# 5

# Central Nervous System Integration of the Psychological Stress Response



**Chapter Objectives**

1. Learn the stages of appraisal that lead to psychological stress responses.
2. Learn how interpretation of ongoing events can be translated into emotional responses and motivations for behavior.
3. Understand the brain structures that are involved in the appraisal process and formation of emotions.
4. Understand the interaction between cognitive and affective information that forms frontal-limbic interactions.
5. Learn the role of outputs from the amygdala in forming physiological outputs to the body during states of stress.

In this chapter, we consider how a person's view of the world can influence his or her emotions and thereby cause psychological stress responses. We will begin with a functional view of how persons evaluate events and then consider how these evaluations may result in negative emotions leading to stress reactions. This discussion will then focus on the neurophysiology of negative affect and its associated neural processes and how these can lead to physiological states accompanying psychological distress. Chapter 3 discussed brain systems underlying the peripheral stress response. It emphasized homeostatic regulation based on activities of the hypothalamus, brainstem, and autonomic nervous system. Chapter 4 introduced the idea that stress responses may arise from psychological threats. We will begin now to formulate a more complete picture of how psychological events can cause stress reactions. We will consider how higher brain systems interact with the regulatory functions of the hypothalamus and brainstem to form psychological stress responses. This discussion will provide further background for the basic question about the ways that ideas can affect the body.

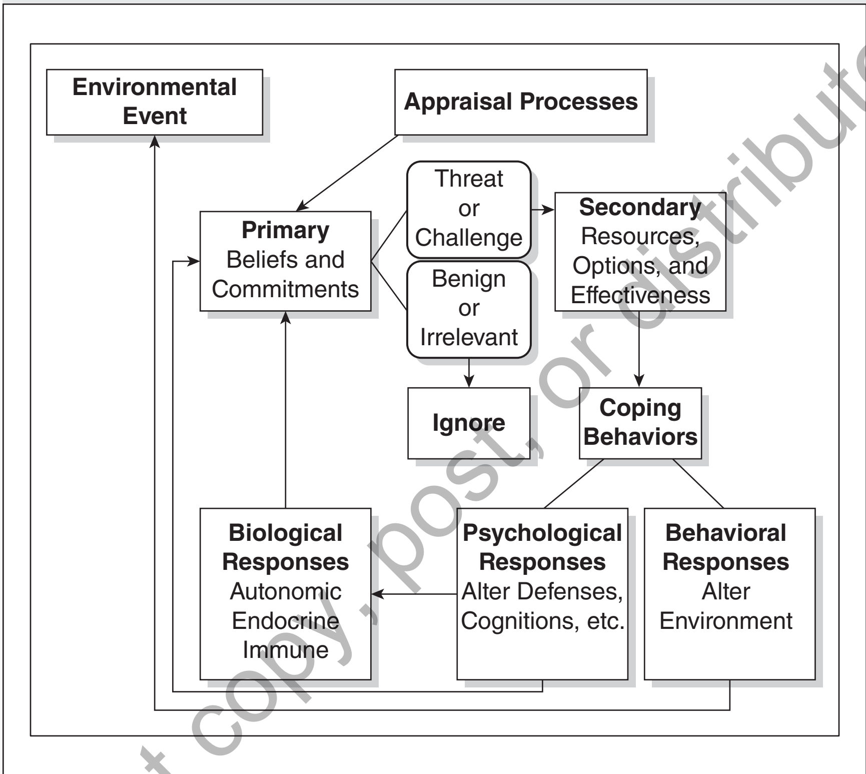
## Appraisals, Psychological Stress, and Negative Emotions

Our responses to things that happen around us are determined by how we think about them. Richard Lazarus and Susan Folkman described how our interactions with the environment could generate emotions that lead to bodily stress responses (Lazarus & Folkman, 1984). They noted that we constantly evaluate the stream of events we encounter. In this *appraisal process,* we classify events as familiar or unfamiliar and threatening or nonthreatening. Similarly, we generate a stream of behavioral strategies to deal with these unfolding events. Along with these appraisals and behavioral adjustments, we experience emotions that signal us about the success of our behavioral strategies and serve to motivate additional behaviors.

## Primary and Secondary Appraisals

Lazarus and Folkman's model of psychological stress takes a cognitive view of how people engage the world. They postulate that we first evaluate events for their threat value. This *primary appraisal* is intended to ensure that we assess each new event so that we do not blindly encounter danger but, instead, recognize it and begin to evolve a plan to deal with it. We next evaluate our options for coping with these presumed threats using *secondary appraisals*. This two-level appraisal process determines our cognitive and behavioral responses, and also our emotional, neurophysiological, autonomic, and endocrine responses to external events. In short, our appraisals determine the nature and magnitude of our psychological reactions and their accompanying physiological adjustments. Figure 5.1 describes the stages in formulating a psychological stress response.

**Figure 5.1** Appraisal model of psychological stress. The process of psychological stress includes both primary appraisals of the threat value of an event and secondary appraisals of the effectiveness of available coping options. These two processes have an impact on physiological responses to the situation.




## Primary Appraisals

Lazarus and Folkman consider the main elements entering into our primary appraisal of an event to be our *beliefs* about how the world should work and our *commitments* to given courses of action. Some events are judged as either benign or irrelevant because they are consistent with our beliefs and commitments, while some events are perceived as *threats or challenges*. Events that are classed as benign can be safely ignored, and they require no special adaptive response. Events that are appraised as threatening require us to prepare to cope with them and perhaps eliminate them.

Lazarus uses beliefs and commitments as the criteria for deciding what events are threatening. This provides a useful means of accounting for cognitive differences between individuals and their emotional and stress reactions to a given event. For example, if I fall and break my arm, I might find this event to be inconvenient, painful, and a disruption to my daily life, but the misfortune would not amount to a personal disaster. On the other hand, imagine this same broken arm happening to an athlete preparing to take part in the Olympic Games. In this instance, the broken arm is appraised as a serious threat to the athlete's commitment to a major goal in life. The otherwise manageable inconvenience of wearing a cast for several weeks turns into a devastating event; the athlete has to stop training and may have a severe psychological response, such as depression. The same event means different things to the athlete and me because we differ in our personal commitments and threat appraisals.

## Secondary Appraisals and Coping Responses

The process of secondary appraisal focuses appropriately on the kinds of responses that might be employed to manage the event in question, and again, people are likely to differ. Events that are potential or known threats require some adaptive response to ensure that harm is limited or avoided. The interventions we employ are referred to as *coping strategies* and *coping behaviors*. These can include both overt and covert activities. If you find yourself feeling chilly on a winter evening, obvious coping behaviors are to put on a sweater or to turn up the thermostat. But other situations in life are not so obviously correctable, and indeed, no simple behavioral strategy may present itself. For example, parents confronted by the news that a young child has a serious, potentially life-threatening illness are likely to receive this as a devastating negative event—one that could have a serious impact on the child and threaten the integrity of the family. This news clearly violates both the beliefs and commitments the parents share. However, the most appropriate responses to the situation are difficult to determine because of the complex questions at hand: Is the illness curable? What is the effect of the treatment on the child? How long will we have to confront this situation? Will there be financial burdens that may affect other children in the family? How will we manage the added time and energy demands possibly imposed by the situation? There are many potential responses, and all have their costs, strengths, and weaknesses.

In such a complex event as a major illness, the parents may use a multilevel strategy to limit the negative impact on themselves and the rest of the family. Such responses may include learning about the disease to assure themselves that everything possible is being done for their child and altering their goals and expectations about the course of the child's development and the life of the family. These responses illustrate adjustments focused on the problem and its emotional impact. Other parents might find themselves overwhelmed by the news and incapable of a directly adaptive response. Instead they might deny that anything is wrong, insisting that the diagnosis is a mistake, even avoiding further treatment for the child. Responses to such a major life stressor may therefore involve cognitive approaches to the situation, behavioral adjustments, realignment of goals and commitments, or purely psychological approaches such as denial.

Lazarus and Folkman have classified coping responses as *problem focused* and *emotion focused*. Problem-focused strategies attack the problem itself, with behaviors designed to gain information, alter the event, and alter beliefs and commitments. Problem-focused strategies increase the person's awareness, level of knowledge, and range of behavioral and cognitive coping options. They can act to reduce the threat value of the event. Emotion-focused strategies call for psychological changes to limit the degree of emotional disruption caused by an event, with minimal effort to alter the event itself.

