

Neurobiology of Sleep

February 18, 2015



History of sleep research

What is sleep?

Sleep cycle

Quantification of sleep

Neural centers for sleep and wakefulness

Dreaming and REM sleep

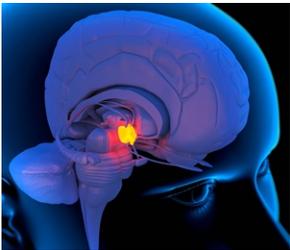
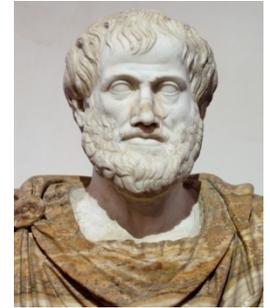
Sleep and circadian rhythm

Sleep homeostasis

Sleep disorders

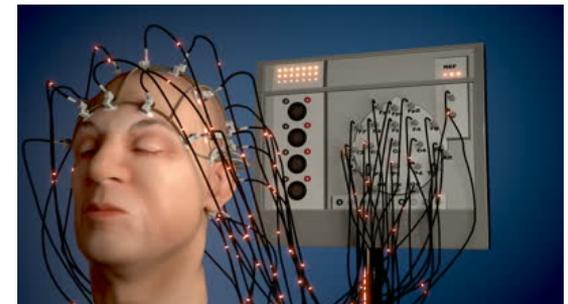
History of Sleep research

Aristotle concocted an interesting (and altogether wrong) theory in the **4th Century BC**. He believed that the digestion of food created warm vapor that rise from the stomach and collect in the head, where they cool and condense, flowing down to the heart (which he believed to be the body's sensory centre), which then caused **sleep** as it cooled.

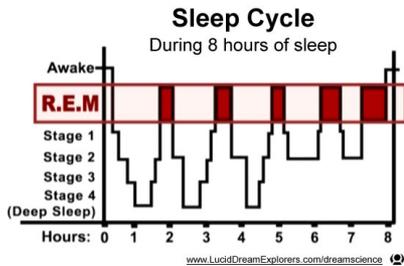
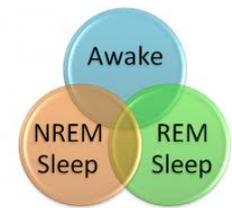


Romanian neurologist **Constantin Von Economo** pinpoints the origin of sleep and wake signals in the **hypothalamus** area of the brain in **1916**.

Invention of the **electroencephalograph** by German **sleep** researcher **Hans Berger** in the late 1920s, and his subsequent realization that **brain waves** change as **wakefulness** gave way to **sleep**, prompted a rapid expansion of **sleep** study in the 1930s, 1940s and 1950s.



Nathaniel Kleitman and his colleagues first pointed out the different types of **REM** and **non-REM sleep** in **1953**



William C. Dement showed that a night's **sleep** consists of several repeating **sleep cycles**, each composed of different **sleep stages**. By **1968**, the different **sleep stages** had become standardized

Romanian-born scientist **Franz Halberg** (the “father of **chronobiology**”) researches **circadian rhythms** and first uses the term “circadian” in **1959**



Japanese-American neurobiologist **Joseph Takahashi** identifies and clones the **CLOCK** circadian gene in **1997**

Present research focus is on:

Treatment of sleep disorders

Maintenance and regulation of circadian rhythm

Neural circuits involved and their neuromodulation



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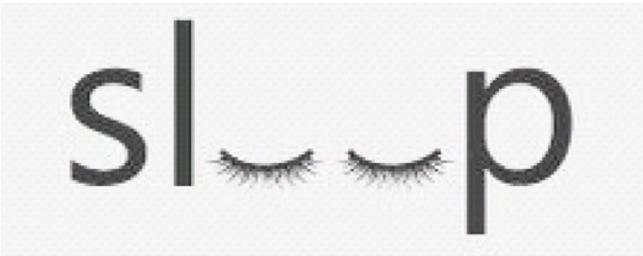
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Sleep is a natural, periodically recurring state of inactivity, characterized by the loss of consciousness and reduced responsiveness to external stimuli.

