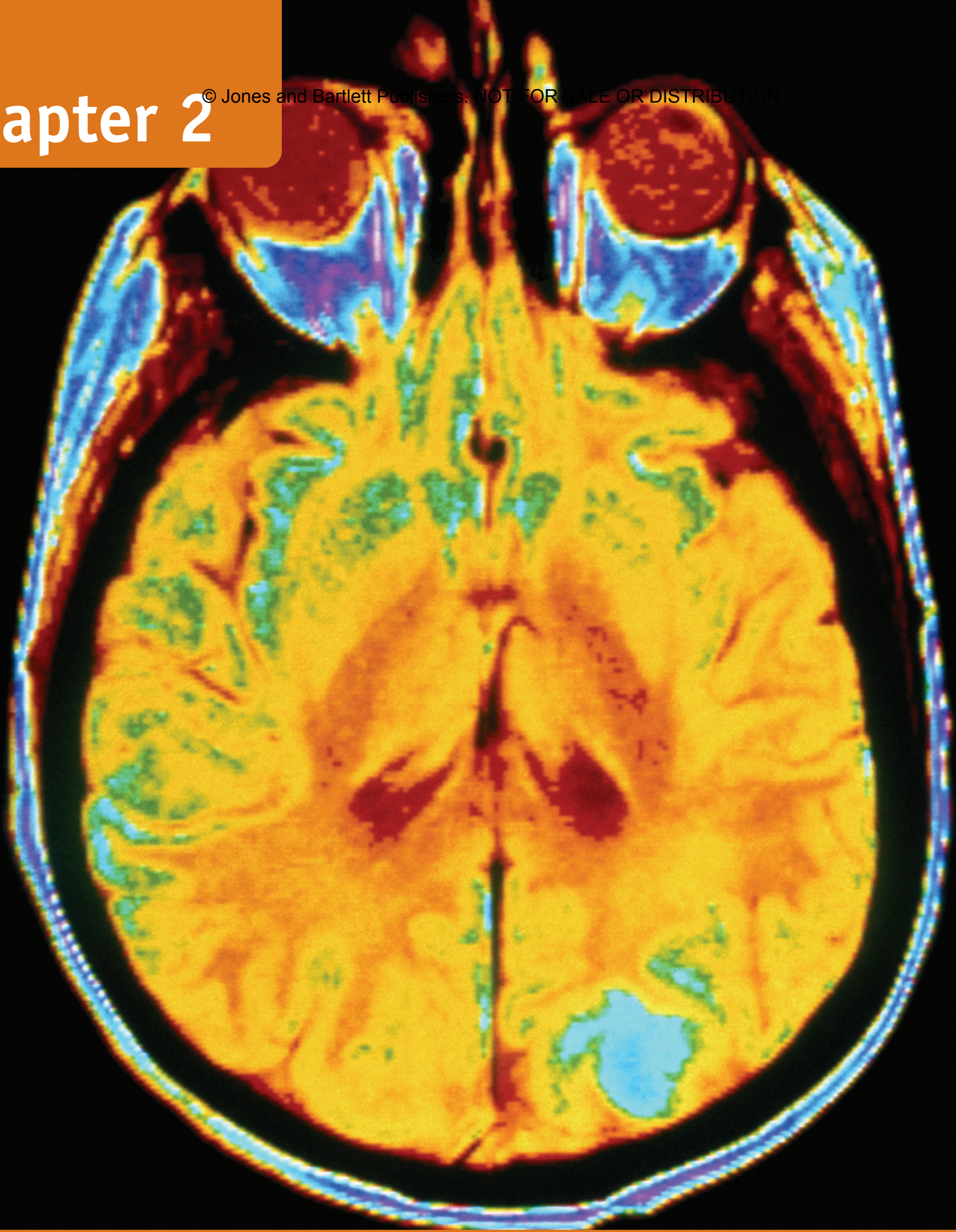
Chapter 2



Physiology of Stress

To understand the stress response, we must possess a fundamental knowledge not only of psychology but of physiology as well.
—George Everly

Hans Selye's discovery of a direct relationship between chronic stress and the excessive wear and tear throughout the body laid the foundation for a clearer understanding of how physiological systems work in an extremely complex and integrative way. Perhaps because of this discovery and the fact that physical deterioration is so noticeable, much attention has been directed toward the physiology of stress. This chapter will take you through some basic concepts that explain the physiological dynamics involved with the stress response—specifically, the immediate, intermediate, and prolonged effects on the body. These processes will be explained in terms of "pathways," which set in action the systematic and integrative steps of the stress response. Because physiology involves specific nomenclature outside the realm of your everyday vocabulary, you may find the nature of this chapter to be very specific and its contents very detailed. Most likely it will merit more than one reading to fully grasp, understand, and appreciate how the body responds to stress. The importance of a strong familiarity with human physiology as influenced by stressful stimuli becomes evident when the necessary steps are taken to effectively deal with the symptoms they produce, especially when using relaxation techniques. For example, it is important to know how the body functions when using specific imagery, visualization, music therapy, and biofeedback.

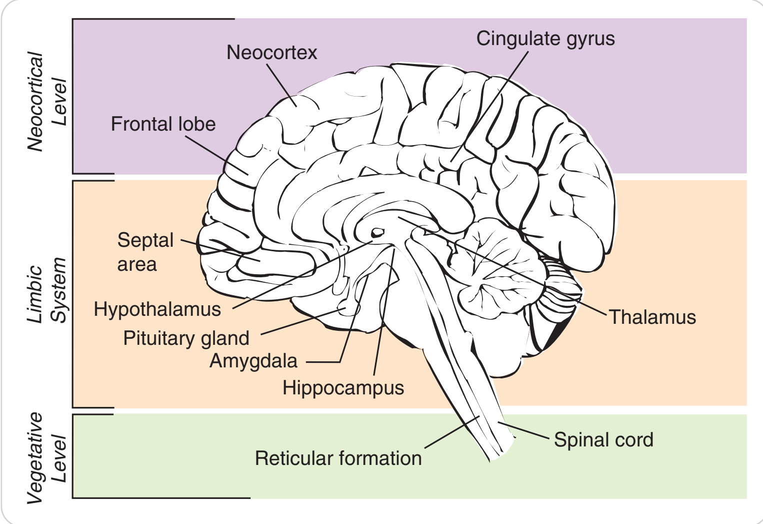


FIGURE 2.1 Three levels of the human brain: vegetative level, limbic system, and neocortical level.

