Question.

Q1

Discuss the physiology of sleep

Q2

Discuss the role of basal ganglia in coordinating movement

Answer.

1. Far from a simple absence of wakefulness, sleep is an active, regulated, and metabolically distinct state, essential for health and well-being. 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.

 There are two types of sleep, non-rapid eye-movement ([NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/)) sleep and rapid eye-movement ([REM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl98/)) 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.

**NREM and REM Sleep Cycles**

A sleep episode begins with a short period of [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) stage 1 progressing through stage 2, followed by stages 3 and 4 and finally to [REM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl98/). 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. 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. 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.

The four stages of [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) sleep are each associated with distinct brain activity and physiology.

#### Stage 1 Sleep

[NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) 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 13Hz

#### Stage 2 Sleep

[Stage 2 sleep](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl118/) 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 12–15 Hz – sleep spindles and K-complexes (large amplitude biphasic waves). 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.

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

Sleep stages 3 and 4 are collectively referred to as slow-wave sleep ([SWS](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl113/)), 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.

The last [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) 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 high amplitude low frequency delta waves (> 75 µV and 0.5–2 Hz) with stage 3 having between 20–50% and stage 4 more than 50% delta activity. EMG activity is low and eye movements are rare.

### REM Sleep

[REM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl98/) sleep is defined by the presence of desynchronized (low-voltage, mixed-frequency) brain wave activity, muscle atonia, and bursts of rapid eye movements. “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. Dreaming is most often associated with [REM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl98/) 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. Approximately 80 percent of vivid dream recall results after arousal from this stage of sleep. REM sleep may also be important for memory consolidation.

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. 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. 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.
* Sympathetic-nerve activity: Sympathetic-nerve activity decreases as [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) 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](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl98/) sleep.
* Respiratory: Ventilation and respiratory flow change during sleep and become increasingly faster and more erratic, specifically during [REM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl98/) sleep. 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](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) sleep. Several factors contribute to hypoventilation during NREM, and possibly REM, sleep such as reduced pharyngeal muscle tone. 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. 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.
* Cerebral blood flow: [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) sleep is associated with significant reductions in blood flow and metabolism, while total blood flow and metabolism in [REM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl98/) sleep is comparable to wakefulness. 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.
* 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](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl113/), while thyroid hormone secretion takes place in the late evening. [Melatonin](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl74/), 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.

**CIRCADIAN RYTHMN**

[Circadian rhythms](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl24/) refer, collectively, to the daily rhythms in physiology and behavior. They control the sleep-wake cycle, modulate physical activity and food consumption, and over the course of the day regulate body temperature, heart rate, muscle tone, and hormone secretion. The rhythms are generated by neural structures in the hypothalamus that function as a biological clock. Animals and plants possess endogenous clocks to organize daily behavioral and physiological rhythms in accord with the external day-night cycle. The basis for these clocks is believed to be a series of molecular pathways involving “clock” genes that are expressed in a nearly 24-hour rhythm.

In mammals, two proteins, Clock and Bmal1, bind together and move into the nucleus of the cell, where they bind to specific sites in the DNA that activate specific genes. Among the genes that they activate are Period and Cryptochrome. The products of these genes also move back into the nucleus, where they disrupt the binding of Clock and Bmal1 to the DNA, thus inhibiting their own synthesis. This results in a rising and falling pattern of expression of the Period and Cryptochrome gene products with a periodicity that is very close to 24 hours.

### The Suprachiasmatic Nucleus

The suprachiasmatic nucleus ([SCN](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl122/)) is responsible for regulating circadian rhythms in all organs. It receives direct inputs from a class of nerve cells in the retina that act as brightness detectors, which can reset the clock genes in the SCN on a daily basis. The SCN then transmits to the rest of the brain and body signals that bring all of the daily cycles in synchrony with the external day-night cycle.

The main influence of the [SCN](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl122/) on sleep is due to a series of relays through the dorsomedial nucleus of the hypothalamus, which signals to the wake-sleep systems to coordinate their activity with the day-night cycles. The SCN also coordinates cycles of feeding, locomotor activity, and hormones, such as corticosteroids. Under some conditions (e.g., limited food availability) when there are changes in the external temperature, or even under conditions of behavioral stress (e.g., the need to avoid a predator), animals must shift their daily cycles to survive. In such circumstances, the dorsomedial nucleus may shift to a new daily cycle, which can be completely out of phase with the SCN and the light-dark cycle, and its signals also shift the daily cycles of sleep, activity, feeding, and corticosteroid hormone secretion.

Another major output of the [SCN](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl122/) is to a pathway that controls the secretion of melatonin, a hormone produced by the pineal gland. [Melatonin](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl74/), which is mainly secreted at night, acts to further consolidate the circadian rhythms but has only limited effects directly on sleep.

