Physiology Team 439

MED439
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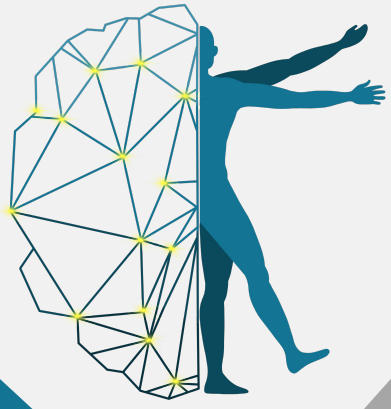


Physiology of Sleep

Objectives:

- Explain the difference between sleep and coma.
- Define NREM and REM sleep.
- Describe how NREM and REM sleep are distributed during a normal night sleep in the average adult human.
- Describe the behavioral and autonomic features associated with NREM and REM sleep.
- Describe EEG, as a physiological tool, is being used to delineate in which stage of sleep (or wakefulness) a person is.
- Appreciate how the total sleep duration and different sleep stages vary with different ages in normal humans.
- Describe the current theories about the neural basis of sleep.

Color index:

- Important.
- Girls slide only.
- Boys slide only.
- Dr's note.
- Extra information.

Editing File

WHAT IS SLEEP?

1

Sleep:
State of unconsciousness from which a subject **can** be aroused by appropriate sensory or other stimuli.also can be defined as a normal, periodic, inhibition of the reticular Activating system.

2

Coma:
State of unconsciousness from which a person **cannot** be aroused by any external stimuli.

3

Awake:
State of readiness/alertness & ability to react consciously to various stimuli.

The difference between coma and sleep is, in sleep state motor/sensory stimuli can wake you up, in coma no external or internal stimuli can't

WHY DO WE SLEEP ? Girls slides only

Females doctor said "just read it"

01

To Rest
To gain relief from this hyperactive state.

02

To Heal
Sleep also allow us to heal our bodies ; the immune system (our ability to fight disease) sleep deprivation affect our metabolism (our internal chemical reactions). It may help us save energy for when we most need it.

03

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

04

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

Theories of sleep

1

Restoration theory:

-Body wears out during the day and sleep is necessary to put it back in shape.

-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.

2

Preservation & protection theory:

-Sleep preserve energy and it provides protection.

-For example, both body temperature and caloric demand decrease during sleep, as compared to wakefulness.

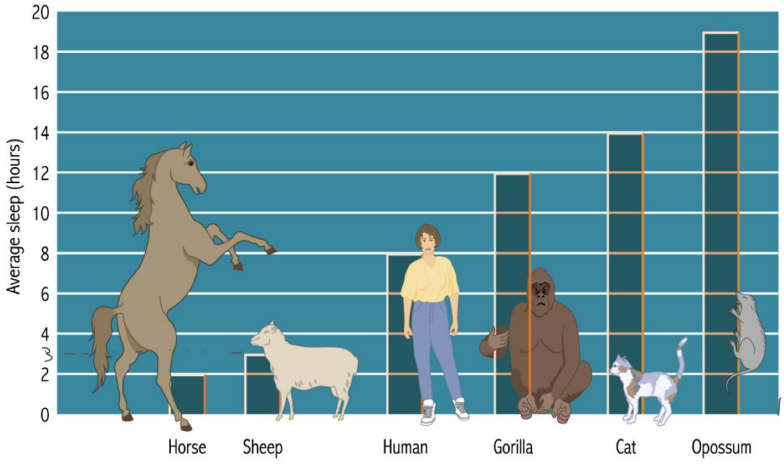
-This theory has studied from animal اللي يدخلون في بيات شتوي، عشان يحفظون طاقتهم

Ultimate goal of sleep :

Sustains our ability to reproduce successfully, by maintaining good health.

