Physiology of Sleep

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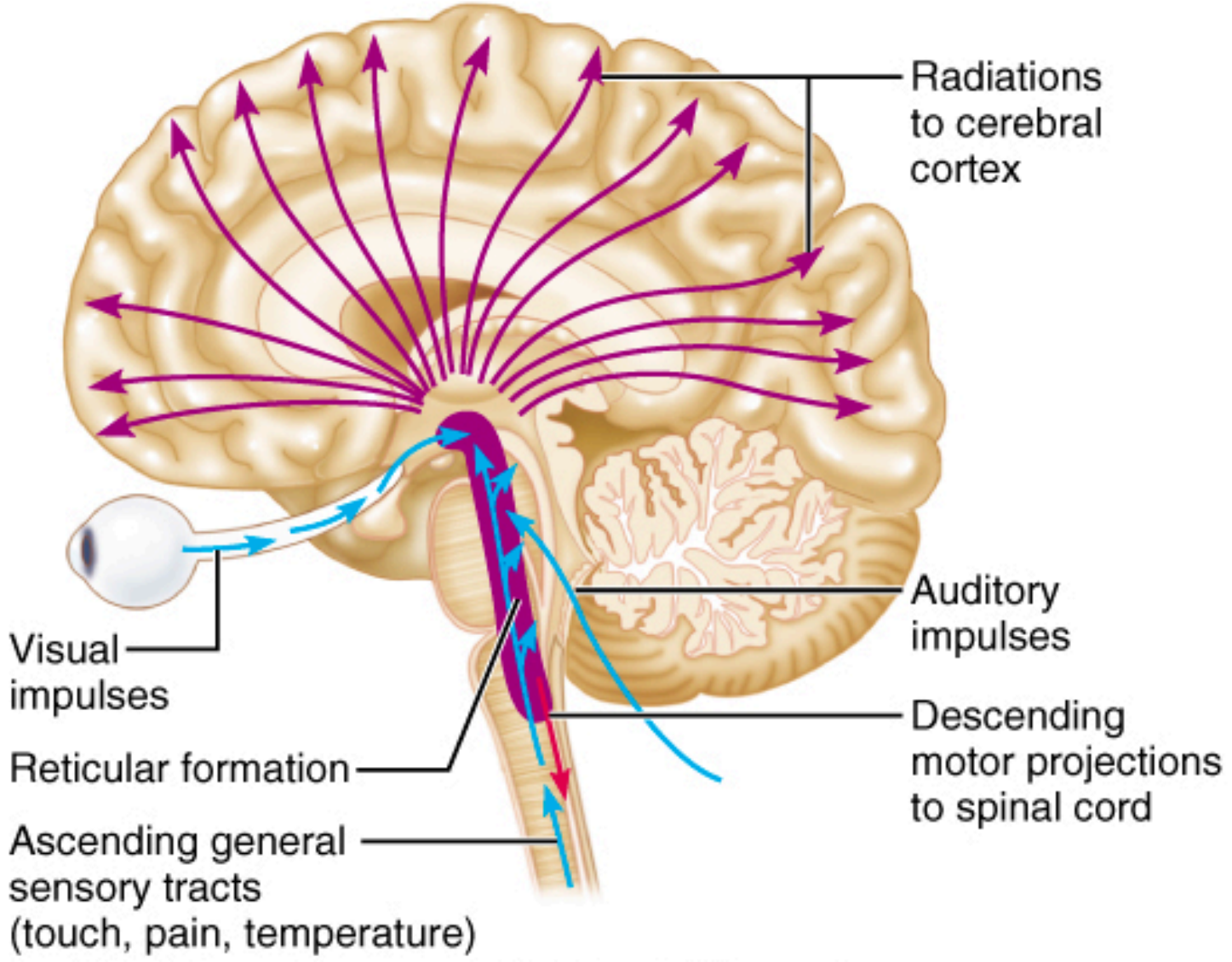
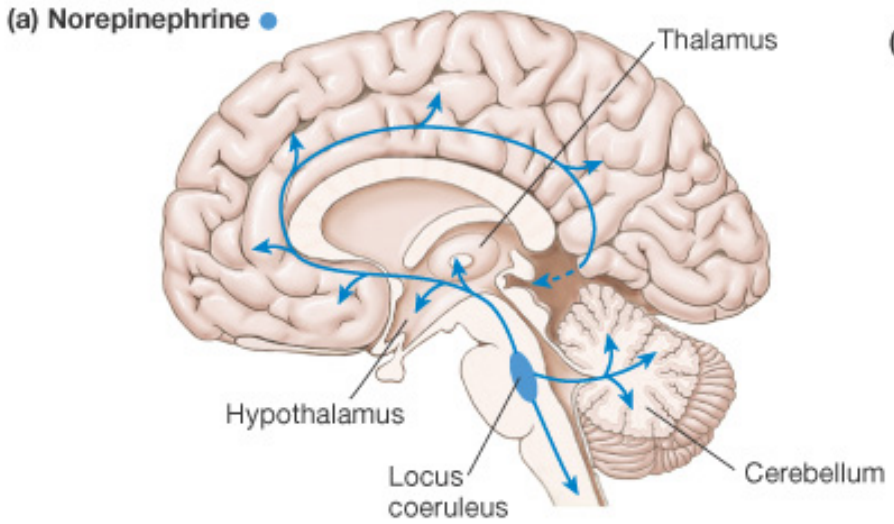
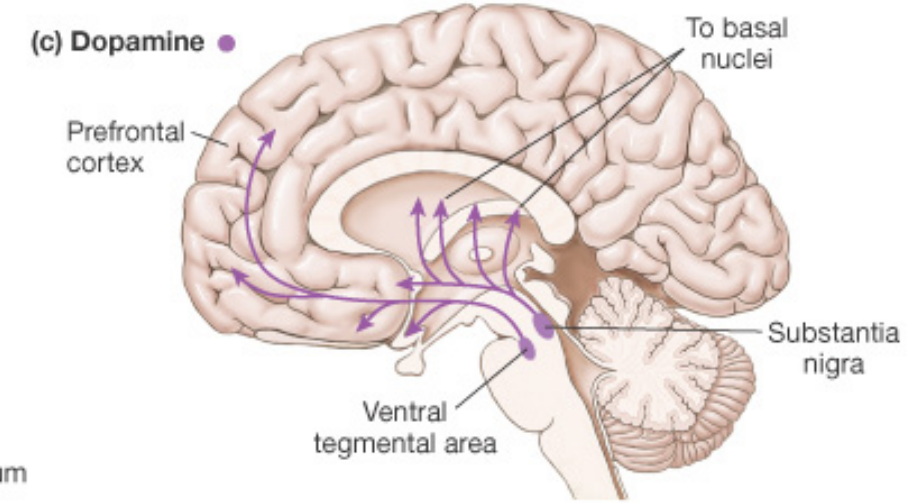
Reticular Formation (Reticular activating system)



