SLEEP and COGNITION

Bruce O'Hara

Bio535 4/17/2012

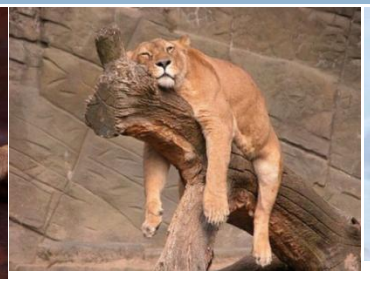
Sleep that knits up the ravel'd sleave of care,
The death of each day's life, sore labor's bath,
Balm of hurt minds, great nature's second course,
Chief nourisher in life's feast.

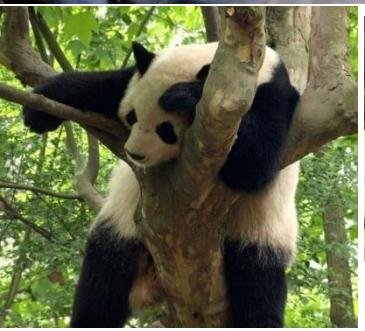
--- William Shakespeare


© Tony Northrup

Sleep is a conserved behavior





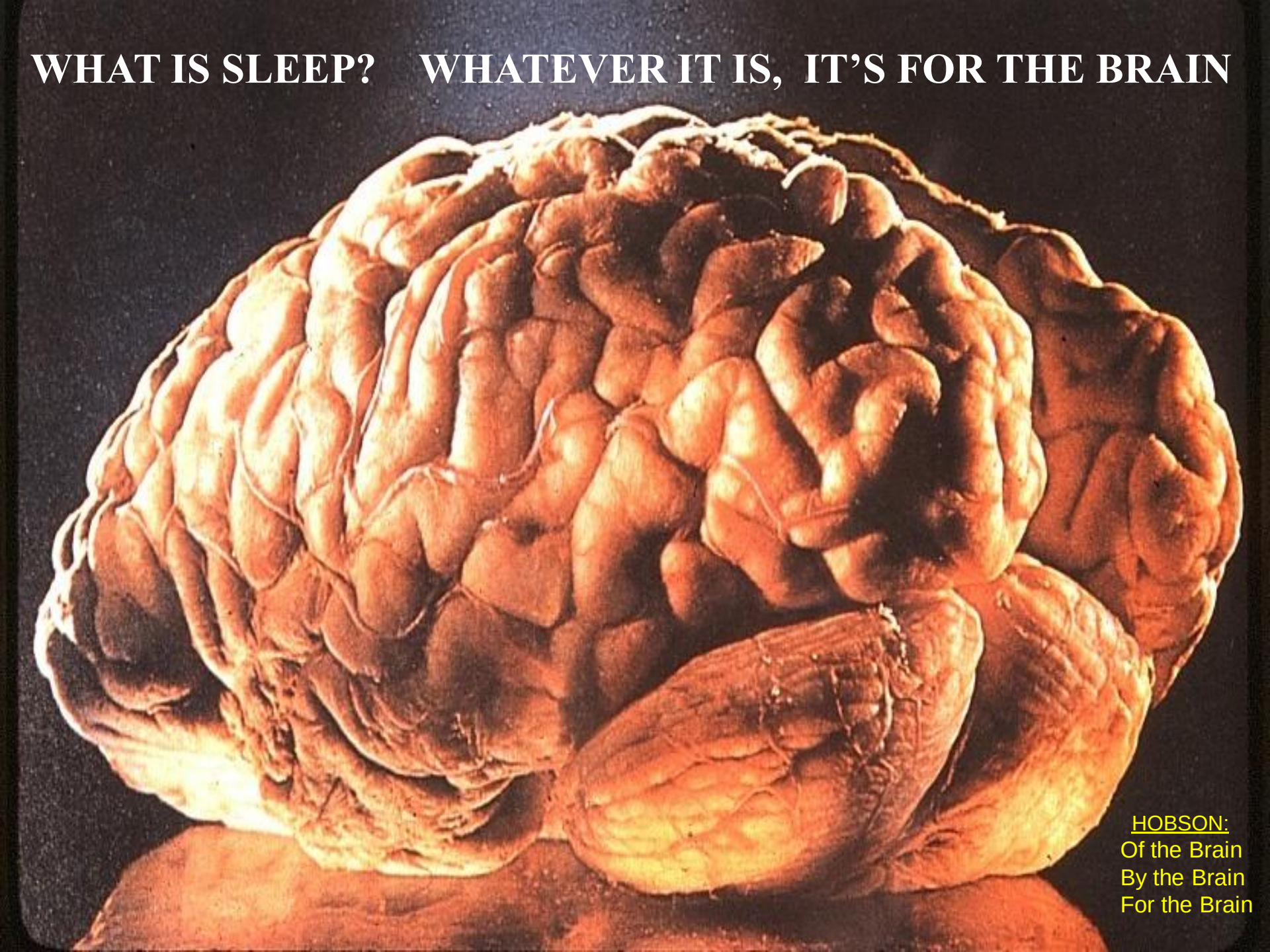






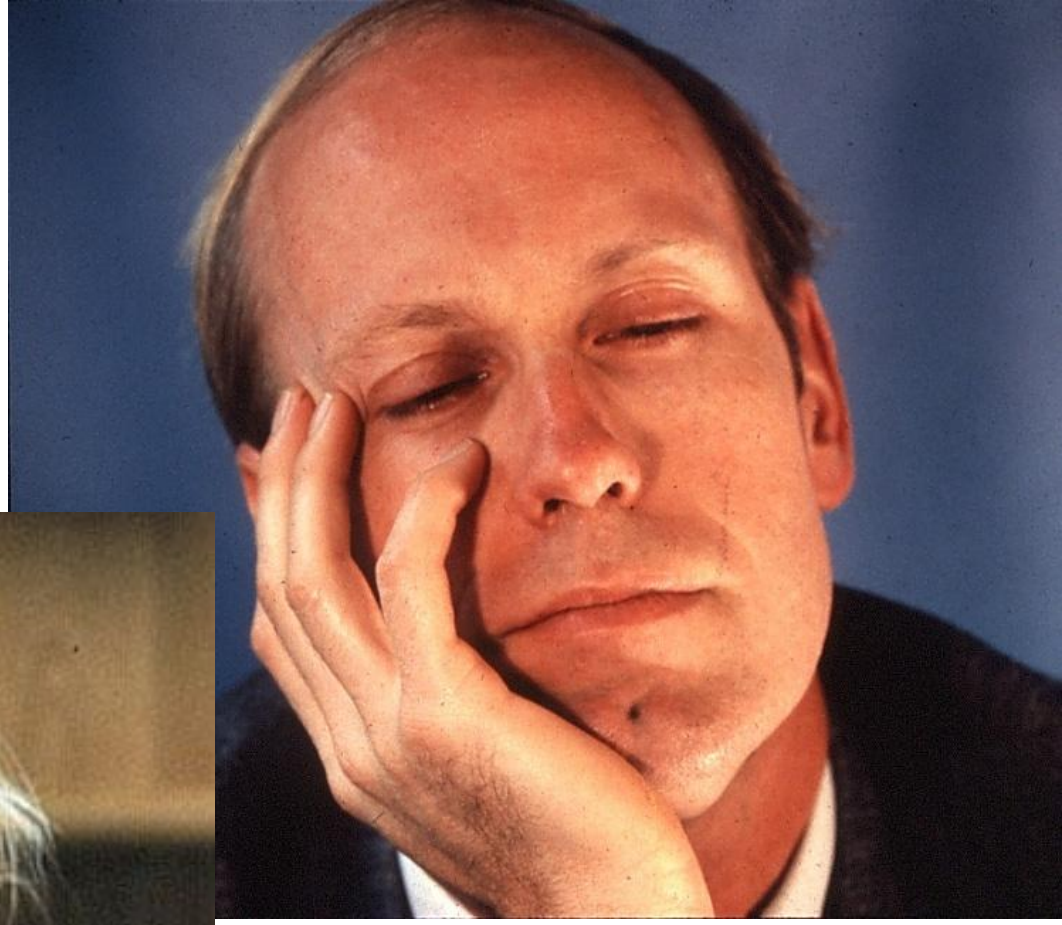


WHAT IS SLEEP? WHATEVER IT IS, IT'S FOR THE BRAIN



HOBSON:
Of the Brain
By the Brain
For the Brain

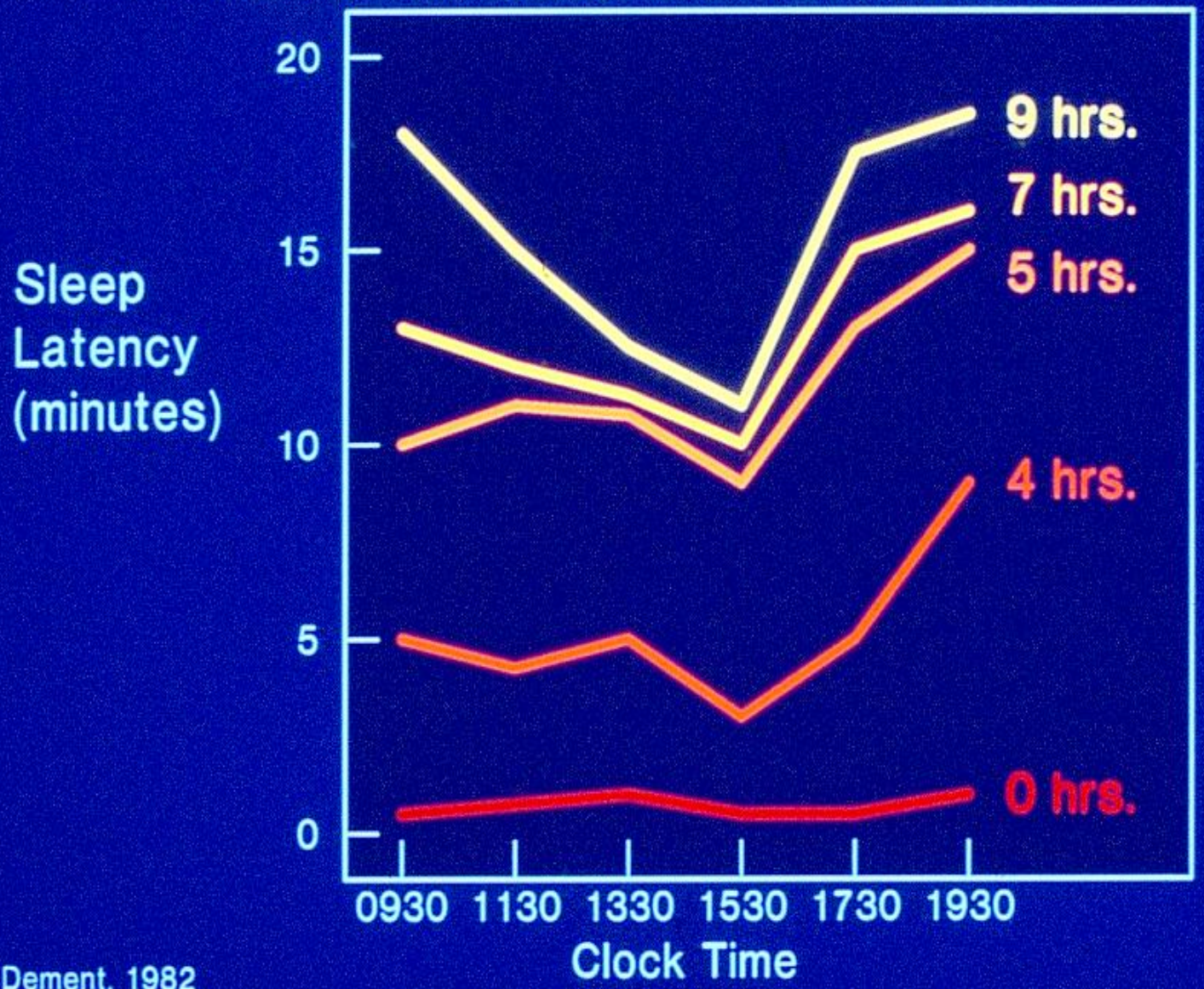
Lack of sleep due to life-style, personal choice, shift work, jet lag, anxiety, or sleep disorders leads to:



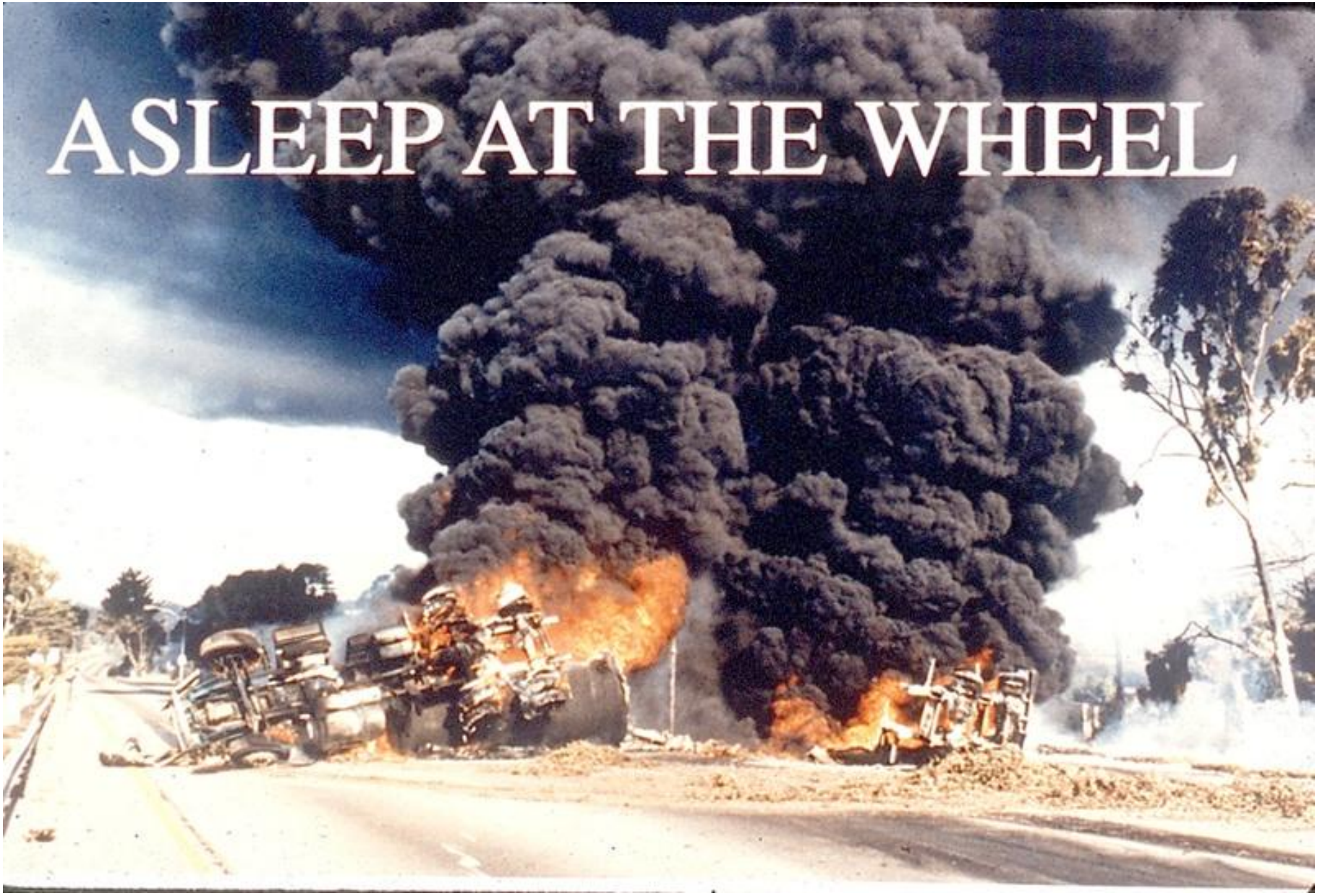
ACCUMULATED SLEEP DEBT AND EXCESSIVE DAYTIME SLEEPINESS

Average Sleep Latency in Young Adults

2nd Day of Measurements for Each Nocturnal Sleep Time Condition



Carskadon & Dement, 1982


ASLEEP AT THE WHEEL

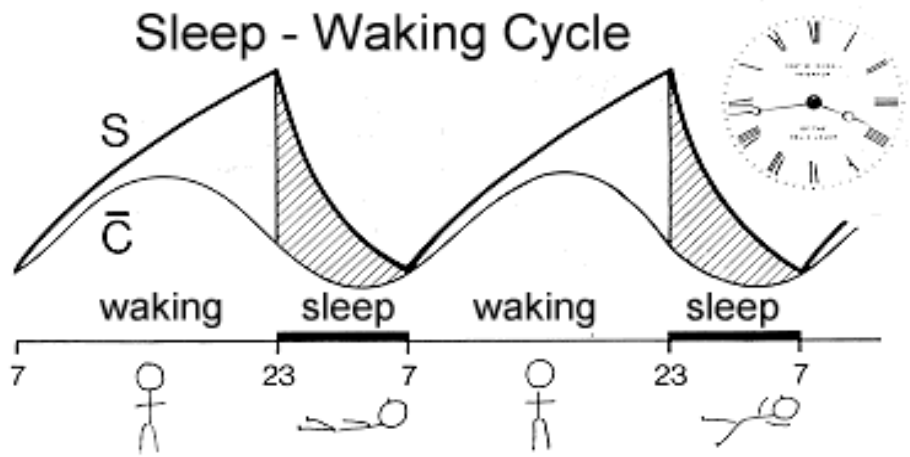
Healthy Sleep and Circadian Rhythms are of Great Importance to Society