Two Types of Sleep

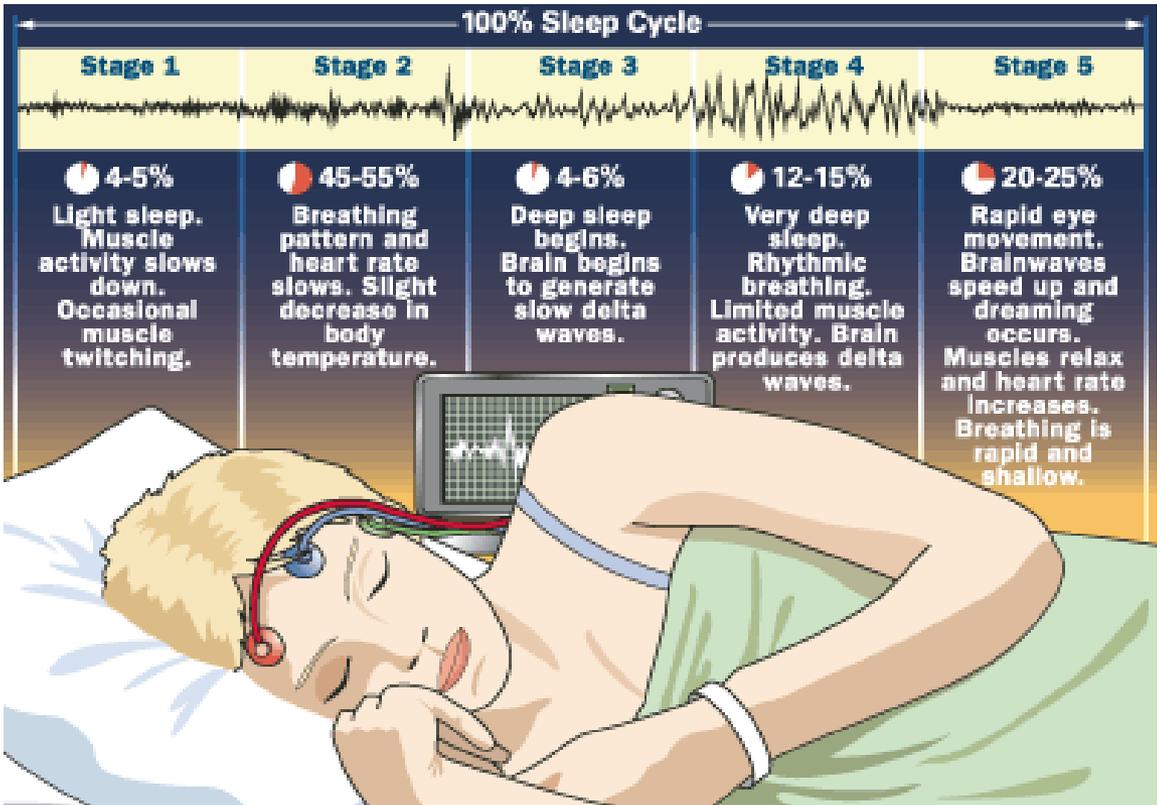
non-REM

- Stage 1
- Stage 2
- Stage 3
- Stage 4

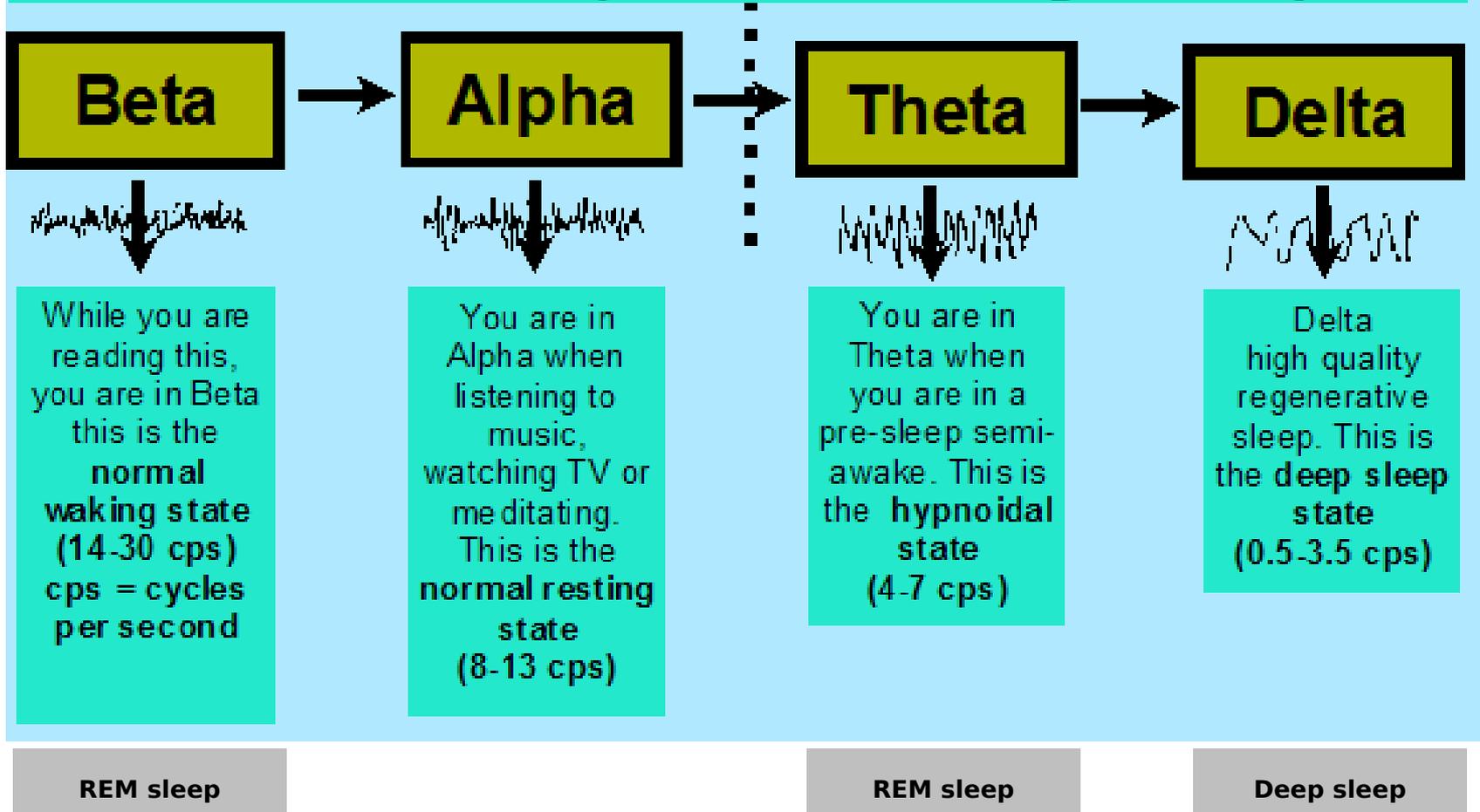
75%

REM

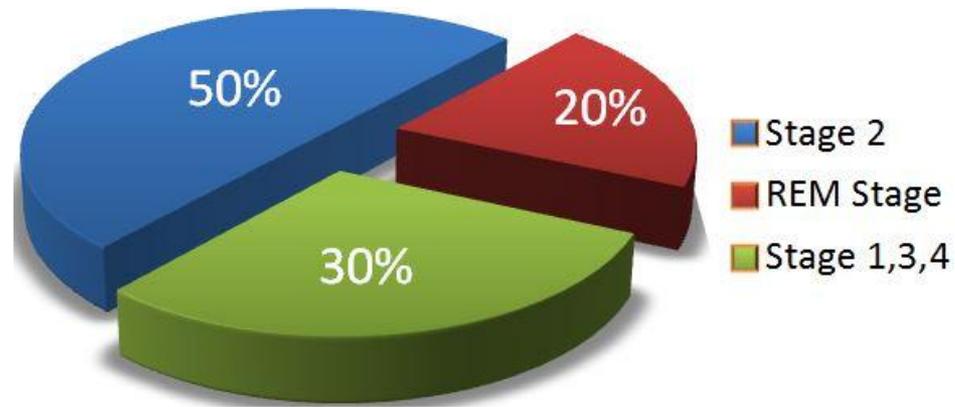
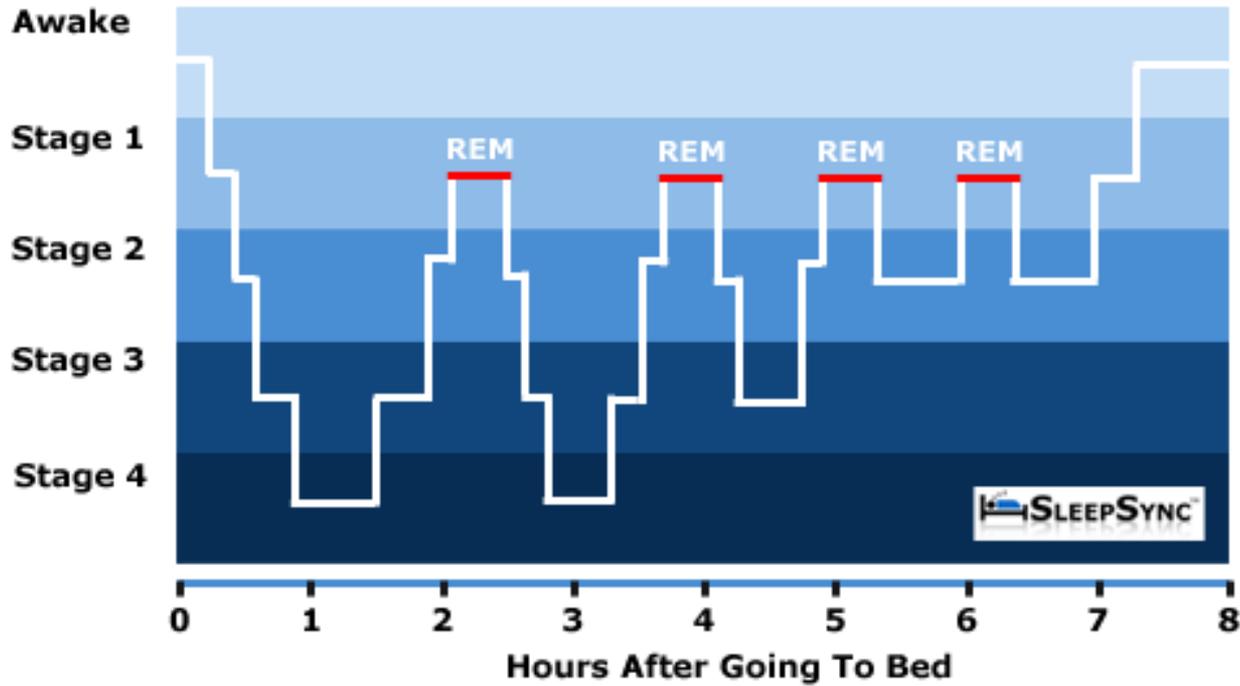
25%



Brain wave frequencies relating to sleep



A Typical 8 Hour Sleep Cycle



Total Sleep Time In Different Sleep Stages



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Polysomnography(PSG)

The Method of Measuring Sleep is Known as Polysomnography

EEG

EOG

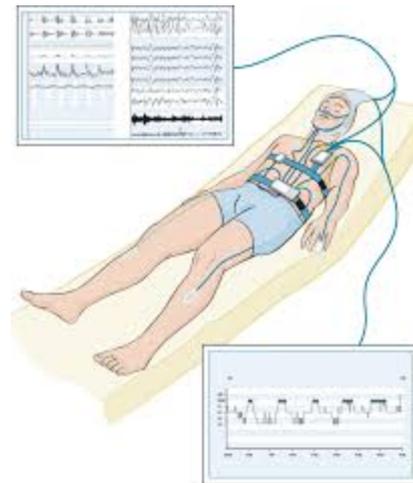
EMG

Electroencephalography Electrooculography Electromyography

Polysomnography(PSG)

Electroencephalography (EEG) is used to differentiate changes in alertness and sleep stages. For the analysis of the states of sleep and wakefulness, EEG frequencies are conveniently grouped into bands:

- Delta, 0.5 to 4 Hz
- Theta, 4 to 8 Hz
- Alpha, 8 to 12 Hz
- Sigma, 12 to 14 Hz
- Beta, 14 to 30 Hz
- Gamma, 30 to 50 Hz



