Comparative physiology and pharmacology of sleep

Sleep regulation (human)

Peter Achermann

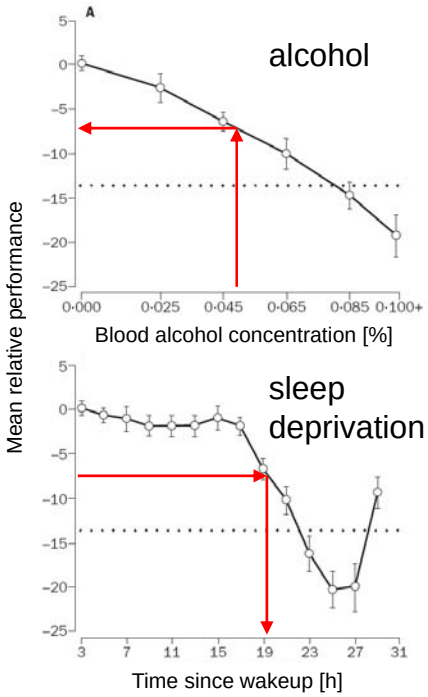
Abteilung Chronobiologie und Schlafforschung
Institut für Pharmakologie und Toxikologie
Zentrum für Integrative Human Physiologie (ZIHP)
Zentrum für Neurowissenschaften Zürich (ZNZ)

BIO 333: HS 2012; 8. Oktober 2012

Learning objectives

At the end of the lecture you should be able to:

- understand the principles of sleep homeostasis



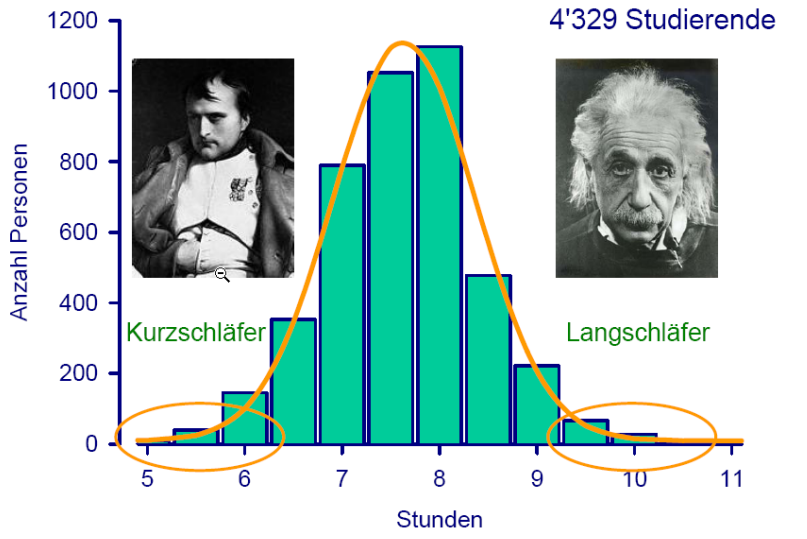
19 h of wakefulness correspond to 0.5 per mille blood alcohol concentration

Lack of sleep may become dangerous

Rajaratnam and Arendt, 2001

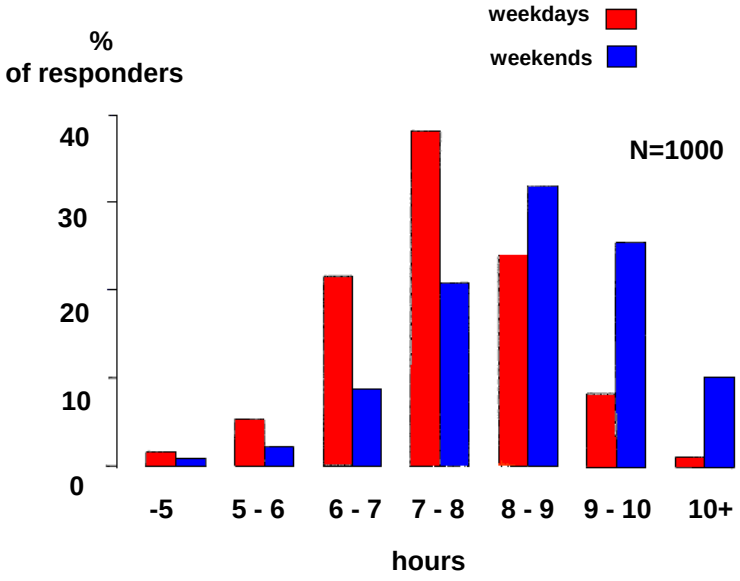
How much sleep do humans need?

