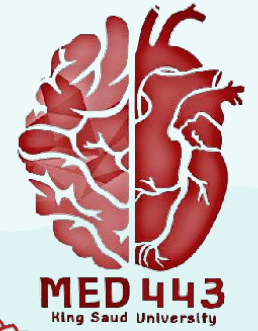
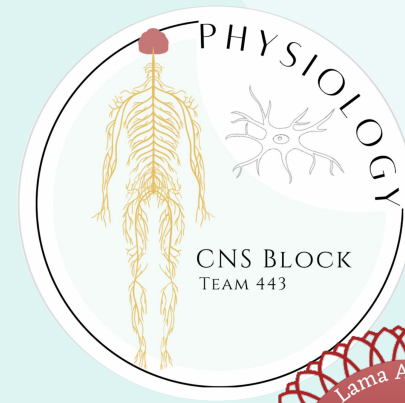




Physiology of sleep

Z z

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Color Index:

- Main text
- **Important**
- Girls Slides
- Boys Slides
- Notes
- Extra

[Editing File](#)



Objectives:

- 1 Explain the difference between sleep and coma.
- 2 Define 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 EEG, as a physiological tool, is being used to delineate in which stage of sleep (or wakefulness) a person is.
- 6 Describe Physiology of Sleep and EEG.
- 7 Appreciate how the total sleep duration and different sleep stages vary with different ages in normal humans.
- 8 Describe the current theories about the neural basis of sleep.



What is sleep?

Sleep: This is the state of unconsciousness from which a subject can be aroused by appropriate sensory or other stimuli.

- Sleep may also be defined as a normal, periodic, inhibition of the reticular Activating system(RAS).

Coma: This is the state of unconsciousness from which a person cannot be aroused by any external stimuli.

Awake: This is the State of readiness/alertness & ability to react consciously to various \ any stimuli.

The difference between coma and sleep is that in coma no external or internal stimuli can wake you up.

Why do we sleep? Female slides

Sleep theory #1: To rest,

- to gain relief from a hyperactive state

Sleep theory #2: To heal,

- Sleep also allows us to heal our bodies ; by helping the immune system (our ability to fight disease), sleep deprivation affect our metabolism(our internal chemical reactions) , it may also help us save energy for when we most need it

Sleep theory #3: To learn,

- sleep may help the human brain get better organized by filing away important memories and discarding unwanted information.

Sleep theory #4: To Dream,

- Dreaming appears to be a by-product of REM sleep. So is it possible that the main reason why we sleep is to dream? If so, why do we dream?

- **Ultimate goal: Sustains our ability to reproduce successfully, by maintaining good health.**



Sleep: introduction

- Transitions between sleep and wakefulness manifest a circadian rhythm consisting of an average of 6–8 h of sleep and 16–18 h of wakefulness.
- Nuclei in both the brainstem and hypothalamus are critical for the transitions between states of consciousness.
- The brainstem ascending arousal system is comprised of groups of neurons that release norepinephrine, serotonin, acetylcholine, or histamine.



Functions of sleep

- 1 Neural maturation.
- 2 Facilitation of learning, memory.
- 3 Cognition.
- 4 Clearance of metabolic waste products generated by neural activity in the awake brain.
- 5 Conservation of metabolic energy.
- 6 Restore natural balances among the neuronal centers.



Theories of sleep

Restoration theory	Preservation and protection theory
<p>-Body wears out during the day and sleep is necessary to put it back in shape \ normal physiological condition.</p> <p>-this is supported by findings that many of the major restorative functions in the body like muscle growth, tissue repair, protein synthesis, and growth hormone release occur mostly, or in some cases only, during sleep.</p>	<p>-Sleep preserve energy and it provides protection \ activity.</p> <p>-for example, both body temperature and caloric demand decrease during sleep, as compared to wakefulness.</p> <p>-This theory has studied from animals. الي يدخلون في بيات شتوي عشان يحفظون طاقتهم</p>



Sleep: Mechanism

Sleep is caused by an **Active Inhibitory Process**.

- **Early theory of sleep:**

The excitatory areas of the upper brain stem, the reticular activating system, simply **became fatigue** during the day activities, waking day and became inactive as a result.

- **Current theory:**

Sleep is caused by an **active inhibitory process**

Stimulation of some specific areas of the brain can produce sleep:

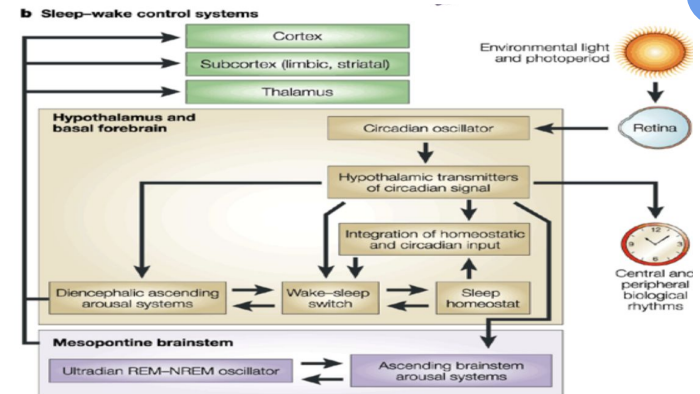
- **Raphe nuclei** in the medulla oblongata: fibers from these raphe neurons secrete serotonin.
 - Drugs that **blocks the formation of serotonin** administered to an animal, the animal cannot sleep for the next several days.
- Serotonin is associated with the production of sleep.**

- Sleep is promoted by a complex set of neural and chemical mechanisms:
- **Daily rhythm** of sleep and arousal suprachiasmatic nucleus of hypothalamus.
 - **Pineal glands** secretion of melatonin (increased melatonin makes you sleepy).
 - **Slow-wave sleep:** Raphe nuclei of the medulla and pons, the secretion of serotonin associated with initiation of sleep.
 - **REM sleep:** Neuron of pons.