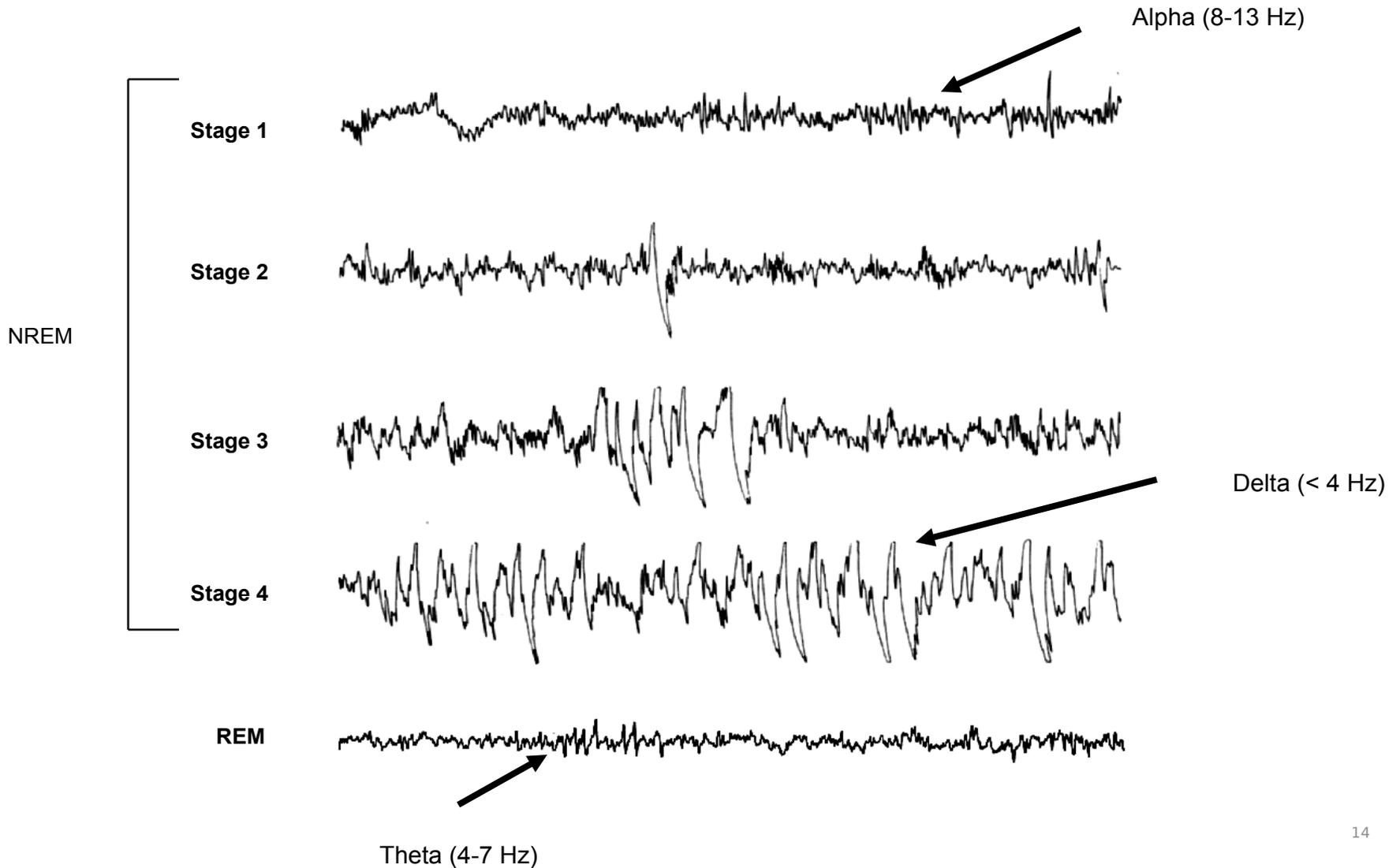
EEG data are combined with those from concurrent recording of eye movements from the electrooculogram (EOG), and muscle tone from the electromyogram (EMG) to define the states of sleep and wakefulness.

This whole system of assessment is usually called polysomnography (PSG).

Additional variables:

respiratory movements, heart rate, blood oxygen, leg movements

EEG waves differ across sleep stages





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Sleep – wake switch

- About a century ago, von Economo predicted a wake-promoting area in the posterior hypothalamus and a sleep-promoting region in the preoptic area.
- Recent studies have identified **ventrolateral preoptic (VLPO)** nucleus as the sleep regulating center and **orexin/hypocretin** neurons in the posterior **lateral hypothalamus** as the wakefulness center.



