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QUESTION 1: Discuss the physiology of sleep.

ANSWER: Sleep is the natural periodic state of rest for mind and body with closed eyes characterized by partial or complete loss of consciousness. Loss of consciousness leads to decreased response to external stimuli and decreased body movements. Depth of sleep is not constant throughout the sleeping period. It varies in different stages of sleep. Sleep requirement is not constant. However, average sleep requirement per day at different age groups is:

1. Newborn infants: 18 to 20 hours

2. Growing children: 12 to 14 hours

3. Adults: 7 to 9 hours

4. Old persons: 5 to 7 hours.

ALPHA, BETA, & GAMMA RHYTHMS

In adult humans who are awake but at rest with the mind wandering and the eyes closed, the most prominent component of the EEG is a fairly regular pattern of waves at a frequency of 8– 13 Hz and amplitude of 50–100 μV when recorded from the scalp. This pattern is the alpha rhythm. It is most marked in the parietal and occipital lobes and is associated with decreased levels of attention. A similar rhythm has been observed in a wide variety of mammalian species. There are some minor variations from species to species, but in all mammals the pattern is remarkably similar. When attention is focused on something, the alpha rhythm is replaced by an irregular 13–30 Hz low-voltage activity, the beta rhythm. This phenomenon is called alpha block and can be produced by any form of sensory stimulation or mental concentration, such as solving arithmetic problems. Another term for this phenomenon is the arousal or alerting response, because it is correlated with the aroused, alert state. It has also been called de-synchronization because it represents breaking up of the obviously synchronized neural activity necessary to produce regular waves. However, the rapid

EEG activity seen in the alert state is also synchronized, but at a higher rate. Therefore, the term de-synchronization is misleading. Gamma oscillations at 30–80 Hz are often seen when an individual is aroused and focuses attention on something. This is often replaced by irregular fast activity as the individual initiates motor activity in response to the stimulus.

PHYSIOLOGICAL CHANGES DURING SLEEP

During sleep, most of the body functions are reduced to basal level. Following are important changes in the body during sleep:

1. PLASMA VOLUME: Plasma volume decreases by about 10% during sleep.

2. CARDIOVASCULAR SYSTEM

   Heart Rate: During sleep, the heart rate reduces. It varies between 45 and 60 beats per minute.

   Blood Pressure: Systolic pressure falls to about 90 to 110 mm Hg. Lowest level is reached about 4th hour of sleep and remains at this level till a short time before waking up. Then, the pressure commences to rise. If sleep is disturbed by exciting dreams, the pressure is elevated above 130 mm Hg.

3. RESPIRATORY SYSTEM: Rate and force of respiration are decreased. Respiration becomes irregular and Cheyne-Stokes type of periodic breathing may develop.

4. GASTROINTESTINAL TRACT: Salivary secretion decreases during sleep. Gastric secretion is not altered or may be increased slightly. Contraction of empty stomach is more vigorous.

5. EXCRETORY SYSTEM: Formation of urine decreases and specific gravity of urine increases.

6. SWEAT SECRETION: Sweat secretion increases during sleep.

7. LACRIMAL SECRETION: Lacrimal secretion decreases during sleep.

8. MUSCLE TONE: Tone in all the muscles of body except ocular muscles decreases very much during sleep. It is called sleep paralysis.

9. REFLEXES: Certain reflexes particularly knee jerk, are abolished. Babinski sign becomes positive during deep sleep. Threshold for most of the reflexes increases. Pupils are constricted. Light reflex is retained. Eyeballs move up and down.

10. BRAIN: Brain is not inactive during sleep. There is a characteristic cycle of brain wave activity during sleep with irregular intervals of dreams. Electrical activity in the brain varies with stages of sleep.

