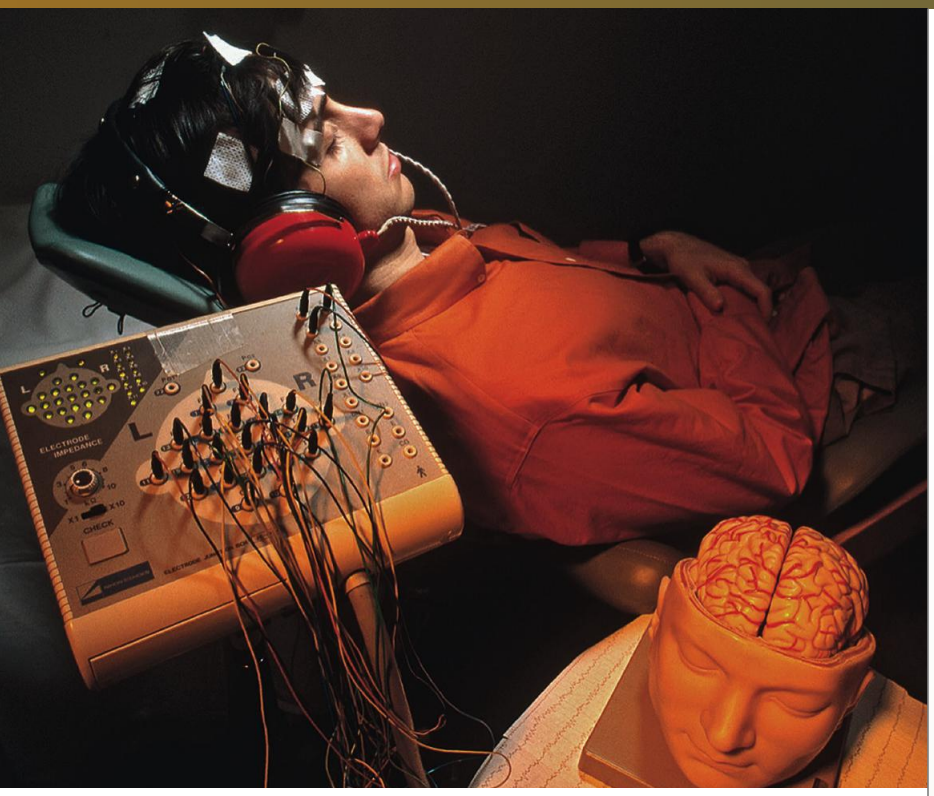
CHAPTER 8

Consciousness, the Brain, and Behavior



Brain function is monitored by an electroencephalogram (EEG).

Chapters 6 and 7 introduced some of the fundamental mechanisms underlying the processing of information in the nervous system. The focus was on the transmission of information within neurons, between neurons, and from the peripheral nervous system (PNS) to the central nervous system (CNS). In this chapter, you will learn about higher-order functions and more complex processing of information that occurs within the CNS. We discuss the general phenomenon of consciousness and its variable states of existence, as well some of the important neural mechanisms involved in the processing of our experiences. Although advances in electrophysiological and brain-imaging techniques are yielding fascinating insights, there is still much that we do not know about these topics. If you can imagine that, for any given neuron, there may be as many as 200,000 other neurons connecting to it through synapses, you can begin to appreciate the complexity of the systems that control even the simplest behavior.

The general principle of physiology most obviously on display in this chapter is that information flow between cells, tissues, and organs is an essential feature of homoeostasis and allows for integration of physiological processes. The nervous system "information" discussed previously involved phenomena like chemical and electrical gradients, graded potentials, and action potentials. Those are the essential

physiological building blocks for the higher-order processes discussed in this chapter, which include our abilities to consciously pay attention, be motivated, learn, remember, and communicate with others. These abilities are essential determinants of many complex behaviors that help us maintain homeostasis. ■

8.1 States of Consciousness

The term *consciousness* includes two distinct concepts: **states of consciousness** and **conscious experiences.** The first concept refers to levels of alertness such as being awake, drowsy, or asleep. The second refers to experiences a person is aware of—thoughts, feelings, perceptions, ideas, dreams, reasoning—during any of the states of consciousness.

A person's state of consciousness is defined in two ways: (1) by behavior, covering the spectrum from maximum attentiveness to comatose; and (2) by the pattern of brain activity that can be recorded electrically. This record, known as the **electroencephalogram** (**EEG**)**,** portrays the electrical potential difference between different points on the surface of the scalp. The EEG is such a useful tool in identifying the different states of consciousness that we begin with it.

Electroencephalogram

Neural activity is manifested by the electrical signals known as graded potentials and action potentials (Chapter 6). It is possible to record the electrical activity in the brain's neurons—particularly those in the cortex near the surface of the brain—from the outside of the head. Electrodes, which are wires attached to the head by a salty paste that conducts electricity, pick up electrical signals generated in the brain and transmit them to a machine that records them as the EEG.

Though we often think of electrical activity in neurons in terms of action potentials, action potentials do not usually contribute directly to the EEG. Action potentials in individual neurons are also far too small to be detected on an EEG recording. Rather, EEG patterns are largely due to synchronous graded potentials—in this case, summed postsynaptic potentials (see Chapter 6) in the many hundreds of thousands of brain neurons that underlie the recording electrodes. The majority of the electrical signal recorded in the EEG originates in the pyramidal cells of the cortex (review Figure 6.39). The processes of these large cells lie close to and perpendicular to the surface of the brain, and the EEG records postsynaptic potentials in their dendrites.

EEG patterns are complex waveforms with large variations in both amplitude and frequency (**Figure 8.1**). (The properties of a wave are summarized in Figure 7.22.) The wave's amplitude, measured in microvolts (μV), indicates how much electrical activity of a similar type is occurring beneath the recording electrodes at any given time. A large amplitude indicates that many neurons are being activated simultaneously. In other words, it indicates the degree of synchronous firing of the neurons that are generating the synaptic activity. On the other hand, a small amplitude indicates that these neurons are less activated or are firing asynchronously. The amplitude may range from 0.5 to 100 μV, which is about 1000 times smaller than the amplitude of an action potential.

The frequency of the wave indicates how often it cycles from the maximal to the minimal amplitude and back. The frequency is measured in hertz (Hz, or cycles per second) and may vary from 0.5 to 40 Hz or higher. Four distinct frequency ranges that define different states of consciousness are characteristic of EEG patterns. In general, lower EEG frequencies indicate less responsive states, such as sleep, whereas higher frequencies indicate increased alertness. As we will see, one stage of sleep is an exception to this general relationship.

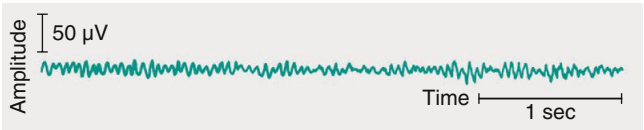


Figure 8.1 EEG patterns are wavelike. This represents a typical EEG recorded from the parietal or occipital lobe of an awake, relaxed person, with a frequency of approximately 20 Hz and an average amplitude of 20 μV.

PHYSIOLOGICAL INQUIRY

■ What is the approximate duration of each wave in this recording?

Answer can be found at end of chapter.

The neuronal networks underlying the wavelike oscillations of the EEG and how they function are still not completely understood. Wave patterns vary not only as a function of state of consciousness but also according to where on the scalp they are recorded. Current thinking is that clusters of neurons in the thalamus are particularly important; they provide a fluctuating action potential frequency output through neurons leading from the thalamus to the cortex. This output, in turn, causes a rhythmic pattern of synaptic activity in the pyramidal neurons of the cortex. As noted previously, the cortical synaptic activity—not the activity of the deep thalamic structures—comprises most of a recorded EEG signal. The synchronicity of the cortical synaptic activity (in other words, the amplitude of the EEG) reflects the degree of synchronous firing of the thalamic neuronal clusters that are generating the EEG. These clusters, in turn, receive input from brain areas involved in controlling the conscious state. Research is also beginning to identify and measure waves of coordinated EEG activity that spread between particular regions of the somatosensory and motor cortex in response to sensory inputs and during the performance of motor tasks.

The EEG is useful clinically in the diagnosis of neurological diseases, as well as in the diagnosis of coma and brain death. It was formerly also used in the detection of brain areas damaged by tumors, blood clots, or hemorrhage. However, the much greater spatial resolution of modern imaging techniques such as ***positron emission tomography*** (***PET***) and ***magnetic resonance imaging*** (***MRI***) make them far superior for detecting and localizing damaged brain areas in such cases (look ahead to Figures 19.6 and 19.7).

A shift from a less synchronized pattern of electrical activity (small-amplitude EEG) to a highly synchronized pattern can be a prelude to the electrical storm that signifies an epileptic seizure. ***Epilepsy*** is a common neurological disease, occurring in about 1% of the population. It manifests in mild, intermediate, and severe forms and is associated with abnormally synchronized discharges of cerebral neurons. These discharges are reflected in the EEG as recurrent waves having distinctive large amplitudes

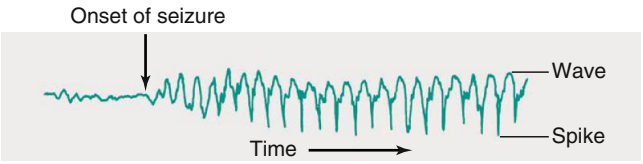


Figure 8.2 Spike-and-wave pattern in the EEG of a patient during an epileptic seizure. Scale is the same as in Figure 8.1.

PHYSIOLOGICAL INQUIRY

- Suppose the patient from which this trace was recorded had a mild form of epilepsy, with the only symptom being vivid visual hallucinations. Where on the patient's head was this measurement most likely taken?

Answer can be found at end of chapter.

(up to 1000 μV) and individual spikes or combinations of spikes and waves (**Figure 8.2**). Epilepsy is also associated with changes in behavior that vary according to the part of the brain affected and severity and can include involuntary muscle contraction and a temporary loss of consciousness. In most cases, the cause of epilepsy cannot be determined. Among the known triggers are traumatic brain injury, abnormal prenatal brain development, diseases that alter brain blood flow, heavy alcohol and illicit drug use, infectious diseases like meningitis and viral encephalitis, extreme stress, sleep deprivation, and exposure to environmental toxins such as lead or carbon monoxide.

The Waking State

Behaviorally, the waking state is far from homogeneous, reflecting the wide variety of activities you may be engaged in at any given moment. The most prominent EEG wave pattern of an awake, relaxed adult whose eyes are closed is an oscillation of 8 to 12 Hz, known as the **alpha rhythm** (**Figure 8.3a**). The alpha rhythm is best recorded over the parietal and occipital lobes and is associated with decreased levels of attention. When alpha rhythms are generated, subjects commonly report that they feel relaxed and happy. However, people who normally experience more alpha rhythm than usual have not been shown to be psychologically different from those with less.

When people are attentive to an external stimulus or are thinking hard about something, the alpha rhythm is replaced by smaller-amplitude, higher-frequency (>12 Hz) oscillations, the **beta rhythm** (**Figure 8.3b**). This transformation, known as the **EEG arousal,** is associated with the act of paying attention to a stimulus rather than with the act of perception itself. For example, if people open their eyes in a completely dark room and try to see, EEG arousal occurs even though they perceive no visual input. With decreasing attention to repeated stimuli, the EEG pattern reverts to the alpha rhythm.

Recent research has described another EEG pattern known as a **gamma rhythm.** These are high-frequency oscillations (30–100 Hz) that spread across large regions of the cortex, which seem in some cases to emanate from the thalamus. They often coincide with the occurrence of combinations of stimuli like hearing noises and seeing objects and are thought to be evidence of large numbers of neurons in the brain actively tying together disparate parts of an experienced scene or event.

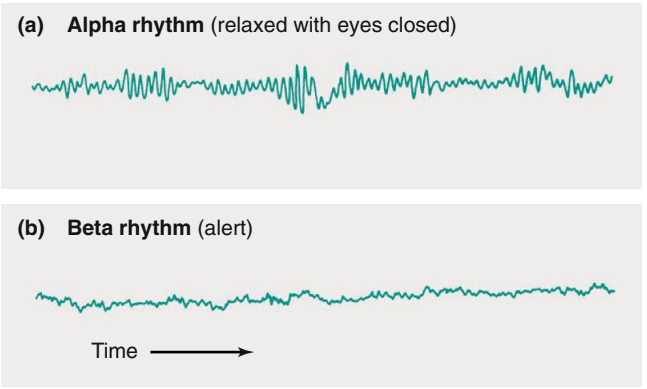


Figure 8.3 EEG recordings of (a) alpha and (b) beta rhythms. Alpha waves vary from about 8 to 12 Hz and have larger amplitudes than beta waves, which have frequencies at or above 13 Hz. Scale is the same as Figure 8.1. Not shown are higher-frequency EEG waves known as gamma waves (30–100 Hz), which have been observed in awake individuals processing sensory inputs.

Sleep

The EEG pattern changes profoundly in sleep, as demonstrated in **Figure 8.4**. As a person becomes increasingly drowsy, his or her wave pattern transitions from a beta rhythm to a predominantly alpha rhythm. When sleep actually occurs, the EEG shifts toward lower-frequency, larger-amplitude wave patterns known as the **theta rhythm** (4–8 Hz) and the **delta rhythm** (slower than 4 Hz). Relaxation of posture, decreased ease of arousal, increased threshold for sensory stimuli, and decreased motor neuron output accompany these EEG changes.

There are two phases of sleep, the names of which depend on whether or not the eyes move behind the closed eyelids: **NREM** (non–rapid eye movement) and **REM** (rapid eye movement) **sleep.** The initial phase of sleep—NREM sleep—is subdivided into three stages. Each successive stage is characterized by an EEG pattern with a lower frequency and larger amplitude than the preceding one. In stage N1 sleep, theta waves begin to be interspersed among the alpha pattern. In stage N2, high-frequency bursts called **sleep spindles** and large-amplitude **K complexes** occasionally interrupt the theta rhythm. Delta waves first appear along with the theta rhythm in stage N3 sleep; as this stage continues, the dominant pattern becomes a delta rhythm, sometimes referred to as slow-wave sleep.

Sleep begins with the progression from stage N1 to stage N3 of NREM sleep, which normally takes 30 to 45 min. The process then changes; the EEG ultimately resumes a small-amplitude, high-frequency, asynchronous pattern that looks very similar to the alert, awake state (see Figure 8.4, bottom trace). Instead of the person waking, however, the behavioral characteristics of sleep continue at this time, but this sleep also includes rapid eye movement (REM).

REM sleep is also called **paradoxical sleep,** because even though a person is asleep and difficult to arouse, his or her EEG pattern shows intense activity that is similar to that observed in the alert, awake state. In fact, brain O_2 consumption is higher during REM sleep than during the NREM or awake states. When awakened during REM sleep, subjects frequently report that they have been dreaming. This is true even in people who usually do not remember dreaming when they awaken on their own.

