

Why Do We Sleep?

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The polar bear, or sea bear (*Ursus maritimus*), has an amazing life style (Figure 12-1). As winter begins in the Arctic and the days become shorter, the bears congregate to prepare for their migration north onto the pack ice. Some bears travel thousands of kilometers. In the continuous darkness of the Arctic winter, the bears hunt seals, walrus, and whales. While the bears are on the ice, they take time to sleep; but their sleep cannot be called either nighttime or daytime sleep, because their world is continuously dark. At the same time as the bears are preparing to go out onto the ice, many other Arctic animals are escaping winter. Arctic terns fly 15,000 kilometers to Antarctica, where it is summer. Lemmings, mice, and ground squirrels cannot travel long distances; these rodents spend the winter in burrows in a sleeplike state called hibernation. When summer comes again, the birds return and the rodents emerge from their burrows. The sea bears return from the ice, dig beds in the earth, and spend the summer in sleep.

The behavior of the sea bears is remarkable to us in two ways. First, we are *diurnal* animals (from the Latin *diaes*, meaning “by day”): we are active in the daylight, and we sleep when it is dark. Our recent evolutionary history places early humans in Africa at latitudes where day and night are almost equal in length. Because we are adapted for daylight vision and have difficulty seeing anything at night, we prefer to avoid darkness. Therefore, it seems strange to us that an animal would seek out and flourish in darkness. Second, as diurnal animals, we obtain our food in daylight and we sleep for about 8 hours each night. Our sleep is characterized by a decline in body temperature and a loss of awareness of our surroundings. The sea bears sleep in the winter, as mentioned, but they will spend the entire summer in a condition of shallow **torpor**—a condition resembling sleep except that the decline in body temperature is greater than that during sleep. Their torpor appears to be voluntary because, if they have access to food throughout the year, they do not enter torpor. It is hard to imagine that we could voluntarily spend all summer in a sleeplike condition.

Despite the very great differences between our behavior and the behavior of sea bears, the environmental pres-

sure to which they and we respond is similar. Our behaviors are adaptations that maximize our ability to obtain food and minimize the loss of energy stores that we obtain from food. In other words, we are active during the day because that is when we can obtain food, and we are inactive at night to conserve body resources. Bears hunt all winter to build up fat supplies, and they enter torpor so that they can extend the period during which they can live on those fat stores. *Hibernation* is a strategy that rodents use to extend fat supplies for as long as possible. It is similar to shallow torpor except that body temperature declines are so extreme that the animals expend almost no energy. The *migratory behavior* of birds is also a strategy used to maximize food acquisition and minimize energy loss, except the objective is achieved by moving to a habitat where food is abundant.

There is one other way in which we are similar to sea bears, rodents, and birds. Our behaviors are not simply responses to the immediate changes that are taking place in our respective environments. We anticipate and prepare for the environmental changes that will result in food abundance or food shortages. The sea bears are clearly prepared to go out on the ice well in advance of its formation because they walk along the Arctic shores for weeks before the ice forms; they also leave the ice before it melts. The birds migrate before food resources are depleted and winter sets in. Rodents gorge themselves, build nests, and store food in their burrows before winter arrives. We retire to



David Myers/Tony Stone

Figure 12-1

In winter polar bears migrate to the Arctic ice, where they hunt in darkness and periodically sleep.

sleeping sites in preparation for sleep, and we frequently get up before it is fully light to prepare for our daily activities. Because we, along with other animals, appear to have warning of impending winter or impending changes in the day–night cycle, there must be signals to which we all respond. In this chapter, we will seek answers to the follow-

ing questions related to biological rhythms and sleep: How is our behavior modified to cope with the day–night cycle? Why have we chosen sleep as a strategy for waiting out the night? What neural mechanisms regulate sleep and waking, and what disorders develop when those mechanisms are disrupted?

A CLOCK FOR ALL SEASONS

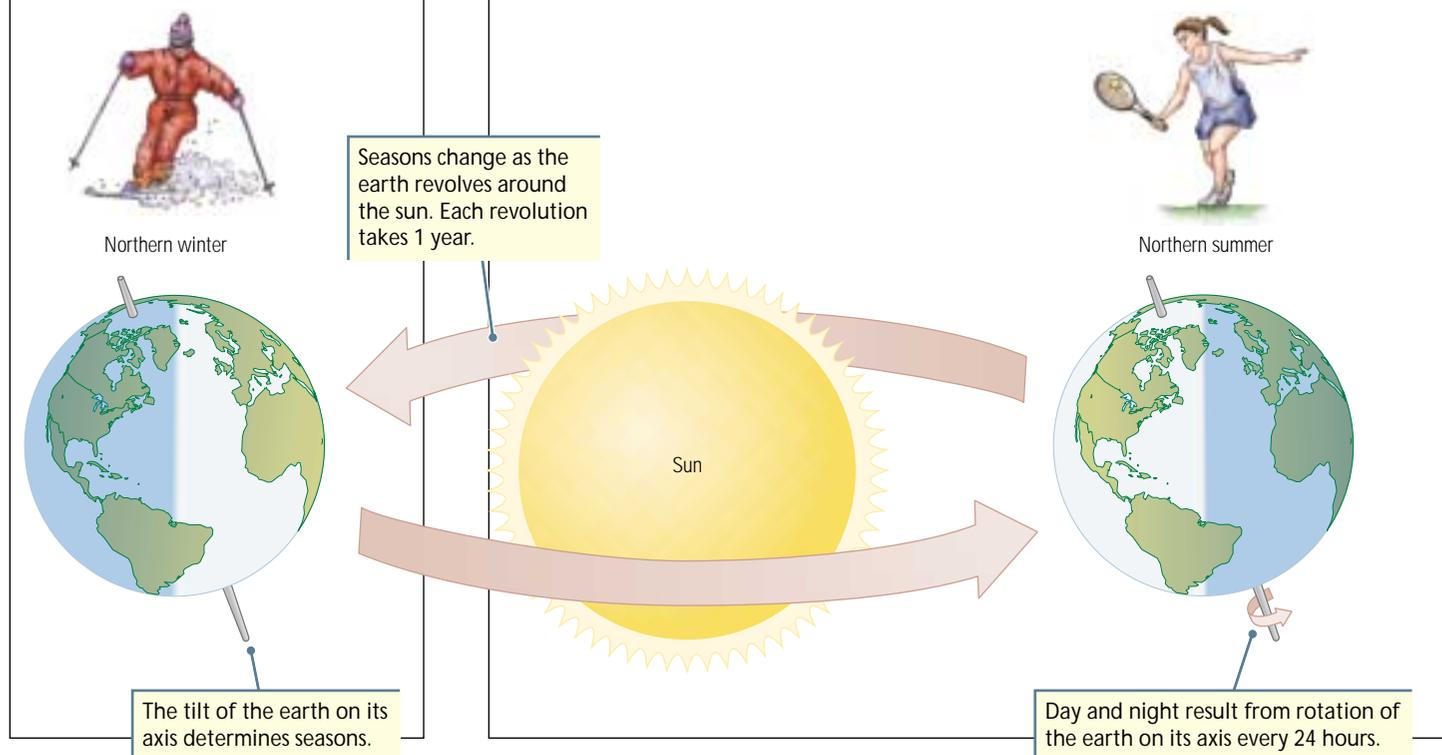
To anticipate daily and seasonal changes, we have biological clocks that respond to cues in our environment. In this section, we will consider the cues that guide our behavior. Because environmental cues themselves are not always consistent, we will examine the role of biological clocks in interpreting environmental cues in an intelligent way. We will also discover how our internal biological clocks adjust our behavior to maintain our schedules.

Figure 12-2

Daily light–dark changes are produced by the daily rotation of the earth on its axis in which each part of the earth faces the sun for part of the rotation cycle (daytime) and faces away from the sun for the other part (nighttime). Seasonal changes in amount of daylight are related to the annual movement of the earth around the sun. Because the axis of the earth is tilted, one pole points toward the sun for part of the year (summertime) and away for the other part of the year (wintertime).

The Origins of Biological Rhythms

The daily and the seasonal changes displayed by animals are called *biological rhythms*. These rhythms are in turn related to the rhythmic cycle of days and seasons produced by the earth's rotation on its axis and the earth's progression around the sun (Figure 12-2). The earth rotates on its axis once every 24 hours, producing a 24-hour cycle of day and night. The axis of the earth is inclined slightly, and so, as the earth orbits the sun, the North Pole is tilted slightly toward the sun for part of the year and is tilted slightly away from the sun for the rest of the year. When inclined toward the sun, the Southern Hemisphere experiences summer and gets more direct sunshine for more hours each day and the climate is warmer. At the same time, the Northern Hemisphere, inclined away from the sun, receives less direct sunlight making the days shorter and



the climate colder. Tropical regions, being near the equator, undergo little climatic change as the earth progresses around the sun.

Because of the seasonal differences in polar and equatorial regions, animals living near the poles are relatively more affected by seasonal changes and animals living near the equator are relatively more affected by day-and-night changes. In addition, the seasonal and daily changes may have combined effects on organisms, inasmuch as the onset and duration of daily changes depend on the season and latitude. Animals living in the polar regions also have to cope with greater fluctuations in daily temperature, light, and food availability than do animals living near the equator.

We humans are equatorial animals in that our behavior is governed more by daily cycles than by seasonal cycles. Our behavior is dominated by a rhythm of daylight activity and nocturnal sleep. Not only does human waking and sleep behavior cycle daily, so also do pulse rate, blood pressure, body temperature, rate of cell division, blood cell count, alertness, urine composition, metabolic rate, sexual drive, and responsiveness to medications. But humans are not unique in this respect. Plants display rhythmic behavior, as exemplified by species in which leaves or flowers open during the day and close at night. Even unicellular algae and fungi display rhythmic behaviors related to the passage of the day. Some animals, including lizards and crabs, change color in a rhythmic pattern. The Florida chameleon, for example, turns green at night, whereas its color matches that of its environment during the day. In short, almost every organism displays changes of some sort that are related to daily or seasonal changes.

Biological Clocks

If the behavior of animals were affected only by seasonal and daily changes, the neural mechanisms that account for changes in behavior would be much simpler to study than they are. That is, behavior would be driven by external cues, which would be easy to identify, and, accordingly, the central processes that respond to those cues also would be easy to identify. That something else is required was first recognized in 1729 by French geologist Jean Jacques D'Ortous de Mairan (see Raven et al., 1992). In an experiment similar to that illustrated in Figure 12-3, De Mairan isolated a plant from daily light and dark cues and from temperature cues and noted that the rhythmic movements of its leaves continued. What concerned de Marain's followers was the possibility that some undetected external cue stimulated the rhythmical behavior of the plant. Such cues could include changes in gravity, changes in electromagnetic fields,

Figure 12-3

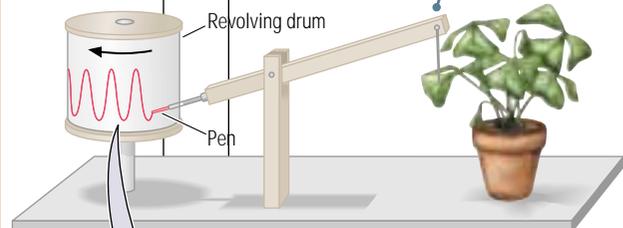
(A) An experimental setup for demonstrating a daily rhythm in wood sorrel. A pen attached to a leaf moves when the leaf moves, producing a record of the leaf's movement on a revolving drum. The plant (B) opens its leaves during the day and (C) closes them at night. The rhythmical activity recorded when the plant is kept in dim light demonstrates that the movement of the leaves is endogenous.

EXPERIMENT

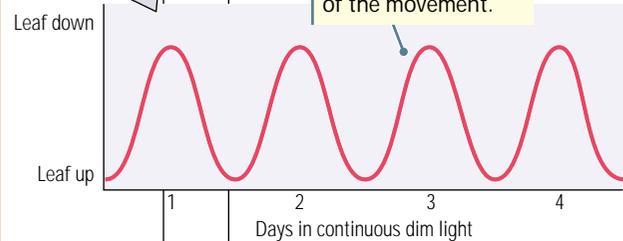
Question: Is plant movement exogenous or endogenous?

Procedure

- (A) The movements of the plant's leaves are recorded in constant dim light. A pen attached to a leaf is moved when the leaf moves,...



Results



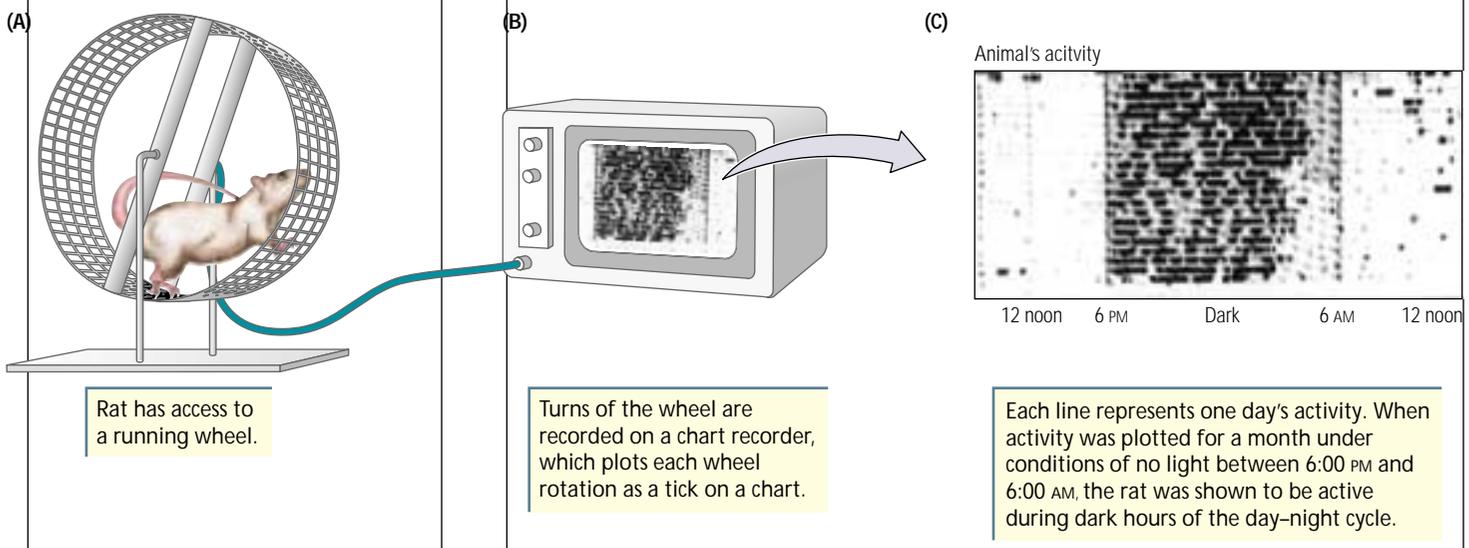
Conclusion

Movement of the plant is endogenous. It is caused by an internal clock that matches the temporal passage of a real day.

Figure 12-4

Creating a record of the daily activity rhythm of a rat. (A) The rat has access to a running wheel. (B) Turns of the wheel are recorded on a chart. (C) The record of each day's activity of a single rat is pasted on a chart. The record of the animal's activity under lighting conditions in which the lights were turned off at 6:00 PM and on at 6:00 AM shows that the animal is active during the dark hours of the day–night cycle.

Adapted from *Biological Clocks in Medicine and Psychiatry* (pp. 12–15), by C. P. Richter, 1965, Springfield, IL: Charles C. Thomas.



and even changes in the intensity of rays from outer space. Nevertheless, it eventually became clear from further experiments that the daily fluctuations were endogenous—that is, they came from within the plant. As we will learn in the following sections, experiments show that most organisms have an **internal clock** that matches the temporal passage of a real day.

A wristwatch or a wall clock enables you to plan and schedule your time. Your internal clock performs these functions, too. A clock allows an animal to anticipate an event: it can migrate before it gets cold rather than waiting until it gets cold. A clock allows an animal to mate at the correct time of the year. A clock allows animals to arrive at the same place at the same time if they are to mate or to begin a migration. Most important, a clock allows an animal to know that if daylight lasts for about 12 hours today, it will last for about 12 hours tomorrow. We can only speculate about how plants and animals evolved internal clocks. Perhaps if behavior were simply driven by external cues, an animal could be tricked into displaying maladaptive behavior. This happens, for example, when plant bulbs begin to grow during a January thaw only to be killed by a subsequent cold spell.

Biological Rhythms

Although the existence of endogenous biological clocks was demonstrated more than 200 years ago, rhythmic behaviors were not studied extensively until quite recently. The detailed study of rhythms had to await the development of procedures that could analyze ongoing behavior over a long period of time. Behavioral analysis requires a method for counting behavioral events and a method for displaying those events in a meaningful way. For example, the behavior of a rodent can be measured by giving the animal access to a running wheel, such as that illustrated in Figure 12-4, in which it can exercise. A chart recorder or a computer records each turn of the wheel and displays the result on a chart. Because rodents are nocturnal, sleeping during light hours and becoming active during dark hours, their wheel-running activity takes place in the dark. If each day's activity is plotted under the preceding day's activity in a column, we can observe a pattern of activity over a period of time. Various details of the record can then be examined, including when the animal was active and how active it was. One of the most important pieces of information that can be obtained from an activity record is the cycle of activity. The time required for a complete cycle of activity to occur is

called a *period*. The period of activity of most rodents is about 24 hours in an environment in which the lights go on and off with regularity. Our own sleep–wake period also is about 24 hours. Many other kinds of behaviors, however, have periods that are more or less than 24 hours.

The results of studies of different species of animals and of different aspects of behavior in a specific animal indicate that a surprisingly large number of biological clocks have varying periods. Two kinds of rhythms typical of most animals are **circannual rhythms** (Latin *circa*, “about,” plus *annual*, “yearly”), of which the migratory cycles of sea bears and Arctic terns are examples, and **circadian rhythms** (Latin *circa*, “about,” plus *dies*, “daily”), which are the day–night rhythms found in almost all animals and cellular processes. These are not the only kinds of rhythms, however. **Ultradian** (Latin *ultra*, “smaller than”) **rhythms** are those that have a period of less than one day. Our eating behavior, which occurs about every 90 minutes to 2 hours, including snacks, is an example of an ultradian rhythm. Rodents, although active throughout the night, are most active at the beginning and end of the dark period. Many sea-dwelling animals have rhythms that are about 12 hours, which match the twice-daily changes in tides produced by the pull of the moon on the earth and its oceans. Therefore, an ultradian rhythm is embedded within their circadian rhythm. Our eye-blink rate, our heart rate, and even the rhythmic action potentials of some of our neurons are other examples of ultradian rhythms. There are also rhythms that have periods of more than a day and less than a year, which are called **infradian** (*infra* meaning “within a year”) **rhythms**. The menstrual cycle of female humans, which has a period of about 28 days, is an example of an infradian rhythm. The term *lunatic* (from the Latin for “moon”) was once used to describe people with mental illness, on the mistaken notion that madness was influenced by the cyclic appearance of a full moon.

In this chapter, we will focus on the circadian rhythm, which is central to our sleep–waking behavior. Note, however, that the fact that a behavior appears to be rhythmic does not mean that it is produced by a clock. There is evidence that sea bears will remain on the ice as long as the ice pack and food supplies last, and many migrating birds will postpone their migrations as long as they have a food supply. Therefore, it is necessary to demonstrate experimentally that a rhythmic behavior is produced by a biological clock. A definitive experiment to support the conclusion that the sea bear does have a clock would be methodologically difficult to conduct, but such demonstrations are not difficult to make with other animals, including ourselves.

