

# 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**

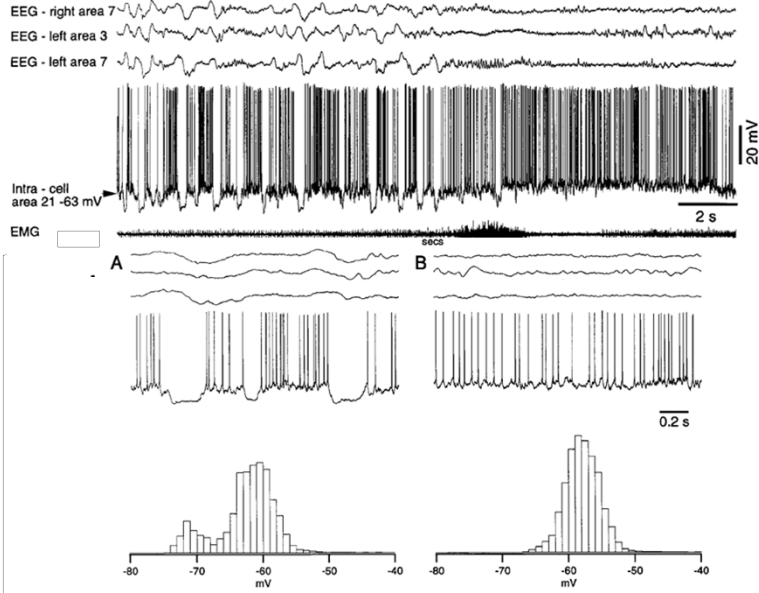
## Stages in human sleep

- Berger 1929: arousal level is related to EEG patterns:  $\delta$ ,  $\theta$ ,  $\alpha$ ,  $\beta$ , later  $\gamma$  
- 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,  $<20 \mu\text{V}$
  - LA2: spindles, K-complexes, slow waves at low amplitude
  - LA3:  $<2 \text{ Hz}$   $>75 \mu\text{V}$  waves 20-50%
  - LA4:  $<2 \text{ Hz}$   $>75 \mu\text{V}$  waves  $>50\%$
  - REM: cortical activation, lack of muscle tone, rapid eye movements, PGO spikes 

## EEG waves

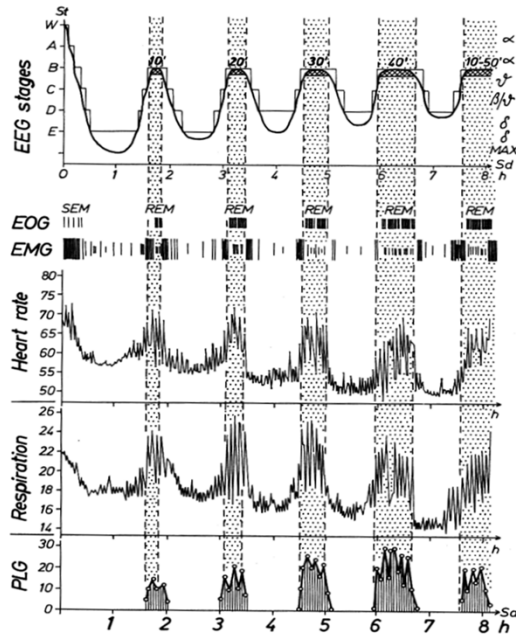
name	frequency	generator	occurrence
slow cortical rhythm	0 - 1 Hz	cortex	sleep, anesthesia
delta waves	1 - 4 Hz	cortex, thalamus?	sleep, anesthesia
theta waves/oscill.	4 - 9 Hz	hippocampus	falling asleep, REM
alpha oscillation	9 - 12 Hz	thalamus	resting state, closed eyes
sigma spindles	12 - 14 Hz	thalamus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

