Introduction – H.M.

- Epileptic patient
- Temporal lobectomy → “Amnesia”
Contents

• Theories of memory
  – Sensory, short-term & long-term memories

• Memory & brain

• Cellular bases of learning & memory
Theory of Memory
Theories of Memory

• Learning
  – The process of acquiring new information
  – Learning happens when a memory is created or is strengthened by repetition.

• Memory
  – Persistence of learning in a state that can be revealed at a later time

• Encoding
  – Processing of incoming information to be stored. Acquisition registers inputs in sensory buffers and sensory analysis stages.
  – Consolidation creates a stronger representation over time.
  – Storage creates and maintains a permanent record.
  – Retrieval utilizes stored information to create a conscious representation.
Sensory and short-term memory mechanisms / Sensory memory

- Sensory memory
  - Decaying relatively swiftly
  - Partial report
  - Echoic memory: audition
  - Iconic memory: vision

Fig 8.1 Partial report experiment

Fig 8.2 MMF
Sensory and short-term memory mechanisms / Short-term memory (1/2)

- Limited capacity
- Seconds ~ minutes

Fig 8.3 Short-term retention of verbal items
Sensory and short-term memory mechanisms / Short-term memory (2/2)

- **Serial position effect**
  - **Primacy effect**
    - At the beginning of the list
    - Enough capacity to transfer from short- to long-term memory
    - Unchanged by adding a distracting task at the end of the list
    - Eliminated if the list items were presented more quickly
  - **Recency effect**
    - At the end of the list
    - Available in short-term memory

Fig 8.4 Serial position effect
Models of short-term memory
/Modal model

Fig 8.5 Modal model of memory
Models of short-term memory
/Levels of processing models

• Levels of processing model
  – The deeper (more meaningful) an item was processed, the more it was consolidated and stored in long-term memory
  – Experiments by Fergus Craik and Robert Lockhart (1972)
    • Superficial level: whether the words were composed of uppercase or lowercase letters
    • Intermediate level: whether a word rhymed with another word
    • Deep level: making a judgment about the meaning of the word
    • Subjects showed better subsequent memory for items more deeply processed during learning
  – Deep or elaborate rehearsal and encoding create meaning-based codes that relate information directly to previously acquired knowledge
Models of short-term memory
/Neuropsychological evidence against the
modal model of memory

• Evidences against the modal model
  – The patient who displayed reduced digit span
    ability still retained the ability to form new long-
    term memories
  – A patient E. E. showed below-normal short-term
    memory ability but preserved long-term memory
  – Information from sensory memory registers can
    be encoded into long-term memory directly
Models of short-term memory
/Working memory models

• A limited-capacity store for retaining information over the short term and for performing mental operations on the contents of this store

• Three-part working memory
  – The central executive mechanism
  – The phonological loop
  – The visuospatial sketchpad

Fig 8.7 Working memory model
Models of long-term memory

Fig 8.9 The hypothesized structure of human memory
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Memory & Brain
Human memory, brain damage, and amnesia
/Brain surgery and memory loss (1/3)

• Neurosurgical procedures
  - Perfrontal lobotomy: removing or disconnecting the prefrontal lobe
  - Corpus callosotomy: surgically sectioning the corpus callosum
  - Amygdalotomies: removing the amygdala
  - Temporal lobe resection: removal of the temporal lobe
Human memory, brain damage, and amnesia
/Brain surgery and memory loss(2/3)

• Patient H.M
  – Bilateral medial temporal lobe resection developed dense amnesia
  – Normal short-term memory, normal digit span abilities
  – What appeared to be disrupted was the transfer of information from short-term storage to long-term memory

Fig 8.10 Digit span for amnesic patients

Fig 8.11 The medial temporal lobe & areas believed to have been removed from H.M.
Human memory, brain damage, and amnesia / Brain surgery and memory loss (3/3)

- A patient R.B.
  - Specific lesion restricted to CA1
  - Hippocampus is crucial in forming new long-term memories.