TYPES OF SLEEP

Sleep is of two types:

1. Rapid eye movement sleep or REM sleep

2. Non-rapid eye movement sleep, NREM sleep or non-REM sleep.

RAPID EYE MOVEMENT SLEEP OR REM SLEEP

REM is the type of sleep associated with rapid conjugate movement of the eyeballs which occurs frequently. Though the eyeballs move, the sleep is deep and thus, called PARADOXICAL SLEEP. High amplitude slow waves seen in EEG during sleep are periodically replaced by rapid, low-voltage EEG activity which resembles that seen in aroused, alert state and in stage 1 sleep. It occupies about 20-30% of sleeping period. It is important because it plays an important role in the consolidation of memory. Sleep is not interrupted. The threshold for arousal by sensory stimuli and by stimulation of the reticular formation is elevated. Another characteristic of REM sleep is the occurrence of large phasic potentials that originate in the cholinergic neurons in the pons and pass rapidly to the lateral geniculate body and from there to the occipital cortex. They are called Pontogeniculo-Occipital (PGO) spikes. The tone of the skeletal muscles in the neck is markedly reduced during REM sleep. Humans aroused at a time when they show the EEG characteristics of REM sleep generally report that they were dreaming, whereas individuals awakened from slow-wave sleep do not. This observation and other evidence indicate that REM sleep and dreaming are closely associated. Positron emission tomography (PET) scans of humans in REM sleep show increased activity in the pontine area, amygdala, and anterior cingulate gyrus, but decreased activity in the prefrontal and parietal cortex. Activity in visual association areas is increased, but there is a decrease in the primary visual cortex. This is consistent with increased emotion and operation of a closed neural system cut off from the areas that relate brain activity to the external world.

NON RAPID EYE MOVEMENT SLEEP OR NREM SLEEP

Non-rapid eye movement (NREM) sleep is the type of sleep without the movements of eyeballs. It is also called slow-wave sleep. It occupies about 70-80% of total sleeping period. NREM sleep is followed by REM sleep.

STAGES OF SLEEP AND EEG PATTERN

RAPID EYE MOVEMENT SLEEP: During REM sleep, electroencephalogram (EEG) shows irregular waves with high frequency and low amplitude. These waves are desynchronized waves.

NON-RAPID EYE MOVEMENT SLEEP: The NREM sleep is divided into four stages, based on the EEG pattern. During the stage of wakefulness, i.e. while lying down with closed eyes and relaxed mind, the alpha waves of EEG appear. When the person proceeds to drowsy state, the alpha waves diminish.

Stage I: Stage of Drowsiness

Alpha waves are diminished and abolished. EEG shows only low voltage fluctuations and infrequent delta waves.