## Outcomes of Coping Efforts and Physiological Responses

As might be expected, each coping strategy has its costs and benefits. Problem-focused strategies may be costly in terms of the energy and time necessary to put them into effect, but they can potentially lessen the stressor value of the event. Emotion-focused strategies are initially less energy consuming but in the long term may be more costly due to a continued drain on coping resources and lack of impact on the event itself. However, some work suggests that emotion-focused coping, denial in particular, can be stress reducing in patients faced with severe cancers where problem-focused strategies might be more anxiety provoking (Kreitler, 1999; Watson, Greer, Blake, & Shrapnell, 1984). Whichever style of coping is employed, we strive to reduce the central nervous system activation associated with negative emotions and to reduce the physiological activation that ensues.

### The Appraisal Process Is Dynamic and Recursive

Once a coping strategy has been used, we again evaluate the event in terms of our (perhaps new) beliefs and commitments and we reassess its threat value. The threat value of an event is therefore continuously modified by our emerging coping strategies. An ultimate goal of the process is to reduce the threat value of events in the environment, to reduce the negative emotions in response to them, and therefore to reduce the inner state associated with stress reactions. This process may be seen as a form of cognitive regulation over emotions and states of distress.

## Psychological Stress Revisited

In our discussion of fight-or-flight responses in Chapter 5, we noted that these represent primitive behaviors designed to aid our survival in a physically hostile environment. However, when we encounter events that threaten our beliefs and commitments, we may well find that we experience negative emotions and generate fight-or-flight responses even when our physical well-being is not at stake. Emotional reactions and physiological responses can result from our perceptions of threat from the environment and perceptions of the success of our coping efforts.

Stress responses that are based on perceptions of threat are considered to be psychological stress responses because the threat value depends largely on our interpretation of the event and its meaning for our own lives. We might say the following things about psychological stressors:

1. They achieve their threat value not through their physical ability to do harm but because of their appraised threat value.
2. They are not equally stressful to all persons.
3. Persons will vary in their ability to cope with perceived stressors.
4. The physiological systems we use to respond to psychological stressors are the same ones that react to physical threats to homeostasis.

If we reflect on the examples of psychological stress in Chapter 4, we will note that some stressors are pure examples of psychologically threatening events, such as performing mental arithmetic in front of an assistant in a laboratory study. The stressor has no intrinsic ability to harm anyone. However, physical stressors usually have a psychological component. When we consider physically threatening events, we see that in conscious persons, these nearly always present a psychological threat as well. Being caught without shelter in a snowstorm will surely challenge the person's homeostatic mechanisms for temperature regulation, but the person is also likely to suffer considerable anxiety and emotional distress due to an awareness of the danger to their well-being. So we might say that persons conscious of their situation are likely to have significant psychological responses to any genuine physical threat.

We noted that Lazarus and Folkman have posed their model in cognitive terms; as though each event encountered during the day is carefully considered and each response selected consciously from a range of options. However, most of our emotional reactions and stress responses do not have this conscious character. So the model works equally well if we exchange the language of cognition for the language of classical conditioning. We could assume that primary appraisals include *implicit appraisals* enacted via classically conditioned responses developed through prior experience. Similarly, we could think of secondary appraisals as being shaped by the enactment of behaviorally conditioned coping strategies from our experience. Appraisals may therefore be relatively automatic, conditioned responses, or they may be highly cognitive, planned ones. Later in this chapter, we will discuss the role of limbic system structures, especially the amygdala and hippocampus, in forming classically conditioned responses and in shaping our cognitive processes.

In this discussion of appraisals and psychological stress, we place much emphasis on the generation of emotions as a result of the appraisals; the particular emotion that results from a situation will depend heavily on the specifics of the two-stage appraisal process. Lazarus has described this relationship at some length (Lazarus, 1991).

The Lazarus and Folkman model does not specify how the psychology of appraisals might link up with physiological outcomes by way of the central nervous system and peripheral outflow. Nevertheless, it is possible to specify plausible neurophysiological mechanisms for three major stages in this top-down model of psychological stress: the primary appraisal process, the accompanying emotions and physiological responses, and modulation of these by coping responses.

## Central Integration of the Response to Psychological Stress

We now turn attention to a model illustrating how encounters with threatening events may be incorporated into neurophysiological changes and autonomic and endocrine outflow. Recall that in Chapter 4, we reviewed the mechanisms responsible for maintaining homeostasis, with the hypothalamus at the top of this core regulatory system. We recognize that the hypothalamus and brainstem can maintain bodily functions within normal limits, and that they also control reflexive and stereotyped behavioral responses. Figure 3.4 showed the integrated sham rage response in the cat that was organized by the hypothalamus and brainstem. What these parts of the brain cannot do for cats, or people, is to *perceive and classify* something at a distance from the body, or consider a *behavioral plan* to obtain or avoid that thing, and to put the plan into *execution.* These activities require the remainder of the brain, the parts above the hypothalamus that can sense external events and shape behavioral responses to them. As we noted before, since these parts of the brain are necessary for survival in a free-living animal, they must form the highest controls over homeostasis. In maintaining homeostasis, the hemispheres are accordingly responsible for stress reactions that may occur to threatening external stimuli or, in humans, to thoughts and ideas. In other words, they carry out the top-down processes that lead to our psychological stress reactions and our fight-or-flight responses. We will review these brain areas and their functions in considering how psychological stress responses are formed.

Figure 5.2 is a guide to the chain of psychophysiological events that lead from an event in the environment to the generation of a reaction in the body. Five major steps occur in this chain:

1. Sensory intake and interpretation of the environment,
2. Generation of emotions based on appraisal processes,
3. Initiation of autonomic and endocrine responses,
4. Feedback to the cortex and limbic system, and
5. Continued autonomic and endocrine outflow.

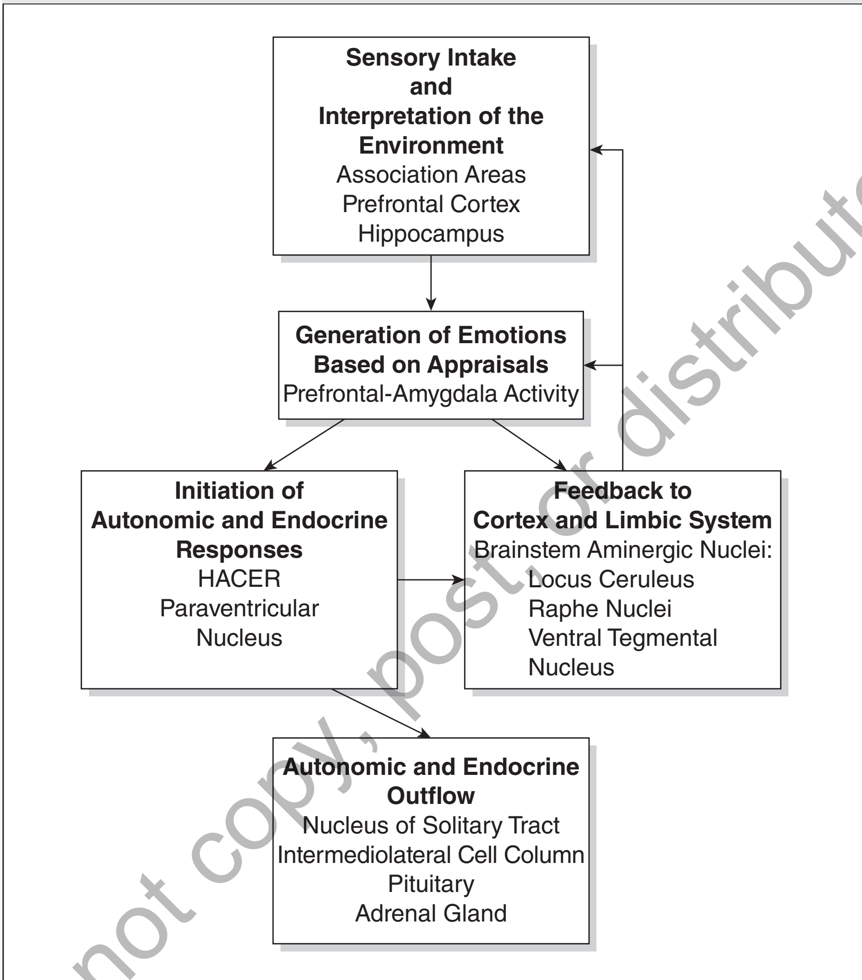
The first four of these steps involve considering how external events affect the regulation of the body. They lead to a consideration of how higher nervous system processes act on the regulatory apparatus involving the hypothalamus and brainstem. As a companion to this simplified diagram, we will review these steps in detail, referring to several related diagrams that describe areas of the brain and its subsystems.