Cont...

Consists of two parts:



Mesencephalic part:

Composed of area of **grey matter of midbrain and pons** when this area is stimulated, nerve impulses going to **thalamus and disperse to the cerebral cortex.**

This greatly affects the cortical activity. **Mesencephalic part causes consciousness.**

Thalamic part

Consists of grey matter in the thalamus. When the thalamic part is stimulated, it develop activity in the cerebral cortex. Thalamic part causes **arousal that is awakening from deep sleep** (sensory input, pain, light).

The RAS and cerebral cortex continue to activate each other through a feedback system. the RAS also has a feedback system with the spinal cord.



Humans (normal sleep durations)

Age group	Duration
New born	15-20 hours
Children	10-15 hours
Adults	6-9 hours
Old age	5-6 hours

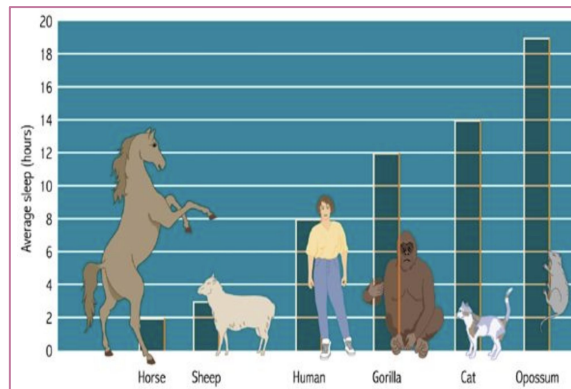


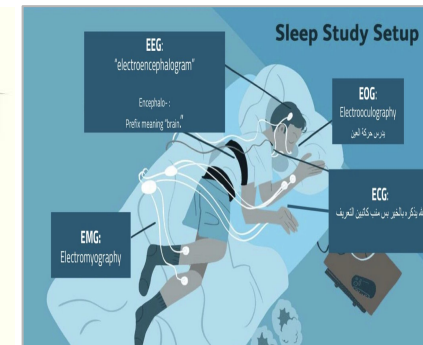
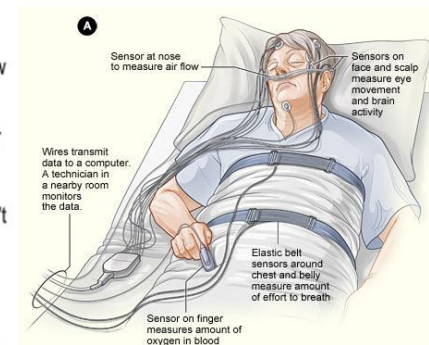
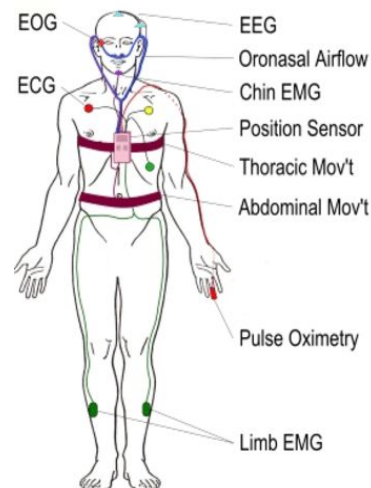
Table 1

Sleep duration recommendations in the US and Canada

National sleep foundation (US)		AASM/SRS (US)
Age group	Recommendation	Age group
Newborns (0-3 months)	14-17 hours	Newborns (0-3 months)
Infants (4-11 months)	12-15 hours	Infants (4-11 months)
Toddlers (1-2 years)	11-14 hours	Toddlers (1-2 years)
Preschoolers (3-5 years)	10-13 hour	Preschoolers (3-5 years)
Children (6-13 years)	9-11 hours	Children (6-12 years)
Teenagers (14-17 years)	8-10 hours	Teenagers (13-17 years)
Young adults (18-25 years)	7-9 hours	Adults (18-60 years)
Adults (26-64 years)	7-9 hours	
Older adults (≥65 years)	7-8 hours	

Polysomnography "sleep study":

Is a test used to diagnose sleep disorders, polysomnography records your brain waves, the oxygen level in your blood, heart rate and breathing as well as eye and leg movements during the study





Sleep Classification

REM (Rapid eye movement) sleep

NREM (NON rapid eye movement)-(SWS) slow wave sleep

There are two types of sleep:

1. Non Rapid Eye Movement Sleep [Slow Wave Sleep- Dreamless]

- EEG waves are generally of low frequency .
- (NREM) sleep is not associated with rapid eye movements .

2. Rapid eye movement sleep [Dreamful].

- this type of sleep rapid eye movements occur (**Neurons of the pons**)

Note: Most sleep during each night is of a slow wave Lasts for 80-90 minutes.

Dreams / nightmare even occur. The difference is that the dreams in slow wave sleep are not remembered but in REM, dreams can be remembered.

Both types alternate with each other.

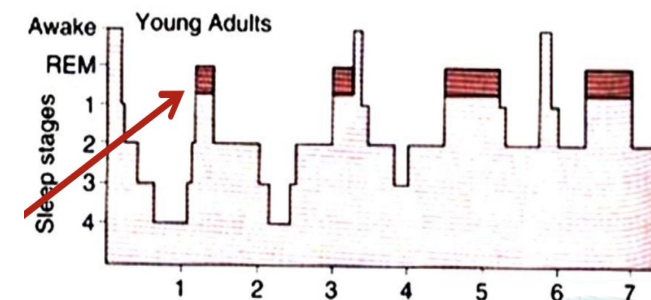
Dr.: NREM has 4 stages while REM has 1 stage. To sum up, the total stages of sleep are 5 stages.