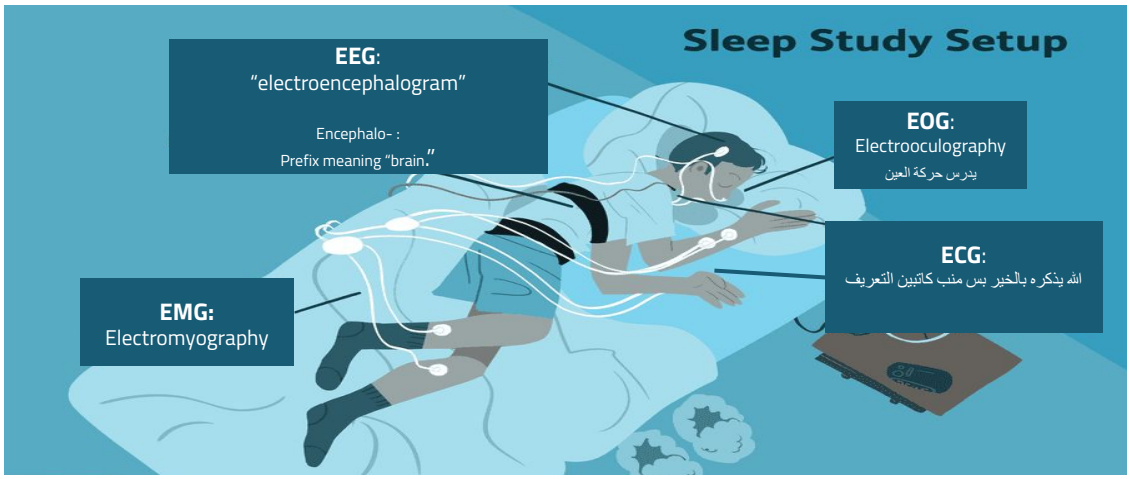
Humans (Sleep Duration)

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



EEG waves

Waves	Frequency*	Type of activity*	Associated with / occurs	
Alpha	8-13 hz	Smooth electrical activity	-Associated with a state of relaxation. -Awake, but non-attentive, large, regular	Alpha 
Beta	14-40 hz	Irregular electrical activity	-Associated with a state of arousal. -Awake and attentive - low amplitude, fast, irregular	Beta 
Theta	4-7 hz	-	Occurs intermittently during early stages of slow wave sleep and REM sleep.	Theta 
Delta	Less than 4 hz	Regular, synchronous(synchronous mean -all together- so these wave will compound together > big waves) electrical activity	Occurs during the deepest stages of slow-wave sleep.	Delta 

*Girls slides only

Sleep classification

NREM
(non-rapid eye movement)

you can dream in NREM but you can't remember the dream

REM
(rapid eye movement,Paradoxical Sleep)

-Also known as **(SWS) slow wave Sleep**
-EEG waves are generally of low frequency .
-Non-Rapid Eye Movement (NREM) sleep is not associated with rapid eye movements .
- SWS occupies most of the total night sleep time (75-80%), it is interrupted by intervening REM sleep periods,~ every 90 minutes .
-dreams in slow wave sleep are not remembered

In a typical night of sleep, a young Adult:
-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 .

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

Possible Cause of REM Sleep:
-It is 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.
-It has been postulated that the large acetylcholine secreting neurons in the upper brain stem reticular formation might, through their extensive efferent fibers, activate brain, even though the signals are not channeled appropriately in the brain to cause normal conscious awareness that is characteristic of wakefulness.
-This mechanism theoretically could cause the excess activity that occurs in certain brain regions in REM sleep.
-REM occupies (20-25%) sleep periods.
-In a normal night of sleep, episodes of REM sleep lasting 5 to 30 minutes usually appear on the average every 90 minutes.
-The first such period occurring 80-100 minutes after the person falls asleep.
-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
-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.
-dreams in REM can be remembered.

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

Stage	Description	E.E.G.findings
1	• This is an initial stage between awakening and sleep. • It normally lasts from 1-7 minutes • the person feels relaxed with eye closed. • If awakened, the person will frequently say that he has not been sleeping.	Alpha waves diminish and Theta waves appear on EEG.
2	• This is the first stage of true sleep. • The person experiences only light sleep. • It is a little harder to awake the person. • Fragment of dream may be experienced. • Eyes may slowly roll from side to side.	Shows sleep spindles (sudden, sharply, pointed waves 12-14-Hz (cycles/sec).
3	• This is the period of moderately deep sleep. • The person is very relaxed. • Body temperature begin to fall. • B.P decreases. • Difficult to awaken the person. • This stage occurs about 20-25 minutes after falling asleep	Shows mixture of sleep spindles and delta waves.
4	• Deep sleep starts Person become fully relaxed. • Respond slowly if awakened.	Dominated by Delta Waves.

