

# Sleep & Memory

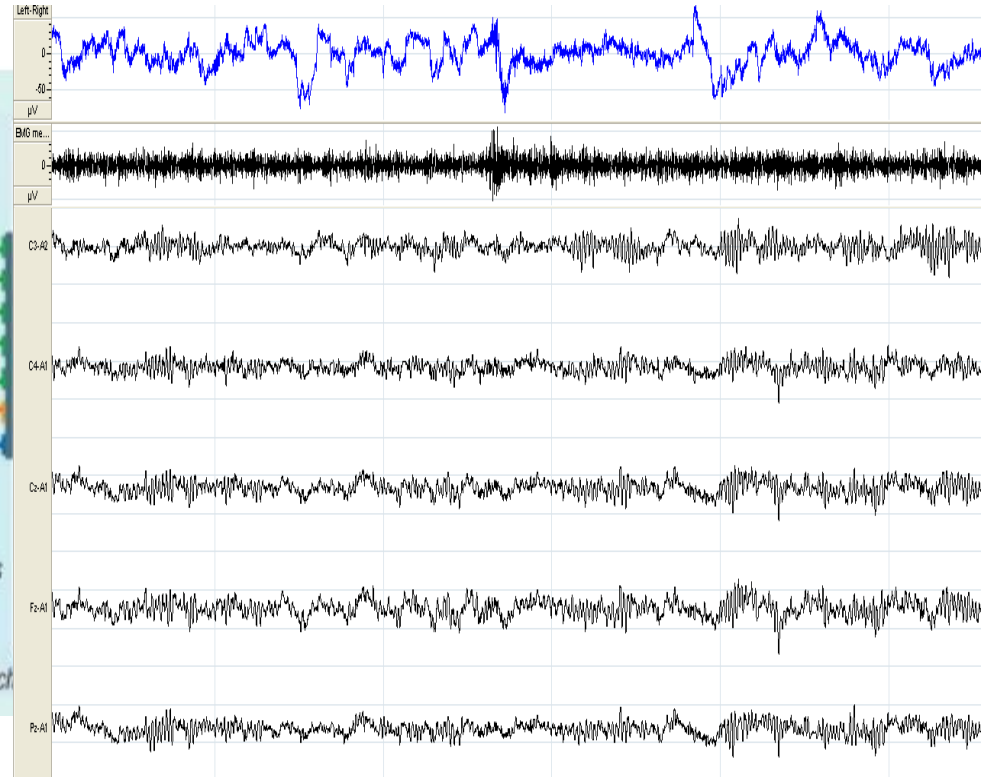
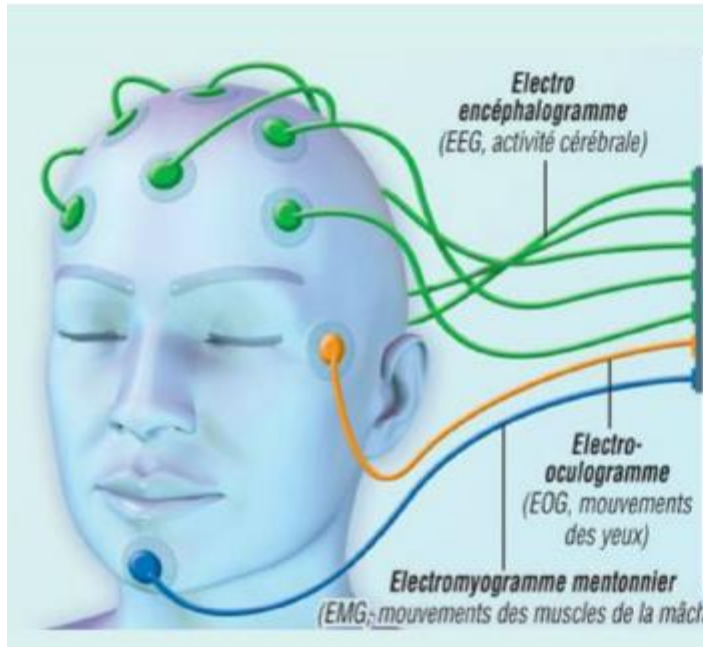
C.Schmidt  
Sleep & Chronobiology Group

GIGA Doctoral School  
December 9<sup>th</sup> 2021

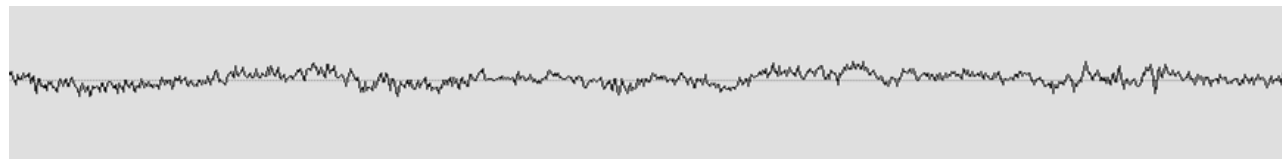
# What is sleep ?

- Periodically recurring behavior
  - Preceded by characteristic searching for a safe, secluded place
  - Characterized by
    - a (recumbant) posture (species-specific)
    - a decrease in responsiveness to external stimuli
    - a rapid state reversibility
  - Characterized by a homeostatic response
    - Sleep deprivation leads to sleep rebound
- + Additional neurophysiological criteria

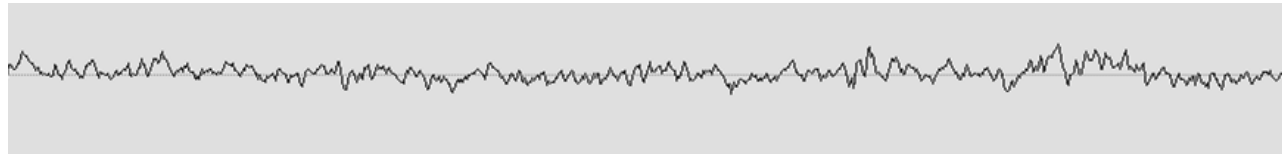
# How do we measure sleep in humans : Polysomnography



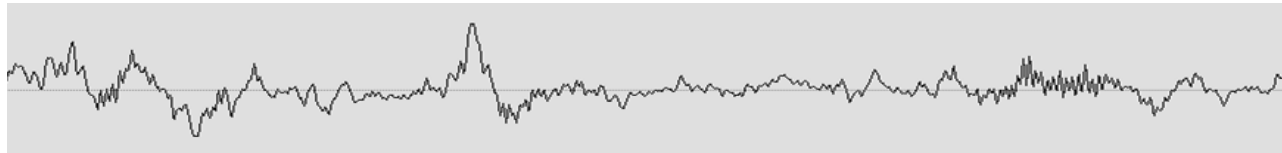
# Brain Waves during Waking and Sleep (EEG)



