Physiology of sleep

Objectives:

1. Explain the difference between sleep and coma.
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.

References:

- Guyton and hall physiology textbook.
- 435 Boys' slides
- 434's Teamwork
- 433's Teamwork

Helpful videos:

- ✓ Step 1 USMLE - Normal Sleep and Sleep Disorders (Duration\ 11:01)
- ✓ Stages of Sleep - Sleep Cycles (Duration\ 2:28)

ملاحظة: الملف مبني على الاوبجكتفز الموجودة بالستيودنت قايد فموب شامل لجميع المعلومات الموجودة بقايتن أو التيمات السابقة، فقط شامل المعلومات الموجودة بسلايدات الطلاب.

1: Explain the difference between sleep and coma.

Sleep and coma:

Sleep	coma
A state of unconsciousness from which one **can be** aroused by a sensory or other stimulus. It may also be defined as a normal, periodic, inhibition of the reticular Activating system.	A state of unconsciousness from which one cannot be aroused by sensory stimulation

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

1- Slow-wave sleep (NREM):

- Deep, restful type of sleep characterized by **decrease in:** peripheral vascular tone, blood pressure, respiratory rate, and metabolic rate.
- In this type: EEG waves are generally of low frequency.
- **Dreams** can occur but they can't be remembered "the consolidation of dream in a memory will not occur", nightmares may also occur.

- **Sleep thought - lacks vivid sensory and motor sensations, is more similar to daytime thinking, and occurs during slow-wave sleep**
- **Raphe nuclei** of the medulla and pons and the secretion **of serotonin**.

2- Rapid eye movement (REM):

- Neurons of the pons.
- **Called:** "**paradoxical sleep**" because the brain is quite active and skeletal muscles contraction occur.
- **Lasts:** 5 to 30 minutes and repeats about 90 minutes' intervals.
- It may be absent if the individual is extremely tired, but it eventually returns as the person becomes more rested.
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- **On EEG:** a low amplitude and a high frequency pattern.
- **It has several important features:**
    - Dreaming occur and can be recalled "at least in part". **True dream - vivid, detailed dreams consisting of sensory and motor sensations experienced during REM**
    - Muscle tone throughout the body "except eye muscles" is exceedingly depressed.
    - Heart rate and respiration become irregular.
    - Despite decreased muscle tone, muscle contraction occurs in addition to **rapid eye movement**.
    - Brain metabolism increased as much and 20% percent, and the EEG shows brain waves that are characteristics of the waking state.

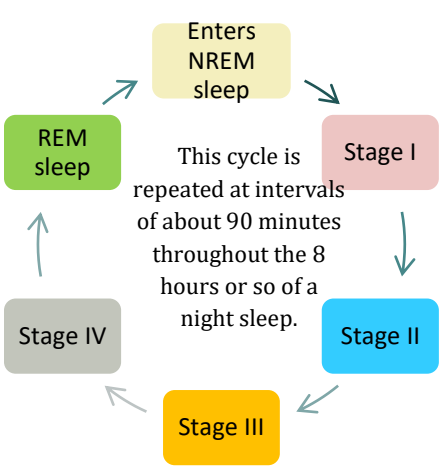
In summary, REM is not as restful as SWS and it is a type of sleep in which the brain is quite active, but this brain:

1- Is not aware cut off the external world.
2- Its activity is not channeled into purposeful external motor activity.

3: Describe how NREM and REM sleep are **distributed** during a normal night sleep in the average adult human.

Distribution of sleep stages:

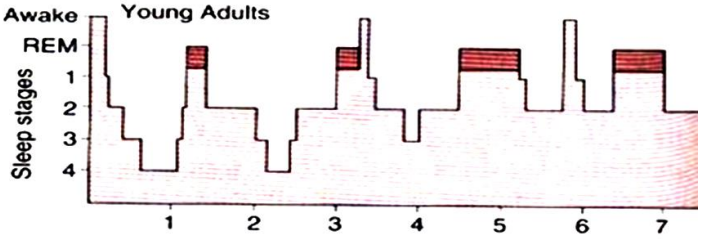
- While SWS occupies most of the total night sleep time (around 75-80%), it is interrupted by intervening[1] REM sleep periods, approximately every 90 minutes.
- **In a typical night of sleep**:
    - A young adult first enters NREM sleep, passes through stages 1, 2, 3 and 4 SWS, and then, 60-100 minutes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



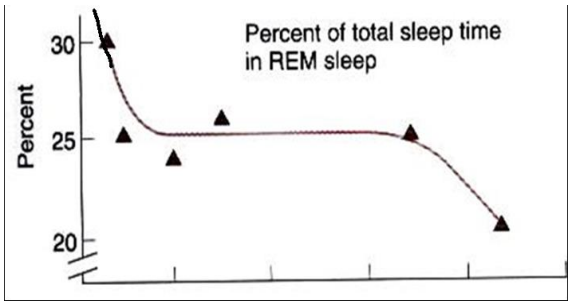
[1] Occur in time between events.

