Comparative physiology and pharmacology of sleep

EEG and neuronal mechanisms

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Learning objectives

At the end of the lecture you should:

- understand the neuronal basis of the EEG
- know the important brain structures of sleep-wake regulation

EEG (1)

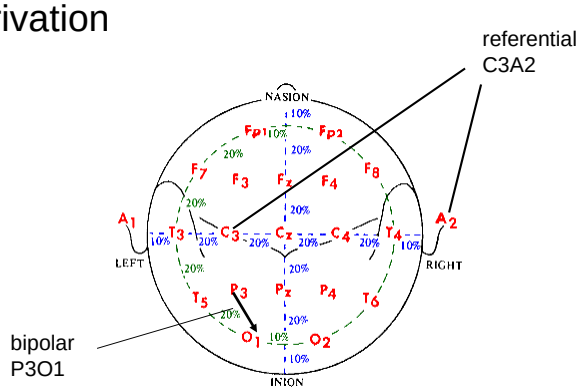
- window to the brain
- collective behavior of cortical neurons
- ~10^8 neurons
- robust, large-scale measure of neocortical dynamics
- closely related to brain state

EEG (2)

- potential difference ⇨ 2 electrodes
  - referential derivation
  - bipolar derivation

10-20 system

odd = left
even = right
z = „zero“



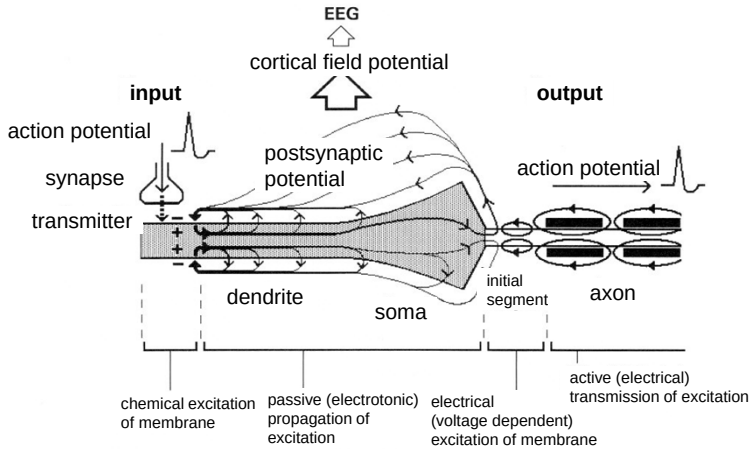
EEG (3)

- electrical potential fluctuations
- generators lie in cortex
  (physiological basics established)
- EEG patterns: complex interactions of neuronal structures in cortical and sub-cortical structures of the brain

Generation of EEG (1)

- postsynaptic summary potentials
  (EPSP, IPSP)
- not sum of action potentials
  (at the level of the cortex not detectable)
- pyramidal cells of cortex
  (perpendicular to surface)

Generation of EEG (2)



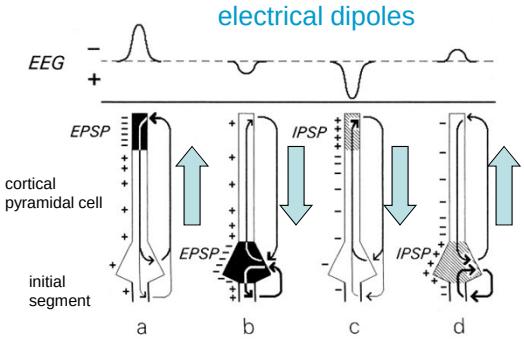
EEG results from postsynaptic cortical field potentials

Zschocke (2002) Klinische Elektroenzephalographie

Generation of EEG (3)

a EPSP at apical dendrite
b EPSP at soma of neuron
c IPSP at apical dendrite
d IPSP at soma

potential fluctuations in EEG mainly resulting from EPSP at apical dendrites



- determinant for EEG: spatial structure and orientation of dipoles
- important potential sources: large pyramidal cells of the cortex

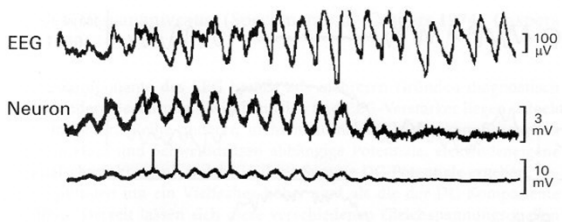
Zschocke (2002) Klinische Elektroenzephalographie

