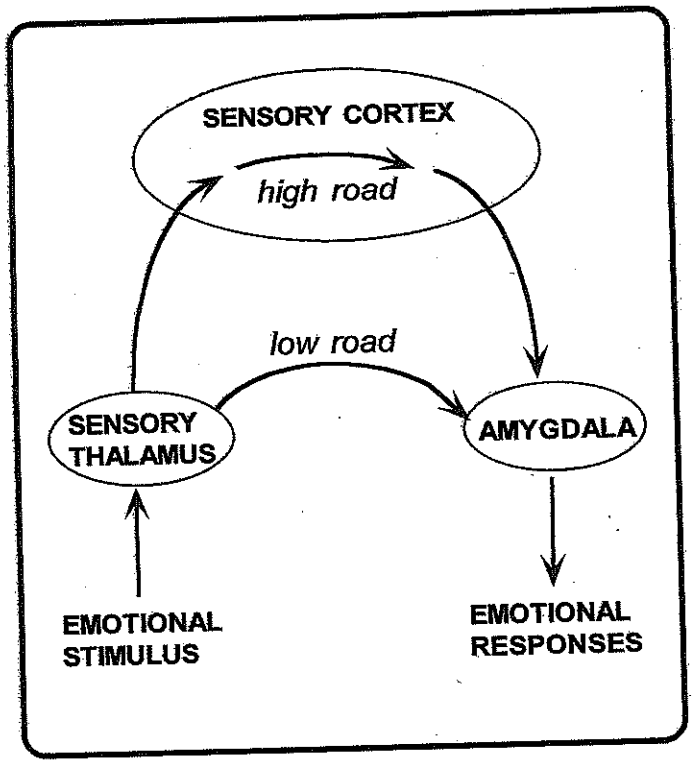

FIGURE 6-13
The Low and the High Roads to the Amygdala.

Information about external stimuli reaches the amygdala by way of direct pathways from the thalamus (the low road) as well as by way of pathways from the thalamus to the cortex to the amygdala. The direct thalamo-amygdala path is a shorter and thus a faster transmission route than the pathway from the thalamus through the cortex to the amygdala. However, because the direct pathway bypasses the cortex, it is unable to benefit from cortical processing. As a result, it can only provide the amygdala with a crude representation of the stimulus. It is thus a quick and dirty *processing pathway. The direct pathway allows us to begin to respond to potentially dangerous stimuli before we fully know what the stimulus is. This can be very useful in dangerous situations. However, its utility requires that the cortical pathway be able to override the direct pathway. It is possible that the direct pathway is responsible for the control of emotional responses that we don't understand. This may occur in all of us some of the time, but may be a predominant mode of functioning in individuals with certain emotional disorders (discussed in more detail in Chapter 8).*

figured this out, the amygdala is already starting to defend against the snake. The information received from the thalamus is unfiltered and biased toward evoking responses. The cortex's job is to prevent the inappropriate response rather than to produce the appropriate one. Alternatively, suppose there is a slender curved shape on the path. The curvature and slenderness reach the amygdala from the thalamus, whereas only the cortex distinguishes a coiled up snake from a curved stick. If it is a snake, the amygdala is ahead of the game. From the point of view of survival, it is better to respond to potentially dangerous events as if they were in fact the real thing than to fail to respond. The cost of treating a stick as a snake is less, in the long run, than the cost of treating a snake as a stick.

So we can begin to see the outline of a fear reaction system. It involves parallel transmission to the amygdala from the sensory thalamus and sensory cortex. The subcortical pathways provide a crude image of the external world, whereas more detailed and accurate representations come from the cortex. While the pathway from the thalamus only involves one link, several links are required to activate the amygdala by way of the cortex. Since each link adds time, the thalamic pathway is faster. Interestingly, the thalamo-amygdala and cortico-amygdala pathways converge in the lateral nucleus of the amygdala. In all likelihood, normally both pathways transmit signals to the lateral nucleus, which appears to play a pivotal role in coordinating the sensory processes that constitute the conditioned fear stimulus. And once the information has reached the lateral nucleus it can be distributed through the internal amygdala pathways to the central nucleus, which then unleashes the full repertoire of defensive reactions. Although I have mainly discussed my own work, research by others (especially Michael Davis, Michael Fanselow, Norman Weinberger, and Bruce Kapp) has also contributed significantly to our understanding of the neural basis of fear conditioning.[53]

