17 Biopsychology of Emotion, Stress, and Health
Fear, the Dark Side of Emotion

17.1 Biopsychology of Emotion: Introduction
17.2 Fear, Defense, and Aggression
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This chapter is about the biopsychology of emotion, stress, and health. It begins with a historical introduction to the biopsychology of emotion, and then it focuses on 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

This section provides a general introduction to the biopsychology of emotion by reviewing several classic early discoveries, 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 intellectu-

ally 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 an 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 body.
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—influences 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 neural structures that he referred to as the limbic system. The **limbic system** is a collection of nuclei and tracts that borders the thalamus (limbic means “border”). Figure 17.4 illustrates some of its key structures: the amygdala, mammillary body, hippocampus, fornix, cortex of the cingulate gyrus, septum, olfactory bulb, and hypothalamus (see Macchi, 1989). Papez proposed that emotional states are expressed through the action of the other limbic structures on the hypothalamus and that they are experienced through the action of the limbic structures on the cortex.

**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. ... He 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.

### TABLE 17.1 Biopsychological Investigation of Emotion: Six Early Landmarks

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case of Phineas Gage</td>
<td>1848</td>
</tr>
<tr>
<td>Darwin’s theory of the evolution of emotion</td>
<td>1872</td>
</tr>
<tr>
<td>James-Lange and Cannon-Bard theories</td>
<td>about 1900</td>
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<tr>
<td>Discovery of sham rage</td>
<td>1929</td>
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<tr>
<td>Limbic system theory of emotion</td>
<td>1937</td>
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<tr>
<td>Discovery of Kluver-Bucy syndrome</td>
<td>1939</td>
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</table>
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 the suspect is guilty or innocent. Consequently, many studies of polygraphy have employed the mock-crime 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 (Lykken, 1959). 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 one 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.

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). The facial expressions in Ekman and Friesen’s atlas are photographs of models who were instructed to contract specific facial muscles on the basis of Ekman and Friesen’s analysis. 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

Despite Darwin’s assertion that human facial expressions are characteristic of the species, it was widely believed that facial expressions are learned and culturally variable. Then, several empirical studies showed that people of different cultures do indeed make similar facial expressions in similar situations and that they can correctly identify the emotional
The significance of facial expressions displayed by people from cultures other than their own (e.g., Ekman, Sorenson, & Friesen, 1969; Hejmadi, Davidson, & Rozin, 2000; Izard, 1971). 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). Although these findings support Darwin's view of the universality of facial expressions, they do not deny the possibility of subtle cultural differences (see Russell, Bachorowski, & Fernandez-Dols, 2003). Nor do they deny the fact that human facial expressions are similar to those of our primate relatives (see Parr, Waller, & Fugate, 2005).

**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. In Figure 17.5, Ekman himself illustrates his 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 it. 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 on page 438). Why don’t you try it? 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, you have just experienced the effect of facial feedback.

**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*...
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 unmasks 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 real time 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 primaries has been recognized. For example, there is evidence for adding contempt and embarrassment to the original six (see Ekman, 1992).

Have you noticed that only one of these 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 to the view that all positive emotions may share the same facial expression. The research on pride by Tracy 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. Expressions of pride were documented across cultures and genders in a study of the victors of judo matches in the Olympic games (Tracy & Matsumoto, in press).

(brief facial expressions) of the real emotion often break through the false one. 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 unmasks a false friend—a fact you would do well to remember. Ekman named the genuine smile the **Duchenne smile** (see Ekman & Davidson, 1993).

**FIGURE 17.6** The effects of facial expression on the experience of emotion. Subjects reported feeling more happy and less angry when they viewed slides while making a happy face, and less happy and more angry when they viewed slides while making an angry face. (Adapted from Rutledge & Hupka, 1985.)

**FIGURE 17.7** The orbicularis oculi and zygomaticus major, two muscles that contract during genuine (Duchenne) smiles. Because the lateral portion of the orbicularis oculi is difficult for most people to contract voluntarily, fake smiles usually lack this component.
occur, and on the putative adaptive functions of such behaviors (see Barrett & Wager, 2006).

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 approaches the stranger and sniffs at its perianal area.... If the intruder is an adult male, the alpha’s sniff leads to piloerection [involuntary bristling of hairs].... Shortly after piloerecting, the alpha male usually bites the intruder, and the intruder runs away. The alpha chases after it, and after one or two additional 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. The next time you play with a cat, take the opportunity to analyze the cat’s behavior in the light of Pellis’s observations.

