Sleep and sleep deprivation

Sleep Basics

• Sleep architecture:
  • Human sleep is composed of stages that repeat in cycles.
  • In adults:
  • Each cycle is 90-120 minutes
  • There are 4-6 cycles in a healthy night’s sleep

Each sleep cycle...

• Consists of REM (i.e., dream sleep) and Non-REM sleep. REM stands for “rapid eye movements.”

Basic Sleep Cycle

For the healthy adult, the first cycle is begins by going from wakefulness to non-REM sleep. The first REM period follows the first period of non REM sleep, and the two sleep states continue to alternate throughout the night with an average period of about 90 minutes. A night of normal human sleep usually consists of 4-6 non REM/REM sleep cycles.

http://www.sleepnet.com/definition.html
• Sleep Architecture: the predictable pattern of alternating REM and NREM sleep that occurs throughout the night, consisting of four NREM phases and one REM phase

• What are the sleep stages again and what basically happens in each sleep stage?

http://www.sleepfoundation.org/site/c.huIXKjM0x/F/b.2419159/k.A817/What_Happens_When_You_Sleep.htm

As we begin to fall asleep, we enter NREM sleep, which is composed of stages 1-4

Stage 1
* Between being awake and falling asleep
* Light sleep

Stage 2
* Onset of sleep
* Becoming disengaged from surroundings
* Breathing and heart rate are regular
* Body temperature drops (so sleeping in a cool room is helpful)
* Sleep spindles are seen on EEG going from stage 2 into stage 3-4 sleep – these are associated with memory enhancement.

Stage 3 and 4
* Deepest and most restorative sleep
* Blood pressure drops
* Breathing becomes slower
* Muscles are relaxed
* Blood supply to muscles increases
* Tissue growth and repair occurs
* Energy is restored
* Hormones are released, such as Growth hormone, essential for growth and development, including muscle development
* Replays of specific brain activity seen with recently learned activities are seen again on MRI. (It is believed the brain is consolidating definitive memories).
First occurs about 90 minutes after falling asleep and recurs about every 90 minutes, getting longer later in the night.

- Heart rate speeds up to waking levels or greater: Provides energy to brain and body.
- Brain is active and dreams occur.
- Eyes dart back and forth “rapid eye movement”.
- Body becomes immobile and relaxed, as muscles are turned off.

In addition, levels of the hormone cortisol dip at bedtime and increase over the night to promote alertness in the morning.

The more cortisol you have, the more alert you are.

The more alert you are, the more information you can take in.

How in the world ...

- Do we know about sleep architecture?
- We know because we can detect electrical impulses.
- We know because of something called an Electroencephalogram or EEG.

How do we know?

EEG

Brain cells communicate by producing tiny electrical impulses.

In an electroencephalogram, also called an EEG, electrodes are placed on the scalp over multiple areas of the brain to detect and record patterns of electrical activity. [http://healthguide.howstuffworks.com/eegdictionary.htm](http://healthguide.howstuffworks.com/eegdictionary.htm)

Howstuffworks.com: EEG

- The test is usually performed by an EEG technician in a specially designed room in a doctor’s office or at a hospital. A technician applies about 16 metal discs (electrodes) to different positions on the scalp using glue. The electrodes are connected by wires to an amplifier and a recording machine.
• The recording machine converts the electrical signals into a series of wavy lines that are drawn onto a moving piece of graph paper imaged into a computer.

• The wavy lines look different for each sleep stage (although REM and Wake can look similar).

A polysomnogram is a series of tests done in a sleep lab. Among other things, it includes the EEG (brain activity), EMG (muscle activity) and ECG (heart activity). It also has an oxygen meter “oximeter” to measure nocturnal oxygen levels.

Note: Most of this lecture is taken from:

• Sleep-Wake Cycle: Its Physiology and Impact on Health
• Copyright © 2006 National Sleep Foundation

www.sleepfoundation.org

Fact or Fiction: The body shuts down to rest during sleep
• First Hint: Look at the wavy lines electrodes. What are they telling you about brain activity, muscle activity and heart activity?

What happens during sleep?

• The voluntary muscles shut down during REM (ie when you are dreaming). This is so you don’t hurt yourself.
• The heart sort of shuts down during deep sleep.
• The brain – the brain not only never shuts down, it is more active during all sleep than it is awake!
**Fact or Fiction:**
The body shuts down during sleep?

- **FICTION**

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- After a good night’s sleep is because **during sleep** ...
  1) the body has actively figured how much stuff (hormones, other chemicals, antibodies) it needs to repair itself and to regulate itself and
  2) has produced these hormones, chemicals and antibodies
  3) has actively repaired itself.

