

Memory & the Brain

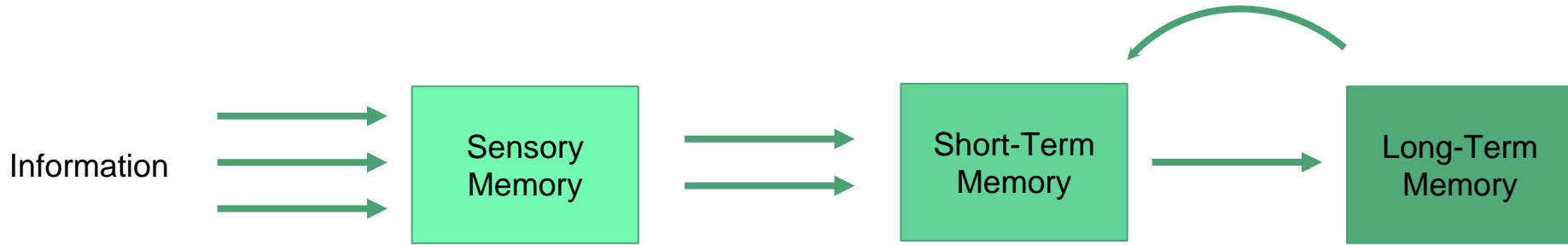
Andrew Bender, Alice Li, Raunak Pillai
OLLI at Vanderbilt, Spring 2018

Why do we forget?

Outline

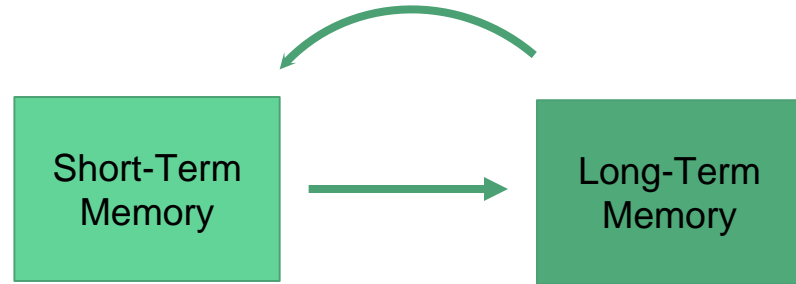
- What is memory?
- When (& why) does it fail?
- Is this really a failure?

What is Memory?

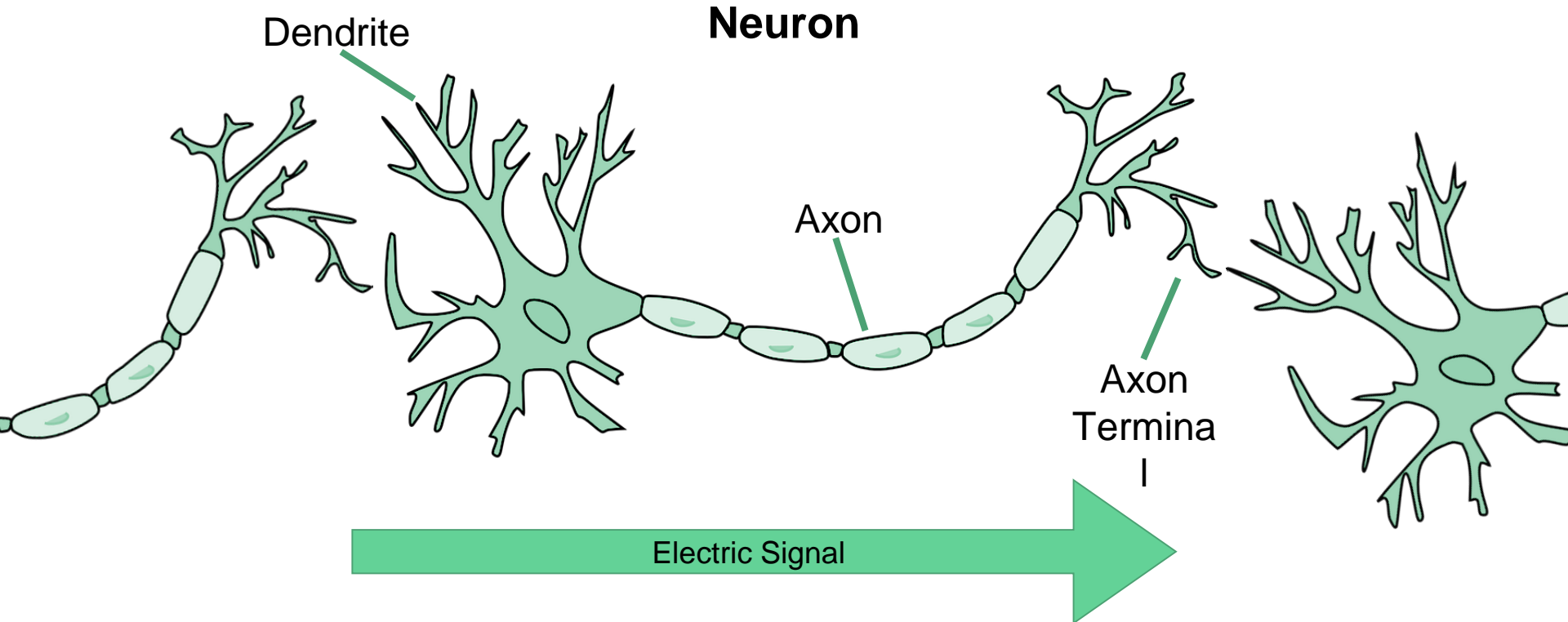


What is Memory?—Tips & Tricks

- 2 kinds of long-term memory
 - “Declarative”
 - “Implicit”
- Long-Term Memory is better when you process it *deeply*:
 - Make connections to what you know
 - Use the material in daily life
 - Organize the information
 - Test yourself

