Biopsychology of Emotion, Stress, and Health

Fear, the Dark Side of Emotion

17.1 Biopsychology of Emotion: Introduction
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This chapter about the biopsychology of emotion, stress, and health begins with a historical introduction to the biopsychology of emotion and then focuses in the next two sections on the dark end of the emotional spectrum: fear. Biopsychological research on emotions has concentrated on fear not because biopsychologists are a scary bunch, but because fear has three important qualities: it is the easiest emotion to infer from behavior in various species; it plays an important adaptive function in motivating the avoidance of threatening situations; and chronic fear induces stress. In the final two sections of the chapter, you will learn how stress increases susceptibility to illness and how some brain structures have been implicated in human emotion.

### 17.1 Biopsychology of Emotion: Introduction

To introduce the biopsychology of emotion, this section reviews several classic early discoveries and then discusses the role of the autonomic nervous system in emotional experience and the facial expression of emotion.

#### Early Landmarks in the Biopsychological Investigation of Emotion

This subsection describes, in chronological sequence, six early landmarks in the biopsychological investigation of emotion. It begins with the 1848 case of Phineas Gage.

#### The Mind-Blowing Case of Phineas Gage

In 1848, Phineas Gage, a 25-year-old construction foreman for the Rutland and Burlington Railroad, was the victim of a tragic accident. In order to lay new tracks, the terrain had to be leveled, and Gage was in charge of the blasting.

His task involved drilling holes in the rock, pouring some gun powder into each hole, covering it with sand, and tamping the material down with a large tamping iron before detonating it with a fuse. On the fateful day, the gunpowder exploded while Gage was tamping it, launching the 3-cm-thick, 90-cm-long tamping iron through his face, skull, and brain and out the other side.

Amazingly, Gage survived his accident, but he survived it a changed man. Before the accident, Gage had been a responsible, intelligent, socially well-adapted person, who was well liked by his friends and fellow workers. Once recovered, he appeared to be as able-bodied and intellectually capable as before, but his personality and emotional life had totally changed. Formerly a religious, respectful, reliable man, Gage became irreverent and impulsive. In particular, his abundant profanity offended many. He became so unreliable and undependable that he soon lost his job, and was never again able to hold a responsible position.

Gage became itinerant, roaming the country for a dozen years until his death in San Francisco. His bizarre accident and apparently successful recovery made headlines around the world, but his death went largely unnoticed and unacknowledged.

Gage was buried next to the offending tamping iron. Five years later, neurologist John Harlow was granted permission from Gage’s family to exhume the body and tamping iron to study them. Since then, Gage’s skull and the tamping iron have been on display in the Warren Anatomical Medical Museum at Harvard University.

In 1994, Damasio and her colleagues brought the power of computerized reconstruction to bear on Gage’s classic case. They began by taking an X-ray of the skull and measuring it precisely, paying particular attention to the position of the entry and exit holes. From these measurements, they reconstructed the accident and determined the likely region of Gage’s brain damage (see Figure 17.1). It was apparent that the damage to Gage’s...
brain affected both medial prefrontal lobes, which we now know are involved in planning and emotion (see Machado & Bachevalier, 2006; Vogt, 2005).

**Darwin’s Theory of the Evolution of Emotion** The first major event in the study of the biopsychology of emotion was the publication in 1872 of Darwin’s book *The Expression of Emotions in Man and Animals*. In it, Darwin argued, largely on the basis of anecdotal evidence, that particular emotional responses, such as human facial expressions, tend to accompany the same emotional states in all members of a species.

Darwin believed that expressions of emotion, like other behaviors, are products of evolution; he therefore tried to understand them by comparing them in different species. From such interspecies comparisons, Darwin developed a theory of the evolution of emotional expression that was composed of three main ideas:

- Expressions of emotion evolve from behaviors that indicate what an animal is likely to do next.
- If the signals provided by such behaviors benefit the animal that displays them, they will evolve in ways that enhance their communicative function, and their original function may be lost.
- Opposite messages are often signaled by opposite movements and postures, an idea called the principle of antithesis.

Consider how Darwin’s theory accounts for the evolution of threat displays. Originally, facing one’s enemies, rising up, and exposing one’s weapons were the components of the early stages of combat. But once enemies began to recognize these behaviors as signals of impending aggression, a survival advantage accrued to attackers that could communicate their aggression most effectively and intimidate their victims without actually fighting. As a result, elaborate threat displays evolved, and actual combat declined.

To be most effective, signals of aggression and submission must be clearly distinguishable; thus, they tended to evolve in opposite directions. For example, gulls signal aggression by pointing their beaks at one another and submission by pointing their beaks away from one another; primates signal aggression by staring and submission by averting their gaze. Figure 17.2 reproduces the woodcuts Darwin used in his 1872 book to illustrate this principle of antithesis in dogs.

**James-Lange and Cannon-Bard Theories** The first physiological theory of emotion was proposed independently by James and Lange in 1884. According to the James-Lange theory, emotion-inducing sensory stimuli are received and interpreted by the cortex, which triggers changes in the visceral organs via the autonomic nervous system and in the skeletal muscles via the somatic nervous system. Then, the autonomic and somatic responses trigger the experience of emotion in the brain. In effect, what the James-Lange theory did was to reverse the usual common-sense way of thinking about the causal relation between the experience of emotion and its expression. James and Lange argued that the autonomic activity and behavior that are triggered by the emotional event (e.g., rapid heartbeat and running away) produce the feeling of emotion, not vice versa.

Around 1915, Cannon proposed an alternative to the James-Lange theory of emotion, and it was subsequently extended and promoted by Bard. According to the Cannon-Bard theory, emotional stimuli have two independent excitatory effects: They excite both the feeling of emotion in the brain and the expression of emotion in the autonomic and somatic nervous systems. That is, the Cannon-Bard theory, in contrast to the James-Lange theory, views emotional experience and emotional expression as parallel processes that have no direct causal relation.
The James-Lange and Cannon-Bard theories make different predictions about the role of feedback from autonomic and somatic nervous system activity in emotional experience. According to the James-Lange theory, emotional experience depends entirely on feedback from autonomic and somatic nervous system activity; according to the Cannon-Bard theory, emotional experience is totally independent of such feedback. Both extreme positions have proved to be incorrect. On the one hand, it seems that the autonomic and somatic feedback is not necessary for the experience of emotion: Human patients whose autonomic and somatic feedback has been largely eliminated by a broken neck are capable of a full range of emotional experiences (e.g., Lowe & Carroll, 1985). On the other hand, there have been numerous reports—some of which you will soon encounter—that autonomic and somatic responses to emotional stimuli can influence emotional experience.

Failure to find unqualified support for either the James-Lange or the Cannon-Bard theory led to the modern biopsychological view. According to this view, each of the three principal factors in an emotional response—the perception of the emotion-inducing stimulus, the autonomic and somatic responses to the stimulus, and the experience of the emotion—can influence the other two (see Figure 17.3).

**Sham Rage** In the late 1920s, Bard (1929) discovered that decorticate cats—cats whose cortex has been removed—respond aggressively to the slightest provocation: After a light touch, they arch their backs, erect their hair, growl, hiss, and expose their teeth.

The aggressive responses of decorticate animals are abnormal in two respects: They are inappropriately severe, and they are not directed at particular targets. Bard referred to the exaggerated, poorly directed aggressive responses of decorticate animals as *sham rage*.
Sham rage can be elicited in cats whose cerebral hemispheres have been removed down to, but not including, the hypothalamus; but it cannot be elicited if the hypothalamus is also removed. On the basis of this observation, Bard concluded that the hypothalamus is critical for the expression of aggressive responses and that the function of the cortex is to inhibit and direct these responses.

**Limbic System and Emotion** In 1937, Papez (pronounced “Payps”) proposed that emotional expression is controlled by several interconnected nuclei and tracts that ring the thalamus. Figure 17.4 illustrates some of the key structures in this circuit, now known as the **limbic system** (*limbic* means “border”): the amygdala, mammillary body, hippocampus, fornix, cortex of the cingulate gyrus, septum, olfactory bulb, and hypothalamus. Papez proposed that emotional states are expressed through the action of the other structures of the circuit on the hypothalamus and that they are experienced through their action on the cortex. Papez’s theory of emotion was revised and expanded by Paul MacLean in 1952 and became the influential **limbic system theory of emotion**.