EEG: sum of cortical field potentials

rhythmic spindle activity (ca. 10 Hz) in EEG generated by rhythmic thalamo-cortical afferents

rhythmic postsynaptic fluctuations of membrane potential

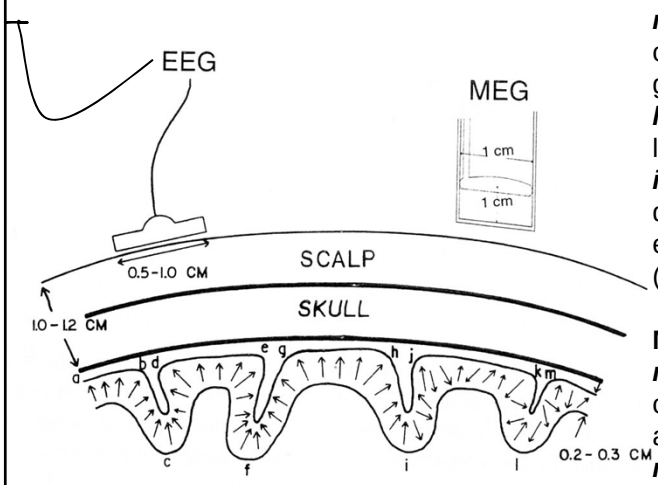
only few action potentials (poor correlation with EEG)



simultaneous recording of EEG and intracellular electrode below EEG electrode (barbiturate anesthesia)

Zschocke (2002) Klinische Elektroenzephalographie

Neocortical sources pictured as dipole layers (folded "dipole sheets")

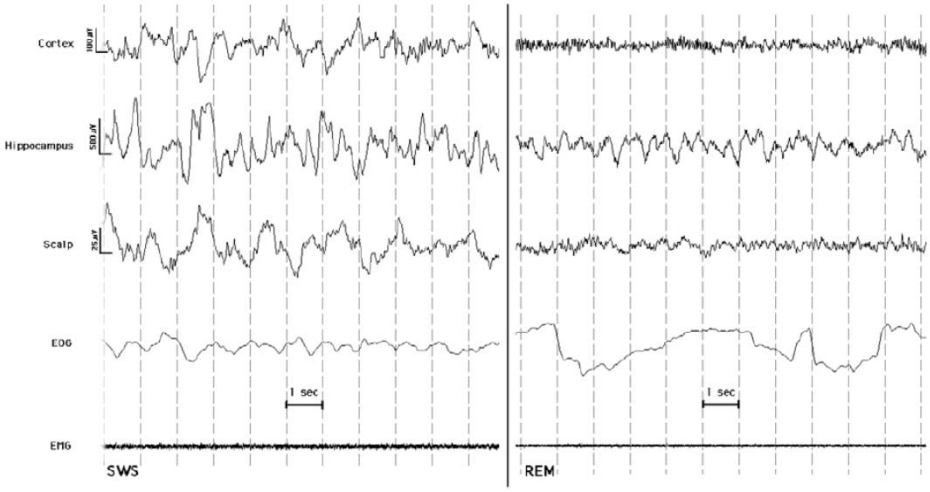


EEG
most sensitive to correlated dipole layer in gyri (regions ab, de, gh)
less sensitive to dipole layer in sulcus (hi)
insensitive to opposing dipole layer in sulci (bcd, efg) or random layer (ijklm)

MEG
most sensitive to correlated & min. apposed dipole layer (hi)
much less sensitive to all other sources shown

Nunez & Srinivasan, 2006

EEG Patterns recorded from intracranial (cortex and hippocampus) and scalp electrodes