Free-Running Rhythms

To determine if a rhythm is produced by a biological clock, researchers must design a test in which they remove all external cues. If light is assumed to be a major cue, there are three ways to set up the experiment: a test can be given in continuous light, it can be given in continuous dark, or the selection of light–dark can be left to the subject.

That the human sleep–waking rhythm is governed by a biological clock was first demonstrated by Jurgen Aschoff and Rutger Weber (see Kleitman, 1965), who allowed subjects to select their light–dark cycle. The experimenters placed individual subjects in an underground bunker in which there were no cues to signal when day began or ended. Thus, the subjects selected the periods when their lights were on or off, when they were active, and when they slept. In short, they selected their own day and night length. By measuring ongoing behavior and recording sleeping periods with sensors on the beds, Aschoff and Weber found that the subjects continued to show daily sleep–activity rhythms. This finding demonstrated that humans have an endogenous biological clock that governs sleep–waking behavior.

Circadian rhythm. An event that occurs with a rhythmic cycle once each day.

Biological rhythm	Time frame	Example
Circannual	Yearly	Migratory cycles of birds
Infradian	Less than a year	Human menstrual cycle
Circadian	Daily	Human sleep cycle
Ultradian	Less than a day	Human eating cycles

Figure 12-5

A free-running rhythm in a human subject. The record for days 1–3 shows the daily sleep period under normal day–night conditions. Days 4–20 show the free-running rhythm that developed while the subject was isolated in a bunker and allowed to control day and night length. The daily activity rhythm shifts from 24 hours to 25.9 hours. On days 21–25, the rhythm frequency returns to 24 hours when the subject is again exposed to a normal light and dark cycle.

Adapted from *Sleep* (p. 33), by J. A. Hobson, 1989, New York: Scientific American Library.

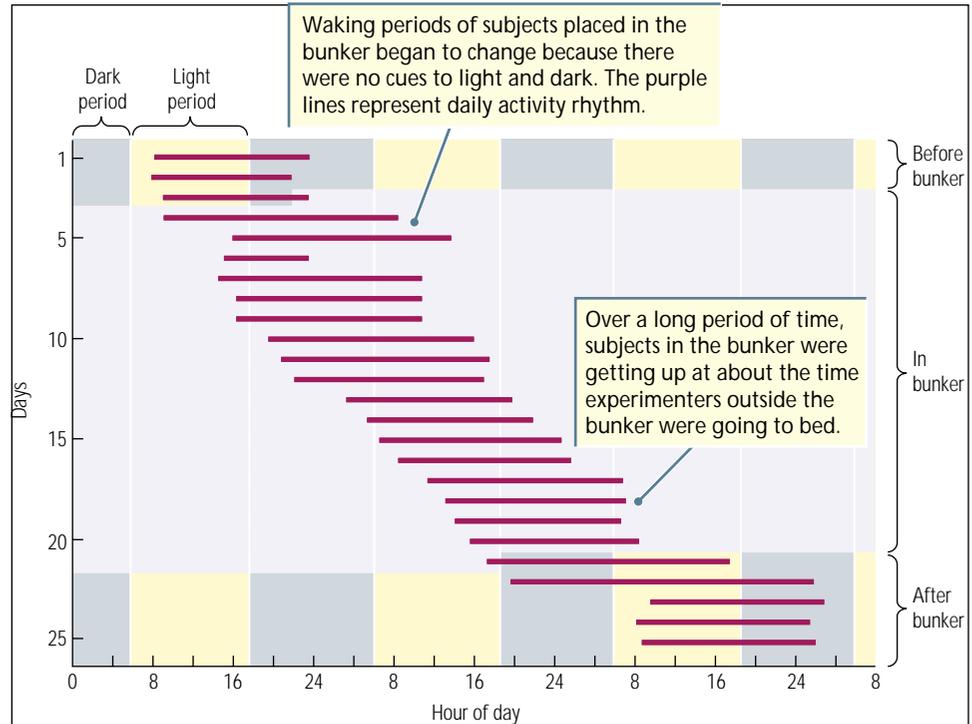
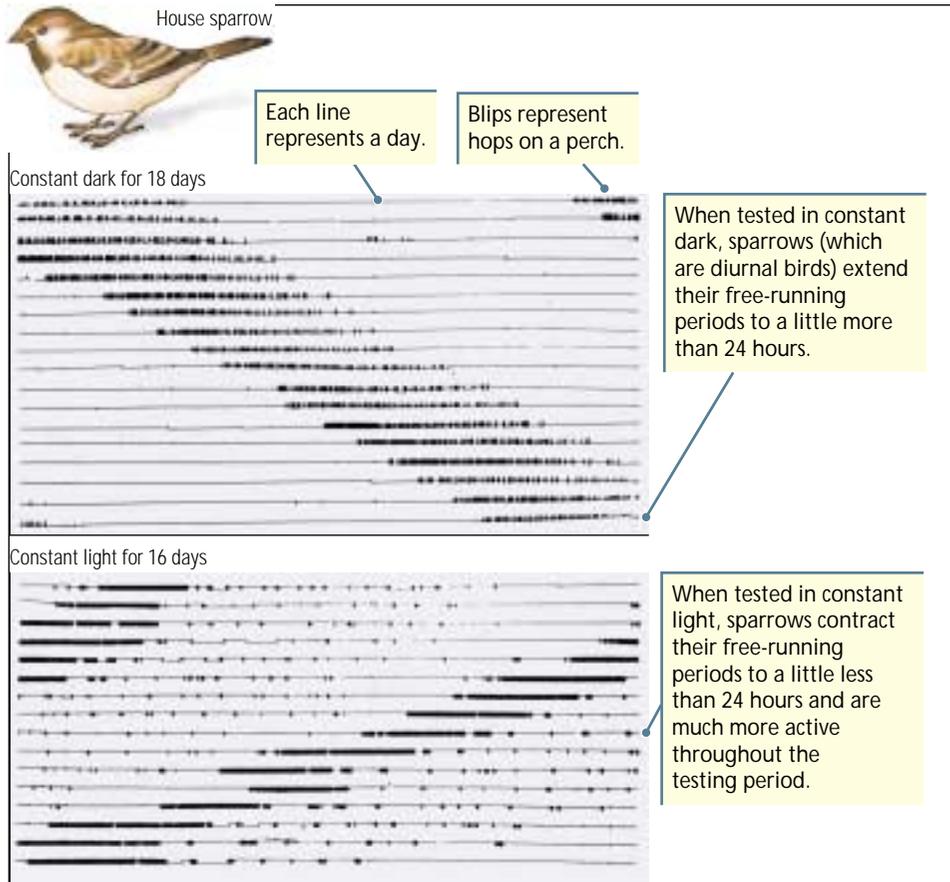


Figure 12-5 shows, however, that the rhythms recorded by Aschoff and Weber were rather peculiar when compared with the rhythms before and after isolation. Although the period of the sleep–wake cycle of Aschoff and Weber’s subjects approximated a normal rhythm of 24 hours before and after the test, during the test it progressively deviated away from clock time. Rather than being 24 hours, the period of the rhythm in the bunker was about 25 to 27 hours, depending on the subject. The subjects were choosing to go to bed from 1 to 2 hours later every night. A shift by an hour or so of sleeping time is not remarkable for a few days, but its cumulative effect over a longer period of time was quite dramatic: soon the subjects were getting up at about the time the experimenters outside the bunker were going to bed. Clearly, the subjects were displaying their own personal rhythms. A rhythm that runs at a frequency of the body’s own devising when environmental cues are absent is called a **free-running rhythm**.

The period of free-running rhythms depends on the way in which external cues are removed. When hamsters, a nocturnal species, are tested in constant darkness, their free-running periods are a little shorter than 24 hours; when they are tested in constant light, their free-running periods are a little longer than 24 hours. This test dependency in hamsters is typical of nocturnal animals. As Figure 12-6 shows, the opposite free-running periods are typical of diurnal animals (Binkley, 1990). When sparrows, which are diurnal birds, are tested in constant dark, their free-running periods are a little longer than 24 hours; when they are tested in constant light, their free-running periods are a little shorter than 24 hours. It is not clear why periods change in different lighting conditions, but a rule of thumb is that animals will expand and contract their sleep periods as the sleep-related lighting period expands or contracts. If you understand this point, you can predict how artificial lighting influences human circadian periods, and you can offer an explanation of why Aschoff and Weber’s subjects displayed periods that were longer than 24 hours. Endogenous rhythmicity is not the only factor that contributes to circadian periods, however. An endogenous rhythm that is just a little slow or a little fast would be useless, so there must also be a mechanism for setting rhythms so that they correspond to environmental events.

Free-running rhythm. A rhythm of the body’s own devising in the absence of all external cues.

**Figure 12-6**

The upper event record shows a house sparrow's free-running rhythm in constant dark (the thicker segments of each link on the record represent the bird's movements on a perch). The lower record shows a sparrow's free-running rhythm in constant light. The differences in a sparrow's responses to constant dark and constant light are characteristic of the free-running rhythms of diurnal animals.

Adapted from *The Clockwork Sparrow* (p. 16), by S. Binkley, 1990, Englewood Cliffs, NJ: Prentice Hall.

Zeitgebers

Because Aschoff and Weber's subjects had a sleep–wake cycle of 24 hours before and after they entered the experiment and because hamsters usually have a 24-hour rhythm, we might wonder how normal rhythms are maintained. There must be some way that the biological clock is kept to a time that matches changes in the day–night cycle. If a biological clock is like a slightly defective wristwatch that runs either too slow or too fast, it will eventually provide times that are inaccurate by hours and so become useless. If we reset the wristwatch each day, however—say, when we awaken—it would then provide useful information even though it is not perfectly accurate. There must be an equivalent way of resetting an errant biological clock. In experiments to determine how clocks are set, researchers have found that cues such as sunrise and sunset, eating times, and other activities can all set the circadian clock. Normally, light is the most potent stimulus for setting a biological clock. Aschoff and Weber called such cues **Zeitgebers** (the German word for “time givers”). When a clock is reset by a zeitgeber, it is said to be **entrained**. The importance of light in entraining circadian rhythms is explained in “Seasonal Affective Disorder” on page 452.

Biological clocks can be reset each day so that they accurately correspond to the season. Remember that, in polar regions, the time of onset and the length of day and night are changing as the seasons progress. To adjust to these changes, an animal needs to anticipate daylight as well as have a good idea of how long the day will last. A biological clock that is reset each day tells an animal that daylight will begin tomorrow at approximately the same time that it began today and that tomorrow will last approximately as long as today did. This information is very useful when we consider

Zeitgeber. An environmental event that entrains biological rhythms; a “time giver.”

Entrain. To make one event occur within the same period as another event occurs; literally, to get on a train.

Seasonal Affective Disorder

Sadness	Later waking
Anxiety	Increased sleep time
Irritability	Interrupted, not refreshing sleep
Decreased physical activity	Daytime drowsiness
Increased appetite	Decreased libido
Carbohydrate craving	Menstrual difficulties
Increased weight	Work difficulties
Earlier sleep onset	Interpersonal difficulties

The symptoms listed above are those observed in more than 66 percent of people who report depression during the winter months in northern latitudes, a condition called *seasonal affective disorder (SAD)*. One explanation of seasonal affective disorder is that the light phase of the circadian rhythm is too short to entrain the circadian rhythms. Consequently, a person's rhythm likely becomes a free-running rhythm. Because people vary in the duration of the phase of their free-running rhythms, some people may be phase retarded, with sleep time coming earlier each day, or phase delayed, with sleep time coming later each day, in relation to the actual day–night cycle. In a diurnal species, the perception of longer nights by the circadian pacemaker most likely results in pressure for increased sleep duration which, if not satisfied, results in cumulative sleep deprivation.

One treatment for SAD is to entrain the circadian rhythm.

The basic idea is to increase the short winter photoperiod by exposing a person to artificial bright light (at least 2500 lux; usual room lighting is not thought to be sufficiently bright). Typically, a person undergoing phototherapy for SAD sits in front of a bank of bright lights. Some investigators recommend the exposure in the morning, others recommend it in the evening, and still others recommend bracketing the day with morning and evening exposure. Investigators consistently report that light is capable of ameliorating depression.



Exposure to a bright light each winter morning entrains the circadian rhythm.

Courtesy of Bio-Light by Enviro-Med, 800-222-3296, www.bio-light.com



Hamster

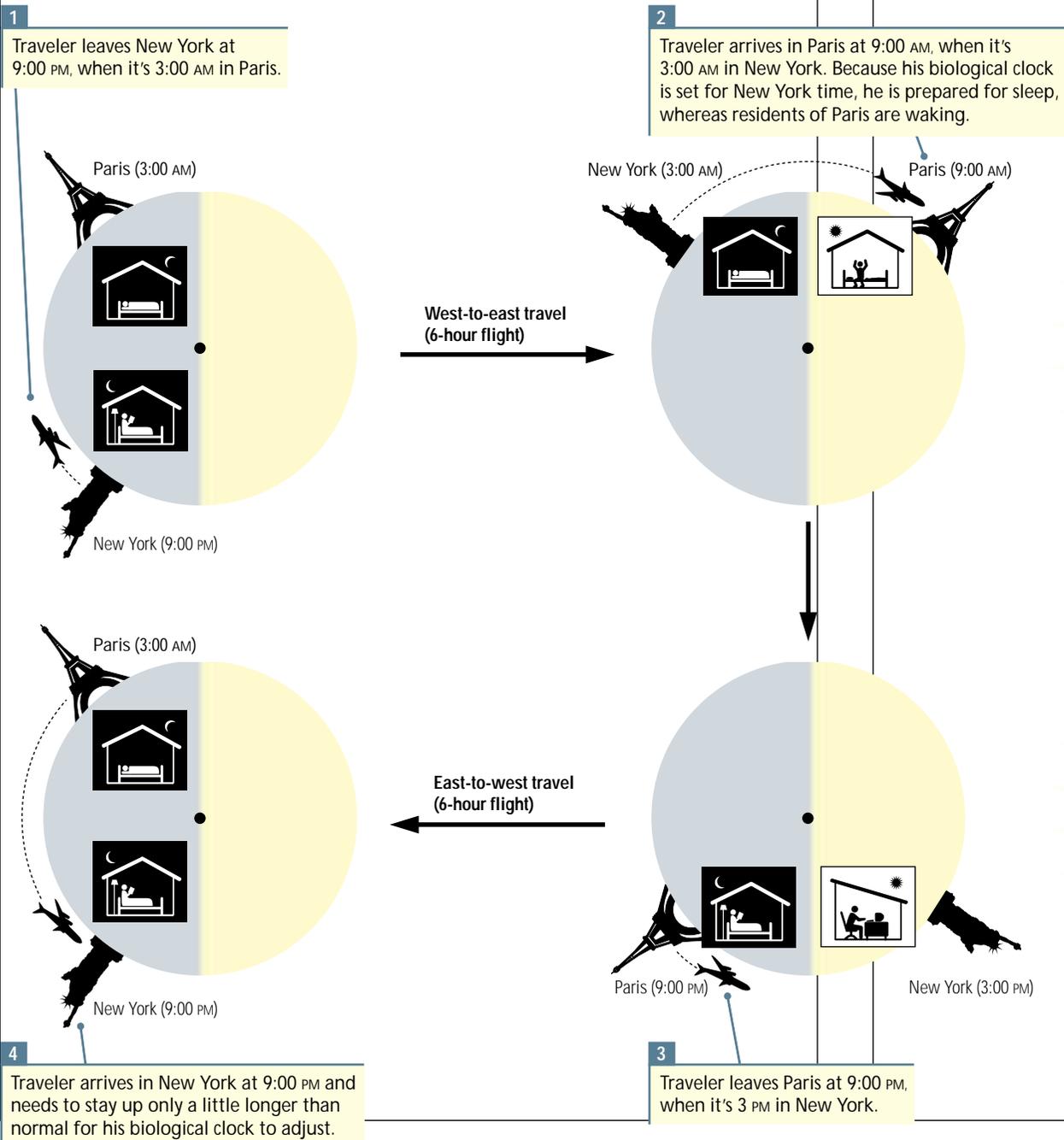
that, in higher latitudes, daylight begins very early in the morning in summer and very late in the morning in winter.

When should the clock be reset? Zeitgebers work best when they are given near the beginning of the light segment of the cycle. The very potent entraining effect of zeitgebers is illustrated by laboratory studies of Syrian hamsters, perhaps one of the most compulsive animals with respect to timekeeping. When given access to running wheels, hamsters exercise during the night segment of the laboratory day–night cycle. A single brief flash of light is an effective zeitgeber for entraining their biological clocks. (If a hamster happens to blink during this zeitgeber, the light will still penetrate its closed eyelids and entrain its biological clock.) Considering the somewhat less compulsive behavior displayed by some of us, we should shudder at the way that we entrain our own clocks when we stay up late in artificial light, sleep late some days, and get up early by using an alarm clock on other days. Such inconsistent behavior with respect to the human biological clock has been associated with job-related fatigue and accidents.

Entrainment also works best if the adjustment to the clock is not too large. People who do shift work are often subject to huge adjustments, especially when they work the graveyard shift (11:00 PM to 8:00 AM), the period when they would normally sleep. Studies show that such a change is difficult to adapt to and is very stressful. Adaptations to shift work are better if workers work the evening shift (3:00 PM to 11:00 PM) before beginning the graveyard shift. Traveling from North America to Europe or Asia also demands a large and difficult time adjustment. For example, travelers flying east from New York to Paris will be beginning their first European day just when their biological clocks are prepared for sleep (Figure 12-7). The difference between a person's circadian rhythm and the daylight cycle in a new environment can produce a feeling of disorientation called "jet lag," referring to jet travel as the cause of such a large, rapid difference. The west-to-east flyer generally has a more difficult adjustment than does the east-to-west traveler, who needs to stay up only a little longer than normal.

Figure 12-7

Jet lag is a disruption in the entrainment of a person's biological clock that may be brought on by jet travel. The disorientation is likely to be more pronounced in west-to-east travel, as from New York to Paris, because the disruption in the person's circadian rhythm is more dramatic. On the return journey, the traveler's biological clock has a much easier adjustment to make.



Traveler arrives in New York at 9:00 PM and needs to stay up only a little longer than normal for his biological clock to adjust.

Traveler leaves Paris at 9:00 PM, when it's 3 PM in New York.

In Review

Many behaviors occur in a rhythmic pattern in relation to time of year or time of day. These rhythmic behaviors are called biological rhythms: the behaviors having a yearly cycle are called circannual rhythms, and the behaviors having a daily cycle are called circadian rhythms. Biological rhythms are timed by regions of the nervous system that serve as biological clocks to time most of our circadian rhythms, especially our sleep–wake cycles. Although biological clocks keep fairly good time, their periods may be slightly shorter or longer than a 24-hour day unless they are reset each day. Their spontaneous periods are called free-running rhythms. The environmental cues that reset the biological clock are called zeitgebers.

THE NEURAL BASIS OF THE BIOLOGICAL CLOCK

Curt Richter (1965) was the first person to attempt to locate biological clocks in the brain. In the 1930s, he captured wild rats and tested them in activity wheels; he found that the animals ran, ate, and drank when the lights were off and were relatively quiescent when the lights were on. Richter's hypothesis was that the rats' rhythmic behavior and the biological clock that was responsible for rhythmicity were separate.

