

Brain Basics: Understanding Sleep

Do you ever feel sleepy or "zone out" during the day? Do you find it hard to wake up on Monday mornings? If so, you are familiar with the powerful need for sleep. However, you may not realize that sleep is as essential for your well-being as food and water.

Sleep: A Dynamic Activity

Until the 1950s, most people thought of sleep as a passive, dormant part of our daily lives. We now know that our brains are very active during sleep. Moreover, sleep affects our daily functioning and our physical and mental health in many ways that we are just beginning to understand.

Nerve-signaling chemicals called *neurotransmitters* control whether we are asleep or awake by acting on different groups of nerve cells, or neurons, in the brain. Neurons in the brainstem, which connects the brain with the spinal cord, produce neurotransmitters such as serotonin and norepinephrine that keep some parts of the brain active while we are awake. Other neurons at the base of the brain begin signaling when we fall asleep. These neurons appear to "switch off" the signals that keep us awake. Research also suggests that a chemical called adenosine builds up in our blood while we are awake and causes drowsiness. This chemical gradually breaks down while we sleep.

During sleep, we usually pass through five phases of sleep: stages 1, 2, 3, 4, and *REM* (rapid eye movement) sleep. These stages progress in a cycle from stage 1 to REM sleep, then the cycle starts over again with stage 1. We spend almost 50 percent of our total sleep time in stage 2 sleep, about 20 percent in REM sleep, and the remaining 30 percent in the other stages. Infants, by contrast, spend about half of their sleep time in REM sleep.

During stage 1, which is light sleep, we drift in and out of sleep and can be awakened easily. Our eyes move very slowly and muscle activity slows. People awakened from stage 1 sleep often remember fragmented visual images. Many also experience sudden muscle contractions called *hypnic myoclonia*, often preceded by a sensation of starting to fall. These sudden movements are similar to the "jump" we make when startled. When we enter stage 2 sleep, our eye movements stop and our brain waves (fluctuations of electrical activity that can be measured by electrodes) become slower, with occasional bursts of rapid waves called *sleep spindles*. In stage 3, extremely slow brain waves called *delta waves* begin to appear, interspersed with smaller, faster waves. By stage 4, the brain produces delta waves almost exclusively. It is very difficult to wake someone during stages 3 and 4, which together are called *deep sleep*. There is no eye movement or muscle activity. People awakened during deep sleep do not adjust immediately and often feel groggy and disoriented for several minutes after they wake up. Some children experience bedwetting, night terrors, or sleepwalking during deep sleep.

When we switch into REM sleep, our breathing becomes more rapid, irregular, and shallow, our eyes jerk rapidly in various directions, and our limb muscles become temporarily paralyzed. Our heart rate increases, our blood pressure rises, and males develop penile erections. When people awaken during REM sleep, they often describe bizarre and illogical tales — dreams.

The first REM sleep period usually occurs about 70 to 90 minutes after we fall asleep. A complete sleep cycle takes 90 to 110 minutes on average. The first sleep cycles each night contain relatively short REM periods and long periods of deep sleep. As the night progresses, REM sleep periods increase in length while deep sleep decreases. By morning, people spend nearly all their sleep time in stages 1, 2, and REM.

People awakened after sleeping more than a few minutes are usually unable to recall the last few minutes before they fell asleep. This sleep-related form of amnesia is the reason people often forget

telephone calls or conversations they've had in the middle of the night. It also explains why we often do not remember our alarms ringing in the morning if we go right back to sleep after turning them off.

Since sleep and wakefulness are influenced by different neurotransmitter signals in the brain, foods and medicines that change the balance of these signals affect whether we feel alert or drowsy and how well we sleep. Caffeinated drinks such as coffee and drugs such as diet pills and decongestants stimulate some parts of the brain and can cause *insomnia*, or an inability to sleep. Many antidepressants suppress REM sleep. Heavy smokers often sleep very lightly and have reduced amounts of REM sleep. They also tend to wake up after 3 or 4 hours of sleep due to nicotine withdrawal. Many people who suffer from insomnia try to solve the problem with alcohol — the so-called night cap. While alcohol does help people fall into light sleep, it also robs them of REM and the deeper, more restorative stages of sleep. Instead, it keeps them in the lighter stages of sleep, from which they can be awakened easily.