In many circles, this topic of study is referred to as *psychophysiology*. This term reflects the fact that a sensory stimulus that prompts the stress response must be processed at the mental level before it can cascade down one or more physiological pathways. In other words, the term **psychophysiology** suggests that there is a mind-body relationship and supports the theory that many diseases and illnesses are psychosomatic, meaning that their origins lie in the higher brain centers. Although the mind-body dualism suggested by Descartes is no longer a viable model for a complete understanding of human physiology, to hold an appreciation of the "whole person" we must first examine the parts to understand how they connect to that whole.

Three systems are directly involved with the physiology of stress: the nervous system, the endocrine system, and the immune system, all of which can be triggered by perceived threats. Because the immune system is so closely linked to the disease process, it will be dealt with separately in Chapter 3.

The Central Nervous System

The nervous system can be divided into two parts: the **central nervous system (CNS)**, which consists of the brain and spinal cord, and the peripheral nervous system (PNS), comprising all neural pathways to the extremities. The human brain is further divided into three levels: the vegetative level, the limbic system, and the neocortical level (FIG. 2.1).

The Vegetative Level

The lowest level of the brain consists of both the reticular formation and the brain stem. The reticular formation, or more specifically the fibers that make up the **reticular activating system (RAS)**, is the link connecting the brain to the spinal cord. Several stress physiologists believe that it is the bridge joining the mind and the

Psychophysiology: A field of study based on the principle that the mind and body are one, where thoughts and perceptions affect potentially all aspects of physiology.

Central nervous system (CNS): Consists of the brain, spinal column, and peripheral nervous system (PNS), comprising all neural pathways to the extremities.

Reticular activating system (RAS): The neural fibers that link the brain to the spinal column.

body as one; this organ functions as a communications link between the mind and the body. The brain stem, consisting of the pons, medulla oblongata, and mesencephalon, is responsible for involuntary functions of the human body, such as heartbeat, respiration, and vasomotor activity. It is considered the automatic-pilot control center of the brain, which assumes responsibility for keeping the vital organs and vegetative processes functioning at all times. This level is thought to be the most primitive section of the human brain, as this portion is similar to those of all other mammals.

The Limbic System

The second or mid-level portion of the brain is called the **limbic system**. The limbic system is the emotional control center. Several tissue centers in this level are directly responsible for the biochemical chain of events that constitute the stress response Cannon observed. The limbic system consists of the thalamus, the hypothalamus, the amygdala, and the pituitary gland, also known as the master endocrine gland. These four glands work in unison to maintain a level of homeostasis within the body. For example, it is the hypothalamus that controls appetite and body-core temperature. The hypothalamus also appears to be the center that registers pain and pleasure; for this reason it is often referred to as the seat of emotions. The combination of these functions in the hypothalamus may explain why hunger decreases when body-core temperature increases in extreme ambient heat, or why appetite diminishes when you are extremely worried. Research evidence is clear that fear is first registered in the amygdala. When a threat is encountered, the hypothalamus carries out four specific functions: (1) it activates the autonomic nervous system; (2) it stimulates the secretion of adrenocorticotropic hormone (ACTH); (3) it produces antidiuretic hormone (ADH) or vasopressin; and (4) it stimulates the thyroid gland to produce thyroxine. All of these will be discussed in greater detail later.

limbic system: The mid-level of the brain, including the hypothalamus and amygdala, which is thought to be responsible for emotional processing.

Autonomic nervous system: Often referred to as the automatic nervous system, the ANS consists of the sympathetic (arousal) and parasympathetic (relaxed) nervous systems. This part of the central nervous system requires no conscious thought; actions such as breathing and heart rate are programmed to function automatically.

The Neocortical Level

The neocortex is the highest and most sophisticated level of the brain. It is at this level that sensory information is processed (decoded) as a threat or a nonthreat and where cognition (thought processes) takes place. Housed within the neocortex are the neural mechanisms allowing one to employ analysis, imagination, creativity, intuition, logic, memory, and organization. It is this highly developed area of brain tissue that is thought to separate humans from all other species.

As Figure 2.1 illustrates, the positions of these structures are such that a higher level can override a lower level of the brain. Thus, conscious thought can influence emotional response, just as conscious thought can intercede in the involuntary control of the vegetative functions to control heart rate, ventilation, and even the flow of blood. This fact will become important to recognize when learning coping skills and relaxation techniques designed to override the stress response and facilitate physiological homeostasis.

Separate from the CNS is a network of neural fibers that feed into the CNS and work in close collaboration with it. This neural tract, the peripheral nervous system (PNS), comprises two individual networks. The first is the somatic network, a bidirectional circuit responsible for transmitting sensory messages along the neural pathways between the five senses and the higher brain centers. These are called the efferent (toward periphery) and afferent (toward brain) neural pathways. The second branch of the PNS is called the **autonomic nervous system (ANS)**. The ANS regulates visceral activities and vital organs, including circulation, digestion, respiration, and temperature regulation. It received the name *autonomic* because this system can function without conscious thought or voluntary control, and does so most, if not all, of the time.

Research conducted by endocrinologist Bruce McEwen indicates that initially a stressful encounter is etched into the memory bank (so as to avoid it down the road), but that repeated episodes of stress decrease memory by weakening hippocampal brain cells. Chronic stress is thought to wither the fragile connection between neurons in this part of the brain, resulting in "brain shrinkage."

Until recently it was believed that, unlike the voluntary somatic system involved in muscle movement, the ANS

FIGURE 2.2 Brain physiology at work. (©Bradford Veley, Marquette, MI.)

