Physiology of Sleep

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References : Guyton and Ganong Textbooks of Medical Physiology

- **Q : What is the difference between sleep and coma ?**

- **Sleep is defined as unconsciousness from which the person can be aroused by sensory stimuli .**
- **If we do an EEG (electroencephalogram) , his EEG will show various waves that are characteristic of different sleep stage .**
- **Coma, on the other hand , is a state of loss of consciousness (LOC) from which the person cannot be aroused ,**
- **If we do EEG in a comatose person , the EEG will be dominated by slow waves .**

Q : What are the types of sleep ?

- Depending on EEG criteria , during each night we go through 2 types of sleep that alternate with each other. They are :
- (1) SWS (Slow-Wave Sleep),
- because in this type of sleep EEG waves are generally of low frequency .
- It is also called Non-Rapid Eye Movement (NREM) sleep because , unlike the other type of sleep , it is not associated with rapid eye movements .
- (2) REM sleep (Rapid Eye Movement),
- because in this type of sleep the the person makes rapid movements by his eyes , in spite of the fact that he is sleeping .

Sleep Classification is Based on EEG Features

(A) NREM Sleep (SWS) :

- ✓ 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 →

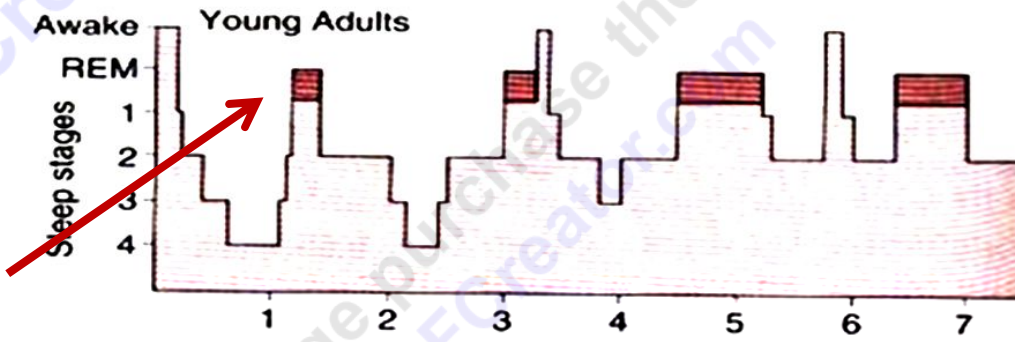
  Still slower frequency (mainly delta) & still higher amplitude waves .

(B) REM Sleep :

- (1) Low-voltage , fast activity

Distribution of Sleep Stages

- While SWS occupies most of the total night sleep time (around 75-80n%) , it is nterrupted by intervening REM sleep periods ,approximately 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 SWS , and then, 60-100 minutes from sleep onset ,
- (3) 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 SWS occupies 75-80% of a night sleep time , & REM sleep occupies 20-25 % of the sleep time