People lose some of the ability to regulate their body temperature during REM, so abnormally hot or cold temperatures in the environment can disrupt this stage of sleep. If our REM sleep is disrupted one night, our bodies don't follow the normal sleep cycle progression the next time we doze off. Instead, we often slip directly into REM sleep and go through extended periods of REM until we "catch up" on this stage of sleep.

People who are under anesthesia or in a coma are often said to be asleep. However, people in these conditions cannot be awakened and do not produce the complex, active brain wave patterns seen in normal sleep. Instead, their brain waves are very slow and weak, sometimes all but undetectable.

How Much Sleep Do We Need?

The amount of sleep each person needs depends on many factors, including age. Infants generally require about 16 hours a day, while teenagers need about 9 hours on average. For most adults, 7 to 8 hours a night appears to be the best amount of sleep, although some people may need as few as 5 hours or as many as 10 hours of sleep each day. Women in the first 3 months of pregnancy often need several more hours of sleep than usual. The amount of sleep a person needs also increases if he or she has been deprived of sleep in previous days. Getting too little sleep creates a "sleep debt," which is much like being overdrawn at a bank. Eventually, your body will demand that the debt be repaid. We don't seem to adapt to getting less sleep than we need; while we may get used to a sleep-depriving schedule, our judgment, reaction time, and other functions are still impaired.

People tend to sleep more lightly and for shorter time spans as they get older, although they generally need about the same amount of sleep as they needed in early adulthood. About half of all people over 65 have frequent sleeping problems, such as insomnia, and deep sleep stages in many elderly people often become very short or stop completely. This change may be a normal part of aging, or it may result from medical problems that are common in elderly people and from the medications and other treatments for those problems.

Experts say that if you feel drowsy during the day, even during boring activities, you haven't had enough sleep. If you routinely fall asleep within 5 minutes of lying down, you probably have severe sleep deprivation, possibly even a sleep disorder. *Microsleeps*, or very brief episodes of sleep in an otherwise awake person, are another mark of sleep deprivation. In many cases, people are not aware that they are experiencing microsleeps. The widespread practice of "burning the candle at both ends" in western industrialized societies has created so much sleep deprivation that what is really abnormal sleepiness is now almost the norm.

Many studies make it clear that sleep deprivation is dangerous. Sleep-deprived people who are tested by using a driving simulator or by performing a hand-eye coordination task perform as badly as or worse than those who are intoxicated. Sleep deprivation also magnifies alcohol's effects on the body,

so a fatigued person who drinks will become much more impaired than someone who is well-rested. Driver fatigue is responsible for an estimated 100,000 motor vehicle accidents and 1500 deaths each year, according to the National Highway Traffic Safety Administration. Since drowsiness is the brain's last step before falling asleep, driving while drowsy can – and often does – lead to disaster. Caffeine and other stimulants cannot overcome the effects of severe sleep deprivation. The National Sleep Foundation says that if you have trouble keeping your eyes focused, if you can't stop yawning, or if you can't remember driving the last few miles, you are probably too drowsy to drive safely.

What Does Sleep Do For Us?

Although scientists are still trying to learn exactly why people need sleep, animal studies show that sleep is necessary for survival. For example, while rats normally live for two to three years, those deprived of REM sleep survive only about 5 weeks on average, and rats deprived of all sleep stages live only about 3 weeks. Sleep-deprived rats also develop abnormally low body temperatures and sores on their tail and paws. The sores may develop because the rats' immune systems become impaired. Some studies suggest that sleep deprivation affects the immune system in detrimental ways.

Sleep appears necessary for our nervous systems to work properly. Too little sleep leaves us drowsy and unable to concentrate the next day. It also leads to impaired memory and physical performance and reduced ability to carry out math calculations. If sleep deprivation continues, hallucinations and mood swings may develop. Some experts believe sleep gives neurons used while we are awake a chance to shut down and repair themselves. Without sleep, neurons may become so depleted in energy or so polluted with byproducts of normal cellular activities that they begin to malfunction. Sleep also may give the brain a chance to exercise important neuronal connections that might otherwise deteriorate from lack of activity.

