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**PHS 305 Assignment; - Neurophysiology.**

**Course Title: - Neurophysiology.**

1) Physiology of Sleep.

Sleep is defined as unconsciousness from which the person can be aroused by sensory or other stimuli. It is to be distinguished from coma, which is unconsciousness from which the person cannot be aroused. There are multiple stages of sleep, from very light sleep to very deep sleep; sleep researchers also divide sleep into two entirely different types of sleep that have different qualities.

Two Types of Sleep.

During each night, a person goes through stages of two types of sleep that alternate with each other. They are called: -

- 1) Slow-wave sleep or Non Rapid eye movement (NREM), because in this type of sleep the brain waves are very strong and very low frequency
- 2) Rapid eye movement sleep (REM sleep), because in this type of sleep the eyes undergo rapid movements despite the fact that the person is still asleep.

Most sleep during each night is of the slow-wave variety; this is the deep, restful sleep that the person experiences during the first hour of sleep after having been awake for many hours. REM sleep, on the other hand, occurs in episodes that occupy about 25 per cent of the sleep time in young adults; each episode normally recurs about every 90 minutes. This type of

sleep is not so restful, and it is usually associated with vivid dreaming.

### Four Stages of NREM Sleep

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

#### 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

This 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, 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.

### Physiology During Sleep.

Physiological changes 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.
- **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

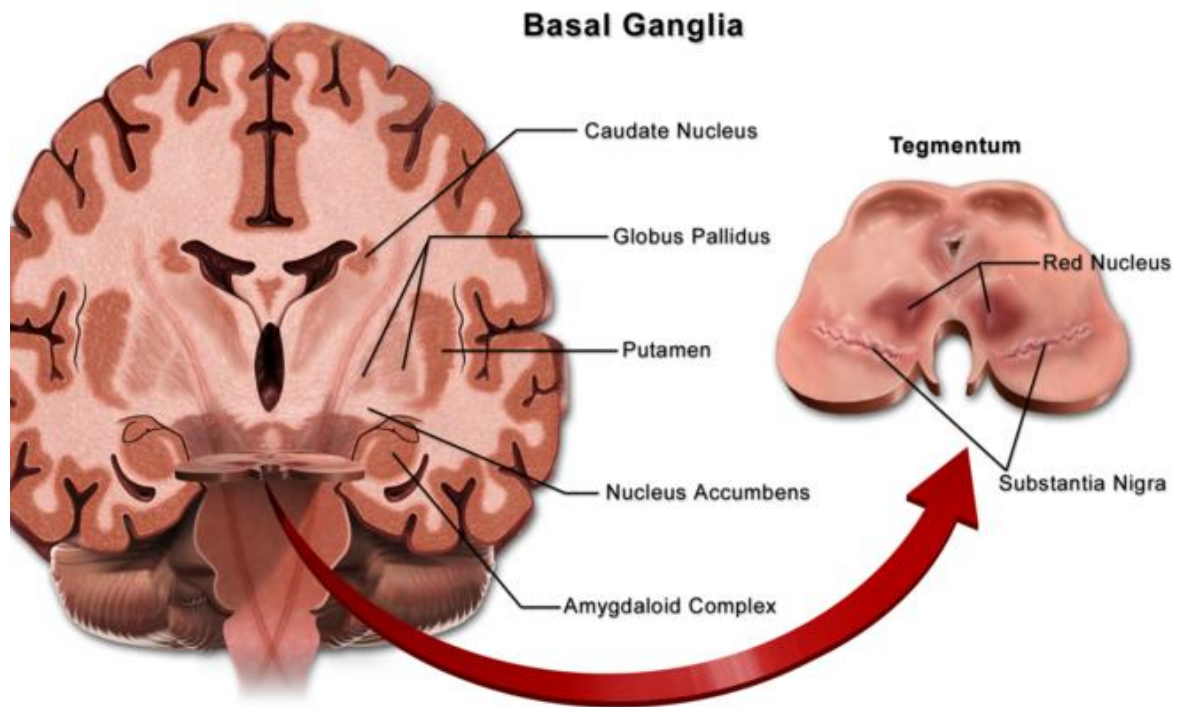
reducing an alerting effect from the suprachiasmatic nucleus, is influenced by the light-dark cycle and is suppressed by light.

## 2) Role of Basal Ganglia in Coordinating Movements.

The basal ganglia, like the cerebellum, constitute another accessory motor system that functions usually not by itself but in close association with the cerebral cortex and corticospinal motor control system. In fact, the basal ganglia receive most of their input signals from the cerebral cortex itself and also return almost all their output signals back to the cortex. On each side of the brain, these ganglia consist of the caudate nucleus, putamen, globus pallidus, substantia nigra, and subthalamic nucleus. They are located mainly lateral to and surrounding the thalamus, occupying a large portion of the interior regions of both cerebral hemispheres. Note also that almost all motor and sensory nerve fibers connecting the cerebral cortex and spinal cord pass through the space that lies between the major masses of the basal ganglia, the caudate nucleus and the putamen. This space is called the internal capsule of the brain. It is important for our current discussion because of the intimate association between the basal ganglia and the corticospinal system for motor control.

