University of Zurich | Clinical Research Priority Program (CRPP) Sleep and Health | University Children's Hospital Zurich

Sleep and Development

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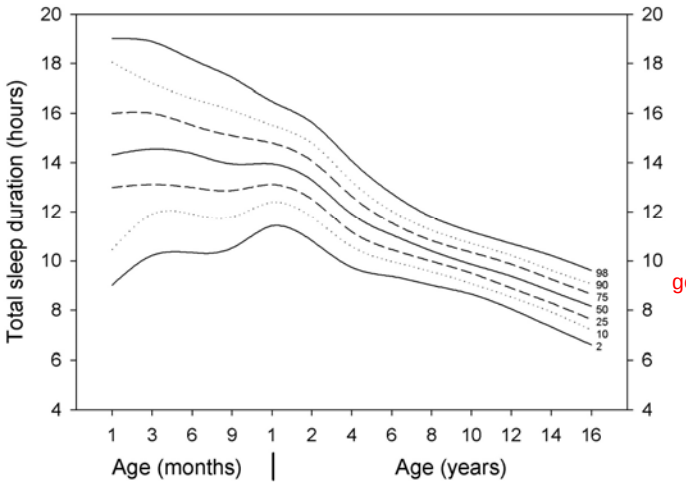
BIO 344: Development of the Nervous System, 27.11.2017

Sleep duration in childhood



goes down obv

Iglowstein et al., 2003

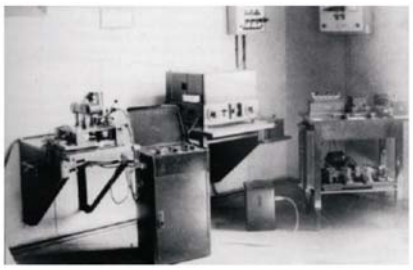
Outline

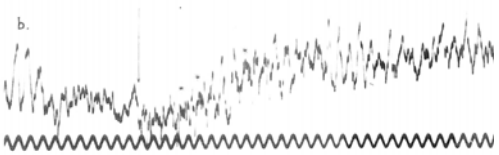
1. How do we measure sleep
2. Development of sleep
3. Similar trajectories
4. Functional relationship?

Endpoints

- Invention of Electroencephalography
- Discovery of REM sleep
- Sleep stages and sleep depth
- Neuronal correlates

Electroencephalography (EEG)





EEG measures potential differences in large cortical networks.

Berger 1929

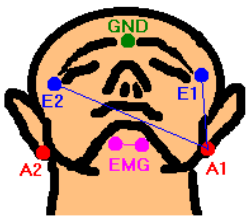
Rapid eye-movement sleep

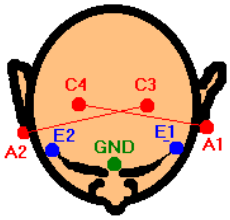
- **Discovered first in humans**
  (*Aserinsky and Kleitman 1953)*
- **Later in cats** *(Dement, 1958)*

Started golden years of sleep research – sleep is not simply a shut-down of brain activity

Sleep recordings

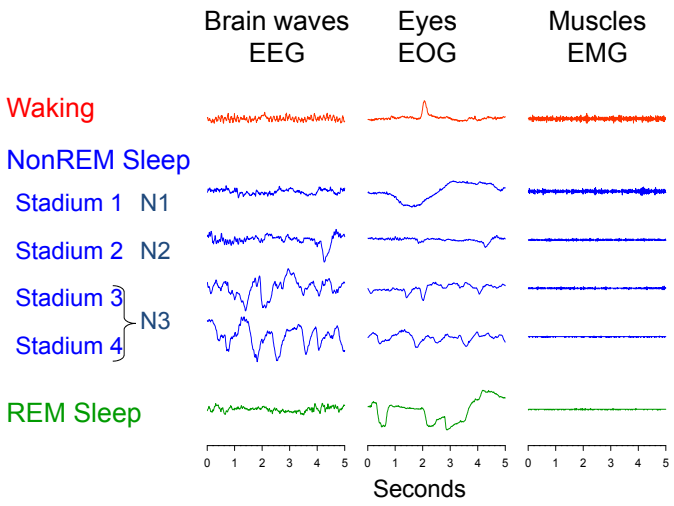
Ground
Electrooculogram (E1E2): eye movement
Electromyogram (EMG): muscel movement
Electroencephalogram (C3A2, C4A1): brain activity





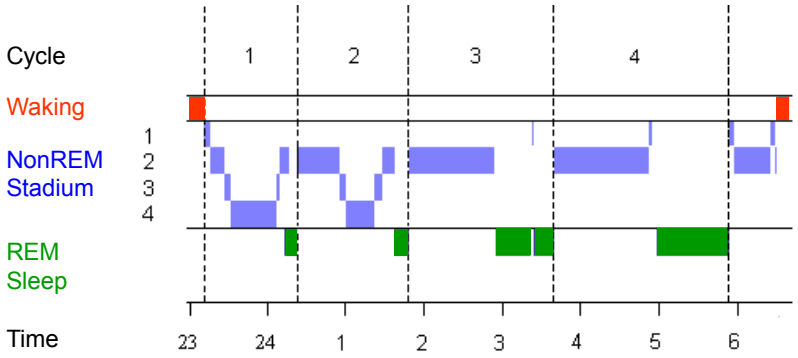
Achermann et al.

Vigilance states



EEG: Electroencephalogram; EOG: Electrooculogram; EMG: Electromyogram

Sleep architecture

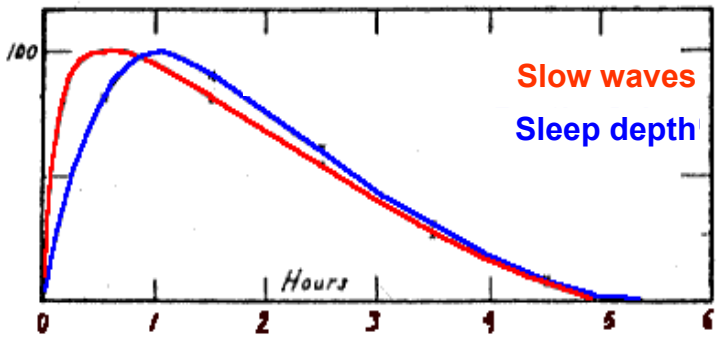


Changes in NonREM-REM sleep cycle characteristics across a sleep period:
-Deep NonREM sleep (3+4) decreases
-REM sleep duration increases

Achermann et al.