Stage II: Stage of Light Sleep

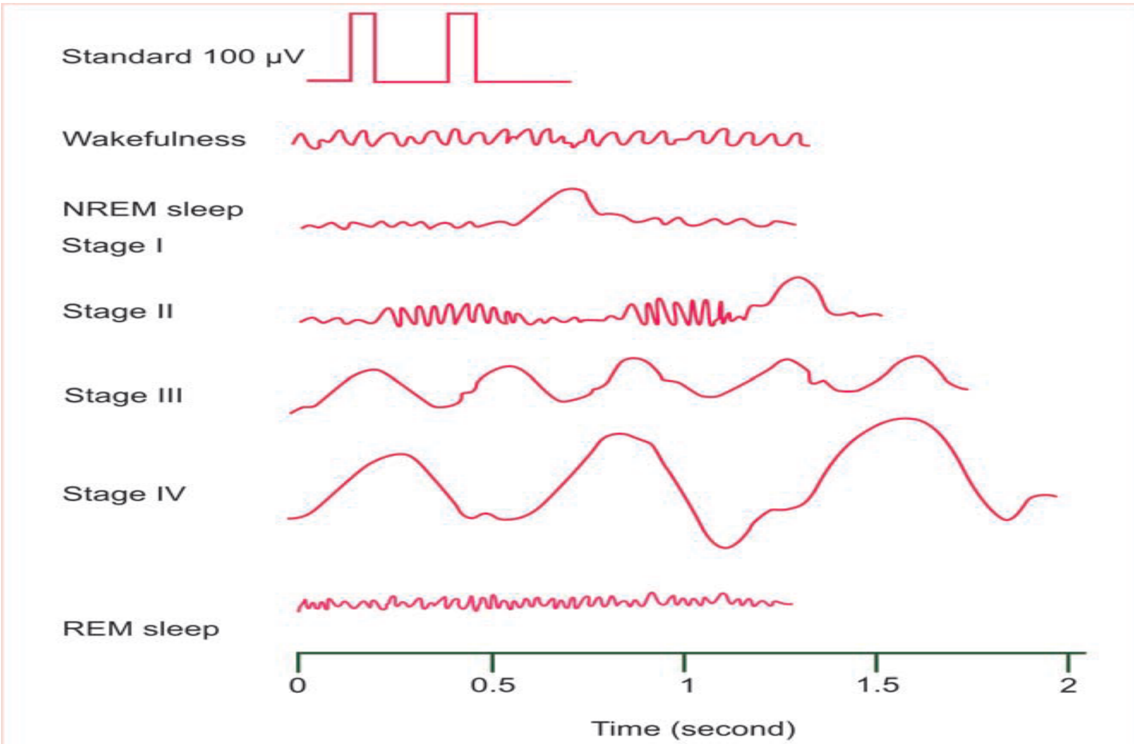
Stage II is characterized by spindle bursts at a frequency of 14 per second, superimposed by low voltage delta waves.

Stage III: Stage of Medium Sleep

During this stage, the spindle bursts disappear. Frequency of delta waves decreases to 1 or 2 per second and amplitude increases to about 100 μV.

State IV: Stage of Deep Sleep

Delta waves become more prominent with low frequency and high amplitude.



CHARACTERISTICS	REM SLEEP	NREM SLEEP
Rapid eye movement	Present	Absent
Dreams	Present	Absent
Muscle twitching	Present	Absent
Heart rate	Fluctuating	Stable
Blood pressure	Fluctuating	Stable
Respiration	Fluctuating	Stable
Body pressure	Fluctuating	Stable
Neurotransmitter	Noradrenaline	Serotonin

Differences between the REM sleep and NREM sleep.

DISTRIBUTION OF SLEEP STAGES

In a typical night of sleep, a young adult first enters NREM sleep, passes through stages 1 and 2, and spends 70–100 minutes in stages 3 and 4. Sleep then lightens, and a REM period follows. This cycle is repeated at intervals of about 90 minutes throughout the night. The cycles are similar, though there is less stage 3 and 4 sleep and more REM sleep toward morning. Thus, four to six REM periods occur per night. REM sleep occupies 80% of total sleep time in premature infants and 50% in full-term neonates. Thereafter, the proportion of REM sleep falls rapidly and plateaus at about 25% until it falls further in old age. Children have more total sleep time and stage 4 sleep than adults.

MECHANISM OF SLEEP

Sleep occurs due to the activity of some sleep-inducing centers in brain. Stimulation of these centers or inhibition of some centers induces sleep. Damage of sleep centers results in sleeplessness or persistent wakefulness called insomnia.

SLEEP CENTERS

Complex pathways between the reticular formation of brainstem, diencephalon and cerebral cortex are involved in the onset and maintenance of sleep. However, two centers which induce sleep are located in brainstem:

1. Raphe nucleus

2. Locus ceruleus of pons.

Recently, many more areas that induce sleep are identified in the brain of animals. Inhibition of ascending reticular activating system also results in sleep. Stimulation of other specific areas of brain can also produce sleep with characteristics near those of natural sleep.