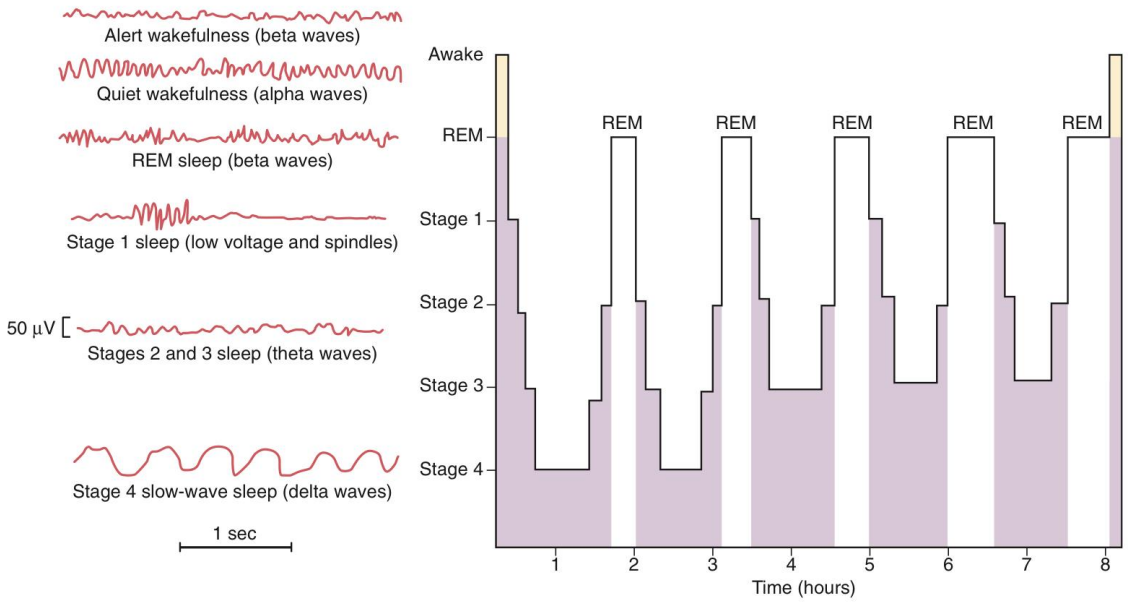
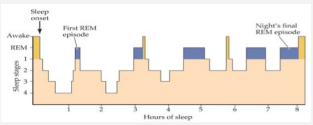


Figure 60-1. Progressive change in the characteristics of the brain waves during alert wakefulness, rapid eye movement *(REM)* sleep, and stages one through four of sleep.

Continuation of **REM 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.



Note about REM sleep:

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.

Physiological changes in sleep

CVS: Pulse Rate, cardiac output, blood pressure & vasomotor tone are decreased but the blood volume is increased.

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

*Basal Metabolic Rate

Urine volume: decreased.

Secretions: **Salivary/lacrimal** secretions are **reduced**, ***gastric/sweat*** secretions are ***increased***.

Muscles: Relaxed.

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

-**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.

Properties of Slow Wave and REM sleep

Properties		Slow wave sleep	REM sleep
Autonomic activities (prof Meo: Im not expecting you to memorize more than 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
Skeletal muscular system	Postural tension: →	Progressively reduced	Eliminated
	Knee jerk reflex: →	Normal	Suppressed
	Phasic twitches: →	Reduced	Increased
	Eye movements: →	Infrequent, slow, uncoordinated	Rapid, coordinated
Cognitive State	-	Vague thoughts	Vivid dreams, well organized
Hormone secretion	Growth hormone: secretion →	High	Low
Neural firing rates	Cerebral cortex (sustained activity): →	Many cells reduced and more phasic	Increased firing rates, tonic
Events related potential	Sensory-Evoked: →	Large	Reduced

Words written in RED were focused on by Females Dr

Mechanism of Sleep

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

1. **Serotonin**, produced by Raphe Nuclei which is in the **medulla oblongata** , induces **SWS.**
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. **Melatonin** (released from Pineal Gland) plays a role in day-night alteration of sleep. (also given as supplements to help induce sleep)

Physiological Mechanisms of Sleep & Waking:

1

Raphe Nucleus (Serotonin):

- Stimulation of Raphe Nuclei (in the lower **Pons & Medulla**) Induces SWS.
- 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 , leave 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, **which indicates** 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 and therefore induces wakefulness. (that's why we sleep in the dark)

3

Acetylcholine:

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

4

Muramyl peptide:

Induces sleep.

