Prevalence of Short Sleep Duration (<7 hours) for Adults Aged ≥ 18 Years, by County, United States, 2014
Consequences of Inadequate Sleep

- Cardiovascular disease, hypertension, stroke
- Diabetes
- Automobile accidents
- Academic failure
- Obesity
- Relationship problems

_Last ditch effort: lack of sleep is gonna make you stupid_
What is MEMORY?

• The INPUT, STORAGE and RECALL of sensory information.
Sensory input

Sensory memory

Unattended information is lost.

Attention

Short-term memory

Unrehearsed information is lost.

Encoding

Long-term memory

Some information may be lost over time.

Maintenance rehearsal

Retrieval
The Issue of
ATTENTION

"It [attention] is the taking possession by
the mind, in clear and vivid form, of one out
of what seem several simultaneously
possible objects or trains of thought...."

- WILLIAM JAMES
One of the primary consequences of inadequate sleep:

**IMPAIRED ATTENTION & CONCENTRATION**

*Why?*
The Issue of ATTENTION

• What exactly is sleep?
• Fragile nature of the wake state
• The "grey area" between sleep and wake
The concept of “MICROSLEEPS”

According to the National Sleep Foundation:

Microsleep occurs when you fall asleep for a period of several seconds. As the name implies, microsleep occurs so quickly that people who have an episode might not even realize they have fallen asleep. During an episode, you may appear to be awake, and even have your eyes open, but your brain does not process information.
Microsleeps are preceded by diminished perception of the world around us
The **LOCUS CERULEUS** is the principal site for brain synthesis of norepinephrine (noradrenaline). Norepinephrine from the locus ceruleus has an excitatory effect on most of the brain, mediating **arousal and attention**...and priming the brain’s neurons to be activated by stimuli.
The projections of the locus ceruleus reach far and wide:

- Brainstem
- Spinal cord
- Cerebellum
- Hypothalamus
- Amygdala
- Cerebral cortex

The norepinephrine from the LC has an excitatory effect on the brain, priming the brain’s neurons to be activated by stimuli.

http://healthysleep.med.harvard.edu/healthy/science/how/neurophysiology
The locus ceruleus is one of the primary brain structures responsible for the ORIENTING REFLEX or ORIENTING RESPONSE:

an organism's immediate response to a change in its environment, when that change is not sudden enough to elicit the startle reflex. The orienting response is a reaction to novel or significant stimuli.
The stereotypic condition of locus ceruleus activation is the orienting response: After a salient stimulus (e.g., a loud sound), we interrupt whatever we were doing before, orient to the stimulus, and then analyze the situation to initiate a new course of action.
Mice were examined following periods of normal rest, short wakefulness, or extended wakefulness, modeling a shift worker’s typical sleep pattern.
There is a protein in the LC called SirT3. It provides an adaptive antioxidant response for the neurons in the LC.

Under normal sleep/wake conditions, this protein is released...metabolic homeostasis is restored...and LC neurons are protected from injury.
Extended Wakefulness: Compromised Metabolics in and Degeneration of Locus Ceruleus Neurons

However, when wakefulness is extended for longer durations, SirT3 protein level declines, which leads to a gradual cell death of LC neurons.

After several days of extended wakefulness, sleep-deprived mice lost 25% of neurons in the locus ceruleus.
▪ Is there lasting injury to the brain after sleep loss?

▪ Can we recover from nights of short sleep by “catching up” on weekends?

▪ Do we ever fully recover from chronic insufficient sleep?
Doesn’t it seem like everyone has **Attention Deficit Disorder** these days?
Percent of children (aged 2–17 years) ever diagnosed with ADHD
The Issue of CONSOLIDATION

Consolidation is the process of creating a memory trace after the initial acquisition, so that it is available for later recall.
Forgetting Curve

Herman Ebbinghaus 1885

We forget 50% of what we learn within one hour of learning it unless we put it into practice or are continuously supported and provided with access to “knowledge.”
Rehearsal & Encoding

Potentiation:

- a synapse increases in strength as increasing numbers of signals are transmitted between two neurons.

- synchronous firing of multiple neurons makes those neurons more likely to fire together in the future.
The Gettysburg Address

Four score and seven years ago our fathers brought forth on this continent a new nation, conceived in Liberty and dedicated to the proposition that all men are created equal.

Now we are engaged in a great civil war, testing whether that nation, or any nation so conceived and so dedicated, can long endure. We are met on a great battlefield of that war. We have come to dedicate a portion of that field as a final resting place for those who here gave their lives that that nation might live. It is our privilege to inter these brave men in that heavey soil.

Four score and seven years ago our fathers brought forth on this continent a new nation, conceived in Liberty and dedicated to the proposition that all men are created equal.

Declaration of Independence

When in the course of human events.....
“You're the One That I Want" (from *Grease*)

I got chills, they’re multiplying...and...
So we’ve seen that rehearsal can consolidate memory.

*But how?*
Dr. Brenda Milner & Patient H. M.
Early Brain Research

- Dr. William Scoville surgically removed entire hippocampus
  - Cured seizures
  - No new memories after surgery
- Dr. Brenda Milner devoted career to studying Patient H. M.
  - Two types of memory: procedural / explicit

The role of the HIPPOCAMPUS in memory
Storage in the hippocampus is temporary...must be consolidated in the neocortex.