### Sleep and Thermoregulation

Body temperature regulation is subject to circadian system influence. An individual’s body temperature is higher during the day than at night. At night there is a gradual decline in body temperature, a decrease in heat production (called the falling phase of the body temperature rhythm), and an increase in heat loss, all which promote sleep onset and maintenance, as well as EEG slow-wave activity. Conversely, there is a gradual increase in body temperature several hours before waking. The brain sends signals to other parts of the body that increase heat production and conservation in order to disrupt sleep and promote waking.

| Physiological Process | [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) | [REM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl98/) |
| --- | --- | --- |
| Brain activity | Decreases from wakefulness | Increases in motor and sensory areas, while other areas are similar to [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) |
| Heart rate | Slows from wakefulness | Increases and varies compared to [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) |
| Blood pressure | Decreases from wakefulness | Increases (up to 30 percent) and varies from [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) |
| Sympathetic nerve activity | Decreases from wakefulness | Increases significantly from wakefulness |
| Muscle tone | Similar to wakefulness | Absent |
| Blood flow to brain | Decreases from wakefulness | Increases from [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/), depending on brain region |
| Respiration | Decreases from wakefulness | Increases and varies from [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/), but may show brief stoppages; coughing suppressed |
| Airway resistance | Increases from wakefulness | Increases and varies from wakefulness |
| Body temperature | Is regulated at lower set point than wakefulness; shivering initiated at lower temperature than during wakefulness | Is not regulated; no shivering or sweating; temperature drifts toward that of the local environment |
| Sexual arousal | Occurs infrequently | Greater than [NREM](https://www.ncbi.nlm.nih.gov/books/n/nap11617/glossary/def-item/gl82/) |

DIFFERNCES BETWEEN NREM AND REM SLEEP.

**Influence of surgery and anaesthesia on sleep.**

Anaesthesia and surgery can have a profound effect upon sleep. On the first night after surgery, sleep architecture is severely disrupted with little or no SWS and REM sleep. The light Stage 2 sleep is fragmented with frequent awakenings. The degree of disruption appears to be related to the severity of the surgical insult. The mechanism is unclear but it is probably due to a combination of the surgical stress and the effects of opioid analgesics. Recovery of lost SWS and REM sleep occurs on postoperative nights 2–5, being later after major surgery. This coincides with the nadir of postoperative pulmonary function and several studies have demonstrated marked hypoxaemia associated with the rebound of REM sleep. It was a logical step to attribute postoperative myocardial ischaemia, myocardial infarction, pulmonary embolism and cerebral impairment (delirium and cognitive impairment) to nocturnal hypoxaemia. However, a number of studies have failed to confirm these presumed associations, although this does not exclude the possibility that the hypoxaemia may be important in some individuals.

1. The basal ganglia or basal nuclei are clumps of gray mass located below the cortex in the depth of both cerebral hemispheres. These nuclei can have different shapes and are involved in the control of movement.

The basal ganglia are surrounded by a white mass of the cerebral hemisphere, and the individual nuclei that enter into their composition build the walls of the lateral cerebral chambers.

The basal ganglia include:

* corpus striatum
* claustrum
* the amygdala
* substantia nigra
* subthalamic sails.

We can classify these nuclei into
the following groups:

* Input nuclei: corpus striatum
(caudate, putamen),
* Intermediary nuclei: Globus Pallidus
Externa, Nigra substance, and Subthalamic Nucleus.
* Output nuclei: Substantia Nigra and
Globus Pallidus.

## **Functions of the basal ganglia**

In order to understand the functions of the basal ganglia, we must mention the extrapyramidal system. This system is the part of the brain and brain stem that participates in motor control except for the corticospinal (pyramid) system. It includes:

* Basal ganglia and their pathways
* Portions of the cerebral cortex that give projections to the basal ganglia
* Parts of the cerebellum that give projections to the basal ganglia
* Parts of the reticular formation that are connected to the basal ganglia and cerebral cortex
* Thalamus nuclei associated with the basal ganglia and reticular formation.

The role of the extrapyramidal system is to control automatic movements, skeletal muscle tone, and maintenance of postural reflexes.

The basal ganglia exert their role in motor control through constant interaction with the cerebral cortex and the corticospinal pathway. They get information mainly from the cerebral cortex and send out information.

Almost all the motor and sensory nerve fibers that connect the cerebral cortex to the spinal cord pass between the major masses of the basal ganglia (nucleus caudatus and putamen) and are called the internal brain capsule.

