LIÈGE université
GIGA institute

CYCLOTRON RESEARCH CENTRE
IN VIVO IMAGING

Sleep & Memory

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GIGA Doctoral School
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What is sleep?

"There is no animal which is always awake or always asleep, such that all sleep is susceptible of awakening and all wake time beyond the natural time limit is susceptible to sleep"

Aristotle: „On Sleep and Sleeplessness"
[~300 BC]

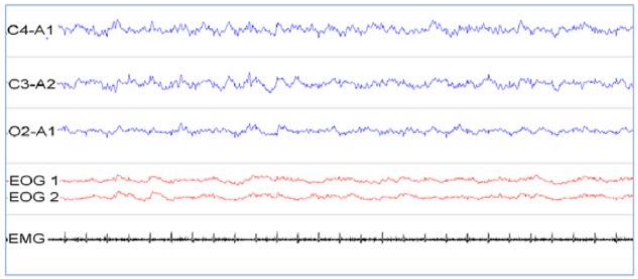
What is sleep?

Behavior/State (of consciousness)
Naturally recurring (periodically)

Characterized by
- a decrease in responsiveness to external stimuli
- a rapid state reversibility

Additional neurophysiological criteria

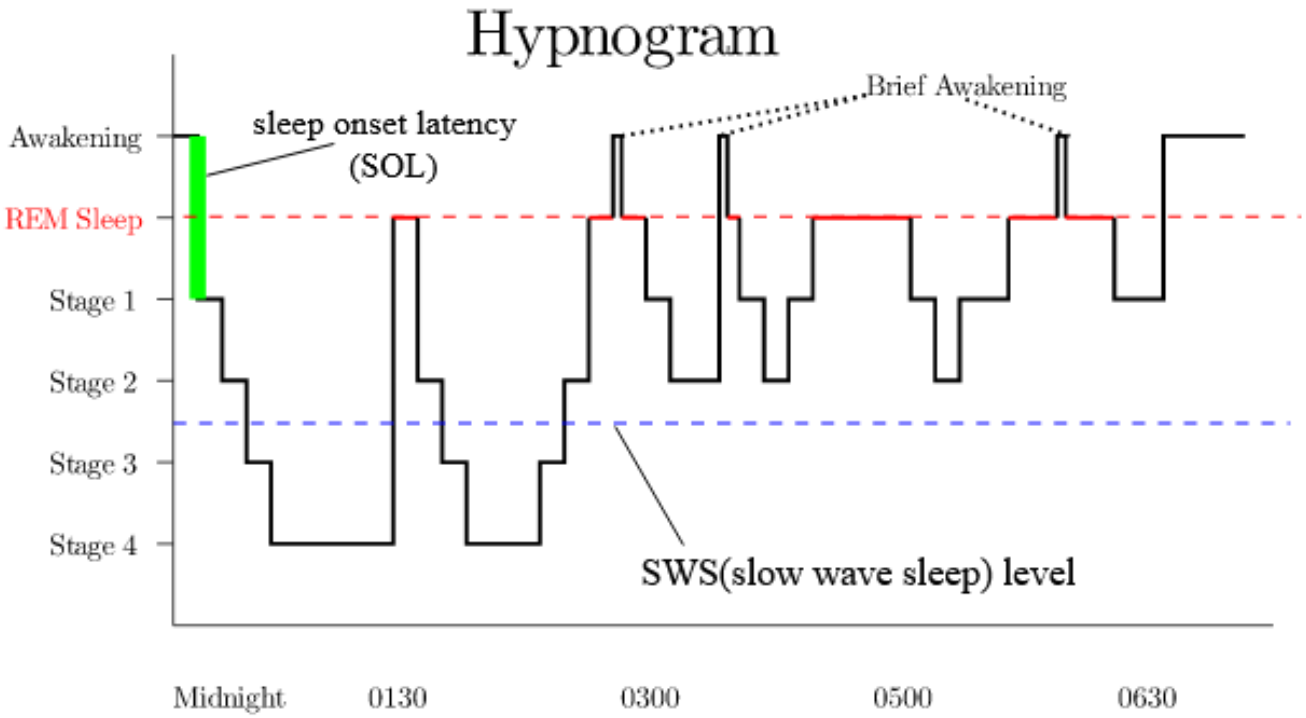
Sleep is not a homogenuous state



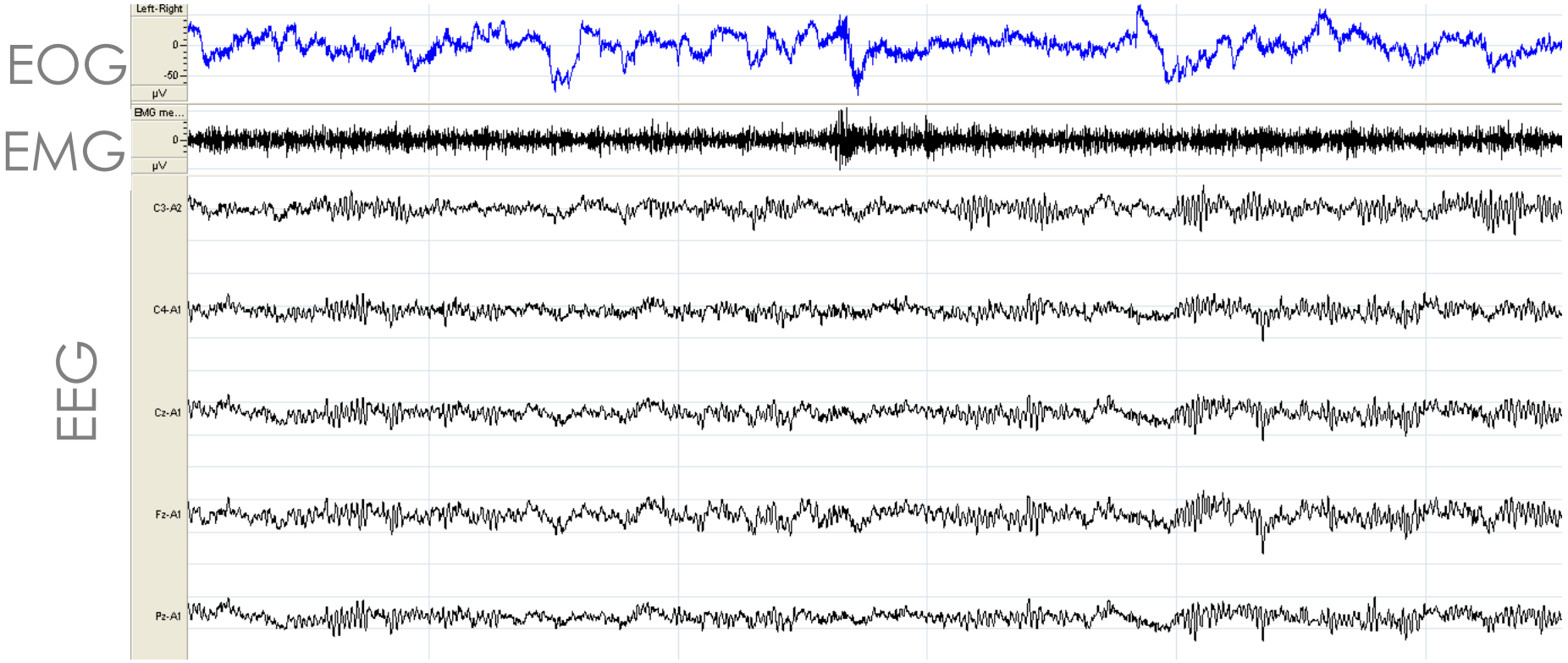
Electro-encephalogram (EEG)

Electro-occulogram (EOG)

Electro-myogram (EMG)