EEG slow waves and sleep depth

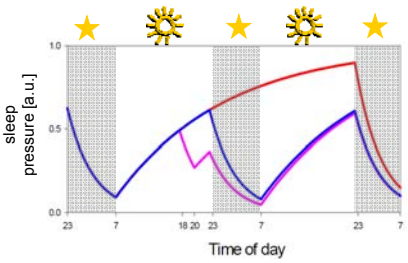
Helen Blake und R. W. Gerard (1937)

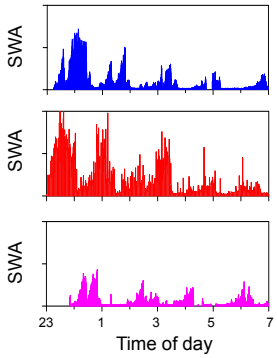


Hours

Number of slow waves and measures of sleep depth decrease in parallel across a sleep period

Slow wave activity reflects sleep homeostasis





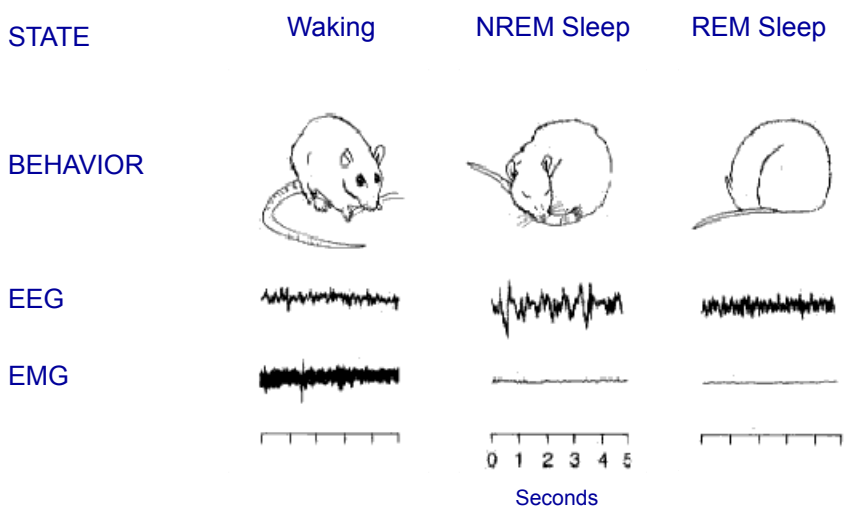
baseline condition
sleep deprivation
daytime nap

Adapted from Achermann & Borbély, 2003

- **Sleep is a regulated process**
- **EEG slow waves reflect sleep homeostasis**

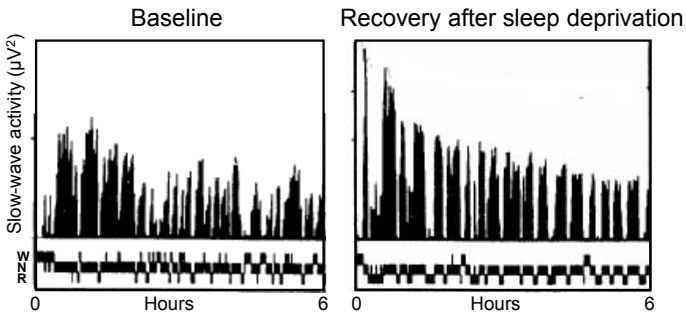
What is going on at the neuronal level?

Vigilance states in rodents



Slow wave activity in rodents

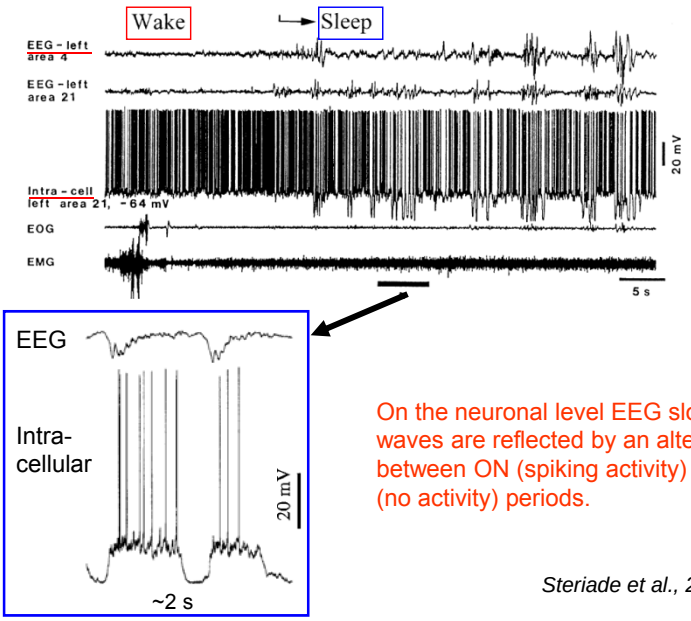
Rat



Also in rodents slow wave activity reflects sleep homeostasis

Franken et al., 1991

Sleep slow oscillations

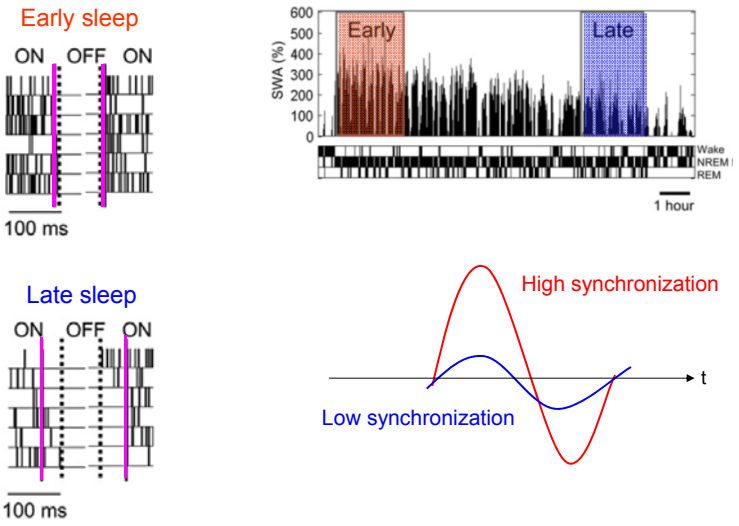


On the neuronal level EEG slow waves are reflected by an alternation between ON (spiking activity) and OFF (no activity) periods.