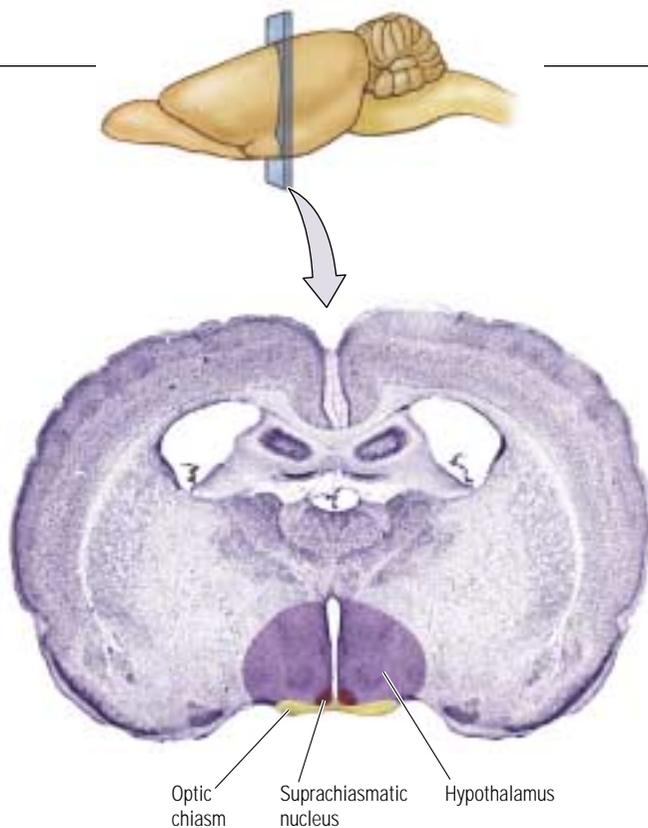
Richter proposed that observable behavior was analogous to the hands of a real clock and was driven by a biological clockwork that was analogous to the springs and wheel inside the clock. The clockwork moved the clock hands and would continue to keep time even if the hands were removed. In other words, he thought that the biological clock acted as a **pacemaker** to instruct other neural structures when they should produce the behaviors for which they were responsible. Thus, behaviors such as running, eating, drinking, and changes in body temperature occur when the pacemaker tells their relevant neural areas that it is time to begin. In support of this idea, Richter found that drugs and changes in body temperature could abolish rhythmic behavior for a number of days, but when the behavior resumed, it occurred at precisely the right time. If an animal was drugged or cooled to decrease its activity, for example, its biological clock still kept the correct time, as indicated by the animal's increased activity when it was warmed up. Many subsequent experiments have confirmed that the time-keeping of the biological clock is resistant to changes in temperature. This finding explains why hibernating animals, whose temperature falls so dramatically, still wake up at the right time in the spring. The finding also demonstrates that the clock and the behavior that it generates are separate, because the biological clock can keep time even though paced behavior does not take place.

Richter further proposed that the biological clock is localized in the brain, rather than being a property of all body or all brain cells. By inserting an electrode into the brain to damage brain tissue with electric current, he found that animals lost their circadian rhythms after damage to the hypothalamus. Subsequently, by making much more discrete lesions, experimenters have shown that a region called the **suprachiasmatic nucleus** is a biological clock (Ralph & Lehman, 1991). As illustrated in Figure 12-8, the suprachiasmatic nucleus is located in the hypothalamus, just above (*supra*) the optic chiasm—hence its name. The suprachiasmatic nucleus receives information about light through its own special visual pathway, the **retinohypothalamic pathway**. This pathway consists of a subset of cone receptors in the retina that are connected to a subset of optic-tract fibers and use glutamate as their primary neurotransmitter. Light signals are carried by this pathway to the suprachiasmatic nucleus to excite and to en-

Pacemaker. A structure that times or determines the period of activity of another structure or an event.

Suprachiasmatic nucleus. A nucleus, located just above the optic chiasm, that is the main pacemaker of circadian rhythms.

Retinohypothalamic pathway. A pathway from a subset of cone receptors in the retina to the the suprachiasmatic nucleus that allows light to entrain the rhythmic activity of the suprachiasmatic nucleus.

**Figure 12-8**

(Top) A lateral view of the rat brain.
 (Bottom) A coronal section through the brain at the level of the optic chiasm, showing the location of the suprachiasmatic nuclei within the hypothalamus and just above the optic chiasm.

train the suprachiasmatic nucleus. Visual fibers carrying information about rhythms also go to an area of the thalamus called the intergeniculate leaflet, but we will limit our consideration of rhythms to the role of the suprachiasmatic nucleus.

Scientists have found another pacemaker in the retina and a third one in the pineal gland. Some behaviors may be paced by widely distributed pacemaker brain cells. Among the other possible pacemakers, the pineal gland has received the most study. It acts as a pacemaker in some species of birds. It is excited by light that enters the brain not through the visual system but through the skull. When the heads of such birds are painted black, the pineal gland's pacemaker activities are blocked. Because the pineal gland can respond directly to light, it has been called the "third eye." In most animals, however, the suprachiasmatic nucleus is the main pacemaker.

Suprachiasmatic Rhythms in a Dish

Further evidence for the role of the suprachiasmatic nucleus in circadian rhythms comes from a remarkable series of experiments demonstrating that the neurons of the nucleus have intrinsic rhythmic activity (Earnest et al., 1999). Following up on Richter's original experiments, investigators have found that if the suprachiasmatic nuclei are selectively lesioned in rodents, the animals still eat, drink, exercise, and sleep a normal amount, but at haphazard times. By itself, disorganized behavior does not definitively demonstrate that the suprachiasmatic nucleus is the clock that gives instructions about when these activities should take place. The suprachiasmatic nucleus could just be a way station between receptors in the eye and a clock located elsewhere in the brain.

Three other lines of evidence do show, however, that the suprachiasmatic nucleus is indeed the biological clock. First, the metabolic activity of the suprachiasmatic nucleus is higher during the light period of the day–night cycle than it is during the dark period of the cycle. If 2-deoxyglucose—a form of glucose that is taken up by metabolically active cells but is not used by them and cannot escape from them—is tagged with

a radioactive label, then cells that are more active will subsequently give off more radioactivity. When 2-deoxyglucose is injected into rodents, its accumulation by the suprachiasmatic nucleus should be relative to the animal's daily rhythm if the neurons in the nucleus are responsible for the rhythm. More tracer is found in the suprachiasmatic nucleus after injections given in the light period of the light–dark cycle than after injections given in the dark period. This experiment demonstrates that suprachiasmatic cells have rhythmic metabolic activity, with their active period correlated with the light period of the light–dark cycle. Other regions of the brain do not show an equivalent rhythmic metabolic pattern; the suprachiasmatic nucleus is special in this respect. Second, recording electrodes placed in the suprachiasmatic nucleus show that neurons in this region are more active during the light period of the cycle than during the dark period, confirming that each neuron has a rhythmic pattern of electrical activity. Third, if all the pathways into and out of the suprachiasmatic nucleus are cut, the neurons of the suprachiasmatic nucleus maintain their rhythmic electrical activity. Together, these experiments show that the suprachiasmatic neurons have a rhythmic pattern of activity that is intrinsic and not a response to rhythmic driving by some other brain structure or to changes in an animal's behavior.

After scientists had demonstrated that the suprachiasmatic nucleus was rhythmically active, the question of how that rhythmicity was generated became central. When the suprachiasmatic nucleus was removed from the brain, maintained in a laboratory dish, and subjected to electrical recording, the neurons were found to maintain their rhythmic activity. Furthermore, if the neurons were isolated from one another, each one was rhythmic. Individual cells did seem to have slightly different rhythms, however. This cellular individuality suggests either that, collectively, the cells express average rhythm or that the suprachiasmatic nucleus has components that are able to produce rhythms with different periods, or both.

Immortal Time

How do suprachiasmatic cells develop their rhythmic activity? One possibility is that the endogenous rhythm is learned. That is, the cells may initially have no rhythm but, after they receive their first exposure to rhythmic stimulation from environmental zeitgebers, they become rhythmic. A number of studies show, however, that rhythmicity is not learned but is genetically specified.

One way of examining whether rhythmicity is learned is to maintain animals from birth in an environment in which there are no zeitgebers. In experiments in which animals are raised in constant darkness, the animals' behavior still becomes rhythmic. It is possible that the animals' fetal suprachiasmatic cells acquired rhythmicity from the mother, but, in experiments in which animals have been maintained without entraining cues for a number of generations, each generation continues to have rhythmic behavior. Even if the mother has received a lesion of the suprachiasmatic nucleus so that her behavior is not rhythmic, the behavior of the offspring is rhythmic. Thus, it seems that rhythmicity is not learned.

A line of evidence supporting the idea that suprachiasmatic cells are genetically programmed for rhythmicity comes from studies performed in Canada by Martin Ralph and his coworkers with the use of transplantation techniques (Ralph & Lehman, 1991). The general design of the experiments is illustrated in Figure 12-9. First, hamsters are tested in constant dim light or in constant dark, to establish their free-running rhythm. They then receive a suprachiasmatic lesion, followed by another test to show that the lesion has abolished their rhythmicity. Finally, the hamsters receive transplants of suprachiasmatic cells obtained from hamster embryos. About 60 days later, the hamsters again show rhythmic activity, demonstrating that the transplanted cells have become integrated into the host brain and are responsible for reestablishing rhythmic behavior.

In further experiments, Ralph and his coworkers identified and selectively bred hamsters that had a 20-hour rhythm. They named the gene that was responsible for the short rhythm *tau*. If they destroyed the suprachiasmatic nucleus in a genetically normal hamster with a 24-hour period and then transplanted cells from a fetal 20-hour hamster into the cavity, the former 24-hour hamster exhibited the 20-hour period of the *tau* hamster.

David Earnest and his coworkers (1999) carried the transplantation methodology one step further. They harvested cells from the rat suprachiasmatic nucleus and used them to produce an immortalized cell line. By treating each generation of cells with 2-deoxyglucose, they were able to demonstrate that the cells' rhythm was passed on from one generation of cells to the next. The transplantation of cells from the immortal cell line into rats that had received suprachiasmatic lesions restored the circadian rhythm in the rats. Thus, the time encoded by the suprachiasmatic neurons is immortal in that it is passed from one hamster generation to the next or from one cultured suprachiasmatic neuron to the next.

Considerable research is being directed toward determining what genes control the ticking of the circadian clock. Because a single suprachiasmatic neuron displays a circadian rhythm, the timing device must be in the neuron itself, possibly entailing an increase and decrease of one or more proteins made by the cell. Just as the back-and-forth swing of a pendulum makes a grandfather clock tick, the increase and decrease in the amount of the protein makes the cell tick once each day. According to this notion, a protein is made until it crests at a certain level, at which point it inhibits its own production; when its level falls to a critical point, production again rises. In turn, the electrical activity of the cell is linked to protein oscillation, allowing the cell to control other cells during a part of the oscillation. The actual way that the oscillation is produced is a little more complex than this description suggests. Studies on mutant and knockout mice suggest that at least a half dozen genes and the proteins that they produce form two interlocking loops to produce the circadian rhythm of suprachiasmatic cells in mammals (Shearman et al., 2000). Although the mechanism has not yet been worked out, the excitation of suprachiasmatic cells through the retinohypothalamic pathway can presumably degrade one of the proteins to entrain the sequence of biochemical steps in the interlocking loops.

Pacemaking

The suprachiasmatic nucleus is of itself not responsible for directly producing behavior. For example, after the suprachiasmatic nucleus is damaged, the behavioral activities of drinking, eating, and sleep and wakefulness still occur. They no longer occur at appropriate times, however. One proposal for how the suprachiasmatic nucleus controls behavior is illustrated in Figure 12-10. In this model, light entrains the suprachiasmatic nucleus, and the pacemaker in turn drives a number of "slave" oscillators. Each slave oscillator is responsible for the rhythmic occurrence of one behavior. In other words, drinking and eating, body temperature, and sleep and wakefulness are each produced by a separate slave oscillator.

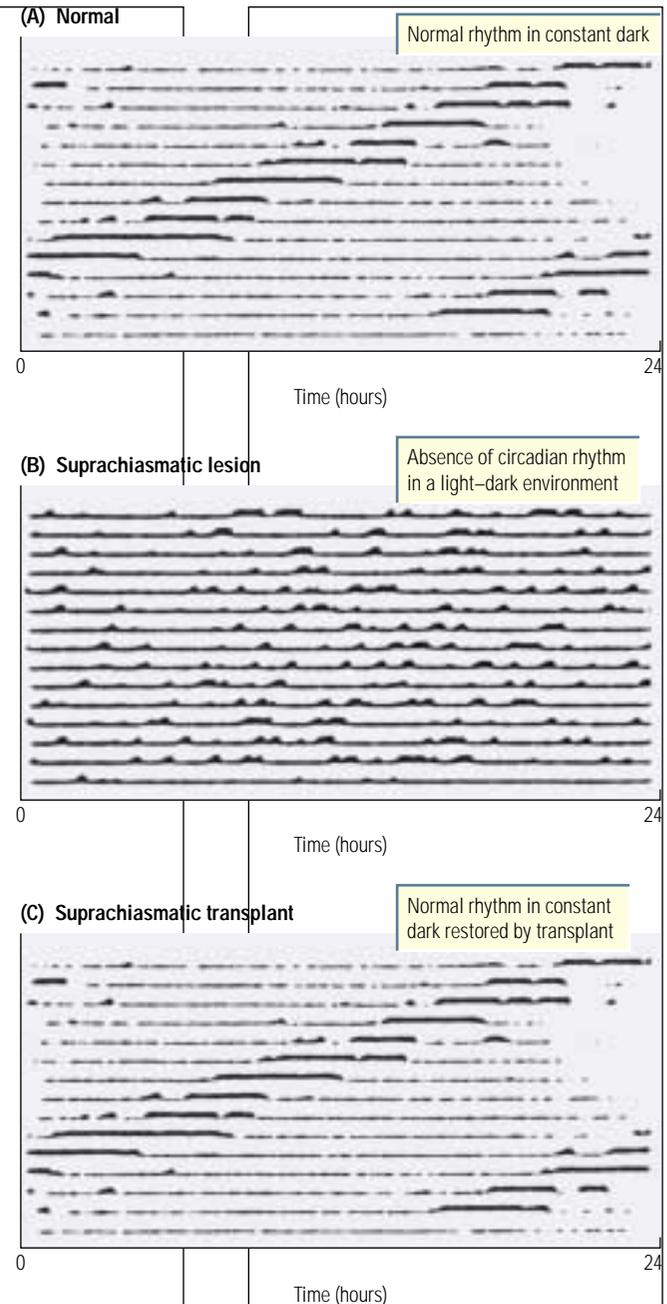


Figure 12-9

Recordings showing that hamsters' circadian rhythms are restored by neural transplantation: (A) free-running rhythm in constant dark; (B) rhythmic behavior eliminated after the suprachiasmatic nucleus has been lesioned; (C) circadian rhythm restored after transplant.

Adapted from "Transplantation: A New Tool in the Analysis of the Mammalian Hypothalamic Circadian Pacemaker," by M. R. Ralph and M. N. Lehman, 1991, *Trends in Neurosciences*, 14, p. 363.

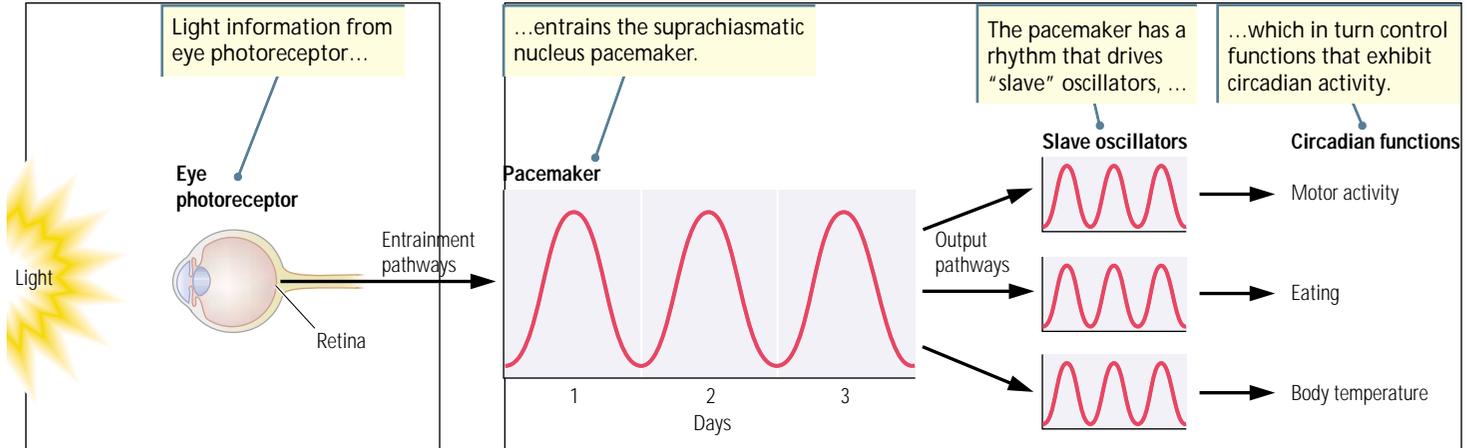


Figure 12-10

A model of the organization of the circadian timing system.

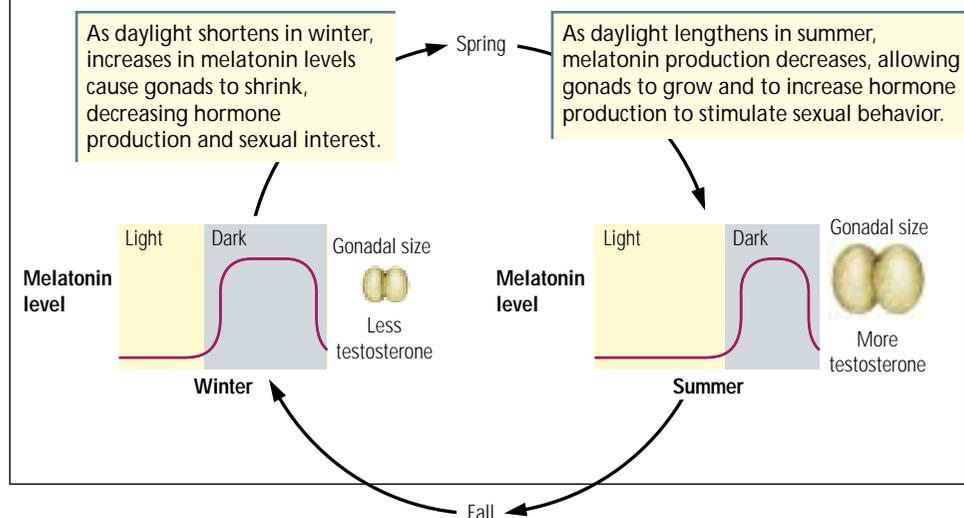
Russel Reiter (1980) showed that the suprachiasmatic circadian pacemaker may also be responsible for some circannual behaviors. Hamsters are summertime, or long-day, breeders. As the days lengthen in springtime, the gonads of male hamsters grow and release hormones that stimulate the males' sexual behavior. As the days shorten in the winter, the gonads shrink, the amount of the hormones that the gonads produce decreases, and the males stop being interested in sexual behavior. As Figure 12-11 shows, when melatonin secretion by the pineal gland during a period of a day is low, gonads enlarge; when melatonin secretion during a period of a day is high, gonads shrink. The control that the pineal gland exerts over the gonads is, in turn, controlled by the suprachiasmatic nucleus. Over a rather indirect pathway that need not concern us here, the suprachiasmatic nucleus drives the pineal gland as a slave oscillator. During the daylight period of the circadian cycle, melatonin secretion by the pineal gland is inhibited by the suprachiasmatic nucleus. Thus, as the days become shorter, the period of inhibition becomes shorter and thus the period during which melatonin is released becomes longer. When the period of daylight is shorter than 12 hours, melatonin release becomes sufficiently long to inhibit the hamster's gonads so that they shrink. In animals, such as sheep and deer, that are short-day breeders and mate in the fall and early winter, melatonin also influences the testes. Its effect on reproductive behavior in these species is the reverse of that in the hamster: reproductive activities begin as melatonin release increases.