Moroni et al., 2007

Oscillatory activity of the Non-REM sleep EEG

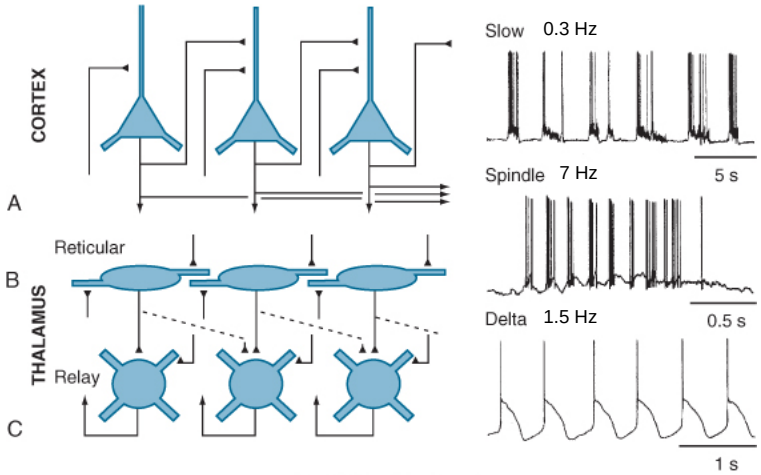
- Delta waves, „slow-wave activity“ (1 – 4 Hz)
- Sleep spindles (~ 14 Hz)
- „Slow oscillations“ (< 1 Hz)
- Alpha activity (~ 10 Hz)

Building blocks of corticothalamic networks

excitatory
GLU

inhibitory
GABA

excitatory
GLU

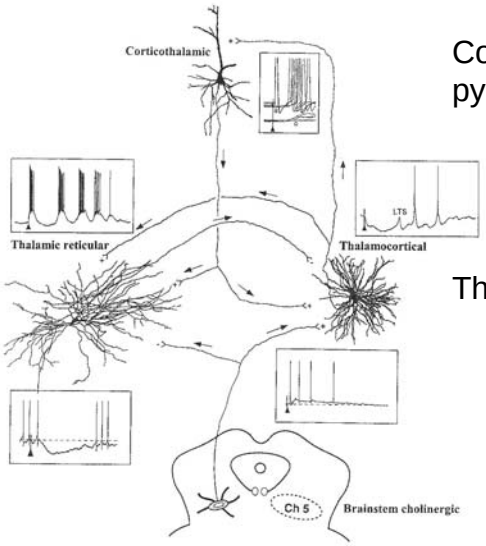


Steriade (2005) Principles and Practice of Sleep Medicine

Neuronal loops in corticothalamic networks

Cortex (Layer VI)
pyramidal cells

Generator of
spindles



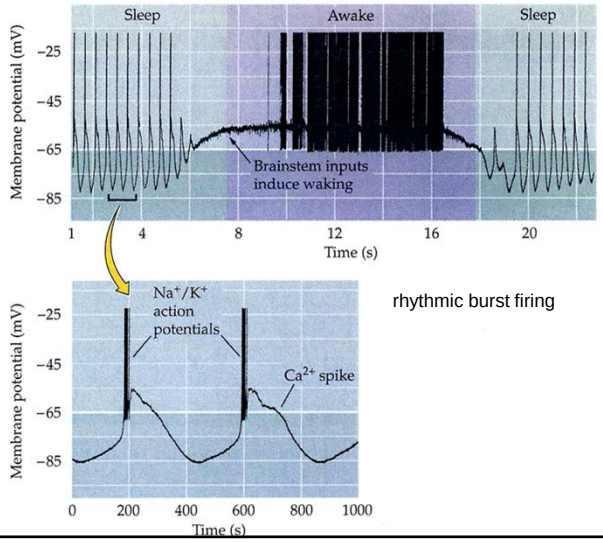
Thalamus

Steriade, Neuroscience, 2000

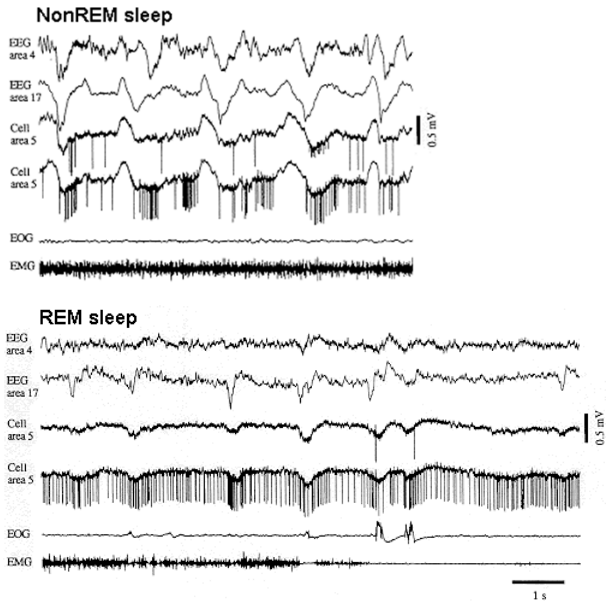
Activity patterns in thalamo-cortical neurons: dependent on membrane potential