Distribution of Sleep Stages

Female slides

In a typical night of sleep, a young Adult

- SWS occupies most of the total night sleep time (75-80%), it is interrupted by intervening REM sleep periods, every 90 minutes . (REM sleep occupies 20-25% of sleep time.)
- first enters into NREM sleep, passes through stages 1 , 2 , 3 & 4 SWS, then, 60-100 min from sleep onset, goes into the first REM sleep episode.
- This cycle is repeated at intervals of about 90 min throughout the 8 hours of night sleep.
- **There are 4-6 sleep cycles/night** (& 4-6 REM periods per night)
- As the night goes on → there is progressive **reduction in stages 3 & 4 sleep and a progressive ↑ in REM sleep .**

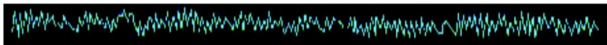



REM sleep periods are shown in red



EEG waves

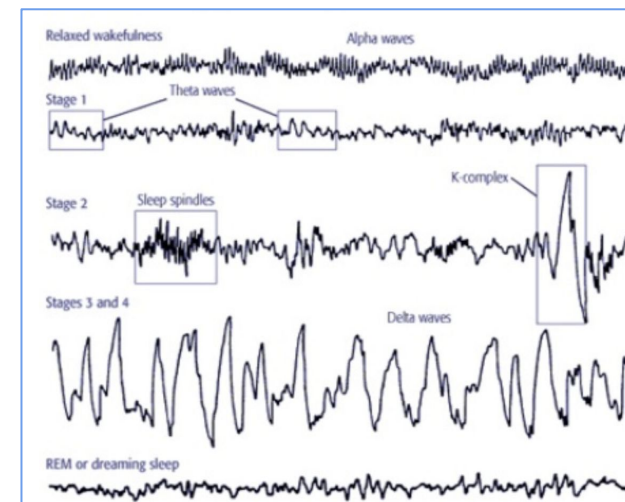
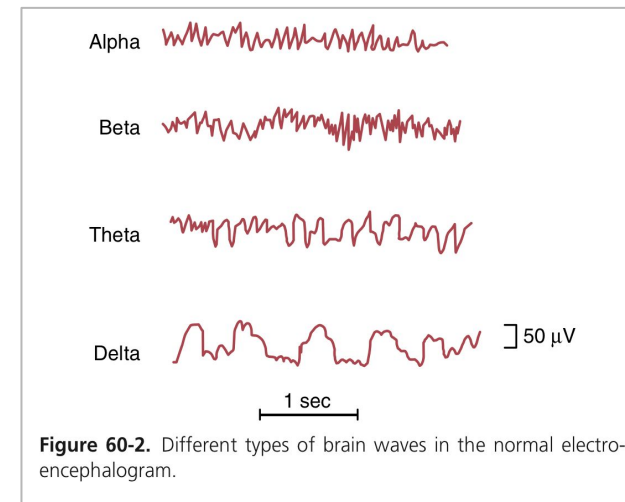
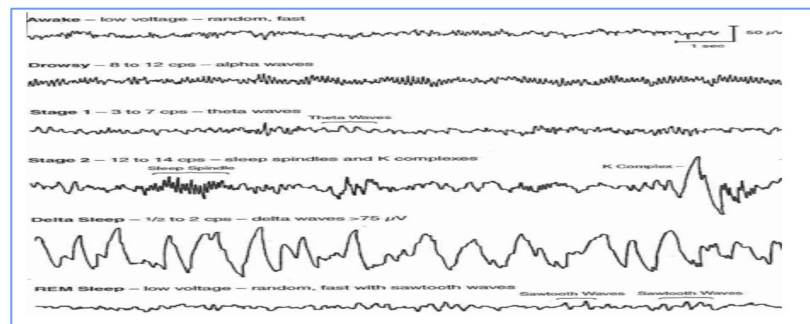
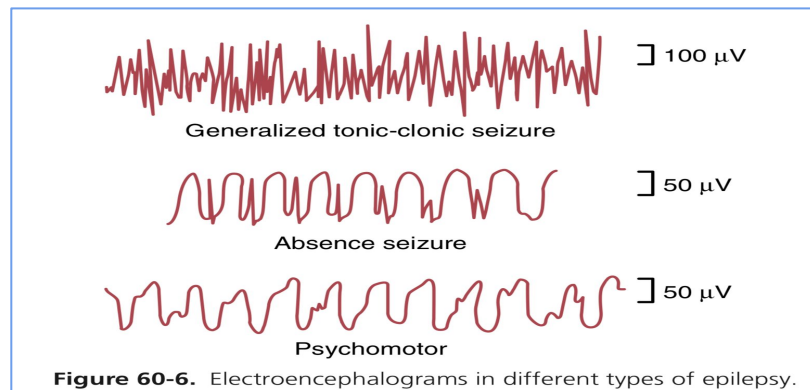
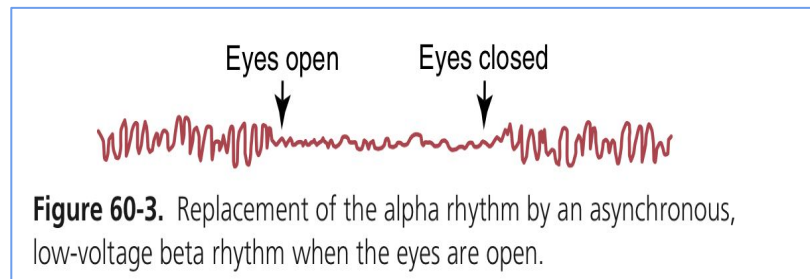
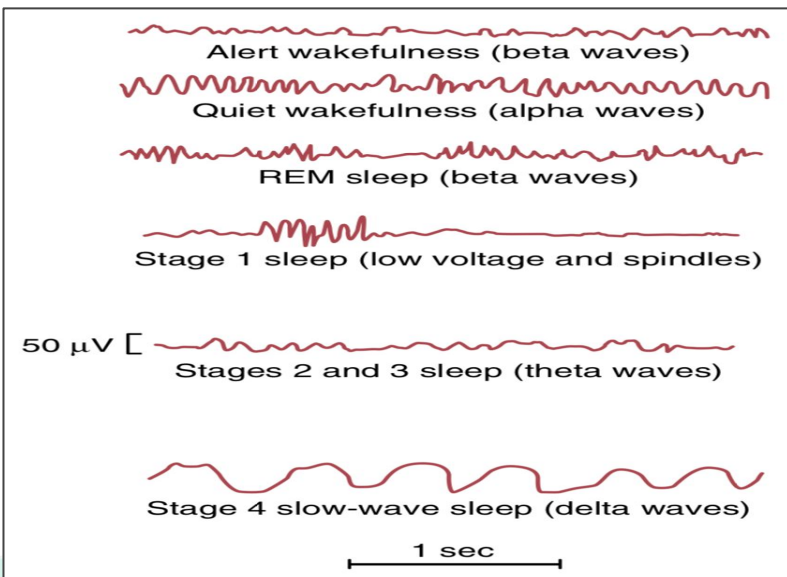
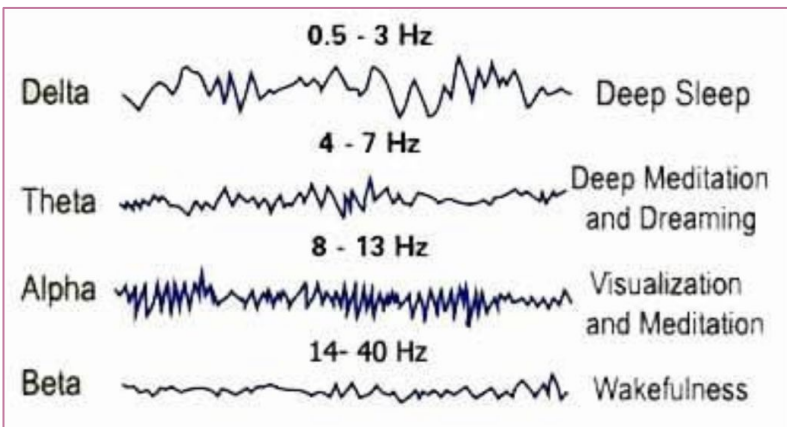
- Stages of Sleep: recorded by EEG