# Slow cortical rhythm



Steriade, M., et al., *J. Neurophysiol.* 85 (2001): 1969-1985

# Physiological variables in sleep



# Polygraphic sleep stages

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



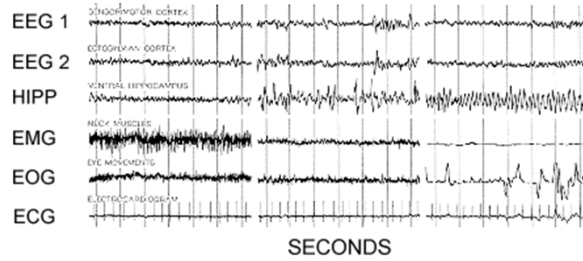
Waking



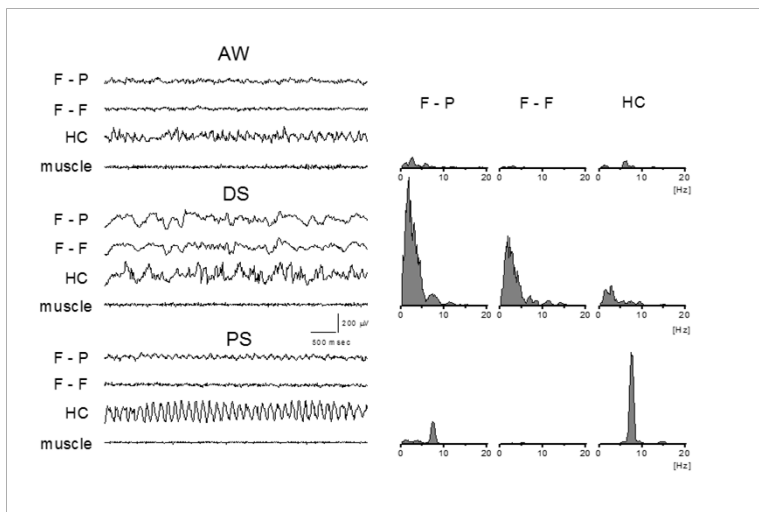
nonREM sleep



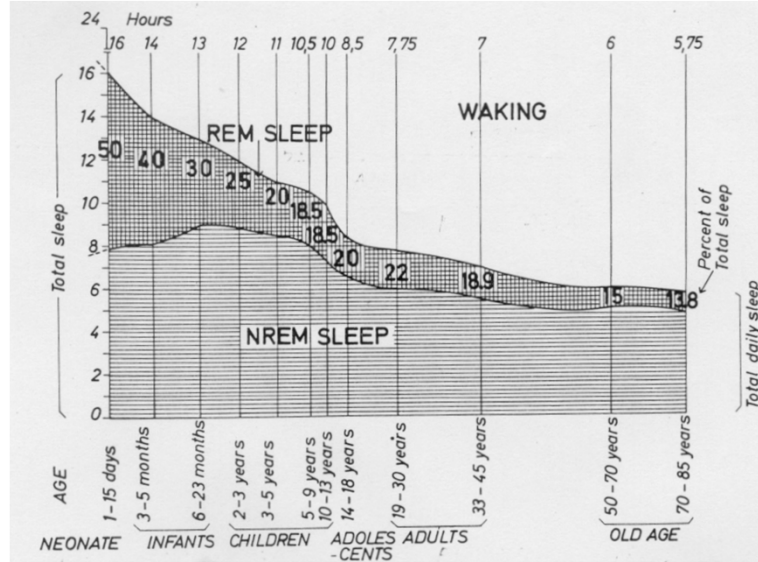
REM sleep



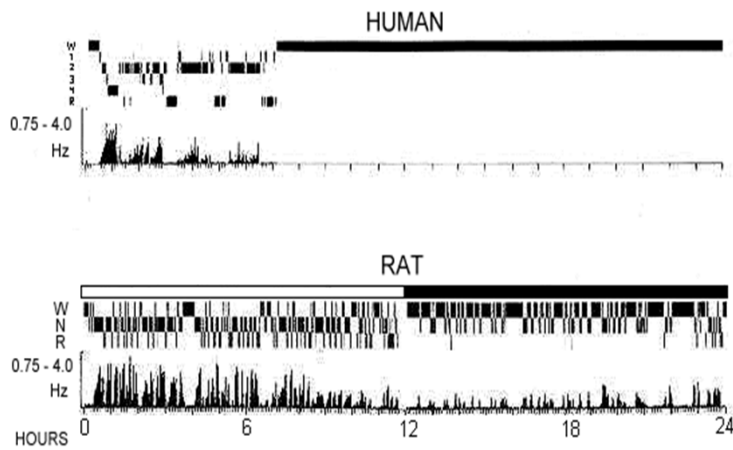
# Sleep stages in rats



# Sleep and age



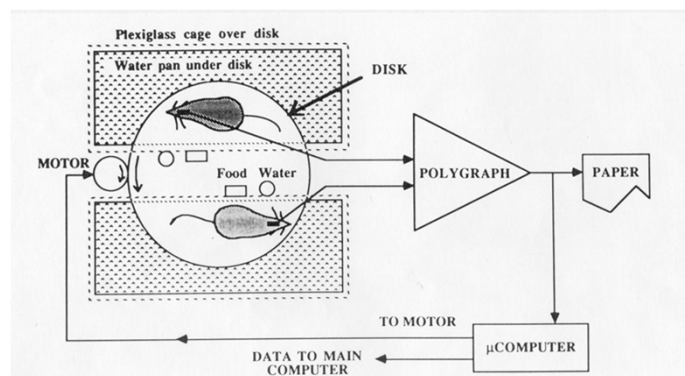
# Diurnal and polycyclic sleep



## 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

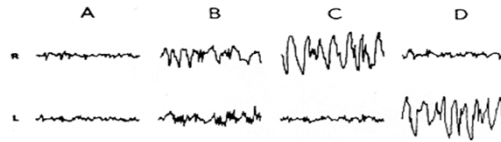
- Ishimori, Pieron, ~1910: dogs kept awake by forced walking for 10 days - successful sleep transfer