Steriade et al., 2000

Relationship between synchronization and SWA

Multi unit recordings in rats

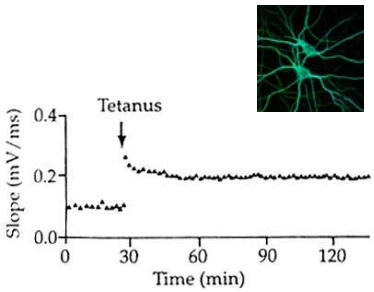


Vyazovskiy et al., Neuron 2009

What causes changes in synchronization?

Changes in synaptic strength (and other factors)

Long term potentiation
(LTP)

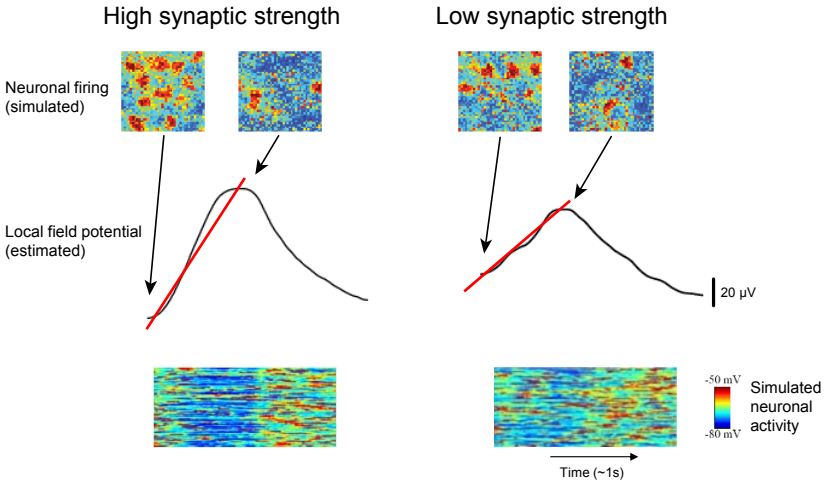


Bliss & Lomo 1973

Synaptic strength and slow waves

Large scale computer model

Esser et al., Sleep 2007

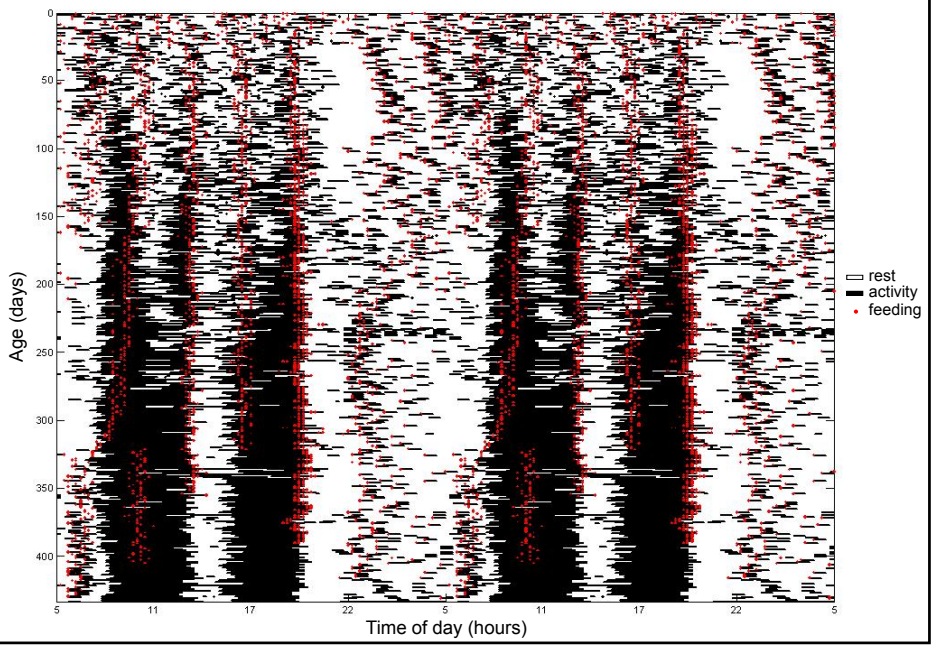


- **On the neuronal level slow waves are reflected by ON and OFF periods**
- **The level of synchronization is determining the size (i.e. amplitude) of slow waves**

Development of sleep

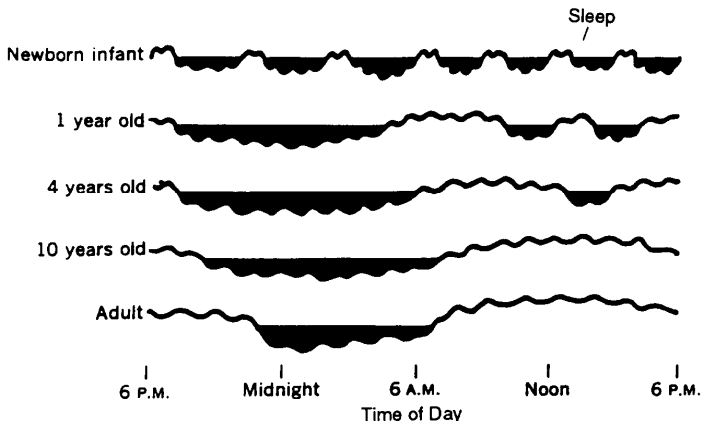
- **Changes in the duration and composition sleep**
- **Changes of EEG slow wave activity**