VLPO

contains GABAergic and galaninergic neurons

active during sleep and are necessary for normal sleep

Lateral hypothalamus

contains orexin/hypocretin neurons

crucial for maintaining normal wakefulness





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Dreaming.. and REM sleep



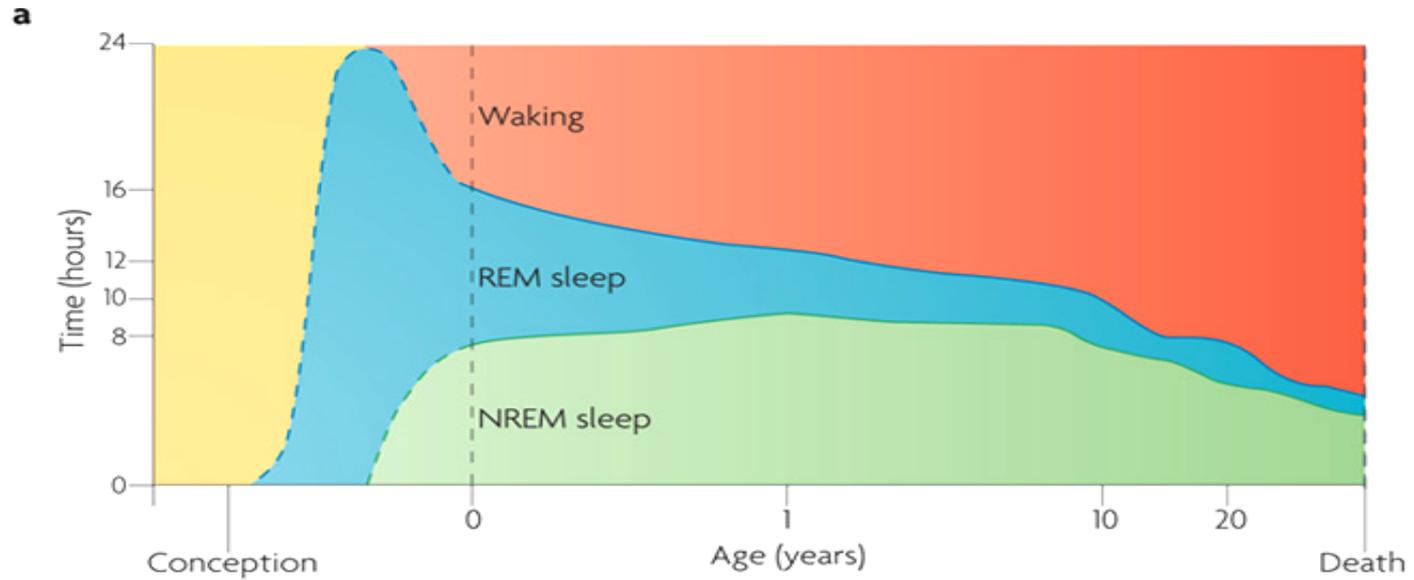
Most dreaming occurs during REM sleep.

During REM sleep, a person's eyes move back and forth rapidly.

REMsleep involves rapid bursts of brainwaves (beta and theta).

HeartRate increases with blood pressure, breathing becomes faster and more irregular, may have twitches in face and hands.

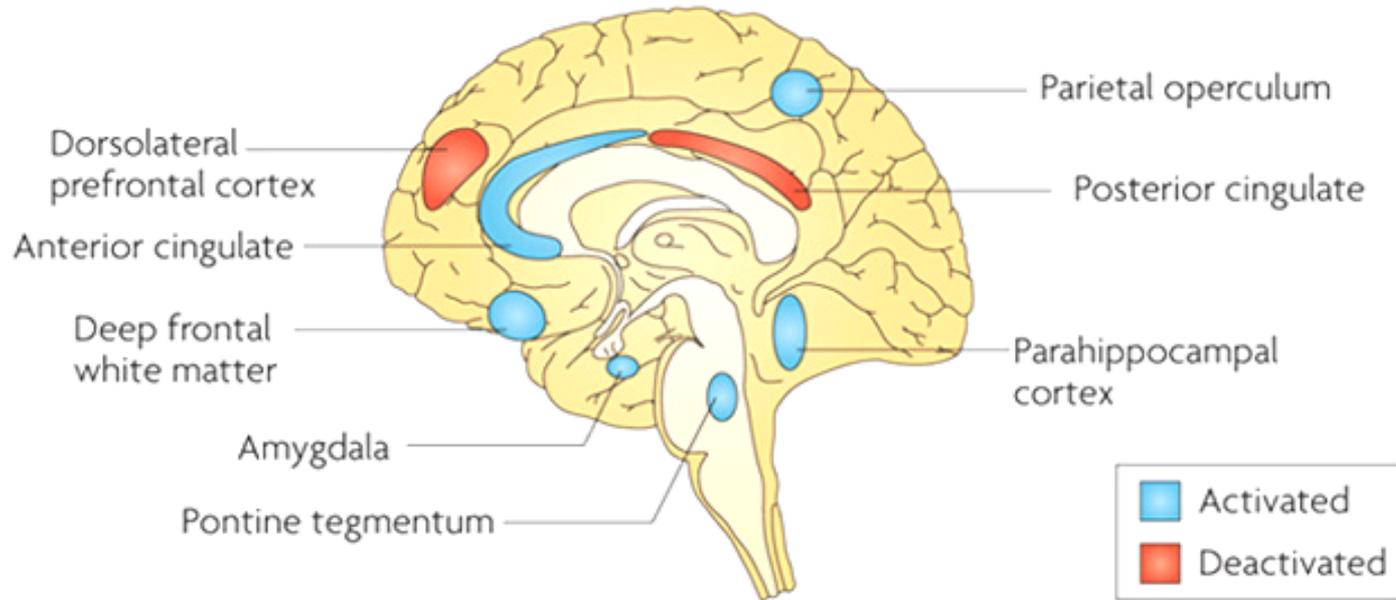
Human sleep and age



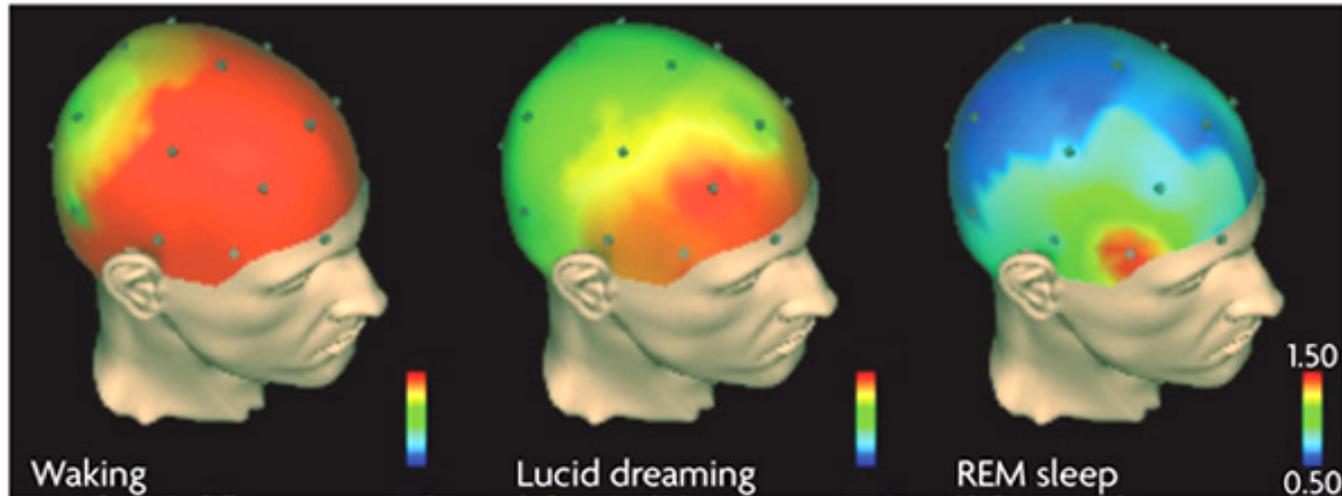
REM plays important role in early brain development and later, is essential for maintenance of brain function.