Role of Raphe Nucleus: The most conspicuous stimulation area for causing almost natural sleep is the raphe nuclei in the lower half of the pons and in the medulla. These nuclei comprise a thin sheet of special neurons located in the midline. Activation of this nucleus results in non-REM sleep. It is due to release of serotonin by the nerve fibers arising from this nucleus .Nerve fibers from these nuclei spread locally in the brain stem reticular formation and also upward into the thalamus, hypothalamus, most areas of the limbic system, and even the neocortex of the cerebrum. In addition, fibers extend downward into the spinal cord, terminating in the posterior horns, where they can inhibit incoming sensory signals, including pain. Many nerve endings of fibers from these raphe neurons secrete serotonin. When a drug that blocks the formation of serotonin is administered to an animal, the animal often cannot sleep for the next several days. Therefore, it has been assumed that serotonin is a transmitter substance associated with production of sleep.

Role of Locus Ceruleus of Pons: Activation of this center produces REM sleep. Noradrenaline released by the nerve fibers arising from locus ceruleus induces REM sleep.

Inhibition of Ascending Reticular Activating System: Ascending reticular activating system (ARAS) is responsible for wakefulness because of its afferent and efferent connections with cerebral cortex. Inhibition of ARAS induces sleep. Lesion of ARAS leads to permanent somnolence, i.e. coma.

Stimulation of some areas in the nucleus of the tractus solitarius can also cause sleep. This nucleus is the termination in the medulla and pons for visceral sensory signals entering by way of the vagus and glossopharyngeal nerves.

Sleep can be promoted by stimulation of several regions in the diencephalon, including (1) the rostral part of the hypothalamus, mainly in the suprachiasmal area, and (2) an occasional area in the diffuse nuclei of the thalamus

IMPORTANCE OF SLEEP

Sleep has persisted throughout evolution of mammals and birds, so it is likely that it is functionally important. Indeed, if humans are awakened every time they show REM sleep, then permitted to sleep without interruption, they show a great deal more than the normal amount of REM sleep for a few nights. Relatively prolonged REM deprivation does not seem to have adverse psychological effects. Rats deprived of sleep for long periods lose weight in spite of increased caloric intake and eventually die. Various studies imply that sleep is needed to maintain metabolic-caloric balance, thermal equilibrium, and immune competence. In experimental animals, sleep is necessary for learning and memory consolidation. Learning sessions do not improve performance until a period of slow-wave or slow-wave plus REM sleep has occurred.

APPLIED PHYSIOLOGY: SLEEP DISORDERS

- Narcolepsy is a chronic neurological disorder caused by the brain’s inability to regulate sleep–wake cycles normally in which there is a sudden loss of voluntary muscle tone (cataplexy), an eventual irresistible urge to sleep during daytime, and possibly also brief episodes of total paralysis at the beginning or end of sleep. Narcolepsy is characterized by a sudden onset of REM sleep, unlike normal sleep which begins with NREM, slow-wave sleep. The prevalence of narcolepsy ranges from 1 in 600 in Japan to 1 in 500,000 in Israel, with 1 in 1000 Americans being affected. Narcolepsy has a familial incidence strongly associated with a class II antigen of the major histocompatibility complex on chromosome 6 at the HLA-DR2 or HLA-DQW1 locus, implying a genetic susceptibility to narcolepsy. The HLA complexes are interrelated genes that regulate the immune system. Brains from humans with narcolepsy often contain fewer hypocretin (orexin) -producing neurons in the hypothalamus. It is thought that the HLA complex may increase susceptibility to an immune attack on these neurons, leading to their degeneration. Cataplexy is the sudden outburst of emotion. Cataplexy and narcoplexy are diseases due to hypothalamic disorders.