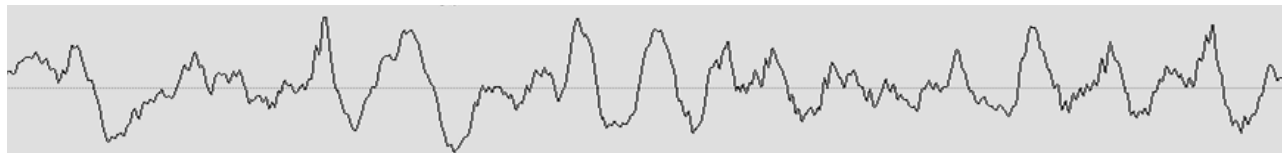
Awake



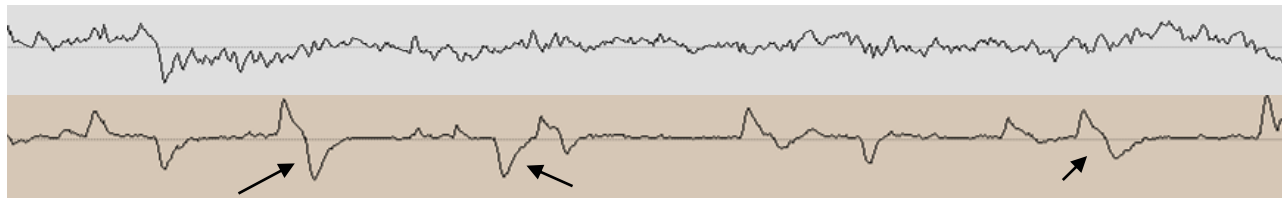
Stage 1



Stage 2



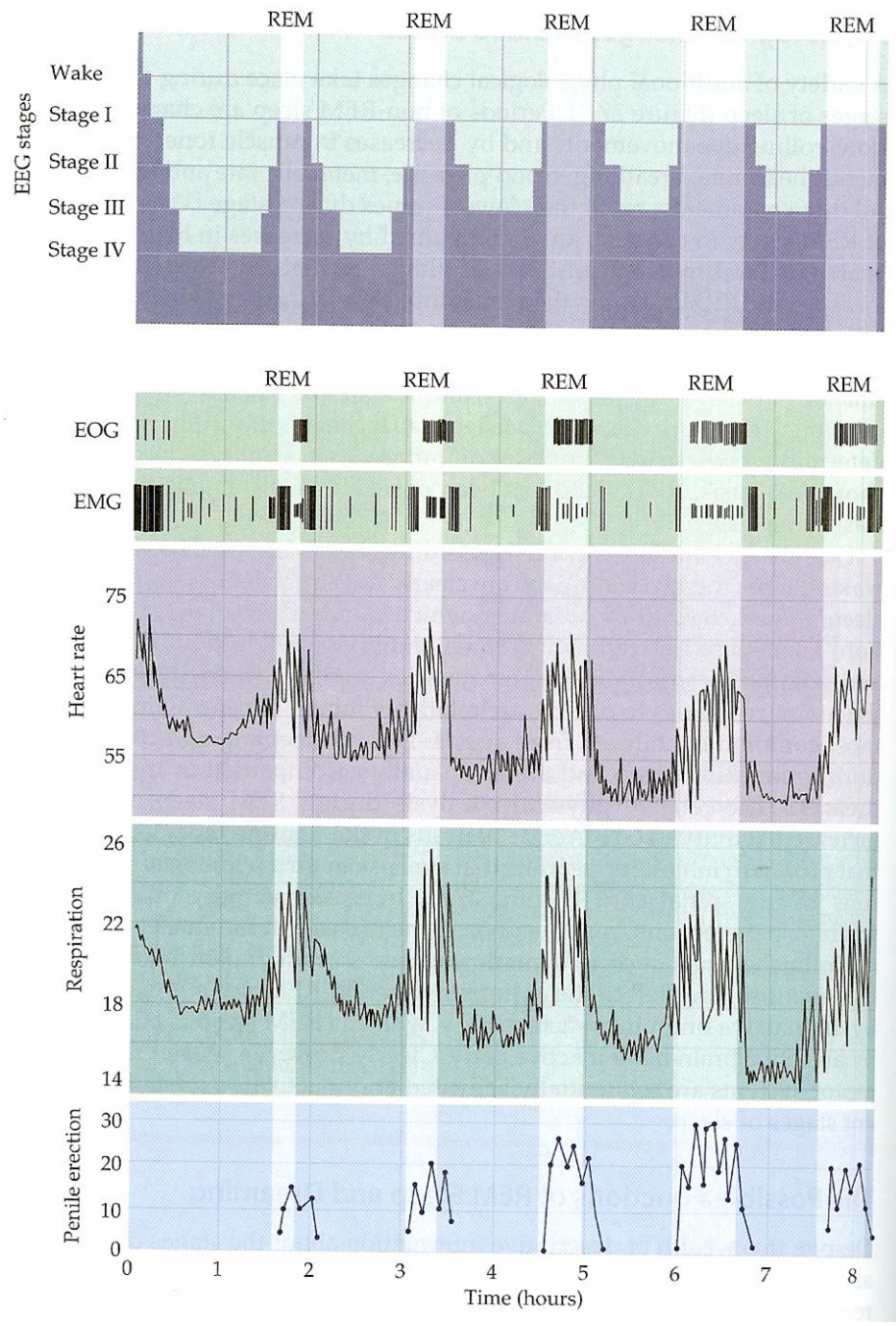
Deep Sleep  
Slow wave sleep



REM Sleep

Eye Movements

← 30 Seconds →



Mechanisms

Regulation

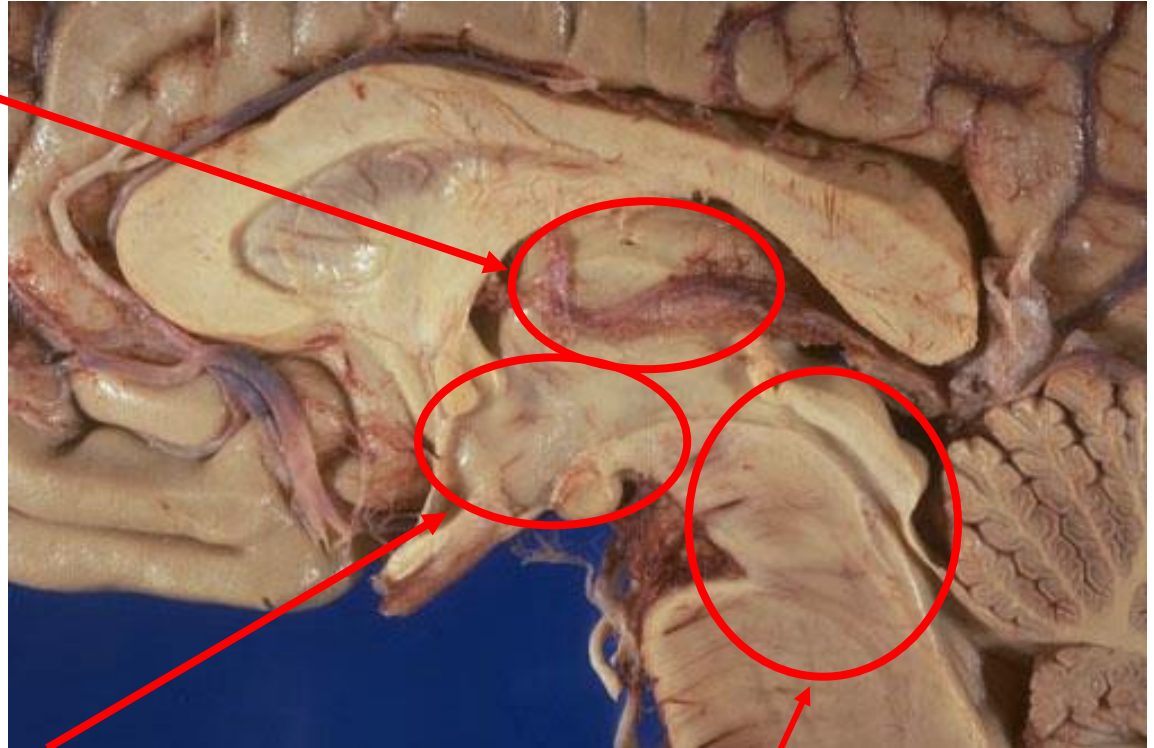
Functions



of sleep

# Ascending arousal system

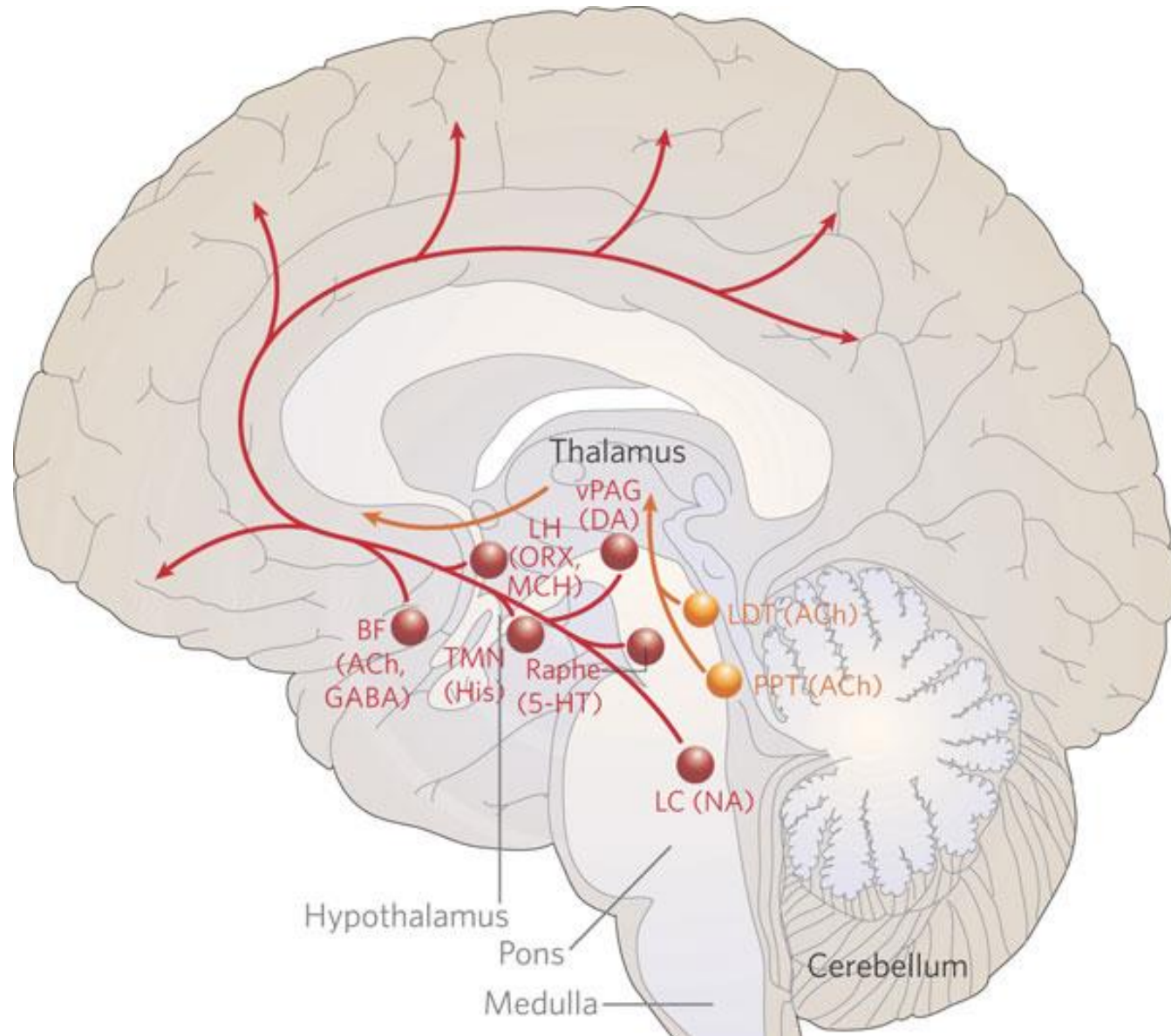