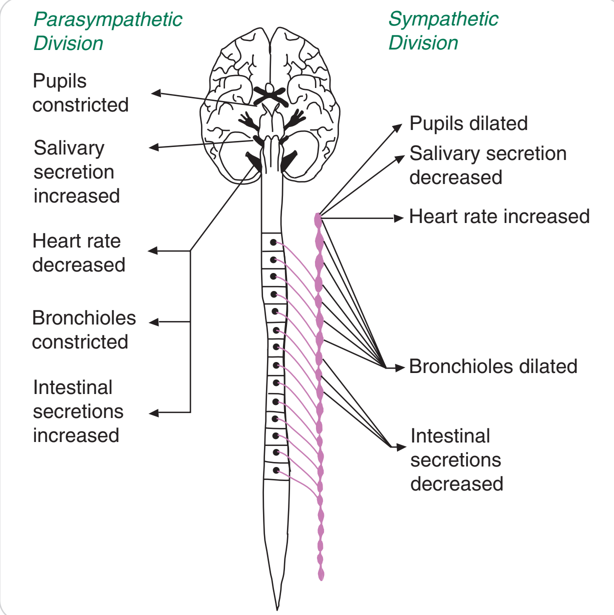


FIGURE 2.3 The sympathetic and parasympathetic systems. Internal organs are typically innervated by neural fibers from both sympathetic and parasympathetic divisions.

could not be intercepted by conscious thought, but now it is recognized that both systems can be influenced by higher mental processes. (This will be discussed more in Chapters 25 and 26.) The ANS works in close coordination with the CNS to maintain a favorable homeostatic condition throughout the body. There are two branches of the ANS that act to maintain this homeostatic balance, the **sympathetic** and **parasympathetic** nervous systems, and these are activated by the hypothalamus. Most organs are innervated (stimulated) by nerve fibers of both the sympathetic and parasympathetic systems.

The Autonomic Nervous System

The Sympathetic and Parasympathetic Nervous Systems

The sympathetic nervous system is responsible for the responses associated with the fight-or-flight response (FIG. 2.3). Through the release of substances called catecholamines, specifically **epinephrine** (adrenaline) and **norepinephrine** (noradrenaline), at various neural synapses, a series of events occurs in several organ tissues to prepare the body for rapid metabolic change and physical movement. Sympathetic drive is associated with energy expenditure, a process known as **catabolic functioning**, where various metabolites are broken down for energy in preparation for movement. It is the release of epinephrine and norepinephrine that

Sympathetic: The branch of the central nervous system that triggers the fight-or-flight response when some element of threat is present.

Parasympathetic: The branch of the central nervous system that specifically calms the body through the parasympathetic response.

Epinephrine: A special neurochemical referred to as a catacholamine, which is responsible for immediate physical readiness for stress including increased heart rate and blood pressure. It works in unison with norepinephrine.

Norepinephrine: A special neurochemical referred to as a catacholamine, which is responsible for immediate physical readiness to stress including increased heart rate and blood pressure. It works in unison with epinephrine.

Catabolic functioning: A metabolic process in which metabolites are broken down for energy in preparation for, or in the process of, exercise (fight or flight).

Stress *with a Human Face*

Perhaps no situation more clearly triggers the fight-or-flight response than face-to-face combat. This was the situation for Geof Steiner, who found himself thrown into the turmoil of the Vietnam War in the late 1960s. Think of how fast your heart beats when you sense someone following you in an unlit parking garage. Then multiply this intensity by the duration of a whole year—a typical tour of duty overseas in wartime. This is the level and duration of stress Geof experienced. Long after his return to the States, Geof found that his memories of the war were still at his coattails, haunting him and ruining his life. It got so bad that the only viable option, he surmised, was suicide. His attempt on his life quickly brought him to a VA psychiatric hospital. But his problems didn't end there: He also battled chronic alcoholism and the ruins of a failed marriage. When all was said and done, all he had to his name was a trailer on a dirt road.

At first glance, the woods of Minnesota don't seem to have anything to do with the jungles of Vietnam. But the call of the forest lured Geof out of his trailer into the woods, where he began to find a peace in nature that had eluded him with his fellow man. It was this bond that gave him a vision and a purpose to live. Inspired by nature's life force, Geof bought open tracts of land near and around his trailer. On this land he vowed to plant a tree for every soldier who died on the soil of Vietnam. Today, in Cushing, Minnesota, stands the Living Memorial Forest, the only living tribute to those who fought in a war that Geof is still trying to understand. He believes that the forest has helped him and other veterans heal the emotional scars and find the inner peace symbolized by the life of each planted tree.

causes the acceleration of heart rate, the increase in the force of myocardial contraction, vasodilation of arteries throughout working muscles, vasoconstriction of arteries to nonworking muscles, dilation of pupils and bronchi, increased ventilation, reduction of digestive activity, released glucose from the liver, and several other functions that prepare the body to fight or flee. It is the sympathetic system that is responsible for supplying skeletal muscles with oxygenated, nutrient-rich blood for energy metabolism. Currently it is thought that norepinephrine serves primarily to assist epinephrine, as the ratio of these two chemical substances released at neural synapses is 5:1 epinephrine to norepinephrine during the stress response. The effects of epinephrine and norepinephrine are very short, lasting only seconds. Because of their rapid release from neural endings, as well as their rapid influence on targeted organ tissue, the effects of the sympathetic nervous system are categorized as **immediate**.

Immediate (effects of stress): A neural response to cognitive processing in which epinephrine and norepinephrine are released, lasting only seconds.

Anabolic functioning: A physiological process in which various body cells (e.g., muscle tissue) regenerate or grow.

Acetylcholine: A chemical substance released by the parasympathetic nervous system to help the body return to homeostasis from the stress response.