**Kluver-Bucy Syndrome** In 1939, Kluver and Bucy observed a striking syndrome (pattern of behavior) in monkeys whose anterior temporal lobes had been removed. This syndrome, which is commonly referred to as the **Kluver-Bucy syndrome**, includes the following behaviors: the consumption of almost anything that is edible, increased sexual activity often directed at inappropriate objects, a tendency to repeatedly investigate familiar objects, a tendency to investigate objects with the mouth, and a lack of fear. Monkeys that could not be handled before surgery were transformed by bilateral anterior temporal lobectomy into tame subjects that showed no fear whatsoever—even in response to snakes, which terrify normal monkeys. In primates, most of the symptoms of the Kluver-Bucy syndrome appear to result from damage to the **amygdala** (see Phelps, 2006), a structure that has played a major role in research on emotion, as you will learn later in this chapter.

The Kluver-Bucy syndrome has been observed in several species. Following is a description of the syndrome in a human patient with a brain infection.

**A Human Case of Kluver-Bucy Syndrome**

He exhibited a flat affect, and although originally restless, ultimately became remarkably placid. He appeared indifferent to people or situations. He spent much time gazing at the television, but never learned to turn it on; when the set was off, he tended to watch reflections of others in the room on the glass screen. On occasion he became facetious, smiling inappropriately and mimicking the gestures and actions of others. Once initiating an imitative series, he would perseverate copying all movements made by another for extended periods of time. . . . He engaged in oral exploration of all objects within his grasp, appearing unable to gain information via tactile or visual means alone. All objects that he could lift were placed in his mouth and sucked or chewed. . . .

Although vigorously heterosexual prior to his illness, he was observed in hospital to make advances toward other male patients. . . . [H]e never made advances toward women, and, in fact, his apparent reversal of sexual polarity prompted his fiancée to sever their relationship. (Marlowe, Mancall, & Thomas, 1985, pp. 55–56)

The six early landmarks in the study of brain mechanisms of emotion just reviewed are listed in Table 17.1.

**Emotions and the Autonomic Nervous System**

Research on the role of the autonomic nervous system (ANS) in emotion has focused on two issues: the degree to which specific patterns of ANS activity are associated with specific emotions and the effectiveness of ANS measures in polygraphy (lie detection).

**Emotional Specificity of the Autonomic Nervous System**

The James-Lange and Cannon-Bard theories differ in their views of the emotional specificity of the autonomic nervous system. The James-Lange theory says...
that different emotional stimuli induce different patterns of ANS activity and that these different patterns produce different emotional experiences. In contrast, the Cannon-Bard theory claims that all emotional stimuli produce the same general pattern of sympathetic activation, which prepares the organism for action (i.e., increased heart rate, increased blood pressure, pupil dilation, increased flow of blood to the muscles, increased respiration, and increased release of epinephrine and norepinephrine from the adrenal medulla).

The experimental evidence suggests that the specificity of ANS reactions lies somewhere between the extremes of total specificity and total generality (Levenson, 1994). There is ample evidence that not all emotions are associated with the same pattern of ANS activity (see Ax, 1955); however, there is insufficient evidence to make a strong case for the view that each emotion is characterized by a different pattern of ANS activity.

**Polygraphy**

Polygraphy is a method of interrogation that employs autonomic nervous system indexes of emotion to infer the truthfulness of the subject’s responses. Polygraph tests administered by skilled examiners can be useful additions to normal interrogation procedures, but they are far from infallible.

The main problem in evaluating the effectiveness of polygraphy is that it is rarely possible in real-life situations to know for certain whether a suspect is guilty or innocent. Consequently, many studies of polygraphy have employed the mock-criminal procedure: Volunteer subjects participate in a mock crime and are then subjected to a polygraph test by an examiner who is unaware of their “guilt” or “innocence.” The usual interrogation method is the control-question technique, in which the physiological response to the target question (e.g., “Did you steal that purse?”) is compared with the physiological responses to control questions whose answers are known (e.g., “Have you ever been in jail before?”). The assumption is that lying will be associated with greater sympathetic activation. The average success rate in various mock-crime studies using the control-question technique is about 80%.

Despite being commonly referred to as lie detection, polygraphy detects emotions, not lies. Consequently, it is less likely to successfully identify lies in real life than in experiments. In real-life situations, questions such as “Did you steal that purse?” are likely to elicit a reaction from all suspects, regardless of their guilt or innocence, making it difficult to detect deception. The guilty-knowledge technique circumvents this problem. In order to use this technique, the polygrapher must have a piece of information concerning the crime that would be known only to the guilty person. Rather than attempting to catch the suspect in a lie, the polygrapher simply assesses the suspect’s reaction to a list of actual and contrived details of the crime. Innocent suspects, because they have no knowledge of the crime, react to all such details in the same way; the guilty react differentially.

In the classic study of the guilty-knowledge technique (Lykken, 1959), subjects waited until the occupant of an office went to the washroom. Then, they entered her office, stole her purse from her desk, removed the money, and left the purse in a locker. The critical part of the interrogation went something like this: “Where do you think we found the purse? In the washroom? . . . In a locker? . . . Hanging on a coat rack? . . .” Even though electrodermal activity was the only measure of ANS activity used in this study, 88% of the mock criminals were correctly identified; more importantly, none of the innocent subjects was judged guilty—see MacLaren (2001) for a review.

**Emotions and Facial Expression**

Ekman and his colleagues have been preeminent in the study of facial expression (see Ekman, 2003). They began in the 1960s by analyzing hundreds of films and photographs of people experiencing various real emotions. From these, they compiled an atlas of the facial expressions that are normally associated with different emotions (Ekman & Friesen, 1975). For example, to produce the facial expression for surprise, models were instructed to pull their brows upward so as to wrinkle their forehead, to open their eyes wide so as to reveal white above the iris, to slacken the muscles around their mouth, and to drop their jaw. Try it.

**Universality of Facial Expression**

Several studies have found that people of different cultures make similar facial expressions in similar situations and that they can correctly identify the emotional significance of facial expressions displayed by people from cultures other than their own. The most convincing of these studies was a study of the members of an isolated New Guinea tribe who had had little or no contact with the outside world (Ekman & Friesen, 1971). However, some studies have identified some subtle cultural differences in facial expressions (see Russell, Bacherowski, & Fernandez-Dols, 2003). Remarkably, human facial expressions are similar.
in many respects to those of our primate relatives (see Parr, Waller, & Fugate, 2005; Parr, Waller, & Vick, 2007).

**Primary Facial Expressions** Ekman and Friesen concluded that the facial expressions of the following six emotions are primary: surprise, anger, sadness, disgust, fear, and happiness (however, see Tracy & Robins, 2004). They further concluded that all other facial expressions of genuine emotion are composed of predictable mixtures of these six primaries. Figure 17.5 illustrates these six primary facial expressions and the combination of two of them to form a nonprimary expression.

**Facial Feedback Hypothesis** Is there any truth to the old idea that putting on a happy face can make you feel better? Research suggests that there is (see Adelmann & Zajonc, 1989). The hypothesis that our facial expressions influence our emotional experience is called the facial feedback hypothesis. In a test of the facial feedback hypothesis, Rutledge and Hupka (1985) instructed subjects to assume one of two patterns of facial contractions while they viewed a series of slides; the patterns corresponded to happy or angry faces, although the subjects were unaware of that. The subjects reported that the slides made them feel more happy and less angry when they were making happy faces, and less happy and more angry when they were making angry faces (see Figure 17.6).

**Voluntary Control of Facial Expression** Because we can exert voluntary control over our facial muscles, it is possible to inhibit true facial expressions and to substitute false ones. There are many reasons for choosing to put on a false facial expression. Some of them are positive (e.g., putting on a false smile to reassure a worried friend), and some are negative (e.g., putting on a false smile to disguise a lie). In either case, it is difficult to fool an expert.

There are two ways of distinguishing true expressions from false ones (Ekman, 1985). First, microexpressions (brief facial expressions) of the real emotion often break through the false one (Porter & ten Brinke, 2008). Such microexpressions last only about 0.05 second, but with practice they can be detected without the aid of slow-motion photography. Second, there are often subtle differences between genuine facial expressions and false ones that can be detected by skilled observers.