- methodological problems - repeated with positive results in goat-rat experiments
- deprivation is not needed for the effect - collection of human urine
- end result: muramyl peptide
- Uchinozo extractions 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, TNF $\alpha$ , PGD $_2$

## Transfer of natural sleep

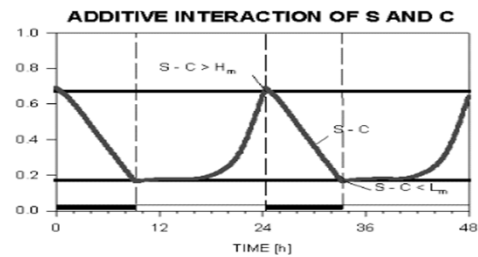
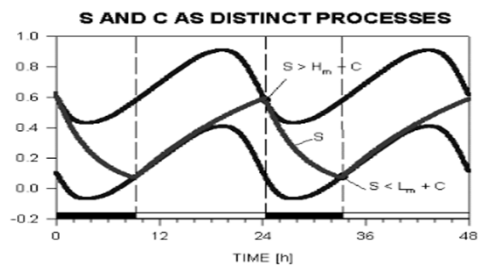
- parabiotic animals: Matsumoto, 1972 - higher synchrony of NREM and REM sleep than between animals joined by their skin only
- de Andres, 1976 - transplantation of an additional head to dogs - independent sleep, 108 h survival
- Siamese twins - independent sleep is possible, but contradicting results 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