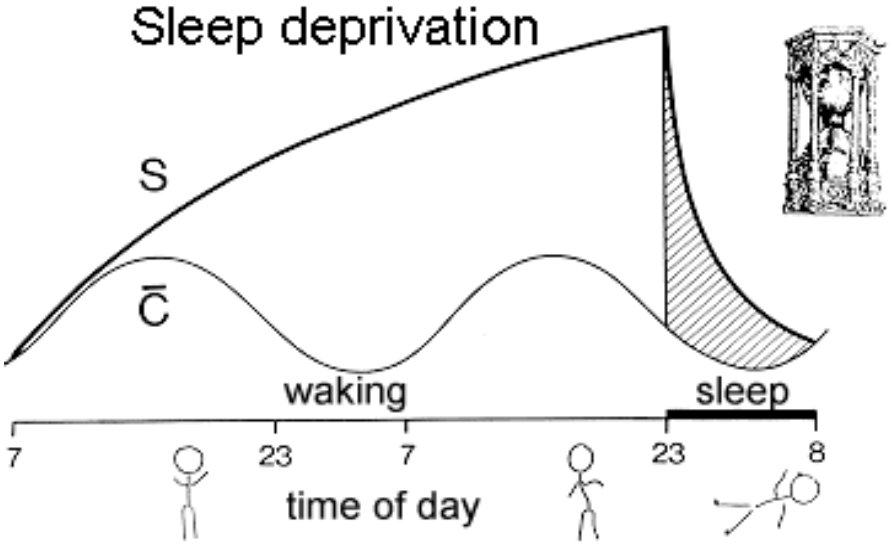
Sleep Disorders
Industrial accidents
Automobile accidents
Poor performances
Life quality
And, even our National Pastime

The Home Team in Baseball can expect a 1.24 run advantage when the visitor has just completed Eastward travel (Nature 377:583, 1995).

Winning percentage jumps from 54% to 63%. Little or no effect of Westward travel.

Sleep Regulation





A Two-Process Model

- Process C: Circadian Regulation

  Behavior independent

  Clock

- Process S: Sleep Homeostasis

  Behavior dependent

  Hourglass

Artwork courtesy of Alexander Borbely

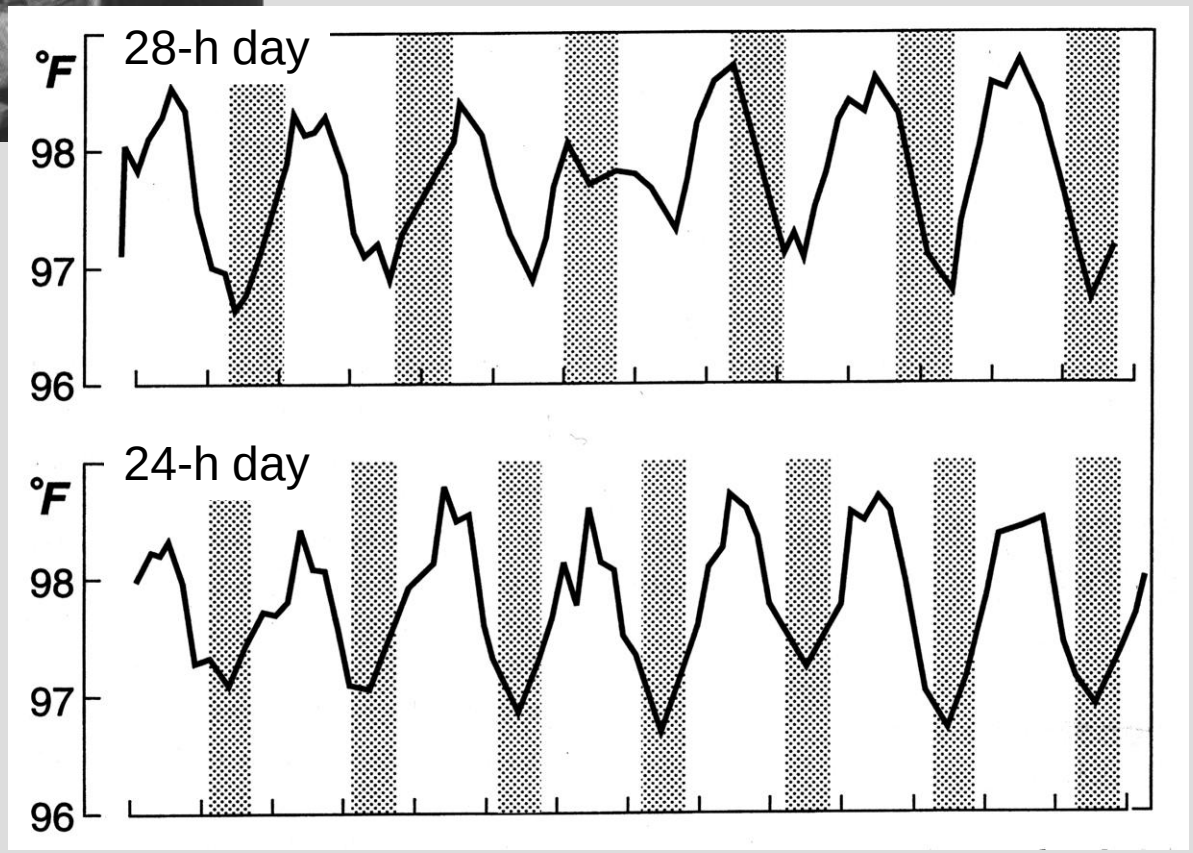
The Earth turning on its axis creates daily cycles in the physical environment.

Endogenous Circadian Clocks presumably evolved to keep time and anticipate these daily cycles.


circa 1937
MAMMOTH CAVE
OF KENTUCKY

Forced Desynchrony:

Living on a 28-h day in
Mammoth Cave, 1938



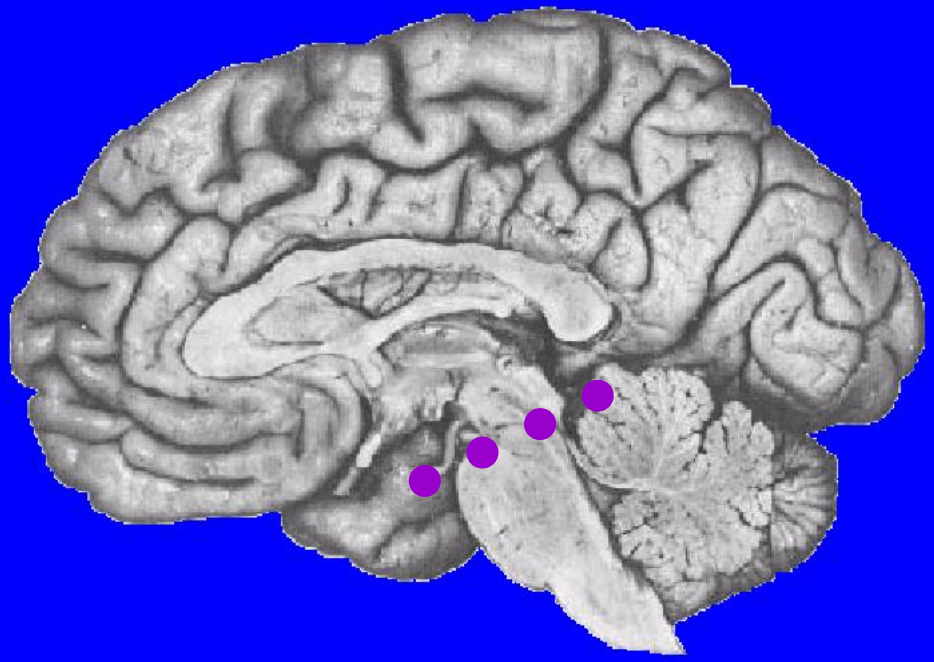
Sleep is the absence of wake.

-Lucretius, 30 BCE

Sleep occurs when sensory input declines.

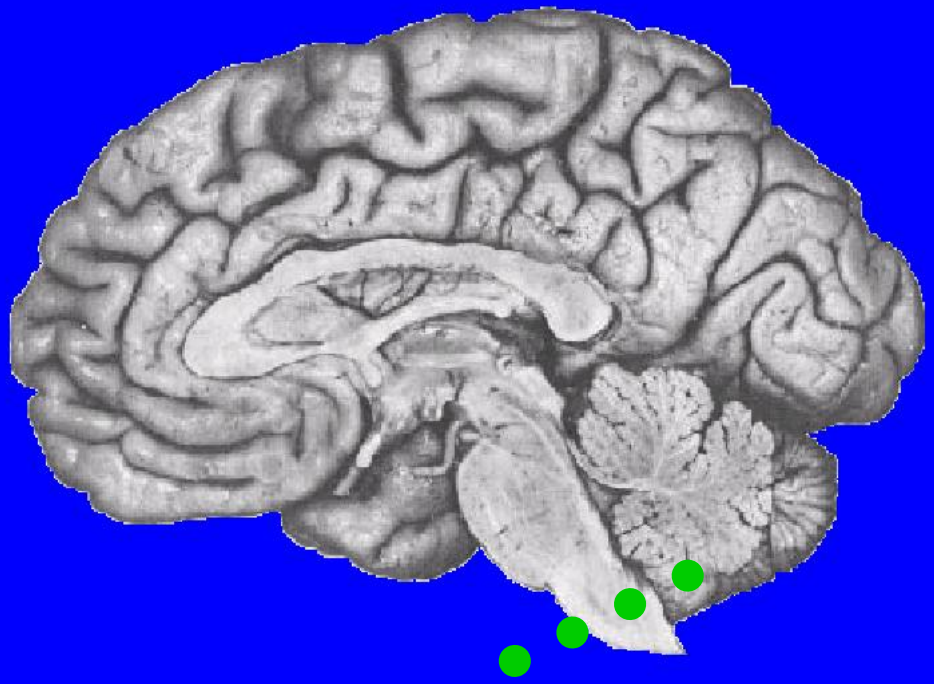
Early 20th Century

Cerveau Isolé – Bremer 1935



Separate brain stem from cortex with cut in midbrain
-– permanent state of somnolence.

Encephale Isolé - Bremer



Separate brain from spinal input
– alternating pattern of sleep and wake.

Bremer's Conclusions

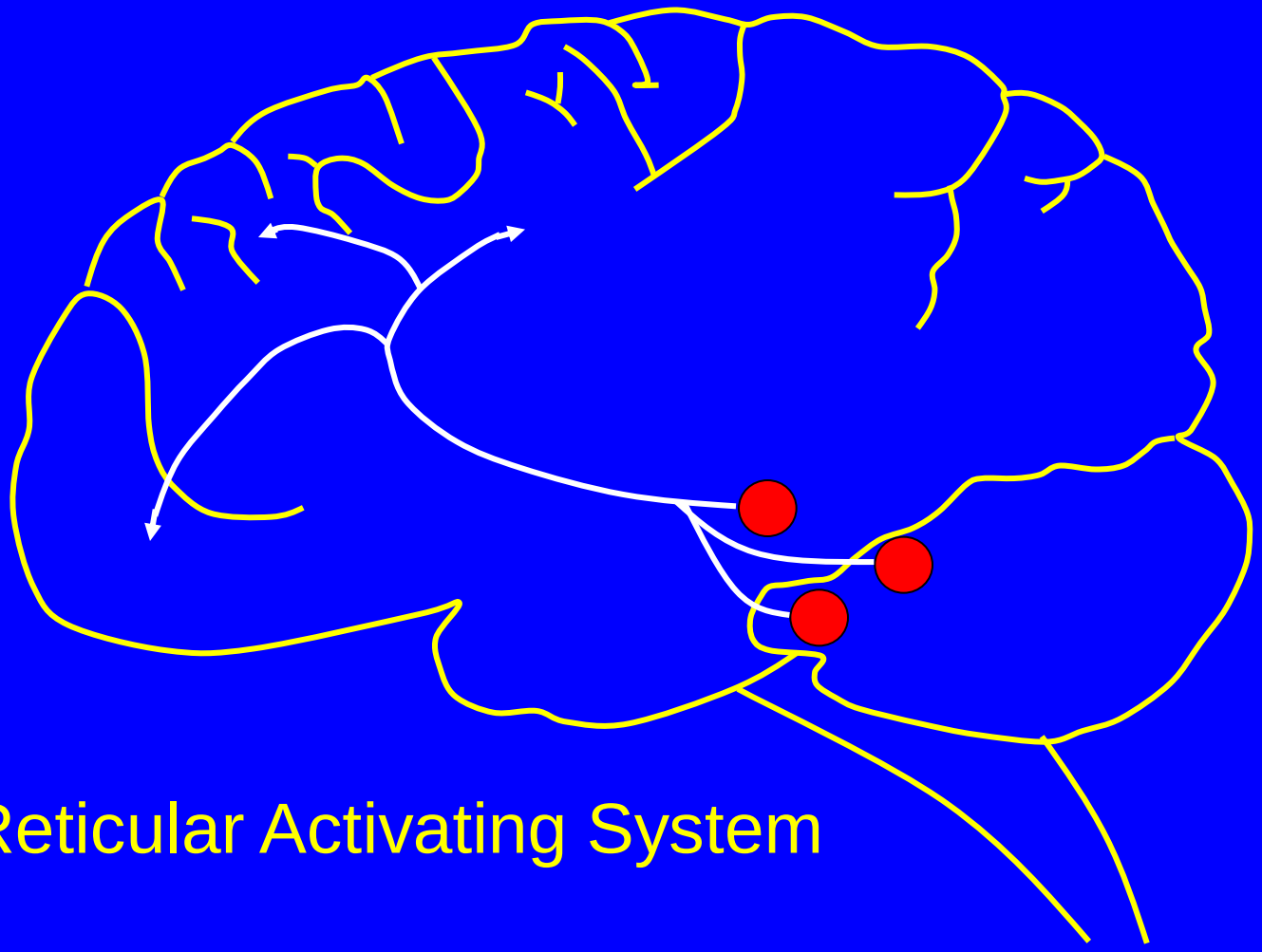
Bremer - Since sleep/wake occurs with sensory input (from cranial nerves) and sleep occurs with no sensory input, sleep is the default condition of the brain and wake is evoked by sensation.

Alternatively, wake promotion could be generated by brain stem mechanisms and sleep could be generated by mechanisms existing above the brain stem (supported by Moruzzi and Magoun's classic 1949 paper, but also earlier by Von Economo's work in 1917 that was largely ignored).

Sleep and wake are actively regulated states.

