How Much Sleep Do We Need?

The vast amount of time spent sleeping suggests that sleep has a significant biological function.

- What is that function?
- What brain mechanisms control sleep?
- How does sleep deprivation impact functioning?
Why do we sleep?

- All mammals, birds and reptiles sleep - fish and amphibians have sleep-like phases
  - Only warm-blooded vertebrates have REM
  - must have an important function
  - Not a special higher-order human function
- Not necessarily needed in large quantities
- No clear relationship between species’ sleep time and activity level

Why do we sleep?

- Some animals sleep with one hemisphere at a time!
- Amount of sleep more predictive of likelihood of being eaten than amount of physical exercise.
Wakefulness

- During wakefulness the EEG of a normal person shows two basic patterns of activity:

  **Alpha activity:**
  - regular, medium-frequency waves of 8-12 Hz
  - present when a person is resting quietly, not aroused or excited and not engaged in demanding mental activity

  **Beta Activity:**
  - irregular, low-amplitude waves of 13-30 Hz
  - Shows desynchrony, reflecting many different neural circuits engaged in active processing
  - Descynchronization is indicative of a person being alert, attentive, and/or thinking
Three Physiological Measures of Sleep

- **Electroencephalogram (EEG)**
  - Reveals “brainwaves”

- **Electrooculogram (EOG)**
  - Records eye movements (such as those seen during rapid eye movement (REM) sleep)

- **Electromyogram (EMG)**
  - Detects activity (and lack thereof) in neck muscles during various sleep stages

Four Stages of Sleep EEG

- EEG voltage and frequency as one progresses from stage 1 through 2, 3, and 4
Four Stages of Sleep EEG

**Stage 1**
- Light sleep
- Muscle activity slows
  - Hypnic myoclonia (myoclonic jerk)
- EEG is similar to awake EEG, but slower
- Low-voltage, high-frequency
- Characterized by theta waves
  - 3.5 - 7.5 Hz waves
  - Eyes closed, preparing to sleep

**Stage 2**
- About 50% of our sleep is spent in stage 2
- Theta activity, but also...
- K complexes - one large negative (upward deflection) wave followed by one large positive wave
  - Precursor to delta activity?
  - Inhibitory mechanism?
- Sleep spindles - bursts of 12-14 Hz waves
Four Stages of Sleep EEG

- Stages 3 and 4 -
  - Together known as “deep sleep” or “SWS”
  - Stage 3 delta waves, large and slow (slower than 3.5 Hz), begin to appear
  - Stage 4 is almost exclusively delta waves

Slow-wave sleep

- Cerebral metabolic rate and blood flow decrease (~75% of waking levels!)
- Areas which show highest activity during waking show highest level of delta waves during sleep, suggesting “resting brain”
- A person who is awoken during SWS is groggy and confused, as if the brain had been ‘off-line’ (contrast with REM).
Four Stages of Sleep EEG

- Progress to stage 4 sleep and then back to stages 3, 2, and REM sleep
  - A cycle takes about 90 minutes
- Durations of REM periods lengthen as night progresses, durations of stages 3 and 4 decrease

Stages of Sleep

[Diagram showing the progression of sleep stages over a 9-hour period, with stages 1 through 4, REM periods, and awake state indicated.]
Four Stages of Sleep EEG

- During REM sleep: REMs, loss of core muscle tone, low-amplitude/high-frequency EEG, increased cerebral and autonomic activity, muscles may twitch
  - ~20% of our sleep is spent in the REM stage
  - Each 90 minute cycle contains about 20-30 mins of REM.

REM Sleep

- neurons within the pons send inhibitory messages to the spinal cord during REM sleep
- this message inhibits motor neurons that project to large muscles
- REM sleep is still observed after damage to the pons
- but, no inhibition of muscle neurons...
REM Sleep and Dreaming

- 80% of awakenings from REM yield reports of story-like dreams
- External stimuli may be incorporated into dreams
- Dreams run on real time
- Everyone dreams
- Sleepwalking and talking are less likely to occur while dreaming

What can possibly go wrong?

- Insomnia
  - Different people require different amounts of sleep
  - People often misjudge the amount of sleep they are getting
  - Important that the cure not be worse than the disease!
What can possibly go wrong?

- **Insomnia**
  - Sleep Apnea: a cessation of breathing while sleeping: causes insomnia because the body panics if blood oxygen levels fall!

What can possibly go wrong?

- **Narcolepsy**
  - Irresistible sleep, cataplexy, sleep paralysis, hypnagogic hallucinations
  - REM during waking, and often go straight to REM (skipping SWS).
What could possibly go wrong?

Causes of Narcolepsy
- Uncertain, but appears to be influenced by a hereditary autoimmune disorder in which orexigenic neurons are attacked by immune system
  - When orexigenic neurons are systematically destroyed in lab rats, narcoleptic behavior results
  - Canine narcolepsy is caused by mutations in one of the orexin receptors

What can possibly go wrong?

REM Sleep Behavior Disorder
- No paralysis observed during REM sleep
  - The result? Dreams can be acted out!
- Appears to have some genetic component
What can possibly go wrong?

**Slow-Wave Sleep Problems:**
- Generally observed in children, and especially during stage 4 sleep
  - Bedwetting
  - Night terrors
  - Sleepwalking

If you *don’t* sleep...

**Effects of sleep deprivation appear to be more cognitive than physiological**
- Complete lack of exercise doesn’t result in diminished need for sleep
- Quadriplegics and paraplegics need sleep

**However, lack of sleep can be fatal!**
- Research with fruit flies
- Fatal familial insomnia
  - Lack of SWS, brief episodes of REM
If you *don’t* sleep...