Thalamus



Hypothalamus

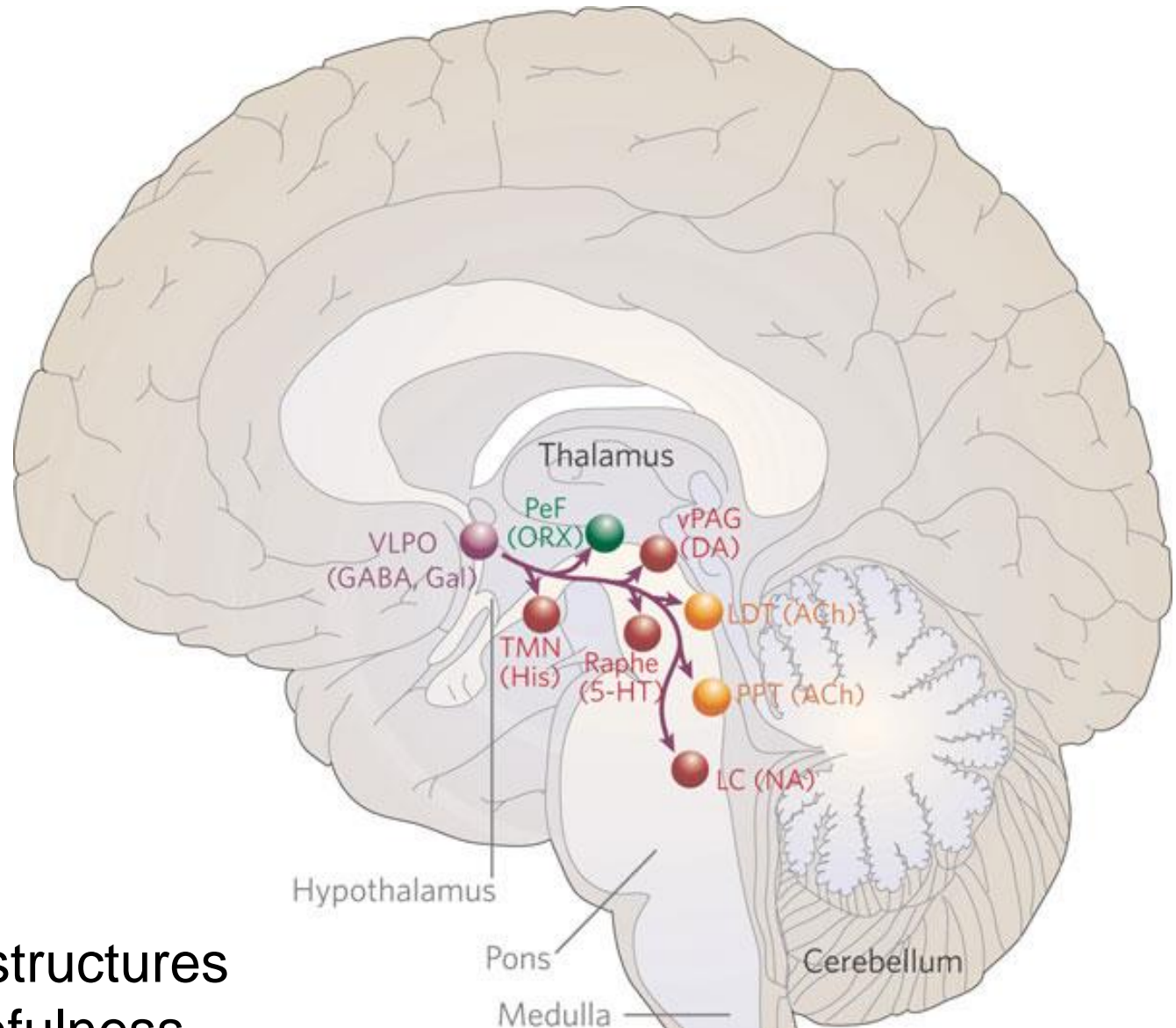
Brainstem  
reticular formation

# Structures maintaining wakefulness



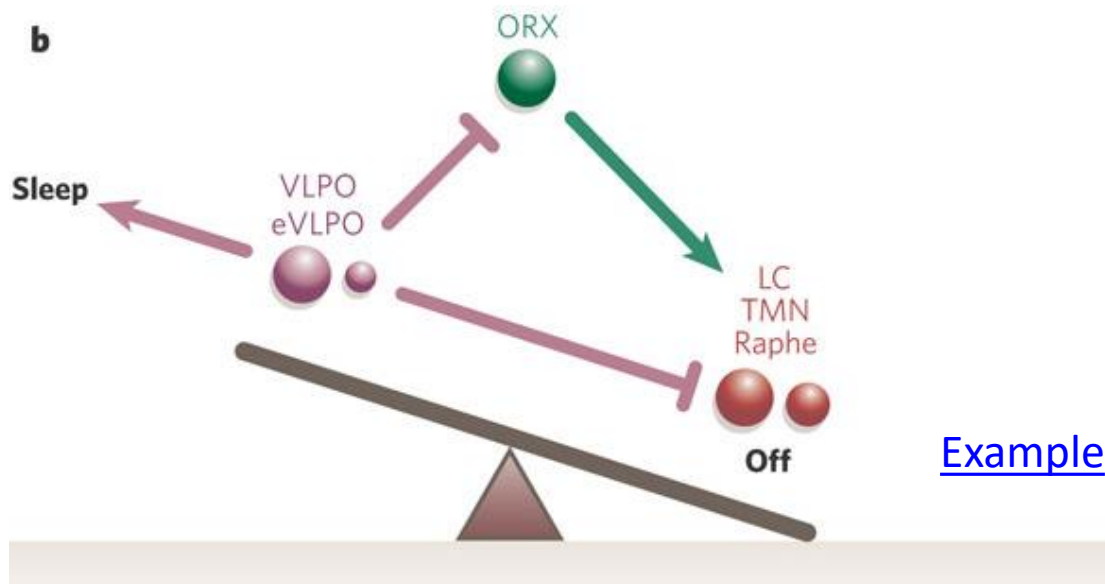
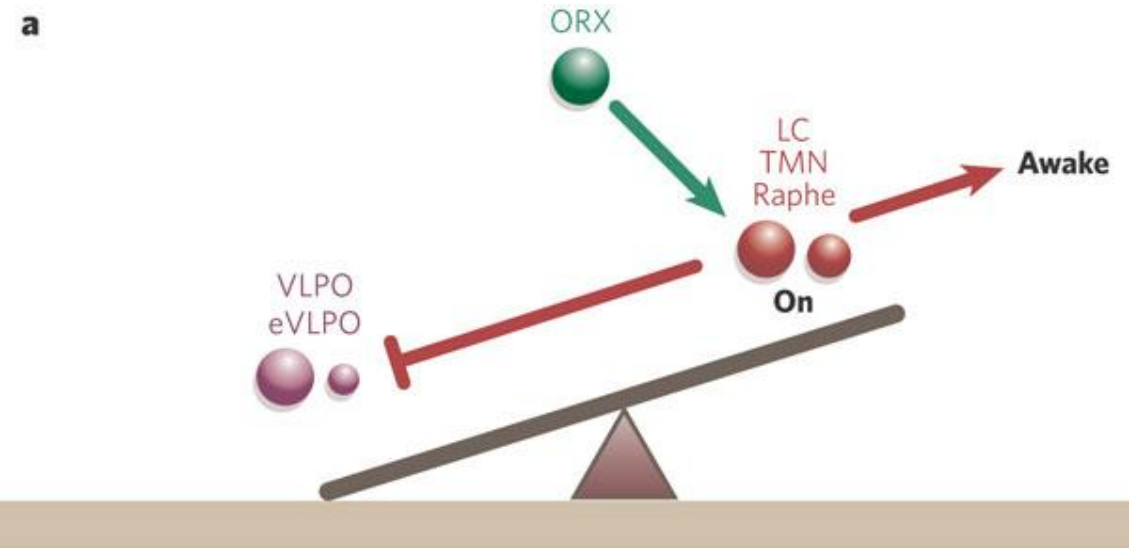


# Structures initiating sleep

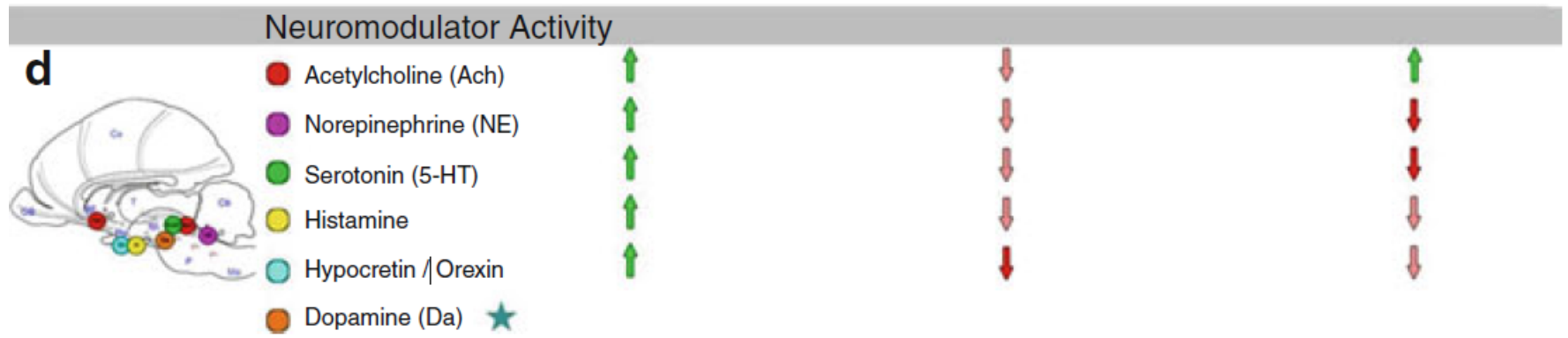
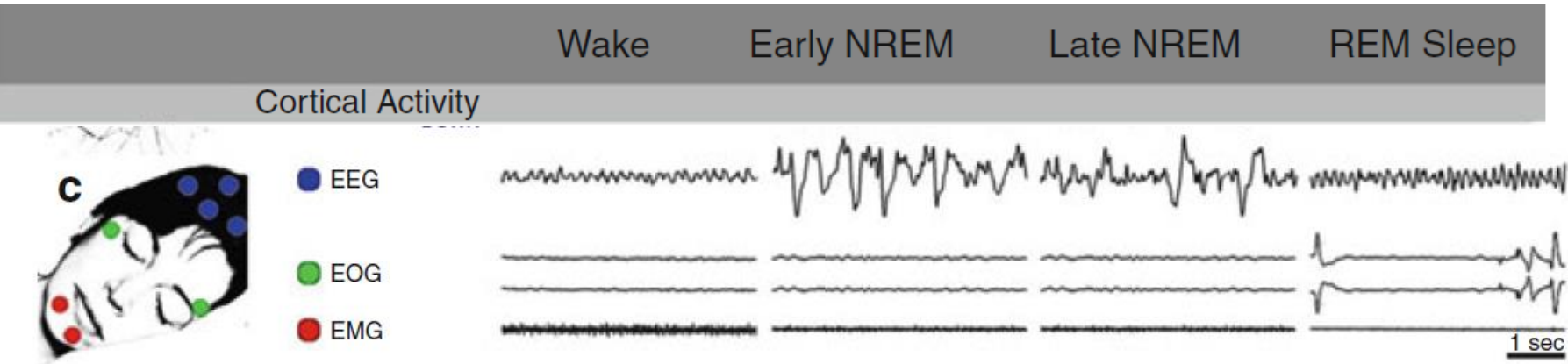