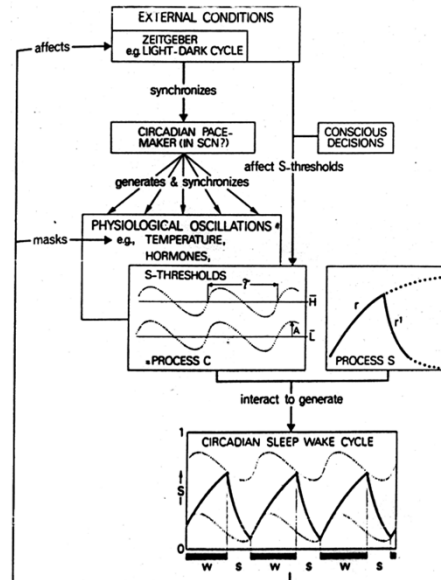
# Unihemispheric sleep in dolphins



# Two process theory of sleep



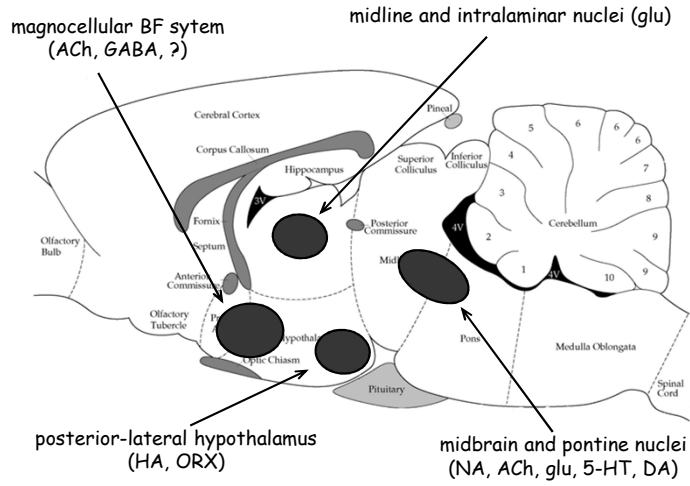
## Synthesis



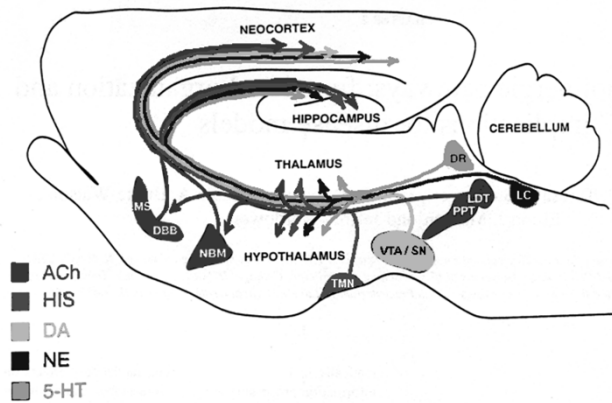
## Neuronal regulation of sleep

- 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 transections of Bremer, 30's
  - Moruzzi and Magoun, 1959
  - Shute and Lewis, 1967
- sleep centers
  - criteria: lesion, stimulation, correlated activity
  - midpontine pretrigeminal transection
  - tractus solitarius - Dell, 1963
  - raphe - Jouvet, 1967
  - thalamus - Andersen and Anderson, 1968
  - basal forebrain - von Economo, 20's

