Sleep and Wakefulness
Topics

• definition and phenomenology of sleep
  - invertebrates
  - vertebrates (humans)

• regulation of sleep
  - circadian
  - homeostatic – humoral regulation – the function of sleep
  - “luxury sleep” – neuronal regulation
Definition of sleep

- rest-activity NOT= sleep-wakefulness

- general criteria of sleep
  - lack of movements
  - elevated sensory threshold
  - full reversibility
  - stereotypic posture
  - specific resting place
  - circadian organization
  - homeostatic regulation: deprivation - rebound

- mammals (and birds) - polygraphic criteria
Sleep in invertebrates

- Sleeping cockroach
- Sleeping scorpion
Stages in human sleep

- **Berger 1929:** arousal level is related to EEG patterns: δ, θ, α, β, later γ
- **Loomis 1937:** 5 stages of the sleep-wakefulness – 1 W and 4 SWS
- **Aserinsky and Kleitman 1953:** discovery of paradoxical sleep related to dreaming
- **Rechtschaffen-Kales criteria**
  - **LA1:** 2-7 Hz, slow eye movements, <20 μV
  - **LA2:** spindles, K-complexes, slow waves at low amplitude
  - **LA3:** <2 Hz >75 μV waves 20-50%
  - **LA4:** <2 Hz >75 μV waves >50%
  - **REM:** cortical activation, lack of muscle tone, rapid eye movements, PGO spikes
# EEG waves

<table>
<thead>
<tr>
<th>name</th>
<th>frequency</th>
<th>generator</th>
<th>occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>slow cortical rhythm</td>
<td>0 – 1 Hz</td>
<td>cortex</td>
<td>sleep, anesthesia</td>
</tr>
<tr>
<td>delta waves</td>
<td>1 – 4 Hz</td>
<td>cortex, thalamus?</td>
<td>sleep, anesthesia</td>
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<tr>
<td>theta waves/oscill.</td>
<td>4 – 9 Hz</td>
<td>hippocampus</td>
<td>falling asleep, REM</td>
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<tr>
<td>alpha oscillation</td>
<td>9 – 12 Hz</td>
<td>thalamus</td>
<td>resting state, closed eyes</td>
</tr>
<tr>
<td>sigma spindles</td>
<td>12 – 14 Hz</td>
<td>thalamus</td>
<td>falling asleep</td>
</tr>
<tr>
<td>beta waves</td>
<td>12 – 20 Hz</td>
<td>cortex</td>
<td>wakefulness, REM</td>
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<tr>
<td>gamma oscillation</td>
<td>20 – 80 Hz</td>
<td>cortical interneurons</td>
<td>attention, activation</td>
</tr>
<tr>
<td>ripple oscilllation</td>
<td>80 – 200 Hz</td>
<td>cortex, hippocampus</td>
<td>attention</td>
</tr>
</tbody>
</table>
Slow cortical rhythm

EEG - right area 7
EEG - left area 3
EEG - left area 7
Intra-cell area 21, -63 mV
EMG

A
B

0.2 s

Physiological variables in sleep

[Diagram showing various physiological variables over a 8-hour period, including EEG stages, EOG, EMG, heart rate, respiration, and PLG.]
Polygraphic sleep stages

- in animals only light and deep NREM sleep and REM sleep are usually distinguished
Sleep stages in rats

AW
F - P
F - F
HC
muscle

DS
F - P
F - F
HC
muscle

PS
F - P
F - F
HC
muscle

[Graphs showing different muscle activities in different sleep stages (AW, DS, PS)]
REM sleep in cats
REM sleep in humans
Sleep and age

The graph illustrates the changes in sleep patterns across different age groups. REM sleep ( Rapid Eye Movement sleep) and NREM sleep (Non-REM sleep) are highlighted for various age categories, from neonates to old age. The graph shows that the duration of sleep decreases with age, with infants and toddlers requiring more sleep than older adults. The graph also indicates the percentage of total sleep time spent in REM sleep, which is higher in infants than in adults.
Diurnal and polycyclic sleep

HUMAN

RAT
Humoral regulation of sleep

- closely related to homeostatic regulation
- something is being accumulated or used up
- sleep can be easily disturbed, but difficult to induce, appropriate control is a main issue

- two approaches:
  - harmful effects of sleep deprivation
    - stress is difficult to eliminate
    - motivation to sleep is almost as strong as motivation to avoid pain – torture
  - isolation of sleep factors
    - following sleep deprivation
    - during natural or experimentally evoked sleep
    - testing prospective signal molecules normally present in our body
Sleep deprivation