- Obstructive sleep apnea (OSA) is the most common cause of daytime sleepiness due to fragmented sleep at night and affects about 24% of middle-aged men and 9% of women in the United States. Breathing ceases for more than 10 s during frequent episodes of obstruction of the upper airway (especially the pharynx) due to reduction in muscle tone. The apnea causes brief arousals from sleep in order to reestablish upper airway tone. Snoring is a common patient complaint. There is actually not a reduction in total sleep time, but individuals with OSA experience a much greater time in stage 1 NREM sleep (from an average of 10% of total sleep to 30–50%) and a marked reduction in slow-wave sleep (stages 3 and 4 NREM sleep). The pathophysiology of OSA includes both a reduction in neuromuscular tone at the onset of sleep and a change in the central respiratory drive. Sleep apnea syndrome occurs in obesity, myxedema, enlargement of tonsil and lesion in brainstem. Common features of this syndrome are loud snoring, restless movements, nocturnal insomnia, daytime sleepiness, morning headache and fatigue. In severe conditions, hypertension, right heart failure and stroke occur.

- Periodic limb movement disorder (PLMD) is a stereotypical rhythmic extension of the big toe and dorsiflexion of the ankle and knee during sleep lasting for about 0.5 to 10s and recurring at intervals of 20 to 90 s. Movements can actually range from shallow, continual movement of the ankle or toes, to wild and strenuous kicking and flailing of the legs and arms. Electromyograph (EMG) recordings show bursts of activity during the first hours of NREM sleep associated with brief EEG signs of arousal. The duration of stage 1 NREM sleep may be increased and that of stages 3 and 4 may be decreased compared to age -matched controls. PLMD is reported to occur in 5% of individuals between the ages of 30 and 50 years and increases to 44% of those over the age of 65. PLMD is similar to restless leg syndrome in which individuals have an irresistible urge to move their legs while at rest all day long. Movement disorders occur immediately after falling asleep. Sleep start or hypnic jerk is the common movement disorder during sleep. It is characterized by sudden jerks of arms or legs. Sleep start is a physiological form of clonus. Other movement disorders are teeth grinding (bruxism), banging the head and restless moment of arms or legs.

- Sleepwalking (somnambulism), bed-wetting (nocturnal enuresis), and night terrors are referred to as PARASOMNIAS, which are sleep disorders associated with arousal from NREM and REM sleep. Episodes of sleepwalking are more common in children than in adults and occur predominantly in males. They may last several minutes. Somnambulists walk with their eyes open and avoid obstacles, but when awakened they cannot recall the episodes. This is associated with PSYCHONEUROSIS in adults. Night terror is a disorder similar to nightmare. It is common in children. It is also called pavor nocturnus or sleep terror. The child awakes screaming in a state of fright and semi-consciousness. The child cannot recollect the attack in the morning. Nightmare occurs shortly after falling asleep and during non-REM sleep. There is no psychological disturbance

- Insomnia: This is the inability to sleep or abnormal wakefulness. It is the most common sleep disorder. It occurs due to systemic illness or mental conditions such as psychiatric problems, alcoholic addiction and drug addiction.

- Hypersomnia: This is the excess sleep or excess need to sleep. It occurs because of lesion in the floor of the third ventricle, brain tumors, encephalitis, chronic bronchitis and disease of muscles. Hypersomnia also occurs in endocrine disorders such as myxedema and diabetes insipidus.

- Nightmare: This is a condition during sleep that is characterized by a sense of extreme uneasiness or discomfort or by frightful dreams. Discomfort is felt as of some heavy weight on the stomach or chest or as uncontrolled movement of the body. After a period of extreme anxiety, the subject wakes with a troubled state of mind. It occurs mostly during REM sleep. Nightmare occurs due to improper food intake, digestive disorders or nervous disorders. It also occurs during drug withdrawal or alcohol withdrawal.

QUESTION 2: Discuss the role of basal ganglia in coordinating movement.

ANSWER:

BASAL GANGLIA

The basal ganglia are deep nuclei of the cerebral hemispheres, and like the cerebellum, have an accessory role to the motor cortex, regulating motor activity to produce smooth movement and maintain posture. They are scattered masses of gray matter submerged in subcortical substance of cerebral hemisphere. Basal ganglia form the part of extra pyramidal system, which is concerned with motor activities.