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 consider it useful to 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) appear to be designed to protect the target site on its back.

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 more attacks at the experimenter if they are left undisturbed. These lesioned rats are more defensive, not more aggressive.

### Table 17.2 Categories of Aggressive and Defensive Behaviors in Rats

<table>
<thead>
<tr>
<th>Aggressive Behaviors</th>
<th>Predatory Aggression</th>
<th>The stalking and killing of members of other species for the purpose of eating them. Rats kill prey, such as mice and frogs, by delivering bites to the back of the neck.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Aggression</td>
<td></td>
<td>Unprovoked aggressive behavior that is directed at a conspecific (member of one’s own species) for the purpose of establishing, altering, or maintaining a social hierarchy. In mammals, social aggression occurs primarily among males. In rats, it is characterized by piloerection, lateral attack, and bites directed at the defender’s back.</td>
</tr>
<tr>
<td>Defensive Behaviors</td>
<td>Intraspecific Defense</td>
<td>Defense against social aggression. In rats, it is characterized by freezing and flight and by various behaviors, such as boxing, that are specifically designed to protect the back from bites.</td>
</tr>
<tr>
<td>Defensive Attacks</td>
<td></td>
<td>Attacks that are launched by animals when they are cornered by threatening members of their own or other species. In rats, they include lunging, shrieking, and biting attacks that are usually directed at the face of the attacker.</td>
</tr>
<tr>
<td>Freezing and Flight</td>
<td></td>
<td>Responses that many animals use to avoid attack. For example, if a human approaches a wild rat, it will often freeze until the human penetrates its safety zone, whereupon it will explode into flight.</td>
</tr>
<tr>
<td>Maternal Defensive Behaviors</td>
<td></td>
<td>The behaviors by which mothers protect their young. Despite their defensive function, they are similar to male social aggression in appearance.</td>
</tr>
<tr>
<td>Risk Assessment</td>
<td></td>
<td>Behaviors that are performed by animals in order to obtain specific information that helps them defend themselves more effectively. For example, rats that have been chased by a cat into their burrow do not emerge until they have spent considerable time at the entrance scanning the surrounding environment.</td>
</tr>
<tr>
<td>Defensive Burying</td>
<td></td>
<td>Rats and other rodents spray sand and dirt ahead with their forepaws to bury dangerous objects in their environment, to drive off predators, and to construct barriers in burrows.</td>
</tr>
</tbody>
</table>
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 nonprimate 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. As a result, it is commonly believed that human aggression—particularly male aggression—is a product of testosterone. Is it?

The answer to this question is not simple (see Wingfield, 2005). Fortunately, Soma and his colleagues have reviewed and insightfully interpreted the extensive research literature on testosterone and aggression in various species (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 of the year.
- 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).
- For understanding the effects of testosterone on aggression, 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 various areas of the brain that show activation. Although studies focusing on brain levels of testosterone are rare, it has been shown that testosterone can be synthesized in particular brain sites in some species from circulating adrenal steroids.

It is unlikely that humans are an exception to the usual involvement of testosterone in social aggression noted in the comparative analysis of Soma and his colleagues. 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 fact that the evidence of the involvement of testosterone in human aggression is unconvincing could mean that hormonal and neural regulation of aggression in humans differs from that in nonprimate mammalian species. However, it could reflect the fact that the human research has not considered brain levels of testosterone, instead focusing on blood levels, often inferred from levels in saliva. Also, the researchers who study human aggression have often failed to appreciate the difference between social aggression, which is related to testosterone in many species, and defensive aggression, which is not. 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.

Fear Conditioning

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). An early study of fear-conditioning was Watson and Rayner’s famous case study of Little Albert, which you likely learned about in an introductory psychology course.

Fear conditioning has been one preferred method of studying fear because the source of fear is always unambiguous (the unconditional stimulus) and because the development of the fear response can be systematically investigated (see Maren, 2001). Efforts to identify the neural mechanisms of fear conditioning almost always involve nonhuman subjects because the studies typically use invasive lesion, stimulation, and recording methods.

In the usual fear-conditioning experiment, the subject, typically 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 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).

![Figure 17.9](image_url)

**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 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). Two kinds of lesion studies have implicated the hippocampus in contextual fear conditioning. First, bilateral hippocampal lesions made before conditioning block the 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). Second, bilateral hippocampal lesions made shortly after conditioning block the retention of the fear response to the context without disrupting retention of the fear response to the explicit conditional stimulus.