Deep sleep coincides with the release of growth hormone in children and young adults. Many of the body's cells also show increased production and reduced breakdown of proteins during deep sleep. Since proteins are the building blocks needed for cell growth and for repair of damage from factors like stress and ultraviolet rays, deep sleep may truly be "beauty sleep." Activity in parts of the brain that control emotions, decision-making processes, and social interactions is drastically reduced during deep sleep, suggesting that this type of sleep may help people maintain optimal emotional and social functioning while they are awake. A study in rats also showed that certain nerve-signaling patterns which the rats generated during the day were repeated during deep sleep. This pattern repetition may help encode memories and improve learning.

Dreaming and REM Sleep

We typically spend more than 2 hours each night dreaming. Scientists do not know much about how or why we dream. Sigmund Freud, who greatly influenced the field of psychology, believed dreaming was a "safety valve" for unconscious desires. Only after 1953, when researchers first described REM in sleeping infants, did scientists begin to carefully study sleep and dreaming. They soon realized that the strange, illogical experiences we call dreams almost always occur during REM sleep. While most mammals and birds show signs of REM sleep, reptiles and other cold-blooded animals do not.

REM sleep begins with signals from an area at the base of the brain called the *pons*. These signals travel to a brain region called the *thalamus*, which relays them to the *cerebral cortex* — the outer layer of the brain that is responsible for learning, thinking, and organizing information. The pons also sends signals that shut off neurons in the spinal cord, causing temporary paralysis of the limb muscles. If something interferes with this paralysis, people will begin to physically "act out" their dreams — a rare, dangerous problem called *REM sleep behavior disorder*. A person dreaming about a ball game, for

example, may run headlong into furniture or blindly strike someone sleeping nearby while trying to catch a ball in the dream.

REM sleep stimulates the brain regions used in learning. This may be important for normal brain development during infancy, which would explain why infants spend much more time in REM sleep than adults. Like deep sleep, REM sleep is associated with increased production of proteins. One study found that REM sleep affects learning of certain mental skills. People taught a skill and then deprived of non-REM sleep could recall what they had learned after sleeping, while people deprived of REM sleep could not.

Some scientists believe dreams are the cortex's attempt to find meaning in the random signals that it receives during REM sleep. The cortex is the part of the brain that interprets and organizes information from the environment during consciousness. It may be that, given random signals from the pons during REM sleep, the cortex tries to interpret these signals as well, creating a "story" out of fragmented brain activity.

Sleep and Circadian Rhythms

Circadian rhythms are regular changes in mental and physical characteristics that occur in the course of a day (*circadian* is Latin for "around a day"). Most circadian rhythms are controlled by the body's biological "clock." This clock, called the *suprachiasmatic nucleus* or *SCN* is actually a pair of pinhead-sized brain structures that together contain about 20,000 neurons. The SCN rests in a part of the brain called the *hypothalamus*, just above the point where the optic nerves cross. Light that reaches photoreceptors in the *retina* (a tissue at the back of the eye) creates signals that travel along the optic nerve to the SCN.

Signals from the SCN travel to several brain regions, including the *pineal gland*, which responds to light-induced signals by switching off production of the hormone melatonin. The body's level of melatonin normally increases after darkness falls, making people feel drowsy. The SCN also governs functions that are synchronized with the sleep/wake cycle, including body temperature, hormone secretion, urine production, and changes in blood pressure.

By depriving people of light and other external time cues, scientists have learned that most people's biological clocks work on a 25-hour cycle rather than a 24-hour one. But because sunlight or other bright lights can reset the SCN, our biological cycles normally follow the 24-hour cycle of the sun, rather than our innate cycle. Circadian rhythms can be affected to some degree by almost any kind of external time cue, such as the beeping of your alarm clock, the clatter of a garbage truck, or the timing of your meals. Scientists call external time cues *zeitgebers* (German for "time givers").

When travelers pass from one time zone to another, they suffer from disrupted circadian rhythms, an uncomfortable feeling known as *jet lag*. For instance, if you travel from California to New York, you "lose" 3 hours according to your body's clock. You will feel tired when the alarm rings at 8 a.m. the next morning because, according to your body's clock, it is still 5 a.m. It usually takes several days for your body's cycles to adjust to the new time.