Rest-activity plot for the first year



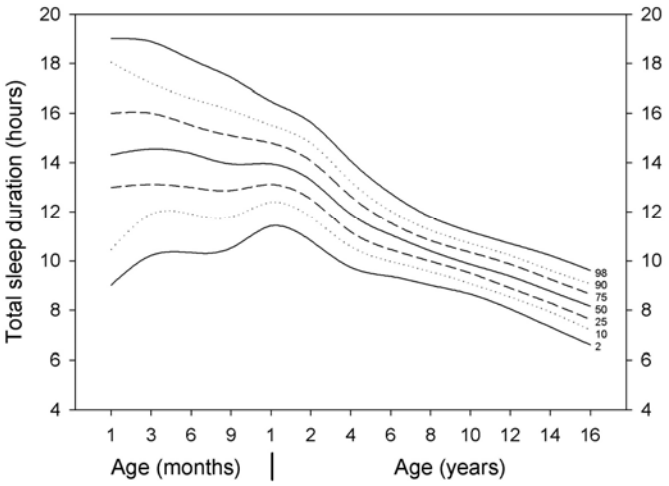
From poly- to monophasic sleep

sleep patterns in different developmental stages: the older the shorter and it becomes basically monophasic



Adapted from Kleitman, 1954

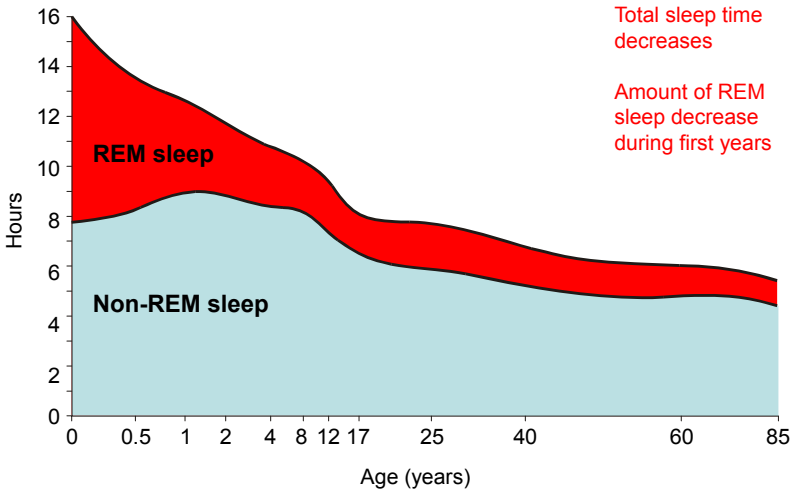
Variability of sleep duration



Age dependent inter-individual differences in sleep duration

Iglowstein et al., 2003

Sleep stages during development

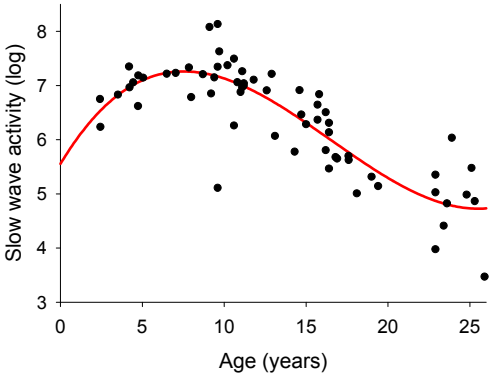


Total sleep time decreases

Amount of REM sleep decrease during first years

Roffwarg et al. 1956

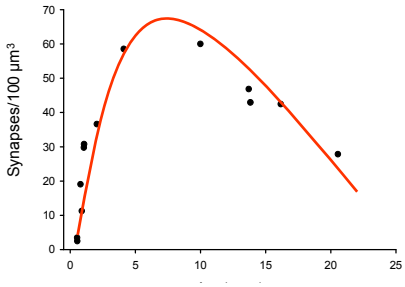
Slow wave activity during development



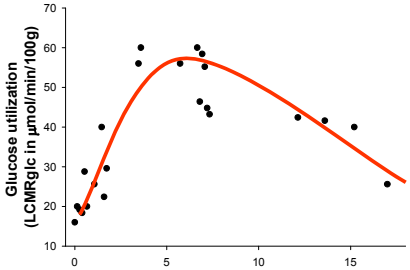
Kurth et al., J Neurosci 2010
Feinberg, J Psych Res 1982

Synapse density and energy consumption

Synapse density



Energy consumption

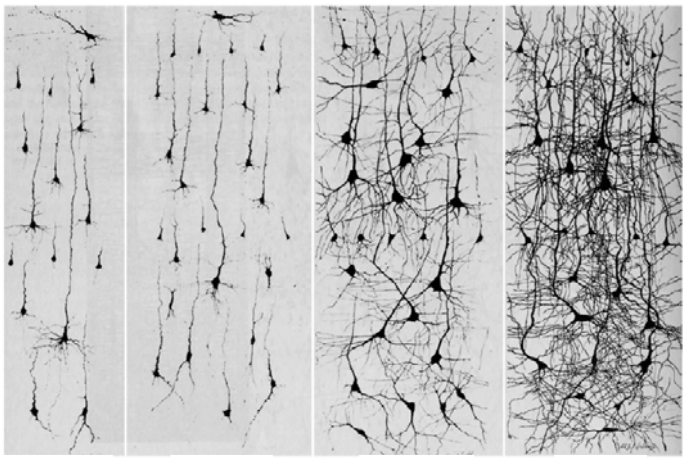


Age (years)

