Pre-Lecture Video

The EEG is a measurement of population activity of the cerebral cortex.

- used extensively in sleep research

Generation of VERY Small Electric Fields

- Detect the <u>summation</u> of MANY neurons (synchronous activity)
- Signal must pass through overlying tissue

Normal EEG

- Alpha rhythms – 8 to 13 Hz ← quiet waking
- Beta rhythyms – 13 - 30 Hz ← active concentration

replace α

See similar brain rhythyms among different species

Two Mechanisms of Synchronous Rhythms

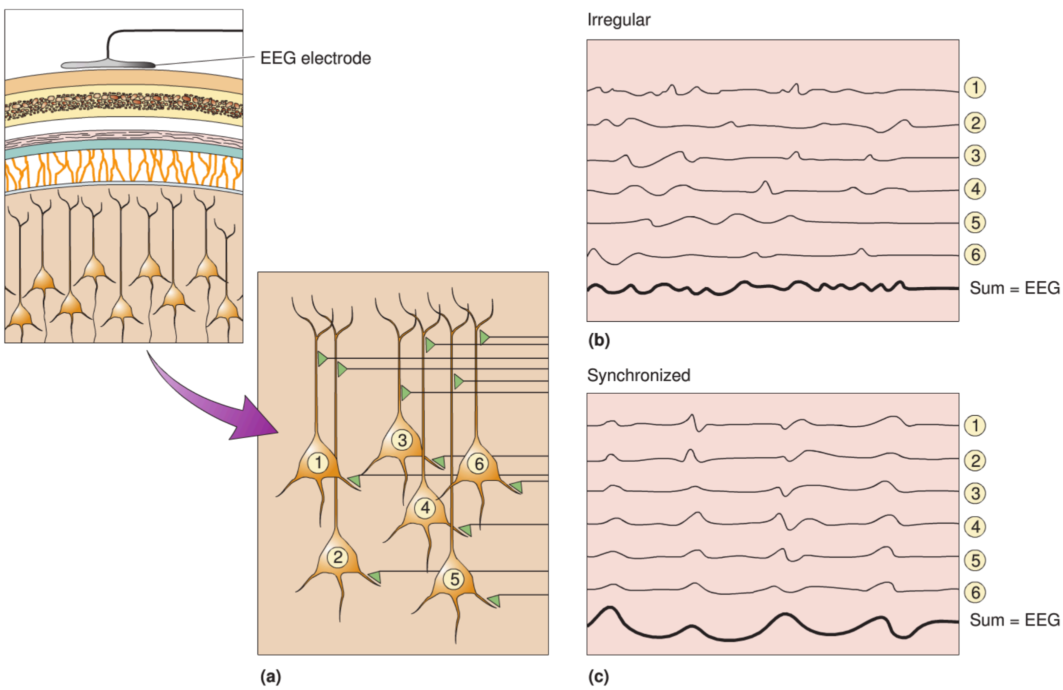
- Two neuron oscillator
- One neuron oscillator

Lecture 36. Sleep

Prof. Melissa Warden

Pre-Lecture Preparation

Watch Video 36-1: Brain rhythms
Understand this figure:



▲ FIGURE 19.5
The generation of large EEG signals by synchronous activity. **(a)** In a population of pyramidal cells located under an EEG electr ode, each neur on receives many syn-aptic inputs. **(b)** If the inputs fir e at irr egular intervals, the pyramidal cell r esponses are not synchr onized, and the summed activity detected by the electr ode has a small amplitude. **(c)** If the same number of inputs fir e within a narr ow time window so the pyramidal cell r esponses are synchronized, the r esulting EEG is much lar ger.

Required Reading

Be able to explain the following figures from Bear et al.: p.649, Fig. 19.5; p.660, Fig. 19.15; p.662, Fig. 19.16; p.667, Fig. 19.18; p.668, Fig. 19.19; p. 669, Box 19.4

Optional Reading

1. Neural substrates of awakening probed with optogenetic control of hypocretin neurons. Adamantidis AR, Zhang F, Aravanis AM, Deisseroth K, de Lecea L. *(hypocretin = orexin)*

Learning Objectives

1. To learn the range of rhythms supported by the neural circuits of the brain, and the neural architectures and firing patterns contribute to these rhythms.
2. To learn the changes in brain physiology that occur during sleep.
3. To learn the functions and mechanisms of REM and non-REM sleep.
4. To learn the mechanisms underlying some common sleep disorders.

Lecture Outline

In this lecture we will discuss the wide range of electrical rhythms supported by the neural circuits of the brain, and how they enable different brain "states" such as sleep and wakefulness. We will discuss the neural mechanisms underlying sleep and dreaming, what happens when you don't sleep, and disorders of sleep.

1. Brain Rhythms
    a. Brain rhythms and how they are measured
    b. How brain anatomy and firing patterns of individual neurons give rise to brain rhythms

2. Sleep
    a. What is sleep, and why we sleep (some hypotheses)
    b. The brain rhythms associated with different stages of sleep
    c. The neural circuits of sleep: orexin, ascending neuromodulatory systems, and the ventrolateral preoptic area

3. Dreaming
    a. Mechanisms of REM sleep
    b. Consequences of not getting enough REM sleep

4. Sleep Disorders
    a. Narcolepsy and orexin neurons
    b. Sleep disorders and psychiatric disease

Study Questions

1. What is a likely explanation for the brain's relative insensitivity to sensory input during REM sleep compared to the waking state?

2. How do neuromodulators affect the function of the thalamus during waking and sleep?

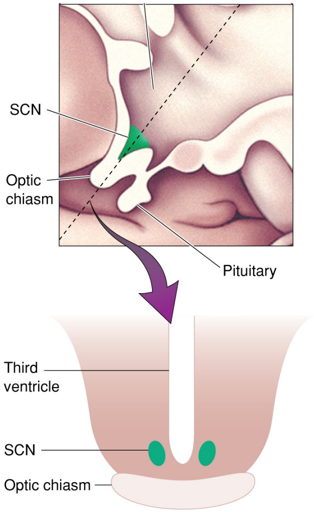
NEUROBIOLOGY AND BEHAVIOR II: INTRODUCTION TO NEUROSCIENCE

BioNB 2220

Lecture 36: Sleep

April 24, 2019

Melissa R. Warden, PhD



What is sleep?

Sleep behavior is conserved and present in essentially all animal species

Characterized by:

Behavioral quiescence (low activity)
Increased arousal threshold
Rapid reversibility
Homeostasis – sleep need builds up
Cyclical

What happens if we don't sleep?

Cognitive deficits

- Increased reaction time
- Decreased accuracy
- Memory impairment
- Increased impulsivity

Depression (although short-term sleep deprivation can have an antidepressant effect)