## The Limbic System and Associated Parts of the Brain

### Anatomical Overview

Figures 5.3 and 5.4 illustrate brain areas associated with appraisals and emotions that are active during psychological stress responses. Figure 5.3 has four views of a human brain with parts of the limbic system and frontal cortex highlighted. In view (a), we see the *orbital prefrontal cortex,* that is, the lower surface of the prefrontal cortex, located just above the eyes. The medial part forms the lower segment of the *ventromedial prefrontal cortex,* also

**Figure 5.2** Major steps in the generation of physiological responses based on perceptions and interpretations of events.

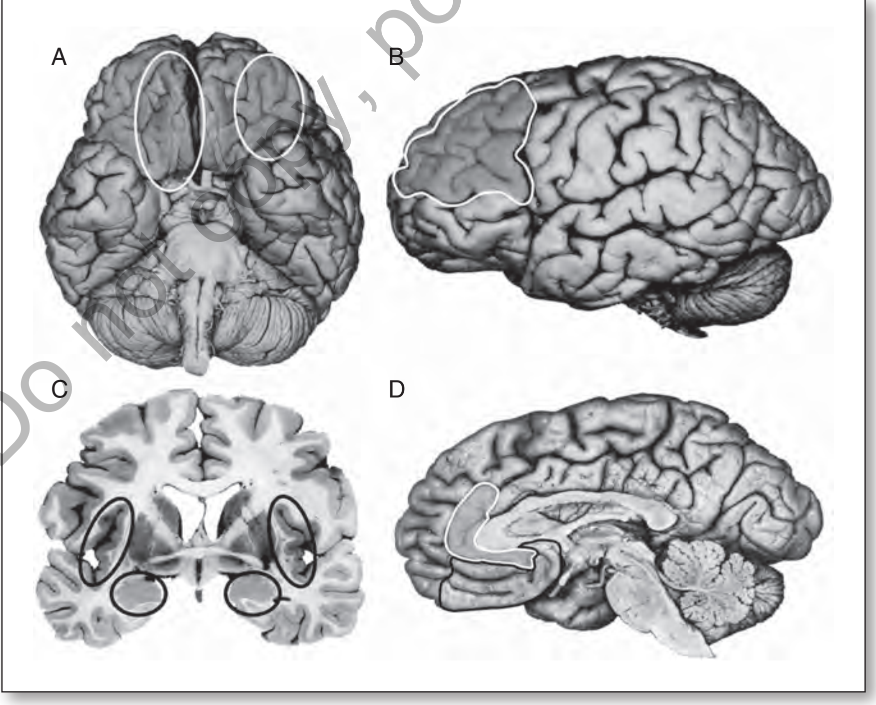





shaded in (d). In contrast, the lateral part has more connections to the lateral and *dorsolateral prefrontal cortex,* highlighted in (b). The ventromedial prefrontal cortex is associated with visceral aspects of decision making (gut feelings, so to speak) whereas the dorsolateral prefrontal cortex is associated with cognitive aspects of decision making, devoid of emotional biases. View (c) shows a vertical slice through the brain indicating where the amygdala is found in the inner convolution of the temporal lobe, and it shows the *insular cortex* buried deeply adjacent to the temporal lobe. The insular cortex is the primary projection area for visceral sensation, and it helps register internal feelings about ongoing events. Finally, in (d) we can see a view of the middle surface of the brain with the shaded *anterior cingulate gyrus,* which terminates just above the medial surface of the ventromedial prefrontal cortex.

Figure 5.4 shows the *limbic lobe* in (a). The term limbic lobe refers to regions of the cortex that relate to *classification and motivational assessment of incoming stimuli.* This system includes the parahippocampal gyrus and cingulate gyrus, along with several subcortical structures and connections. The parahippocampal gyrus overlies the hippocampus and amygdala, and it transmits sensory inputs to these structures. The cingulate gyrus communicates along its entire length to several adjacent areas of sensory and motor cortex. Finally, the anterior cingulate gyrus assimilates information about ongoing sensory processes, motor behaviors, and motivational states. The anterior cingulate gyrus in turn communicates with the prefrontal cortex, especially the ventromedial prefrontal cortex, as outlined in Figure 5.3.

**Figure 5.3** Brain areas associated with emotions and evaluations of current events: (a) the orbital frontal cortex showing the medial and lateral areas, (b) the dorsolateral prefrontal cortex, (c) the amygdala, and (d) the anterior cingulate gyrus just above the ventromedial prefrontal cortex.



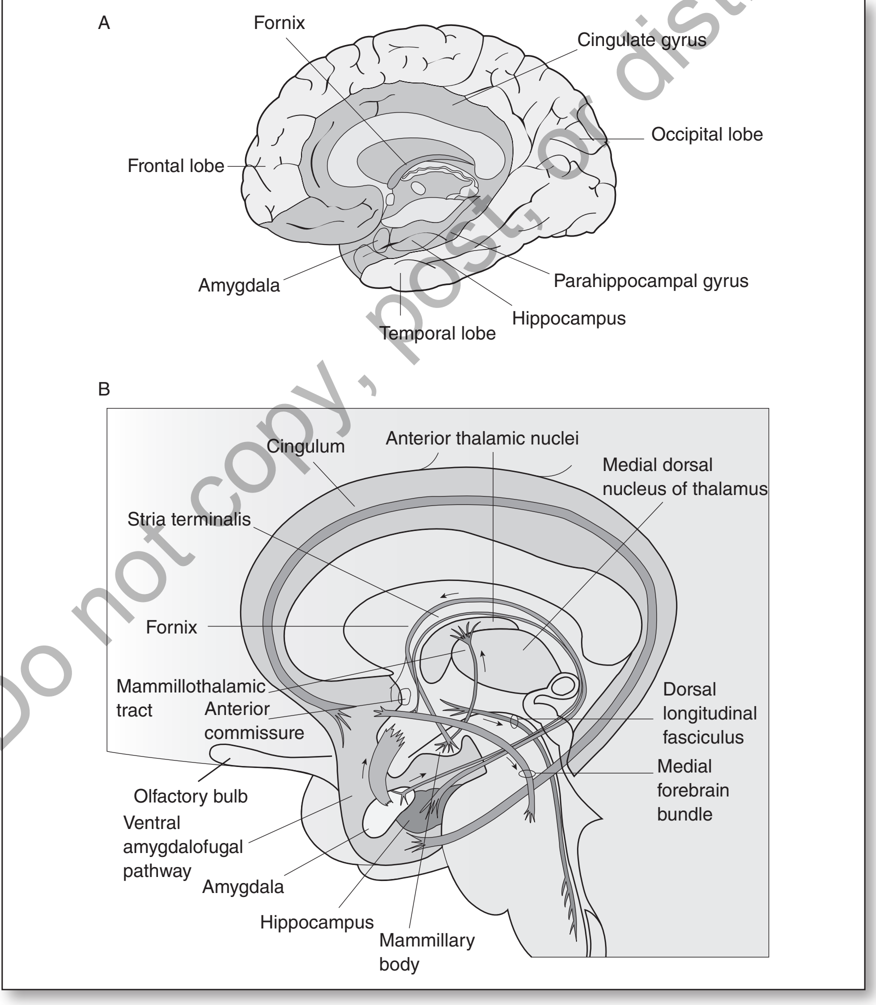
Several key limbic system structures and their interconnections are below the surface of the cortex, as shown in (b). The principal connections are from the amygdala to the *bed nuclei of the stria terminalis* and the *nucleus accumbens,* which are associated with forming positive and negative subjective responses to events. The primary pathways from the amygdala to these structures are *the stria terminalis* and *ventral amygdalofugal pathway.* The second important set of pathways connects the hippocampus to the mammillary bodies by way of the fornix.

