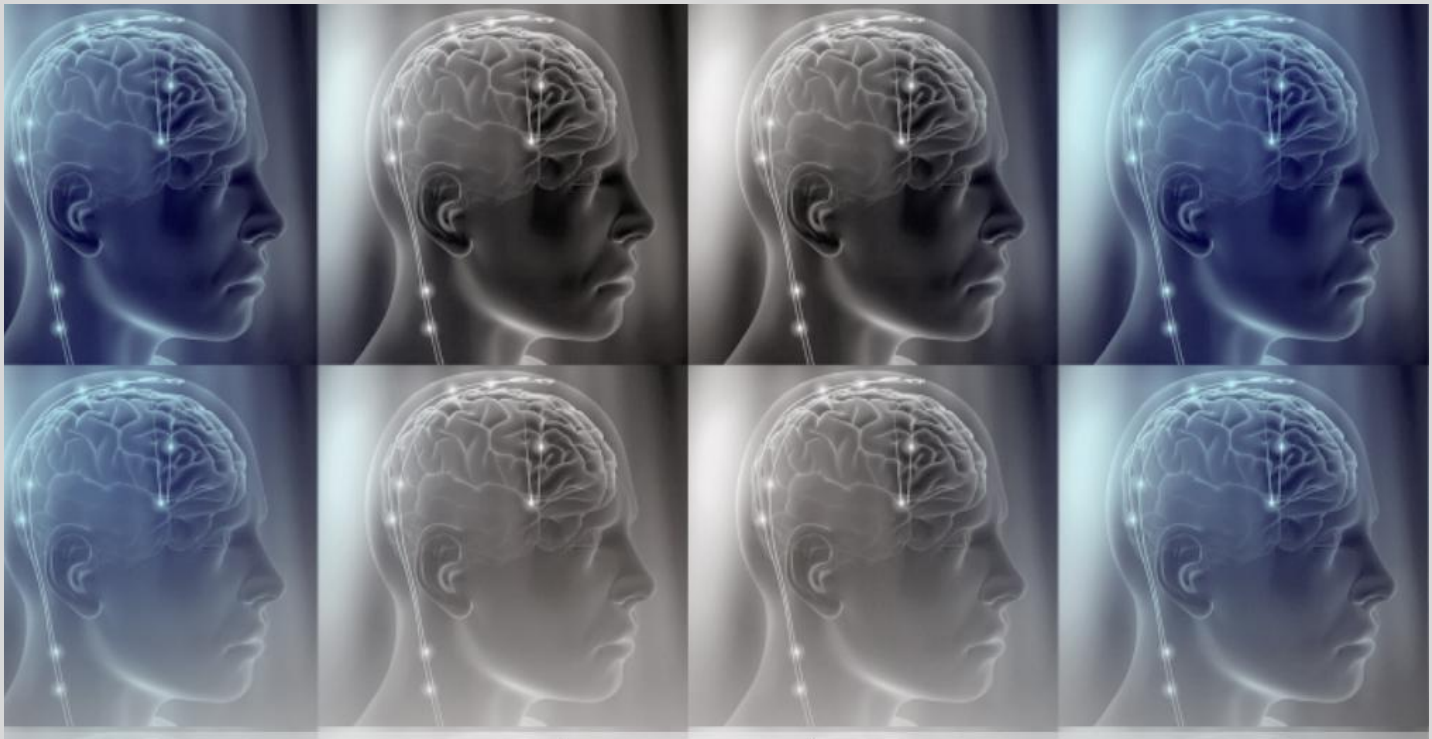

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CNS Central Nervous System

Block

Physiology Team

Female Side Male side

Done By: Abdullah AL-Anazi

Revised By: Mohammed Asiri

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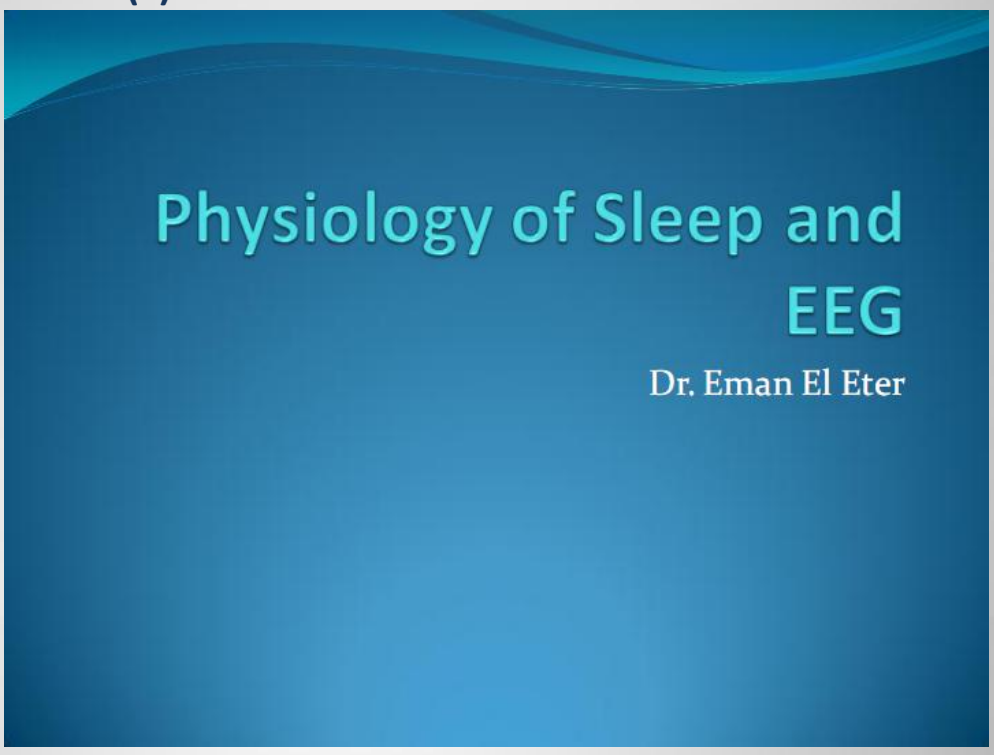

Team Notes :

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Objectives:

- Difference between sleep & coma.
- Why do we sleep?
- Types of sleep: NREM & REM.
- EEG waves.
- Stages of NREM sleep.
- Importance of REM sleep.
- Sleep cycle and effect of age.
- Sleep/awake cycle (Role of SCN).
- Mechanism of sleep (centers/ neurotransmitters).
- Sleep disorders.

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Definition

- Sleep is a state of loss of consciousness from which a subject can be aroused by appropriate stimuli.
- Coma is a state of unconsciousness from which a subject cannot be aroused

Team Notes :

The EEG in coma is generally unreactive , and there are several EEG patterns of coma .

However, the medical student is required to know that the commonest EEG pattern of coma is continuous slow waves

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Why do we sleep?

- Restoration, or repair:
  - Waking life disrupts homeostasis
  - Sleep may conserve some energy
- Protection with the circadian cycle
- Circadian synthesis of hormones, ...
- Consolidation of learning?
- Remodelling of synaptic function

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EEG waves

- The frequencies of brain waves range from 0.5-500 Hz.
- The most clinically relevant waves:
- *Alpha waves* - 8-13 Hz
