Biological Psychology
Learning and Memory

OUTLINE

- Learning
  - Classical Conditioning
  - Operant Conditioning
- Neural Mechanisms of Memory
  - LTP
  - Reconsolidation
- Types of Memory
- Amnesia
Learning

“...relatively permanent changes in behavior produced by experience”

- Learning involves changes in the nervous system produced by experiences
- Nervous system changes are physical
- Learning allows us to adapt our behaviors to the environment
- Learning involves interactions among the motor, sensory, and memory systems

Types of Learning

- **Habituation** - decrease in innate responsiveness due to experience
- **Sensitization** - increase in sensitivity due to experience
- **Pavlovian (classical) conditioning** - associative conditioning
  - Unconditioned Stimulus (UCS)
  - Unconditioned Response (UCR)
  - Conditioned Stimulus (CS)
  - Conditioned Response (CR)
- **Operant Conditioning** - response important
  - Punishment
  - Contingency
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PROCEDURES FOR CLASSICAL CONDITIONING

At first

<table>
<thead>
<tr>
<th>Conditioned stimulus (CS)</th>
<th>Followed by</th>
<th>Food</th>
<th>Automatically elicits</th>
<th>Unconditioned response (UCR)</th>
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After some number of repetitions

<table>
<thead>
<tr>
<th>Conditioned stimulus (CS)</th>
<th>Conditioned response (CR)</th>
<th>Salivation</th>
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(a) Classical conditioning
CLASSICAL CONDITIONING TERMS:

- **UCS** - unconditioned stimulus → stimulus with a natural response
- **UCR** - unconditioned response → natural response to the **UCS**
- **CS** - conditioned stimulus → stimulus with unrelated response prior to conditioning
- **CR** - conditioned response → the response to the **CS** after conditioning

CLASSICAL CONDITIONING TERMS

- **Acquisition** – period of first learning
CLASSICAL CONDITIONING TERMS

- Extinction – weakening of the conditioned association through repeated CS presentation

- Spontaneous Recovery – reappearance of a previously extinguished association
UCS and UCR have a pre-existing strong connection
CS does not normally have a strong connection with the UCS or UCR.

Through pairing the CS and UCS a connection is strengthened between these two brain areas.
**INSIDE THE BRAIN**

- Through pairing the CS and UCS a connection is strengthened between these two brain areas.
- CS → CR, when the connection is strong enough.

**SINGLE TRIAL LEARNING**

- *Conditioned* Taste Aversions - example of one pairing of the CS and UCS being effective for conditioning.

| Food (CS) + Virus (UCS) = Nausea (UCR) = Food (CS) produces Nausea (CR) |
|---|---|---|---|
| [Food image] + [Virus image] = [Nausea image] = [No food image] |

*Problem during chemotherapy*
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PROcedures FOR OPERANT CONDITIONING

- In operant conditioning the learner’s behavior controls the presentation of reinforcement or punishment
**REINFORCEMENT**

- Reinforcement = activation of brain mechanisms that increase the likelihood that a response will occur

- Electrical stimulation of rat brain induces reinforcement (Olds study)

- Dopamine plays a critical role in reinforcement and, thus, learning

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**NUCLEUS ACCUMBENS AND REINFORCEMENT**

- Mesolimbic DA pathway → nucleus accumbens

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*Image description*:
- Diagram showing the mesolimbic DA pathway connecting the frontal cortex to the nucleus accumbens.
- Key functions of the nucleus accumbens and mesolimbic DA pathway are highlighted, including reward, pleasure, motor function, and compulsion.
- The diagram also indicates the involvement of dopamine and serotonin pathways in these processes.
NUCLEUS ACCUMBENS AND REINFORCEMENT

- Rats will self-inject dopamine agonists directly into the nucleus accumbens
- Drugs of abuse and natural reinforcers increase Dopamine in the nucleus accumbens
- What what happen if you administered dopamine receptor antagonists?

WHAT TYPE OF LEARNING?

1. Every time someone flushes a toilet in the apartment building, the shower becomes very hot and causes the person to jump back. Over time, the person begins to jump back automatically after hearing the flush, before the water temperature changes.