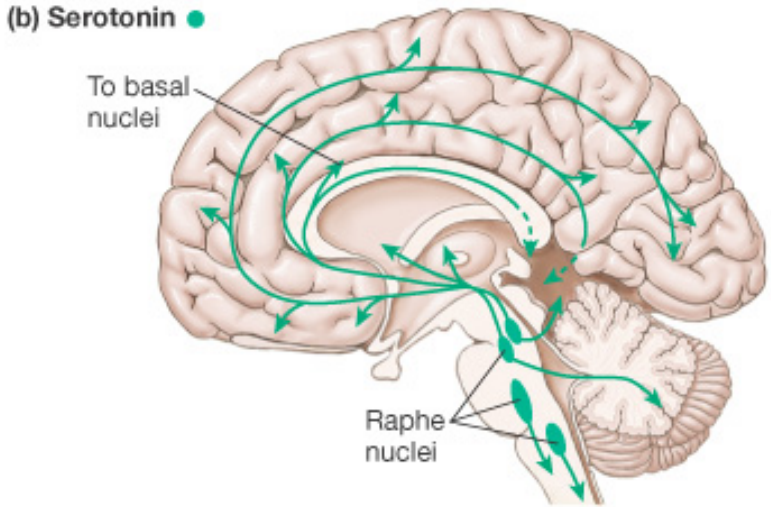
Neuromodulator Systems



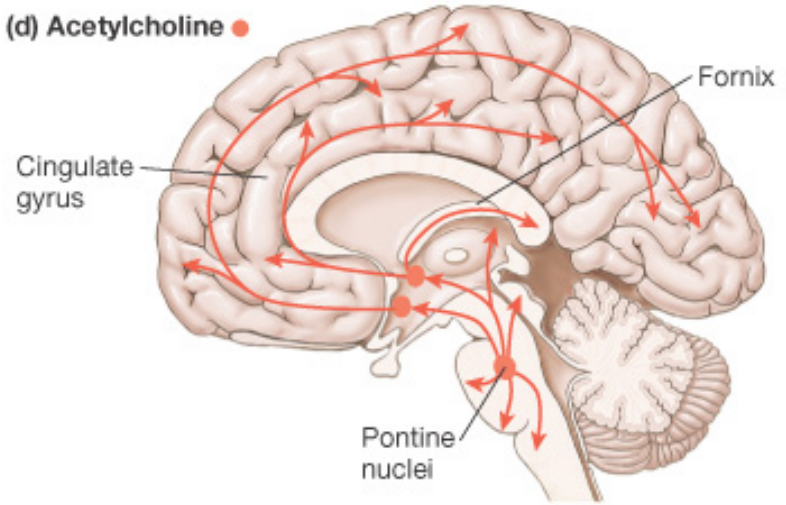
Arousal, Reward system



Motor systems, reward, cognition, endocrine control



Mood, satiety, body temperature, introversion; pain inhibition



Learning, short-term memory, arousal, reward

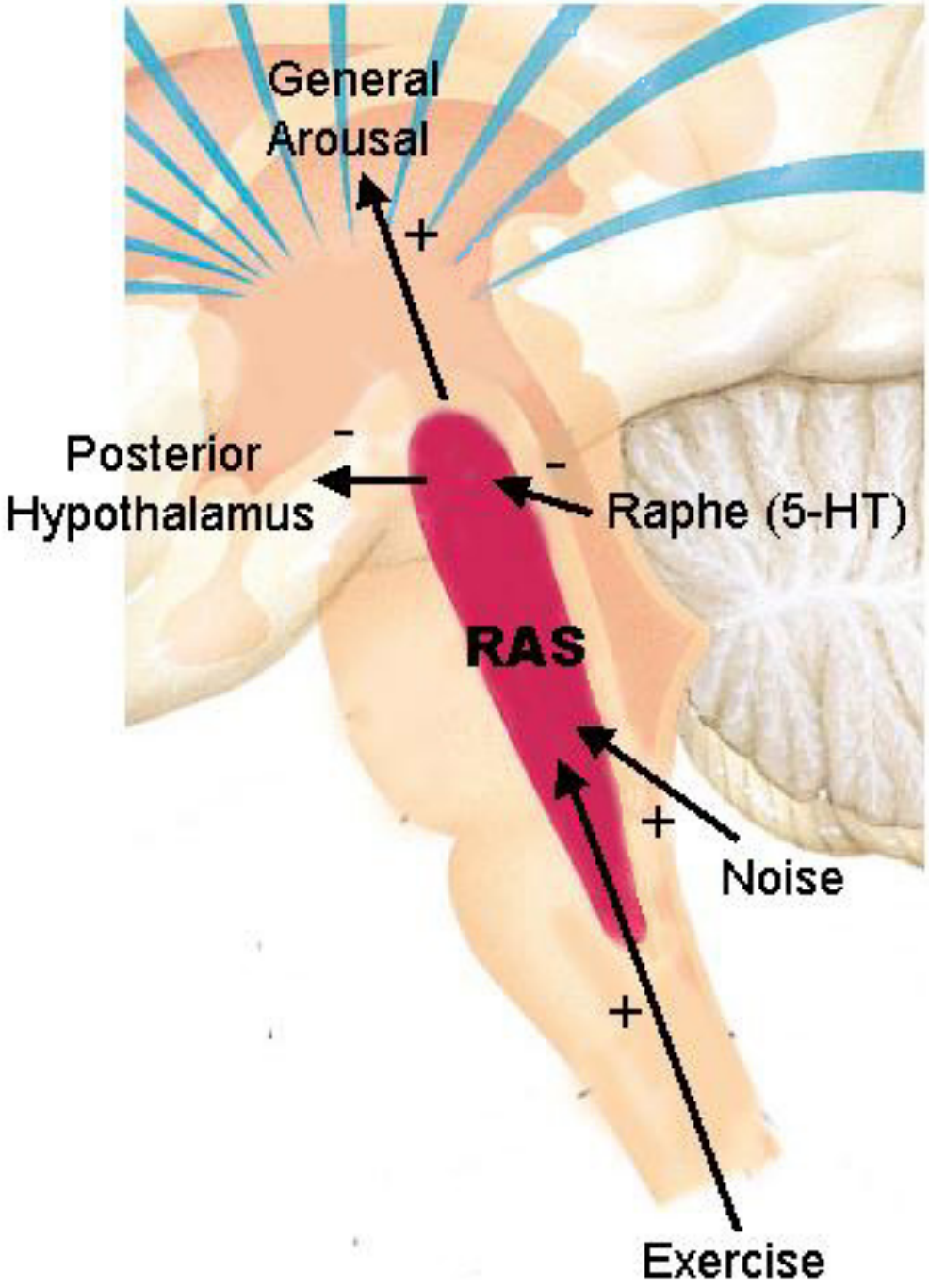
Sleep

- Loss of wakefulness
- A fundamental function for physical and mental health
- Not loss of conciousness; only a “shift”
- An unconcious state which can be in part modified by sensory stimulations

Sleep centers

Areas causing sleep when stimulated:

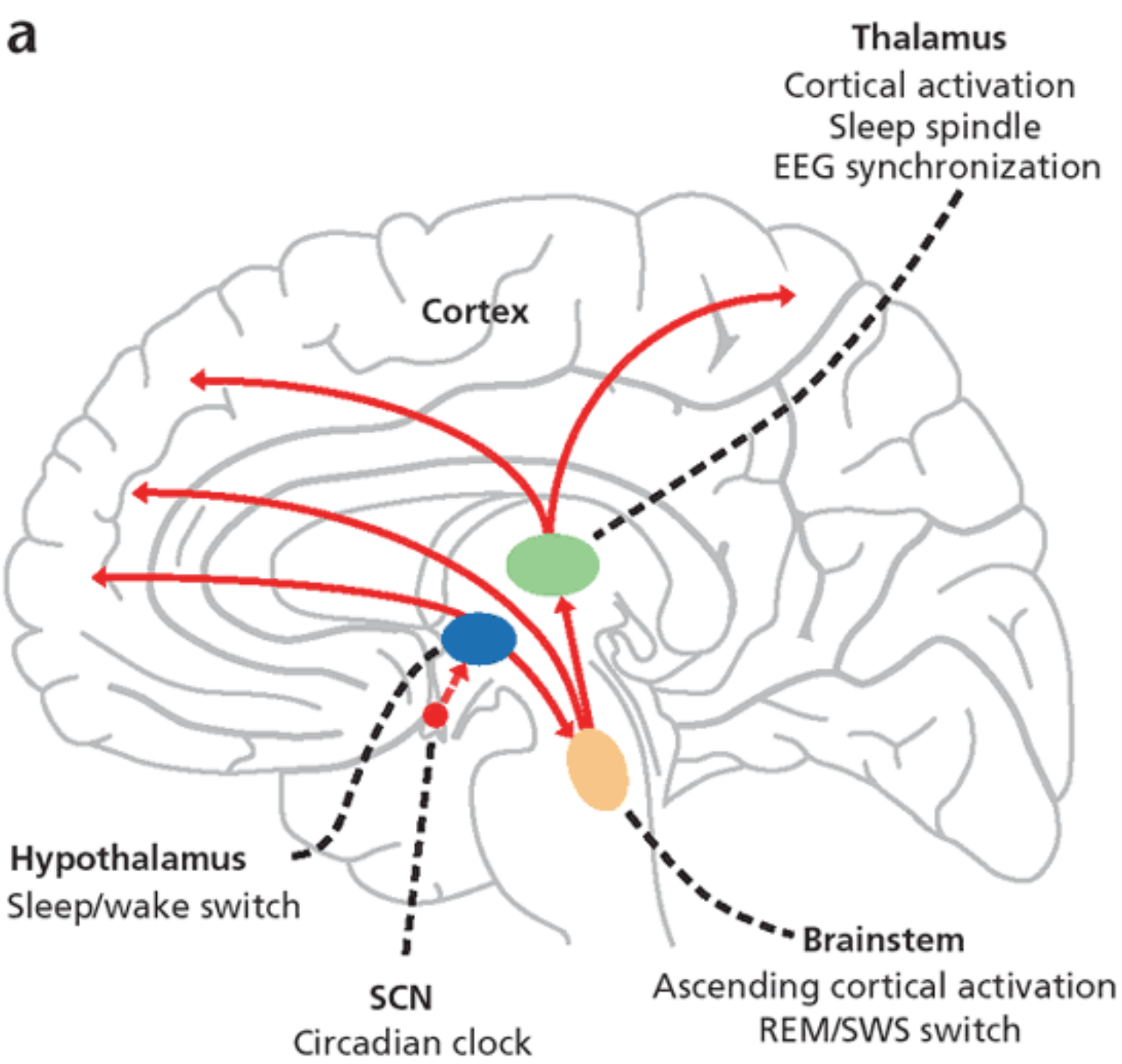
1. **Raphe nuclei in lower pons and medulla**
   - Targets (efferents): Reticular formation, thalamus, neocortex, hypothalamus, limbic system, dorsal roots of spinal cord
   - Neurotransmitter: **Serotonin (5HT)**


General
Arousal
+
Posterior
Hypothalamus
-
-
Raphe (5-HT)
RAS
+
Noise
+
Exercise

Sleep centers

2. *“**Medullary synchronization area**” in nuc. tractus solitarius level:
   - May stimulate the Raphe nuclei?
3. ***Diencephalic sleep areas**:
   1. Rostral of hypothalamus, especially the suprachiasmatic area
   2. Intralaminar and anterior thalamic nuclei
4. **Basal forebrain sleep area**:
   1. Preoptic area and Broca’s diagonal band.

*low freq stimulation (8/s) leads to sleep; while high freq. causes to wake up


a
Thalamus
Cortical activation
Sleep spindle
EEG synchronization
Cortex
Hypothalamus
Sleep/wake switch
SCN
Circadian clock
Brainstem
Ascending cortical activation
REM/SWS switch

Some factors known to interfere with sleep

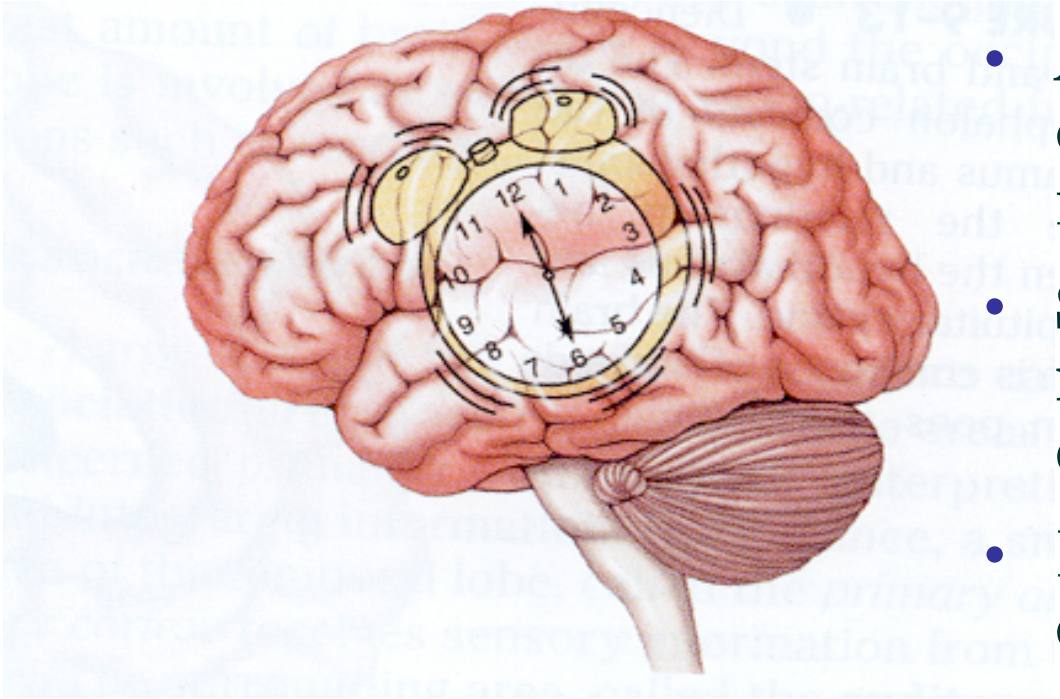
- **Adenosine** - Inhibits the specific cholinergic neurons of RAS which stimulates the cortex
- **PgD2**-Increases tendency to sleep when released from **medial preoptic area** of hypothalamus
- **PgE2**-wakefulness
- **IL-1**
- **Δ-sleep inducing factor**
- **Muramil Peptide**
- Rythmic stimulation of **mechanoreceptors** (10 Hz or lower)

Why do we sleep?

