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1. ***Discuss the physiology of sleep***

Sleep refers to a state of unconsciousness from which the individual can be aroused by sensory or other stimuli. During sleep, the stimulus pulse transfer becomes less frequent between the reticular formation and cerebral cortex.

SLEEP-WAKE CYCLE

Sleep and wakefulness, like many of the body's regulatory mechanisms, have circadian rhythm of about 24 h. A newborn infant has many cycles of sleep and wakefulness in 24 h, but after the age of 2 years a single sleep-wake cycle is established. In a normal adult, the sleep-wake cycle consists of 7–8 h of sleep and 16–17 h of wakefulness.

CONTROL OF SLEEP-WAKE CYCLE

- Sleep-wake cycle, like other circadian rhythms, is endogenous.
- The biological clock controlling the circadian rhythms is the suprachiasmatic nucleus of the anterior hypothalamus.
- The circadian rhythms are endogenous and can persist without environmental cues; however, under normal circumstances the rhythms are modulated by external timing cues called zeitgebers (time givers) that adapt the rhythm to the environment.
- Sunlight is a powerful timing cue; light entrains this rhythm by means of retinohypothalamic tract.
- Although the suprachiasmatic nucleus regulates the timing of sleep, it is not responsible for sleep itself.

FACTORS AFFECTING SLEEP

The factors which minimize sensory stimulation and favour the onset of natural sleep are:

- Darkened room
- Comfortable surrounding temperature
- Silence
- Physical and mental relaxation
- Consumption of a basic urge, such as hunger or sex

- Low-frequency stimulation, such as by patting or knocking in a cradle or sitting in a moving vehicle.

TYPES AND STAGES OF SLEEP

Sleep is of two types: non-REM sleep and REM sleep, which alternate in a sleep cycle.

Non-REM sleep

Non-REM sleep, i.e. non-rapid eye movement sleep is also known as slow wave sleep (SWS), because in this type of sleep brain waves are very slow. In normal adults, sleep mostly begins with non-REM sleep. It is the type of sleep which a person experiences during first hour of sleep after having been kept awake for many hours. The non-REM sleep alternates with REM sleep during the sleep cycle.

Stages and EEG patterns of non-REM sleep

1. **Stage of wakefulness**

- The state of wakefulness and consciousness results due to stimulatory impulses from RAS to cerebral cortex.
- EEG pattern during wakefulness is characterized by asynchronous and low-amplitude brain waves called β waves.

2. **State of quiet, awake rest with eyes closed**

- State of quiet, awake rest with eyes closed is the period in between the stage of wakefulness and stage of sleep.
- EEG pattern during quiet awake resting stage is characterized by α waves which are highly synchronized, large waves having a frequency of 8–13 cycles/s.

3. **State of non-REM sleep**

- When an individual from the state of quiet rest with eyes closed enters the state of non-REM sleep, the consciousness is reduced.
- The non-REM sleep also known as slow-wave sleep progresses in an orderly way from light to deep sleep in four stages as:

Stage 1 of non-REM sleep (stage of very light sleep): EEG pattern in this stage is characterized by low amplitude mixed frequency activity. There is still considerable sensitivity to sensory stimuli. However, the mild to moderate stimuli are often unable to produce a full arousal.

Stage 2 of non-REM sleep (stage of light sleep): This is characterized by the appearance of sleep spindles. These are bursts of α-like 10–14 Hz, 50 μV waves, which periodically interrupt the α rhythm. Auditory stimuli during this phase readily evoke the K-complexes in the EEG. They also occur spontaneously during this stage. The K-complex consists of one or two high-voltage waves followed by a brief 14 Hz activity.

Stage 3 of non-REM sleep or stage of moderate deep sleep: This is characterized by an EEG that display high amplitude slow (0.5–2 Hz) waves called δ waves.

Stage 4 of non-REM sleep or stage of deep sleep: This produces EEG pattern dome-like very slow, large waves called δ waves. Thus, the characteristic of deep sleep is a pattern of rhythmic slow waves, indicating marked synchronization.

Physiological changes during non-REM sleep

- Muscle tone decreases progressively.
- Heart rate and blood pressure are decreased.
- Respiration rate is also decreased.
- Eyes begin slow, rolling movement until they finally stop in stage 4 (deep sleep) with eyes turned upwards.
- Body metabolism is lowered.
- Pituitary shows pulsatile release of growth hormone and gonadotropin.

Behavioural changes during non-REM sleep

- Progressive reduction in consciousness.
- An increasing resistance to being awakened, it is more difficult to wake up a person from stage 3 and 4 than from stage 1 and 2 of non-REM sleep.
- It is more difficult to wake up a young person than elderly from sleep because elderly person spends very little time in stage 3 and 4 of non-REM stage.
- When awaken, person does not report dreaming.
- There is some response to meaningful stimuli even in sleep, which indicates that sensory processing continues at some level after the onset of sleep.