- REM sleep occupies 80 % of total sleep time in premature infants , and 50 % in full-term nenates .
- Thereafter , the proportion of REM sleep falls rapidly and plateaus at about 25 % until it falls further in old age .
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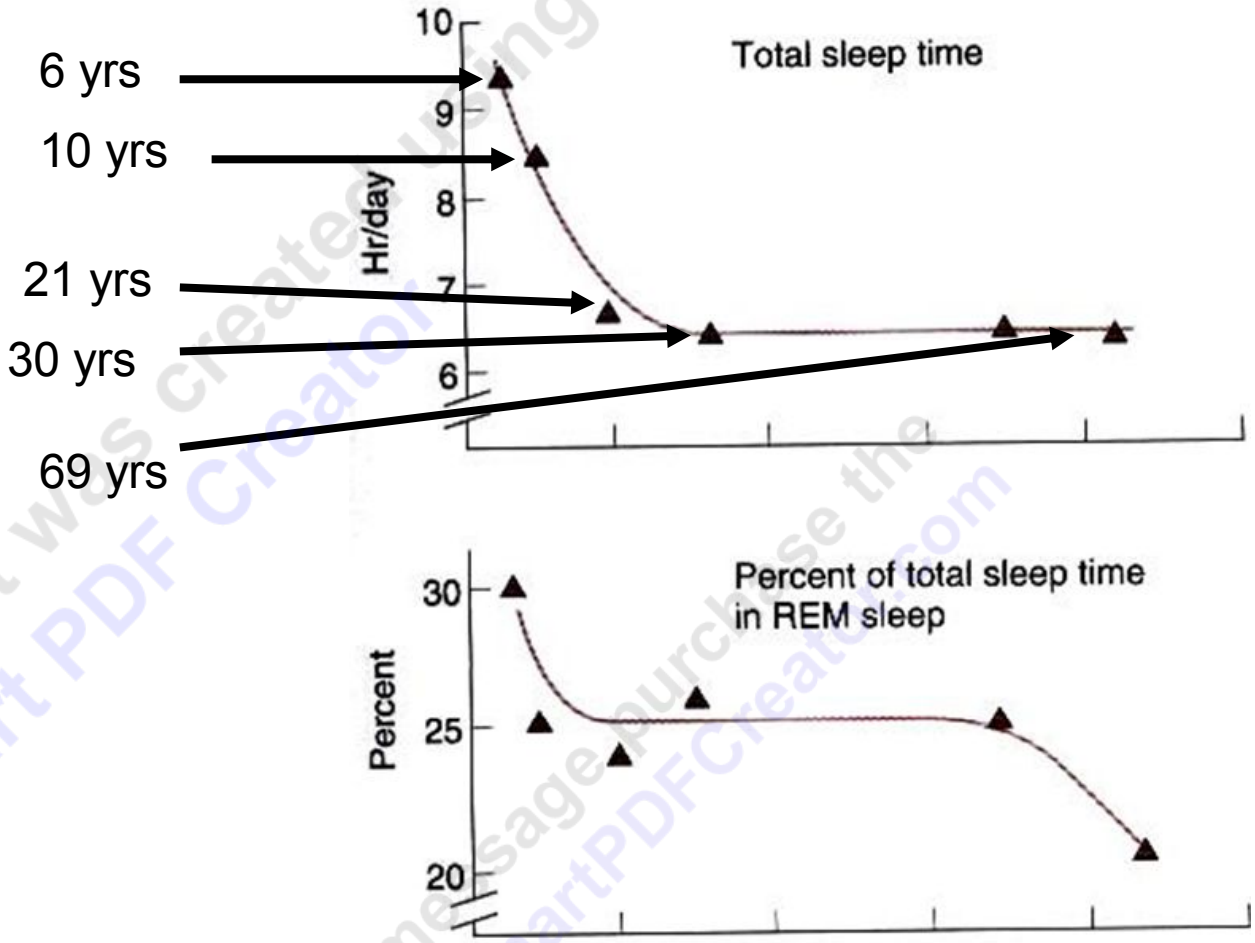
- Children have more total sleep time and stage 4 sleep than adults .



SWS (NREM Sleep (Slow-Wave Sleep , SWS)

- SWS sleep is an exceedingly restful type of sleep .
- It is typically exemplified in the first hour of sleep hat follows a prolonged period of sleep deprivation .
- It is associated with decrease in peripheral vascular resistance (there is 10 - 30 % decreases in BP) , decrease in respiratory rate, and BMR (Basal Metabolic Rate)
- Sometimes dreams , even nightmares , occur during SWS sleep .
- However , the difference between the dreams that occur in SWS and dreams of REM sleep is that :

  (1) REM dreams are vivid dreams ,

  (2) REM dreams are associated with more bodily muscle activity, &

  (3) the dreams of SWS usually are not remembered .

REM Sleep (Paradoxical Sleep)

- In a normal night of sleep, bouts of REM sleep lasting

5 to 30 minutes usually appear on the average every 90 minutes.

- REM sleep is not as restful as SWS .
- When the person is extremely sleepy, each bout of REM sleep is short, and it may even be absent.
- Conversely, as the person becomes more rested through the night, the durations of the REM bouts increase.
- There are several important characteristics of REM sleep:

(1) There are rapid eye movements .

(2) Muscle tone throughout the body is exceedingly depressed, indicating strong inhibition of the spinal muscle control areas.