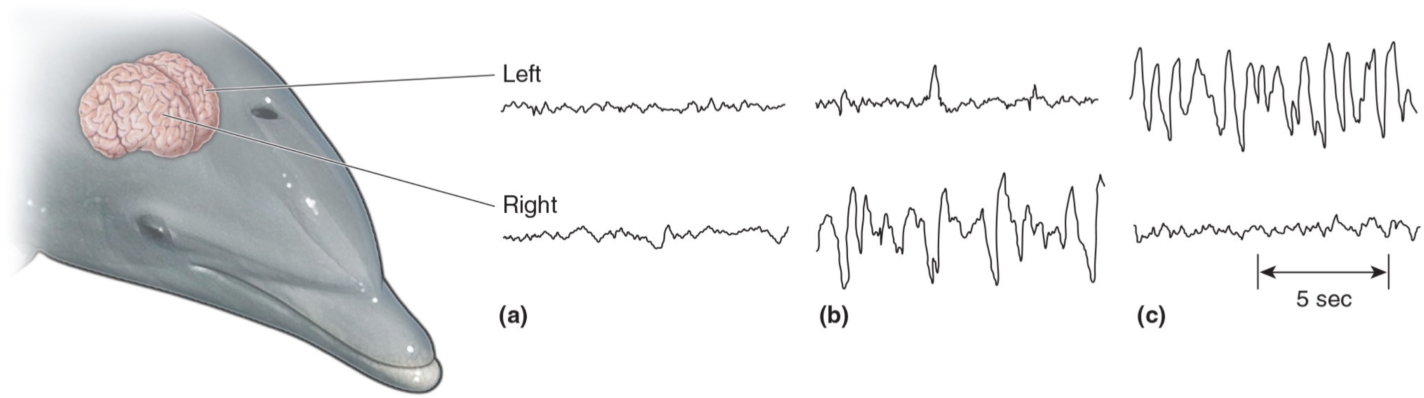
Hallucinations

Impaired immune function

Diabetes and obesity

Death (fatal familial insomnia)

Sleep in a bottlenose dolphin



- Dolphins and whales live their entire lives in water, but must breathe air every minute or so. Even so, they sleep just as much as humans do.
- Bottlenose dolphins sleep with only one hemisphere at a time.
  - 2 hours non-REM on one side
  - 1 hour both awake
  - 2 hours non-REM on the other side
  - Repeat this for 12 hours. No REM sleep.
- Dolphins have evolved clever mechanisms to make sure they get enough sleep. Why is sleep so important?

Why do we sleep?

Major theories:

Synaptic Homeostasis

- Memory encoding during wakefulness promotes the formation of synapses
- Many synapses shrink during sleep. But large, well-established synapses are spared
- Potential mechanism for memory consolidation

Sleep is restorative.

- We sleep in order to repair the brain and body.

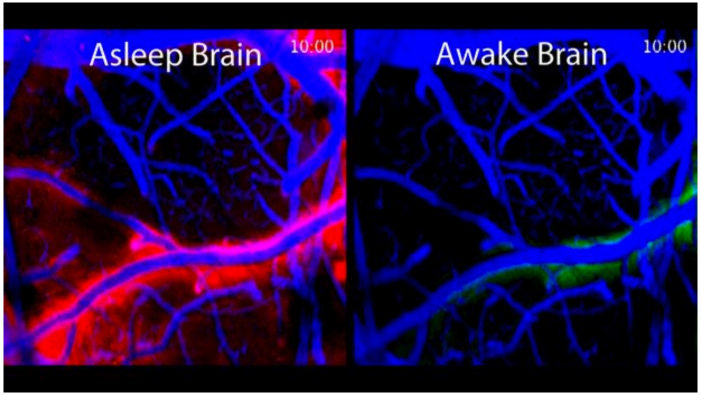
Evidence for sleep theories

Memory consolidation

- declarative memories are enhanced by deep (non-REM) sleep
- non-declarative memories are enhanced by REM sleep

Sleep is restorative

- Space between neurons expands during sleep
- Extra space enables β-amyloid and other potential toxins to be cleared more quickly



Maiken Nedergaard
University of Copenhagen

Brain states, sleep, and the electroencephalogram

Distinct patterns of brain rhythms associated with distinct sleep/wake brain states:

Awake/Dreaming

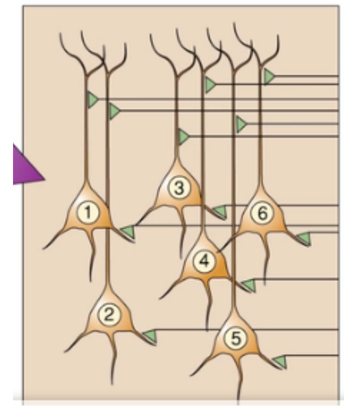
Deep sleep

Brain can generate rhythms 0.05 Hz – 500 Hz

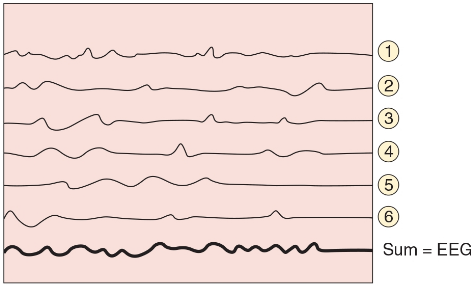
CLICKER QUESTION

What does this figure SPECIFICALLY suggest about EEG recordings?

A. EEGs that are similar between two brain areas means that there are direct neural connections between these brain areas.
B. That the more powerful the oscillations are in the EEG recording, the greater the number of cells that you are recording from.
C. That the EEG is an indicator of how synchronized neurons are in the recorded region.
D. That the morphology of the cells in a given area will influence the EEG signal.

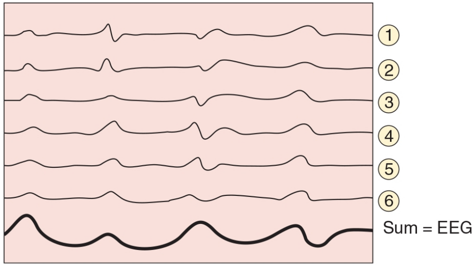


Irregular



(b)

Synchronized



(c)

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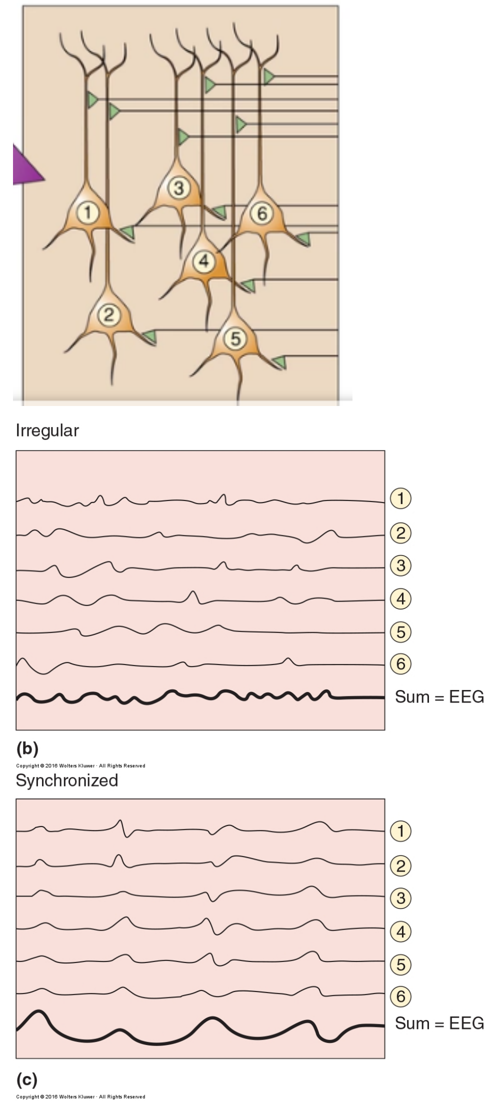

CLICKER QUESTION

Which of the following is true regarding EEG recordings from different types of mammals?

A. Different species have vastly different brain structures, and because of that very different EEG patterns.
B. Although categories of brain oscillations appear similar, they cannot be compared directly across species because our behavioral repertoires are too different.
C. Categories of brain oscillations during particular behaviors are highly conserved across mammals.
D. Larger mammals have prominent EEG rhythms; smaller animals don’t.

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D. Larger mammals have prominent EEG rhythms; smaller animals don't.

EEG rhythms and brain states

The EEG can't tell us WHAT someone is thinking, but it can tell us IF someone is thinking.