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**During sleep, the body produces hormones...**

- The best known is growth hormone.
- Aside Question: A long face may not be genetic, but caused by sleeping with the mouth open as an infant. An infant that always sleeps with it’s mouth open will likely develop a long face. **Fact or Fiction?**

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**Answer: FACT.**
It grows the way it is set during sleep.

A long face is caused by sleeping with the mouth open as an infant.

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**Example**

- “Children with severe allergic rhinitis often have facial manifestations of itching and obstructed breathing, including a gaping mouth, chapped lips, evidence of sleep deprivation, a long face, dental malocclusions, and the allergic shiner, allergic salutre, or allergic crease.”

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**Aside:**

- Definition: Rhinitis = runny nose. Children with chronic runny nose due to allergy, have trouble breathing while they are sleeping and they sleep with their mouth open.
There are many causes of a "long face". One of the primary causes, however, is upper airway compromise. This may be a result of enlargement of the tonsils, adenoids, nasal turbinate, nasal polyps, hemangioma, allergies, nasal septal deviations, nasal floor narrowing, etc. The reason is they sleep with their mouth open to breathe more easily. Children grow when they sleep.

The body produces hormones that regulate both appetite and metabolism. One of these hormones is called Leptin.

Claim: Sleep deprivation, especially during childhood and adolescence is a risk factor for obesity. If you don't sleep well, this can cause you to gain weight. Fact or Fiction?

Fact: Sleep-Wake Cycle: Its Physiology and Impact on Health

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"Why is the nation getting fatter? Most experts attribute it to our sedentary lifestyle combined with our caloric intake. But we’re also getting less sleep than we used to, a factor whose role in obesity is just coming to light."

..... studies have found a correlation between inadequate sleep and insufficient levels of the hormone leptin, which regulates carbohydrate metabolism.

Low levels of leptin cause the body to crave carbohydrates regardless of the amount of calories consumed.”

Sleep deprivation causes weight gain: Fact or Fiction?

Fact

From: Sleep-Wake Cycle: Its Physiology and Impact on Health

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Aside

What is BMI?

• What is BMI?
• Body mass index, the most widely used measure of obesity.
• Calculated as (weight in kg) divided by (height-in-meters-squared)
• 25 kg/m² is normal. 30 kg/m² is the cutoff for obesity.
• When you don’t sleep well, hormones that regulate both your metabolism and your appetite are not produced in appropriate amounts. Thus you have slower metabolism and your appetite is increased, causing you to gain weight.

Again...

Example #1

During sleep, the body produces antibodies and fights infection

Example #1: To the editor:

"Popular wisdom holds that not getting enough sleep increases the propensity of catching a cold or other ailments. In America, sleep duration has steadily declined from nearly 9 hours in 1960 to less than 7 currently. Although adverse effects of sleep deprivation on immune parameters have been documented, the clinical implications of these findings are unclear. We examined the effect of sleep deprivation on immune response to influenza vaccination."

Example #2

"Flu shots were administered to men who had been restricted to just four hours of sleep per night for four straight nights and to those who had slept normally. Ten days after vaccination, those in the sleep deprived group had a substantially lower immune response compared with those who got adequate sleep, producing less than half as many flu-fighting antibodies."

What happened?

Example #2

• Similar to example #1, but with the HepatitisA vaccine often given to health care workers. Lange T. Perrus B. Fehm HL. Born J. Sleep enhances the human antibody response to hepatitis A vaccination. Psychosomatic Medicine. 65(5):831-5; 2003 Sep-Oct.

• Abstract

• OBJECTIVE: METHODS: Two groups of healthy humans (N = 19) not previously infected with hepatitis A virus (HAV) were studied. On the night after primary vaccination with inactivated HAV, which took place at 0900 hours, one group had regular sleep. The other group stayed awake, and did not sleep before 2100 hours the following day.

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What happened?

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Example #2 continued

• **RESULTS**: Subjects who had regular sleep after vaccination, displayed a nearly twofold higher HAV antibody titer after 4 weeks than subjects staying awake on this night \((p=0.018)\). Compared with wakefulness, sleep after vaccination distinctly increased release of several immune-stimulating hormones including growth hormone, prolactin, and dopamine \((p < 0.01)\). **CONCLUSIONS**: Data suggest that sleep compared with sleep deprivation on the night after vaccination improves the formation of antigen-specific immune defense as reflected by antibody production in humans.

Notice the brain activity especially during deep sleep it’s thinking – that’s why people wake up knowing things. (This is not a myth)

How do we know people (and animals) think during sleep?

