Physiology of Sleep

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عفا الله عنه وعن والديه

-اللهم بارك-

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Objectives

- At the end of this lecture the student should be able to :

(1) appreciate the difference between sleep and coma .

(2) describe the neural basis of sleep .

(2) define what is meant by NREM (non-rapid eye movement,SWS) and REM (rapid eye movement) sleep .

(3) describe how NREM and REM sleep are distributed during a normal night sleep in the average adult human

(4) describe the behavioral and autonomic features associated with NREM and REM sleep .

(5) describe how the EEG , as a physiological tool , is being used to delineate in which stage of sleep (or wakefulness) a person is

(6) appreciate how the total sleep duration and different sleep stages vary with different ages in normal humans .

(7) describe the current theories about the neural basis of sleep .

Resources

(1) Ganong's Review of Medical Physiology , 23rd edition . p 192 .
(2) GuytonTextbooks of Medical Physiology ,11th edition p.739 .

• Q : What is the difference between sleep and coma ?

- Sleep is temporary physiological state of unconsciousness from which the person can be aroused (awaken) by sensory stimuli .
- If we do an EEG in a sleeping person , it shows various types of transients (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 •
- 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 •

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 f requency .
- 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). يبدو كأنه صاح
- because in this type of sleep 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): S 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.

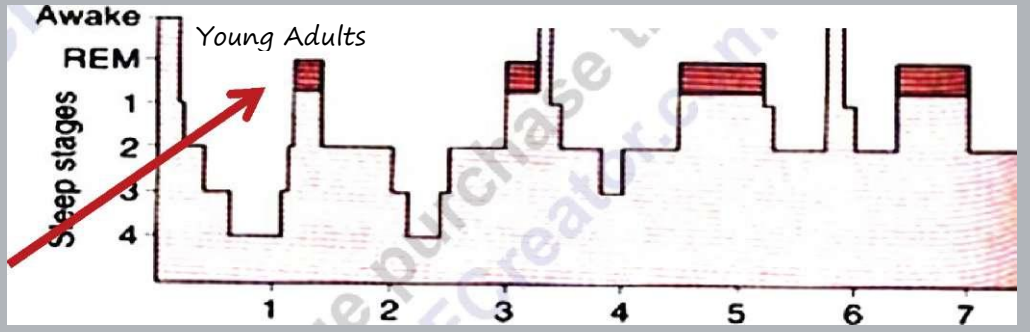
(B) REM Sleep :

- Low-voltage, fast activity كأنه صاح، وهنا تكون الأحلام غالبا

Distribution of Sleep Stages

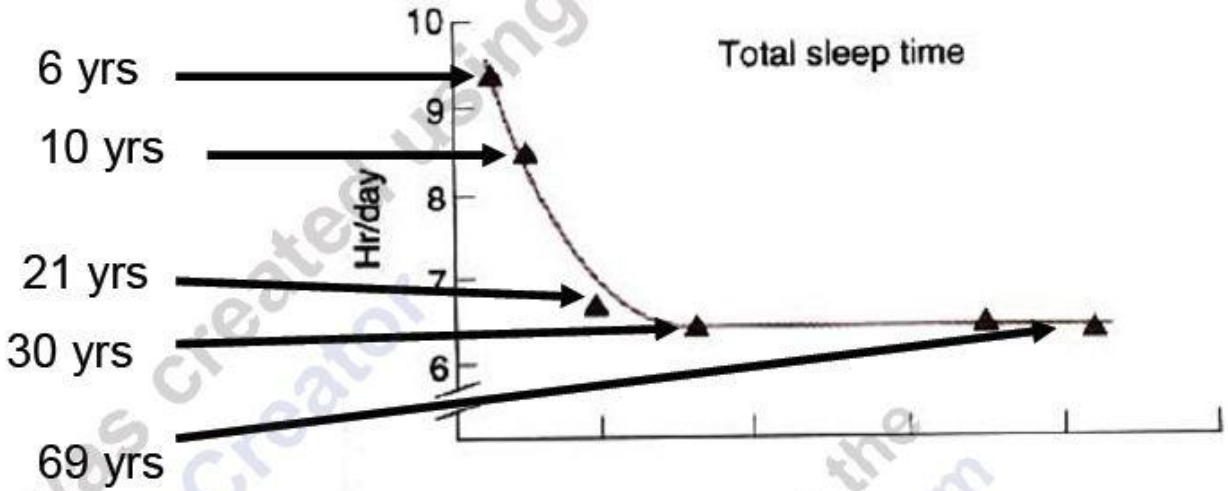
- While SWS occupies most of the total night sleep time (around 75-80n%), it is interrupted by intervening REM sleep periods, approximately every 90 minutes .
- In a typical night of sleep, a young adult (1) first enters NREM sleep, passes through stages 1 , 2 , 3 and 4 SWS, and then, 60-100 minutes 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)