Differentiated regional activation may underlie the phenomenological distinction between the states of REM sleep, lucid dreaming and waking

a

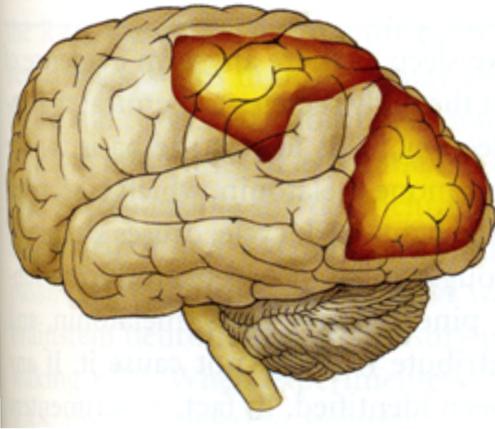


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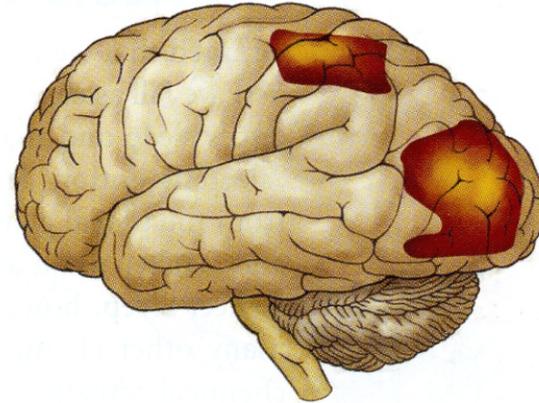
REM sleep in learning and memory consolidation

(A) Reaction-time task



Subjects are trained on a reaction-time task, and brain activity is recorded with PET.

(B) REM sleep that night



Subjects display a similar pattern of brain activity during subsequent REM sleep.

<http://tonks.disted.camosun.bc.ca/>

On doing a PET scan,
similar areas show brain activity during REM sleep as well as during a reaction time
task given earlier that day!



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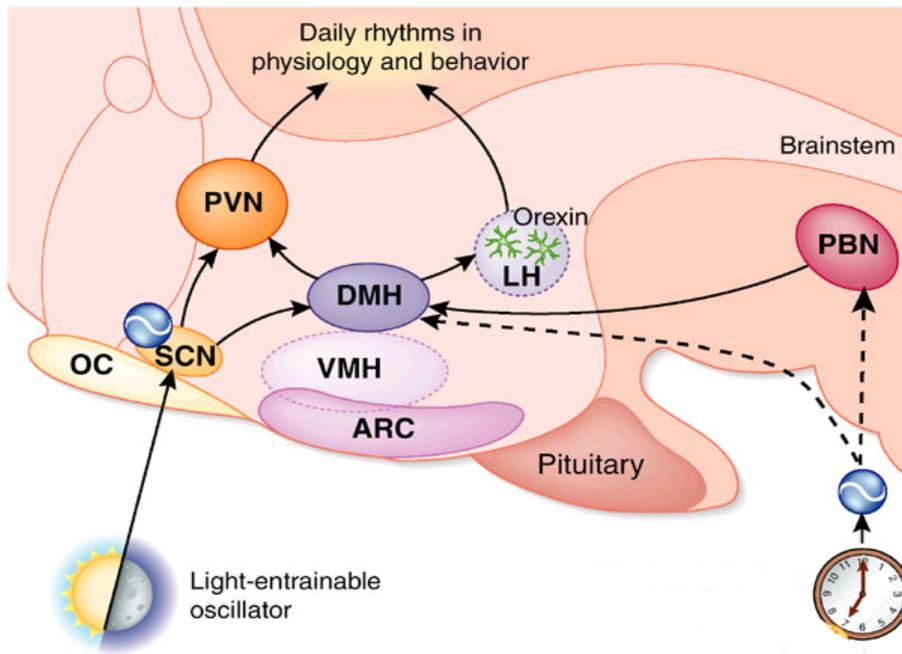
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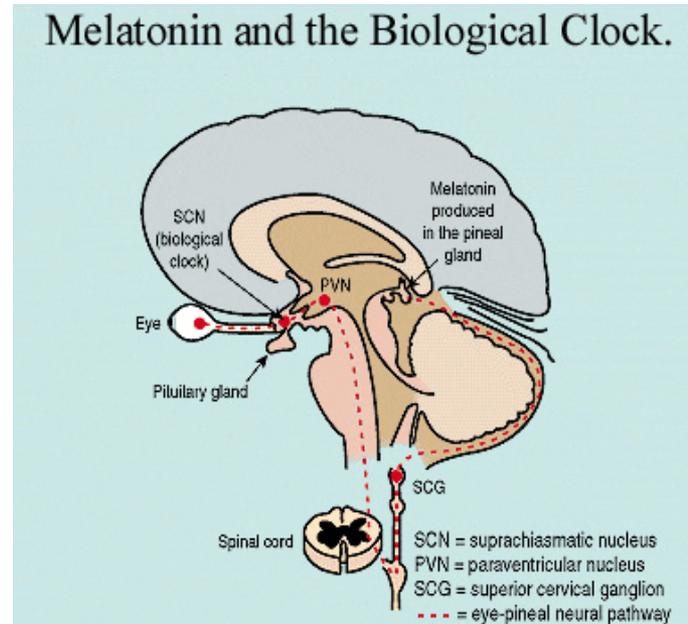
BODY CLOCK!