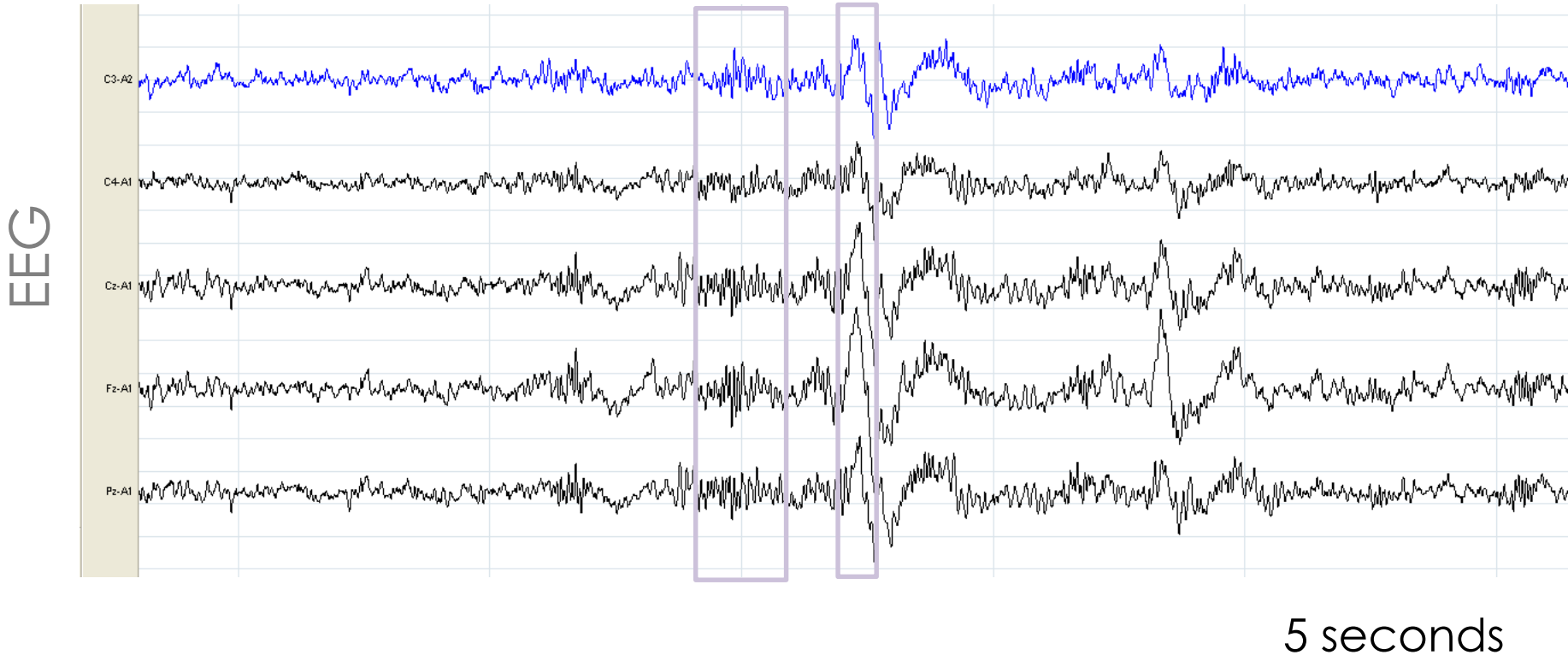
WAKEFULNESS



5 seconds

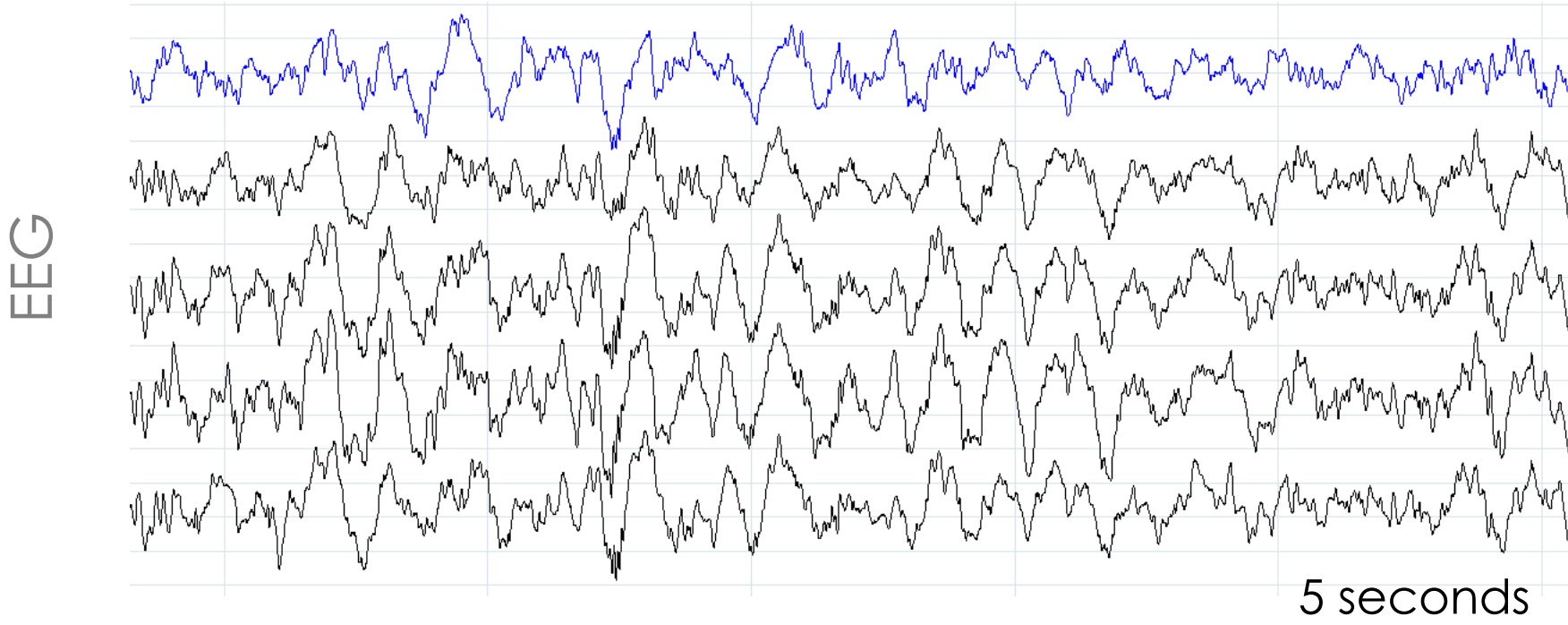
- Fast and low amplitude EEG activity
- Non stereotyped eye movements
- High muscular tone

LIGHT NON RAPID EYE MOVEMENT SLEEP
STAGE 2 SLEEP



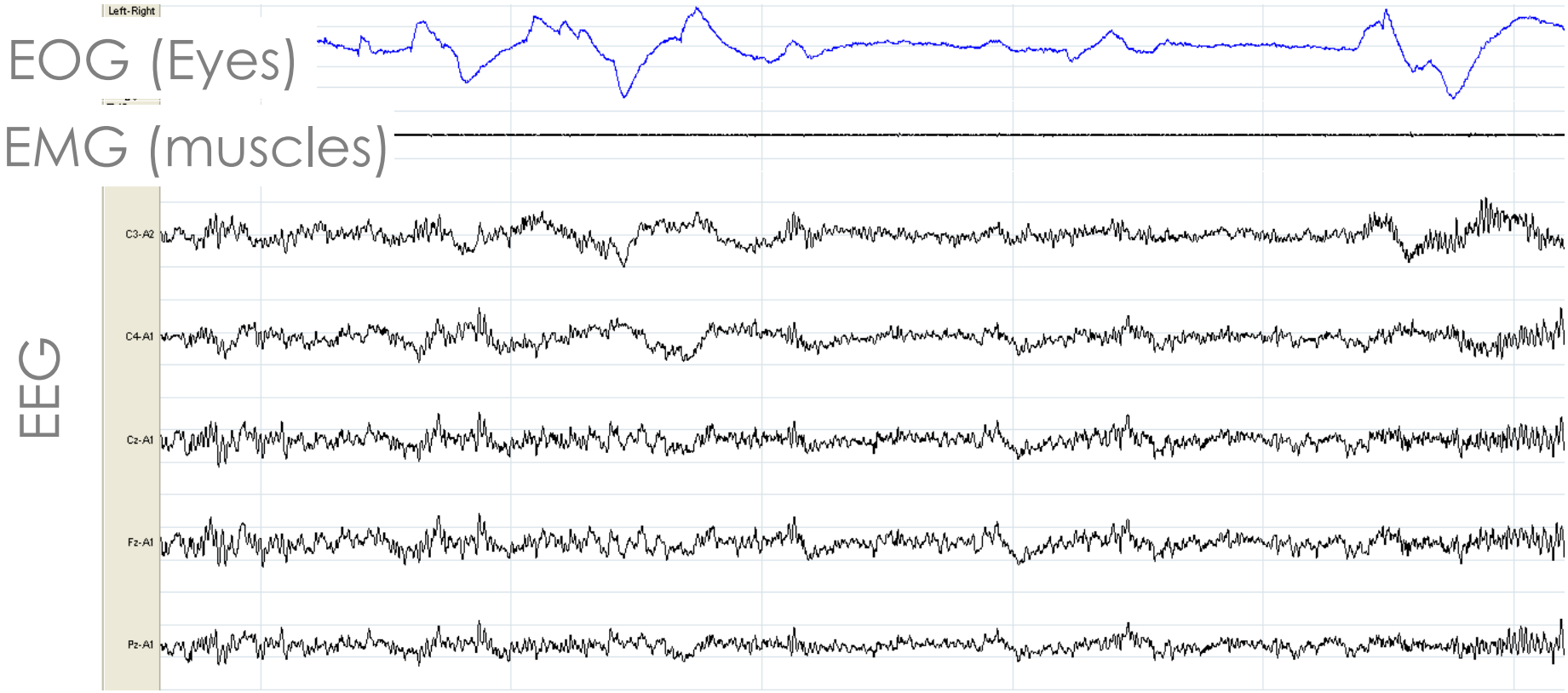
- Slower and higher amplitude EEG activity than wake
- K complexes
- Spindles

