PART 1: Using ‘Brain Games’ to Make Inferences about Memory Systems

Katherine L. Possin, Ph.D.

BIOGRAPHY:

Dr. Katherine Possin is a neuropsychologist with expertise in the cognitive changes associated with neurodegenerative diseases. Her research program aims to elucidate the visuospatial and memory changes that emerge in the early stages of neurodegenerative diseases, including Alzheimer’s disease and Parkinson’s disease. The neural bases of these changes are investigated using multimodal neuroimaging. As part of this research, she is developing novel tests to evaluate these cognitive changes including virtual reality tests of spatial navigation that are analogous to rodent paradigms. Dr. Possin also evaluates patients for neurodegenerative diseases at the Memory and Aging Center Clinic.

Dr. Possin earned her B.A. in psychology from Tufts University (magna cum laude) and her Ph.D. in clinical psychology from the University of California, San Diego. She completed her clinical internship in the UCSF Department of Psychiatry and her postdoctoral fellowship at the UCSF Memory and Aging Center in the Department of Neurology. She is currently an Assistant Professor at the Memory and Aging Center.

BIBLIOGRAPHY:


PART 2: Brain Games and Physical Exercise: Forestalling Cognitive Decline

Brianne M. Bettcher, PhD

BIOGRAPHY:

Brianne Bettcher, PhD is an Assistant Professor in Neurology and works as a neuropsychologist at the Memory and Aging Center. After receiving her PhD in clinical psychology and neuroscience at Temple University, she completed her clinical neuropsychology internship at the Palo Alto Veterans Affairs Hospital as well as a neuropsychology fellowship at UCSF. Her research focuses on the role of inflammation in cognitive aging and utilizes cognitive neuroscience techniques to understand how vascular and inflammatory risk factors may impact brain structure. Her research is funded by an NIH/NIA K23 Career Development Award to study the relationship between peripheral inflammation, cognitive functions and white matter microstructure in healthy, community dwelling older adults.

BIBLIOGRAPHY:


PART 3: What Neuroscience Tells Us About the Self

Winston Chiong, MD, PhD

BIOGRAPHY:

Winston Chiong, MD PhD is an Instructor and Clinical Fellow in Neurology at the UCSF Memory and Aging Center, and is a Postdoctoral Fellow in the UC Berkeley Helen Wills Neuroscience Institute. After receiving his undergraduate degree in philosophy at Berkeley, he received his PhD in philosophy from New York University, and his MD from UCSF. He subsequently completed residency training in neurology at UCSF. His research interests lie at the intersections between philosophy, medicine and cognitive neuroscience. He has written about the ethics of medical education, clinical research and brain death. His current research focuses on human decision-making, and how it is affected by normal aging and neurodegenerative disease.

BIBLIOGRAPHY:


Brain Games that Capture Brain Circuits

Part 1: Using ‘Brain Games’ to Make Inferences about Memory Systems

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I have a memory problem.
- I have trouble finding words or names when I need them.
- Sometimes I can’t remember why I walked into a room, especially if I get distracted on the way.
- I forget where I put my keys or glasses, or where I parked my car.
- I can’t remember the meanings of words, or what objects are used for.
- I sometimes forget what I did yesterday or last week. Even when reminded, I still don’t remember.

“HM” – the famous patient who taught us about the role of the hippocampus in memory

- Dr. William Scoville performed a bilateral medial temporal lobe resection in 1953, curing HM’s seizures
- He could no longer commit new events to long-term memory

HM’s impaired memory system

- Long-term memory consolidation
  - What we usually mean when we say “memory”
  - Memory for events or facts
  - Permanent, unlimited capacity

HM’s spared memory abilities

- Learning a new skill (‘procedural memory’)
  - Learn skills or habits, knowing how to do something
  - Learning is unconscious

- Short-term memory (also called ‘working memory’)
  - Temporary, small capacity

Short-term “working” memory

- Working Memory holds information in conscious awareness so we can use it
- The information comes from our senses and from long term memory stores
- Duration: seconds, or as long as you rehearse the information “on-line”
- Capacity: very small
  - About 5-7 items in memory at a time
  - If you chunk, you can hold more information
  - The better you inhibit irrelevant information, the more relevant information you can hold
- Impaired by stress
A working memory test

- Say the letters in order followed by the numbers in order

Hippocampus degeneration in Alzheimer’s disease

Cardinal symptom is decreased memory consolidation

Let’s try a memory test.