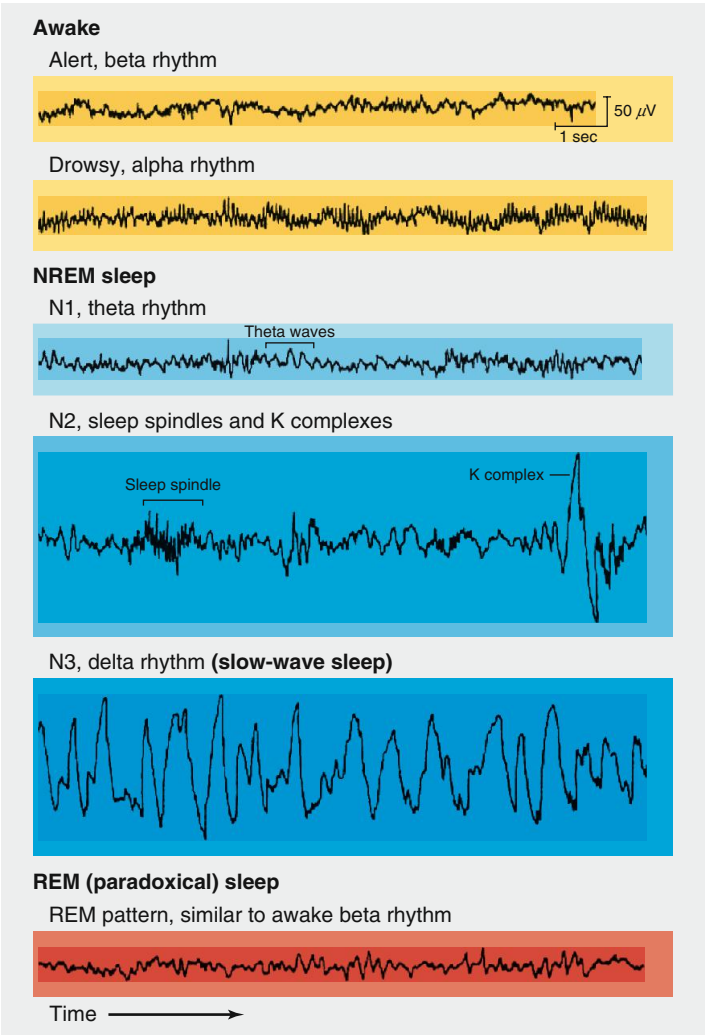


Figure 8.4 The EEG record of a person passing from an awake state through the various stages of sleep. The large-amplitude delta waves of slow-wave sleep demonstrate the synchronous activity pattern in cortical neurons. The asynchronous pattern during REM sleep is similar to that observed in awake individuals.

If uninterrupted, the stages of sleep occur in a cyclical fashion, tending to move from NREM stages N1 to N2 to N3, then back up to N2, and then to an episode of REM sleep. Continuous recordings of adults show that the average total night's sleep comprises four or five such cycles, each lasting 90 to 100 min (**Figure 8.5**). Significantly more time is spent in NREM during the first few cycles, but time spent in REM sleep increases toward the end of an undisturbed night. In young adults, REM sleep constitutes 20% to 25% of the total sleeping time; this fraction tends to decline progressively with aging. Initially, as you transition from drowsiness to stage N1 sleep, there is a considerable tension in the postural muscles, and brief muscle twitches called hypnic jerks sometimes occur. Eventually, the muscles become progressively more relaxed as NREM sleep progresses. Sleepers awakened during NREM sleep report dreaming less frequently than sleepers awakened during REM sleep. REM dreams also tend to seem more "real" and be more emotionally intense than those occurring in NREM sleep.

With several exceptions, skeletal muscle tension, already decreased during NREM sleep, is markedly inhibited during

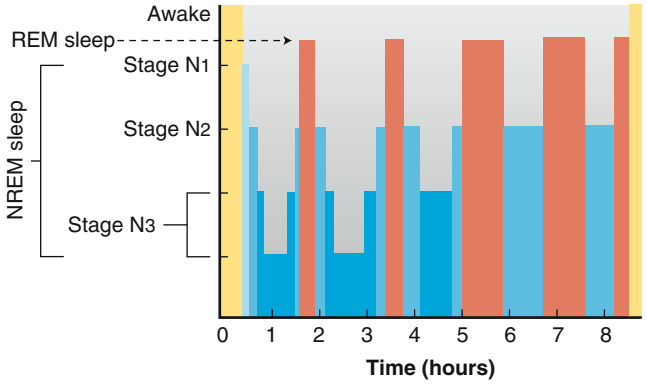


Figure 8.5 Schematic representation of the timing of sleep stages in a young adult. Bar colors correspond to the EEG traces shown in Figure 8.4.

REM sleep. Exceptions include the eye muscles, which undergo rapid bursts of contractions and cause the sweeping eye movements that give this sleep stage its name. The significance of these eye movements is not understood. Experiments suggest that they do not seem to rigorously correlate with the content of dreams; that is, what the sleeper is "seeing" in a dream does not seem to affect the eye movements. Furthermore, eye movements also occur during REM sleep in animals and humans that have been blind since birth and thus have no experience tracking objects with eye movements. Other groups of muscles that are active during REM sleep are the respiratory muscles; in fact, the rate of breathing is frequently increased compared to the awake, relaxed state. In one form of a disease known as ***sleep apnea,*** however, stimulation of the respiratory muscles temporarily ceases, sometimes hundreds of times during a night. The resulting decreases in oxygen levels repeatedly awaken the apnea sufferer, who is deprived of both slow-wave and REM sleep. As a result, this disease is associated with excessive—and sometimes dangerous—sleepiness during the day (refer to Chapter 13 for a more complete discussion of sleep apnea).

During the sleep cycle, many changes occur throughout the body in addition to altered muscle tension, providing an excellent example of the general principle of physiology that the functions of organ systems are coordinated with each other. During NREM sleep, for example, there are pulsatile releases of hormones from the anterior pituitary gland such as growth hormone and the gonadotropic hormones (Chapter 11), so adequate sleep is essential for normal growth in children and for regulation of reproductive function in adults. Decreases in blood pressure, heart rate, and respiratory rate also occur during NREM sleep. REM sleep is associated with an increase and irregularity in blood pressure, heart rate, and respiratory rate.

Although we spend about one-third of our lives sleeping, the functions of sleep are not completely understood. Many lines of research, however, suggest that sleep is a fundamental necessity of a complex nervous system. Sleep, or a sleeplike state, is a characteristic found throughout the animal kingdom, including insects, reptiles, birds, mammals, and others. Studies of sleep deprivation in humans and other animals suggest that sleep is a homeostatic requirement, similar to the need for food and water. Deprivation of sleep impairs the immune system, causes cognitive and memory deficits, and ultimately leads to psychosis and

even death. Much of the sleep research on humans has focused on the importance of sleep for learning and memory formation. EEG studies show that during sleep, the brain experiences reactivation of neural pathways stimulated during the prior awake state, and that subjects deprived of sleep show less effective memory retention. Based on these and other findings, many scientists believe that part of the restorative value of sleep lies in facilitating chemical and structural changes responsible for dampening the overall activity in the brain's neural networks while conserving and strengthening synapses in pathways associated with information that is important to learn and remember.

Table 8.1 summarizes the sleep states.

Neural Substrates of States of Consciousness

Periods of sleep and wakefulness alternate about once a day; that is, they manifest a circadian rhythm consisting on average of 8 h asleep and 16 h awake. Within the sleep portion of this circadian cycle, NREM sleep and REM sleep alternate, as we have seen. As we shift from the waking state through NREM sleep to REM sleep, attention shifts to internally generated stimuli (dreams) so that we are largely insensitive to external stimuli. Although sleep facilitates our ability to retain memories of experiences occurring in the waking state, dreams are generally forgotten relatively quickly. The tight rules for determining reality also become relaxed during dreaming, sometimes allowing for bizarre dreams.

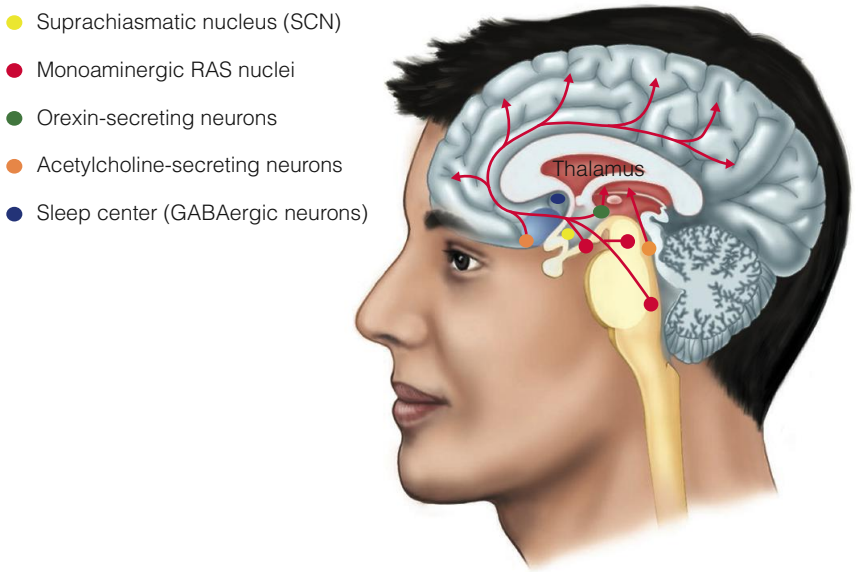
What physiological processes drive these cyclic changes in states of consciousness? Nuclei in both the brainstem and hypothalamus are involved.

Recall from Chapter 6 that a diverging network of brainstem nuclei called the reticular formation connects the brainstem with widespread regions of the brain and spinal cord. This network is essential for life and integrates a large number of physiological functions, including motor control, cardiovascular and respiratory control, and—relevant to the present discussion—states of consciousness. The brainstem reticular formation and all other components involved in regulating consciousness are sometimes referred to as the **reticular activating system (RAS).** This system consists of clusters of neurons and neural pathways originating in the brainstem and hypothalamus, distinguished by both their anatomical distribution and the neurotransmitters they release (**Figure 8.6**). Neurons of the RAS project widely throughout the cortex, as well as to areas of the thalamus that influence the EEG. Varying activation and inhibition of distinct groups of these neurons mediate transitions between waking and sleeping states.

The awake state is characterized by widespread activation of the cortex and thalamus by ascending pathways of the RAS (see Figure 8.6). Neurons originating in the brainstem release the monoaminergic neurotransmitters norepinephrine, serotonin, and histamine, which in this case function principally as neuromodulators (see Chapter 6). Their axon terminals are distributed widely throughout the brain, where they enhance excitatory synaptic activity. The drowsiness that occurs in people using certain antihistamines may be a result of blocking the histaminergic inputs of this system. In addition, acetylcholine from neurons in the pons and basal forebrain facilitates transmission of ascending sensory information through the thalamus and also enhances communication between the thalamus and cortex.

TABLE 8.1 Sleep–Wakefulness Stages

Stage	Behavior	EEG (See Figures 8.3 and 8.4)
Alert wakefulness	Awake, alert with eyes open.	Beta rhythm (greater than 12 Hz).
Relaxed wakefulness	Awake, relaxed with eyes closed.	Mainly alpha rhythm (8–12 Hz) over the parietal and occipital lobes. Changes to beta rhythm in response to internal or external stimuli.
Relaxed drowsiness	Fatigued, tired, or bored; eyelids may narrow and close; head may start to droop; momentary lapses of attention and alertness. Sleepy but not asleep.	Decrease in alpha-wave amplitude and frequency.
NREM (slow-wave) sleep		
Stage N1	Light sleep; easily aroused by moderate stimuli or even by neck muscle jerks triggered by muscle stretch receptors as head nods; continuous lack of awareness.	Alpha waves reduced in frequency, amplitude, and percentage of time present; gaps in alpha rhythm filled with theta (4–8 Hz) and delta (slower than 4 Hz) activity.
Stage N2	Further lack of sensitivity to activation and arousal.	Alpha waves replaced by random waves of greater amplitude.
Stage N3	Deep sleep; in stage N3, activation and arousal occur only with vigorous stimulation.	Much theta and delta activity; progressive increase in amount of delta.
REM (paradoxical) sleep	Greatest muscle relaxation and difficulty of arousal; begins 50–90 min after sleep onset, episodes repeated every 60–90 min, each episode lasting about 10 min; dreaming frequently occurs, rapid eye movements behind closed eyelids; marked increase in brain O_2 consumption.	EEG resembles that of alert awake state.



AP|R **Figure 8.6** Brain regions involved in regulating states of consciousness. Red arrows indicate principal pathways of ascending activation of the thalamus and cortex by the reticular activating system (RAS) during the awake state. Additional pathways not shown that are important in maintaining cortical arousal include excitatory inputs to the monoaminergic RAS nuclei from orexinergic neurons, and inhibitory inputs to the sleep center from the monoaminergic RAS nuclei. Monoamines from the RAS nuclei include histamine, norepinephrine, and serotonin. Orexin neurons and GABAergic neurons of the sleep center are hypothalamic nuclei, and the acetylcholine neurons are in the basal forebrain and pons.

PHYSIOLOGICAL INQUIRY

- Explain why some drugs prescribed to treat allergic reactions cause drowsiness as a side effect.

Answer can be found at end of chapter.

Recently discovered neuropeptides called **orexins** (a name meaning "to stimulate appetite") also have an important contribution in maintaining the awake state. They are produced by neurons in the hypothalamus that have widespread projections throughout the cortex and thalamus. (Some scientists also refer to these neuropeptides as **hypocretins** because they are made in the *hypo*thalamus and share some amino acid sequence similarity with the hormone se*cretin*.) Orexin-secreting neurons also densely innervate and stimulate action potential firing by the monoaminergic neurons of the RAS. Experimental animals and humans that lack orexins or their receptors suffer from ***narcolepsy***, a condition characterized by sudden attacks of sleepiness that unpredictably occur during the normal wakeful period. The importance of orexins in wakefulness has been recently validated by experiments showing that sleep is promoted in people ingesting a drug that blocks binding of orexins to their receptors. Loss of orexinergic neurons that occurs with age may explain why older people sometimes have difficulty sleeping.

Sleep is characterized by a markedly different pattern of neuronal activity and neurotransmitter release. Of central importance is the active firing of neurons in the "sleep center," a group of neurons in the ventrolateral preoptic nucleus of the hypothalamus (see Figure 8.6). These neurons release the inhibitory neurotransmitter GABA (gamma-aminobutyric acid) onto neurons throughout the brainstem and hypothalamus, including those that secrete orexins and monoamines. Inhibition of these regions reduces the levels of orexin, norepinephrine, serotonin, and histamine throughout the brain. Each of these substances has been associated with alertness and arousal; therefore, inhibition of their secretion by GABA tends to promote sleep. This accounts for the sleep-inducing effects of ***benzodiazepines*** such as ***diazepam*** (***Valium***) and ***alprazolam*** (***Xanax***), which are GABA agonists and are used to treat anxiety and insomnia in some people.