DEEP NON RAPID EYE MOVEMENT SLEEP
SLOW WAVE SLEEP



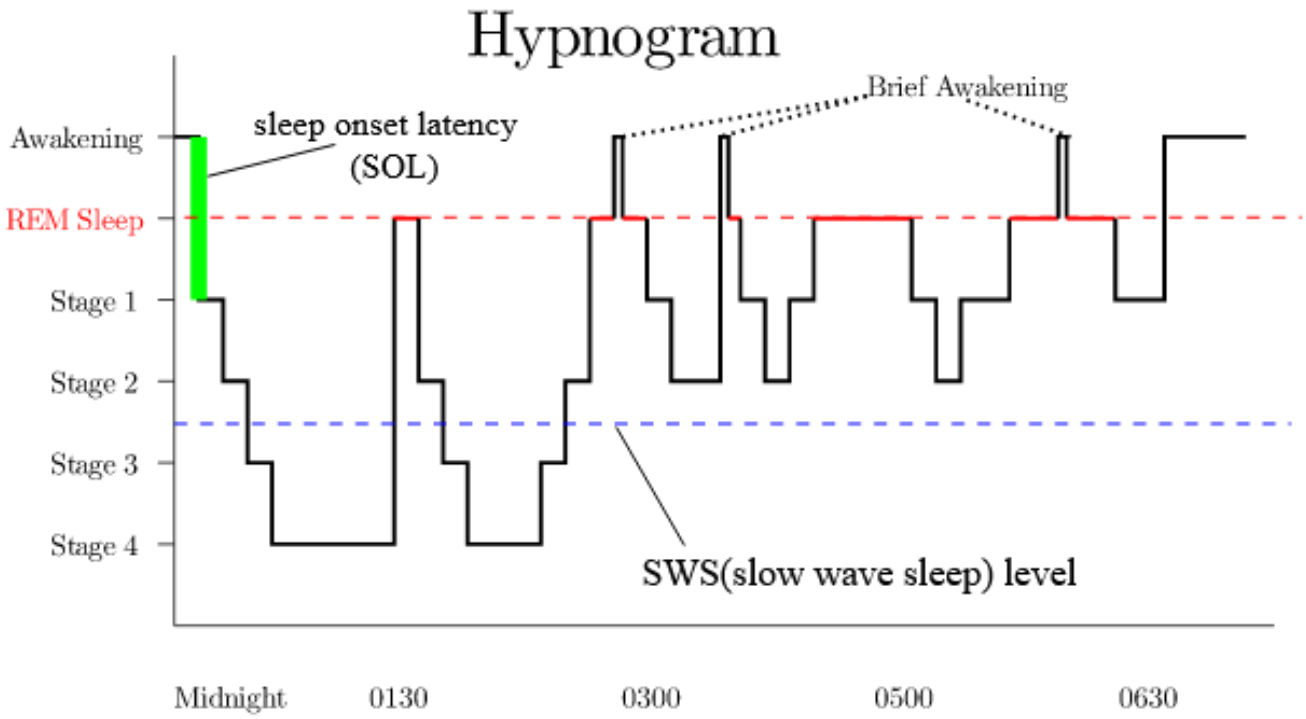
- Slow and high amplitude EEG activity

RAPID EYE MOVEMENT SLEEP
REM sleep – Paradoxical sleep



5 seconds

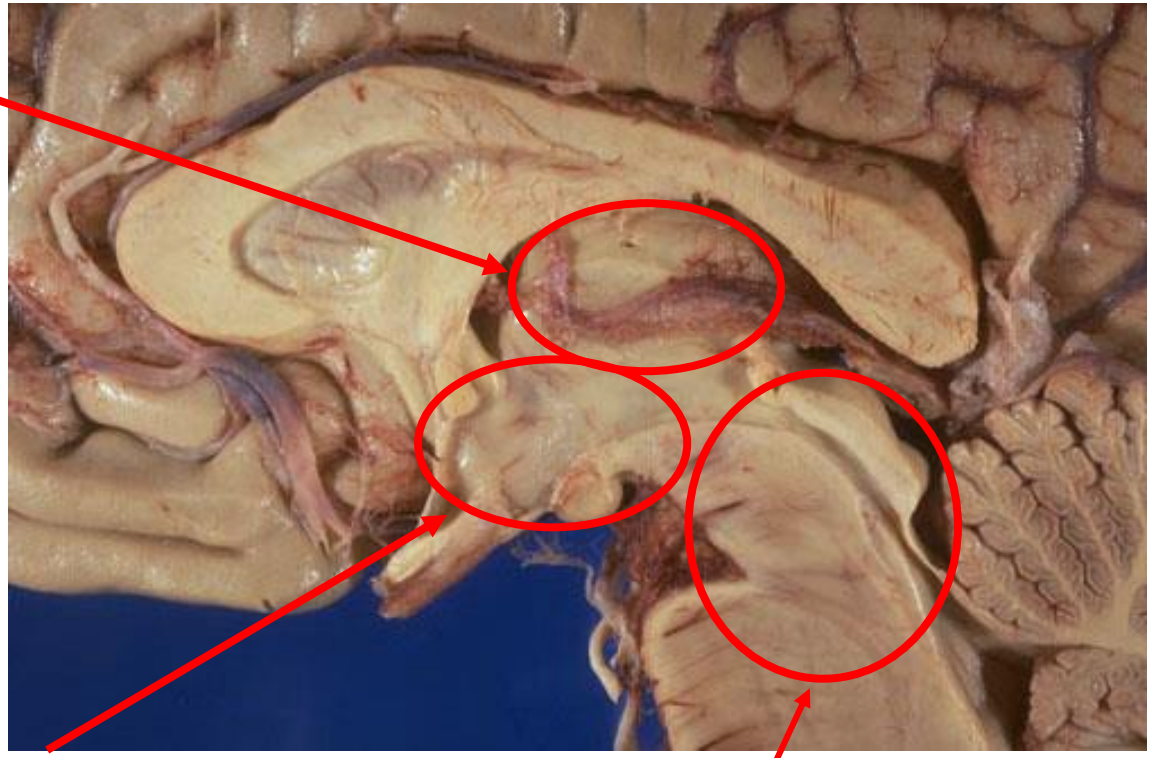
- Fast and low amplitude EEG activity
- Stereotyped/saccadic rapid eye movements (REM)
- Low muscular tone
- Most of oniric activity


Hypnogram
Brief Awakening
sleep onset latency
(SOL)
Awakening
REM Sleep
Stage 1
Stage 2
Stage 3
Stage 4
SWS(slow wave sleep) level
Midnight
0130
0300
0500
0630