2. Your hands are cold so you put your gloves on. In the future, you are more likely to put gloves on when it’s cold.

3. A prairie dog usually lets out a loud cry when another large animal passes by. However, prairie dogs that are near a hiking trail stop sounding the warning call when humans pass by.
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THE HEBB RULE

- Donald Hebb:
- Synapses that are active at the same time that the postsynaptic neuron fires, are strengthened over time
- “Neurons that fire together are wired together”
HEBBIAN SYNAPSES

Incoming action potential arrives at same time as...

postsynaptic neuron has action potential

Later...

this synapse strengthened

ARE YOU DOWN WITH LTP?

http://www.youtube.com/watch?v=BwZfLv3Z96A
LTP ANIMATION

- http://www.sumanasinc.com/webcontent/animations/content/receptors.html

LONG-TERM POTENTIATION

- LTP = changes in glutamate receptors
  - NMDA and AMPA subtype in the hippocampus
  - AMPA = typical ionotropic
  - NMDA = special
NMDA Receptors

- NMDA receptor controls a calcium channel which is blocked by Mg$^{2+}$ ions.
- Mg$^{2+}$ ions are ejected from the calcium channel when the membrane is depolarized.
- To open an NMDA channel you need:
  - presence of glutamate
  - a depolarized membrane

AMPA and NMDA receptors during LTP

If one or (better) more AMPA receptors have been repeatedly stimulated, enough sodium enters to largely depolarize the dendrite’s membrane. Doing so displaces the magnesium ions and therefore enables glutamate to stimulate the NMDA receptor. Both sodium and calcium enter through the NMDA receptor’s channel.
**Calcium is the Key to LTP**

- Calcium activates a protein: CaMKII
- CaMKII is necessary and sufficient for LTP
- It increases the number of AMPA channels = stronger connection next time
- Also activates retrograde messenger (Nitric Oxide) to strengthen the presynaptic neuron

**Overview of LTP**

- Increased glutamate release
- NMDA/AMPA receptors
- Calcium entry into dendritic spine
- Nitric Oxide feedback onto presynaptic cell
THOUGHT EXPERIMENT

- You have a mouse and you want to BLOCK its ability to learn
- Think through the steps of LTP
- What could you do at each step to block learning?

EVIDENCE FOR AN LTP/LEARNING LINK

- Mice with abnormal NMDA receptors have difficulty learning
- Mice with more than normal NMDA receptors have “super” memory
- Drugs that block LTP block learning
- Drugs that facilitate LTP facilitate learning
MECHANISMS OF LTP

http://www.youtube.com/watch?v=GMehTI6DPYI&feature=related

ACTIVITY-DEPENDENT CHANGES IN THE NERVOUS SYSTEM

- Neural activity can shape neural connections (e.g., through long-term potentiation)
- Behavior can change the brain as well as brain influencing behavior

- Carlson, 1998
Sprouting of new neural connections

LTP vs. LTD
- **LTP**: increases synaptic excitability by AMPA receptor insertion due to action of protein kinase stimulated by Ca\(^{2+}\) influx
- **LTD**: decreases synaptic excitability by AMPA receptor removal due to kinase activation
QUIZ YOURSELF

- What does it mean that “neurons that fire together wire together?”
- What are the steps for LTP?

1. Activate NMDA receptors by…
   - repeatedly stimulate nearby AMPA glutamate receptors, and depolarizing the dendrite.
   - Depolarization repels the magnesium ions and allows glutamate to open NMDA channels so that sodium and calcium ions can enter the cell.

2. Calcium ions → protein production
   - Proteins alter the activities of more than a hundred other known chemicals within the dendrites.
   - increases the future responsiveness of these glutamate receptors.
3. Calcium activates a protein called CaMKII and ....
   • The dendrite may build more AMPA receptors or move them into a better position.
   • Neurons make more NMDA receptors.
   • The dendrite may make more branches, thus forming additional synapses with the same axon.
   • The AMPA receptors become more responsive than before.
4. LTP causes presynaptic changes through the release of a Nitric Oxide

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- Learning
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  • LTP
- Phases of Memory
- Types of Memory
- Amnesia
Three Phases of Memory

- **Encoding**
- **Consolidation**
- **Retrieval**

Cognitive & neural processes that initially transform an experience into a memory trace.