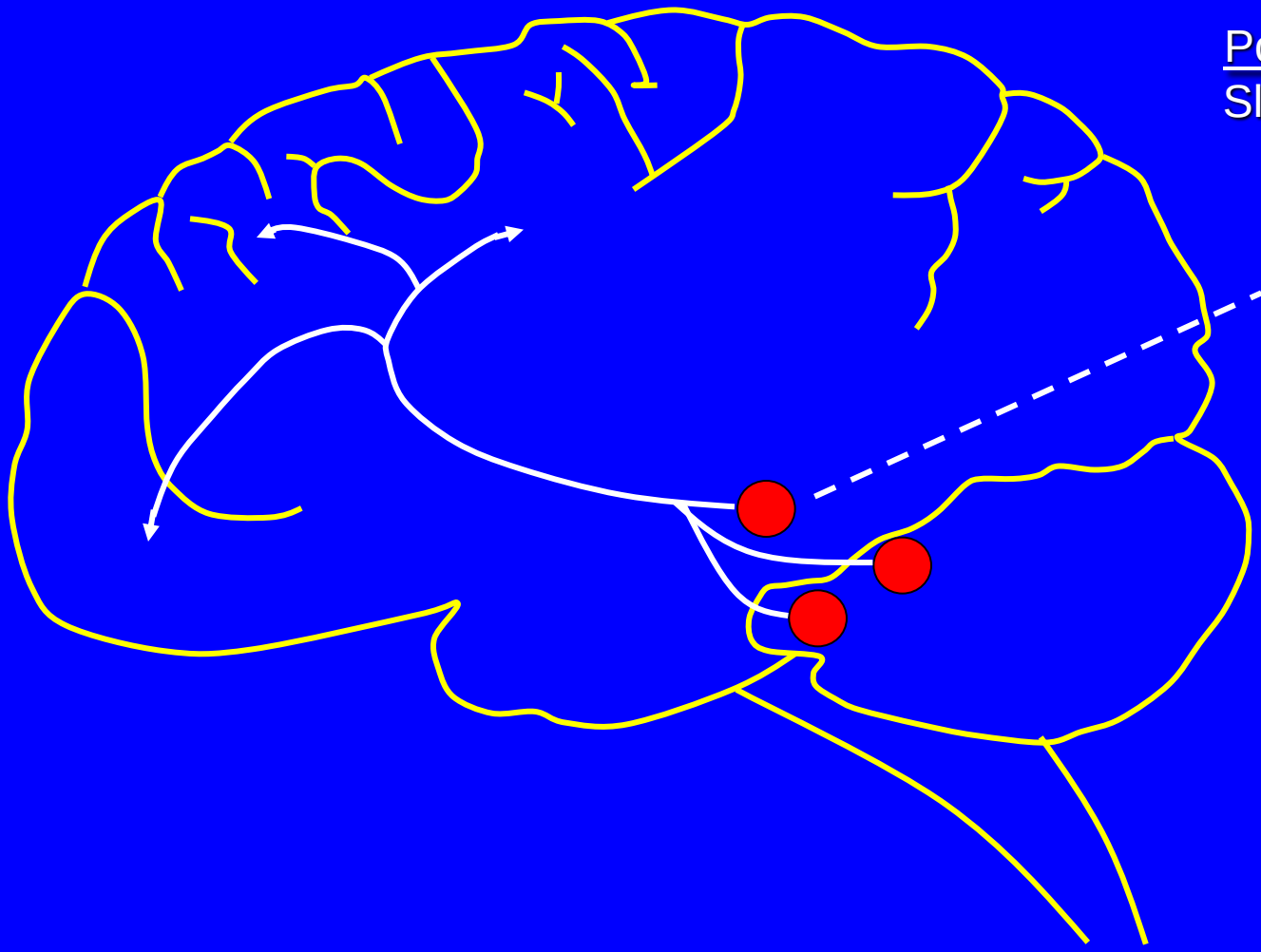
Modern Viewpoint

How is wake regulated by the brain?



Reticular Activating System

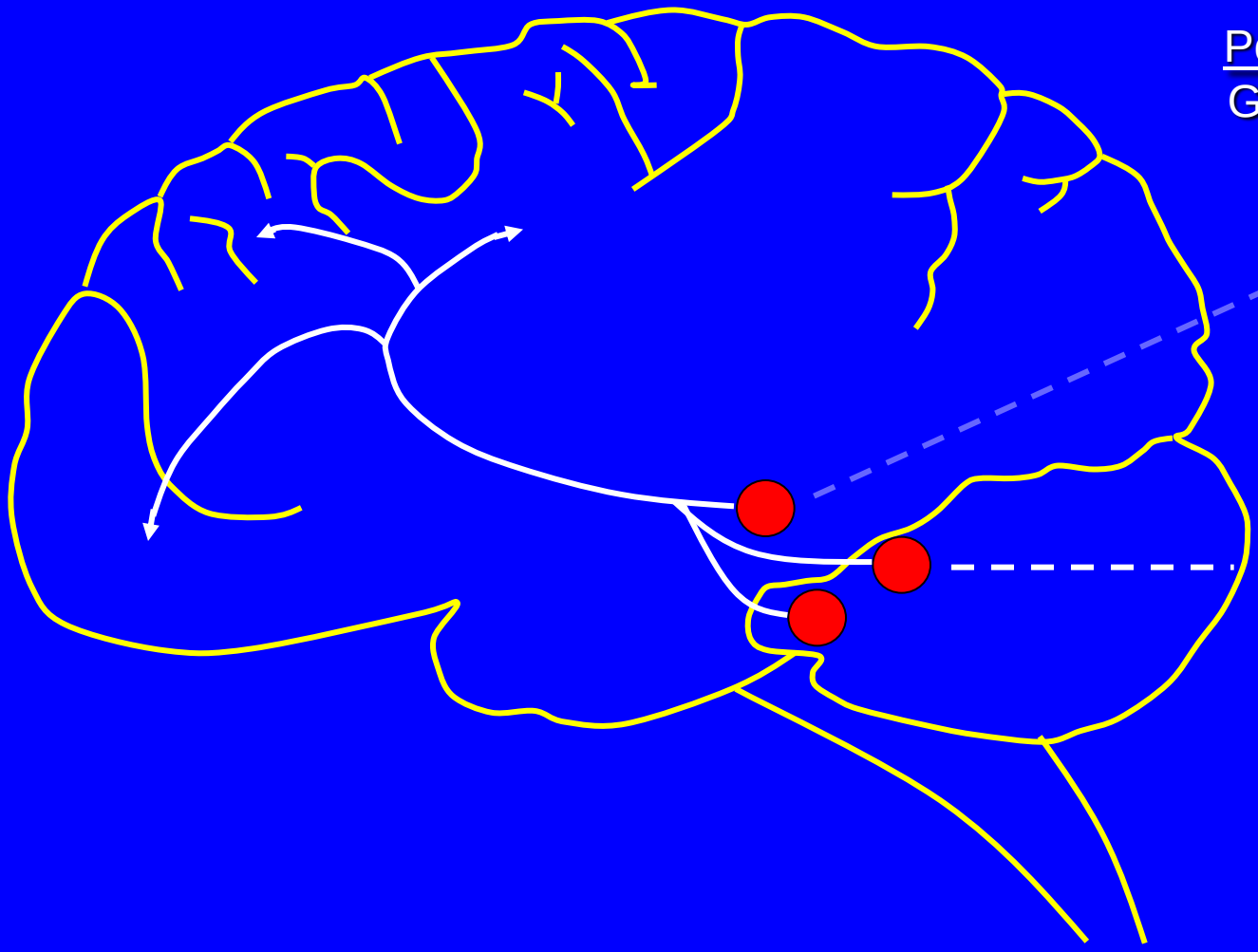
How is wake regulated by the brain?



Possible Function
Sleep/Wake State

Serotonergic
Raphe Nuclei

How is wake regulated by the brain?

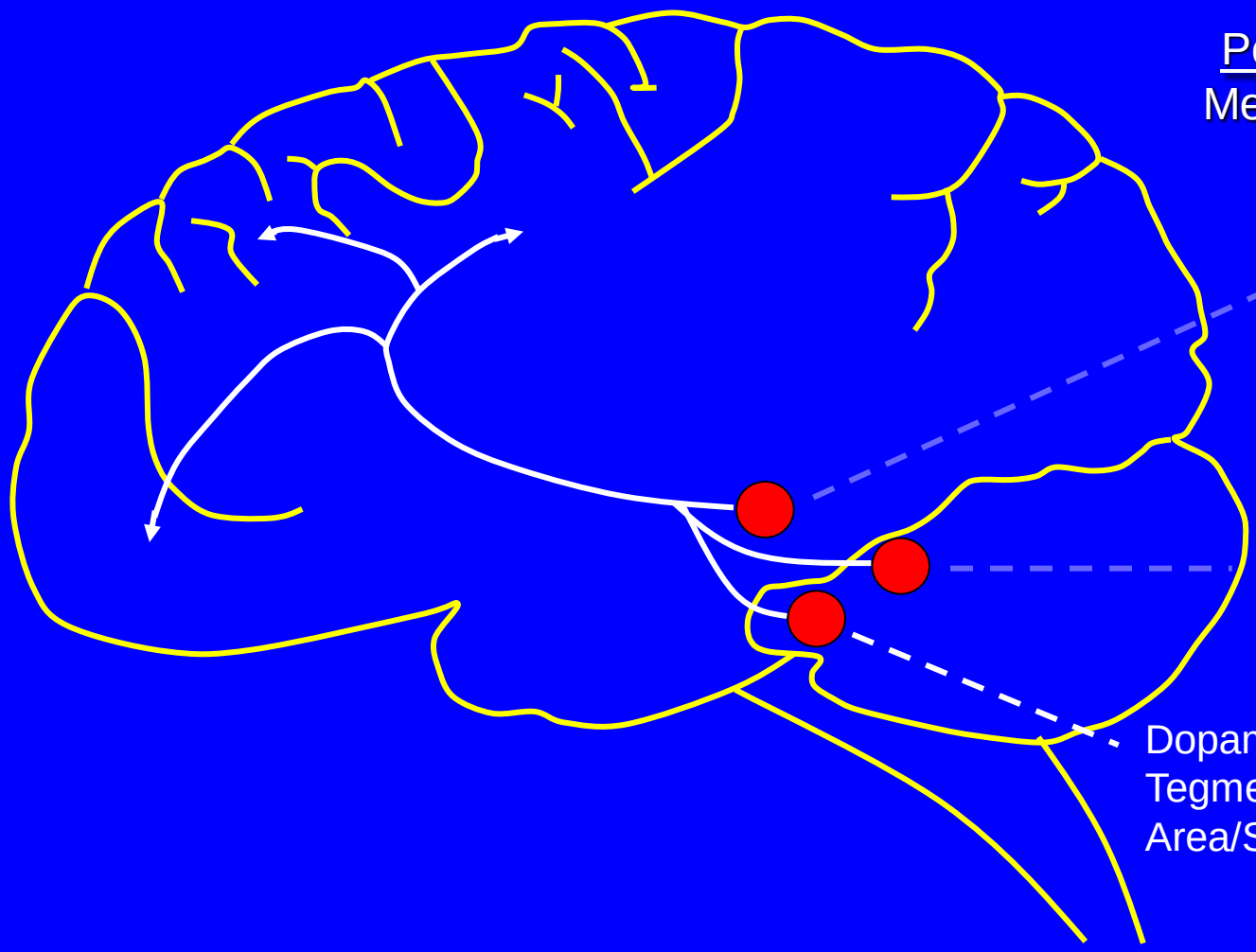


Possible Function
General Attention

Serotonergic
Raphe Nuclei

Noradrenergic
Locus Coeruleus

How is wake regulated by the brain?



Possible Function
Memory Acquisition

Serotonergic
Raphe Nuclei

Noradrenergic
Locus Coeruleus

Dopaminergic Ventral
Tegmental
Area/Substantia Nigra

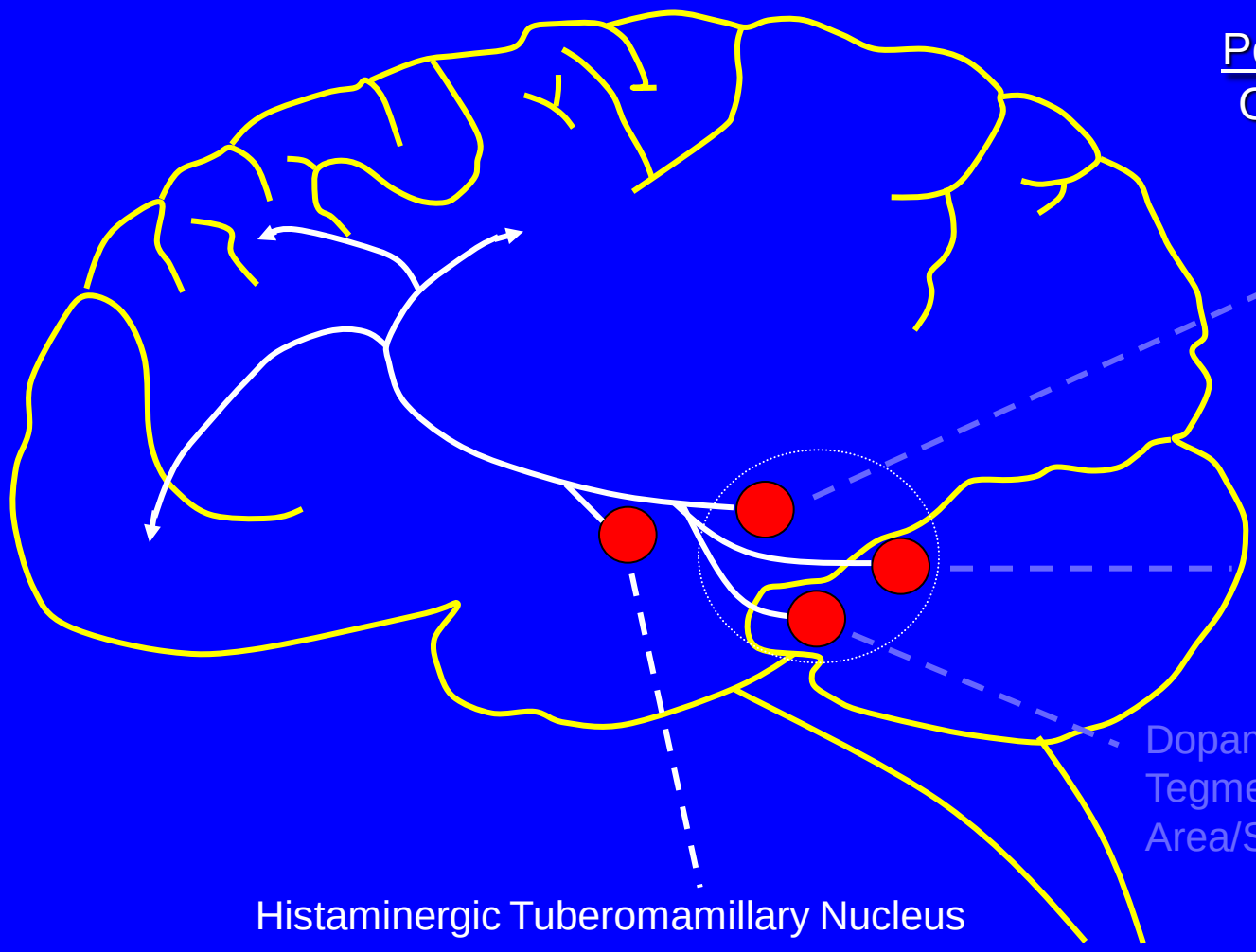
Von Economo - Observations

Viral encephalitis (encephalitis lethargica) outbreak of 1917 had three forms:

- Akinesia
- Hypersomnolence with ophthalmoplegia
  - associated with *posterior* hypothalamic lesions
- Insomnia with chorea
  - associated with *anterior* hypothalamic lesions

Von Economo's observations of the importance of the posterior hypothalamus for wake promotion went largely unheeded until recently.

How is wake regulated by the brain?



Possible Function
General Arousal

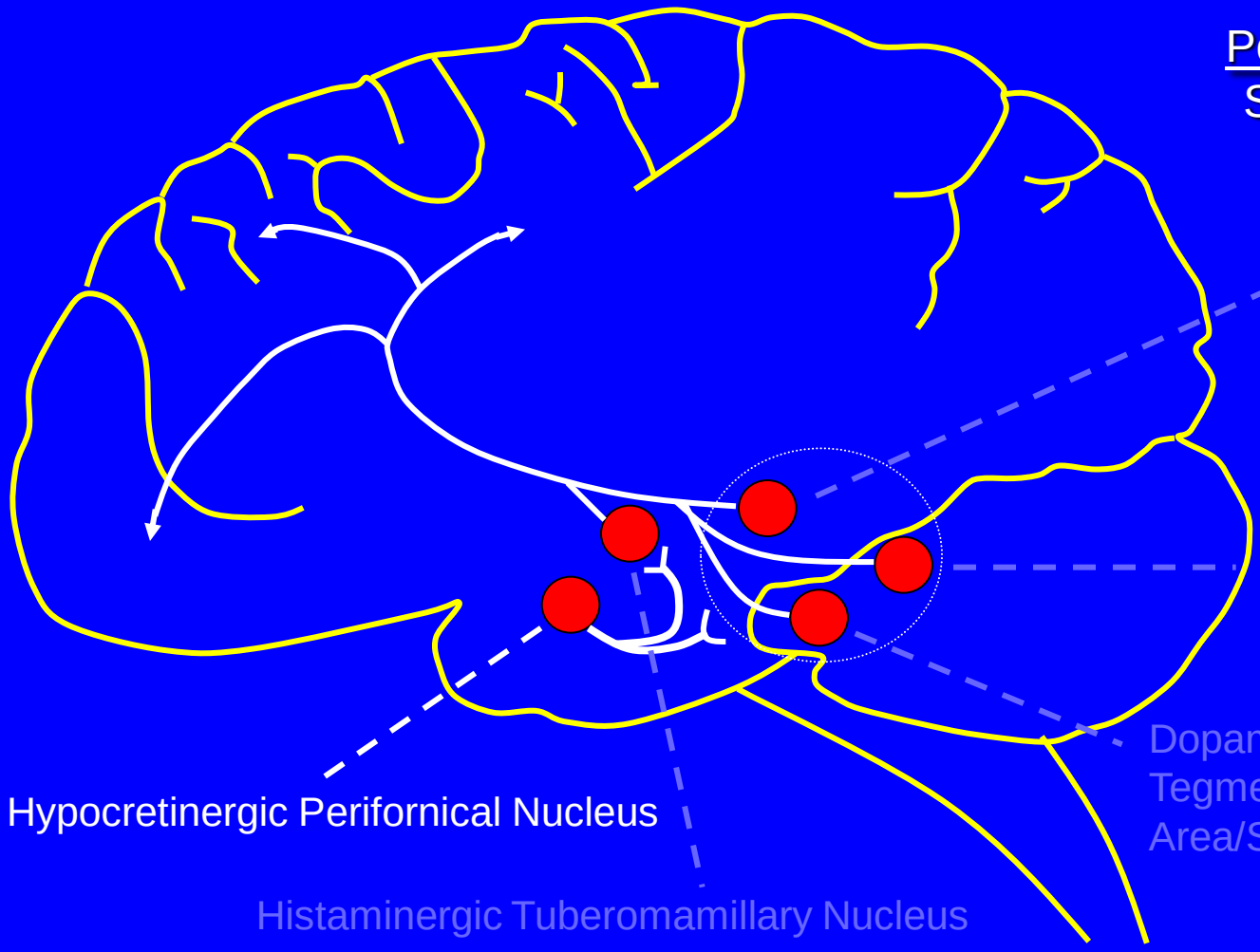
Serotonergic
Raphe Nuclei

Noradrenergic
Locus Coeruleus

Dopaminergic Ventral
Tegmental
Area/Substantia Nigra

Histaminergic Tuberomamillary Nucleus

How is wake regulated by the brain?



