PHYSIOLOGY

SHEET NO. 11

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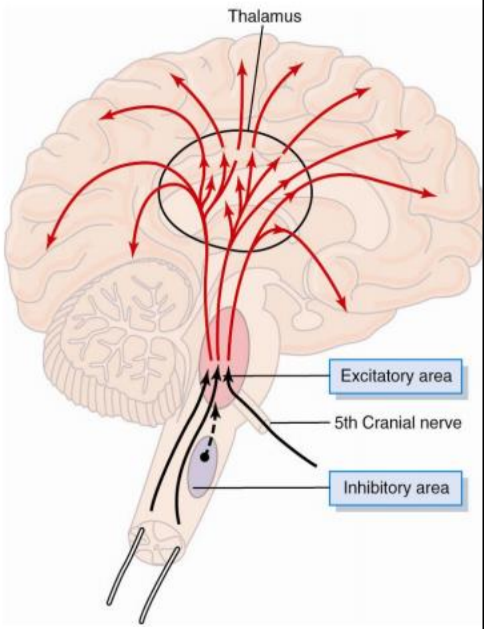
Brain activity and sleep:

Before we start talking about our main topic “sleep”, let me introduce our main character in this wonderful process, please say hi to “**the reticular activating system - RAS**”. This system is concerned mainly with controlling and regulating sleep and wakefulness, it is found in <u>the brain stem reticular formation</u>. And it works with a great group of excitatory and inhibitory areas of the brain.

We need the reticular activating system because the cerebrum requires a constant input to remain active.

Location of excitatory and inhibitory areas of the brain:



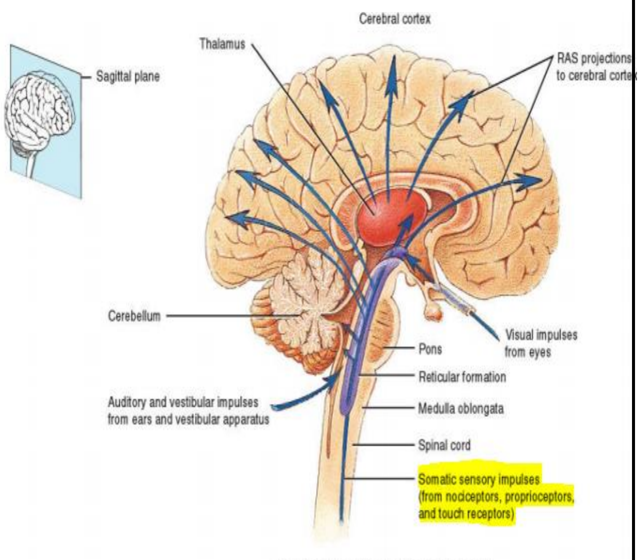
We will talk mainly about one excitatory area and one inhibitory area.

1-Excitatroy signals from the brain stem:

bulboreticular (excitatory/ faciliatory) area: an area found in the midbrain and pons. It sends excitatory signals to the thalamus then to every part of the cortex to awake/ arouse/ activate it. It also sends excitatory signals to the antigravity muscles. It uses the excitatory neurotransmitter **Ach**.

➔ remember that the pontine reticulospinal tract is excitatory to the antigravity muscles and it has a very high basal rate of firing.

➔Please notice that signals from the brainstem activate **wide areas of the cortex (background activation),** but that is not always the case, it may also activate **specific areas to perform discrete tasks,** like activating specific part of the thalamus that will activate specific area in the cerebral cortex.



Sagittal section through brain and spinal cord

Bulboreticular area is excited by signals from the periphery, <u>especially pain signals</u>. That means there are some lower (ascending) fibers that come up **to activate the bulboreticular area**. Examples on these ascending tracts: anterolateral spinothalamic tract (**ALS**), dorsal column medial lemniscus tract (**DCML**). (there are also fibers coming from the cortex downward (descending) **to activate the bulboreticular area** acting as a positive feedback system. Example on these descending tracts: **corticospinal tract**).

For ex walking while you are sleepy will excite this area to increase your alertance level and you wake up!