The most widely studied difference between a genuine and a false facial expression was first described by the French anatomist Duchenne in 1862. Duchenne said that the smile of enjoyment could be distinguished from...
deliberately produced smiles by consideration of the two facial muscles that are contracted during genuine smiles: orbicularis oculi, which encircles the eye and pulls the skin from the cheeks and forehead toward the eyeball, and zygomaticus major, which pulls the lip corners up (see Figure 17.7). According to Duchenne, the zygomaticus major can be controlled voluntarily, whereas the orbicularis oculi is normally contracted only by genuine pleasure. Thus, inertia of the orbicularis oculi in smiling unmask a false friend—a fact you would do well to remember. Ekman named the genuine smile the Duchenne smile (see Ekman & Davidson, 1993).

**Facial Expressions: Current Perspectives** Ekman’s work on facial expression began before video recording became commonplace. Now, video recordings provide almost unlimited access to natural facial expressions made in response to real-life situations. As a result, it is now clear that Ekman’s six primary facial expressions of emotion rarely occur in pure form—they are ideals with many subtle variations. Also, the existence of other primary emotions has been recognized. For example, Ekman (1992) agrees that there is evidence for adding contempt and embarrassment to his original six.

Have you noticed that only one of the eight primary emotions, happiness, has a positive emotional valence? (Emotional valence refers to the general positive or negative character of an emotion.) This imbalance has led some to hypothesize that all positive emotions may share the same facial expression. The research on pride by Tracy

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**Check It Out**

**Experiencing Facial Feedback**

Why don’t you try the facial feedback hypothesis? Pull your eyebrows down and together; raise your upper eyelids and tighten your lower eyelids, and narrow your lips and press them together. Now, hold this expression for a few seconds. If it makes you feel slightly angry and uncomfortable, you have just experienced the effect of facial feedback.
and Robins (2004, 2007a, 2007b) argues against this view. The expression of pride is readily identified by individuals of various cultures, cannot be created from a mixture of other primary expressions, and involves postural as well as facial components (Tracy & Robins, 2007a). Pride is expressed through a small smile, with the head tilted back slightly and the hands on the hips, raised above the head, or clenched in fists with the arms crossed on the chest—see Figure 17.8.

**Types of Aggressive and Defensive Behaviors**

Considerable progress in the understanding of aggressive and defensive behaviors has come from the research of Blanchard and Blanchard (see 1989, 1990) on the colony-intruder model of aggression and defense in rats. Blanchard and Blanchard have derived rich descriptions of rat intraspecific aggressive and defensive behaviors by studying the interactions between the alpha male—the dominant male—of an established mixed-sex colony and a small male intruder:

The alpha male usually bites the intruder [on the back], and the intruder runs away. The alpha chases after it, and after one or two additional [back] bites, the intruder stops running and turns to face its attacker. It rears up on its hind legs, using its forelimbs to push off the alpha. . . . However, rather than standing nose to nose with the “boxing” intruder, the attacking rat abruptly moves to a lateral orientation, with the long axis of its body perpendicular to the front of the defending rat. . . . It moves sideways toward the intruder, crowding and sometimes pushing it off balance. If the defending rat stands solid against this “lateral attack” movement, the alpha may make a quick lunge forward and around the defender’s body to bite at its back. In response to such a lunge, the defender usually pivots on its hind feet, in the same direction as the attacker is moving, continuing its frontal orientation to the attacker. If the defending rat moves quickly enough, no bite will be made. (From “Affect and Aggression: An Animal Model Applied to Human Behavior,” by D. C. Blanchard and R. J. Blanchard, in Advances in the Study of Aggression, Vol. 1, 1984, edited by D. C. Blanchard and R. J. Blanchard. San Diego: Academic Press. Copyright 1984 by Academic Press. Reprinted by permission.)

Another excellent illustration of how careful observation of behavior has led to improved understanding of aggressive and defensive behaviors is provided by the study of Pellis and colleagues (1988) of cats. They began by videotaping interactions between cats and mice. They found that different cats reacted to mice in different ways: Some were efficient mouse killers, some reacted defensively, and some seemed to play with the mice. Careful analysis
of the “play” sequences led to two important conclusions. The first conclusion was that, in contrast to the common belief, cats do not play with their prey; the cats that appeared to be playing with the mice were simply vacillating between attack and defense. The second conclusion was that one can best understand each cat’s interactions with mice by locating the interactions on a linear scale, with total aggressiveness at one end, total defensiveness at the other, and various proportions of the two in between.

Pellis and colleagues tested their conclusions by reducing the defensiveness of the cats with an antianxiety drug. As predicted, the drug moved each cat along the scale toward more efficient killing. Cats that avoided mice before the injection “played with” them after the injection, those that “played with” them before the injection killed them after the injection, and those that killed them before the injection killed them more quickly after the injection.

Based on the numerous detailed descriptions of rat aggressive and defensive behaviors provided by the Blanchards and other biopsychologists who have followed their example, most researchers now distinguish among different categories of such behaviors. These categories of rat aggressive and defensive behaviors are based on three criteria: (1) their topography (form), (2) the situations that elicit them, and (3) their apparent function. Several of these categories are described in Table 17.2 (see also Blanchard et al., 2001; Dielenberg & McGregor, 2001; Kavaliers & Choleris, 2001).

The analysis of aggressive and defensive behaviors has led to the development of the target-site concept—the idea that the aggressive and defensive behaviors of an animal are often designed to attack specific sites on the body of another animal while protecting specific sites on its own. For example, the behavior of a socially aggressive rat (e.g., lateral attack) appears to be designed to deliver bites to the defending rat’s back and to protect its own face, the likely target of a defensive attack. Conversely, most of the maneuvers of the defending rat (e.g., boxing and pivoting) appear to be designed to protect the target site on its back.

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<th>TABLE 17.2 Categories of Aggressive and Defensive Behaviors in Rats</th>
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The discovery that aggressive and defensive behaviors occur in a variety of stereotypical species—common forms was the necessary first step in the identification of their neural bases. Because the different categories of aggressive and defensive behaviors are mediated by different neural circuits, little progress was made in identifying these circuits before the categories were delineated. For example, the lateral septum was once believed to inhibit all aggression, because lateral septal lesions rendered laboratory rats notoriously difficult to handle—the behavior of the lesioned rats was commonly referred to as septal aggression or septal rage. However, we now know that lateral septal lesions do not increase aggression: Rats with lateral septal lesions do not initiate attacks at an experimenter unless they are threatened.

**Aggression and Testosterone**

The fact that social aggression in many species occurs more commonly among males than among females is usually explained with reference to the organizational and activational effects of testosterone. The brief period of testosterone release that occurs around birth in genetic males is thought to organize their nervous systems along masculine lines and hence to create the potential for male patterns of social aggression to be activated by the high testosterone levels that are present after puberty. These organizational and activational effects have been demonstrated in some mammalian species. For example, neonatal castration of male mice eliminates the ability of testosterone injections to induce social aggression in adulthood, and adult castration eliminates social aggression in males that do not receive testosterone replacement injections. Unfortunately, research on testosterone and aggression in other species has not been so straightforward (see Wingfield, 2005).

Soma and his colleagues have reviewed the extensive comparative research literature on testosterone and aggression (Demas et al., 2005; Soma, 2006). Here are their major conclusions:

- Testosterone increases social aggression in the males of many species; aggression is largely abolished by castration in these same species.
- In some species, castration has no effect on social aggression; in still others, castration reduces aggression during the breeding season but not at other times.
- The relation between aggression and testosterone levels is difficult to interpret because engaging in aggressive activity can itself increase testosterone levels—for example, just playing with a gun increased the testosterone levels of male college students (Klinesmith, Kasser, & McAndrew, 2006).
- The blood level of testosterone, which is the only measure used in many studies, is not the best measure.

What matters more are the testosterone levels in the relevant areas of the brain. Although studies focusing on brain levels of testosterone are rare, it has been shown that testosterone can be synthesized in particular brain sites and not in others.

It is unlikely that humans are an exception to the usual involvement of testosterone in mammalian social aggression. However, the evidence is far from clear. In human males, aggressive behavior does not increase at puberty as testosterone levels in the blood increase; aggressive behavior is not eliminated by castration; and it is not increased by testosterone injections that elevate blood levels of testosterone. A few studies have found that violent male criminals and aggressive male athletes tend to have higher testosterone levels than normal (see Bernhardt, 1997); however, this correlation may indicate that aggressive encounters increase testosterone, rather than vice versa.

The lack of strong evidence of the involvement of testosterone in human aggression could mean that hormonal and neural regulation of aggression in humans differs from that in many other mammalian species.