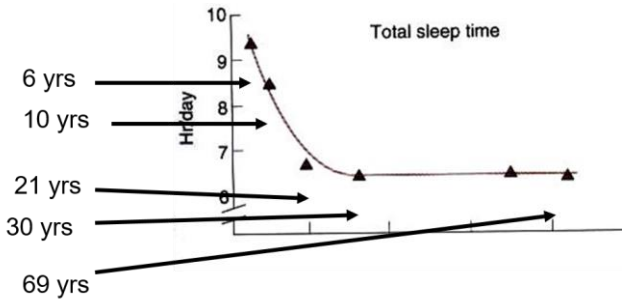
- **As the night goes on → there is progressive reduction in stages 3 and 4 sleep and progressive increase in REM sleep.**

✓ In a young adult SWS (NREM sleep) 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.
- 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.





4: Describe the **behavioral** and **autonomic** features associated with **NREM** and **REM** sleep.

TABLE 14.1 *Properties of Slow-Wave and REM Sleep*

Property	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
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
EVENT-RELATED POTENTIALS		
Sensory-evoked	Large	Reduced

BIOLOGICAL PSYCHOLOGY, Fourth Edition, Table 14.1 © Sinauer Associates, Inc.

Physiological changes during sleep:

- **CVS:** Pulse Rate, cardiac output, blood pressure, and vasomotor tone are decreased but the blood volume is increased.
- **Respiration:** Tidal volume and rate of respiration is decreased. BMR is decreased 10-15%.
- **Urine volume:** Urine volume is decreased.
- **Secretions:** Salivary / lacrimal secretions are reduced; gastric/sweet secretions are increased.

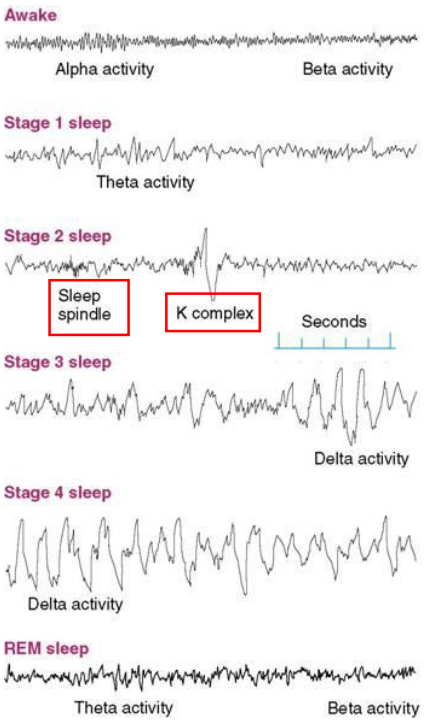
TABLE 14.2 *Neural Activity of Neurotransmitter Systems during Sleep and Arousal*

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

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

EEG (electroencephalogram) waves:

Alpha waves activity:	A smooth electrical activity of **8 – 12 Hz** recorded from the brain.	Generally associated with a state of **relaxation**. "awake but rested"
Beta waves activity:	Irregular electrical activity of **13 – 30 Hz** recorded from the brain	Generally associated with a state of **arousal**.
Theta waves activity:	EEG activity of **3.5 – 7.5 Hz**.	Occurs intermittently during early stages of slow wave sleep and REM sleep.
Delta waves activity:	Regular, synchronous electrical activity of less than 4 Hz recorded from the brain.	occurs during the **deepest stages** of slow-wave sleep. "deep sleep + infants + organic brain disease"



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. Alpha waves diminish and Theta waves appear on EEG.
2. **Stage 2 NREM →** This is the **first stage of true sleep**.
   Marked by appearance of **Sleep Spindles**. These are bursts of alpha-like 10-14z , 50 uV waves .
3. **Stage 3 NREM →** Lower frequency (mainly theta), higher amplitude EEG waves. Body temperature begin to fall. B.P decreases. Difficult to awaken the person. This stage occurs about 20-25 minutes after falling asleep.
4. **Stage 4 NREM →** Still slower frequency (mainly delta) & still higher amplitude waves. The difference is that the dreams in slow wave sleep are not remembered but in REM, dreams can be remembered.