Possible mechanisms of sleep-wake cycle

- **Wakefulness**: Excitatory effects of RAS and thalamus
- Stimultion of RAS reinforced by the positive feedback from cortex and peripheral nervous system
- RAS gets “tired” during the day.
- **Sleep**: Diminished RAS activity allows sleep centers to inhibit RAS - - - - and *drowsiness* begin…

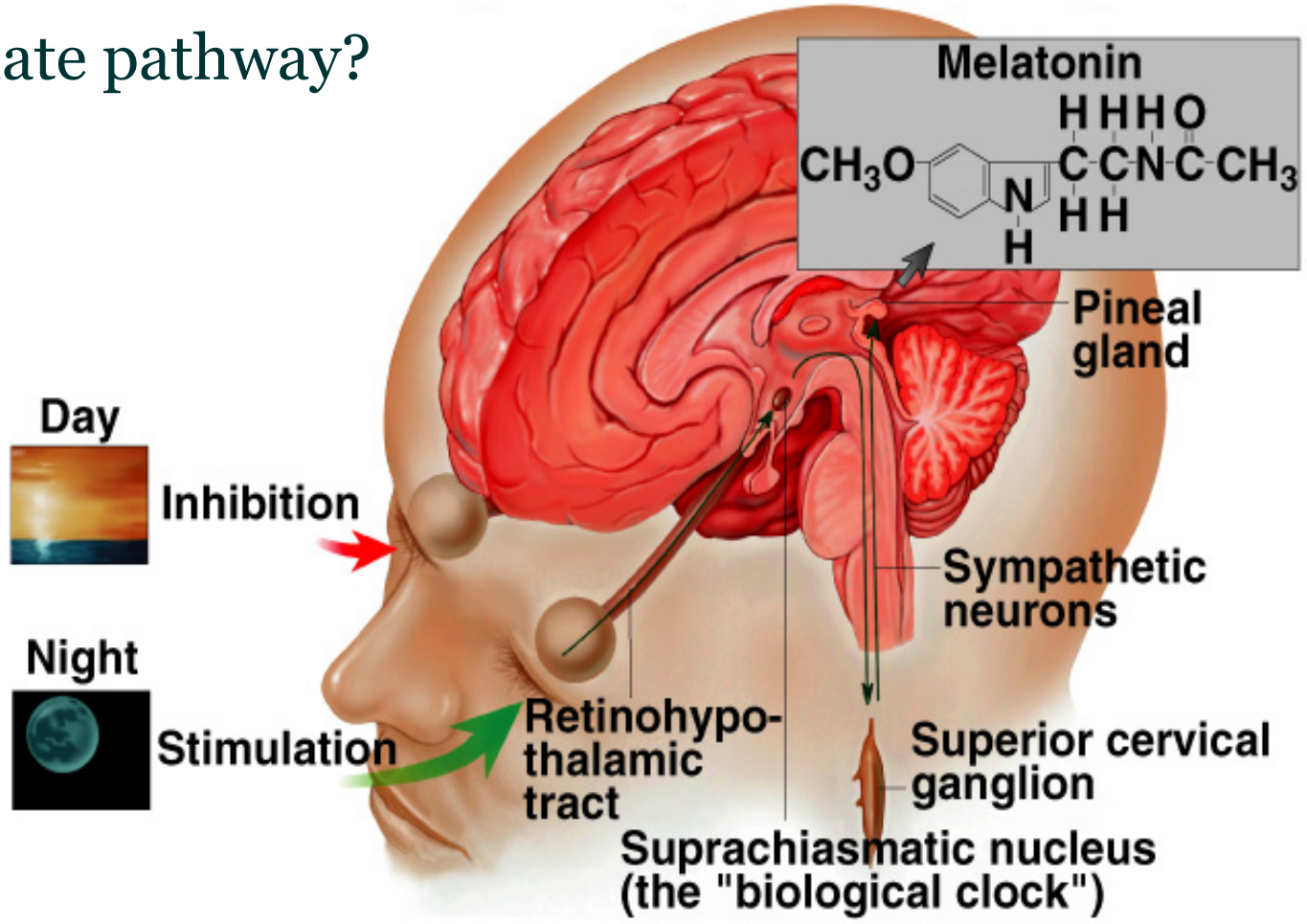
Sleep-Wake Cycle: Biological Rythms



- A part of **circa**(about)**dian**(a day) rythms
- **Suprachiasmatic nucleus** – Biological clock
- Related to **natural light-dark cycle**

Sleep-Wake Cycle: Biological Rythms

- 1. Retinohypothalamic pathway-Pineal gland-Melatonin
- 2. **Humoral fototransduction**-circulating receptors?
- 3. Intergeniculate pathway?



Phases of Sleep

1. Slow-wave sleep (*NonREM*):
    - Phase 1-4
2. Paradoxal/desynchronized sleep (REM- *Rapid Eye Movements*)

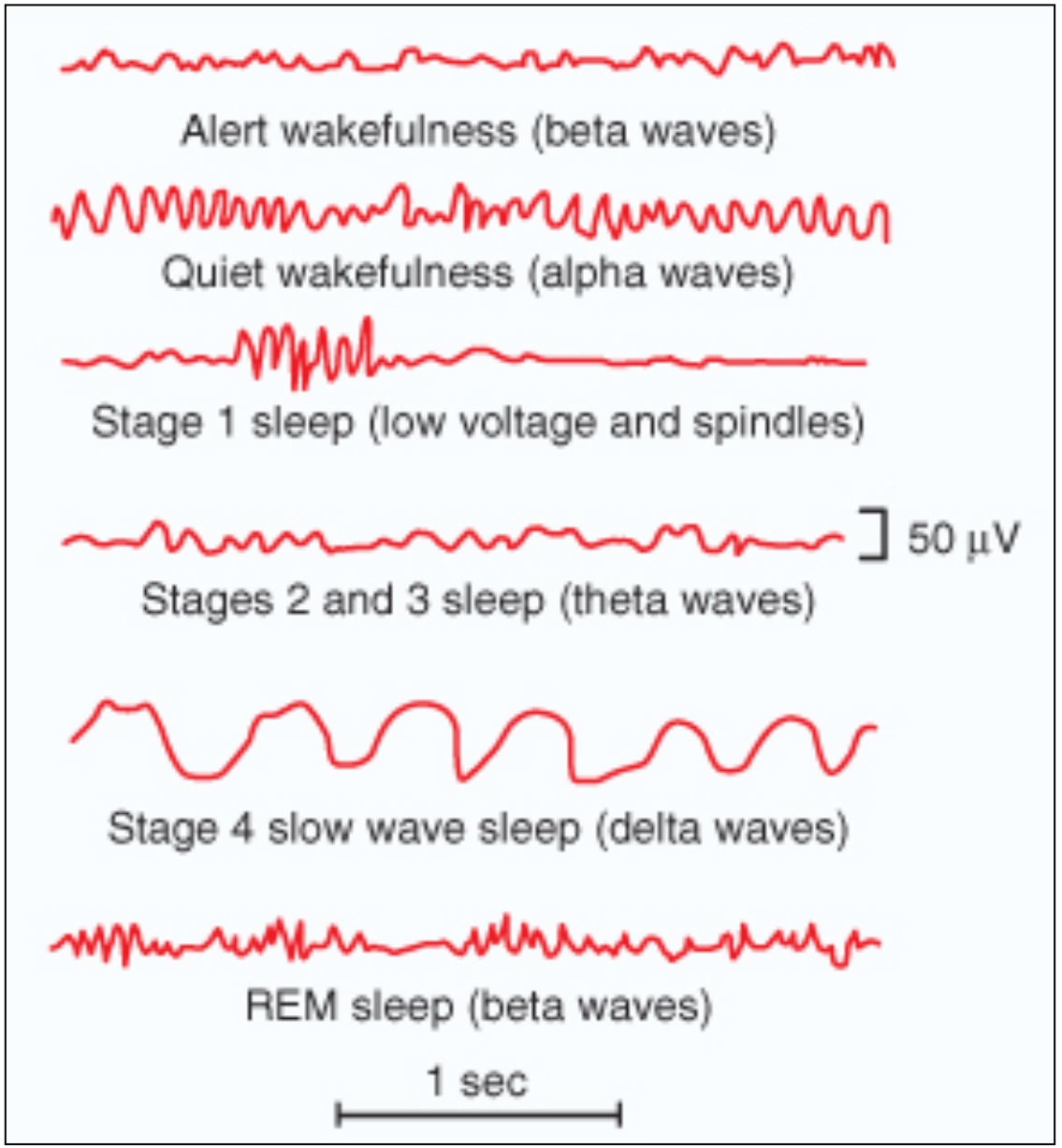
Slow-Wave (nonREM) Sleep

- Entrance to sleep
- Takes appr. 90 minutes with 5-20 minutes intervals
- Peripheral vessel tone and vegetative body functions decrease
- Muscle tone decreases
- 10-30% decrease in blood pressure, respiration rate and basal metabolism
- Spinal reflexes can be elicited but strech (deep tendon) reflexes are absent.

Slow-Wave (nonREM) Sleep

- Dreams cannot be remembered
- Theta and delta waves in EEG
- Duration and frequency decrease with age
- Has 4 different stages