Mechanisms
Regulation
Functions
} of sleep

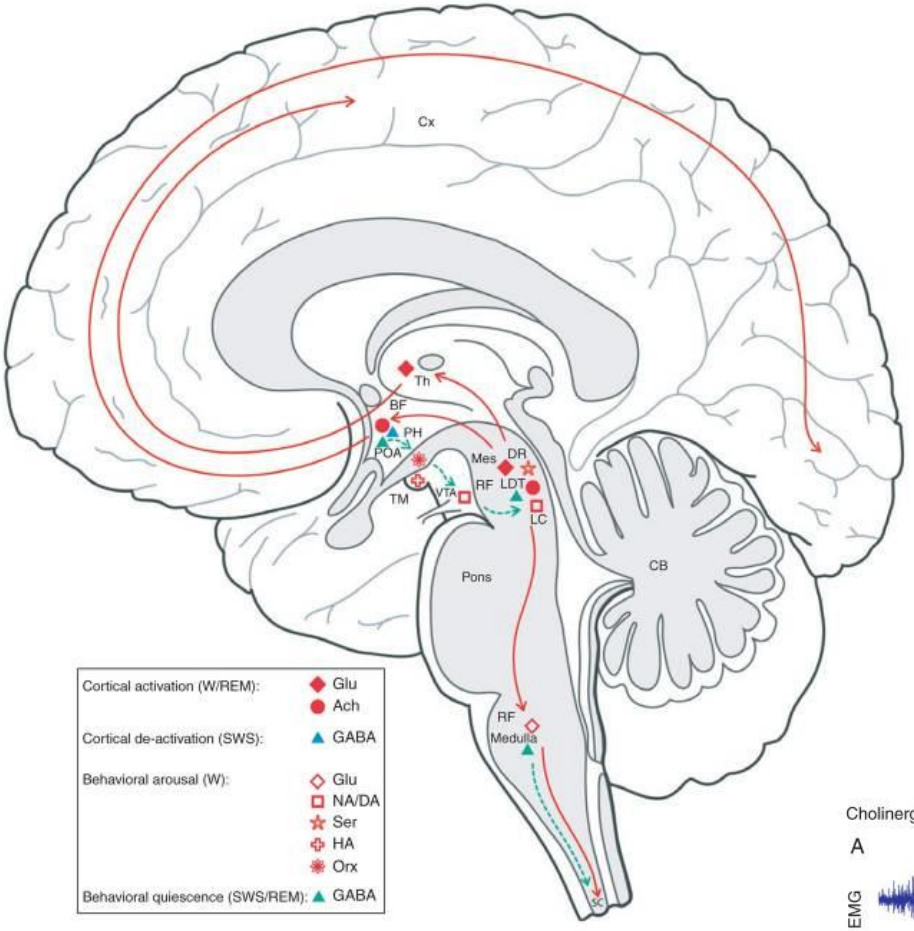
Ascending arousal system

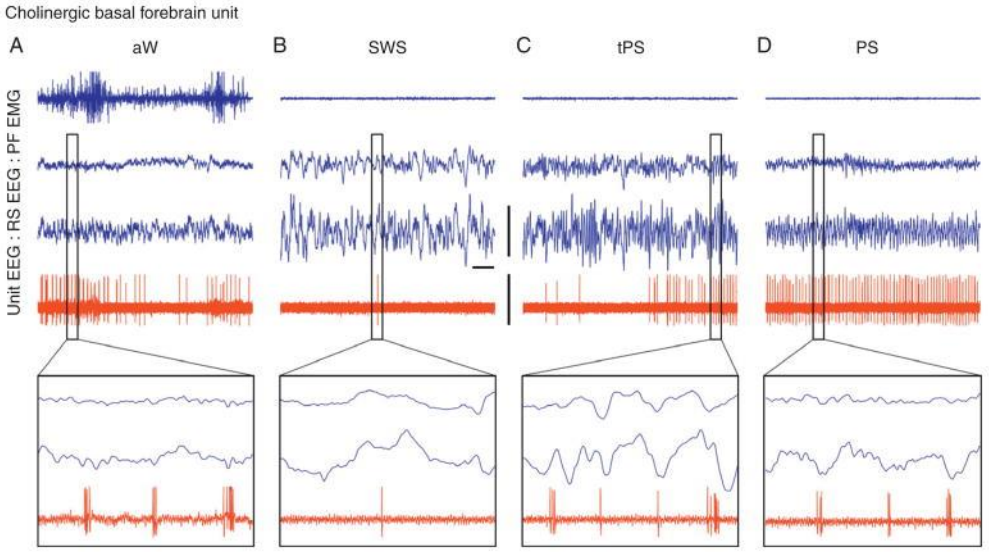
Thalamus



Hypothalamus

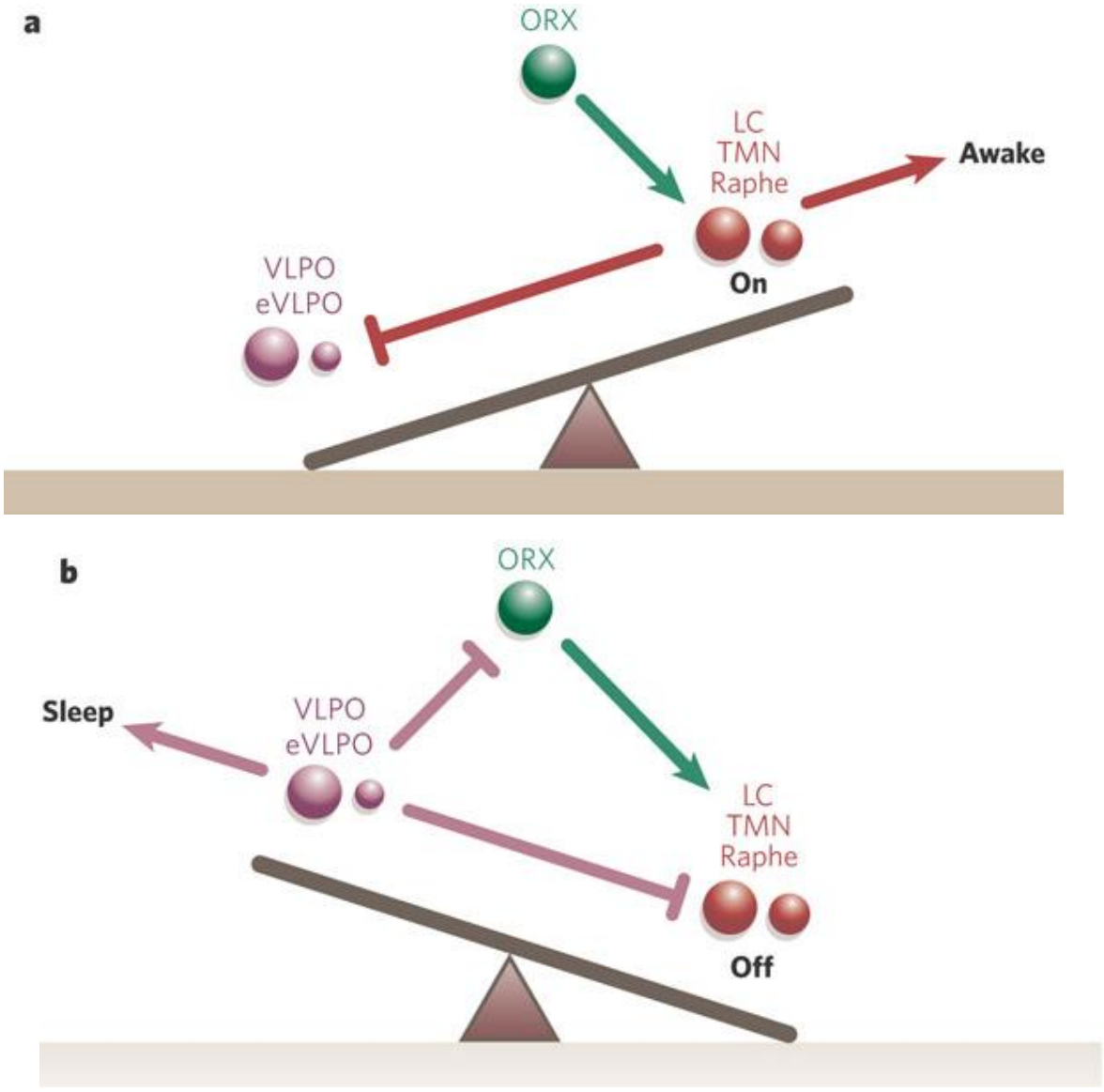
Brainstem
reticular formation





Jones, B.E., Handbook of Clinical Neurology,2010

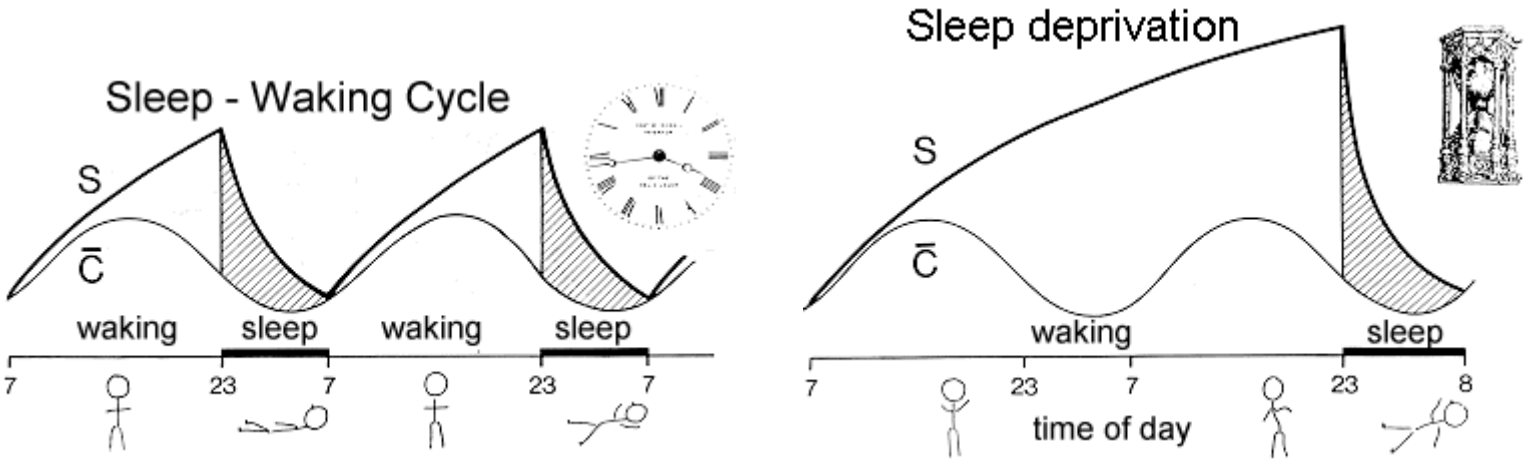
Sleep/wakefulness as a flip-flop system stabilized by Orexinergic neurons



Saper et al. 2005

Mechanisms
Regulation
Functions
} of sleep

Regulation of the sleep-wake cycle: Sleep Homeostasis and Circadian Rhythmicity

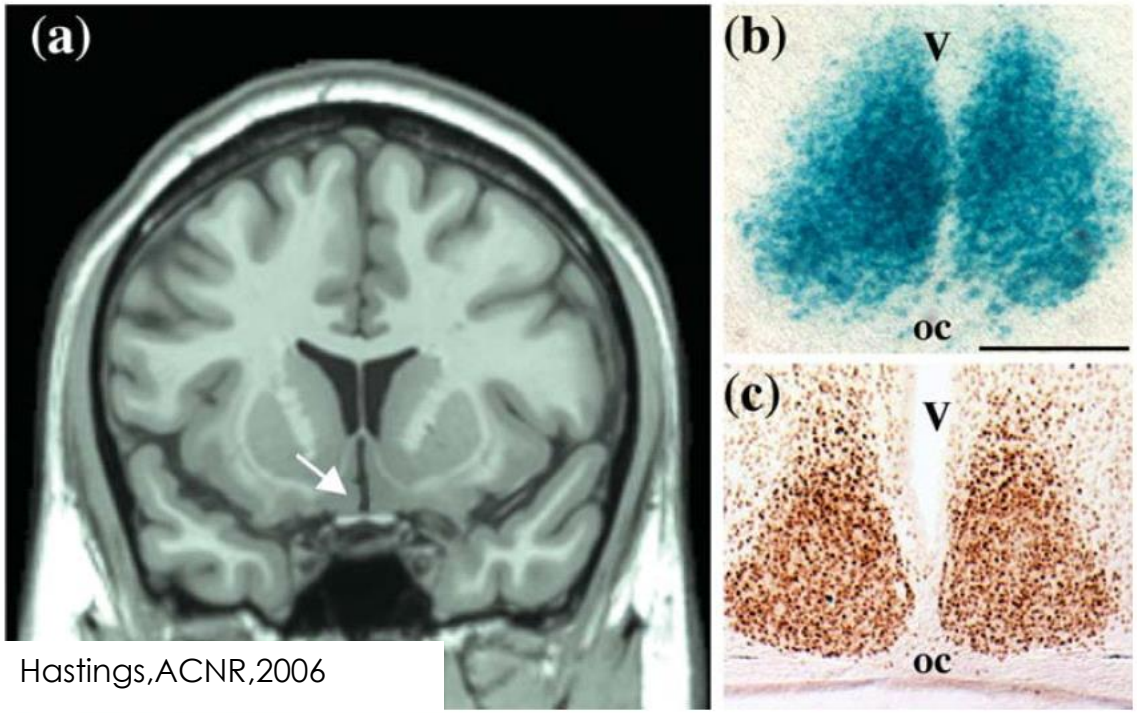


<u>Circadian timing system</u>: endogenuous, nearly 24-hour modulation in sleep-wake propensity

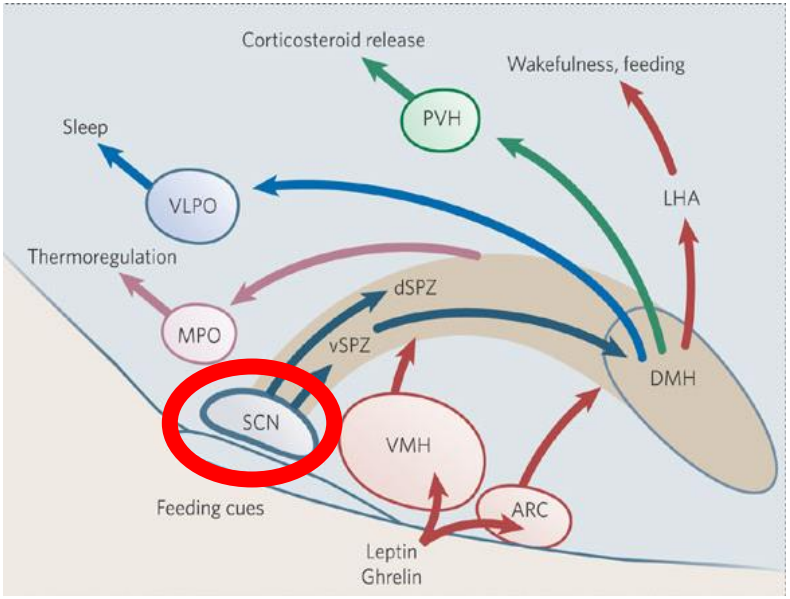
<u>Sleep homeostatic process</u>: hour-glass process, depending on prior sleep-wake history (sleep pressure built-up during wakefulness and its dissipation during (slow wave) sleep)

Borbély AA. A two process model of sleep regulation Hum Neurobiol. 1982;1(3):195-204.

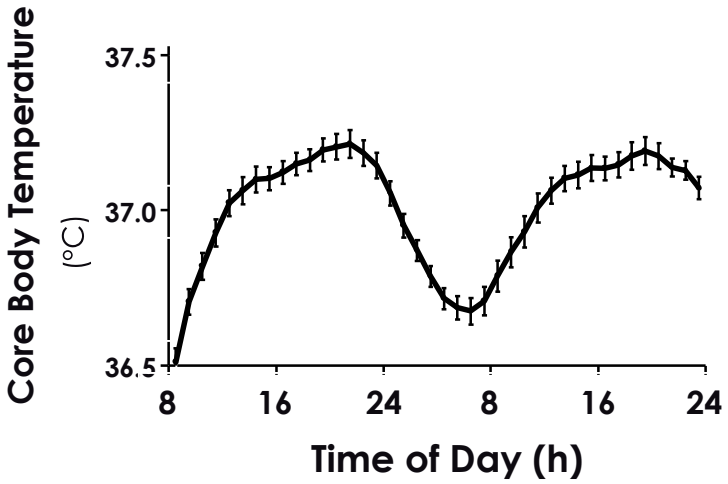
Circadian masterclock: Suprachiasmatic nucleus (SCN)

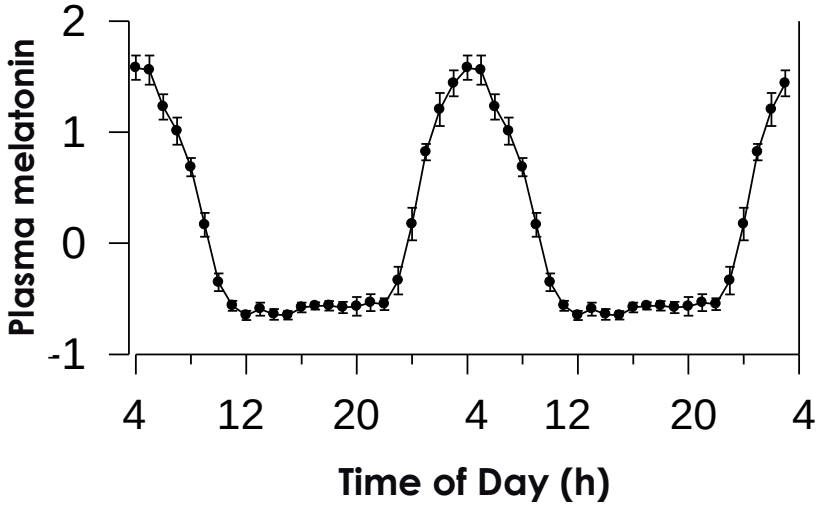


Hastings,ACNR,2006



Measuring the hands of the clock in humans





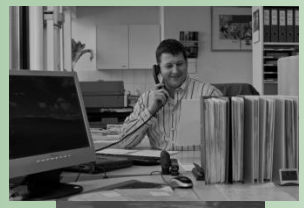
Modified from Dijk et al. 1992, 1997

Exogenuous – Endogenuous clocks

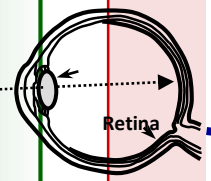
24-h rhythms

«Zeitgeber»