The pattern of acetylcholine release varies in different sleep stages. It is decreased in NREM sleep, but in REM sleep it is increased to levels similar to those in the awake state. The increase in acetylcholine during REM sleep facilitates communication between the thalamus and cortex and increases the cortical activity and dreaming that occur in this state.

Figure 8.7 shows a model of factors involved in regulating the transition between waking and sleeping states. Transition to the wakeful state is favored by three main inputs to orexin-secreting cells: (1) action potential firing from the suprachiasmatic nucleus (SCN), (2) indicators of negative energy balance, and (3) arousing emotional states signaled by the limbic system (see Figure 6.40 and Section 8.3 of this chapter). The SCN is the principle circadian pacemaker of the body (see Chapter 1). Entrained to a 24-hour cycle by light and other daily stimuli, it activates orexin cells in the morning. It also triggers the secretion of melatonin at night from the pineal gland in the brain. Although melatonin has been used as a "natural" substance for treating insomnia and jet lag, it has not yet been demonstrated unequivocally to be effective as a sleeping pill. It has, however, been shown to induce a decrease in body temperature, a key event in falling asleep.

The metabolic and limbic system inputs to orexinergic neurons provide adaptive behavioral flexibility to the initiation of wakefulness, so that under special circumstances our sleep and wake patterns can vary from the typical pattern of sleeping at night and being awake during the day. Metabolic indicators of negative energy balance resulting from a prolonged fast include decreased blood glucose concentration, increased plasma concentrations of an appetite-stimulating hormone called ghrelin, and decreased concentrations of the appetite-suppressing hormone leptin (see Chapter 16 for a description of these hormones). These conditions all stimulate orexin release, which may be adaptive because the resulting arousal would allow you to seek out food at times when you would otherwise be asleep. This link between metabolism and wakefulness is an excellent example of the general principle of physiology that the functions of organ systems—in this case, the nervous and endocrine systems—are coordinated with each other. Limbic system inputs coding strong emotions such as fear or anger also stimulate orexin neurons. This may be adaptive by interrupting sleep

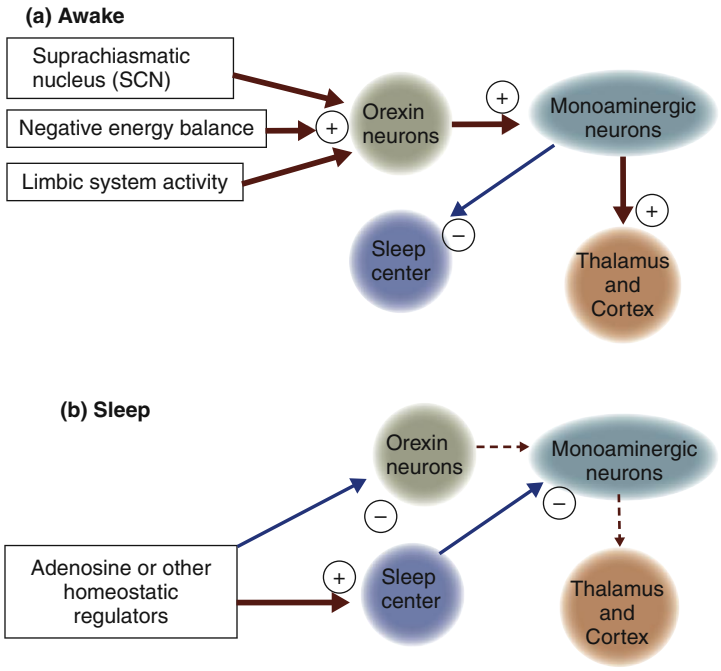


Figure 8.7 A model for the regulation of transitions to (a) the awake state and (b) sleep. Red arrows and "+" signs indicate stimulatory influences, blue arrows and "−" signs indicate inhibitory pathways. Orexin neurons and the sleep center are in the hypothalamus. Monoaminergic neurons release norepinephrine, serotonin, and histamine. Adapted from Sakurai, Takeshi. Nature Reviews, *Neuroscience* (8): pp. 171–181, March 2007.

PHYSIOLOGICAL INQUIRY

- As mentioned in the text, interleukin 1, a fever-inducing cytokine that increases in the circulation during an infection, promotes the sleep state. Speculate about some possible adaptive advantages of such a mechanism.

Answer can be found at end of chapter.

at times when we need to respond to situations affecting our well-being and survival.

The factors that activate the sleep center are not completely understood, but it is thought that homeostatic regulation by one or more chemicals is involved. The need for sleep behaves like other homeostatic demands of the body. Individuals deprived of sleep for a prolonged period will subsequently experience prolonged bouts of "catch-up" sleep, as though the body needs to rid itself of some chemical that has built up. Adenosine (a metabolite of ATP) is one likely candidate. Its concentration is increased in the brain after a prolonged waking period, and it has been shown to reduce firing by orexinergic neurons. This in part explains the stimulatory effect of caffeine, which blocks adenosine receptors. Buildup of adenosine or other homeostatic regulators can also facilitate the transition to the sleep state at times when you may normally be awake, like when you take an afternoon nap after being up late studying for an exam. Another potential sleep-inducing chemical candidate is interleukin 1, one of the cytokines in a family of intercellular messengers with important functions in the immune system (Chapter 18). It fluctuates in parallel with normal sleep–wake cycles and has also been shown to facilitate the sleep state.

Coma and Brain Death

The term ***coma*** describes an extreme decrease in mental function due to structural, physiological, or metabolic impairment of the brain. A person in a coma exhibits a sustained loss of the capacity for arousal even in response to vigorous stimulation. There is no outward behavioral expression of any mental function, the eyes are usually closed, and sleep–wake cycles disappear. Coma can result from extensive damage to the cerebral cortex; damage to the brainstem arousal mechanisms; interruptions of the connections between the brainstem and cortical areas; metabolic dysfunctions; brain infections; or an overdose of certain drugs, such as sedatives, sleeping pills, narcotics, or ethanol. Comas may be reversible or irreversible, depending on the type, location, and severity of brain damage. Experiments using high-density EEG arrays in some coma patients suggest that even though they exhibit no outward behaviors or responses, they may have some level of consciousness.

Patients in an irreversible coma often enter a ***persistent vegetative state*** in which sleep–wake cycles are present even though the patient is unaware of his or her surroundings. Individuals in a persistent vegetative state may smile, cry, or seem to react to elements of their environment. However, there is no definitive evidence that they can comprehend these behaviors.

A coma—even when irreversible—is not equivalent to death. We are left, then, with the question, When is a person actually dead? This question often has urgent medical, legal, and social consequences. For example, with the need for viable tissues for organ transplantation, it becomes important to know just when a donor is legally dead so that the organs can be removed as soon after death as possible.

Brain death is currently accepted by the medical and legal establishment as the criterion for death, despite the viability of other organs. Brain death occurs when the brain no longer functions and appears to have no possibility of functioning again.

The problem now becomes practical. How do we know when a person (e.g., someone in a coma) is brain-dead? Although there is some variation in how different hospitals and physicians determine brain death, the criteria listed in **Table 8.2** lists the generally agreed-upon standards. Notice that the cause of a coma must be known, because comas due to drug poisoning and other conditions are often reversible. Also, the criteria specify that there be no evidence of functioning neural tissues above the spinal cord because fragments of spinal reflexes may remain for several hours or longer after the brain is dead (see Chapter 10 for spinal reflex examples). The criterion for lack of spontaneous respiration (apnea) must be assessed with caution. Machines supplying artificial respiration must be turned off, and arterial blood gas levels monitored carefully (see Figure 13.21 and Table 13.6). Although arterial carbon dioxide levels must be allowed to increase above a critical point for the test to be valid, it is of course not advisable to allow arterial oxygen levels to decrease too much because of the danger of further brain damage. Therefore, apnea tests are generally limited to a duration of 8 to 10 minutes.

TABLE 8.2 Criteria for Brain Death

I. The nature and duration of the coma must be known.
   A. Known structural damage to brain or irreversible systemic metabolic disease
   B. No chance of drug intoxication, especially from paralyzing or sedative drugs
   C. No severe electrolyte, acid–base, or endocrine disorder that could be reversible
   D. Patient not suffering from hypothermia

II. Cerebral and brainstem function are absent.
   A. No response to painful stimuli other than spinal cord reflexes
   B. Pupils unresponsive to light
   C. No eye movement in response to stimulation of the vestibular reflex or corneal touch
   D. Apnea (no spontaneous breathing) for 8–10 minutes when ventilator is removed and arterial carbon dioxide levels are allowed to increase above 60 mmHg
   E. No gag or cough reflex; purely spinal reflexes may be retained
   F. Confirmatory neurological exam after 6 hours

III. Supplementary (optional) criteria
   A. Flat EEG for 30 min (wave amplitudes less than 2 mV)
   B. Responses absent in vital brainstem structures
   C. Greatly reduced cerebral circulation

Source: Table adapted from American Academy of Neurology, *Neurology* 74: 1911–1918 (2010).

8.2 Conscious Experiences

Conscious experiences are those things we are aware of—either internal, such as an idea, or external, such as an object or event. The most obvious aspect of this phenomenon is sensory awareness, but we are also aware of inner states such as fatigue, thirst, and happiness. We are aware of the passing of time, of what we are presently thinking about, and of consciously recalling a fact learned in the past. We are aware of reasoning and exerting self-control, and we are aware of directing our attention to specific events. Not least, we are aware of "self."

Basic to the concept of conscious experience is the question of selective attention.

Selective Attention

The term **selective attention** means avoiding the distraction of irrelevant stimuli while seeking out and focusing on stimuli that are momentarily important. Both voluntary and reflex mechanisms affect selective attention. An example of voluntary control of selective attention familiar to students is ignoring distracting events in a busy library while studying there.

Another example of selective attention occurs when a novel stimulus is presented to a relaxed subject showing an alpha EEG pattern. This causes the EEG to shift to the beta rhythm. If the stimulus has meaning for the individual, behavioral changes also occur. The person stops what he or she is doing, listens intently, and turns toward the stimulus source, a behavior called the **orienting response.** If the person is concentrating hard and is not distracted by the novel stimulus, the orienting response does not occur. It is also possible to focus attention on a particular stimulus without making any behavioral response.

For attention to be directed only toward stimuli that are meaningful, the nervous system must have the means to evaluate the importance of incoming sensory information. Thus, even before we focus attention on an object in our sensory world and become aware of it, a certain amount of processing has already occurred. This so-called **preattentive processing** directs our attention toward the part of the sensory world that is of particular interest and prepares the brain's perceptual processes for it.

If a stimulus is repeated but is found to be irrelevant, the behavioral response to the stimulus progressively decreases, a process known as **habituation.** For example, when a loud bell is sounded for the first time, it may evoke an orienting response because the person may be frightened by or curious about the novel stimulus. After several rings, however, the individual has a progressively smaller response and eventually may ignore the bell altogether. An extraneous stimulus of another type or the same stimulus at a different intensity can restore the orienting response.

Habituation involves a depression of synaptic transmission in the involved pathway, possibly related to a prolonged inactivation of Ca^{2+} channels in presynaptic axon terminals. Such inactivation results in a decreased Ca^{2+} influx during depolarization and, therefore, a decrease in the amount of neurotransmitter released by a terminal in response to action potentials.

Neural Mechanisms for Selective Attention

Directing our attention to an object involves several distinct neurological processes. First, our attention must be disengaged from its present focus. Then, attention must be moved to the new focus. Attention must then be engaged at the new focus. Finally, there must be an increased level of arousal that produces prolonged attention to the new focus.

An area that has an important function in orienting and selective attention is in the brainstem, where the interaction of various sensory modalities in single cells can be detected experimentally. The receptive fields of the different modalities overlap. For example, a visual and auditory input from the same location in space will significantly enhance the firing rates of certain of these so-called multisensory cells, whereas the same type of stimuli originating at different places will have little effect on or may even inhibit their response. Thus, weak clues can add together to enhance each other's significance so we pay attention to the event, whereas we may ignore an isolated small clue.

The locus ceruleus is one of the monoaminergic RAS nuclei. It is located in the pons, projects to the parietal cortex and many other parts of the central nervous system, and is also implicated in selective attention. The system of fibers leading from the locus ceruleus helps determine which brain area is to gain temporary predominance in the ongoing stream of the conscious experience. These neurons release norepinephrine, which acts as a neuromodulator to enhance the signals transmitted by certain sensory inputs. The effect is to increase the difference between the sensory inputs and other, weaker signals. Thus, neurons of the locus ceruleus improve information processing during selective attention.

The thalamus is another brain region involved in selective attention. It is a synaptic relay station for the majority of ascending sensory pathways (see Figure 7.20). Inputs from regions of the cerebral cortex and brainstem can modulate synaptic activity in

the thalamus, making it a filter that can selectively influence the transmission of sensory information.

There are also multisensory neurons in association areas of the cerebral cortex (see Figure 7.13). Whereas the brainstem neurons are concerned with the orienting movements associated with paying attention to a specific stimulus, the cortical multisensory neurons are more involved in the perception of the stimulus. Researchers are only beginning to understand how the various areas of the attentional system interact.

Some insights into neural mechanisms of selective attention are being gained from the study of individuals diagnosed with ***attention-deficit/hyperactivity disorder*** (***AD/HD***). This condition typically begins early in childhood and is the most common neurobehavioral problem in school-aged children (estimates range from 3% to 7%). AD/HD is characterized by difficulty in maintaining selective attention and/or impulsiveness and hyperactivity. Investigation has yet to reveal clear environmental causes, but there is some evidence for a genetic basis because AD/HD tends to run in families. Functional imaging studies of the brains of children with AD/HD have indicated dysfunction of brain regions in which catecholamine signaling is prominent, including the basal nuclei and prefrontal cortex. In support of this, the most effective medication used to treat AD/HD is ***methylphenidate*** (***Ritalin***), a drug that increases synaptic concentrations of norepinephrine (and dopamine).

Neural Mechanisms of Conscious Experiences

Conscious experiences are popularly attributed to the workings of the "mind," a word that conjures up the image of a nonneural "me," a phantom interposed between afferent and efferent impulses. The implication is that the mind is something more than neural activity. The mind represents a summation of neural activity at any given moment and does not require anything more. However, scientists are only beginning to understand the mechanisms that give rise to conscious experiences.

We will speculate about this problem in this section. The thinking begins with the assumption that conscious experience requires neural processes—either graded potentials or action potentials—somewhere in the brain. At any moment, certain of these processes correlate with conscious awareness, and others do not. A key question here is, What is different about the processes we are aware of?

