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**CLASS: 300 LEVEL**

**COURSE: NEUROPHYSIOLOGY**

**ASSIGNMENT:**

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

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

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

**The Physiology Of Sleep**

**SLEEP**

Sleep refers to a state of unconsciousness from which the individual can be aroused by sensory or other stimuli. When asleep, an individual is not aware of the environment and is unable to perform activities that require consciousness. During sleep, the stimulus pulse transfer becomes less frequent between the reticular formation and cerebral cortex.

**SLEEP-WAKE CYCLE AND FACTORS AFFECTING SLEEP**

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 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**

Sleep time remains fairly stable from day to day even under widely varying conditions and is only modestly affected by variations in activity and sensory stimulation. However, the factors which minimize sensory stimulation and favour the onset of natural sleep are:

1. Darkened room,
2. Comfortable surrounding temperature,
3. Silence,
4. Physical and mental relaxation,
5. Consumption of a basic urge,

**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 rest 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.

**Physiological changes during non-REM sleep**

1. Muscle tone decreases progressively.
2. Heart rate and blood pressure are decreased.
3. Respiration rate is also decreased.
4. Eyes begin slow, rolling movement until they finally stop in stage 4 (deep sleep) with eyes turned upwards.
5. Body metabolism is lowered.

**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’ (as explained below). In adults, the REM sleep follows non-REM sleep, while in adults entry into sleep occurs via REM sleep.

**Physiological changes during REM sleep**

1. 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.
2. Heart rate and respiration rate become irregular.
3. 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.
4. 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.
5. Middle ear muscles are also active during REM sleep.
6. Penile erection in males and engorgement of clitoris in females may occur during REM sleep.

**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**

1. 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:
2. 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.
3. About 25% of entire sleep period is passed in REM sleep.
4. Duration of REM sleep, which is about 5 min (out of total 90 min) in first cycle increases progressively in the next cycle.
5. 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.
6. 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.
7. As morning approaches, the individual may be periodically awaken during later sleep cycles.

**GENESIS OF SLEEP**

The sleep state does not result from the passive withdrawal of arousal due to fatigue of RAS as thought earlier. Now, it is established that the sleep is produced by an active process which is different for non-REM sleep and REM sleep.

**Genesis of non-REM sleep**

The non-REM sleep is generated by interaction of neurons which are grouped as:

1. Diencephalic sleep zone lies in the hypothalamus and the nearby intra-laminar and anterior thalamic nuclei. A sleep facilitatory centre is considered to be located in the anterior hypothalamus, as its stimulation causes sleep. Posterior hypothalamus acts as a waking centre, as its stimulation causes wakefulness. The diencephalic sleep zone must be stimulated at low frequency (about 8 Hz) to produce sleep.
2. Medullary synchronizing zone is in the reticular formation of medulla oblongata at the level of nucleus of the tractus solitarius. Like diencephalic sleep zone, this zone also produces sleep when stimulated at low frequency.
3. Basal forebrain sleep zone includes the pre-optic area and the diagonal band of Broca. Unlike the other two zones, stimulation of this zone at low as well as high frequency produces sleep.

**Activity of non-REM on cells**

The non-REM on cells are GABAergic inhibitory neurons that mediate sleep-inducing action of the above described sleep zones. These cells are thought to produce sleep by inhibiting the histaminergic cells in the posterior hypothalamus as well as cells of nucleus reticularis pontis oralis (RPO) in the mid brain that mediate arousal.

**Mechanism of production of sleep spindles and slow waves of non-REM sleep**

The non-REM sleep is characterized by the EEG spindles and slow waves that are produced by synchronized postsynaptic potentials in the cortical neurons. These synchronized synaptic potentials are generated by the rhythmic firing of thalamic relay neurons that project to the cortex. The rhythmic firing of relay neurons is a result of action of GABAergic inhibitory neurons in the nucleus reticularis that forms a shell around the thalamus.

**Genesis of REM sleep**

Rapid eye movement sleep is generated by the interaction of neurons in the caudal mid brain and pons with the neurons in the medulla and forebrain. REM sleep as described earlier is characterized by:

**Blockage of EEG spindles and slow waves,**

1. Occurrence of PGO waves,
2. Muscle atonia and
3. Phasic motor action.

**Genesis of the above components of REM sleep is discussed.**

Role of cholinergic neurons of mid brain and the adjacent dorsal pons

These cells form an important component of the mid-brain arousal system and are maximally active during waking and REM sleep. Their activity contributes to the blocking of the slow waves of EEG.