Possible Function
Sleep or Wake?

Serotonergic
Raphe Nuclei

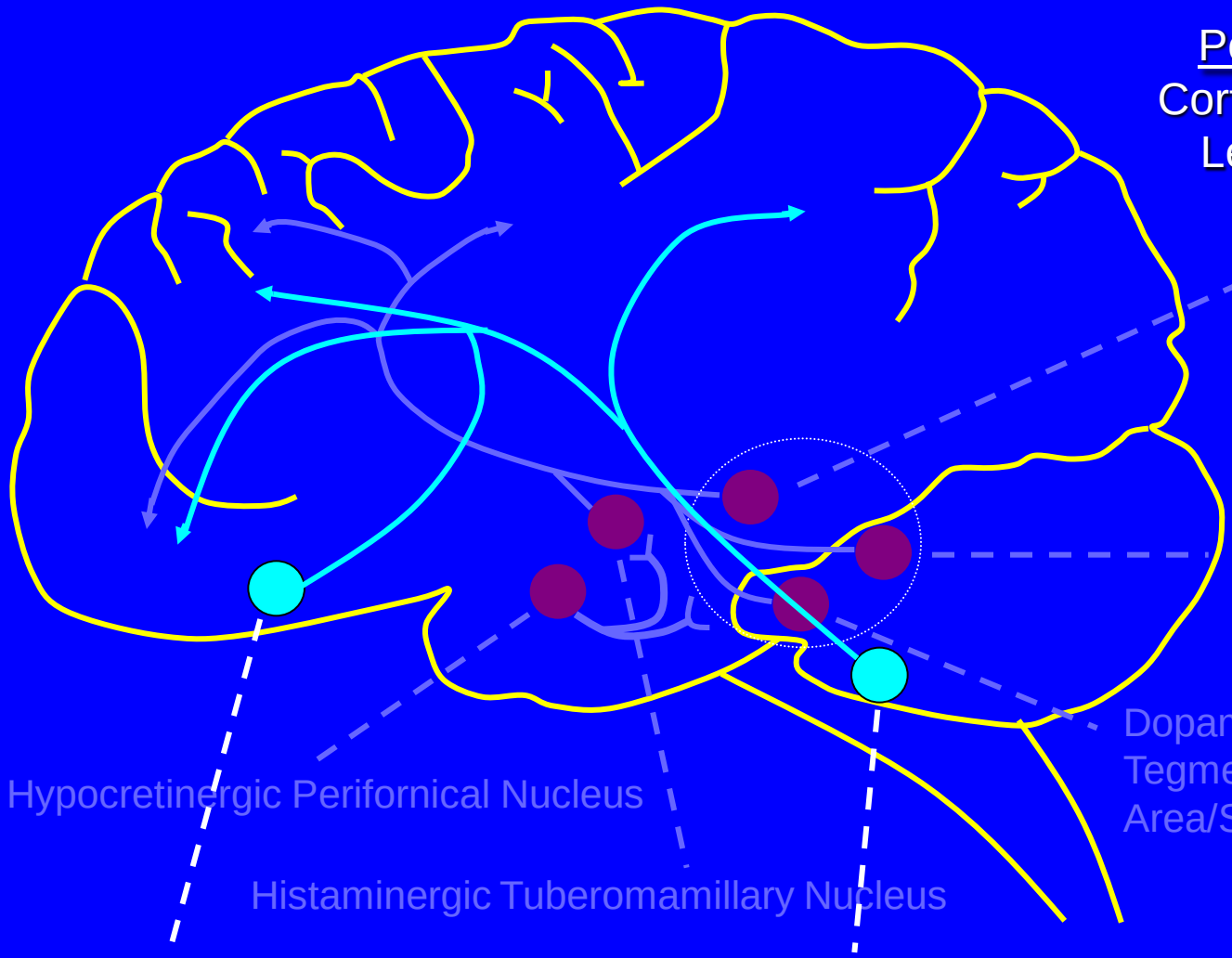
Noradrenergic
Locus Coeruleus

Dopaminergic Ventral
Tegmental
Area/Substantia Nigra

Hypocretinergic Perifornical Nucleus

Histaminergic Tuberomamillary Nucleus

How is wake regulated by the brain?



<u>Possible Function</u>
Cortical Desynchrony,
Learning/Memory

Serotonergic
Raphe Nuclei

Noradrenergic
Locus Coeruleus

Dopaminergic Ventral
Tegmental
Area/Substantia Nigra

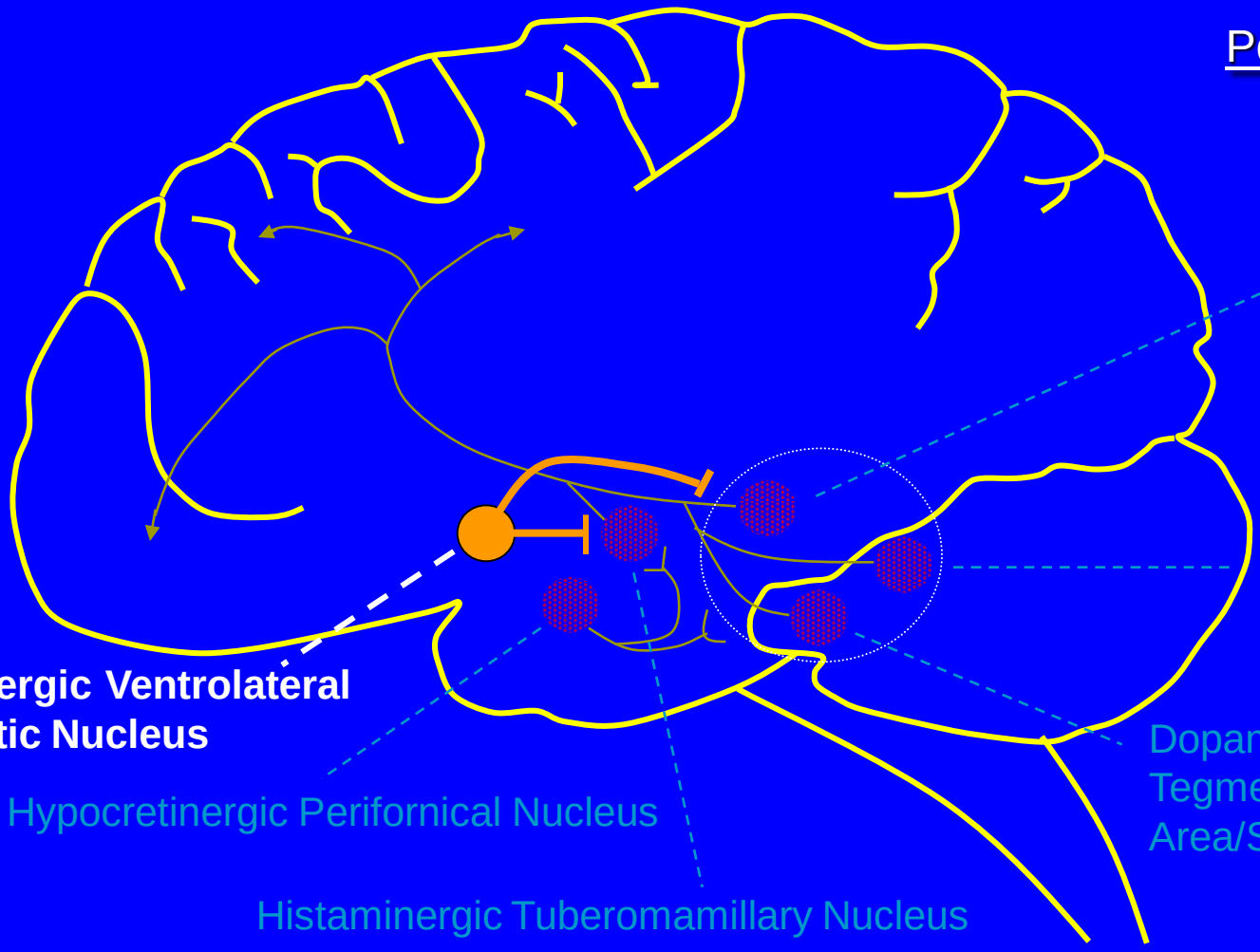
Hypocretinergic Perifornical Nucleus

Histaminergic Tuberomamillary Nucleus

Cholinergic Basal Forebrain

Cholinergic Pedunculopontine/Laterodorsal Tegmentum

How is NREM regulated by the brain?



Possible Function
Suppresses monoamines, histamine

Serotonergic Raphe Nuclei

Noradrenergic Locus Coeruleus

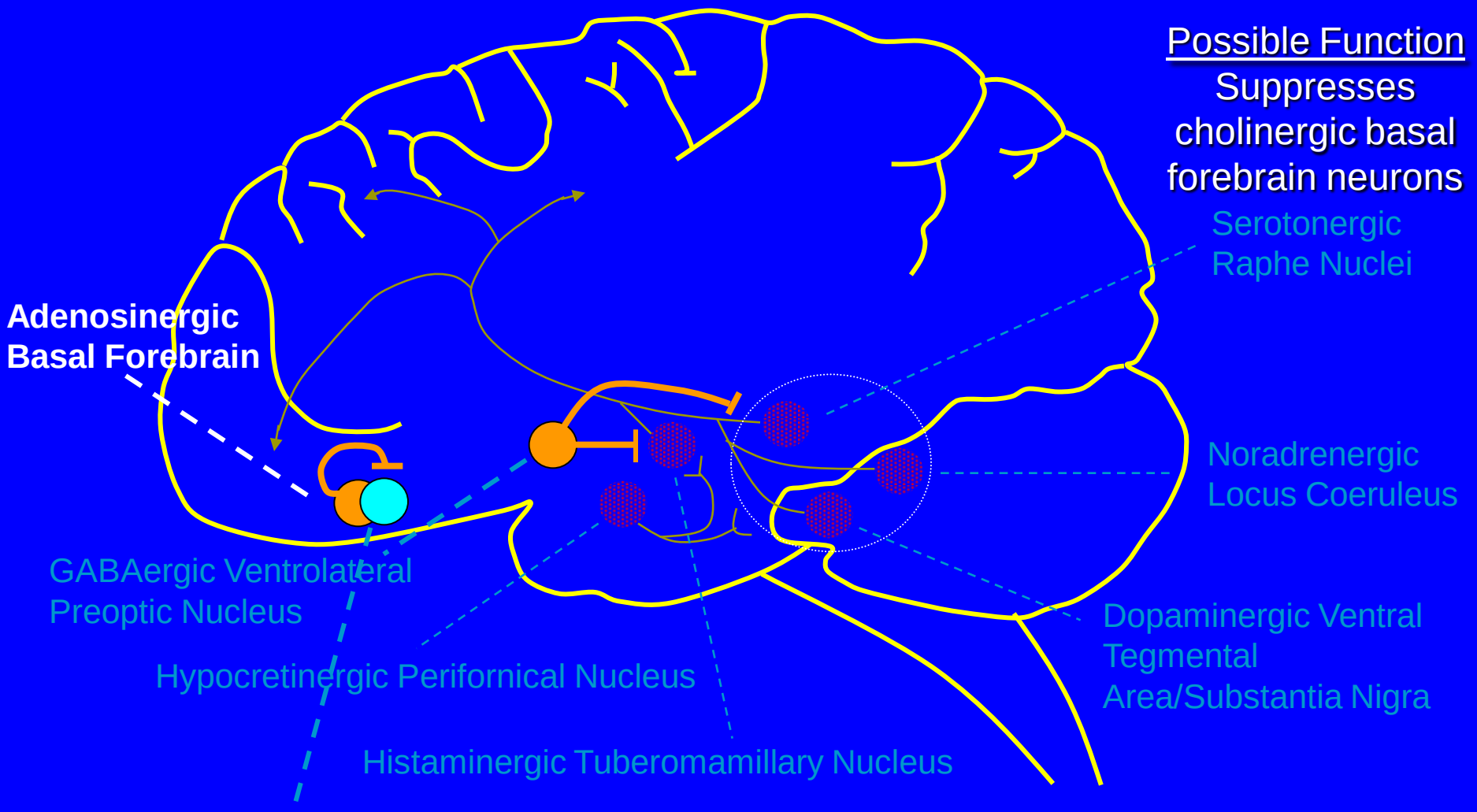
GABAergic Ventrolateral Preoptic Nucleus

Dopaminergic Ventral Tegmental Area/Substantia Nigra

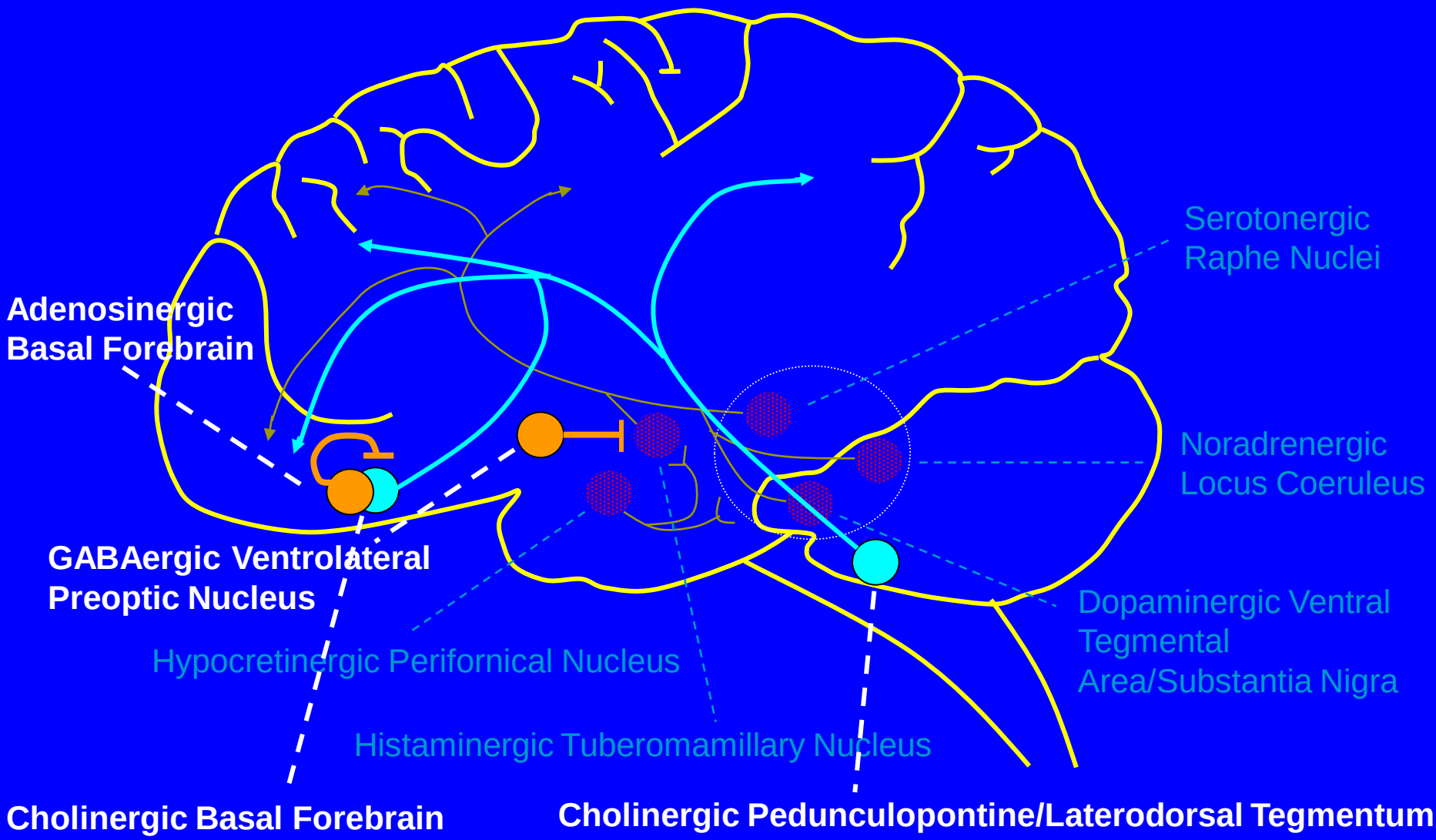
Hypocretinergic Perifornical Nucleus

Histaminergic Tuberomamillary Nucleus

How is NREM regulated by the brain?