A further assumption is that the neural activity that corresponds to a conscious experience resides not in a single anatomical cluster of "consciousness neurons" but rather in a set of neurons that are temporarily functioning together in a specific way. Because we can become aware of many different things, we further assume that this grouping of neurons can vary—shifting, for example, among parts of the brain that deal with visual or auditory stimuli, memories or new ideas, emotions, or language.

Consider the visual perception of an object. Different aspects of something we see are processed by different areas of the visual cortex—the object's color by one part, its motion by another, its location in the visual field by another, and its shape by still another—but we see *one* object. Not only do we perceive it; we may also know its name and function. Moreover, as we see an object, we can sometimes also hear or smell it, which requires participation of brain areas other than the visual cortex.

The simultaneous participation of different groups of neurons in a conscious experience can also be inferred for the olfactory system. Repugnant and alluring odors evoke different reactions, although they are both processed in the olfactory pathway. Neurons involved in emotion are also clearly involved in this type of perception.

Neurons from the various parts of the brain that simultaneously process different aspects of the information related to the object we see are said to form a "temporary set" of neurons. It is suggested that the synchronous activity of the neurons in the temporary set leads to conscious awareness of the object we are seeing.

As we become aware of still other events—perhaps a memory related to the object—the set of neurons involved in the synchronous activity shifts, and a different temporary set forms. In other words, it is suggested that specific relevant neurons in many areas of the brain function together to form the unified activity that corresponds to awareness.

What parts of the brain may be involved in such a temporary neuronal set? Clearly, the cerebral cortex is involved. Removal of specific areas of the cortex abolishes awareness of only specific types of consciousness. For example, in a syndrome called ***sensory neglect***, damage to association areas of the parietal cortex causes the injured person to neglect parts of the body or parts of the visual field as though they do not exist. Stroke patients with parietal lobe damage often do not acknowledge the presence of a paralyzed part of their body or will only be able to describe some but not all elements in a visual field. **Figure 8.8** shows an example of sensory neglect as shown in drawings made by a patient with parietal lobe

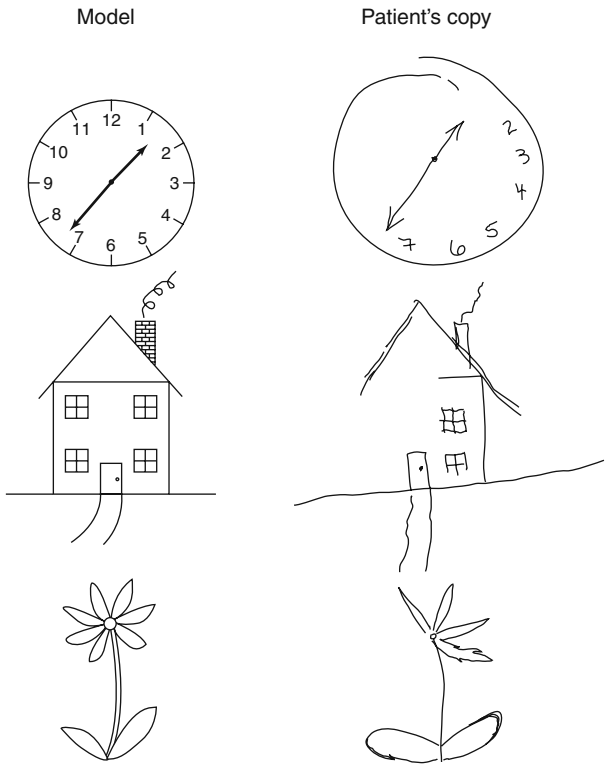


Figure 8.8 Unilateral visual neglect in a patient with right parietal lobe damage. Although patients such as these are not impaired visually, they do not perceive part of their visual world. The drawings on the right were copied by the patient from the drawings on the left.

damage on the right side of the brain. Patients such as these are completely unaware of the left-hand parts of the visual image. Subcortical areas such as the thalamus and basal nuclei may also be directly involved in conscious experience, but it seems that the hippocampus and cerebellum are not.

Saying that we can use one set of neurons and then shift to a new set at a later time may be the same as saying we can focus attention on—that is, bring into conscious awareness—one object or event and then shift our focus of attention to another object or event at a later time. Thus, the mechanisms of conscious awareness and attention are intimately related.

8.3 Motivation and Emotion

Motivation is a factor in most, if not all, behaviors, and emotions accompany many of our conscious experiences. Motivated behaviors such as sexual behaviors are involved in controlling much of our day-to-day behavior, and emotions may help us to achieve the goals we set for ourselves as well as express our feelings.

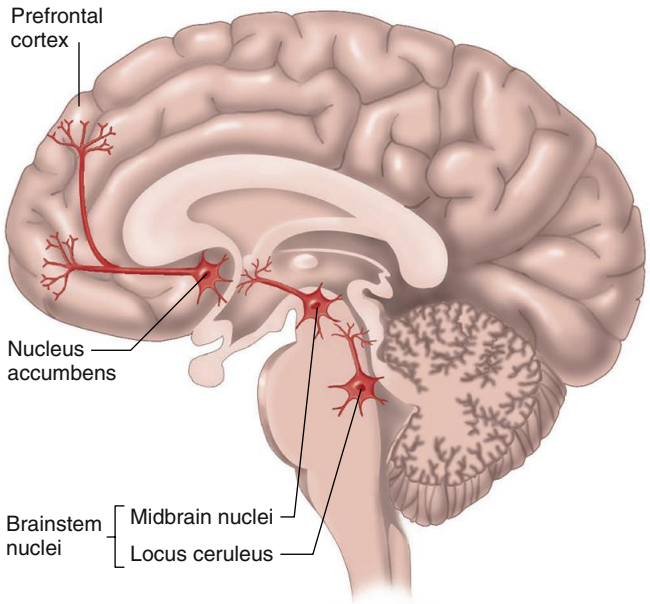
Motivation

Those processes responsible for the goal-directed quality of behavior are the **motivations,** or "drives," for that behavior. Motivation can lead to hormonal, autonomic, and behavioral responses. **Primary motivated behavior** is behavior related directly to homeostasis—that is, the maintenance of a relatively stable internal environment, such as getting something to drink when you are thirsty. In such homeostatic goal-directed behavior, specific body "needs" are satisfied. Thus, in our example, the perception of need results from a decrease in total body water, and the correlate of need satisfaction is the return of body water volume to normal. We will discuss the neurophysiological integration of much homeostatic goal-directed behavior later (thirst and drinking, Chapter 14; food intake and temperature regulation, Chapter 16).

In many kinds of behavior, however, the relation between the behavior and the primary goal is indirect. For example, the selection of a particular flavor of beverage has little if any apparent relation to homeostasis. The motivation in this case is secondary. Much of human behavior fits into this latter category and is influenced by habit, learning, intellect, and emotions—factors that can be lumped together under the term "incentives." Often, it is difficult to distinguish between primary and secondary goals. For instance, although some salt in the diet is required for survival, most of your drive to eat salt is hedonistic (for enjoyment).

The concepts of reward and punishment are inseparable from motivation. Rewards are things that organisms work for or things that make the behavior that leads to them occur more often—in other words, positive reinforcement. Punishments are the opposite.

Neural Pathways The neural system subserving reward and punishment is part of the reticular activating system, which you will recall arises in the brainstem and comprises several components. The component involved in motivation is known as the **mesolimbic dopamine pathway:** *meso-* because it arises in the midbrain (mesencephalon) area of the brainstem; *limbic* because it sends its fibers to areas of the limbic system, such as the prefrontal cortex, the nucleus accumbens, and the undersurface



APR **Figure 8.9** Schematic drawing of the mesolimbic dopamine pathway. Various psychoactive substances are thought to work in these areas to enhance brain reward.

of the frontal lobe (**Figure 8.9**); and *dopamine* because its fibers release the neurotransmitter dopamine. The mesolimbic dopamine pathway is implicated in evaluating the availability of incentives and reinforcers (asking, Is it worth it? for example) and translating the evaluation into action.

Much of the available information concerning the neural substrates of motivation has been obtained by studying behavioral responses of animals to rewarding or punishing stimuli. One way in which this can be done is by using the technique of **brain self-stimulation.** In this technique, an awake experimental animal regulates the rate at which electrical stimuli are delivered through electrodes implanted in discrete brain areas. The small electrical charges given to the brain cause the local neurons to depolarize, thus mimicking what may happen if these neurons were to fire spontaneously. The experimental animal is placed in a box containing a lever it can press (**Figure 8.10**). If no stimulus is delivered to the brain when the bar is pressed, the animal usually presses it occasionally at random.

However, if a stimulus is delivered to the brain as a result of a bar press, different behaviors occur, depending on the location of the electrodes. If the animal increases the bar-pressing rate above the level of random presses, the electrical stimulus is by definition rewarding. If the animal decreases the press rate below the random level, the stimulus is punishing. Thus, the rate of bar pressing with the electrode in different brain areas is taken to be a measure of the effectiveness of the reward or punishment. Different pressing rates are found for different brain regions.

Scientists expected the hypothalamus to have a function in motivation because the neural centers for the regulation of eating, drinking, temperature control, and sexual behavior are there. Indeed, it was found that brain self-stimulation of the lateral regions of the hypothalamus serves as a positive reward. Animals with electrodes in these areas have been known to press a bar to stimulate their brains 2000 times per hour continuously for 24 h until they collapse from exhaustion. In

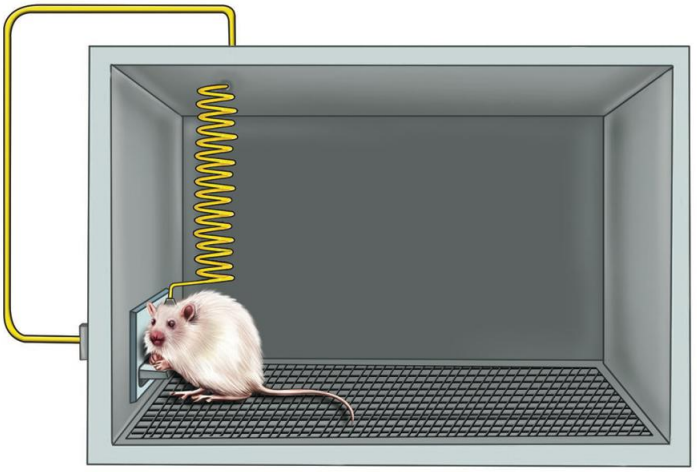


Figure 8.10 Apparatus for self-stimulation experiments. Rats like the one shown here do not appear to be bothered by the implanted electrode. In fact, they work hard to get the electrical stimulation.

PHYSIOLOGICAL INQUIRY

- A general principle of physiology states that physiological processes are dictated by the laws of chemistry and physics. How is this exemplified in the experiment depicted in this figure?

Answer can be found at end of chapter.

fact, electrical stimulation of the lateral hypothalamus is more rewarding than external rewards. Hungry rats, for example, often ignore available food for the sake of stimulating their brains at that location.

Although the rewarding sites—particularly those for primary motivated behavior—are more densely packed in the lateral hypothalamus than anywhere else in the brain, self-stimulation can occur in a large number of brain areas. Motivated behaviors based on learning also involve additional integrative centers, including the cortex, and limbic system, brainstem, and spinal cord—in other words, all levels of the nervous system can be involved.

Recently, scientists demonstrated that an animal's behavior could be altered by electrically manipulating the reward pathways of its brain. For example, the scientists could alter whether a rat chose a risky or safe behavior by stimulating or inhibiting reward pathways at the moment a behavior was chosen. This influenced the future behavior of the rat such that it preferred whichever type of behavior for which the investigators provided an electrical reward.

Chemical Mediators Dopamine is a major neurotransmitter in the pathway that mediates the brain reward systems and motivation. For this reason, drugs that increase synaptic activity in the dopamine pathways increase self-stimulation rates—that is, they provide positive reinforcement. Amphetamines are an example of such a drug because they increase the presynaptic release of dopamine. Conversely, drugs such as chlorpromazine, an antipsychotic drug that blocks dopamine receptors and lowers activity in the catecholamine pathways, are negatively reinforcing. The catecholamines, as we will see, are also implicated in the pathways involved in learning. This is not unexpected, because rewards and punishments are believed to constitute incentives for learning.

Emotion

Emotion can be considered in terms of a relation between an individual and the environment based on the individual's evaluation of the environment (is it pleasant or hostile?), disposition toward the environment (am I happy and attracted to the environment or fearful of it?), and the actual physical response to it. While analyzing the physiological bases of emotion, it is helpful to distinguish (1) the anatomical sites where the emotional value of a stimulus is determined; (2) the hormonal, autonomic, and outward expressions and displays of response to the stimulus (so-called **emotional behavior**); and (3) the conscious experience, or **inner emotions,** such as feelings of fear, love, anger, joy, anxiety, hope, and so on.

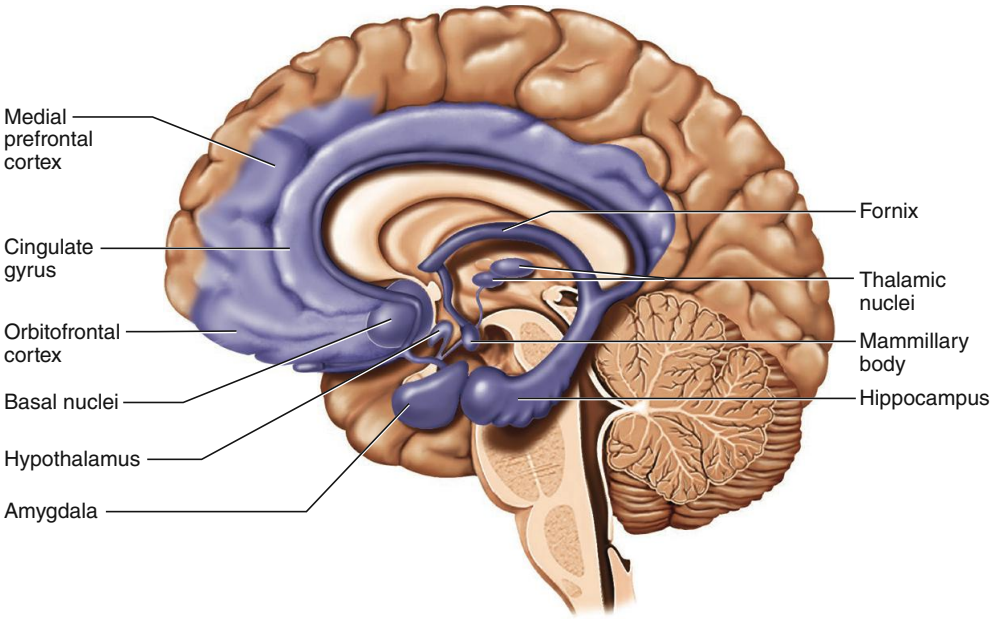
Emotional behavior can be studied more easily than the anatomical systems or inner emotions because it includes responses that can be measured externally (in terms of behavior). For example, stimulation of certain regions of the lateral hypothalamus causes an experimental animal to arch its back, puff out the fur on its tail, hiss, snarl, bare its claws and teeth, flatten its ears, and strike. Simultaneously, its heart rate, blood pressure, respiration, salivation, and plasma concentrations of epinephrine and fatty acids all increase. Clearly, this behavior typifies that of an enraged or threatened animal. Moreover, the animal's behavior can be changed from savage to docile and back again simply by activating different areas of the limbic system (**Figure 8.11**).