The hippocampus is critical for memory consolidation

List learning in AD

Photo Researchers, Inc
How to be a good consolidator

We remember when we pay attention
  • Focus and reduce distractions

We remember when we make it meaningful
  • Make associations that give new information context or significance in terms of all the other things you have in your mind

Elaborative Encoding

Hi, My Name is Bri

Hi, My Name is Winston

Memory Consolidation Strategies

- Pay attention
- Make associations
  - We consolidate long-term memories in terms of their associations to other memories or concepts
  - The most effective associations are original, engage multiple senses, engage emotions, or are personally salient

Brain Bases of Long-term Memory

- Frontal-parietal circuits
- Hippocampus and related structures

Navigation Memory

- How will you navigate home after this talk?
Allocentric v. Egocentric Navigation

- Allocentric ("other-centered"): represent locations relative to major landmarks
  - "my house is northeast of UCSF, between Coit Tower and Fisherman’s Wharf"
  - Hippocampus
- Egocentric ("self-centered"): represent locations relative to your body
  - "To get to my house, I take a left on 3rd st. I take a right on King St and follow along the water. After I pass the Ferry Building, I take a left."
  - Caudate nucleus

Morris Water Maze

Insights and paradigms from rodent work can guide anatomically-focused test development

Video courtesy of Gladstone Behavioral Core

Allocentric Morris Maze Test

Egocentric Route Learning Test
Take Home Points

• There are several types of memory

• Each type of memory relies on a set of brain regions and circuits

• By measuring the function of different types of memory, neuropsychologists can make inferences about the integrity of the underlying brain circuits

Why do we need to understand the links between memory and brain circuits?

• Memory disorders tend to target specific circuits

• To treat these diseases, we need to understand how these memory systems work and why they fail

• Even healthy people can maximize their memories by understanding how memory systems work
Brain Games and Physical Exercise
Forestalling Cognitive Decline

Brianne M. Bettcher, PhD
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How Do We Slow Cognitive Aging?
Evolving Field of Cognitive Aging Research

Outline

• Cognitive Engagement
  – Plasticity
  – Cognitive Exercise and Games

• Physical Exercise
  – Physical Activity
  – Mechanisms of Physical Exercise

Plasticity and Cognitive Reserve
The Nun Study

• Longitudinal Study of Aging

• Available Data:
  – Annual examinations
  – Convent archives of early and middle life
  – Brain autopsies upon death

Plasticity and Cognitive Reserve

“Brain Pathology”
Under the Microscope

“Clinical Manifestation”
Face-Face Presentation

Alzheimer’s Disease Dementia
Clinically Normal, No Dementia

Cognitive Reserve (CR)
Yaakov Stern, Columbia University

• Cognitive Reserve -
  – Accounts for the noted differences between severity of brain pathology and clinical presentation.

  – Proposes that differences in how tasks are mentally processed can help some people cope better than others with brain changes (Stern, 2002).

Sister Matthia, a model of healthy aging in the Nun Study, at 104 years of age, 3 months before she died.
Snowdon DA Ann Intern Med 2003;139:450-454

©2003 by American College of Physicians

Image courtesy of William Seely & Stephen DeArmond
Cognitive Reserve

- Patients with **CR** may handle a larger amount of brain damage before showing the same level of impairment.

Cognitive Exercise & Brain Games

- Cognitive Leisure Activity
- Cognitive Interventions
  - Cognitive Training

Findings: Promising, but Mixed

Brain Games: Gazzaley Lab Studies

- First Day: Lab EEG testing
- Last Day: Lab EEG testing
- One Month: Home Training

Collaboration with Colleagues at Lucas Arts (Funded by Robert Wood Johnson Foundation)