How is REM regulated by the brain?

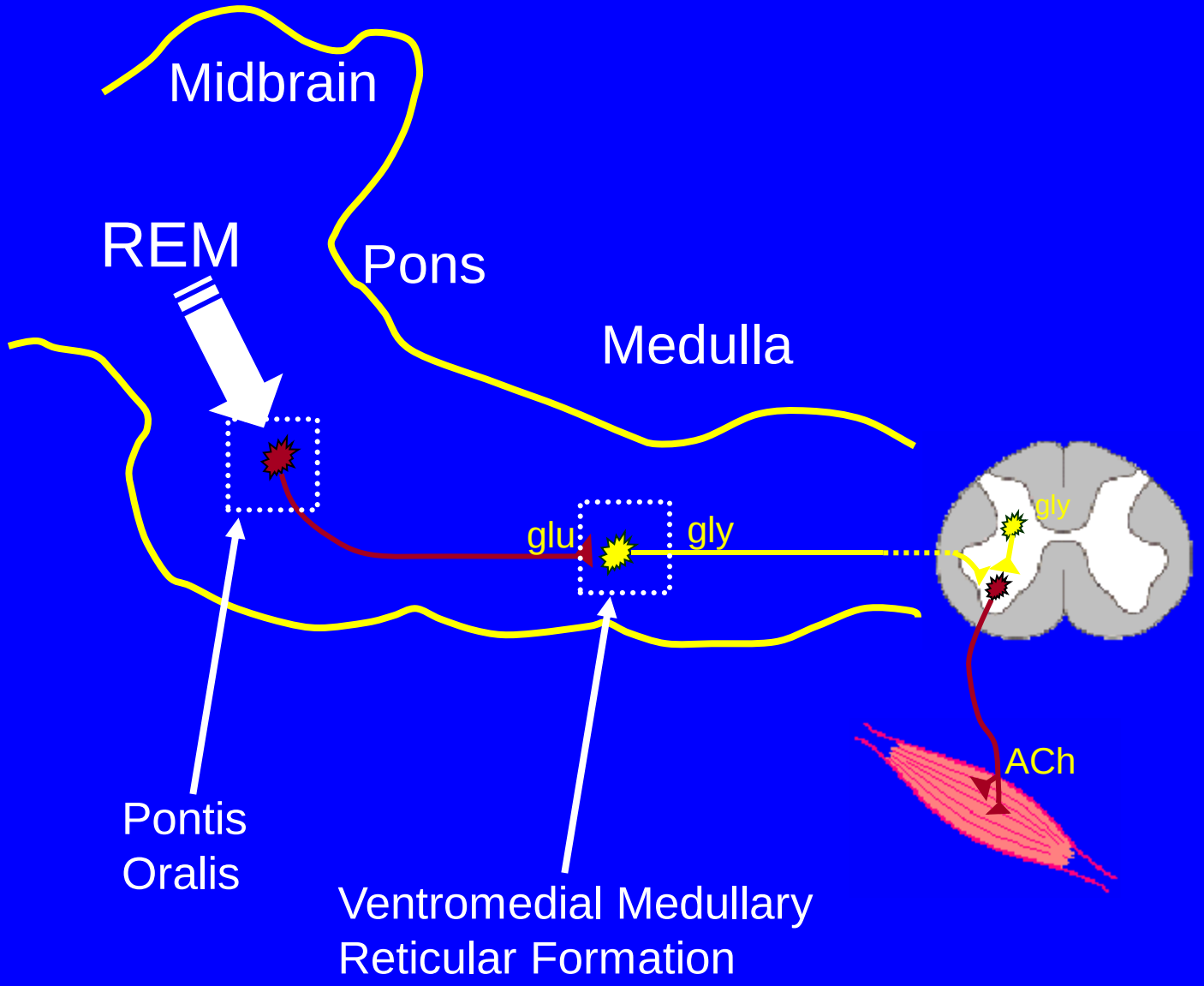


Muscle Tone

NREM Sleep:
Decreased (akin to relaxed wakefulness)

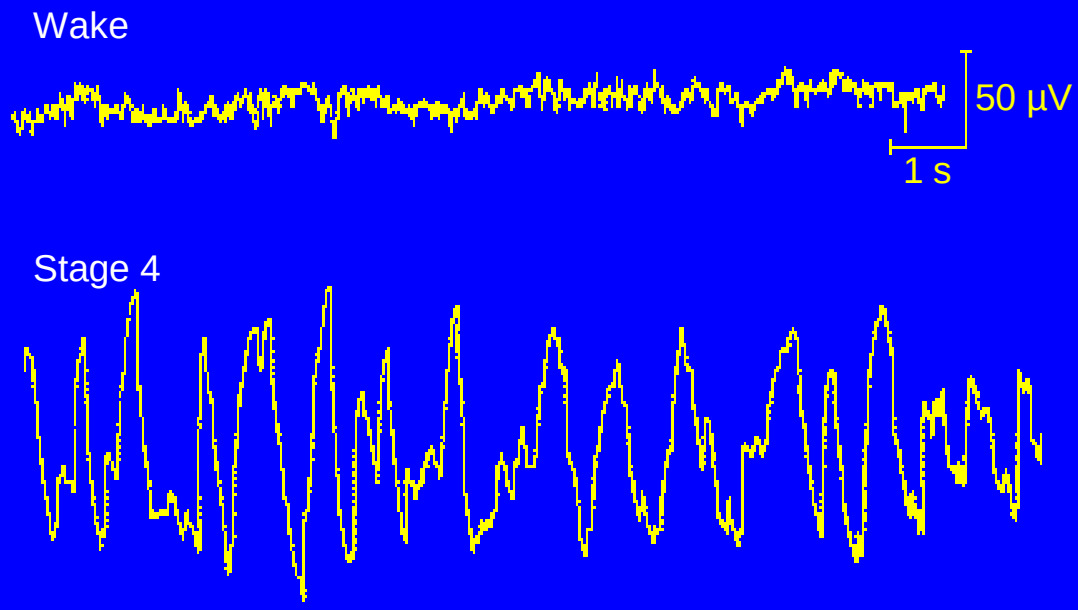
REM Sleep:
Active inhibition of all spinal motor activity (cranial nerves *not* affected)

Muscle Tone


Midbrain
REM
Pons
Medulla
glu
gly
gly
ACh
Pontis
Oralis
Ventromedial Medullary
Reticular Formation

What Is EEG amplitude?

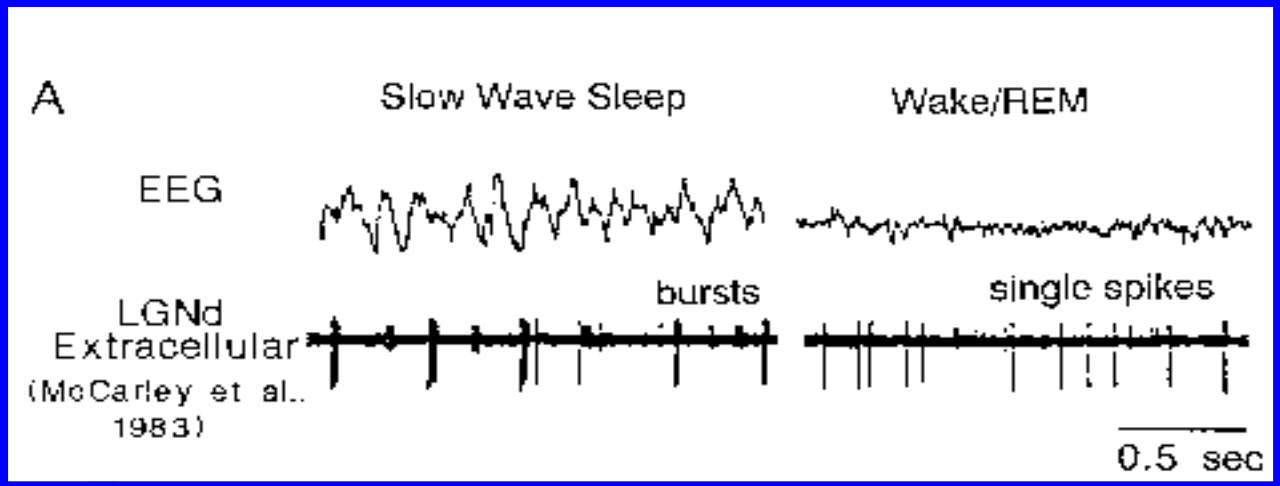
Low “amplitude” and high “amplitude” EEG indicates the degree of synchrony between cortical neurons, not the amount of activity. Desynchronized firing leads to destructive interference. Synchronicity additively combines waveforms.



From whence the EEG?

What causes cortical neurons to fire in synchrony?

Thalamocortical neurons synchronize cortical networks



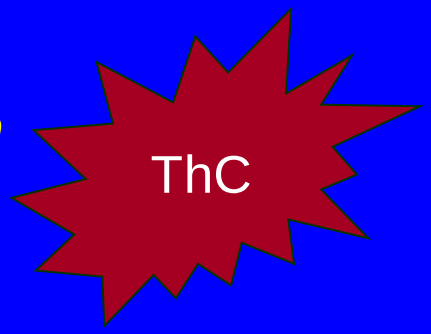
Thalamocortical Neurons Have Two Firing Modes

How do neuromodulators lead to EEG patterns?

Wake

NE
DA
5-HT
ACh

excitation →

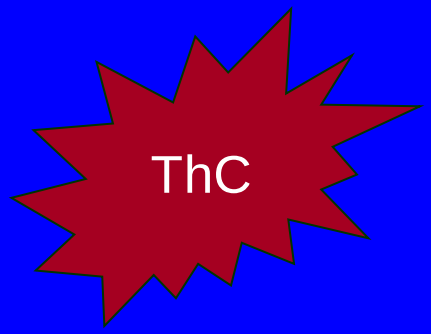


Raises membrane potential (Vm) and shifts ThC neurons to single spike firing.

How do neuromodulators lead to EEG patterns?

NREM

NE
DA
5-HT
ACh

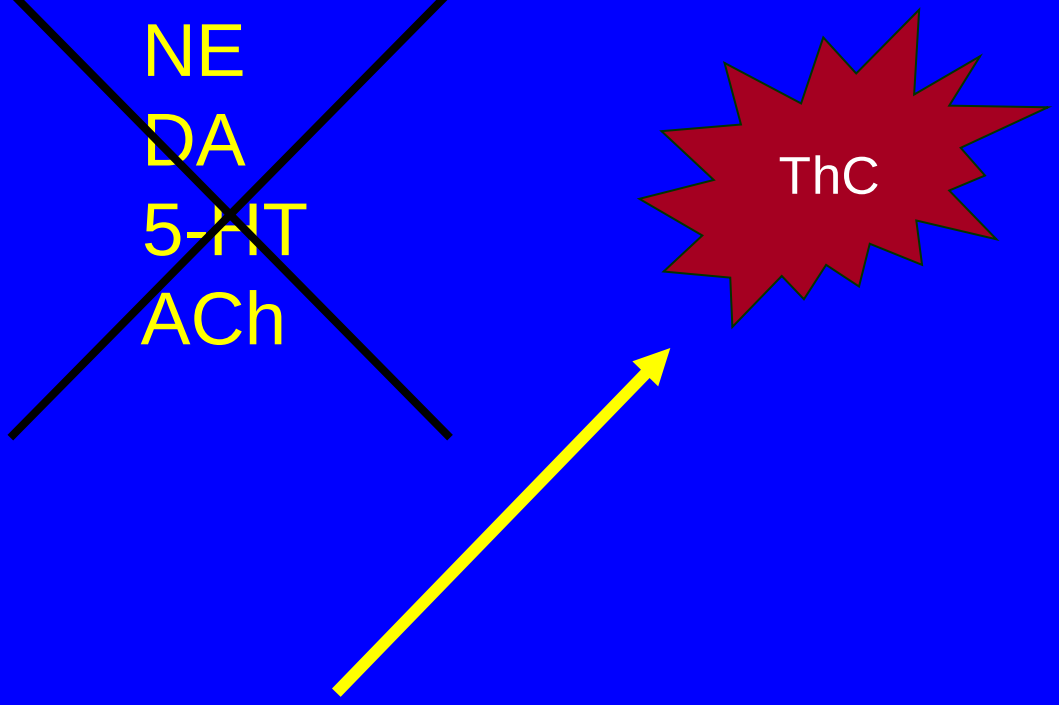


Loss of excitation lowers Vm and allows expression of T- and H-currents. This shifts ThC neurons to intrinsic burst firing.

How do neuromodulators lead to EEG patterns?

REM

NE
DA
5-HT
ACh



Acetylcholine elevates Vm enough to switch back to single spike firing.

All mammals divide their existence among three unique states of the brain:

Wakefulness

Rapid-Eye-Movement (REM) Sleep

non Rapid-Eye-Movement (NREM) Sleep

Sleep states are determined by observing:

Behavior/Posture

Muscle Activity (EMG)

Heart rate / blood pressure

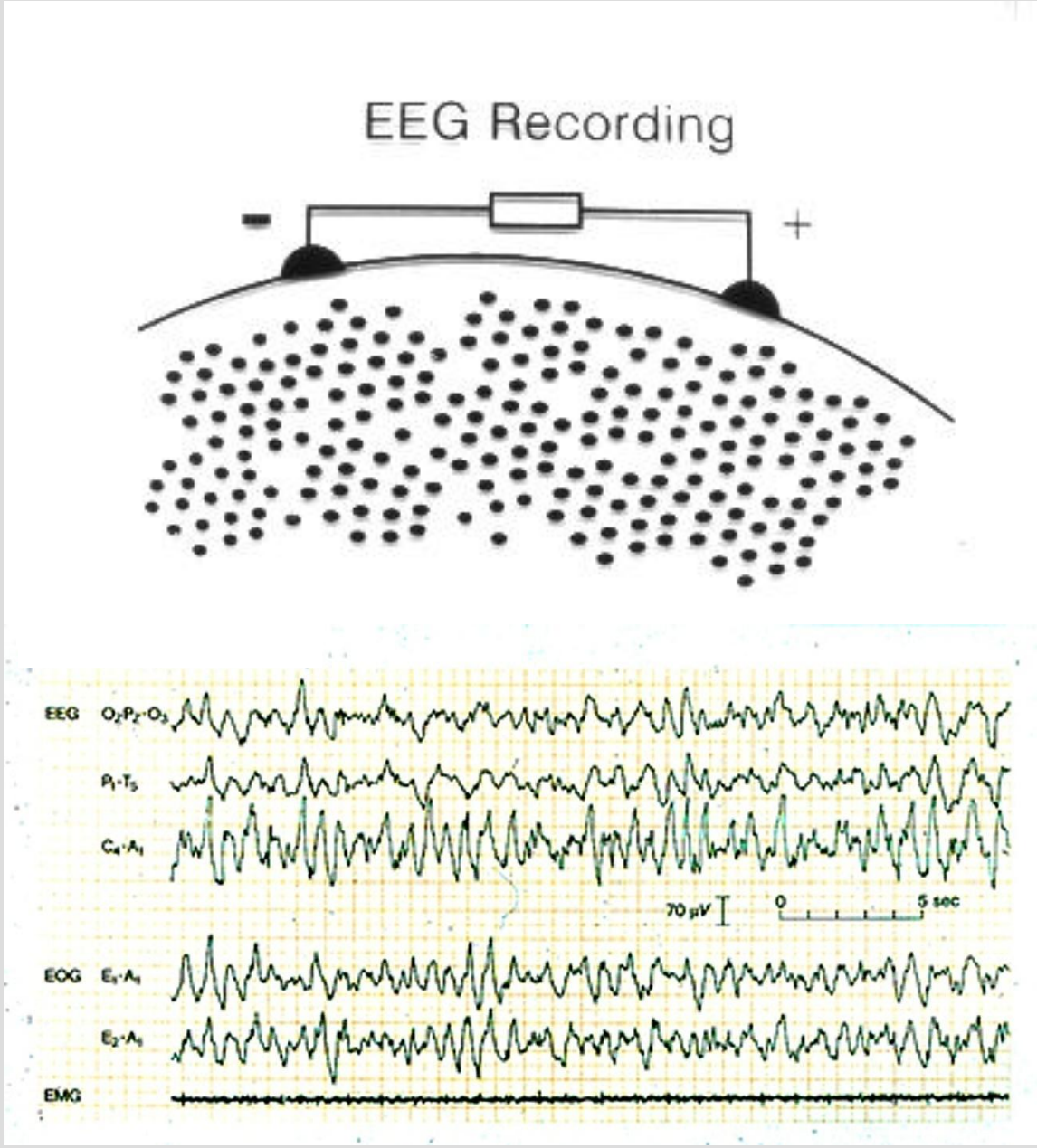
Temperature

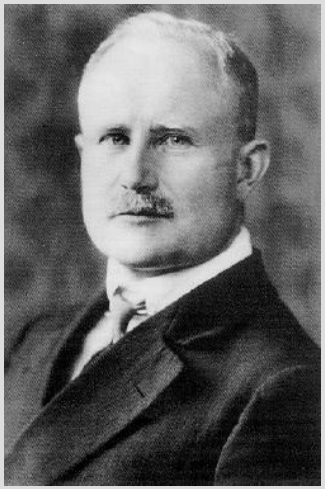
Brain Activity (EEG)