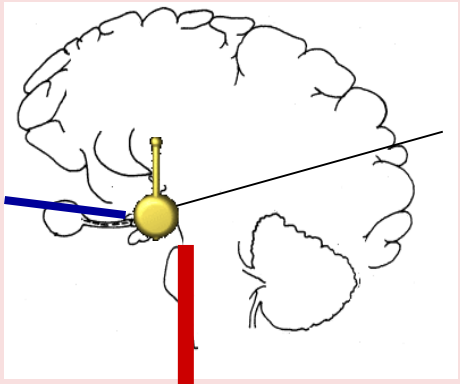
Entrainment



Eye



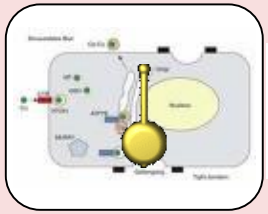
Endogenuous circadian rhythms



SCN = master clock

SYNCHRONISATION

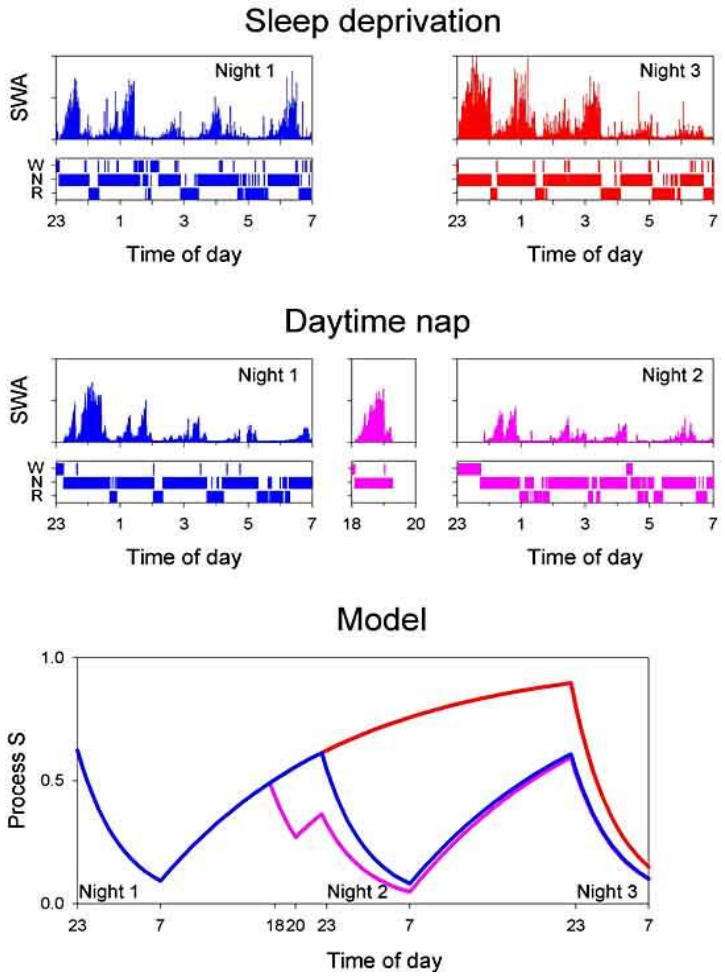
Oscillation in organs



Oscillation in cells (genes)

Sleep Homeostasis

reflected in the levels of **slow wave activity observable during NREM sleep**



Sleep Homeostasis

+ Local and activity-dependent component
+ Not uniform across the brain
+ dependent on behavioral and cognitive content of waking

Diffuse system implicating processes occurring at a cellular or local network level

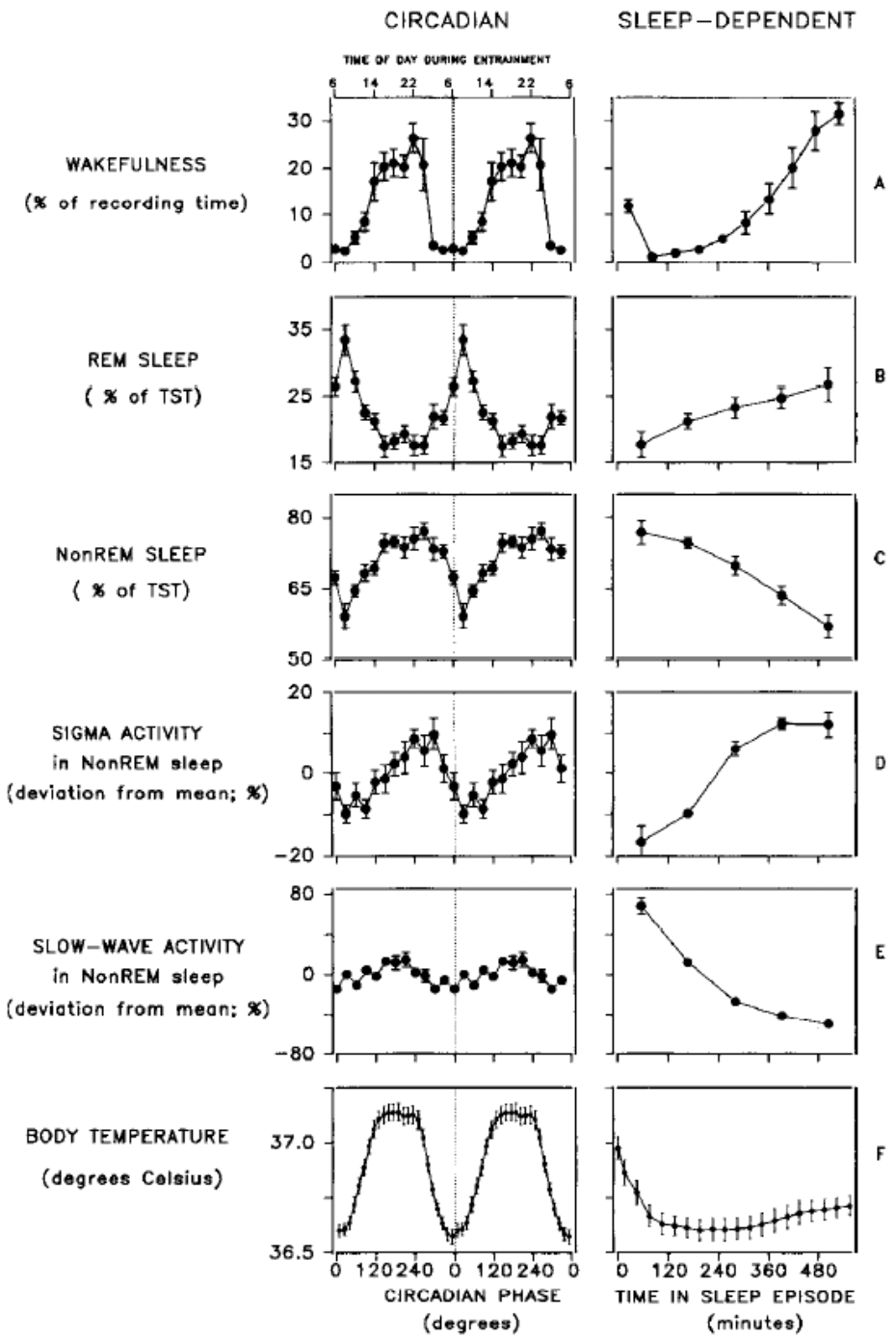
- maintenance of cellular homeostasis
- the replenishment of energy stores (adenosine or cytokines regulation of imbalanced synaptic strengths)

Thomas et al., Elife, 2020

Some sleep parameters are strongly modulated by circadian rhythm (e.g. REM sleep)

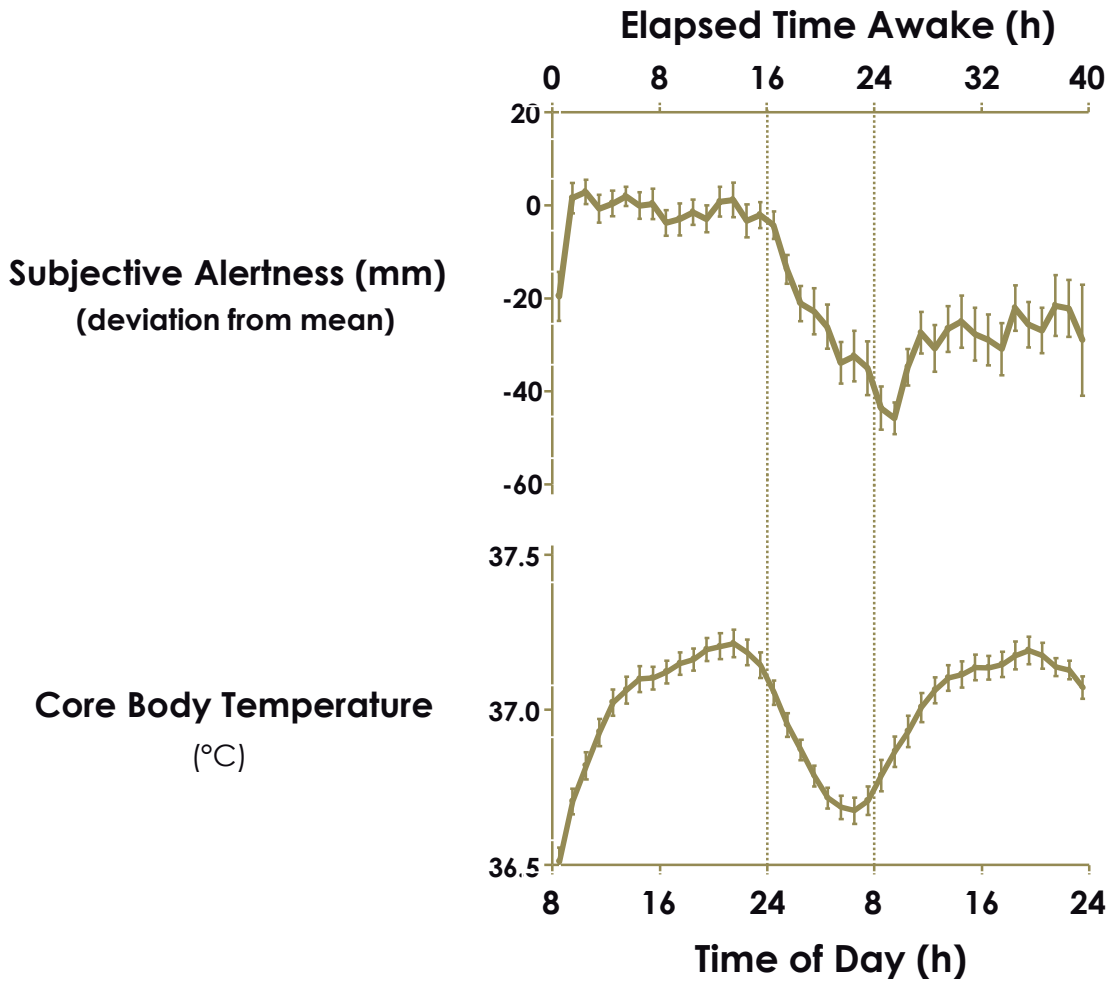
Others are modulated by homeostatic regulation (e.g. slow wave activity during NREM)