Large variation in sleep duration

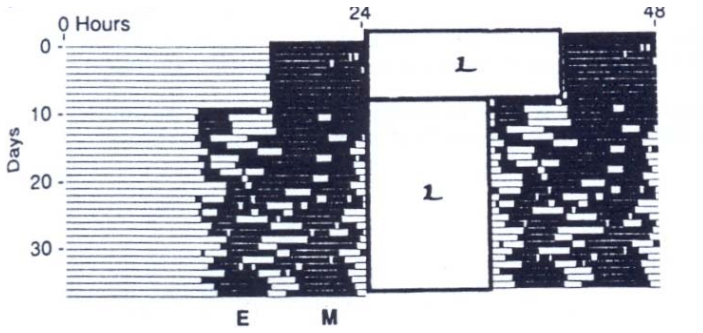


Landolt (2008)

How long do we sleep ?



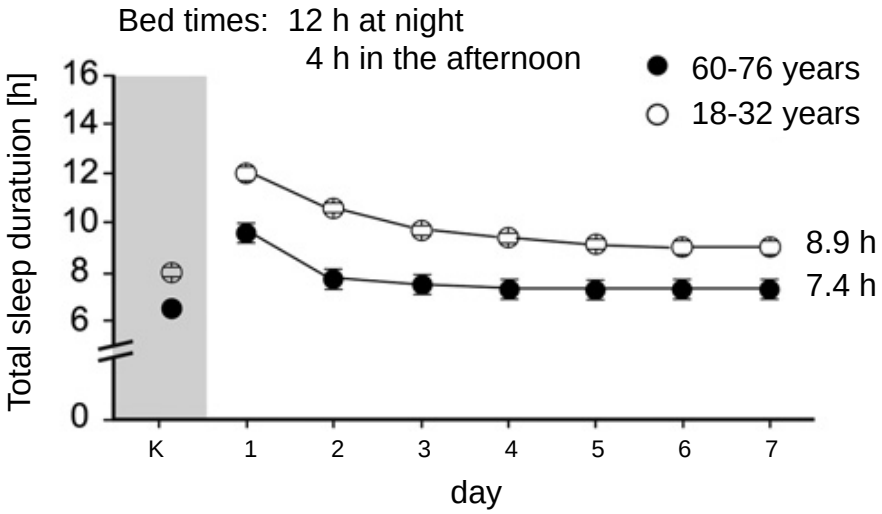
Changes in day length:
Summer (long day; 16 h) vs. winter (short day; 10 h)



L: light
E: evening-, M: morning component

Wehr, 1991

Sleep duration reaches asymptote



Klerman and Dijk (2008)