Awake states and dreaming states:

- Cortex is processing information
- Cortical firing rates are high and neurons are desynchronized
- High frequency, low amplitude EEG
- Gamma and beta rhythms dominate

Non-dreaming sleep states, some drugged states, coma:

- Cortex is 'offline'
- Cortical firing rates are low and neurons are synchronized – excited by slow, rhythmic input from the thalamus
- Low frequency, high amplitude EEG
- Delta rhythms dominate

Categorization of EEG rhythms based on frequency

Delta: slow, less than 4 Hz, large amplitude. Deep sleep.

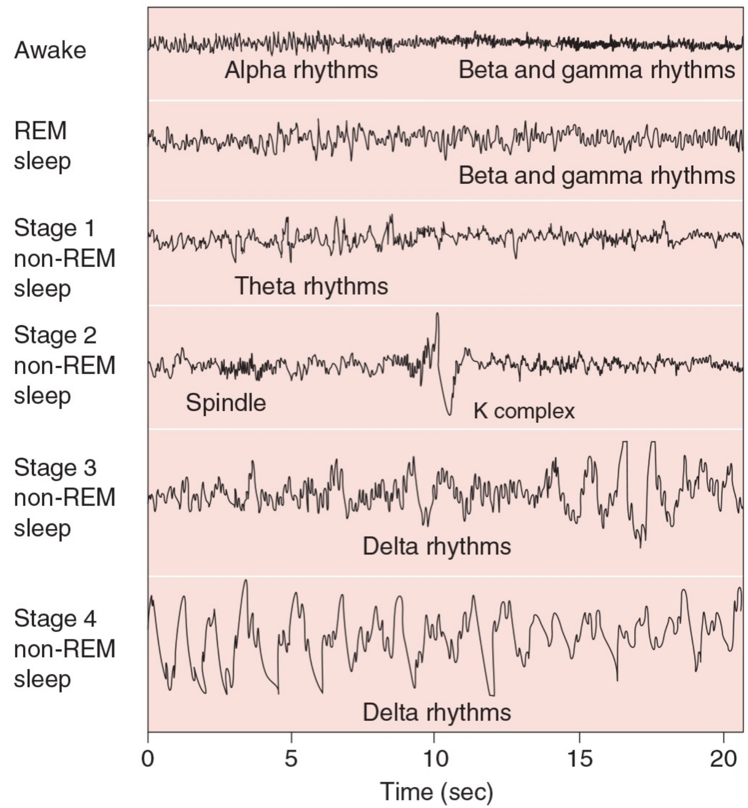
Theta: 4-7 Hz. Light sleep.

Alpha: 8-13 Hz. Quiet waking states.

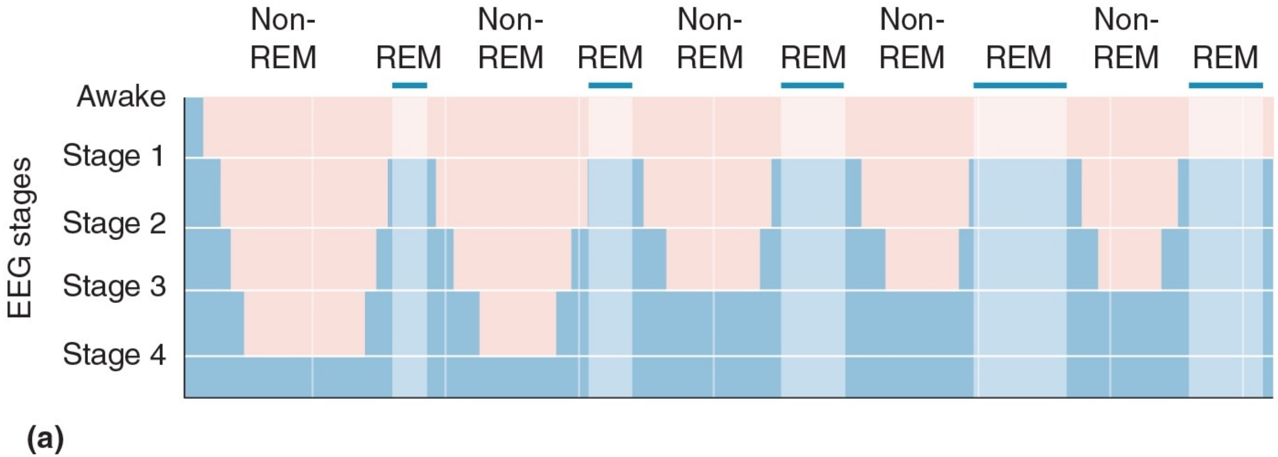
Beta: 15-30 Hz. Active states.

Gamma: 30-90 Hz. Attentive states.

Spindles: brief 8-14 Hz waves associated with sleep



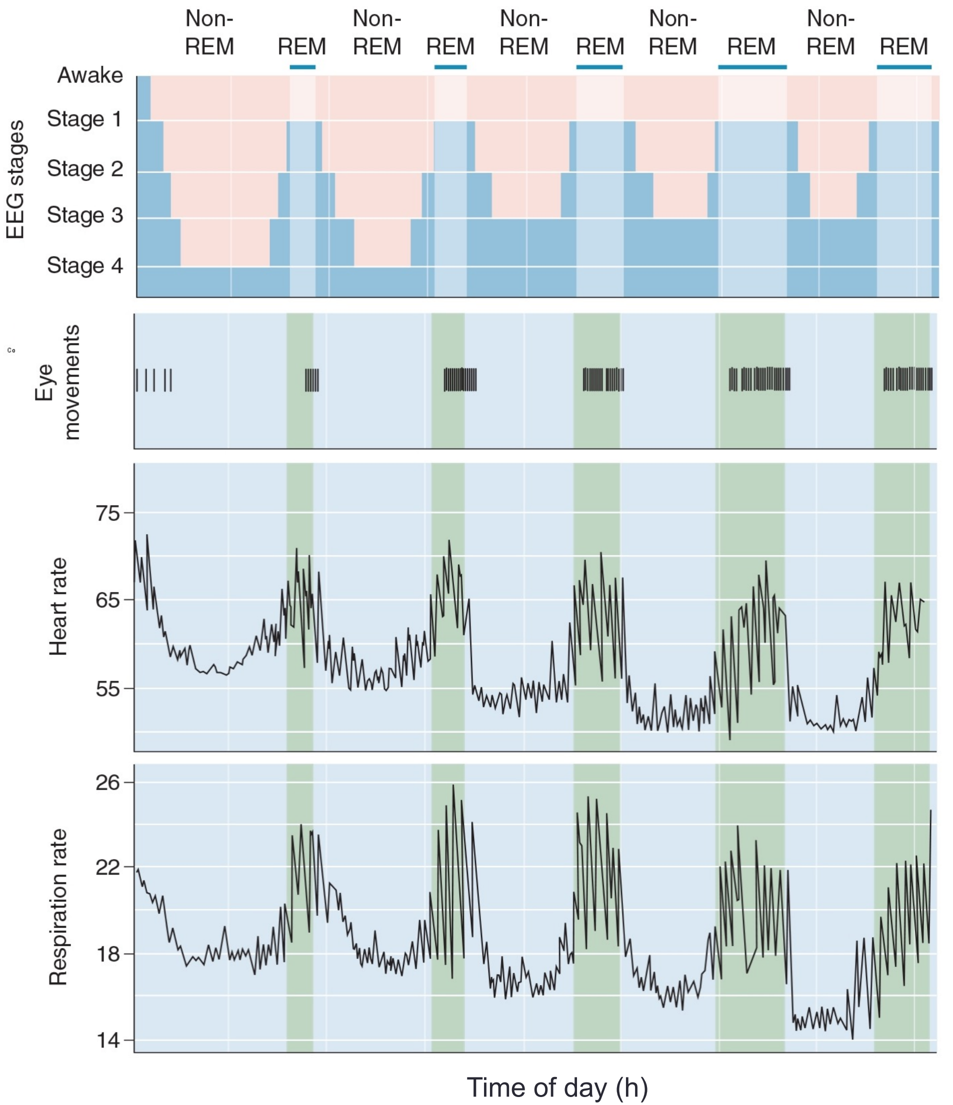
Sleep Cycle



- ~90 minutes per cycle in adults
- Oscillations in EEG, eye movements, and physiological functions (heart and respiration rate).
- 75% time spent in non-REM sleep, ~25% time spent in REM sleep.
- Non-REM sleep divided into 4 stages: 1 is lightest, 4 is deepest.