A Sea Horse for All Occasions: Consider another example. You are walking down the street and notice someone running toward you. The person, upon reaching you, hits you on the head and steals your wallet or purse. The next time someone is running toward you, chances are a set of standard fear responses will be set into play. You will probably freeze and prepare to defend yourself, your blood pressure and

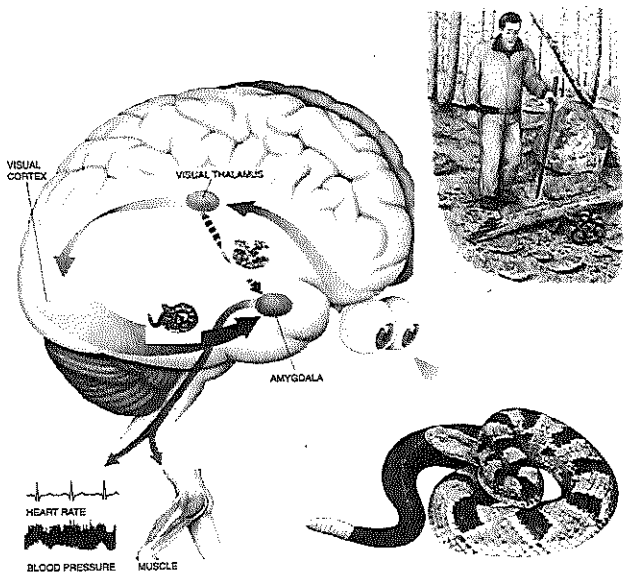

FIGURE 6-14
Brain Pathways of Defense.

As the hiker walks through the woods, he abruptly encounters a snake coiled up behind a log on the path (upper right inset). The visual stimulus is first processed in the brain by the thalamus. Part of the thalamus passes crude, almost archetypal, information directly to the amygdala. This quick and dirty transmission allows the brain to start to respond to the possible danger signified by a thin, curved object, which could be a snake, or could be a stick or some other benign object. Meanwhile, the thalamus also sends visual information to the visual cortex (this part of the thalamus has a greater ability to encode the details of the stimulus than does the part that sends inputs to the amygdala). The visual cortex then goes about the business of creating a detailed and accurate representation of the stimulus. The outcome of cortical processing is then fed to the amygdala as well. Although the cortical pathway provides the amygdala with a more accurate representation than the direct pathway to the amygdala from the thalamus, it takes longer for the information to reach the amygdala by way of the cortex. In situations of danger, it is very useful to be able to respond quickly. The time saved by the amygdala in acting on the thalamic information, rather than waiting for the cortical input, may be the difference between life and death. It is better to have treated a stick as a snake than not to have responded to a possible snake. Most of what we know about these pathways has actually been learned by studies of the auditory as opposed to the visual system, but the same organizational principles seem to apply. (From J.E. LeDoux, Emotion, memory and the brain. *Scientific American* [June 1994], vol 270, p. 38. © 1994 by Scientific American Inc., all rights reserved.)

heart rate will rise, your palms and feet will sweat, stress hormones will begin to flow through your bloodstream, and so on. The sight of someone running toward you has become a conditioned fear stimulus. But suppose you later find yourself on the street where you were mugged. Although there is no one running toward you, your body may still be going through its defense motions. The reason for this is that not only did you get conditioned to the immediate stimulus directly associated with the trauma (the sight of the mugger running toward you), but also to the other stimuli that just happen to have been there. These made up the occasion or context in which the mugging took place, and like the sight of the mugger they too were conditioned by the traumatic experience.

Psychologists have studied contextual conditioning extensively. If you place a rat in a box and give it a few exposures to a mild shock in the presence of a tone, the rat will become conditioned to the tone, as we've already seen, but will also get conditioned to the box. So the next time the rat is placed in the box, the conditioned fear responses—freezing, autonomic and endocrine arousal, pain suppression, reflex potentiation—will occur, even in the absence of the tone. The context has become a CS.

In a contextual fear conditioning experiment, the context is made up of all of the stimuli present, other than the explicit CS. In other words, the CS is in the foreground—it is the most salient and predictive stimulus with respect to the shock. All other stimuli are in the background of the CS and constitute the context. The context is always there, but the CS only comes on sometimes. For this reason, it is often necessary to test the effects of a CS in a novel context, one that has not been associated with the shock, since fear responses elicited by the ever-present context can prevent the detection of responses that occur to the occasionally occurring CS.