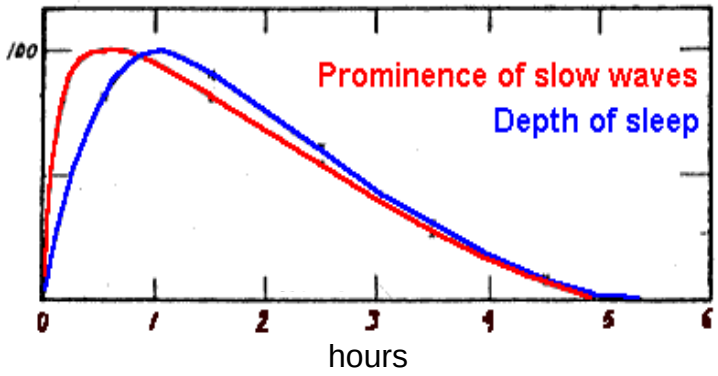
Sleep regulation

Investigation of the *function* of sleep

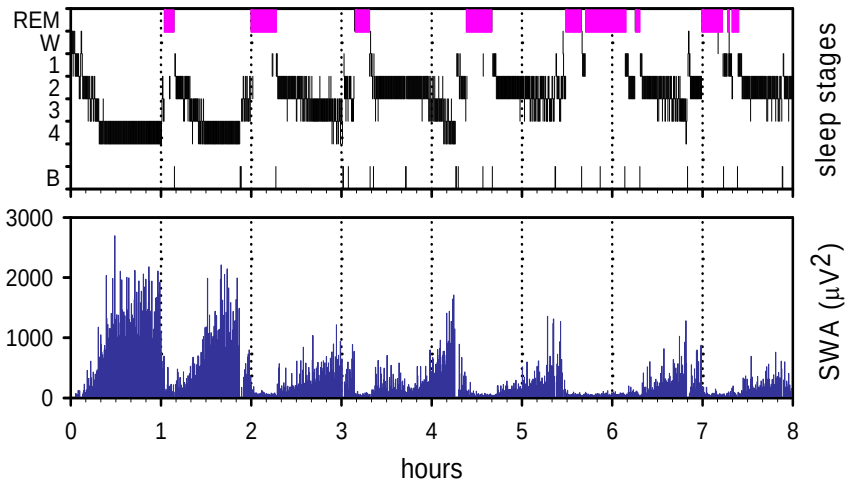
- *Manipulation of the „system“*
- *Sleep deprivation*
  - *acute*
  - *chronic*
  - *selectiv*

Important discovery in the 1930ies: Association between slow waves and sleep depth

Blake und Gerard (1937)



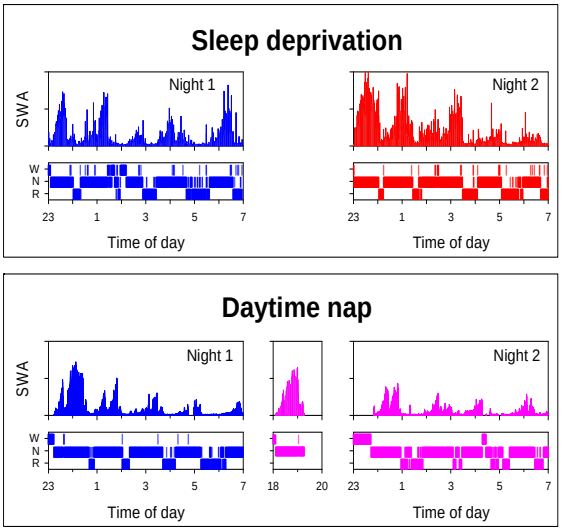
Slow-wave activity (SWA; 0.75-4.5 Hz) declines in course of sleep is modulated by non-REM-REM sleep cycle



World record staying awake

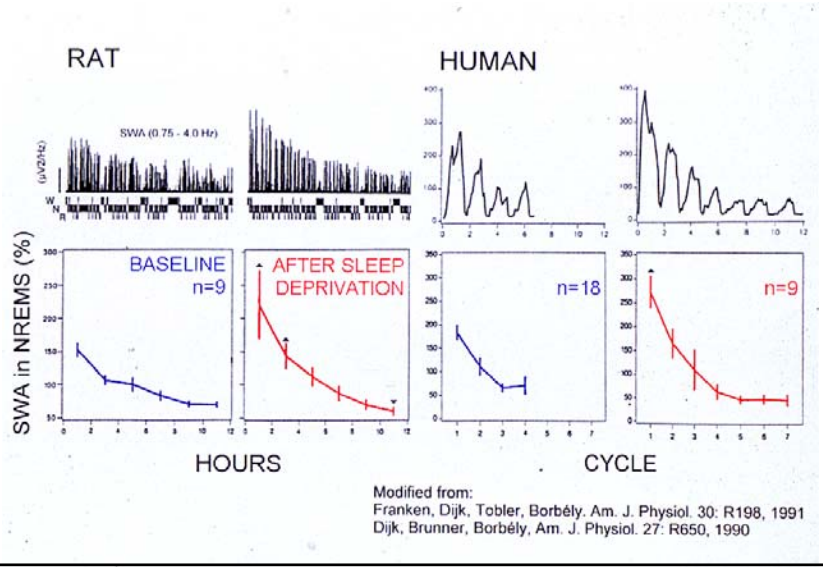
- 1965: 17-year-old Randy Gardner
- stayed awake for 11 days (264 hours)
- missed approx. 88 h of sleep
- first sleep episode lasted 14 hours

EEG delta activity (SWA; 0.75-4.5 Hz) marker of sleep intensity



Achermann & Borbély, 2003

After sleep deprivation: increase of slow waves in non-REM sleep EEG
similar in human and animals



The EEG is an indicator of “sleep pressure” and sleep depth

Specifically: sleep pressure and sleep depth are manifest in power of low frequency EEG waves

