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COURSE:PHYS 305( Neurophysiology assignment )

1. Discuss the physiology of sleep.

Humans spend about one-third of their lives asleep, yet most individuals know little about sleep. Although its function has not been completely discovered sleep is a universal need of all higher life forms including humans, absence of which has serious physiological consequences.

## **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.

### **Two Types of Sleep**

#### Over the course of a period of sleep, NREM( Non- rapid eye movement) and REM(Rapid eye movement) sleep alternate cyclically. 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. 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. 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.

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

The four stages of NREM sleep are each associated with distinct brain activity and physiololgy.

#### **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.

#### **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. 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), 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 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.

### **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. “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. 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. Approximately 80 percent of vivid dream recall results after arousal from this stage of sleep.REM sleep may also be important for memory consolidation.

### **Physiology During Sleep**

### 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. 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 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.
* Respiratory: Ventilation and respiratory flow change during sleep and become increasingly faster and more erratic, specifically during REM 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 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 during 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 sleep is associated with significant reductions in blood flow and metabolism, while total blood flow and metabolism in REM 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, 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.

## **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) .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. 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. Importantly, through synchronization of the circadian system, process C assists in keeping sleep-wakefulness cycles coordinated with environmental light-dark cycles.

### **Sleep-Generating Systems in the Brainstem**

Sleep process S is regulated by neurons that shut down the arousal systems, thus allowing the brain to fall asleep. Many of these neurons are found in the preoptic area of the hypothalamus. These neurons, containing molecules that inhibit neuronal communication, turn off the arousal systems during sleep. Loss of these nerve cells causes profound insomnia. Inputs from other regions of the brain also greatly influence the sleep system. These include inputs from the lower brainstem that relay information about the state of the body (e.g., a full stomach is conducive to falling asleep), as well as from emotional and cognitive areas of the forebrain. In addition, as described further in the next section, there are inputs from the circadian system that allow the wake-sleep system to synchronize with the external day-night cycle, but also to override this cycle when it is necessitated by environmental needs.

The sleep-generating system also includes neurons in the pons that intermittently switch from NREM to REM sleep over the course of the night. These neurons send outputs to the lower brainstem and spinal cord that cause muscle atonia, REMs, and chaotic autonomic activity that characterize REM sleep. Other outputs are sent to the forebrain, including activation of the cholinergic pathways to the thalamus to activate the EEG.

### **Wake-Generating Systems in the Brainstem**

Wakefulness is generated by an ascending arousal system from the brainstem that activates forebrain structures to maintain wakefulness. The main source for the ascending arousal influence includes two major pathways that originate in the upper brainstem. The first pathway, which takes origin from cholinergic neurons in the upper pons, activates parts of the thalamus that are responsible for maintaining transmission of sensory information to the cerebral cortex. The second pathway, which originates in cell groups in the upper brainstem that contain the monoamine neurotransmitters (norepinephrine, serotonin, dopamine, and histamine), enters the hypothalamus, rather than the thalamus, where it picks up inputs from nerve cells that contain peptides (orexin or hypocretin and melanin-concentrating hormone). These inputs then traverse the basal forebrain, where they pick up additional inputs from cells containing acetylcholine and gamma-aminobutyric acid. Ultimately, all of these inputs enter the cerebral cortex, where they diffusely activate the nerve cells and prepare them for the interpretation and analysis of incoming sensory information.

## **CIRCADIAN RHYTHMS, THE 24-HOUR CLOCK**

Circadian rhythms 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.

Many other genes are also regulated by Clock and Bmal1, and these genes cycle in this way in many tissues in the body, giving rise to daily patterns of activity. These rhythmically expressed genes contribute to many aspects of cellular function, including glucose and lipid metabolism, signal transduction, secretion, oxidative metabolism, and many others, suggesting the importance of the circadian system in many central aspects of life.

### **The Suprachiasmatic Nucleus**

The suprachiasmatic nucleus (SCN) 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 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 is to a pathway that controls the secretion of melatonin, a hormone produced by the pineal gland. Melatonin, 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.

## **SLEEP PATTERNS CHANGE WITH AGE**

Sleep architecture changes continuously and considerably with age. From infancy to adulthood, there are marked changes in how sleep is initiated and maintained, the percentage of time spent in each stage of sleep, and overall sleep efficiency (i.e., how successfully sleep is initiated and maintained). A general trend is that sleep efficiency declines with age. Although the consequences of decreased sleep efficiency are relatively well documented, the reasons are complex and poorly understood. Examination of sleep characteristics by age, however, allows a closer understanding of the function of sleep for human development and successful aging.