Both factors interact in many cases



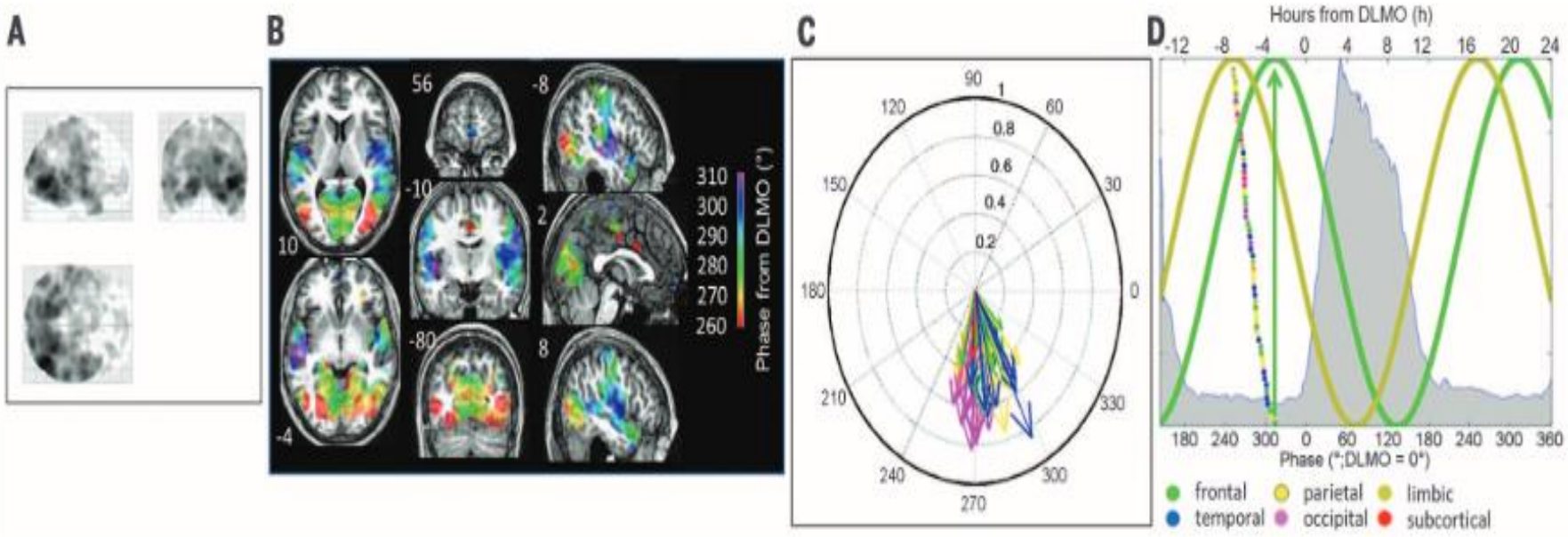
Dijk et al.,JNeurosci,1995

Circadian and Sleep-Wake dependent Modulation of Alertness during the wake state



Modified from Dijk et al. 1992

Local modulation of human brain responses by circadian rhythmicity and sleep debt



Muto et al., Science, 2016

Mechanisms
Regulation
Functions

} of sleep

Sleep function(s) are not completely specified yet

- Brain detoxication / restoration
- Energy balance / thermoregulation
- Restauration of system brain function and synaptic/neural function
- **Learning and memory** (focus on human studies)

Sleep & Memory

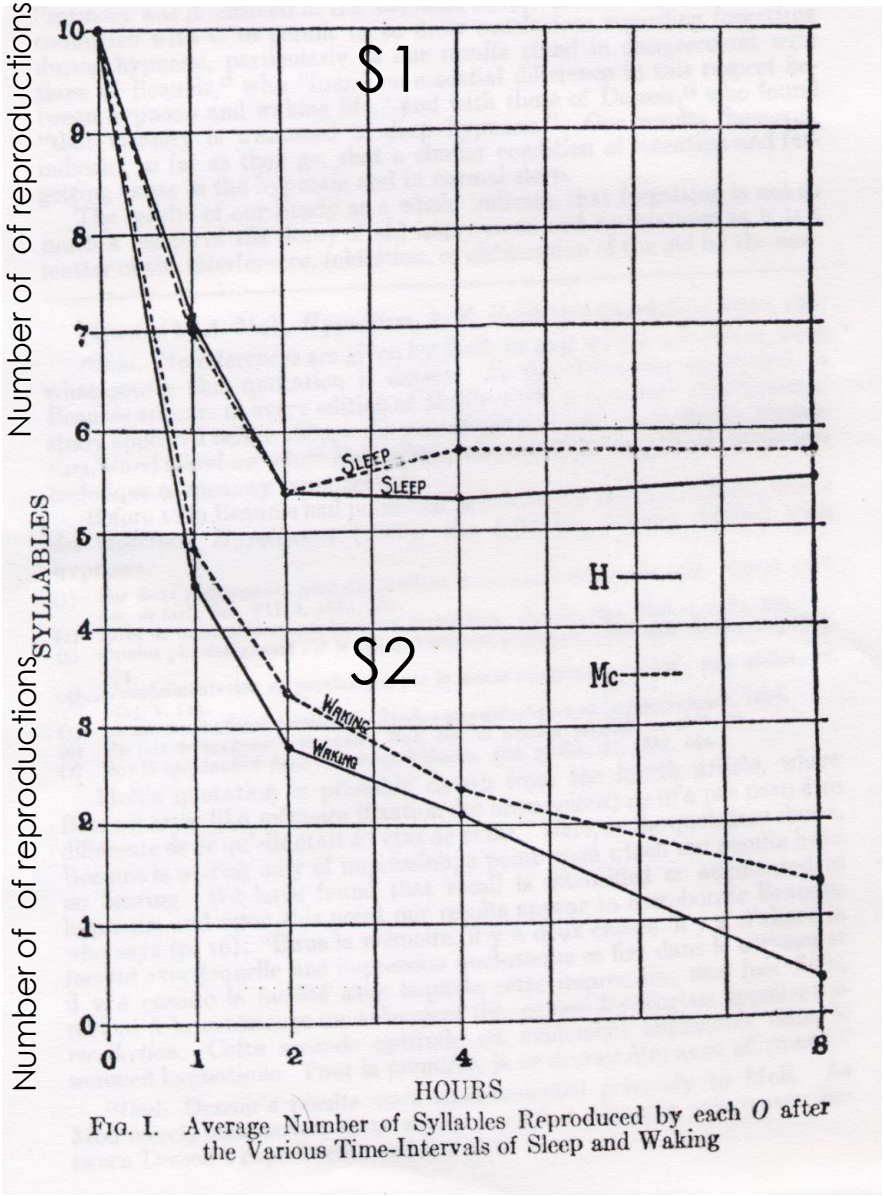


FIG. I. Average Number of Syllables Reproduced by each *O* after the Various Time-Intervals of Sleep and Waking

2Ss
Nonsense syllables

evening learning : 23.00-1.00
morning learning: 8.00-10.00

Sleep has
a beneficial effect
on memory

Jenkins & Dallenbach, 1924

Sleep has a beneficial effect on memory

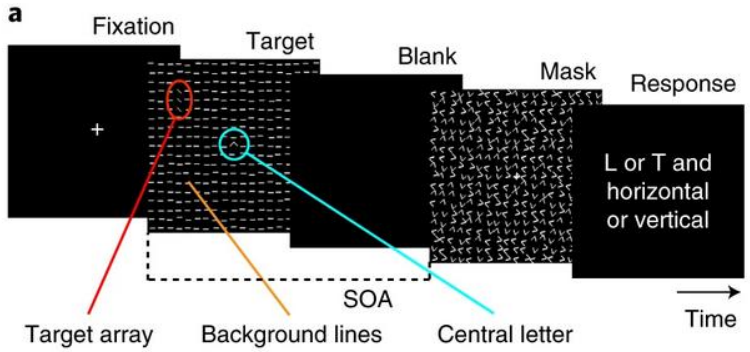
Role of sleep stages (NREM-REM)?

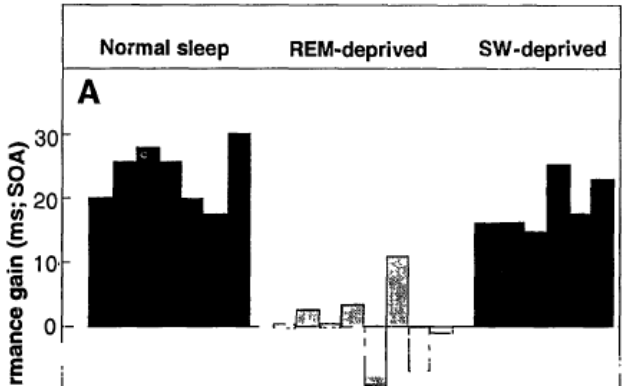
Slow-wave-rich sleep (early night) benefits declarative memory traces while REM-rich (late night) sleep benefits procedural learning (e.g. Plihal and Born, J.Cogn.Neurosciences,1997)

Low acetylcholine during slow-wave sleep is critical for declarative memory consolidation (Gais & Born, PNAS, 2004)

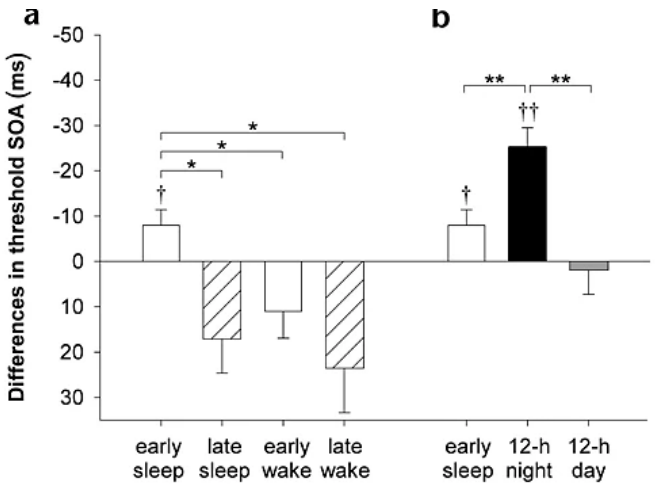
Role of sleep stages (NREM-REM)?

Visual discrimination task: Improvement after practicing visual texture discrimination does not occur until several hours after practice has ended. The improvement strongly depends on sleep.