They consist of the:

- caudate nucleus
- putamen
- globus pallidus

The caudate nucleus and putamen are referred to as the striatum, based on their striated appearance. The substantia nigra of the midbrain and subthalamic nucleus of the diencephalon are functionally associated with, and sometimes classified as, components of the basal ganglia.

The input to the basal ganglia is from the motor cortex, the output to the cortex is through the thalamus. A complex series of interactions between components of the basal ganglia and associated structures leads to this output, which then regulates the level of excitation in the motor cortex. These interactions form an indirect pathway that inhibits cortical excitation and a direct pathway that is excitatory. The balance of these opposing pathways is responsible for coordinating smooth movement and maintenance of posture.

FUNCTIONS OF BASAL GANGLIA

Basal ganglia form the part of extrapyramidal system, which is concerned with integration and regulation motor activities. Various functions of basal ganglia are:

1. CONTROL OF MUSCLE TONE: Basal ganglia control the muscle tone. In fact, gamma motor neurons of spinal cord are responsible for development of tone in the muscle. Basal ganglia decrease the muscle tone by inhibiting gamma motor neurons through descending inhibitory reticular system in brainstem. During the lesion of basal ganglia, muscle tone increases leading to rigidity.

2. CONTROL OF MOTOR ACTIVITY:

i. Regulation of Voluntary Movements: Movements during voluntary motor activity are initiated by cerebral cortex. However, these movements are controlled by basal ganglia, which are in close association with cerebral cortex. During lesions of basal ganglia, the control mechanism is lost and so the movements become inaccurate and awkward. Basal ganglia control the motor activities because of the nervous (neuronal) circuits between basal ganglia and other parts of the brain involved in motor activity. Neuronal circuits arise from three areas of the cerebral cortex:

a. Premotor area b. Primary motor area c. Supplementary motor area.

All these nerve fibers from cerebral cortex reach the caudate nucleus. From here, the fibers go to putamen. Some of the fibers from cerebral cortex go directly to putamen also. Putamen sends fibers to globus pallidus. Fibers from here run towards the thalamus, subthalamic nucleus of Luys and substantia nigra. Subthalamic nucleus and substantia nigra are in turn, projected into thalamus. Now, the fibers from thalamus are projected back into primary motor area and other two motor areas, i.e. premotor area and supplementary motor area.

ii. Regulation of Conscious Movements: Fibers between cerebral cortex and caudate nucleus are concerned with regulation of conscious movements. This function of basal ganglia is also known as the cognitive control of activity. For example, when a stray dog barks at a man, immediately the person, understands the situation, turns away and starts running.

iii. Regulation of Subconscious Movements Cortical fibers reaching putamen are directly concerned with regulation of some subconscious movements, which take place during trained motor activities, i.e. skilled activities such as writing the learnt alphabet, paper cutting, nail hammering, etc.

3. <u>CONTROL OF REFLEX MUSCULAR ACTIVITY</u>: Some reflex muscular activities, particularly visual and labyrinthine reflexes are important in maintaining the posture. Basal ganglia are responsible for the coordination and integration of impulses for these reflex activities. During lesion of basal ganglia, the postural movements, especially the visual and labyrinthine reflexes become abnormal. These abnormal movements are associated with rigidity. Rigidity is because of the loss of inhibitory influence from the cerebral cortex on spinal cord via basal ganglia.

4. <u>CONTROL OF AUTOMATIC ASSOCIATED MOVEMENTS</u>: Automatic associated movements are the movements in the body, which take place along with some motor activities. Examples are the swing of the arms while walking, appropriate facial expressions while talking or doing any work. Basal ganglia are responsible for the automatic associated movements.

Lesion in basal ganglia causes absence of these automatic associated movements, resulting in poverty of movements. Face without appropriate expressions while doing any work is called mask-like face. Body without associated movements is called statue-like body.