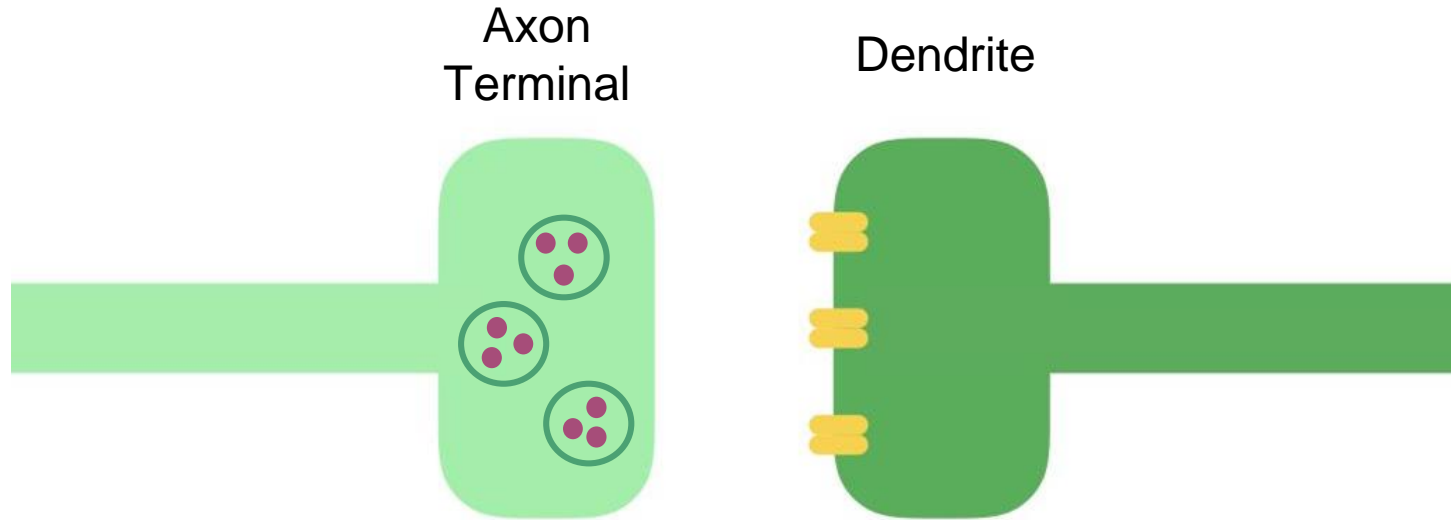


What is Memory?—Neuroscience



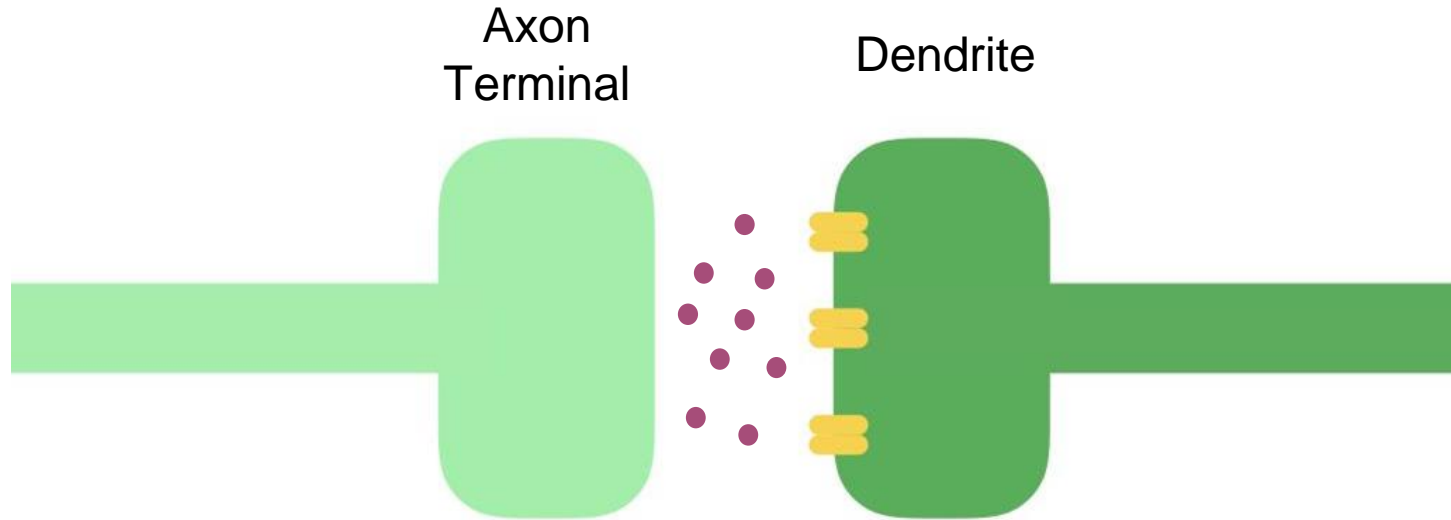
What is Memory?—Neuroscience

- Neurons communicate through *synapses*



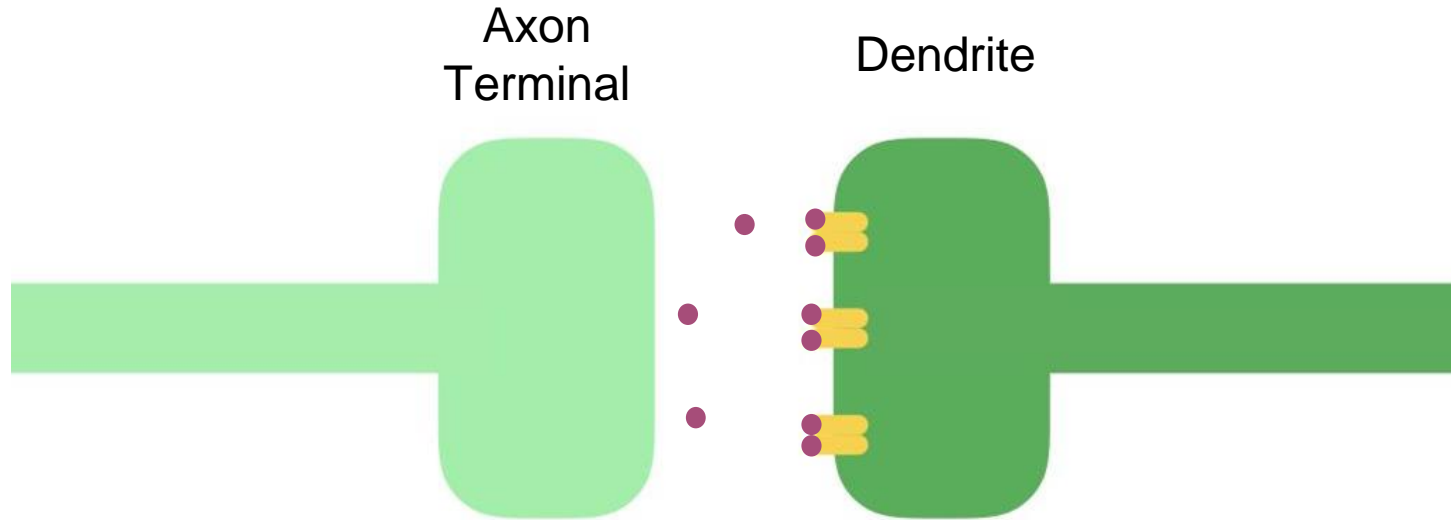
What is Memory?—Neuroscience

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What is Memory?—Neuroscience

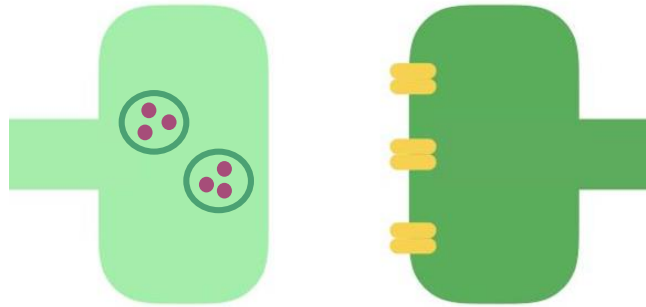
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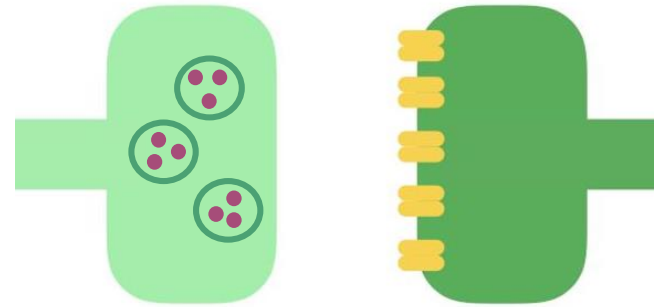
What is Memory?—Neuroscience

- Neurons communicate through *synapses*
- Synapses *change* during learning
 - “Neurons that fire together, wire together” - Donald Hebb

