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Questions:

1. Discuss the physiology of sleep.
2. Discuss the role of ganglia in coordinating system.

**A**- **THE PHYSIOLGY OF SLEEP**

Humans spend about one-third of their lives asleep, yet most individuals know little about sleep. Although its function remains to be fully elucidated, sleep is a universal need of all higher life forms including humans, absence of which has serious physiological consequences. This chapter provides an overview of basic sleep physiology and describes the characteristics of REM and NREM sleep. Sleep and circadian-generating systems are also reviewed. The chapter ends with a discussion about how sleep patterns change over an individual’s life span.

## **SLEEP ARCHITECTURE**

Sleep architecture refers to the basic structural organization of normal sleep. There are two types of sleep, non-rapid eye-movement (NREM) sleep and rapid eye-movement (REM) sleep. NREM sleep is divided into stages 1, 2, 3, and 4, representing a continuum of relative depth. Each has unique characteristics including variations in brain wave patterns, eye movements, and muscle tone. Sleep cycles and stages were uncovered with the use of electroencephalographic (EEG) recordings that trace the electrical patterns of brain activity ([Loomis et al., 1937](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00092); [Dement and Kleitman, 1957a](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00062)).

### **Two Types of Sleep**

Over the course of a period of sleep, NREM and REM sleep alternate cyclically ([Figure 2-1](https://www.ncbi.nlm.nih.gov/books/NBK19956/figure/a2000f7efmmm00003/?report=objectonly)). The function of alternations between these two types of sleep is not yet understood, but irregular cycling and/or absent sleep stages are associated with sleep disorders ([Zepelin et al., 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00124)). For example, instead of entering sleep through NREM, as is typical, individuals with narcolepsy enter sleep directly into REM sleep

#### **NREM and REM Sleep Cycles**

A sleep episode begins with a short period of NREM stage 1 progressing through stage 2, followed by stages 3 and 4 and finally to REM. However, individuals do not remain in REM sleep the remainder of the night but, rather, cycle between stages of NREM and REM throughout the night ([Figure 2-1](https://www.ncbi.nlm.nih.gov/books/NBK19956/figure/a2000f7efmmm00003/?report=objectonly)). NREM sleep constitutes about 75 to 80 percent of total time spent in sleep, and REM sleep constitutes the remaining 20 to 25 percent. The average length of the first NREM-REM sleep cycle is 70 to 100 minutes. The second, and later, cycles are longer lasting—approximately 90 to 120 minutes ([Carskadon and Dement, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00052)). In normal adults, REM sleep increases as the night progresses and is longest in the last one-third of the sleep episode. As the sleep episode progresses, stage 2 begins to account for the majority of NREM sleep, and stages 3 and 4 may sometimes altogether disappear.

### **Four Stages of NREM Sleep**

The four stages of NREM sleep are each associated with distinct brain activity and physiology. [Figure 2-2](https://www.ncbi.nlm.nih.gov/books/NBK19956/figure/a2000f7efmmm00004/?report=objectonly)shows the EEG patterns characteristic of the four NREM stages. Other instruments are used to track characteristic changes in eye movement and muscle tone.

#### **Stage 1 Sleep**

NREM stage 1 sleep serves a transitional role in sleep-stage cycling. Aside from newborns and those with narcolepsy and other specific neurological disorders, the average individual’s sleep episode begins in NREM stage 1. This stage usually lasts 1 to 7 minutes in the initial cycle, constituting 2 to 5 percent of total sleep, and is easily interrupted by a disruptive noise. Brain activity on the EEG in stage 1 transitions from wakefulness (marked by rhythmic alpha waves) to low-voltage, mixed-frequency waves. Alpha waves are associated with a wakeful relaxation state and are characterized by a frequency of 8 to 13 cycles per second ([Carskadon and Dement, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00052)).

#### **Stage 2 Sleep**

Stage 2 sleep lasts approximately 10 to 25 minutes in the initial cycle and lengthens with each successive cycle, eventually constituting between 45 to 55 percent of the total sleep episode. An individual in stage 2 sleep requires more intense stimuli than in stage 1 to awaken. Brain activity on an EEG shows relatively low-voltage, mixed-frequency activity characterized by the presence of sleep spindles and K-complexes ([Figure 2-2](https://www.ncbi.nlm.nih.gov/books/NBK19956/figure/a2000f7efmmm00004/?report=objectonly)). It is hypothesized that sleep spindles are important for memory consolidation. Individuals who learn a new task have a significantly higher density of sleep spindles than those in a control group ([Gais et al., 2002](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00073)).