Intellectual Functions During non-REM Sleep

- Thoughts become illogical and incoherent towards the onset of sleep.
- Retrograde amnesia occurs during transition from wakefulness to sleep. This is because sleep inactivates the consolidation of short-term into long-term memory. An example of retrograde amnesia includes not remembering the ringing of alarm clock.

REM sleep

REM sleep, i.e. 'rapid eye movement' sleep is also called 'fast wave (desynchronized) sleep, or 'paradoxical sleep' or 'dream sleep' or 'deepest sleep'. In adults, the REM sleep follows non-REM sleep, while in adults entry into sleep occurs via REM sleep.

EEG pattern of REM sleep

During REM sleep, EEG is characterized by a high-frequency and low-amplitude pattern (β rhythm), i.e. some desynchronized pattern that is seen in the waking state. Hence, REM sleep is also called 'fast wave sleep' or 'desynchronized sleep'. However, the individual clearly is unresponsive to environment stimuli and thus is asleep. Further, it is usually more difficult to awake in REM sleep than in non-REM sleep.

Behavioural changes during REM sleep

Arousal: As mentioned above, it is difficult to arouse an individual from REM sleep as it is from deep sleep. However, when awakened from REM sleep, the individual is immediately alert and aware of the environment. Dreaming occurs during REM sleep, so it is also called 'dream sleep'. There is vivid dream recall from approximately 80% of arousals from REM sleep.

Physiological changes during REM sleep

I. Rapid eye movements are the hallmark of this state of sleep and that is why the name REM sleep. Rapid eye movements (saccadic eye movements) are bursts of small jerky movements that bring the eye from one fixation point to another to allow a sweeping of visual images of dreams.
II. Heart rate and respiration rate become irregular.
III. Muscle tone is reduced due to inhibition of spinal motor neurons via brain stem mechanisms. Snoring during sleep results from partial obstruction of airways caused by relaxed tongue (due to muscular atonia) in supine position.
IV. Twitching of limb musculature occurs occasionally. Because muscle tone is reduced tremendously during REM sleep, frequency and intensity of muscle twitching do not produce injuries or awaken the individual.
V. Middle ear muscles are also active during REM sleep.
VI. Penile erection in males and engorgement of clitoris in females may occur during REM sleep.
VII. Impaired thermoregulation. Sweating or shivering during sleep in response to ambient temperature occurs in non-REM sleep and ceases in REM sleep.
VIII. Teeth grinding (bruxism) may be seen in children.

SLEEP CYCLE

In a normal adult individual, the average sleep period of about 7–8 h is divided into about 5 cycles during which non-REM sleep and REM sleep alternate with each other. There is an orderly progression of sleep states and stages during a typical sleep cycle.

Duration of sleep cycles and sleep stages

The average duration of each sleep cycle is about 90 min (range 70–120 min). Duration of different sleep stages are different in different cycles:

- Duration of non-REM sleep which is about 85 min (out of total 90 min) in first cycle decreases progressively in the next sleep cycles. ————————————
- About 25% of entire sleep period is passed in REM sleep.
- Duration of REM sleep, which is about 5 min (out of total 90 min) in first cycle increases progressively in the next cycle.
- Duration of deeper stages (3 and 4) of non-REM sleep is maximum during first cycle and then decreases progressively and may even disappear altogether from the later cycles.
- Duration of second stage of non-REM sleep increases progressively from first cycle onwards and may even occupy most of the non-REM portion of the later cycles. About 50% of the entire sleep period is spent in second stage of non-REM sleep.

- As morning approaches, the individual may be periodically awaken during later sleep cycles.

Variations in sleep cycles

Variations in sleep cycle, from the typical adult pattern depicted in, occur under certain circumstances. In adults, onset of sleep with REM sleep occurs under special circumstances, such as in jet lag, chronic sleep deprivation, narcolepsy, acute withdrawal of REM suppressing drugs and endogenous depressions.

Variations in total sleep duration

Average sleep time per day differs according to the age:

i. During infancy: 16 h
ii. During childhood: 10 h
iii. During adulthood: 7–8 h
iv. During old age: <8 h.

Variation in time period of different stages of sleep

Effect of age:

i. Prematurely born infants spend about 80% of their sleep time in REM sleep.
ii. Full-term infants spend only 50% of their sleep time in REM sleep.
iii. The total time spent in REM sleep is reduced to about 1.5–2 h by puberty and remains unchanged there further.
iv. In adulthood, reduction in total sleep time to 8 h (2 h REM and 6 h non-REM sleep).
v. In old age, there is very high variability in the type and duration of sleep.