The origins of many biological rhythms are not yet understood. In his 1965 book titled *Biological Clocks in Medicine and Psychiatry*, Curt Richter summarized a lifetime

Figure 12-11

The circadian pacemaker of the hamster controls circannual sexual activity. In winter, as daylight shortens and night lengthens, there is an increase in total nighttime melatonin secretion, which in turn inhibits testicular growth.

Adapted from "The Pineal and Its Hormones in the Control of Reproduction in Mammals," by R. J. Reiter, 1980, *Endocrinology Review*, 7, p. 120.



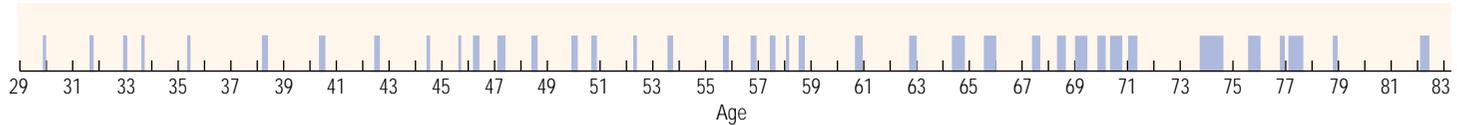


Figure 12-12

The attacks of mental illness displayed by the English writer Mary Lamb appear to have had a cyclical component. Such observations would be difficult to obtain today, because the drugs used to treat psychiatric disorders can mask abnormal rhythms.

Adapted from *Biological Clocks in Medicine and Psychiatry* (p. 92), by C. P. Richter, 1965, Springfield, IL: Charles C Thomas.

of recording various normal and abnormal rhythms. Richter recorded rhythmic activity in many bodily functions—including body temperature, hormone levels, eating, and drinking—that were associated but not *in phase*, or perfectly coordinated, with the sleep–wake cycle. He suggested that rhythms with similar periods but different phases might be controlled by different clocks. For example, although body temperature is generally low during sleep, the fact that it does not correlate perfectly with sleep suggests that the two are paced by different biological clocks. Richter also reviewed evidence of peripheral clocks—clocks that are not controlled by the brain. One such example was a patient whose knee swelled up every few days. The person was an accomplished athlete, and the managers of the rugby team for which he played measured the phase of knee swelling and scheduled matches for periods when his knee was functioning normally. Richter hypothesized that many physical and behavioral disorders might be caused by “shocks,” either physical or environmental, that upset the timing of biological clocks. Richter’s legacy includes a rich line of research that examines the relation between various kinds of illness and biological clocks. For example, the record of psychotic attacks suffered by the English writer Mary Lamb, illustrated in Figure 12-12, is one of many rhythmic records that Richter thought represented the action of a biological clock.

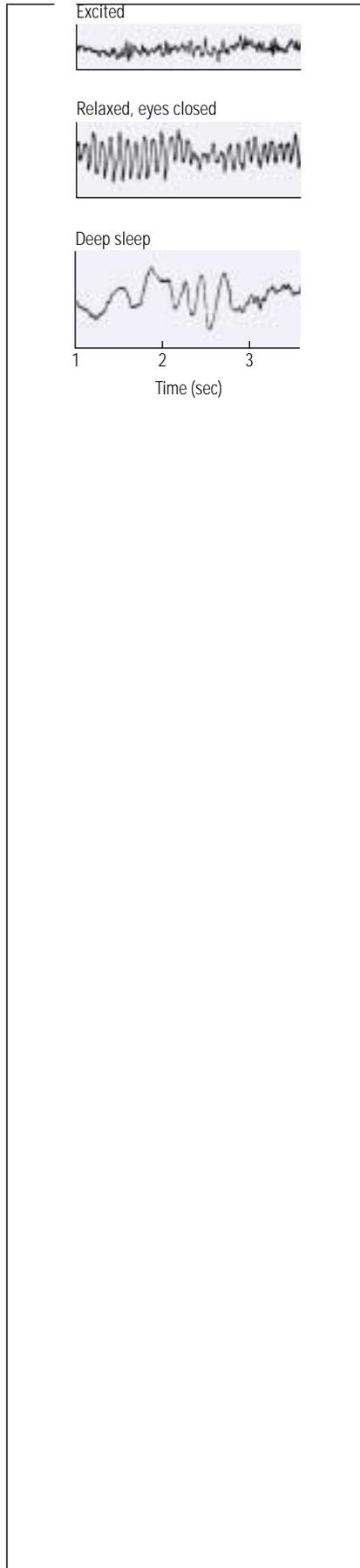
In the next section, we will consider some of the events of sleeping and waking behavior and the neural mechanisms that control them. Understanding circadian rhythms is important for understanding sleeping and waking. If the circadian pacemaker function of the suprachiasmatic nucleus is disrupted, then sleep will be disrupted. Consequently, many sleep disorders may be due not to the mechanisms that control sleep but to a malfunction of the pacemaker.

In Review

A number of nuclei in the brain serve as biological clocks, including the suprachiasmatic nucleus of the hypothalamus and the pineal gland of the thalamus. Damage to the suprachiasmatic nucleus disrupts the rhythm of daily behaviors. We know that the timing produced by the suprachiasmatic nucleus is a product of its cells because, if removed and cultured in a dish, the cells continue their rhythmic behavior and even pass on their rhythms to offspring cells cultured in a dish. If such cells are transplanted back into a brain from which the suprachiasmatic nucleus has been removed, they restore the animal’s rhythmic behavior.

SLEEP STAGES AND DREAMS

Most people are awake during the day and asleep at night. Both of these behavioral states, which we call *waking* and *sleeping*, are more complex than suggested by our daily experiences. Waking behavior encompasses some periods in which we sit relatively still, other periods when we are still but mentally active, and still other periods when we are physically active. Each of these different conditions is associated with different neural activity. Our sleep behavior is similarly variable in that it consists of periods of



resting, napping, long bouts of sleep, and various sleep-related events including snoring, dreaming, thrashing about, and even sleepwalking. Each of these conditions, too, is associated with different neural activity. This section describes some of the behavioral events of waking and sleeping and some of the neural processes that underlie them.

We will begin with the measurement of sleep and waking behavior. A crude measure is to have people record in a diary when they are awake and when they are asleep. Such measures show that there is considerable variation in sleep-waking behavior. People do sleep more when they are young than when they are old. Most people sleep about 7 to 8 hours per night, but some people sleep much more or less than that. There are recorded cases of people who even sleep for less than 1 hour each day. Some people nap for a brief period in the daytime, and others never nap. For example, one of the authors of this textbook can close his eyes and nap almost anytime, including during important lectures, while riding in a car, and even while riding on a ski lift. The other author never naps and finds his colleague's behavior amazing. Benjamin Franklin is credited with the statement, "Early to bed and early to rise makes a man healthy, wealthy, and wise," but measures of sleep behavior indicate that the correlation does not actually exist. Apparently, variations in sleeping time are quite normal.

Experimental studies in which sleep behavior is measured by observing sleeping subjects indicate that diaries are not always accurate. Many people who complain that they have insomnia and are unable to sleep are found, when their sleep is observed, to sleep a normal amount. Many others who report that they sleep a normal amount but are always tired are observed to have such disturbed sleep that they can be described as sleeping hardly at all. Even direct observations of one person by another are not completely accurate, however. We are remarkable dissemblers. We frequently pretend to be more awake than we are or more asleep than we are. Many legal cases revolve around the "state of consciousness" of a car operator or a worker involved in an accident, attesting to the difficulty of determining whether someone is awake or asleep. It is even more difficult to determine sleep-waking behavior in other animals. After examining how sleep can be objectively measured, we will turn to the stages of sleep and dreams.

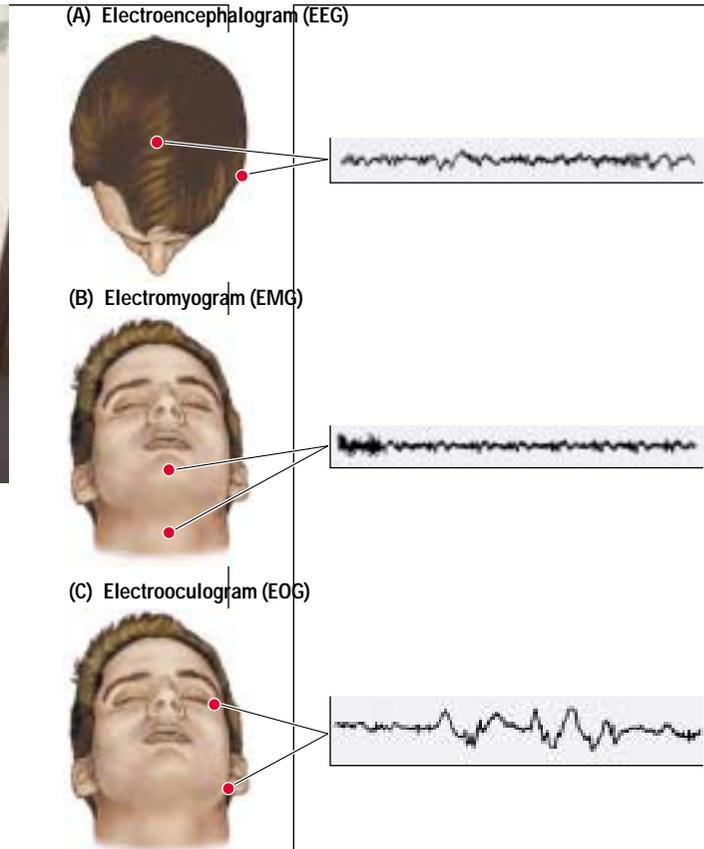
Measuring Sleep

Reliable measures of sleep and waking behavior can be obtained by recording the electrical activity of the brain and body with a polygraph, a machine that graphs many biological events (*poly* meaning "many"). Figure 12-13 illustrates a typical polygraph setup and some commonly used measures. Electrodes are pasted onto a number of standard locations on the skull's surface for an electroencephalogram (EEG, a record of brain-wave activity), onto muscles of the neck for an electromyogram (EMG, a record of muscle activity), and above the eyes for an electrooculogram (EOG, a record of eye movements). A thermometer also may be used, to measure body temperature. Together, these measures provide a comprehensive description of sleep-waking states.

The EEG record is the primary measure of sleep states. The electroencephalograph records patterns from different parts of the brain; we will look at the patterns of the neocortex. When a person is awake, the EEG of the neocortex consists of small-amplitude waves with a fast frequency. This pattern of activity is usually referred to as fast activity, activated EEG, or waking EEG—or, more formally, as a **beta rhythm** (which means that the rhythm of the waves has a frequency, or period, ranging from 15 to 30 hertz, or times per second). When a person becomes drowsy, the fast-wave activity of the neocortex changes in two ways: (1) the amplitude (height) of the waves becomes greater, and (2) the frequency (period) of the waves becomes slower. Usually the two changes occur together. When subjects relax and close their eyes, they may produce a

**Figure 12-13**

The setup for a polygraph recording. The electronic equipment in the foreground records the various readings from the electrodes attached to the subject. (A) Electroencephalogram made from a point on the skull relative to a neutral point on the ear. (B) Electromyogram made between two muscles, such as those on the chin and throat. (C) Electrooculogram made between the eye and a neutral point on the ear.



particular rhythmic pattern called an **alpha rhythm** (large waves whose rhythms have a frequency ranging from 7 to 11 hertz). As subjects go to sleep, they produce slower, larger EEG waves known as slow-wave activity, resting activity, or sleeplike activity—or, more formally, as **delta rhythms** (waves with a frequency of 1 to 3 hertz). The relation of EEG patterns to behavior is correlational, not causative; that is, the waves are not producing the behavior, nor is the behavior producing the waves. That accepted, a rule of thumb is that fast-wave activity is associated with waking behavior, and slow-wave activity is associated with sleeping behavior.

Observers of sleep have long known that sleep consists of segments in which a sleeper is relatively still and segments in which twitching movements of the mouth, fingers, and toes occur. These two different aspects of sleep are readily observable in household pets and bed partners. In 1955 Eugene Aserinsky and Nathaniel Kleitman (see Dement, 1972), working at the University of Chicago, discovered that the twitching periods were also associated with rapid eye movements, or REMs, in which the eyes can be observed flickering back and forth behind the sleeper's closed eyelids. More remarkably, they discovered that, during REMs, the neocortical EEG record displays a fast-wave pattern. That is, the EEG record suggested that the subjects were awake, even though Aserinsky and Kleitman were able to confirm that the subjects really were asleep.

This phase of sleep, in which fast-wave activity occurs in association with REMs, was designated as **REM sleep**. The other phase of sleep, associated with slowing of the EEG, is called **NREM** (for non-REM) **sleep** and sometimes **slow-wave sleep**. With these distinctions in mind, we can turn now to the EEG patterns associated with a typical night's sleep.

Visit the section on the EEG in the Research Methods module of your CD to learn more about the EEG and the stages of sleep and waking.

A Typical Night's Sleep

Figure 12-14 is a record of brain activity from one subject during a typical night's sleep. Figure 12-14A displays the EEG patterns associated with waking and with sleep. Sleep is divided into four stages on the basis of EEG records. Notice that the main change characterizing these stages is that the EEG waves become larger and slower in a progression from stage 1 sleep through stage 4 sleep. The designation of these stages assumes that the sleeper moves from relatively shallow sleep in stage 1 to deeper sleep in stage 4.

Figure 12-14B illustrates graphically when these different stages of sleep occur and how long they last in the course of a night's sleep. Notice that the depth of sleep changes several times. The subject gradually descends from a waking state to stage 4 sleep in about one-half hour, stays in stage 4 sleep for about one-half hour, and then ascends to stage 1 sleep. This sequence lasts approximately 90 minutes and is typically repeated four times, except that, as the night progresses, the stages of sleep associated with the slowest EEG patterns are less frequent.

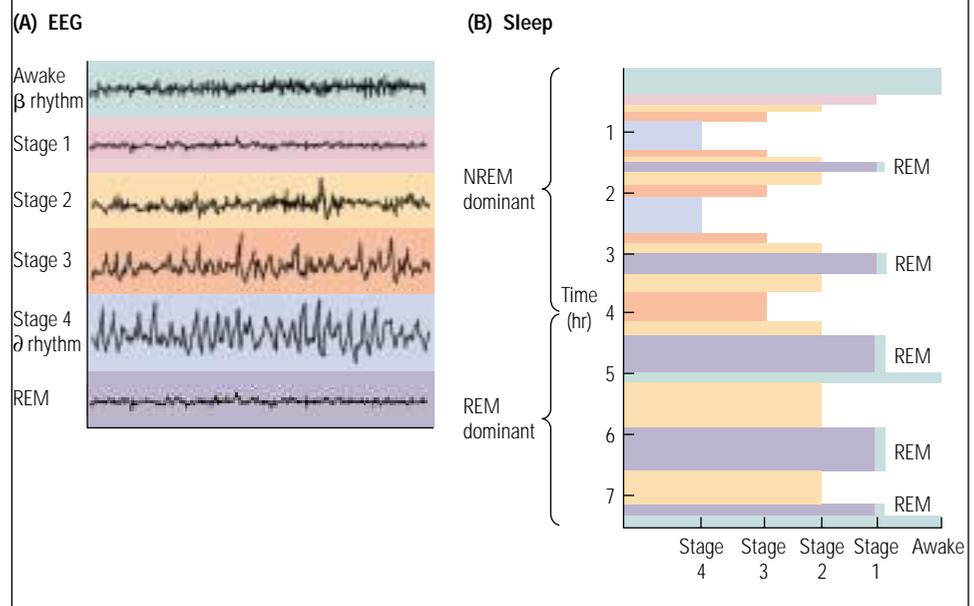
As already mentioned, the EEG of stage 1 sleep is similar to the EEG of waking, but the subject is asleep. The oculograph indicates that the subject's eyes are moving during stage 1, meaning that it is REM sleep. Therefore, the duration of the different stages of sleep roughly divides a night's sleep into two parts, the first dominated by NREM sleep and the second dominated by REM sleep. Body temperature is lowest (about 1.5 degrees below a normal temperature of 37.7°C) during the first part of a night's sleep and rises during the second part. Self-reports of subjects who are awakened from sleep at different times suggest that stage 4, the deepest sleep, occurs early. Subjects are difficult to awaken at this time and act groggy when disturbed. When subjects are awakened in the second half of sleep, they appear more alert and attentive.

In considering a "typical" night's sleep, we should bear in mind that the behavior of individual people is very variable and most variations are not abnormal. Adults typically sleep about 8 hours with about 2 of those hours spent in REM, but some people sleep less than 8 hours and others sleep more. A person's sleep patterns may also vary at different times of life. The time that we spend asleep increases during growth spurts and in conjunction with physical exertion. Sleep durations also increase for women

Figure 12-14

(A) Electroencephalographic patterns associated with waking and four stages of sleep. Stage 1 has the same EEG pattern as REM sleep, and stages 2 to 4 are called NREM sleep. (B) In a typical night's sleep, a person undergoes a number of sleep-state changes. NREM sleep dominates the early sleep hours, and REM sleep dominates the later sleep hours. The depth of sleep is indicated by the relative lengths of the bars, and the duration of each stage of sleep is indicated by the thickness of the bars. The time spent in REM sleep is indicated by dark purple bars.

Adapted from "Sleep and Dreaming," by D. D. Kelley, in E. R. Kandel, J. H. Schwartz, and T. M. Jessell (Eds.), *Principles of Neuroscience*, 1991, New York: Elsevier, p. 794.



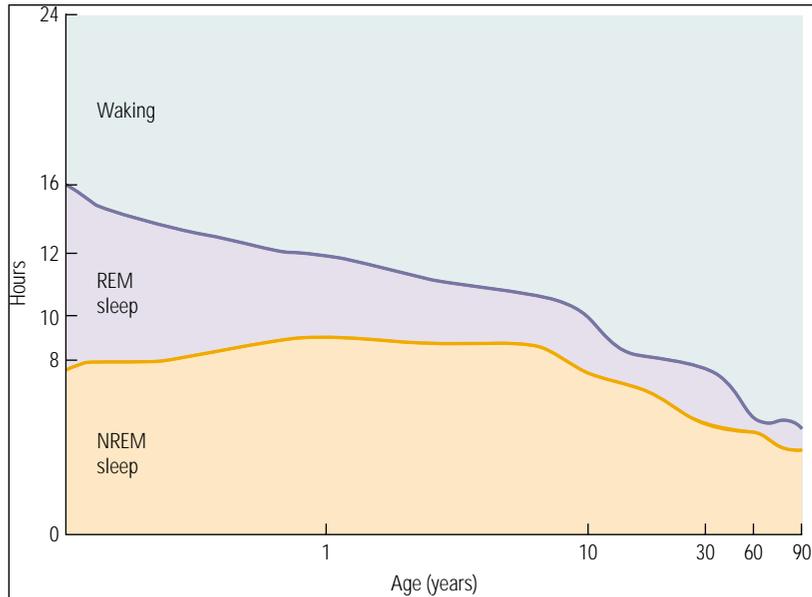


Figure 12-15

The amount of time that humans spend sleeping decreases with age. The amount of REM sleep is especially high in the first few years of life.