To reduce the effects of jet lag, some doctors try to manipulate the biological clock with a technique called light therapy. They expose people to special lights, many times brighter than ordinary household light, for several hours near the time the subjects want to wake up. This helps them reset their biological clocks and adjust to a new time zone.

Symptoms much like jet lag are common in people who work nights or who perform shift work. Because these people's work schedules are at odds with powerful sleep-regulating cues like sunlight, they often become uncontrollably drowsy during work, and they may suffer insomnia or other problems when they try to sleep. Shift workers have an increased risk of heart problems, digestive disturbances,

and emotional and mental problems, all of which may be related to their sleeping problems. The number and severity of workplace accidents also tend to increase during the night shift. Major industrial accidents attributed partly to errors made by fatigued night-shift workers include the Exxon Valdez oil spill and the Three Mile Island and Chernobyl nuclear power plant accidents. One study also found that medical interns working on the night shift are twice as likely as others to misinterpret hospital test records, which could endanger their patients. It may be possible to reduce shift-related fatigue by using bright lights in the workplace, minimizing shift changes, and taking scheduled naps.

Many people with total blindness experience life-long sleeping problems because their retinas are unable to detect light. These people have a kind of permanent jet lag and periodic insomnia because their circadian rhythms follow their innate cycle rather than a 24-hour one. Daily supplements of melatonin may improve night-time sleep for such patients. However, since the high doses of melatonin found in most supplements can build up in the body, long-term use of this substance may create new problems. Because the potential side effects of melatonin supplements are still largely unknown, most experts discourage melatonin use by the general public.

Sleep and Disease

Sleep and sleep-related problems play a role in a large number of human disorders and affect almost every field of medicine. For example, problems like stroke and asthma attacks tend to occur more frequently during the night and early morning, perhaps due to changes in hormones, heart rate, and other characteristics associated with sleep. Sleep also affects some kinds of epilepsy in complex ways. REM sleep seems to help prevent seizures that begin in one part of the brain from spreading to other brain regions, while deep sleep may promote the spread of these seizures. Sleep deprivation also triggers seizures in people with some types of epilepsy.

Neurons that control sleep interact closely with the immune system. As anyone who has had the flu knows, infectious diseases tend to make us feel sleepy. This probably happens because *cytokines*, chemicals our immune systems produce while fighting an infection, are powerful sleep-inducing chemicals. Sleep may help the body conserve energy and other resources that the immune system needs to mount an attack.

Sleeping problems occur in almost all people with mental disorders, including those with depression and schizophrenia. People with depression, for example, often awaken in the early hours of the morning and find themselves unable to get back to sleep. The amount of sleep a person gets also strongly influences the symptoms of mental disorders. Sleep deprivation is an effective therapy for people with certain types of depression, while it can actually cause depression in other people. Extreme sleep deprivation can lead to a seemingly psychotic state of paranoia and hallucinations in otherwise healthy people, and disrupted sleep can trigger episodes of mania (agitation and hyperactivity) in people with manic depression.

Sleeping problems are common in many other disorders as well, including Alzheimer's disease, stroke, cancer, and head injury. These sleeping problems may arise from changes in the brain regions and neurotransmitters that control sleep, or from the drugs used to control symptoms of other disorders. In patients who are hospitalized or who receive round-the-clock care, treatment schedules or hospital routines also may disrupt sleep. The old joke about a patient being awakened by a nurse so he could take a sleeping pill contains a grain of truth. Once sleeping problems develop, they can add to a person's impairment and cause confusion, frustration, or depression. Patients who are unable to sleep also notice pain more and may increase their requests for pain medication. Better management of sleeping problems in people who have other disorders could improve these patients' health and quality of life.

Sleep Disorders

At least 40 million Americans each year suffer from chronic, long-term sleep disorders each year, and an additional 20 million experience occasional sleeping problems. These disorders and the resulting sleep deprivation interfere with work, driving, and social activities. They also account for an estimated \$16 billion in medical costs each year, while the indirect costs due to lost productivity and other factors are probably much greater. Doctors have described more than 70 sleep disorders, most of which can be managed effectively once they are correctly diagnosed. The most common sleep disorders include insomnia, sleep apnea, restless legs syndrome, and narcolepsy.

