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?

Information → Sensory Memory → Short-Term Memory → Long-Term 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

Dendrite

Neuron

Axon

Axon Terminal

Electric Signal

Image from pixabay.com
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
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

- 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?
Why Does Memory Fail?—Answer 2

- 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?
When Does Memory Fail?—7 Sins

- Absent-mindedness
- Transience
- Blocking
- Persistence
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

http://mercercognitivepsychology.pbworks.com
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

Excerpt from Clive Wearing’s diary in 1990

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

http://www.pbs.org/
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 Disease

- 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

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

THE ALZHEIMER’S TIMELINE

1. Early brain changes
2. Subtle decline in thinking
3. Memory changes, confusion
4. Inability to bathe, dress or eat without help
5. Loss of ability to communicate and recognize loved ones
Current Treatments

- 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

### FDA-Approved Drugs for Alzheimer’s Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulations</th>
<th>Usual Daily Dosage</th>
<th>Starting Dose / Titration</th>
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<tr>
<td>Acetylcholinesterase Inhibitors</td>
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<tr>
<td>Donepezil - Aricept (Eisai/PD-RX)</td>
<td>5 or 10 mg tabs; 5 or 10 mg orally dispersible tabs</td>
<td>5-10 mg once</td>
<td>5 mg once / d; after 4-6 wks increase to 10 mg once / d</td>
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<tr>
<td>Aclonzep (Eisai/PD-RX)</td>
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<tr>
<td>Galantamine - immediate-release generic</td>
<td>4, 8 or 12 mg tabs; 4 mg/mL soln</td>
<td>16-24 mg divided bid</td>
<td>8 mg / d divided bid; after 4 wks increase to 16 mg / d, then after 4 wks to 24 mg / d</td>
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<tr>
<td>Donepezil (Eisai/PD-RX)</td>
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<tr>
<td>Rivastigmine - Exelon (Novartis)</td>
<td>1.5, 3, 4.5 or 6 mg caps; 2 mg/mL soln</td>
<td>6-12 mg divided bid</td>
<td>3 mg / d divided bid; increased in increments of 3 mg / d q2wks2 to 12 mg / d</td>
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<tr>
<td>Transdermal - Exelon Patch (Novartis)</td>
<td>4.6 mg / 24 hours or 9.5 mg / 24 hours</td>
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<td>4.6 mg / 24 hours; after 4 weeks if tolerated, increase to 9.5 mg / 24 hours</td>
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<tr>
<td>Tacrine - Cognex (Shionogi)</td>
<td>10, 20, 30, 40 mg caps</td>
<td>120-160 mg / day divided qid</td>
<td>10 mg / 4x/day; after 4 weeks increase to 20 mg qid</td>
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<tr>
<td>Memantine - Namenda (Forest/PD-Rx)</td>
<td>5 or 10 mg tabs; 2 mg/mL soln</td>
<td>20 mg, once or divided bid</td>
<td>5 mg once / d; increase to 20 mg / d, increments of 5 mg q wk</td>
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1. Finaflex Reminyl.
2. Every 4 weeks for dementia associated with Parkinson’s disease.

Source: Treatment Guidelines from The Medical Letter, Vol. 58 (91) March 2010
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

- **Sagramostim**
  - FDA-approved for leukemia treatment
  - Stimulates innate immune system
  - Phase II study expected to be completed in 2017

Pictures from drugbank.ca and drugline.org
# Genetics and Alzheimer’s Disease

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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