Adapted from "Ontogenetic Development of the Human Sleep-Dream Cycle," by H. P. Roffward, J. Muzio, and W. C. Dement (1966), *Science*, 152.

during pregnancy. The time that is spent in different stages of sleep changes dramatically over the life span. As is illustrated in Figure 12-15, most people sleep less as they grow older. Furthermore, in the first 2 years of life, REM sleep makes up nearly half of sleep time, but it declines proportionately until, in middle age, it constitutes little more than 10 percent of sleep time.

Another aspect of "typical" patterns of sleep has to do with the fact that we modern humans, because much of our time is spent indoors, are exposed to less outdoor light than our ancestors were. This difference is important because outdoor light is much brighter than indoor light, and bright light may be necessary for setting our circadian rhythms. Therefore, we cannot really be sure if our patterns of sleep would be the same as those of people living in "natural" environments. Some scientists have commented on the fact that we are the only primates to take all of our sleep in one block. They speculate that if we were exposed to natural light, we might divide our sleep into two parts, an early evening part and an early morning part, with a period of waking in between.

NREM Sleep

Although many people may think that sleep is an inactive period, a remarkable range of activities take place during sleep (see "Restless Legs Syndrome" on page 464). During NREM sleep, body temperature declines, heart rate decreases, blood flow decreases, we perspire and lose body weight owing to water loss, and our levels of growth hormone increase. It was once thought that we do not dream during NREM sleep, but recent studies show that, when subjects are aroused from NREM sleep, they do report dreams. NREM sleep is also the time during which we toss and turn in bed, pull on the covers, and engage in other movements. If we talk in our sleep, we will do so during NREM sleep. If we make flailing movements of the limbs, such as banging with an arm or kicking with a foot, we will usually do so in NREM sleep. Some people even get up and walk during sleep, and this "sleepwalking" is thought to occur in NREM sleep. Children may experience brief, very frightening dreams called night terrors, which also occur in NREM sleep. All these conditions are inconsistent with a period that is often described as quiet and inactive.

🎯 To learn more about night terrors, visit the Web site at www.worthpublishers.com/kolb/chapter12.

Restless Legs Syndrome

I've always been a fairly untalented sleeper. Even as a child, it would take me some time to fall asleep, and I would often roll around searching for a comfortable position before going under. But my real difficulties with sleeping did not manifest themselves until early adulthood. By that time, my father had been diagnosed with Restless Legs Syndrome (RLS) and I was suffering the same symptoms.

Initially, my symptoms consisted of a mild tingling in my legs. It caused me to be fidgety and made it hard to fall asleep. Eventually, I went through a number of days without much sleep and reached a point where I simply could not function. I went to a doctor who prescribed a small course of sleeping medication (a benzodiazepine). I was able to get good sleep and my sleep cycle seemed to get back on track. Over the next decade I had periodic bouts of tingling in my legs which caused me to be fidgety and interfered with sleep. As time passed, the bouts occurred with increasing frequency and the symptoms became more noticeable and uncomfortable. I would simply suffer through these bouts, sleeping poorly and paying the consequences, or I would seek medical help. Being a student, I did not have a regular doctor. Unfortunately, most physicians I met did not know about RLS, and thought I was “drug seeking” or merely stressed out. I received a variety of patronizing responses and found these experiences insulting and demeaning. It would have been easy to give up and try to deal with it on my own, but because of my father's diagnosis, I knew the true source of the problem and was determined to get help.

When I took my current position, I started seeing a doctor on a regular basis. By this time, my sleep was being seriously affected by RLS. The sensations in my legs were something like a combination of an ache in

my muscles (much like one gets after exercising) and an electrical, tingling sensation. They would be briefly relieved with movement, such as stretching, rubbing, contracting my muscles, or changing position, but would return within seconds. In fact, my wife says my cycle is about 13 to 15 seconds between movements. I do this either when awake or during sleep. Trying not to move greatly increases the discomfort—much like trying to not scratch a very bad itch. The symptoms get worse in the evening and at night. Most nights, I have trouble falling asleep. Other nights, I wake up after an hour or so and then have trouble going back under.

Now my doctor takes me seriously. We exchanged research articles and thoroughly discussed treatment options. As part of this process, my wife met with my physician to relate her experiences. I was stunned to learn how severely my RLS was interfering with her sleep. I think she was being compassionate and not complaining so I wouldn't feel any more upset than I already was about my sleeping difficulties. My doctor started me on a regular course of sleeping medication (again, a benzodiazepine) and encouraged me to stay on it. This was a life-changing event. For the first time in my adult life, I was getting good sleep on a regular basis. My wife and I also got separate beds.

On the down side, RLS is a chronic and progressive condition. Over the years I've had to slowly increase dosages, switch to new medicines, and am now on two medications. I have always communicated openly and honestly with my physician, and we have worked together to monitor issues such as tolerance and medication dosages. I have gone for consultation with a neurologist experienced with RLS. I still get good sleep, but I have had to make many significant adjustments.

REM Sleep and Dreaming

REM sleep is no less exciting and remarkable than NREM sleep. During REM sleep, our eyes move and our toes, fingers, and mouths twitch, and males have penile erections. Still, we are paralyzed, as indicated by the absence of muscle activity on an EMG. You can get an idea of what REM sleep is like by observing a cat or dog. At the onset of REM sleep, the animal usually subsides into a sprawled posture as the paralysis of its

I am very up front about the fact that I have RLS. In fact, whenever I teach the topic of sleep and sleep disorders in my brain and behavior classes, I always make some time to talk about my experiences with RLS. Occasionally, students approach me with their own difficulties, and I try to provide them with information and resources.

—Stuart Hall, Ph.D., University of Montana

Restless legs syndrome (RLS) is a sleep disorder in which a person experiences unpleasant sensations in the legs described as creeping, crawling, tingling, pulling, or pain. The sensations are usually in the calf area but may be felt anywhere from the thigh to the ankle. One or both legs may be affected; for some people, the sensations are also felt in the arms. People with RLS describe an irresistible urge to move the legs when the sensations occur. Many people with RLS have a related sleep disorder called *periodic limb movement in sleep* (PLMS). It is characterized by involuntary jerking or bending leg movements in sleep that typically occur every 10 to 60 seconds. Some people experience hundreds of such movements per night, which can wake them, disturb their sleep, and annoy bed partners. People with these disorders get less sleep at night and may feel sleepy during the day.

These symptoms affect both sexes, and symptoms can begin at any time but are more severe among older people. Young people who experience symptoms are sometimes thought to have “growing pains” or may be considered hyperactive because they cannot easily sit still in school. There is no laboratory test for these disorders, and a doctor cannot detect anything abnormal in a physical examination. In mild cases of the disorders, massage, exercise, stretching, and hot baths may be helpful. For more severe cases, patients can re-



Bill Aron/PhotoEdit

Insomnia like that shown in this time-lapse photograph is a frequent consequence of restless legs syndrome, a sleep disorder characterized by painful sensations in the legs.

strict their intake of caffeine, take benzodiazepines to help them get to sleep, and take L-dopa, a drug that is also used to treat Parkinson's disease. These treatments reduce symptoms, but at present there is no cure for the condition.

muscles sets in. Figure 12-16 illustrates the sleep postures of a horse. Horses can sleep while standing up by locking their knee joints, and they can sleep while lying down with their heads held slightly up. At these times, they are in NREM sleep; when they are completely sprawled out, they are in REM sleep. During REM sleep, animals' limbs twitch visibly, and, if you look carefully at the face of a dog or cat, you will also see the skin of the snout twitch and the eyes move behind the eyelids. It might seem strange

Courtesy of Ian Wishaw



Courtesy of Ian Wishaw

Courtesy of Ian Wishaw



Figure 12-16

Horses usually seek an open, sunny area in which to take brief periods of sleep. Ian's horse, Lady Jones, illustrates three sleep postures. At top left she displays NREM sleep, standing with legs locked and head down, and at top right she displays NREM sleep lying down with head up. At bottom left she is in REM sleep, in which all posture and muscle tone is lost.

Courtesy of Ian Wishaw

that an animal that is paralyzed can make small twitching movements, but the neural pathways that mediate these twitches are presumably spared the paralysis. One explanation for the twitching movements of the eyes, face, and distal parts of the limbs is that such movements may help to maintain blood flow in those parts of the body. An additional change resulting from the absence of muscle activity during REM sleep is that mechanisms that regulate body temperature stop working and body temperature moves toward room temperature. The sleeper may wake up from REM sleep feeling cold or hot, depending on the temperature of the room.

The most remarkable aspect of REM sleep was discovered by William Dement and Nathaniel Kleitman in 1957 (Dement, 1972). When subjects were awakened from REM sleep, they reported that they had been having vivid dreams. In contrast, subjects aroused from NREM sleep were much less likely to report that they had been dreaming, and the dreams that they did report were much less vivid.

The technique of electrical recording from a sleeping subject in a sleep laboratory made it possible to subject dreams to experimental analysis, and such studies provided some objective answers to a number of interesting questions concerning dreaming. The first question that studies of dreaming answered was, How often do people dream? Reports by people on their dreaming behavior had previously suggested that dreaming was quite variable, with some people reporting that they dreamed frequently and others reporting that they never dreamed. Waking subjects up during periods of REM showed that everyone dreams, that they dream a number of times each night, and that dreams last longer as a sleep session progresses. Those who claimed not to dream were presumably forgetting their dreams. Perhaps people who forget their dreams do so because they do not wake up during or immediately after a dream, thus allowing a subsequent NREM sleep session to erase the memory of the dream.

Another interesting question that objective measures answered was, How long do dreams last? There had been suggestions that dreams last but an instant. By waking people up at different intervals after the onset of a REM period and matching the reported dream content to the previous duration of REM sleep, researchers were able to show that dreams appear to take place in real time. That is, an action that a person performed in a dream lasts about as long as it would take to perform while awake.

What Do We Dream About?

The study of dreaming in sleep laboratories also allowed researchers to study the content of dreams. Past explanations of dreaming have ranged from messages from the gods to indigestion. The first modern treatment of dreams was described by the founder of psychoanalysis, Sigmund Freud, in *The Interpretation of Dreams*, published in 1900. Freud reviewed the early literature on dreams, described a methodology for studying dreams, and provided a theory to explain their meaning. We will briefly consider Freud's theory inasmuch as it remains popular in psychoanalysis and in the arts.

Freud suggested that the function of dreams was the symbolic fulfillment of unconscious wishes. His theory of personality was that people have both a conscious and an unconscious. Freud proposed that the unconscious contains unacknowledged desires and wishes, many of which are sexual. He further proposed that dreams have two levels of meaning. The *manifest content* of a dream consists of a series of often bizarre images and actions that are only loosely connected. The *latent content* of the dream contains its true meaning, which, when interpreted by a psychoanalyst, provides a coherent account of the dreamer's unconscious wishes.

Freud provided a method for interpreting symbols and reconstructing the latent content of dreams. For example, he pointed out that a dream usually began with an incident from the previous day, incorporated childhood experiences, and included ongoing unfulfilled wishes. He also identified a number of types of dreams, such as those that dealt with childhood events, anxiety, and wish fulfillment. The content of the dream was important to Freud and other psychoanalysts in clinical practice because, when interpreted, dreams were a source of insight into a patient's problems.

Other psychoanalysts, unhappy with Freud's emphasis on sexual desire, developed their own methods of interpretation. Carl Jung, another psychoanalyst and contemporary of Freud, for example, proposed that the symbolism of dreams signified distant human memories that were encoded in the brain but had long since been lost to conscious awareness. Jung proposed that dreams allowed a dreamer to relive the history of the human race. As more theories of dream interpretation developed, their central weakness became apparent: it was difficult, if not impossible, to know which interpretation was correct.

The dream research of Freud and his contemporaries was impeded by their reliance on a subject's memory of a dream and by the fact that many of their subjects were patients. This unquestionably resulted in the selection of the unusual by both the patient and the analyst. Now that researchers study dreams more objectively by waking subjects and questioning them, one might think that the meaning of dreams might be better understood. Certainly, knowledge of the content of dreams has improved. Research suggests that most dreams are about events that happened quite recently and concern ongoing problems. Colors of objects, symbols, and emotional content most often relate to events taking place in a person's recent waking period. Calvin Hall documented more than 10,000 dreams of normal people and found that more than 64 percent were associated with sadness, anxiety, or anger. Only about 18 percent were happy. Hostile acts against the dreamer outnumbered friendly acts by more than two to one. Surprisingly, in light of Freud's theory, only about 1 percent of dreams included sexual feelings or acts.

Contemporary dream theories fall into two groups—continuity and discontinuity theories. Continuity theories propose that as we pass from waking into NREM and then into REM sleep, we continue to ruminate and worry (that is, daydream), but the worrying becomes more bizarre as we lose conscious control over our thoughts. Discontinuity theories propose that both the content and the neural basis of ruminating,

Click on the Web site to investigate more about research on dreams at www.worthpublishers.com/kolb/chapter12.

of NREM dreams, and of REM dreams are different. Two discontinuity theories that represent opposing views of the meaning of REM dreams are described next.

J. Allen Hobson (1989) proposed what he calls the *activation-synthesis hypothesis* of dreaming. According to this view, during a dream the cortex is bombarded by signals from the brainstem, and these signals produce the pattern of waking (or activated) EEG. The cortex, in response to this excitation, generates images, actions, and emotion from personal memory stores. In the absence of external verification, these dream events are fragmented and bizarre and reveal nothing more than that the cortex has been activated. According to the activation-synthesis hypothesis, dreams are nevertheless personal in that a person's memories and experiences are activated, but they have no meaning. So, for example, the following dream, with its bizarre, delusional, and fragmented elements, would be representative of images that are synthesized to accompany brain activation. According to this hypothesis, any meaning that the dream might seem to have is created by the dreamer after the fact, as was perhaps done by the middle-aged dreamer who recounted this dream:

I found myself walking in a jungle. Everything was green and fresh and I felt refreshed and content. After some time I encountered a girl whom I did not know. The most remarkable thing about her was her eyes, which had an almost gold color. I was really struck by her eyes not only because of their unique color but also because of their expression. I tried to make out other details of her face and body but her eyes were so dominating that was all I could see. Eventually, however, I noticed that she was dressed in a white robe and was standing very still with her hands at her side. I then noticed that she was in a compound with wire around it. I became concerned that she was a prisoner. Soon, I noticed other people dressed in white robes and they were also standing still or walking slowly without swinging their arms. It was really apparent that they were all prisoners. At this time I was standing by the fence that enclosed them, and I was starting to feel more concerned. Suddenly it dawned on me that I was in the compound and when I looked down at myself I found that I was dressed in a white robe as well. I remember that I suddenly became quite frightened and woke up when I realized that I was exactly like everyone else. The reason that I remembered this dream is the very striking way in which my emotions seemed to be going from contentment, to concern, to fear as the dream progressed. I think that this dream reflected my desire in the 1970's to maintain my individuality. (Recounted by A. W.)

Anttio Revonsuo (2000) of Finland agrees with Hobson about the content of dreams but uses content analysis to argue that dreams are biologically important in that they lead to enhanced performance in dealing with threatening life events. In his *evolutionary hypothesis of dreams*, Revonsuo argues that this enhanced performance would have been especially important for early humans, whose environment included frequent dangerous events that constituted extreme threats to their reproductive success. He notes that dreams are highly organized and are significantly biased toward threatening images (as, for example, in the preceding dream). People seldom dream about reading, writing, and calculating, even though these behaviors may occupy much of their day. The threatening events of dreams are the same ones that are threatening in real life (Figure 12-17). For example, animals and strange men who could be characterized as "enemies" figure prominently in dreams. Revonsuo notes that there is overwhelming evidence that dream content incorporates the current emotional problems of the dreamer. He also reviews evidence to suggest that depressed dreamers who dream about their focal problems are better adjusted than those who do not. Revonsuo also notes that recurrent dreams and nightmares generally begin in childhood, when a



Erich Lessing/Art Resource

Figure 12-17

The terrifying visions that may persist even after awakening from a frightening dream are represented in this painting titled *The Night*, by the Swiss artist Ferdinand Hodler.

The Night, by Ferdinand Hodler (1853–1918), oil on canvas, 116 x 299 cm., Kunstmuseum, Berne, Switzerland.

person is most vulnerable, and are associated with anxiety, threats, and pursuit. In them, the dreamer is usually watching, hiding, or running away. Revonsuo therefore proposes that the experience of dealing with threats in dreams is adaptive because it can be applied to dealing with real-life threats. To illustrate, a student provided the following account of a dream from childhood that she had dreamed subsequently a few times:

When I was five years old, I had a dream that at the time frightened me but that I now find somewhat amusing. It took place in the skating rink of my small hometown. There was no ice in the rink, but instead the floor consisted of sod. The women, my mother included, were working in the concession booth, and the men were in the arena, dressed in their work clothes. I was among the children of the town who were lined up in the lobby of the rink. None of the children, including myself, knew why we were lined up. The adults were summoning the children two at a time. I decided to take a peek through the window, and this is what I saw. There was a large circus-ride type metal chair that was connected to a pulley, which would raise the chair to about 20 feet into the air. The seat would be lowered and two children at a time would be placed in it. A noose was then placed around the neck of each and the chair was again raised. Once the chair reached its greatest height, the bottom would drop out of the chair and the children would be hanged (I did not see this but I thought that is what happened to them.) At this point, I turned to a friend and said, "Here, Ursula, you can go ahead of me" and I went to my mother and told her what was going on. She smiled as if I were just being difficult and told me that I was to get back in the line. At this point I thought, "Forget it," and I found a place to hide underneath the big wooden bleachers in the lobby. It was dark and I could hear everyone out looking for me. (Recounted by N. W.)

When asked what she thought this dream meant, this student said that she really did not know. When told that it could be an anxiety dream, something common in children, that might represent an activity that she considered stressful, such as competing in figure skating and failing, she said that she did not think that was it. She volunteered, however, that her community's skating rink was natural ice and that it was bitterly cold whenever there was enough ice to go skating. When she had to skate, her feet got cold and her mother almost had to lift her up and drag her out onto the ice. Being dropped out of the chair may have been a symbolic representation of being pushed out onto the ice. Elements of the dream did represent what went on at the skating rink. Men did prepare the ice and the women did run a confection booth, and she did resist being sent out to skate. The recurrence of the dream could be due to the

conflict that she felt about having to do something that exposed her to the cold and her solution in hiding.

In Review

The average length of a night's sleep is from 7 to 8 hours, but some people sleep much less or much more. Sleep is divided into four stages on the basis of the EEG record. The first three stages are characterized by progressive slowing of the EEG record, whereas the fourth stage is characterized by a waking EEG record. Because rapid eye movements accompany stage 4 sleep, it is called REM sleep; the other three stages are grouped together as NREM sleep. There are about four REM sleep periods each night, with each period getting longer as sleep progresses. REM sleep is also marked by muscle paralysis and dreams that are more vivid than those of NREM sleep. There are various interpretations of the function of dreams. The activation-synthesis hypothesis suggests that they are simply a by-product of the brain's activity and so have no meaning, whereas the evolutionary hypothesis suggests that dreams help people to work out solutions to threatening problems and events.