(3) Despite the extreme inhibition of the peripheral muscles, irregular , active bodily muscle movements do occur.

(4) Heart rate (HR) and respiratory rate (RR) usually become irregular, which is characteristic of the dream state

(5) It is usually associated with active , sometimes vivid , dreaming .

(6) The person is more difficult to arouse by sensory stimuli than during NREM sleep , and yet people usually awaken spontaneously in the morning during an episode of REM sleep (and frequently remember bits & pieces of the dream) .

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

(8) The EEG shows a pattern of brain waves similar to those that occur during wakefulness.

- Therefore , it is not surprising that REM sleep is also called paradoxical sleep : the paradox being that the person is asleep although he looks awake
- In summary, REM sleep is a type of sleep in which the brain is quite active , but this brain →.
- (1) is not aware cut off the external world
- (2) its activity is not channeled into purposeful external motor activity .

Theories of Sleep

What Makes Us Fall Asleep Sleep ?

- **Theories of sleep : old and modern :**
- **The old theory of sleep states that sleep is caused only by a passive process due to fatigue of RAS neurons after discharging for many hours of wakefulness .**
- **This theory was abandoned after experiments in laboratory animals led to development of a new theory stating that in addition , a strong active sleep-inducing inhibitory process that inhibits the RAS to produce sleep . It is mediated by the neurotransmitter serotonin (produced by the Raphe Nuclei) and the hormone Melatonin (released from the Pineal Gland) .**

- **Experimental findings supporting the modern theory are :**

✓ **(1) Transecting the brainstem at the level of the midpons , leaves the animal in a state of intense wakefulness for a period of days , at the end of which the animal passes into coma (possibly from exhaustion of the Bulboreticular Excitatory (Facilitory)Area), and then it eventually dies .**

- **The above-mentioned transection cuts the nerves going from the inhibitory serotonin-secreting Raphe Nuclei to the Bulboreticular Facilitory Area .**
- **What does this mean ? It means that the serotonin-secreting Raphe fibers normally inhibit the <u>Bulboreticular</u> Facilitory Area to produce sleep .**

✓ **(2) lesions that destroy the Raphe Nuclei themselves make the animal sleepless for days .**

- ✓ **(3) Serotonin agonists suppress sleep and serotonin antagonst increases SWS in humans. This proves that serotonin**

  (which is synthesized in the Raphe Nuclei) is necessary for induction of sleep .

- ✓ **(4) Stimulation of the Suprachiasmal Nucleus (SCN) of hypothalamus (which inhibits Melatonin release) produces sleep.**

Melatonin as Circadian Controller of Sleep-Wake Cycles

- Altenating " Sleep-Wake Cycles " are **under marked Circadian Control .**
- **" Circadian Control " : means regulation of a biological rhythm**

  (e.g. sleep-wakefulness , hormone secretion , etc) by day-night cycles .

- Melatonin is a hormone secreted by the Pineal Gland during darkness . It inhibits RAS & thereby induces sleep .
- The Suprachiasmatic Nucleus (SCN) inhibits melatonin secretion → thereby inhibits sleep & promotes wakefulness .

Why do we have sleep-waking cycles ?

- 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 Facilitory 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.

- **Then, after the brain remains activated for many hours, the activating neurons in the Bulboreticular Facilitory Area gradually become fatigued.**
- **Consequently, the positive feedback cycle between the mesencephalic reticular nuclei 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 → leading to rapid transition from wakefulness back to sleep.**

Possible Mechanisms for Genesis (Generation) of REM Sleep

- The mechanism that triggers REM sleep is believed to be Cholinergic Neurons located in the Pons .
- This is because animal experiments have shown that → at the onset of REM sleep , large groups of spikes originate in the Pontine RF (Lateral Pontine Tegmentum)
- These spikes discharges rapidly spread from the Pons to the Lateral Geniculate Nucleus (LGN) (i.e., thalamus) & from there the Occipital cortex . Hence they are called Ponto-Geniculo-Occipital (PGO) spikes .
- These PGO discharges initiate REM sleep .

Physiologic Functions of Sleep

- 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) may become psychotic .
- It seems that sleep restores both normal levels of brain activity and normal “balance” among the different functions of the CNS .