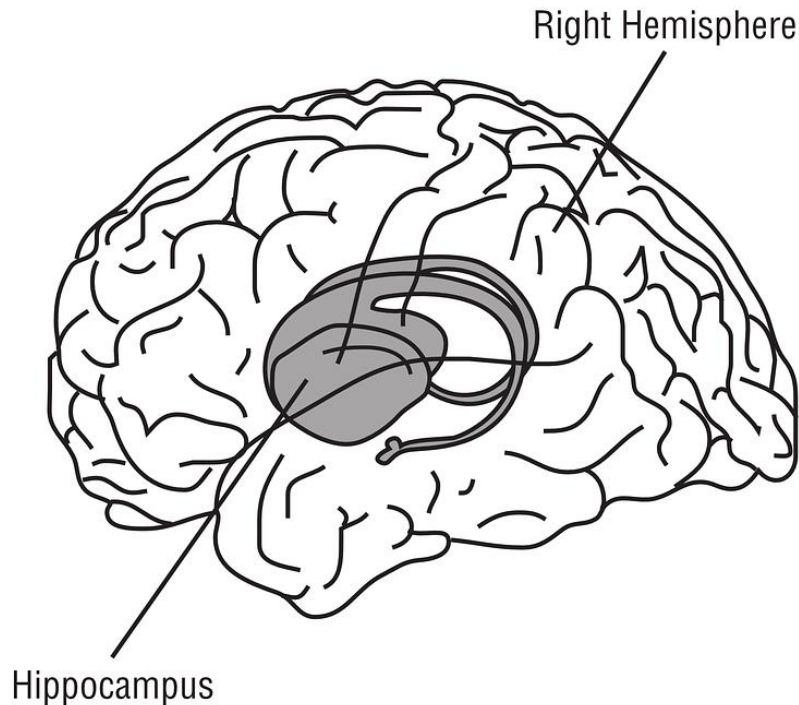
Synapse before
learning



Synapse after
learning



What is Memory?—Neuroscience



- The *hippocampus* is involved in memory
- One theory:
 - Hippocampus forms *connections* between different brain areas

What is Memory?—Review

- Different kinds of memory
- Long Term Memory is better with *deeper processing*

- *Within* a neuron, electrical signaling from dendrite to axon terminal
- *Between* neurons, chemical signaling through synapses
- Learning makes our synapses *change*
- The hippocampus uses this to help make & recall memories

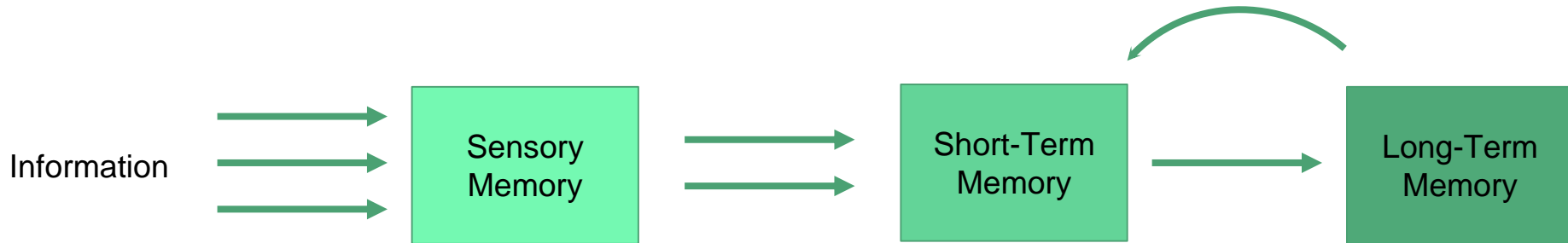
When Does Memory Fail?