Hippocampus is not the final resting place for memory....it is a temporary weigh station

This is what happens during rehearsal...this is what happens during sleep.
Waking vs. Sleeping Rehearsal

- **Waking Rehearsal** is simply practice and repetition
- In a sense, purposeful repetition of the initial stimuli or piece of information

- **What exactly then is Sleeping Rehearsal?**
• During sleep, there is continual activation between the hippocampus and the cerebral cortex (with a number of relay stations along the way).
• Activation patterns in the sleeping brain mimic those recorded during the learning of the task during the previous day
Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation

Richard Boyce
Stephen D. Glasgow
Sylvain Williams
Antoine Adamantidis

*Science* 13 May 2016:

- **OPTOGENICS**: technology that allows scientists to control the activity of specific neurons by LIGHT
- Mice were trained to spot a new object placed in a field with two other objects of similar size and shape
- The exact neurons within the hippocampus were identified (i.e., those activated during the learning process)
- Using optogenics, the researchers then turned off these same neurons while the mice were in REM sleep
- Compared to a control group, the experimental mice failed the next day at the same task, suggesting their memory of the task had been erased or impaired.
SLOW WAVE SLEEP seems to play more of a role in DECLARATIVE MEMORY:

Remembering Basic Factual Information

REM SLEEP plays a stronger role in PROCEDURAL MEMORY:

Remembering HOW to do something
Without adequate sleep, rehearsal and encoding suffer.

Again, a single night of insufficient sleep may impair the retention of information learned or acquired the previous day.

Better to get some sleep before a big test than to pull an all-nighter.
Retrieval returns a memory from long-term storage to short-term, or working memory, where it can be more easily accessed.
The Issue of RETRIEVAL

• Recall or retrieval of a memory refers to accessing information from the past which has previously been encoded and stored in the brain.

• Commonly known as “remembering”

• Retrieval involves re-visiting (or reactivation of) the nerve pathways the brain formed when the information was first encoded.
Energy & Waste

Cardiovascular system

Lymphatic system
How are nutrients supplied to the brain?

The brain uses about 25% of the body’s energy supply, even though it occupies only 2% of body’s mass.
LYMPHATIC SYSTEM

A parallel collection of vessels that extends throughout the body...collects proteins and waste products...sends to circulatory system for removal.
Given the supply of nutrients the brain needs to function, it creates a tremendous amount of waste.

...but the brain has very little lymphatic involvement.
Cerebrospinal Fluid (CSF)

- CSF fills spaces that surround the brain.
- CSF doesn’t stay on the outer surface of the brain, but rather is pumped into the inner regions of brain.
- It flows along the outsides of the blood vessels, and cleans away the waste from spaces between brain cells.
- Access to entire brain volume.
• The extracellular space between brain neurons increased by approximately 60% in the sleeping brain compared to the waking baseline.

• Accomplished by brain cells actually shrinking in size during sleep
Awake
- Reduced interstitial space
- Restricted CSF flow
- Metabolites accumulate

Asleep
- 60% increase in interstitial space
- Better CSF flow
- Effective clearance of metabolites
The restorative function of sleep may be a consequence of the enhanced removal of neurotoxic waste products that accumulate in the awake central nervous system.
Challenging cognitive tasks require mental activity and resources. After continued focus on one type of task, the brain becomes depleted.

One potential mechanism for this phenomenon is that continued synaptic activity triggers the release of **BETA-AMYLOID**, a brain peptide that suppresses local neuronal activity.
• When the researchers injected beta-amyloid into the brains of mice, the CSF cleared away this “debris” twice as quickly during sleep as during wake.

• Impaired quality & quantity of sleep leaves beta-amyloid behind.

• When beta-amyloid peptides accumulate, they begin to clump together and form plaques.

These plaques are classic biological markers for Alzheimer’s disease.
Poor sleep is associated with CSF biomarkers of amyloid pathology in cognitively normal adults

Kate S. Sprecher, MS, Rebecca L. Koscik, PhD, Cynthia M. Carlsson, MD, Henrik Zetterberg, PhD, MD, Kaj Blennow, PhD, MD, Ozioma C. Okonkwo, PhD, Mark A. Sager, MD, Sanjay Asthana, MD, Sterling G. Johnson, PhD, Ruth M. Benca, MD, PhD and Barbara B. Bendlin, PhD

Self-reported sleep and Alzheimer disease CSF biomarkers
A wake-up call

Adam P. Spira, Yo-EI S. Ju

First published July 5, 2017, DOI: https://doi.org/10.1212/WNL.0000000000004189
Inadequate sleep results in inadequate cleansing of the brain.

The buildup of debris and waste products blocks cell-to-cell signaling between synapses.

Recovery of information previously stored is impaired.
Sensory memory

Unattended information is lost.

Short-term memory

Unrehearsed information is lost.

Long-term memory

Some information may be lost over time.

Sensory input

Attention

Maintenance rehearsal

Encoding

Retrieval
So here we are at the 1 hour mark. How’s your memory for what we’ve covered this morning?

You’ve got two choices to help you remember it all?

We forget 50% of what we learn within one hour of learning it unless we put it into practice or are continuously supported and provided with access to “knowledge.”