Thinking Creatively

Most aggressive outbursts in humans are overreactions to real or perceived threat, and thus they are more appropriately viewed as defensive attack, not social aggression.

**17.3 Neural Mechanisms of Fear Conditioning**

Much of what we know about the neural mechanisms of fear has come from the study of fear conditioning (Olsson & Phelps, 2007). **Fear conditioning** is the establishment of fear in response to a previously neutral stimulus (the *conditional stimulus*) by presenting it, usually several times, before the delivery of an aversive stimulus (the *unconditional stimulus*).

In the usual fear-conditioning experiment, the subject, often a rat, hears a tone (conditional stimulus) and then receives a mild electric shock to its feet (unconditional stimulus). After several pairings of the tone and the shock, the rat responds to the tone with a variety of defensive behaviors (e.g., freezing and increased susceptibility to startle) and sympathetic nervous system responses (e.g., increased heart rate and blood pressure). LeDoux and his colleagues have mapped the neural mechanism
that mediates this form of auditory fear conditioning (see Schafe & LeDoux, 2004).

**Amygdala and Fear Conditioning**

LeDoux and his colleagues began their search for the neural mechanisms of auditory fear conditioning by making lesions in the auditory pathways of rats. They found that bilateral lesions to the **medial geniculate nucleus** (the auditory relay nucleus of the thalamus) blocked fear conditioning to a tone, but bilateral lesions to the auditory cortex did not. This indicated that for auditory fear conditioning to occur, it is necessary for signals elicited by the tone to reach the medial geniculate nucleus but not the auditory cortex. It also indicated that a pathway from the medial geniculate nucleus to a structure other than the auditory cortex plays a key role in fear conditioning. This pathway proved to be the pathway from the medial geniculate nucleus to the amygdala. Lesions of the amygdala, like lesions of the medial geniculate nucleus, blocked fear conditioning. The amygdala receives input from all sensory systems, and it is believed to be the structure in which the emotional significance of sensory signals is learned and retained.

Several pathways (see Balleine & Killcross, 2006; LaBar, 2007) carry signals from the amygdala to brain-stem structures that control the various emotional responses. For example, a pathway to the periaqueductal gray of the midbrain elicits appropriate defensive responses (see Bandler & Shipley, 1994), whereas another pathway to the lateral hypothalamus elicits appropriate sympathetic responses.

The fact that auditory cortex lesions do not disrupt fear conditioning to simple tones does not mean that the auditory cortex is not involved in auditory fear conditioning. There are two pathways from the medial geniculate nucleus to the amygdala: the direct one, which you have already learned about, and an indirect one that projects via the auditory cortex (Romanski & LeDoux, 1992). Both routes are capable of mediating fear conditioning to simple sounds; if only one is destroyed, conditioning progresses normally. However, only the cortical route is capable of mediating fear conditioning to complex sounds (Jarrell et al., 1987).

**Contextual Fear Conditioning and the Hippocampus**

Environments, or **contexts**, in which fear-inducing stimuli are encountered can themselves come to elicit fear. For example, if you repeatedly encountered a bear on a particular trail in the forest, the trail itself would elicit fear in you. The process by which benign contexts come to elicit fear through their association with fear-inducing stimuli is called **contextual fear conditioning**.

Contextual fear conditioning has been produced in the laboratory in two ways. First, it has been produced by the conventional fear-conditioning procedure, which we just discussed. For example, if a rat repeatedly receives an electric shock following a conditional stimulus, such as a tone, the rat will become fearful of the conditional context (the test chamber) as well as the tone. Second, contextual fear conditioning has been produced by delivering aversive stimuli in a

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**Figure 17.9** The structures that are thought to mediate the sympathetic and behavioral responses conditioned to an auditory conditional stimulus.
particular context in the absence of any other conditional stimulus. For example, if a rat receives shocks in a distinctive test chamber, the rat will become fearful of that chamber.

In view of the fact that the hippocampus plays a key role in memory for spatial location, it is reasonable to expect that it would be involved in contextual fear conditioning. This seems to be the case (see Antoniadis & McDonald, 2000). Bilateral hippocampal lesions block the subsequent development of a fear response to the context without blocking the development of a fear response to the explicit conditional stimulus (e.g., a tone).

Amygdala Complex and Fear Conditioning

The preceding discussion has probably left you with the impression that the amygdala is a single brain structure; it isn’t. It is actually a cluster of many nuclei, often referred to as the amygdala complex. The amygdala is composed of a dozen or so major nuclei, which are themselves divided into subnuclei. Each of these subnuclei is structurally distinct, has different connections (see LeDoux, 2000b), and is thus likely to have different functions.

The study of fear conditioning provides a compelling demonstration of the inadvisability of assuming that the amygdala is a single structure. Evidence has been accumulating that it is actually the lateral nucleus of the amygdala—not the entire amygdala—that is critically involved in the acquisition, storage, and expression of conditioned fear (see Kim & Jung, 2006; Maren & Quirk, 2004). Both the prefrontal cortex and the hippocampus project to the lateral nucleus of the amygdala: The prefrontal cortex is thought to act on the lateral nucleus of the amygdala to suppress conditioned fear, and the hippocampus is thought to interact with that part of the amygdala to mediate learning about the context of fear-related events.

When the body is exposed to harm or threat, the result is a cluster of physiological changes that is generally referred to as the stress response—or just stress. All stressors (experiences that induce the stress response) produce the same core pattern of physiological changes, whether psychological (e.g., dismay at the loss of one’s job) or physical (e.g., long-term exposure to cold). However, it is chronic psychological stress that has been most frequently implicated in ill health (see Kiecolt-Glaser et al., 2002; Natelson, 2004), which is the focus of this section.

The Stress Response

Hans Selye (pronounced “SELL-yay”) first described the stress response in the 1950s, and he emphasized its dual nature. In the short term, it produces adaptive changes...
that help the animal respond to the stressor (e.g., mobilization of energy resources); in the long term, however, it produces changes that are maladaptive (e.g., enlarged adrenal glands)—see de Kloet, Joëls, and Holsboer (2005).

Selye attributed the stress response to the activation of the anterior-pituitary adrenal-cortex system. He concluded that stressors acting on neural circuits stimulate the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary, that the ACTH in turn triggers the release of glucocorticoids from the adrenal cortex, and that the glucocorticoids produce many of the components of the stress response (see Erickson, Drevets, & Schulkin, 2003; Schulkin, Morgan, & Rosen, 2005). The level of circulating glucocorticoids is the most commonly employed physiological measure of stress.

Selye largely ignored the contributions of the sympathetic nervous system to the stress response. However, stressors activate the sympathetic nervous system, thereby increasing the amounts of epinephrine and norepinephrine released from the adrenal medulla. Most modern theories of stress acknowledge the roles of both the anterior-pituitary adrenal-cortex system and the sympathetic-nervous-system adrenal-medulla system (see Gunnar & Quevedo, 2007; Ulrich-Lai & Herman, 2009). Figure 17.10 illustrates the two-system view.

The major feature of Selye’s landmark theory is its assertion that both physical and psychological stressors induce the same general stress response. This assertion has proven to be partly correct. There is good evidence that all kinds of common psychological stressors—such as losing a job, taking a final exam, or ending a relationship—act like physical stressors. However, Selye’s contention that there is only one stress response has proven to be a gross simplification. Stress responses are complex and varied, with the exact response depending on the stressor, its timing, the nature of the stressed person, and how the stressed person reacts to the stressor (e.g., Joëls & Baram, 2009; Miller, Chen, & Zhou, 2007; Smith, 2006). For example, in a study of women awaiting surgery for possible breast cancer, the levels of stress were lower in those who had convinced themselves that they could not possibly have cancer, that their prayers were certain to be answered, or that it was counterproductive to worry (Katz et al., 1970).

In the 1990s, there was an important advance in the understanding of the stress response (see Fleschner & Laudenslager, 2004). It was discovered that brief stressors produce physiological reactions that participate in the body’s inflammatory responses. Most notably, it was found that brief stressors produced an increase in blood levels of cytokines, a group of peptide hormones that are released by many cells and participate in a variety of physiological and immunological responses, causing inflammation and fever. The cytokines are now classified with the adrenal hormones as major stress hormones.