- SWS appears to be crucial for brain rest
- REM appears to involve mental ‘house cleaning’
  - REM deprivation results in rebound
    - Suggests brain needs a certain amount of REM
  - REM time decreases over development

Learning is ‘development’...

- Research with both humans and non-human animals suggests that sleep aids in consolidation of long-term memories
- SWS and REM each play an important role
Memory

- Declarative memory vs non-declarative memory

**SWS vs SWS + REM**

![Graph showing discrimination improvement for SWS and SWS + REM](Mednick et al, 2003)
No Sleep vs. SWS vs. SWS + REM

Karni et al, 1991

No sleep vs. SWS only

Tucker et al., 2006

No Sleep vs. SWS vs. SWS + REM

Karni et al, 1991

No Sleep vs. SWS only

Tucker et al., 2006
Sleep and Memory

- REM sleep appears to facilitate consolidation of *non-declarative* memories
- SWS seems to facilitate consolidation of *declarative* memories

Peigneux et al., 2004
During SWS (but not REM sleep), same hippocampal and para-hippocampal areas were activated as when learning the route!

Peigneux et al., 2004

Chemical control of sleep

Sleep is regulated:
- If deprived of SWS or REM sleep, an organism will try to ‘make up’ the missed sleep.
- If SWS is obtained in a nap, that amount will be ‘deducted’ from the following nights sleep.

This suggests that something ‘knows’ how much sleep we are getting!
Regulating mechanism

- **Adenosine** - a neuromodulator that inhibits neural activity

  - Astrocytes have glycogen
  - During SWS astrocytes regain glycogen
  - **Adenosine** inhibits neural activity
  - When brain is active, glycogen is used by neurons for energy
  - Being awake depletes glycogen
  - Fall in glycogen level -> increase in extracellular adenosine

  **Caffeine blocks adenosine receptors!**

Neurotransmitters of sleep and arousal

- Acetylcholine
- Norepinephrine
- Serotonin
- Histamine
- Orexin
Neurotransmitters of sleep and arousal

- **Acetylcholine**
  - Produced in dorsal pons and basal forebrain and then widely distributed
  - Acetylcholine *increases* arousal (greater desynchronization)
  - High levels of Ach found both in REM and awake states

- **Norepinephrine**
  - Produced in the dorsal pons and then widely distributed
  - Part of the “fight or flight” system
  - Increases ability to pay attention to stimuli
  - Highest levels when awake, lower in SWS, lowest in REM
Activity of NE neurons in LC of DP

- Serotonin
  - Produced in the *raphe nuclei* of the reticular formation and widely distributed
  - Higher serotonin levels associated with greater arousal.
Activity of serotonergic neurons in raphe nuclei

<table>
<thead>
<tr>
<th>State</th>
<th>Mean firing rate (spikes/sec)</th>
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<tbody>
<tr>
<td>Active waking</td>
<td>4</td>
</tr>
<tr>
<td>Quiet waking</td>
<td>3</td>
</tr>
<tr>
<td>Drowsy</td>
<td>2</td>
</tr>
<tr>
<td>Stage 1 sleep</td>
<td>1</td>
</tr>
<tr>
<td>Stage 2 sleep</td>
<td>1</td>
</tr>
<tr>
<td>Stage 3 sleep</td>
<td>1</td>
</tr>
<tr>
<td>Pre-REM sleep</td>
<td>1</td>
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<tr>
<td>REM sleep</td>
<td>5</td>
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<td>First second after REM sleep</td>
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Sleep-Waking State

The neurotransmitters of sleep

- **Histamine**
  - Produced in hypothalamus and widely distributed
  - High when awake, low during both REM and SWS
The neurotransmitters of sleep

- Orexin
  - Produced in lateral hypothalamus and broadly distributed
  - Promotes wakefulness

Acetylcholine: arousal
- Levels high during wakefulness and REM

Norepinephrine: arousal (vigilance)
- Levels high when alert, low during SWS and REM

Serotonin: arousal
- Levels high when awake, lowering increasingly as you head towards REM

Histamine: arousal
- Levels high when awake, low during SWS and REM

Orexin: arousal
- Levels high when alert, low during rest and all sleep states
Neural Control of SWS

- Ventrolateral preoptic area
  - Destruction of this area produced insomnia (and eventually death) in rats

- Receives inhibitory inputs from:
  - Locus coeruleus
  - Raphe nuclei
  - Hypothalamus

- Ventrolateral preoptic area
  - Contains inhibitory GABA-secreting neurons which project to:
    - Dorsal pons (acetylcholine)
    - Locus coeruleus (norepinephrine)
    - Raphe nuclei (serotonin)
    - Hypothalamus (histamine, orexin)
Neural Control of SWS

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Neural Control of SWS

- Ventrolateral preoptic area
  - Receives inhibitory inputs from:
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    - Raphe nuclei
    - Hypothalamus
So...

- **Either** the ventrolateral preoptic area is **inhibited**, or it is **inhibiting**.

- **Orexin** helps tip the scale towards “awake”

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The REM flip-flop

- **REM-ON** and **REM-OFF** neurons
  
  - During awake states, REM-OFF neurons are **activated by**
    
    - Orexin
    - Serotonin
    - Norepinephrine
The REM flip-flop

- **REM-ON and REM-OFF neurons**
  - Once sleep has begun, this excitatory activity decreases... REM-OFF neuronal activity decreases too.
  - So REM-ON system kicks in!