**Lateral Nucleus of the Amygdala 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 and has different connections. Making things potentially even more confusing is the fact that the anatomy of the amygdala is so complex that there is no general consensus about how to divide it into its components (see LeDoux, 2000b).

Don’t worry! I don’t expect you to master the intricacies of amygdalar anatomy. I merely want you to be able to put what I am about to say in context. You see, evidence suggests that it is 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). The prefrontal lobe 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.

**Scan Your Brain**

This chapter is about to change direction. The remaining two sections focus on the effects of stress on health and on the neural mechanisms of human emotion. This is a good point for you to scan your brain to see whether it has retained the introductory material on emotion and fear. Fill in each of the following blanks with the most appropriate term. The correct answers are provided below. Before continuing, review material related to your errors and omissions.

1. The theory that the subjective experience of emotion is triggered by ANS responses is called the _______ theory.
2. The pattern of aggressive responses observed in decorticate animals is called _______.
3. Between the amygdala and the fornix in the limbic ring is the _______.
4. A Duchenne smile, but not a false smile, involves contraction of the _______.
5. Aggression directed by the alpha male of a colony at a male intruder is called _______ aggression.
6. The usual target site of rat defensive attacks is the _______ of the attacking rat.
7. Testosterone increases _______ aggression in rats.
8. In humans, most violent outbursts that are labeled as aggression are more appropriately viewed as _______ attacks.
9. The historic case study of Little Albert was the first study of fear _______.
10. In the typical auditory fear conditioning experiment, the _______ is a tone.
11. Auditory fear conditioning to simple tones depends on a pathway from the _______ to the amygdala.
12. Unlike auditory fear conditioning to simple tones, fear conditioning to complex sounds involves the _______.
13. The prefrontal lobe is thought to act on the _______ of the amygdala to inhibit conditioned fear.

**Stress and Health**

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), whether psychological (e.g., dismay at the loss of one’s job) or physical (e.g., long-term exposure to cold), produce a similar core pattern of physiological changes; however, it is chronic psychological stress (e.g., in the form of chronic fear) that has been most frequently implicated in ill health (see Kiecolt-Glaser et al., 2002; Krantz & McCeney, 2002; Natelson, 2004).
The Stress Response

Hans Selye (pronounced “SELL-yay”) first described the stress response in the 1950s, and he quickly recognized 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 effects 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.

With his emphasis on the role of the anterior-pituitary adrenal-cortex system in stress, Selye largely ignored the contributions of the sympathetic nervous system. Stressors also 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 major roles of both systems (see Figure 17.10).

The magnitude of the stress response depends not only on the stressor and the individual; it also depends on the strategies the individual adopts to cope with the stress (McEwen, 1994). 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 to think about their problem in certain ways. 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 about it experienced less stress (Katz et al., 1970).

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., Cresswell et al., 2005; Miller, Chen, & Zhou, 2007; Smith, 2006).

In the 1990s, there was an important advance in the understanding of the stress response (see Fleshner & 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 have taken their place 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 Fleshner & Laudenslager, 2004; Koolhass, de Boer, & Buwalda, 2006).

Many current 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? Male rats exposed to subordination stress are more likely to attack juveniles, to have testes that are smaller than normal, to have shorter life spans, and to have lower levels of testosterone and higher levels of glucocorticoids.

**Stress and Gastric Ulcers**

Stress has long been implicated in the development of many disorders—for example, heart disease, asthma, and depression (Miller & Blackwell, 2006). The involvement of stress in gastric ulcers is currently of particular interest to researchers because of a recent breakthrough in identifying stress in gastric ulcers is currently of particular interest to depression (Miller & Blackwell, 2006). The involvement of many disorders—for example, heart disease, asthma, and stress has long been implicated in the development of such studies to common human stressors (see Fleshner & Laudenslager, 2004; Koolhass, de Boer, & Buwalda, 2006).

In the United States alone, about 500,000 new cases are reported each year. Gastric ulcers occur more commonly in people living in stressful situations, and stressors (e.g., confinement to a restraint tube for a few hours) can produce gastric ulcers in laboratory animals.

For decades, gastric ulcers were regarded as the prototypical psychosomatic disease (a physical disease with evidence of a psychological cause). However, this view seemed to change with the report that gastric ulcers are caused by bacteria. Indeed, it has been claimed that the ulcer-causing 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 in gastric ulcers, but a consideration of the evidence suggests otherwise (Overmier & Murison, 1997).

