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300l, Mobs

17/MHS01/169

Neuro-physiology assignment

Physiology of sleep

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

Stages of sleep

There are two kinds of sleep:

1. Rapid eye movement (REM) sleep
2. non-REM (NREM) or slow-wave sleep

REMsleep is so named because of the characteristic eye movements that occur during this stage of sleep.

REMsleep

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

EEG pattern of REMsleep

During REMsleep, 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 (Fig. 10.11-9G). 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. Because of EEG pattern of wakefulness, the REM is also called ' paradoxical sleep'

The PGO (ponto-geniculooccipital) waves are not detectable in humans by scalp EEG, but are recordable by depth EEG recordings. These waves originate in pons and pass rapidly to lateral geniculate body and then to cerebral cortex and hence the name PGO. These waves activate the reticular inhibiting area in the medulla producing hypotonia. 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

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. Heart rate and respiration rate become irregular.
2. 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.
3. 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.

4. Middle ear muscles are also active during REM sleep.
5. Penile erection in males and engorgement of clitoris in females may occur during REM sleep

NREM sleep is divided into four stages. A person falling asleep first enters stage 1, the EEG begins to show a low-voltage, mixed frequency pattern. A theta rhythm (4– 7 Hz) can be seen at this early stage of slow wave sleep. Throughout NREM sleep, there is some activity of skeletal muscle but no eye movements occur. Stage 2 is marked by the appearance of sinusoidal waves called sleep spindles (12– 14 Hz) and occasional high voltage biphasic waves called K complexes.

In stage 3, a high-amplitude delta rhythm (0.5– 4 Hz) dominates the EEG waves. Maximum slowing with large waves is seen in stage 4. Thus, the characteristic of deep sleep is a pattern of rhythmic slow waves, indicating marked synchronization; it is sometimes referred to as slow-wave sleep. Whereas theta and delta rhythms are normal during sleep, their appearance during wakefulness is a sign of brain dysfunction.

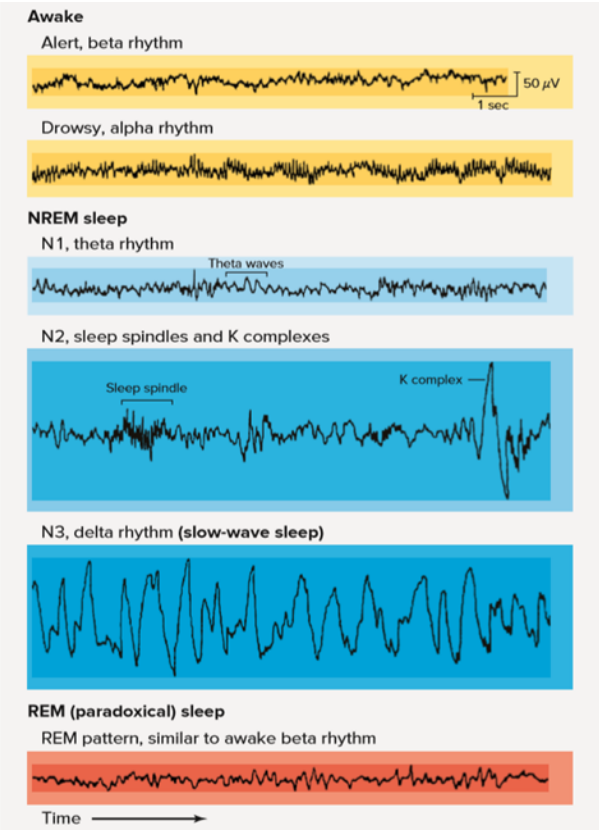
Sleep cycle

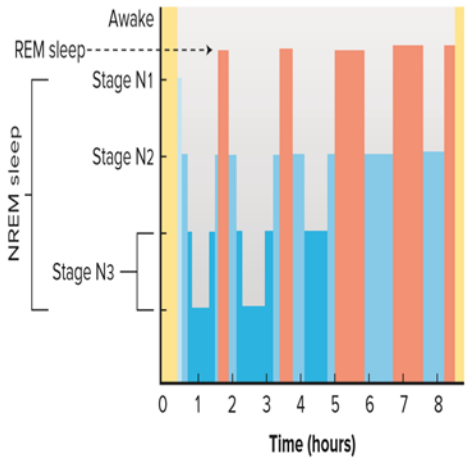
In a normal adult individual, the average sleep period of about 7– 8 h is divided into about 5 cycles during which non-REM sleep and REM sleep alternate with each other. There is an orderly progression of sleep states and stages during a typical sleep cycle. When an individual falls asleep, the N1 stage of SWS sleep is entered first. During next hour or so the person