Insomnia

Almost everyone occasionally suffers from short-term insomnia. This problem can result from stress, jet lag, diet, or many other factors. Insomnia almost always affects job performance and well-being the next day. About 60 million Americans a year have insomnia frequently or for extended periods of time, which leads to even more serious sleep deficits. Insomnia tends to increase with age and affects about 40 percent of women and 30 percent of men. It is often the major disabling symptom of an underlying medical disorder.

For short-term insomnia, doctors may prescribe sleeping pills. Most sleeping pills stop working after several weeks of nightly use, however, and long-term use can actually interfere with good sleep. Mild insomnia often can be prevented or cured by practicing good sleep habits (see "*Tips for a Good Night's Sleep*"). For more serious cases of insomnia, researchers are experimenting with light therapy and other ways to alter circadian cycles.

Sleep Apnea

Sleep apnea is a disorder of interrupted breathing during sleep. It usually occurs in association with fat buildup or loss of muscle tone with aging. These changes allow the windpipe to collapse during breathing when muscles relax during sleep. This problem, called *obstructive sleep apnea*, is usually associated with loud snoring (though not everyone who snores has this disorder). Sleep apnea also can occur if the neurons that control breathing malfunction during sleep.

During an episode of obstructive apnea, the person's effort to inhale air creates suction that collapses the windpipe. This blocks the air flow for 10 seconds to a minute while the sleeping person struggles to breathe. When the person's blood oxygen level falls, the brain responds by awakening the person enough to tighten the upper airway muscles and open the windpipe. The person may snort or gasp, then resume snoring. This cycle may be repeated hundreds of times a night. The frequent awakenings that sleep apnea patients experience leave them continually sleepy and may lead to personality changes such as irritability or depression. Sleep apnea also deprives the person of oxygen, which can lead to morning headaches, a loss of interest in sex, or a decline in mental functioning. It also is linked to high blood pressure, irregular heartbeats, and an increased risk of heart attacks and stroke. Patients with severe, untreated sleep apnea are two to three times more likely to have automobile accidents than the general population. In some high-risk individuals, sleep apnea may even lead to sudden death from respiratory arrest during sleep.

An estimated 18 million Americans have sleep apnea. However, few of them have had the problem diagnosed. Patients with the typical features of sleep apnea, such as loud snoring, obesity, and excessive daytime sleepiness, should be referred to a specialized sleep center that can perform a test called *polysomnography*. This test records the patient's brain waves, heartbeat, and breathing during an entire night. If sleep apnea is diagnosed, several treatments are available. Mild sleep apnea frequently can be overcome through weight loss or by preventing the person from sleeping on his or her back. Other people may need special devices or surgery to correct the obstruction. People with sleep apnea should never take sedatives or sleeping pills, which can prevent them from awakening enough to breathe.

Restless Legs Syndrome

Restless legs syndrome (RLS), a familial disorder causing unpleasant crawling, prickling, or tingling sensations in the legs and feet and an urge to move them for relief, is emerging as one of the most common sleep disorders, especially among older people. This disorder, which affects as many as 12 million Americans, leads to constant leg movement during the day and insomnia at night. Severe RLS is most common in elderly people, though symptoms may develop at any age. In some cases, it may be linked to other conditions such as anemia, pregnancy, or diabetes.

Many RLS patients also have a disorder known as *periodic limb movement disorder* or *PLMD*, which causes repetitive jerking movements of the limbs, especially the legs. These movements occur every 20 to 40 seconds and cause repeated awakening and severely fragmented sleep. In one study, RLS and PLMD accounted for a third of the insomnia seen in patients older than age 60.

RLS and PLMD often can be relieved by drugs that affect the neurotransmitter dopamine, suggesting that dopamine abnormalities underlie these disorders' symptoms. Learning how these disorders occur may lead to better therapies in the future.