Eye Movements (EOG)

Respiratory Rate

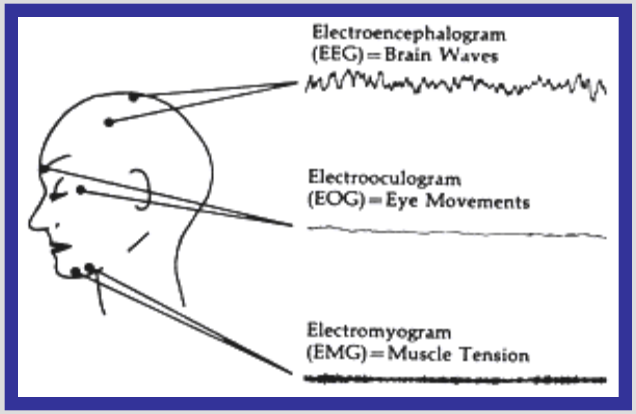
First Electroencephalogram (EEG) Recording in humans in 1928

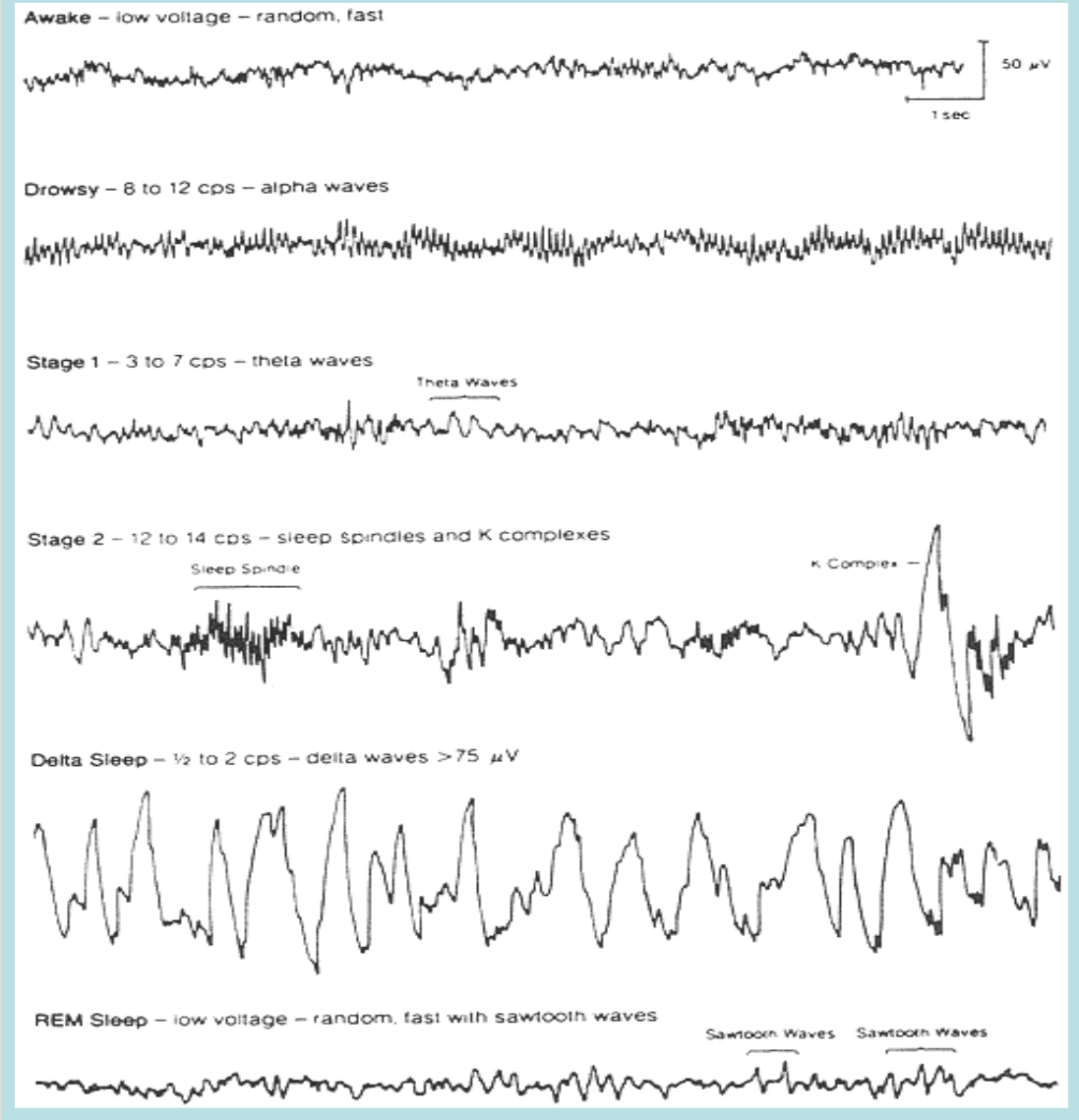




Hans Berger (1873 – 1941)

SLEEP STATES CAN BE DEFINED BY EEG ACTIVITY





The Duality of Sleep

REM Sleep

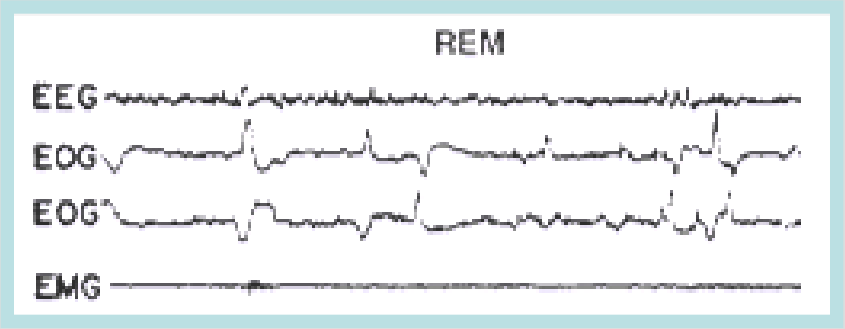
An active brain in a paralyzed body
(paradoxical sleep)

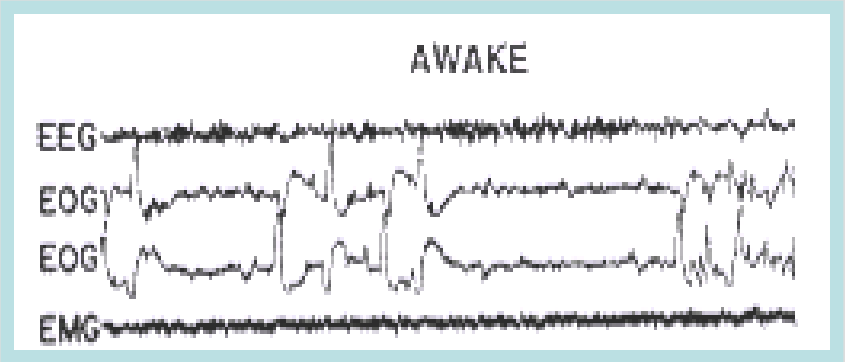
NREM Sleep

An quiescent brain in a movable body

REM Sleep

- ***Binocularly synchronous REMs, sawtooth waves**
- ***Dreaming**
- ***Muscle Atonia (Paralysis)**
- ***High metabolic activity in brain**
- ***Irregular breathing**
  - **increased risk of apnea or hypoxic events**
- ***Increased heart rate variability**
  - **increased risk of arrhythmias, pulmonary hypertension, and heart attack**





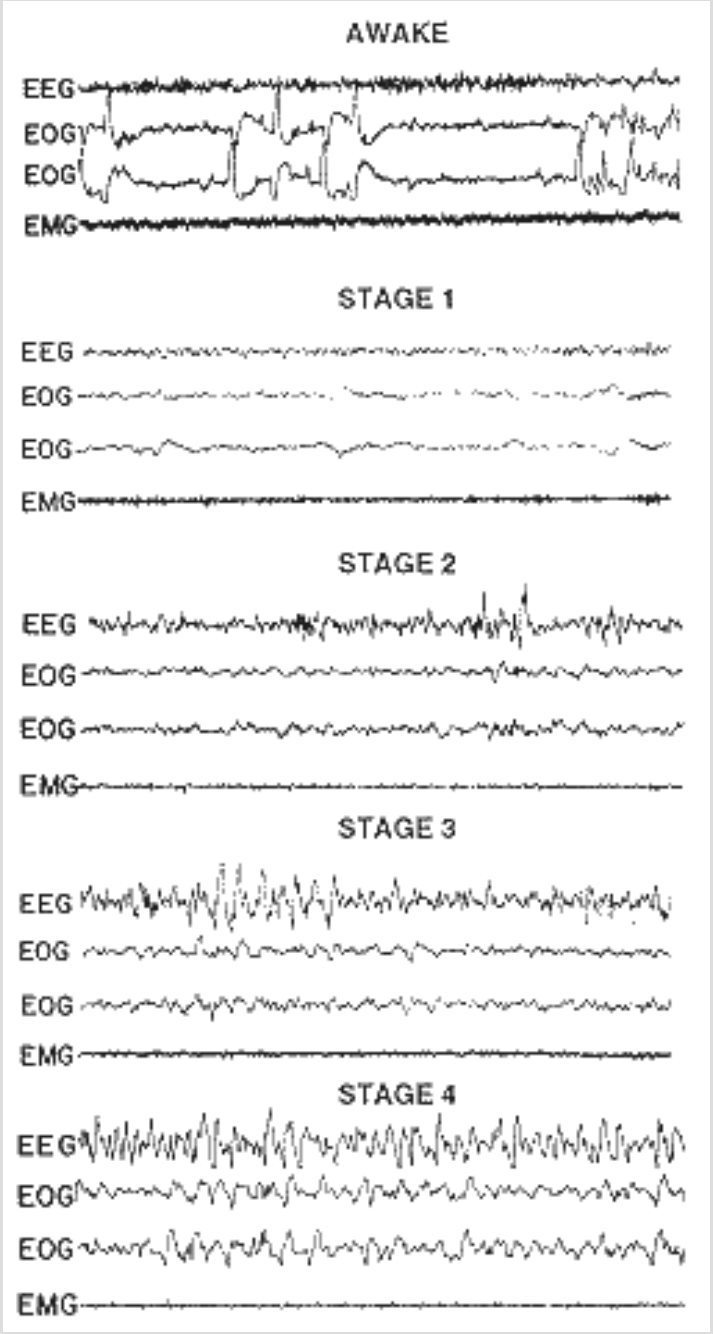
NREM Sleep

- STAGE 1
  Alpha activity decreases, mostly of low voltage, mixed frequency activity, much of it at 3-7 Hz. Slow rolling eye movements appear. The EMG is moderate to low.

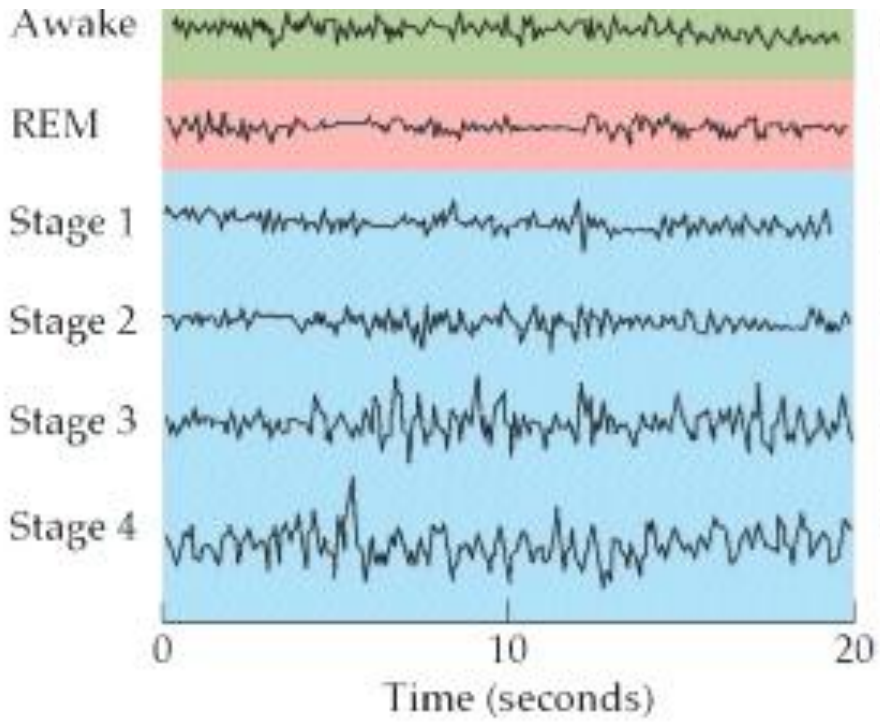
- STAGE 2
  Low voltage, mixed frequency background activity, bursts of distinctive 12-15 Hz sinusoidal waves (sleep spindles). Eye movements are rare, and the EMG is low to moderate.

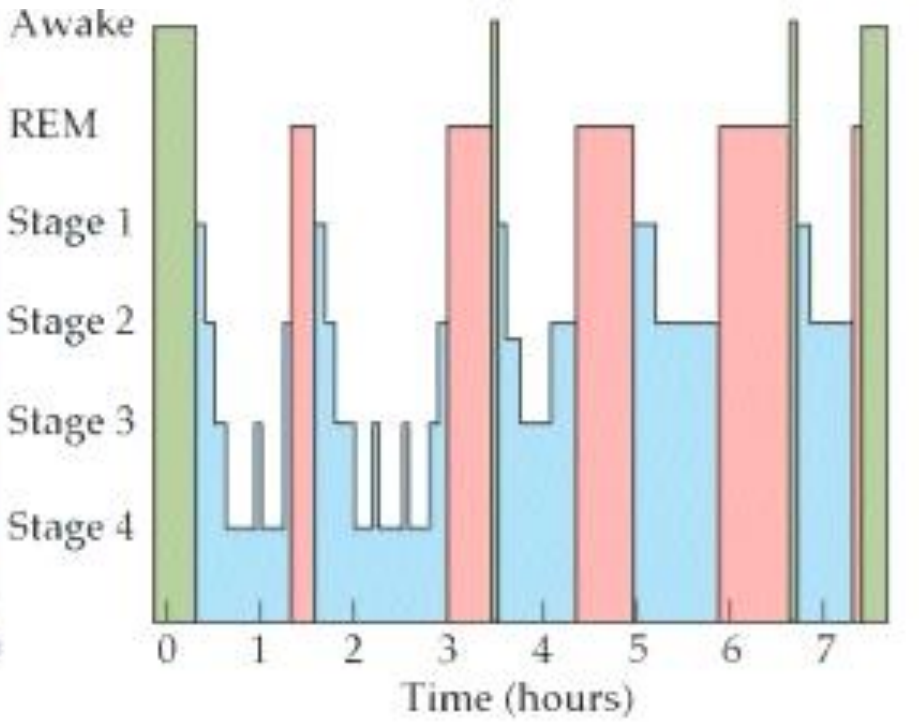
- STAGE 3
  High amplitude (>75 mV), slow (0.5-4 Hz) "delta waves" appear in the EEG.

- STAGE 4
  There is a quantitative increase in delta waves so that they come to dominate the EEG tracing.



