

8 Physiology of Sleep and EEG

CNS



Sources

- Female slides
- Guyton & Hall Text book

Objectives

1. Difference between sleep & coma.
2. Why do we sleep?
3. Types of sleep: NREM & REM.
4. EEG waves.
5. Stages of NREM sleep.
6. Importance of REM sleep.
7. Sleep cycle and effect of age.
8. Sleep/awake cycle (Role of SCN).
9. Mechanism of sleep (centers/ neurotransmitters).
10. Sleep disorders.

New Terms

LC : locus coeruleus

DR : dorsal raphe

TMN : tuberomammillary nucleus

Definitions

- ❖ **Sleep** : is a state of loss of consciousness from which a subject **can** be **aroused** by appropriate stimuli.
- ❖ **Coma** : is a state of unconsciousness from which a subject **cannot** be **aroused** .

EEG waves

- ❖ The frequencies of brain waves range from **0.5-500 Hz**.
- ❖ The most clinically relevant waves:
- ❖ **Alpha waves** - **8-13 Hz**
- ❖ **Beta waves** - Greater than **13 Hz**
- ❖ **Theta waves** - **3.5-7.5 Hz**
- ❖ **Delta waves** - **3 Hz or less**

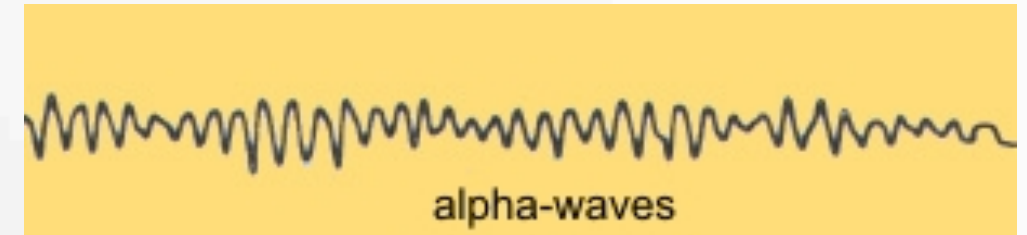
• Why do we sleep?

- ❖ **Restoration** (repair):
 - Waking life disrupts homeostasis.
 - Sleep may conserve some energy.
- ❖ **Protection** with the circadian cycle.
- ❖ Circadian **synthesis** of hormones
- ❖ **Consolidation** of learning.
 - Remodelling of synaptic function



Alpha waves

- Seen in **all age** groups but are **most common in adults**.
- **Most** marked in the **parieto-occipital area**.
- Occur **rhythmically** on both sides of the head but are often slightly higher in amplitude on the **non-dominant** side, especially in **right-handed** individuals .
- Occur with **closed eyes , relaxation, wondering mind**.



Alpha block (Arousal response)

- Alpha activity **disappears** normally with **attention** (eg, mental arithmetic, stress, opening eyes, any form of sensory stimulation).
- Then become **replaced** with irregular **low** voltage activity.
- **Desynchronization** as it represents **breakup** of synchronized neuronal activity.

An abnormal exception is **alpha coma**, most often caused **by hypoxic-ischemic encephalopathy** of destructive processes in the pons (eg, intracerebral hemorrhage). In alpha coma, alpha waves are distributed **uniformly** both anteriorly and posteriorly in patients who are unresponsive to stimuli

Beta waves

- ❖ Seen in **all** age groups.
- ❖ **Small** in amplitude , usually **symmetric** and more evident anteriorly.
- ❖ **> 13 Hz/sec**

Theta waves

- ❖ **Normally** seen during **sleep** at any age.
- ❖ In **awake** adults, these waves are **abnormal** if they occur in excess.
- ❖ **Theta and delta** waves are known collectively as **slow waves**.

Delta waves

- ❖ **Slow waves**, have a frequency of $\leq 3\text{Hz}$ or less.
- ❖ Normally seen in **deep sleep in adults** as well as in **infants** and **children**.
- ❖ Delta waves are **abnormal** in the **awake** adult.
- ❖ Often, have the **largest amplitude** of all waves.
- ❖ Delta waves can be **focal** (local pathology) or **diffuse** (generalized dysfunction).