Sleep and EEG waves

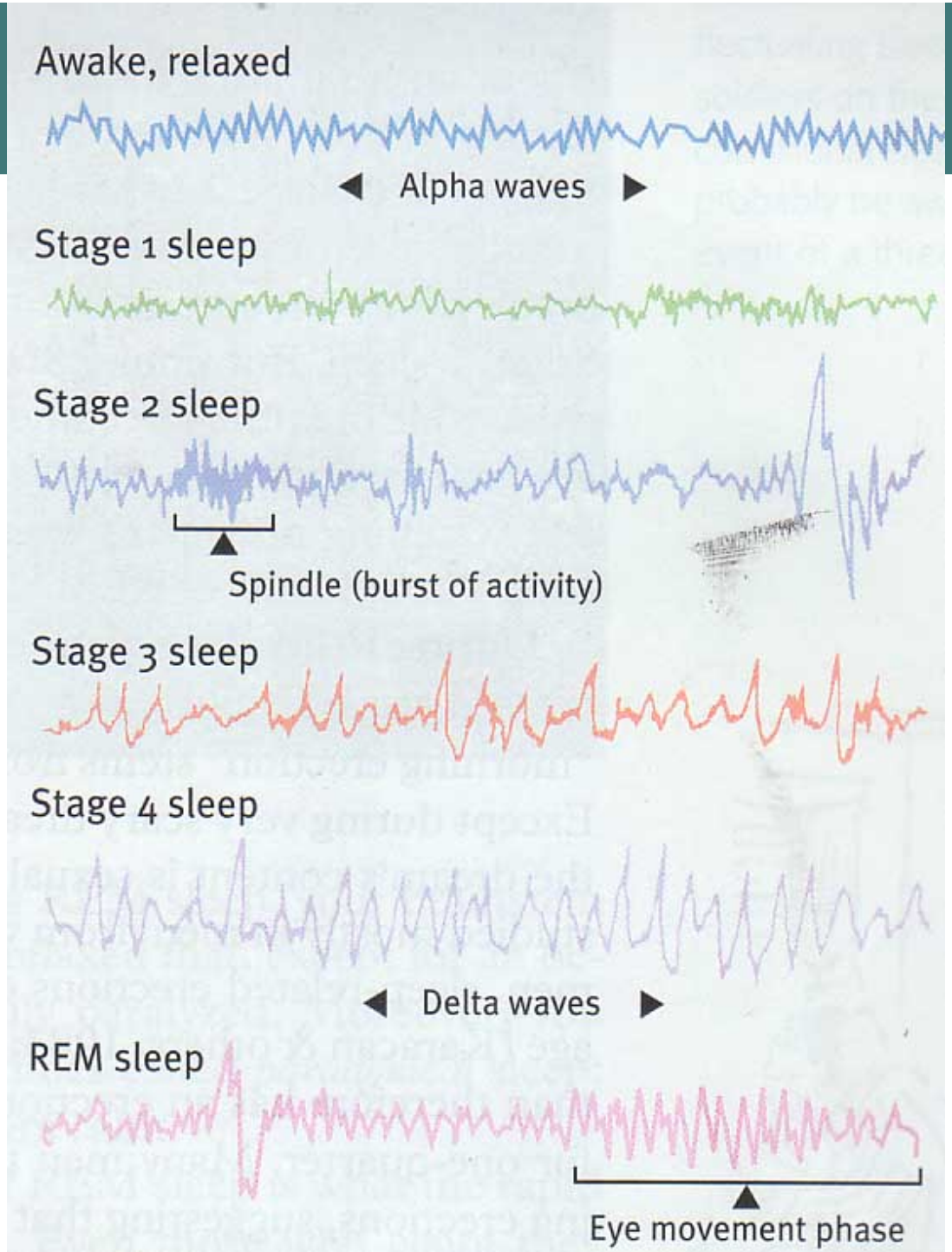


Phase-1 nonREM

- Transition period between wakefulness and sleep; takes approximately 1-15 minutes.
- Eyes closed and relaxed…
- Light sleep, hallucination-like visions…
- α (alpha) waves weaken, slower θ (delta) waves emerge.

Phase-2 nonREM

- First stage of the real sleep; takes about 20 minutes…
- Sleep spindles: 12-14 Hz sharp waves appear for 1-2 seconds…
- Slow eye movements…
- Hard to awaken…
- Fragments of dreams?


Awake, relaxed
Alpha waves
Stage 1 sleep
Stage 2 sleep
Spindle (burst of activity)
Stage 3 sleep
Stage 4 sleep
Delta waves
REM sleep
Eye movement phase

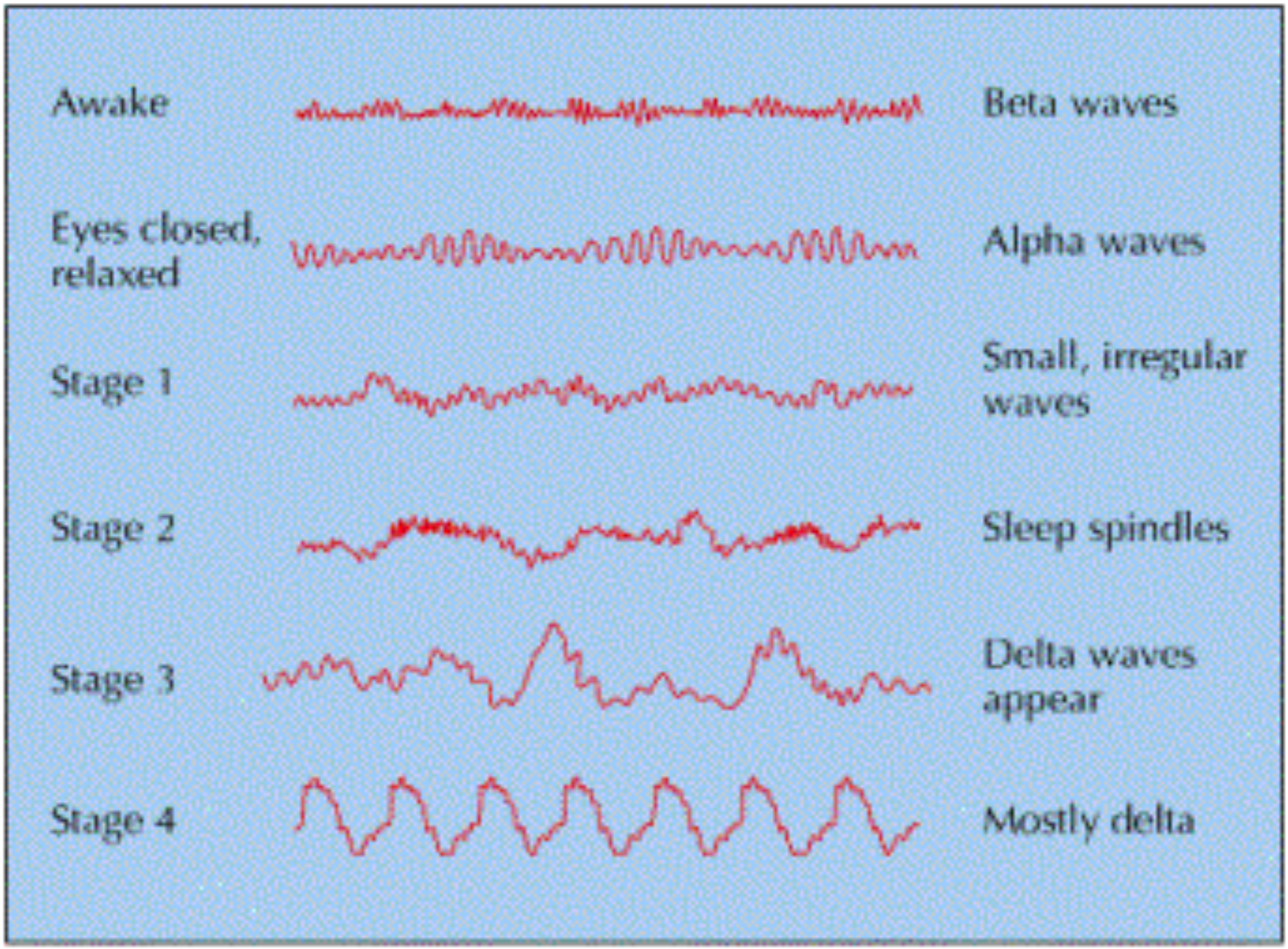
Phase-3 nonREM

- Half-way deep sleep
- Body temperature and blood pressure decreases
- Harder to awaken
- Low frequency δ **(theta) waves**
- Sleep spindles are decreased
- No slow eye movements

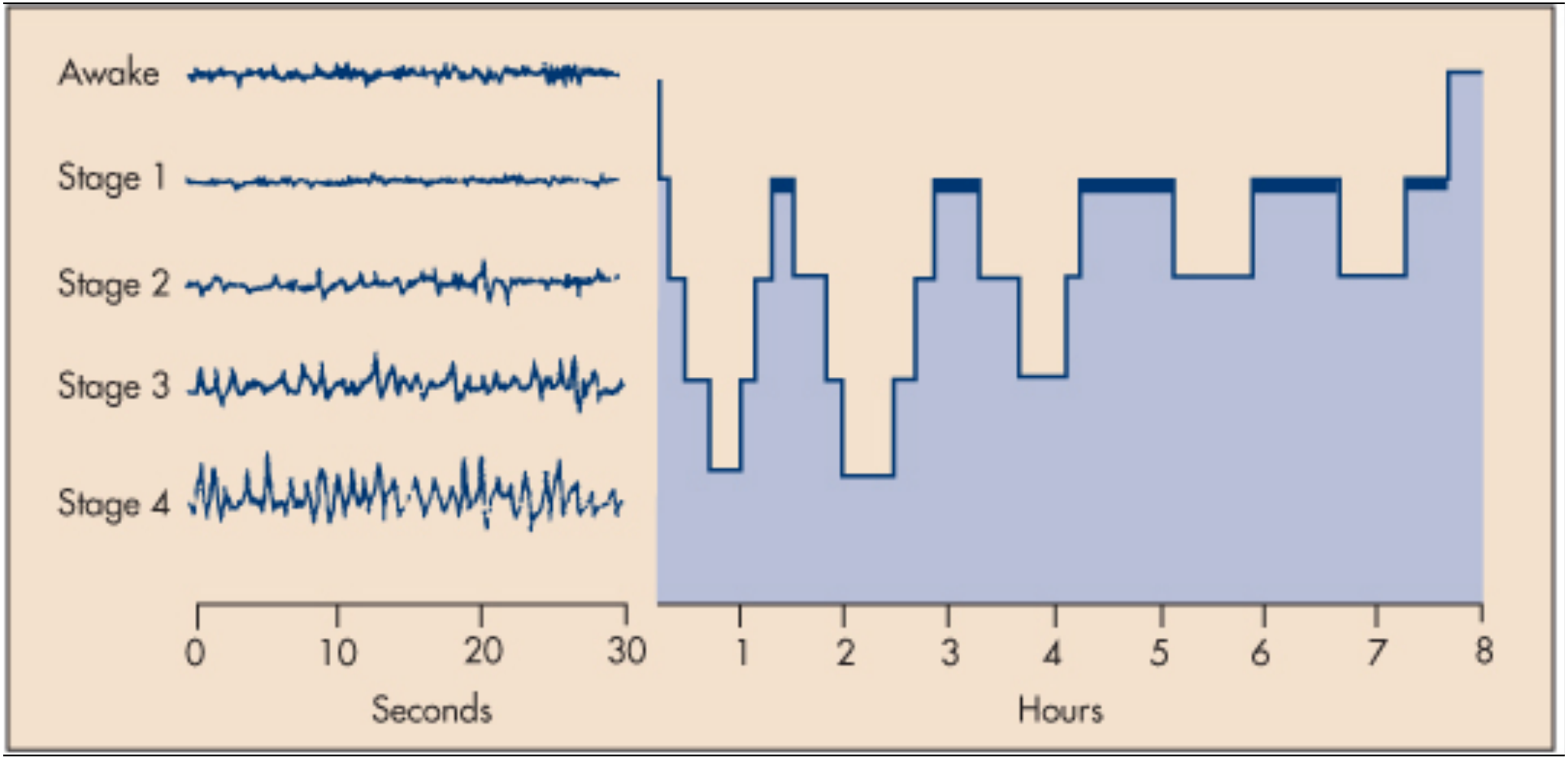
Phase-4 nonREM

- Deepest sleep; takes about 30-40 mins.
- **δ (theta) waves** predominate
- Most reflexes are intact; muscle tone slightly decreased
- Sleep-walking; sleep-talking; snoring and bedwetting generally occurs at this stage.