In a sense contextual conditioning is incidental learning. During conditioning, the subject is paying attention to the most obvious stimulus (the tone CS) but the other stimuli get bought for the same purchase price. This is very useful from an evolutionary point of view. Our rabbit that escaped from the fox got conditioned not only to the stimuli that were immediately and directly associated with the arrival of the fox—its sight and smell and the sounds it made when attacking—but also to the place where the fox encounter took place—the

watering hole and its surroundings. These extra stimuli are very useful in expanding the impact of conditioning beyond the most obvious and direct stimuli, allowing the organism to use even remotely related cues to avoid or escape from danger.

The interesting thing about a context is that it is not a particular stimulus but a collection of many. For some time it has been thought that the integration of individual stimuli into a context that no longer contains the individual elements is a function of the hippocampus.[54] Unlike the amygdala, the hippocampus does not get information from brain regions that process individual sensory stimuli, like lights and tones.[55] Instead, the sights and sounds of a place are pooled together before reaching the hippocampus, and one job of this brain region is to create a representation of the context that contains not individual stimuli but relations between stimuli.[56]

With this view of the hippocampus in mind, Russ Phillips and I, as well as Mike Fanselow and colleagues, examined whether the hippocampus might play a crucial role in the conditioning of fear responses to background contextual events.[57] In other words, we examined whether damage to the hippocampus might interfere with the conditioning of fear responses to the chamber in which tone-shock pairings occurred. Normal rats froze as soon as they were placed in the conditioning box. Rats with hippocampal lesions showed little freezing to the conditioning box. But as soon as the tone came on, the lesioned rats started freezing. The hippocampal lesion, in other words, selectively eliminated fear responses elicited by contextual stimuli without affecting fear responses elicited by a tone. The tone still worked because the tone could get to the amygdala directly. We reasoned that the hippocampal lesioned animals showed no fear responses to the box because they couldn't form the contextual representation and send it to the amygdala. Indeed, amygdala damage interfered with contextual conditioning just as it did with tone conditioning.[58]

A Hub in the Wheel of Fear: The amygdala is like the hub of a wheel. It receives low-level inputs from sensory-specific regions of the thalamus, higher level information from sensory-specific cortex, and still higher level (sensory independent) information about the general situation from the hippocampal formation. Through such

connections, the amygdala is able to process the emotional significance of individual stimuli as well as complex situations. The amygdala is, in essence, involved in the appraisal of emotional meaning. It is where trigger stimuli do their triggering.

It is not unreasonable to suggest that by knowing what the different inputs to the amygdala are, and having some idea of what function those areas play in cognition, we can get some reasonable hypotheses about what kinds of cognitive representations can arouse fear responses. And by the same token, if we know how the brain achieves some cognitive function, and we can determine how the brain regions involved in that function are connected with the amygdala, we can come up with some plausible ideas about how fear might be aroused by that kind of cognition.

It is easy to imagine how malfunctions of the amygdala and its neural partners might lead to emotional disorders. If in some individuals (for genetic or acquired reasons) thalamic pathways are dominant or otherwise uncoupled from the cortical pathways, these persons might form emotional memories on the basis of stimulus events that do not coincide with their ongoing conscious perceptions of the world mediated by the cortex. That is, because thalamic pathways to the amygdala exit the sensory system before conscious perceptions are created at the cortical level, the processing that occurs through these subcortical pathways, which can only represent features and fragments of stimuli, does not necessarily coincide with the perceptions occurring in the cortex. Such people would have very poor insight into their emotions. At the same time, if the hippocampal system were uncoupled from the thalamic and cortical projections to the amygdala, we might have persons who express emotions that are inappropriate to the immediate context, including possibly the social context. These are purely speculative suggestions at this point, but they are consistent with the facts now available.

Same as It Ever Was

Through studies of fear conditioning in rats, we have been able to map out in great detail the brain mechanisms that underlie fear reactions. The reason we study fear in rats is obvious—we want to learn