- *Beta waves* - Greater than 13 Hz
- *Theta waves* - 3.5-7.5 Hz
- *Delta waves* - 3 Hz or less

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Alpha waves

- Seen in all age groups but are most common in adults.
- Most marked in the parieto-occipital area.
- Occur rhythmically on both sides of the head but are often slightly higher in amplitude on the **nondominant** side, especially in right-handed individuals
- Occur with closed eyes , relaxation, wondering mind.

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Alpha block

- Alpha activity disappears normally with attention (eg, mental arithmetic, stress, opening eyes, any form of sensory stimulation).
- Then become replaced with irregular low voltage activity.
- Called arousal or alerting response.
- Also called desynchronization as it represents breakup of synchronized neuronal activity!!!!
- An abnormal exception is alpha coma, most often caused by hypoxic-ischemic encephalopathy of destructive processes in the pons (eg, intracerebral hemorrhage). In alpha coma, alpha waves are distributed uniformly both anteriorly and posteriorly in patients who are unresponsive to stimuli

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Beta waves

- Seen in all age groups.
- Small in amplitude , usually symmetric and more evident anteriorly.
- Drugs, such as barbiturates and benzodiazepines, augment beta waves.
- > 13 Hz/sec

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Theta waves

- Normally seen during sleep at any age.
- In awake adults, these waves are abnormal if they occur in excess.
- Theta and delta waves are known collectively as slow waves.