Just as the sympathetic neural drive is associated with energy expenditure, the parasympathetic drive is responsible for energy conservation and relaxation. This is referred to as **anabolic functioning**, during which body cells are allowed to regenerate. The parasympathetic nervous system is dominated by the tenth cranial, or vagus, nerve, which in turn is influenced by the brain stem. When activated, the parasympathetic nervous system releases **acetylcholine** (ACh), a neurological agent that decreases metabolic activity and returns the body to homeostasis. The influence of the parasympathetic drive is associated with a reduction in heart rate, ventilation, muscle tension, and several other functions. Both systems are partially active at all times; however, the sympathetic and parasympathetic systems are mutually exclusive in that they cannot dominate visceral activity simultaneously. These two systems allow for the precise regulation of visceral organ activity, much like the use of the accelerator and brake when driving. Sympathetic arousal, like a gas pedal pushed to the car floor, becomes

BOX 2.1 **Hormonal Imbalance**

The endocrine system is an amazing yet delicate system of chemical properties aligned to ensure physiological homeostasis. The stress hormone dehydroepiandrosterone (DHEA), for example, is secreted from the adrenal gland. DHEA is known as a sex hormone that decreases in both production and secretion throughout the aging process. Speculation suggests that supplementation of DHEA might increase stamina and memory, and may decrease the aging process in much the same way as antioxidants; beta-carotene, vitamin C, vitamin E, and selenium. Results of a host of studies revealed that no significant changes in these aspects occurred in either animals or humans. Some scientists actually suggested that increased amounts of DHEA, above what the body normally produces, might actually promote cancer. Supplementation is recommended only on the advice of your physician.

Serotonin and **melatonin** are not stress hormones, yet they do seem to have an effect on mood. Decreases in both serotonin and melatonin are thought to be related to bouts of depression. Many things affect serotonin levels in the brain—from the natural and synthetic chemicals in the foods you eat, to the amount of sunlight you receive in the course of a day, to perhaps things we still don't know. Research is inconclusive about how serotonin affects mood. Most likely, stress affects serotonin levels as well.

the dominant force during stress, and parasympathetic tone holds influence over the body at all other times to promote homeostasis. In other words, you cannot be physically aroused and relaxed at the same time.

But there are exceptions to the dynamics of these biochemical reactions. For example, it is sympathetic nerves, not parasympathetic nerves, that release ACh in the sweat glands to decrease body-core temperature during arousal. And sympathetic and parasympathetic stimulation of salivary glands is not antagonistic; both influence the secretion of saliva. In addition, all blood vessels are influenced by sympathetic dominance, with the exception of the vasculature of the penis and clitoris, which is activated by parasympathetic innervation.

The Endocrine System

The endocrine system consists of a series of glands located throughout the body that regulate metabolic functions requiring endurance rather than speed. The endocrine system is a network of four components: glands, hormones, circulation, and target organs. Endocrine glands manufacture and release biochemical substances called hormones. Hormones are chemical messengers made up of protein compounds that are programmed to attach to specific cell receptor sites to alter (increase or decrease) cell metabolism. Hormones are transported through the bloodstream from the glands that produced them to the target organs they are called upon to influence. The heart, skeletal muscle, and arteries are among the organs targeted by hormones for metabolic change.

The glands that are most closely involved with the stress response are the pituitary, thyroid, and adrenal glands. The **pituitary gland** is called the master gland due to the fact that it manufactures several important hormones, which then trigger hormone release in other organs. The **hypothalamus** appears to have direct influence over it (FIG. 2.4). The thyroid gland increases the general metabolic rate. Perhaps the gland that has the most direct impact on the stress response, however, is the

Serotonin: A neurotransmitter that is associated with mood. A decrease in serotonin levels is thought to be related to depression. Serotonin levels are affected by many factors including stress hormones and the foods you consume.

Melatonin: A hormone secreted in the brain that is related to sleep, mood, and perhaps several other aspects of physiology and consciousness.

Pituitary gland: An endocrine gland located below the hypothalamus, which, upon command from the hypothalamus, releases ACTH and then commands the adrenal glands to secrete their stress hormones.

Hypothalamus: Often called the "seat of the emotions," the hypothalamus is involved with emotional processing. When a thought is perceived as a threat, the hypothalamus secretes a substance called corticotrophin-releasing factor to the pituitary gland to activate the fight-or-flight response.

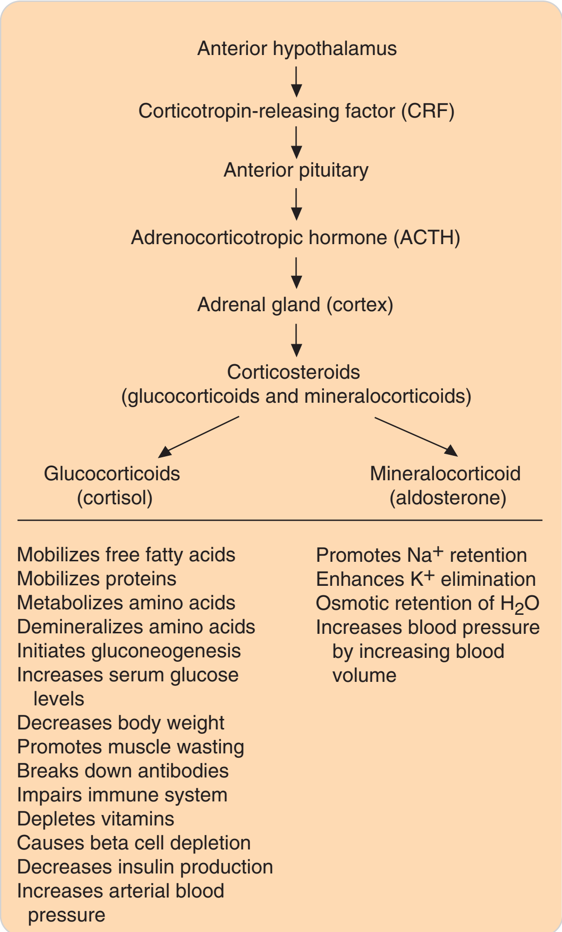


FIGURE 2.4 The physiological response to stress.