Three Phases of Memory

- **Encoding**
- **Consolidation**
- **Retrieval**

Process by which recent memories are crystallized into long-term memory.
Three Phases of Memory

Encoding  Consolidation  Retrieval

Re-accessing information stored in memory

Forgetting
Three Phases of Memory

Encoding  Consolidation  Retrieval

Forgetting

Unless you RECONSOLIDATE the information

Forgetting
RECONSOLIDATION

Control group
Day 1: Training tone + shock

Rat learns to fear tone

Nader, Schafe, & Le Doux, 2000

RECONSOLIDATION

Test group
Day 1: Training tone + shock

Rat learns to fear tone

Nader, Schafe, & Le Doux, 2000
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ATKINSON-SHIFFRIN MEMORY MODEL

Three stages of memory storage

- **Sensory register** - 0.5-1 second
- **Short-term store/working memory** - 10-15 seconds
- **Long-term store** - relatively permanent
  - Interference
  - Memory attributes - external stimuli
  - Retrieval to short-term store for processing can modify - reconsolidation
Long-term Memory Systems

- MEMORY
  - Declarative
    - Episodic memory
    - Semantic memory
  - Nondeclarative
    - Classical conditioning
    - Skills and habits
    - priming

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**Anterograde Amnesia**

- Korsakoff’s Syndrome
- H.M.
DEGENERATION OF MAMMILLARY BODIES WITH KORSAKOFF’S SYNDROME

• Loss of declarative not procedural memory
• Lack of awareness of memory deficit (tend to confabulate)

KORSAKOFF’S SYNDROME

Korsakoff’s syndrome is a severe form of anterograde amnesia associated with chronic alcoholism
• Thiamine deficiency produces brain damage
Clive Wearing
Anterograde Amnesia

http://www.youtube.com/watch?v=wDNDRDJy-vo

H. M. (Henry Molaision) An Unforgettable Amnesiac
PROMINENT INVESTIGATORS OF H.M.

Brenda Milner  Suzanne Corkin  Elizabeth Kensinger

PREOPERATIVE HISTORY OF H.M.

- Born 1926
- Only child of working-class parents
- Hit by bicycle at age 7 and was unconscious for 5 minutes
- Major seizure on 16th birthday
- Graduated H.S and worked on an assembly line as a “motor winder” until seizures became incapacitating
- 10 petit mal seizures/day and 1-2 grand mal seizures per week
BRAIN OPERATION

- Dr. William Scoville
- Performed when H.M. was 27
- Bilateral 1.5” supraorbital trephine holes
- Elevated frontal lobes
- Retracted temporal lobes laterally to allow access to the medial portion
- Spared temporal neocortex

Location of H.M.’s lesion: Medial Temporal Lobe (MTL)
H.M. ANATOMICAL DAMAGE: MRI DATA

- Approximately 8cm of temporal lobe removed
  - Amygdala, hippocampus, prepyriform gyrus, parahippocampal gyrus

H.M.’s MRI
THE HIPPOCAMPUS AND LIMBIC SYSTEM

Short-term versus Long-term Memory
• Spared short-term memory; impaired long-term memory
Long-term Memory Systems

MEMORY

Declarative

Episodic memory

Semantic memory

Classical conditioning

priming

Nondeclarative

Skills & habits

priming

Long-term Memory Systems

MEMORY

Declarative

Episodic memory

Semantic memory

Classical conditioning

priming

Nondeclarative

Skills and habits

priming
H.M. demonstrated poor memory for words and phrases that entered the language after the onset of his amnesia.

<table>
<thead>
<tr>
<th>Word/Phrase</th>
<th>Free Recall</th>
</tr>
</thead>
<tbody>
<tr>
<td>angel dust</td>
<td>“dust made by angels, we call it rain”</td>
</tr>
<tr>
<td>biodegradable</td>
<td>“two grades”</td>
</tr>
<tr>
<td>flower child</td>
<td>“a young person who grows flowers”</td>
</tr>
<tr>
<td>Watergate</td>
<td>“a city or town in Pennsylvania or Ohio”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Word/Phrase</th>
<th>Four-choice Recognition</th>
</tr>
</thead>
<tbody>
<tr>
<td>brain wash</td>
<td>the fluid that surrounds and bathes the brain</td>
</tr>
<tr>
<td>granola</td>
<td>a portable keyboard wind instrument</td>
</tr>
<tr>
<td>software</td>
<td>expensive clothing made of a soft, twilled fabric</td>
</tr>
</tbody>
</table>

Long-term Memory Systems

- **MEMORY**
  - Declarative
    - Episodic memory
    - Semantic memory
  - Nondeclarative
    - Classical conditioning
      - Skills and habits
    - priming
H.M. HAS ABILITY TO STORE SOME INFORMATION: *IMPLICIT LEARNING WITHOUT EXPLICIT KNOWLEDGE*?