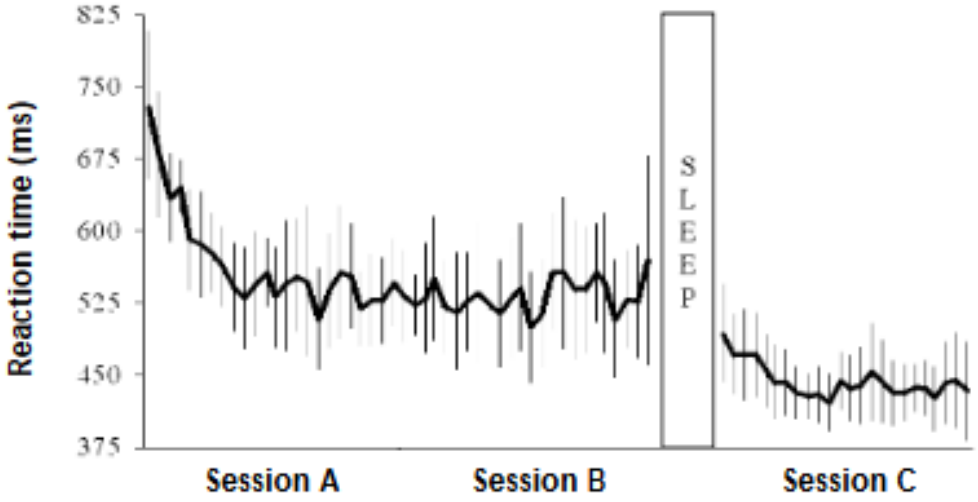
Karni et al., Science, 1994

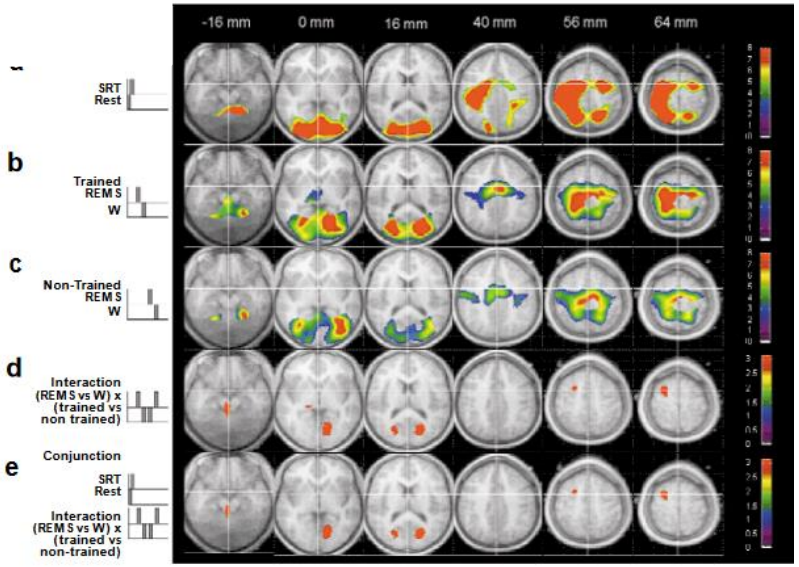


Gais et al., Nature Neurosciences, 2001

Role of sleep stages (NREM-REM)?

Experience-dependent changes in cerebral activation during human REM sleep

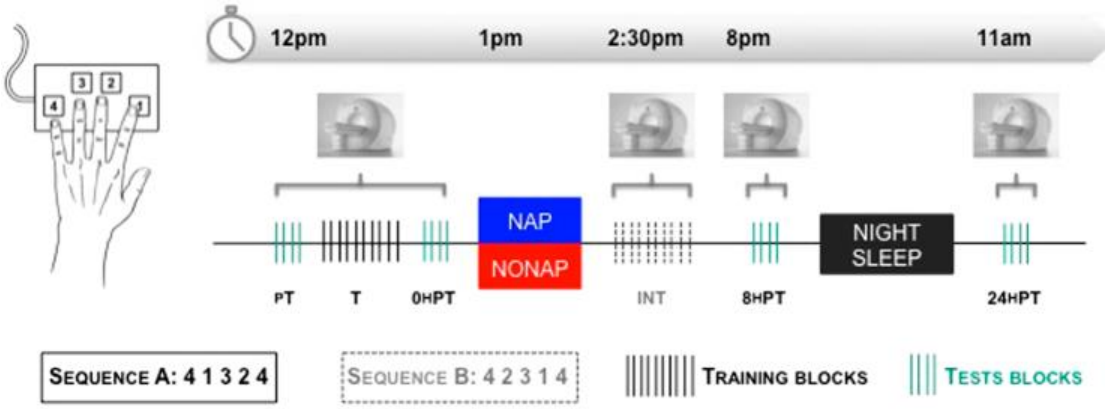




Note. Sleep-dependent reorganisation (e.g. of remote emotional memories) (Sterpenich et al., JNS, 2009)

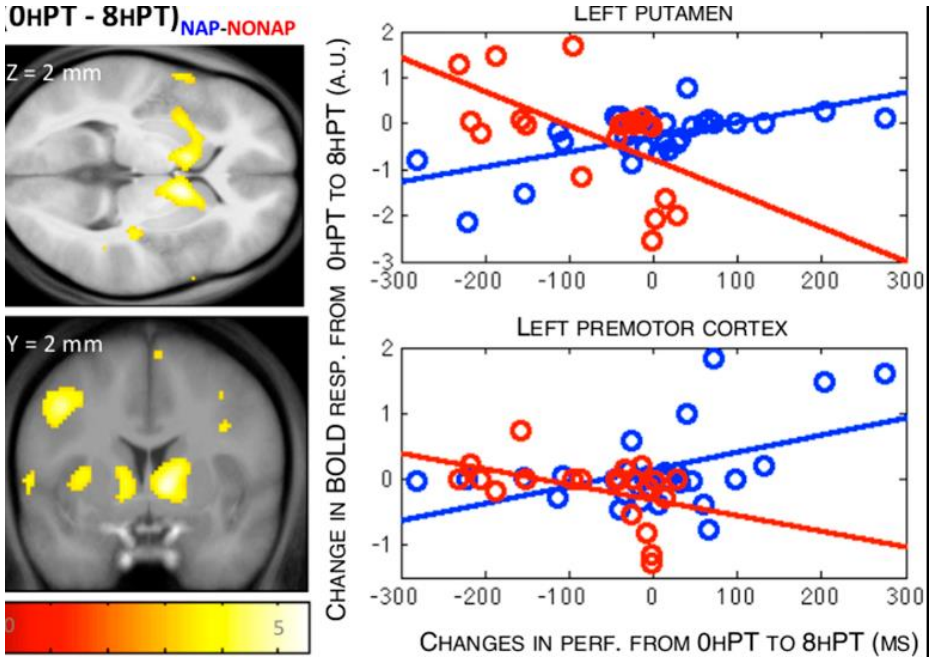
Maquet et al., Nature Neurosciences, 2000

Off-line performance gains or resilience to interference?



Post-training nap

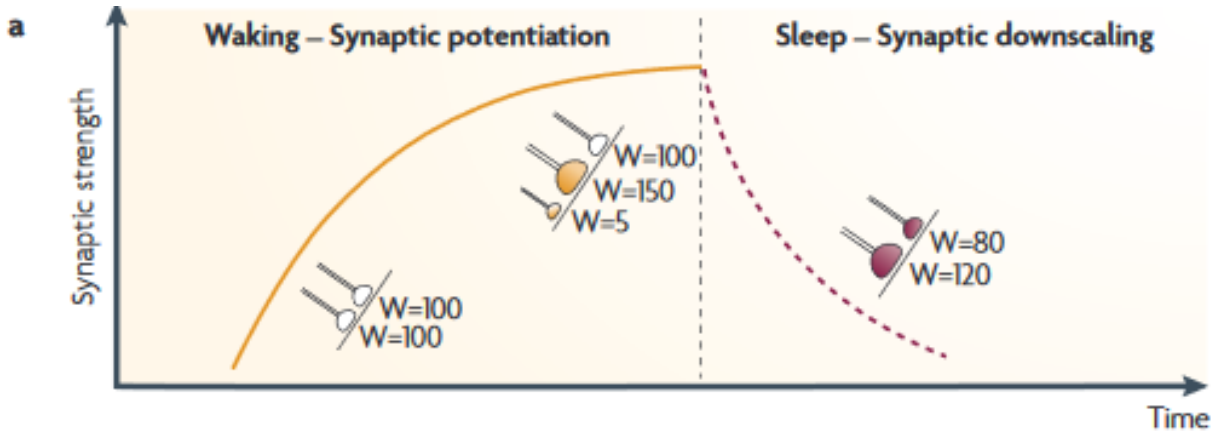
- transiently protects memory against interference
- modulates the link between cerebral activity and behavior (smaller post-interference decrease in cortico-striatal activity is associated with better performance when allowed to sleep)



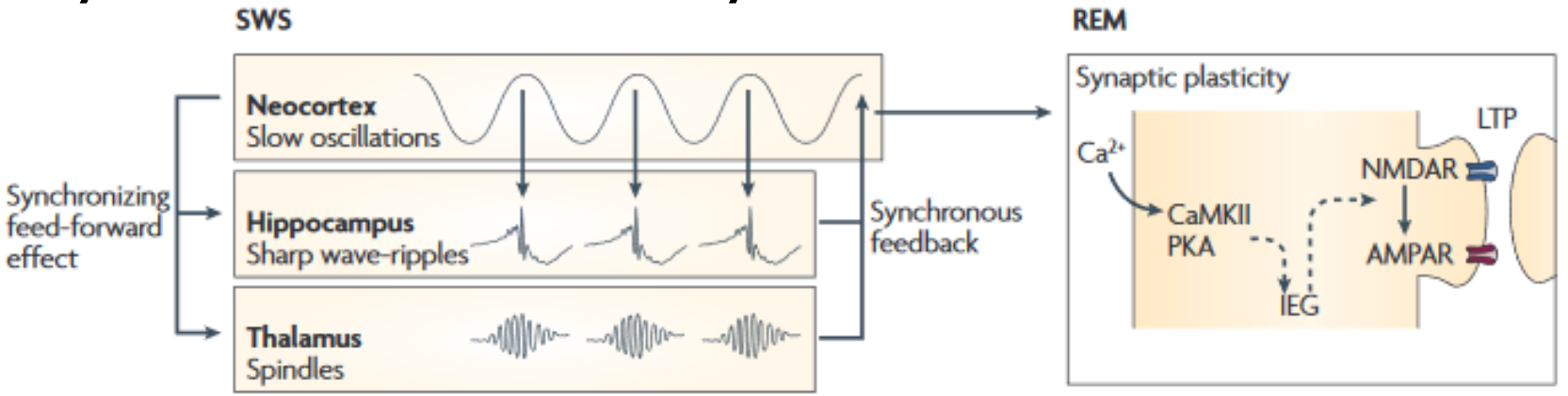
Albouy et al., SciRep, 2016

Facilitation in a learning-independent or learning-specific manner?