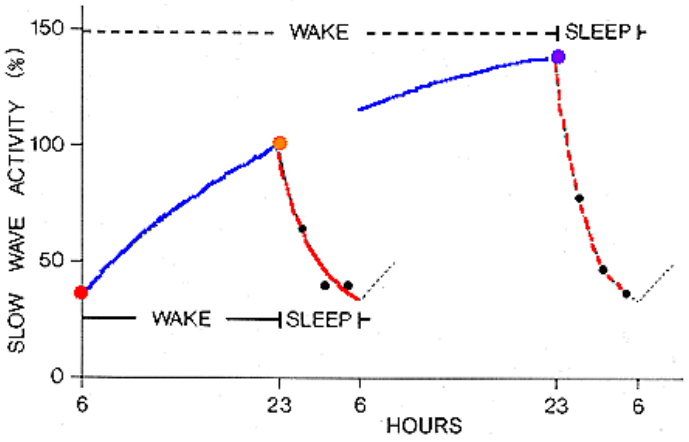
= delta activity (or SWA)

„sleep pressure“

builds up during wakefulness

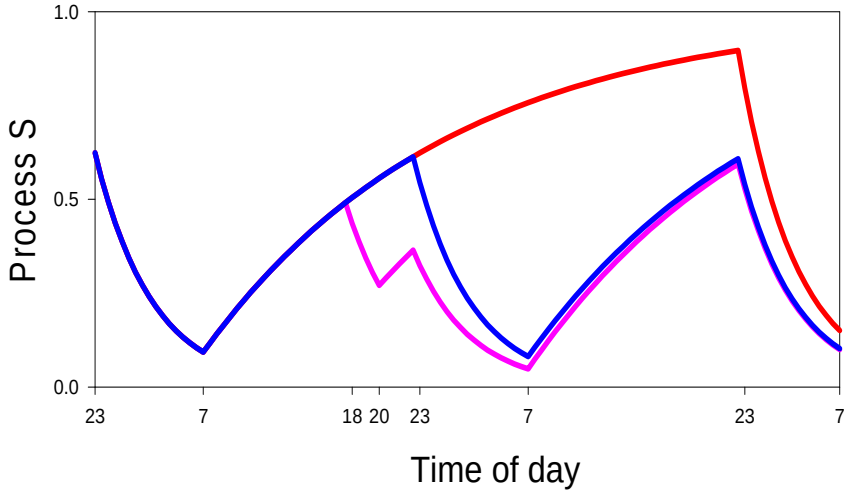
decreases during sleep

Homeostatic sleep regulation:
Hypothetical "Process S" builds up during wakefulness and declines during sleep and is manifest as SWA



Daan et al., 1984

Model of sleep homeostasis
(exponential functions)



Achermann & Borbély, Frontiers in Biosci., 8, 2003

Sleep homeostasis

- Sleep-wake dependent aspect of sleep regulation
- Homeostatic mechanisms
  - counteract deviations from an average ‘‘reference level’’ of sleep
  - augment sleep propensity when sleep is curtailed or absent, and
  - reduce sleep propensity in response to excess sleep
- Intensity and duration