- What did you have for breakfast last Tuesday?
- What is the capital of Canada?
- What kind of clothing is the person in front of you wearing?

There are *many* things we don't remember

Why Does Memory Fail?—Answer 1

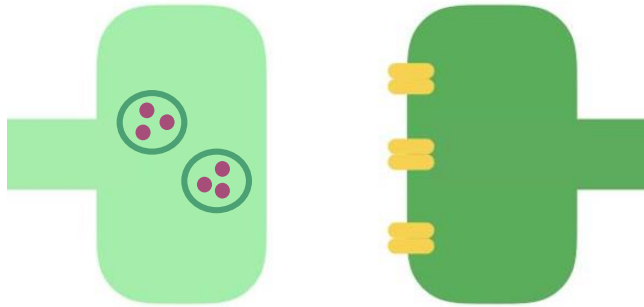
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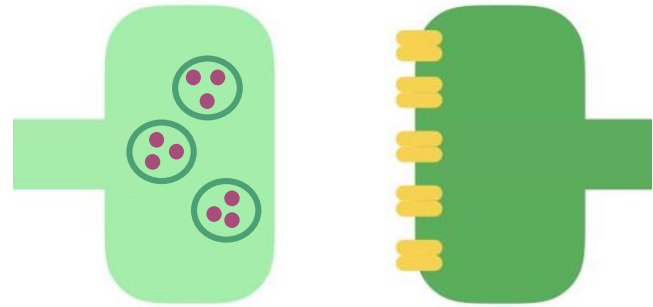
Why Does Memory Fail?—Answer 2

- What did you have for breakfast last Tuesday?
- What is the capital of Canada?
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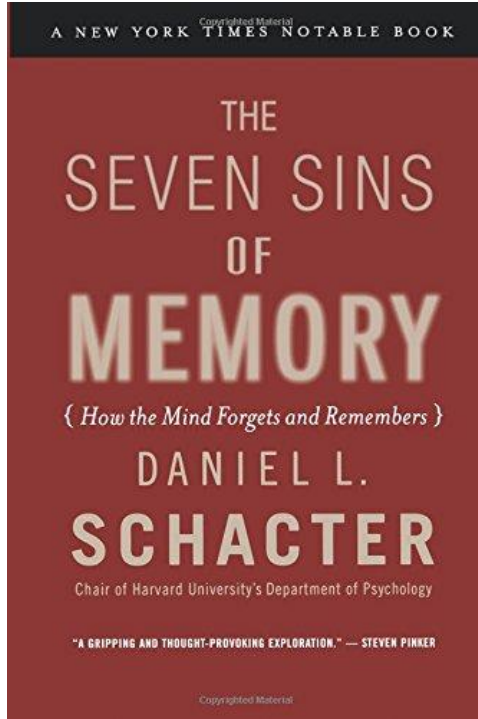
Synapse before
learning



Synapse after
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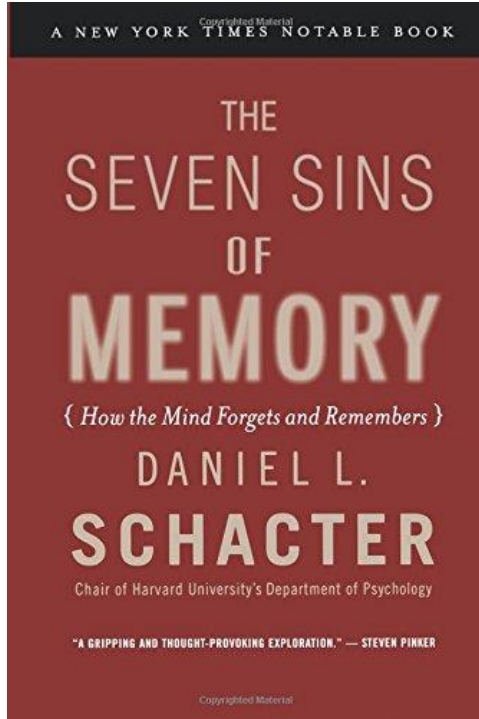


When Does Memory Fail?—7 Sins



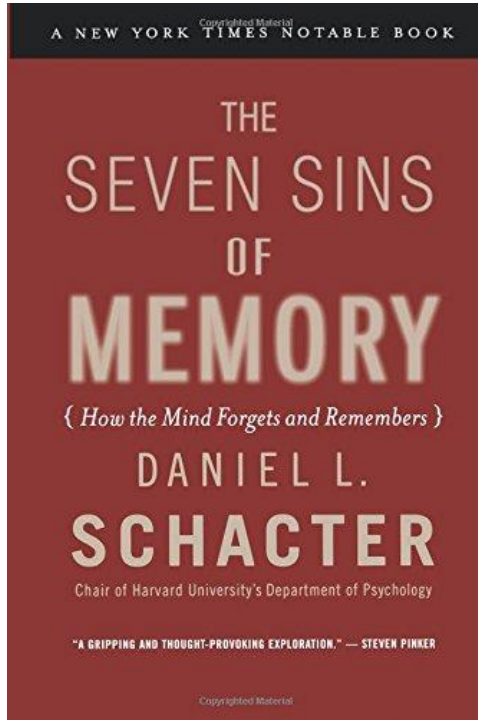
- Absent-mindedness
- Transience
- Blocking
- Persistence

Is This Really A Failure?



- No, in fact *remembering everything* might be bad
- Our memory lets us go on *auto-pilot*

Is This Really A Failure?



- Absent-mindedness
 - Helps us only remember what we pay attention to
- Transience
 - Helps us forget irrelevant details
- Blocking
 - Accident of our mind bringing forth important info
- Persistence
 - Helps us avoid forgetting important mistakes

So Maybe Forgetting Isn't So Bad....