Huttenlocher, J Comp Neurol 1997

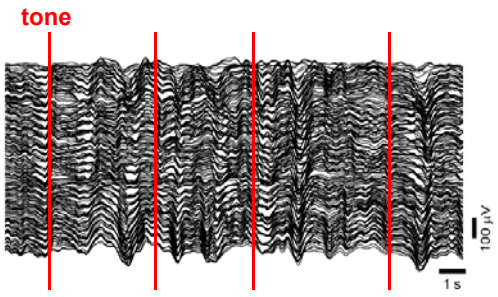
Chugani, Prev Med 1998

Cortical maturation in early years

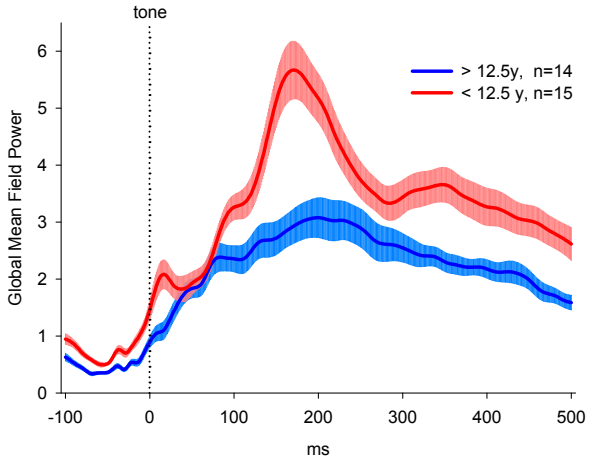


Conel's Atlanten in Courchesne 2007

Evoked responses in children



Changes in cortical excitability

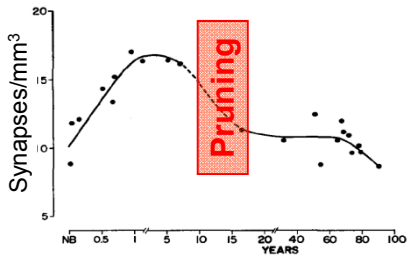


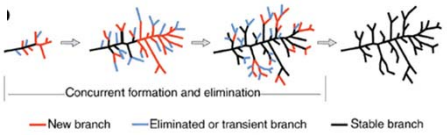
Increased cortical excitability in pre-pubertal children

- **More synapses use more energy**
- **More synapses lead to increased network synchronization and larger slow waves**

Pruning: Refining process during adolescence

Pruning during adolescence



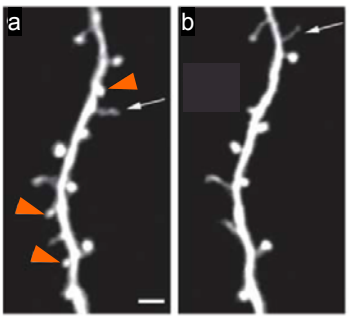


During adolescence more synapses are eliminated than newly formed

Huttenlocher 1979
Hua et al. 2004

Structural changes

Two photon imaging in mice

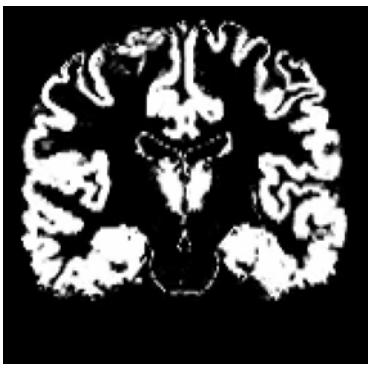


Zuo et al., Nature 2005

MRI cortical thickness

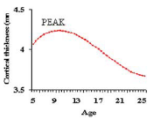
Structural magnetic resonance imaging (MRI)

Girl, 9.5 years



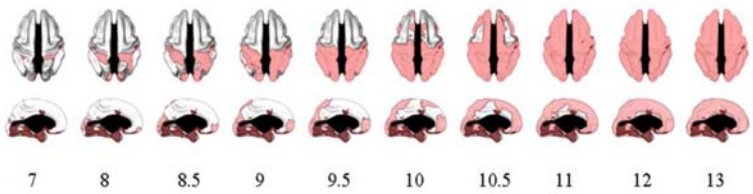
Woman, 28.3 years

Local maturation



Cortical gray matter maturation starts in the back and ends in the front

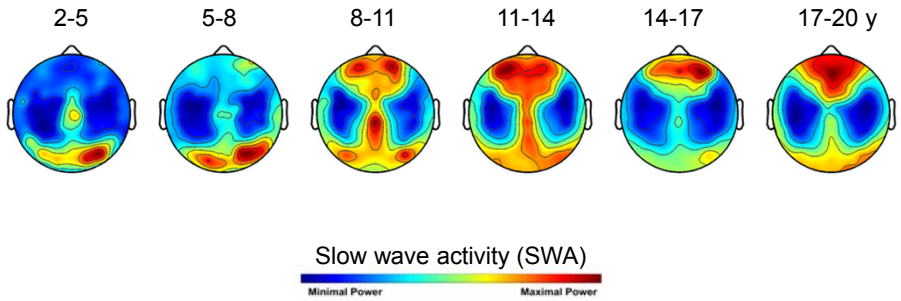
Age of peak cortical thickness



years

Shaw et al., J Neurosci 2008

Age dependent SWA topography

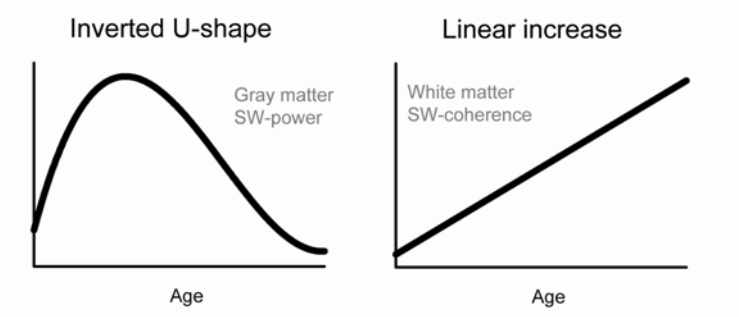


Kurth et al., J Neurosci 2010

- **Gray matter maturation parallels changes in slow wave activity**

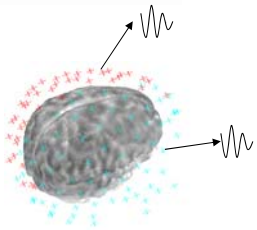
What about white matter?