**Animal Models of Stress**

Most of the early research on stress was conducted with nonhumans, and even today most lines of stress research begin with controlled experiments involving nonhumans before moving to correlational studies of humans. Early stress research on nonhumans tended to involve extreme forms of stress such as repeated exposure to electric shock or long periods of physical restraint. There are two problems with this kind of research. First is the problem of ethics. Any research that involves creating stressful situations is going to be controversial, but many of the early stress studies were “over the top” and would not be permitted today in many countries. The second problem is that studies that use extreme, unnatural forms of stress are often of questionable scientific value. Responses to extreme stress tend to mask normal variations in the stress response, and it is difficult to relate the results of such studies to common human stressors (see Fleschner & Laudenslager, 2004; Koolhass, de Boer, & Buwalda, 2006).
Some animal models of stress involve the study of threat from conspecifics (members of the same species). Virtually all mammals—particularly males—experience threats from conspecifics at certain points in their lives. When conspecific threat becomes an enduring feature of daily life, the result is subordination stress (see Berton et al., 2006; Sapolsky, 2005). Subordination stress is most readily studied in social species that form stable dominance hierarchies (pecking orders; see Chapter 2). What do you think happens to subordinate male rodents who are continually attacked by more dominant males? They are more likely to attack juveniles, and they have small testes, shorter life spans, lower blood levels of testosterone, and higher blood levels of glucocorticoids.

### Psychosomatic Disorders: The Case of Gastric Ulcers

Interest in pathological effects of stress has increased as researchers have identified more and more psychosomatic disorders (medical disorders that have psychological causes). So many adverse effects of stress on health (e.g., in heart disease, asthma, and skin disorders) have been documented that it is now more reasonable to think of most, if not all, medical disorders as psychosomatic (Miller & Blackwell, 2006; Wargo, 2007).

Gastric ulcers were one of the first medical disorders to be classified as psychosomatic. Gastric ulcers are painful lesions to the lining of the stomach and duodenum, which in extreme cases can be life-threatening. About 500,000 new cases are reported each year in the United States.

The view of gastric ulcers as the prototypical psychosomatic disorder changed with the discovery that they seemed to be caused by bacteria. It was claimed that bacteria (Helicobacter pylori) are responsible for all cases of gastric ulcers except those caused by nonsteroidal anti-inflammatory agents such as aspirin (Blaser, 1996). This seemed to rule out stress as a causal factor, but a consideration of the evidence suggests otherwise.

There is no denying that H. pylori damage the stomach wall or that antibiotic treatment of gastric ulcers helps many sufferers. The facts do, however, suggest that H. pylori infection alone is insufficient to produce the disorder in most people. Although it is true that most patients with gastric ulcers display signs of H. pylori infection, so too do 75% of healthy individuals. Also, although it is true that antibiotics improve the condition of many patients with gastric ulcers, so do psychological treatments—and they do it without reducing signs of H. pylori infection. Apparently, there is another factor that increases the susceptibility of the stomach wall to damage from H. pylori, and this factor appears to be stress. Gastric ulcers occur more commonly in people living in stressful situations, and stressors produce gastric ulcers in laboratory animals.

### Psychoneuroimmunology: Stress, the Immune System, and the Brain

A major change in the study of psychosomatic disorders came in the 1970s with the discovery that stress can increase susceptibility to infectious diseases. Up to that point, infectious diseases had been regarded as “strictly physical.” The discovery that stress can increase susceptibility to infection led in the early 1980s to the emergence of a new field of research: psychoneuroimmunology—the study of interactions among psychological factors, the nervous system, and the immune system (see Fleschner & Lader, 2004). Psychoneuroimmunological research is the focus of this subsection. Let’s begin with an introduction to the immune system.

**Immune System** Microorganisms of every description revel in the warm, damp, nutritive climate of your body. Your immune system keeps your body from being overwhelmed by these invaders, but, before it can take any action against an invading microorganism, the immune system must have some way of distinguishing foreign cells from body cells. That is the function of antigens—protein molecules on the surface of a cell that identify it as native or foreign.

There are two divisions of the mammalian immune system: the innate immune system and the adaptive immune system (see Iwasaki & Medzhitov, 2010; O’Neill, 2005). The innate immune system is the first line of defense. It acts near entry points to the body and attacks general classes of molecules produced by a variety of pathogens (disease-causing agents). If the general innate immune system fails to destroy a pathogen, it is dealt with by the specific adaptive immune system. The adaptive immune system mounts a targeted attack by binding to the antigens on foreign cells and destroying them or marking them for destruction by other cells. An important feature of the adaptive immune system is that it has a memory; once particular pathogens have been recognized and destroyed, they are promptly eliminated if they invade again (see Littman & Singh, 2007; Reiner, Sallusto, & Lanzavecchia, 2007). The memory of the adaptive immune system is the mechanism that gives vaccinations their prophylactic (preventive) effect—vaccination involves administering a weakened form of a virus so that if the virus later invades, the adaptive immune system is prepared to act against it. For example, smallpox has been largely eradicated by programs of vaccination with the weaker virus of its largely benign relative, cowpox. The process of creating immunity through vaccination is termed immunization.

Until recently, most immunological research has focused on the adaptive immune system; however, the discovery of the role of cytokines in the innate immune system stimulated interest in that system (O’Neill, 2005).
The innate immune system is activated by **toll-like receptors** (receptors that are similar in structure to a receptor called **toll**, which had previously been discovered in fruit flies). Various kinds of **phagocytes** (cells, such as macrophages and microglia, that destroy and ingest pathogens) have toll-like receptors in their membranes, and upon binding to pathogens, the toll-like receptors trigger two responses (see Kettenmann, 2006; Pocock & Kettenmann, 2007). First, the phagocytes destroy and consume the pathogens (see Deretic & Klionsky, 2008)—in Figure 17.11, you see a macrophage about to engage in **phagocytosis** (the destruction and ingestion of foreign matter) of a bacterium. Then, the phagocytes release cytokines, which trigger an inflammatory response that results in swelling and redness at sites of local infection and produces the fever, body aches, and other flu-like symptoms that often accompany infections. Cytokines also attract more phagocytes from the blood into the infected area.

Another important effect of the cytokines is that they activate lymphocytes. **Lymphocytes** are cells of the adaptive immune system, specialized white blood cells that are produced in **bone marrow** and the **thymus gland** and are stored in the lymphatic system until they have been activated (see Terszowski et al., 2006; von Boehmer, 2006). There are many kinds of lymphocytes, but they are considered to be of two general types: T lymphocytes and B lymphocytes. Each is involved in a different adaptive immune reaction. **Cell-mediated immunity** is directed by **T cells** (T lymphocytes); **antibody-mediated immunity** is directed by **B cells** (B lymphocytes)—see Figure 17.12 on page 458.

The cell-mediated immune reaction begins when a macrophage ingests a foreign microorganism. The macrophage then displays the microorganism’s antigens on the surface of its cell membrane, and this display attracts T cells. Each T cell has two kinds of receptors on its surface, one for molecules that are normally found on the surface of macrophages and other body cells, and one for a specific foreign antigen. There are millions of different receptors for foreign antigens on T cells, but there is only one kind on each T cell, and there are only a few T cells with each kind of receptor. Once a T cell with a receptor for the foreign antigen binds to the surface of an infected macrophage, a series of reactions is initiated (Grakoui et al., 1999; Malissen, 1999). Among these reactions is the multiplication of the bound T cell, creating more T cells with the specific receptor necessary to destroy all invaders that contain the target antigens and all body cells that have been infected by the invaders.

The antibody-mediated immune reaction begins when a B cell binds to a foreign antigen for which it contains an appropriate receptor. This causes the B cell to multiply and to synthesize a lethal form of its receptor molecules. These lethal receptor molecules, called **antibodies**, are released into the intracellular fluid, where they bind to the foreign antigens and destroy or deactivate the microorganisms that possess them. Memory B cells for the specific antigen are also produced during the process; these cells have a long life and accelerate antibody-mediated immunity if there is a subsequent infection by the same microorganism (see Ahmed & Gray, 1996). The recent discovery of **T-reg cells** (regulatory T cells) is potentially of major clinical significance (Fehervari & Sakaguchi, 2006). Sometimes T cells start to attack the body’s own tissue, mistaking it for a pathogen, thus producing **autoimmune diseases**—for example, T cells sometimes attack the body’s own myelin, causing **multiple sclerosis** (see Chapter 10). T-reg cells combat autoimmune diseases by identifying and destroying T cells that engage in such attacks.