(B) REM Sleep:

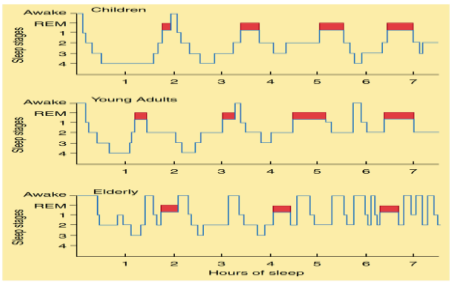
Low-voltage, fast activity.

Stages of sleep "from 434 and 433"				
	REM	Stage 1	Stage 2	Stage 3&4
Experience:	Very active stage of dream. **Vivid dreams can occur.**	**Falling asleep** and transition stage between waking & sleep.	**Base line of sleep**	**Deep sleep.**
Duration:	20-25% of normal night sleep.	1-5 minutes. ~2.5% of a normal night sleep.	- 90 minute. - ~45-60% of a normal night sleep.	- 15-30 minutes. - ~40% of all sleep.
Signs:	-	Eye begins to roll slightly.	-	Slowing of heart rate, breathing rate, and brain activity.
Waveform:	Irregular, low-voltage and fast activity.	Irregular, jagged, low voltage wave.	**- Sleep spindles. - K-complex.**	- EEG recording of slow, large amplitude wave. - Highly synchronized neuronal activity.
	Beta waves	**Alpha waves**		**- stage 3 → mainly theta. - stage 4 → mainly delta.**
Notes:	Length of rem stages increases as the night progresses.	- Start when sleep has just begun, - Brain activity begins to decline.	-	Stages 3&4 sleep predominance in the night, and length will increase as night progress.

*To remember the brain waves: "**b**uying **a** **t**iny **d**og".

6: Appreciate how the **total sleep duration** and **different sleep stages** vary with different ages in normal humans.

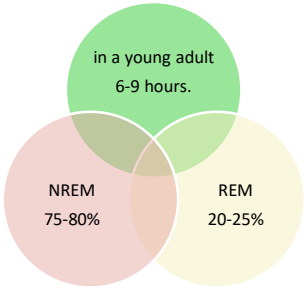
Normal sleep cycle at different ages:



- Rem sleep is indicated in red.
- In a typical night of sleep, a **young adult** first enters NREM sleep → passes through stages 1&2, and spends **70-100 min in stages 3&4** → sleep the lightens, and a REM period follows.

- REM sleep occupies:

Premature infants	80% of total sleep.
Full-term neonates	50% of total sleep. 15 - 20 hours.
Elderly	20% of total sleep. "from 20-69ys" 5-6 hours.
Children	More sleep time and stage 4 than adults. 10 -15 hours



*Note: this topic is present in the guide's objectives and in both 433's and 434's teamwork but **not in** the boys' slides.

7: Describe the **current theories** about the neural basis of sleep.

Theories of Sleep:

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

(1) Serotonin, produced by the **Raphe Nuclei**, 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.

(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:

- **Raphe nucleus:**
  - **Stimulation of** Raphe Nuclei (which are situated in the lower pons & medulla) **induces SW.**
  - **Destruction of** the Raphe Nuclei makes 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 the mid pons**, 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.

- **Injections 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 → produces wakefulness.

Melatonin as a 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.

In Boys' slides but not in the objectives!

Why Do We Sleep?

- **Proximate Explanation:**
  - Because we begin to "feel" tired..melatonin ↑
  - Need to consolidate energy and experiences.
  - Need to avoid predators.
  - Need to restore body cells and promote protein anabolism;
  - Maintain hormonal secretions, immune function.
- **Ultimate Explanation:**
  - sustains our ability to reproduce successfully, by maintaining good health.

Awake: This is the state of readiness / alertness and ability to react consciously to various stimuli.

DREAMS AND REMS

- **What are true dreams for?**

  Although research has yet to answer this question, a prevalent view today is that dreams don't serve any purpose at all, but are side effects of REM.
  To exercise groups of neurons during sleep some are in perceptual and motor areas REM occurs in other mammals and to a much greater extent in fetuses and infants than adults REM sleep may help consolidate memories.