EXCEPT FOR THIS PRESENTATION

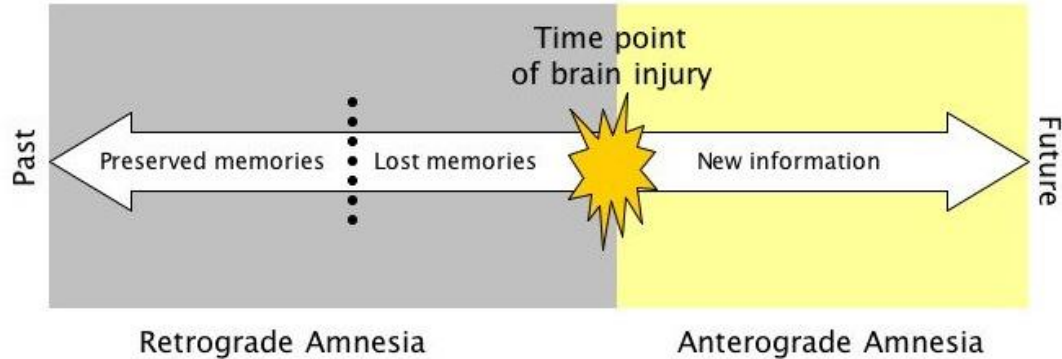
Amnesia

What is amnesia?

- Loss of memories
- Preserved intelligence, awareness, attention span
- Caused by brain injury or emotional shock/trauma

Types of amnesia

- Retrograde amnesia
- Anterograde amnesia
- Dissociative amnesia



Retrograde amnesia

- Case study: Patient E.F.
 - 33-year-old married locksmith without children
 - Went unconscious for unknown reasons
 - Awoke with amnesia
 - Did not recognize his wife
 - Last memories of himself were 12-14 years prior to the incident
 - Was able to re-learn recent public facts and events

Anterograde amnesia

- Movie: *Memento*
- Directed by Christopher Nolan
- Premiered in 2000



Anterograde amnesia

- The case of Clive Wearing
 - Brain infection in 1985
 - Musical ability remained intact despite losing the ability to retain recent info

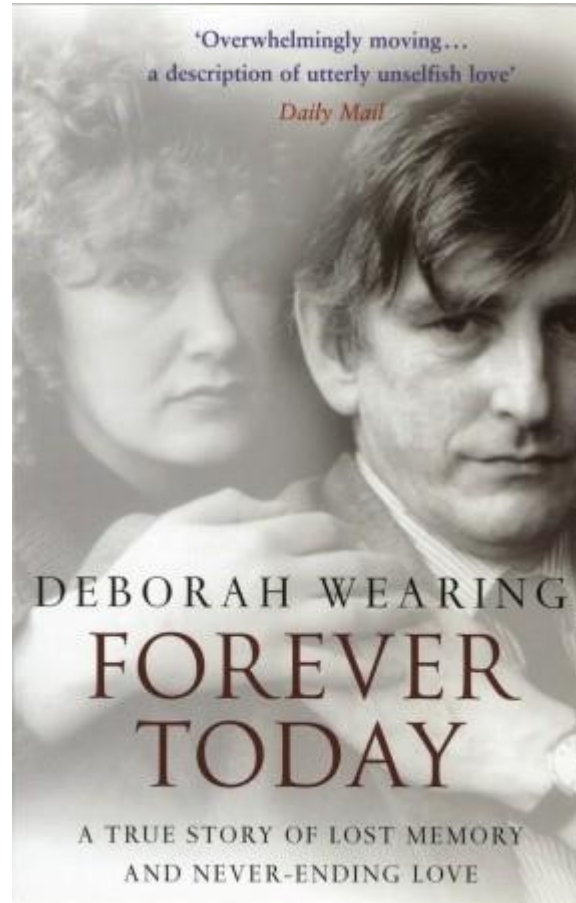


<http://www.bbc.com/news/magazine-15791973>

Excerpt from Clive Wearing's diary in 1990

Now I am ~~totally~~^{almost} PERFECTLY AWAKE (1st time). PA
Now I am ~~subliminally~~^{subliminally} PERFECTLY AWAKE (2nd time). PA
Now I am ~~almost~~^{almost} PERFECTLY AWAKE (3rd time). PA
Now I am ~~completely~~^{completely} PERFECTLY AWAKE (4th time). PA
Now I am ~~almost~~^{almost} PERFECTLY AWAKE (5th time). PA
Now I am ~~subliminally~~^{subliminally} REALLY AWAKE (6th time). PA
Now I am ~~completely~~^{completely} PERFECTLY AWAKE (7th time). PA
The Food Arrives - A DELICIOUS PIECE OF CHOCOLATE
1st PATIENCE GAME ENDS - I AM REALLY AWAKE. APPLET
Hello Darling! I love you x x x
I am ~~completely~~^{almost} AWAKE - FIRST TIME, BUT I CAN'T
DARLING GOES HOME JUST AS I WAKE UP COMPLETELY
" DELIVERES A LOVE LETTER