There is no denying that *H. pylori* damages 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 control subjects. 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.

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

A major change in the study of stress and health came in the 1970s with the discovery that stress can increase susceptibility to infectious diseases, which up to that point had been regarded as “strictly physical.” This discovery that stress can increase susceptibility to infection led in the early 1980s to the emergence of a new field of biopsychological research. That field is psychoneuroimmunology—the study of interactions among psychological factors, the nervous system, and the immune system (see Fleshner & Laudenslager, 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 (see Ploegh, 1998). Your immune system keeps your body from being overwhelmed by these invaders. 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 why antigens—protein molecules on the surface of a cell that identify it as native or foreign—play a major role in specific immune reactions (see Matzinger, 2002; Medzhitov & Janeway, 2002).

There are two divisions of the mammalian immune system: the innate immune system and the adaptive immune system (see O’Neill, 2005). The innate immune system is the first line of defense. It acts near entry points to the body and attacks generic classes of molecules produced by a variety of pathogens (disease-causing agents). If the innate immune system fails to destroy a pathogen, it is dealt with by the 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. The memory of the adaptive immune system is the mechanism by which vaccinations have their prophylactic (preventive) effect—\textit{vaccination} involves administering weakened forms 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 \textit{immunization}.

Until recently, most immunological research has focused on the adaptive immune system—researchers found its specificity and memory particularly interesting. However, the discovery of the role of cytokines in the innate immune system eliminated this bias, and much is now being discovered about the innate immune system (O’Neill, 2005).

Here is how the innate immune system is thought to work. Its immune response is initiated by \textit{toll-like receptors}, receptors that are synthesized by many cells of the innate immune system for the purpose of detecting generic pathogens. (They were called \textit{toll-like} because they are similar in structure to a receptor called \textit{toll}, which had previously been discovered in fruit flies.) For example, various kinds of \textit{phagocytes} (cells, such as macrophages and microglia, that destroy and ingest pathogens) have toll-like receptors in their membranes that trigger two types of responses upon detecting pathogens (see Kettenmann, 2006). First, the phagocytes destroy and consume the pathogens—in Figure 17.11 you see a \textit{macrophage} engaging in \textit{phagocytosis} (the destruction and ingestion of foreign matter) of a “poor” 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 flulike symptoms that often accompany general body infections. Cytokines also attract more phagocytes from the blood into the infected area.

Another important effect of the cytokines is that they activate the cells of the second division of the immune system, the adaptive immune system. These cells are \textit{lymphocytes}, specialized white blood cells that are produced in the \textit{bone marrow} and \textit{thymus gland} and are stored in the lymphatic system until they are 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. \textit{Cell-mediated immunity} is directed by \textit{T cells} (T lymphocytes); \textit{antibody-mediated immunity} is directed by \textit{B cells} (B lymphocytes)—see Figure 17.12.

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 \textit{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
What Effect Does Stress Have on Immune Function?

It is widely believed that stress disrupts immune function. I am sure that you have heard this point made by family members, friends, and even by physicians. But is this true? By this point in the book, I am sure you appreciate that the ultimate criterion of truth is empirical evidence, not popular opinion.

One of the problems with the view that stress disrupts immune function is that it is inconsistent with the principles of evolution. 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 spandrel (a nonadaptive by-product of an adaptive evolutionary change; see Chapter 2).

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.

Until the mid-1990s, researchers were puzzled by the highly coordinated nature of immune reactions. Then, an important discovery provided an insight into the mechanism by which immune cells can communicate. High-resolution microscopic images of immune cells revealed connections between them that looked like synapses (see Davis, 2006).

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Two major events have helped clarify the relation between stress and immune function. The first was the meta-analysis (combined analysis of previously published studies) of Segerstrom and Miller (2004), which involved the combined analysis of 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 a demented loved one, living with a handicap, or experiencing a period of unemployment, adversely affected the adaptive immune system.

The second helpful event was the discovery of the critical role played by the cytokines in the innate immune system. The discovery that the release of cytokines and the resulting inflammatory responses that are triggered by stress are adaptive, at least in the short term, challenged the assumption that stress is always bad for the health. Short-term stress-induced inflammatory responses help the body combat infection; only during long-term stress does cytokine release come to be 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. It also has initiated a new line of psychoneuroimmunological research: one that focuses on complex interactions between stress and immune function and is not based on the assumption that all stress adversely affects all aspects of immune function (Robles, Glaser, & Kiecolt-Glaser, 2005).