VLPO: inhibits structures promoting wakefulness

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



Example: Narcolepsy



Mechanisms

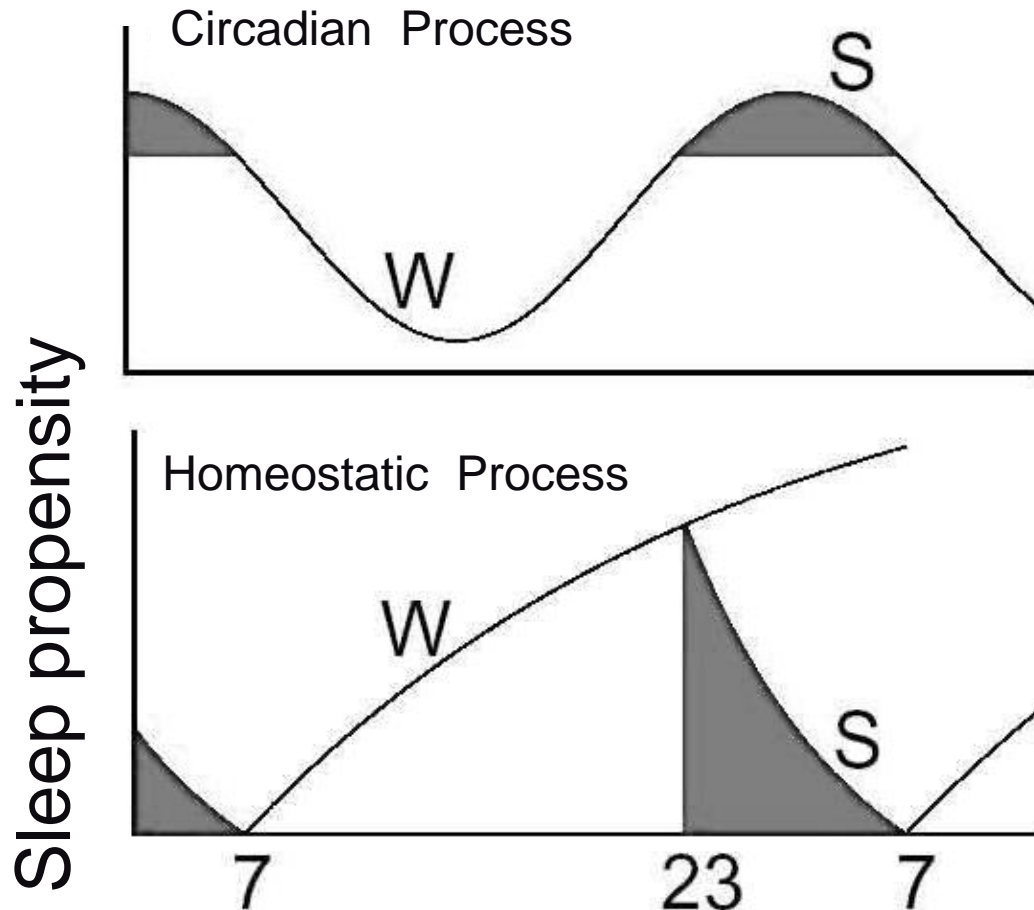
Regulation

Functions

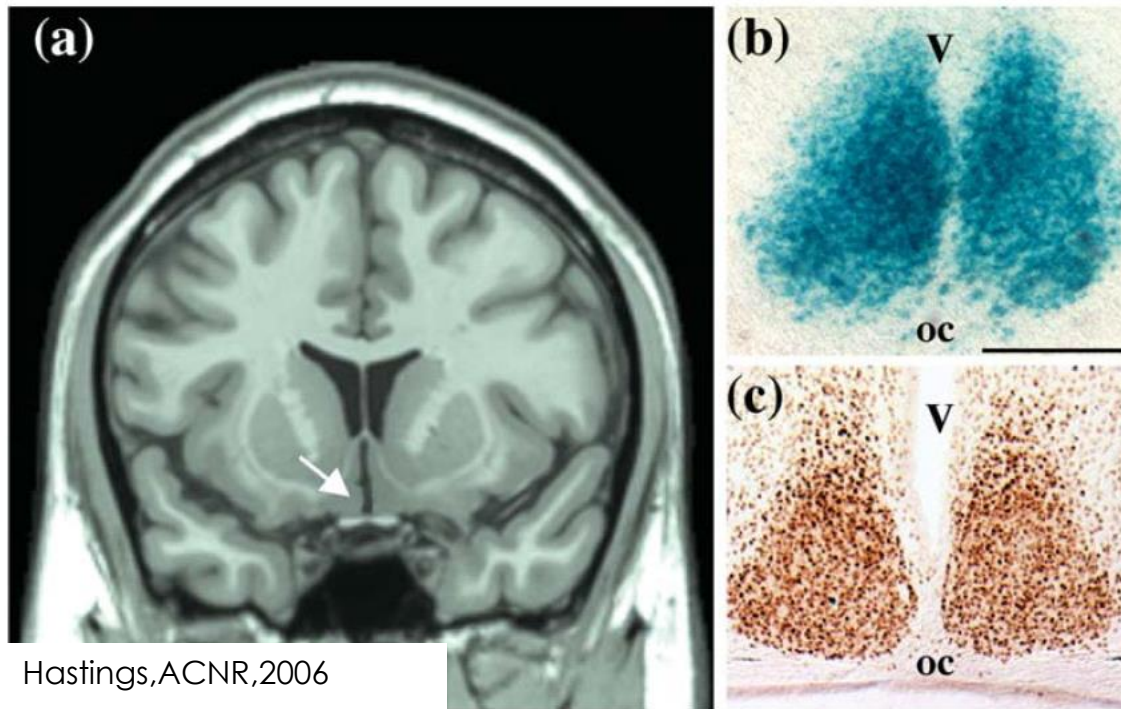


of sleep

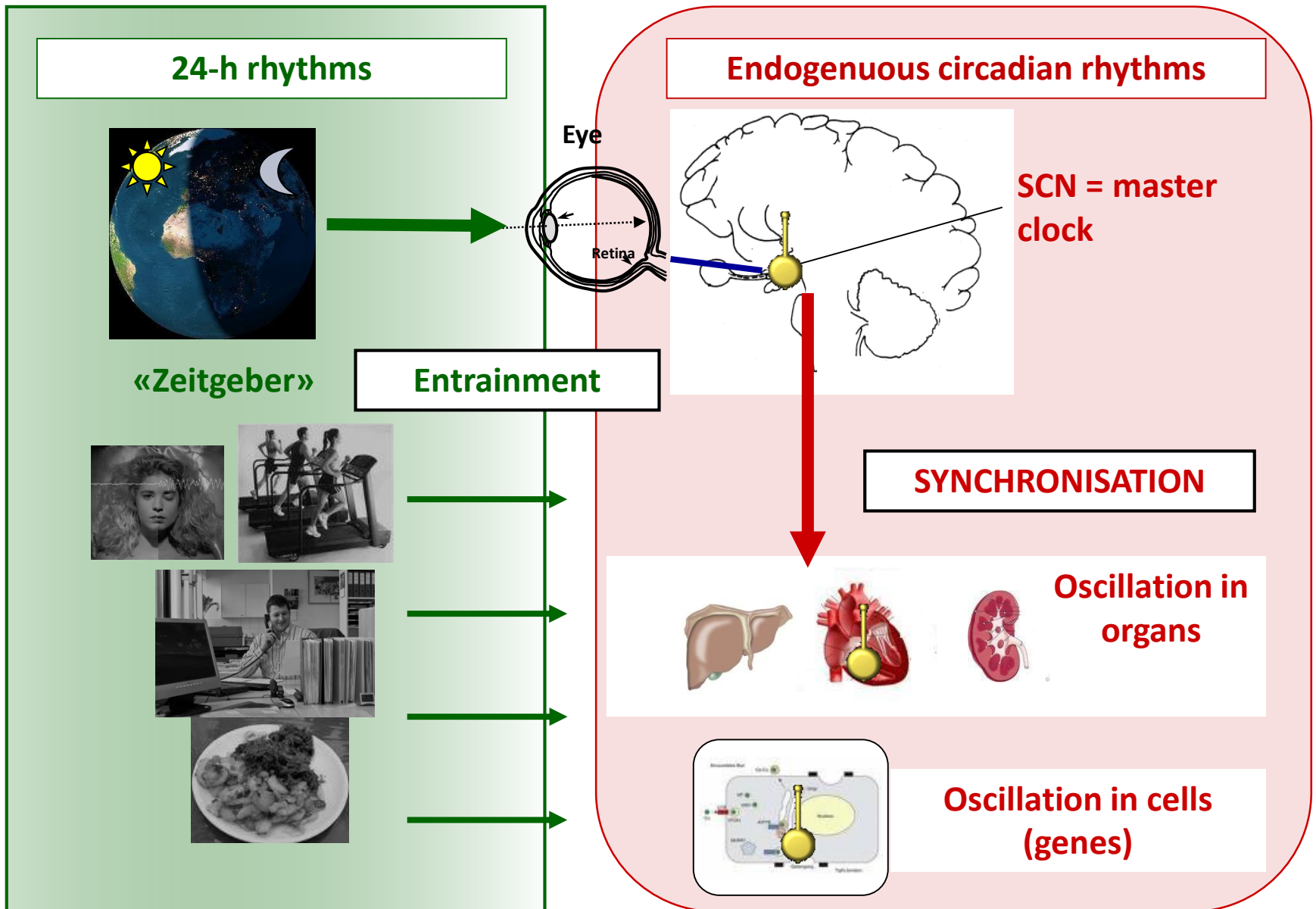
# Sleep-Wake Regulation: Sleep Homeostasis and Circadian Rhythmicity

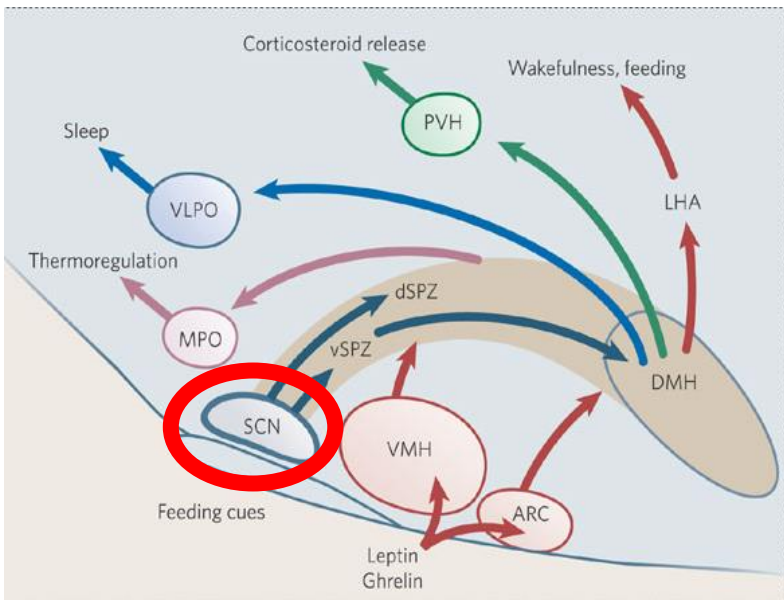


# Circadian masterclock: Suprachiasmatic nucleus (SCN)

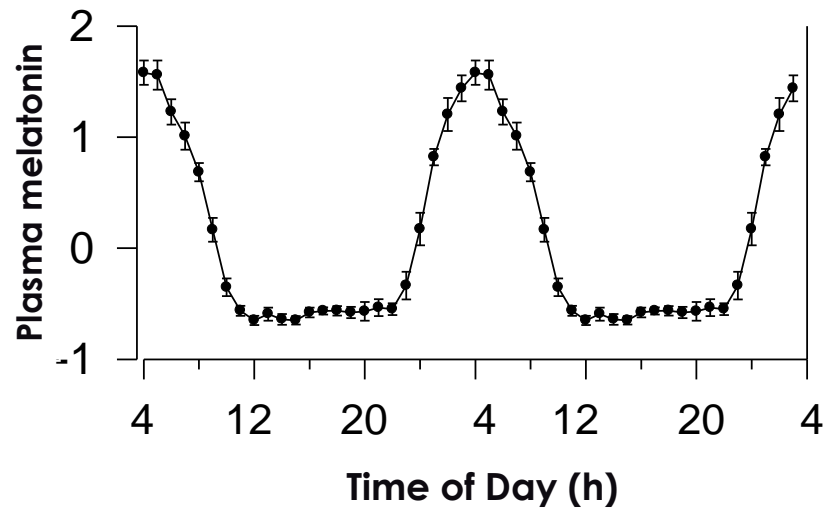
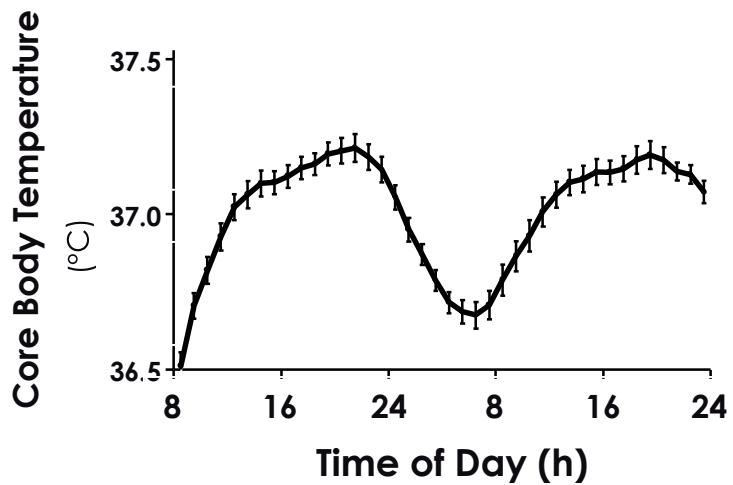


# Exogenous – Endogenous clocks





## Measuring the hands of the clock in humans

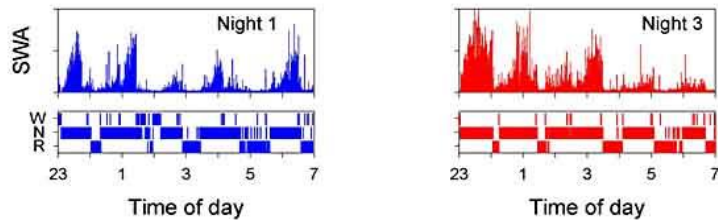




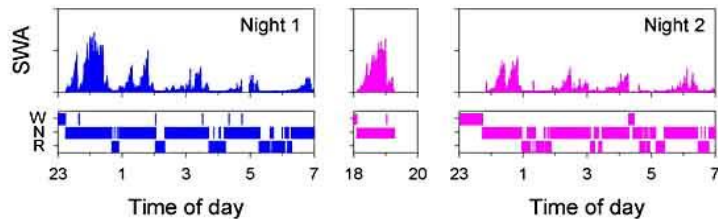
# Sleep Homeostasis

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

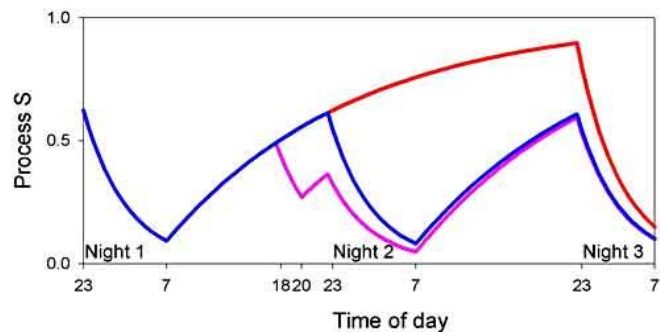
### Sleep deprivation



### Daytime nap



### Model



# Sleep Homeostasis

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

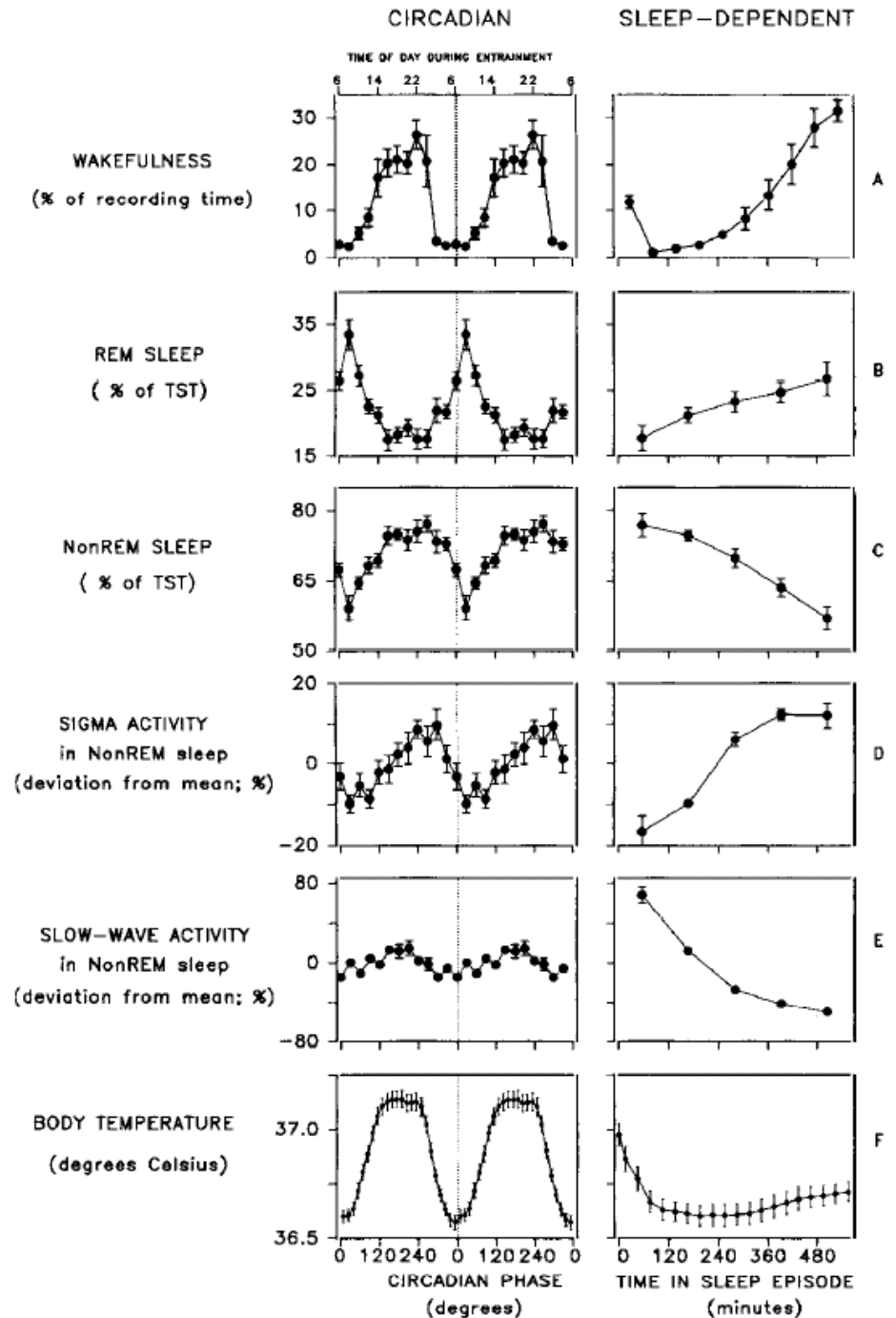
Diffuse system implicating processes occurring at a cellular or local network level