2- Inhibitory signals from the brainstem:

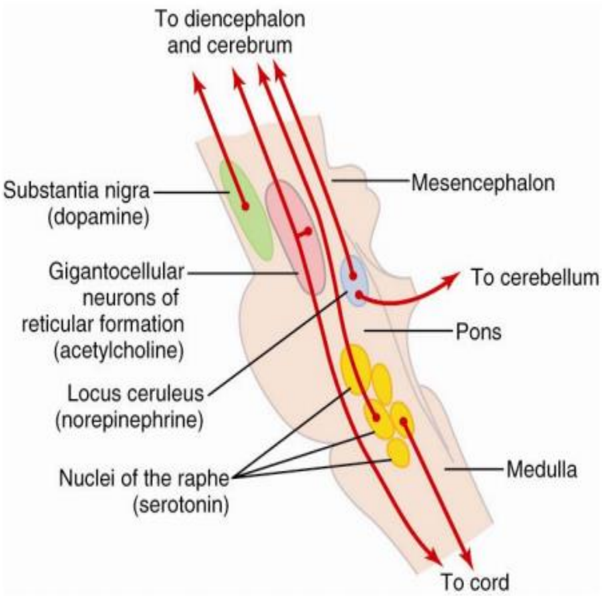
Reticular inhibitory area: an area found in medulla; when activated, **it inhibits the bulboreticular area** and decreases the activity of the cortex. (Unconsciousness :either sleep or coma.)

Let's end this introduction by discussing the neurohormonal control of the brain activity and how it is related to the reticular activating system.

Neurohumoral Control of Brain Activity

1.as we mentioned before, the **bulboreticular area** uses **Ach** as the excitatory neurotransmitter. Another excitatory area, the **Locus coeruleus** uses **norepinephrine** [important in REM sleep, will be discussed later].

2. inhibitory areas like the **raphe magnus nucleus** (part of the endogenous analgesic system) uses **serotonin** as the inhibitory neurotransmitter. While **Substantia nigra** (part of the basal ganglia) uses **dopamine**.



Sleep:

It is a state of unconsciousness from which one can be aroused by sensory stimulus and that is what makes it different from coma in which one cannot be aroused.

We learned that the bulboreticular area can be activated by a lot of somatic sensory impulses; you can awake someone from sleep by touch, pain, temperature and even high sound. And it is activated by the corticospinal tract; you can stay awake if you continue to walk because this will send impulses to the bulboreticular area activating it.

Why do we sleep?

mechanism is unknown.

1.probably an **active** inhibitory process in which the excitatory reticular neurons are inhibited: stimulation of **the raphe nuclei** causes sleep; these nuclei release **serotonin** which is thought to induce sleep.

Some drugs work by inhibiting the release of serotonin causing prolonged wakefulness. Blockade of serotonin formation causes prolonged wakefulness in animals; however, blood levels of serotonin are lower during sleep.

Lesion of raphe nuclei can prevent sleep.

stimulation of other brain regions can also **induce sleep,** examples:

a. **Nucleus of the solitary tract:** there is inter-relation between raphe nuclei and nucleus of the solitary tract; solitary tract stimulation will not produce sleep if the raphe nuclei are destroyed. therefore, solitary tract may be stimulating release of serotonin from the raphe nuclei.

b. **Suprachiasmatic area of the rostral hypothalamus:** through the optic tract it knows if there is light or not, so it is responsible for the circadian rhythm (day-night cycle). It induces sleep by knowing when the night is, and sends to raphe nuclei to secrete serotonin.

c. **Diffuse thalamic nuclei**

2. accumulation of sleep factors [mostly they are peptide]:

a. **muramyl peptide** - found in CSF and urine of animals kept awake for prolonged periods, it will cause sleep when injected into third ventricle of another animal.

b. also a peptide isolated from the blood of sleeping animals.

c. also certain substances extracted from the brain stem [bulboreticular area] of animals kept awake.

Sleep cycle:

no explanation for the sleep - wakefulness cycle

however, there are many theories:

1- sleep cycle may be caused by fatigue of the excitatory areas (keeps a person awake) and this induces sleep while fatigue of the inhibitory areas of the lower brain awakens the person. [and that's probably not true, because those areas don't become fatigued]

2- sleep probably is an **active** process driven by a center below the midpontine level of the brain stem. [peptides that inhibit bulboreticular area and activate reticular inhibitory area]

Physiological Effects of Sleep:

little on the body itself [decrease in sympathetic and increase in parasympathetic tone= decrease heart rate and respiration, decrease in muscle tone, fall in arterial pressure].

profound effects on the brain [lack of sleep can lead to altered mental states, paranoia, and psychosis].