Role of nucleus reticularis pontis oralis

The nucleus RPO forms another important neuronal machinery for genesis of REM sleep. Three classes of neurons in the RPO of particular interest are:

1. Cholinergic PGO-on cells. The discharge of these neurons produces the so-called PGO spikes that are characteristic of REM sleep

2. REM-waking-on-cells of RPO fire at high rate during active waking as well as during REM sleep. Some of these cells project to the motor neurons in the spinal cord and others project to the motor neurons that drive the extraocular muscles.

Burst firing of REM-waking-on cells during REM sleep produces rapid eye movements and muscle twitches.

3. REM-on-cells. REM-on-cells of RPO show high level of activity during REM sleep but have a very little or no activity during waking and non-REM sleep. Although few in number, these cells play a key role in REM sleep.

**Chemical mediators of sleep**

Neurotransmitters employed by the neurons forming the neural substrate of sleep as discussed above include:

1. Serotonin,
2. Acetylcholine and
3. Noradrenaline.

The substances that have been identified by an experiment on sleep-deprived animals as sleep-producing substances (S/S) are:

Muramyl dipeptide, a chemical related to substances found in the bacterial cell walls,

Interleukin-1, a cytokine that may mediate the effects of muramyl dipeptides as well as immune response,

* Adenosine,
* Delta sleep-inducing peptide, a substance isolated from the blood of sleeping rabbits,
* Prostaglandin D2 and
* Arginine vasotoxin.

**PHYSIOLOGICAL SIGNIFICANCE OF SLEEP**

Sleep is an indispensable phenomenon. Its physiological significance is highlighted.

1. Sleep may serve as a period of body’s rest and metabolic restoration as evidenced by following physiological changes during non-REM sleep:

* Pulsatile release of growth hormone and gonadotropins from the pituitary and
* Decrease in blood pressure, heart rate and respiration.

2. Sleep is necessary for certain forms of learning. In experimental animals, learning sessions do not improve performance until a period of SWS or SWS plus REM sleep has occurred. However, it is not known why sleep is necessary and there is as yet no clinical correlate to this experimental observation.

3. REM sleep is necessary for mental well-being. The correlation between dreaming and REM sleep indicates that the brain is highly active at this time. This may allow for the expression, through dreams, of concern in the subconscious and for long-term chemical and structural changes that brain must undergo to make learning and memory possible.

4. REM sleep plays an important role in homeostatic mechanism. It is evident from the observation that when the experimental animals are completely deprived of REM sleep for long periods, they loose weight in spite of increased caloric intake and finally die.

**SLEEP DISORDERS**

1. Insomnia refers to an inability to have sufficient or restful sleep despite an adequate opportunity for sleep. It is a subjective problem that occurs at one time or another in almost all adults. Insomnia can be relieved temporarily by sleeping pills, especially benzodiazepines. Prolonged use of these drugs can be habit-forming and can compromise day time performance.

2. Fatal familial insomnia is a serious disorder characterized by worsening insomnia, impaired autonomic and motor functions, dementia and eventually death. It is a progressive disease that occurs in both an inherited and a sporadic form.

3. Narcolepsy refers to an irresistible urge to sleep. As mentioned in the sleep cycle, in adults the sleep onset occurs with non-REM sleep, which is followed by REM sleep. However, in narcolepsy, REM sleep is entered directly from the waking states. Narcolepsy may manifest as:

* Episodes of sudden sleep. The individuals go to sleep while performing day time tasks.
* Cataplexy. In some narcoleptics, the profound reduction in the muscle tone characteristic of REM sleep can occur without loss of consciousness. During such an attack, called cataplexy, the individual suddenly becomes paralysed, falls to the ground and is unable to move.
* Dream-like state during wakefulness is another mode of manifestation of narcolepsy. Narcoleptics describe it as a hallucination.

4. Some sleep disorders associated with non-REM sleep (slow wave sleep), or more specifically, occurring during arousal from slow wave sleep are:

Sleep walking (somnambulism). Episodes of sleep walking are more common in children than in adults and occur predominantly in males. These episodes may last for several minutes. Such individuals walk with their eyes open and avoid obstacles, but when awakened, they cannot recall the episode

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

**The Role Of Basal Ganglia In Movement.**

**CONTROL OF MOTOR ACTIVITY**

1. **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:
   * Premotor area
   * Primary motor area
   * 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.

1. **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.
2. **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. skill ed activities such as writing the learnt alphabet, paper cutting, nail hammering, etc.