This slide is a bit similar to the previous slide with a few more additional notes from males slides.

Sleep: Mechanism

1

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

Early theory of sleep:

The excitatory areas of the upper brain stem, the reticular activating system (RAS), 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

2

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 block 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.**

3

Sleep is promoted by a complex set of neural and chemical mechanisms:

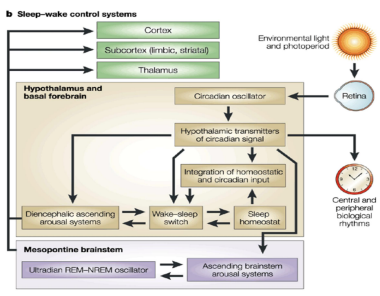
- Daily rhythm of sleep and arousal suprachiasmatic nucleus of hypothalamus.
- **Pineal glands** secretion of melatonin (increased melatonin makes you sleepy).
- **SWS:** Raphe nuclei of the medulla and pons, the secretion of serotonin associated with initiation of sleep.
- **REM sleep:** Neuron of pons.

Mesencephalic part:

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

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

Consists of two parts:



Thalamic part:

Consists of grey matter in the thalamus. When the thalamic part is stimulated, it develop activity in the cerebral cortex.

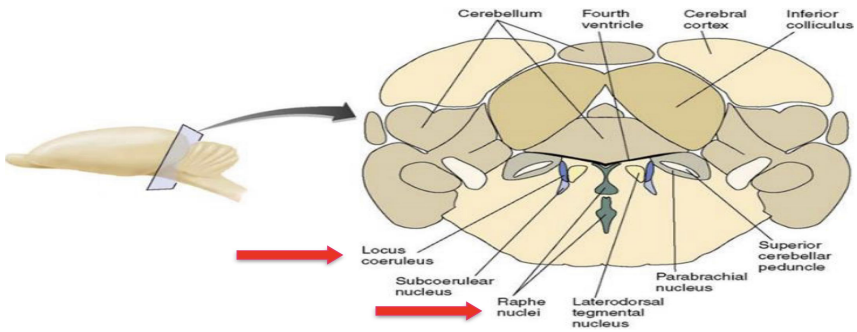
Thalamic part causes **arousal that is awakening from deep sleep** (sensory input, pain, light).

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.

Neural Activity of Neurotransmitter Systems during Sleep and Arousal

Table is important:

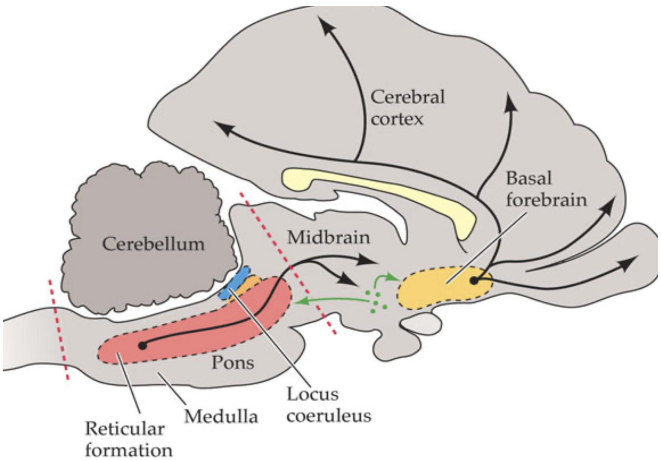
Neurotransmitter	Site of cell bodies	Activity During		
		Wakefulness	SWS	REM
Serotonin	Raphe Nuclei	High	Low	Very low
Norepinephrine	Locus Coeruleus	High	Low	Very low
Acetylcholine	Brainstem	High	Low	High