Fig 8.14 Section of brain from R.B. & normal
Human memory, brain damage, and amnesia
/Memory consolidation and the hippocampus

• Memory consolidation
  – memories are solidified in long-term stores over long-term period

• The hippocampal region is critical for the consolidation of information in long-term memory
  – Evidence: amnesics have retrograde amnesia for memories from one to a few years prior to the damage to the medial temporal lobe or diencephalon, a pattern that does not support a storage role but rather a role in consolidation
  – Consolidation strengthens the associations between multiple stimulus inputs and activations of previously stored information
  – Once consolidation is complete, the hippocampus is no longer required for storage or retrieval
Human memory, brain damage, and amnesia
/ Anterior and lateral temporal lobes and memory

• Lesions that damage the lateral cortex of the anterior temporal lobe lead to a dense amnesia that includes severe retrograde amnesia

• The lateral and anterior regions of the temporal lobe: the sites of storage of long-term declarative memories or regions for retrieval of information from long-term stores
Human memory, brain damage, and amnesia

Amnesics can learn new information (1/2)

• Medial temporal lobe damage generally is associated with the inability to learn new information

• Is it true that damage to the medial temporal lobe memory systems affects both episodic and semantic memory?

• Amnesic’s learning of new information includes semantic knowledge
Human memory, brain damage, and amnesia

Amnesics can learn new information

- Patient K. C.
  - His retrograde amnesia involved episodic information from his entire life
  - Intact semantic memory for general world knowledge
  - K. C. demonstrated perceptual priming effects & procedural learning.

Fig 8.17 K.C.’s lesions

Fig 8.19 Sequence learning paradigm
Human memory, brain damage, and amnesia
/Deficits in forming new nondeclarative
memories

• The dissociations in what amnestics can learn
indicate that distinct neural systems mediate
different forms of memory
  – One alternative interpretation: the differential
demands that different types of knowledge place on a
single cognitive-neural memory system
    • Declarative memory is more cognitively demanding and
thus is first affected by partial damage to a hypothesized
unitary memory system
  – Double associations are the strongest evidence for
two separate systems
Human memory, brain damage, and amnesia
/ The perceptual representation system (PRS) (1/3)

Fig 8.20 A word-priming study
Human memory, brain damage, and amnesia

The perceptual representation system (PRS) (2/3)

• Information is remembered better on recall or recognition tests if it is processed more deeply during encoding
  – Subjects complete fragments of words and perform better with words previously viewed even without explicitly recognizing them
  – When the initial words are presented auditorily, and then perform the implicit tests visually, priming from auditory to visual is reduced for the implicit tests
  – Implicit memory in priming reflects a PRS that subserves structural, visual, and auditory word form representations
Human memory, brain damage, and amnesia
/The perceptual representation system (PRS) (3/3)

- Possible and impossible objects
  - Subjects were better at deciding on objects previously viewed
    - This occurred only for possible objects, and only when subjects were instructed to pay attention to the global form of the stimulus at the time of encoding
- The PRS apparently mediates word and nonword forms of priming, and so implicit memory of this type is not based on conceptual systems but rather is perceptual in nature
- Patient M. S.
  - Removing most of areas 18 and 19 of his right occipital lobe<그림 8.23>
  - Explicit tests of memory (recognition and cued recall) and implicit memory (perceptual priming)
  - The test materials were words presented briefly and then read aloud
  - The amnesic patients displayed the expected impairment of explicit word recognition, but they did not show impairment in the implicit perceptual priming
  - M. S. had the novel pattern of normal performance on explicit recognition but impairment in the implicit perceptual priming test
Animal models of memory

- What structures of the medial temporal lobe systems are involved in episodic memory?