#### **Stages 3 and 4, Slow-Wave Sleep**

Sleep stages 3 and 4 are collectively referred to as slow-wave sleep (SWS), most of which occurs during the first third of the night. Each has distinguishing characteristics. Stage 3 lasts only a few minutes and constitutes about 3 to 8 percent of sleep. The EEG shows increased high-voltage, slow-wave activity ([Figure 2-2](https://www.ncbi.nlm.nih.gov/books/NBK19956/figure/a2000f7efmmm00004/?report=objectonly)).

The last NREM stage is stage 4, which lasts approximately 20 to 40 minutes in the first cycle and makes up about 10 to 15 percent of sleep. The arousal threshold is highest for all NREM stages in stage 4. This stage is characterized by increased amounts of high-voltage, slow-wave activity on the EEG ([Carskadon and Dement, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00052)).

### **REM Sleep**

REM sleep is defined by the presence of desynchronized (low-voltage, mixed-frequency) brain wave activity, muscle atonia, and bursts of rapid eye movements ([Carskadon and Dement, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00052)). “Sawtooth” wave forms, theta activity (3 to 7 counts per second), and slow alpha activity also characterize REM sleep. During the initial cycle, the REM period may last only 1 to 5 minutes; however, it becomes progressively prolonged as the sleep episode progresses ([Carskadon and Dement, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00052)). There are numerous physiological differences between NREM and REM sleep.  Dreaming is most often associated with REM sleep. Loss of muscle tone and reflexes likely serves an important function because it prevents an individual from “acting out” their dreams or nightmares while sleeping (see [Chapter 3](https://www.ncbi.nlm.nih.gov/books/n/nap11617/a2000f7efddd00072/?report=reader)) ([Bader et al., 2003](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00043)). Approximately 80 percent of vivid dream recall results after arousal from this stage of sleep ([Dement and Kleitman, 1957b](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00063)). REM sleep may also be important for memory consolidation ([Crick and Mitchison, 1983](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00060); [Smith and Lapp, 1991](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00116)).

### **Physiology During Sleep**

In addition to the physiological changes listed in [Table 2-1](https://www.ncbi.nlm.nih.gov/books/NBK19956/table/a2000f7efttt00003/?report=objectonly), there are other body system changes that occur during sleep. Generally, these changes are well tolerated in healthy individuals, but they may compromise the sometimes fragile balance of individuals with vulnerable systems, such as those with cardiovascular diseases ([Parker and Dunbar, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00106)). Physiological changes also occur in the following systems:

* Cardiovascular: Changes in blood pressure and heart rate occur during sleep and are primarily determined by autonomic nervous system activity. For instance, brief increases in blood pressure and heart rate occur with K-complexes, arousals, and large body movements ([Lugaresi et al., 1978](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00093); [Catcheside et al., 2002](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00057); [Blasi et al., 2003](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00046); [Tank et al., 2003](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00119)). Further, there is an increased risk of myocardial infarction in the morning due to the sharp increases in heart rate and blood pressure that accompany awakening ([Floras et al., 1978](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00071); [Mulcahy et al., 1993](https://www.ncbi.nlm.nih.gov/books/NBK19956/" \l "a2000f7efrrr00103)).
* Sympathetic-nerve activity: Sympathetic-nerve activity decreases as NREM sleep deepens; however, there is a burst of sympathetic-nerve activity during NREM sleep due to the brief increase in blood pressure and heart rate that follows K-complexes. Compared to wakefulness, there is a rise in activity during REM sleep ([Somers et al., 1993](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00117)).
* Respiratory: Ventilation and respiratory flow change during sleep and become increasingly faster and more erratic, specifically during REM sleep ([Krieger, 2000](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00086); [Simon et al., 2002](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00115)). Ventilation data during REM sleep are somewhat unclear, but they suggest that hypoventilation (deficient ventilation of the lungs that results in reduction in the oxygen content or increase in the carbon dioxide content of the blood or both) occurs in a similar way as during NREM sleep ([NLM, 2006](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00105)). Several factors contribute to hypoventilation during NREM, and possibly REM, sleep such as reduced pharyngeal muscle tone ([Krieger, 2000](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00086); [Simon et al., 2002](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00115)). Further, during REM sleep, there is reduced rib cage movement and increased upper airway resistance due to the loss of tone in the intercostals and upper airway muscles ([Parker and Dunbar, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00106)). More generally, ventilation and respiratory flow show less effective adaptive responses dur ing sleep. The cough reflex, which normally reacts to irritants in the airway, is suppressed during REM and NREM sleep. The hypoxic ventilatory response is also lower in NREM sleep than during wakefulness and decreases further during REM sleep. Similarly, the arousal response to respiratory resistance (for example, resistance in breathing in or out) is lowest in stage 3 and stage 4 sleep ([Douglas, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00067)).
* Cerebral blood flow: NREM sleep is associated with significant reductions in blood flow and metabolism, while total blood flow and metabolism in REM sleep is comparable to wakefulness ([Madsen et al., 1991b](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00095)). However, metabolism and blood flow increase in certain brain regions during REM sleep, compared to wakefulness, such as the limbic system (which is involved with emotions), and visual association areas ([Madsen et al., 1991a](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00094)).
* Renal: There is a decreased excretion of sodium, potassium, chloride, and calcium during sleep that allows for more concentrated and reduced urine flow. The changes that occur during sleep in renal function are complex and include changes in renal blood flow, glomerular filtration, hormone secretion, and sympathetic neural stimulation.
* Endocrine: Endocrine functions such as growth hormone, thyroid hormone, and melatonin secretion are influenced by sleep. Growth hormone secretion typically takes place during the first few hours after sleep onset and generally occurs during SWS, while thyroid hormone secretion takes place in the late evening. Melatonin, which induces sleepiness, likely by reducing an alerting effect from the suprachiasmatic nucleus, is influenced by the light-dark cycle and is suppressed by light ([Parker and Dunbar, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00106)).

## **SLEEP-WAKE REGULATION**

### **The Two-Process Model**

The sleep-wake system is thought to be regulated by the interplay of two major processes, one that promotes sleep (process S) and one that maintains wakefulness (process C) ([Gillette and Abbott, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00076)). Process S is the homeostatic drive for sleep. The need for sleep (process S) accumulates across the day, peaks just before bedtime at night and dissipates throughout the night.

Process C is wake promoting and is regulated by the circadian system. Process C builds across the day, serving to counteract process S and promote wakefulness and alertness. However, this wake-promoting system begins to decline at bedtime, serving to enhance sleep consolidation as the need for sleep dissipates across the night ([Gillette and Abbott, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00076)). With an adequate night’s rest, the homeostatic drive for sleep is reduced, the circadian waking drive begins to increase, and the cycle starts over. In the absence of process C, total sleep time remains the same, but it is randomly distributed over the day and night; therefore, process C also works to consolidate sleep and wake into fairly distinct episodes ([Gillette and Abbott, 2005](https://www.ncbi.nlm.nih.gov/books/NBK19956/#a2000f7efrrr00076)). Importantly, through synchronization of the circadian system, process C assists in keeping sleep-wakefulness cycles coordinated with environmental light-dark cycles.

**B- THE ROLE OF BASAL GANGLIA IN COORDINATING SYSTEM.**

The basal ganglia (or basal nuclei) are a group of nuclei of varied origin in the brains of vertebrates that act as a cohesive functional unit. They are situated at the base of the forebrain and are strogly connected with the cerebral cortex, thalamus and other brain areas. The basal ganglia are associated with various of functions, including voluntary motor control, procedural learning relating to routine behaviors or habits such as bruxism, and eye movements, as well as cognitive and emotional functions.

## Action Selection

Currently popular theories hold that the basal ganglia play a primary role in action selection. Action selection is the decision of which of several possible behaviors to execute at a given time.

Experiemental studies show that the basal ganglia exert an inhibitory influence on a number of motor systems and that a release of this inhibition permits the motor to become active. The behavior switching that takes place within the basal ganglia is influenced by signals from many parts of the brain, including the prefrontal cortex which plays a key role in executive functions.