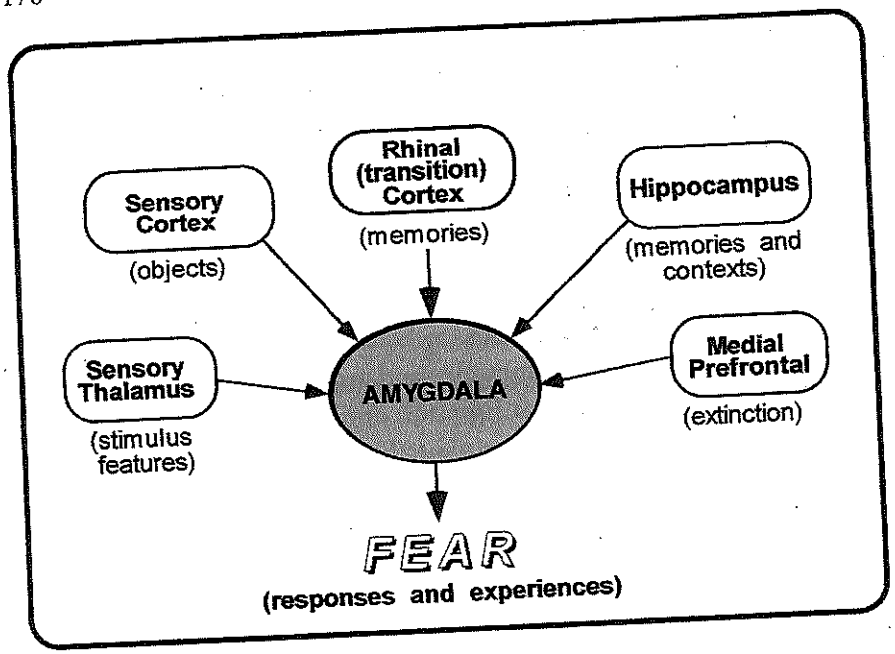

FIGURE 6-15
The Amygdala: Hub in the Wheel of Fear.

The amygdala receives inputs from a wide range of levels of cognitive processing. By way of inputs from sensory areas of the thalamus, the emotional functions of the amygdala can be triggered by low-level stimulus features, whereas inputs from cortical sensory processing systems (especially the late stages of processing in these systems) allow more complex aspects of stimulus processing (objects and events) to activate the amygdala. Inputs from the hippocampus play an important role in setting the emotional context. In addition, as we'll see in Chapter 7, the hippocampus and related areas of the cortex (including the rhinal or transitional cortical areas) are involved in the formation and retrieval of explicit memories, and inputs to the amygdala from these areas may allow emotions to be triggered by such memories. The medial prefrontal cortex has been implicated in the process known as extinction, whereby the ability of conditioned fear stimuli to elicit conditioned fear responses is weakened by repeated exposure to the conditioned stimulus without the unconditioned stimulus. Inputs to the amygdala from the medial prefrontal cortex appear to contribute to this process (see Chapter 8). By knowing which cortical areas project to the amygdala, and knowing the functions in which those areas participate, we can make predictions about how those functions might contribute to fear reactions. Anatomy can, in other words, illuminate psychology.

how human fear works. Less obvious, perhaps, is whether this is a reasonable approach. Can we really learn something about human fear by studying the brain of a rat? I believe we can.

Although no other creature has been studied as thoroughly with fear conditioning as the rat, and though no other technique has been used to study fear more extensively than fear conditioning, if we compile the evidence across species and experimental approaches we reach the inescapable conclusion that the basic brain mechanisms of fear are essentially the same through many levels of evolutionary development.

Let's start with our basic model of fear, fear conditioning. The effects of amygdala lesions on fear conditioning have been studied in birds, rats, rabbits, monkeys, and people using autonomic nervous system activity as the conditioned response. In each of these species, damage to the amygdala interferes with conditioned fear reactions—the CS fails to elicit the CR when the amygdala is damaged.

Pigeons are the only nonmammalian species in which the effects of amygdala lesions on fear conditioning have been examined. The similarity of the effects in pigeons and mammals means either that the amygdala was selected as a key component of the defense system of the vertebrate brain before birds and mammals separated from reptiles, or that the amygdala evolved to perform this function separately in the two post-reptilian lines. The best way to resolve this issue would be to know whether amygdala lesions interrupt fear conditioning in reptiles. Unfortunately, this experiment has not been performed. As a result, we need to turn to some other kind of evidence in search of an answer.

Another technique that has been used to map the brain pathways of fear or defensive behavior is brain stimulation. These techniques have been applied to reptiles as well as mammals and birds, and might thus be able to help us piece together an answer as to whether the amygdala has been involved in defense since at least the time when birds and mammals diverged from reptiles.