Forever Today
by Deborah Wearing



Dissociative amnesia

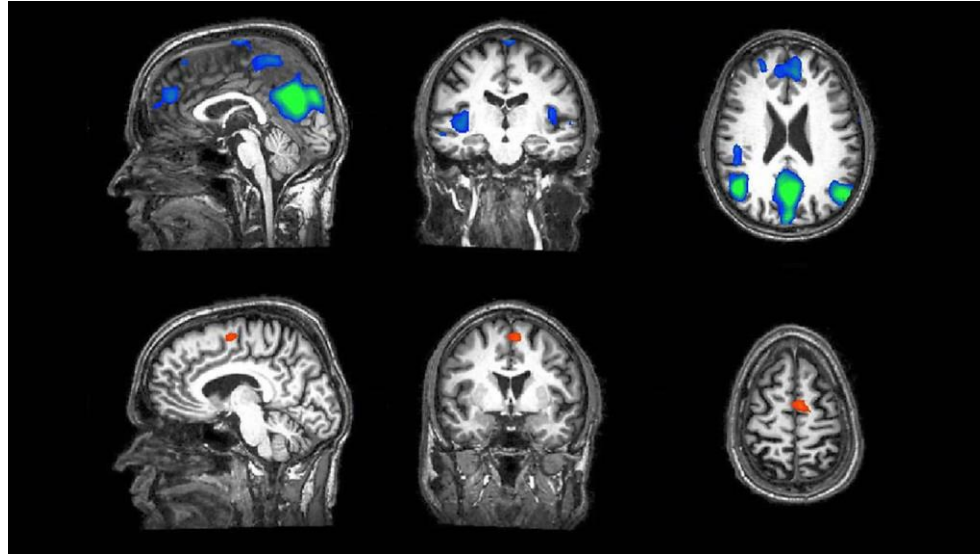
- Dissociative fugue
- Case study: Jane Dee Williams
 - Found wandering in a Colorado mall in May 1985 with a green coat, a Toyota key, a copy of *Watership Down*, two green pens, a notebook, and no clue who she was
 - Discovered 12 years after her disappearance by a former co-worker who saw her photograph in newspaper stories
 - Real name: Jody Roberts, reporter for a news organization in Washington
- Controversial diagnosis

Malingering

- What is it?
- What are some motivations for malingering?
- How do we uncover malingering?

fMRI

- Functional magnetic resonance imaging
- Technique used to look at the brain



Treatment

- Occupational therapy
- Technological assistance
- Targeted nutrition (for special cases only)

Dementia

ALZHEIMER'S DISEASE IS THE

6TH

leading cause of death
in the United States

16.1 MILLION AMERICANS

provide unpaid care for people with
Alzheimer's or other dementias

These caregivers provided an estimated

18.4 BILLION HOURS
of care valued at over
\$232 BILLION

Between 2000 and
2015 deaths from heart
disease have decreased

11% 

while deaths from Alzheimer's
disease have increased

 **123%**



1 IN 3

seniors dies
with Alzheimer's
or another
dementia

It kills more than
breast cancer and
prostate cancer
COMBINED

EARLY AND ACCURATE DIAGNOSIS COULD SAVE UP TO

\$7.9 TRILLION

in medical and care costs

IN 2018, Alzheimer's and other
dementias will cost the nation

\$277 BILLION

BY 2050, these costs
could rise as high as

\$1.1 TRILLION



5.7 MILLION

Americans are living
with Alzheimer's

BY 2050, this
number is projected
to rise to nearly

14 MILLION



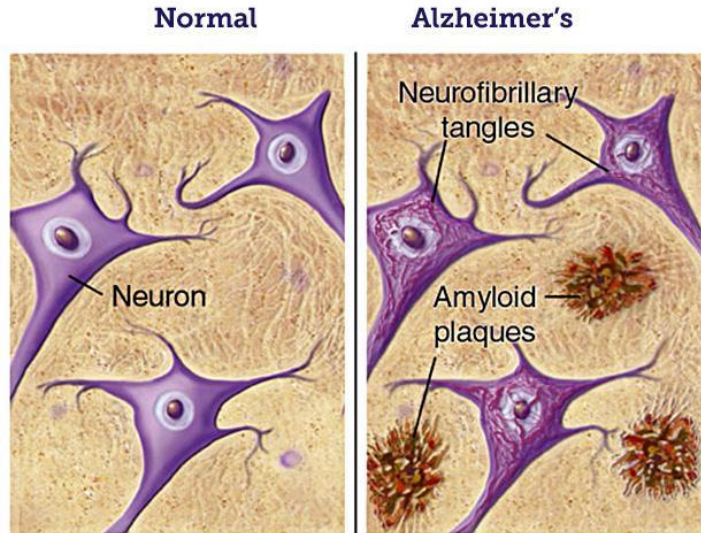
**EVERY
65 SECONDS**
someone in the
United States
develops the
disease

alzheimer's  association®

THE BRAINS BEHIND SAVING YOURS.™

Alzheimer's Disease

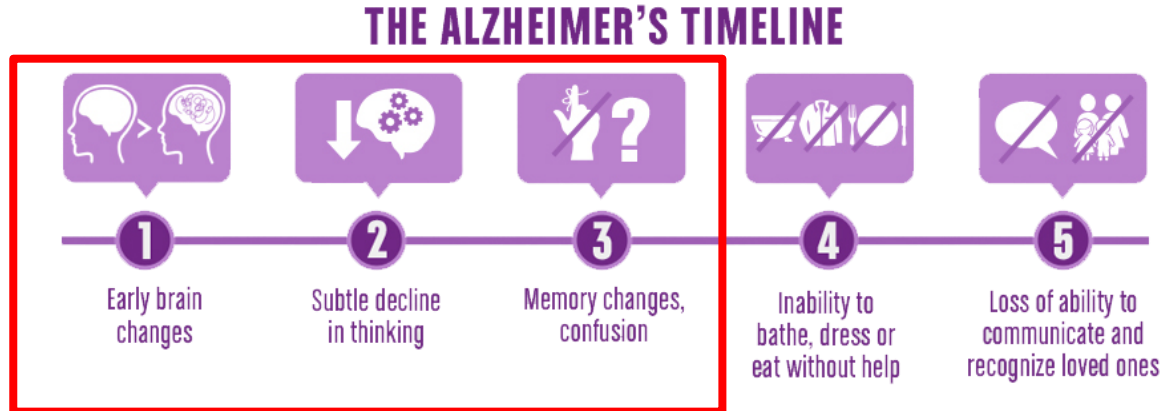
Normal vs. Alzheimer's Diseased Brain



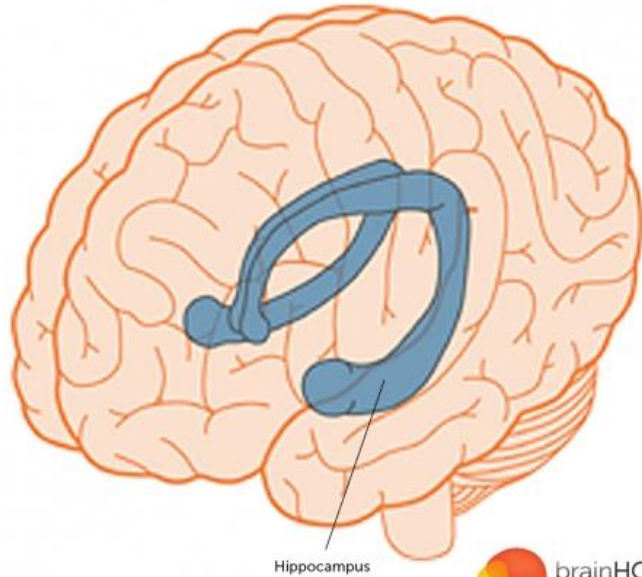
- Most common causes of dementia among older adults
- Dr. Alois Alzheimer in 1906
- Amyloid plaques
- Neurofibrillary tau tangles
- Decreased connections in brain
- Inflammation