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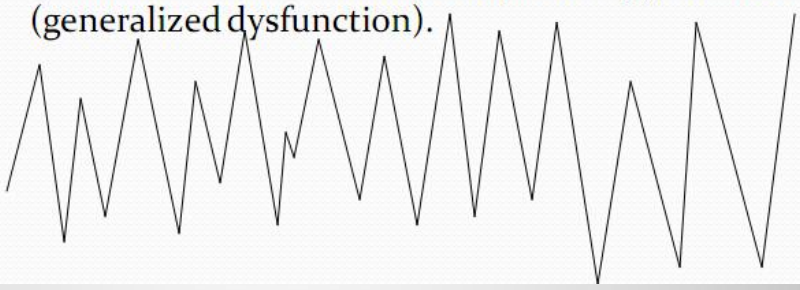
Delta waves

- Slow waves, have a frequency of ≤ 3Hz or less.
- Normally seen in deep sleep in adults as well as in infants and children.
- Delta waves are abnormal in the awake adult.
- Often, have the largest amplitude of all waves.
- Delta waves can be focal (local pathology) or diffuse (generalized dysfunction).



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Sleep spindles

- Spindles are groups of waves that occur during many sleep stages but especially in stage 2.
- They have frequencies in the upper levels of alpha or lower levels of beta.
- Lasting for a second or less, they increase in amplitude initially and then decrease slowly. The waveform resembles a spindle.
- They usually are symmetric and are most obvious in the parasagittal regions.

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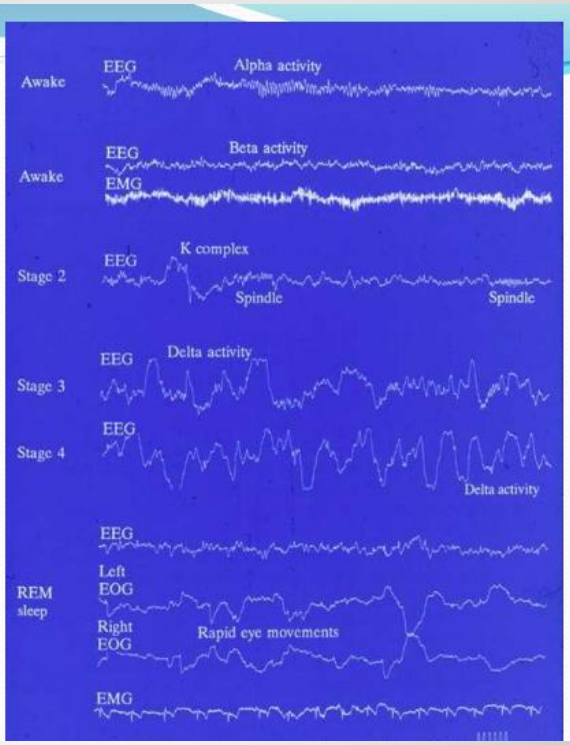

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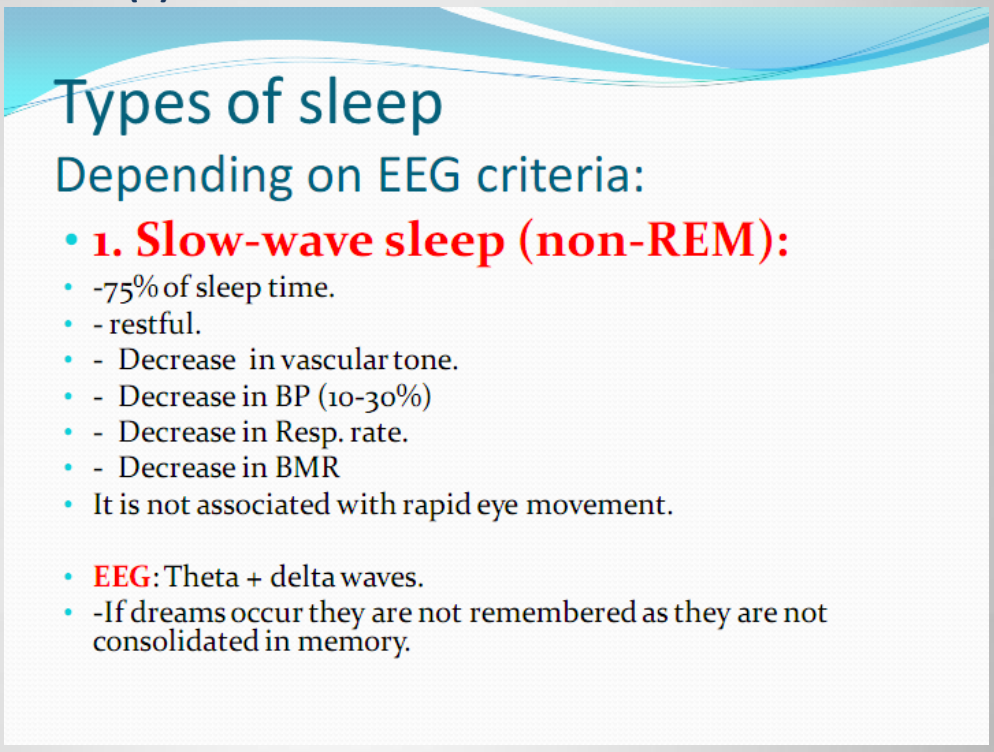