The first step we need to take, though, is to be certain that brain stimulation identifies the same pathways of fear reactivity that studies of fear conditioning have in the mammalian brain, where fear conditioning has been most clearly related to brain pathways. There is a long and interesting history to studies of brain stimulation in

mammals, which we will only be able to touch on here.[59] Our main concern is whether stimulation of the amygdala, the heart and soul of the fear system revealed by fear conditioning studies, gives rise to defense responses in mammals. Clearly this occurs. It is well established that stimulation of the amygdala in anesthetized mammals elicits autonomic nervous system responses, and in awake mammals such stimulations elicit freezing, escape, and defensive attack responses, in addition to autonomic changes.[60] These kinds of studies have been performed in rats, cats, dogs, rabbits, and monkeys, all with similar results. Further, defense responses can be elicited from the central nucleus of the amygdala, the region by which the amygdala communicates with brain stem areas that control conditioned fear responses. And interruption of the pathways connecting the amygdala with these brain stem pathways interferes with the expression of the defense responses. Studies of fear conditioning and brain stimulation reveal similar output pathways in the expression of fear responses.

Let's now descend the phyletic tree and see what happens when we stimulate the amygdala of reptiles. It's tricky business to use living reptiles as examples of what reptiles might have been like when mammals diverged, as current reptiles themselves come from lines that have diverged from the ancestral lines. Nevertheless, since brain and behavior are not preserved in fossil records, this is the only way comparative studies of brain function can be conducted. Stimulation of the amygdala in lizards elicits the defensive behaviors these animals characteristically show when they are threatened by a predator, and lesions of the same regions reduce the expression of these behaviors in response to natural trigger stimuli.[61]

Now going up the branching evolutionary tree, we can consider the effects of stimulation of the human amygdala.[62] Such studies are performed in conjunction with brain surgery for otherwise untreatable epilepsy. Since the stimuli are delivered to the amygdala while the subjects are awake, it is possible to not only record expressive responses that are elicited, but also to ask the subjects to report on their experiences. Interestingly, the most common experience reported is a sense of foreboding danger, of fear. Fear is also the most commonly reported experience occurring in association with epileptic seizures, which are in essence spontaneous electrical stimulations that originate in the amygdala.

Recent studies of humans with amygdala damage also suggest that it plays a special role in fear. It is extremely rare to encounter patients with damage to only the amygdala, but it is not that rare to come across patients with damage that includes the amygdala. This is particularly common in patients who undergo surgery to remove epileptic regions of their temporal lobe. Kevin LaBar, Liz Phelps, and I conducted a study of fear conditioning in patients of this type.[63] Because we were studying humans rather than rats, we chose to use a very loud obnoxious noise as the US instead of electric shock. This worked just fine for conditioning autonomic nervous system responses to a softer, non-noxious sound in the control subjects. Importantly, we found that autonomic conditioned responses were reduced in the temporal lobe lesioned group. Interestingly, the patients consciously "knew" the relationship between the CS and US: when asked what went on in the experiment, they typically said, "Oh, there was a sound followed by this other really loud sound." This knowledge was not enough to transform the meaningless sound into a trigger stimulus. Although the lesions included areas other than the amygdala, we know from the animal studies that of all the areas included in the lesion, damage to the amygdala is the likely cause of the deficit in fear conditioning. This is a good example of why animal studies are so important. Without the animal studies the human experiment would be uninterpretable.

Although damage restricted to the human amygdala is very rare, Antonio Damasio and his colleagues at the University of Iowa have come across such a patient.[64] They have performed some extremely important and fascinating studies on her. For example, in one study they examined her ability to detect the emotional expression on faces. She was able to correctly identify most classes of expressions, except when the faces showed fear. And most importantly they have recently examined whether the capacity for fear conditioning is interfered with. Indeed, it was. Unlike the temporal lobe lesioned patients, this case unequivocally implicates the amygdala. Again, though, this study was inspired by the body of animal research that had already implicated the amygdala. If this study had been performed twenty

years ago, before any of the animal conditioning studies had been done, we would have little understanding of the pathways through which the amygdala contributes to fear conditioning. In point of fact, though, the human studies might not have even been performed had the animal studies not set the stage for them—without the known effects of amygdala damage on conditioned fear in experimental animals, why would anyone consider doing such a study in humans with amygdala pathology?

The point of this discussion is to illustrate that the amygdala seems to do the same thing—take care of fear responses—in all species that have an amygdala. This is not the only function of the amygdala,[65] but it is certainly an important one. The function seems to have been established eons ago, probably at least since dinosaurs ruled the earth, and to have been maintained through diverse branches of evolutionary development. Defense against danger is perhaps an organism's number one priority and it appears that in the major groups of vertebrate animals that have been studied (reptiles, birds, and mammals) the brain performs this function using a common architectural plan.