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

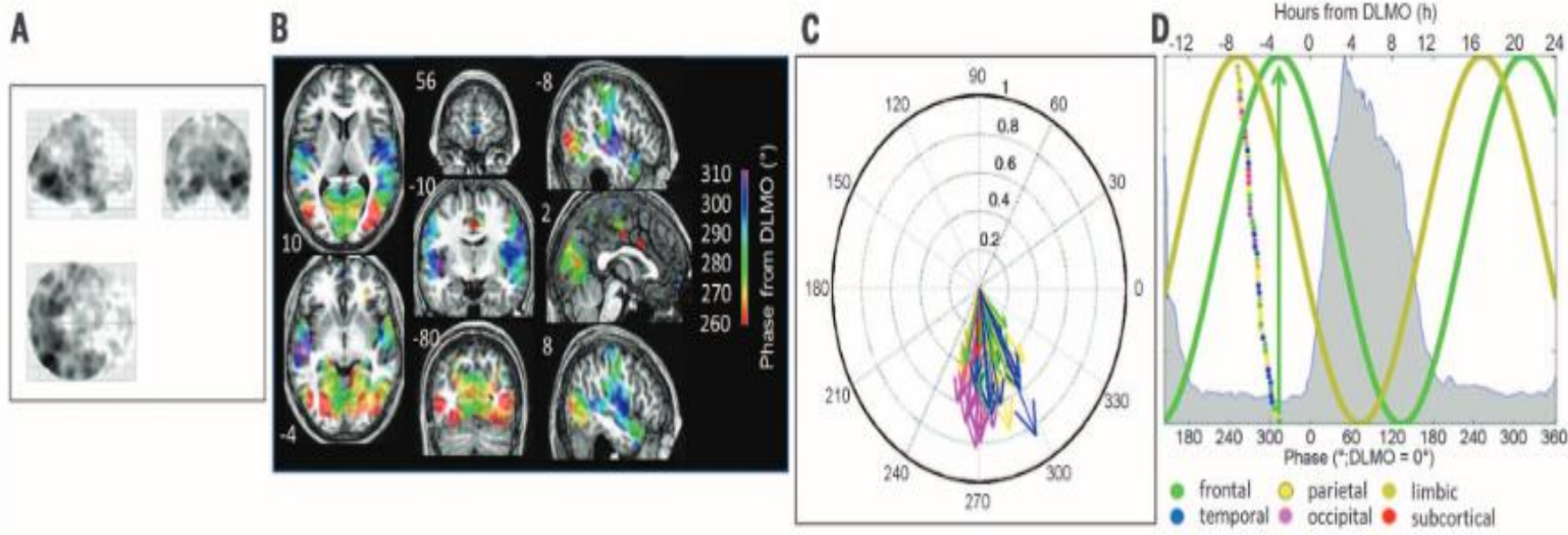
Some sleep parameters are strongly modulated by circadian rhythm (e.g. REM sleep)

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

Both factors interact in many cases



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



Mechanisms  
Regulation  
Functions



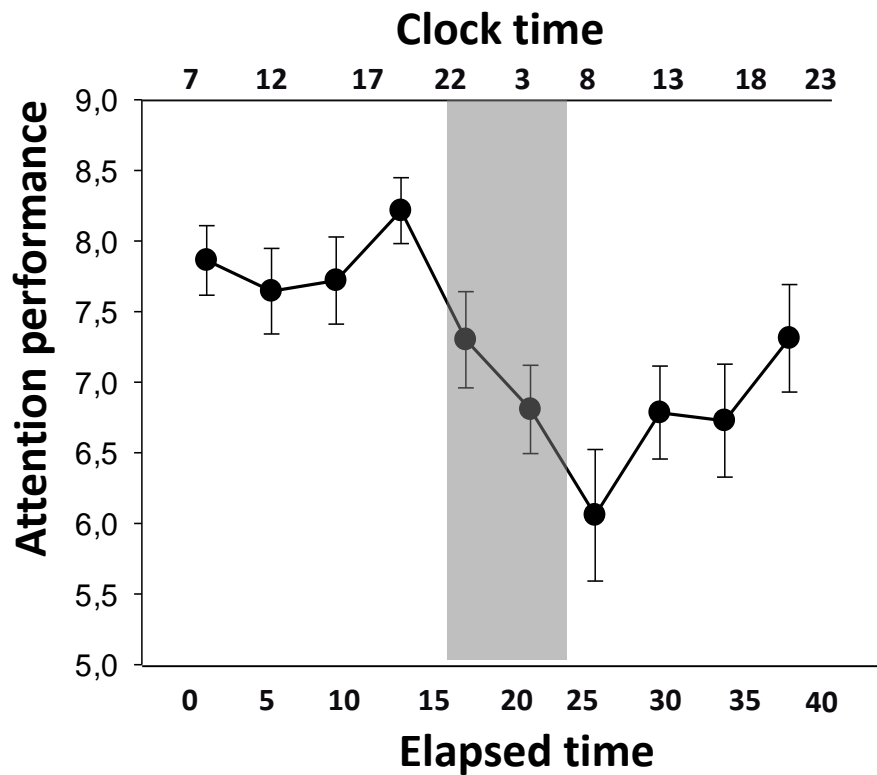
of sleep

# Sleep function(s)

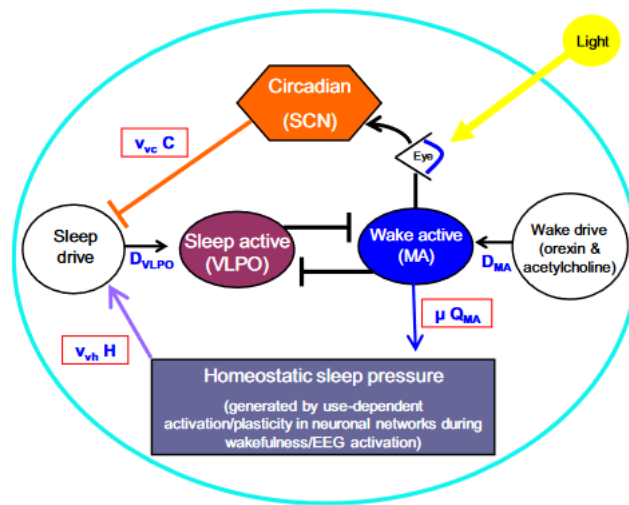
- Brain detoxification / restoration
- Energy balance / thermoregulation
- Restoration of system function
- Restoration of synaptic function  
(synaptic homeostasis)
- Plasticity / Learning and memory
- ...

# Restoration of system function

Lack of sleep leads to attention and cognitive deficits.