Physiological changes during REM and non-REM sleep

Regular increases in heart rate and respiration rate



How does our brain create sleeping and waking states?

Mechanisms of sleep control

Circadian rhythms

Sleep homeostasis (sleep need)

Voluntary – frontal cortex

Neural mechanisms of sleep

Until 1940's it was thought that sleep was a passive process: deprive the brain of sensory input, and it will fall asleep.

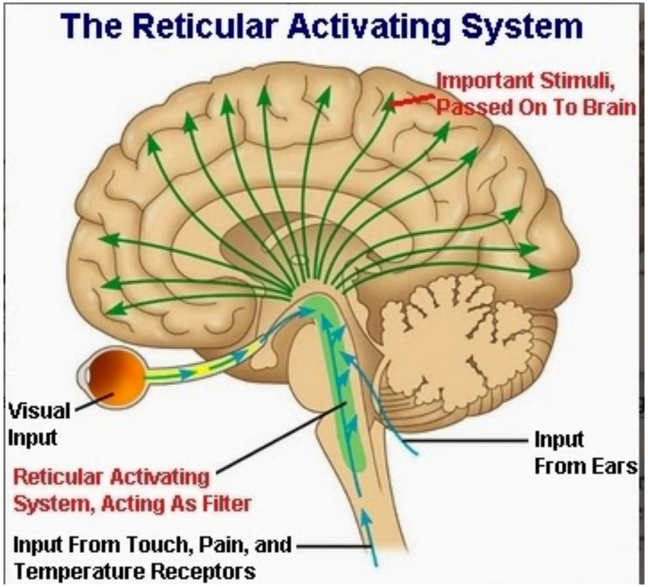
BUT if sensory afferents to brain are blocked, the animal will still have cycles of sleeping and waking.

Some of the neurons most critical to control of sleep and waking are part of the diffuse modulatory neurotransmitter systems

Reticular activating system

1940s and 50s

- Lesions in midline structures of the brainstem causes coma.
- Electrical stimulation of this region produced waking (desynchronized) EEG signal

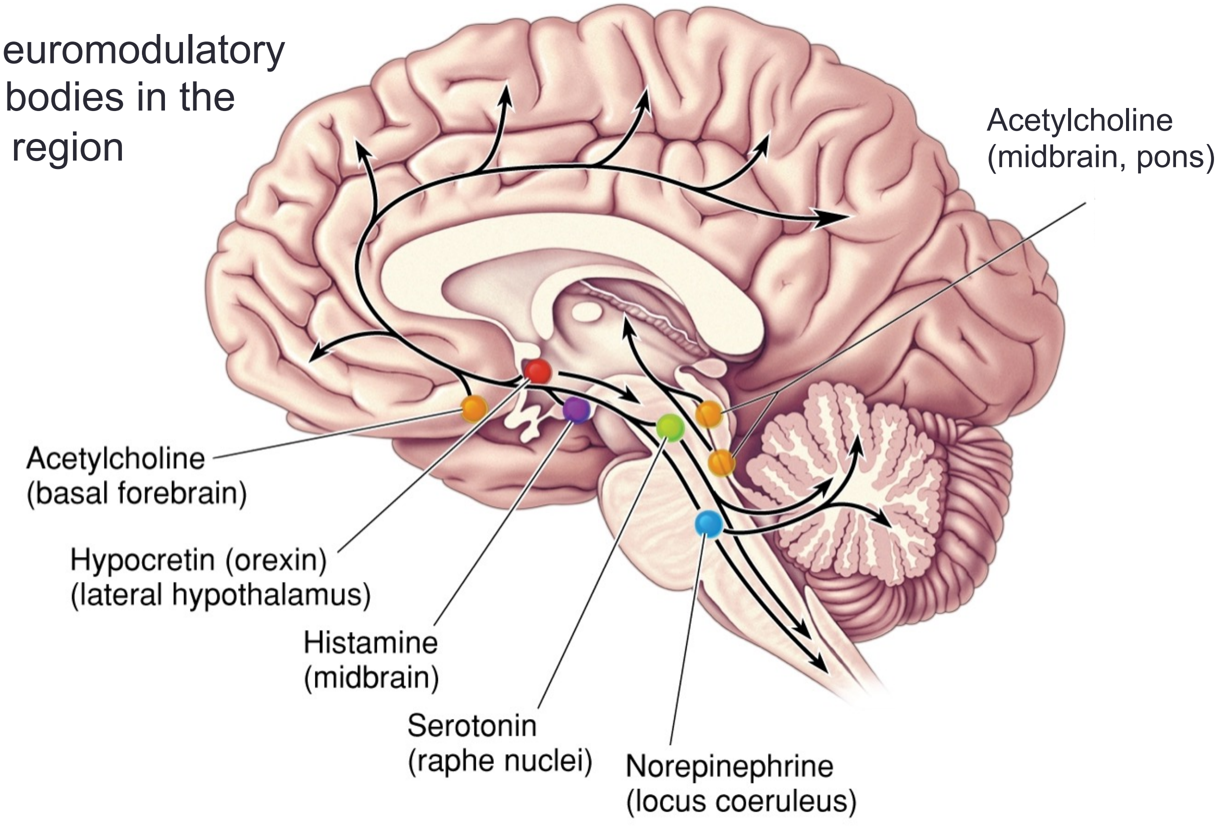


This large region is called the <u>reticular activating system</u>

The reticular activating system contains many different kinds of neurons that have different roles in sleep regulation

The neuromodulatory systems that regulate waking and sleeping

Many ascending neuromodulatory systems have cell bodies in the reticular activating region



Neuromodulators promote wakefulness

Histamine (hypothalamus). This is why antihistamines make you sleepy.

Hypocretin (hypothalamus). Neuropeptide. Modafinil (Provigil) causes hypocretin and histamine release

Norepinephrine (locus coeruleus)

Serotonin (raphe nuclei)

Acetylcholine (brainstem and basal forebrain)

The modulatory systems that regulate waking and sleeping

Neuromodulators increase their activity during the awake state:

- Hypocretin (hypothalamus).
- Histamine (midbrain)
- Norepinephrine (locus coeruleus)
- Serotonin (raphe nuclei)
- Acetylcholine (brainstem and basal forebrain)

Neurons in these systems

- Increase their firing rates during waking
- Project to the entire thalamus, cerebral cortex, and many other brain regions
- Suppress synchronization, promote waking desynchronized EEG

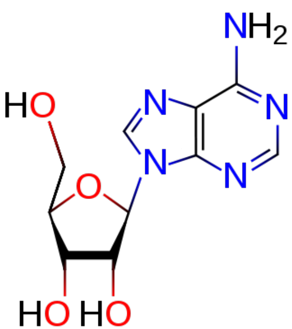
How does caffeine keep us awake?

How does caffeine work?