The remarkable fact is that at the level of behavior, defense against danger is achieved in many different ways in different species, yet the amygdala's role is constant. It is this neural correspondence across species that no doubt allows diverse behaviors to achieve the same evolutionary function in different animals. This functional equivalence and neural correspondence applies to many vertebrate brains, including human brains. When it comes to detecting and responding to danger, the brain just hasn't changed much. In some ways we are emotional lizards.[66] I am quite confident in telling you that studies of fear reactions in rats tell us a great deal about how fear mechanisms work in our brains as well.

Beyond Evolution

By way of the amygdala and its input and output connections, the brain is programmed to detect dangers, both those that were routinely experienced by our ancestors and those learned about by each of us as individuals, and to produce protective responses that are

most effective for our particular body type, and for the ancient environmental conditions under which the responses were selected.

Prepackaged responses have been shaped by evolution and occur automatically, or as Darwin pointed out, involuntarily.[67] They take place before the brain has had the chance to start thinking about what to do. Thinking takes time, but responding to danger often needs to occur quickly and without much mulling over the decision. Recall Darwin's encounter with the puff adder at the Zoological Gardens—the snake struck and Darwin recoiled back quick as a flash. If the snake had not been behind glass, Darwin's life would have been at the mercy of his involuntary responses—if they were quick enough, he would have survived; if they were too slow, he would have perished. He certainly had no time to decide whether or not to jump once the snake started to strike. And even though he had resolved not to jump, he could not stop himself.

While many animals get through life mostly on emotional automatic pilot, those animals that can readily switch from automatic pilot to willful control have a tremendous extra advantage. This advantage depends on the wedding of emotional and cognitive functions. So far we've emphasized the role of cognitive processes as a source of signals that can trigger prepackaged emotional reactions. But cognition also contributes to emotion by giving us the ability to make decisions about what kind of action should occur next, given the situation in which we find ourselves now. One of the reasons that cognition is so useful a part of the mental arsenal is that it allows this shift from *reaction* to *action*. The survival advantages that come from being able to make this shift may have been an important ingredient that shaped the evolutionary elaboration of cognition in mammals and the explosion of cognition in primates, especially in humans.

In responding first with its most-likely-to-succeed behavior, the brain buys time. This is not to say that the brain responds automatically first for the purpose of buying time. The automatic responses came first, in the evolutionary sense, and cannot exist for the purpose of serving responses that evolved later. Buying time is a fortunate by-product of the way information processing is constrained by brain organization.

Imagine that you are a small mammal, say a prairie dog. You come out of your burrow to look for dinner. You begin exploring around,

and all of a sudden you spot a bobcat, which you know to be a serious enemy. You immediately stop all movement. Freezing is evolution's gift to you. You do it without having to weigh decisions. It just happens. The sight or sound of the bobcat goes straight to your amygdala and out comes the freezing response. If you had to make a deliberate decision about what to do, you would have to consider the likelihood of each possible choice succeeding or failing and could get so bogged down in decision making that you might be eaten before you made the choice. And if you started fidgeting around or pacing while trying to decide, you would surely attract the predator's attention and certainly decrease your likelihood of surviving. Freezing, of course, is not the only automatic response. But it is a fairly universal initial response to detection of danger throughout the animal kingdom (see Chapter 5). Automatic responses like freezing have the advantage of having been test-piloted through the ages; reasoned responses do not come with this kind of fine-tuning.

Presumably, evolution could work toward making cognition faster, so that thought could always precede action, eliminating involuntary action altogether from the behavioral repertoire. But this would be quite costly. There are many things that we are better off not having to think about, like putting one foot in front of the other when we walk, blinking when objects come near the eye, getting the glove to just the right spot to catch a fly ball, inserting the subject and verb in the correct place when we speak, responding quickly and appropriately to danger, and so forth. Behavioral and mental functions would slow down to a crawl if every response had to be preceded by a thought.

But no matter how useful automatic reactions are, they are only a quick fix, especially in humans. Eventually you take control. You make a plan and carry it out. This requires that your cognitive resources be directed to the emotional problem. You have to stop thinking about whatever you were thinking about before the danger occurred and start thinking about the danger you are facing (and already responding to automatically). Robert and Caroline Blanchard call this behavior "risk assessment."[68] This is something we do all the time. We're always sizing up situations and planning how to maximize our gains and minimize our losses. Surviving is not just something we

do in the presence of a wild beast. Social situations are often survival encounters.