The connections of the motor cortex, the thalamus and the joint circuits of the brain stem and cerebellum are very important. Namely, the main circuit of the basal ganglia system involves a huge number of connections between the basal ganglia themselves, as well as numerous entry and exit pathways between the motor regions of the brain and the basal ganglia.

The most prominent functions of the
basal ganglia include:

* Represents the accessory motor system. Mediates between neocortical motor centers and the "elderly" motor areas of the brainstem Selects the purposeful and desired motor activity and suppresses unwanted movements.
* Acts by modifying ongoing neural activity in motor projections
* Delivers an inhibitory role in motor control
* Inhibits muscle tone (balance of excitatory and inbound input signals according to PMN terminating on skeletal muscle)
* Monitor and adjust slow and continuous contractions (equilibrium, body position, etc.)
* Regulates attention and individual cognitive processes
* Participates in motor planning and learning
* Assisting the cerebral cortex in making subconscious, learned movements
* Temporal pattern of movement and gradation of the intensity of movement.

One of the major roles of the basal ganglia is to participate in the control of complex patterns of motor activity such as: letter writing, cutting paper with scissors, throwing a ball into a basket, adding the ball in football, many aspects of vocalization, controlled eye movements, or literally all our other skilled movements.

Cognitive control of motor activity in which the nucleus caudatus plays a major role is another important function of the basal ganglia. Likewise, planning which movement patterns will be used together, or in what order in order to achieve a complex goal, is another role of the basal ganglia.

The basal ganglia are particularly associated with movement disorders. Associated with damage to the BG are: tremors; involuntary muscle movements; abnormal increase in tone; difficulty initiating movements; abnormal posture.

Movement disorders comprise a variety of motor problems, not all of which are associated with dysfunction of the basal ganglia. Those that have a clearly established pathological basis and are caused by pathophysiological mechanisms directly involving the basal ganglia include:

* **Parkinson's**

Parkinson's is the most notorious disease of the basal ganglia. Classic clinical symptoms include bradykinesia, resting tremor, postural instability, and shuffling gait. This disease is a result of neurodegeneration of the SNpc dopaminergic neurons. Often found in the Parkinsonian striatum, alpha-synuclein protein aggregates form toxic “Lewy bodies,” which are inclusions within neurons. The substantia nigra, due to degeneration, loses its grossly visible dark pigmentation, a concomitant sign of dopamine biosynthesis dysfunction. This loss of dopamine depresses the nigrostriatal pathway. With decreased dopaminergic input the striatum exerts less positive motor activity and more negative motor inhibition. This gives the characteristic hypokinetic dysfunction found in these patients.

* **Huntington Disease**

[Huntington disease](https://www.physio-pedia.com/Huntington_Disease) is a hyperkinetic movement disorder. Its cause is a genetic defect manifesting as a CAG repeat on chromosome 4p on the HTT gene. This creates an abnormally long Huntington gene which leads to neuronal death in the caudate and the putamen. The indirect pathway is interrupted and leads to a hyperkinetic presentation. Symptoms include involuntary movements such as chorea, cognitive degeneration, and psychiatric dysfunction.

* **Hemiballism**

Hemiballism (from the Greek “to throw”) is used to describe hyperkinetic, involuntary, forceful movements of the ipsilateral arm and leg. Commonly, a lesion in the contralateral subthalamic nuclei causes hemiballism. Given that the subthalamus is part of the indirect pathway this lesion reduces or eliminates indirect pathway signalling, leading to a relative overabundance of activity in the direct pathway. Such causes include [stroke](https://www.physio-pedia.com/Stroke), [traumatic brain injury](https://www.physio-pedia.com/Overview_of_Traumatic_Brain_Injury), [amyotrophic lateral sclerosis](https://www.physio-pedia.com/Motor_Neurone_Disease_MND), nonketotic hyperglycemia, neoplasm, vascular malformation, and other causes.

* **Tourette Syndrome**

Tourette syndrome has been shown to have a significant neurological basal ganglia component which manifests as sudden, repetitive uncontrolled movements and vocalizations, called “tics.” These tics have been associated with dysfunction of the GABAergic projections from the striatum, leading to a relative increase in dopaminergic activity much like in hemiballism and Huntington’s disease.

Additionally, parts of the basal ganglia play a key role in reward and reinforcement, addictive behaviours and habit formation. Pathophysiological processes underlying psychiatric disorders such as [depression](https://www.physio-pedia.com/Depression) and obsessive-compulsive disorder involve the basal ganglia and their connections with many other structures (particularly to the prefrontal cortex and the limbic system). In terms of cognitive disorders, basal ganglia abnormalities have been found in individuals with [schizophrenia](https://www.physio-pedia.com/Schizophrenia) and may explain have learning deficits associated with the disorder.