Sleep probably functions to balance the activity of the various areas of the brain, to reset/re-zero/reboot neuronal circuits.

Types of sleep: REM= Rapid Eye Movement

Delta waves Slow wave / deep sleep / non-REM sleep	Beta waves REM sleep / paradoxical sleep Paradoxical means containing two opposite facts or characteristics. In this type of sleep the person is sleepy but his eyes are moving and this opposite to what is known about sleep and that it does not come with movements. متناقض
Makes up 75% of sleep period.	Makes up 25% of sleep period. In children it makes >50% / thought to be important for the growth of CNS. Function of REM sleep is unknown. But it may be important for neuronal development and in testing the cortex to see if it can be brought to activity. May be involved in memory consolidation.
Restful sleep at the beginning of the sleep period. We start with slow sleep. **Takes 60 to 90 minutes** depending on the tiredness. If the person isn't tired = 60min, if the person is tired = 90 min.	Comes after the slow wave sleep/ begin about 60 to 90 minutes after falling asleep and reappear at 60 to 90 minutes interval. **takes 10 to 30 minutes** depending on the tiredness. If the person isn't tired = 30 min, if the person is tired = 10 min.
Last for progressively **shorter** periods of time each time they occur.	Last for progressively **longer** periods of time each time they occur, a few minutes at first, 30 minutes toward the end of the sleep period.
Associated with a **decrease** in vegetative functions. Heart rate, respiratory rate and temperature are **much lower and stable**. (Parasympathetic stimulation that also induces salivation!)	Associated with an increase in cortical activity and metabolism. Heart rate and respiratory rate are **lower but irregular** increasing and decreasing throughout this type of sleep.

*Sleeping when you are tired -> more slow sleep and less REM sleep.

Usually not associated with dreaming; dreams do occur, but they are not remembered. [nightmares/ not vivid/ rational] Why? Because the cerebral cortex isn't active, and for remembering anything the cerebral cortex must be active. And here we come to an important advice, don't stay awake for the late night to continue studying, your cerebral cortex will get tired whenever you feel you're sleepy and will not memorize anything!!	Associated with **active dreaming**; Dreams can be remembered because the cerebral cortex is active, and the evidence is the movement of the eye which is controlled by the cerebral cortex. + vivid/clear, emotional dreams + Genital arousal → You remember the dream with its details "Almost totally inhabited!"
So night walking happens here! Peripheral muscle tone is inhibited but less than in REM sleep ➔ **easier** to arouse by sensory stimulation. = muscle tone is present [toss and turn]	Peripheral muscle tone is inhibited much more than in slow wave sleep [paralysis]. ➔ **difficult** to arouse by sensory stimulation. Physiological arousal threshold **increases.**

Note: Locus coeruleus secretes norepinephrine which is excitatory and important in the REM sleep. *Damage to the locus ceruleus prevents REM sleep*.

EEG Waves / Brain Waves:

Electroencephalogram

electrical recordings [local potentials not action potential] from the surface of the brain characterized as alpha, beta, theta, and delta **depending on the frequency**. frequency is inversely proportional to amplitude.

each functional state of the brain has a characteristic pattern of brain waves (sleep, wakefulness, epilepsy, psychoses, etc.)

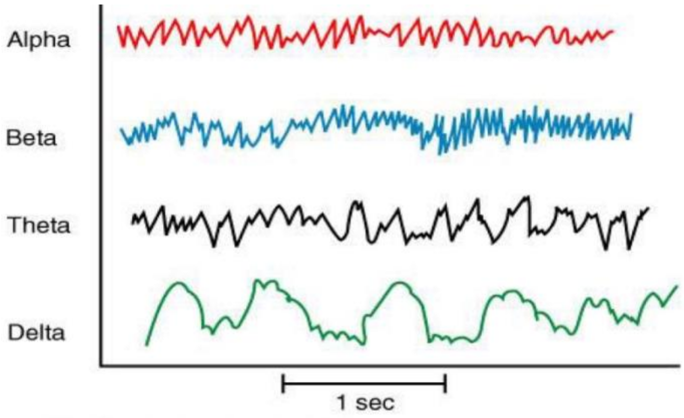
It is difficult to do EEG [we use about >20 electrodes to record potential in different areas] but easy to read it. The opposite is with ECG which is easy to do but difficult to read.