The limbic system and its connections with the cortex function to help us form motivations to avoid things that are dangerous, to approach and obtain things that are needed for survival, and to remember motivationally relevant experiences for future reference. In cases of real or imagined danger, the limbic system, especially outputs from the amygdala, is responsible for integrating a state of fight-or-flight. This pattern is the key component of an acute stress reaction. In order to gain an appreciation for the development of an acute psychological stress response, it is useful to first consider how information arriving from the environment is processed and interpreted.

## Primary Appraisals: Sensory Intake and Interpretation of the Environment

In considering how events affect the internal state of our bodies during stress responses, it is helpful to trace the path of sensory information through the central nervous system. Sensory information is relayed from the sense organs to the thalamus, which acts as the central way station for most incoming information. The thalamus directs information to the primary cortical projection areas, dedicated specifically to each of the various sense modalities. Figure 5.5 illustrates the flow of visual and auditory information. The primary projection area for vision is located in the occipital lobe at the back of the cortex, and the projection area for auditory sensation is on the upper surface of the temporal lobe. These two streams of incoming information pass from the primary projection areas through a series of *association areas* of the cortex, during which time raw sensory information is increasingly elaborated and connected with stored memories relating to that sense modality. These elaborations of sensory input in combination with memories are responsible for giving percepts their object-like qualities that we may recognize as familiar or unfamiliar. In addition, the visual and auditory inputs converge at the junction of the parietal and temporal lobes. This convergence of different streams of sensory information forms a highly elaborated *polymodal association* area.

**Figure 5.4** The limbic lobe and limbic system with related structures. (a) The areas of cortex collectively known as the limbic lobe. These include the parahippocampal gyrus in the medial temporal lobe, the cingulate gyrus, and ventromedial prefrontal cortex. (b) The limbic system. The amygdala is shown with its major outputs, the stria terminalis and the ventral amygdalofugal pathway terminating at the bed nuclei of the stria terminalis and the n. accumbens. From: Iversen, S., Iversen, L., & Saper, C. B. (2000). The autonomic nervous system and the hypothalamus. In E. R. Kandel, J. H. Schwartz & T. M. Jessell (Eds.), *Principles of Neural Science* (4th ed., pp. 960–981). New York: McGraw-Hill.



Finally, this highly elaborated visual and auditory information stream is passed along the inferior temporal gyrus.

## What Is It? And Where Is It?

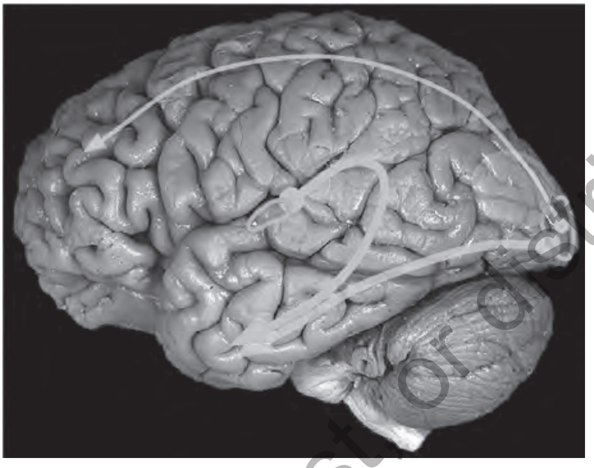
During primary appraisals, we have to answer questions such as "What is out there?" "Where is it?" and "Does it mean anything for me?" Sensory pathways in the brain are designed to help answer these questions. Figure 5.5 shows visual information traveling along two pathways. The first pathway travels from visual association areas to language perception areas in the superior temporal lobe. This path allows things to be identified by name if they are familiar, and this is useful for answering the question "What is it?" This step is essential for assigning meaning to an event. The second visual pathway is shown travelling forward toward the prefrontal cortex, and studies show that this is essential for identifying where an object is and how it is moving in space. In cases of so-called blindsight, patients with damage to the pathway to the temporal lobe will deny seeing identifiable objects, but they are able to move around obstacles as if they could see. In fact, they can unconsciously perceive one part of the visual stream. They know where things are, but they can't tell what things are.

The third question is concerned with assigning personal meaning to the event in question. On the *affective* side of the appraisal process are the structures of the inferior temporal lobe, the basal forebrain, and their own separate connections to the ventromedial prefrontal cortex. As shorthand, we can refer to the coming together of information at the prefrontal cortex and the outputs of the limbic system as *frontal-limbic* connections. We will deal with each of these in turn as this chapter progresses. The key point here is that the evaluation of events, as to meaning and significance and then giving them an affective flavor, captures the essence of the appraisal process. The appraisals then determine how we form emotions and stress reactions.

## Cognition and Emotion: Generating Emotions Based on Appraisal Processes

The appraisal process therefore leads us to consider both the cognitive and the affective sides of things in developing a model of events leading up to psychological stress reactions. Before exploring the more affective side of things, it is worthwhile to consider the cognitive functions of the prefrontal cortex. Figure 5.5 indicates pathways that lead to the frontal lobes, areas of the brain that participate in assessing the meaning and significance of inputs. In relation to appraisal processes, the dorsolateral

**Figure 5.5** Flow of sensory information to the limbic system. Left view of a human brain showing the flow of visual and auditory information to form polymodal sensory inputs to the inferior temporal cortex along with visual pathways to the frontal lobes.





prefrontal cortex is especially important for our ability to consciously work through complex problems. There is much evidence that this is the area most specialized for working memory, studied extensively by the late Patricia Goldman-Rakic (Goldman-Rakic, 1996) and others (Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998). Carrying out arithmetic problems "in your head" or mentally rotating a recalled image of a baseball glove are two examples of working memory tasks. Working memory is a set of processes that allows us to direct our attention as needed, to allow events to be evaluated in consciousness, and to consider alternative courses of action—just the sorts of cognitive skills necessary to carry out primary and secondary appraisals.

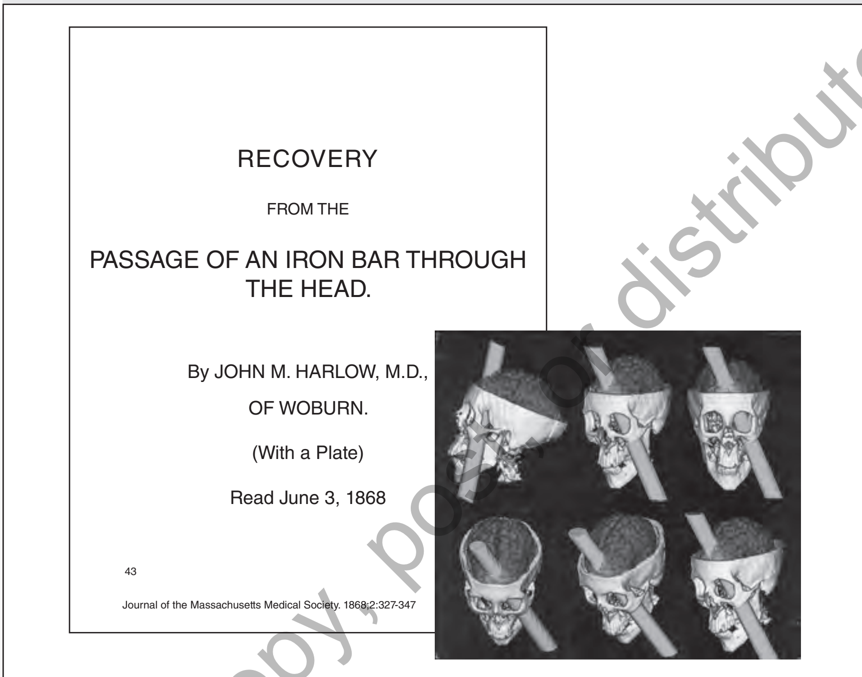
The importance of frontal lobe functioning, in this cognitive sense, is that it is crucial for assessing the meaning of ongoing events. However, purely cognitive processes are sterile things that are not entirely useful in making real decisions. To make effective decisions leading to action in our daily lives, we also need to know how we feel about things. For this reason, the frontal lobes also have abundant visceral inputs that tell our decision-making apparatus how the body is responding as events are experienced and courses of action considered. These visceral inputs depend on the ventromedial prefrontal cortex.