Brain Games: Gazzaley Lab Studies

Interference Diagnostic

Single-task

Multitask

Multitasking Cost: ((Single task - Multitask) / Single task) X 100

Courtesy of Dr. Joaquin A. Anguera, and Dr. Adam Gazzaley’s Lab

Brain Games: Gazzaley Lab Studies

Multitasking Cost

Decades of Life

57%

27%

-27%

-63%

No Cost

Decades of Life

Courtesy of Dr. Joaquin A. Anguera, and Dr. Adam Gazzaley’s Lab
Cognitive Engagement Review

- Plasticity and Cognitive Reserve
  - Strong evidence that our brains continue to change and adapt
  - Research has uncovered many risk and protective factors
- Cognitive Engagement and Brain Games
  - New research suggests that brain games targeting specific cognitive processes may be helpful
  - Promising area of research, although still in its infancy

Course Outline

- Cognitive Engagement
  - Cognitive Reserve
  - Cognitive Exercise, Games, and Leisure
- Physical Exercise
  - Physical Activity
  - Mechanisms of Physical Exercise

Physical Exercise

- Physical activity, particularly aerobic activity, is associated with a significant reduction in risk of dementia.

Middleton et al. JAGS. 2010, 58, 132201326.

Physical Exercise and BDNF

- Women who report being physically active, particularly during teenage years, show a lower likelihood of cognitive impairment in late life.
- Individuals who became active later in life also showed lower risk than those who were never active.

Physical Exercise and the Hippocampus

Figure: Voluntary exercise induces BDNF.
Physical Exercise: Mechanisms

- Inflammation is related to lower integrity of white matter in brain

Physical Exercise Review

- Physical Activity
  - Considerable evidence that you can reap the benefits of exercise at any age.
- Mechanisms of Physical Exercise
  - Exercise reduces vascular risk factors, obesity, & inflammatory markers, and improves neuronal function.
  - Exercise may alter brain structure as well.

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What Neuroscience Tells Us about the Self

Winston Chiong, MD PhD
UCSF Mini Medical School – November 15, 2012

Brain diseases teach us about how the healthy brain is organized

Psalm 137 (King James Version):
If I forget thee, O Jerusalem,
    let my right hand forget her cunning.
If I do not remember thee,
    let my tongue cleave to the roof of my mouth;
    if I prefer not Jerusalem above my chief joy.

What’s the connection here?

Focal vs. distributed

• Focal lesions: strokes, tumors, neurosurgery
  • Vision
  • Language
  • Memory
  • Control of movement
  • Sense of touch
• More distributed in the brain (?)
  • How are these different functions brought together to make us who we are?

“The self”

• Seems to refer to many different things
  • Individuality: myself, yourself, self vs. other
  • Reflexivity: self-awareness
  • Personhood: being a self
  • Identity: remaining the same person over time
  • Autonomy: to be a law to oneself
• Related to global processes that integrate the activity of different parts of the brain
Controversy: loss of self in dementia

Two problems of integration
- "Synchronic unity" – at a given time
- Many different things compete for our attention
- We have conflicting aims and desires
- Must focus, prioritize, and allocate attention
- "Diachronic unity" – across different times
- Plan for the future
- Recall prior intentions and completed tasks
- "Mental time travel"

Two causes of dementia
- Frontotemporal dementia
  - disinhibition, distractibility
  - loss of concern for other people
  - compulsive/repetitive movements
  - overeating (especially sweets)
  - loss of insight
- Alzheimer’s disease
  - forgetting episodic memories
  - impaired learning
  - disorientation in time
  - difficulties with navigation

Two brain networks
- Salience network:
  - Value and emotion
  - Motivation
  - Attention/alertness
  - Staying on task
- Default network
Two brain networks

Default network:
• Autobiographical memory
• Envisioning the future
• Navigation
• Adopting other perspectives
• Mind-wandering (Dynamic simulation?)

Conclusions

• Two distributed networks
• Coordinate/organize the activity of the other parts of the brain
• Give coherence to our thoughts, motivations and actions
• Synchronic unity: salience network
• Diachronic unity: default network

Conclusions

• Is the self lost in dementia?
  • need to distinguish different kinds of unity
• Alzheimer’s: loss of unity across time
  • trouble linking one moment to the next
  • but can be very present in the moment
• FTD: loss of unity at a given time
  • distracted, emotionally disengaged, bizarre
  • but memory of past events (if paying attention) can be preserved