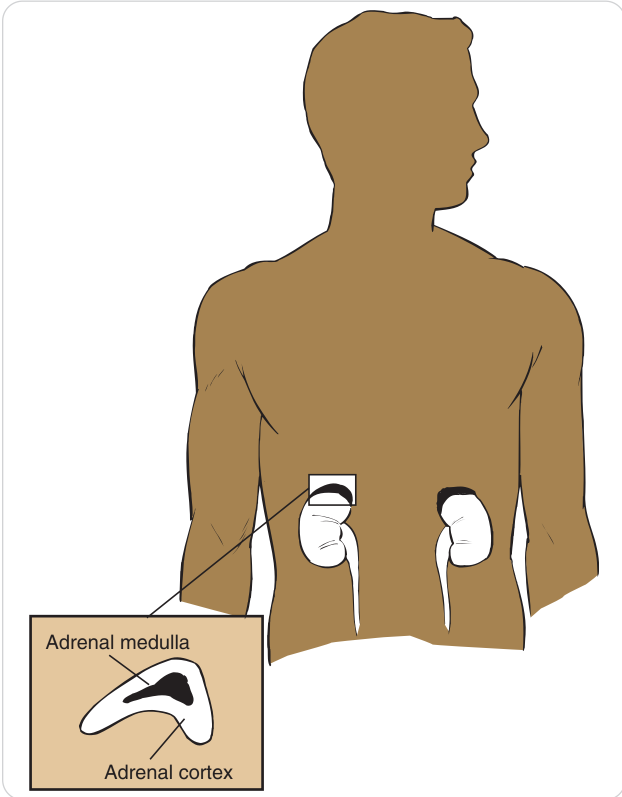


FIGURE 2.5 The adrenal gland, made up of the adrenal cortex and medulla, sits upon the top of each kidney, and is cone-shaped in appearance.

adrenal gland (FIG. 2.5). The adrenal gland, a cone-shaped mass of tissue about the size of a small grapefruit, sits on top of each kidney. The adrenal gland has two distinct parts, each of which produces hormones with very different functions. The exterior of the adrenal gland is called the adrenal cortex, and it manufactures and releases hormones called corticosteroids. There are two types of **corticosteroids**: glucocorticoids and mineralocorticoids. **Glucocorticoids** are a family of biochemical agents that includes cortisol and cortisone, with cortisol being the primary one. Its function is to help to generate glucose, through the degradation of proteins (amino acids) during a process called gluconeogenesis in the liver, as an energy source for both the central nervous system (the brain) and skeletal muscles during physical exercise. **Cortisol** is also involved in the process of lipolysis, or the mobilization and breakdown of fats (fatty acids) for energy. Recent clinical studies have linked increased levels of cortisol with suppression of the immune system. It appears that cortisol metabolizes (degrades) white blood cells. A metaphor to illustrate this process is the situation in which you resort to burning the furniture to keep warm once you exhaust your supply of firewood. As the

Adrenal gland: The endocrine glands that are located on top of each kidney that house and release several stress hormones including the catecholamines epinephrine and norepinephrine, cortisol.

Corticosteroids: Stress hormones released by the adrenal cortex, such as cortisol and cortisone.

Glucocorticoids: A family of biochemical agents that includes cortisol and cortisone, produced and released from the adrenal gland.

Cortisol: A stress hormone released by the adrenal glands that helps the body prepare for fight or flight by promoting the release of glucose and lipids in the blood for energy metabolism.

BOX 2.2 **Adrenal Fatigue and Adrenal Failure**

With the alarming rate of chronic fatigue syndrome, the word in some medical circles is that many Americans suffer from adrenal fatigue, due to prolonged stress. What is adrenal fatigue? Because of the amount of chronic stress many people admit to experiencing, the adrenal glands begin to work overtime. Signs of exhaustion and the inability to produce and release the host of catecholamines and hormones for fight or flight, appear to give credence to Hans Selye's General Adaptation Syndrome. The symptoms of adrenal insufficiency include fatigue, dizziness, low blood sugar (resulting in cravings and subsequent weight gain), and depression. Weak adrenals are associated with the incidence of autoimmune diseases, ranging from chronic fatigue syndrome and lupus to rheumatoid arthritis. Due to the complexities of human physiology, poor adrenal function is also associated with aggravated symptoms of menopause. Addison's disease is the name given to those with adrenal failure, a condition where the adrenal glands are no longer able to produce and secrete the necessary hormones for metabolic function.

number of white blood cells decreases, the efficiency of the immune system decreases, setting the stage for illness and disease. (This will be discussed in greater detail in Chapter 3.) It has also come to light that increased cortisol can direct excess amounts of cholesterol into the blood, thereby adding to associated artery plaque buildup and leading to hypertension and coronary heart disease. **Mineralocorticoids**, specifically aldosterone, are secreted to maintain plasma volume and electrolyte (sodium and potassium) balance, two essential functions in the regulation of circulation. (The exact mechanisms will be discussed later in this chapter.)

The inside of the adrenal gland is called the **adrenal medulla**. This portion of the gland secretes catecholamines (epinephrine and norepinephrine), which act in a similar fashion as those secreted at the endings of sympathetic nerves. The adrenal medulla releases 80 percent epinephrine and 20 percent norepinephrine. Under the influences of stress, up to three hundred times the amount of epinephrine can be found in the blood compared to the amount in samples taken at rest.