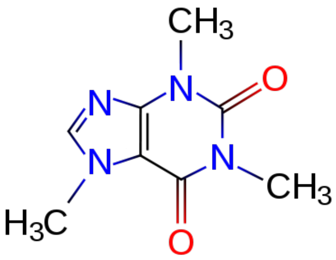
Caffeine is an antagonist of the adenosine receptor

To understand how caffeine inhibits sleep, we need to understand what adenosine does in the brain

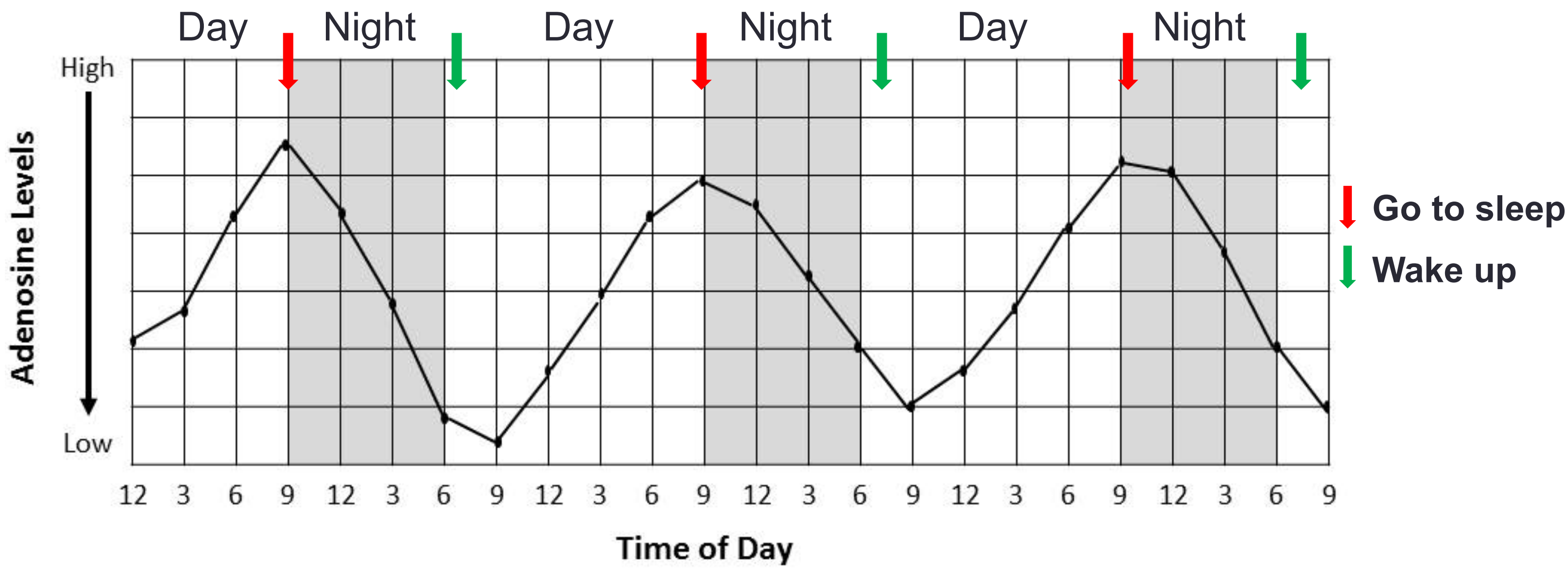
Adenosine



Caffeine



Adenosine Levels Cycle

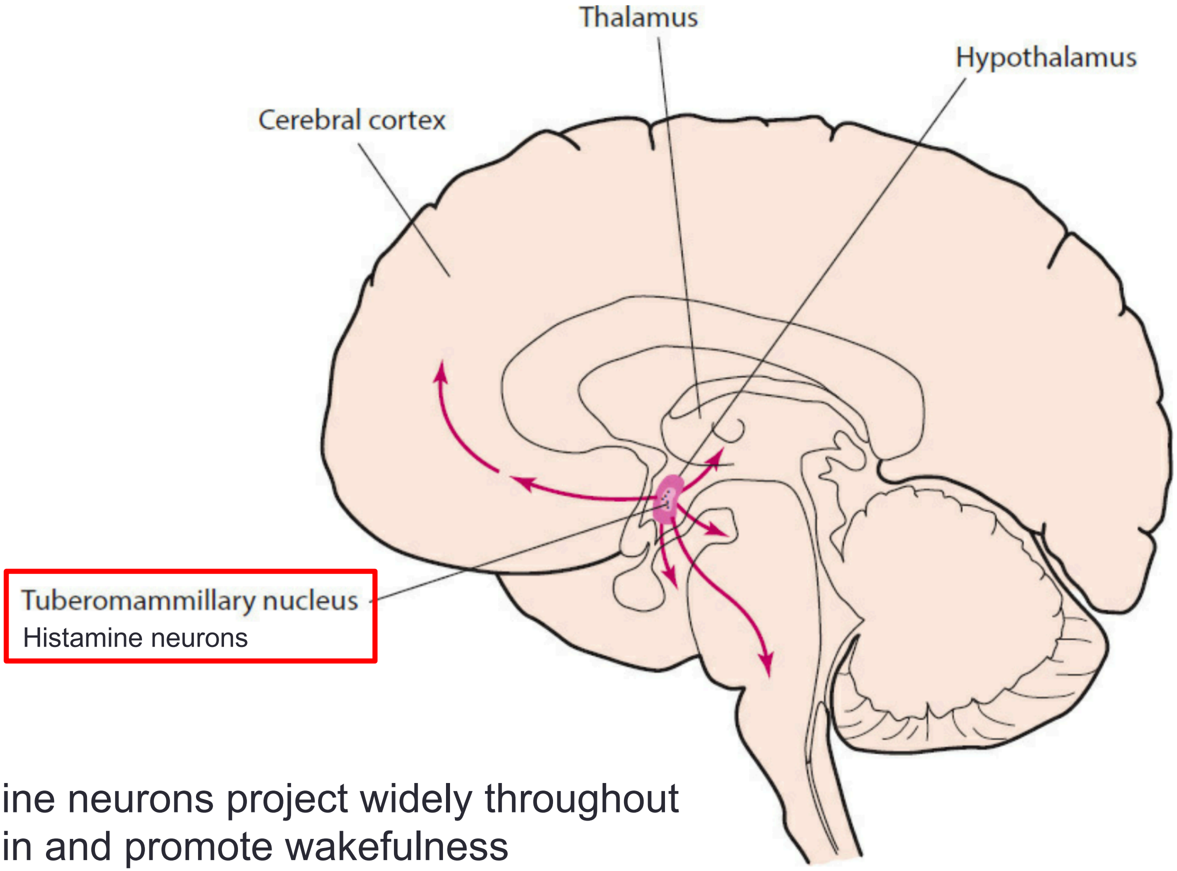


Adenosine builds up in the brain during wakefulness

- Cells use ATP (adenosine triphosphate) for energy – adenosine is a breakdown product of ATP
- Adenosine accumulates inside the cell as energy is used and ATP is depleted
- Excess adenosine is transported outside the cell to the extracellular space

Ascending neuromodulatory neurons express adenosine receptors and detect rising adenosine levels