Team Notes :

is divided into 4 stages :

(1) Stage 1 NREM → when a person is initially falling asleep . • Characterized by low-amplitude, fast activity

(2) Stage 2 NREM → •

Marked by appearance of Sleep Spindles . These are bursts of alpha-like 10-14 z , 50 uV waves .

(3) Stage 3 NREM → •

Lower frequency (mainly theta) , higher amplitude EEG waves .

(4) Stage 4 NREM → •

Still slower frequency (mainly delta) & still higher amplitude waves

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Types of sleep, continued,...

- **2- Rapid Eye Movement Sleep (REM):**
- **Is so called because of rapid eye moevement.**
- -Occur in episodes of 5-30 min, recurring every 90 min.
- -Tiredness shortens the duration of each episode.
- -As you become restful through the night, the duration of each episode increases.
- -Active dreaming, remembered later.

Team Notes :

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REM, continued,....

- Decrease in muscle tone (due to excitation of reticular inhibitory centers).
- HR & RR are irregular.
- Rapid rolling movement of the eyes.
- Erection of penis.
- Engorgement of clitoris.
- Twitches of facial & limb muscles.
- More difficult to awake a person than in slow-wave sleep.

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REM, continued,...

- EEG: B-waves, indicating a high level of activity in the brain during REM (That is why it is called paradoxical sleep).

PGO spikes stimulate the Inhibitory Reticular Area leading to Hypotonia:

Exception: Respiratory + Eye muscles.

In sleep apnea, respiratory muscles are inhibited.

Team Notes :

The brain is highly active in REM sleep, and overall brain metabolism may be increased as much as 20 %

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Importance of REM sleep

- 1. Expression of concerns in the sub-consciousness (Through dreams),
- 2. Long-term chemical and structural changes that the brain need to make learning & memory possible.

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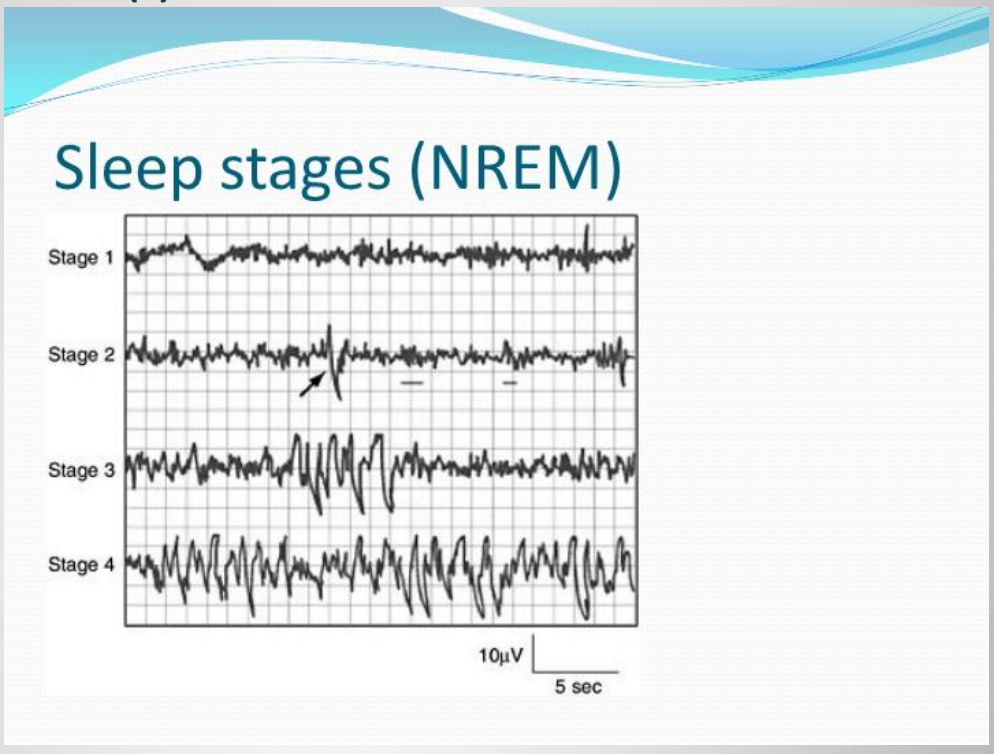