Waves	Frequency	Type of activity	Associated with/occurs
<p>alpha</p> 	8-13hz	Smooth electrical activity	<ul style="list-style-type: none">-associated with a state of relaxation.-awake but non-attentive.-large ,regular Alpha waves.
<p>beta</p> 	14-40hz	Irregular electrical activity	<ul style="list-style-type: none">-associated with a state of arousal.-awake and attentive-low amplitude, fast,irregular Beta waves.
<p>theta</p>	4-7hz	-	<ul style="list-style-type: none">-occurs intermittently during early stages of slow wave sleep, and REM sleep.
<p>delta</p>	less than 4hz	Regular synchronous electrical activity (synchronous means all together so these waves will join together to form a big wave)	<ul style="list-style-type: none">-Occurs during the deepest stages of slow-wave sleep.



EEG waves

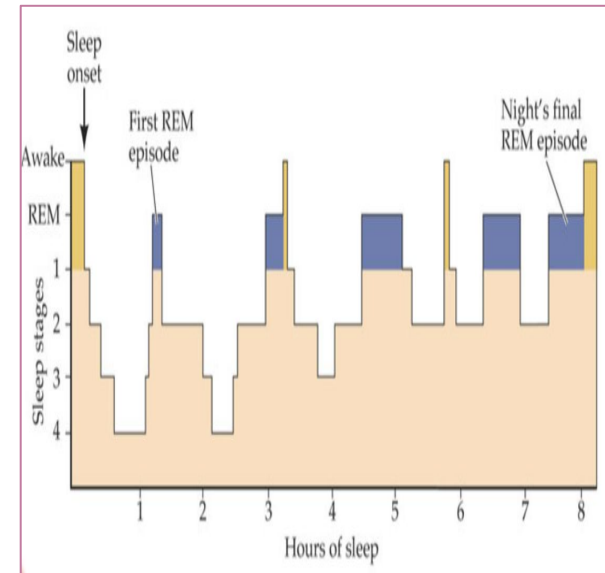
from Beta to Delta the Amplitude of the waves increase





REM Sleep (Paradoxical sleep) (Desynchronized sleep)

- In a normal night of sleep, episodes (bouts) of REM sleep lasting for 5 to 30 minutes usually appear on the average after every 90 minutes (The first such period occurring 80-100 minutes after the person falls asleep)
- REM sleep is not as restful as SWS.
- When the person is extremely sleepy, each episode of REM sleep is short (the duration of each bout of REM is very short), and it may even be absent.
- Conversely, as the person becomes more rested through the night, the durations of the REM episodes (bouts) increase.



- Possible cause of REM sleep: it's not understood why slow wave sleep is broken periodically by REM sleep.

- Drugs that mimic the action of acetylcholine increase the occurrence of REM sleep.

*REM sleep also called dreamful sleep.

- It has been postulated that the large acetylcholine secreting neurons in the upper brain stem reticular formation might through their extensive efferent fibers activate the brain, even though the signals are not channeled appropriately in the brain to cause normal conscious that is characteristic of wakefulness.