Alzheimer's: Changes in the Brain

- Preclinical stage: brain damage starts 10 years or more prior to symptoms
- Damage first to hippocampus
 - Essential to memory formation
 - Memory problems are typically one of first symptoms



Hippocampus



Hippocampus



- “Seahorse” in Greek
- Part of limbic system
- Bilateral
- Important for memory consolidation

Front Page of the NY Times - Dec 4, 2008

U.S.

H. M., an Unforgettable Amnesiac, Dies at 82

By BENEDICT CAREY DEC. 4, 2008

He knew his name. That much he could remember.

He knew that his father's family came from Thibodaux, La., and his mother was from Ireland, and he knew about the 1929 stock market crash and World War II and life in the 1940s.

But he could remember almost nothing after that.

In 1953, he underwent an experimental brain operation in Hartford to correct a [seizure disorder](#), only to emerge from it fundamentally and irreparably changed. He developed a syndrome neurologists call profound [amnesia](#). He had lost the ability to form new memories.

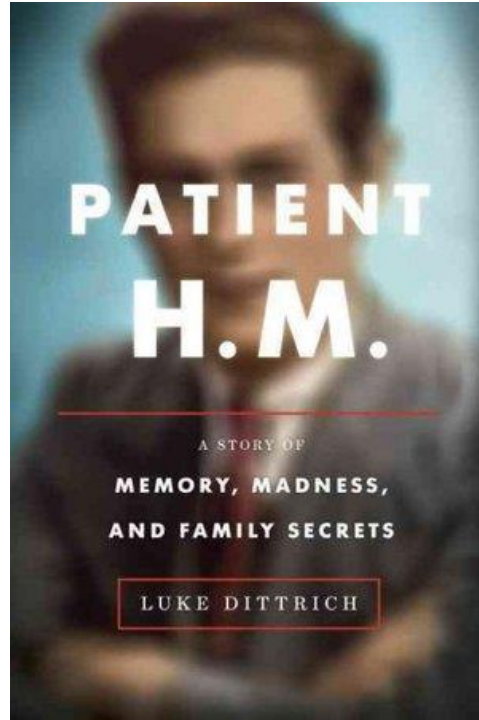
For the next 55 years, each time he met a friend, each time he ate a meal, each time he walked in the woods, it was as if for the first time.

Henry Molaison (HM)

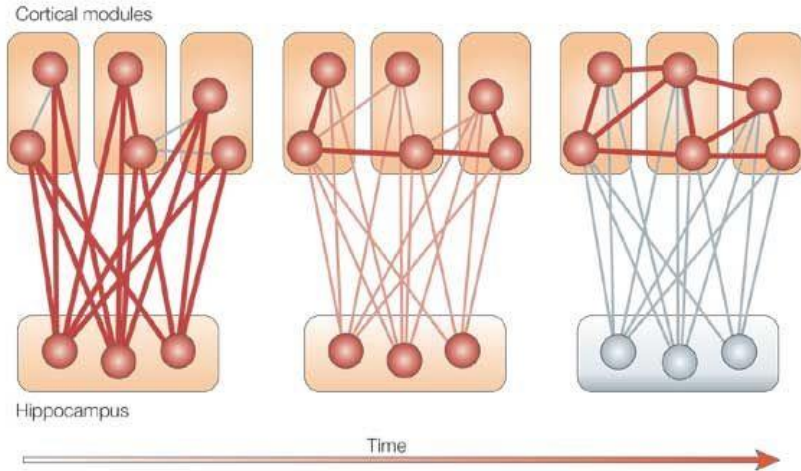


- Most studied mind in history
- Suffered from seizures
- Dr. William Beecher Scoville removed hippocampus
- Seizures resolved
- Personality was unaffected
- IQ actually improved
- Could not form new memories

Interested in learning more about HM?



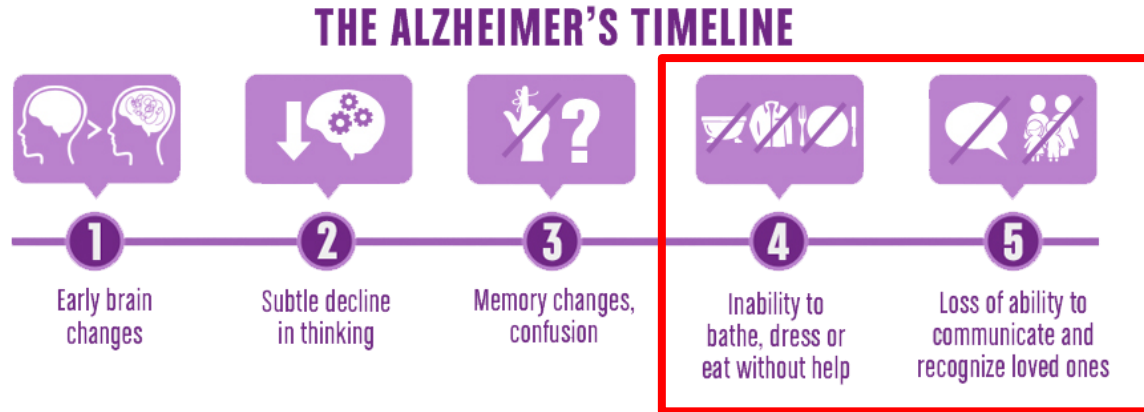
Hippocampus and Memory



- Short-term → Long-term
- Experience activates different areas of cortex
- Cortical areas activate hippocampus
- Hippocampus strengthens connections between cortical areas