Sleep Stages-EEG



Sleep Stages



REM Sleep

- 5-30 minutes with 90 minute-intervals
- Active dreaming (dreams are remembered)
- **Active body movements**
- **More difficult to wake up with sensory stimulations**
- Waking up in the morning generally coincides with the last REM period.
- **Decrease in muscle tone** (except respiratory and eye muscles)
- Irregularity in heart and respiration rate.
- **20% increase in brain met**abolism

REM Sleep

- Atonia in neck muscles
- Rapid eye movements
- Beta waves in EEG

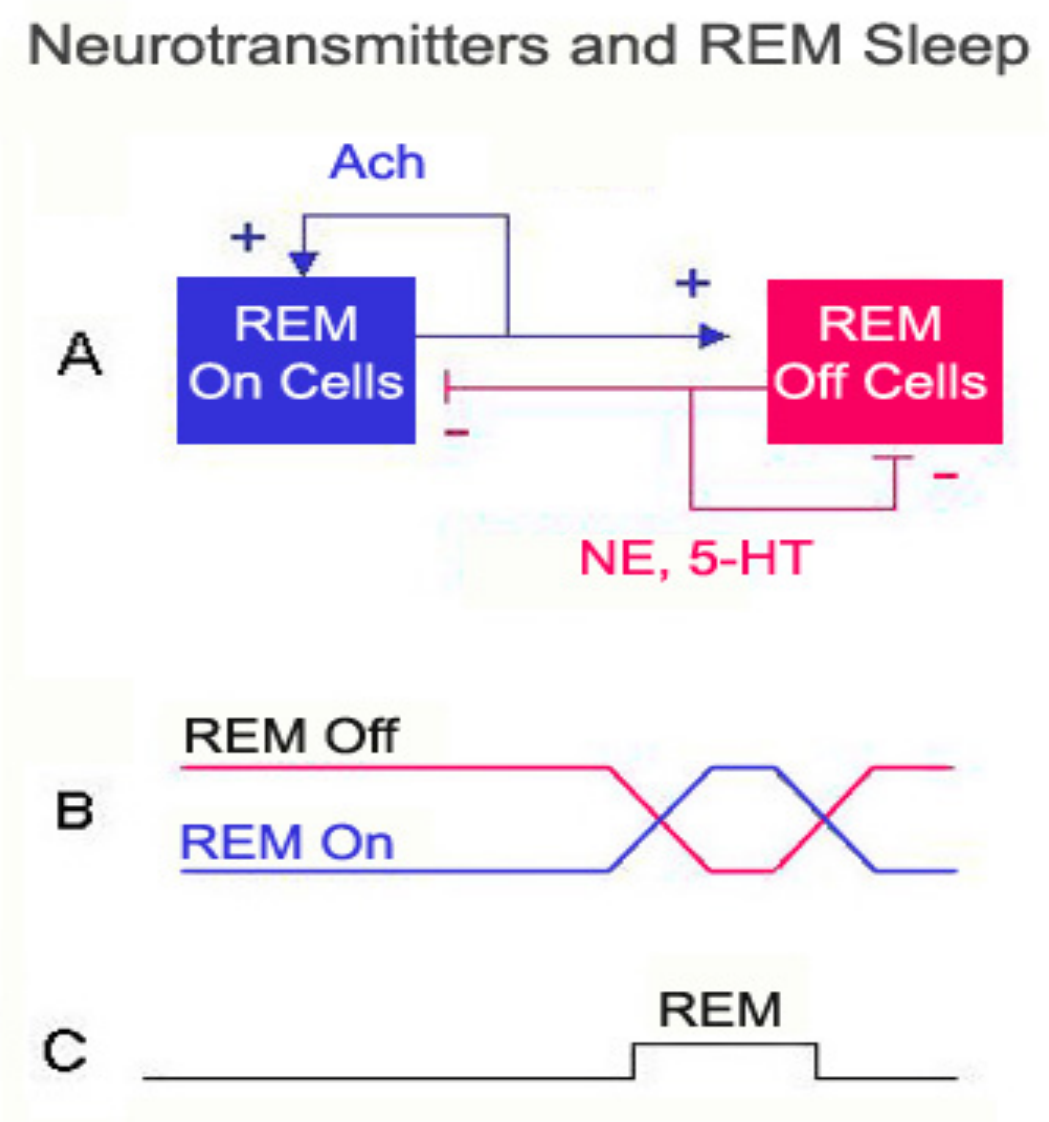
=paradoxal sleep, =desynchronized sleep

Possible causes of REM Sleep

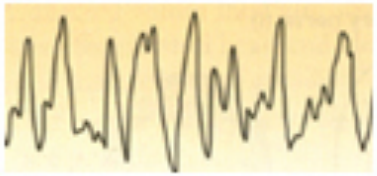
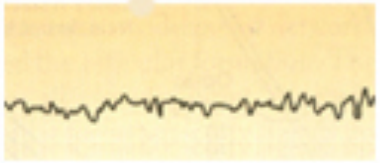
- ACh neurons in rostral reticular formation
  - Lateral tegmentum→lateral geniculate body→occipital cortex:

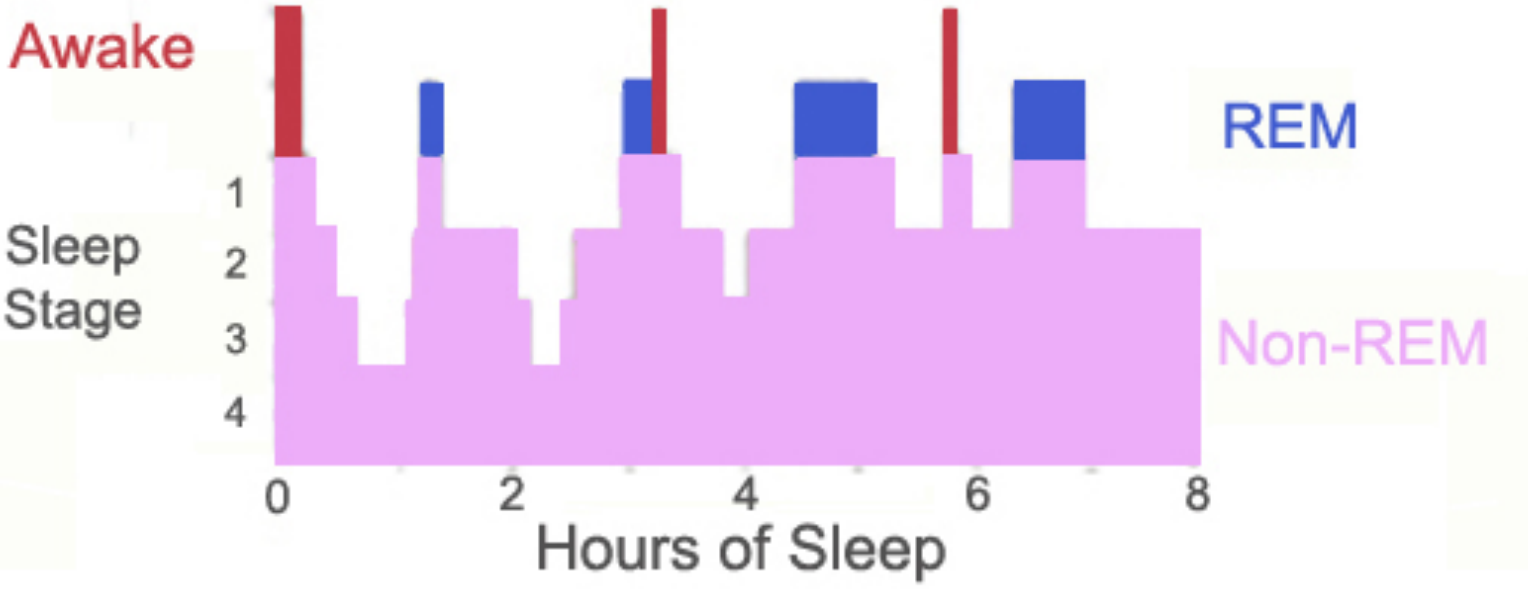
  = Ponto-geniculo-occipital spikes in EEG

Possible causes of REM Sleep

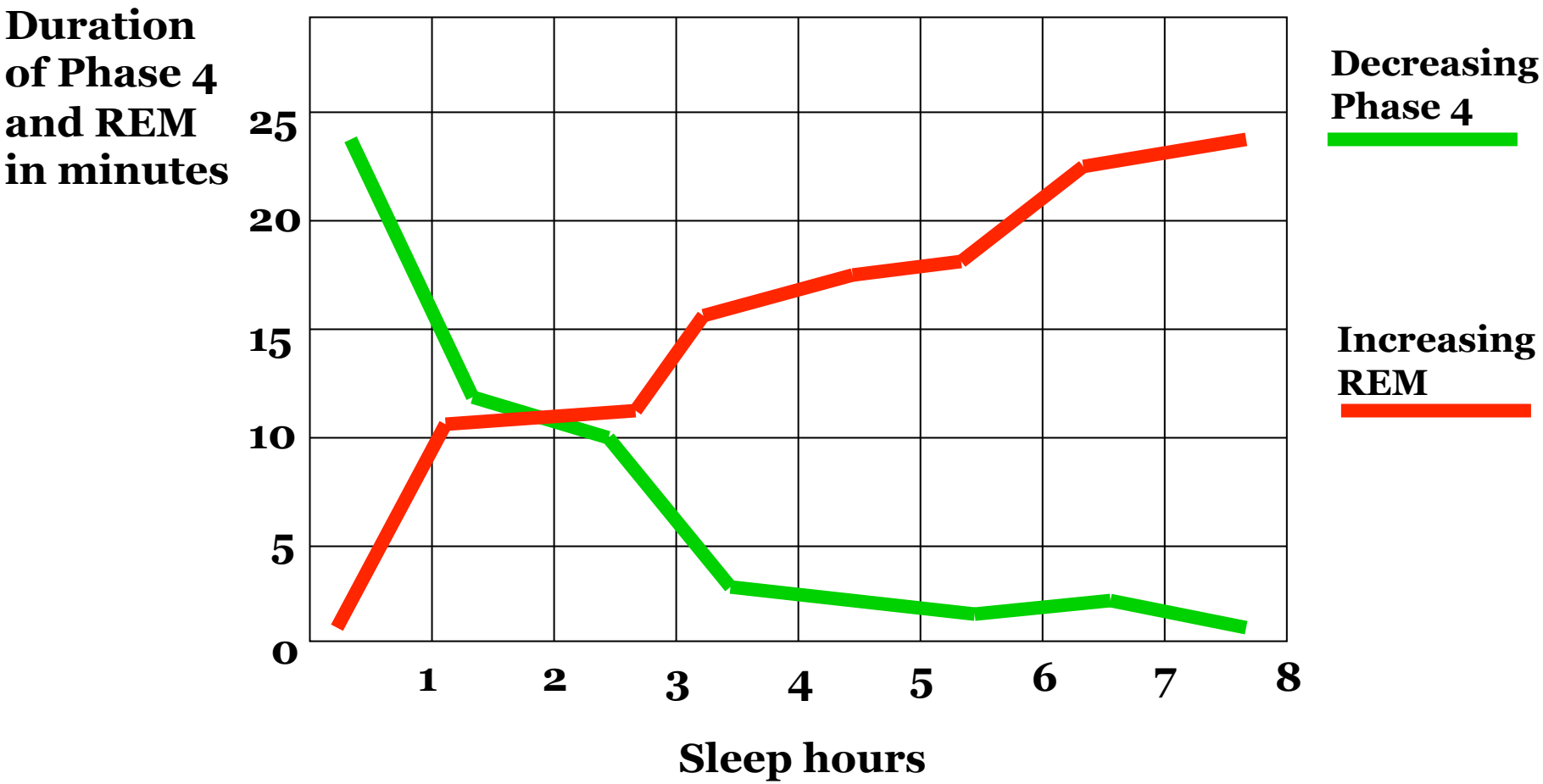


Characteristics of REM and Non-REM Sleep

Non-REM	REM (Paradoxical)
Slow EEG	EEG similar to awake person
	
Muscular activity	No movement
Dreaming rare	Dreaming common
Easily awakened	Hard to arouse easily
80% of sleep time	20% of sleep time