Researchers had been puzzled by the complex and highly coordinated nature of immune reactions. Then, high-resolution microscopic images of immune cells revealed connections between them that looked like synapses (see Biber et al., 2007; Davis, 2006).

**What Effect Does Stress Have on Immune Function: Disruptive or Beneficial?** It is widely believed that the main effect of stress on immune function is disruptive. I am sure that you have heard this from family members, friends, and even physicians. But is this true?
One of the logical problems with the view that stress always disrupts immune function is that it is inconsistent with the principles of evolution (see Segerstrom, 2007). Virtually every individual organism encounters many stressors during the course of its life, and it is difficult to see how a maladaptive response to stress, such as a disruption of immune function, could have evolved—or could have survived if it had been created by a genetic accident or as a \textit{spandrel} (a nonadaptive by-product of an adaptive evolutionary change; see Chapter 2).

Two events have helped clarify the relation between stress and immune function. The first was the \textit{meta-analysis} of Segerstrom and Miller (2004), which reviewed about 300 previous studies of stress and immune function. Segerstrom and Miller found that the effects of stress on immune function depended on the kind of stress. They found that acute (brief) stressors (i.e., those lasting less than 100 minutes, such as public speaking, an athletic competition, or a musical performance) actually led to improvements in immune function. Not surprisingly, the improvements in immune function following acute stress occurred mainly in the innate immune system, whose components can be marshaled quickly. In contrast, chronic (long-lasting) stressors, such as caring for an ill relative or experiencing a period of unemployment, adversely affected the adaptive immune system. Stress that disrupts health or other aspects of functioning is called \textit{distress}, and stress that improves health or other aspects of functioning is called \textit{eustress}.

The second event that has helped clarify the relation between stress and immune function was the discovery of the bidirectional role played by the cytokines in the innate immune system. Short-term cytokine-induced inflammatory responses help the body combat infection, whereas long-term cytokine release is associated with a variety of
adverse health consequences (Robles, Glaser, & Kiecolt-Glaser, 2005). This finding provided an explanation of the pattern of results discovered by Segerstrom and Miller’s meta-analysis.

**How Does Stress Influence Immune Function?** The mechanisms by which stress influences immune function have been difficult to specify because there are so many possibilities (see Dustin & Colman, 2002). Stress produces widespread changes in the body through its effects on the anterior-pituitary adrenal-cortex system and the sympathetic-nervous-system adrenal-medulla system, and there are innumerable mechanisms by which these systems can influence immune function. For example, both T cells and B cells have receptors for glucocorticoids; and lymphocytes have receptors for epinephrine, norepinephrine, and glucocorticoids. In addition, many of the neuropeptides that are released by neurons are also released by cells of the immune system. Conversely, cytokines, originally thought to be produced only by cells of the immune system, have been found to be produced in the nervous system (Salzet, Vieau, & Day, 2000). In short, the physiological mechanisms by which the nervous system and the immune system can interact are innumerable.

It is important to appreciate that there are behavioral routes by which stress can affect immune function. For example, people under severe stress often change their diet, exercise, sleep, and drug use, any of which could influence immune function. Also, the behavior of a stressed or ill person can produce stress and illness in others. For example, Wolf and colleagues (2007) found that stress in mothers aggravates asthmatic symptoms in their children; conversely, asthma in the children increases measures of stress in their mothers.

**Does Stress Affect Susceptibility to Infectious Disease?** You have just learned that stress influences immune function. Most people assume that this means that stress increases susceptibility to infectious diseases. But it doesn’t, and it is important that you understand why. There are three reasons why decreases in immune function may not be reflected in an increased incidence of infectious disease:

- The immune system seems to have many redundant components; thus, disruption of one of them may have little or no effect on vulnerability to infection.
- Stress-produced changes in immune function may be too short-lived to have substantial effects on the probability of infection.
- Declines in some aspects of immune function may induce compensatory increases in others.

It has proven difficult to show unequivocally that stress causes increases in susceptibility to infectious diseases in humans. One reason for this difficulty is that only correlational studies are possible. Numerous studies have reported positive correlations between stress and ill health in human subjects; for example, students in one study reported more respiratory infections during final exams (Glaser et al., 1987). However, interpretation of such correlations is never straightforward: Subjects may report more illness during times of stress because they expect to be more ill, because their experience of illness during times of stress is more unpleasant, or because the stress changed their behavior in ways that increased their susceptibility to infection.

Despite the difficulties of proving a causal link between stress and susceptibility to infectious disease in humans, the evidence for such a link is strong. Three basic types of evidence, when considered together, are almost persuasive:

- Correlational studies in humans—as you have just learned—have found correlations between stress levels and numerous measures of health.
- Controlled experiments conducted with laboratory animals show that stress can increase susceptibility to infectious disease in these species.
- Partially controlled studies conducted with humans, which are rare for ethical reasons, have added greatly to the weight of evidence.

One of the first partially controlled studies demonstrating stress-induced increases in the susceptibility of humans to infectious disease was conducted by Cohen and colleagues (1991). Using questionnaires, they assessed psychological stress levels in 394 healthy participants. Then, each participant randomly received saline nasal drops that contained a respiratory virus or only the saline. Then, all of the participants were quarantined until the end of the study. A higher proportion of those participants who scored highly on the stress scales developed colds.

**Early Experience of Stress**

Early exposure to severe stress can have a variety of adverse effects on subsequent development. Children subjected to maltreatment or other forms of severe stress display a variety of brain and endocrine system abnormalities (Evans & Kim, 2007; Teicher et al., 2003). As you will learn in Chapter 18, some psychiatric disorders are thought to result from an interaction between an inherited susceptibility to a disorder and early exposure to severe stress. Also, early exposure to stress often increases the intensity of subsequent stress responses (e.g., increases the subsequent release of glucocorticoids in response to stressors).

It is important to understand that the developmental period during which early stress can adversely affect neural and endocrine development begins before birth. Many experiments have demonstrated the adverse effects of prenatal stress in laboratory animals; pregnant females have been exposed
Thinking Creatively

One particularly interesting line of research on the role of early experience in the development of the stress response began with the observation that handling of rat pups by researchers for a few minutes per day during the first few weeks of the rats’ lives has a variety of salutary (health-promoting) effects (see Sapolsky, 1997). The majority of these effects seemed to result from a decrease in the magnitude of the handled pups’ responses to stressful events. As adults, rats that were handled as pups displayed smaller increases in circulating glucocorticoids in response to stressors (see Francis & Meaney, 1999). It seemed remarkable that a few hours of handling early in life could have such a significant and lasting effect. In fact, evidence supports an alternative interpretation.

Liu and colleagues (1997) found that handled rat pups are groomed (licked) more by their mothers, and they hypothesized that the salutary effects of the early handling resulted from the extra grooming, rather than from the handling itself. They confirmed this hypothesis by showing that unhandled rat pups that received a lot of grooming from their mothers developed the same profile of increased glucocorticoid release that was observed in handled pups.

The research on the effects of early grooming on the subsequent neural and behavioral development of rat pups is important because it is a particularly well-documented case of epigenetic transmission of a trait (see Parent et al., 2005). I hope you remember from earlier chapters that traits can be passed from parents to offspring by epigenetic mechanisms—literally, epigenetic means “not of the genes.” In this case, the female rat pups of fearful, poor grooming mothers or foster mothers are themselves fearful, poor grooming mothers as adults.

In contrast, early separation of rat pups from their mothers seems to have effects opposite to those of high levels of early grooming (see Cirulli, Berry, & Alleva, 2003; Pryce & Feldon, 2003; Rhees, Lephart, & Eliason, 2001). As adults, rats that are separated from their mothers in infancy display elevated behavioral and hormonal responses to stress.

### Stress and the Hippocampus

Exposure to stress affects the structure and function of the brain in a variety of ways (see Rodrigues, LeDoux, & Sapolsky, 2009). However, the hippocampus is particularly susceptible to stress-induced effects. The reason for this susceptibility may be the particularly dense population of glucocorticoid receptors in the hippocampus (see McEwen, 2004).

Stress has been shown to reduce dendritic branching in the hippocampus, to reduce adult neurogenesis in the hippocampus, to modify the structure of some hippocampal synapses, and to disrupt the performance of hippocampus-dependent tasks (see Sandi, 2004). These effects of stress on the hippocampus appear to be mediated by elevated glucocorticoid levels: They can be induced by corticosterone (a major glucocorticoid) and can be blocked by adrenalectomy (surgical removal of the adrenal glands)—see Brummelte, Pawluski, and Galea (2006), Gould (2004), and McEwen (2004).
This final section of the chapter deals with the brain mechanisms of human emotion. We still do not know how the brain controls the experience or expression of emotion, or how the brain interprets emotion in others, but progress has been made. Each of the following subsections illustrates an area of progress.