1. Rat studies: Rats exposed to environmental enrichment develop larger brains and more synaptic connections **IF AND ONLY IF** they are allowed to sleep normally.

2. Many studies that wake people up during NREM sleep indicate mentation (thinking). 50% can remember what they were thinking about right before they were woken up. These thoughts are not dream-like (they are not bizarre) but often related to a current problem the person is experiencing.

3. Studies show the following:
   - Significantly better absorption of information when someone is alert vs someone who is sleep deprived
   - Significantly better synthesis of learned information after a good night’s sleep vs before going to sleep.
   - In particular, skills like playing chess are consolidated and incorporated into the brain during sleep

4. Sleep "spindles" – vertical lines going from phase 2 to phase 3 sleep that are seen on EEG are associated better recall of information learned the previous day.
5. You can actually see thinking on MRI! We know what parts of the brain light up when specific types of tasks are being learned. These same parts light up during sleep.

Some references for sleep thinking and memory:

• Catherine M Hill, Alexandra M Hogan, Annette Karmiloff-Smith To sleep, perchance to enrich learning? Arch Dis Child 2007;92:637–643. “There is evidence that sleep enhances memory and learning. ... and minor but persistent disruption of sleep may have long-term implications for cognitive performance.”

Some references for sleep thinking and memory:

• Nielsen, T A. A review of mentation in REM and NREM sleep: "covert" REM sleep as a possible reconciliation of two opposing models. Behavioral & Brain Sciences. 23(6):851-66; discussion 904-1121, 2000 Dec. “Numerous studies have replicated the finding of mentation in both rapid eye movement (REM) and non-rapid eye movement (NREM) sleep.”

How much sleep does a person optimally need?

• Infants >14 hours. Newborns spend up to 20 of every 24 h asleep, reducing to 14 h by 4 months, 11 h by 6 months and to around 10 h for the rest of the first 2 years.
• Adolescents 9-10 hours
• Middle age 7-9 hours
• Old age 7-9 hours, but they don’t get it

What happens to people who are sleep deprived?

• All of the following have been shown in studies
  - Become irritable and emotional
  - Lose some of their moral compass
  - Cognition is impaired
  - More likely to get sick
  - Become accident prone
  - Fall asleep while driving
  - Medical residents are 6X more likely to make serious mistakes w.r.t patients
  - Risk of heart attack and stroke increase

Chronic sleep deprivation is a strong risk factor for...

• Accidents
• Depression (RR > 30)
• Heart disease
Why don’t people sleep enough?

- “Voluntary”/Societal Sleep deprivation
- Sleep disorders

Introduction to Sleep Disorders

- Big three, because they are highly prevalent.
  - Insomnia
  - Obstructive sleep apnea
  - Restless legs
- Less prevalent
  - REM behavioral disorder/night terrors
  - Narcolepsy
  - Sleep walking

Start with sleep disorders: Insomnia

- Insomnia:
  - Trouble with falling asleep or staying asleep that causes noticeable daytime symptoms
    - Inability to concentrate; eyes feel tired
  - Treated (not very effectively) with hypnotic medicines and/or behavioral therapy

Insomnia

- Primary behavioral therapy is “stimulus control” which basically says to avoid your bedroom until you are sleepy enough to fall asleep. As simple as this sounds, it has actually been shown to produce better quality sleep on polysomnogram, after being followed for a few weeks.

Why would a person have insomnia?

- The medical profession considered insomnia solely symptom of something else and not a disorder in and of itself. (Pain, Depression).
- Examples:
- Stress, worry – especially about finances, obviously causes insomnia.
- Pain, heart disease

It used to be:
Why does a person have insomnia (newer viewpoints)?

• They may have “hyperarousal” disorder: The ultimate light sleeper. The person’s brain responds to noises while the EEG says he/she is asleep.

Why does a person have insomnia (newer viewpoints)?

• They may be a “night-owl.” A night owl doesn’t get sleepy until 4:00 am. The medical term for night-owlness is “delayed circadian phase shift disorder.” When a night-owl is forced to get up early for school or work, chronic insomnia may develop.

Question Fact or Fiction:

• Claim: Night-owlness is a state of mind, probably related to depression or laziness. Night owls can become “morning larks” with simple behavioral exercises.

Fact or Fiction?