### **Neuronal Circuitry of the Basal Ganglia.**

The anatomical connections between the basal ganglia and the other brain elements that provide motor control are complex.



One of the principal roles of the basal ganglia in motor control is to function in association with the corticospinal system to control complex patterns of motor activity. An example is the writing of letters of the alphabet. When there is serious damage to the basal ganglia, the cortical system of motor control can no longer provide these patterns. Instead, one's writing becomes crude, as if one were learning for the first time how to write. Other patterns that require the basal ganglia are cutting paper with scissors, hammering nails, shooting a basketball through a hoop, passing a football, throwing a baseball, the movements of shovelling dirt, most aspects of vocalization, controlled movements of the eyes, and virtually any other of our skilled movements, most of them performed subconsciously.

Principal pathways through the basal ganglia for executing learned patterns of movement begin mainly in the premotor and supplementary areas of the motor cortex and in the somatosensory areas of the sensory cortex. Next they pass to the putamen (mainly bypassing the caudate nucleus), then to the internal portion of the globus pallidus, next to the ventroanterior and ventrolateral relay

nuclei of the thalamus, and finally return to the cerebral primary motor cortex and to portions of the premotor and supplementary cerebral areas closely associated with the primary motor cortex. Thus, the putamen circuit has its inputs mainly from those parts of the brain adjacent to the primary motor cortex but not much from the primary motor cortex itself. Then its outputs do go mainly back to the primary motor cortex or closely associated premotor and supplementary cortex. Functioning in close association with this primary putamen circuit are ancillary circuits that pass from the putamen through the external globus pallidus, the subthalamus, and the substantia nigra—finally returning to the motor cortex by way of the thalamus.

### **Neurotransmitters.**

In most regions of the brain, the predominant classes of neurons use glutamate as the neurotransmitter and have excitatory effects on their targets. In the basal ganglia, however, the great majority of neurons uses gamma-aminobutyric acid (GABA) as the neurotransmitter and have inhibitory effects on their targets.

The inputs from the cortex and thalamus to the striatum and subthalamic nucleus are glutamatergic, but the outputs from the striatum, pallidum, and substantia nigra pars reticulata all use GABA. Thus, following the initial excitation of the striatum, the internal dynamics of the basal ganglia are dominated by inhibition and disinhibition.

Other neurotransmitters have important modulatory effects. Dopamine is used by the projection from the substantia nigra pars compacta to the dorsal striatum and also in the analogous projection from the ventral tegmental area to the ventral striatum (nucleus accumbens).

Acetylcholine also plays an important role, as it is used both by several external inputs to the striatum and by a group of striatal interneurons. Although cholinergic cells make up only a small

fraction of the total population, the striatum has one of the highest acetylcholine concentrations of any brain structure.

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.

### **Pathways.**

The basal nuclei modulate **motor function** through various pathways in order to initiate, terminate, or modulate the extent of the movement.

These are the following:

- **Direct pathway:** which is responsible for the initiation of the movement. In order to make this happen, the direct pathway



funnels the information from the striatum to GPi/SNr via GABAergic inhibitory projections. This inhibition releases the firing from the thalamocortical neurons to initiate the movement.

- **Indirect pathway**, which has a net excitatory effect on the same structures. The neurons from the external part of globus pallidus send inhibitory fibers to the subthalamic nucleus instead of sending directly to the thalamus (hence its name “indirect”). From the subthalamic nucleus, neurons send their axons to the internal part of the globus pallidus and reticular part of the substantia nigra and then continue as the direct pathway with GABAergic inhibitory neurons to the thalamus and glutamate excitatory efferents to the cortex. So, functionally, the striatum inhibits the external globus pallidus, and that causes disinhibition of the subthalamus.
- **Hyperdirect pathway**, via which the internal part of globus pallidus and reticular part of the substantia nigra receive strong excitatory signals from the cortex directly through STN and has a shorter conduction time compared to the direct and indirect pathways. The hyperdirect pathway consists of neurons projecting from the cortex directly to the subthalamic nucleus (STN), skipping the striatum. Therefore, the glutamatergic excitatory neurons of the STN can then excite the GPi/SNr thus suppressing thalamic activity on the cerebral cortex and increasing inhibitory influences on the upper motor neurons.

Considering the conduction path and time, we can say that the **hyperdirect** and **indirect pathways** make clear initiation and termination of the selected motor program, while at the same time cancelling other competing motor programs.