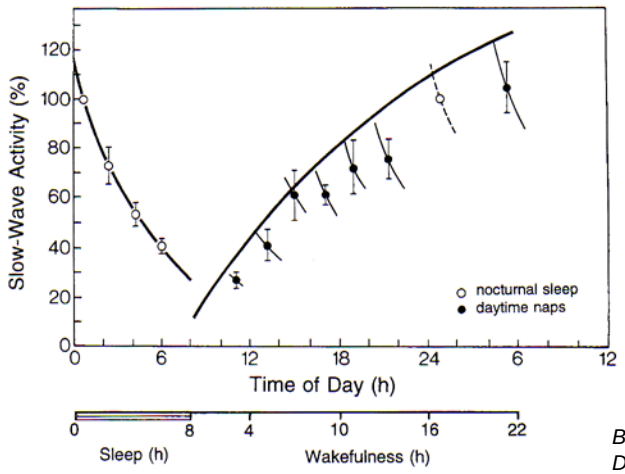
Definition of sleep

- **Behavior**
- **Physiology**

Sleep is homeostatically regulated

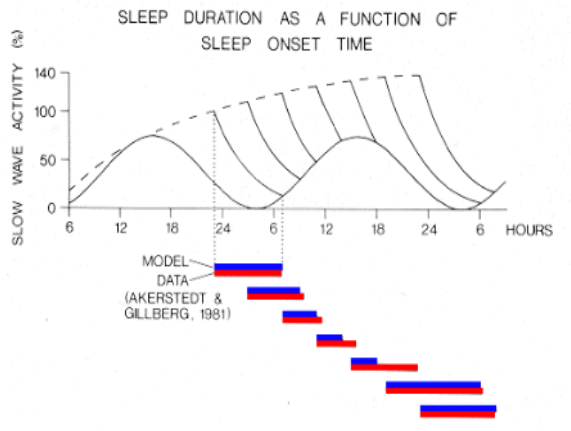
Sleep: active, regulated process
Sleep EEG: important indicator

Build-up of homeostatic process measured by naps: Level of SWA determined by duration of prior wakefulness and sleep



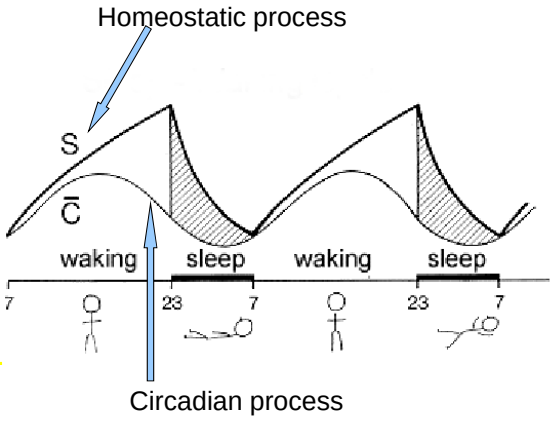
Beersma et al., 1987
Dijk 1995

Circadian effects: displaced sleep

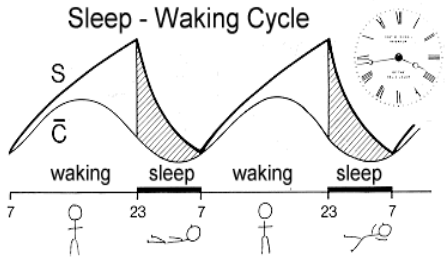


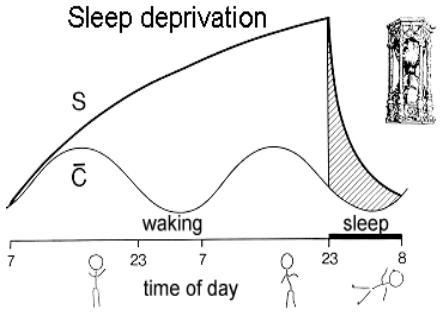
Borbély, 1982

Two process model of sleep regulation



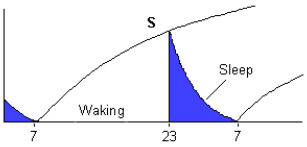
Borbély, Human Neurobiol,1982
Daan et al., Am J Physiol, 1984



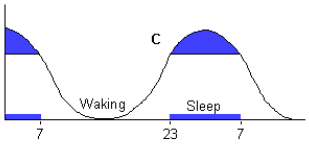


Two process model of sleep regulation

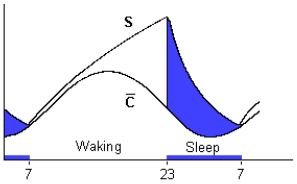
Homeostatic process



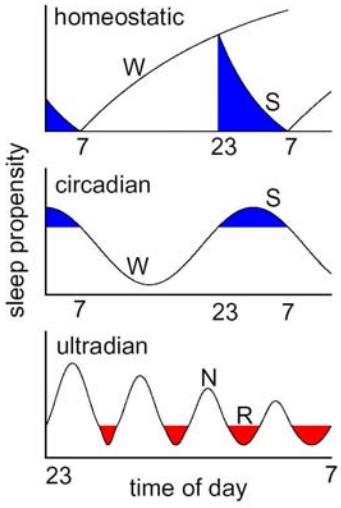
Circadian process



Interaction



Three major processes underlying sleep regulation



Achermann & Borbély, 2003

Sleep pressure

Alteration of periods with high and low sleep propensity (independent of preceding sleep and wakefulness)

Cyclic alternation of non-REM and REM sleep

W: wake; S: sleep;
N:non-REM sleep; R: REM sleep