- This mechanism theoretically could cause the excess activity that occurs in certain brain regions in REM sleep.



Stages of slow-wave(non rapid eye movement) sleep

stage	Description	EEG Findings
1	<ul style="list-style-type: none">• This is an initial stage between awakening and sleep• It normally lasts from 1-7 min• The person feels relaxed with eyes closed• If awakened, the person will frequently say that he has not been sleeping	Alpha waves diminished and Theta waves appear on EEG.
2	<ul style="list-style-type: none">• This is the first stage of true sleep• The person only experiences only light sleep• It's a little harder to awake the person• Fragment of a dream may be experienced• Eyes may slowly roll from side to side	Shows sleep spindles (sudden,sharply pointed waves) 12-14 hz (cycles/second).
3	<ul style="list-style-type: none">• This is the period of moderately deep sleep• The person is very relaxed• Body temperature begins to fall, B.P decreases• Difficult to wake the person up• This stage occurs about 20-25 min after falling asleep	Shows mixture of sleep spindles and delta waves.
4	<ul style="list-style-type: none">• Deep sleep starts person become fully relaxed, Respond slowly if awakened	Dominant by delta waves.



Cont...

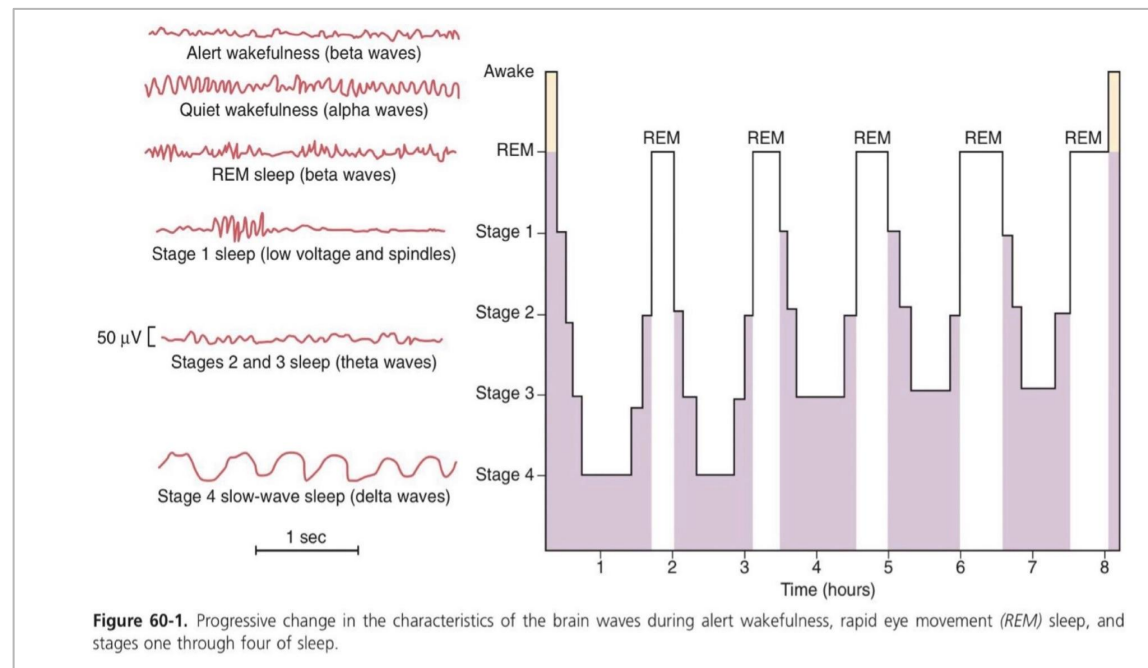
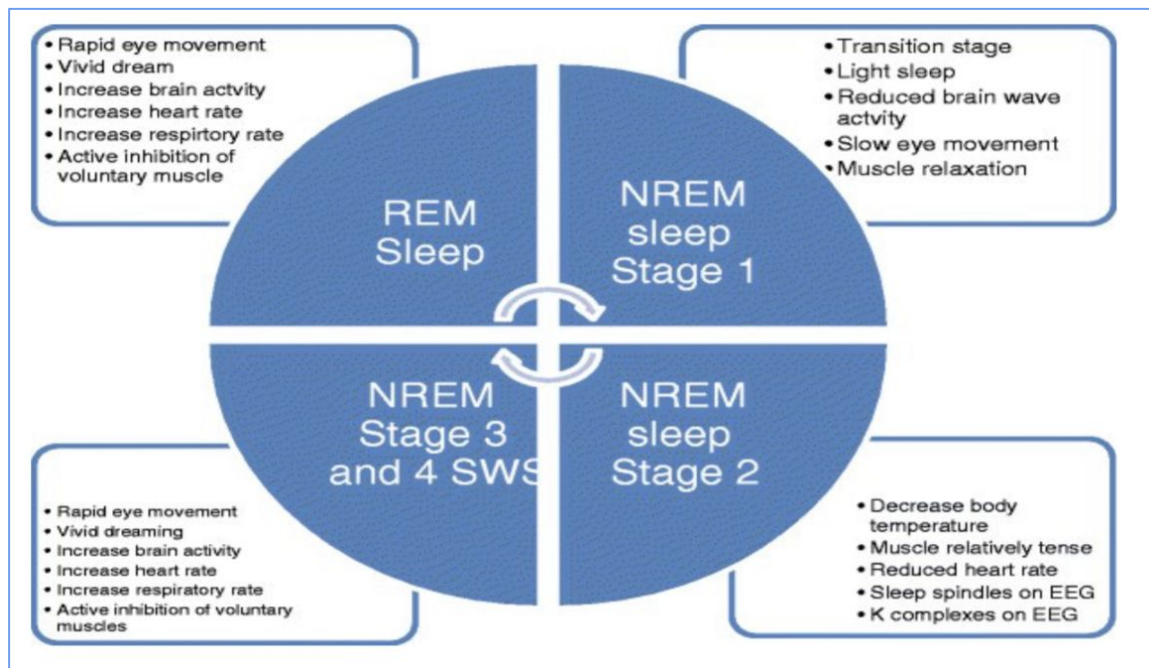


Figure 60-1. Progressive change in the characteristics of the brain waves during alert wakefulness, rapid eye movement (REM) sleep, and stages one through four of sleep.