We don't really fully understand how the human brain sizes up a situation, comes up with a set of potential courses of action, predicts possible outcomes of different actions, assigns priorities to possible actions, and chooses a particular action, but these activities are unquestionably amongst the most sophisticated cognitive functions. They allow the crucial shift from reaction to action. From what we currently know, it seems likely that regions like the prefrontal cortex may be involved.[69] The prefrontal cortex is the part of the cerebral cortex that has expanded the most in primates, and it may not even exist in other mammals.[70] When this region is damaged in people, they have great difficulty in planning what to do.[71] So-called frontal lobe patients tend to do the same thing over and over again. They are glued to the present and unable to project themselves into the future. Some regions of the prefrontal cortex are linked with the amygdala, and together these regions, and possibly others, may play key roles in planning and executing emotional actions. We'll again consider the role of the prefrontal cortex in emotion when we turn to the topic of emotional consciousness in Chapter 9. Another brain region that may be involved is the basal ganglia, a collection of areas in the subcortical forebrain. These regions have long been implicated in controlling movement, and recent work has shown that interactions between the amygdala and the basal ganglia may be important in instrumental emotional behavior, which is essentially what I am calling emotional actions.[72]

Emotional plans are a wonderful addition to emotional automaticity. They allow us to be emotional *actors*, rather than just *reactors*. But the capacity to make this switch has a price. Once you start thinking, not only do you try to figure the best thing to do in the face of several possible next moves that a predator (including a social predator) is likely to make, you also think about what will happen if the plan fails. Bigger brains allow better plans, but for these you pay in the currency of anxiety, a topic that we'll return to in Chapter 8.

The appraisal theorist Lazarus has talked about emotional coping.[73] In the scheme presented here, emotional coping represents the cognitive planning of voluntary *actions* once we find ourselves in the

midst of an involuntarily elicited emotional *reaction*. Evolutionary programming sets the emotional ball rolling, but from then on we are very much in the driver's seat. How effectively we deal with this responsibility is a matter of our genetic constitution, past experience, and cognitive creativity, to name but a few of the many factors that are important. And while we will need to understand all of these before we understand "emotion," it seems to me that the way to start understanding emotion is by elucidating the first step in the sequence—the elicitation of prepackaged emotional *reactions* by innate or learned trigger stimuli. We clearly need to go beyond evolution in order to understand emotion, but we should get past it by understanding its contribution rather than ignoring it. I think we have now done that, at least for the emotion fear, or at least for those aspects of the emotion fear that are captured by studies of fear conditioning.

7

REMEMBRANCE OF EMOTIONS PAST

"Every man has reminiscences which he would not tell to everyone but only to his friends. He has other matters in his mind which he would not reveal even to his friends, but only to himself, and that in secret. But there are other things which a man is afraid to tell even to himself, and every decent man has a number of such things stored away in his mind."

Fyodor Dostoevsky, *Notes from the Underground*[1]

BICYCLING. SPEAKING ENGLISH. The Pledge of Allegiance. Multiplication by 7s. The rules of dominoes. Bowel control. A taste for spinach. Immense fear of snakes. Balancing when standing. The meaning of "halcyon days." The words to "Subterranean Homesick Blues." Anxiety associated with the sound of a dentist drill. The smell of banana pudding.

What do all of these have in common? They are each things I've learned and stored in my brain. Some I've learned to do, or learned to expect; others are remembered personal experiences; and still others are just rote facts.

For a long time, it was thought that there was one kind of learning system that would take care of all the learning the brain does. During the behaviorist reign, for example, it was assumed that psychologists could study any kind of learning in any kind of animal and find out how humans learn the things we learn. This logic was not only applied to those things that humans and animals both do, like

finding food and avoiding danger, but also to things that humans do easily and animals do poorly if at all, like speaking.

It is now known that there are multiple memory systems in the brain, each devoted to different memory functions. The brain system that allowed me to learn to hit a baseball is different from the one that allows me to remember trying to hit the ball and failing, and this is different still from the system that made me tense and anxious when I stepped up to the plate after having been beaned the last time up. Though these are each forms of long-term memory (memory that lasts more than a few seconds), they are mediated by different neural networks. Different kinds of memory, like different kinds of emotions and different kinds of sensations, come out of different brain systems.