Gray versus white matter maturation



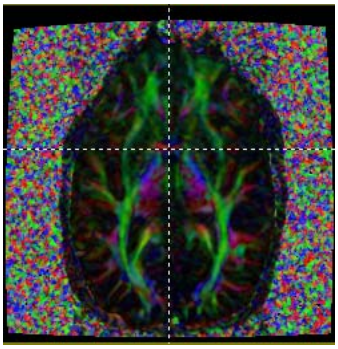
Cortical white matter shows
a linear increase across age

Coherence

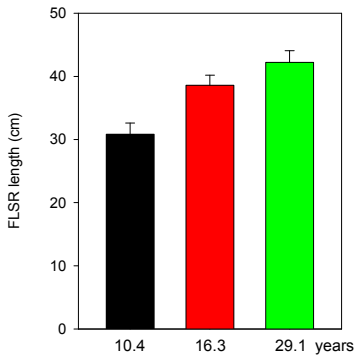


Diffusion tensor imaging

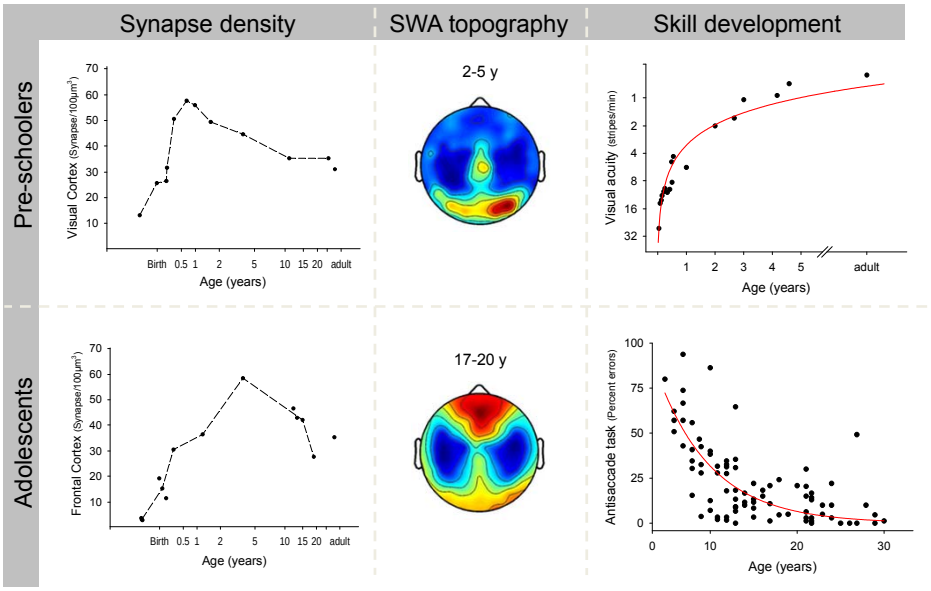
Novel magnetic resonance imaging technique



directed movement of H_2O
estimation of fiber bundles

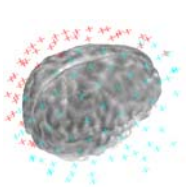


Relationship to connectivity and behavior

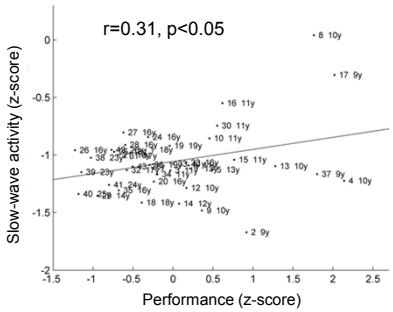


Ringli and Huber, Prog Brain Res, 2011

Direct relationship?



Zurich Neuromotor Assessment Battery



Relationship between the maturation of SWA topography and motor development

Kurth et al., NeuroImage 2012

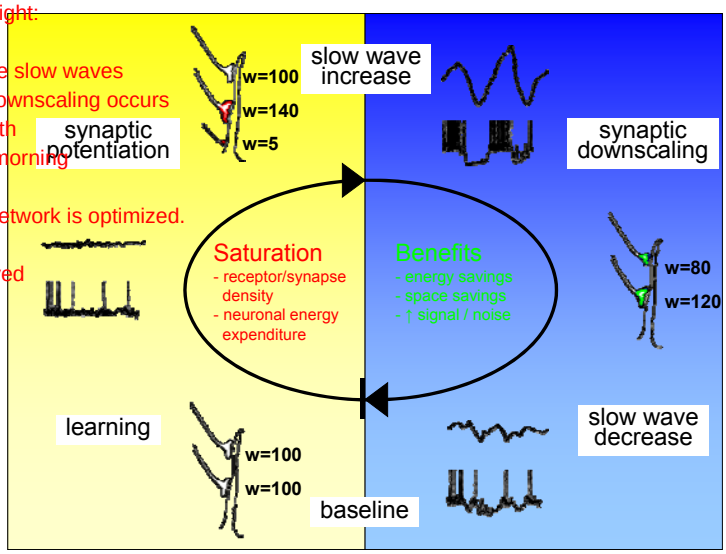
- **Predominance of SWA shifts from back to front**
- **Parallels anatomical and behavioral maturation**

How could this be explained?

what we see here: when we wake up, we have a network - synapses are connected differently, we can assign them different weights. overnight, synapses are sterngthened, the overall weight increases then, stronger synapses consume more energy though, to establish them and to maintain them. if we cannot supply enough energy to a synapse or neuron, it cannot fulfill its task.
Stronger synapses grow bigger, but they can reach a limit, also: space limiatations: not possible to grow infinite synpases.

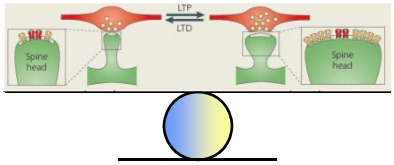
Synaptic homeostasis hypothesis

model of synaptic scaling:
synpases are reduced in terms of their weight:
this happens during sleep.
the stronger the connections the bigger the slow waves
when enter NREM sleep. then, synaptic downscaling occurs
for all synpases, such that synaptic strength
in the next morning is the same as in the morning
before (see numbers of the example).
it's not that we forgot everything, but the network is optimized.
this process is self-limiting.
Also, noise or learned mistakes are removed
which is good.