Characteristics of REM sleep:

- There are rapid eye movements
 - Muscle tone throughout the body (except eye muscles) is exceedingly depressed
 - Active form of sleep associated with dreaming
 - Difficult to arouse by sensory stimuli.
 - Heart rate and respiration become irregular which is characteristic of a dream state.
 - Brain is highly active in REM sleep and brain metabolism may be increased by 20%.
 - EEG.: Pattern shows brain wave of wakefulness, REM sleep is a type of sleep in which the brain is quite active, but this brain :
 - is not aware cut-off the external world.
 - its activity is not channeled into purposeful external motor activity.
- REM sleep occupies 80% of total sleep time in premature infants & 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 & stage 4 sleep than adults.



Physiological Changes in Sleep



CVS: Pulse Rate, cardiac output, blood pressure & vasomotor tone are decreased but the blood volume is increased because of reabsorption (fluids enter circulation)



Respiration: Tidal volume & respiratory rate are decreased. BMR is decreased 10-15%.



Urine volume: Decreased



Secretions: Salivary/lacrimal secretions are reduced, gastric/sweat secretions are increased. Due to digestion



Reflexes: Superficial reflexes are unchanged except plantex reflex, but Deep reflexes are reduced.



Muscles: Relaxed

-Effects produced by awakening after 60-100 Minutes:

1. Equilibrium disturbed.
2. Neuromuscular junction fatigue.
3. Threshold for pain is lowered.
4. Some cells shrink.

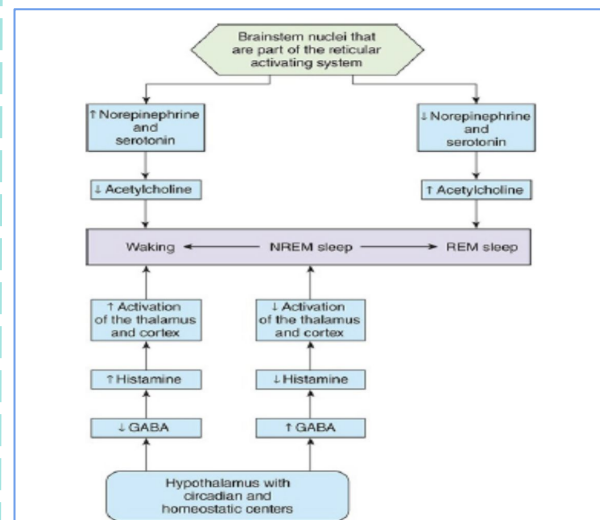


FIGURE 14-4 A model of how alternating activity of brainstem and hypothalamic neurons may influence the different states of consciousness. In this model, wakefulness and REM sleep are at opposite extremes. When the activity of norepinephrine- and serotonin-containing neurons (locus coeruleus and raphe nuclei) is dominant, there is a reduced level of activity in acetylcholine-containing pontine neurons leading to wakefulness. The reverse of

-Growth hormone, melatonin, cortisol, leptin, and ghrelin levels are highly correlated with sleep and circadian rhythmicity.



Properties of Slow wave and REM Sleep

Properties		Slow wave sleep	REM sleep
Autonomic activities	Heart rate: →	Slow decline	Variable with high bursts
	Respiration: →	Slow decline	Variable with high bursts
	Thermoregulation: →	Maintained	Impaired
	Brain temperature: →	Decreased	Increased
	Cerebral blood flow: →	Reduced	High
Cognitive State	—	Vague thoughts	Vivid dreams, well organized
Hormone secretion	Growth hormone: secretion →	High	Low



Cont...

Properties		Slow wave sleep	REM sleep
Skeletal muscular system	Postural tension: →	Progressively reduced	Eliminated
	Knee jerk reflex: →	Normal	Suppressed
	Phasic twitches: →	Reduced	Increased
	Eye movements: →	Infrequent, slow, uncoordinated	Rapid, coordinated
Neural firing rates	Cerebral cortex (sustained) activity: →	Many cells reduced and more phasic	Increased firing rates, tonic
Events related potential	Sensory-Evoked: →	Large	Reduced



Mechanisms of Sleep

Although several theories of sleep have been proposed, most current evidence is in favor of the following:



Serotonin, produced by **Raphe Nuclei** which is in the **medulla oblongata**, induces **SWS Sleep**.



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.



Melatonin (released from Pineal Gland) plays a role in day-night alteration of sleep. (also given as supplements to help induce sleep)



Role of Serotonin & Melatonin in SWS

1 Raphe Nucleus (Serotonin)

- Stimulation of Raphe Nuclei (**in the lower Pons & Medulla**) Induces SW.
- Destruction of **Raphe Nuclei** renders the animal Sleepless for several days until it dies.
- Administration of drugs that **block Serotonin formation** make the animal sleepless for several days.
- Transecting the brainstem at the level of **mid pons** of an animal, leaves the animal in a state of intense wakefulness for a period of days.
- The Transection cuts the nerves going from the inhibitory Serotonin-Secreting Raphe Nuclei to the Bulboreticular Facilitatory area of the RAS, **indication** that the Serotonin-Secreting Raphe fibers normally **Inhibit** the Bulboreticular Facilitatory area to produce sleep.