### **Newborns and Infants**

At birth, sleep timing is distributed evenly across day and night for the first few weeks, with no regular rhythm or concentration of sleeping and waking. Newborns sleep about 16 to 18 hours per day; however, it is discontinuous with the longest continuous sleep episode lasting only 2.5 to 4 hours. Newborns have three types of sleep: quiet sleep (similar to NREM), active sleep (analogous to REM), and indeterminate sleep. Sleep onset occurs through REM, not NREM, and each sleep episode consists of only one or two cycles . This distinctive sleep architecture occurs mostly because circadian rhythms have not yet been fully entrained. Circadian rhythms begin to arise around 2 to 3 months of age, leading to sleep consolidation that manifests in greater durations of wakefulness during the day and longer periods of sleep at night .Circadian rhythm development in the first 3 months includes: emergence of the 24-hour core body temperature cycle (1 month of age); progression of nocturnal sleeping (2 months of age); and cycling of melatonin and cortisol hormones in a circadian rhythm (3 months of age).

Sleep cycles also change because of the emergence of the circadian rhythm and a greater responsiveness to social cues (such as breast-feeding and bedtime routines). By 3 months of age, sleep cycles become more regular: sleep onset now begins with NREM, REM sleep decreases and shifts to the later part of the sleep cycle, and the total NREM and REM sleep cycle is typically 50 minute. By 6 months of age, total sleep time reduces slightly and the longest continuous sleep episode lengthens to approximately 6 hours. As sleep cycles mature, the typical muscle paralysis of REM sleep replaces the propensity for movement in what was called “active sleep” as a newborn. By 12 months old, the infant typically sleeps 14 to 15 hours per day with the majority of sleep consolidated in the evening and during one to two naps during the day.

### **Young Children**

There are a limited number of studies that address normal sleep architecture in young children; however, one trend that appears to be consistent is that sleep amounts decrease as a child gets older. The reduction cannot be attributed solely to physiologic requirements, because cultural environments and social changes also influence changing sleep characteristics in young children. Total sleep time decreases by 2 hours from age 2 to age 5 (13 hours to 11) .Socially, the decrease in time asleep may be a result of decreased daytime napping, as most children discontinue napping between 3 and 5 years old .Other social and cultural factors that begin to influence sleep include how, with whom, and where children sleep and the introduction of school time routines.

Physiologically, it has been suggested that by the time children enter school (typically 6 years old) they begin to manifest circadian sleep phase preferences—a tendency to be a “night owl” or “morning bird”.Older children, however, are significantly more likely to experience challenges in initiating and maintaining sleep than younger children. In addition, older children are more likely to have nightmares, which usually disrupt sleep, making it discontinuous .One study found that children appear to have longer REM sleep latencies than adolescents and consequently spend a greater percentage of sleep time in stages 3 and 4.

### **Adolescents**

A complex and bidirectional relationship exists between pubertal development and sleep. Studies underscore the importance of using pubertal stage, rather than chronologic age as the metric in understanding sleep, as has been found for other physiologic parameters in the second decade of life. It has been determined that adolescents require 9 to 10 hours of sleep each night, though few adolescents obtain adequate sleep. In the United States, the average total sleep time in a sample of eighth-grade students was found to be 7.9 hours .Over a quarter of high school and college students were found to be sleep deprived.

SWS and sleep latency time progressively declines with advancing pubertal development; however, time spent in stage 2 increases .These changes are likely in part due to pubertal and hormonal changes that accompany the onset of puberty .For instance, at midpuberty, there is significantly greater daytime sleepiness than at earlier stages of puberty. Afternoon sleepiness is greater than that in late afternoon and evening in more mature adolescents than in younger subjects. With increasing age, the total time spent sleeping decreases, as does REM sleep. However, if bedtime is fixed, the duration of REM sleep remains constant.

### **Adults**

Sleep architecture continues to change with age across adulthood. Two major attributes of age-related sleep changes are earlier wake time and reduced sleep consolidation .A hallmark change with age is a tendency toward earlier bedtimes and wake times. Older adults (approximately ages 65 to 75) typically awaken 1.33 hours earlier, and go to bed 1.07 hours earlier, than younger adults (approximately ages 20 to 30). There are no conclusive studies that demonstrate why older adults experience earlier wake times, despite decreased sleep efficiency, but one hypothesis may be an advanced circadian pacemaker that accompanies age .It is unclear if this is due to older adults experiencing an increased sensitivity to light. Nonetheless, the consequences of an advanced circadian rhythm are a 1-hour advance in body temperature increase in the early morning and misaligned melatonin and cortisol secretion rhythms with the circadian clock.

Younger adults may experience brief awakenings, but they are usually minor and occur close to an REM sleep transition; thus, sleep remains relatively consolidated. Arousal occurring mostly from REM sleep in young adults suggests that there is a protective mechanism to keep from awakening during NREM sleep; however, this protective effect appears to also decline with age .As an individual ages (between the ages of 20 to 60), SWS declines at a rate of about 2 percent per decade. Because arousal thresholds are typically highest during SWS, and because SWS declines with age, older adults experience more frequent awakenings during a sleep episode. Another important variable may be an age-related reduction both in homeostatic sleep pressure and circadian pacemaker effectiveness during the night.

