Normal Sleep, Sleep Physiology, and Sleep Deprivation: General Principles

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NORMAL SLEEP IN ADULTS, INFANTS, AND THE ELDERLY

Normal sleep is divided into non–rapid eye movement (NREM) and rapid eye movement (REM) sleep. The stages of sleep are stage I (light sleep), stage II, stages III and IV (deep or delta-wave sleep), and REM sleep; NREM sleep comprises stages I-IV. Sleep is an active process that cycles at an ultradian rhythm of about 90 minutes.

Waking usually transitions into NREM sleep. REM follows NREM sleep and occurs 4-5 times during a normal 8- to 9-hour sleep period. The first REM period of the night may be less than 10 minutes in duration, while the last may exceed 60 minutes.

For the purpose of analysis, overnight sleep has been divided into 3 equal time periods: sleep in the first third of the night, which comprises the highest percentage of NREM; sleep in the middle third of the night; and sleep in the last third of the night, the majority of which is REM. Awakening after a full night's sleep is usually from REM sleep.

Sleep in adults

In adults, sleep of 8-8.4 hours is considered fully restorative. In some cases, total sleep often is divided into an overnight sleep period of 6-7 hours and a midafternoon nap of 1-2 hours.

Stage I is considered a transition between wake and sleep. It occurs upon falling asleep and during brief arousal periods within sleep and usually accounts for 5-10% of total sleep time. Stage II occurs throughout the sleep period and represents 40-50% of total sleep time. Stages III and IV delta sleep occur mostly in the first third of the night. They are distinguished from each other only by the percentage of delta activity and represent up to 20% of total sleep time. REM represents 20-25% of total sleep time.

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Sleep in infants

Infants have an overall greater total sleep time than any other age group; their sleep time can be divided into multiple periods. In newborns, the total sleep duration in a day can be 14-16 hours.

Over the first several months of life, sleep time decreases; by age 5-6 months, sleep consolidates into an overnight period with at least 1 nap during the day. REM sleep in infants represents a larger percentage of the total sleep at the expense of stages III and IV. Until age 3-4 months, newborns transition from wake into REM sleep. Thereafter, wake begins to transition directly into NREM.

Overnight, electrocardiographic recorded voltage remains high during sleep, as it does during periods of wakefulness. Sleep spindles begin appearing in the second month of life with a density greater than that seen in adults (see Sleep Physiology). After the first year, the spindles begin decreasing in density and progress toward adult patterns. K complexes begin by the sixth month of life.

Sleep in elderly persons

In elderly persons, the time spent in stages III and IV sleep decreases by 10-15% and the time in stage II increases by 5% compared to young adults, representing an overall decrease in total sleep duration. Latency to fall asleep and the number and duration of overnight arousals increase. Thus to have a fully restorative sleep, the total time in bed must increase. If the elderly person does not increase the total time in bed, complaints of insomnia and chronic sleepiness may occur. Sleep fragmentation results from the increase in overnight arousals and may be exacerbated by the increasing number of geriatric medical conditions, including sleep apnea, musculoskeletal disorders, and cardiopulmonary disease.
Sleep is a state of unconsciousness in which the brain is relatively more responsive to internal than to external stimuli. The predictable cycling of sleep and the reversal of relative external unresponsiveness are features that assist in distinguishing sleep from other states of unconsciousness. The brain gradually becomes less responsive to visual, auditory, and other environmental stimuli during the transition from wake to sleep, which is considered by some to be stage 1 of sleep.

Historically, sleep was thought to be a passive state that was initiated through withdrawal of sensory input. Currently, withdrawal of sensory awareness is believed to be a factor in sleep, but an active initiation mechanism that facilitates brain withdrawal also is recognized.

NREM sleep is controlled by complex initiating and maintenance mechanisms. The extent of which is not fully elaborated. Probably no single sleep-generating center exists. A more likely mechanism is sleep-generating circuits with inputs from brainstem and hypothalamic neuronal groups. Within these circuits, sleep initiation may begin with the emergence of inhibitory signals from the anterior hypothalamic preoptic nucleus directed caudally toward the brainstem reticular core and posterior hypothalamus. The preoptic nucleus inhibits the histaminergic posterior hypothalamic tuberoinfundibular region through GABA and probably acetylcholine.