2 Melatonin

- **Injection of melatonin** Induce sleep.
- Stimulation of the **supra-Chiasmal Nucleus (SCN)** of Hypothalamus **By light** falling on the retina **Inhibits Melatonin release** From Pineal Gland & produce wakefulness. (that's why we sleep in the dark)



Physiological mechanisms of sleep & waking

1

Acetylcholine

- One of the most important neurotransmitters involved in arousal.
- Two groups of acetylcholinergic neurons are located in **Pons & basal forebrain**

2

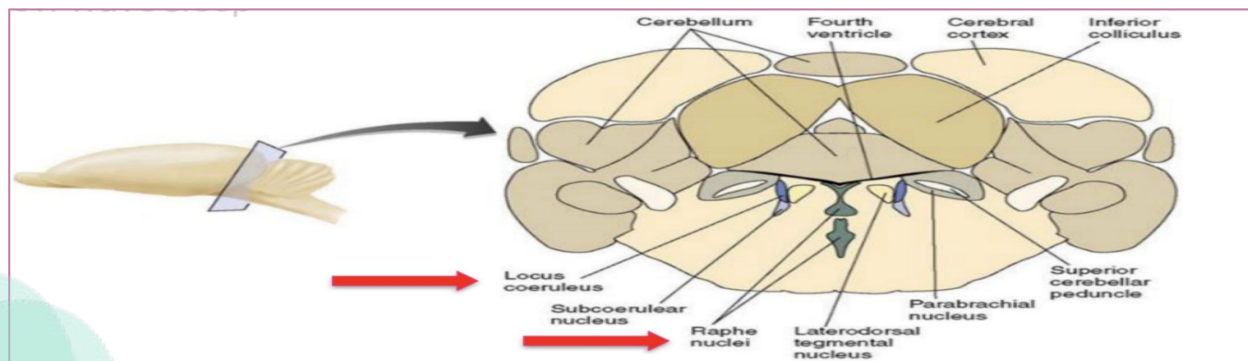
Muramyl peptide

- induces sleep



Neural Activity of Neurotransmitter Systems During Sleep and Arousal

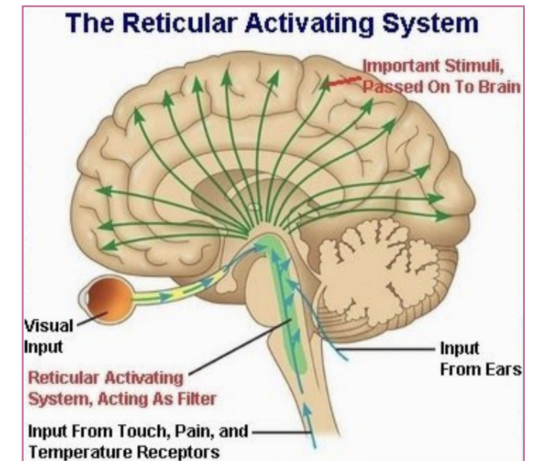
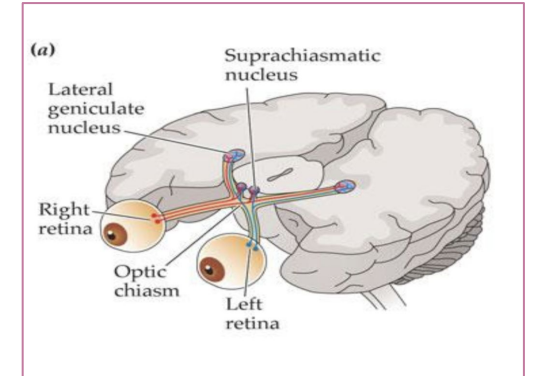
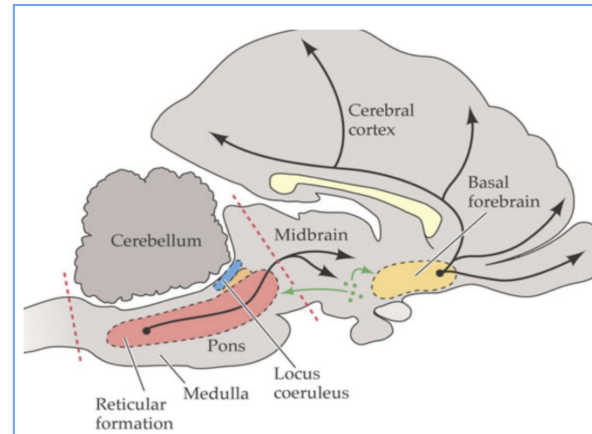
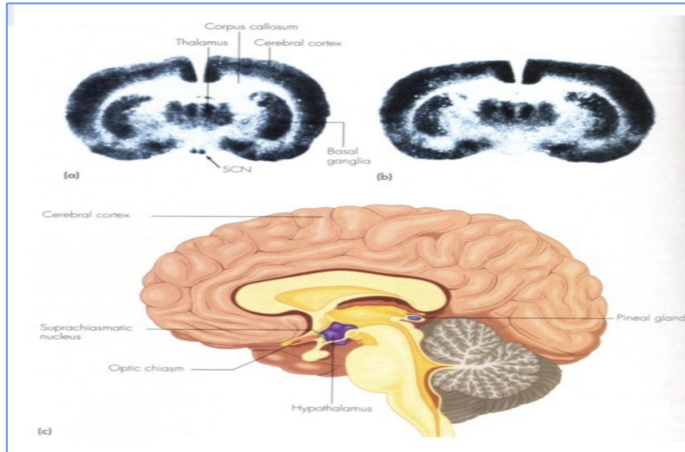
Neurotransmitter	Site of cell bodies	Activity During		
		Wakefulness	SWS	REM
Serotonin	Raphe Nuclei	High	Low	Very Low
Norepinephrine	Locus Coeruleus	High	Low	Very Low
Acetylcholine	Brainstem	High	Low	High