An early case study that shed light on neurological structures involved in emotional behavior was that of a patient known as S.M. This patient suffered from a rare disorder (***Urbach–Wiethe disease***) in which the amygdala was destroyed bilaterally. Intelligence and memory formation remained intact. However, this individual lacked the ability to express fear in appropriate situations and could not recognize fearful expressions on other people's faces, demonstrating the importance of the amygdala in humans for the emotion of fear.

Emotional behavior includes such complex behaviors as the passionate defense of a political ideology and such simple actions as laughing, sweating, crying, or blushing. Emotional behavior is achieved by the autonomic and somatic nervous systems under the influence of integrating centers such as those we just mentioned and provides an outward sign that the brain's "emotion systems" are activated.

The cerebral cortex has a major function in directing many of the motor responses during emotional behavior (for example, whether you approach or avoid a situation). Moreover, forebrain structures, including the cerebral cortex, account for the modulation, direction, understanding, or even inhibition of emotional behaviors.

Although limbic areas of the brain seem to handle inner emotions, there is no single "emotional system." The amygdala



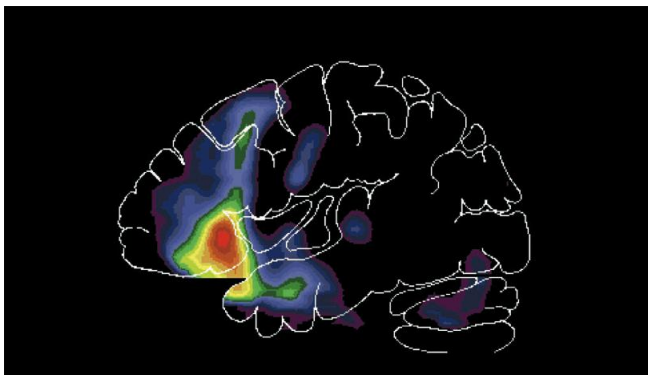
AP|R **Figure 8.11** Brain structures including elements of the limbic system that are involved in emotion, motivation, and the affective disorders. Individual basal nuclei are not shown in this view.

PHYSIOLOGICAL INQUIRY

- What might have favored the evolution of emotions?

Answer can be found at end of chapter.

(see Figure 8.11), and the region of association cortex on the lower surface of the frontal lobe, however, are central to most emotional states (**Figure 8.12**). The amygdala, in addition to being responsible for the emotion of fear, interacts with other parts of the brain via extensive reciprocal connections that can influence emotions about external stimuli, decision making, memory, attention, homeostatic processes, and behavioral responses. For example, it sends output to the hypothalamus, which is central to autonomic and hormonal homeostatic processes.



AP|R **Figure 8.12** Computer image of a human brain scan showing increased activity (red and yellow areas) in the prefrontal cortex during a sad thought. Marcus E. Raichle, M.D., Washington University School of Medicine.

The limbic areas have been stimulated in awake human beings undergoing neurosurgery. These patients reported vague feelings of fear or anxiety during periods of stimulation to certain areas. Stimulation of other areas induced pleasurable sensations that the subjects found hard to define precisely. In normal functioning, the cerebral cortex allows us to connect such inner emotions with the particular experiences or thoughts that cause them.

8.4 Altered States of Consciousness

States of consciousness may be different from the commonly experienced ones like wakefulness and drowsiness. Other, more unusual sensations, such as those occurring with hypnosis, mind-altering drugs, and certain diseases, are referred to as ***altered states of consciousness.*** These altered states are also characteristic of psychiatric illnesses.

Schizophrenia

One of the diseases that induces altered states of consciousness is ***schizophrenia,*** in which information is not properly regulated in the brain. The amazingly diverse symptoms of schizophrenia include hallucinations, especially "hearing" voices, and delusions, such as the belief that one has been chosen for a special mission or is being persecuted by others. Schizophrenics become withdrawn, are emotionally unresponsive, and experience inappropriate moods. They may also experience abnormal motor behavior, which can include total immobilization (***catatonia***). The symptoms vary from person to person.

The causes of schizophrenia remain unclear. Studies suggest that it reflects a developmental disorder in which neurons migrate or mature abnormally during brain formation. The abnormality may be due to a genetic predisposition or multiple environmental factors such as viral infections and malnutrition during fetal life or early childhood. The brain abnormalities involve diverse neural circuits and neurotransmitter systems that regulate basic cognitive processes. A widely accepted explanation for schizophrenia suggests that certain mesocortical dopamine pathways are overactive. This hypothesis is supported by the fact that amphetamine-like drugs, which enhance dopamine signaling, make the symptoms worse, as well as by the fact that the most therapeutically beneficial drugs used in treating schizophrenia act at least in part to block dopamine receptors.

Schizophrenia affects approximately 1% of people over the age of 18, with the typical age of onset in the late teens or early 20s just as brain development nears completion. Currently, there is no prevention or cure for the disease, although drugs can often control the symptoms.

The Mood Disorders: Depression and Bipolar Disorders

The term **mood** refers to a pervasive and sustained inner emotion that affects a person's perception of the world. In addition to being part of the conscious experience of the person, others can observe it. In healthy people, moods can be normal, elevated, or depressed, and people generally feel that they have some degree of control over their moods. That sense of control is lost, however, in the ***mood disorders*****,** which include depressive disorders and bipolar disorders. Along with schizophrenia, the mood disorders represent the major psychiatric illnesses.

Depression

Some of the prominent features of ***depressive disorder*** (***depression***) are a pervasive feeling of emptiness or sadness; a loss of energy, interest, or pleasure; anxiety; irritability; an increase or decrease in appetite; disturbed sleep; and thoughts of death or suicide. Depression can occur on its own, independent of any other illness, or it can arise secondary to other medical disorders. It is associated with decreased neuronal activity and metabolism in the anterior part of the limbic system and nearby prefrontal cortex.

Although the major biogenic amine neurotransmitters (norepinephrine, dopamine, and serotonin) and acetylcholine have all been implicated, the causes of the mood disorders are unknown.

Current treatment of the depressive disorders emphasizes drugs and psychotherapy. The classical antidepressant drugs are of three types. The ***tricyclic antidepressant drugs*** such as ***amitriptyline*** (***Elavil***)**,** ***desipramine*** (***Norpramin***)**,** and ***doxepin*** (***Sinequan***) interfere with serotonin and/or norepinephrine reuptake by presynaptic endings. The ***monoamine oxidase*** (***MAO***) ***inhibitors*** interfere with the enzyme responsible for the breakdown of these same two neurotransmitters. A third class of antidepressant drugs, the ***serotonin-specific reuptake inhibitors*** (***SSRIs***)**,** includes the most widely used antidepressant drugs—including ***escitalopram*** (***Lexapro***)**,** ***fluoxetine*** (***Prozac***)**,** ***paroxetine*** (***Paxil***)**,** and ***sertraline*** (***Zoloft***)**.** As the name of this class of drugs suggests, they selectively inhibit serotonin reuptake by presynaptic terminals. In all three classes, the result is an increased concentration of serotonin and (except for the third class) norepinephrine in the extracellular fluid at synapses. SSRIs are currently the most commonly prescribed of the three types, due to a better safety record and fewer side effects and interactions with other medications. Recent research suggests that combining psychotherapy with drug therapy provides the maximum benefit to most patients with depression.

The biochemical effects of antidepressant medications occur immediately, but the beneficial antidepressant effects usually appear only after several weeks of treatment. Thus, the known biochemical effect must be only an early step in a complex sequence that leads to a therapeutic effect of these drugs. Consistent with the long latency of the antidepressant effect is the recent evidence that these drugs may ultimately stimulate the growth of new neurons in the hippocampus. Chronic stress is a known trigger of depression in some people, and it has also been shown to inhibit hippocampal neurogenesis in animals. In addition, careful measurements of the hippocampus in chronically depressed patients show that it tends to be smaller than in matched, nondepressed individuals. Finally, though antidepressant drugs normally have measurable effects on behavior in animal models of depression, it was recently shown that those effects disappear completely when steps are taken to prevent neurogenesis.

Alternative treatments used when drug therapy and psychotherapy are not effective include electrical stimulation of the brain. One such treatment is ***electroconvulsive therapy*** (***ECT***). As the name suggests, pulses of electrical current applied through the skull are used to activate a large number of neurons in the brain simultaneously, thereby inducing a convulsion, or seizure. The patient is under anesthesia and prepared with a muscle relaxant to minimize the effects of the convulsion on the musculoskeletal system. A series of ECT treatments is believed to act via changes in neurotransmitter function by causing changes in the sensitivity of certain serotonin and adrenergic postsynaptic receptors. Despite good evidence that it can be an effective treatment, ECT tends to be utilized as a treatment of last resort in patients with depression who do not respond to medication.

A recent alternative to drug therapy used to treat depression involves stimulation of the brain with electromagnets and is called ***repetitive transcranial magnetic stimulation*** (***rTMS***)**.** In rTMS, circular or figure-eight-shaped metallic coils are placed against the skull overlying specific brain regions; brief, powerful electrical currents are then applied at frequencies between 1 and 25 pulses per second. The resulting magnetic field induces current to flow through cortical neuronal networks directly beneath the coil. The immediate effect is similar to ECT—neural activity is transiently disordered or sometimes silenced in that brain region. However, no anesthesia is required and no pain, convulsion, or memory loss occurs. Depending on the frequency and treatment regimen applied, the lasting effects of rTMS can cause either an increase or a decrease in the overall activity of the targeted area. In recent clinical trials, 2 to 4 weeks of daily rTMS stimulation of the left prefrontal cortex resulted in marked improvement of patients with major depression who had not responded to medication. However, rTMS has not yet shown the same level of clinical effectiveness as ECT. Medical scientists are hopeful that refinements in rTMS techniques in the future could lead to breakthroughs in the treatment of obsessive-compulsive disorder, mania, schizophrenia, and other psychiatric illnesses.

Bipolar Disorder

The term ***bipolar disorder*** describes swings between mania and depression. Episodes of ***mania*** are characterized by an abnormally and persistently elevated mood, sometimes with euphoria (that is, an exaggerated and unrealistic sense of well-being), racing thoughts, excessive energy, overconfidence, impulsiveness, significantly decreased time spent sleeping, and irritability.

A major drug used in treating patients with bipolar disorder is the chemical element ***lithium*** (***Eskalith, Lithobid***)**,** sometimes given in combination with anticonvulsant drugs. It is highly specific, normalizing both the manic and depressed moods and slowing down thinking and motor behavior without causing sedation. In addition, it decreases the severity of the swings between mania and depression that occur in the bipolar disorders. In some cases,

lithium is even effective in depression not associated with mania. Although it has been used for more than 50 years, the mechanisms of lithium action are not completely understood. It may help because it interferes with the formation of signaling molecules of the inositol phosphate family (Chapter 5), thereby decreasing the response of postsynaptic neurons to neurotransmitters that utilize this signal transduction pathway. Lithium has also been found to chronically increase the rate of glutamate reuptake at excitatory synapses, which would be expected to reduce excessive nervous system activity during manic episodes.

Psychoactive Substances, Dependence, and Tolerance

In the previous sections, we mentioned several drugs used to combat altered states of consciousness. Psychoactive substances are also used as "recreational" drugs in a deliberate attempt to elevate mood and produce unusual states of consciousness ranging from meditative states to hallucinations. Virtually all the psychoactive substances exert their actions either directly or indirectly by altering neurotransmitter–receptor interactions in the biogenic amine pathways, particularly those of dopamine and serotonin. For example, the primary effect of cocaine comes from its ability to block the reuptake of dopamine into the presynaptic axon terminal. Psychoactive substances are often chemically similar to neurotransmitters such as dopamine, serotonin, and norepinephrine, and they interact with the receptors activated by these transmitters (**Figure 8.13**).

Dependence

Substance dependence, the term now preferred to *addiction,* has two facets that may occur either together or independently: (1) a ***psychological dependence*** that is experienced as a craving for a substance and an inability to stop using the substance at will; and (2) a ***physical dependence*** that requires one to take the substance to avoid ***withdrawal***, which is the spectrum of unpleasant physiological symptoms that occur with cessation of substance use. Substance dependence is diagnosed if three or more of the characteristics listed in **Table 8.3** occur within a 12-month period. **Table 8.4** lists rates of use and risk of dependence for some commonly used substances.

Several neuronal systems are involved in substance dependence, but most psychoactive substances act on the mesolimbic dopamine pathway (see Figure 8.9). In addition to the actions of this system mentioned earlier in the context of motivation and emotion, the mesolimbic dopamine pathway allows a person to experience pleasure in response to pleasurable events or in response to certain substances. Although the major neurotransmitter implicated in substance dependence is dopamine, other neurotransmitters, including GABA, enkephalin, serotonin, and glutamate, may also be involved.

Tolerance

Tolerance to a substance occurs when increasing doses of the substance are required to achieve effects that initially occurred in response to a smaller dose. That is, it takes more of the substance to do the same job. Moreover, tolerance can develop to another substance as a result of taking the initial substance, a phenomenon called ***cross-tolerance***. Cross-tolerance may develop if the physiological actions of the two substances are similar. Tolerance and cross-tolerance can occur with many classes of substances, not just psychoactive substances.