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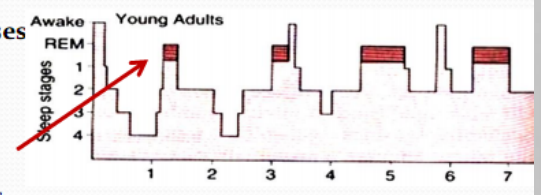
Distribution of Sleep Stages

- While NREM occupies (around 75-80n%) , it is interrupted by intervening REM sleep periods, every 90 minutes .
- In a typical night of sleep , a young adult (1) first enters NREM sleep , passes through stages 1 , 2 , 3 and 4 , then
- (2) goes into the first REM sleep episode.
- This cycle is repeated at intervals of about 90 minutes throughout the 8 hours or so of a night sleep.
- Therefore , there are 4-6 sleep cycles per night (and 4-6 REM periods per night)
- As the night goes on → there is progressive reduction in stages 3 and 4 sleep and a progressive increase in REM sleep .



REM sleep periods are shown in red

In a young adult NREM occupies 75-80% of a night sleep time , & REM sleep occupies 20-25 % of the sleep time

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Distribution of sleep stages in a typical night

- Premature infants:
- REM sleep occupies 80% of total sleep time.
- Full term neonates:
- 50% of sleep time is occupied by REM.
- Aged/elderly:
- Thereafter , the proportion of REM sleep falls rapidly and plateaus at about 25 % (20-69ys) until it falls further in old age .
- Children have more sleep time and stage 4 than adults

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Sleep/wakefulness rhythm

- Periods of sleep and wakefulness alternate about once a day.
- A circadian rhythm consist typically of 8h sleep and 16 h awake.
- This rhythm is controlled by the biological clock function of suprachiasmatic (SCN) nucleus in the hypothalamus.
- Within sleep portion of this circadian cycle NREM and REM sleep alternate.

Team Notes :

- During the morning , and after a restful night sleep , the Bulboreticular Facilitory Area becomes maximally active , and overcomes any inhibition by the Raphe Nuclei . Moreover , Melatonin falls to very low levels in the morning .
- This release of the Bulboreticular Facilitory Area from inhibition (1) activates (through the thalamic nuclei) the cerebral cortex to increased vigilance , and also

  (2) excites the Peripheral Nervous System (PNS) to become more receptive to incoming sensory stimuli + be more ready to respond by increasing muscle tone .

, Both (1) and (2) above send numerous positive feedback signals back to the Bulboreticular Facilitotry Area to activate it still further.

- Therefore, once wakefulness begins, it has a natural tendency to sustain itself because of all this positive feedback activity.

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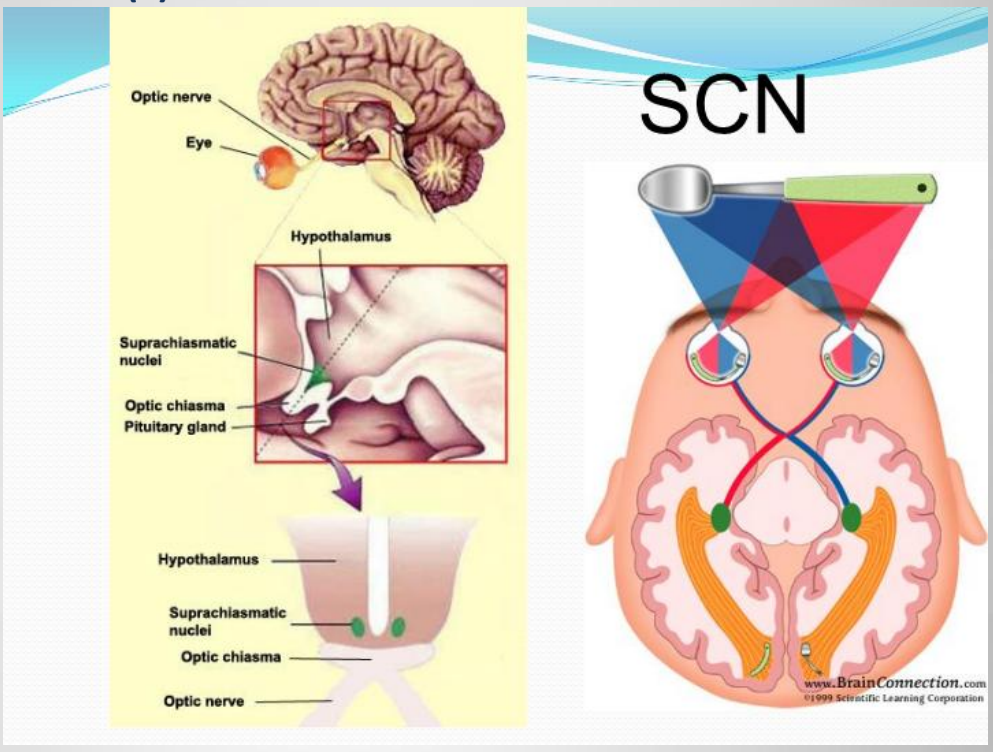