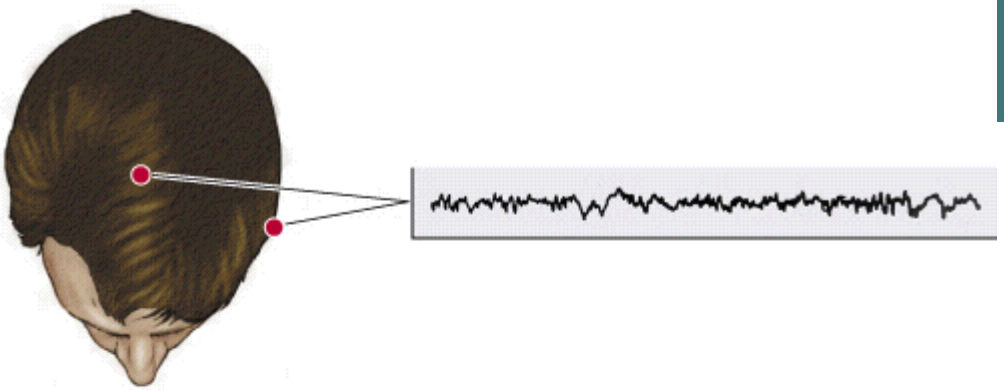


Typical sleep phases in night sleep

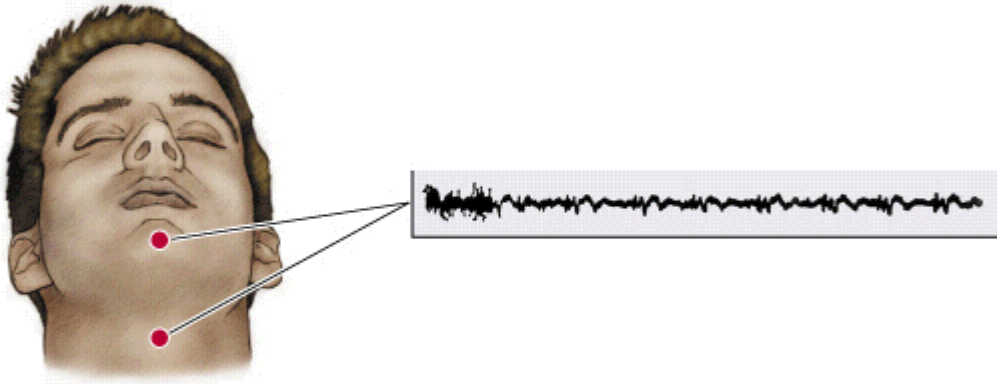


EEG / EMG / EOG

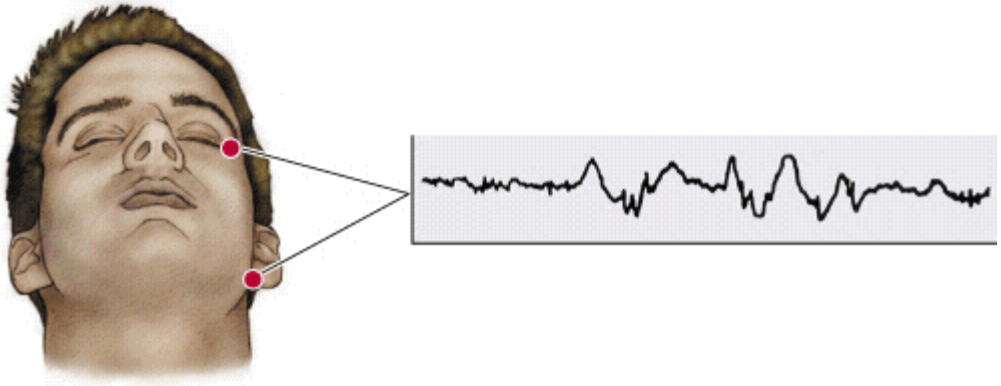
(A) Electroencephalogram (EEG)

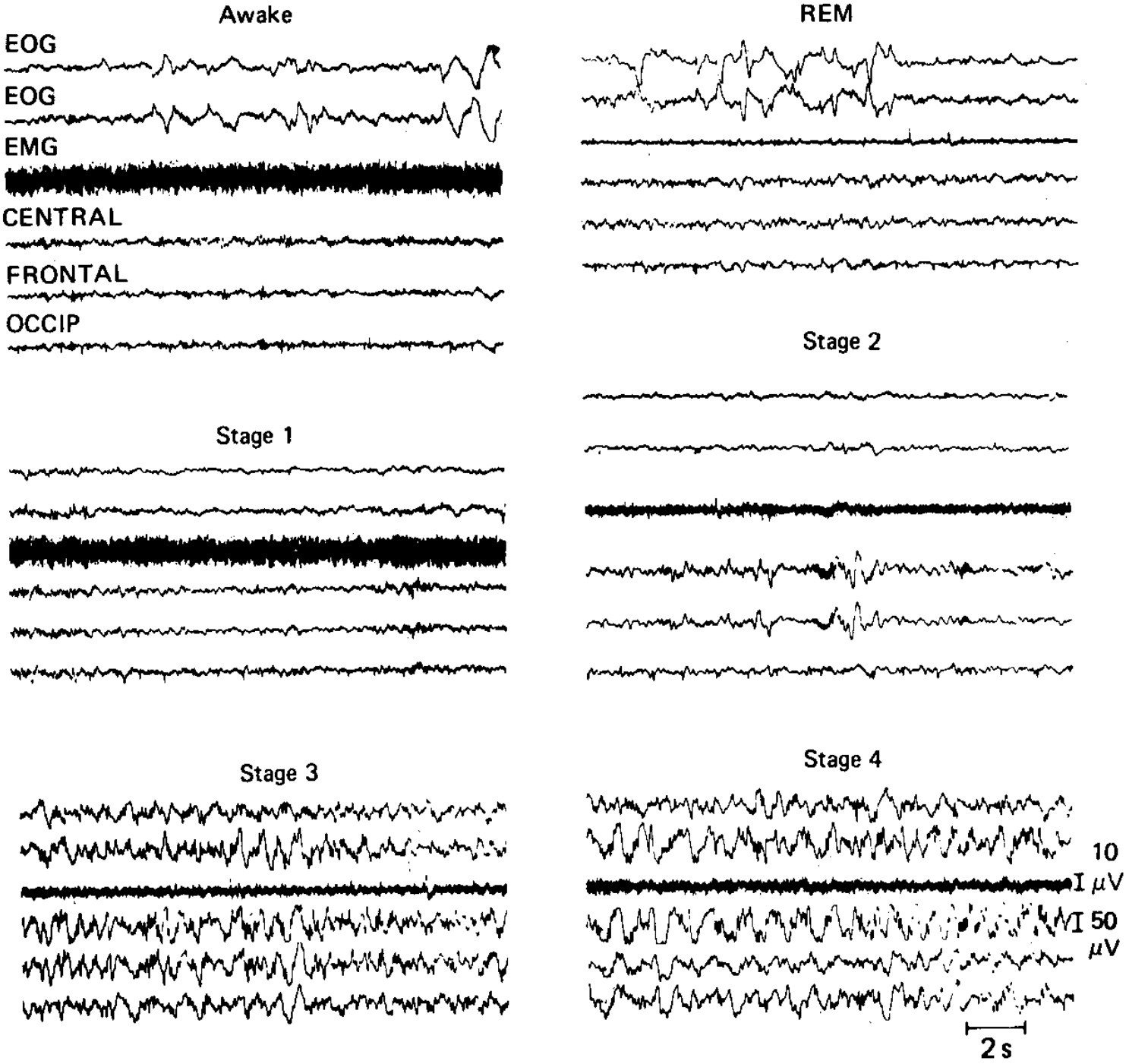


(B) Electromyogram (EMG)



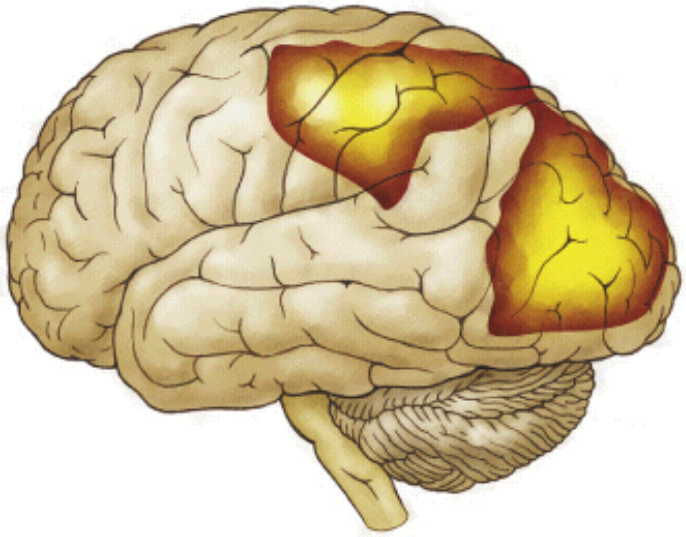
(C) Electrooculogram (EOG)




Awake
EOG
EOG
EMG
CENTRAL
FRONTAL
OCCIP
REM
Stage 1
Stage 2
Stage 3
Stage 4
10 μV
50 μV
2 s