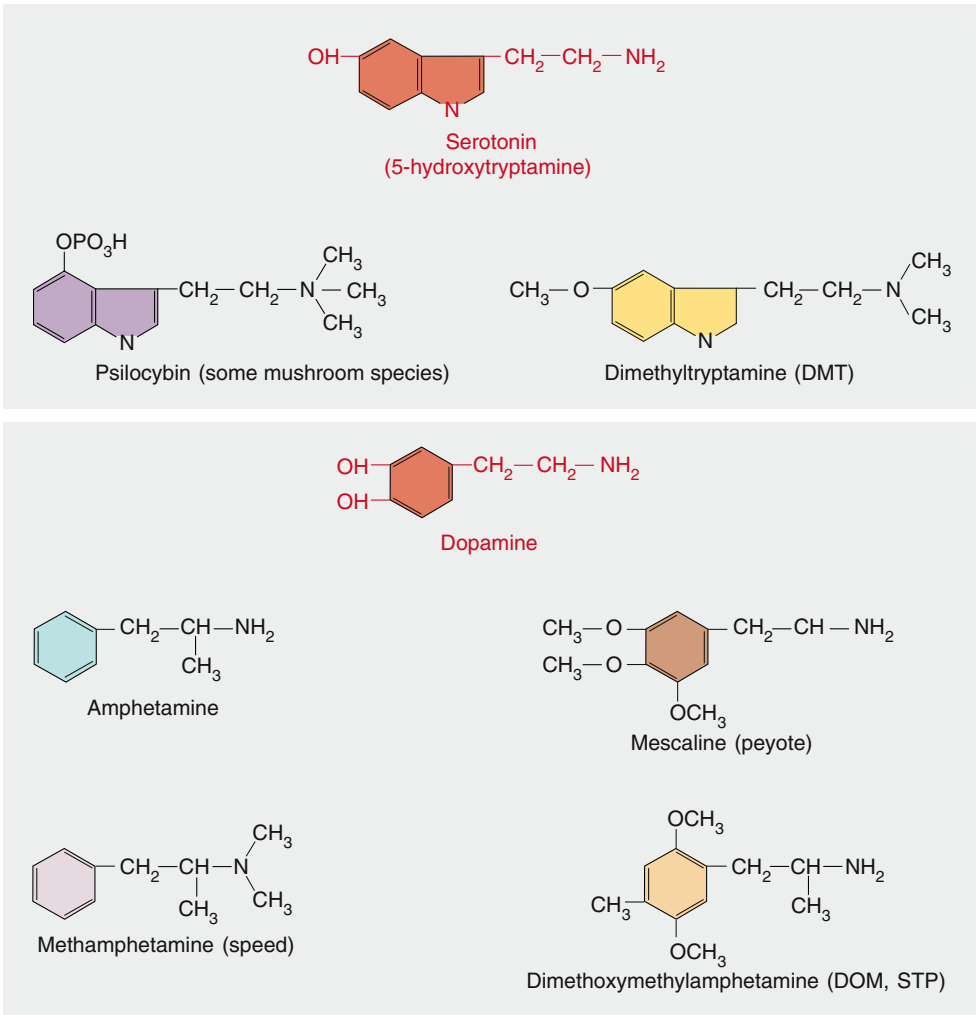


Figure 8.13 Molecular similarities between neurotransmitters (orange) and some substances that elevate mood. At high doses, these substances can cause hallucinations.

PHYSIOLOGICAL INQUIRY

- How would you expect dimethyltryptamine (DMT) to affect sleeping behavior?

Answer can be found at end of chapter.

TABLE 8.3 Diagnostic Criteria for Substance Dependence

Substance dependence is indicated when three or more of the following occur within a 12-month period.

I. Tolerance, as indicated by
   A. a need for increasing amounts of the substance to achieve the desired effect, or
   B. decreasing effects when continuing to use the same amount of the substance.

II. Withdrawal, as indicated by
   A. appearance of the characteristic withdrawal symptoms upon terminating use of the substance, or
   B. use of the substance (or one closely related to it) to relieve or avoid withdrawal symptoms.

III. Use of the substance in larger amounts or for longer periods of time than intended.

IV. Persistent desire for the substance; unsuccessful attempts to cut down or control use of the substance.

V. A great deal of time is spent in activities necessary to obtain the substance, use it, or recover from its effects.

VI. Occupational, social, or recreational activities are given up or reduced because of substance use.

VII. Use of the substance is continued despite knowledge that one has a physical or psychological problem that the substance is likely to exacerbate.

Source: Table adapted from *The Diagnostic and Statistical Manual of Mental Disorders,* 4th ed., American Psychiatric Association, Arlington, VA, 2000.

Tolerance may develop because the presence of the substance stimulates the synthesis of the enzymes that degrade it. With persistent use of a substance, the concentrations of these enzymes increase, so more of the substance must be administered to produce the same plasma concentrations and, therefore, the same initial effect.

Alternatively, tolerance can develop as a result of changes in the number and/or sensitivity of receptors that respond to the substance, the amount or activity of enzymes involved in neurotransmitter synthesis, the activity of reuptake transport molecules, or the signal transduction pathways in the postsynaptic cell.

8.5 Learning and Memory

Learning is the acquisition and storage of information as a consequence of experience. It is measured by an increase in the likelihood of a particular behavioral response to a stimulus. Generally, rewards or punishments are crucial ingredients of learning, as are contact with and manipulation of the environment. **Memory** is the relatively permanent storage form of learned information, although, as we will see, it is not a single, unitary phenomenon. Rather, the brain processes, stores, and retrieves information in different ways to suit different needs.

Memory

The term **memory encoding** defines the neural processes that change an experience into the memory of that experience—in other words, the physiological events that lead to memory formation. This section addresses three questions. First, are there different kinds of memories? Second, where do they occur in the brain? Third, what happens physiologically to make them occur?

New scientific information about memory is being generated at a tremendous pace; there is as yet no unifying theory as to how memory is encoded, stored, and retrieved. However, memory can be viewed in two broad categories called declarative and procedural memory. **Declarative memory** (sometimes also referred to as "explicit" memory) is the retention and recall of conscious experiences that can be put into words (declared). One example is the memory of having perceived an object or event and, therefore, recognizing it as familiar and maybe even knowing the specific time and place the memory originated. A second example would be the general knowledge of the world, such as names and facts. The hippocampus, amygdala, and other parts of the limbic system are required for the formation of declarative memories.

The second broad category of memory, **procedural memory,** can be defined as the memory of how to do things (sometimes this is also called "implicit" or "reflexive" memory).

TABLE 8.4 Substance Use and Dependence

Substance	Percentage of Population Using at Least Once	Percentage of Population Who Meet Dependence Criteria	Percentage of Those Using Who Become Dependent
Tobacco	75.6	24.1	31.9
Heroin	1.5	0.4	23.1
Cocaine	16.2	2.7	16.7
Alcohol	91.5	14.1	15.4
Amphetamines	15.3	1.7	11.2
Marijuana	46.3	4.2	9.1

Source: Table adapted from Laurence L. Brunton, John S. Lazo, and Keith L. Parker, eds., *Goodman and Gilman's The Pharmacological Basis of Therapeutics,* 11th ed., McGraw-Hill, NY, 2006.

This is the memory for skilled behaviors independent of conscious understanding, as, for example, riding a bicycle. Individuals can suffer severe deficits in declarative memory but have intact procedural memory. One case study describes a pianist who learned a new piece to accompany a singer at a concert but had no recollection the following morning of having performed the composition. He could remember how to play the music but could not remember having done so. Procedural memory also includes learned emotional responses, such as fear of spiders, and the classic example of Pavlov's dogs, which learned to salivate at the sound of a bell after the sound had previously been associated with food. The primary areas of the brain involved in procedural memory are regions of sensorimotor cortex, the basal nuclei, and the cerebellum.

Another way to classify memory is in terms of duration—does it last for a long or only a short time? **Short-term memory** registers and retains incoming information for a short time—a matter of seconds to minutes—after its input. In other words, it is the memory that we use when we keep information consciously "in mind." For example, you may hear a telephone number in a radio advertisement and remember it only long enough to reach for your phone and enter the number. Short-term memory makes possible a temporary impression of one's present environment in a readily accessible form and is an essential ingredient of many forms of higher mental activity. When short-term memory is used in a context such as a cognitive task, it is often referred to as "working memory." The distinctions between short-term and working memory are continually evolving as neuroscientists learn more about them; we will simply refer to all such memories as "short-term." Short-term memories may be converted into **long-term memories,** which may be stored for days to years and recalled at a later time. The process by which short-term memories become long-term memories is called **consolidation.**

Focusing attention is essential for many memory-based skills. The longer the span of attention in short-term memory, the better the chess player, the greater the ability to reason, and the better a student is at understanding complicated sentences and drawing inferences from texts. In fact, there is a strong correlation between short-term memory and standard measures of intelligence. Conversely, the specific memory deficit that occurs in the early stages of ***Alzheimer's disease,*** a condition marked by dementia and serious memory losses, may be in this attention-focusing component of short-term memory.

The Neural Basis of Learning and Memory

The neural mechanism and parts of the brain involved vary for different types of memory. Short-term encoding and long-term memory storage occur in different brain areas for both declarative and procedural memories (**Figure 8.14**).

What is happening during memory formation on a cellular level? Conditions such as coma, deep anesthesia, electroconvulsive shock, and insufficient blood supply to the brain, all of which interfere with the electrical activity of the brain, also interfere with short-term memory. Therefore, it is assumed that short-term memory requires ongoing graded or action potentials. Short-term memory is interrupted when a person becomes unconscious from a blow on the head, and memories are abolished for all that happened for a variable period of time before the blow, a condition called ***retrograde amnesia.*** (***Amnesia*** is the general term for loss of memory.) Short-term memory is also susceptible to external interference, such as an attempt to learn conflicting information. On the other hand, long-term memory can survive deep anesthesia, trauma, or electroconvulsive shock, all of which disrupt the normal patterns of neural conduction in the brain. Thus, short-term memory requires electrical activity in the neurons.

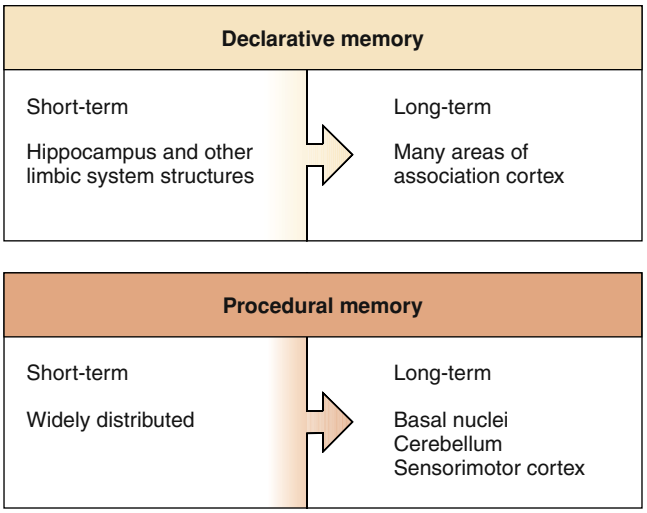


Figure 8.14 Brain areas involved in encoding and storage of declarative and procedural memories.

PHYSIOLOGICAL INQUIRY

- After a brief meeting, you are more likely to remember the name of someone you are strongly attracted to than the name of someone for whom you have no feelings. Propose a mechanism.

Answer can be found at end of chapter.

Another type of amnesia is referred to as ***anterograde amnesia.*** It results from damage to the limbic system and associated structures, including the hippocampus, thalamus, and hypothalamus. Patients with this condition lose their ability to consolidate short-term declarative memories into long-term memories. Although they can remember stored information and events that occurred before their brain injury, after the injury they can only retain information as long as it exists in short-term memory.

The case of a patient known as H.M. illustrates that formation of declarative and procedural memories involves distinct neural processes and that limbic system structures are essential for consolidating declarative memories. In 1953, H.M. underwent bilateral removal of the amygdala and large parts of the hippocampus as a treatment for persistent, debilitating epilepsy. Although his epileptic condition improved after this surgery, it resulted in anterograde amnesia. He still had a normal intelligence and a normal short-term memory. He could retain information for minutes as long as he was not distracted; however, he could not form long-term memories. If he was introduced to someone on one day, on the next day he did not recall having previously met that person. Nor could he remember any events that occurred after his surgery, although his memory for events prior to the surgery

was intact. Interestingly, H.M. had normal procedural memory and could learn new puzzles and motor tasks as readily as normal individuals. This case was the first to draw attention to the critical importance of temporal lobe structures of the limbic system in consolidating short-term declarative memories into long-term memories. Additional cases since have demonstrated that the hippocampus is the primary structure involved in this process. Because H.M. retained memories from before the surgery, his case showed that the hippocampus is not involved in the *storage* of declarative memories.

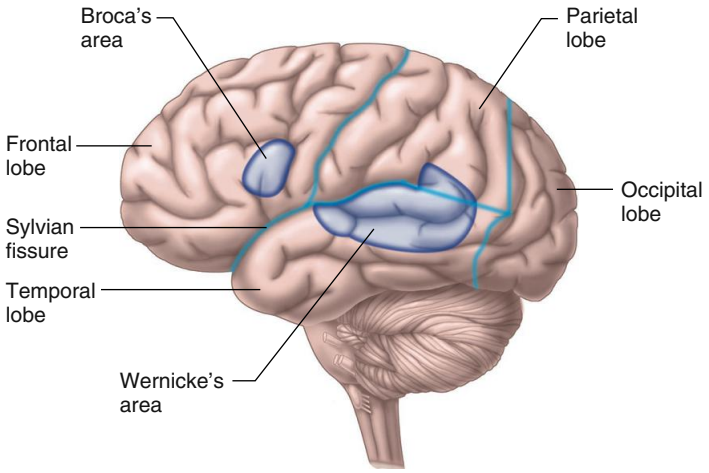
The problem of exactly how memories are stored in the brain is still unsolved, but some of the pieces of the puzzle are falling into place. One model for memory is **long-term potentiation (LTP),** in which certain synapses undergo a long-lasting increase in their effectiveness when they are heavily used. Review Figure 6.36, which details how this occurs at glutamatergic synapses. An analogous process, **long-term depression (LTD),** *decreases* the effectiveness of synaptic contacts between neurons. The mechanism of this suppression of activity appears to be mainly via changes in the ion channels in the postsynaptic membrane.

It is generally accepted that long-term memory formation involves processes that alter gene expression. This is achieved by a cascade of second messengers and transcription factors that ultimately leads to the production of new cellular proteins. These new proteins may be involved in the increased number of synapses that have been demonstrated after long-term memory formation. They may also be involved in structural changes in individual synapses (e.g., by an increase in the number of receptors on the postsynaptic membrane). This ability of neural tissue to change because of activation is known as **plasticity.**

8.6 Cerebral Dominance and Language

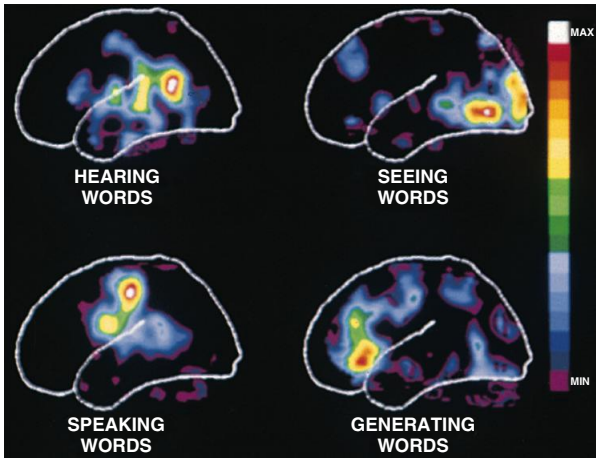
The two cerebral hemispheres appear to be nearly symmetrical, but each has anatomical, chemical, and functional specializations. We have already mentioned that the left hemisphere deals with the somatosensory and motor functions of the right side of the body, and vice versa. In addition, specific aspects of language use tend to be controlled by predominantly one cerebral hemisphere or the other. In 90% of the population, the left hemisphere is specialized to handle specific tasks involved in producing and comprehending language—the conceptualization of the words you want to say or write, the neural control of the act of speaking or writing, and recent verbal memory. This is even true of the sign language used by some deaf people. Conversely, the right cerebral hemisphere in most people tends to have dominance in determining the ability to understand and express affective, or emotional, aspects of language.