The tuberoinfundibular region projects rostrally to the intralaminar nuclei of the thalamus and to the cerebral cortex. Inhibition of the tuberoinfundibular region is a critical step toward falling asleep because it results in functional disconnection between the brain stem and the more rostral thalamus and cortex. A decrease in ascending thalamic cholinergic transmissions occurs in association with decreasing cortical responsiveness. In addition to inhibiting higher cortical consciousness, the tuberoinfundibular tract projects caudally into the pontine reticular system and inhibits afferent transmissions from ascending cholinergic tracts.

NREM is an active state that is maintained partly through oscillations between the thalamus and the cortex. The 3 major oscillation systems are sleep spindles, delta oscillations, and slow cortical oscillations. Sleep spindles, a hallmark of stage II sleep, are generated by bursts of hyperpolarizing GABAergic thalamic reticular neurons. These bursts inhibit thalamocortical projection neurons. As deafferentation spreads, cortical-thalamic projections back to the thalamus synchronize. As hyperpolarization of the thalamic reticular neurons progresses, delta waves are produced by interactions from both thalamic reticular and cortical pyramidal sources. Slow cortical oscillations are produced in neocortical networks by cyclic hyperpolarizations and depolarizations.

Although the functions of NREM sleep remain speculative, several theories have been put forth. One theory proposes that decreased metabolic demand facilitates replenishment of glycogen stores. Another theory, which utilizes neuronal plasticity, suggests that the oscillating depolarizations and hyperpolarizations consolidate memory and remove redundant or excess synapses.

REM sleep is generated by mesencephalic and pontine cholinergic neurons, hence these are referred to as REM-on neurons. As REM sleep initiates, monoaminergic locus ceruleus and serotonergic raphe neurons become inactive and are called REM-off neurons.

REM is characterized by muscle atonia, cortical activation, low-voltage desynchronization of the EEG, and rapid eye movements. REM may be considered to have both tonic and phasic characteristics. Tonic muscle atonia is present throughout REM sleep. It results from inhibition of alpha motor neurons by clusters of peri–locus ceruleus neurons, which are referred to collectively as the dorsolateral small cell reticular group.

Projection of the presumed cholinergic dorsolateral small cell reticular group is through the medullary reticular formation, which projects through the ventrolateral reticulospinal tract to inhibitory spinal and bulbar interneurons. Glycinergic interneurons produce postsynaptic inhibition and hyperpolarization of the spinal alpha motor neurons. Tonic cortical activation with EEG desynchronization is promoted by phasic discharges of reticulospinal neurons to the thalamic nuclei. Other projections through brainstem reticular formation neurons are likely to be involved as well.

Phasic rapid eye movements are composed of lateral saccades generated in the paramedian pontine reticular formation and vertical saccades thought to be generated in the mesencephalic reticular formation. REM density is a term used to describe the frequency per minute of the eye movement bursts.

Phasic pontine-geniculate-occipital (PGO) spikes are another neurophysiological feature of REM sleep. These spikes appear to be generated by lateral dorsal tegmental and pedunculopontine tegmental neuronal bursts. They are projected to the lateral geniculate and other thalamic nuclei, and then to the occipital cortex. PGO bursts precede rapid eye movements by several seconds. Increases in PGO bursts are seen after REM sleep deprivation.

Other phasic features of REM sleep include periodic skeletal muscle twitches, increased heart rate variability, pupil dilation, and increased respiratory rate.

During NREM sleep, the metabolic demand of the brain decreases. This is supported by oxygen positron emission tomography (PET) studies, which show that, during NREM sleep, the blood flow throughout the entire brain progressively decreases. PET studies also show that, during REM sleep, blood flow increases in the thalamus and the primary visual, motor, and sensory cortices, while remaining comparatively decreased in the prefrontal and parietal associational regions. The increase in blood flow to the primary cortical regions may explain the vivid nature of REM dreaming, while the continued decrease in blood flow to the prefrontal cortex may explain the unquestioning acceptance of even the most bizarre dream content.