	When alert and relaxed	When doing activities		
	Alpha waves	Beta waves	Theta waves	Delta waves
Frequency	8 -13 Hz	14 - 80 Hz	4 - 7 Hz	below 3.5 Hz
	-mostly occipital cortex but can also be found in frontal and parietal regions as well. -will not occur without cortical connection to thalamus	High rate (frequency) Low amplitude (magnitude)	parietal and temporal regions in children Not in adults; as it may represent an abnormality (eg,sign of epilepsy) if it was observed in a certain part of the brain.	Highest magnitude Slowest rate (Slow)
	quiet **resting** states of cerebrum, <u>they disappear when there is a specific mental activity (opening</u>	occur during **intense mental activity** or	occur during **emotional stress in adults** particularly in response to	occur during deep sleep thought to be activity of the cortex

Hz (hertz) = cycle/second

<u>of the eyes, intense mental concentration, or stress) or during sleep</u>	**stress** [during REM]	**disappointment, frustration, or depression**	independent of signals from lower brain areas

EEG Sleep Patterns:



We can conclude that **deep sleep/ non-REM sleep** is called **slow-wave sleep (SWS)** because <u>delta waves</u> which are the slowest wave can be found in this type of sleep.

Summary ➔ *Desynchronised =there is sleep and some sort of activity

In REM sleep: high-frequency, low-amplitude oscillations/waves. Similar to wakefulness (**beta waves**)= <u>desynchronized EEG pattern</u>. Pontine-Geniculate-Occipital [PGO] waves?

In non-REM (resting) sleep: low-frequency, high amplitude waves (**delta waves**)= <u>synchronized EEG patterns</u>. But alpha and theta activity is also present in the EEG record [why?] because non-REM sleep has 4 stages, in stages 1 and 2: Alpha waves, in stages 3 and 4: delta waves.

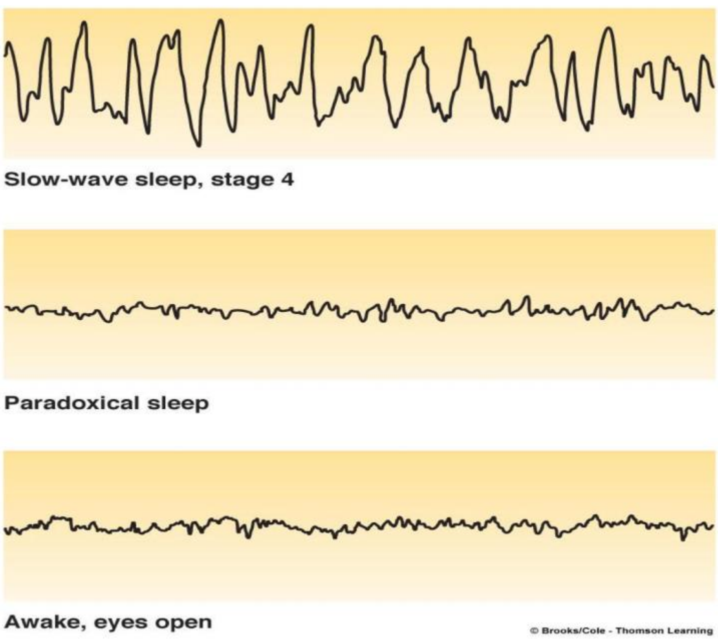
Stages of non-REM sleep:

Stage 1 – eyes are closed, and relaxation begins; the EEG shows **alpha waves**; one can be easily aroused. This is when you put your head on the pillow and start thinking [day dreams أحلام اليقظة]

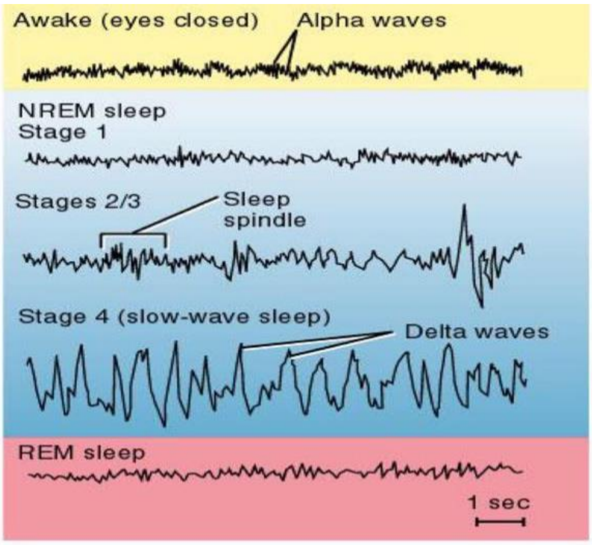
Stage 2 – EEG pattern is **irregular with sleep spindles** (high-voltage wave bursts); arousal is more difficult.