The Neuroendocrine Pathways

Evolutionary adaptations have provided several backup systems to ensure the survival of the human organism. Not all pathways act at the same speed, yet the ultimate goal is the same: physical survival. First, not only does the hypothalamus initiate activation of the sympathetic nervous system to cause an immediate effect (Table 2.1), but the posterior hypothalamus also has a direct neural pathway, called the sympathetic preganglionic neuron, that links it to the adrenal medulla. Next, upon stimulation by the posterior hypothalamus, the adrenal medulla secretes both epinephrine and norepinephrine. Once in the bloodstream, these catecholamines reinforce the efforts of the sympathetic drive, which has already released these same substances through sympathetic neural endings throughout the body. The release of epinephrine and norepinephrine from the adrenal medulla acts as a backup system for these biochemical agents to ensure the most efficient means of physical survival. The hormonal influences brought about by the adrenal medulla are called **intermediate stress effects**. Because their release is via the bloodstream rather than neural endings, travel time is longer (approximately twenty to thirty seconds), and unlike the release of these substances from sympathetic neural endings, the effects of catecholamines from the adrenal medulla can last as long as two hours when high levels of secretions are circulating in the bloodstream.

In addition, there is a third and potentially more potent system joining the efforts of the nervous and endocrine systems to prepare the body for real or perceived danger. Neural impulses received by the hypothalamus as potential threats create a chain of biochemical messages,

Mineralocorticoids: A class of hormones that maintain plasma volume and electrolyte balance, such as aldosterone.

Adrenal medulla: The portion of the adrenal gland responsible for secreting epinephrine and norepinephrine.

Intermediate stress effects: The hormonal response triggered by the neural aspects of the adrenal medulla that are released directly into the blood, lasting minutes to hours.

TABLE 2.1 Pathways of Stress Response

Effects	Reaction	Time
The body has several backup dynamics to help ensure physical survival. Here, these dynamics are broken down into categories based on the duration of their metabolic reactions.		
Immediate effects	Epinephrine and norepinephrine from the sympathetic nervous system	2–3 seconds
Intermediate effects	Epinephrine and norepinephrine from adrenal medulla	20–30 seconds
Prolonged effects	ACTH, vasopressin, and thyroxine neuroendocrine pathways	Minutes, hours, days, or weeks

SOURCE: R. Allen, *Human Stress: Its Nature and Control* (Minneapolis, MN: Burgess, 1983).

which like a line of falling dominos cascade through the endocrine-system glands. Because the half-life of these hormones and the speed of their metabolic reactions vary in length from hours to weeks in some cases, this chain of reactions is referred to as the **prolonged effect of stress**.

The ACTH Axis

Physiologically speaking, a biochemical pathway is referred to as an axis. In this section we will discuss the ACTH axis. The other two axes, the **vasopressin axis** and the **thyroxine axis**, are covered in the following sections.

The **ACTH axis**, also known as the hyphothalmic-pituitary-adrenal **(HPA) axis** (FIG. 2.6), begins with the release of corticotropin-releasing factor (CRF) from the anterior hypothalamus. This substance activates the pituitary gland to release ACTH, which travels via the bloodstream to in turn activate the **adrenal cortex**. Upon stimulation by ACTH, the adrenal cortex releases a set of corticosteroids (cortisol and aldosterone), which act to increase metabolism and alter body fluids, and thus blood pressure, respectively. The effects of hormones released by the adrenal cortex are considered to be prolonged because they activate their functions for minutes to hours. Note that increased secretions of cortisol in the blood act primarily to ensure adequate supplies of blood sugar for energy metabolism. However, when increasingly high levels of cortisol are observed due to chronic stress, this hormone compromises the integrity of several physiological systems.

The Vasopressin Axis

Vasopressin or antidiuretic hormone (ADH) is synthesized in the hypothalamus but is released by the pituitary through a special portal system. The primary purpose of vasopressin is to regulate fluid loss through the urinary tract. It does this in a number of ways, including water reabsorption and decreased perspiration. By altering blood volume, however, it also has a pronounced effect on stroke volume, or the amount of blood that is pumped through the left ventricle of the heart with each contraction. Consequently ADH has a pronounced effect on blood pressure. Under normal circumstances, ADH

Prolonged effect of stress: Hormonal effects that may take days or perhaps more than a week to be fully realized from the initial stress response.

Vasopressin axis: A chain of physiological events stemming from the release of vasopressin or antidiuretic hormone (ADH).

Thyroxine axis: A chain of physiological events stemming from the release of thyroxine.

ACTH axis: A physiological pathway whereby a message is sent from the hypothalamus to the pituitary, then on to the adrenal gland to secrete a flood of stress hormones for fight or flight.

(HPA) axis: The hypothalamic-pituitary-adrenal axis, a term synonymous with the ACTH axis.

Adrenal cortex: The portion of the adrenal gland that produces and secretes a host of corticosteroids (e.g., cortisol and aldosterone).