## The Case of Phineas Gage

A most impressive demonstration of what happens when our cognitive and affective capacities are disconnected from each other comes from studying patients who have sustained brain damage to the ventromedial prefrontal cortex, where the two types of information come together. The most famous such patient is Phineas Gage (Figure 5.6). As recounted by his physician, John Harlow (Harlow, 1868), Gage was foreman of a blasting crew cutting a new railroad through the mountains of Vermont. His job called for setting blasting powder charges in holes drilled into the rock by his crewmen. On September 13, 1848, he was briefly distracted while setting a charge, and his iron tamping rod slipped from his hands into the hole his assistant had just filled with blasting powder. The resulting detonation propelled the tamping rod upward and entirely through Gage's skull. The extraordinary aspect of this case is that Gage lost consciousness only for a matter of minutes. He remained lucid after coming to. He could describe the accident in detail, and an hour afterward he walked upstairs to his room at a nearby boarding house. Testing by Harlow and others indicated that he was cognitively intact and fully aware of his surroundings. He retained his rational faculties, but as his friends observed, "Gage was no longer Gage." What they were referring to was that Gage had undergone a personality change. He became socially boorish, he lost his social inhibitions, and he lost his previous goal-oriented approach to life. Although he supported himself until his death on May 21, 1861, he became a shiftless drifter, going from one menial job to another. Dr. Harlow followed Gage through the remaining 12 years of his life, obtained his skull and the tamping rod after his death, and donated them to the Warren Anatomical Museum at Harvard College. Through John Harlow's extraordinary writing and an innovative reconstruction of Gage's injury by Hannah Damasio and her colleagues (Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994), we now know that the injury "involved both left and right prefrontal cortices in a pattern that, as confirmed by Gage's modern counterparts, causes a defect in rational decision making and the processing of emotion." That is, Gage lost his ventromedial prefrontal cortex on both sides of the path of the tamping rod. Patients with such damage find it difficult to invest events with meaning and to make informed choices about future actions based on feelings about their consequences.

Insight into Phineas Gage's deficit comes from studies of modern patients with similar lesions. This work is summarized engagingly by Antonio Damasio (Damasio, 1994), who reports that patients with frontal lesions, particularly bilateral damage to the ventromedial prefrontal cortex and related areas, are often fully conscious and able to perform normally on tests of intelligence. But

**Figure 5.6** Phineas Gage's reconstructed skull and brain and Harlow's classic paper. Reprinted with permission from *Science Magazine*. From: Damasio, H., Grabowski, T., Frank, R., Galaburda, A. M., & Damasio, A. R. (1994). The return of Phineas Gage: Clues about the brain from the skull of a famous patient. *Science, 264*, 1102–1105.






these people have a dramatic deficit in making decisions. Damasio provides the striking example of a patient with ventromedial prefrontal damage who was given a simple choice of two dates for a follow-up appointment about a month later. Most persons would think for a moment and state a preference for one of the options. But in this case, the patient began a lengthy discussion of each option, rationally stating their pros and cons, but in spite of this rational evaluation, he was unable to decide which date would be "better" until his physician, in desperation, suggested a date. The patient immediately agreed to that date and happily left the office as though his former monologue was irrelevant! In Damasio's words: "We might conclude that the result of these patients' lesions is the discarding of what their brains have acquired through education and socialization. One of the most distinctive human traits is the ability to learn to be guided by future prospects rather than by immediate outcomes . . ." (Damasio, 1994). We should also note that such patients are not necessarily devoid of emotional experience. Often they may exhibit emotional reactions that are inappropriate for the times or situations, as did Phineas Gage. What these patients lack is the ability to have normal emotional responses in relation to present thoughts and events—a lack of normal appraisals.

## Prefrontal-Limbic Interactions and Thoughts and Feelings

As the discussion above shows, the ventromedial prefrontal cortex and the closely associated anterior cingulate gyrus are crucial for forming the visceral coloration of thoughts and ideas needed to help us choose a course of action. These prefrontal-limbic connections help us to feel about things. This reasoning leads us to place the connections from the limbic system, especially those projecting from the amygdala toward the basal ganglia and the prefrontal cortex, at the beginning of the chain of events resulting in normal emotional responses and perhaps leading to physiological stress responses.

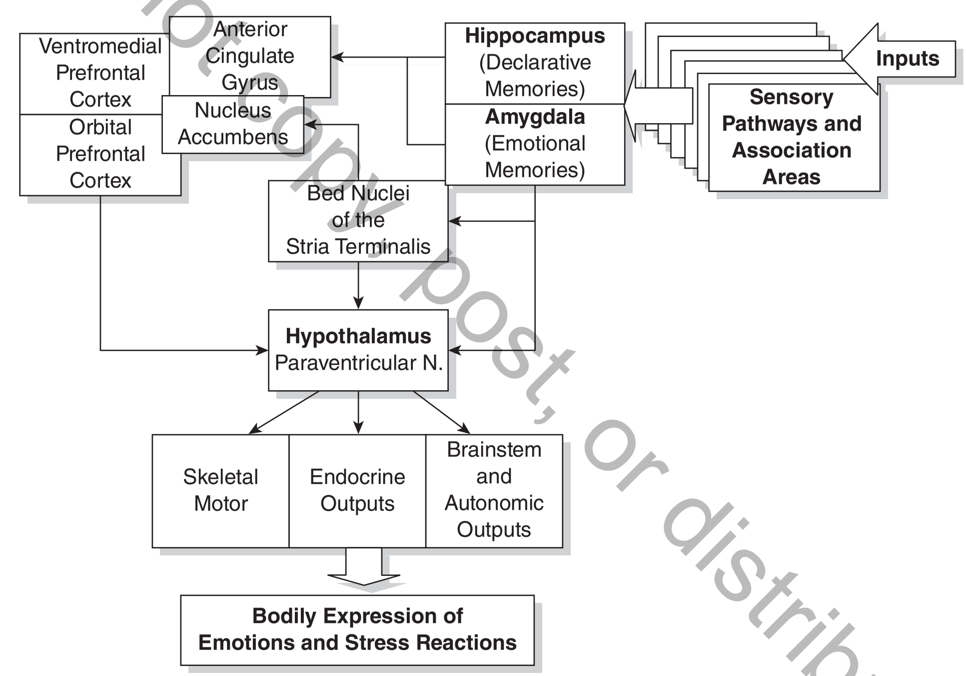
## Secondary Appraisals: How Well Did Our Coping Attempt Work?

The previous discussion indicates that when we perceive events, we have the decision-making capacity to know how we feel about them based on our beliefs and commitments. During secondary appraisals, we must be able to invest alternative coping strategies with both meaning and emotional content in order to choose the best alternative. In addition, we have to decide if the primary appraisal and the coping effort altered the threat value of the initial event. In the case of secondary appraisals, it seems reasonable that the same set of neural structures and cognitive-affective processes comes into play to evaluate the outcome of our initial coping efforts. In this manner, an encounter with a meaningful event becomes a recursive process of evaluation, behavioral choice and coping efforts, and reevaluation.

## Physiological Correlates of Primary and Secondary Appraisal Processes

Figure 5.7 illustrates the neural structures involved in processing sensory inputs, appraising them, forming emotions, deciding on coping strategies, and generating bodily outputs to support our behaviors.

**Figure 5.7** Neurophysiologically based model of the primary brain processes determining autonomic and endocrine responses to psychological stress.



The right part of the diagram indicates sensory information being processed through successively higher levels of association cortex and the convergence of information at the inferior temporal gyrus. Here information is passed to the parahippocampal gyrus on the medial surfaces of the temporal lobe. At this point, the highly processed inputs become available to both the hippocampus and the amygdala. We should note that these structures have parallel and complementary functions. The hippocampus is associated with the formation of declarative memories. Damage to, or surgical removal of, the hippocampus will impair or eliminate the ability of a person to form new memories of their daily experiences. Brenda Milner's reports on the famous patient, H. M., who had bilateral surgical removal of his hippocampal regions, dramatically illustrate the devastating impact of such a deficit (Milner & Penfield, 1955; Scoville & Milner, 1957). Even after years of living in a new neighborhood, H. M. was unable to develop a cognitive map of his surroundings and had to be accompanied on walks. Because he lacked the ability to form long-term memories, he was also unable to carry out plans of action in his life; instead, he lived constantly in the present.