For excellent patient education resources, visit eMedicine's Sleep Disorders Center. Also, see eMedicine's patient education article on Sleep: Understanding the Basics.
Melatonin has been implicated as a modulator of light entrainment. It is secreted maximally during the night by the pineal gland. Prolactin, testosterone, and growth hormone also demonstrate circadian rhythms, with maximal secretion during the night.

Circadian Rhythms That Influence Sleep

Glucose-PET studies in individuals deprived of sleep have shown that after 24 hours of sustained wakefulness, the metabolic activity of the brain decreases significantly (up to 6% for the whole brain and up to 11% for specific cortical and basal ganglionic areas). In humans, sleep deprivation also results in a decrease in core body temperature, a decrease in immune system function as measured by white cell count and activity, and a decrease in the release of growth hormone. Sleep deprivation has been implicated as a cause of increased heart rate variability.

As the function of sleep has not been fully determined, the absolute number of hours necessary to fulfill its function is still unknown. Some individuals claim full effectiveness with only 3-5 hours of sleep per night, while some admit needing at least 8 hours of sleep per night (or more) to perform effectively. Sleep deprivation is best defined at this point by group means and in terms of the tasks impaired.

With decreased sleep, higher-order cognitive tasks are affected early and disproportionately. Tests requiring both speed and accuracy demonstrate considerably slowed speed before accuracy begins to fail. Total sleep duration of 7 hours per night over 1 week has resulted in decreased speed in tasks of both simple reaction time and more demanding computer-generated mathematical problem solving. Total sleep duration of 5 hours per night over 1 week shows both decrease in speed and the beginning of accuracy failure.

Total sleep duration of 7 hours per night over 1 week leads to impairment of cognitive work requiring simultaneous focus on several tasks. In driving simulations, for example, accidents increase progressively as total sleep duration is decreased to 7, 5, and 3 hours per night over 1 week. In the same simulations, 3 hours total sleep duration was associated with loss of ability to simultaneously appreciate peripheral and centrally presented visual stimuli, which could be termed as a form of visual simultanagnosia and peripheral visual neglect.

In tasks requiring judgment, increasingly risky behaviors emerge as the total sleep duration is limited to 5 hours per night. The high cost of an action seemingly is ignored as the sleep-deprived individual focuses on limited benefit.

One explanation for decreasing performance in sleep deprivation is the occurrence of microsleep. Microsleep is defined as brief (several seconds) runs of theta or delta activities that break through the otherwise beta or alpha EEG of waking. It has been seen to increase with sleep deprivation. In studies in which polysomnography is recorded simultaneously, microsleep impairs continuity of cognitive function and occurs prior to performance failure. However, the occurrence of microsleep has not been shown in most instances of polysomnographic correlated performance failure. Other explanations for performance impairments include sensory perceptual impairments such as the development of visual neglect phenomena.

These experimental findings can be explained by glucose-PET studies, which show that individuals deprived of sleep for 24 hours have a decrease in metabolism in the prefrontal and parietal associative areas. The areas most important for judgment, impulse control, attention, and visual association are disproportionally hypometabolic compared to the primary sensory and motor areas necessary for receiving and acting upon the environmental inputs. This finding leads to the hypothesis that the areas of the brain most responsible for higher-order cognition are to some degree less functional during sleep-deprived waking activity.

Sleep deprivation is a relative concept. Small amounts of sleep loss (eg, 1 hour per night over many nights) have subtle cognitive costs, which appear to go unrecognized by the individual experiencing the sleep loss. More severe restriction of sleep for a week leads to profound cognitive deficits similar to those seen in some stroke patients, which also appear to go unrecognized by the individual. The lack of recognition of the effects of sleep deprivation appears to be a constant feature, one which, it is hoped, will be overcome by further research and education.

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