Tononi and Cirelli, 2003;2014

Synaptic homeostasis



Holtmaat and Svoboda, Nat Rev Neurosci 2009

Synaptic strength is balanced across 24 hours (=synaptic homeostasis). (at least in adults)

Wakefulness favors synaptic potentiation (overall gain)

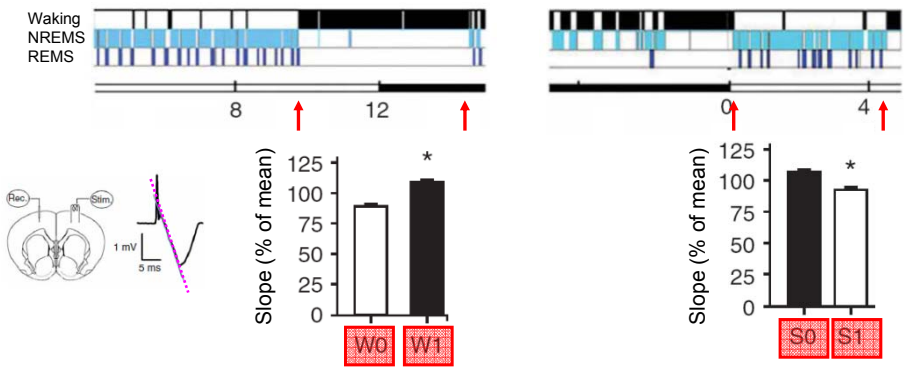
Sleep favors synaptic depression (opposite function as in wakefulness - overall loss respectively normalization actually)

Tononi and Cirelli, Neuron 2014

Changes in synaptic strength

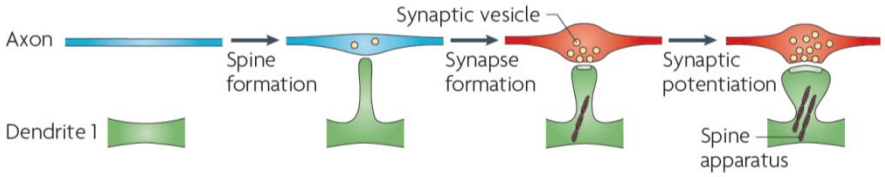
Rats

Vyazovskiy et al., Nat Neurosci 2008



Wakefulness is associated with a net increase in synaptic strength
Sleep is favoring synaptic depression

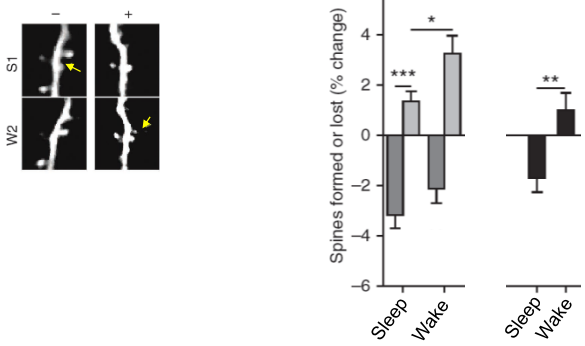
From spines to synapses



Holtmaat and Svoboda, Nat Rev Neurosci 2009

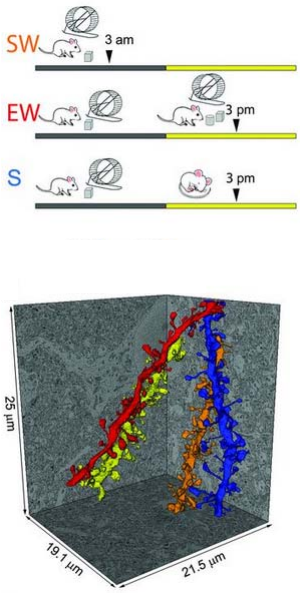
Net change in the number of spines

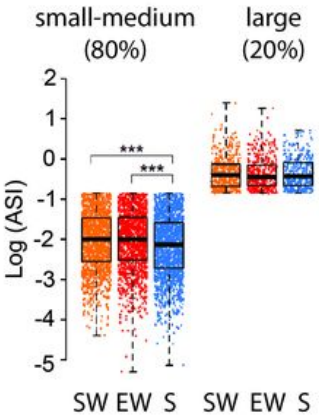
Two photon imaging in adolescent mice



Maret et al., Nat Neurosci 2011

Changes in EM reconstructed axon-spine interface (ASI) across sleep





de Vivo et al., Science 2017

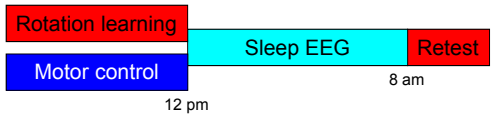
- **Potentiation/synapse formation predominates during wakefulness**
- **Sleep favors synaptic depression (downscaling)/synapse elimination**

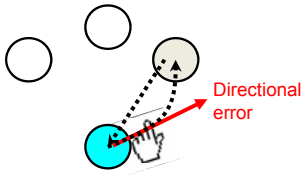
Is this related to performance?

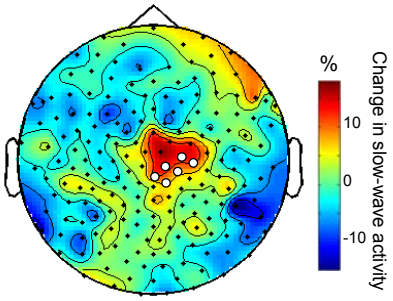
Local increase in slow-wave activity

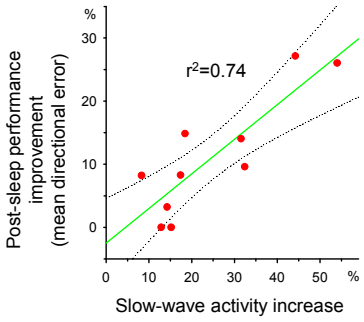
Huber et al., Nature 2004

subject perofrms better after sleep (next morning)