About night-owls: Talk with sleep specialist Dr. Phyllis Zee

• Dr. Zee is a foremost specialist in circadian rhythm as it relates to sleep. What is circadian rhythm?
• “Circadian rhythms refer to the cyclical changes—like fluctuations in body temperature, hormone levels, and sleep—that occur over a 24-hour period, driven by the brain’s biological “clock.” In humans, the biological clock consists of a group of neurons in the hypothalamus of the brain called the suprachiasmatic nucleus (SCN).”

Claim: Night-owlness is just a state of mind. Fact or Fiction?

• Dr. Zee is a foremost specialist in circadian rhythm as it relates to sleep. What is circadian rhythm?
• “Circadian rhythms refer to the cyclical changes—like fluctuations in body temperature, hormone levels, and sleep—that occur over a 24-hour period, driven by the brain’s biological “clock.” In humans, the biological clock consists of a group of neurons in the hypothalamus of the brain called the suprachiasmatic nucleus (SCN).”

Fiction!

• Just as owls are nocturnal by genetics, a person’s circadian rhythm is genetically determined. Humans have a “split gene” for circadian rhythm. This means some of us are naturally day-larks and some of us are naturally night owls. In night owls, the entire sleep-wake cycle is delayed. For example, melatonin production always starts about three hours before peak sleepiness. “Normal” people start producing melatonin at about 8-9 pm. Night owls don’t start producing melatonin until about 1-2 am.
• Many become chronically sleep deprived, because they have to work in the morning when they should be sleeping.
• There is an effective treatment to get night owls to start the sleep cycle earlier. This was developed by sleep specialist Dr. Phyllis Zee. It uses a combination of bright light and melatonin, but it is (1) expensive; (2) long term; and (3) highly limited in the number of physicians who are competent to prescribe the treatment.

What is the best prescription for night owls?
• Because of sleep debt, many owls are able to switch to a daytime schedule if careful to never stay up late.
• But if you can’t... then
• Get a job where you can sleep until noon.
• Get a nighttime job.
• If have a daytime job, and the situation permits, negotiate with employer for latest possible flex-time. May be possible to work from 11am-7pm. (Be very careful – you don’t want to get fired – maybe wait a couple of years to ask).

What causes OSA?
• A reduced space for air to get through from your mouth/nose to your lungs. During wakefulness, the throat muscles keep the airway open. During sleep, muscle tone, especially during REM, is greatly weakened.

What causes OSA?
• Primary cause: Obesity – excess fatty tissue takes up space in the airway.
• Other causes: anatomical
  • Any jaw structure or palate that is associated with a narrow airway
  • Tonsils can also block the airway
“Retrognathia” or Receding Jaw is a strong risk factor for OSA

Air blockage because of the tonsils. (Bottom right – airway is blocked)

Is OSA serious?

• Very serious – every apneic event causes blood-vessel injury and inflammation.
• In time, repetitive damage to blood vessels can become severe.
• Adverse outcomes include hypertension, heart attacks and stroke
• OSA may be on the causal pathway between obesity and hypertension – it may be a major reason why obese people develop hypertension

In addition:

• Severe OSA results in severe sleep deprivation, which itself is a risk factor for depression and heart attacks.

But, good news!

• OSA is effectively treated with a device that provides continuous positive airway pressure “CPAP”. For short the device is just called a CPAP. Most patients will be able to sleep essentially apnea-free as long as they wear the device.
• Efficacy of CPAP is profound!
• Sleepiness and depression disappear; blood pressure and weight may be reduced.
Restless Legs Syndrome

- Restless legs is a creepy-crawling sensation in the legs that primarily occurs when sitting or lying down. Often most notable when trying to fall asleep. Often relieved when patient gets up and starts walking.
- Maybe (in some cases) caused by mild dopamine deficiency and/or moderate-severe iron deficiency. Otherwise cause is unknown.

Sleep questions

- If you choose sleep for your written presentation, answer the 2 questions on the next slide. Determine by searching the original medical literature if each claim is probably true or not. You may supplement the medical literature with other online or written sources. Do not exceed five pages not including references, double spaced, Times New Roman, font size 11, default margins.
- See syllabus for Rubric.

Fact or Fiction:

1. In children, large tonsils may diminish the capacity for learning and/or are associated with attention deficit disorder (hint: what do large tonsils have to do with sleep?)
2. Sleepwalkers, while in deep sleep, have murdered persons in their vicinity (if true, do the courts hold the sleepwalker responsible?)

For students assigned to the Sleep Project

- CPAP is only effective for OSA if the patient uses it. You are charged with counseling patients with moderate to severe OSA who do not use their CPAP, though they have been prescribed one. You should research CPAPs and CPAP masks and determine ways to make the CPAP more comfortable. You may have mock-interviews with patients.