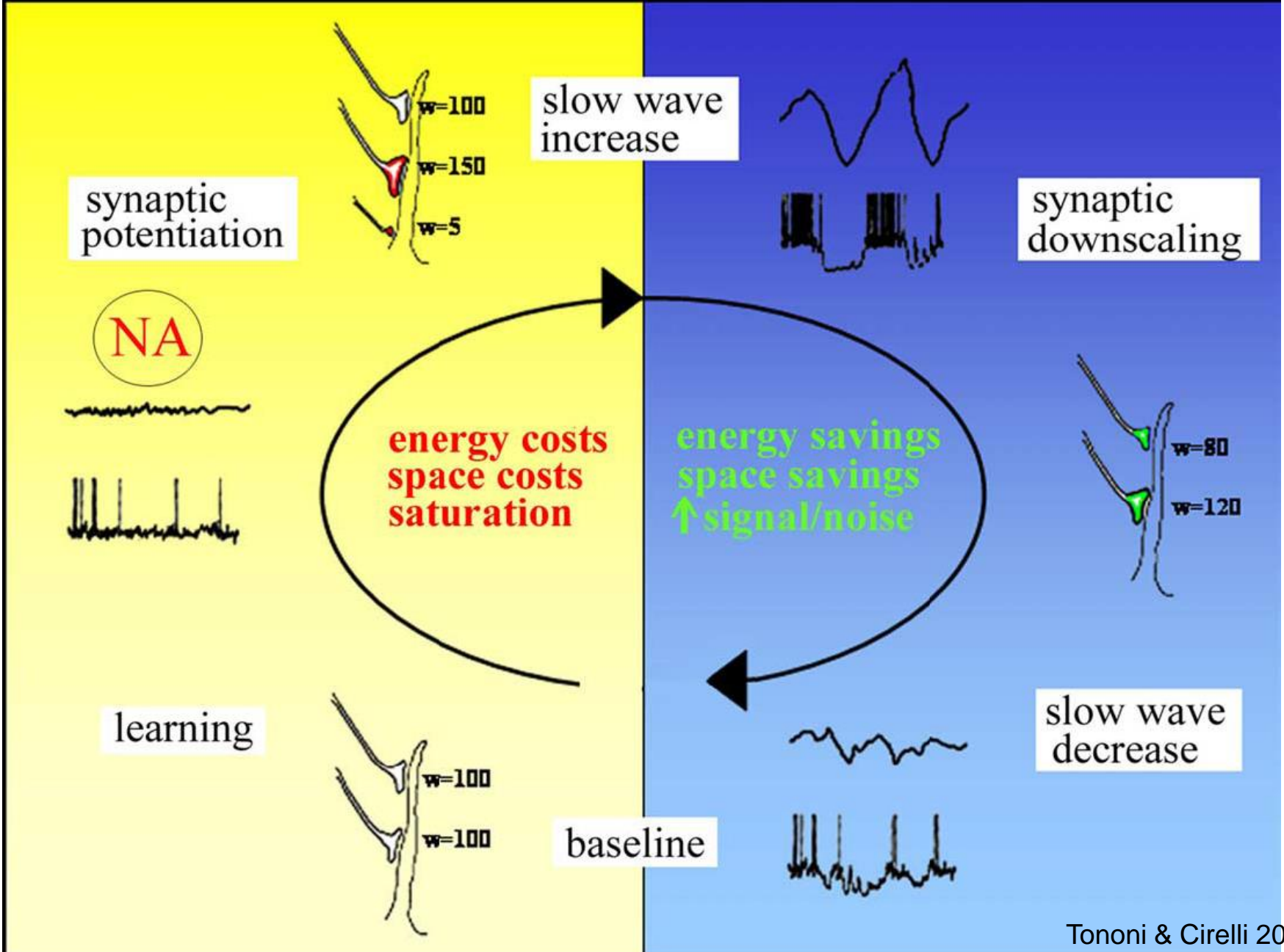
## Model of arousal state dynamics



Postnova et al., 2016, 2018  
Skeldon et al., 2016

Muto et al., 2016  
Maire et al., 2017  
Vandewalle et al., 2007

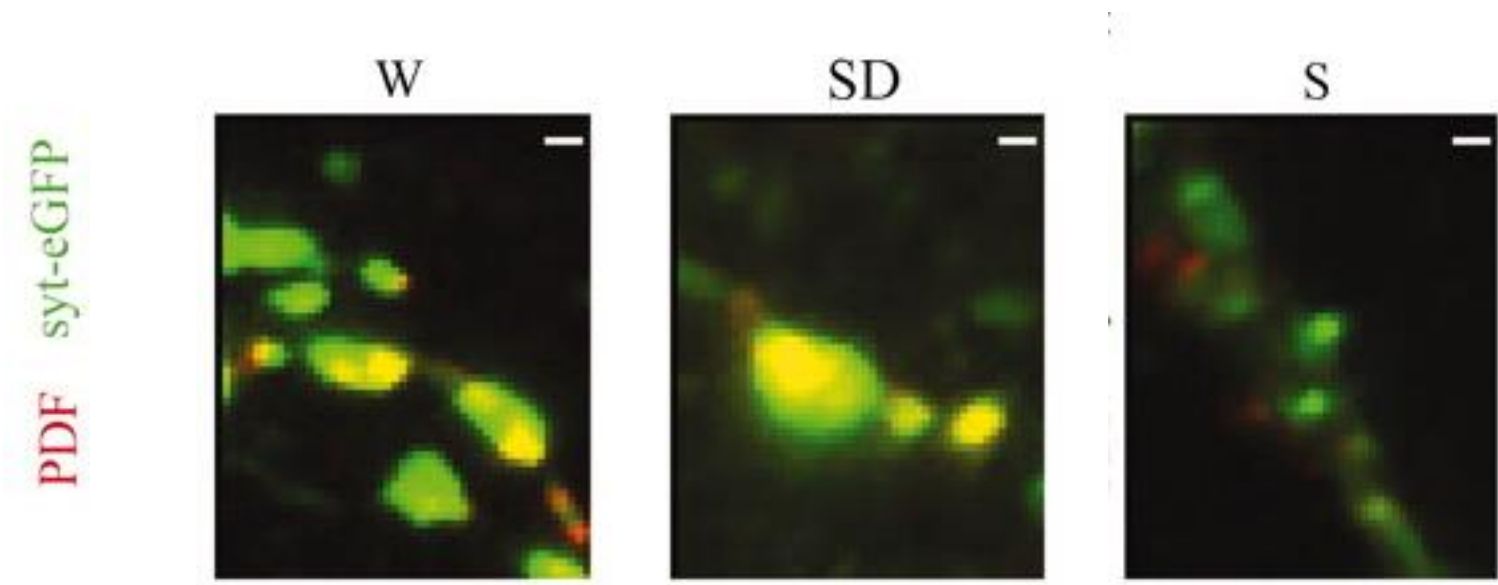
# Restoration of synaptic function



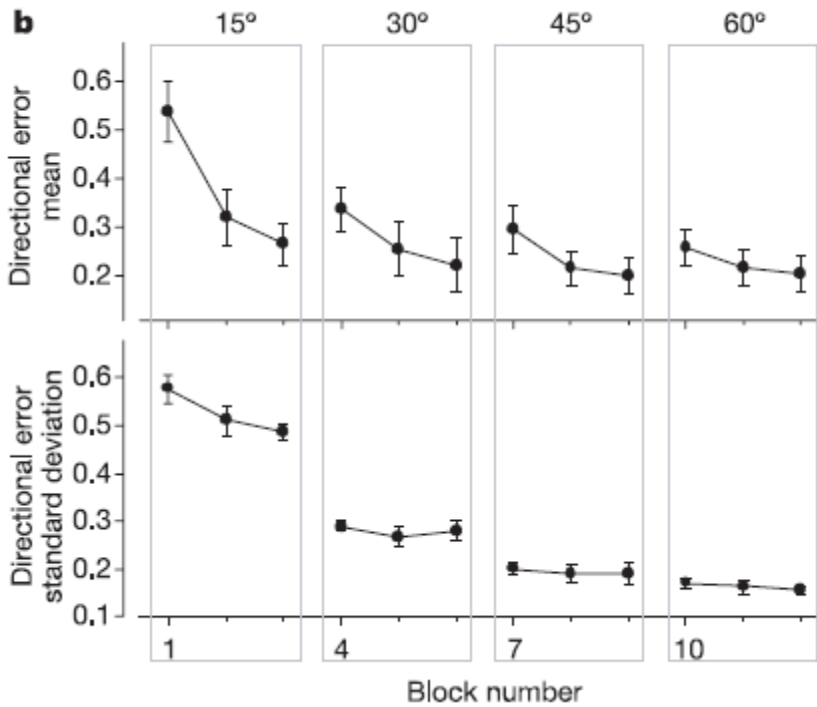
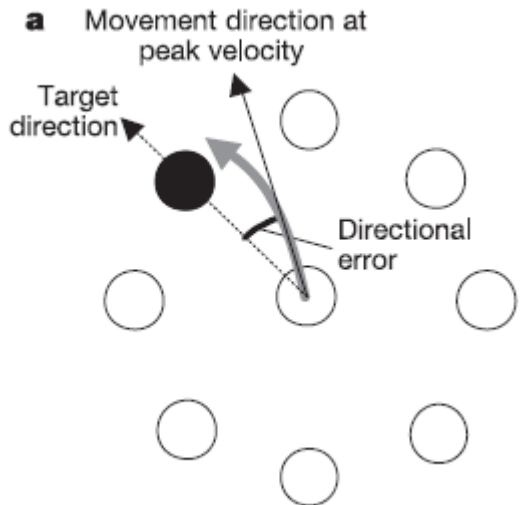


# Restoration of synaptic function

Synapse size increases with wakefulness and decreases with sleep in flies

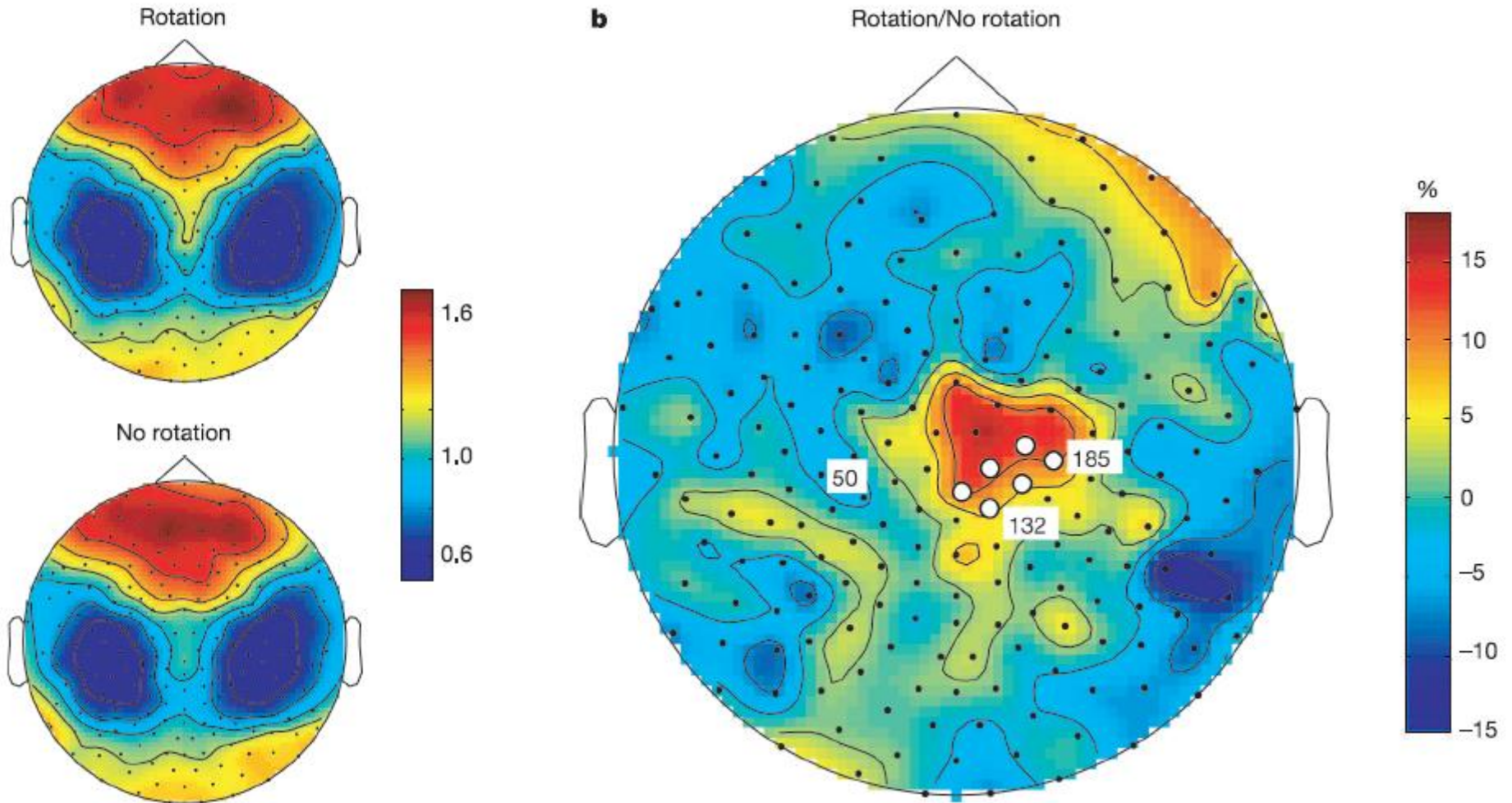


# Restoration of synaptic function



# Restoration of synaptic function

## Region-specific increase of slow waves after learning



# Plasticity / Learning and memory

2Ss  
Nonsense syllables

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

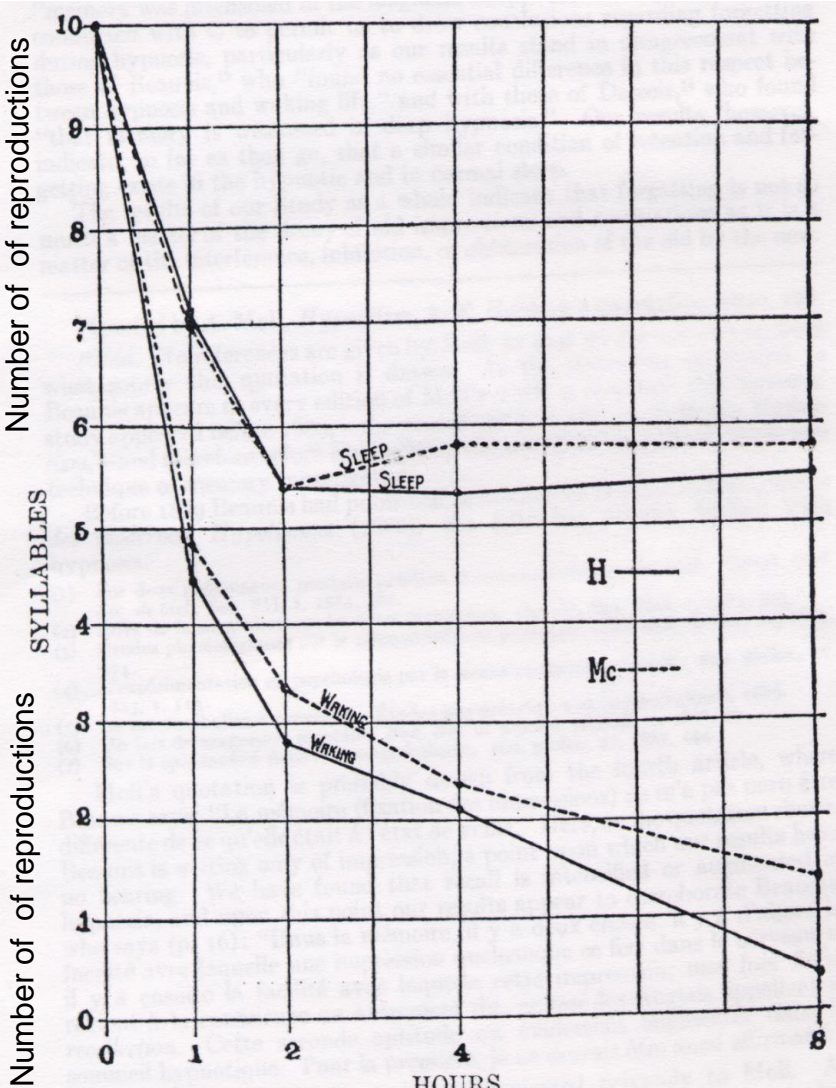


FIG. I. Average Number of Syllables Reproduced by each O after the Various Time-Intervals of Sleep and Waking

