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 →

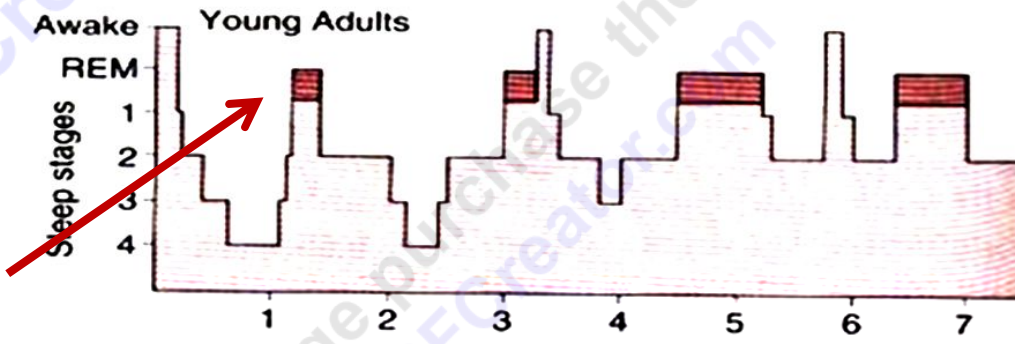
  Still slower frequency (mainly delta) & still higher amplitude waves .

(B) REM Sleep :

- Low-voltage , fast activity

Distribution of Sleep Stages

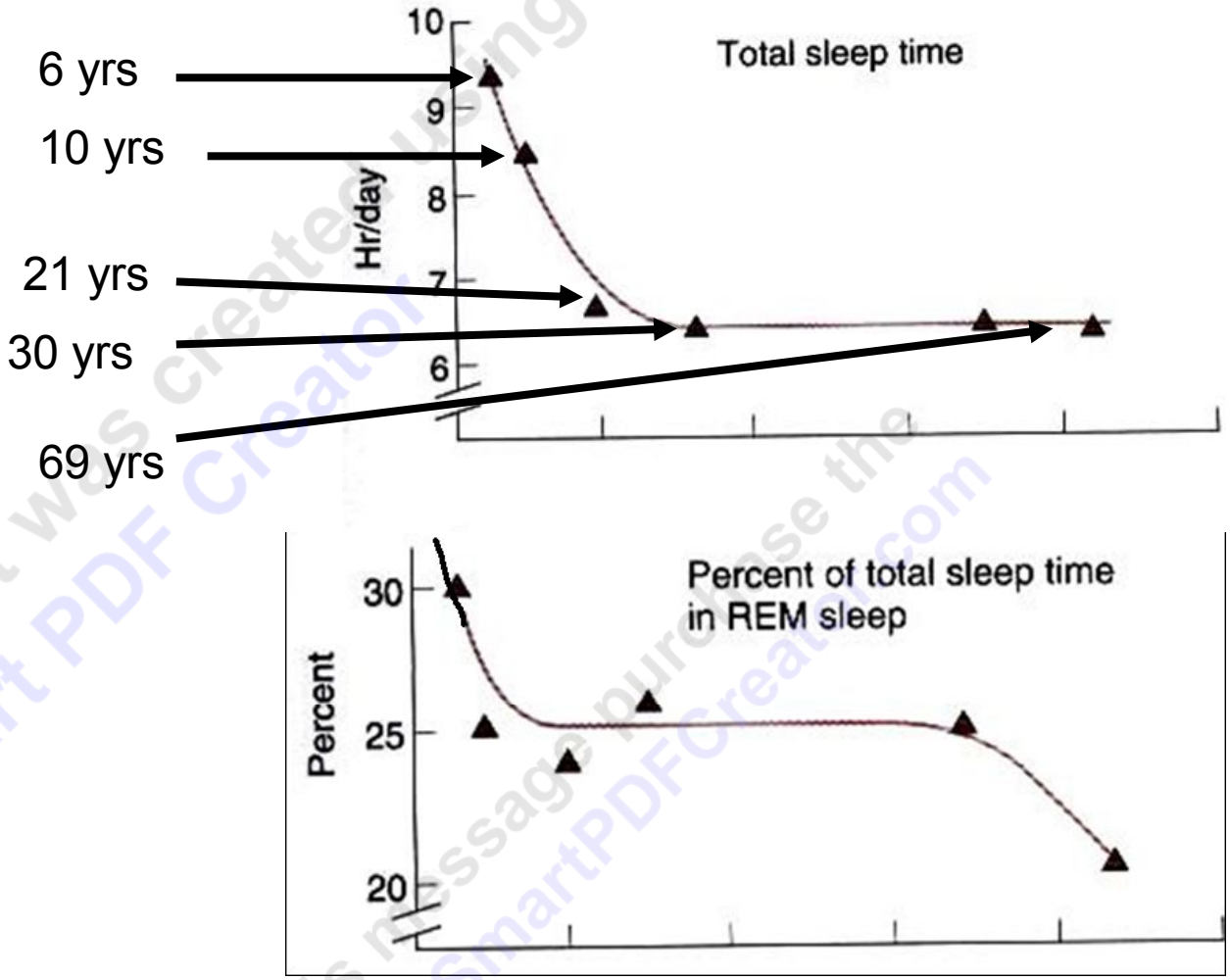
- While SWS occupies most of the total night sleep time (around 75-80n%) , it is nterrupted by intervening REM sleep periods ,approximately every 90 minutes .
- In a typical night of sleep , a young adult (1) first enters NREM sleep , passes through stages 1 , 2 , 3 and 4 SWS , and then, 60-100 minutes 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 neonates .
- Therefafter , the proportion of REM sleep falls rapidly and plateaus at about 25% until it falls further in old age .
- 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 , dreams are more characteristic of REM sleep

REM Sleep (Paradoxical Sleep)

- In a normal night of sleep, episodes 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 (except eye muscles) is exceedingly depressed .

(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 + BP fluctuations may occur 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 .

Q : If dreams do occur during SWS : how do they differ from those of REM sleep ?

- SWS dreams if they occur , differ from those of REM sleep in that :

(1) REM dreams are vivid dreams ,

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

(3) the dreams of SWS are not remembered , usually , on waking up .

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 .**
- **Sleep is an active field of ongoing research , and many chemicals (e.g., adenosine , orexin etc) are claimed by different sleep researchers to play a role , but what all Researcher Scientists and Medical doctors agree upon are 3 things :**
- **(1) that the neurotransmitter serotonin (produced by the Raphe Nuclei) plays an important role in SWS sleep ,**
- **(2) that Ponto-Geniculo-Occipital circuit plays an important role in generation of REM sleep.**
- **(3) that the hormone Melatonin (released from the Pineal Gland) plays an important role in day-night entrainment of sleep .**

- **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**

- **The above-mentioned transection cuts the nerves going from the inhibitory serotonin-secreting Raphe Nuclei to the Bulboreticular Facilitory Area**
- **(N.B .: the Bulboreticular Facilitory Area + intralaminar thalamic nuclei constitute the reticular activating system , RAS) .**
- **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 and antagonists greatly influence SWS in humans.**
- ✓ **(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**

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- Thanks !