Team Notes :

Then, after the brain remains activated for many hours during the day , the activating neurons in the Bulboreticular Facilitory Area gradually become fatigued.

Consequently, the positive feedback cycle between the Bulboreticular Facilitotry Area and the cerebral cortex fades,

and then the effects of →

(1) the sleep-promoting centers (Raphe Nuclei) , and

(2) the rising melatonin levels ,

take over (dominate) → leading to rapid transition from

wakefulness to sleep.

CNS central Nervous System

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Mechanism of Sleep

Genesis of slow-wave sleep:

- Active process produced by inhibition of areas in RAS responsible for alert conscious state of wakefulness.
- **Sleep Zones:**
- Stimulation of the following sites will lead to sleep and synchronization of slow –wave sleep EEG:
- 1. Diencephalon :
- -suprachiasmatic region of post hypothalamus.
- -diffuse thalamic nuclei: intra-laminal & ant.thalamic

Team Notes :

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Mechanism of sleep, continue.,

- Slow frequency stim of diencephalon.....sleep.
- High frequency stim of diencephalon.....arousal.
- 2. Medulla oblongata:

Medullary synchronizing zone at the level of NTS.

3. Basal forebrain: pre-optic area:

High or slow frequency stim.....synchronization + sleep.

1,2&3 are connected together and with reticular area of the brain stem.

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Genesis of REM sleep

- The mechanism producing REM sleep is located in pontine reticular formation.
- Large cholinergic ponto-geniculo-occipital (PGO) spikes arise in this area and are thought to initiate sleep.
- Discharge of noradrenergic neurons of locus ceruleus + discharge of serotonergic neurons of midbrain raphe causes wakefulness. They become silent when PGO active during REM.

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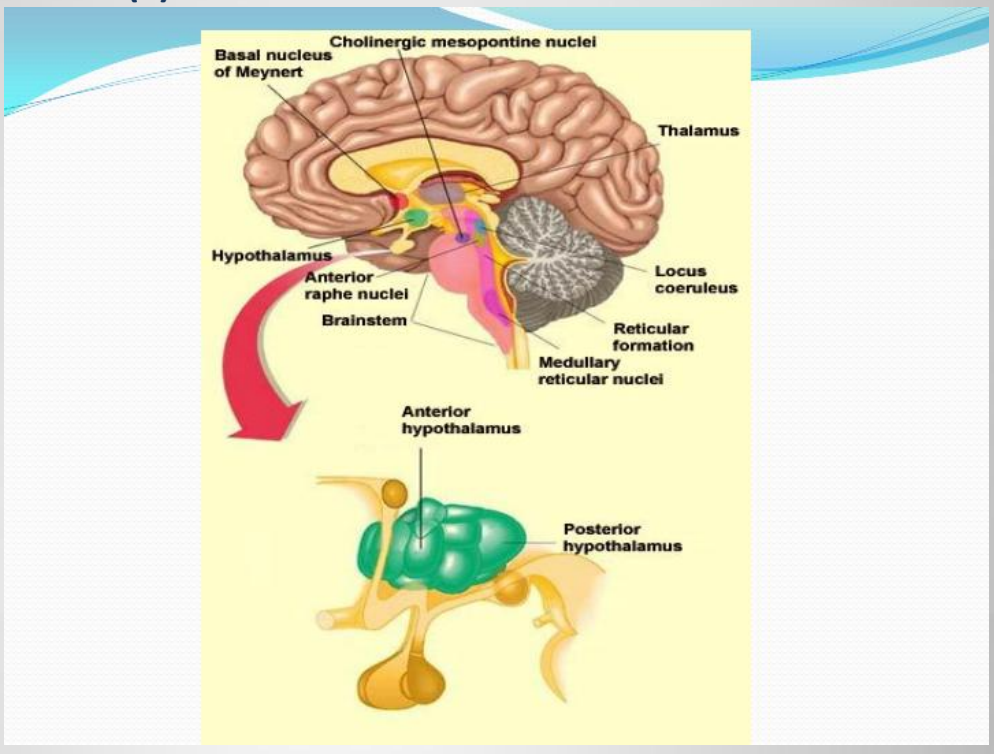