passes progressively in deeper stages of sleep until deep sleep is reached. After about 15 minutes of deep sleep, depth of sleep starts decreasing and continues to do so until the person re-enters the N1 stage of sleep about 90 minutes after the start of the first sleep cycle. At this point, individual passes fromSWS to REMsleep. This cycle repeats itself about 5 times during night. After the second cycle, the intervals between periods of REMsleep become shorter and the duration of each of period of REMsleep becomes longer. As morning approaches, an individual spends less time in the deeper stages of SWS and periodically awakens. This sleep cycle is typical of adult.

Average sleep time per day differs according to the age:

- During infancy: 16 h,
- During childhood: 10 h,
- During adulthood: 7– 8 h and
- During old age: <8 h.





Stage	Behavior	EEG (See Figures 8.3 and 8.4)
Alert wakefulness	Awake, alert with eyes open.	Beta rhythm (greater than 12 Hz).
Relaxed wakefulness	Awake, relaxed with eyes closed.	Mainly alpha rhythm (8–12 Hz) over the parietal and occipital lobes. Changes to beta rhythm in response to internal or external stimuli.
Relaxed drowsiness	Fatigued, tired, or bored; eyelids may narrow and close; head may start to droop; momentary lapses of attention and alertness. Sleepy but not asleep.	Decrease in alpha-wave amplitude and frequency.
NREM (slow-wave) sleep		
Stage N1	Light sleep; easily aroused by moderate stimuli or even by neck muscle jerks triggered by muscle stretch receptors as head nods; continuous lack of awareness.	Alpha waves reduced in frequency, amplitude, and percentage of time present; gaps in alpha rhythm filled with theta (4–8 Hz) and delta (slower than 4 Hz) activity.
Stage N2	Further lack of sensitivity to activation and arousal.	Alpha waves replaced by random waves of greater amplitude.
Stage N3	Deep sleep; in stage N3, activation and arousal occur only with vigorous stimulation.	Much theta and delta activity; progressive increase in amount of delta.
REM (paradoxical) sleep	Greatest muscle relaxation and difficulty of arousal; begins 50–90 min after sleep onset, episodes repeated every 60–90 min, each episode lasting about 10 min; dreaming frequently occurs, rapid eye movements behind closed eyelids; marked increase in brain O_2 consumption.	EEG resembles that of alert awake state.

Sleep-wake up 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 rhythmto the environment. Sunlight is a powerful timing cue. Light entrains this rhythmby means of retinohypothalamic tract. Although the suprachiasmatic nucleus regulates the timing of sleep, it is not responsible for sleep itself

Importance of Sleep

Although we spend about one-third of our lives sleeping, the functions of sleep are not completely understood. Many lines of research, however, suggest that sleep is a fundamental necessity of a complex nervous system Studies of sleep deprivation in humans and other animals suggest that sleep

is a homeostatic requirement, similar to the need for food and water. Deprivation of sleep impairs the immune system, causes cognitive and memory deficits, and ultimately leads to psychosis and even death. Part of the restorative mechanism of sleep may arise from removal of protein fragments, waste products, and neurotransmitters that accumulate from brain activity in the awake state. During sleep, the space between neurons increases more than 60% due to transient shrinking of glial cells, allowing a significant increase in the flow of cerebrospinal fluid between neurons

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:

- Darkened room,
- Comfortable surrounding temperature,
- Silence,
- Physical and mental relaxation,
- Consumption of a basic urge, such as hunger or sex and
- Low-frequency stimulation, such as by patting or knocking in a cradle or sitting in a moving vehicle.cerebrospinal fluid between neurons.

Clinical Correlates

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.

4. REM behaviour disorder. It is a newly recognized condition in which REM sleep is not associated with inhibition of muscle tone. Consequently, such persons act out their dreams, that is, they thrash about and may even jump out off the bed, ready to do battle with imagined aggression. The generalized or localized muscle contraction associated with vivid visual imagery, i.e. the motor response to some of the dream events is referred to a hypnoeic myoclonia.