## The Amygdala Performs a Parallel Memory Function

The amygdala, frequently seen as the center of emotional experience, is really a memory structure. It is essential to the formation of classically conditioned associations, and in relation to these associations, it is essential in forming appropriate motivational states (emotions) with regard to the external world and our feelings about that world. Recall that in classical conditioning, two types of sensory events come to be associated with each other. According to the usual example, Pavlov's dog was given numerous pairings of a sounding bell and placement of food into its mouth via a feeding tube. This involved, therefore, the pairing of a sound, an exteroceptive sensation (arriving from outside by way of our touch, smell, hearing, or vision) and an interoceptive sensation (arriving from the viscera, by way of the insular cortex). Finally, the dog learned to salivate in anticipation of the food when the bell sounded. We now know that the formation of such associations is impossible if the amygdala is destroyed (Davis & Whalen, 2001). Similarly, destruction of specific sets of neurons in the amygdala eliminates established fear memories in rats (Han et al., 2009). These findings show that the amygdala is essential for us to use and retain experiences that attach *motivational significance* to things we perceive.

Together, the hippocampus and the amygdala are essential to building up a normal store of familiar experiences and their motivational meanings. The hippocampus allows us to remember what happened, and the amygdala allows us to remember what it felt like the last time we had that experience.

## The Amygdala Triggers Warning Systems by Classifying Incoming Stimuli

Research using animal models has indicated the importance of the amygdala in generating appropriate responses to threatening situations. A special case of the appraisal process is when we encounter something we have never seen before. Much research shows that novel events are normally stressful. In Chapter 4, we noted that stress-related endocrine responses occur in primates exposed to novel events in the lab. Our own work has shown that humans brought into the lab for the first time have higher levels of cortisol than they do on future visits. However, animals that have had their amygdalae surgically removed do not hesitate to approach and explore unfamiliar or threatening objects. For example, young primates are afraid of snakes. Primates shown snake photographs have extremely rapid and robust responses in the pulvinar of the thalamus, an area with heavy visual input and the ability to direct visual attention (Van Le et al., 2013). But an amygdalectomized young monkey will approach a rubber snake and pick it up and try to eat it, something a normal monkey will not do. An amygdalectomized rat will climb on and explore a sedated cat. Human patients with no amygdalae due to disease usually have to be supervised to keep them out of danger.

The amygdala gives us the ability to shape emotional memories and to modify our responses based on experience. Without an amygdala, we are deprived of our ability to anticipate negative consequences of our behavior. A detailed discussion is provided by Davis (Davis, 2000). Since this book focuses on stress, it is easy to overlook the fact that the amygdala together with the hippocampus also serves to prime our responses to events that are positive in nature, as in Pavlov's dog salivating at the prospect of food.

## Outputs From the Amygdala and Hippocampus Provide Essential Information to the Prefrontal Cortex

Figure 5.7 also indicates a pair of pathways from the hippocampus and amygdala to the anterior cingulate gyrus. The functions of this part of the cingulate gyrus are complex, but one role for this region is in helping animals choose behavioral alternatives under motivational conditions. This is a function that is disturbed in patients with damage to the ventromedial prefrontal cortex. This relationship is consistent with the role of the hippocampus as registering contextual information and the amygdala as providing motivational value to specific cues, both pieces of information being important in making informed behavioral choices or selecting coping strategies.

A second set of connections in Figure 5.7 shows outputs from the amygdala to the bed nuclei of the stria terminalis (which are way stations from the amygdala) and then on to the nearby nucleus accumbens. These structures are located beneath the surface of the ventromedial prefrontal cortex, near where it is joined by the anterior cingulate gyrus (Figure 5.3d and Figure 5.4b). This appears to be a place where inputs have begun to obtain motivational significance and where they begin to give rise to conscious awareness of the relationships between contextual cues in light of the prevailing motivational context. We might also think of this as an area where the dialogue between experience and emotion is carried out. The diagram shows the areas representing the prefrontal cortex, nucleus accumbens, and anterior cingulate gyrus as overlapping. This is a visual shorthand indicating that the interconnections are extensive. Recalling the consequences for patients with damage to the ventromedial prefrontal cortex, we begin to understand more clearly why they make poor decisions and fail to adaptively guide their behavior; they are unable to put the cognitive information about an event together with how they feel about it.

### Frontal-Limbic Interactions and Appraisals

We might consider these frontal-limbic interactions as critical for both primary and secondary appraisals as outlined in Lazarus and Folkman's model of psychological stress. Primary appraisals involve recognizing whether something is dangerous. Secondary appraisals involve reviewing the available coping responses, evaluating a plan of action, and examining possible outcomes in view of their costs and benefits. The frontal-limbic connections specified in the model suggest that the psychological processes postulated by Folkman and Lazarus have reasonable neurophysiological candidates.



## Internal Sources of Amygdaloid Activity and Internally Generated Emotional Responses

We have discussed of psychological stressors as though they always begin as external events. But we all know from personal experience that some of the most consistent sources of psychological distress are our own thoughts and ruminations. Jay Schulkin, Bruce McEwen, and Phil Gold have described how we may agonize over future events or past actions and how distressing mental activity may generate the same frontal-limbic responses that would occur if we were confronting a genuine external threat (Schulkin, McEwen, & Gold, 1994). These recalled or imagined events are certainly able to engage the limbic system and the related bodily outputs. Understanding the frontal-limbic mechanisms underlying the generation of emotions helps us appreciate the very close association we have between our ability to evaluate the world and formulate coping strategies, and thus to shape our emotional experience.

## Initiation of Behavioral, Autonomic, and Neuroendocrine Responses to Psychological Stressors

The next steps in our model concern how our appraisals and associated emotions lead to changes in our peripheral physiology by way of autonomic and endocrine outputs. Considering the amygdala's position in the path of sensory input and its extensive connections to frontal areas and to the hypothalamus and brainstem, we may say that the amygdala is a focal point of transition from information arriving as sensory inputs to the addition of affective coloration and the formulation of our autonomic and endocrine responses. Figure 5.7 indicates that the hypothalamus receives inputs from the amygdala, the bed nuclei of the stria terminalis, and the orbital prefrontal cortex. The hypothalamus, as noted in Chapter 4, can shape all three components of emotional expression, motor functions such as posture and facial expression, endocrine outputs, and autonomic activity.

Chapter 6 discusses the endocrine outputs. The autonomic and motor outputs from the hypothalamus project to the pons and medulla, and these outputs incorporate two functional subsystems. The first is the *central feedback subsystem,* which includes the pontine reticular formation and its aminergic nuclei. The second subsystem is the *brainstem response subsystem, which* includes the descending pathways that arrive at the muscles and viscera of our bodies. They include the nucleus paragigantocellularis, the nucleus of the solitary tract, and the intermediolateral cell column.

## Feedback to the Cortex and Limbic System: The Central Feedback Subsystem

Once incoming information has been categorized and appraised and an initial response formulated, it may be important to *reset the state* of the central nervous system so that it may act in unison to meet a serious threat or to attain a highly desirable goal. This resetting is accomplished by a network of nuclei in the brainstem that we term the *central feedback subsystem*. These nuclei provide feedback to the rest of the central nervous system about its own activities and so the system sets the global behavioral state of the person. The central feedback subsystem consists of three *aminergic nuclei* that are the sources of nerve fibers releasing norepinephrine, dopamine, and serotonin. Depending on commands from the amygdala and hypothalamus, it can prepare us to meet an emergency if we need to respond to one, or it can put us to sleep if it is safe to do so. Its functions are not simply activational, however. This system's outputs to frontal-limbic areas determine our threshold for experiencing positive and negative affect in given situations. They also determine our longer term sense of well-being or dysphoria.

These nuclei are located in an area of the pons known as the reticular formation, first recognized for its importance in controlling sleep and waking in cats. The pontine reticular formation is a diffuse collection of fibers and specialized nuclei. It is phylogenetically very old, and in primitive species it connects sensory systems with systems allowing the formation of behavioral and physiological responses. It plays a similar role in humans, with considerably greater integration and control from higher centers, especially motor and decision-making systems controlled by the cortex.