Alpha



Beta



Theta



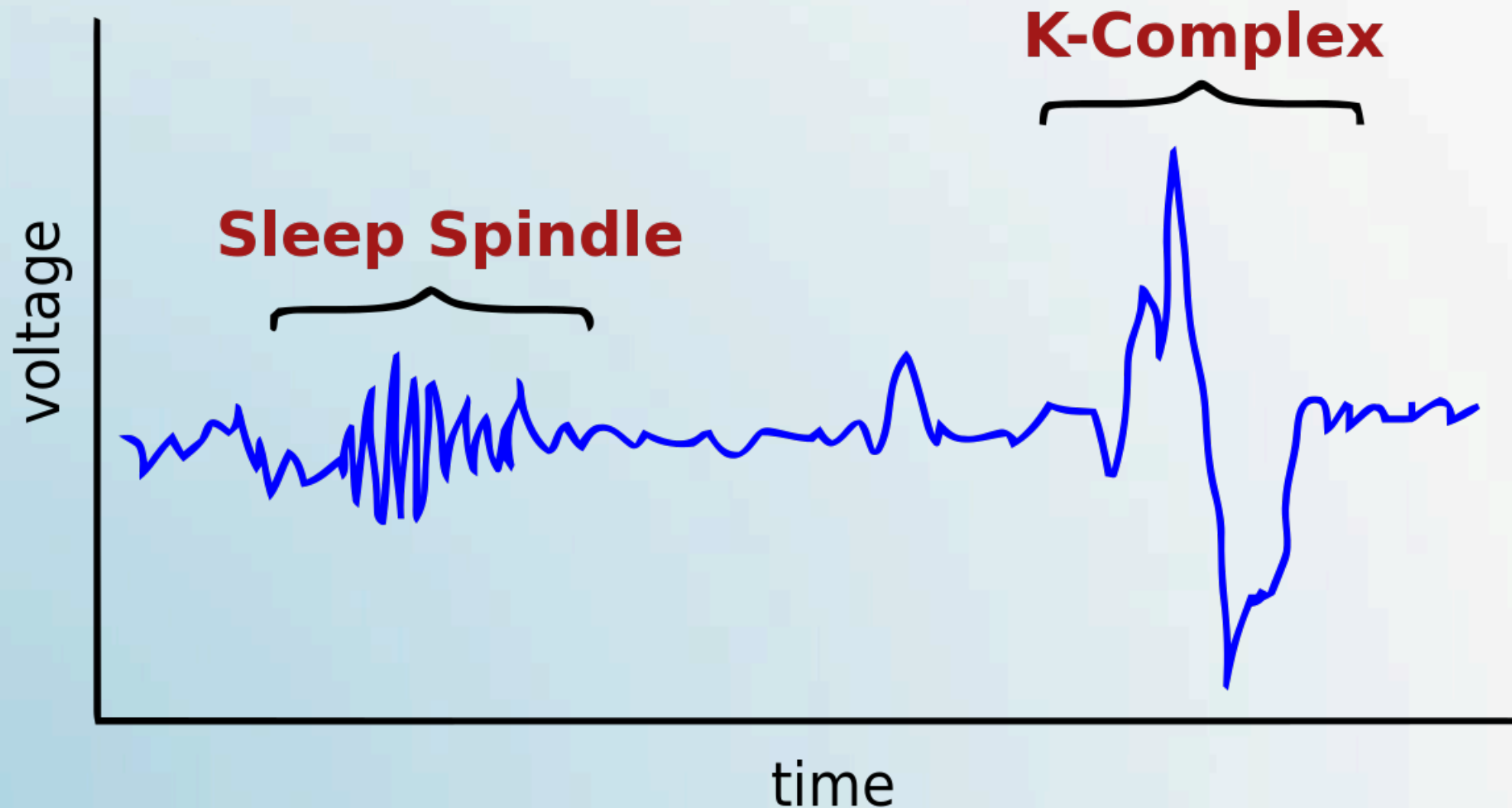
Delta



50 μ V

Sleep spindles

- ❖ Spindles are **groups** of waves that occur during many sleep stages but especially in **stage 2**.
- ❖ They have **frequencies** in the **upper** levels of alpha or **lower** levels of beta.
- ❖ Lasting for a **second** or less, they increase in **amplitude** initially and then decrease slowly. The waveform resembles a **spindle**.
- ❖ They usually are **symmetric** and are most obvious in the **parasagittal** regions.