Hyperpolarization: oscillatory mode

Depolarization: tonic mode (single spike mode)



rhythmic burst firing



Non-REM sleep:

tonic hyperpolarization

⇨ burst mode

⇨ slow waves in EEG, large amplitude

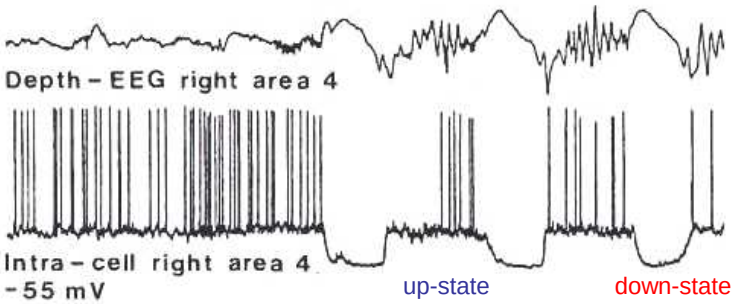
REM sleep and waking:

partially depolarized

⇨ single spike mode

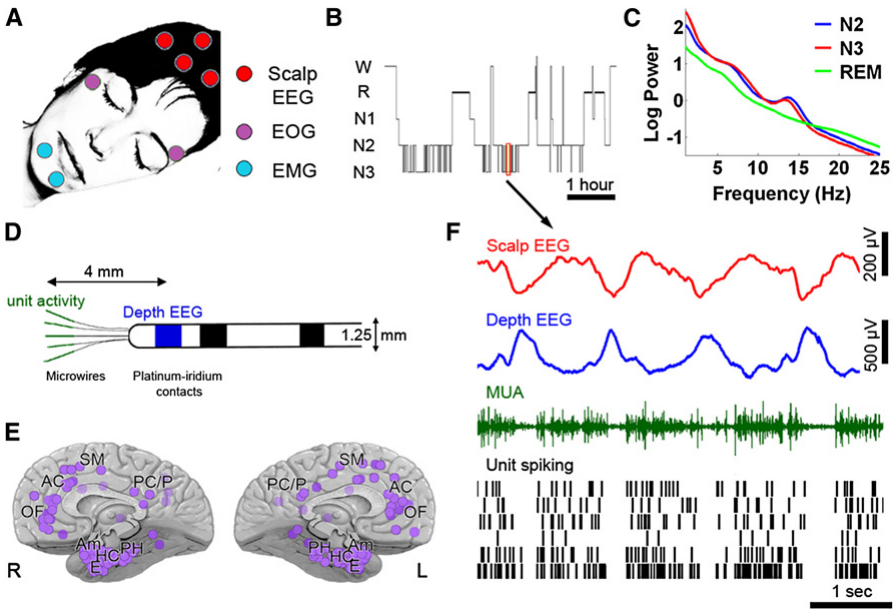
⇨ fast waves in EEG, small amplitude

Slow oscillation (< 1 Hz)



First recordings in the cat (Steriade at al., 1993)