### **Gender Differences**

Although there have been few systematic studies, there appear to be gender-based differences in sleep and circadian rhythms. Available evidence is strongest in adults; however, gender differences have also been observed in infancy, childhood ), and adolescence. In adults, men spend greater time in stage 1 sleep and experience more awakenings. Although women maintain SWS longer than men, they complain more often of difficulty falling asleep and midsleep awakenings. In contrast, men are more likely to complain of daytime sleepiness. In women, the menstrual cycle may influence sleep-wake activity; however, methodological challenges have limited the number of conclusive findings .There have been a number of studies that suggest that women’s sleep patterns are greatly affected during pregnancy and the postpartum period. For example, women often experience considerable daytime sleepiness during pregnancy.

### **Elderly People**

Problematic sleep has adverse effects on all individuals, regardless of age; however, older people typically show an increase in disturbed sleep that can create a negative impact on their quality of life, mood, and alertness .Elderly individuals sleep 36 percent less than children at age 5 .Although the ability to sleep becomes more difficult, the need to sleep does not decrease with age .Difficulty in initiating and maintaining sleep is cited in 43 percent of the elderly although these problems are more commonly among adults suffering from depression, respiratory symptoms, and physical disability, among others . However, declining sleep efficiency and quality has also been observed in healthy older people.

Changes in sleep patterns affect males and females differently. The progressive decrease in SWS is one of the most prominent changes with aging; however, it appears to preferentially affect men. The gender difference is unclear, but it has been suggested that older women have “better-preserved” SWS than men .Women ages 70 and older spend around 15 to 20 percent of total sleep time in stages 3 and 4; men of the same age spend only around 5 percent of total sleep time in stages 3 and 4 .Another gender contrast is that older women go to bed and wake up earlier than older men, which suggests that body temperature rhythms are phase-advanced in elderly women. However, both men and women have increased stage 1 and decreased REM sleep.

Older people also experience a decrease in melatonin levels, which may be due to the gradual deterioration of the hypothalamic nuclei that drive circadian rhythms .The inability to maintain long sleep episodes and bouts of wakefulness may reflect, in addition to other medical factors, a continuously decreasing sleep homeostasis . Other prominent factors are the continuous increase in sleep latency and nighttime awakenings and inconsistency of external cues such as light exposure (which tends to be low), irregular meal times, nocturia, and decreased mobility leading to a reduction in exercise.

1. Discuss the role of basal ganglia in coordinating movement.

 The basal ganglia are large subcortical structures comprising several interconnected nuclei in the forebrain, diencephalon, and midbrain. Historically, the basal ganglia have been viewed as a component of the motor system.The basal ganglia (BG) are interconnected nuclei located in the white matter of both hemispheres. They include the caudate nucleus, the putamen, the nucleus accumbens, the globus pallidus, the substantia nigra, and the subthalamic nucleus. The primary role of the BG involves coordination of motor function, but they are also thought to be involved in the processing of pain. This is exemplified by clinical disorders that feature both movement disturbance and chronic pain.

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 c**erebral cortex** and the corticospinal pathway ([1](https://www.ncbi.nlm.nih.gov/books/NBK537141/)). 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.

## **Movement**

The greatest source of insight into the functions of the basal ganglia has come from the study of two neurological disorders, Parkinson’s disease and Huntington’s disease. For both of these disorders, the nature of the neural damage is well-understood and can be correlated with the resulting symptoms.

Parkinson’s disease involves the major loss of dopaminergic cells in the substantia nigra. Huntington’s disease involves the massive loss of medium spiny neurons in the striatum.

The symptoms of the two diseases are virtually opposite: Parkinson’s disease is characterized by a gradual loss of the ability to initiate movement, whereas Huntington’s disease is characterized by an inability to prevent parts of the body from moving unintentionally.

It is noteworthy that, although both diseases have cognitive symptoms, especially in their advanced stages, the most salient symptoms relate to the ability to initiate and control movement. Thus, both are classified primarily as movement disorders.

A different movement disorder, called hemiballismus, may result from damage restricted to the subthalamic nucleus. Hemiballismus is characterized by violent and uncontrollable flinging movements of the arms and legs.

## **Function in Eye Movement**

One of the most intensively studied functions of the basal ganglia is their role in controlling eye movements. Eye movement is influenced by an extensive network of brain regions that converge on a midbrain area called the superior colliculus (SC).

The SC is a layered structure whose layers form two-dimensional retinotopic maps of visual space. A bump of neural activity in the deep layers of the SC drives eye movement toward the corresponding point in space.

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.