Types of sleep

(non-REM) 1-Slow-Wave sleep

(REM) 2-Rapid Eye movement

Overview: Guyton “Additional Reading”

- The two types of sleep alternate with each other.
- Slow-wave-sleep in which the brain waves are strong and of low frequency.
- Rapid Eye movement sleep (REM-sleep), in which eyes undergo reapid movements despite the fact that the person is still asleep.
- The slow-wave-sleep is the deep, restful sleep that a person experiences during the first hour of sleep after having been awake for many hours.
- The REM sleep, occurs in episodes that occupy 25 % of the sleep time in young adults.
- Each episode normally recurs about every 90 minutes.
- The REM is not so restful, and it is usually associated with vivid dreaming.

Slow-Wave Sleep (non-REM) “dreamless sleep”

75% of sleep time , restful type of sleep . There is a decrease in vascular tone.

Decrease: in blood pressure (10-30%) , respiratory rate, and basal metabolic rate.

The dreams in SWS



The dreams of slow-wave-sleep are usually not remembered because consolidation of the dreams in memory does not occur.

* Sometimes, nightmares “الكوابيس” occur during Slow-wave-sleep

Rapid Eye movement (REM)

Occur in episodes of 5-30 min, recurring every 90 min.

Decrease

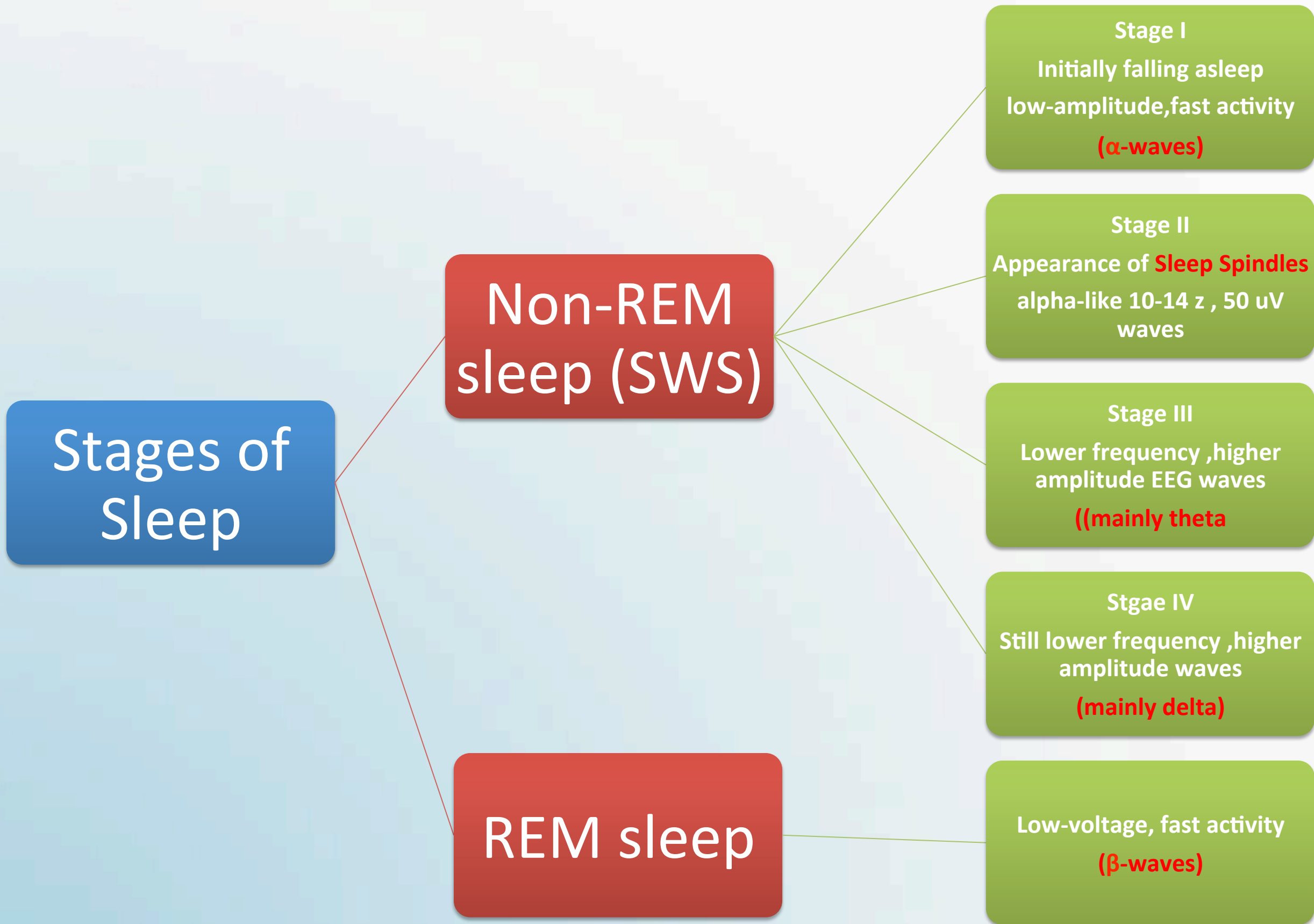
Tiredness : When the person is extremely sleepy, each bout of REM sleep is **short** and may even be **absent**.