**Cognitive Neuroscience of Emotion**

Cognitive neuroscience is currently the dominant approach being used to study the brain mechanisms of human emotion. There have been many functional brain-imaging studies of people experiencing or imagining emotions or watching others experiencing them. These studies have established three points that have advanced our understanding of the brain mechanisms of emotion in fundamental ways (see Bastiaansen, Thioux, & Keysers, 2009; Niedenthal, 2007):

- Brain activity associated with each human emotion is diffuse—there is not a center for each emotion. Think “mosaic,” not “center,” for locations of brain mechanisms of emotion.
- There is virtually always activity in motor and sensory cortices when a person experiences an emotion or empathizes with a person experiencing an emotion (see Figure 17.13).
- Very similar patterns of brain activity tend to be recorded when a person experiences an emotion, imagines that emotion, or sees somebody else experience that emotion.

These three fundamental findings are influencing how researchers are thinking about the neural mechanisms of emotion. For example, the activity observed in sensory and motor cortex during the experience of human emotions is now believed to be an important part of the mechanism by which the emotions are experienced. The re-experiencing of related patterns of motor, autonomic, and sensory neural activity during emotional experiences is generally referred to as the embodiment of emotions (see Niedenthal, 2007).

These three fundamental findings may also help explain the remarkable ability of humans to grasp the emotional states of others (see Bastiaansen et al., 2009). You may recall that mirror neurons, which have been identified in nonhuman primates, are neurons that fire when a specific response is performed by a subject or the subject watches the response being performed. The discovery that certain patterns of brain activity are observed on fMRI scans when individuals experience an emotion or watch somebody else experience the same emotion suggests that a mirror-like system might be the basis for human empathy (Fabbri-Destro & Rizzolatti, 2008; Iacoboni, 2009; Keysers & Gazzola, 2009; Oberman & Ramachandran, 2007).

**Amygdala and Human Emotion**

You have already learned that the amygdala plays an important role in fear conditioning in rats. Numerous functional brain-imaging studies have found the amygdala to be involved in human emotions—particularly in fear and other negative emotions (see Adolphs, 2008; Cheng et al., 2006; Sergerie, Lepage, & Armony, 2006). Furthermore, the amygdala appears to be involved in only some aspects of human fear. It seems to be more involved in the perception of fear in others.

**FIGURE 17.13** Horizontal, sagittal, and coronal functional MRIs show areas of increased activity in the primary motor cortex (M1) and the premotor cortex (PMC) when volunteers watched facial expressions of emotion. The same areas were active when the volunteers made the expressions themselves. (From Carr et al., 2003.)
than in its experience. The following case illustrates these points.

The Case of S.P., the Woman Who Couldn’t Perceive Fear

At the age of 48, S.P. had her right amygdala and adjacent tissues removed for the treatment of epilepsy. Because her left amygdala had been damaged, she in effect had a bilateral amygdalar lesion.

Following her surgery, S.P. had an above average I.Q., and her perceptual abilities were generally normal. Of particular relevance was the fact that she had no difficulty in identifying faces or extracting information from them (e.g., information about age or gender). However, S.P. did have a severe postsurgical deficit in recognizing facial expressions of fear and less striking deficits in recognizing facial expressions of disgust, sadness, and happiness.

In contrast, S.P. had no difficulty specifying which emotion would go with particular sentences. Also, she had no difficulty using facial expressions upon request to express various emotions (Anderson & Phelps, 2000). This case is consistent with previous reports that the human amygdala is specifically involved in perceiving facial expressions of emotion, particularly of fear (e.g., Broks et al., 1998; Calder et al., 1996).

The case of S.P. is similar to reported cases of Urbach-Wiethe disease (see Aggleton & Young, 2000). Urbach-Wiethe disease is a genetic disorder that often results in calcification (hardening by conversion to calcium carbonate, the main component of bone) of the amygdala and surrounding anterior medial temporal-lobe structures in both hemispheres (see Figure 17.14). One Urbach-Wiethe patient with bilateral amygdalar damage was found to have lost the ability to recognize facial expressions of fear (Adolphs, 2006). Indeed, she could not describe fear-inducing situations or produce fearful expressions, although she had no difficulty on tests involving other emotions. Although recent research has focused on the role of the amygdala in the recognition of negative facial expressions, patients with Urbach-Wiethe disease sometimes have difficulty recognizing other complex visual stimuli (Adolphs & Tranel, 1999).

Medial Prefrontal Lobes and Human Emotion

Emotion and cognition are often studied independently, but it is now believed that they are better studied as components of the same system (Phelps, 2004, 2006; Beer, Knight, & Esposito, 2006). The medial portions of the prefrontal lobes (including the medial portions of the orbitofrontal cortex and cingulate cortex) are the sites of emotion-cognition interaction that have received the most attention. Functional brain-imaging studies have found evidence of activity in the medial prefrontal lobes when emotional reactions are being cognitively suppressed or re-evaluated (see Quirk & Beer, 2006). Most of the studies of medial prefrontal lobe activity employ suppression paradigms or reappraisal paradigms. In studies that use suppression paradigms, participants are directed to inhibit their emotional reactions to unpleasant films or pictures; in studies that use reappraisal paradigms, participants are instructed to reinterpret a picture to change their emotional reaction to it. The medial prefrontal lobes are active when both of these paradigms are used, and they seem to exert their cognitive control of emotion by interacting with the amygdala (see Holland & Gallagher, 2004; Quirk & Beer, 2006).

Many theories of the specific functions of the medial prefrontal lobes have been proposed. The medial prefrontal lobes have been hypothesized to monitor the difference between outcome and expectancy (Potts et al., 2006), to respond to personal choices that result in losses (Gehring & Willoughby, 2002), to predict the likelihood of error (Brown & Braver, 2005), to guide behavior based on previous actions and outcomes (Kennerly et al.,

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**FIGURE 17.14** Bilateral calcification of the amygdalae in twins with Urbach-Wiethe disease. The red circles indicate the areas of calcification. (From Hurlemann et al., 2007.)
2006), and to respond to social rejection (Somerville, Heatherton, & Kelley, 2006). Which hypothesis is correct? Perhaps all are; the medial prefrontal lobes are large and complex, and they likely perform many functions. This point was made by Kawasaki and colleagues (2005).

Kawasaki and colleagues used microelectrodes to record from 267 neurons in the anterior cingulate cortices of four patients prior to surgery. They assessed the activity of the neurons when the patients viewed photographs with emotional content. Of these 267 neurons, 56 responded most strongly and consistently to negative emotional content. This confirms previous research linking the medial prefrontal lobes with negative emotional reactions, but it also shows that not all neurons in the area perform the same function—neurons directly involved in emotional processing appear to be sparse and widely distributed in the human brain.

**Clinical Implications**

**Lateralization of Emotion**

There is considerable evidence that emotional functions are lateralized, that is, that the left and right cerebral hemispheres are specialized to perform different emotional functions (e.g., Kim et al., 2004; Shaw et al., 2005)—as you learned in Chapter 16. This evidence has led to several theories of the cerebral lateralization of emotion (see Demaree et al., 2005); the following are the two most prominent:

- The *right-hemisphere model* of the cerebral lateralization of emotion holds that the right hemisphere is specialized for all aspects of emotional processing: perception, expression, and experience of emotion.
- The *valence model* proposes that the right hemisphere is specialized for processing negative emotion and the left hemisphere is specialized for processing positive emotion.

Most studies of the cerebral lateralization of emotion have employed functional brain-imaging methods, and the results have been complex and variable. Wager and colleagues (2003) performed a meta-analysis of the data from 65 such studies. Which of the theories does the analysis support?

The main conclusion of Wager and colleagues was that the current theories of lateralization of emotion are too general from a neuroanatomical perspective. Overall comparisons between left and right hemispheres revealed no interhemispheric differences in either the amount of emotional processing or the valence of the emotions being processed. However, when the comparisons were conducted on a structure-by-structure basis, they revealed substantial evidence of lateralization of emotional processing. Some kinds of emotional processing were lateralized to the left hemisphere in certain structures and to the right in others. Functional brain-imaging studies of emotion have commonly observed lateralization in the amygdalae—more activity is often observed in the left amygdala (Baas, Aleman, & Kahn, 2004). Clearly, neither the right-hemisphere model nor the valence model of the lateralization of emotion is supported by the evidence. The models are too general.

