Brain Imaging Applied to Memory & Learning

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Levels of Analysis
Molecules/Synapses/Neurons/Networks/Maps/Systems/CNS
Is memory in the brain distributed or localized???

“It is not possible to demonstrate the isolated localization of a memory trace anywhere in the nervous system...The engram is represented throughout the region”

*Karl Lashley 1950*
Maze
more cortical brain injury results in worse learning and memory regardless of lesion (injury) location

mass action for distributed memory

Figure 16B. Relationship between extent of neocortical lesion and errors in learning or relearning the Lashley III maze. Top. Original learning (N = 37). The ordinate indicates for each animal the percentage of cortex removed, and the abscissa indicates the number of errors made during learning. Bottom. Relearning of the same maze task in rats with lesions made about 2 weeks after original learning (N = 59). The ordinate indicates the percentage of cortex removed, and the abscissa indicates the number of errors made during the postoperative retention test. (From Lashley, 1929.)
Location of hippocampus
Hippocampus of Human Brain

a sea horse
“HM”
Henry Molaison
1926-2008
THE AMNESIC PATIENT H.M.

1926 Birth
1942 Age 16, First major seizure
1953 Age 27, Bilateral medial temporal-lobe resection
1955 Report of pervasive and profound anterograde amnesia by Dr. Brenda Milner
1962 Neuropsychological examinations characterizing the amnesic syndrome

Figure 14.20 The hippocampus of H.M. The hippocampus (H) and entorhinal cortex (EC) are present in the brain of a normal subject (right), but absent bilaterally in the brain of H.M. (left).

What were the consequences of bilateral removal of H.M.’s hippocampus? (p. 441)
High Average Intelligence
Intact Short Term Memory (7 digits)
Normal Conversation, Math Performance
Good Memory of Distant Past (his name, his school, his parents)
Personality Maintained
Unable to Acquire New Memories for Events & Facts (people, places, news)
  - all modalities
  - all materials (verbal & nonverbal)

Retrograde Amnesia  Anterograde Amnesia
1953 surgery
HM’s Reflections

“Every day is alone in itself, whatever joy I’ve had and whatever sorrow I’ve had.”
(Milner et al, 1968)

“Right now I’m wondering. Have I done or said anything amiss? You see, at this moment everything looks clear to me, but what happened just before? That’s what worries me. It’s like waking from a dream; I just don’t remember.” (Milner, 1970)
Declarative (Explicit) Memory Neural Systems

• medial temporal lobe (global amnesia)

Amnesic Patient H.M.
HM - Henry Molaison
1926-2008

http://thebrainobservatory.ucsd.edu/content/120209

2600 slices/70 microns
PERMANENT PRESENT TENSE

The UNFORGETTABLE LIFE of the AMNESIC PATIENT, H.M.

SUZANNE CORKIN
Alzheimer’s disease

AD

neurofibrillary tangles

amyloid plaques

Typical

Typical

AD
Declarative (Explicit) Memory Neural Systems

- medial temporal lobe
- dorsolateral prefrontal cortex
Declarative (Explicit) Memory Neural Systems

- dorsolateral prefrontal cortex
  (deficits in source, recency, frequency)
Magnetic Resonance Imaging - MRI

Magnet aligns some atoms in the body; Radio frequency fields systematically alter alignment of magnetization; Nuclei produce rotating magnetic field detectable by the scanner
MRI – Lateral Views
Structure – Brain Changes with Learning

Three-ball juggling routine 3 month
hMT/V5
Functional Magnetic Resonance Imaging (fMRI) – Brain Function

- increased blood flow to active region
- hemoglobins become deoxygenated as neurons use up the supplies of $O_2$
- fMRI measures ratio of Oxy:Deoxy
- Blood Oxygenation Level Dependent effect (BOLD effect)
Stages of Memory

Encoding → Storage → Retrieval

behavior

Functional neuroimaging
A Penny for Your Thoughts

Ages 5-30

3 pennies/day $\times$ 365 days/year $\times$ 25 years

= 27,375 pennies
1. Does the Lincoln on the penny face right or left?

2. Is anything above his head? What?

3. Is anything below his head? What?

4. Is anything to his left? What?

5. Is anything to his right? What?
Fig. 1. Examples of drawings obtained from people who tried to reproduce a penny from memory.