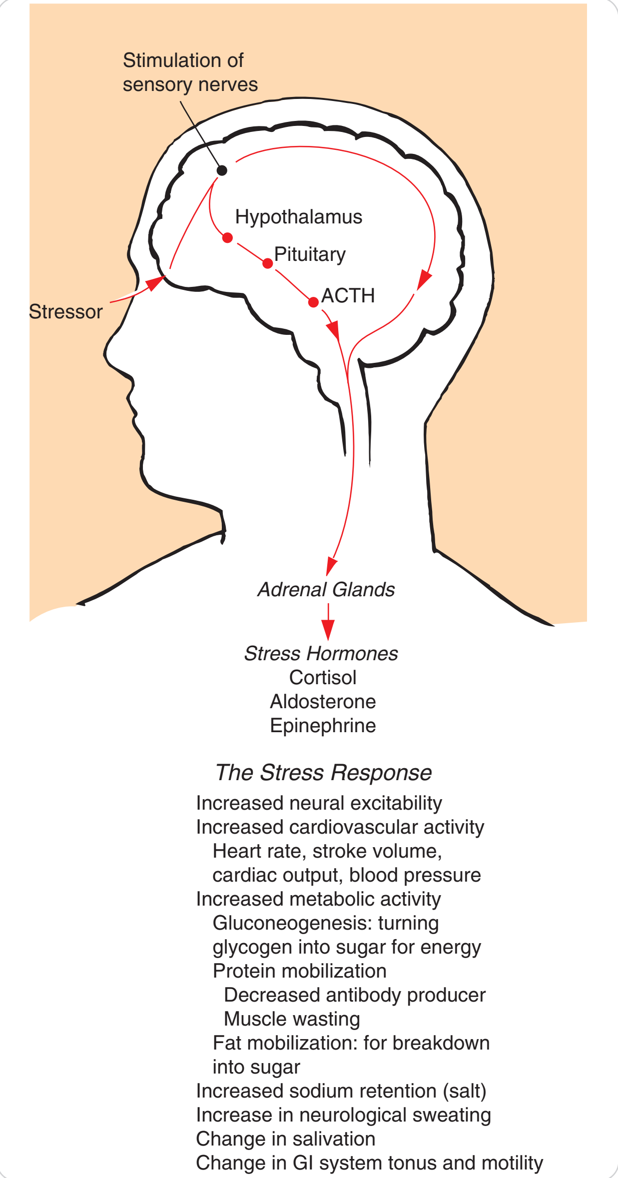


FIGURE 2.6 The ACTH axis.

regulates blood pressure by either increasing blood volume (changing the concentration of water in the blood) should it be too low, or decreasing blood volume when it becomes too high. Under the influence of chronic stress, however, many regulatory mechanisms in the body lose their ability to maintain physiological homeostasis. Consequently, the increased secretions of vasopressin produced under duress will increase blood pressure even when someone already has elevated resting values; this is known as hypertension. The purpose of vasopressin as well as aldosterone, epinephrine, and norepinephrine is to increase blood pressure to ensure that active muscles receive oxygenated blood, but under chronic stress in a resting state this hormonal response—the abundance of stress hormones—is literally overkill, leading to hypertension and death due to CHD.

The Thyroxine Axis

Stimulation in the hypothalamus triggers the release of thyrotropic hormone–releasing factor (TRF). TRF is transported through a special portal system to the anterior portion of the pituitary, where it stimulates the secretion of thyrotropic hormone (TTH). Once in the bloodstream, TTH follows a path to the thyroid gland, which stimulates the release of two more hormones: thyroxine and triiodothyronine. The purpose of these two hormones is to increase overall metabolism, or basal metabolic rate (BMR). Thyroxine is powerful enough to double one's rate of metabolism. Note that the effects of this pathway are very prolonged. Because the production of thyroxine takes several days, it may be ten days to two weeks before visible signs manifest as significant symptoms through this pathway. This explains why you may come down with a cold or flu a week after a very stressful encounter rather than the day after. The metabolic effects of thyroxine released through this pathway are increased workload on the heart muscle, increased gastrointestinal activity (e.g., gastritis), and, in some cases, a condition called **cerebration** or cerebral excitivity, which is associated with anxiety attacks and/or insomnia.

A Parable of Psychophysiology

A metaphor can be used to illustrate the three pathways discussed earlier (FIG. 2.7). Let us say that your life is in danger because of a classified CIA document you inadvertently stumbled across, and you now pose a threat to national security. You want to deliver a message and a copy of this document to your family, who live a few hundred miles away, to let them know your life is in danger. This message is, of course, very important and you want to make sure your family gets it, so you use a couple of methods to ensure its delivery. First you immediately place a phone call to your parents'

Cerebration: A term used to describe the neurological excitability of the brain, associated with anxiety attacks and insomnia.

BOX 2.3 Insomnia and Brain Physiology

Brain chemistry is a complicated subject and our understanding of it is embryonic at best, but some facts are clear with regard to how brain physiology works. Not only does an "active" mind release epinephrine and norepinephrine in the brain, compromising the ability to fall sleep, but other neurotransmitters—specifically, melatonin and serotonin—are affected by a host of daily rituals and behaviors, ranging from nutritional habits, caffeine intake, and sunlight exposure to cell phone use. Melatonin is a hormone secreted in the pituitary of the brain. This neurotransmitter is not only affected by real and artificial light, but is also thought to be associated with both sleep patterns and skin pigmentation. As daylight decreases, the melatonin level increases, giving rise to the belief that increases in melatonin help promote sleep.

The brain neurotransmitter serotonin is partially affected by light. Decreases in light decrease serotonin levels, a factor associated with seasonal affective disorder (SAD) and depression.

While the use of artificial evening light can alter serotonin levels, it can decrease melatonin levels, thus affecting natural sleep patterns (sleep patterns have changed dramatically since the turn of the twentieth century with the use of electricity). Cell phone use is thought to decrease melatonin with similar results. Increased consumption of carbohydrates (late-night snacks) can increase serotonin levels, which may, in turn, affect melatonin levels. Medications for depression include selective serotonin reuptake inhibitors (SSRIs), which act to increase serotonin levels. This activity may, in fact, act to decrease melatonin levels, thus affecting a full night's sleep.

house because it is the quickest way to deliver the message, and the message is received instantaneously on their answering machine. This is like the action of the sympathetic nervous system. As a backup, you send a wire via Western Union in case no one listens to the answering machine. This form of communication is fairly quick, taking perhaps minutes to hours, and is equivalent to the preganglionic nerve to the adrenal medulla. And because you also need to send a copy of the document to further explain the contents of your message, you ship a package via overnight mail delivery. This means of communication allows more comprehensive information to be sent, but it takes much longer. It is like the neuroendocrine pathways. Similarly, our bodies are composed of several communication systems, each with its own time element and function, the overall purpose being to prepare the body for physical survival. As illustrated by this story, there are many backup systems, fast and slow, to get the message through.

Immediate effects	Intermediate effects	Prolonged effects
Phone call	Western Union telegram	Overnight delivery

FIGURE 2.7 Like communication networks that send and receive messages, the human body has several complex messenger systems, which not only see that the information gets through but also ensure that the body will survive the perceived threat after the message is received.