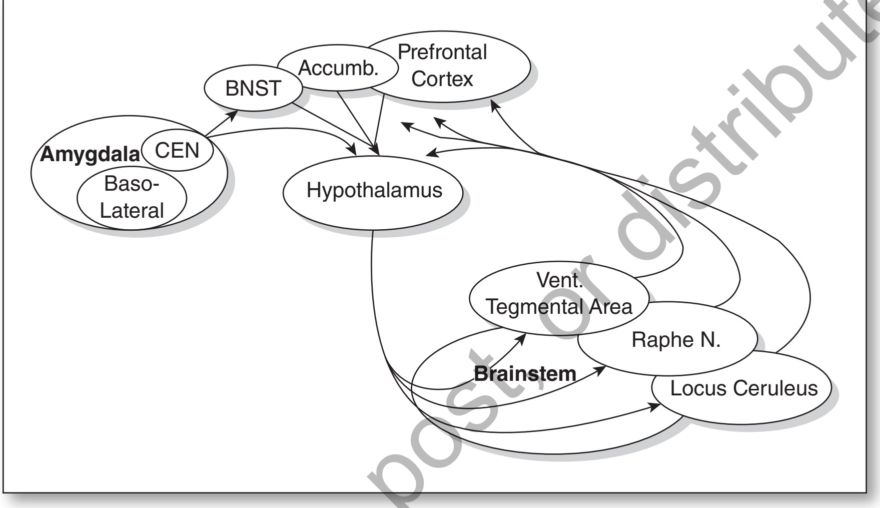
The aminergic nuclei contain cell bodies that synthesize the monoamine neurotransmitters: norepinephrine, serotonin, and dopamine. Figure 5.8 schematizes the inputs and outputs from these nuclei. In general, their inputs arise from frontal-limbic areas. In turn, these nuclei send fibers to all parts of the central nervous system to set our behavioral state. These small groupings of cell bodies are therefore extremely important in shaping the interplay of emotional experience, brain states, and autonomic and motor outflow. Each set of nuclei has a different role to play. The *locus ceruleus* contains norepinephrine cell bodies; the *raphe nuclei* have serotonin-producing neurons; and the *ventral tegmental area* has neurons that produce dopamine.

Each set of nuclei and their accompanying transmitter systems perform different, but complementary functions, as described in the following paragraphs.

## Locus Ceruleus

The locus ceruleus contains 90% of the norepinephrine-synthesizing cell bodies in the central nervous system, and these cell bodies send fibers to the

**Figure 5.8** The central feedback subsystem. The outputs from the central nucleus of the amygdala (CEN) to the bed nucleus of the stria terminalis (BNST) and nucleus accumbens (Accumb.) and descending pathways to and through the hypothalamus to the brainstem aminergic nuclei. The ascending projections are directed to all parts of the cerebral hemispheres, with especially heavy representation to hypothalamus and frontal-limbic areas.



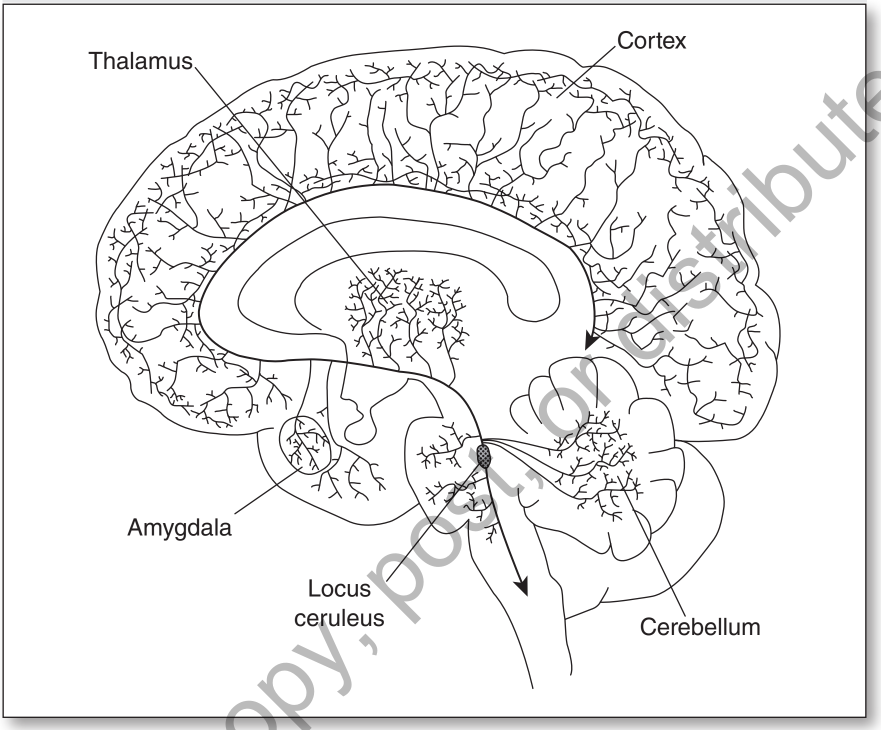



cortex, limbic structures, and spinal cord (Aston-Jones, Ennis, Pieribone, Nickell, & Shipley, 1986). The extent of the distribution of these nerve fibers is indicated in Figure 5.9. The norepinephrine fiber system functions most clearly as the brain's global arousal mechanism. The locus ceruleus is most active during aroused behavioral states, such as states of fight-or-flight, and it is nearly silent during deep stages of sleep. The locus ceruleus responds to signals of danger that can arise from the amygdala, and it responds to signals from the body indicating that a homeostatic need has arisen. The simplest example of this process is the sense of anxiety and attentional focus caused by a full bladder and a need to visit the restroom.

## Raphe Nuclei

The raphe nuclei have serotonin-containing fibers that ascend to frontal-limbic areas, including the amygdala, the hypothalamus, the anterior cingulate gyrus, and the orbital prefrontal cortex. It is noteworthy that affective balance and mood disorders are strongly associated with functioning of this

**Figure 5.9** Projections of noradrenergic fibers from the locus ceruleus to the rest of the central nervous system. Reprinted from "Volume Transmission in the Brain," by L. F. Agnati, B. Bjelke, & K. Fuxe, 1992, *American Scientist, 80,* pp. 362–373. Reprinted with permission.




system. Several major psychoactive medications, particularly the selective serotonin-reuptake-inhibiting antidepressants, act on the serotonin transmitter system. So we associate this system with long-term regulation of affect, and its dysregulation is associated with mood disorders.

## Ventral Tegmental Nuclei

The ventral tegmental area of the pons has a set of nuclei that are a major source of the brain's dopaminergic fibers. This fiber system is associated with motivation (attention to incoming stimuli, direction of motor behaviors toward goals, and avoidance of danger), cognitive processing (working memory), and the experience of reward (including the attraction to drugs of abuse). The attentional, motivational, and subjective effects of dopamine are determined by its release in the prefrontal cortex and the nucleus accumbens, sometimes referred to as the brain's reward center. Dopamine release at the nucleus accumbens is associated with euphoria during drug intake (Comings & Blum, 2000) and in response to playing a thrilling video game (Koepp et al., 1998). The dopaminergic system also affects our moods over the long term. For these reasons, the dopaminergic system is thought to generate the experience of pleasure associated with states of reward. Clearly it acts to influence how we process incoming information and shapes affective responses, especially positively hedonic aspects of our experience (Blum, Cull, Braverman, & Comings, 1996).

Since the aminergic nuclei receive abundant inputs from the amygdala, and because they feed back on frontal-limbic areas, we might expect them to be involved in our mood states. This is the case. For example, reduced norepinephrine in the locus ceruleus has been implicated in animal models of depression. Similarly, reduced function of the raphe nuclei, shown by low serotonin levels, is associated with defective social interactions and increased hostility and violent behavior (Brown, Goodwin, Ballenger, Goyer, & Major, 1986). Persons deficient in dopaminergic receptors are also characteristically more irritable than those with a greater receptor density.

Chapter 7 will focus more on the locus ceruleus and raphe nuclei, but we can see that the amygdala, acting directly on these nuclei, can alter the functional state of the central nervous system and organize responses appropriate to such negative moods.

