Loss of Recent Memory After Bilateral Hippocampal Lesions

William Beecher Scoville and Brenda Milner (1957)
Tips for reading primary literature

Abstract

Introduction

Results ↔ Figures ↔ Methods

Discussion
Abstract
Abstract

• Patients with removal of a large portion of the medial temporal lobe exhibit a grave and unexpected memory deficit

• Memory deficit merits further investigation (i.e., characterize extent of memory deficit and probe for other deficits)

• What the study did: carries out formal memory and intelligence testing

• What the study found: hippocampal complex is important for normal memory function
Introduction
Introduction

• For each patient:
  – What was the patient’s relevant history (i.e., why was the operation performed)?
  – What brain regions were removed?
  – What impairments were observed post-operatively (i.e., what prompted the formal memory investigation)?
Patient HM
Patient HM

• What was the relevant history?
  – Knocked down by bicycle at age 9
  – Was unconscious for 5 minutes and sustained a head injury
  – Seizures
    – Minor seizures since the age of 10
    – Major, incapacitating seizures since the age of 16
  – Unresponsive to medication
Patient HM

- What brain regions were removed?
  - Medial portion of the temporal lobe, bilaterally, extending 8cm posteriorly from the temporal pole
    - MRI now shows this to be 5cm bilaterally, not 8cm
  - Removed brain structures: amygdala, uncus, anterior two thirds of the hippocampus, anterior portion of hippocampal gyrus
HM’s Lesion (Figure 2)
H.M.’s presumed lesion

Amygdala
Subicular Complex
Entorhinal Cortex
Perirhinal and Parahippocampal Cortices
Hippocampus
Dentate Gyrus

Courtesy of Squire, L.R.
Patient HM

What impairments were observed post operatively? Just a few examples…

- Could no longer recognize hospital staff or find his way around hospital
- Recalled nothing of daily events, such as what he ate for lunch
- Reads same magazines and does the same puzzles day after day
- Did not remember events in the recent past, such as the death of an uncle three years before
- Early memories appeared intact
You test a patient with a lesion of the MTL on a certain task. They do as well as normal people. What can you say?

You test the same patient on another task. They don’t do as well as normal people. What can you say?
Methods, Results, Figures
Methods

• Formal testing of each patient to obtain a detailed description of functional deficit
  – Tests of intelligence and perception
  – Tests of memory
Results and Figures
# Tests of Intelligence

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intelligence Quotient (IQ)</td>
<td>✔️</td>
<td></td>
</tr>
<tr>
<td>Perception</td>
<td>✔️</td>
<td></td>
</tr>
<tr>
<td>Abstract thinking and reasoning</td>
<td>✔️</td>
<td></td>
</tr>
<tr>
<td>Personality and motivation</td>
<td>✔️</td>
<td></td>
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</tbody>
</table>
Tests of Intelligence

RESULT: No impairment of personality or general intelligence following bilateral removal of the medial temporal lobe
Tests of Memory

<table>
<thead>
<tr>
<th>Sample Question</th>
<th>Normal</th>
<th>Impaired</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>
## Tests of Memory

<table>
<thead>
<tr>
<th>Sample Question</th>
<th>Normal</th>
<th>Impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is current date?</strong></td>
<td></td>
<td><strong>X</strong></td>
</tr>
<tr>
<td>(HM’s answer: March 1953 Correct: April 26, 1955)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Tests of Memory

<table>
<thead>
<tr>
<th>Sample Question</th>
<th>Normal</th>
<th>Impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is your age? (HM’s answer: 27 Correct: 29)</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
# Tests of Memory

<table>
<thead>
<tr>
<th>Sample Question</th>
<th>Normal</th>
<th>Impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td>View a drawing&lt;br&gt;Then draw it as accurately as possible from memory</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

Does impairment on this task imply a memory impairment? What else would you like to see as a control?
Rey-Osterrieth Complex Figure

Hippocampal Lesion  MTL Lesion (HM)  Control

Courtesy of Squire, L.R.
A Short Number Sequence

Task: remember the number “584”.

A few minutes later, when asked for the number, HM said “584”.

How did HM remember the number sequence?

“It’s easy. You just remember 8. You see 5, 8, and 4 add to 17. You remember 8, subtract it from 17, and it leaves 9. Divide 9 in half and you get 5 and 4 and there you are: 584. Easy.”

A few minutes later, after he had been engaged in another task, HM had no recollection of the number or of his train of thought about it. Thus, there is another (immediate) memory system that is intact in HM and is independent of the hippocampus.
Mirror Tracing Task

- Mirror tracing task, Milner, 1965
How would you expect a normal person to perform on mirror tracing across a number of practice sessions?

So, this task involves learning?

