Physiology of Sleep

Assoc. Prof. Sinan Canan
sinancanan@gmail.com
www.sinancanan.net
Reticular Formation (Reticular activating system)
Neuromodulator Systems

(a) Norepinephrine
- Arousal, Reward system

(b) Serotonin
- Mood, satiety, body temperature, introversion; pain inhibition

(c) Dopamine
- Motor systems, reward, cognition, endocrine control

(d) Acetylcholine
- Learning, short-term memory, arousal, reward
Sleep

• Loss of wakefulness
• A fundamental function for physical and mental health
• Not loss of consciousness; only a “shift”
• An unconscious state which can be in part modified by sensory stimulations
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)**
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
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
- Stimulation 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 Rhythms

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 stretch (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

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)

50 μV

1 sec
Phase-1 nonREM

- Transition period between wakefulness and sleep; takes approximately 1-15 minutes.
- Eyes closed and relaxed...
- Light sleep, hallucination-like visions...
- $\alpha$ (alpha) waves weaken, slower $\theta$ (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

Stage 1 sleep

Stage 2 sleep

Stage 3 sleep

Stage 4 sleep

REM sleep

Alpha waves

Spindle (burst of activity)

Delta waves

Eye movement phase
Phase-3 nonREM

- Half-way deep sleep
- Body temperature and blood pressure decreases
- Harder to awaken
- Low frequency $\delta$ (theta) waves
- Sleep spindles are decreased
- No slow eye movements
Phase-4 nonREM

- Deepest sleep; takes about 30-40 mins.
- $\delta$ (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

- Awake: Beta waves
- Eyes closed, relaxed: Alpha waves
- Stage 1: Small, irregular waves
- Stage 2: Sleep spindles
- Stage 3: Delta waves appear
- Stage 4: Mostly delta
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 metabolism
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 $\rightarrow$ lateral geniculate body $\rightarrow$ occipital cortex:
    - Ponto-geniculoo-occipital spikes in EEG
Possible causes of REM Sleep

Neurotransmitters and REM Sleep

A

REM On Cells

REM Off Cells

Ach

+

+

--;

NE, 5-HT

B

REM Off

REM On

C

REM
Characteristics of REM and Non-REM Sleep

Non-REM
- Slow EEG
- Muscular activity
- Dreaming rare
- Easily awakened
- 80% of sleep time

REM (Paradoxical)
- EEG similar to awake person
- No movement
- Dreaming common
- Hard to arouse easily
- 20% of sleep time

![Graph showing sleep stages and hours of sleep]
Typical sleep phases in night sleep

- **Duration of Phase 4 and REM in minutes**

- **Sleep hours**

- **Decreasing Phase 4**

- **Increasing REM**
EEG / EMG / EOG

(A) Electroencephalogram (EEG)

(B) Electromyogram (EMG)

(C) Electrooculogram (EOG)
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

![Graph showing the decrease in total sleep time with age, separating REM sleep and NREM sleep.](image-url)
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
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 disruption 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 syndrome
  • Recurrent 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
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!