Another approach to studying the lateralization of emotions is based on observing the asymmetry of facial expressions. In most people, each facial expression begins on the left side of the face and, when fully expressed, is more pronounced there—which implies right-hemisphere dominance for facial expressions (see Figure 17.15). Remarkably, the same asymmetry of facial expressions has been documented in monkeys (Hauser, 1993). A right-hemisphere dominance for the recognition of facial expressions has also been demonstrated—people base their judgments of facial expression more on the right side of an observed face (Coolican et al., 2007).

**Individual Differences in the Neural Mechanisms of Emotion**

In general, more complex brain functions tend to show more individual differences in cerebral localization. For example, in Chapter 16, you learned that the cortical localization of language

![FIGURE 17.15](https://devlrn.developmentandlearning.org/17/08.jpg)
processes varies substantially from person to person. Nevertheless, few studies of the neural mechanisms of emotion have focused on individual differences (see Leppänen & Nelson, 2009; Samanez-Larkin et al., 2008). Let’s consider two studies and one notorious case that have a bearing on this issue.

First, Adolphs and colleagues (1999) tested the ability of nine neuropsychological patients with bilateral amygdalar damage to correctly identify facial expressions of emotion. As others had reported, these researchers found that the group of patients as a whole had difficulty identifying facial expressions of fear. However, there were substantial differences among the patients: Some also had difficulty identifying other negative emotions, and two had no deficits whatsoever in identifying facial expressions of emotions. Remarkably, structural MRIs revealed that both of these latter two patients had total bilateral amygdalar lesions.

Second, Canli and colleagues (2002) used functional MRIs to compare the reactions of healthy participants who scored high on extraversion with those of healthy participants who scored high on neuroticism. These personality dimensions were selected because of their relation to emotion—people high on the extraversion scale have a tendency toward positive emotional reaction; people high on the neuroticism scale have a tendency toward negative emotional reaction. Although all the participants displayed increased activity in the amygdala when viewing fearful faces, only the extraverts displayed increased amygdalar activity when viewing happy faces.

The following case study ends the chapter by emphasizing the point that the brain mechanisms of emotion differ from person to person. Fortunately, the reactions of Charles Whitman to brain damage are atypical.

The Case of Charles Whitman, the Texas Tower Sniper

After having lunch with his wife and his mother, Charles Whitman went home and typed a letter of farewell—perhaps as an explanation for what would soon happen. He stated in his letter that he was having many compelling and bizarre ideas. Psychiatric care had been no help. He asked that his brain be autopsied after he was through; he was sure that they would find the problem.

By all reports, Whitman had been a good person. An Eagle Scout at 12 and a high school graduate at 17, he then enlisted in the Marine Corps, where he established himself as an expert marksman. After his discharge, he entered the University of Texas to study architectural engineering.

Nevertheless, in the evening of August 1, 1966, Whitman killed his wife and mother. He professed love for both of them, but he did not want them to face the aftermath of what was to follow.

The next morning, at about 11:30, Whitman went to the Tower of the University of Texas, carrying six guns, ammunition, several knives, food, and water. He clubbed the receptionist to death and shot four more people on his way to the observation deck. Once on the deck, he opened fire on people crossing the campus and on nearby streets. He was deadly, killing people as far as 300 meters away—people who assumed they were out of range.

At 1:24 that afternoon, the police fought their way to the platform and shot Whitman to death. All told, 17 people, including Whitman, had been killed, and another 31 had been wounded (Helmer, 1986).

An autopsy was conducted. Whitman was correct: They found a walnut-sized tumor in his right amygdala.

Themes Revisited

All four of the book’s themes were prevalent in this chapter. The clinical implications theme appeared frequently, both because brain-damaged patients have taught us much about the neural mechanisms of emotion and because emotions have a major impact on health. The evolutionary perspective theme also occurred frequently because comparative research and the consideration of evolutionary pressures have also had a major impact on current thinking about the biopsychology of emotion.

The thinking creatively theme appeared where the text encouraged you to think in unconventional ways about the relation between testosterone and human aggression, the interpretation of reports of correlations between stress and ill health, and the possibility of susceptibility to stress being passed from generation to generation by maternal care.

Neuroplasticity was the major theme of the discussion of the effects of stress on the hippocampus.
Think about It

1. With practice, you could become an expert in the production and recognition of facial expressions. How could you earn a living with these skills?
2. Does the target-site concept have any relevance to human aggression, defense, and play fighting?
3. Genes are not the only means by which behavioral tendencies can be passed from generation to generation. Discuss, with reference to maternal care and susceptibility to stress.
4. It is misleading to think of the amygdala as a single structure. Discuss.
5. Evidence suggests that emotion is a right-hemisphere phenomenon. Discuss.
6. Research on emotion has focused on fear. Why?

Key Terms

17.1 Biopsychology of Emotion: Introduction
James-Lange theory (p. 444)
Cannon-Bard theory (p. 444)
Decorticate (p. 445)
Sham rage (p. 445)
Limbic system (p. 446)
Kluver-Bucy syndrome (p. 446)
Amygdala (p. 446)
Polygraphy (p. 447)
Control-question technique (p. 447)
Guilty-knowledge technique (p. 447)
Facial feedback hypothesis (p. 448)
Duchenne smile (p. 449)

17.2 Fear, Defense, and Aggression
Fear (p. 450)
Defensive behaviors (p. 450)
Aggressive behaviors (p. 450)
Alpha male (p. 450)
Target-site concept (p. 451)

17.3 Neural Mechanisms of Fear Conditioning
Fear conditioning (p. 452)
Contextual fear conditioning (p. 453)
Hippocampus (p. 454)
Lateral nucleus of the amygdala (p. 454)
Prefrontal cortex (p. 454)

17.4 Stress and Health
Stress (p. 454)
Stressors (p. 454)
Adrenocorticotropic hormone (ACTH) (p. 455)
Glucocorticoids (p. 455)
Adrenal cortex (p. 455)
Adrenal medulla (p. 455)
Cytokines (p. 455)
Subordination stress (p. 456)
Psychosomatic disorder (p. 456)
Gastric ulcers (p. 456)
Psychoneuroimmunology (p. 456)
Immune system (p. 456)
Antigens (p. 456)
Innate immune system (p. 456)
Pathogens (p. 456)
Adaptive immune system (p. 456)
Vaccination (p. 456)
Immunization (p. 456)
Toll-like receptors (p. 457)
Phagocytes (p. 457)
Macrophage (p. 457)
Phagocytosis (p. 457)
Lymphocytes (p. 457)
Cell-mediated immunity (p. 457)
T cells (p. 457)
B cells (p. 457)
Antibodies (p. 457)
T-reg cells (p. 457)
Autoimmune diseases (p. 457)
Epigenetic (p. 460)
Corticosterone (p. 460)
Adrenalectomy (p. 460)

17.5 Brain Mechanisms of Human Emotion
Mirror-like system (p. 461)
Urban-Wiethe disease (p. 462)
Suppression paradigm (p. 462)
Reappraisal paradigm (p. 462)

Quick Review

Test your comprehension of the chapter with this brief practice test. You can find the answers to these questions as well as more practice tests, activities, and other study resources at www.mypsychlab.com.

1. Sham rage was first observed in
   a. Papez’s circuit.
   b. wild rats.
   c. decorticate cats.
   d. monkeys with no limbic system.
   e. patients with Kluver-Bucy syndrome.

2. When an alpha male rat attacks a submissive male intruder, he
   a. directs his attack at the intruder’s face.
   b. directs his attack at the intruder’s back.
   c. moves toward the “boxing” intruder with a lateral (side-ways) attack.
   d. both a and c
   e. both b and c

3. A genuine smile
   a. involves the orbicularis oculi.
   b. involves the zygomaticus major.
   c. is called a Duchenne smile.
   d. all of the above
   e. both a and c

4. The most commonly used measure of stress is
   a. the level of glucocorticoids circulating in the blood.
   b. blood pressure.
   c. heart rate.
   d. the release of glucocorticoids from the pituitary.
   e. both b and c

5. T cells and B cells are
   a. phagocytes.
   b. lymphocytes.
   c. antibodies.
   d. antigens.
   e. macrophages.