Language is a complex code that includes the acts of listening, seeing, reading, speaking, and expressing emotion. The major centers for the technical aspects of language function are in the left hemisphere in the temporal, parietal, and frontal cortex next to the Sylvian fissure, which separates the temporal lobe from the frontal and parietal lobes (**Figure 8.15**). Each of the various regions deals with a separate aspect of language. For example, distinct areas are specialized for hearing, seeing, speaking, and generating words (**Figure 8.16**). There are even



AP|R **Figure 8.15** Areas of the left cerebral hemisphere found clinically to be involved in the comprehension (Wernicke's area) and motor (Broca's area) aspects of language. Blue lines indicate divisions of the cortex into frontal, parietal, temporal, and occipital lobes. Similar regions on the right side of the brain are involved in understanding and expressing affective (emotional) aspects of language.

distinct brain networks for different categories of things, such as "animals" and "tools." Although the regions responsible for the affective components of language have not been as specifically mapped, it appears they are in the same general region of the right cerebral hemisphere. There is variation between individuals in the regional processing of language, and some research even suggests that males and females may process language slightly



AP|R **Figure 8.16** PET scans reveal areas of increased blood flow in specific parts of the temporal, occipital, parietal, and frontal lobes during various language-based activities. Courtesy of Dr. Marcus E. Raichle.

PHYSIOLOGICAL INQUIRY

- Note the various brain areas of increased metabolic activity as revealed by the PET scan in this figure. How does this reflect the general principle of physiology that information flow between cells, tissues, and organs is an essential feature of homeostasis and allows for integration of physiological processes?

Answer can be found at end of chapter.

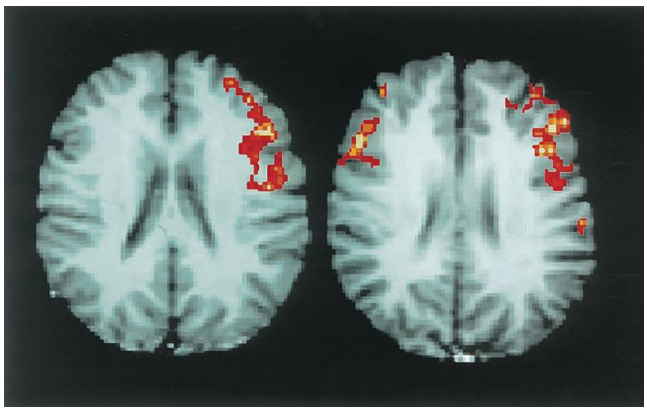
differently. Females are more likely to involve areas of both hemispheres for some language tasks, whereas males generally show activity mainly on the left side (**Figure 8.17**).

Much of our knowledge about how language is produced has been obtained from patients who have suffered brain damage and, as a result, have one or more defects in language, including ***aphasia*** (from the Greek, "speechlessness") and ***aprosodia***. (**Prosody** includes aspects of communication such as intonation, rhythm, pitch, emphasis, gestures, and accompanying facial expressions, so aprosodia refers to the absence of those aspects.)

The specific defects that occur vary according to the region of the brain that is damaged. For example, damage to the left temporal region known as **Wernicke's area** (see Figure 8.15) generally results in aphasias that are more closely related to *comprehension*—the individuals have difficulty understanding spoken or written language even though their hearing and vision are unimpaired. Although they may have fluent speech, they scramble words so that their sentences make no sense, often adding unnecessary words, or even creating made-up words. For example, they may intend to ask someone on a date but say, "If when going movie by fleeble because have to watch would." They are often unaware that they are not speaking in clear sentences. In contrast, damage to **Broca's area,** the language area in the frontal cortex responsible for the articulation of speech, can cause *expressive* aphasias. Individuals with this condition have difficulty carrying out the coordinated respiratory and oral movements necessary for language even though they can move their lips and tongues. They understand spoken language and know what they want to say but have trouble forming words and sentences. For example, instead of fluidly saying, "I have two sisters," they may hesitantly utter, "Two . . . sister . . . sister." Patients with damage to Broca's area can become frustrated because they generally are aware that their words do not accurately convey their thoughts. Aprosodias result from damage to language areas in the right cerebral hemisphere or to neural pathways connecting the left and right hemispheres. Though they can form and understand words and sentences, people with these conditions have impaired ability to interpret or express emotional intentions, and their social interactions suffer greatly as a result. For example, they may not be able to distinguish whether a person who said "thank you very much" was expressing genuine appreciation for a thoughtful compliment or delivering a sarcastic retort after feeling insulted.

The potential for the development of language-specific mechanisms in the two hemispheres is present at birth, but the assignment of language functions to specific brain areas is fairly flexible in the early years of life. Thus, for example, damage to the language areas of the left hemisphere during infancy or early childhood causes temporary, minor language impairment until the right hemisphere can take over. However, similar damage acquired during adulthood typically causes permanent, devastating language deficits. By puberty, the brain's ability to transfer language functions between hemispheres is less successful, and often language skills are lost permanently.

Differences between the two hemispheres are usually masked by the integration that occurs via the corpus callosum and other pathways that connect the two sides of the brain. However, the separate functions of the left and right hemispheres have been uncovered by studying patients in whom the two hemispheres have been separated surgically for treatment of severe epilepsy. These so-called **split-brain** patients participated in studies in which they were asked to hold and identify an object such as a ball in their left or right hand behind a barrier that prevented them from seeing the object. Subjects who held the ball in their right hand were able to say that it was a ball, but persons who held the ball in their left hand were unable to name it. Because the processing of sensory information occurs on the side of the brain opposite to the sensation, this result demonstrated conclusively that the left hemisphere contains a language center that is not present in the right hemisphere. ■



AP|R **Figure 8.17** Images of the active areas of the brain in a male (left) and a female (right) during a language task. (In scans of this type, the patient's left is displayed on the right of the image.) Note that both sides of the woman's brain are used in processing language, but the man's brain is more compartmentalized. Shaywitz et al., 1995 NMR Research/Yale Medical School.

PHYSIOLOGICAL INQUIRY

- Based on typical patterns of cerebral dominance of language tasks, how may you explain the difference in how these two individuals processed this task?

Answer can be found at end of chapter.

SUMMARY

States of Consciousness

I. The electroencephalogram (EEG) provides one means of defining the states of consciousness.
   a. Electrical currents in the cerebral cortex due predominantly to summed postsynaptic potentials are recorded as the EEG.
   b. Slower EEG wave frequencies correlate with less responsive behaviors.
   c. Rhythm generators in the thalamus are probably responsible for the wavelike nature of the EEG.
   d. EEGs are used to diagnose brain disease and damage.

II. Alpha rhythms and, during EEG arousal, beta rhythms characterize the EEG of an awake person.

III. NREM sleep progresses from stage N1 (higher-frequency, smaller-amplitude waves) through stage N3 (lower-frequency, larger-amplitude waves) and then back again, followed by an episode of REM sleep. There are generally four or five of these cycles per night.

IV. Wakefulness is stimulated or regulated by groups of neurons originating in the brainstem and hypothalamus that activate

cortical arousal by releasing orexins, norepinephrine, serotonin, histamine, and acetylcholine. A sleep center in the hypothalamus releases GABA and inhibits these activating centers.

V. Extensive damage to the cerebral cortex or brainstem arousal mechanisms can result in coma or brain death.

Conscious Experiences

I. Brain structures involved in selective attention determine which brain areas gain temporary predominance in the ongoing stream of conscious experience.

II. Conscious experiences may occur because a set of neurons temporarily function together, with the neurons that compose the set changing as the focus of attention changes.

Motivation and Emotion

I. Behaviors that satisfy homeostatic needs are primary motivated behaviors. Behavior not related to homeostasis is a result of secondary motivation.
   a. Repetition of a behavior indicates it is rewarding, and avoidance of a behavior indicates it is punishing.
   b. The mesolimbic dopamine pathway, which goes to prefrontal cortex and parts of the limbic system, mediates emotion and motivation.
   c. Dopamine is the primary neurotransmitter in the brain pathway that mediates motivation and reward.

II. Three aspects of emotion—anatomical and physiological bases for emotion, emotional behavior, and inner emotions—can be distinguished. The limbic system integrates inner emotions and behavior.

Altered States of Consciousness

I. Hyperactivity in a brain dopaminergic system is implicated in schizophrenia.

II. Mood disorders may be caused by disturbances in transmission at brain synapses mediated by dopamine, norepinephrine, serotonin, and acetylcholine.

III. Many psychoactive drugs, which are often chemically related to neurotransmitters, result in substance dependence, withdrawal, and tolerance. The mesolimbic dopamine pathway is implicated in substance abuse.

Learning and Memory

I. The brain processes, stores, and retrieves information in different ways to suit different needs.

II. Memory encoding involves cellular or molecular changes specific to different memories.

III. Declarative memories are involved in remembering facts and events. Procedural memories are memories of how to do things.

IV. Short-term memories are converted into long-term memories by a process known as consolidation.

V. Prefrontal cortex and limbic regions of the temporal lobe are important brain areas for some forms of memory.

VI. Formation of long-term memory probably involves changes in second-messenger systems and protein synthesis.

Cerebral Dominance and Language

I. The two cerebral hemispheres differ anatomically, chemically, and functionally. In 90% of the population, the left hemisphere dominates the technical aspects of language production and comprehension such as word meanings and sentence structure, while the right hemisphere dominates in mediating the emotional content of language.

II. The development of language functions occurs in a critical period that ends shortly after the time of puberty.

III. After damage to the dominant hemisphere, the opposite hemisphere can acquire some language function—the younger the patient, the greater the transfer of function.

REVIEW QUESTIONS

1. State the two criteria used to define one's state of consciousness.
2. What type of neural activity is recorded as the EEG?
3. Draw EEG records that show alpha and beta rhythms, the stages of NREM sleep, and REM sleep. Indicate the characteristic wave frequencies of each.
4. Distinguish NREM sleep from REM sleep.
5. Briefly describe a neural mechanism that determines the states of consciousness.
6. Name the criteria used to distinguish brain death from coma.
7. Describe the orienting response as a form of directed attention.
8. Distinguish primary from secondary motivated behavior.
9. Explain how rewards and punishments are anatomically related to emotions.
10. Explain what brain self-stimulation can tell about emotions and rewards and punishments.
11. Name the primary neurotransmitter that mediates the brain reward systems.
12. Distinguish inner emotions from emotional behavior. Name the brain areas involved in each.
13. Describe the role of the limbic system in emotions.
14. Name the major neurotransmitters involved in schizophrenia and the mood disorders.
15. Describe a mechanism that could explain tolerance and withdrawal.
16. Distinguish the types of memory.
17. Describe the major brain regions involved in comprehension and motor aspects of language.

KEY TERMS

8.1 States of Consciousness

alpha rhythm
beta rhythm
conscious experiences
delta rhythm
EEG arousal
electroencephalogram (EEG)
gamma rhythm
hypocretins
K complexes
NREM sleep
orexins
paradoxical sleep
REM sleep
reticular activating system (RAS)
sleep spindles
states of consciousness
theta rhythm

8.2 Conscious Experiences

habituation
orienting response
preattentive processing
selective attention

8.3 Motivation and Emotion

brain self-stimulation
emotional behavior
inner emotions
mesolimbic dopamine pathway
motivations
primary motivated behavior

8.4 Altered States of Consciousness

mood

8.5 Learning and Memory

consolidation
declarative memory
learning
long-term depression (LTD)
long-term memories
long-term potentiation (LTP)
memory
memory encoding
plasticity
procedural memory
short-term memory

8.6 Cerebral Dominance and Language

Broca's area
prosody
split-brain
Wernicke's area

CLINICAL TERMS

8.1 States of Consciousness

alprazolam (Xanax)
benzodiazepines
brain death
coma
diazepam (Valium)
epilepsy
magnetic resonance imaging (MRI)
narcolepsy
persistent vegetative state
positron emission tomography (PET)
sleep apnea

8.2 Conscious Experiences

attention-deficit/hyperactivity disorder (AD/HD)
methylphenidate (Ritalin)
sensory neglect

8.3 Motivation and Emotion

Urbach–Wiethe disease

8.4 Altered States of Consciousness

altered states of consciousness
amitriptyline (Elavil)
bipolar disorder
catatonia
cross-tolerance
depressive disorder (depression)
desipramine (Norpramin)
doxepin (Sinequan)
electroconvulsive therapy (ECT)
escitalopram (Lexapro)
fluoxetine (Prozac)
lithium (Eskalith, Lithobid)
mania
monoamine oxidase (MAO) inhibitors
mood disorders
paroxetine (Paxil)
physical dependence
psychological dependence
repetitive transcranial magnetic stimulation (rTMS)
schizophrenia
serotonin-specific reuptake inhibitors (SSRIs)
sertraline (Zoloft)
substance dependence
tolerance
tricyclic antidepressant drugs
withdrawal

8.5 Learning and Memory

Alzheimer's disease
amnesia
anterograde amnesia
retrograde amnesia

8.6 Cerebral Dominance and Language

aphasia
aprosodia

CHAPTER 8

Clinical Case Study: Head Injury in a Teenage Soccer Player

In the final minute of the high-school state championship match, with the score tied 1 to 1, the corner kick sailed toward the far post. Lunging for a header and the win, the 17-year-old midfielder was kicked solidly in the right side of her head by a defender. She crumpled to the ground and lay motionless. The team physician rushed onto the field, where the girl lay on her back with her eyes closed. She was breathing normally but failed to respond to the sound of her name or a touch on her arm. An ambulance was immediately summoned. After a few moments, her eyes fluttered open, and she looked up at the doctor and her teammates with a confused expression on her face. Asked how she was feeling, she said "fine" and attempted to sit up but winced in pain and put her hand to her head as the physician told her to remain lying down. It was an encouraging sign that all four limbs and her trunk muscles had moved normally in her attempt to sit up, suggesting she did not have a serious injury to her spinal cord.

The physician then asked her a series of questions. Did she remember how she had been injured? She responded with a blank look and a small shake of her head "no." Did she know what day this was and where she was? After a long pause and a look at her surroundings, she replied that it was Saturday and this was the championship soccer match. How much time was left in the game, and what was the score? Another long pause, and then "It's almost halftime, and it's zero to zero." Before he could ask the next question, her eyes rolled back in their sockets and her body stiffened for several seconds, after which she once again looked around with a confused expression.

Reflect and Review #1

- What are the two general types of amnesia, and which type did this person appear to have?