THEORIES OF SLEEP

The simplest question that we can ask about sleep is, Why do we sleep? Any satisfactory explanation has a lot to account for. As we have seen, sleep is complex, consisting as it does of at least four stages. Sleep also seems to have within it a rhythmic component lasting about 90 minutes in which the EEG gradually slows and then speeds up again. Finally, in one of these stages, the sleeping brain has a waking EEG, the motor system is paralyzed except for twitching movements, and people have more vivid dreams than those in other stages of sleep. An adequate theory of sleep must account for all these phenomena. This section summarizes four theories of why we sleep.

Sleep as a Passive Process

One of the earliest theories views sleep as a passive process that takes place as a result of a decrease in sensory stimulation. According to the theory, as evening approaches, there are fewer stimuli to maintain alertness, so sleep sets in. This theory does not account for the complexity of sleep, nor is it supported by direct experimental investigations. It predicts that if subjects are deprived of all stimulation they will go to sleep. Experiments reveal, however, that when subjects are isolated in bedrooms, they spend less, not more, time asleep. These results do not support the idea that sleep sets in because there is nothing to do.

Although the passive-process theory of sleep originally did not consider biological rhythms as a contributing factor to sleep, what we now know about biological rhythms provides some support for a weak version of this idea. Shimir Amir and Jane Steward (1996) showed that initially neutral stimuli can be conditioned to be zeitgebers, which entrain more regular circadian rhythms and thus more regular periods of sleep. In other words, the activities that we engage in before we sleep and after we wake up will become zeitgebers by being associated with light–dark changes. Therefore, exposure to darkness and quiet in the evening and to light and other kinds of stimulation in the morning is one way of synchronizing biological rhythms.

Sleep as a Biological Adaptation

The biological theory of sleep holds that it is an adaptive behavior that is influenced by the many ways in which a species adapts to its environment. First, sleep is designed as an energy-conserving strategy to cope with times when food is scarce. In other words, each animal species gathers food at optimal times and conserves energy the rest of the time. If the nutrient value of the food that a species eats is high, it can spend less time foraging and more time sleeping. Second, an animal species' behavior is influenced by whether the species is predator or prey. If an animal is a predator, it can sleep at its ease; if it is a prey, its sleep time is reduced because it must remain alert as much as possible. Third, an animal that is strictly nocturnal or diurnal will likely also sleep when it cannot travel easily. Dement has stated this idea as follows: "We sleep to keep from bumping into things in the dark" (Figure 12-18).

The sleep patterns of most animal species are consistent with the adaptive theory. Figure 12-19 illustrates the average sleep time of a number of common mammals. Because herbivores—including donkeys, horses, and cows—consume food that is poor in nutrients, they have to spend a long time collecting enough food to sustain themselves, which reduces their sleep time. Because they are also prey, their sleep time is further reduced as they watch for predators. Carnivores, including domestic cats and dogs, eat nutrient-rich foods and usually consume most of a day's or even a week's food at a single meal. Thus, because they do not need to eat constantly and because by resting they can conserve energy, carnivores spend a great deal of time each day sleeping. The behavior of some animals does appear odd, however. Opossums, which spend much of their time asleep, may have specialized in energy conservation as a survival strategy. We humans are average in our sleep time, which is presumably indicative of an evolutionary pattern in which food gathering was not an overwhelming preoccupation and predation was not a major concern.



Lynn Hoffman/Photo Researchers

Figure 12-18

Biological theories of sleep suggest that sleep is an energy-conserving strategy and also serves other functions, such as staying safe during the night.

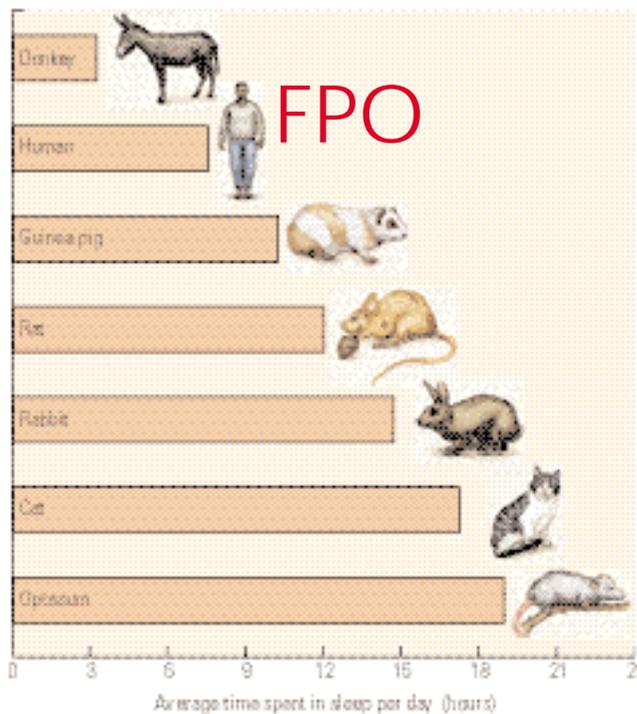
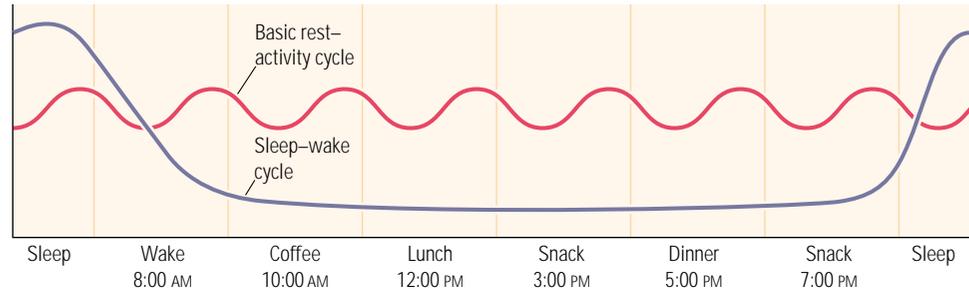


Figure 12-19

The average amount of time spent sleeping each day by different animal species. Sleep time is affected both by the amount of time required to obtain food and by the risk of predation.

Figure 12-20

Our behavior is dominated by a basic rest-activity cycle (red) in which our activity level changes in the course of the day and by an NREM-REM sleep cycle (purple) in the course of the night.



Sleep can contribute to energy conservation in a number of ways. Inactivity is a way of conserving energy because energy is not being expended in moving the body or supporting posture. The brain is a major user of energy, so switching off the brain during sleep—especially NREM sleep—is another good way to conserve energy. The drop in body temperature that typically accompanies sleep also contributes to energy conservation.

A good theory of sleep must explain not only sleep but also NREM and REM sleep. Before the discovery of REM sleep, Kleitman had suggested that animals, including humans, have a **basic rest-activity cycle** (BRAC) that has a period of about 90 minutes (see Dement, 1972). He based his hypothesis on the observation that human infants have frequent feeding periods between which they sleep. As is illustrated in Figure 12-20, the behavior of adult humans also suggests that activity and rest are organized into temporal packets. School classes, work periods, meal times, coffee breaks, and snack times appear to be divided into intervals of 90 minutes or so. The later discovery that REM sleep occurs at intervals of about 90 minutes added support to Kleitman's hypothesis, because the REM periods could be considered to be a continuation into sleep of the 90-minute BRAC cycle. The hypothesis now assumes that periods of eating are periods of high brain activity, just as are periods of REM. Kleitman proposes that the BRAC rhythm is so fundamental that it cannot be turned off. Accordingly, in order for a night's sleep to be uninterrupted by periodic waking (and perhaps snacking), the body is paralyzed and only the brain is allowed to be active. In other words, to use an analogy, rather than turning off the engine of an automobile stopped at a red light, the driver disengages the transmission and sets the brakes so that the car cannot move. Although Kleitman's hypothesis has not been subjected to serious experimentation, it does not seem to be seriously challenged by any competing explanation.

Sleep as a Restorative Process

The idea that sleep has a restorative function is widely held among poets, philosophers, and the public, as illustrated by Macbeth's description of sleep in Shakespeare's *Macbeth*:

Sleep that knits up the ravell'd sleeve of care,
The death of each day's life, sore labour's bath,
Balm of hurt minds, great nature's second course,
Chief nourisher in life's feast.

It is also an idea that we can understand from a personal perspective. Toward the end of the day, we become tired, and when we awaken from sleep, we are refreshed. If we do not get enough sleep, we often become irritable. Nevertheless, fatigue and alertness may simply be aspects of the circadian rhythm and have nothing at all to do with wear and tear on the body or depletion of essential bodily resources. To evaluate whether sleep is essential for one or another bodily process, many studies of sleep deprivation have been conducted. The studies fall into three types: total sleep deprivation, deprivation of slow-wave sleep, and deprivation of REM sleep.

Sleep-deprivation studies have not identified any function for which sleep is essential. One well-known case study on sleep deprivation described by Dement illustrates this point. In 1965, as part of a science-fair project, a student named Randy Gardner planned to break the world record of 260 hours (almost 11 days) of consecutive wakefulness with the help of two classmates, who would keep him awake. Gardner did break the record, then slept for 14 hours and reported no ill effects. The world record now stands at a little more than 18 days. A number of reviews of sleep-deprivation research are consistent in concluding that, at least for these limited periods of sleep deprivation, no marked physiological alterations ensue.

Although sleep deprivation does not seem to have adverse physiological consequences, it is associated with poor cognitive performance. The decreases in performance contribute to many accidents at work and on the road. The sleep-deprivation deficit does not manifest itself in an inability to do a task, because sleep-deprived subjects can perform even very complex tasks. Rather, the deficit is revealed when sustained attention is required and when a task is repetitive or boring. Even short periods of sleep deprivation, amounting to the loss of a few hours of sleep, can increase errors on tasks requiring sustained attention. A confounding factor in cognitive performance is that sleep-deprived subjects will take **microsleeps**, which are brief sleeps lasting a few seconds. During microsleep, subjects may remain sitting or standing, but their eyelids droop briefly and they become less responsive to external stimuli. Many people who have driven a car while tired have experienced a microsleep and awakened just in time to prevent themselves from driving off the road.

Some studies have focused on the selective contributions of REM sleep. To deprive a subject of REM sleep, researchers allow subjects to sleep but awaken them as they start to go into REM sleep. REM-sleep deprivation has two effects. First, subjects show an increased tendency to go into REM sleep in subsequent sleep sessions, so awakenings must become more and more frequent. Second, subsequent to REM deprivation, subjects experience “REM rebound,” showing more than the usual amount of REM sleep in the first available sleep session. Some early REM-deprivation studies reported that subjects could begin to hallucinate and display other abnormalities in behavior, but these reports have not been confirmed.

Two kinds of observations, however, suggest that there are no adverse effects of prolonged or even complete deprivation of REM sleep. Virtually all antidepressant drugs, including MAO inhibitors, tricyclic antidepressants, and selective serotonin reuptake inhibitors, suppress REM sleep either partly or completely. In fact, the clinical effectiveness of these drugs may derive from their REM-depressant effects (Vogel et al., 1990). There are no reports, however, of adverse consequences of prolonged REM deprivation as a consequence of antidepressant drug treatments. A number of cases have been reported of people who have suffered lower brainstem damage that results in a complete loss of REM sleep. Some of these people suffer from a condition termed the “locked-in” syndrome: they are fully conscious, alert, and responsive but are quadriplegic and mute. O. N. Markand and M. L. Dyken (1976) reported that REM sleep was completely absent in five of seven patients with locked-in syndrome without apparent ill effects. I. Osorio and R. B. Daroff (1980) also described patients who had more selective lesions that abolished REM but left them ambulatory and verbally communicative; they lived quite satisfactorily without REM sleep.

Sleep and Memory Storage

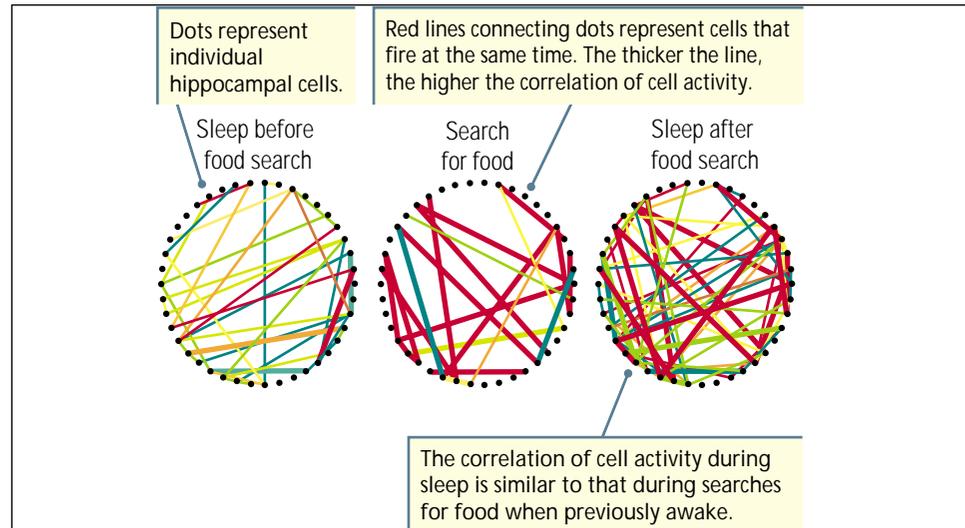
Two groups of experiments have proposed that dreams play a role in solidifying and organizing events so that we can remember them. One group proposes that dreams in NREM sleep store events in memory, whereas researchers in the other group propose that dreams in REM sleep fulfill this function.

Microsleep. A brief period of sleep lasting a second or so.

Figure 12-21

Are waking events replayed in sleep? The activity of hippocampal cells suggests that rats dream about previous experiences. The dots on the periphery of the circle represent 42 hippocampal cells that were recorded at the same time under three conditions: (1) a session of slow-wave sleep before a food-searching task, (2) the food-searching task, and (3) during slow-wave sleep after the food-searching task. The red lines connecting cells indicate cells whose discharge occurred at the same time. There were no strong correlations between cells during the slow-wave sleep that preceded the food-searching task, but the correlations between cells during the food search and during the subsequent slow-wave sleep were similar.

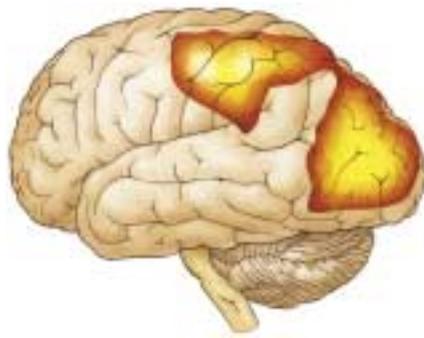
Adapted from "Reactivation of Hippocampal Ensemble Memories During Sleep," by M. A. Wilson and B. L. McNaughton, 1994, *Science*, 165, p. 678.



To examine whether rats “dream” about their experiences, Matthew Wilson and Bruce McNaughton (1994) made use of the finding that many hippocampal cells fire when a rat is in a certain location in an environment. These cells, called place cells, are relatively inactive until the rat passes through a particular place in its environment, whether it spontaneously walks through that place or is carried through it by the experimenter. The experimenters trained rats to look for food in a circular container or to search for food on a four-arm maze. Recordings were made from as many as 100 place cells at the same time in three conditions: during slow-wave sleep, during a session in the food-searching task, and during slow-wave sleep after a session in the food-searching task. The experimenters then used computer methodology to look for cells whose discharge was correlated—that is, cells that discharged at the same time. As is illustrated in Figure 12-21, the activity of only a few cells was strongly correlated in the sleep session that preceded the food-searching task. During food searching, quite a number of cells discharged at the same time as a rat visited different locations in the apparatus. In the sleep session that followed the food-searching experience, correlations that were remarkably similar to those observed during food searching were observed. In short, the rats appeared to be dreaming about their previous food-searching experience. In addition to demonstrating that rats dream, Wilson and McNaughton propose that dreaming during slow-wave sleep helps to store the memory of the previous food-searching experience, so that, if given the opportunity, the animal would know where to look for the food. This group also proposes that REM sleep may be important for storing memories (Poe et al., 2000), but we will look at an example from a study on human subjects that demonstrates this possibility.

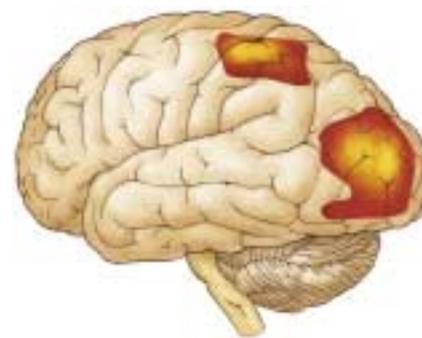
To determine whether humans dream about their experiences, Pierre Maquet and his coworkers in Belgium trained subjects on a serial reaction task and observed regional blood flow in the brain with PET scans during training and during REM sleep on the subsequent night (Maquet et al., 2000). The subjects faced a computer screen on which were six positional markers. The subjects were to push one of six keys when a corresponding positional marker was illuminated. The subjects did not know that the sequence in which the positional markers were illuminated was predetermined. Consequently, as training progressed, the subjects indicated that they were learning because their reaction time improved on trials on which one positional marker was correlated with a preceding marker. On the PET scan measures of brain activation, a similar pattern of neocortical activation was found during task acquisition and during REM sleep (Figure 12-22). On the basis of this result, Maquet and coworkers suggest,

(A) Reaction-time task



Subjects are trained on a reaction-time task, and brain activity is recorded with PET.

(B) REM sleep that night



Subjects display a similar pattern of brain activity during subsequent REM sleep.

first, that the subjects were dreaming about their learning experience and, second, that the replay while dreaming strengthened the memory of the task.

The interpretation of dreaming given to these two experiments is quite different from the psychoanalytical and activation-synthesis interpretations of dreaming. The conclusion from both of these studies is that dreams, whether in slow-wave sleep or in REM sleep, in rats or in humans, are important for storing memories. This is a rich area of study, with additional experimental support. Substantial evidence suggests both that sleep increases after a session of learning and that memory improves after a sleep session. Other research shows that sleep deprivation impairs memory formation.

The results of some natural experiments raise questions about the memory-storing functions of sleep. There are many documented cases of people who sleep less than a couple of hours each day yet remain active and healthy. These cases raise the question of why most people need much longer periods of sleep. Many people who take minor tranquilizers as a way of improving sleep have changes in sleep without corresponding complaints about learning. Although the drugs do improve the onset and duration of sleep, they also suppress stage 4 sleep, a result that raises questions about the importance of stage 4 for memory. P. Lavie and coworkers (1984) reported the case of a 33-year-old man who suffered a head injury at age 20 and subsequently displayed little REM sleep, as documented in sleep-recording sessions in a sleep laboratory. The lack of REM sleep did not appear to cause serious effects: the subject completed high school, attended law school, and subsequently practiced law. Human infants spend a great deal of time sleeping in their first year or so, but they remember nothing of this period of life. Finally, the sloth is one of nature's great sleepers but is not noted to be among its great learners. In conclusion, we can say that memory-storing theories of sleep are extremely interesting, and it is certainly possible that, just as sleep appears to contribute to well-being, it may also contribute to memory.

In Review

Several theories have been put forward to explain why we sleep. The biological theory, that sleep is an adaptive strategy for conserving energy during times when food resources are hard to obtain, has replaced the passive theory, that sleep results from lack of sensory stimulation. Scientists are examining the ideas that sleep is a restorative process and that sleep has a role in storing and sorting memory, but so far the evidence in favor of these ideas is not strong.