- Delayed non-matching to sample task

Fig 8.26 The medial temporal lobe of the monkey

Fig 8.25 Memory task
Animal models of memory

- Delayed nonmatching to sample task
  - Memory was impaired only if the lesion included the hippocampus and amygdala
  - The presence of absence of the amygdala lesion did not affect the monkey’s memory
    → the amygdala could not be part of the system that support the acquisition of long-term memory

Fig 8.27 The delayed nonmatching for normal monkey vs. monkeys with lesions
Animal models of memory

- The hippocampus cannot function properly if the parahippocampal and perihinal regions are damaged.
- These regions are involved in much processing themselves.
- Lesions restricted to the hippocampus do not produce as severe a form of amnesia as do lesions that include surrounding cortex.

Fig 8.28 Information flow between neocortex & hippocampus

Fig 8.29 The hippocampal memory system in monkeys & rats
Imaging the human brain and memory
/Episodic encoding and retrieval (1/3)

• Whether the hippocampus becomes active when encoding new information
  – The right hippocampal region was activated during encoding of the face but not during recognition, where retrieval processes should have been engaged
  – Encoding also activated the left prefrontal cortex, whereas recognition activated the right prefrontal cortex
  – When subjects were asked to perform a retrieval task for episodic memories, the right, not the left, hemisphere was activated

• The left prefrontal region and hippocampal region were active during the intentional encoding of information, whereas the right prefrontal region was activated during episodic retrieval
Imaging the human brain and memory / Episodic encoding and retrieval (2/3)

Fig 8.30-31 A PET study of encoding and retrieval of face information

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Imaging the human brain and memory
/Episodic encoding and retrieval (3/3)

Fig 8.32-34 Brain imaging:
Brain activation
by episodic encoding & retrieval
Imaging the human brain and memory
/Procedural memory encoding and retrieval

• Experiment
  – The subjects responded to stimulus sequences by pushing a button with their right hand while monitoring a sequence of tones and counting those of lower frequency
  – Activated region: the motor cortex, the supplementary motor area of the left hemisphere, the putamen in the basal ganglia bilaterally, the rostral prefrontal cortex, and parietal cortex
  – When the auditory task was removed: the right dorsolateral prefrontal cortex, right premotor cortex, right putamen, and parieto-occipital cortex

Fig 8.35 Activations corresponding to implicit learning of motor sequences
Imaging the human brain and memory
/Procedural memory encoding and retrieval

• Motor cortex is critical for implicit procedural learning of movement patterns
• The supplementary motor cortex may be part of the cortical-subcortical motor loop, which regulates voluntary movements
• Explicit learning and awareness of the sequences required increased activity in the right premotor cortex, the dorsolateral prefrontal cortex associated with working memory, the anterior cingulate, areas in the parietal cortex concerned with voluntary attention, and the lateral temporal cortical areas that store explicit memories
Imaging the human brain and memory
/Perceptual priming and implicit and explicit memory (1/2)

• Experiment
  – Schacter et al. showed the subjects the words but required them to process the words only for surface perceptual features
  – Subjects were assigned an implicit stem-completion task in which some experimental blocks had stems from previously presented words and other blocks had stems of new words
  – Result
    • Subjects manifested implicit priming behaviorally
    • No activations or deactivations were noted in the hippocampus, but blood flow in the bilateral occipital cortex (area 19) decreased
    • The hippocampus was not activated, even though implicit perceptual priming was obtained

Fig 8.36 PET scans during recall of words
• Implicit and explicit retrieval of information is subserved by separate brain systems
• The hippocampus is activated most when explicit retrieval includes significant experience with the material, not merely an attempt to retrieve information
• The hippocampus encodes new information but also retrieves recent information when explicit recollection is involved
• Deactivation of the visual cortex for previously seen words is a correlate of perceptual priming
Cellular Bases of Learning & Memory
Long-term potentiation and the hippocampus (1/4)

- Three major excitatory neural components of the hippocampus
  - **Perforant pathway**
    - forms excitatory connections between the parahippocampal cortex and the granule cells of the dentate gyrus
  - **Mossy fibers**
    - connect the granule cells of the dentate gyrus to the CA3 pyramidal cells
  - **Schaffer collaterals**
    - connect the CA3 pyramidal cells to the CA1 pyramidal cells