The Distribution of Sleep Stages Throughout the Night



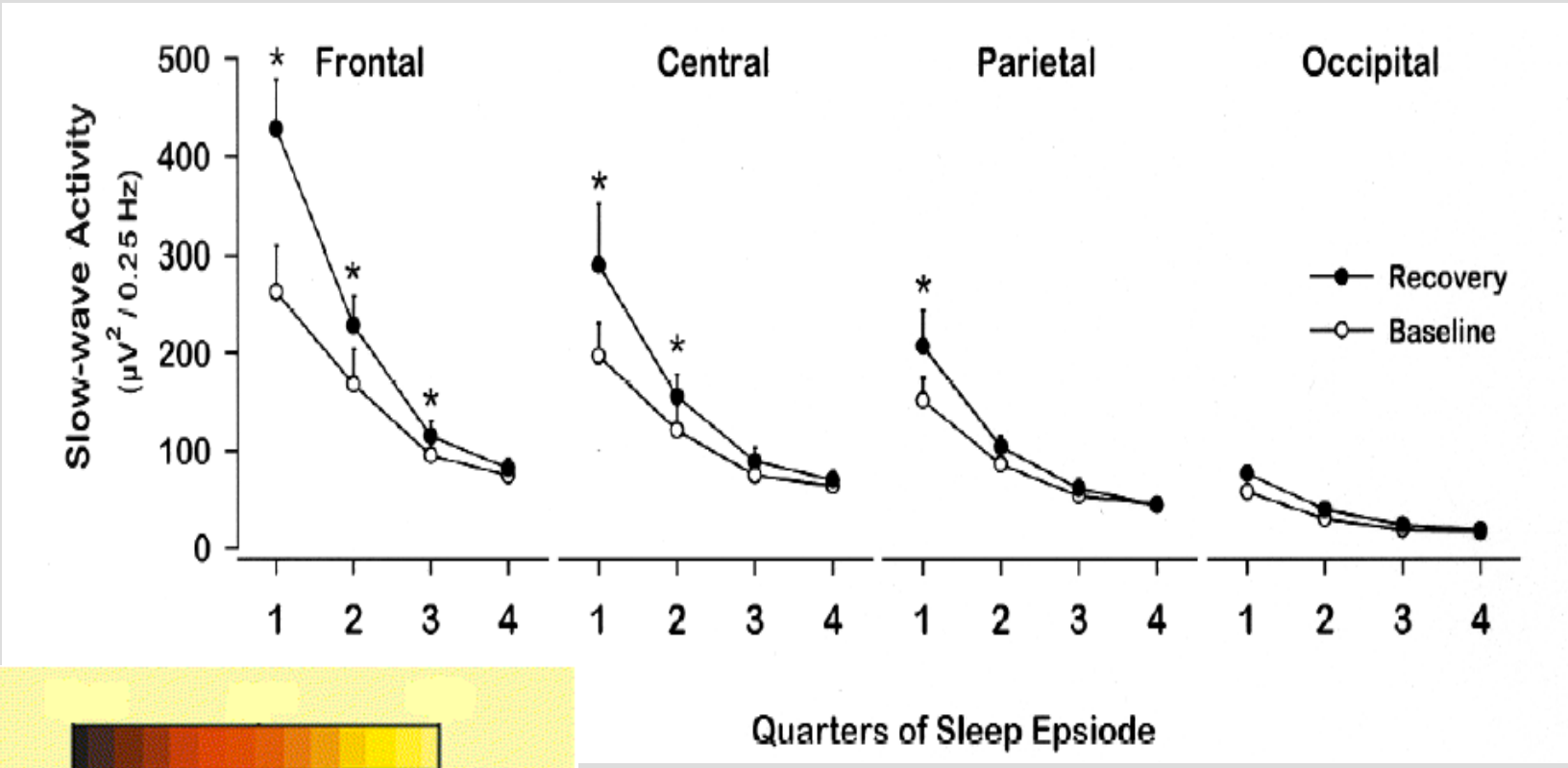


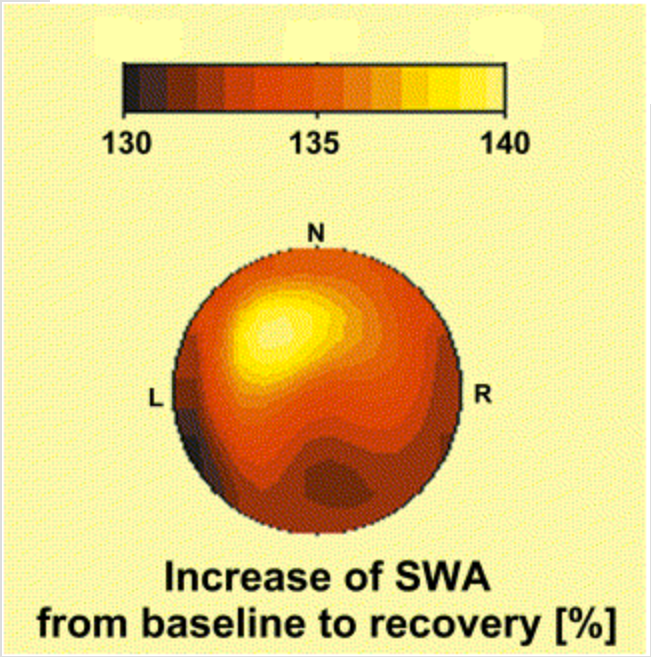
Sleep is regulated by Circadian, Homeostatic, and Ultradian Processes

Local vs. Global Aspects of Sleep

Does Sleep Homeostasis reflect a Use-Dependent Process?

Krueger & Obal, JSR, 1993
Benington & Heller, Prog Neurobiol, 1995





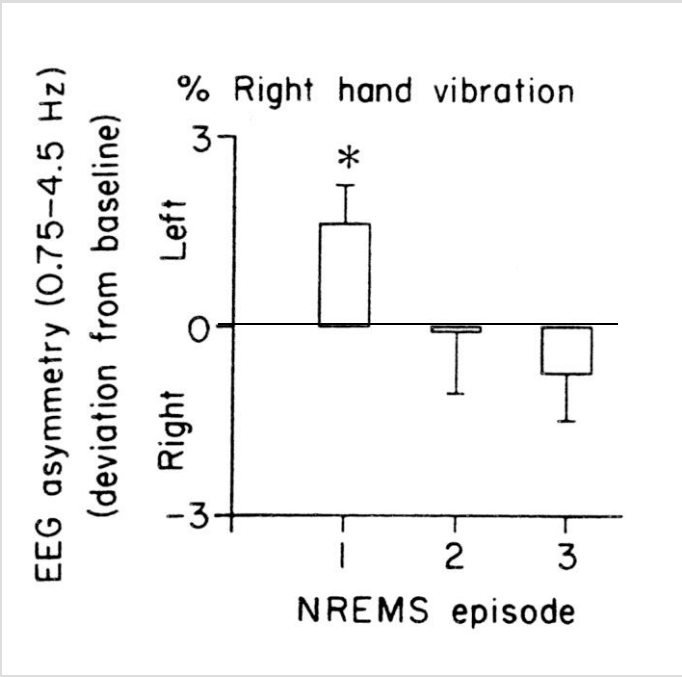
Frontal predominance of the relative increase in EEG delta power after sleep deprivation

Cajochen et al. 1999
Finelli et al. 2000

Right hand stimulation (vibration) in humans for 6-h prior to sleep

Only in the central EEG derivation (over the somato-sensory cortex) and only in the delta frequency range, a shift in EEG power towards the stimulated, left hemisphere was observed.

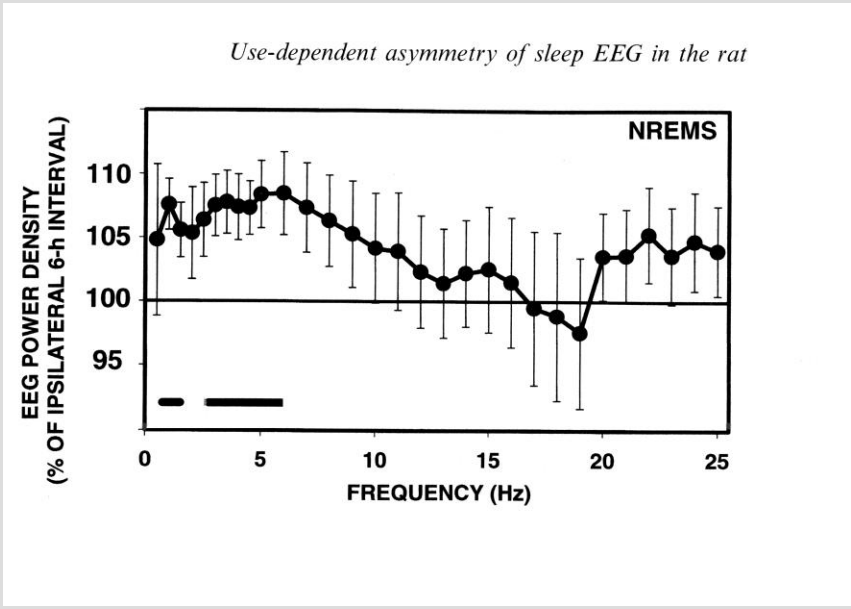
Kattler *et al.* JSR 1994



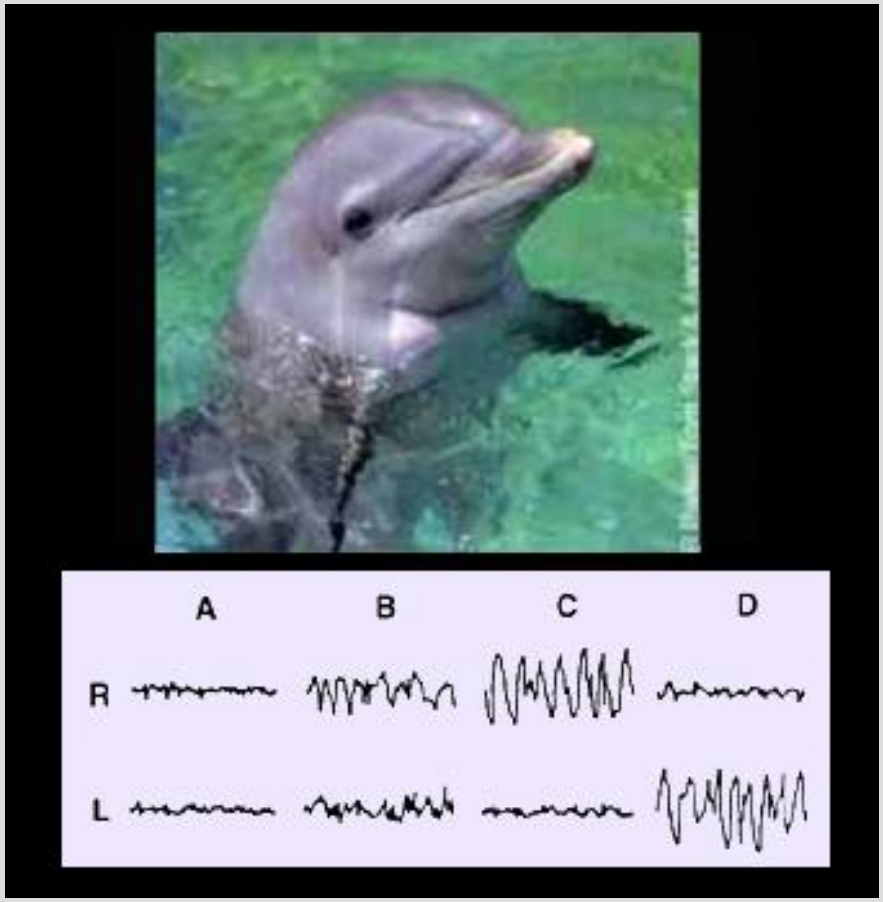
Unilateral vibrissae stimulation in the mouse for 6-h prior to sleep

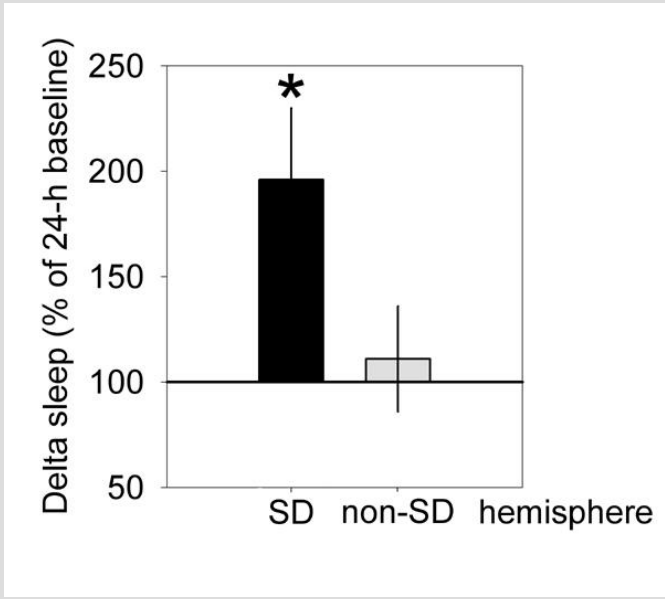
The hemisphere contra-lateral to the uncut whiskers showed increased EEG power in the delta frequency range.

Vyazovskiy *et al.* JSR 2000



Unihemispheric Sleep and Unihemispheric Sleep Deprivation in the Bottlenose Dolphin





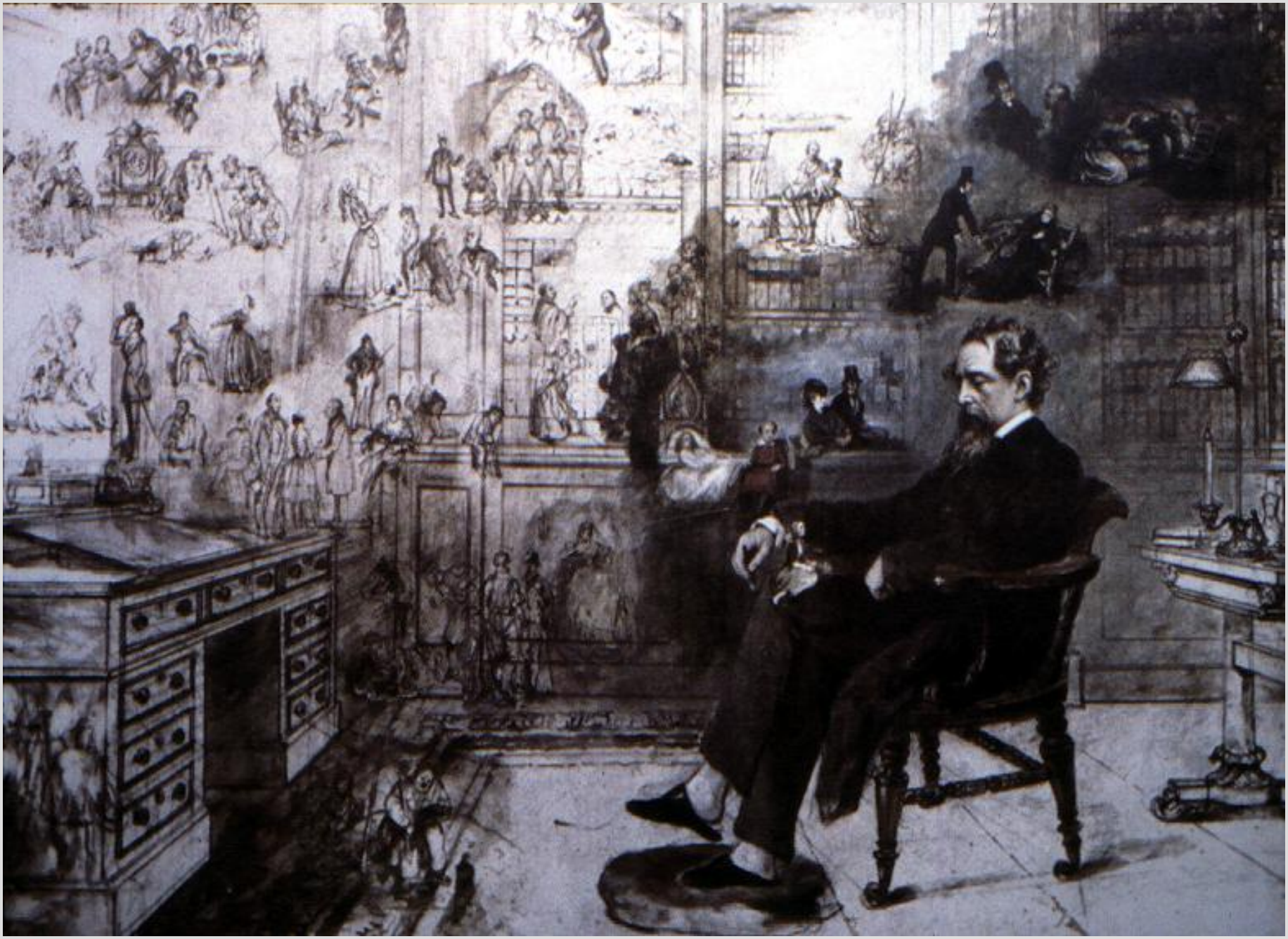
Delta sleep during the 24-h following a 4-day unihemispheric delta-sleep deprivation (SD). Average of 9 trials in 5 animals