Disorders of Sleep:

- **Insomnia (habitual sleeplessness; inability to sleep.)**
  - Reported to affect approximately 25% of the population occasionally, and 9% regularly.
  - There appears to be no single definition of insomnia.
  - One of the most important causes of insomnia seems to be sleeping medication.
  - Insomnia is not a disease, but rather may be a symptom of pain, discomfort, or other physical ailment.
- **Drug dependency insomnia:**
  - An insomnia caused by the side effects of ever increasing doses of sleeping medications.
- **Sleep apnea:**
  - Cessation of breathing while sleeping.

- Disorders of Sleep
  - **Narcolepsy:**
    - A sleep disorder characterized by periods of irresistible sleep, attacks of cataplexy, sleep paralysis, and hypnagogic hallucinations.
      - **Sleep attack:**
        - A symptom of narcolepsy; an irresistible urge to sleep during the day, after which the person awakes feeling refreshed.
      - **Cataplexy:**
        - A symptom of narcolepsy; complete paralysis that occurs during waking.
      - **Sleep paralysis:**
        - A symptom of narcolepsy; paralysis occurring just before a person falls asleep.
      - **Hypnagogic hallucination:**
        - A symptom of narcolepsy; vivid dreams that occur just before a person falls asleep; accompanied by sleep paralysis.
      - **REM sleep behavior:**
        - A neurological disorder in which the person does not become paralyzed during REM sleep and thus acts out dreams.

Physiological Mechanisms of Sleep and Waking :

Neural Control of Arousal	
Acetylcholine:	- One of the most important neurotransmitters involved in arousal. - Two groups of acetyl cholinergic neurons located in the pons and basal forebrain, produce activation and cortical desynchrony when they are stimulated.
Norepinephrine:	Catecholamine agonists produce arousal and sleeplessness; effects appear to be mediated by the locus coeruleus in the dorsal pons.
Locus ceoruleus:	A dark-colored group of noradrenergic cell bodies located in the pons near the rostral end of the floor of the fourth ventricle; involved in arousal and vigilance.

Serotonin (5-HT):	Appears to play a role in activating behavior; almost all of the brain's serotonergic neurons are found in the raphe nucleus, located in the medullary and pontine regions of the brain.
Raphe nucleus:	A group of nuclei located in the reticular formation of the medulla, pons, and midbrain, situated along the midline; contain serotonergic neurons.
Histamine	A neurotransmitter implicated in control of wakefulness and arousal; a compound synthesized from histidine, an amino acid.
Tuberomammillary nucleus	A nucleus in the ventral posterior hypothalamus, just rostral to the mammillary bodies; contains histaminergic neurons involved in cortical activation and behavioral arousal.
Hypocretin	A peptide also known as orexin, produced by neurons whose cell bodies are located in the hypothalamus; their destruction causes narcolepsy.
Neural Control of Slow-Wave Sleep	
Ventrolateral preoptic area (VLPA):	- A group of GABAergic neurons in the preoptic area whose activity suppresses alertness and behavioral arousal and promotes sleep. - Destruction of this area has been reporter to result in total insomnia, coma, and eventual death in rats.
Neural Control of REM sleep	
PGO wave (Pontine, Geniculate, Occipital):	Bursts of phasic electrical activity originating in the pons, followed by activity in the lateral geniculate nucleus and visual cortex, a characteristic of REM sleep.
The Executive Mechanism	
Peribrachial area	The region around the brachium conjunctivum, located in the dorsolateral pons; contains acetyl cholinergic neurons involved in the initiation of REM sleep.
Carbachol	A drug that stimulates acetylcholine receptors
Medial pontine reticular formation (MPRF):	A region that contains neurons involved in the initiation of REM sleep; activated by acetyl cholinergic neurons of the peribrachial area.
Magnocellular nucleus:	A nucleus in the medulla; involved in the atonia (muscular paralysis) that accompanies REM sleep.

Biological Clocks	
Suprachiasmatic nucleus	A nucleus situated atop the optic chiasm. It contains a biological clock responsible for organizing many of the body's circadian rhythms
Melanopsin	A photopigment present in ganglion cells in the retina whose axons transmit information to the SCN, the thalamus, and the olivary pretectal nucleus.
Intergeniculate leaflet (IGL):	A part of the lateral geniculate nucleus that receives information from the retina and projects to the SCN; terminals release neuropeptide Y at the SCN.

Done by: Shahad AlEnezi.

إن احسنت فمن الله عز وجل، وإن أسأت أو أخطأت فمن نفسي والشيطان.