![Synaptic organization of the rat hippocampus](image)

Fig 8.37 Synaptic organization of the rat hippocampus
Long-term potentiation and the hippocampus (2/4)

• LTP (long-term potentiation)
  - Stimulation of axons of the perforant pathway leads to greater synaptic strength in the perforant pathway such that later simulation created larger postsynaptic responses in the granule cells of the dentate gyrus

• LTD (long-term depression)

Fig 8.38 LTP in perforant pathways
Long-term potentiation and the hippocampus (3/4)

• Hebbian learning
  - If a synapse is active when a postsynaptic neuron is active, the synapse will be strengthened

• Associative LTP
  - If a weak and a strong input act on a cell at the same time, the weak synapse becomes stronger
  - When two weak inputs (W1 and W2) and one strong input (S1) are given to the same cell, and when W1 and S1 are active together, W1 is strengthened whereas W2 is not. Subsequently, if W2 and S1 are active together, W1 is not affected by the LTP induced from W2 and S1
Long-term potentiation and the hippocampus (4/4)

• Three rules for associative LTP
  – Cooperativity: more than one input must be active at the same time
  – Associativity: weak inputs are potentiated when co-occurring with stronger inputs
  – Specificity: only the stimulated synapse shows potentiation

• LTP production
  – For LTP to be produced, the postsynaptic cells must be depolarized in addition to receiving excitatory inputs
  – If an input that is normally not strong enough to induce LTP is paired with a depolarizing current to the post-synaptic cell, LTP can be induced

• LTP prevention
  – LTP is reduced by inhibitory inputs to postsynaptic cells
  – When postsynaptic cells are hyperpolarized, LTP is prevented
Long-term potentiation and the hippocampus
/The NMDA receptor (1/3)

Fig 8.39 NMDA receptor
Long-term potentiation and the hippocampus
/The NMDA receptor (2/3)

• NMDA receptors are central to producing LTP but not maintaining it
  - When AP5 is introduced to CA1 neurons, NMDA receptors are chemically blocked and LTP induction is prevented. But the AP5 treatment does not produce any effect on previously established LTP in these cells
  - NMDA receptors are normally blocked by Mg$^{2+}$
  - The Mg$^{2+}$ ions can be ejected from the NMDA receptors only when the neurotransmitter glutamate binds to the receptors and when the membrane is depolarized $\rightarrow$ Mg$^{2+}$ is ejected and Ca$^{2+}$ can enter the cell
  - Ca$^{2+}$ acts as an intracellular messenger conveying the signal which changes enzyme activities that influence synaptic strength
Long-term potentiation and the hippocampus
/The NMDA receptor (3/3)

• LTP induction likely include presynaptic and postsynaptic mechanisms
  – Hypothesis 1
    • LTP raises the sensitivity of postsynaptic non-NMDA glutamate receptors and prompts more glutamate to be released presynaptically
  – Hypothesis 2
    • Changes in the physical characteristics of the dendritic spines transmit EPSPs more effectively to the dendrites
    • Via a postsynaptic to presynaptic cell message, the efficiency of presynaptic neurotransmitter release is increased
Long-term potentiation and the hippocampus
/Long-term potentiation and memory performance

• LTP and spatial learning
  – Chemically blocking LTP in the hippocampus of normal mice impairs their ability to demonstrate normal place learning
  – Genetic manipulations that block the cascade of molecular triggers for LTP also impair spatial learning

• Conclusions
  – NMDA receptors may be needed to learn a spatial strategy but not to encode a new map
  – The pretraining merely allowed the motor-related side effects of NMDA receptor blockage to be avoided

• LTP does exist at the cellular level and that NMDA receptors play a crucial role in LTP induction in many pathways of the brain
Summary

Fig 8.40 Relationships of long-term memory systems

- 기억력의 천재들
  - http://wnetwork.hani.co.kr/newyorker/view.html?&cline=20&log_no=926

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## Key Terms

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