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Role of neurotransmitters

- Serotonin:
- -Agonist: (-) sleep.
- -antagonist: (+) slow-wave sleep.
- Serotonin appears to modulate sleep through its effect on other hypnogenic factors in the anterior hypothalamus and suprachiasmatic nucleus
- Serotonin is a melatonin precursor

Team Notes :

Serotonin , produced by the Raphe Nuclei , induces SWS sleep

<u>Melatonin as Circadian Controller of Sleep-Wake Cycles</u>

Alternating " Sleep-Wake Cycles " are under marked Circadian Control .

" Circadian Control/Rhythm " : means regulation of a biological rhythm (e.g. sleep-wakefulness , hormone secretion , etc) by day-night cycles .

Darkness (e.g., at night) stimualtes the Pineal Gland to secrete the hormone melatonin .

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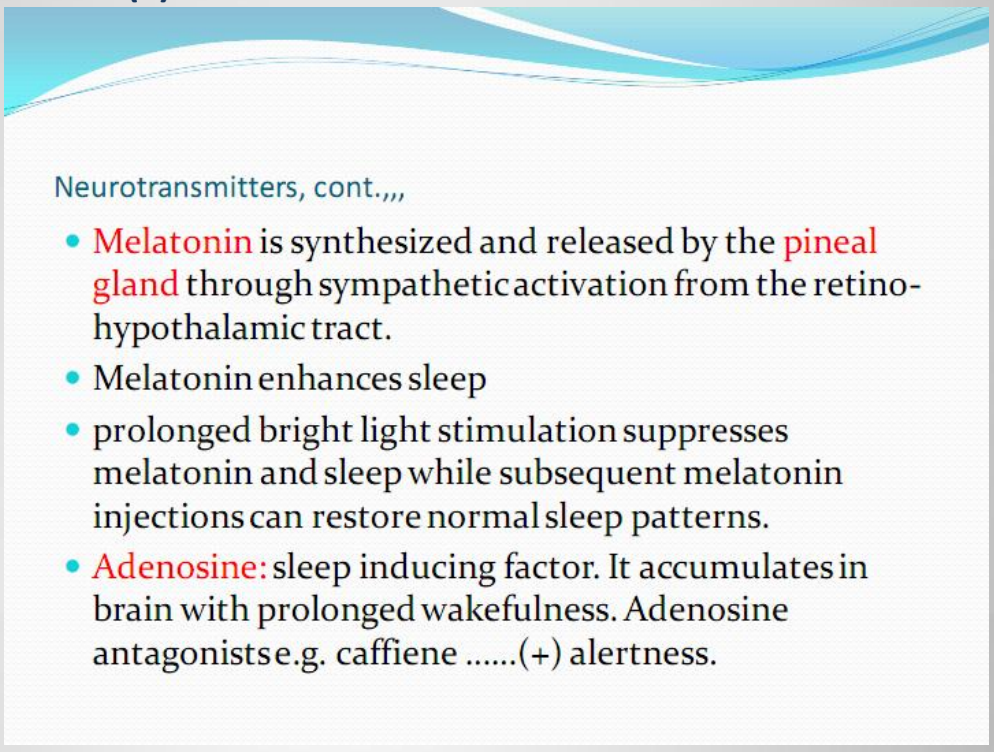

Team Notes :

Melatonin inhibits the RAS & thereby induces SWS .

Daylight falling on the retina stimulates the Suprachiasmal Nucleus (SCN) of hypothalamus .

SCN inhibits melatonin secretion by the Pineal Gland , & thereby it inhibits sleep and promotes wakefulness .