Progression of Alzheimer's

- Damage to other cortical areas beyond hippocampus
- Mild AD: memory loss and cognitive difficulties
- Moderate AD: language, reasoning, recognition of family/friends
- Severe AD: cannot communicate, completely dependent on others



Current Treatments

FDA-Approved Drugs for Alzheimer's Disease

Drug	Formulations	Usual Daily Dosage	Starting Dose/ Titration
Acetylcholinesterase Inhibitors			
Donepezil - <i>Aricept</i> (Eisai/PD-RX) <i>Aricept ODT</i> (Eisai/PD-RX)	5 or 10 mg tabs 5 or 10 mg orally disintegrating tabs	5-10 mg once	5 mg once/d; after 4-6 wks increase to 10 mg once/d
Galantamine - immediate-release generic <i>Razadyne</i> ¹ (Ortho-McNeil)	4, 8 or 12 mg tabs; 4 mg/mL soln	16-24 mg divided bid	8 mg/d divided bid; after 4 wks increase to 16 mg/d, then after 4 wks to 24 mg/d
Extended-release generic <i>Razadyne ER</i> (Ortho-McNeil)	8, 16 or 24 mg caps	16-24 mg once	8 mg once/d; after 4 wks increase to 16 mg/d, then after 4 wks more to 24 mg/d
Rivastigmine - <i>Exelon</i> (Novartis)	1.5, 3, 4.5 or 6 mg caps; 2 mg/mL soln	6-12 mg divided bid	3 mg/d divided bid; increased in increments of 3 mg/d q2wks ² to 12 mg/d
Transdermal - <i>Exelon Patch</i> (Novartis)	4.6 mg/24 hours or 9.5 mg/24 hours	9.5 mg/24 hours	4.6 mg/24 hours; after 4 weeks if tolerated, increase to 9.5mg/24 hours
Tacrine - <i>Cognex</i> (Shionogi)	10, 20, 30, 40 mg caps	120-160 mg/day divided qid	10 mg 4x/day; after 4 weeks increase to 20 mg qid
NMDA-Receptor Antagonist			
Memantine - <i>Namenda</i> (Forest/PD-RX)	5 or 10 mg tabs; 2 mg/mL soln	20 mg, once or divided bid	5 mg once/d; increase to 20mg/d, increments of 5 mg q wk

1. Formerly Reminyl.

2. Every 4 weeks for dementia associated with Parkinson's disease.

Source: Treatment Guidelines from The Medical Letter, Vol. 8 (91) March 2010

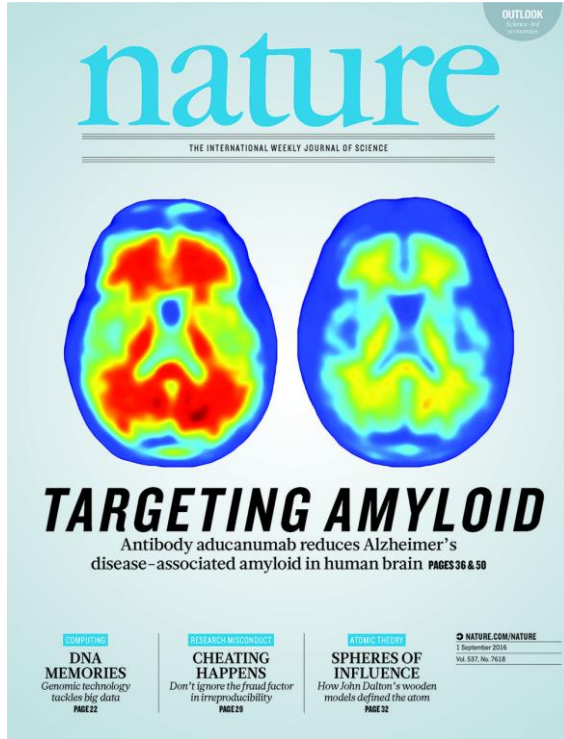
- AD is only top 10 cause of death that cannot be prevented, cured or even slowed
- 5 FDA-approved treatments
 - Treat symptoms
 - Help memory and cognitive functioning
 - Do not treat underlying causes

National Alzheimer's Plan



- Congress increased funding for AD by \$400 million in 2017
- According to the Alzheimer's Association, \$1.4 billion invested in AD in 2017
- National Alzheimer's Plan: achieve breakthroughs in prevention and treatment by 2025

Hope for Future Drugs



- Aducanumab
 - Antibody that targets amyloid before it becomes plaque
 - Phase III clinical trials expected to finish in 2019
- JNJ-54861911
 - Inhibits enzyme that makes amyloid
 - Phase III clinical trials expected to finish in 2024

Hope for Future Drugs



- AADvac1
 - Vaccine that stimulates immune system to attack abnormal form of tau protein
 - Phase II clinical trial expected to finish in 2019
- Sargramostim
 - FDA-approved for leukemia treatment
 - Stimulates innate immune system
 - Phase II study expected to be completed in 2017

Genetics and Alzheimer's Disease

	Early-Onset AD (Dominantly Inherited)	Early-Onset AD (Complex Inheritance)	Late-Onset AD (Complex Inheritance)
Cause:	Inherited Genetic Mutations	Genetic and Environmental Risk Factors	Genetic and Environmental Risk Factors
Age at Onset:	Usually 30-60 years	<65 years	>65 years
Proportion of Cases:	~1%	~4%	~95%

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What can you do? - Convincing Evidence

1. Exercise

- a. 30 minutes of aerobic exercise, 3-4 days/week

2. Healthy Eating

- a. Mediterranean diet has been shown to thwart Alzheimer's or slow its progression

3. Sleep

- a. More sleep → greater amyloid clearance from the brain



What can you do? - Some Evidence



1. Cognitive Stimulation

- a. Builds a cognitive reserve, so damage is less debilitating

2. Social Connection

- a. Social activities stimulate the brain

Questions?

References

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