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

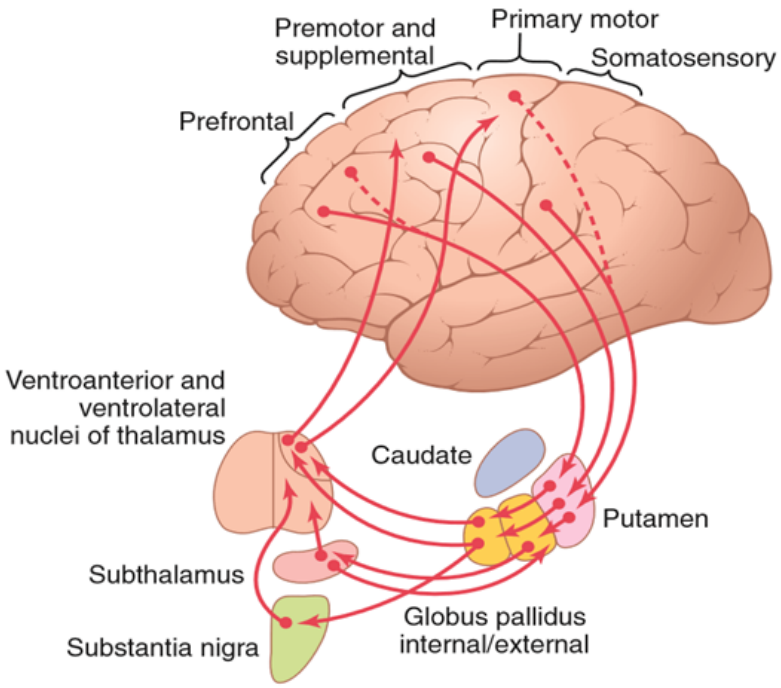
The direct pathway of movement is a neural pathway within the central nervous system(CNS) through the basal ganglia which facilitates the initiation and execution of voluntary movement. It works in conjunction with the indirect pathway. Both of these pathways are part of the cortico-basal gangliathalamo-cortical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



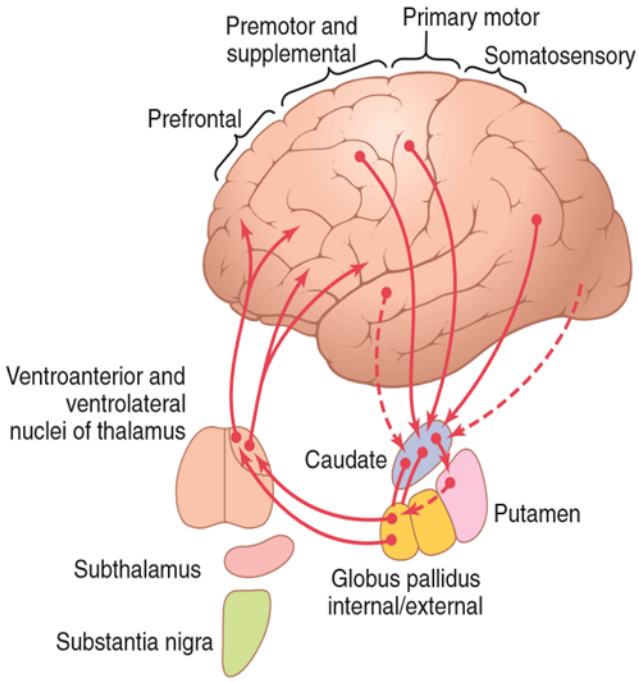
Diagramof pitman circuit

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 fromcompeting 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 fromparts 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.



Diagramof caudate circuit

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

Clinical Correlates

Parkinson's disease: This is a syndrome whereby dopaminergic neurons of the substantia nigra degenerate. When this happens, the ability of the basal ganglia to promote or inhibit movement is affect. This causes difficulty in initiating movement. Symptoms include rigidity, slow movement tremor, postural instability. Thinking and behavioral problems occur in the advance stage. The cause is unknown although it is believed to be genetic and environmental. There is no cure. Treatment involves medications such as levodopa, dopamine agonists.