Sleep has a beneficial effect on memory

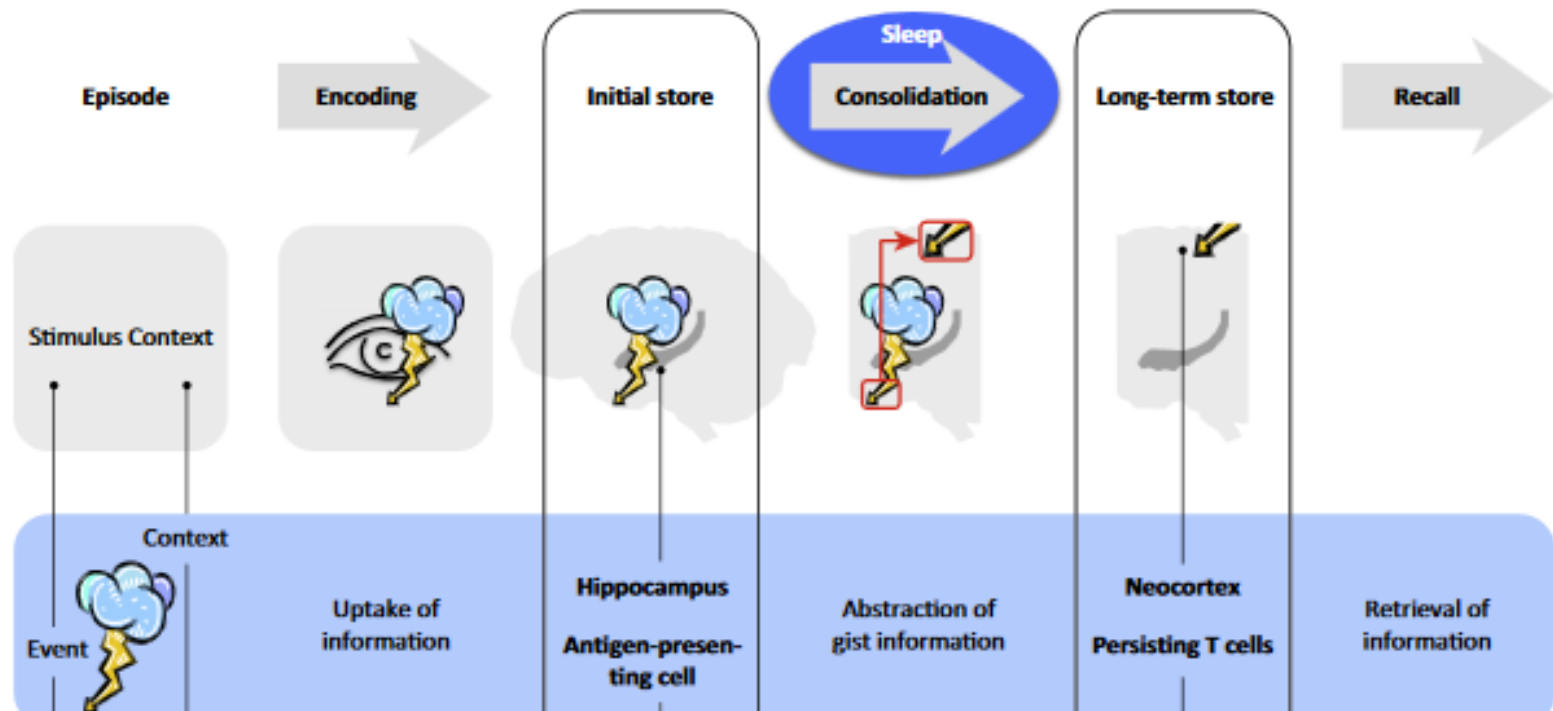
# Sleep has a beneficial effect on memory

## 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)

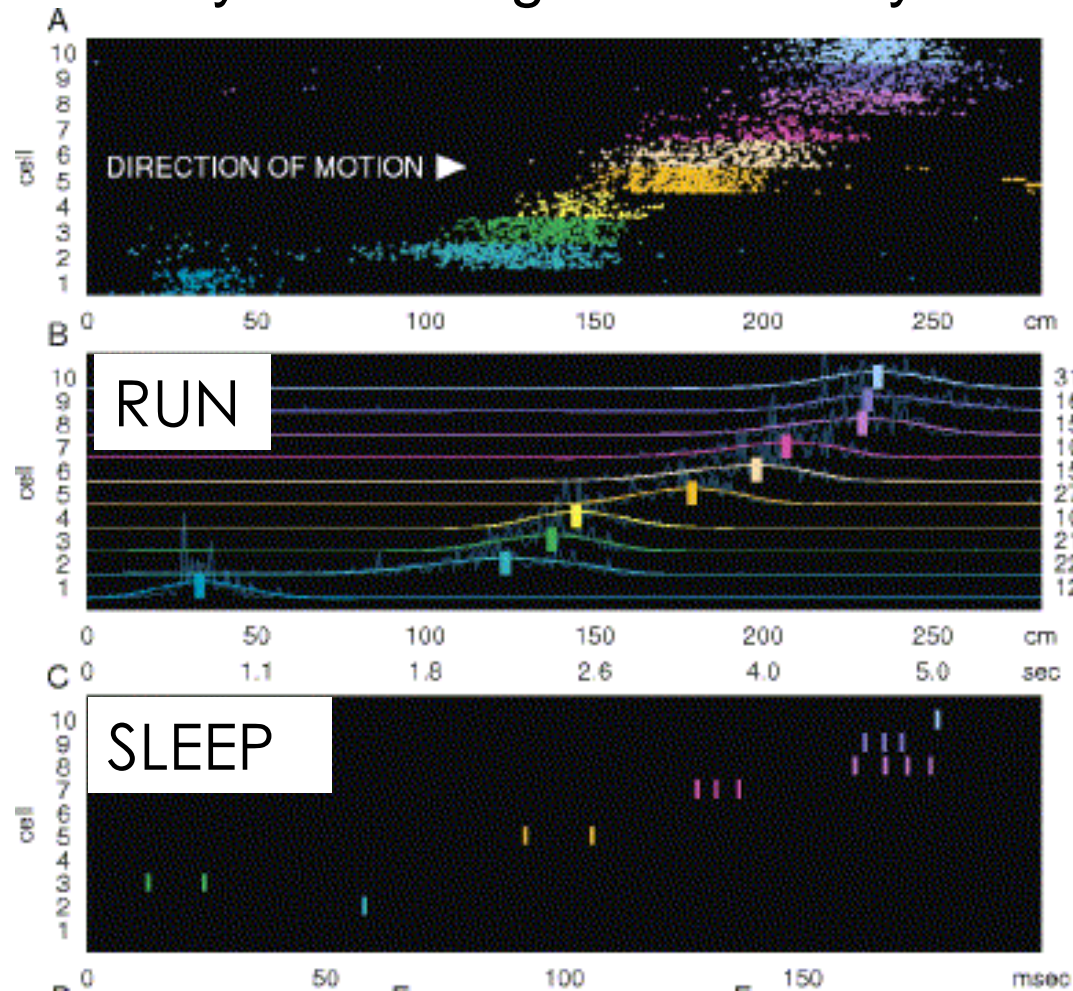
Low acetylcholine during slow-wave sleep is critical for declarative memory consolidation (Gais & Born, PNAS, 2004)

# System Consolidation



Westermann et al.,  
Nat.Reviews Neur., 2015

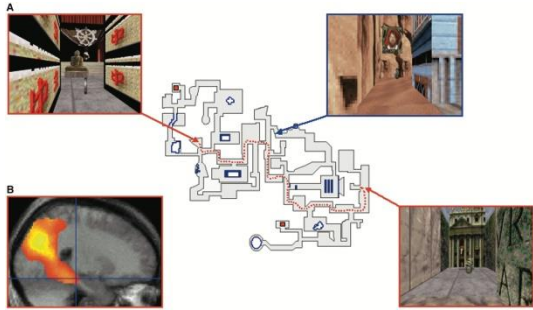
# Plasticity / Learning and memory



Neural activities are replayed during sleep

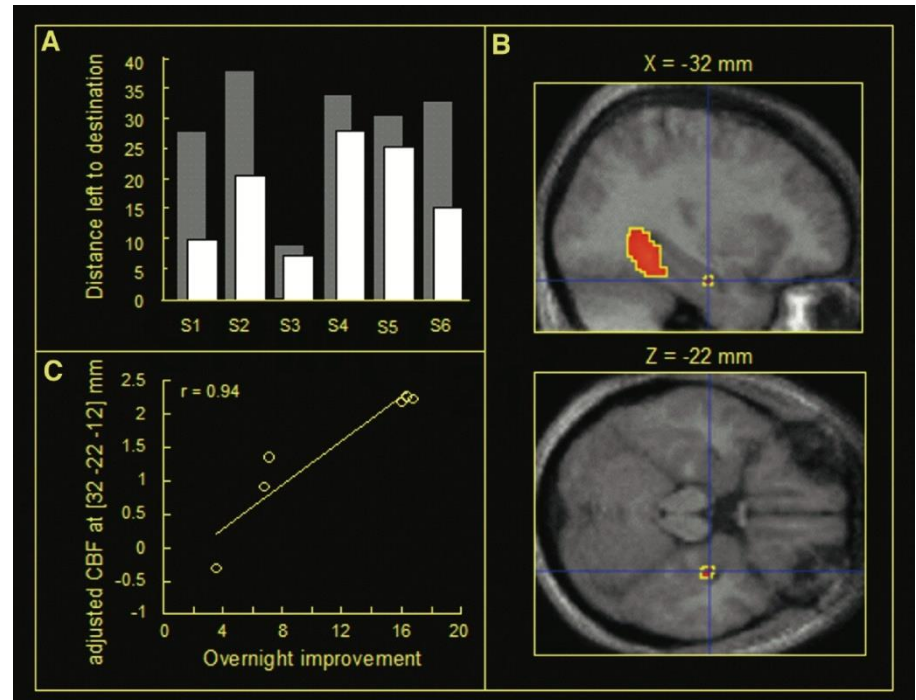
Here in the place cells of the rat hippocampus

# Spatial memories strengthened in the human hippocampus during slow wave sleep



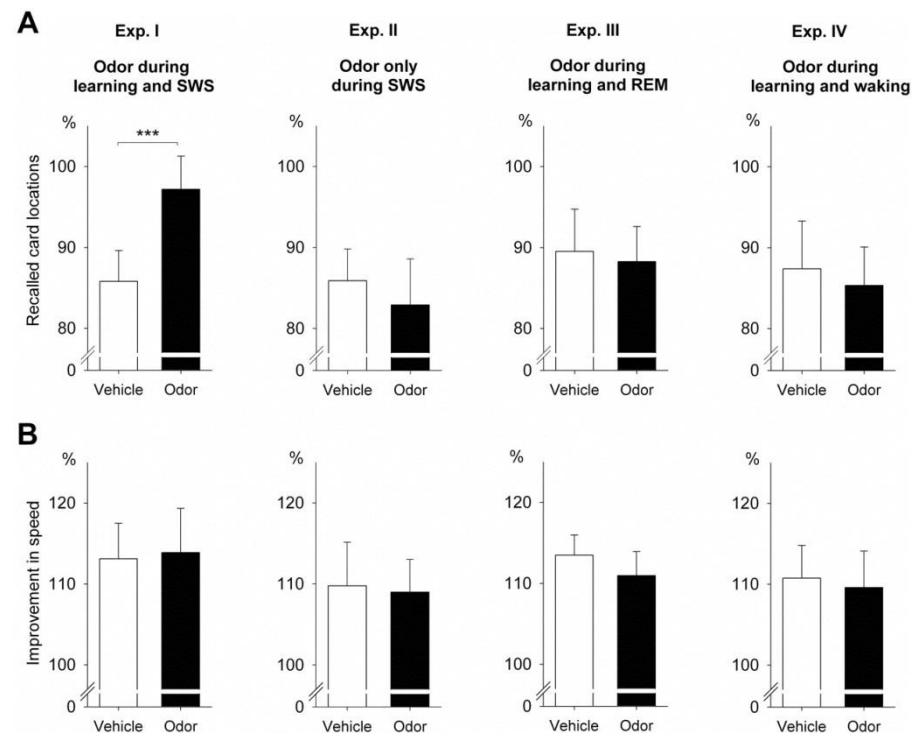
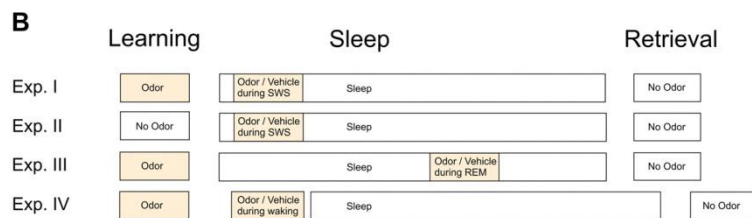
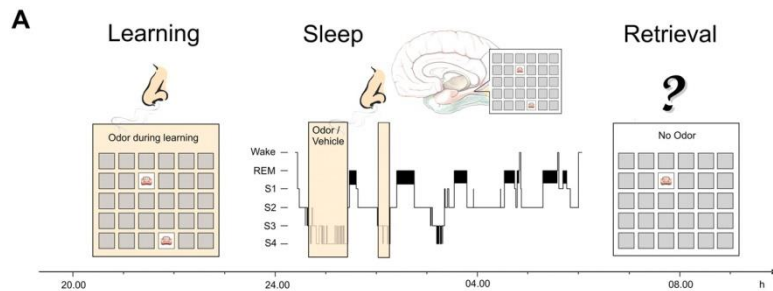
Peigneux, 2004