Stage 3 – sleep deepens; **theta and delta waves** appear; vital signals decline; dreaming is common but can't be remembered.

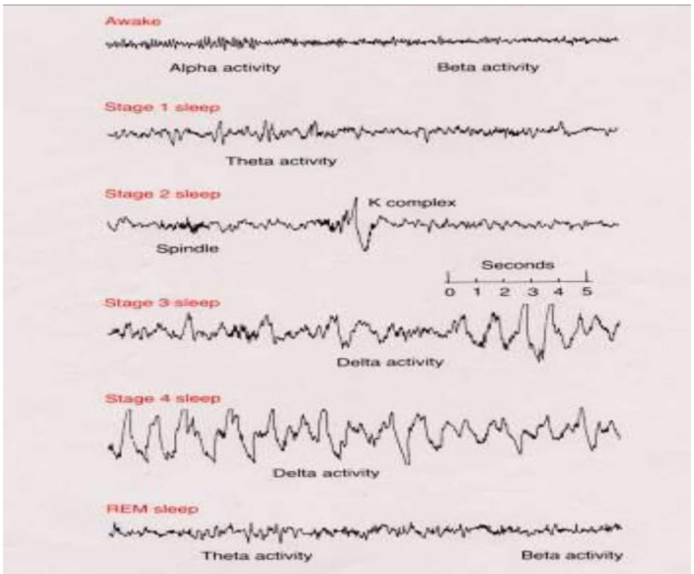
Stage 4 – EEG pattern is dominated by **delta waves;** skeletal muscles are relaxed; arousal is difficult.

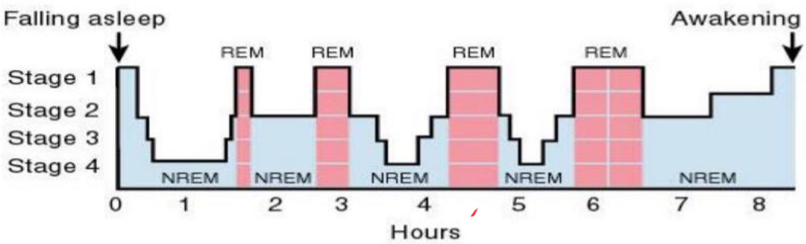


CHARACTERISTIC	TYPE OF SLEEP: Slow-wave sleep	TYPE OF SLEEP: Paradoxical sleep
EEG	Displays slow waves	Similar to EEG of alert, awake person
Motor Activity	Considerable muscle tone; frequent shifting	Abrupt inhibition of muscle tone; no movement
Heart Rate, Respiratory Rate, Blood Pressure	Minor reductions	Irregular
Dreaming	Rare (mental activity is extension of waking-time thoughts)	Common
Percentage of Sleeping Time	80%	20%
Other Important Characteristics	Has four stages; sleeper must pass through this type of sleep first	Rapid eye movements



(a) EEG waves during sleep stages





(b) Pattern of NREM and REM sleep over one sleep period

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Note that REM is progressively increasing .

Quiz

1. An Individual Is displaying rapid eye movement , suppressed muscle tone , and Its difficult to wakeup . When he does awake , he reports dreaming . The cycle of sleep he was experiencing Is ;

A. Slow sleep wave

B. Stage 1 sleep

C. Stage 2 sleep

D. REM sleep

2. This stage of sleep Is characterized by the presence of delta waves :

A. Stage 1 sleep

B. Stage 2 sleep

C. REM sleep

D. Slow wave sleep

3. A transection made through the pons would cut off the influence of the ———— , thereby causing lack of sleep state .

A.ascending reticular activating system

B. Ventrolateral preoptic area

c. Basal forebrain area

D. Raphe nuclei

4. Which one of the following statements regarding REM sleep is true:

A. During REM sleep , ECG patterns show a dominance of delta waves

B. During REM sleep , brain activity and physiological arousal are significantly lees than they are during active wakefulness

C. During REM sleep , ECG patterns show a dominance of theta waves

D. During REM sleep , brain activity and physiological arousal are similar to that of active wakefulness

D, D, A, D

good luck !