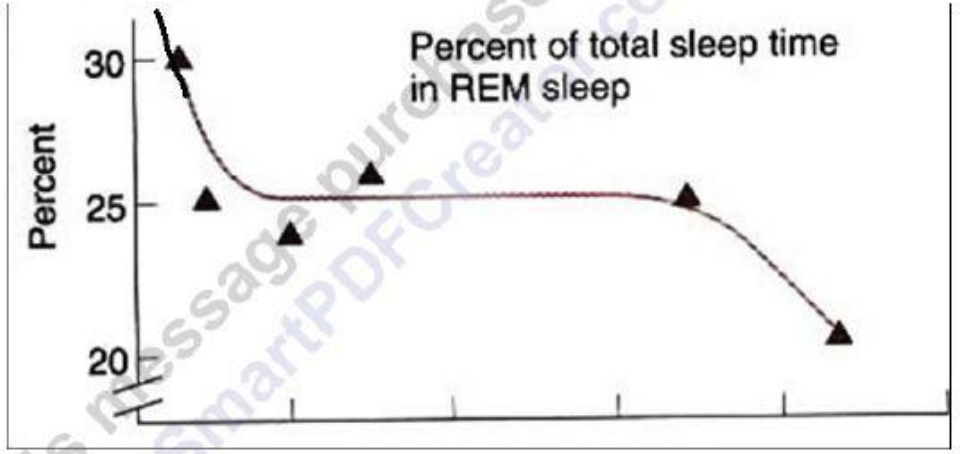
- As the night goes on -> there is progressive reduction in stages 3 and 4 sleep and a progressive increase in REM sleep.



REM sleep periods are shown in red

- In a young adult SWS (NREM sleep) occupies 75-80% of a night sleep time , & REM sleep occupies 20-25 % of the sleep time الصورة الآتية مهمة (المهم فيها أن الصغار نومهم كثير، وعكس الشباب الريم)





- REM sleep occupies 80 % of total sleep time in premature infants , and 50 % in full-term neonates .
- Thereafter , 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 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 episode 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 episodes 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 .

لو كان العكس.. لمثل وطبق حلمه !

(3) Despite the extreme inhibition of the peripheral muscles, Irregular, active bodily muscle movements do occur, BUT without tone!!

(4) Heart rate (HR) and respiratory rate (RR) usually become irregular بسبب الحلم + 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 لأنه عايش في عالمه الداخلي , 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** نائم صاح : the paradox being that although the person is asleep , he may **seem** (because of his eye movements , etc) 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 أما لو صحيته على الريم سيتذكر

Theories of Sleep

- Although several theories of sleep have been proposed , most current evidence is in favour of the following :
- (1) Serotonin, produced by the Raphe Nuclei, induces SWS sleep ,
- (2) The mechanism that triggers REM sleep is located in the Pontine Reticular Formation; & the Ponto-Geniculo-Occipital circuit is instrumental in generation of REM sleep.
- (3) The hormone Melatonin (released from the Pineal Gland) plays an important role in day-night entrainment of sleep.

- **Role of Serotonin & Melatonin in SWS :**

(1) Stimulation of Raphe Nuclei (which are situated in the lower pons & medulla) induces SW

(2) Destruction of the Raphe Nuclei makes the animal sleepless for several days until it dies

(3) Administrations of drugs that block serotonin formation make the animal sleepless for several days.

(4) 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 of the RAS.
- What does this mean? It means that the serotonin-secreting Raphe fibers normally inhibit the Bulboreticular Facilitory Area to produce sleep.

(5) Injections of melatonin induce sleep.

(6) Stimulation of the Suprachiasmal Nucleus (SCN) of hypothalamus by light falling on the retina -> inhibits Melatonin release from Pineal Gland -> produces wakefulness .

Melatonin as Circadian Controller of Sleep-Wake Cycles

- 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) stimulates the Pineal Gland to secrete the hormone melatonin.
- 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.

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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 اليقظة , 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.

- 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 ,

takeover (dominate) -> leading to rapid transition from wakefulness to sleep.

Possible Mechanisms for Genesis ولا أزيرا؟ (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 Reticular Formation .
- These spikes rapidly spread from the Pons to the Lateral Geniculate Nucleus (LGN) & from there the Occipital cortex. Hence they are called "Ponto-Geniculo-Occipital (PGO) spikes " .
- These PGO 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) 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.

مهماااات

- أهم حاجة في الريم البونز وأنه يكون فيه PGO spikes
- أهم حاجة في قسيم الريم السيروتونين
- أهم حاجة في الميلاتونين هو تنظيم نوم الليل والنهار
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- Thanks!