Increase

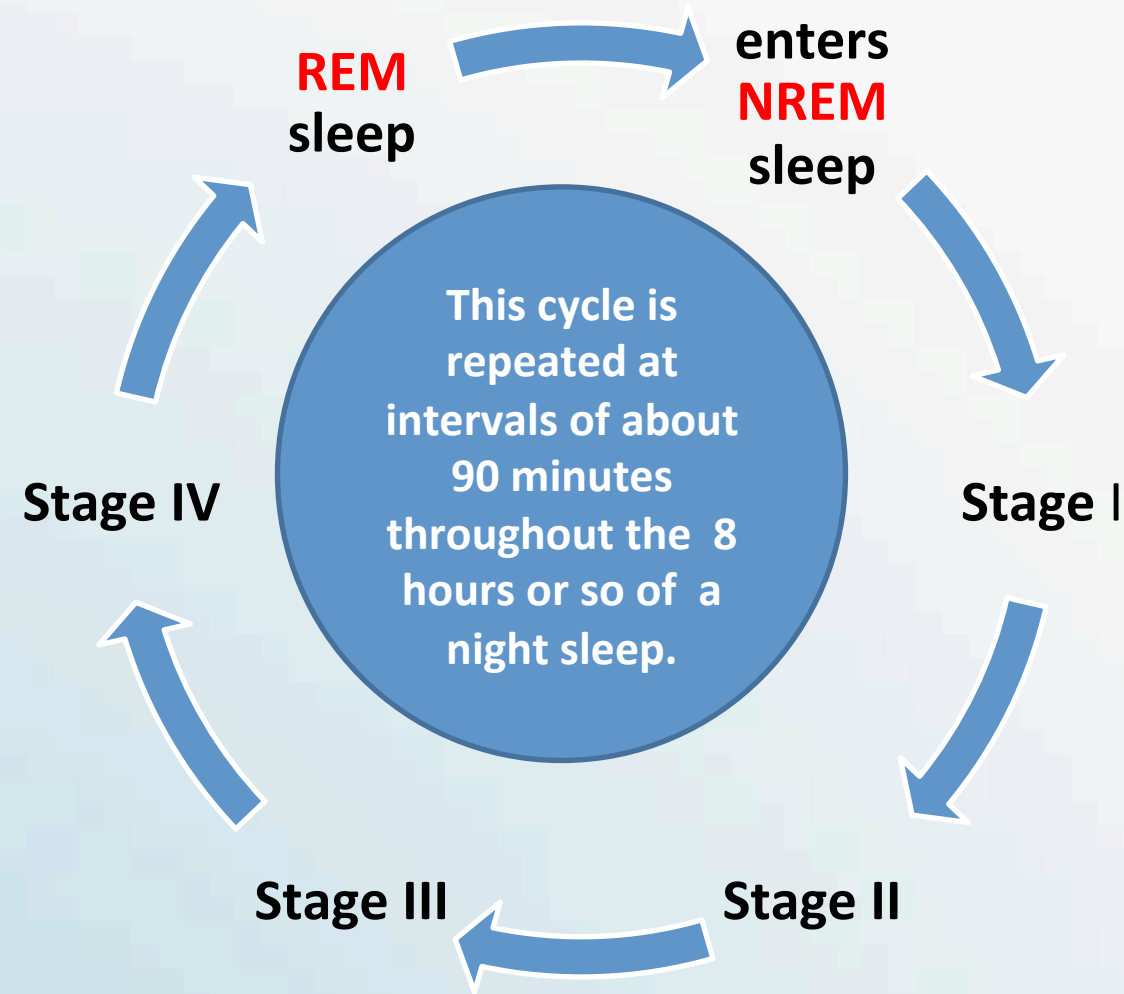
Conversely, as the person becomes more rested through the night, the durations of REM bouts **increase**.