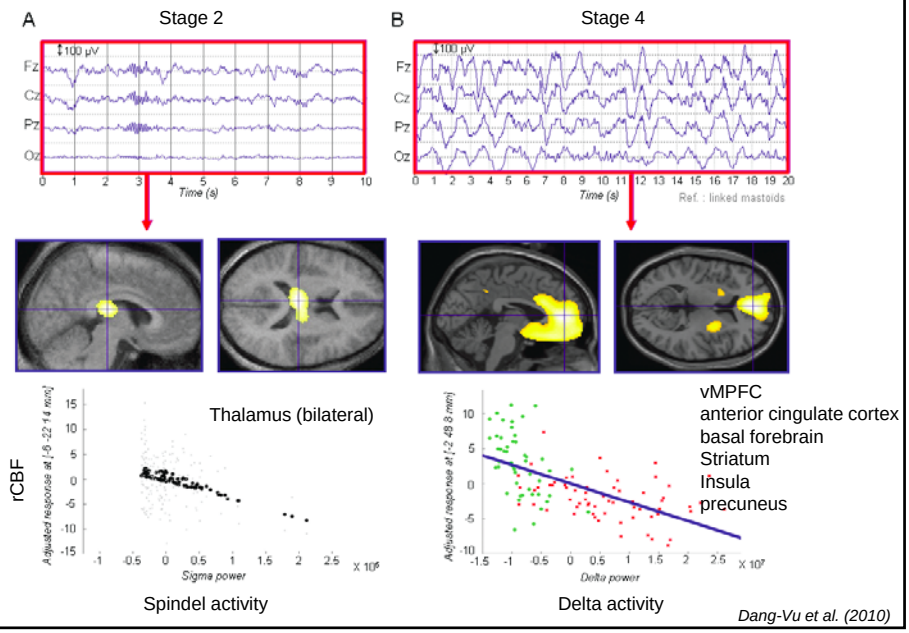
Slow oscillations of membran potential
hyperpolarisation: „down-state“
depolarisation: „up-state“



Nir et al (2011)

Neural correlates of NREM sleep oscillations

($H_2{}^{15}O$ PET studies)

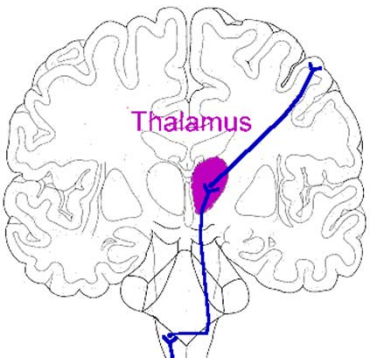


Spindel activity

Delta activity

Dang-Vu et al. (2010)

Thalamus important sensory relais station



Sensory information reaches the cortex via the thalamus. The relay neurons in the specific thalamic nuclei act as gatekeepers:

In **waking**, the gate is open (depolarizing influence: Ach, NA, HA, 5-HT, Glu)

In **sleep**, the gate is closed (reduced depolarizing influence of transmitters)

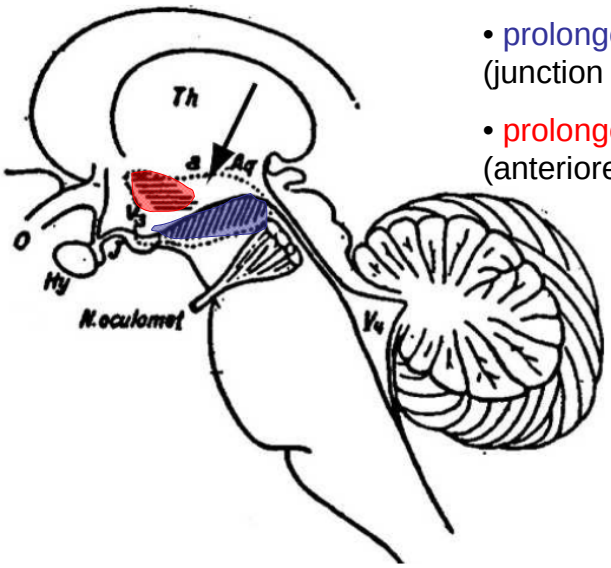
Sleep

- passive

process ?

- active

- Bremer (1892-1959): wakefulness can be maintained only as long as sensory stimuli from the environment impinge upon the brain
- Hess (1881-1973): stimulation of deep brain structures (diencephalon) induced sleep



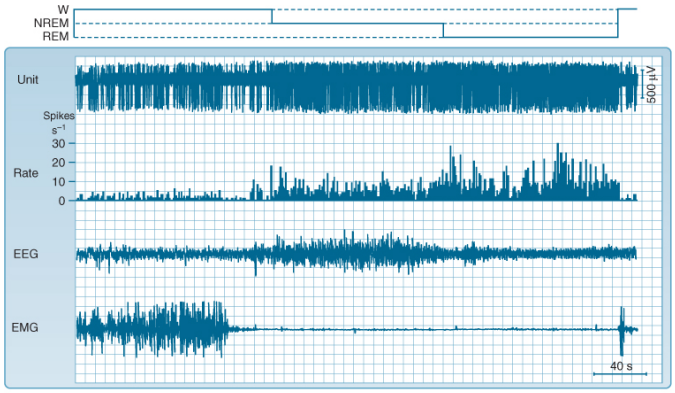
Brain stem

- prolonged sleepiness (junction brainstem/forebrain)
- prolonged insomnia (anteriorer hypothalamus)