Suprachiasmatic nucleus

The circadian timing system is regulated by the suprachiasmatic nucleus, a small group of nerve cells in the hypothalamus that acts as a master clock.



Nature Neuroscience 9, 300 - 302 (2006)

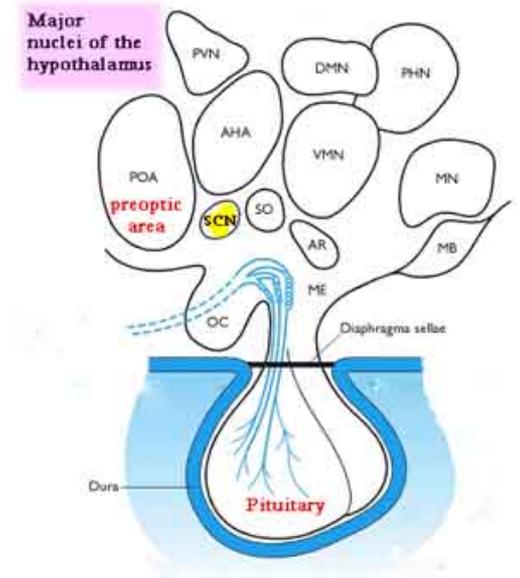


Melatonin

The body's level of melatonin (produced in Pineal gland) normally rises after darkness falls, making people feel sleepy

The suprachiasmatic nucleus (SCN)

- It synchronizes with environmental cycles in light-dark
- Light that reaches photoreceptors in the retina creates signals that travel along the optic nerve to the suprachiasmatic nucleus.
- Neurons in the SCN fire action potentials in a 24-hour rhythm. At mid-day, the firing rate reaches a maximum, and, during the night, it falls again.
- The circadian rhythm in the SCN is generated by a gene expression cycle in individual SCN neurons.
- CLOCK (circadian locomotor output cycles kaput) genes. How the gene expression cycle (so-called the core clock) connects to the neural firing remains unknown.



Sleep homeostasis



ATP - ADP - AMP - Adenosine recycling is common in cells!

Dependent on glucose, glycogen, and O_2

Brain glycogen falls with sleep deprivation

Adenosine concentration rises during wake and falls during sleep

Caffeine blocks adenosine receptors

Sleep is in sync with the body's metabolism!



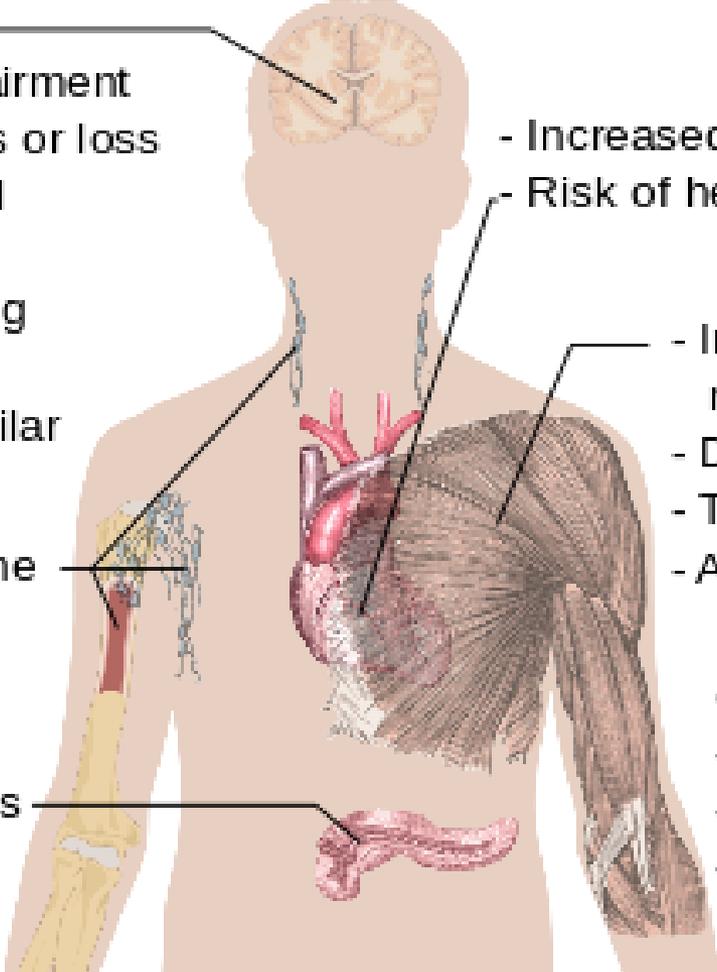
^{morning}
~~Every~~night I go to sleep late