The finding that stress can sometimes have beneficial effects on health has led some investigators to consider stress to be of two different types: distress (stress that reduces health) and eustress (stress that improves health). This dichotomy is useful because it emphasizes that the effects of stress on health are not all negative. However, it is important not to take these categories too literally. The very same stress can have adverse effects in some people and beneficial effects in others. Even in the same person, a stressful experience can produce both beneficial and adverse effects at the same time.

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 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 display changed patterns of diet, exercise, sleep, and drug use, any or all of which could influence immune function.

It is also important to appreciate that stress or illness in one 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. In children with asthma, life stresses markedly increase cytokine levels (Chen et al., 2006) and reduce the expression of genes that encode glucocorticoid receptors (Miller & Chen, 2006).

Does Stress Affect Susceptibility to Infectious Disease? You have just learned that stress influences immune function, but this does not prove that stress increases susceptibility to infectious diseases. These are related but separate issues that require different lines of research to resolve them. 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 conclusive:

- Correlational studies in humans, which—as you have just learned—are suggestive but unconvincing on their own.
- Controlled experiments conducted with laboratory animals, which prove that stress can increase susceptibility to infectious disease but do not prove that it happens in humans.
- Partially controlled studies conducted with humans, which are rare for ethical reasons, but add greatly to the weight of evidence.

One of the first partially controlled studies demonstrating stress-induced decreases 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 received saline nasal drops that contained a respiratory virus; controls received only saline. Then, all of the participants were quarantined until the end of the study. A higher proportion of those participants who 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 (Teicher, 2002; 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. Because early exposure to stress often increases the intensity of subsequent stress responses (e.g., increases the subsequent release of glucocorticoids in response to stressors), such exposure likely amplifies the adverse effects of subsequent stress.

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 to stressors, and the adverse effects of that exposure on their offspring have subsequently been documented (see Avishai-Eliner et al., 2002; Kofman, 2002; Maccari et al., 2003).

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. This effect seems to have been produced by decreased negative feedback from greater numbers of glucocorticoid receptors in the hippocampus, resulting from changes in hippocampal gene expression (Meaney & Szyf, 2005).

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). Epigenetic means "not of the genes," and epigenetic mechanisms of transmission are nongenetic means by which traits are passed from parents to offspring. 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

Many studies of the effects of stress on the brain suggest that 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). Surprisingly, the reduction of neurogenesis by stress tends to be greater in males than females (e.g., Falconer & Galea, 2003)—perhaps because estradiol has neuroprotective effects that testosterone lacks (see Kambo & Galea, 2006; Ormerod & Galea, 2001b).

Pause here to review the preceding section on stress and health. Fill in each of the following blanks. The correct answers are provided below. Review material related to your errors or omissions before proceeding.

1. Glucocorticoids are released from the ________ as part of the stress response.
2. Stressors increase the release of epinephrine and norepinephrine from the ________.
3. Brief stressors trigger the release of ________, which participate in the body’s inflammatory responses.
4. When threats from conspecifics become an enduring feature of daily life, the result is ________.
5. Gastric ulcers have recently been shown to be caused by H. pylori, but it still seems likely that ________ is a causal factor in their development.
6. The study of the interactions among psychological factors, the nervous system, and the immune system is called ________.
7. There are two immune systems: the ________ immune system and the adaptive immune system.
8. Disease-causing agents are known as ________.
10. T cells and B cells are involved in cell-mediated and ________ immune reactions, respectively.
11. Rat pups groomed intensely by their mothers display decreased ________ release from the adrenal cortex in response to stressors in adulthood.
12. Corticosterone is a ________.
13. In laboratory animals, stress has been shown to reduce adult neurogenesis in the ________.

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 expressing various emotions using facial expressions upon request (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 temporal-lobe structures in both hemispheres. 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, subjects with bilateral amygdalar damage sometimes have some difficulty recognizing a variety of other stimuli (e.g., patterns, landscapes), particularly those stimuli that the subjects report liking the least (Adolphs & Tranel, 1999).

**Specific Role of the Medial Prefrontal Lobes in 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). 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. Recent 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 recent studies of medial prefrontal lobe activity have employed 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).