Characterized By:

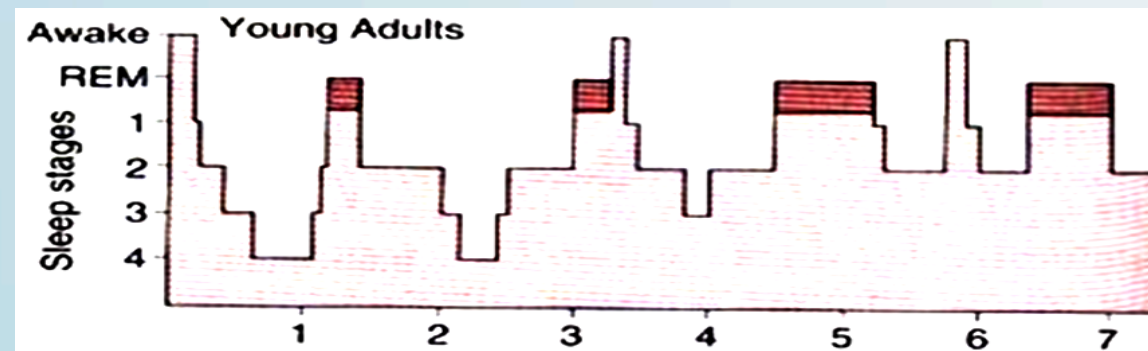
- Active dreaming, remembered later.
- Decrease in muscle tone .
- Rapid rolling movement of the eyes.
- The person is more difficult to arouse by sensory stimuli than during NREM sleep , and yet people usually awoken spontaneously in the morning during an episode of REM sleep.
- Associated with more bodily muscle activity.
- HR & RR are irregular. (characteristic of dream state)
- Twitches of facial & limb muscles.

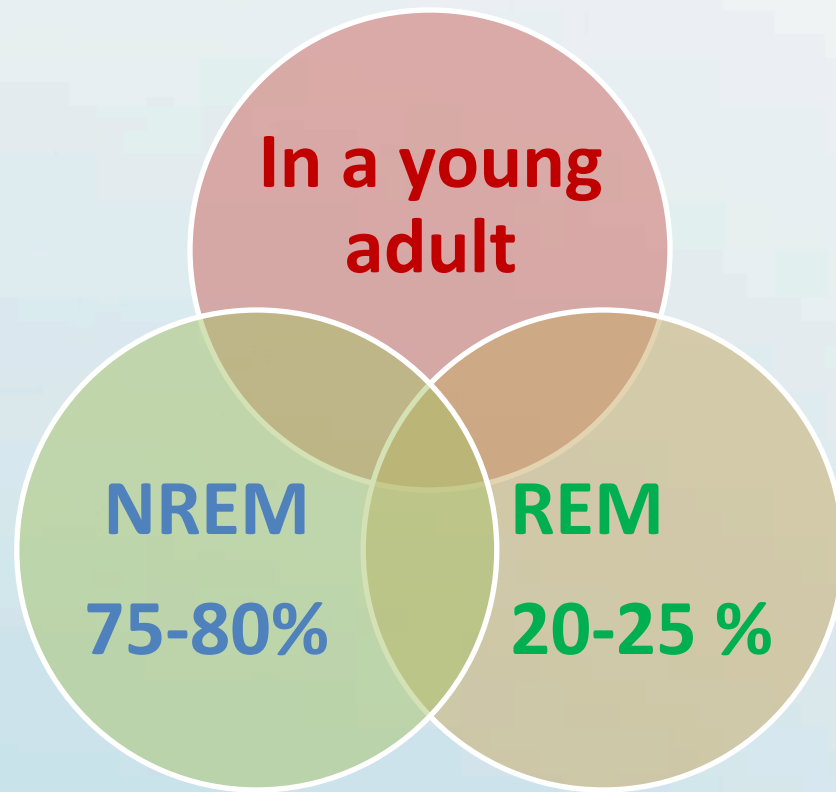


Distribution of Sleep Stages



- 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 .