These signs suggested that she had suffered an injury to her brain and should undergo a thorough neurological exam. The ambulance arrived, she was placed on a rigid backboard with her head supported and restrained, and she was transported to the hospital for further assessment and observation.

By the time she reached the emergency room, she was less disoriented and had no nausea but still complained that her head hurt. Her pulse rate and blood pressure were normal. A series of neurological tests was then performed. When a light was shone into either eye, both pupils constricted equally, which is normal. She was also able to smoothly track a moving object with her eyes. Her sense of balance was good, and she was able to feel a vibrating tuning fork, light pinpricks, and warm and cold objects on the skin of all of her extremities. Muscle tone, strength, and reflexes were also normal. Asked again about the collision, she still was unsure what had happened. However, suddenly straightening in her chair, she said, "Wait—the game was almost over and we were tied one to one. Did we win?"

The blow to this soccer player's head resulted in a ***concussion,*** an injury suffered by more than 300,000 athletes each year in the United States (and as many as 5–10 times that number in the general population). Concussion occurs after some form of head

—Continued next page

—Continued

trauma and often, but not always, causes a brief loss of consciousness. It sometimes results in temporary retrograde amnesia, which varies in extent with the severity of the injury, and also in brief epileptic-like seizures. The mechanism of the loss of consciousness, amnesia, and seizures is thought to be a transient electrophysiological dysfunction of the reticular activating system in the upper midbrain caused by rotation of the cerebral hemispheres on the relatively fixed brainstem. The relatively large size and inertia of the brains of humans and other primates make them especially susceptible to such injuries. By comparison, animals adapted for cranial impact like goats, rams, and woodpeckers are able to withstand 100-fold greater force than humans without sustaining injury. Computed tomography and magnetic resonance imaging scans of most concussion patients show no abnormal swelling or vascular injury of the brain. However, widespread reports of persistent memory and concentration problems have increasingly raised concerns that in some cases concussion injuries may involve lasting damage in the form of microscopic shearing lesions in the brain.

More serious than a concussion is ***intracranial hemorrhage,*** which results from damage to blood vessels in and around the brain. It can be associated with skull fracture, violent shaking, and sudden accelerative forces such as those that would occur during an automobile accident.

Reflect and Review #2

- Recall how the brain sits within the skull (see Figure 6.47); considering that anatomy, why is a hemorrhage in the brain so serious?

Blood may collect between the skull and the dura mater (an ***epidural hematoma,*** **Figure 8.18**), or between the arachnoid mater and the surrounding meninges or within the brain (***subdural hematoma***). Intracranial hemorrhage often occurs without loss of consciousness; symptoms such as nausea, headache, motor dysfunction, and loss of pupillary reflexes may not occur until several hours or days afterward. Because it is encased in tough membranes and surrounded by bone, there is no room for hemorrhaging blood to "leak out;" thus, the excess fluid compresses brain tissue. This can cause serious and possibly permanent damage to the brain. One reason that it is important to closely monitor the condition of a person with concussion for some time after the injury, therefore, is to be able to recognize whether the initial trauma has resulted in an intracranial hemorrhage.

Concussion injuries in sports are receiving increased attention. Some neurologists suspect that concussions have the potential to cause long-term physical, cognitive, and psychological changes, and that the risk is magnified in those who experience multiple concussions. Suspicions have been fueled by high-profile cases of professional boxers who have developed symptoms similar to those seen in the neurodegenerative conditions Parkinson's disease (see Chapter 10) and Alzheimer's disease (see Chapter 6). Recent histological studies of the brains of deceased professional football players have shown significant microscopic damage in those who have suffered multiple concussions. Even more disconcerting are the recent findings in teenage football players, that milder repetitive blows to the head that do not meet the clinical criteria of a concussion may also lead to lasting brain damage. To address issues such as these, research is currently under way in which athletes are being assessed for attention span, memory, processing speed, and reaction time—both before and after suffering concussions. Other initiatives include developing more sensitive diagnostic tests, creating guidelines on when to allow athletes to return to competition following a head injury, and the design of protective headgear.

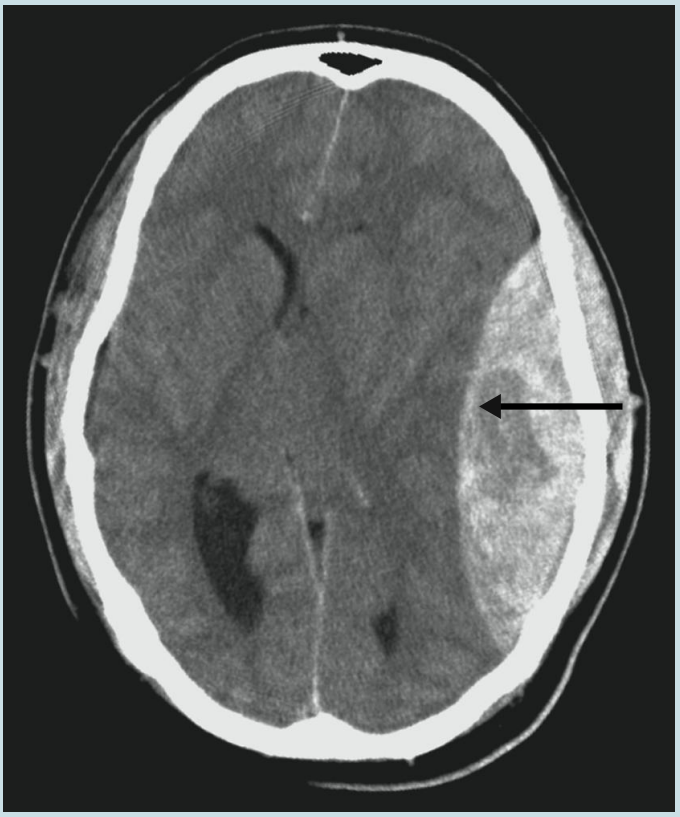


Figure 8.18 CT scan of a large, left-side epidural hematoma resulting from a motorcycle crash in which the rider was not wearing a helmet. Arrow shows where blood pooling within the cranium has compressed the brain tissue. Patient's left side is on the right side of the image. Courtesy of Lee Faucher, M.D., University of Wisconsin SMPH.

The soccer player in this case was given pain medication and kept in the hospital overnight for observation. She had a head CT scan performed, the result of which was normal. She suffered no further seizures, showed no signs of hemorrhage, and by morning her memory had completely returned and other neurological test results were normal. She was sent home with instructions to return for a follow-up examination the next week, or sooner if her headache did not steadily improve. She was also advised to avoid competing for a minimum of 2 weeks. A person who receives a second blow to the head prior to complete healing of a first concussion injury has an elevated risk of suffering life-threatening brain swelling.

Clinical terms: concussion, epidural hematoma, intracranial hemorrhage, subdural hematoma

See Chapter 19 for complete, integrative case studies.

CHAPTER 8 TEST QUESTIONS *Recall and Comprehend*

Answers appear in Appendix A.

These questions test your recall of important details covered in this chapter. They also help prepare you for the type of questions encountered in standardized exams. Many additional questions of this type are available on Connect and LearnSmart.

1–4: Match the state of consciousness (a–d) with the correct electroencephalogram pattern (use each answer once).

State of consciousness:

a. relaxed, awake, eyes closed
b. stage N3 non–rapid eye movement (NREM) sleep
c. rapid eye movement (REM) sleep
d. epileptic seizure

Electroencephalogram pattern:

1. Very large-amplitude, recurrent waves, associated with sharp spikes
2. Small-amplitude, high-frequency waves, similar to the attentive awake state
3. Irregular, slow-frequency, large-amplitude, "alpha" rhythm
4. Regular, very slow-frequency, very large-amplitude "delta" rhythm
5. Which pattern of neurotransmitter activity is most consistent with the awake state?
   a. high histamine, orexins and GABA; low norepinephrine
   b. high norepinephrine, histamine and serotonin; low orexins
   c. high histamine and serotonin; low GABA and orexins
   d. high histamine, GABA and orexins; low serotonin
   e. high orexins, histamine and norepinephrine; low GABA
6. Which best describes "habituation"?
   a. seeking out and focusing on momentarily important stimuli
   b. decreased behavioral response to a persistent irrelevant stimulus
   c. halting current activity and orienting toward a novel stimulus
   d. evaluation of the importance of sensory stimuli that occur prior to focusing attention
   e. strengthening of synapses that are repeatedly stimulated during learning
7. The mesolimbic dopamine pathway is most closely associated with
   a. shifting between states of consciousness.
   b. emotional behavior.
   c. motivation and reward behaviors.
   d. perception of fear.
   e. primary visual perception.
8. Antidepressant medications most commonly target what neurotransmitter?
   a. acetylcholine
   b. dopamine
   c. histamine
   d. serotonin
   e. glutamate
9. Which is a true statement about memory?
   a. Consolidation converts short-term memories into long-term memories.
   b. Short-term memory stores information for years, perhaps indefinitely.
   c. In retrograde amnesia, the ability to form new memories is lost.
   d. The cerebellum is an important site of storage for declarative memory.
   e. Destruction of the hippocampus erases all previously stored memories.
10. Broca's area
    a. is in the parietal association cortex and is responsible for language comprehension.
    b. is in the right frontal lobe and is responsible for memory formation.
    c. is in the left frontal lobe and is responsible for articulation of speech.
    d. is in the occipital lobe and is responsible for interpreting body language.
    e. is part of the limbic system and is responsible for the perception of fear.

CHAPTER 8 TEST QUESTIONS *Apply, Analyze, and Evaluate*

Answers appear in Appendix A.

These questions, which are designed to be challenging, require you to integrate concepts covered in the chapter to draw your own conclusions. See if you can first answer the questions without using the hints that are provided; then, if you are having difficulty, refer back to the figures or sections indicated in the hints.

1. Explain why patients given drugs to treat Parkinson's disease (Chapter 6) sometimes develop symptoms similar to those of schizophrenia. *Hint:* Recall the role of dopamine in these disorders.
2. Explain how clinical observations of individuals with various aphasias help physiologists understand the neural basis of language. *Hint:* Review Section 8.6 for a reminder about aphasias.

CHAPTER 8 TEST QUESTIONS *General Principles Assessment*

Answers appear in Appendix A.

These questions reinforce the key theme first introduced in Chapter 1, that general principles of physiology can be applied across all levels of organization and across all organ systems.

1. Review the general principles of physiology presented in Chapter 1. Which of those eight principles is best demonstrated by the two parts of Figure 8.7, and why?
2. How does the regulation of sleep exemplify the general principle of physiology that *homeostasis is essential for health and survival*?

CHAPTER 8 ANSWERS TO PHYSIOLOGICAL INQUIRY QUESTIONS

Figure 8.1 If the frequency of the waveform is 20 Hz (20 waves per second), then the duration of each wave is 1/20 sec, or 50 msec.

Figure 8.2 The primary visual cortex and related association areas are in the occipital lobes of the brain (review Figure 7.13), so it is most likely that this abnormal rhythm was recorded by electrodes placed on the scalp at the back of the patient's head.

Figure 8.6 Among the drugs used to treat allergic reactions are antihistamines, which block the histamine receptor. They are prescribed because of their ability to block histamine's contributions to the inflammatory response, which include vasodilation and leakiness of small blood vessels (see Table 18.12). Because histamine is associated with the awake state, drowsiness is a common side effect of antihistamines.

Fortunately, antihistamines have been developed that do not cross the blood–brain barrier and thus do not have this side effect (e.g., loratadine [Claritin, Alavert]).

Figure 8.7 There are a number of possible reasons it may be adaptive for cytokines to induce sleep. For example, the decreased physical activity associated with sleep may conserve metabolic energy when running a fever and fighting an infection. Sleeping more and eating less may also help by decreasing intake and plasma concentrations of specific nutrients needed by invading organisms to replicate, like iron (see Chapter 1). From a population health perspective, more time spent in sleep may be adaptive by reducing the number of others with which an infected individual comes into contact.

Figure 8.10 Behavior and all brain-mediated phenomena are the result of changes in electrical properties of neurons. The physical principles that govern electrical signaling apply here, such as the generation of local currents (ion fluxes), movement of current across a resistance (lipid bilayers of plasma membranes), transmission of current (axons), and so on. Note that there is no relevant stimulus causing this animal's behavior; it reflects the electrical events artificially induced in the brain by the implanted electrode.

Figure 8.11 There are many ways emotions could potentially contribute to survival and reproduction. The perception of fear aids survival by stimulating avoidance or caution in potentially dangerous situations, like coming into contact with potentially venomous spiders or snakes or walking near the edge of a high cliff. Our tendency to be disgusted by the smell of rotting food and fecal matter might have evolved as a protection against infection by potentially harmful bacteria or pathogens. Anger and rage could contribute to both survival and reproduction by facilitating our ability to fight for mates or territory or for self-defense. Emotions like happiness and love might have been selected for because of the advantage they provided in kinship safety and pair bonding with mates.

Figure 8.13 An increase in serotonin concentrations is associated with the waking state (refer back to Figure 8.7), so sleep is inhibited by DMT and other drugs that simulate serotonin action. For this same reason, sleeplessness is also a common side effect of antidepressant medications discussed earlier in the text (e.g., serotonin-specific reuptake inhibitors) because they increase serotonin levels in the brain.

Figure 8.14 The involvement of the limbic system in the formation of declarative memories (like remembering names) provides a clue. Experiences that generate strong emotional responses cause greater activity in the limbic system and are more likely to be remembered than emotionally neutral experiences.

Figure 8.16 It is clear from these images that a language task (for example, speaking and listening to words) activates many different parts of the cerebral cortex at the same time. As you have learned in Chapters 6 through 8, different regions of the cortex communicate extensively with each other via fiber tracts. The images in this figure indicate that each specific type of language task is associated with considerable information flow in the form of electrical signals between different regions (lobes) of the cerebral cortex. Other tasks, such as motor tasks or interpretation of various types of sensory input, would also generate complex patterns of activation throughout parts of the cortex.

Figure 8.17 The left side of the brain is responsible for technical aspects of language like the definitions of words, sentence construction, and motor programs for speaking; the right side of the brain is responsible for encoding and expressing affective, or emotional, aspects. The individual showing right-hemisphere activity might have invested greater emotional content in the language task than the individual showing only left-hemisphere activity.

ONLINE STUDY TOOLS

Test your recall, comprehension, and critical thinking skills with interactive questions about higher brain function assigned by your instructor. Also access McGraw-Hill LearnSmart®/SmartBook® and Anatomy & Physiology REVEALED from your McGraw-Hill Connect® home page.

Do you have trouble accessing and retaining key concepts when reading a textbook? This personalized adaptive learning tool serves as a guide to your reading by helping you discover which aspects of higher brain function you have mastered, and which will require more attention.

A fascinating view inside real human bodies that also incorporates animations to help you understand higher brain function.