Figure 12-22

Do we store memories during REM sleep? (A) Regional blood flow in the brain as measured by PET during learning on a reaction-time task. (B) A very similar pattern of blood flow during REM sleep on the subsequent night suggests that subjects were dreaming about their learning experience. Adapted from "Experience Dependent Changes in Cerebral Activation During Human REM Sleep," by P. Maquet et al., 1998, *Nature Neuroscience*, 3, p. 832.



Sloth

THE NEURAL BASIS OF SLEEP

Granted that we do not yet know for sure *why* we sleep, is there any firm evidence of *how* we fall asleep? An early popular idea held that the body secretes a chemical that induces sleep and that can be removed only by sleeping. This idea is the basis for the “sleeping potion” featured in many stories. The hormone melatonin, which is secreted from the pineal gland during the dark phase of the light–dark cycle, causes sleepiness and is taken as an aid for sleep, so it might be thought to be the sleep-producing substance. Sleep, however, survives removal of the pineal gland. Thus, melatonin, and many other chemical substances, may only contribute to sleep, not cause it. If any chemical actually regulates sleep, it has not yet been identified. In fact, experimenters who have studied sleep in various species of animals have obtained evidence that sleep is *not* produced by a compound circulating in the bloodstream. When dolphins and birds sleep, only one hemisphere sleeps at a time. This ability presumably allows an animal’s other hemisphere to remain behaviorally alert. Because any blood-borne substance would affect both hemispheres, this finding suggests that sleep is not caused by a chemical that circulates in the bloodstream. This observation also strongly suggests that sleep is produced by the action of some region within each hemisphere.

In this section, we consider two points about the neural basis of sleep. First, we examine evidence that sleep is produced by activity in a region of the brainstem. Second, we look at evidence that the various events associated with sleep, including events associated with REM and NREM sleep, are controlled by a number of different brainstem nuclei.

The Reticular Activating System and Sleep

A dramatic experiment and a clever hypothesis by Giuseppe Moruzzi and Horace Magoun (1949) provide the beginnings of an answer to the question of which areas of the brain regulate sleep. Moruzzi and Magoun were recording the cortical EEG from anesthetized cats while electrically stimulating the cats’ brainstems. They discovered that, in response to the electrical stimulation, the large, slow cortical EEG typical of the condition of anesthesia was dramatically replaced by the low-voltage, fast-wave EEG typical of waking. The waking pattern of EEG activity outlasted the period of stimulation, demonstrating that it was produced by the activity of neurons in the region of the stimulating electrode. During the “waking period,” the cat did not become behaviorally aroused because it was anesthetized, but its cortical EEG appeared to indicate that it was awake. This pattern of EEG is referred to as a *desynchronized EEG*, meaning that the large, synchronized waves of sleep were replaced by low-voltage, fast activity. Subsequent experiments by Moruzzi and Magoun and by others showed that desynchronized EEG could be induced from a large area running through the center of the brainstem. Anatomically, this area of the brainstem is composed of a mixture of nuclei and fibers forming a *reticulum* (from the Latin word *rete*, meaning “net”). Moruzzi and Magoun named this brainstem area the *reticular activating system (RAS)* and proposed that this area of the brain is responsible for sleep–waking behavior. The location of the RAS is illustrated in Figure 12-23.

We know that if someone disturbs us when we are asleep, we usually wake up. To explain how sensory stimulation and the RAS are related, Moruzzi and Magoun proposed that sensory pathways entering the brainstem have collateral axons that synapse with neurons in the RAS. They proposed that sensory stimulation is conveyed to RAS neurons by these collaterals, and then RAS neurons produce the desynchronized EEG by axons that project to the cortex. Subsequent experiments with sleeping cats showed that stimulation would produce waking EEG activity and behavioral arousal in the animals just as if they had been provided with sensory stimulation to wake them up.

Moruzzi and Magoun further proposed that the cortex sends axons to the RAS, providing a route for people to stimulate their own reticular activating systems in order to stay awake. In sum, both sensory stimulation and conscious effort could activate the RAS to maintain waking.

Two other lines of experimental evidence support the idea that the RAS is responsible for desynchronized EEG. Because it was possible that Moruzzi and Magoun had stimulated various sensory pathways passing through the brainstem, it was necessary to demonstrate that brainstem neurons and not sensory pathway stimulation produced the waking EEG. When experimenters cut the brainstem just behind the RAS, thereby severing incoming sensory pathways, RAS stimulation still produced a desynchronized EEG. This result strengthened the argument that RAS neurons, not sensory pathways running through the region, are responsible for producing a desynchronized EEG. Furthermore, if the cut was made through the brainstem just in front of the RAS, the desynchronized EEG activity no longer occurred in response to electrical stimulation of the RAS. Together these experiments demonstrated that RAS neurons acting through axons projecting to the cortex produce the waking EEG.

A different line of evidence obtained from humans who have suffered brainstem injury supports this conclusion. Damage that affects the RAS results in **coma**, a state of deep unconsciousness resembling sleep. In a well-publicized case, a 21-year-old woman named Karen Ann Quinlan (Quinlan & Quinlan, 1977), after taking a minor tranquilizer and having a few drinks at a birthday party, sustained RAS damage that put her in a coma. She was hospitalized, placed on a respirator to support breathing, and fed by tubes. Her family fought a protracted legal battle to have her removed from life support, which was finally won before the Supreme Court of New Jersey. Even after being removed from life support, however, Quinlan lived for 10 more years in a perpetual coma.

Despite substantial evidence that the RAS has a role in sleep–waking behavior, attempts to localize sleep to a particular structure or group of neurons within the RAS have not been successful. Many studies have demonstrated that discrete lesions at various locations within the RAS can produce periods of sleep that last for days; but, with care, animals in the laboratory and human brain-injured patients recover from these acute symptoms. These findings suggest that sleep–waking behavior is due to the activity of a diffuse network of fibers and cells rather than being regulated by a single nucleus. As described in the next section, there are at least two routes through which patterns of a waking EEG are produced.

The Neural Basis of the EEG Changes Associated with Waking

A series of experiments performed on rats by Case Vanderwolf and his coworkers suggest that two brain structures are responsible for producing the waking EEG of the neocortex (Vanderwolf, 1988). Figure 12-24 illustrates the location of these structures, both of which are ascending neural pathways (described in Chapter 6).

One of the structures, the basal forebrain, contains large cholinergic cells whose axons project diffusely to the neocortex. When these cells secrete acetylcholine from their terminals, they stimulate neocortical neurons that then change their activity pattern to produce a waking EEG. The other structure, the median raphé, contains serotonin neurons whose axons also project diffusely to the neocortex. When these cells secrete serotonin (5-HT) from their terminals, they also stimulate neocortical cells to

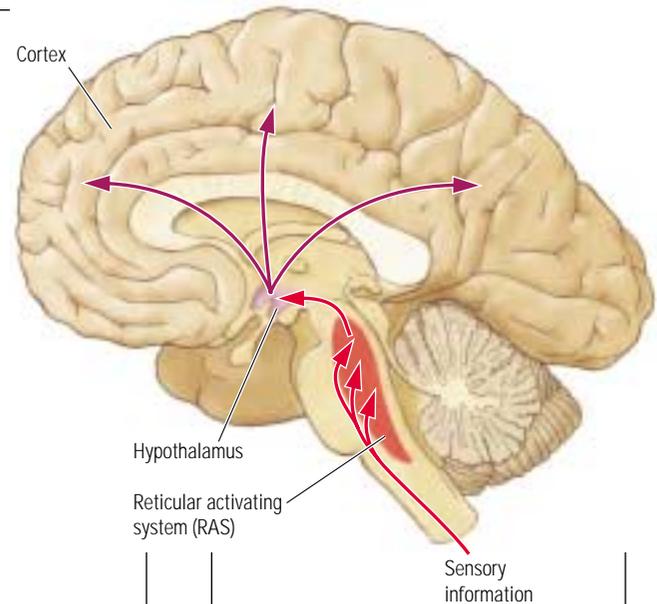


Figure 12-23

The reticular activating system is a region in the middle of the brain characterized by a mixture of cells and fiber pathways. Stimulation of the RAS produces a waking EEG, whereas damage to it produces a slow-wave, sleeplike EEG.

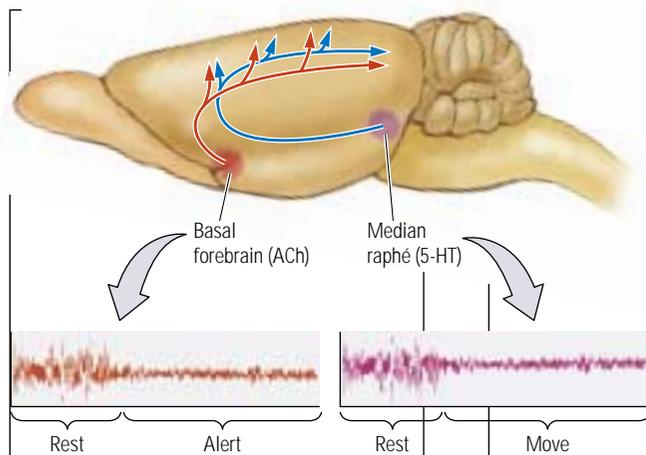


Figure 12-24

The cells of two ascending systems are responsible for an activated (beta) EEG in the rat. Basal forebrain acetylcholine (ACh) cells produce an activated EEG pattern when a rat is alert but immobile. The serotonergic raphe cells of the midbrain produce an activated EEG pattern when the rat moves.

produce a waking EEG. Although both pathways produce a very similar pattern of EEG activity, the relations of the two types of desynchronized EEG to behavior are different. If the activity of the cholinergic projection is blocked with drugs or with lesions to the cells of the basal forebrain, the normal waking EEG that should be recorded from an immobile rat is replaced by EEG activity resembling that of NREM sleep. If the rat walks or is otherwise active, a waking EEG is obtained from the neocortex. These findings suggest that the cholinergic EEG is responsible for the waking EEG when the rat is still and alert, whereas serotonergic activation is additionally responsible for the waking EEG when the animal moves.

It is important to note that neither the basal forebrain system nor the median raphe system is responsible for behavior. In fact, if both structures are pharmacologically or surgically destroyed, a rat can still stand and walk around. Its neocortical EEG, however, resembles that of a sleeping animal. As long as one of the systems is producing a waking EEG, rats can learn simple tasks. If both systems are destroyed, however, an animal, although still able to walk around, is no longer able to learn or display intelligent behavior. In a sense, the cortex is like a house in which the lights are powered by two separate power sources: both power sources must fail for the house to be left in darkness.

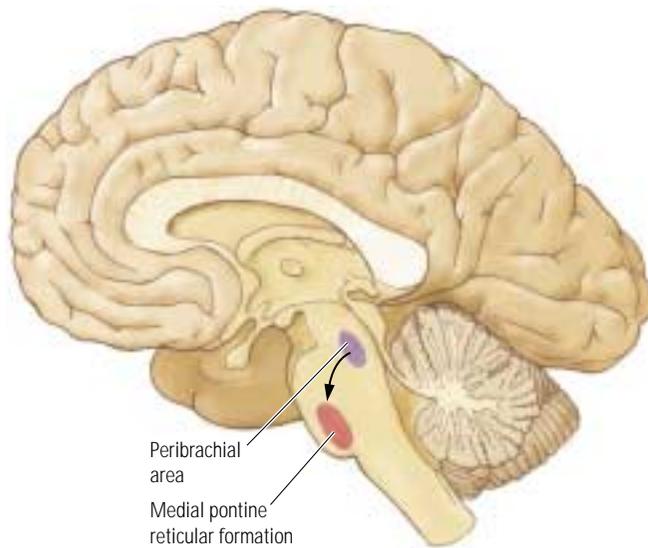
We do not know if the basal forebrain and median raphe produce the same two desynchronized patterns of EEG activity in humans as they do in rats, but it is likely that they do. Consequently, it is likely that, when we are alert, the cholinergic neurons are active and, when we move, the serotonin neurons are additionally active. You may have had the experience, when you felt sleepy in a class or behind the wheel of a car, of being able to wake yourself up by moving around a little—shaking your head or stretching. Presumably, your arousal level decreased as your cholinergic neurons became inactive; but, when you moved, your serotonergic neurons became active and restored your level of arousal. When we enter sleep, both cholinergic and serotonergic neurons become less active, allowing slow waves to appear in the cortical record.

The Neural Basis of REM Sleep

When we were looking at evidence related to the function of REM sleep, we considered a number of clinical cases in which people who had suffered brainstem damage no longer displayed REM sleep. This observation suggests that REM sleep is produced by the action of a neural area that is distinct from the RAS, which produces NREM sleep.

Barbara Jones (1993) and her colleagues described a group of cholinergic neurons known as the **peribrachial area**, which appears to be implicated in REM sleep. This area is located in the dorsal part of the brainstem just anterior to the cerebellum. Jones selectively destroyed these cells by injecting the neurotoxin kainic acid onto them and found that REM sleep in her experimental animal subjects was drastically reduced. This result suggested that the peribrachial area is responsible for producing REM sleep and REM-related behaviors. The peribrachial area extends into a more ventrally located nucleus called the **medial pontine reticular formation (MPRF)**. Lesions of the MPRF also abolish REM sleep, and injections of cholinergic agonists (drugs that act like acetylcholine) into the MPRF induce REM sleep. Thus, both the peribrachial area and the MPRF, illustrated in Figure 12-25, take part in the production of REM sleep.

If these two brain areas are responsible for producing REM sleep, how do other events related to REM sleep take place? Such events include: (1) an EEG pattern similar to the waking EEG pattern; (2) eye movements, or REMs; (3) sharp EEG spikes recorded from the pons, the lateral geniculate nucleus, and the visual cortex, called

**Figure 12-25**

The location of the two brainstem structures responsible for REM sleep. Damage to either area will reduce or abolish REM sleep.

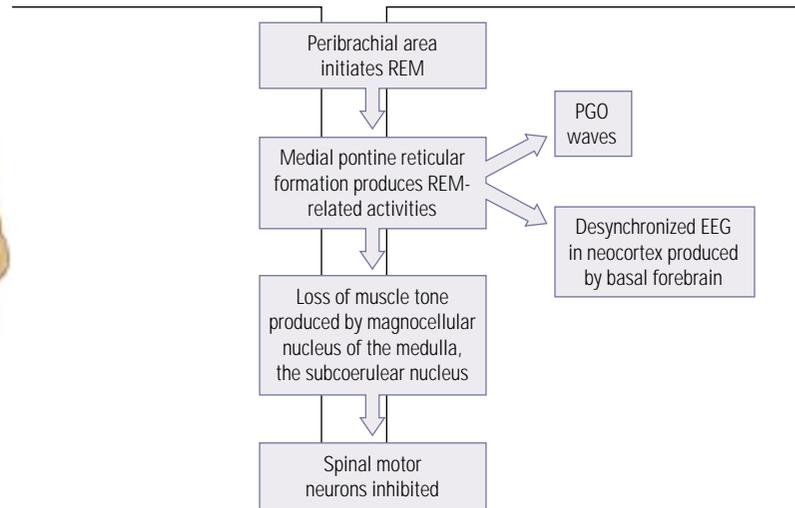
PGO (pons, geniculate, occipital) waves after the structures in which they are found; and (4) **atonia**, an absence of muscle tone due to the inhibition of motor neurons. These REM-related activities are likely to be found in humans, although, at present, PGO waves have not been confirmed in humans.

One explanation of how other REM-related activities take place is illustrated in Figure 12-26. The MPRF sends projections to basal forebrain cholinergic neurons to activate them and so produce the activated EEG of the cortex. Then the peribrachial area excites the PGO pathway to produce PGO waves and eye movements. Finally, the atonia of REM sleep is produced by the MPRF through a pathway that sends input to the **subcoeruleus nucleus**, located just behind it. The subcoeruleus nucleus excites the **magnocellular nucleus of the medulla**, which sends projections to the spinal motor neurons to inhibit them so that paralysis is achieved during the REM-sleep period.

French researcher Michael Jouvet (1972) observed that cats with lesions in the subcoeruleus nucleus displayed a remarkable behavior when they entered REM sleep. Rather than losing muscle tone and stretching out in the paralysis that typically accompanies REM sleep, they stood up, looked around, and made movements of catching an imaginary mouse or running from an imaginary threat. If cats dream about catching mice or dream about escaping from a threat, then it appeared that these cats were acting out their dreams.

In Review

Separate neural regions are responsible for sleep. The reticular activating system (RAS) in the central region of the brainstem is responsible for NREM sleep, whereas the peribrachial area and the medial pontine reticular formation (MPRF) are responsible for REM sleep. The last two areas, through pathways to the neocortex and spinal cord, are responsible for producing the waking EEG and the muscular paralysis that are associated with REM sleep.

**Figure 12-26**

The neural control of events related to REM sleep.

SLEEP DISORDERS

Disturbances of sleep are annoying and result in impaired performance during the following day. Some people suffer from sleep disorders almost every night that leave them chronically tired and unproductive. Some people are also visited by unwanted attacks of sleep in the daytime. In this section, we will consider abnormalities of sleep—some related to NREM sleep and others related to REM sleep.

Disorders of NREM Sleep

The two most common sleep disorders are **insomnia**, the inability to sleep, and **narcolepsy** (from the Greek *narco*, “a stupor,” and *lepsy*, “to be seized”), falling asleep at inconvenient times. They are considered disorders of slow-wave sleep. About 15 percent of people complain of ongoing sleep problems; an additional 20 percent complain of occasional sleep problems. As people age, the incidence of complaints about problems with sleep increases. Insomnia and narcolepsy are related, as anyone who has stayed up late at night can confirm: a short night’s sleep is often accompanied by a tendency to fall asleep at inconvenient times the next day.

Our understanding of insomnia is complicated by a large variation in how much time people spend asleep. Some short sleepers may think that they should sleep more, and some long sleepers may think that they should sleep less; yet, for each, the sleeping pattern may be appropriate. It is also possible that, for some people, circadian rhythms are disrupted by subtle life-style choices. Staying up late may set a person’s circadian rhythm forward, encouraging a cascade of late sleep followed by still later staying up.

Some sleep problems are brought on by shift work or by international travel. Institutions that use shift workers attempt to schedule shifts so that they disrupt sleep patterns as little as possible, usually by having workers change to shifts forward in time rather than backward. Disruptions caused by international travel are an inconvenience for the occasional traveler, but, for airline crews who travel regularly, especially on west-to-east flights, light–dark changes and time-zone changes can seriously disrupt sleep. Other common causes of sleep disorders are stress, long hours of work, and irregular life styles. Even worrying about insomnia is thought to play a major role in about 15 percent of insomnia cases.

Sleep disorders are a complicating factor in other conditions, including depression, a condition in which people may sleep too much or too little. Anxiety and depression may account for about 35 percent of insomnias. There are also quantitative differences in the sleep of depressed patients, because they enter REM sleep very quickly. It is possible, however, that entering REM sleep quickly is secondarily related to sleep deprivation, rather than being related directly to depression, because people who are sleep deprived also enter REM very quickly. Irregular sleeping patterns are also common in schizophrenia.

Insomnia may be brought on by sedative-hypnotic drugs, including secobarbital, sodium amytal, and many minor tranquilizers. These “sleeping pills” do help people get to sleep, but they cause additional problems. People may sleep under one of these drugs, but they are likely to feel groggy and tired the next day, which defeats the purpose of taking the drug. In addition, people develop tolerance to these medications, become dependent on them, and display rebound insomnia when they stop taking them. A person may increase the dose of the drug each time the drug fails to produce the desired effect. The syndrome in which patients unsuccessfully attempt to sleep by increasing their dosage of a drug is called **drug-dependency insomnia**.

