**NEUROPHYSIOLOGY**

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**Question**

Q1. Discuss the physiology of sleep

Q2. Discuss the role of basal ganglia in coordinating movement

**Answers**

**Q1.** Sleep is a state of unconsciousness in which the brain is relatively more responsive to internal than 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, somatosensory, and other environmental stimuli during the transition from wake to sleep, which is considered by some to be stage I of sleep.

The "switch" for sleep is considered to be the ventrolateral preoptic nucleus (VLPO) of the anterior hypothalamus. This area becomes active during sleep and uses the inhibitory neurotransmitters GABA and galanin to initiate sleep by inhibiting the arousal regions of the brain. The VLPO innervates and can inhibit the wake-promoting regions of the brain including the tubero-mammillary nucleus, lateral hypothalamus, locus coeruleus, dorsal raphe, laterodorsal tegmental nucleus, and pedunculopontine tegmental nucleus. The hypocretin (orexin) neurons in the lateral hypothalamus help stabilize this switch and the loss of these neurons results in narcolepsy. The tuber infundibular 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 a 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 N2 sleep, are generated by bursts of hyperpolarizing GABAnergic neurons in the reticular nucleus of the thalamus. These bursts inhibit thalamocortical projection neurons. As deafferentation spreads, corticothalamic 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 the 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 the cholinergic mediated "REM-on neurons" in the mesencephalic and pontine cholinergic neurons. The pedunculopontine tegmental nucleus (PPT) and the lateral dorsal tegmental (LDT) neurons use acetylcholine to trigger cortical desynchrony via the thalamus. Cortical desynchrony (also described as low voltage mixed frequency) is the EEG hallmark of REM sleep. An additional EEG hallmark of REM sleep is "sawtooth waves." A pharmacologic offshoot of the cholinergic mediation of REM sleep is stage R increasing with cholinergic agonists and decreasing with anticholinergics.

"REM-off neurons" are the noradrenergic locus coeruleus and serotonergic raphe neurons. The REM-off neurons use norepinephrine, serotonin, and histamine to inhibit the REM-on cholinergic cells and stop REM sleep. These REM-off neurons become inactive during REM sleep. Medications, such as antidepressants, that increase the amount of norepinephrine or serotonin can cause a pharmacologic suppression of REM sleep. REM sleep (stage R) is characterized by muscle atonia, cortical activation, low-voltage desynchronization of the EEG, and rapid eye movements. REM sleep has a parasympathetically medicated tonic component and a sympathetically mediated phasic component. The phasic portion of REM sleep is characterized by skeletal muscle twitches, increased heart rate variability, pupillary dilation, and increased respiratory rate. Muscle atonia is present throughout REM sleep, except for phasic muscle twitches. It results from inhibition of alpha motor neurons by clusters of peri–locus coeruleus 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 projections from cholinergic lateral dorsal tegmental and pedunculopontine tegmental 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 seen in animals, but not humans. 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. In humans, intracerebral recordings, noninvasive PET, fMRI, and magnetoencephalography scanning in healthy volunteers indicate that the rapid eye movements observed during REM sleep are generated by mechanisms similar or identical to PGO waves in animals.

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 visual regions of the cortex 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.

**Q2.** 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 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. 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

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.

Basal Ganglia Neurotransmitter Systems

This advanced system consists of several important segments or systems. Those are:

* A system of dopamine neurons located in the substantia nigra, and give projections to the nucleus caudatus and putamen.
* A system of GABA-containing neurons located in nucleus caudatus and putamen, and give projections in substance nigra.
* A system of acetylcholine neurons located in the cerebral cortex, and they give the projections to the nucleus caudatus and the putamen.
* Noradrenergic, serotonin and other neuronal systems are located outside the basal ganglia system, and yield projections into this system.