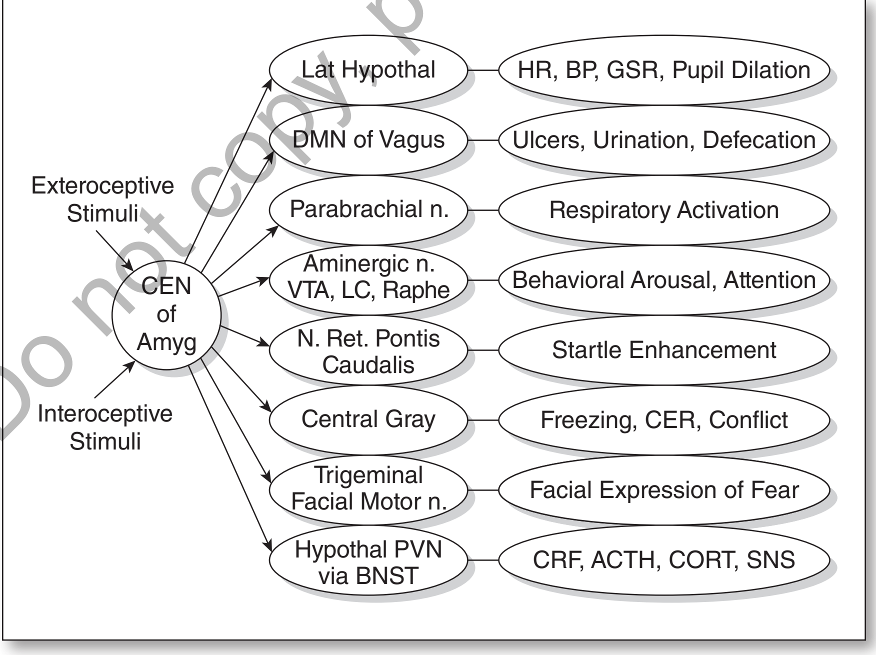
The central feedback subsystems associated with the brainstem aminergic nuclei therefore serve to coordinate the level of arousal and the affective tone and behavioral state of the entire central nervous system in response to the commands of the amygdala and of frontal-limbic processes. We can think of them as bringing the separate elements in the central nervous system into line, whether the situation calls for fight-or-flight, approach, avoidance, or sleep.

## Autonomic and Endocrine Outflow: The Emotional Response Subsystem

In accordance with the role of the hypothalamus and brainstem as way stations to the body, the outputs described above have extensive influence on a large number of peripheral response systems involved in stress responses and emotions. Figure 5.10 indicates the extensive role played by the amygdala in shaping bodily outputs associated with the emotions and states of stress. Michael Davis (Davis, 2000) has summarized a large number of anatomical and neurophysiological studies that show a central role for the amygdala in a wide range of bodily expressions of the emotions. The pathways from the central nucleus of the amygdala arrive directly or indirectly at two areas of the hypothalamus, the lateral hypothalamus and the paraventricular nucleus (PVN).

The lateral hypothalamus is a key area for sympathetic outflow to regions of the brainstem. The term HACER (the Hypothalamic Area Controlling Emotional Responses, pronounced ah-SEHR) was coined by Orville Smith (Smith, DeVito, & Astley, 1982) to capture the emotional role of this region of the hypothalamus. The HACER corresponds anatomically to the lateral portion of the hypothalamus in the area surrounding the fornix. This area affects heart rate, blood pressure, and pupillary

**Figure 5.10** Outputs from the central nucleus of the amygdala (CEN) to hypothalamus and brainstem with effects on peripheral physiology. HR = heart rate, BP = blood pressure, GSR = galvanic skin response, CER = conditioned emotional responses, CRF = corticotropin-releasing factor, ACTH = adrenocorticotropin, CORT = cortisol, and SNS = sympathetic nervous system. The role of the amygdala in unconditioned fear and anxiety. Davis in Aggleton, J.P./2000/The Amygdala, 2/e. Oxford University Press.



dilation, all components of the sympathetic part of the acute fight-or-flight response. Studies in rats and primates have shown that autonomic responses to aversive events, including threat of capture or electric shock, are absent when the areas corresponding to the HACER have been destroyed. However, the behavioral correlates of threat, such as muscular tensing and facial grimacing, are present, indicating that the animal is aware of the impending threat and is experiencing the event appropriately. What appears to be missing are links to physiological outputs to the periphery. In such animals, the usual cardiovascular changes associated with such threats are greatly diminished. The term HACER is used here in favor of more traditional anatomical designations because several hypothalamic nuclei are involved, and the collection does not correspond directly to a single anatomical designation.

Concerning other hypothalamic targets of the central nucleus of the amygdala, the PVN will be discussed in more detail in Chapter 6. Areas of the brainstem listed in Figure 5.10 that are affected by the central nucleus of the amygdala include areas regulating emotional *behaviors* such as freezing, *sympathetic responses* such as cardiovascular activation, and *parasympathetic* outputs to the visceral organs.

## Summary

In this chapter, we have considered how our perceptions of the world and our sense of our own ability to cope with challenges can become the basis for emotional states. Through a process of primary and secondary appraisals, we begin to formulate our physiological responses to psychologically challenging events. Chapter 4 described the layers of control we can use to maintain physiological homeostasis. We now see that we can use our higher cognitive functions, involving the prefrontal cortex, to evaluate external events in conjunction with goals and commitments. The outcome of the appraisal process can activate critical structures of the limbic system. These evaluative processes form the basis for emotions and also for the formulation of behavioral, autonomic, and endocrine responses to threatening events. We may therefore think of these psychological appraisal processes as exerting the highest level of control over our homeostatic functions. More generally, we may think of the appraisal process and its effects on stress responses as being central to our basic question of how ideas can come to have power over our bodies.

## FURTHER READING

Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus coeruleus-norepinephrine function: Adaptive gain and optimal performance. *Annual Review of Neuroscience, 28,* 403–450.

An integrated discussion of the locus ceruleus in arousal, attention, and integrated activity with the prefrontal cortex.

Lazarus, R. S. (1991). *Emotion and adaptation.* New York, NY: Oxford University Press.

Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal, and coping.* New York, NY: Springer.

There is a large literature on coping processes, psychological stress, and health. Lazarus and Folkman (1984) present a valuable, extended consideration of coping processes and psychological stress. Lazarus (1991) presents an extensive update of his views of emotion in relation to appraisals, coping processes, and adaptive behavior.

Smith, C. A., & Kirby, L. D. (2011). The role of appraisal and emotion in coping and adaptation. In R. J. Contrada & A. Baum (Eds.), *The handbook of stress science* (pp. 195–208). New York, NY: Springer.

An overview of appraisal and coping theories.

Carver, C. S. (2011). Coping. In R. J. Contrada & A. Baum (Eds.), *The handbook of stress science* (pp. 221–229). New York, NY: Springer.

A concise taxonomy of coping strategies in relation to stress.

Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science, 279,* 1347–1351.

Evidence that specific regions of the dorsolateral prefrontal cortex serve different kinds of working memory tasks. The paper notes that these areas are shifted more posteriorly in humans than in other primates. The authors speculate that the presence in humans of processes such as planning and intentionality may account for the anatomical reorientation of these functions.

Damasio, A. R. (1994). *Descartes' error: Emotion, reason, and the human brain.* New York, NY: G.P. Putnam's Sons.

This book on reason and emotion is a rich account of the clinical consequences of frontal lobe damage and the importance of prefrontal areas for evaluative processes.

Smith, O. A., & DeVito, J. L. (1984). Central neural integration for the control of autonomic responses associated with emotion. *Annual Review of Neurosciences, 7,* 43–65.

A well-written account of the organization of higher influences on autonomic outflow in relation to the emotions.

## DISCUSSION POINTS

1. What was the critical injury to Phineas Gage? How did this impair his ability to make decisions and form plans for his life?
2. What was the role of the hippocampus in the famous case of H. M., and how did his deficit prevent him from making long-term plans for his behavior?
3. Compare the memory functions served by the hippocampus and the amygdala.
4. Why would damage to the amygdala affect a person's ability to make choices?
5. What forms of information are integrated at the ventromedial prefrontal cortex, and how does this integration form the basis for appraisals and coping responses?