MECHANISM OF SLEEP

Sleep occurs due to the activity of some sleep-inducing centers in brain. Stimulation of these 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:

i. **Raphe Nucleus:** Raphe nucleus is situated in lower pons and medulla. Activation of this nucleus results in non-REM sleep. It is due to release of serotonin by the nerve fibers arising from this nucleus. Serotonin induces non-REM sleep.
ii. **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.

APPLIED PHYSIOLOGY – SLEEP DISORDERS

Insomnia: Insomnia 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: Hypersomnia 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.

2. *Discuss the role of basal ganglia in coordinating movement*

The basal ganglia are a group of structures found deep within the cerebral hemispheres. The structures generally included in the basal ganglia are the:

- Caudate nucleus, putamen, and globus pallidus in the cerebrum
- The substantia nigra in the midbrain
- The subthalamic nucleus in the diencephalon

The basal ganglia are best known for their role in movement.

DIRECT PATHWAY OF MOVEMENT

The direct pathway of movement is a neural pathway within the central nervous system (CNS) through the basal ganglia which facilitates the initiation and execution of voluntary movement. It works in conjunction with the indirect pathway. Both of these pathways are part of the cortico-basal gangliathalamo-cortical loop.

The direct pathway passes through the **caudate nucleus, putamen, and globus pallidus**, which are parts of the basal ganglia. It also involves another basal ganglia component the **substantia nigra**, a part of the midbrain. In a resting individual, a specific region of the globus pallidus, the internal globus pallidus (GPi), and a part of the substantia nigra, the pars reticulata (SNpr), send spontaneous inhibitory signals to the ventral lateral nucleus (VL) of the thalamus, through the release of GABA, an inhibitory neurotransmitter. Inhibition of the inhibitory neurons that project to the ventral anterior nucleus (VA), which project to the motor regions of the cerebral cortices of the telencephalon, leads to an increase in activity in the motor cortices, thereby promoting muscular action.

The pre-frontal region of the cerebral cortex sends activating signals to the motor cortices. The motor cortices send signals through the basal ganglia to refine the choice of muscles that will participate in the movement and to amplify the activity in the motor cortices that will drive the muscle contractions.

In the direct pathway, the motor cortices send activating signals to the caudate and putamen (which together form the dorsal striatum). The cells of the direct pathway in the caudate and putamen that receive these signals are inhibitory and, once they become activated, send inhibitory signals to the GPi and SNpr and stop activity there. The net effect is to allow the activation of the ventral lateral nucleus which, in turn, sends activating signals to the motor cortices. These events amplify motor cortical activity that will eventually drive muscle contractions.

INDIRECT PATHWAY

The indirect pathway of movement is a neuronal circuit through the basal ganglia and several associated nuclei within the central nervous system (CNS) which helps to prevent unwanted muscle contractions from competing with voluntary movements.

The indirect pathway passes through the caudate, putamen, and globus pallidus. It traverses the subthalamic nucleus and enters the substantia nigra. In a resting individual, the internal globus pallidus and the pars reticulata send spontaneous inhibitory signals to the ventrolateral nucleus (VL) of the thalamus, through the release of GABA, an inhibitory neurotransmitter. Inhibition of the excitatory neurons within VL, which project to the motor regions of the cerebral cortices of the telencephalon, leads to a reduction of activity in the motor cortices, and a lack of muscular action.

The pre-frontal region of the cerebral cortex sends activating signals to the motor cortices. The motor cortices send activating signals to the direct pathway through the basal ganglia, which stops inhibitory outflow from parts of the globus pallidus internus and the substantia nigra pars reticulata. The net effect is to allow the activation of the ventrolateral nucleus of the thalamus which, in turn, sends activating signals to the motor cortices. These events amplify motor cortical activity that will eventually drive muscle contractions.

Simultaneously, in the indirect pathway, the motor cortices send activating signals to the caudate and putamen. The cells of the indirect pathway in the caudate and putamen that receive these signals are inhibitory and, once activated, they send inhibitory signals to the globus pallidus externus, reducing the activity in that nucleus.

The globus pallidus externus normally sends inhibitory signals to the subthalamic nucleus. On activation of the indirect pathway, these inhibitory signals are reduced, which allows more activation of the subthalamic nucleus. Subthalamic nucleus cells can then send more activating signals to some parts of the globus pallidus internus and substantia nigra pars reticulata. Thus, parts of these two nuclei are driven to send more inhibitory signals to the ventrolateral nucleus of the thalamus, which prevents the development of significant activity in the motor cerebral cortices. This behavior prevents the activation of motor cortical areas that would compete with the voluntary movement.