Mukhametov *et al.* Neirofiziologiia,1988
Oleksenko *et al.* JSR, 1992

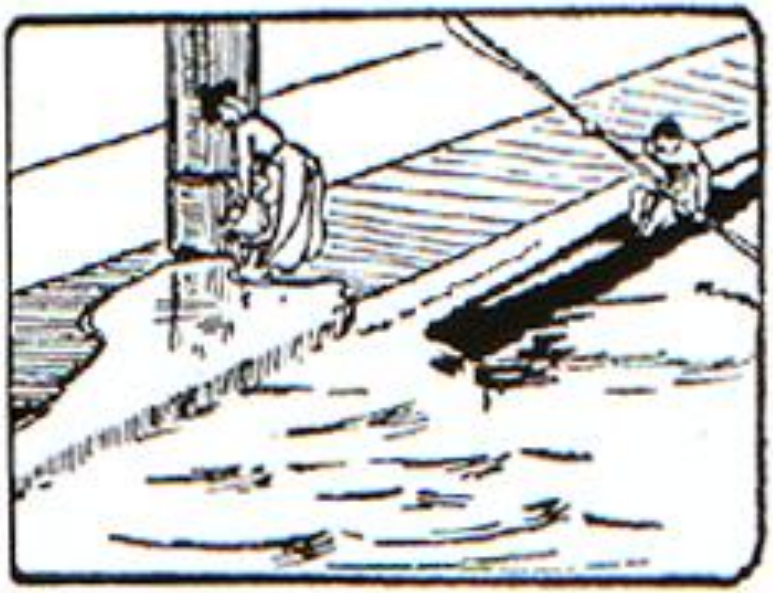
SLEEP
Hobson, 1988

Also wrote:
The Dreaming Brain - 1988

The Chemistry of Conscious States – 1994



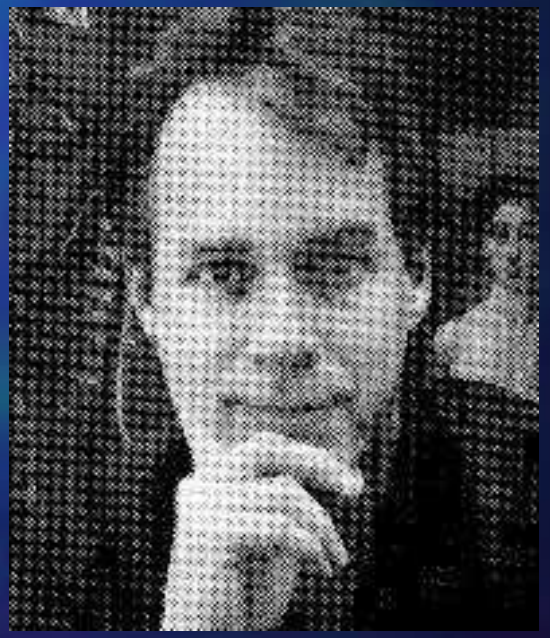
These drawings from an early edition of *The Interpretation of Dreams* illustrate Freud's belief that the dream is "the guardian of sleep." The drawings depict the dream of a nursemaid whose charge cries during the night because he wants to go to the lavatory. The dream tries to guard her sleep by showing him doing so. But the child continues to cry and she dreams that the pool of urine floods the town and becomes a sea, until finally the dream can no longer prevent her waking.



Lucid dreaming: Evidence that REM sleep can support unimpaired cognitive function and a methodology for studying the psychophysiology of dreaming

Stephen LaBerge

The Lucidity Institute



What is Lucid Dreaming?

Lucid dreaming is *dreaming while knowing that you are dreaming*. This fascinating state of consciousness allows you to control your dreams and experience anything imaginable, from the sublime to the impossible.

http://www.lucidity.com

What is Lucid Dreaming?

- Possess clear cognizance that one is dreaming
- Reason clearly
- Remember conditions of waking life
- Act upon reflection or in accordance with plans decided upon before sleep

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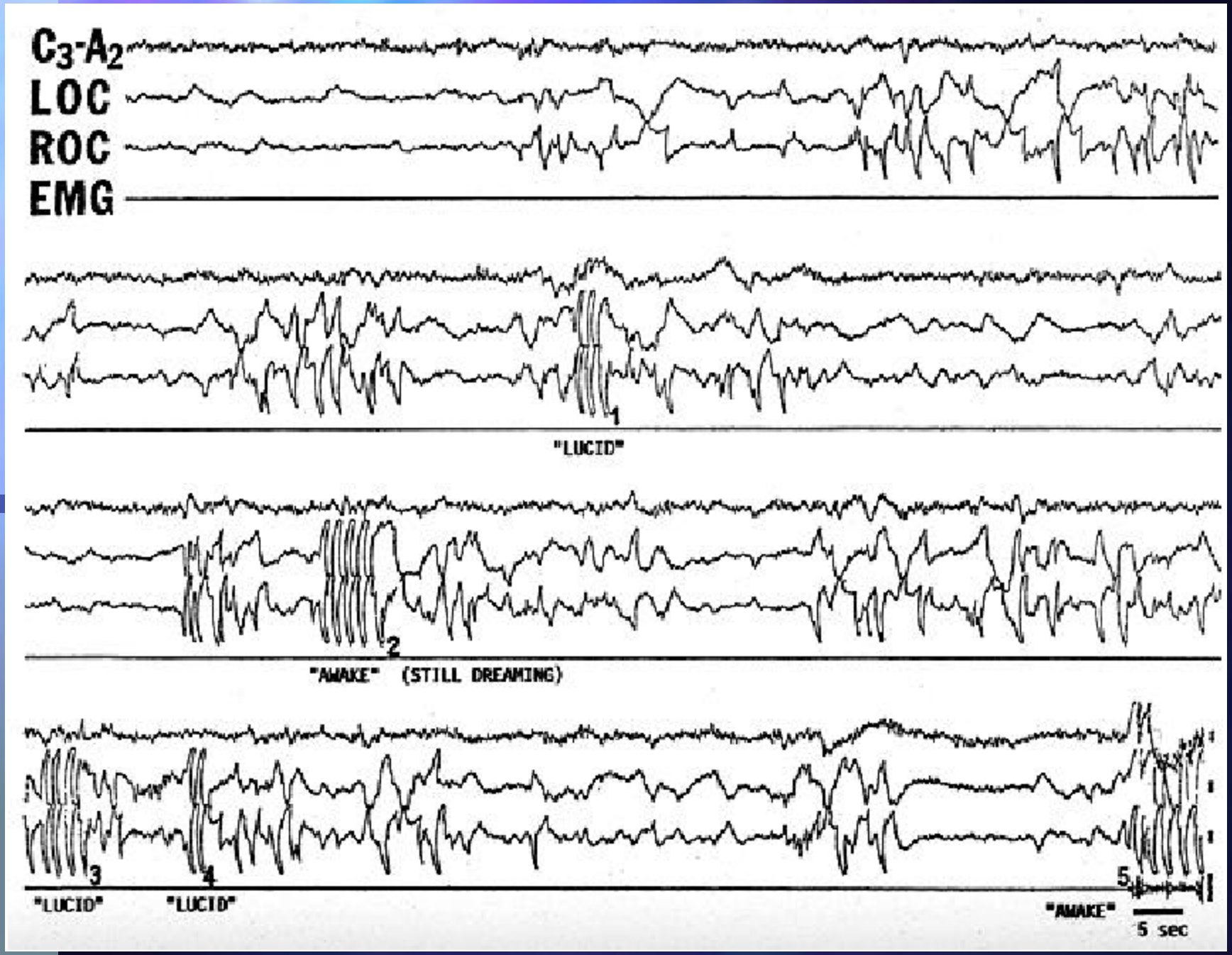
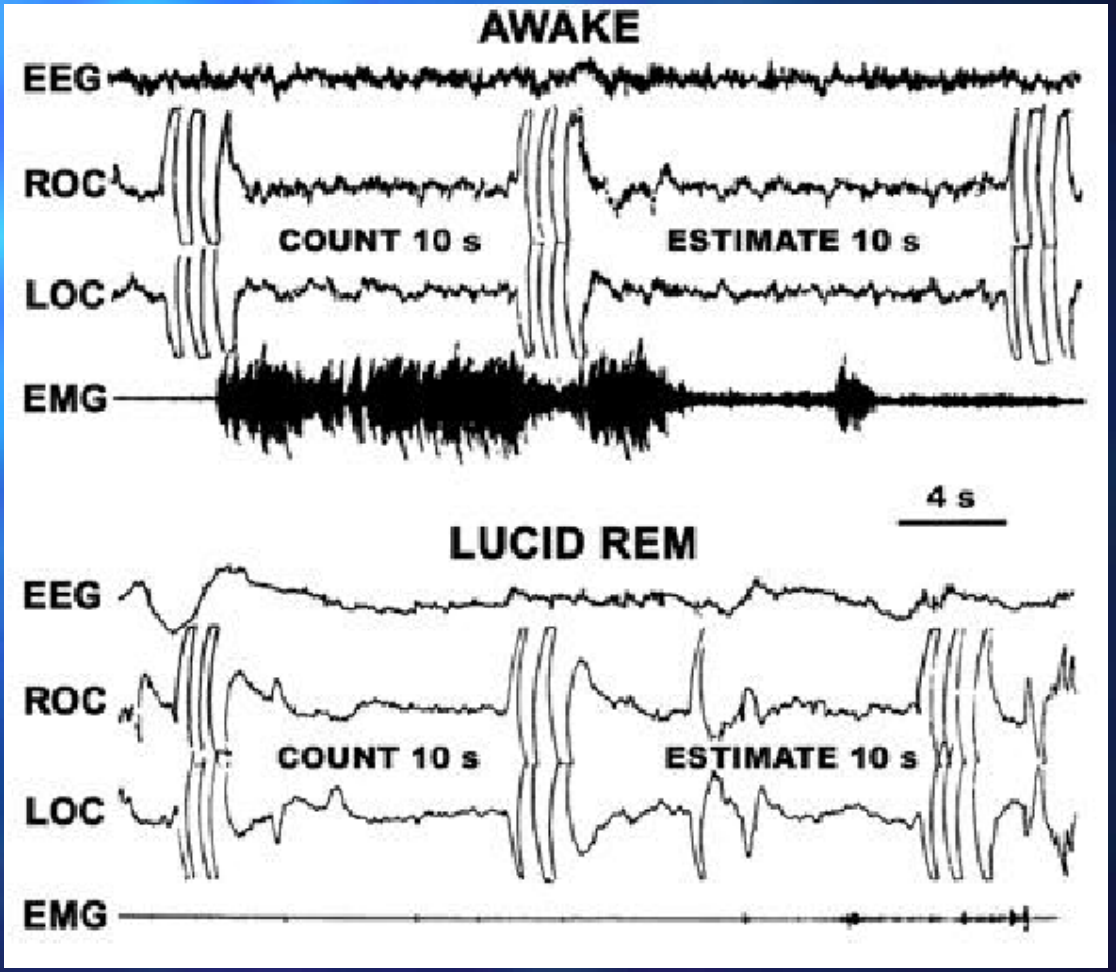
Allow precise correlations between physiology and the subjective reports and enabling the methodical testing of hypotheses


C3-A2
LOC
ROC
EMG
1
"LUCID"
2
"AWAKE" (STILL DREAMING)
3
"LUCID"
4
"LUCID"
5
"AWAKE"
5 sec

Eye Movement Control



Theories of dreaming that do not account for lucidity are incomplete, and theories that do not allow for lucidity are incorrect.

“A dream is real while it lasts. Can we say more of life?”

Havelock Ellis


EASY TWIST OFF
100%
NATURAL
ELLIOTT'S
Amazing™
EASY TWIST OFF


Dreaming
permits each and
every one of us to
be quietly and safely
insane every night of
our lives.
Dr. William Dement

Some describe memory as a “heterogeneous entity,” involving two main divisions:

Declarative (explicit):

The subject is aware the information exists and is being accessed.

Ex. Direct memorization of information from a textbook.

Non-declarative (implicit):

The subject’s behavior is affected by the new memory, though he/she may not be aware of it.

Ex. Someone may have the ability to speak a complete sentence without being able to describe the grammatical rules used. Or, learning to ride a bicycle.

Memory Consolidation:

One definition:

"The time dependent process that converts labile memory traces into more permanent and/or enhanced forms."

So, how does sleep consolidate memories?

Two of the major hypotheses:

The ***dual process*** hypothesis suggests that REM and nonREM sleep act differently on different memory traces, depending on the memory system in which the information/behavior belongs.

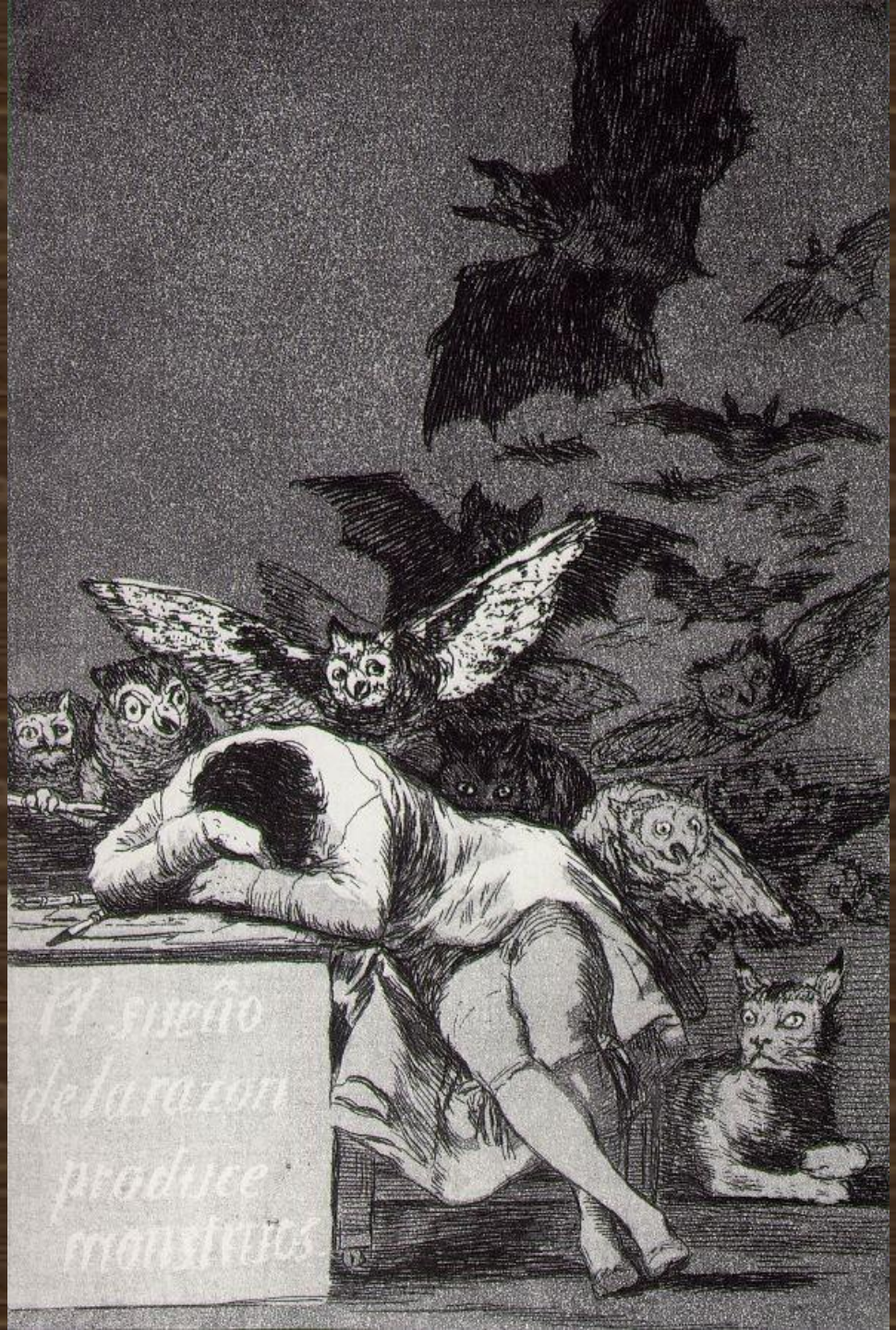
One example is the hypothesis that SWS (NREM) facilitates consolidation of declarative memory, while REM sleep consolidates non-declarative memory.

In the ***double step*** hypothesis, it is believed that REM and NREM sleep complement each others' roles in memory consolidation.

This is achieved by the position that specific sleep stage sequences act in the brain's consolidation of memory in successive steps.

Studies in humans and in rodents models have shown that sleep improves learning and memory.

- 1. Sleep deprivation after learning affects memory consolidation.
- 2. Learning affects post-learning sleep.
- 3. Stimulation during sleep and altering the sleep pattern affects overnight memories.
- 4. Neural patterns of specific behaviors are re-expressed during post-training sleep.


El sueño
de la razon
produce
monstruos