In this chapter we are going to be concerned with two learning systems that the brain uses to form memories about emotional experiences. The separate existence of these two kinds of memories in the brain is nicely illustrated by considering a famous case study in which one of these systems was damaged, but the other continued to function normally.

Is That a Pin in Your Hand or Are You Just Glad to See Me?

In the early part of this century, a French physician named Edouard Claparede examined a female patient who, as a result of brain damage, had seemingly lost all ability to create new memories.[2] Each time Claparede walked into the room he had to reintroduce himself to her, as she had no recollection of having seen him before. The memory problem was so severe that if Claparede left the room and returned a few minutes later, she wouldn't remember having seen him.

One day, he tried something new. He entered the room, and, as on every other day, he held out his hand to greet her. In typical fashion she shook his hand. But when their hands met, she quickly pulled hers back, for Claparede had concealed a tack in his palm and had pricked her with it. The next time he returned to the room to greet her, she still had no recognition of him, but she refused to shake his hand. She could not tell him why she would not shake hands with him, but she wouldn't do it.

Claparede had come to signify danger. He was no longer just a man, no longer just a doctor, but had become a stimulus with a specific emotional meaning. Although the patient did not have a conscious memory of the situation, subconsciously she learned that shaking Claparede's hand could cause her harm, and her brain used this stored information, this memory, to prevent the unpleasantness from occurring again.

These instances of memory sparing and loss were not easily interpreted in Claparede's time and until recently were thought of as reflecting the survival and breakdown of different aspects of one learning and memory system. But modern studies of the brain mechanisms of memory have given us a different view. It now seems that Claparede was seeing the operation of two different memory systems in his patient—one involved in forming memories of experiences and making those memories available for conscious recollection at some later time, and another operating outside of consciousness and controlling behavior without explicit awareness of the past learning.

Conscious recollection is the kind of memory that we have in mind when we use the term "memory" in everyday conversation: to remember is to be conscious of some past experience, and to have a memory problem (again, in everyday parlance) is to have difficulty with this ability. Scientists refer to conscious recollections as declarative or explicit memories.[3] Memories created this way can be brought to mind and described verbally. Sometimes we may have trouble dredging up the memory, but it is potentially available as a conscious memory. As a result of brain damage, Claparede's patient had a problem with this type of memory.

But the patient's ability to protect herself from a situation of potential danger by refusing to shake hands reflects a different kind of memory system. This system forms implicit or nondeclarative memories about dangerous or otherwise threatening situations. Memories of this type, as we saw in the last chapter, are created through the mechanisms of fear conditioning—because of its association with the painful pinprick, the sight of Claparede became a *learned trigger* of defensive behavior (a conditioned fear stimulus). We also saw that

conditioned fear responses involve implicit or unconscious processes in two important senses: the learning that occurs does not depend on conscious awareness and, once the learning has taken place, the stimulus does not have to be consciously perceived in order to elicit the conditioned emotional responses. We may become aware that fear conditioning has taken place, but we do not have control over its occurrence or conscious access to its workings. Claparede's patient shows us something similar: as a result of brain damage, she had no conscious memory of the learning experience through which the conditioned fear stimulus implicitly acquired the capacity to protect her from being pricked again.

Through brain damage we can thus see the operation of an implicit emotional memory system in the absence of explicit conscious memory of the emotional learning experience. Normally, though, in the undamaged brain, explicit memory and implicit emotional memory systems are working at the same time, each forming their own special brand of memories. So if you met Claparede today and he was, after all these years, still up to his old tricks, you would form an explicit conscious memory of being pricked by the old codger, as well as an implicit or unconscious memory. We are going to call the implicit, fear-conditioned memory an "emotional memory" and the explicit declarative memory a "memory of an emotion." Having already explored how fear conditioning works, we will now examine the neural organization of the explicit or declarative memory system, and also take a look at interactions between this conscious memory network and the unconsciously functioning fear conditioning system.

Henry Mnemonic: The Life and Times of Case H.M.

Karl Lashley, the father of modern physiological psychology and one of the most influential brain researchers in the first half of the twentieth century, conducted an extensive series of investigations attempting to find the locus of memory in the rat brain. His conclusion, that memory is not mediated by any particular neural system but is instead diffusely distributed in the brain, was widely accepted. By mid-century researchers had quit looking for the location of memory in the brain—it seemed that this was a fruitless and even