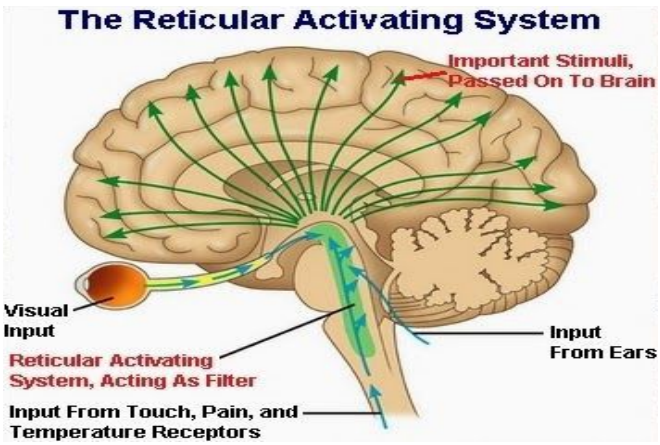


The Reticular Activating System (RAS)

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 the control of the reticular activating system in the upper brain and diencephalon.





Sleep Disorders/Burden (females slides only)

70 million people in the US suffer from sleeping problems (50% have chronic sleep disorders).

Insomnia = 30 million **(most common)**
Sleep apnea = 18 million
Narcolepsy = 250 thousand Americans
Motor car accidents = 100 thousand
Traffic fatalities = 1500 drowsy driving/annum (per year)

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

1 Disorders of SWS:

1- Sleep talking/Sleepwalking (common in children)
2- Night tremors: Are seen in Ⅰ Ⅰ Ⅰ, Ⅰ Ⅴ stage of SWS (common in children)
3- Night terrors: Sudden arousal from sleep and intense fear accompanied by physiological reactions (ex: rapid heart rate, perspiration/sweating) that occur during SWS*

2 Disorders of REM sleep:

1-Nightmare: Frightening dream
2-Sleep paralysis: subject awake but unable to speak or move
3- Sleeping sickness*

3 Insomnia:

Inability to sleep 

4 Somnolence:

Extreme sleepiness

5 Somnambulism:

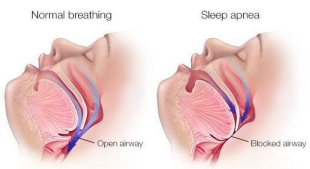
Walking during sleep* 

6 Drug dependency Insomnia:

An insomnia caused by the side effect of ever increasing doses of sleeping medications*

7 Sleep apnea:

Cessation of breathing while sleeping
(Mostly to obese patients and usually leads to them not getting enough sleeping time)



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*

Symptoms of Narcolepsy: Females slide* (just know the definition of each)

Sleep attack:

An irresistible urge to sleep during the day, after which the person awakes feeling refreshed.

Cataplexy:

Complete paralysis that occurs **during waking.**

Sleep paralysis:

Paralysis occurring just **before a person falls asleep.**

males slides*
Females slide*

MCQ & SAQ:

Q1: State of unconsciousness from which a subject can be aroused by appropriate sensory or other stimuli.

A. Sleep
B. Coma
C. Awake
D. Cataplexy

Q2: which of the following is associated with a state of arousal

A.Beta
B. Alpha
C. Theta
D. Delta

Q3: 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

Q4: Which of the following pattern of changes in central neurotransmitters or neuromodulators are associated with the transition from non-REM to wakefulness?(extra)
A.Decreased serotonin
B. Increased GABA
C.Decreased Histamine
D.Increased Orexin

Q5: Stimulation of the Supra-chiasmal nucleus of hypothalamus by light falling on the retina inhibits which of the following?
A. Serotonin
B. Acetylcholine
C. Melatonin
D. Muramyl peptide

Q6: Walking during sleep is also known as?

A. Somnolence
B. Somnambulism
C. Sleep apnea
D. Insomnia

answer key:
1: A
2: A
3: B
4: D
5: C
6: B

1- enumerate the Theories of sleep

2- explain how sleep preserve energy and provides protection.

3- Mention the physiological changes in sleep regarding secretions

4- Mention two symptom of narcolepsy and define them.

A1: slide 4

A2: slide 4

A3:Salivary/lacrimal secretions are **reduced**, ***gastric/sweat*** secretions are ***increased***.

A4: Cataplexy: Complete paralysis that occurs **during waking.**
Sleep paralysis: Paralysis occurring just **before a person falls asleep.**

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