Neurobiology of Sleep

February 18, 2015
Objectives

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 vaporsthat 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.


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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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

Beta

While you are reading this, you are in Beta this is the normal waking state (14-30 cps) cps = cycles per second

Alpha

You are in Alpha when listening to music, watching TV or meditating. This is the normal resting state (8-13 cps)

Theta

You are in Theta when you are in a pre-sleep semi-awake. This is the hypnoidal state (4-7 cps)

Delta

Delta high quality regenerative sleep. This is the deep sleep state (0.5-3.5 cps)

REM sleep

REM sleep

Deep sleep
A Typical 8 Hour Sleep Cycle

- Awake 50%
- Stage 2 30%
- REM Stage 20%
- Stage 1, 3, 4 20%

Total Sleep Time In Different Sleep Stages
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Polysomnography (PSG)

The Method of Measuring Sleep is Known as Polysomnography

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

- Alpha (8-13 Hz)
- Theta (4-7 Hz)
- Delta (< 4 Hz)

NREM

Stage 1
Stage 2
Stage 3
Stage 4
REM

Theta (4-7 Hz)
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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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Most dreaming occurs during REM sleep.

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

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

REM sleep and dreaming: towards a theory of protoconsciousness

J. Allan Hobson

Nature Reviews Neuroscience 10, 803-813 (November 2009)
Differentiated regional activation may underlie the phenomenological distinction between the states of REM sleep, lucid dreaming and waking.
REM sleep in learning and memory consolidation

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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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.

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 O₂

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!
Everynight I go to sleep late
And in the morning I realize it was a bad idea
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 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

Continuous Positive Airway Pressure (CPAP)
Narcolepsy causes excessive daytime sleepiness and sleep attacks. Those with narcolepsy tend to get to REM earlier than those with normal sleep.

Symptoms:
- Excessive daytimesleepiness
- Sudden loss of muscletone
- Sleepparalysis
- Hallucinations

Cause: Low levels of Hypocretin

No cure. Medications and lifestyle changes may help.
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**!