In the short term, the combination of these various neural and hormonal pathways serves a very important purpose: physical survival. However, when these same pathways are employed continuously due to the influence of chronic stressors, the effects can be devastating to the body. In light of the fact that the body prepares physically for threats, whether they are of a physical, mental, emotional, or spiritual nature, repeated physical arousal suggests that the activation of the stress response is an obsolete mechanism for dealing with stressors that do not pertain to physical survival. The inability of the body to return to homeostasis can have significant effects on the cardiovascular system, the digestive system, the musculoskeletal system, and, research now indicates, the immune system. Organs locked into a pattern of overactive metabolic activity will eventually show signs of dysfunction. For instance, constant pressure and repeated wear and tear on the arteries and blood vessels can cause tissue damage to the inner lining of these organs. Numerous changes can also occur throughout the digestive system, including constipation, gastritis, diarrhea, and hemorrhoids. As was observed by Selye, the inability of the body to return to homeostasis can set the stage for signs and symptoms of disease and illness.

A Decade of Brain Imaging Research

Prior to the start of each decade, the medical profession selects one area of human physiology to study in-depth. In 1990, the brain was chosen as the target of this research. With the advancement of electromagnetic technology and magnetic resonance imaging (neuroimaging), scores of studies have been conducted to determine which aspects of the brain are active in a variety of mental states and thought processes (Zimmer, 2003). Only recently have the dots been connected to provide a more accurate understanding of this most complex human organ. Bruce McEwen is one researcher working in this area. In his book *The End of Stress as We Know It,* McEwen synthesizes much of this information, including the work of his protégé Robert Sapolsky, author of the acclaimed book *Why Zebras Don't Get Ulcers.* Here are some highlights from McEwen's research:

- The hippocampus and the amygdala together form conscious memories of emotional events.
- The hippocampus is highly sensitive to the stress hormone cortisol, which aids in memory formation of stress.
- The hippocampus region is rich in receptor sites for glucocorticoids.
- The amygdala is responsible for the emotional content of memory, particularly fear.
- Repeated excessive exposure to cortisol accelerates the aging process of the hippocampus and may, in fact, damage or shrink brain cells. Moreover, chronic stress may affect memory and learning processes [in Vietnam vets with post-traumatic stress disorder (PTSD), this region of the brain was 26 percent smaller than in their peers without PTSD].
- Research by Sapolsky reveals that damage to brain cells (in animals) due to chronic stress appears to be irreversible.

McEwen concludes that the human brain is, indeed, wired for stress, or "**allostatic load**" as he calls it. While some neurophysiologists have been investigating the stress response in the brain, however, others have been looking at states of consciousness. This vein of research will be discussed in Chapter 18.

Allostatic load: A term coined by stress researcher Bruce McEwen to replace the expression "stressed out"; the damage to the body when the allostatic (stress) response functions improperly or for prolonged states, causing physical damage to the body.

SUMMARY

- Psychophysiology is a term to describe the body's physiological reaction to perceived stressors, suggesting that the stress response is a mind-body phenomenon.
- There are three physiological systems that are directly involved in the stress response: the nervous system, the endocrine system, and the immune system.
- The nervous system comprises two parts: the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS includes three levels: the vegetative, the limbic, and the neocortical.
- The limbic system houses the hypothalamus, which controls many functions, including appetite and emotions. The neocortical level processes and decodes all stimuli.
- The most important part of the PNS regarding the stress response is the autonomic nervous system, which activates sympathetic and parasympathetic neural drives. Sympathetic drive causes physical arousal (e.g., increased heart rate) through the secretion of epinephrine and norepinephrine, whereas parasympathetic drive maintains homeostasis through the release of ACh. The two neural drives are mutually exclusive, meaning that you cannot be aroused and relaxed at the same time.
- The endocrine system consists of a series of glands that secrete hormones that travel through the circulatory system and act on target organs. The major stress gland is the adrenal gland.
- The adrenal gland has two parts, each performing different functions. The cortex (outside) secretes cortisol and aldosterone, while the medulla (inside) secretes epinephrine and norepinephrine.
- The nervous system and endocrine system join together to form metabolic pathways or axes. There are three pathways: the ACTH axis, the vasopressin axis, and the thyroxine axis.
- The body has several backup mechanisms to ensure physical survival. These systems are classified as immediate, lasting seconds (sympathetic drive); intermediate, lasting minutes (adrenal medulla); and prolonged, lasting hours if not weeks (neuroendocrine pathways). Each system is involved in several metabolic pathways.
- Stress is considered one of the primary factors associated with insomnia. Good sleep hygiene consists of behaviors that help promote a good night's sleep rather than detract from it, including decreased caffeine consumption, consistent bed times, and a host of effective relaxation techniques that enhance sleep quality.
- A decade of brain research reveals that humans are hard-wired for stress through an intricate pattern of neural pathways designed for the fight-or-flight response. Research also suggests that chronic stress appears to atrophy brain tissue, specifically the hippocampus.

STUDY GUIDE QUESTIONS

1. What role does the nervous system play in the stress response?
2. What role does the endocrine system play in the stress response?
3. Name and explain the three pathways (axes) of stress physiology.
4. What does new brain imaging tell us about stress physiology?

SELF-ASSESSMENT

As noted in this chapter, the stress response has immediate, intermediate, and prolonged effects. To reinforce your understanding of each type, reflect on how your body reacts to stress through these three processes.

1. What do you feel when immediately threatened?

	Yes	No
a. Tingling sensations	_______	_______
b. Sweating	_______	_______
c. Muscle tension	_______	_______
d. Rapid heart rate	_______	_______
e. Rapid breathing (or holding your breath)	_______	_______
f. Rush of blood to the head and face (feelings of being flushed)	_______	_______

g. Other ____

2. How would you best classify your body's intermediate (within hours) response to stress?

a. Tension headache

b. Stomachache

c. Sore neck and shoulders

d. Sore throat

e. Other ______________________

f. Other ______________________

g. Other ______________________

h. Other ______________________

3. What do you notice as long-term effects of prolonged (5–10 days) stress?

a. Cold or flu

b. Broken-out face

c. Herpes breakout (around lips)

d. Menstrual period

e. Other ______________________

f. Other ______________________

g. Other ______________________

h. Other ______________________

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