Nickerson and Adams, 1979
Visual Encoding Task

“indoor or outdoor?”

Event

Event

Event

Event

15.84 s

2.88 s 10.08 s

0 s 380 s

24 events X 4 runs...

380 s
Event-Related Design
For Subsequent Memory

Separate response recorded for each stimulus

Later memory test

Compare fMRI responses leading to successful vs unsuccessful memory encoding
Greater Activation at Encoding Predicts Subsequent Memory

Brewer et al., Science, 1998
Greater Medial Temporal Lobe and Frontal Lobe Activation Correlated with Successful Memory Formation

Brewer et al., Science, 1998
How do declarative memory systems develop in the brain?
9.5 year old girl, scanned 3 times over 6 months

You have let me have more fun in 3 days than I could have in any other place. Just think of it. I'm playing a game when at the same time I'm a researcher. Ginny pig. And who knows I might help someone else my age if they have any brain problems. While still earning money. And what do you think beats that? Nothing.
Experimental Design

Participants: 14 adults (ages 19-24 years), 35 children (ages 8-17 years)

Memory Task:

Encoding (scanned):

250 scenes

Recognition test: Item

500 scenes

Response Condition

Old; Remembered R
Old; Familiar K
New F
Behavioral Results

\[ r = 0.29^*, p < 0.05 \]

\[ r = -0.01, \text{n.s.} \]

\[ r = 0.33^*, p = .02 \]
Regions of Interest: Remembered > Forgotten
Remembered > Forgotten

Ofen et al., *Nature Neuroscience*, 2007
Controlling Human Learning

Yoo et al., *NeuroImage*, 2012

Yoo et al., *NeuroImage*, 2012
Better Learning in good versus bad brain states
Fear & The Amygdala
Selective Amygdala Lesions

Cute and cuddly or fearsome predator?

Blanchard & Blanchard (1972)
Human Amygdala:
Emotional Influences on Recollection

(Urbach-Wiethe Disease)
Cahill et al., 1995
Hamann et al, 1996

- View story with emotional middle section
- Test recall 1-week later
- Intact emotional reactions
- No enhanced memory
Visual Encoding Task

“How emotionally intense do you find this picture?”

Event: fixation point

15.84 s

2.88 s

10.08 s

380 s

24 events
X 4 runs
Emotional Experience

![Brain Image]

Percent Activation

Stimulus Presentation Period

L ←→ R

Legend:
- 3
- 2
- 1
- 0
Decline of Fluid Skills and Preservation of Crystallized Skills across the Life Span

Park et al., 2002, *Psychology and Aging*
Memory for emotionally positive, negative, and neutral pictures

Mather et al., *Psychological Science*, 2004
Recall Proportions

Younger
Positive: 0.38
Negative: 0.30
Neutral: 0.20

Older
Positive: 0.45
Negative: 0.32
Neutral: 0.25
Amygdala Activation

% signal change

younger

positive
neutral
negative
Amygdala Activation

% signal change

-0.06 -0.04 -0.02 0 0.02 0.04 0.06 0.08 0.1

younger older

positive neutral negative

Diagram showing the % signal change in the amygdala activation for positive, neutral, and negative stimuli in younger and older groups.
Maintaining Cognition in Older Adulthood

- Cardiovascular Exercise
- Cognitive Exercise?
PHYSICAL EXERCISE
(Erickson et al., 2011)

• 120 adults
  60 aerobic & 60 stretching
  3 days/wk, 7 weeks, up to 40 min/session
Increase in hippocampus volume (2%) for aerobic exercise group and a decrease in volume for stretching control group.

A. Hippocampus

B. Caudate Nucleus

C. Thalamus
Improved Spatial Memory After Aerobic Physical Exercise

Erickson K I et al. PNAS 2011;108:3017-3022
Education & Learning: Achievement Gap
High-Stakes Statewide Standardized Tests

Massachusetts Comprehensive Assessment System
MCAS – Math & ELA
Cortical Thickness Analysis
Greater Cortical Thickness Correlates with Better Standardized Test Scores

Cluster-corrected, $Z > 1.3$, $p < .05$, 2 hemispheres
Greater Cortical Thickness With Higher SES (Paid Lunch > Free Lunch)

Cluster-corrected, $Z > 1.3, p < .05, 2$ hemispheres