Narcolepsy

Narcolepsy affects an estimated 250,000 Americans. People with narcolepsy have frequent "sleep attacks" at various times of the day, even if they have had a normal amount of night-time sleep. These attacks last from several seconds to more than 30 minutes. People with narcolepsy also may experience cataplexy (loss of muscle control during emotional situations), hallucinations, temporary paralysis when they awaken, and disrupted night-time sleep. These symptoms seem to be features of REM sleep that appear during waking, which suggests that narcolepsy is a disorder of sleep regulation. The symptoms of narcolepsy typically appear during adolescence, though it often takes years to obtain a correct diagnosis. The disorder (or at least a predisposition to it) is usually hereditary, but it occasionally is linked to brain damage from a head injury or neurological disease.

Once narcolepsy is diagnosed, stimulants, antidepressants, or other drugs can help control the symptoms and prevent the embarrassing and dangerous effects of falling asleep at improper times. Naps at certain times of the day also may reduce the excessive daytime sleepiness.

In 1999, a research team working with canine models identified a gene that causes narcolepsy—a breakthrough that brings a cure for this disabling condition within reach. The gene, hypocretin receptor 2, codes for a protein that allows brain cells to receive instructions from other cells. The defective versions of the gene encode proteins that cannot recognize these messages, perhaps cutting the cells off from messages that promote wakefulness. The researchers know that the same gene exists in humans, and they are currently searching for defective versions in people with narcolepsy.

The Future

Sleep research is expanding and attracting more and more attention from scientists. Researchers now know that sleep is an active and dynamic state that greatly influences our waking hours, and they realize that we must understand sleep to fully understand the brain. Innovative techniques, such as brain imaging, can now help researchers understand how different brain regions function during sleep and how different activities and disorders affect sleep. Understanding the factors that affect sleep in health and disease also may lead to revolutionary new therapies for sleep disorders and to ways of overcoming jet lag and the problems associated with shift work. We can expect these and many other benefits from research that will allow us to truly understand sleep's impact on our lives.

Tips for a Good Night's Sleep:

Adapted from "When You Can't Sleep: The ABCs of ZZZs," by the National Sleep Foundation.

- Set a schedule:

Go to bed at a set time each night and get up at the same time each morning. Disrupting this schedule may lead to insomnia. "Sleeping in" on weekends also makes it harder to wake up early on Monday morning because it re-sets your sleep cycles for a later awakening.

- Exercise:

Try to exercise 20 to 30 minutes a day. Daily exercise often helps people sleep, although a workout soon before bedtime may interfere with sleep. For maximum benefit, try to get your exercise about 5 to 6 hours before going to bed.

- Avoid caffeine, nicotine, and alcohol:

Avoid drinks that contain caffeine, which acts as a stimulant and keeps people awake. Sources of caffeine include coffee, chocolate, soft drinks, non-herbal teas, diet drugs, and some pain relievers. Smokers tend to sleep very lightly and often wake up in the early morning due to nicotine withdrawal. Alcohol robs people of deep sleep and REM sleep and keeps them in the lighter stages of sleep.

- Relax before bed:

A warm bath, reading, or another relaxing routine can make it easier to fall asleep. You can train yourself to associate certain restful activities with sleep and make them part of your bedtime ritual.

- Sleep until sunlight:

If possible, wake up with the sun, or use very bright lights in the morning. Sunlight helps the body's internal biological clock reset itself each day. Sleep experts recommend exposure to an hour of morning sunlight for people having problems falling asleep.

- Don't lie in bed awake:

If you can't get to sleep, don't just lie in bed. Do something else, like reading, watching television, or listening to music, until you feel tired. The anxiety of being unable to fall asleep can actually contribute to insomnia.

- Control your room temperature:

Maintain a comfortable temperature in the bedroom. Extreme temperatures may disrupt sleep or prevent you from falling asleep.

- See a doctor if your sleeping problem continues:

If you have trouble falling asleep night after night, or if you always feel tired the next day, then you may have a sleep disorder and should see a physician. Your primary care physician may be able to help you; if not, you can probably find a sleep specialist at a major hospital near you. Most sleep disorders can be treated effectively, so you can finally get that good night's sleep you need.

For information on other neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

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