Von Economo, 1930

Sleep and brain

- Sleep: aktive process



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sleep active neuron

median preoptic nucleus (hypothalamus)

McGinty & Szymusiak (2005) Principles and Practice of Sleep Medicine

Basis of sleep-wake states

- Neurophysiology
- Neuroanatomy
- Neurochemistry

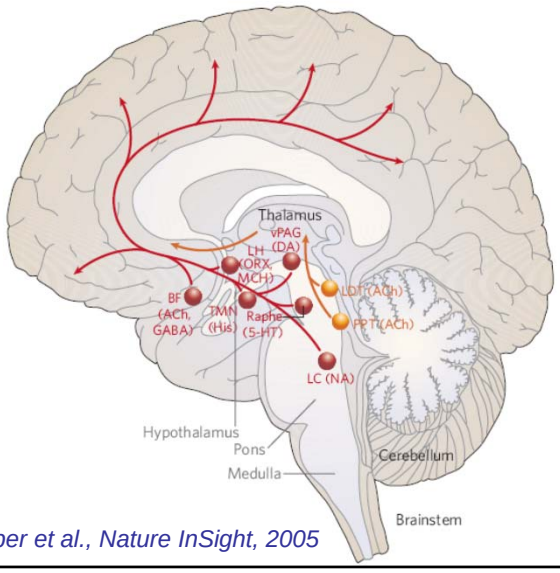
Reticular arousal system

(ARAS: ascending reticular arousal system)

- electric stimulation in brain stem: immediate awakening of a sleeping animal

(Moruzzi, G. and Magoun, H. (1949) Brain stem reticular formation and activation of the EEG. *Electroenceph. Clin. Neurophysiol*. 1, 455)

Key elements of "ascending reticular arousal system"

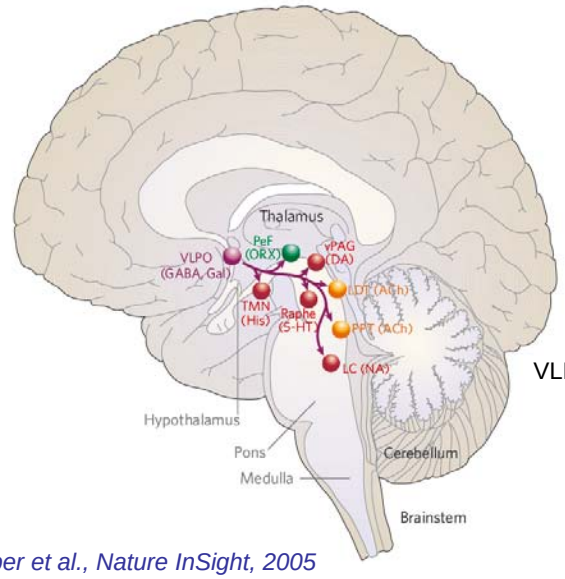


Saper et al., Nature InSight, 2005

Activation of thalamus: Facilitation of thalamo-cortical transmission

Activation of cortex: Facilitation of processing of inputs from the thalamus

Projections of the VLPO to the ascending reticular arousal system



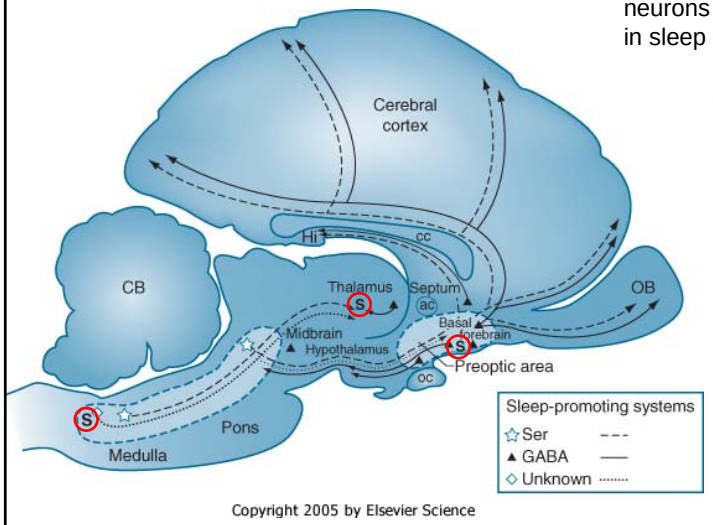
VLPO:
ventrolateral preoptic nucleus

VLPO neurons activ during sleep

Saper et al., Nature InSight, 2005

Non-REM sleep

S Stimulation induces sleep; neurons with higher activity in sleep than waking



Structures:

- brain stem (raphe nuclei, solitary tract nuclei)
- forebrain (ant. hypothalamus, preoptic area, basal forebrain)

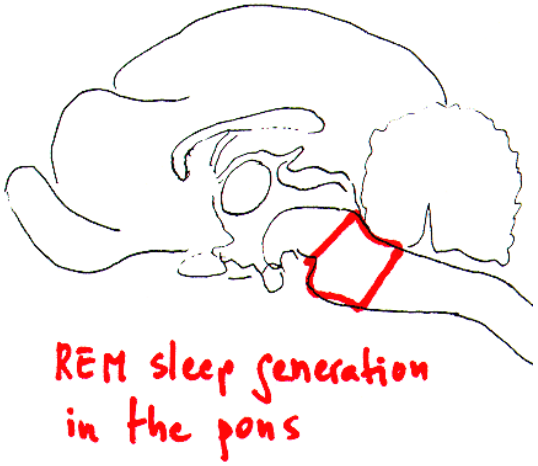
Neurotransmitter:

- Serotonin (5-HT)
- Adenosin
- GABA

Outlined areas: large lesions -> chronic reduction or loss of non-REM sleep

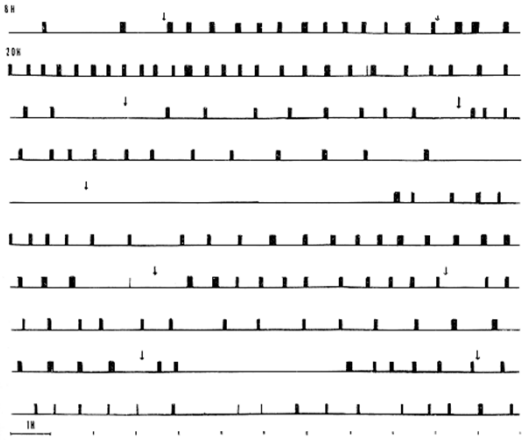
Jones (2005) Principles and Practice of Sleep Medicine

REM sleep



Isolated pons generates periodic episodes of REM sleep

Pons: necessary and sufficient for generating essential signs of REM sleep



Isolated pons generates periodic episodes of REM sleep

(ponteine cat)

Five-day continuous recording (12 h per line)

REM sleep (black bars) occurs at regular intervals

- Non-REM sleep: large brain areas
- REM sleep: pons; nearby structures of midbrain

- brain never «sleeps»
- neuronal activity in waking and sleep
- wake vs. sleep:
  different activity patterns of neurons

Dreams and the Brain

- Lesion in pons
  Loss of REM sleep
  Ability to dream preserved

- Lesion in forebrain
  „Loss of dreams“
  REM sleep preserved

(neurophysiological results M. Solms)

REM sleep behavior disorder

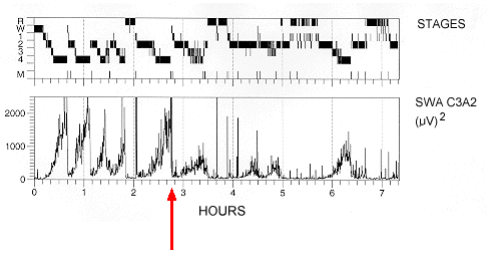
50-year old patient

REM sleep parasomnia

“Oneirism" or "acting out of dreams".

Characterized by intermittent loss of REM sleep muscle atonia and by appearance of elaborate motor activity associated with dream mentation.

rare



23-year old man

Sleepwalking

Non-REM sleep parasomnia
Mild form of the arousal disorders

Somnambulism

Occurs during non-REM sleep, in particular in slow-wave sleep (stages 3 and 4)

Common in children; disappears with time