NREM deprivation: set-point of thermo-regulation increases
REM deprivation: heat dissipation increases
energy homeostasis becomes disturbed
Sleep factors

• **Ishimori, Pieron, ~1910:** dogs kept awake by forced walking for 10 days - successful sleep transfer
• methodological problems - repeated with positive results in goat-rat experiments
• deprivation is not needed for the effect - collection of human urine
• **end result:** muramyl peptide
• **Uchinozo** extractions from the brainstem of sleep deprived rats - uridine, oxidized glutathione (glu-cys-gly)
• **Monnier** sleep induced by thalamic stimulation in rabbits: DSIP (9 aa-s)
• these are not natural sleep factors
• **natural signal molecules:** GHRH, adenosine, interleukin-1, TNFα, PGD2
Transfer of natural sleep

- parabiotic animals: Matsumoto, 1972 - higher synchrony of NREM and REM sleep than between animals joined by their skin only

- de Andres, 1976 - transplantation of an additional head to dogs - independent sleep, 108 h survival

- Siamese twins - independent sleep is possible, but contradicting results exist

- Mukhametov, 1985-87 sleep in dolphins - the two hemispheres can sleep separately

- described in other animals as well: birds, whale, etc. - complete decussation of the visual pathway is a prerequisite
Unihemispheric sleep in dolphins
Two process theory of sleep
Synthesis

EXTERNAL CONDITIONS

ZEITGEBER
e.g. LIGHT-DARK CYCLE

synchronizes

CIRCADIAN PACE-MAKER (IN SCN?)

affects

CONSCIOUS DECISIONS

generates & synchronizes

masks

PHYSIOLOGICAL OSCILLATIONS*
e.g., TEMPERATURE,
HORMONES,

S-THRESHOLDS

*PROCESS C

interact to generate

CIRCADIAN SLEEP WAKE CYCLE
Neuronal regulation of sleep

- ancient theories about sleep (Mesopotamia)
- neuronal and humoral theories
- active hypothesis - basal state: wakefulness
  - Pavlov: irradiation of inhibition
  - von Economo: encephalitis plague
- passive hypothesis - basal state: sleep
  - classical transsections of Bremer, 30's
  - Moruzzi and Magoun, 1959
  - Shute and Lewis, 1967
- sleep centers
  - criteria: lesion, stimulation, correlated activity
  - midpontine pretrigeminal transsection
  - tractus solitarius - Dell, 1963
  - raphe - Jouvet, 1967
  - thalamus - Andersen and Anderson, 1968
  - basal forebrain - von Economo, 20’s
Arousing areas

- Magnocellular BF system (ACh, GABA, ?)
- Posterior-lateral hypothalamus (HA, ORX)
- Midline and intralaminar nuclei (glu)
- Midbrain and pontine nuclei (NA, ACh, glu, 5-HT, DA)
Ascending activating systems
Thalamo-cortical connections
Functional states of thalamus
Role of the basal forebrain

- von Economo: BF-POA promotes sleep, posterior HT promotes wakefulness
- Sterman and Clemente 1962- lesion causes decreased or fragmented sleep
- stimulation - sleep (also at high frequency!)
- conditioned response to sounds
- warming, ACh crystals - sleep
- late 70's, early 80's - description of the cholinergic system
- cholinergic cells disappear or shrink in Alzheimer's disease
- electrical - excitotoxic - selective lesion
- corticopetal projection is not exclusively cholinergic
- SCN, thermoregulation, proximity of HT, VLPO, prefrontal cortex - high importance
Unilateral lesion of BF I.
Unilateral lesion of BF II.

Before lesion

- No drug
- Scopolamine

After R. NB lesion

- No drug
- Scopolamine

Modified from Buzsáki et al., J. Neurosci 8 (1988): 4007-4026
Berger - 1929
Sleep stages

Awake: low voltage-random, fast

Drowsy: 8 to 12 cps- alpha waves

Stage 1: 3 to 7 cps- theta waves

Stage 2: 12 to 14 cps- sleep spindles and K complexes

Deep sleep: 1/2 to 2 cps- delta waves > 75 V

REM sleep: low voltage-random, fast with sawtooth waves
Brainstem transsections

A: 'encephale isole'
B: 'cervau isole'
The cholinergic system