## Hippocampal Reactivation during SWS and Memory Consolidation



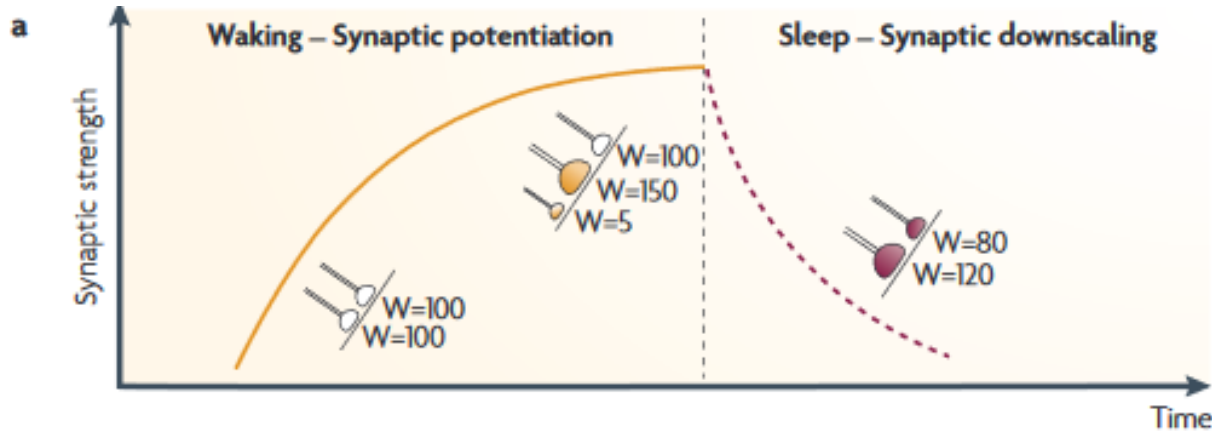


# Odor Cues During Slow-Wave Sleep Prompt Declarative Memory Consolidation

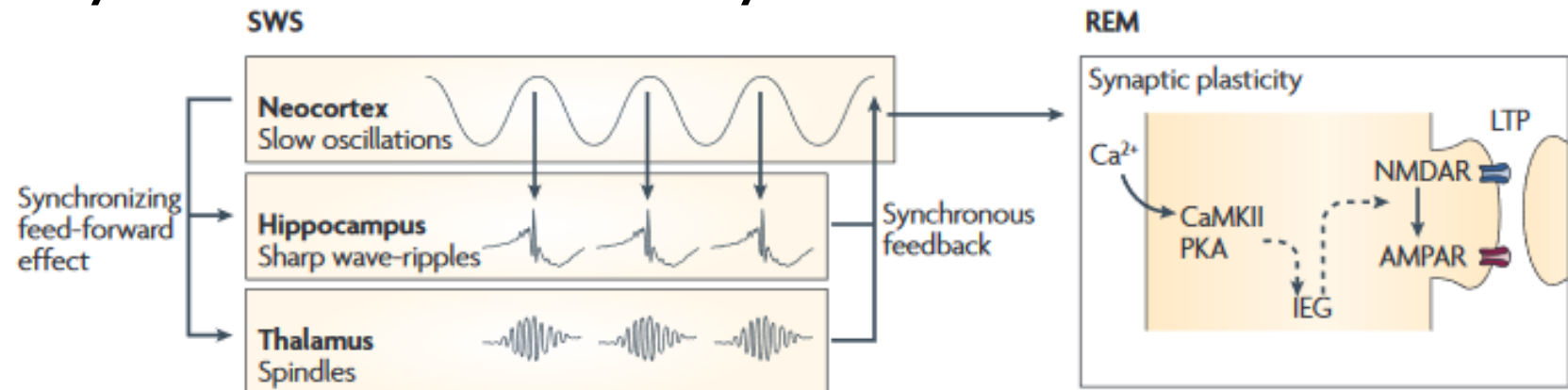


# Facilitation in a learning-independent or learning-specific manner?

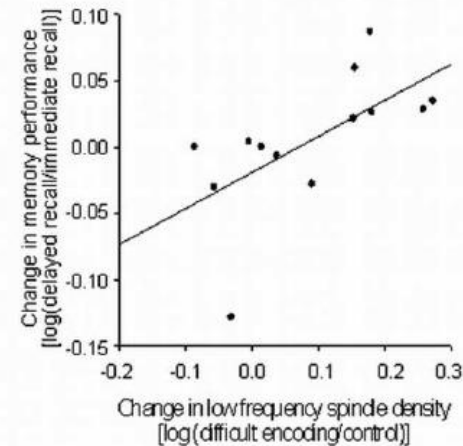
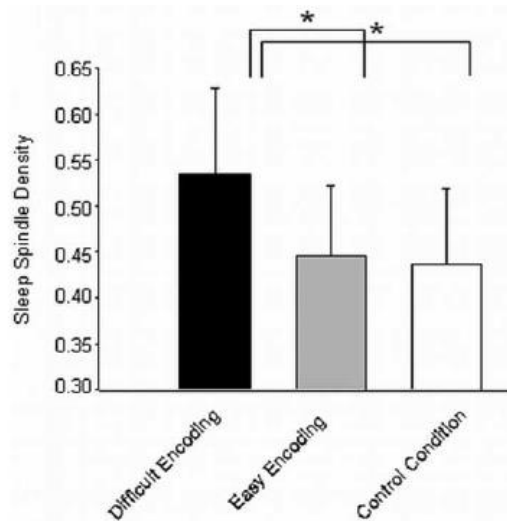
## Synaptic homeostasis theory



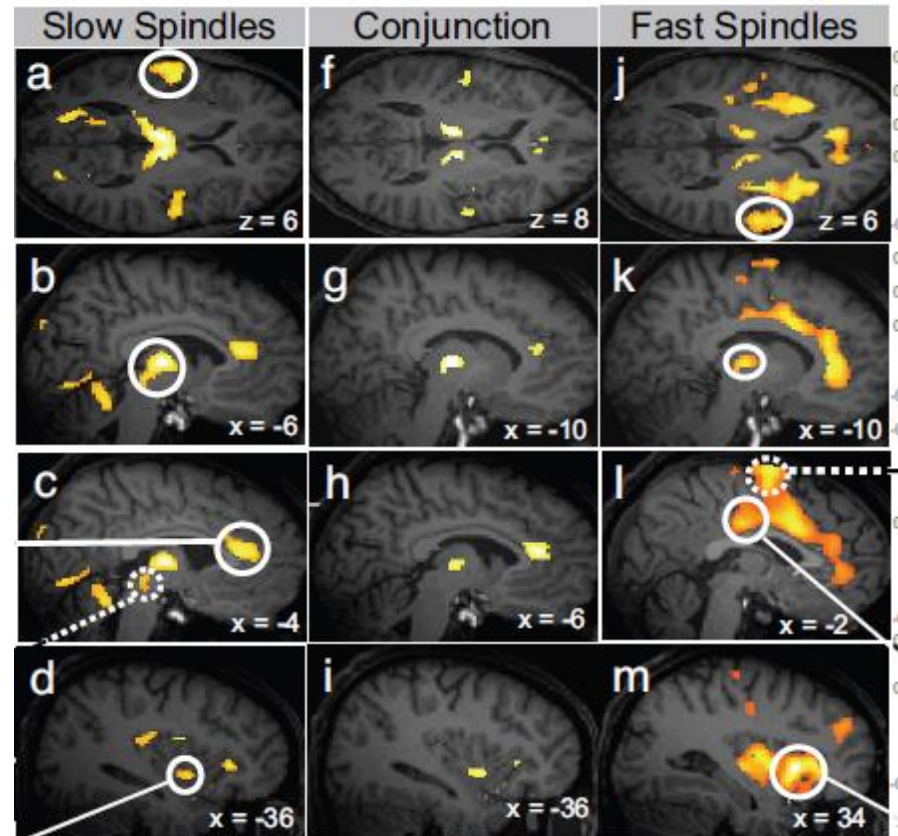
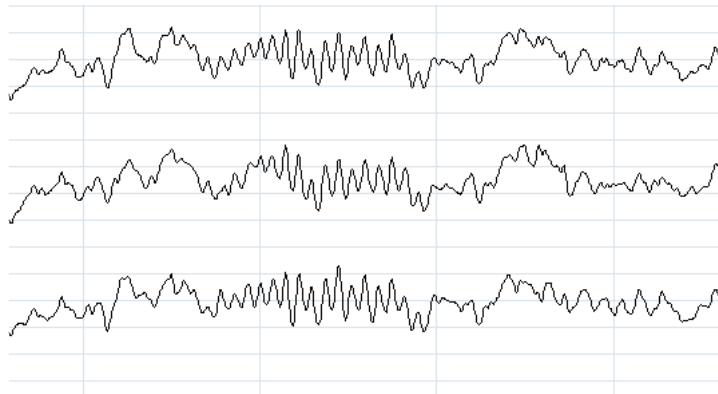
## b Systems consolidation theory



# Sleep Spindles: Facilitators of Memory Formation and Learning?

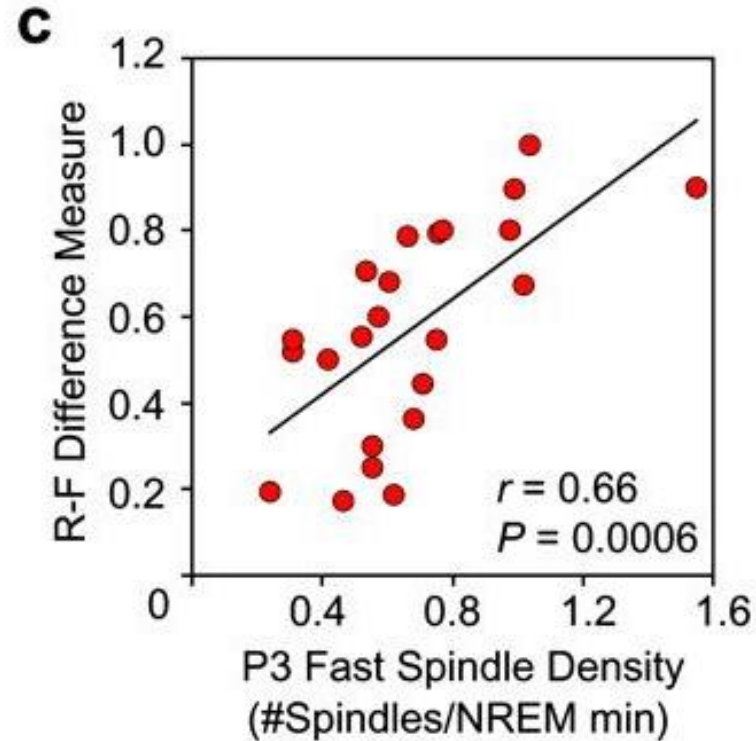
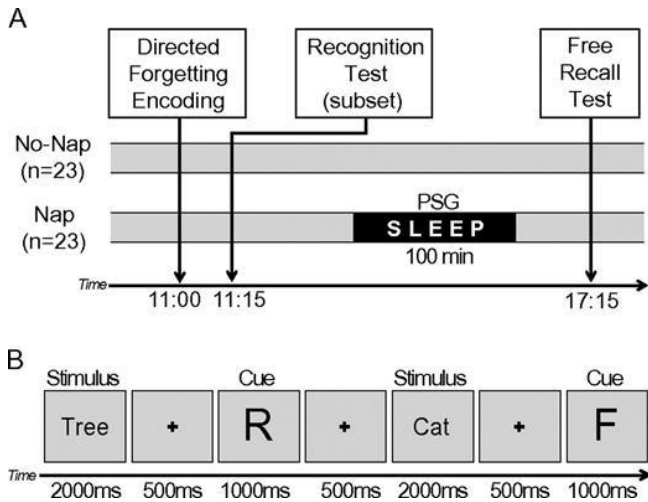


Sleep is a state of overall decreased brain activity, but **sleep spindles** are hallmarked by increased brain activity



Increased activity associated with (slow and fast) spindles

# The Role of Sleep in Directed Forgetting and Remembering of Human Memories



Saletin, 2011

# 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