CNS Central Nervous System

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Working Together in Sleep

Brainstem Nucleus	Neurotransmitter	Activity State of Nucleus
Wakefulness		
Pedunculopontine	ACh	Active
Locus coeruleus	NE	Active
Raphe	5-HT	Active
Non-REM Sleep		
Pedunculopontine	ACh	Silent
Locus coeruleus	NE	Decreased Activity
Raphe	5-HT	Decreased Activity
REM Sleep On		
Pedunculopontine	ACh	Active as REM Approaches
Locus coeruleus	NE	Become Silent
Raphe	5-HT	Inactive
REM Sleep Off		
Locus coeruleus	NE	Become Active
Raphe	5-HT	Become Active

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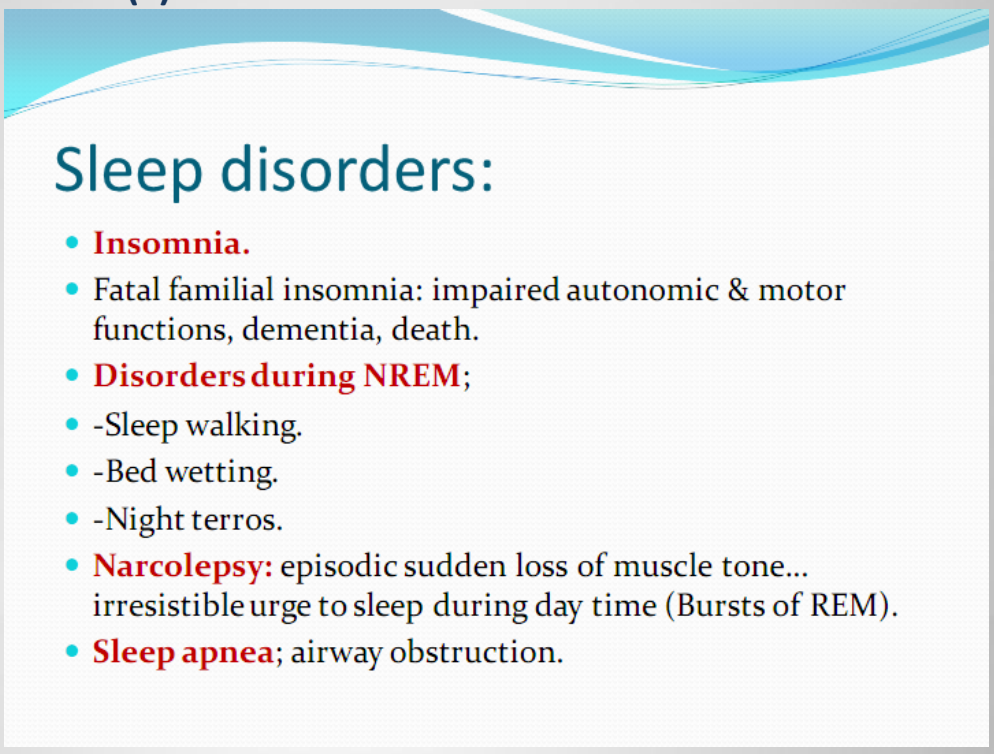

Team Notes :

Sleep deprivation (forced lack of sleep) experiments in humans have shown that the subject :

(1) experiences at first progressively increasing sluggishness of thought , & later

(2) becomes markedly irritable , & later still

(3) develops mental confusion & psychosis-like features .

It seems that sleep restores both normal levels of brain activity and normal "balance" among the different hormones , neurotransmitters & functions of the CNS

Q1: All of the following are the characteristics of Slow Wave Sleep Except:

- Decrease heart rate
- Decrease Respiratory rate
- Increase growth hormone secretion
- **Increased cerebral blood flow**

Q2: Which of the following is true about NREM (Non-REM) sleep:

- **It is also known as slow wave sleep**
- It is associated with dreaming
- It is not restful
- It has five stages

Q3: The Rapid Eye Movement Sleep (REM) sleep:

- **The first bout occurs 80-100 minutes after the person falls asleep**
- Bouts/episodes usually appear on the average after every 30 minutes
- Subject is easy to arouse by sensory stimuli
- Heart rate and respiration usually become regular

Q4: Which of the following is a characteristic of REM sleep:

- It occupies most of the night sleep time in adults
- **Its first episode occurs 60-100 minutes after a person falls asleep**
- It has 8-10 episodes during a normal night sleep
- The EEG shows delta waves all over the brain

Q5: Slow wave sleep:

- Is frequently called dreamful sleep
- **Lasts for most of the period of night**
- Eyes undergoes rapid movements
- Brain is highly active with increase metabolism by about 20%

Q6: The mechanisms that triggers REM sleep is located in:

- Auditory cortex
- Motor area 4
- **Pontine reticular formation**
- Pituitary gland