The Reticular Activating System

- **RAS:** Is a diffuse network of nerve pathways in the brainstem connecting the spinal cord, cerebrum, cerebellum and mediating overall level of consciousness.
- Normal sleep is under control of the reticular activating system in the upper brainstem and diencephalon





Sleep disorders \ burden

-70 million people in the US suffer from sleep problems [50% have chronic sleep disorder]

Insomnia = 30 million (most common)

sleep apnea= 18 million

Narcolepsy= 250,000 Americans have

Motor Car Accidents= 100,000

traffic fatalities =1500 drowsy driving/annum (Per year)

-Approximately \$16 billion annually the cost of healthcare in USA & result in \$50 billion annually in lost productivity.

- 1 Disorder of slow wave sleep:
- 1- **Sleep talking / sleep walking**
[common in children]
 - 2- **Night tremors:** Are seen in III, IV stage of slow wave sleep [common in children].
 - 3- **Night terrors:** Sudden arousal from sleep and intense fear accompanied by physiological reactions (e.g., rapid heart rate, perspiration) that occur in SWS.

- 2 Disorder of REM sleep:
- 1- **Nightmare:** Frightening dream (Awake from REM).
 - 2- **Sleep Paralysis:** Subject awake but unable to speak or move.
 - 3- **Sleeping Sickness.**

3 **Insomnia:**
inability to sleep
Causes stress, affect social life

4 **Drug dependency insomnia:**
An insomnia caused by the side effect of ever increasing doses of sleeping medications

5 **Somnolence:**
Extreme sleepiness



Cont...

6

Somnambulism:
Walking during sleep

7

Sleep apnea:
Cessation of breathing while sleeping (failure to breathe when asleep) Especially in obese patients, causes heart and other serious diseases

8

Narcolepsy:

A sleeping disorder characterized by periods of **irresistible sleep**, attacks of **cataplexy**, **sleep paralysis**, and **hypnagogic hallucinations**.

Excessive sleepiness may occur while talking, sitting, decreased ability to regulate sleep.

Female slides

Symptoms of Narcolepsy

1- Sleep attack	2- Cataplexy	3- Sleep paralysis
An irresistible urge to sleep during the day, after which the person awakes feeling refreshed.	Complete paralysis that occurs during walking .	Paralysis occurring just before a person falls asleep .



TEST YOURSELF !

From team 439

1- State of unconsciousness from which a subject can be aroused by appropriate sensory or other stimuli.

A) Coma

B) Sleep

C) Cataplexy

D) Awake

2- Which of the following is true about REM sleep?

A) High muscle tone

B) Increased phasic twitches

C) Occurrence is directly proportional with fatigue

D) Normal heart rate

3- which of the following is associated with a state of arousal?

A) Beta

B) Alpha

C) Theta

D) Delta

4- Stimulation of the Supra-chiasm nucleus of hypothalamus by light falling on the retina inhibits which of the following?

A) Serotonin

B) Acetylcholine

C) Melatonin

D) Muramyl peptide



SAQ

1- what is the difference between sleep and coma ?

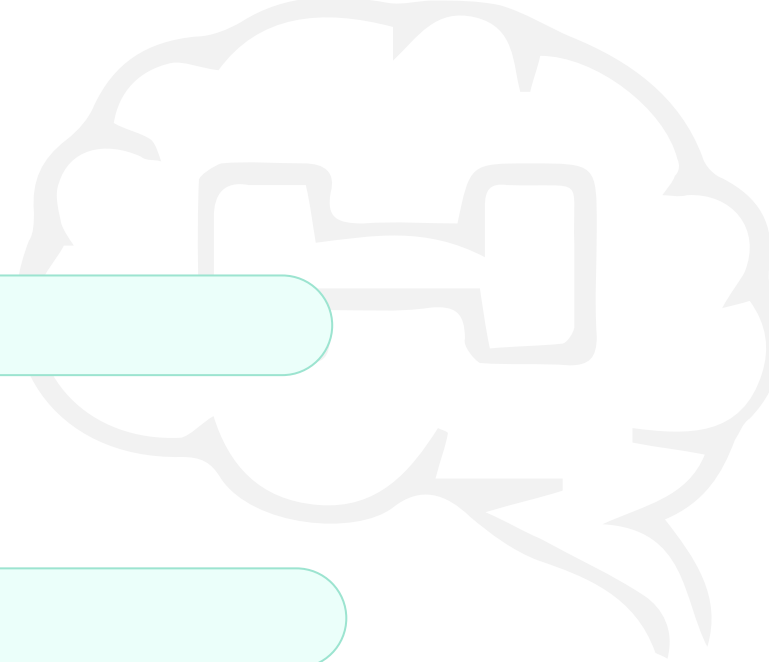
In slide 3

2- define NREM and REM sleep ?

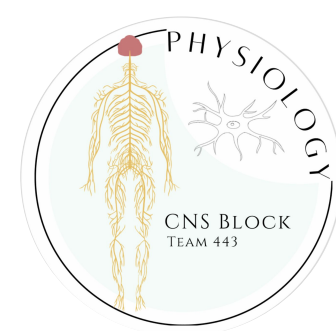
In slide 9

3- mention some of the physiological changes in sleep?

In slide 16



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💡 Special Thanks to Physiology Team441
💡 Team logo and design was done by Rafan Alhazzani
💡 Thanks to ALEEN ALKULYAH for Helping with the design!

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