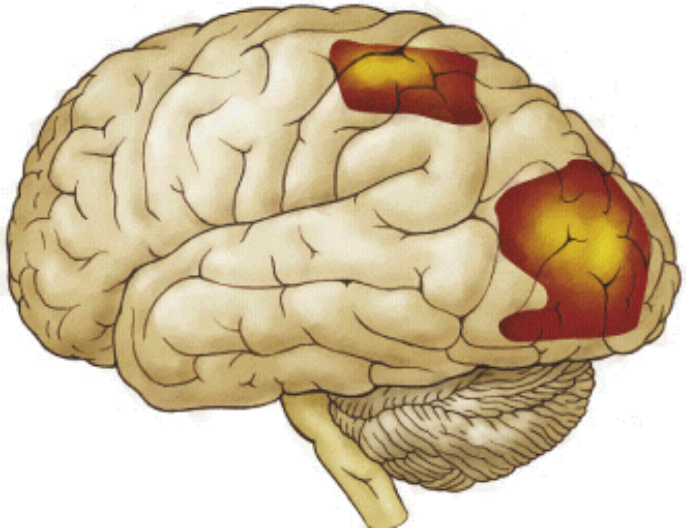
Cortical activity during sleep

(A) Reaction-time task



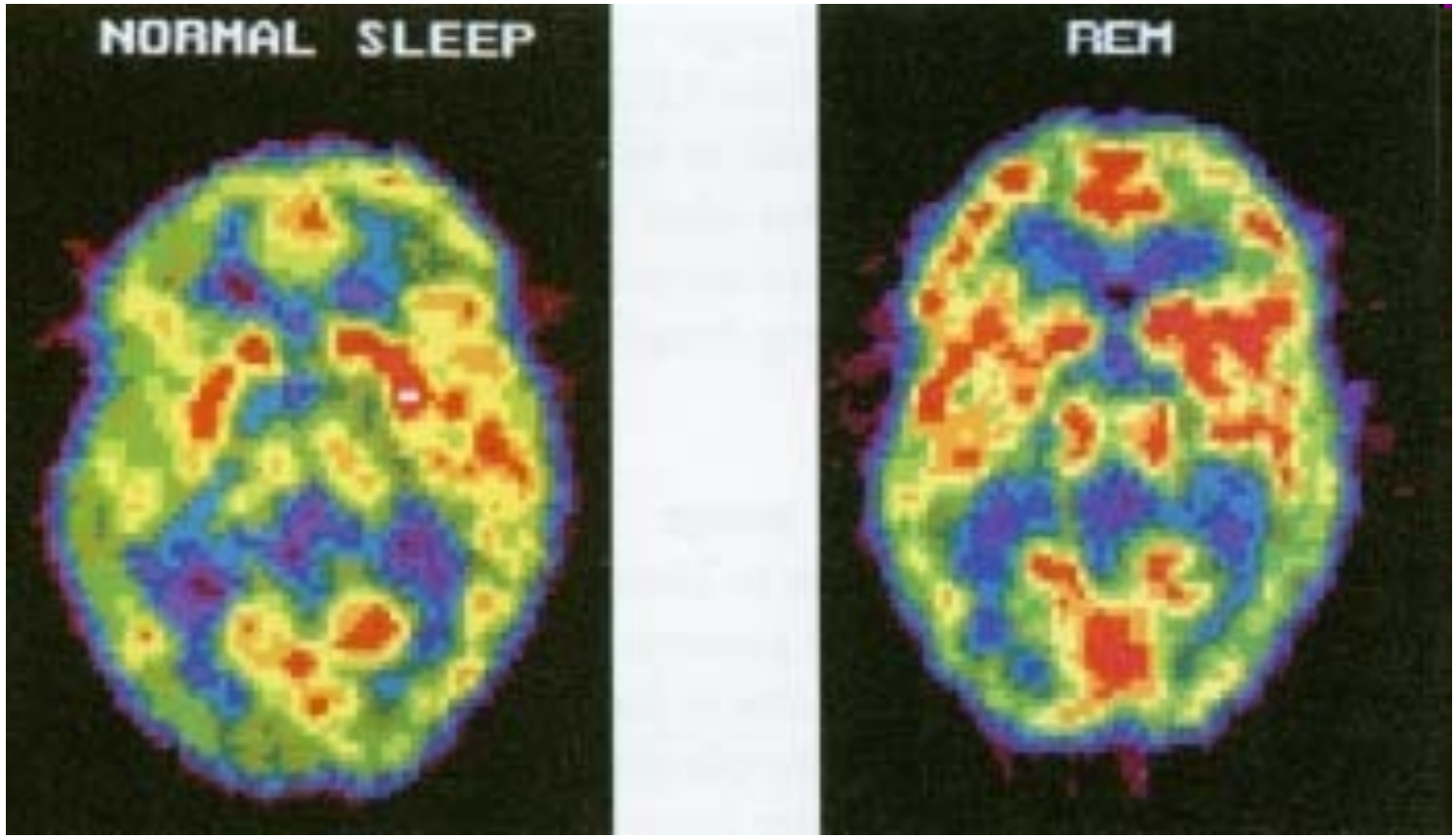
Subjects are trained on a reaction-time task, and brain activity is recorded with PET.

(B) REM sleep that night



Subjects display a similar pattern of brain activity during subsequent REM sleep.

Cortical activity during sleep



Waking up

- It is hard to wake up in nonREM Phase 4.
- Spontaneous arousal occurs in REM
- In thalamic neurons:
  - “Hyperpolarized” phasic firing during sleep;
  - “Depolarized” tonic firing due to sensory input…

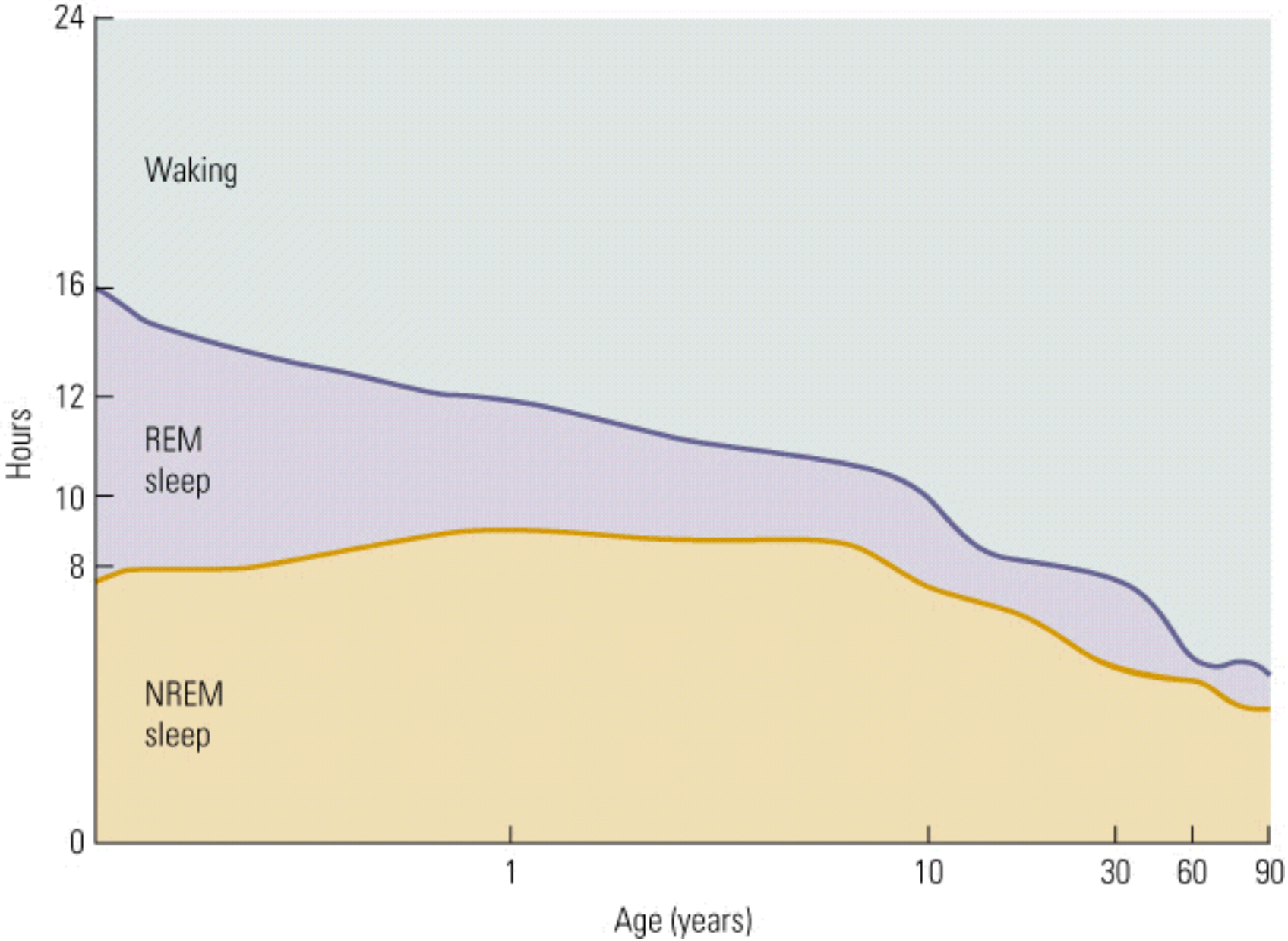
Physiological effects of sleep

- Sleep,
  - Helps the maintenance of normal activity level of CNS.
  - Helps to maintain the “balance” between the different parts of the CNS.
- Increased sympathetic activity and muscle tone during the awake period decreases with sleep…

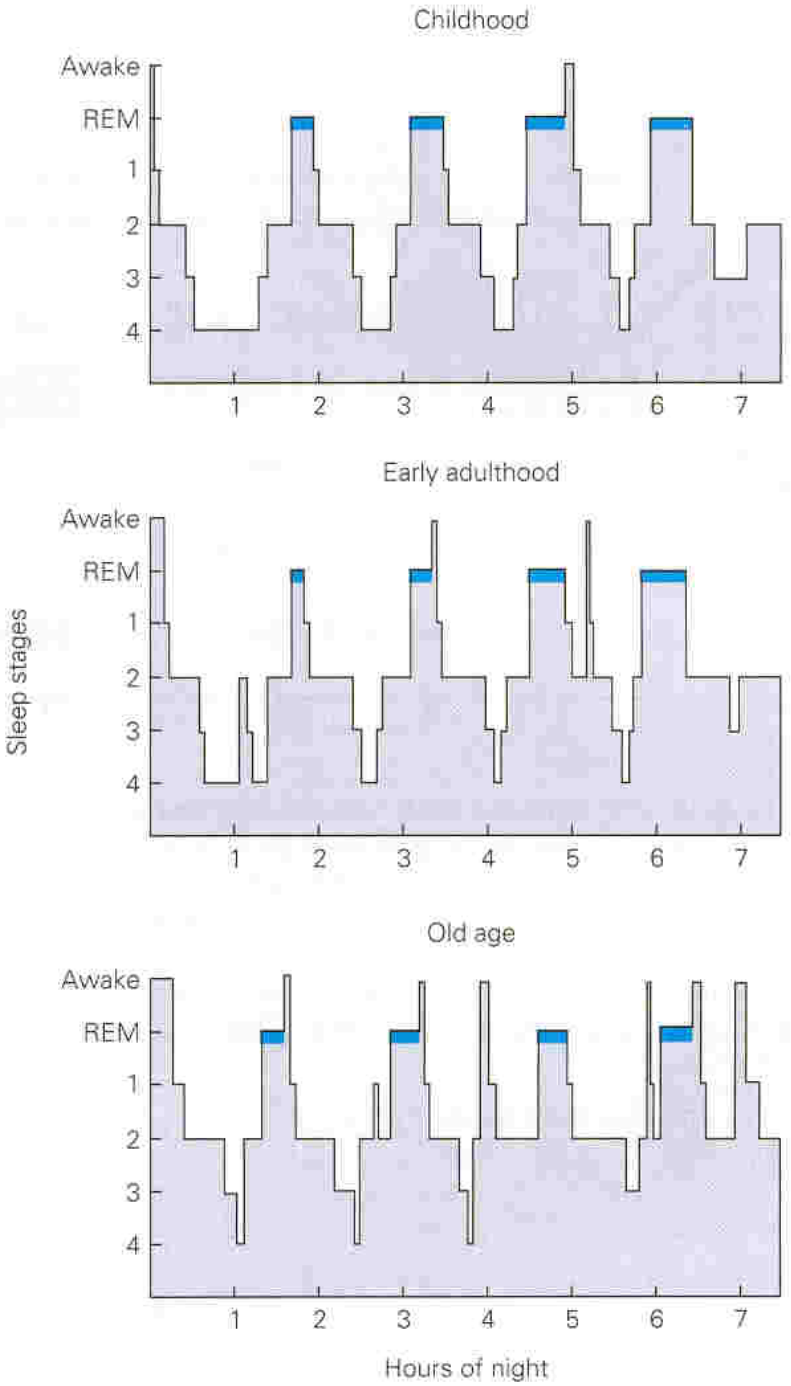
Physiological effects of sleep

- Body temperature drops, energy loss decreases
- Growth hormone and cortisol secretion
- Phosphate excretion from kidneys increase
- Melatonin secretion increases
- Skin and tissue repair