Many theories of the specific functions of the medial prefrontal lobes have been proposed, including the following: The medial prefrontal lobes are thought 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., 2006), and to respond to social rejection (Somerville, Heatherton, & Kelley, 2006). Which is correct? Perhaps all are; the medial prefrontal lobes are large and complex, and they likely perform many functions. This point was made by a study by Kawasaki and colleagues (2005).

Kawasaki and colleagues used microelectrodes to record from 267 neurons in the anterior cingulate cortices in the medial prefrontal lobes of four patients prior to surgery. They assessed the activity of the neurons when the patients viewed photographs with emotional content. Of these 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 involved in emotional processing are sparse and widely distributed in this area of the human brain.

**Lateralization of Emotion**

There is a lot of 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) — you read a bit about this in Chapter 16. The results of these studies have led to several different theories of the cerebral lateralization of emotion (see Demaree et al., 2005); the following are the two most prominent:

- **The right-hemisphere model** 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.

However, neither of these general theories is strongly supported by the results of recent research. Recently, most studies of the cerebral lateralization of emotion have employed functional brain-imaging methods. Although the results of functional brain-imaging studies of emotion have been complex and variable, it is possible to derive some general conclusions about the cerebral lateralization of emotion from Wager and colleagues’ (2003) meta-analysis of the data from 65 of these studies.
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, all kinds of evidence of lateralization of emotional processing emerged. Some kinds of emotional processing were lateralized to the left hemisphere in particular structures and to the right in others. Moreover, there was a tendency for some emotional processes to be more lateralized in males than in females. New theories of the lateralization of emotion need to focus on particular brain structures and on sex differences.

Before leaving the topic of lateralization of emotion, I would like to mention a finding that has been linked to it. Human facial expressions tend to be asymmetrical. Each facial expression begins on the left side of the face and, when fully expressed, is more pronounced there—which implies right-hemisphere dominance. Remarkably, the same asymmetry of facial expressions has been documented in monkeys (Hauser, 1993)—see Figure 17.13. This observed asymmetry of facial expressions is sometimes used to argue for the right-hemisphere model of emotion.

**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 control of language varies substantially from person to person, and you just learned that males tend to display more lateralization of emotional functions than females. Nevertheless, few studies of the neural mechanisms of emotion have focused on individual differences. 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 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 clearly theme appeared where the text discussed the use of polygraphy in lie detection, the relation between testosterone and aggression in men, the critical interpretation of reports of correlations between stress and ill health, the possibility of susceptibility to stress being communicated from generation to generation by maternal care, and the complex structure of the amygdala.

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. 433)
Cannon-Bard theory (p. 433)
Decorticate (p. 434)
Sham rage (p. 434)
Limbic system (p. 435)
Kluver-Bucy syndrome (p. 435)
Amygdala (p. 435)
Polygraphy (p. 436)
Control-question technique (p. 436)
Guilty-knowledge technique (p. 436)
Facial feedback hypothesis (p. 437)
Duchenne smile (p. 438)

17.2 Fear, Defense, and Aggression
Fear (p. 439)
Defensive behaviors (p. 439)
Aggressive behaviors (p. 439)
Alpha male (p. 439)
Target-site concept (p. 440)

17.3 Neural Mechanisms of Fear Conditioning
Fear conditioning (p. 441)
Contextual fear conditioning (p. 442)
Hippocampus (p. 443)
Lateral nucleus of the amygdala (p. 443)
Prefrontal lobe (p. 443)

17.4 Stress and Health
Stress (p. 443)
Stressors (p. 443)
Adrenocorticotropic hormone (ACTH) (p. 444)
Glucocorticoids (p. 444)
Adrenal cortex (p. 444)
Adrenal medulla (p. 444)
Cytokines (p. 444)
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Gastric ulcers (p. 445)
Psychoneuroimmunology (p. 445)
Immune system (p. 445)
Antigens (p. 445)
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Pathogens (p. 445)
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Toll-like receptors (p. 446)
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Cell-mediated immunity (p. 446)
T cells (p. 446)
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B cells (p. 446)
Antibodies (p. 446)
T-reg cells (p. 447)
Autoimmune diseases (p. 447)
Epigenetic (p. 449)
Corticosterone (p. 450)
Adrenalectomy (p. 450)

17.5 Brain Mechanisms of Human Emotion
Urbach-Wiethe disease (p. 451)
Suppression paradigm (p. 451)
Reappraisal paradigm (p. 451)