Hypothalamic histamine neurons are part of the ascending neuromodulatory system

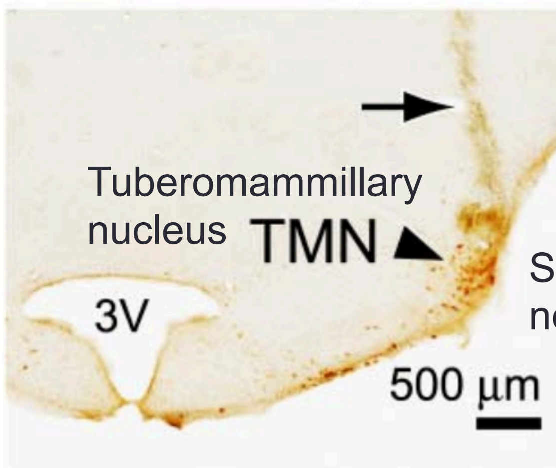


Histamine neurons project widely throughout the brain and promote wakefulness

Antihistamines promote sleep

Blocks wakefulness-promoting functions of histamine

Hypothalamic histamine neurons express adenosine receptors

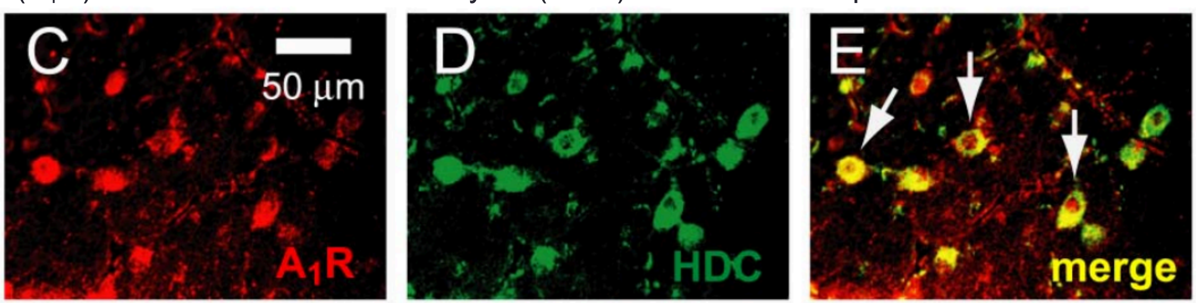


Stained for histamine neurons

Adenosine receptor (A_1R)

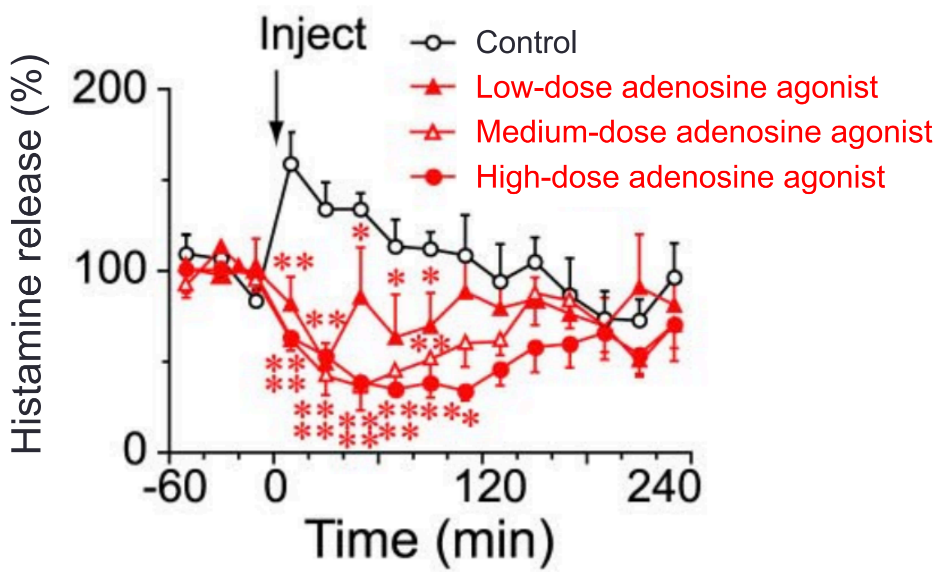
Histamine-producing enzyme (HDC)

Stains overlap – neurons express both markers



Histidine decarboxylase (HDC)

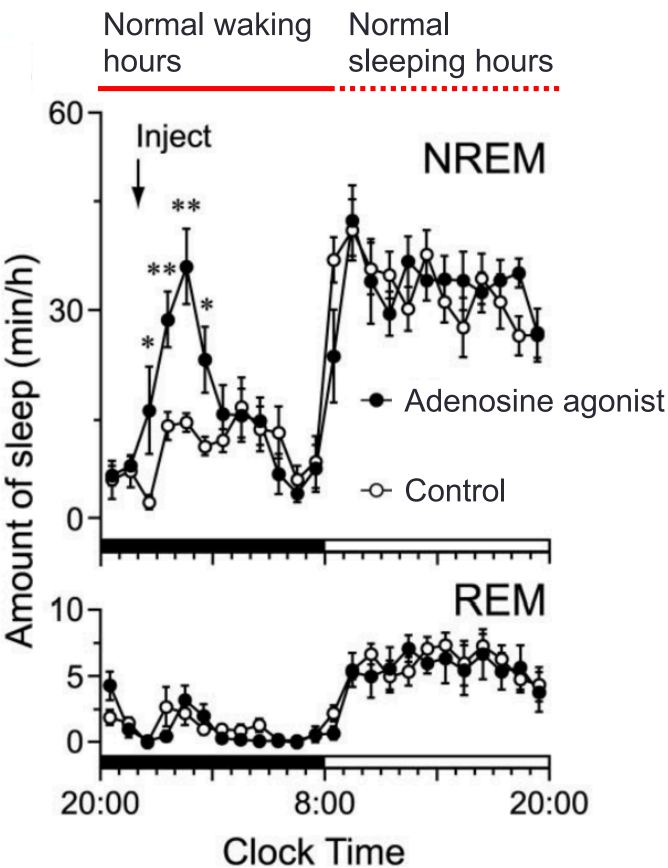
Adenosine inhibits histamine release



Injected adenosine agonist directly into the hypothalamic tuberomammillary nucleus (where histamine neurons are located)

Measured histamine release in the cortex

Adenosine promotes sleep by inhibiting histamine release



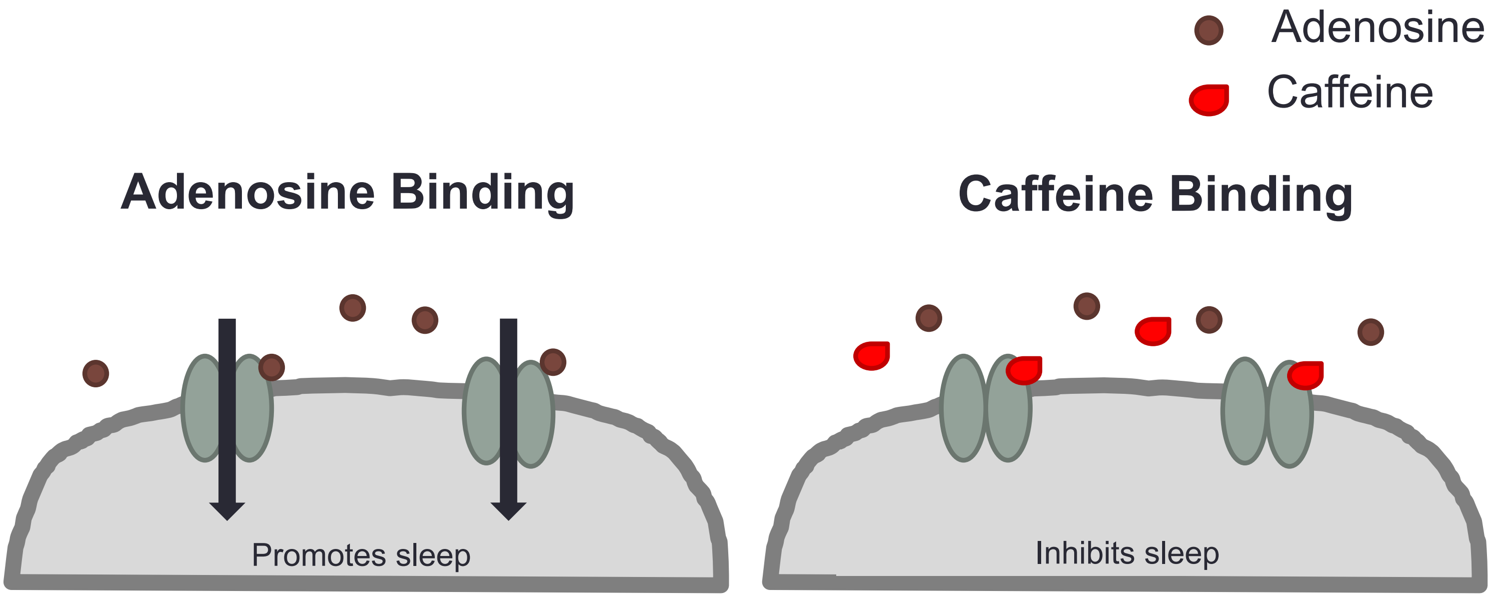
Injected adenosine agonist into the hypothalamic tuberomammillary nucleus (where histamine neurons are located)