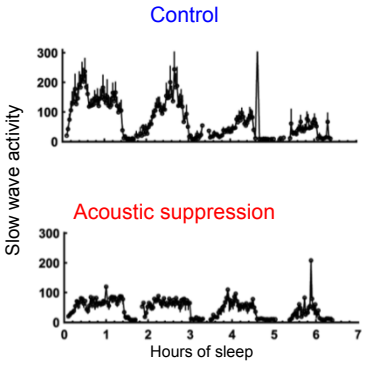


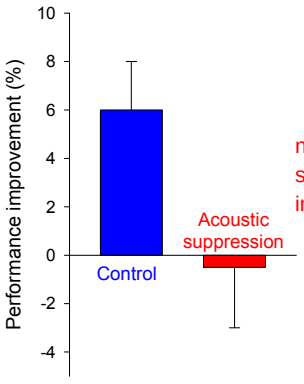




Suppression of slow waves

Evidence for a causal relationship between slow wave activity and sleep dependent performance improvements





no improvement when slow waves are suppressed - evidence for slow wave improtance for performance improvement

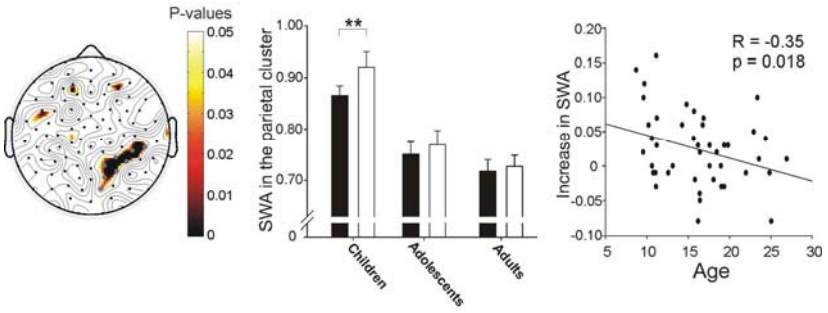
Landsness et al., Sleep 2009

Slow waves are related to sleep dependent performance changes.

How does this look like in children?

Local slow wave activity after learning

in children, adolescents and adults

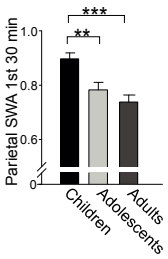


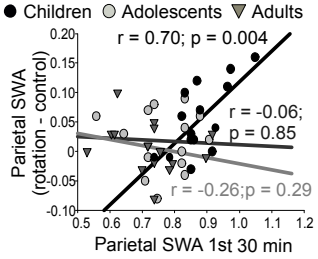
Wilhelm et al., J Neurosci 2014

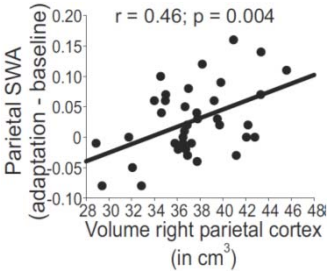
Relationship to markers of maturation

EEG Slow wave activity

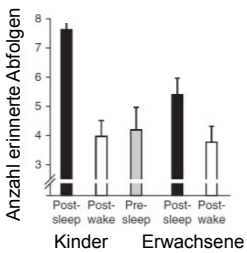
Cortical gray matter volume

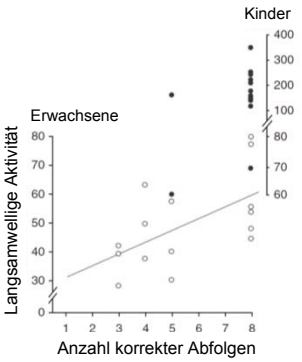






Does children's performance benefit from sleep?





Wilhelm et al., Nat Neurosci 2014

children benefit even more from sleep than adults do.

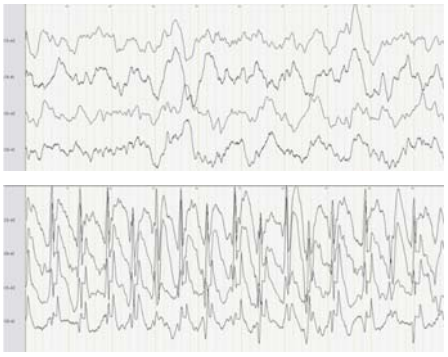
Experience dependent increase in SWA is larger in children.

Children seem to benefit more from sleep.

How does this translate into clinical population?

Continuous spike-wave epilepsy in NREM sleep

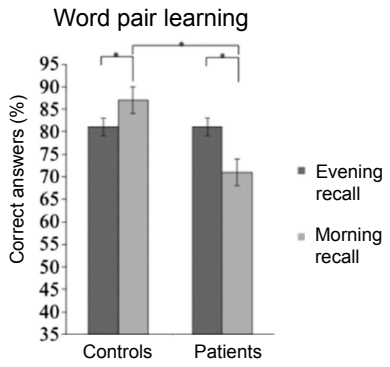
Slow waves during sleep



Epileptic spike waves during sleep

Developmental retardations are associated with this form of childhood epilepsy
(Roulet Perez et al., 1993; Holmes and Lenck-Santini, 2006; Tassinari and Rubboli, 2006)

No sleep dependent performance improvement



Galer et al., Epilepsy&Behavior 2015

Contents lists available at ScienceDirect
Epilepsy & Behavior
22 (2011) 380-384
journal homepage: www.elsevier.com/locate/yebeh

Is sleep-related consolidation impaired in focal idiopathic epilepsies of childhood? A pilot study

Charline Urbain [a,b,*], Tiziana Di Vincenzo [a], Philippe Peigneux [a], Patrick Van Bogaert [b,c]

4 Patients with activation of spike waves during slow wave sleep

No improvement after sleep

1 Patients without spike waves during sleep after treatment

Improvement after sleep

Conclusions

- Sleep quantity and quality changes during development
- Sleep slow waves mirror cortical maturation
- Synaptic homeostasis may play a role during development

on REM sleep:
Blumberg: researcher, REM sleep, muscle activity.
isolated muscles are activated during REM sleep: this locala activation is very ccritical for the development of the motor system (established during REM sleep, to probe every single muscle, because there is no noise during complete silence).

Do we sleep enough (slide)?:
during working days - dont sleep enough. weekend: sleep too much (to catch up lost sleep)
consequnces: being sleepy during the day has negative consquences on performance (more sleep ~> better marks/better performance)