And in the morning I realize it was a bad idea



SLEEP DEPRIVATION

Effects of Sleep deprivation

- 
- Irritability
 - Cognitive impairment
 - Memory lapses or loss
 - Impaired moral judgement
 - Severe yawning
 - Hallucinations
 - Symptoms similar to ADHD
 - Impaired immune system
 - Risk of diabetes Type 2
 - Increased heart rate variability
 - Risk of heart disease
 - Increased reaction time
 - Decreased accuracy
 - Tremors
 - Aches
- Other:*
- Growth suppression
 - Risk of obesity
 - Decreased temperature



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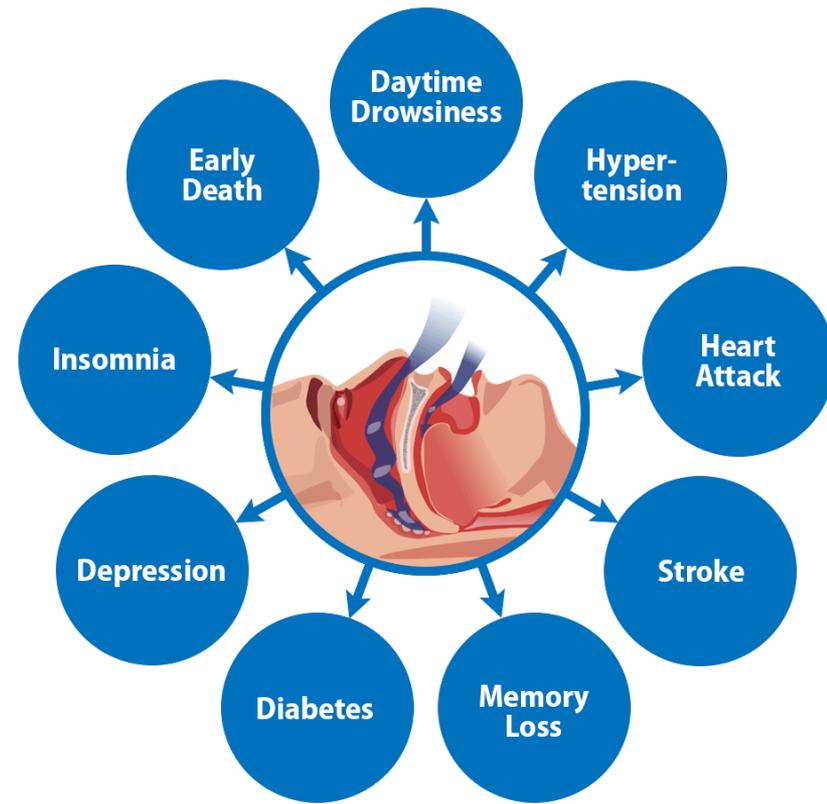
Sleep disorders

Sleep Apnea

There are two main types of sleep apnea:

Obstructive sleep apnea, the more common form that occurs when throat muscles relax

Central sleep apnea, which occurs when your brain doesn't send proper signals to the muscles that control breathing



normal airway



obstructed airway

Continuous Positive Airway Pressure (CPAP)



Narcolepsy

Narcolepsy causes excessive daytime sleepiness and sleep attacks. Those with narcolepsy tend to get to REM earlier than those with normal sleep.

Symptoms:

Excessive daytime sleepiness

Sudden loss of muscle tone

Sleep paralysis

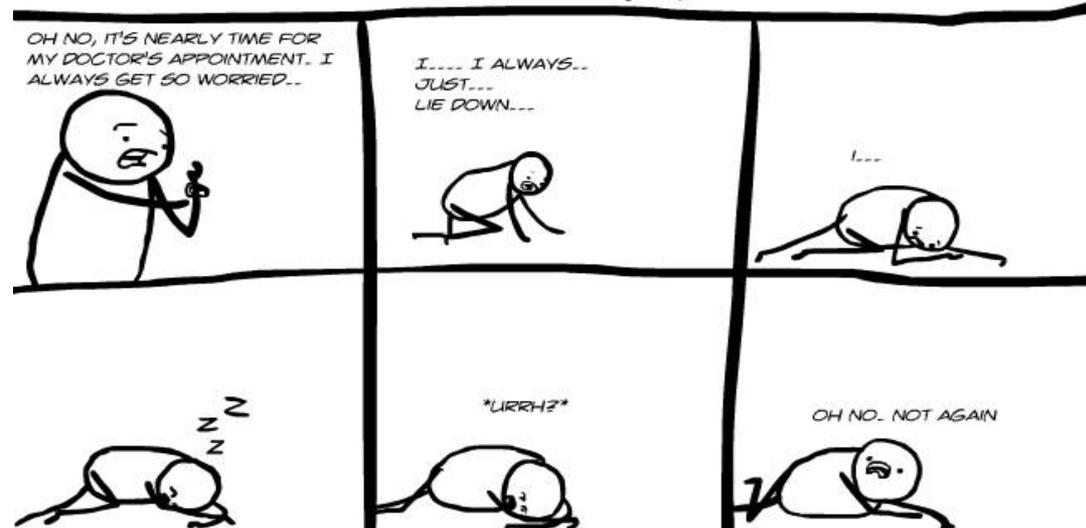
Hallucinations

Cause: Low levels of Hypocretin

No cure. Medications and lifestyle changes may help.



The Adventure Of Narcolepsy Man



Restless Leg Syndrome (RLS)

Restless Leg Syndrome is the uncontrollable urge to move your legs. Most people experience "creepy" sensations on their legs like 'itching' or 'pins and needles'.

It is also known as Willis-Ekbom disease (WED)

These sensations can go on even in your sleep causing constant sleep disturbances.

Most individuals with RLS suffer from periodic limb movement disorder (limbs jerking during sleep), which is an objective physiologic marker of the disorder and is associated with sleep disruption.

It can be caused by low iron levels
and/or imbalance in dopamine levels



Thanks for staying**awake!**