Synaptic homeostasis theory



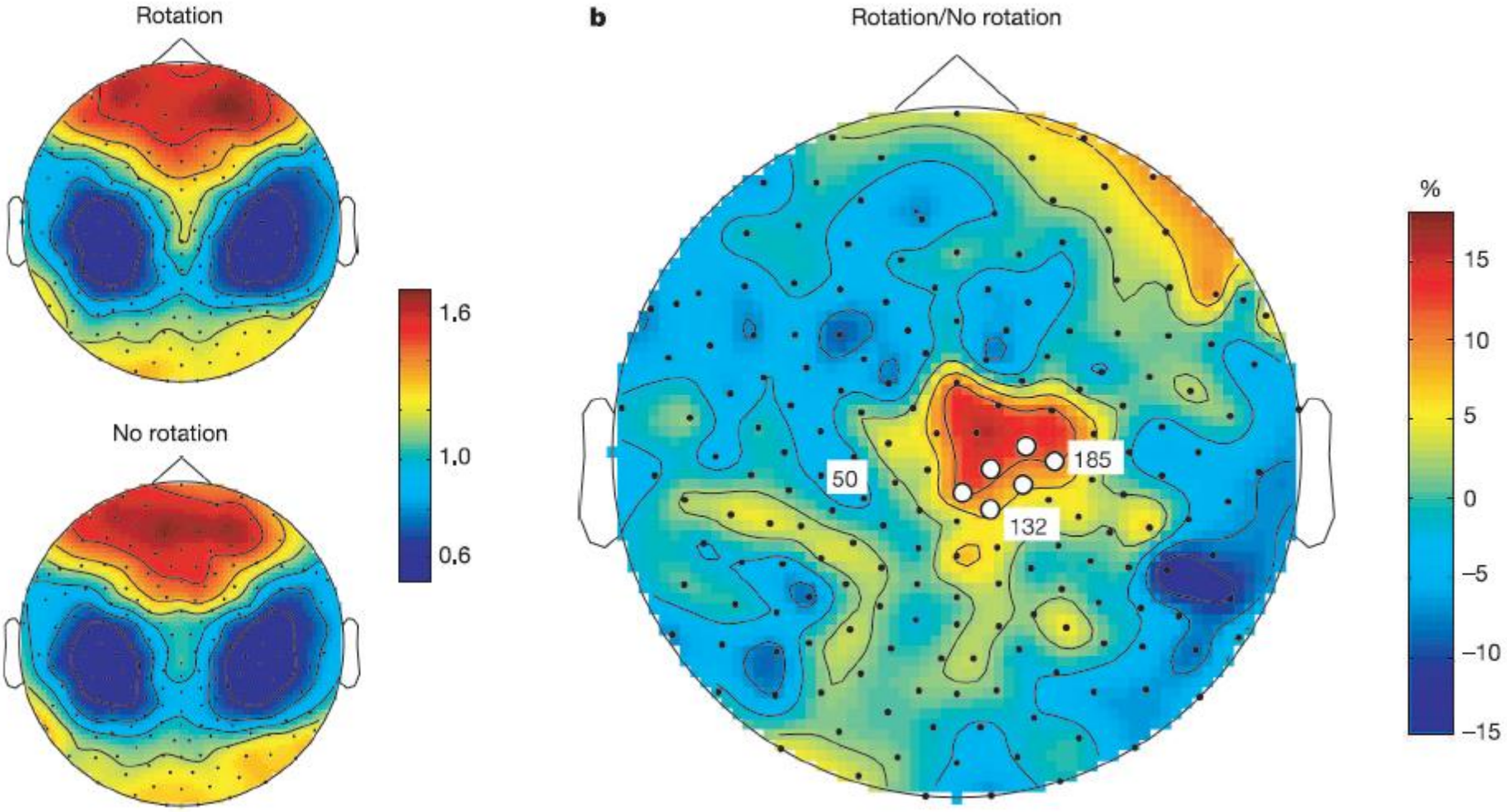
b Systems consolidation theory



Diekelmann & Born, Nature Reviews Neurosciences, 2010

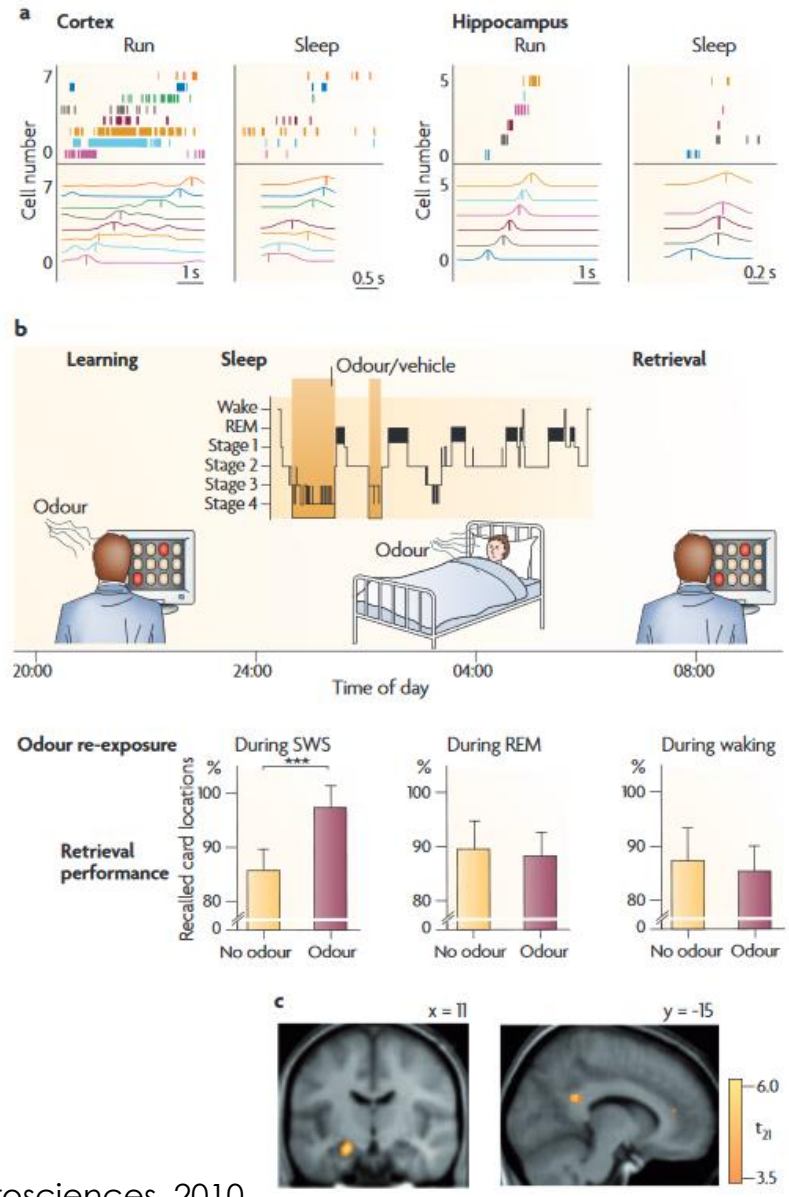
Synaptic homeostasis theory
(Example)

Region-specific increase of slow waves after learning



Huber et al., Nature, 2004

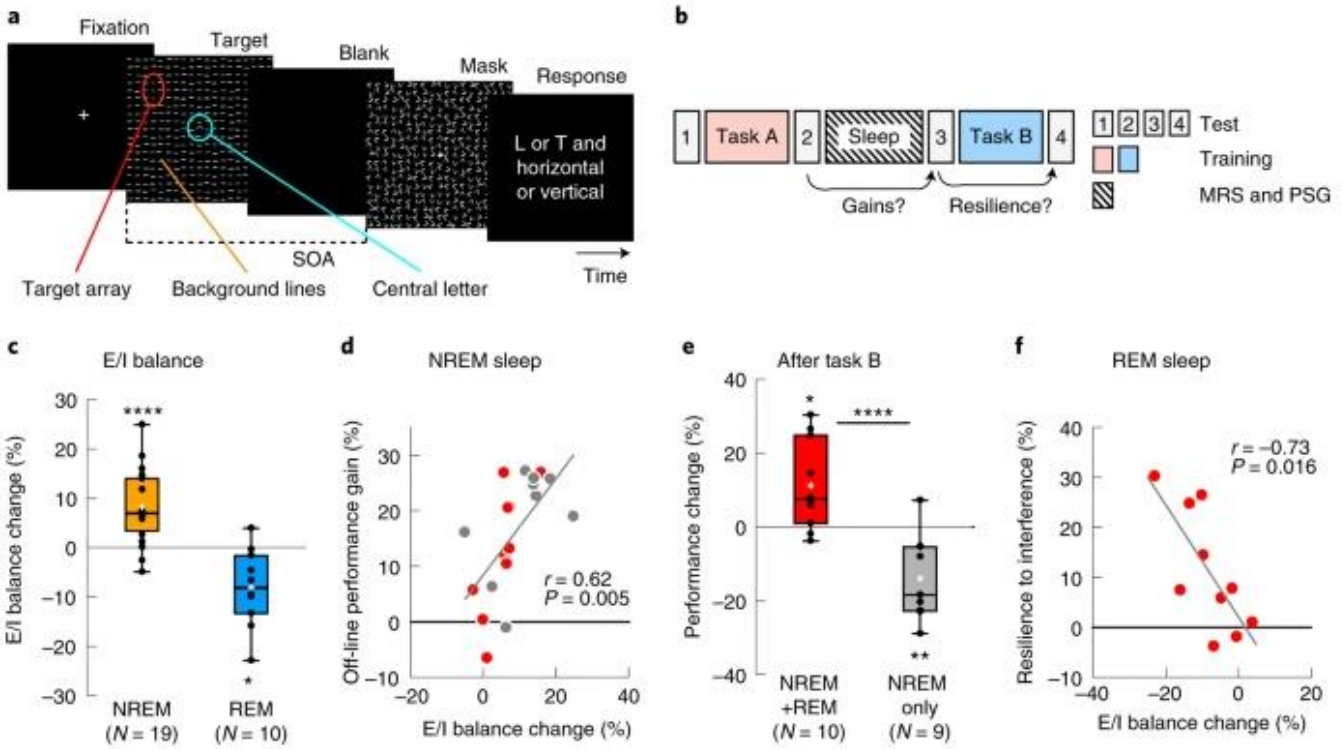
Systems consolidation theory
(Example)



Lee et al., Neuron, 2002
Rasch et al, Science, 2007
From Diekelmann, Nature Review Neurosciences, 2010

Complementary contributions of

- Non-REM and REM sleep
- Learning-specific and unspecific processes
- Resilience to interference and offline gains



Tamaki et al., Nature Neurosciences, 2020

Summary

- Sleep is initiated through interactions of hypothalamic, (basal forebrain) and brainstem structures
- Sleep is under the control of 2 regulatory factors
  - Circadian
  - Homeostatic
- Sleep functions are still under discussion
  - Synaptic homeostasis
  - Memory/Plasticity
  - Circadian contribution?