Age group	REM sleep
Premature infants	80%
Full term neonates	50%
Aged/elderly	Falls rapidly to 25% (From 20-69ys)
Children	more sleep time and stage 4 than adults



- A circadian rhythm consist typically of 8h sleep and 16 h awake.
- This rhythm is controlled by the biological clock function of **suprachiasmatic (SCN) nucleus** in the hypothalamus.



Alert wakefulness (beta waves)



Quiet wakefulness (alpha waves)



Stage 1 sleep (low voltage and spindles)



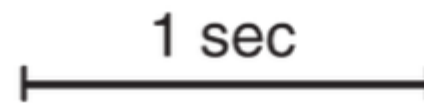
Stages 2 and 3 sleep (theta waves)



Stage 4 slow wave sleep (delta waves)



REM sleep (beta waves)



Mechanism of Sleep

NREM Sleep promoting systems:

<p>Preoptic area:</p>	<p>Ventrolateral preoptic area (VLPO) & Median preoptic area (MNPO) contain inhibitory neurotransmitters GABA and the inhibitory neuropeptide Galanin, and they innervate all the arousal-promoting regions (including: LTD/PPT, LC, DR, TMN and Orexin neurons). Thus, the VLPO and MNPO are hypothesized to promote sleep by coordinating the inhibition of arousal regions during NREM and REM sleep.</p>
<p>Lateral Hypothalamus & Basal forebrain:</p>	<p>Contain scattered GABAergic neurons that are active during NREM sleep. Some of these cells may directly innervate the cortex, and it is possible that they modulate cortical networks to promote slow wave activity.</p>
<p>Medulla Oblongata:</p>	<p>Medullary synchronizing zone at the level of nucleus tractus solitarius (NTS).</p>

Genesis of REM sleep is located in the Pons :

The mechanism producing REM sleep is located in pontine reticular formation.

Large cholinergic ponto-geniculo-occipital (PGO) spikes arise in this area and are thought to initiate REM sleep (by inhibiting noradrenergic neurons of locus ceruleus + serotonergic neurons of midbrain raphe).

REM sleep promoting systems:

Acetylcholine:	<p>Neurons in the laterodorsal and pedunculo pontine tegmental nuclei (LDT/PPT) may help generate the cortical activation and atonia of REM sleep. The LDT/PPT is the main source of ACh to the thalamus which will depolarize thalamic neurons to promote the transmission of information (including dreams) from the cortex through the thalamus.</p> <p>LDT/PPT neurons may also activate atonia-promoting neurons in the ventromedial medulla, by releasing GABA and Glycine inhibitory neurotransmitters to the motor neurons in the spinal cord and brainstem.</p>
Monoamines:	<p>Monoamines such as NE and 5-HT (Serotonin) increase muscle tone by directly exciting motor neurons, so atonia during REM sleep is probably due to a combination of inhibition by (GABA and glycine) and a loss of excitation caused by (NE and 5-HT).</p>
Melanin-concentrating hormone (MCH):	<p>The amount of REM sleep is increased by infusions of MCH (into the lateral ventricles) “by inhibiting the arousal regions”</p>

Other neurotransmitters induces sleep:

- **Melatonin:** synthesized and released by the **pineal gland**, and it enhances sleep. Prolonged bright light suppresses melatonin and sleep, while subsequent melatonin injections can restore normal sleep patterns.
- **Adenosine:** sleep inducing factor. It accumulates in brain with prolonged wakefulness. Adenosine antagonists e.g. caffeine cause alertness.

REM sleep effector neurons:

Eye movements are controlled by a group of medial pontine reticular formation neurons, while muscle atonia is caused by a group of neurons in the lateral pontine reticular formation, which send inhibitory projections to the motor neurons in the spinal cord. (Note, eyes and respiratory muscles are not inhibited during REM sleep)

Sleep disorders:

- **Insomnia:** Fatal familial insomnia: impaired autonomic & motor functions, dementia, death.
- **Disorders during NREM:**
 - -Sleep walking.
 - -Bed wetting.
 - -Night terrors. (Panic)
- **Narcolepsy:** episodic sudden loss of muscle tone and irresistible urge to sleep during day time (Bursts of REM).
- **Sleep apnea:** airway obstruction (might be because of inhibition of respiratory muscles during REM sleep).

Clinical Application:

GABAergic neurons: are active during NREM sleep, so many medications used to treat insomnia work by promoting GABA signaling e.g. **Benzodiazepine, Barbiturate.**



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CNS Block