Result: decreased histamine release and increased sleep

Adenosine acts as a natural antihistamine

How does caffeine work?

Caffeine is an antagonist of the adenosine receptor



Circadian rhythms

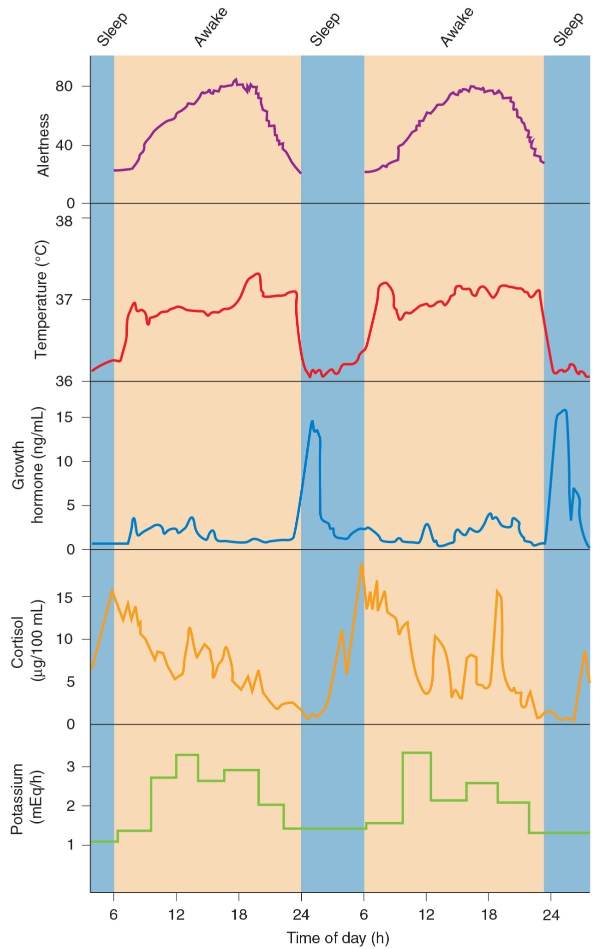
Circadian rhythms

Behavior coordinated with daily cycles of daylight and darkness. (Circa = approximately; Dies = day)

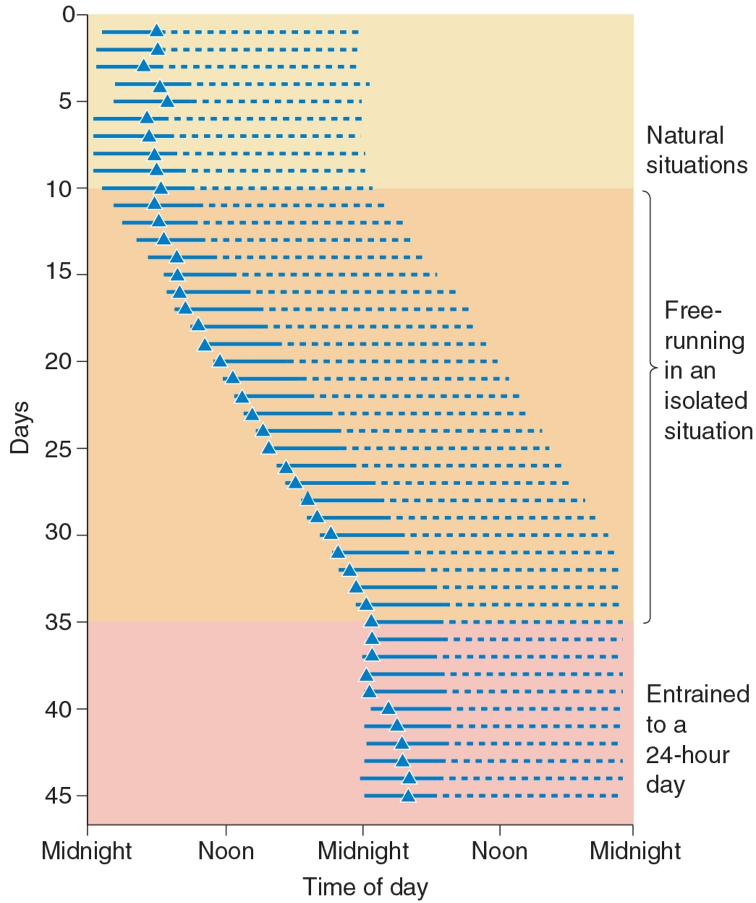
Daily fluctuations of physiological and biochemical processes.

When daylight/darkness cycles are removed, circadian rhythms continue on more or less the same schedule.

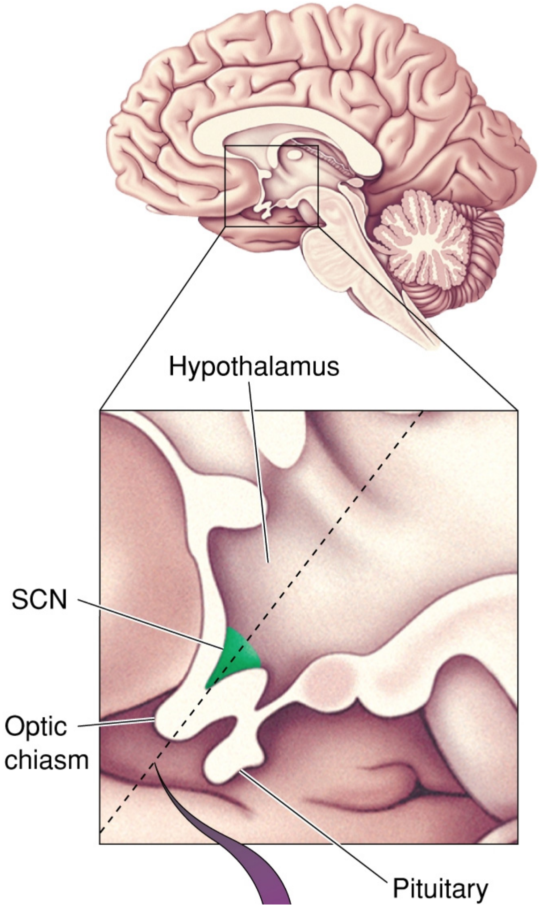
Circadian rhythms of physiological functions



Circadian rhythms contribute to daily rhythms of animals, but other cues are used to adjust cycle