How do you expect HM to do on mirror tracing?
HM’s Performance on Mirror Tracing

• Before each session, HM would claim that he had never done the task.

• Yet, once he performed the task…

Milner 1965
### Summary of 10 Patients (Table 1)

<table>
<thead>
<tr>
<th>Cases</th>
<th>Age at Time of Follow-up (yr)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Operation</th>
<th>Bi- or Unilateral</th>
<th>Approximate Extent of Removal along Medial Temporal Lobes (cm)</th>
<th>Time between Operation and Testing (mo)</th>
<th>Wechsler Scale Intelligence Quotient</th>
<th>Memory Quotient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe memory defect</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1, H. M.</td>
<td>29</td>
<td>M</td>
<td>Epilepsy</td>
<td>Medial temporal</td>
<td>B</td>
<td>8</td>
<td>20</td>
<td>112</td>
<td>67</td>
</tr>
<tr>
<td>Case 2, D. C.</td>
<td>47</td>
<td>M</td>
<td>Paranoid schizophrenia</td>
<td>Medial temporal and orbital undercutting</td>
<td>B</td>
<td>5.5</td>
<td>20</td>
<td>122</td>
<td>70</td>
</tr>
<tr>
<td>Case 3, M. B.</td>
<td>55</td>
<td>F</td>
<td>Manic-depressive psychosis</td>
<td>Medial temporal</td>
<td>B</td>
<td>8</td>
<td>28</td>
<td>78</td>
<td>60</td>
</tr>
<tr>
<td>Group II:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Moderate memory defect</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Case 4, A. Z.</td>
<td>35</td>
<td>F</td>
<td>Paranoid schizophrenia</td>
<td>Medial temporal</td>
<td>B</td>
<td>5</td>
<td>40</td>
<td>96</td>
<td>84</td>
</tr>
<tr>
<td>Case 5, M. R.</td>
<td>40</td>
<td>F</td>
<td>Paranoid schizophrenia</td>
<td>Medial temporal and orbital undercutting</td>
<td>B</td>
<td>5</td>
<td>39</td>
<td>123</td>
<td>81</td>
</tr>
<tr>
<td>Case 6, A. R.</td>
<td>38</td>
<td>F</td>
<td>Hebephrenic schizophrenia</td>
<td>Medial temporal and orbital undercutting</td>
<td>B</td>
<td>4.5</td>
<td>47</td>
<td>Incomplete</td>
<td></td>
</tr>
<tr>
<td>Case 7, C. G.</td>
<td>44</td>
<td>F</td>
<td>Schizophrenia</td>
<td>Medial temporal</td>
<td>B</td>
<td>5.5</td>
<td>41</td>
<td>Incomplete</td>
<td></td>
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<tr>
<td>Case 8, A. L.</td>
<td>31</td>
<td>M</td>
<td>Schizophrenia</td>
<td>Medial temporal</td>
<td>B</td>
<td>6</td>
<td>38</td>
<td>Incomplete</td>
<td></td>
</tr>
<tr>
<td>Group III:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No memory defect</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Case 9, I. S.</td>
<td>54</td>
<td>F</td>
<td>Paranoid schizophrenia</td>
<td>Uncectomy</td>
<td>B</td>
<td>4</td>
<td>53</td>
<td>122</td>
<td>125</td>
</tr>
<tr>
<td>Case 10, E. G.</td>
<td>55</td>
<td>F</td>
<td>Incisural herniation</td>
<td>Inferior temporal lobectomy</td>
<td>U-Rt.</td>
<td>9</td>
<td>16</td>
<td>93</td>
<td>90</td>
</tr>
</tbody>
</table>

- All patients with bilateral MTL damage have impaired memory.
- The patient with unilateral damage and the patient with damage outside of the hippocampal region did not have a memory impairment.
Discussion
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• The ability to acquire new memories is a distinct function (separate from functions such as perception or reasoning), and it is localized to the medial temporal lobes.

• The medial temporal lobes are not required for immediate memory.

• The medial temporal lobe and the hippocampus cannot be the site of final storage for long-term memory of knowledge that was acquired before lesion.

• The medial temporal lobe is not necessary for acquiring some kind of knowledge. This suggested that there is more than one type of memory in the brain.
Subdivisions of Human Memory

HUMAN MEMORY

DECLARATIVE (EXPLICIT)
- FACTS
- EVENTS

NONDECLARATIVE (IMPLICIT)
- PROCEDURAL (SKILLS AND HABITS)
- PRIMING
- SIMPLE CLASSICAL CONDITIONING
- NONASSOCIATIVE LEARNING
  - EMOTIONAL RESPONSES
  - SKELETAL MUSCULATURE

MEDIAL TEMPORAL LOBE
- STRIATUM
- NEOCORTEX
- AMYGDALA
- CEREBELLUM
- REFLEX PATHWAYS