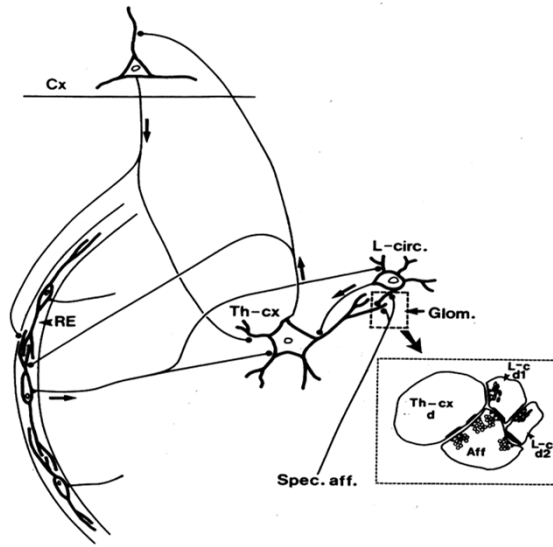
# Arousing areas



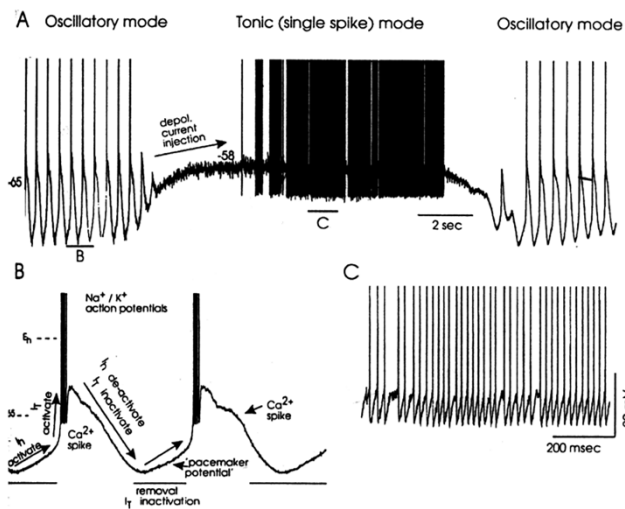
# Ascending activating systems



# Thalamo-cortical connections



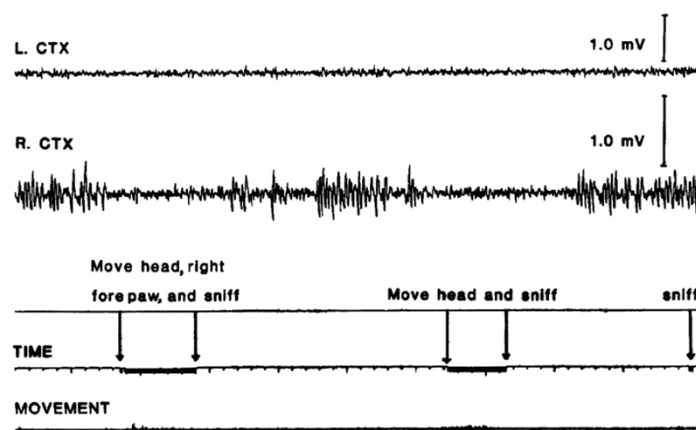
# Functional states of thalamus



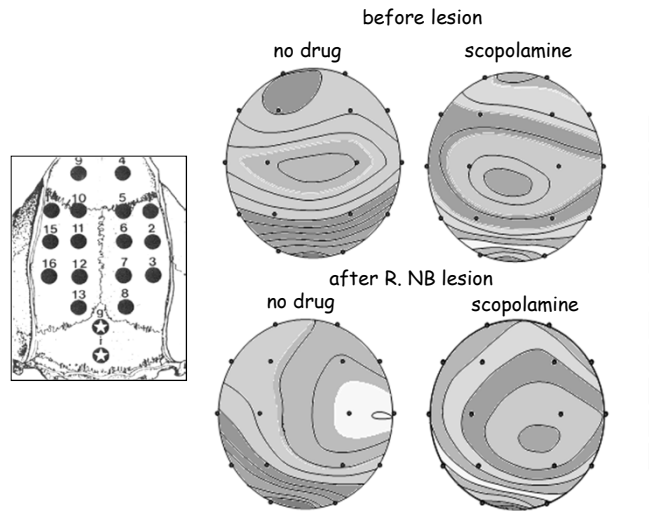
## Role of the basal forebrain

- von Economo: BF-POA promotes sleep, posterior HT promotes wakefulness
- Serman 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 *et*
- 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.

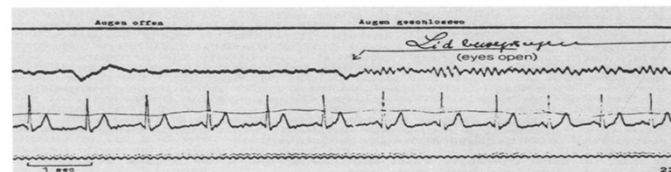
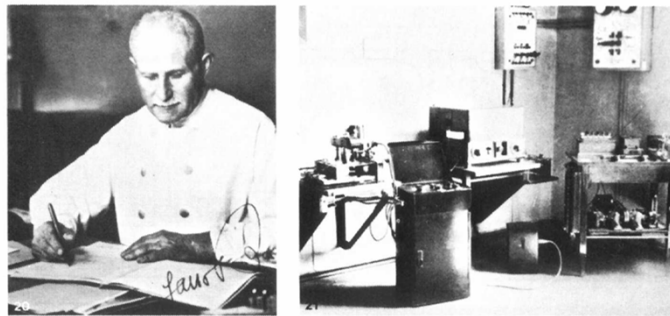


## Unilateral lesion of BF II.



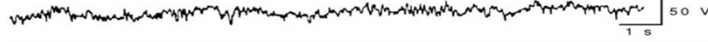
modified from Buzsáki et al., *J. Neurosci.* 8 (1988): 4007-4026

## Berger - 1929

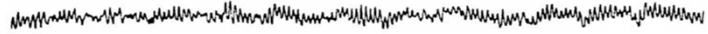


# Sleep stages

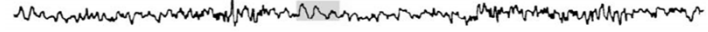
Awake: low voltage-random, fast



Drowsy: 8 to 12 cps- alpha waves



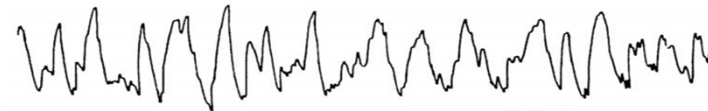
Stage 1: 3 to 7 cps- theta waves



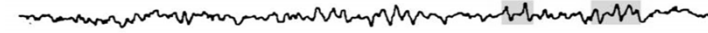
Stage 2: 12 to 14 cps- sleep spindles and K complexes



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



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

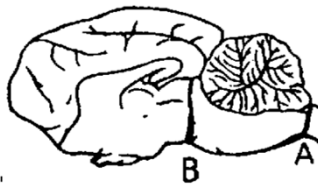


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# Brainstem transections



C



B: 'cervau isole'

A: 'encephale isole'

# The cholinergic system