Sleep across life span

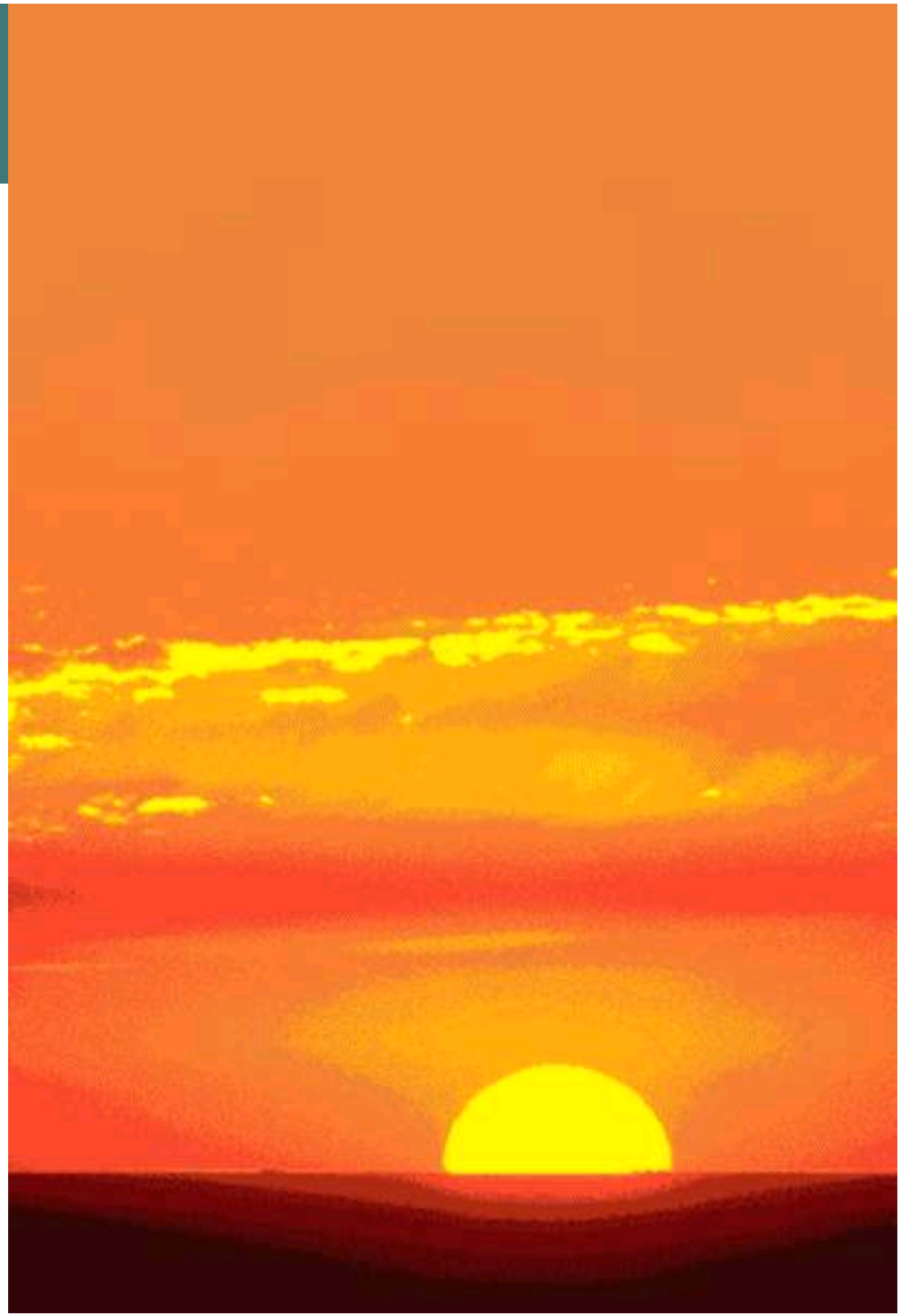


Sleep across life span



Sleep disorders

- Insomnia
  - Disturbances in sleep onset or maintenance
- Fatal Familial Insomnia
  - Unable to sleep, emotional instability, hallucinations, stupor- coma and death



Sleep deprivation

- Prolonged wakefulness may result in irritability, confusion and psychotic symptoms
- Fatigue, prostration, depression…
- **Unability to direct attention**
- **Hypersensitivity to pain**
- Visceral problems including **anorexia** and **distruption of excretion**
- **Defects in skin repair**
  - Collagen fibres loose their flexibility and may display color changes

REM sleep deprivation

- Confusion
- Paranoia
- Affective disorders
- Decrease in motor performance
- Memory consolidation impairments?
- Loss of balance
- Decreased immune efficiency

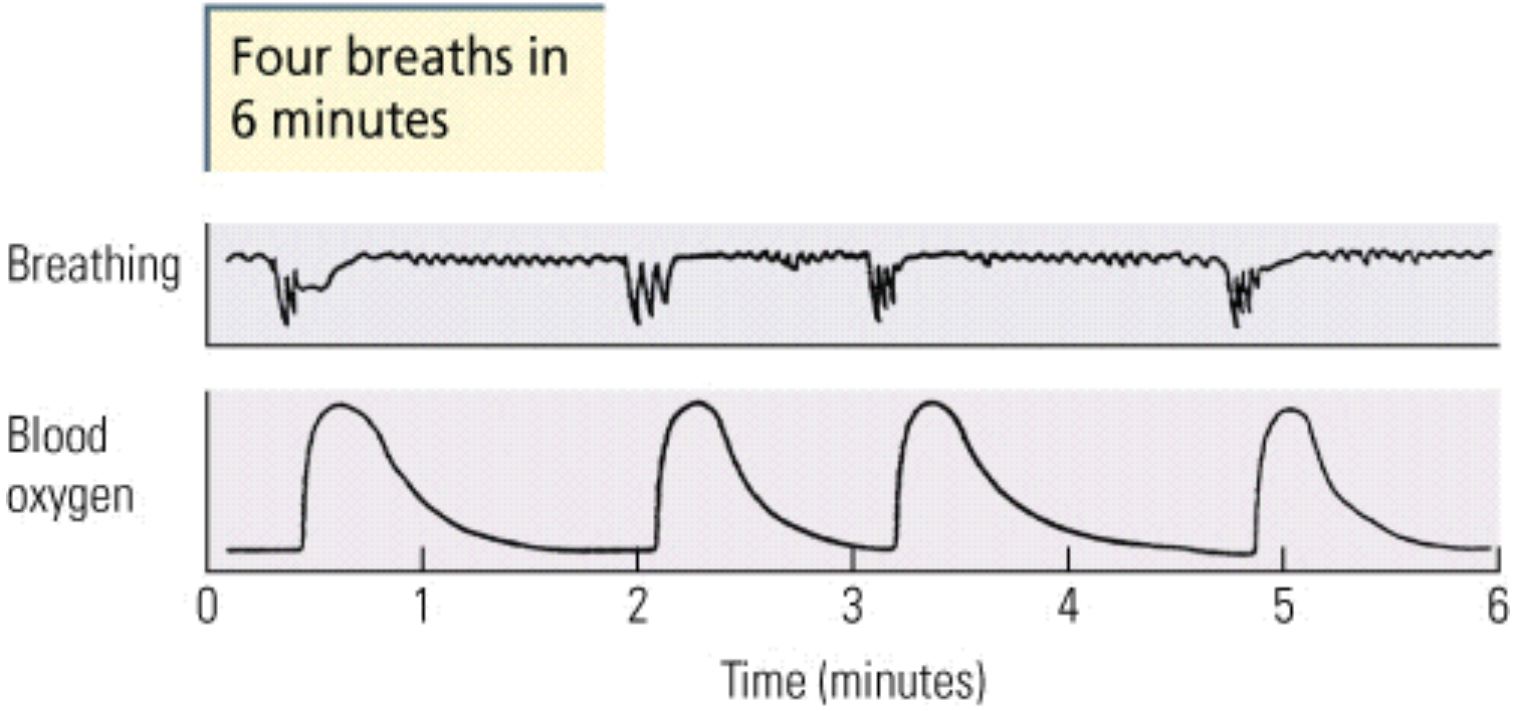
  - Work, traffic and home accidents!

Sleep disorders

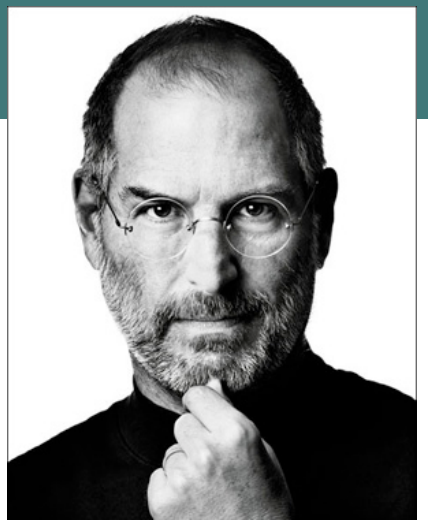
- **Parasomnias**
  - Sleep walking (somnanbulism), talking, etc..
- **Behavioral disorders** in REM sleep
  - Excess motor activity in REM.
- **Narcolepsy**
- **Restless leg sydrome**
  - Reccurrent leg movements like shaking or withdrawal-extension
- **Sleep paralysis**
  - Unable to move for a couple of minutes right after sleep onset or after waking up.

Sleep disorders

- **Obstructive Sleep Apnea Syndrome**
  - Collapse in the upper airways, interruption of respiration, snoring…
  - May cause restlessness and day sleep



Quote:



For you to sleep well at night,
the aesthetic,
the quality,
has to be carried all the way through…

(Steve Jobs)

- *Have a nice sleep!*