Like many other people, you may have had the experience of being suddenly overcome with an urge to sleep at an inconvenient time, such as while attending a lecture.

Narcolepsy. A sleep disorder in which a person falls asleep at inappropriate times of the day.

Drug-dependency insomnia. A condition that results from continuous use of “sleeping pills” in which a person becomes tolerant of the drug while the drug also results in deprivation of either REM or NREM sleep, leading the person to increase the drug dosage.

For some people, such experiences with narcolepsy are common and disruptive. J. S., a junior in college, sat in the front row of the classroom for his course on the brain; within a few minutes of the beginning of each class, he dropped off to sleep. The instructor became concerned about his abilities as a lecturer, but one day he heard another instructor describe the sleeping behavior of a student who turned out to be J. S. The instructor then asked J. S. to stay after class to discuss his sleeping behavior. J. S. reported that sleeping in classes was a chronic problem. Not only did he sleep in class, but he fell asleep whenever he tried to study. He even fell asleep at the dinner table and in other inappropriate locations. His sleeping problem had made it a challenge to get through high school and was making it very difficult for him to pass his college courses.

About 1 percent of people suffer from narcolepsy, which takes a surprising number of forms. J. S. had a form of narcolepsy in which he fell asleep while sitting still, and his sleeping bouts consisted of brief bouts of NREM sleep lasting from 5 to 10 minutes. This pattern was very similar to napping and to dropping off to sleep in class after a late night, but it was distinguishable as narcolepsy by its frequency and by the disruptive effect that it had on his academic career. J. S. eventually discussed his problem with his physician and received a prescription for Ritalin, an amphetamine-like drug that stimulates dopamine transmission (see Chapter 6), which proved very helpful.

Some people who suffer from daytime sleepiness attend a sleep clinic to get help in sleeping better at night. Studies of narcoleptic people in sleep clinics have resulted in one surprising discovery concerning the causes of narcolepsy. “Sleep Apnea,” on page 482, describes a person who had to wake up in order to breathe; his *sleep apnea* left him extremely tired and caused him to nod off in the daytime.

Disorders of REM Sleep

Recall from the description of REM sleep that it is associated with muscular atonia and dreaming. REM-sleep atonia can occur when a person is not asleep, as in the case of L. M., a college senior who, after hearing a lecture on narcoleptic disorders, recounted the following experience. She had just gone to sleep when her roommate came into their room. She woke up and intended to ask her roommate if she wanted to go skating the next morning, but found herself completely unable to speak. She tried to turn her head to follow her roommate’s movements across the room but found that she was paralyzed. She had the terrifying feeling that some kind of monstrous creature was hiding in the bathroom waiting for her roommate. She tried to cry out but could produce only harsh, gurgling noises. Her roommate knocked her out of her paralysis by hitting her with a pillow.

This form of narcolepsy, called **sleep paralysis**, is extremely common. In informal class surveys, almost a third of students state that they have had such an experience. The atonia is typically accompanied by an unpleasant feeling of dread or fear. It seems likely that, in sleep paralysis, a person has entered REM sleep and atonia has occurred, but the person remains partly conscious or has partly awakened.

The atonia of REM sleep may also occur while a person is awake; this form is called **cataplexy** (from the Greek *cata*, “to fall,” and *plexus*, “seized”). In cataplexy, an awake, alert person suddenly loses all muscle tone and falls to the floor. These attacks are frequently reported to be triggered by excitement or laughing. Suddenly, the jaw drops, the head sinks, the arms go limp, the legs buckle, and the person falls down. The collapse can be so sudden that there is a real risk of injury. While in an atonic condition, the person may see imaginary creatures or hear imaginary voices. These hallucinations are called **hypnogogic** (Greek *hypno*, “sleep,” and *agogic*, “leading into”) hallucinations. People who fall into a state of cataplexy with hypnogogic hallucinations give every appearance of having fallen into REM sleep while remaining conscious.

 Link to the Web site at www.worthpublishers.com/kolb/chapter12 to learn more about narcolepsy.

Sleep paralysis. An inability to move owing to the brain’s inhibition of motor neurons.

Cataplexy. A condition in which a person collapses owing to the loss of all muscle activity or tone.

Hypnogogic. Referring to a hallucinogenic or dreamlike event at the beginning of sleep.

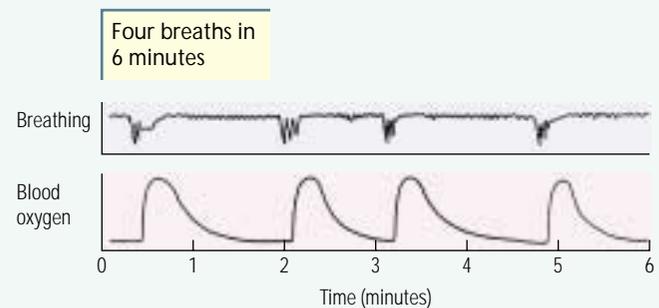
Sleep Apnea

The first time I went to a doctor for my insomnia, I was twenty-five—that was about thirty years ago. I explained to the doctor that I couldn't sleep; I had trouble falling asleep, I woke up many, many times during the night, and I was tired and sleepy all day long. As I explained my problem to him, he smiled and nodded. Inwardly, this attitude infuriated me—he couldn't possibly understand what I was going through. He asked me one or two questions: Had any close friend or relative died recently? Was I having any trouble in my job or at home? When I answered no, he shrugged his shoulders and reached for his prescription pad. Since that first occasion I have seen I don't know how many doctors, but none could help me. I've been given hundreds of different pills—to put me to sleep at night, to keep me awake in the daytime, to calm me down, to pep me up—have even been psychoanalyzed. But still I cannot sleep at night. (In Dement, 1992, p. 73).

This patient went to the Stanford University Sleep Disorders Clinic in 1972. He had recording electrodes attached so that brain, muscle, eye, and breathing activity could be recorded while he slept. The experimenters were amazed to find that he had to wake up to breathe. They observed that he would go for more than a minute and a half without breathing, wake up and gasp for breath, and then return to sleep, at which time the sequence was repeated. This condition is called sleep apnea (*a*, “not,” and *pnea*, “breathing”). It may be produced by a central problem, such as a weak command to the respiratory muscles, or it may be obstructive, caused by collapse of the upper airway. When people suffering from sleep apnea stop breathing, they either wake up completely and

have difficulty getting back to sleep or they make repeated partial awakenings throughout the night to gasp for breath.

Because sufferers are apparently unaware of their sleep apnea, it must be diagnosed by someone who watches them sleep. Sleep apnea affects all ages and both sexes, and 30 percent of people older than 65 years of age may have some form of it. Sleep apnea is thought to be more common among people who are overweight and who snore, conditions in which air flow is restricted. Surgery to expand the upper airway, weight loss, and face masks that deliver negative pressure to open the airway are all treatments for sleep apnea. Sleep apnea may also be related to sudden infant death syndrome, or crib death, in which otherwise healthy infants inexplicably die in their sleep.



A 6-minute record of two measures taken from a person with sleep apnea, taken when the person was in REM sleep. The breathing record shows points at which the person inhaled. The record of blood oxygen shows that blood oxygen increased after each breath and then continued to fall until another breath was taken. This person breathed only 4 times in the 6-minute period; a normal sleeper would breathe more than 60 times in the same interval.

Conditions in which REM-sleep atonia occurs frequently may have a genetic basis. In 1970, William Dement was given a litter of Doberman pinscher dogs and, later, a litter of Labrador retrievers, all of whom had cataplexy. The disease is transmitted as a recessive trait; so, to develop the disease, a dog must inherit the trait from both its mother and its father. The descendants of those dogs provide animal models for

investigating the neural basis of the disease as well as its treatment. When a dog is excited, such as when it is running for a piece of food, it may suddenly collapse, as is illustrated in Figure 12-27. Jerome Siegel (2000) investigated the cause of narcolepsy in dogs and found that neurons in the subcoerulear nucleus become inactive and neurons in the magnocellular nucleus of the medulla become active during attacks of cataplexy, just as they do during REM sleep. For some reason, the neurons responsible for paralysis during REM were producing cataplexy during waking. On the basis of anatomical examinations of the brains of narcoleptic dogs, Siegel suggested that the death of neurons in the amygdala and adjacent forebrain areas occurs as a one-time event just before the onset of the disease early in life. Presumably, the loss of these neurons somehow results in the loss of inhibition in the brainstem areas that produce paralysis. It is important to note that, although a genetic basis for cataplexy has been identified in dogs, there is as yet no evidence that all cases of human cataplexy are genetic. Like some forms of narcolepsy, cataplexy is treatable with Ritalin.

Recall Jouvet's experiment, in which he reported that cats with lesions to the subcoerulear region of the brainstem entered REM sleep without the accompanying atonia and apparently acted out their dreams. A similar condition has been reported in people and may either have a genetic basis or be caused by

Figure 12-27

Dog and man with narcolepsy having an attack of cataplexy, with complete loss of muscle tone, while awake and conscious. In both, the attack causes the head to droop and the back and legs to sag, and it can progress to a complete loss of muscle tone. Cataplexy is distinct from the sleep attacks that afflict most narcoleptics in that people hear and remember what is said around them and dogs can track a moving object with their eyes.

James Aronovsky (dog sequence), Joel Deutsch (human sequence), Slim Films.



brain damage. The condition has been named *REM without atonia*. The behavior of people who have REM without atonia suggests that they are acting out their dreams. The following two accounts are those of a 67-year-old patient described by Carlos Schenck and his coworkers (1986):

I was on a motorcycle going down the highway when another motorcyclist comes up alongside me and tries to ram me with his motorcycle. Well, I decided I'm going to kick his motorcycle away and at that point my wife woke me up and said, "What in heavens are you doing to me?" because I was kicking the hell out of her.

I had a dream where someone was shooting at me with a rifle and it was in a field that had ridges in it, so I decided to crawl behind a ridge—and I then had a gun too—and I look over the ridge so when he showed up I would shoot back at him and when I came to [i.e., awakened] I was kneeling alongside the bed with my arms extended like I was holding the rifle up and ready to shoot.

In both of these dreams, the patient had vivid pictorial images, but he heard nothing and he felt afraid. Although a large number of patients who have had such experiences have been described, most are elderly and suffer from brain injury or other brain-related disorders. REM without atonia can be treated with benzodiazepines, which block REM sleep.

Sleep and Consciousness

Many scientists interested in the neural basis of consciousness study sleep and sleep-related disorders because the many different kinds of waking and sleep conditions suggest that consciousness is not a unitary condition, either neurally or behaviorally. Rather, there are a variety of "states of consciousness," some of which can occur simultaneously. René Descartes, whose theory of mind was described in Chapter 1, conceived of his idea of a mind through a dream. He dreamed that he was interpreting the dream as it occurred. Later, when awake, he reasoned that, if he could think and analyze a dream while asleep, the mind must be able to function during both waking and sleep. Therefore it must be independent of the body that underwent sleep and waking transitions.

More recent research is a source of additional insight into consciousness. For example, what we colloquially refer to as waking comprises at least two different states, one in which there is alert consciousness and one in which there are movement and consciousness. People attempting to go to sleep or attempting to stay awake appear to realize that they can take advantage of these different conditions to achieve their objective. People who are tired and wish to fall asleep usually seek out a dark, quiet room, where they lie still. In doing so, they are removing themselves from a condition of "moving consciousness." People who want to stay awake, especially if they are tired, can apparently do so as long as they keep moving. By walking around and otherwise remaining active, they can stay awake indefinitely.

Similarly, sleep consists of a number of NREM conditions and a REM-sleep condition. People in both NREM sleep and REM sleep are at least in some sense conscious when they dream. Dream consciousness can also occur in conjunction with waking consciousness, as witnessed by reports that people who fall into a state of cataplexy are conscious of being awake while experiencing the visual and emotional features of dreams when they have hypnagogic hallucinations.

Besides being a source of insight into the neural basis of consciousness, the study of sleep states and events may help to explain some psychiatric and drug-induced con-

ditions. For example, among the symptoms of schizophrenia are visual and auditory hallucinations. Are these dream events that occur unexpectedly during waking? Many people who take hallucinogenic drugs such as LSD report that they have visual hallucinations. Does the drug initiate the visual features of dreams? People who have panic attacks suffer from very real fright that has no obvious cause. Are they experiencing the fear attacks that commonly occur during sleep paralysis and cataplexy? The answers to these questions are incomplete, but the similarities in symptoms between some waking and some sleep conditions do suggest that some waking disturbances may be sleep events that occur during waking.

In Review

Disorders of NREM sleep include insomnia, in which a person has difficulty falling asleep at night, and narcolepsy, in which a person falls asleep involuntarily in the daytime. Treating insomnia with sleeping pills, usually sedative hypnotics, may cause drug-dependent insomnia, in which progressively higher doses must be taken to achieve sleep. Disorders of REM sleep include sleep paralysis, in which a person awakes but is paralyzed and experiences a sense of fear, and cataplexy, in which a person may lose muscle tone and collapse in the daytime. Cataplexy may be associated with hypnagogic hallucinations, in which a person experiences dreams while paralyzed but awake.

SUMMARY

1. *What are biological rhythms?* Biological rhythms are cyclic patterns of behavior of varying length that are displayed by animals, plants, and even single-celled organisms. Mammals display a number of biological rhythms including circadian, or daily, rhythms and circannual, or yearly, rhythms. In the absence of environmental cues, circadian rhythms are free running, lasting a little more or a little less than their usual period of 24 hours, depending on the individual or the environmental conditions. Cues that reset a biological clock to a 24-hour rhythm are called zeitgebers.
2. *What is a biological clock?* A biological clock is a neural structure responsible for producing rhythmic behavior. There are a number of biological clocks in the brain, including the suprachiasmatic nucleus and the pineal gland. The suprachiasmatic nucleus is the mammalian biological clock responsible for circadian rhythms, and it has its own free-running rhythm with a period that is a little more or a little less than 24 hours. Stimuli from the environment such as sunrise and sunset entrain the free-running rhythm so that its period is 24 hours.
3. *How does a biological clock keep time?* Neurons of the suprachiasmatic nucleus have an activity rhythm in which they are active in the daytime and inactive at night. These neurons display their rhythmicity when disconnected from other brain structures, when removed from the brain and cultured in a dish, and after being cultured for a number of generations in a dish. When reimplanted into a brain without a suprachiasmatic nucleus, they restore the animal's circadian rhythms. The different aspects of circadian rhythms of neurons, including their period, are under genetic control.
4. *How is sleep measured?* Sleep events are measured by recording the brain's activity to produce an electroencephalogram, or EEG; muscular activity to produce an electromyogram, or EMG; and eye movements to produce an electrooculogram,

neuroscience interactive



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Try some self-tests to reinforce your mastery of the material. Look at some of the updates reflecting current research on the brain. You'll also be able to link to other sites which will reinforce what you've learned.

■ www.rls.org

Link to this site to learn more about restless legs syndrome and current research to help people suffering from this disorder.

■ www.sleepfoundation.org

The headquarters of the National Sleep Foundation can be a fascinating starting point for investigation about sleep disorders and normal sleep patterns.

On your CD-ROM you can review some of the research methods useful to understanding sleep in the three-dimensional research lab.

- or EOG. A typical night's sleep consists of four stages, as indicated by physiological measures, which take place in a number of cycles in the course of the night. During one stage of sleep, the EEG has a waking pattern and, because the sleeper displays rapid eye movements, this stage is called REM sleep. The other stages of sleep, in which the EEG has a slower rhythm, are called non-REM (NREM) sleep. NREM-sleep and REM-sleep intervals alternate four or five times each night; the duration of NREM sleep is longer in the early part of sleep, whereas the duration of REM sleep is longer in the later part of sleep.
5. *What events are associated with REM sleep?* A sleeper in slow-wave sleep has muscle tone, may toss and turn, and has dreams that are not especially vivid. A sleeper in REM sleep has no muscle tone and so is paralyzed, and has vivid dreams whose duration coincides with the duration of the REM period. There are several hypotheses about why we dream. The activation-synthesis hypothesis proposes that dreams are not meaningful and are only a by-product of the brain's state of excitation during REM. The evolutionary hypothesis suggests that dreams evolved as a mechanism to cope with real threats and fears posed by the environment.
 6. *Why do we sleep?* There are several theories of sleep, including the propositions that sleep results from the absence of sensory stimulation, that it is a biological adaptation that conserves energy resources, and that it is a restorative process that fixes wear and tear in the brain. Sleep may also organize and store each day's memories.
 7. *What is the neural basis of sleep?* Separate neural regions of the brain are responsible for NREM and REM sleep. The reticular activating system (RAS) located in the central area of the brainstem is responsible for NREM sleep. If it is stimulated, a sleeper awakes; if it is damaged, a person may enter a condition of coma. The peribrachial area and the medial pontine reticular formation of the brainstem are responsible for REM sleep. If these areas are damaged, REM sleep may no longer occur. Pathways from these areas project to the cortex to produce the cortical activation of REM and to the brainstem to produce the muscular paralysis of REM.
 8. *What disorders are associated with sleep?* There are several disorders of NREM sleep, including insomnia, the inability to sleep at night, and narcolepsy, inconveniently falling asleep in the daytime. The administration of sedative hypnotics to induce sleep may induce drug-dependency insomnia, a sleep disorder in which progressively larger doses of the drug are required to produce sleep. Disorders of REM sleep include sleep paralysis, in which a person awakens but remains paralyzed and sometimes feels fear and dread. Cataplexy is a disorder in which an awake person collapses into a state of paralysis. At the same time, the person may remain awake and have hypnagogic hallucinations similar to dreaming while awake.

KEY TERMS

cataplexy, p. 481

circadian rhythm, p. 449

drug-dependency

insomnia, p. 480

entrain, p. 451

free-running rhythm,
p. 450

hypnagogic, p. 481

microsleep, p. 473

narcolepsy, p. 480

pacemaker, p. 454

retinohypothalamic

pathway, p. 454

sleep paralysis, p. 481

suprachiasmatic nucleus,
p. 454

zeitgeber, p. 451

REVIEW QUESTIONS

1. Why are circadian and circannual rhythms such prominent rhythms in mammals?
2. Describe some of the details of the circadian clock that allow it to be easily studied.
3. In what ways are NREM sleep and REM sleep organized differently in the brain?
4. Describe the various theories of sleep.
5. What are some of the most common sleep disorders, and what are their causes and treatments?

FOR FURTHER THOUGHT

What ways can you suggest to combine the different theories of why we sleep into a unified theory?

RECOMMENDED READING

- Dement, W. C. (1972). *Some must watch while some must sleep*. New York: Norton. This short book is written in an engaging style for the beginning student of sleep. Nevertheless, instructors and even experts in sleep find it to be an excellent introduction by one of the pioneers of sleep research.
- Hobson, J. (1989). *Sleep*. New York: Scientific American Library. This book covers most of the main ideas that have developed from research into sleep. It also covers areas of psychology, ethology, neuroscience, and molecular biology, and it provides an overview of the disorders of sleep. Hobson presents his own theory of dreams, the theory of activation synthesis.
- Kleitman, N. (1965). *Sleep and wakefulness*. Chicago: University of Chicago Press. This book is an exhaustive description of research into sleep and covers all the major findings produced by the first decades of sleep research.