The human suprachiasmatic nuclei



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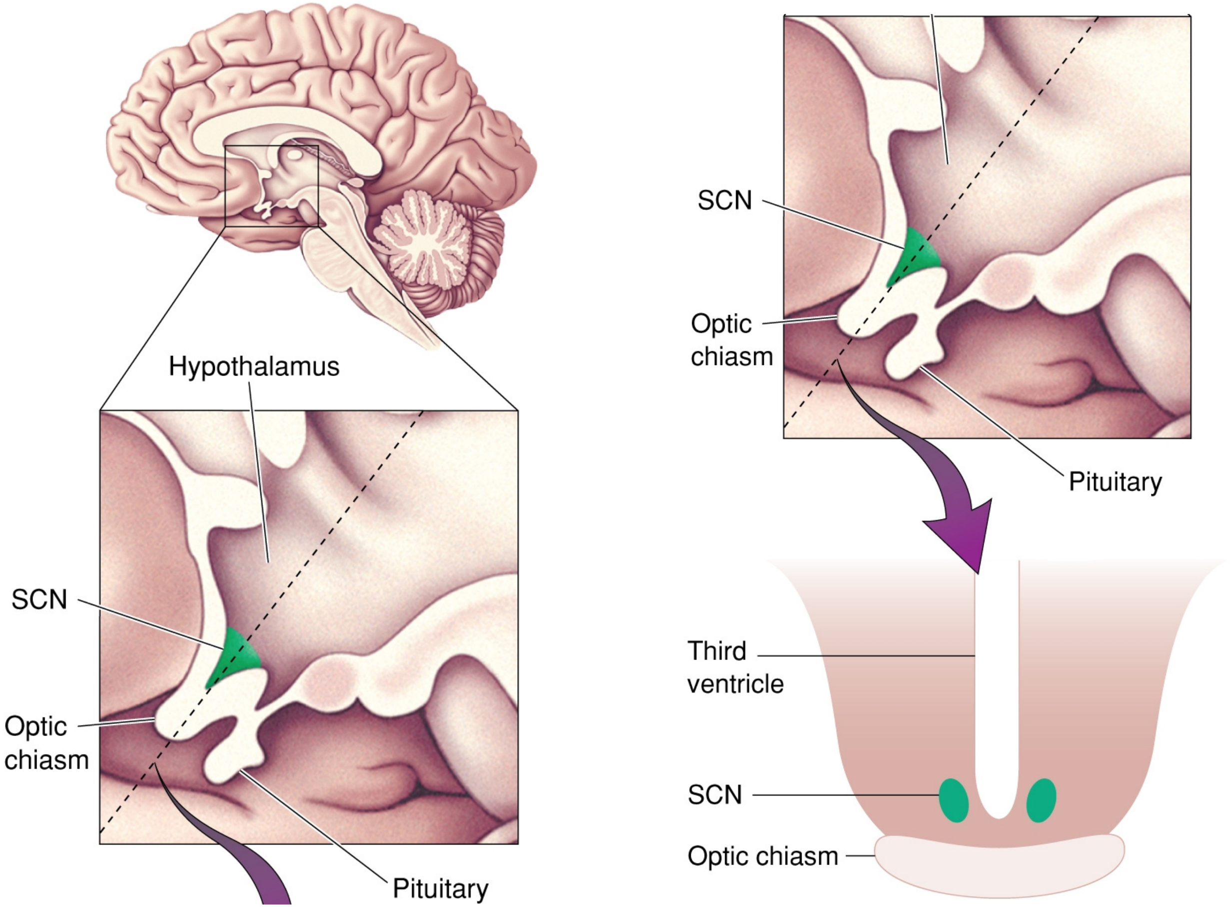
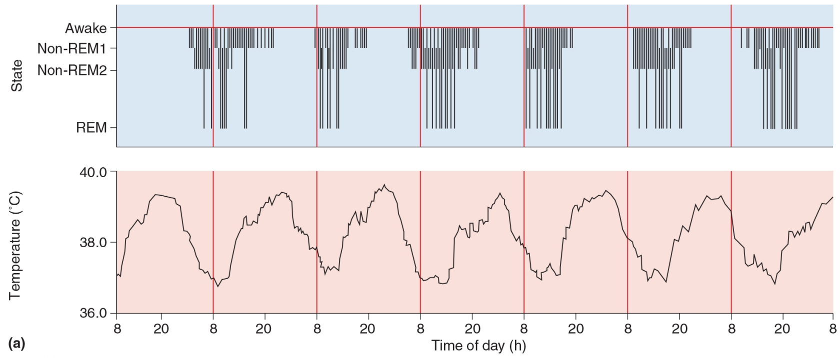


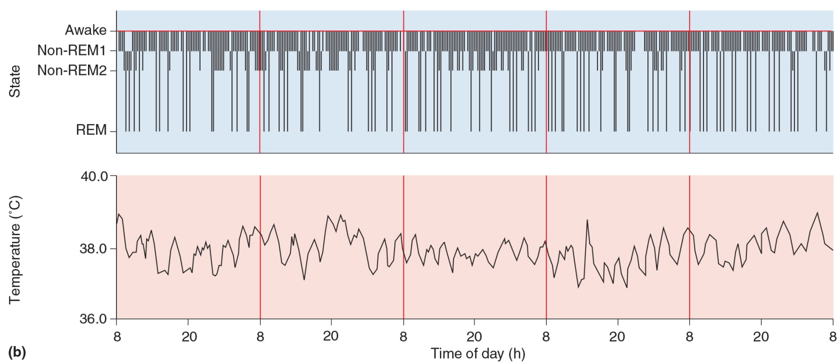
Suprachiasmatic nucleus (SCN) is essential for normal sleep rhythms

Squirrel monkey kept in a constantly lit environment

Bilateral SCN lesions lead to abnormal, rapid cycling sleep and physiological rhythms

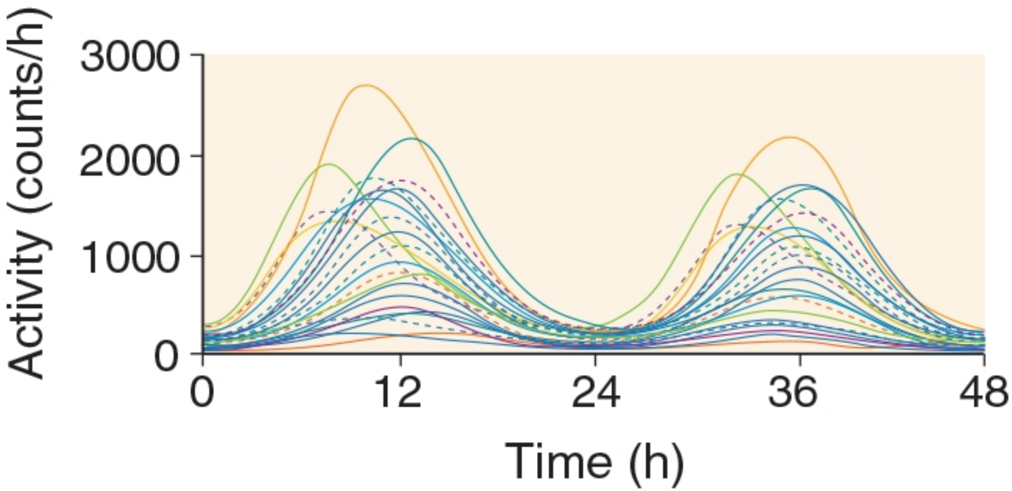


Normal squirrel monkey



Squirrel monkey with SCN lesion

Circadian rhythms of the SCN isolated from the rest of the brain



Individual cultured SCN cells will continue to cycle when removed from the body and from each other! Daily fluctuations in firing rate.

SCN rhythms can be adjusted by external inputs. For example, the retina sends a direct projection to the SCN.

SCN control of sleep cycles

SCN activity controls the activity of the ascending neuromodulatory systems

Indirect control – via intermediate nuclei