- **Priming tasks (limited)**
  - Shown word “DEFINE” and later given the stem DEF and asked to complete it with the first word that comes to mind
  - But unable to pick out word just seen from a list of words
Long-term Memory Systems

MEMORY

Declarative

- Episodic memory
- Semantic memory

Nondeclarative

- Classical conditioning
- Skills and habits
- priming

Skill Learning

Milner, 1962

(3) Performance of H.M. on mirror-tracing task

- Errors per trial
- Day 1
- Day 2
- Day 3
- Trials
**CONCLUSIONS**

- The experiments done on H.M. and other amnesic patients suggest that the Hippocampus and amygdala (and other temporal lobe structures):
  - Are required to move Short term memory into Long term memory
  - Are required for explicit learning (“Knowing that”: Declarative memories = Episodic or Semantic)
  - Are not required for implicit learning (“Knowing how” Procedural memories/skills; Priming)
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**COMING UP....**

- Data and Lab Report Intro and Methods Due 8am Tuesday
- Review Ch. 12 (learning and memory)
COMING UP....
- Read Ch. 13 – Lateralization and Language
- Stats lab tomorrow
- Peer review due Thursday

MORE ON H.M.
- If you’re interested, read on!
**LIVING SITUATION AND DAILY ACTIVITIES**

- Returned home to live with mother and father
- Helped with errands, mow lawn, crossword puzzles
- Attended rehabilitative workshop for 10 years – simple repetitive tasks
- Father died 1967; Mother died 1981
  - When asked where he lived in 1986 he said “In a house with my mother”
  - Are your parents alive? “I don’t know.”

**MOTIVATION AND AFFECT**

- H.M. spent last years in a nursing home
  - Clothes laid out; Dresses self
  - Reminded to shave, brush teeth and comb hair
  - Participated in daily activities of home
- Rarely complained about anything
- No GSR to electric shocks
- When observed to be acting “differently”: nursing home personnel needed to run through list: “toothache, headache, stomach ache”? 
- Did not spontaneously say that he “has a headache”
MOTIVATION AND AFFECT

- Unless questioned, did not say that he is full or tired
- Did not ask for food or drink
  - Sometimes asked to “go the bathroom”
- Described as even tempered and well behaved
  - No swearing
- Occasional bouts of anger
  - Another patient in nursing home liked to annoy him (calls him names, disturbs bingo card)
  - Shook bed, walks around in circles
  - As soon as distracted, his anger dissipated immediately

MOTIVATION AND AFFECT

- Appeared to have no interest in sexual relationships
  - Did not talk about sexual topics
  - Did not seek sexual satisfaction
  - Did not flirt
  - Never had a girlfriend
  - Did not masturbate
  - Anticonvulsants may have contributed to hypososexuality
SENSORY AND SENSORIMOTOR FUNCTION
- Mild to moderate somatosensory dysfunction
  - Pressure sensitivity
  - Two point discrimination
  - Pain sensitivity
- Most visual function normal
- Olfactory
  - Could detect weak odors (compared to DI water)
  - Discriminated odor intensity
  - Adapted to strong odors
  - Impaired in the perception of odor quality

MOONEY’S FACE PERCEPTION TEST
- H.M.: only 4 errors (40 out of 44) in eight minutes
- Age-matched controls: Mean: 36.2 out of 44 in 9 minutes 53 seconds

Milner et al., 1968
H.M.’s Memory Functions

- **Spared**
  - Immediate memory
  - Implicit

- **Impaired**
  - Long-term memory (new learning)
  - Explicit memory
    - Verbal and nonverbal
    - Semantic
    - Episodic

H.M. has intact implicit memory
Fig. 13-6d, p. 395

Fig. 13-6e, p. 396
H.M.’s Memory Functions

- **Spared**
  - Immediate memory
  - Implicit

- **Impaired**
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A Typical Conversation with H.M.

*(Ogdën & Corkin, 1991)*

- Q: Do you know why you are here at MIT?
- A: I wonder at times, but I know one thing. What is learned about me will help other people.
- Q: Yes, it has helped other people.
- A: And that is the important thing. Because at one time that’s what I wanted to be, a brain surgeon.
- Q: Really? A brain surgeon?
- A: And I said “no” to myself, before I had any kind of epilepsy.
- Q: Did you. Why is that?
A: Because I wore glasses. I said, suppose you are making an incision in someone – [pause] – and you could get blood on your glasses, or an attendant could be mopping your brow and go too low and move your glasses over. You could make a wrong movement then.

Q: And then what would happen?
A: And that person would be dead, or paralyzed.

Q: So it’s a good job you decided not to be a brain surgeon.
A: Yeah. I thought mostly dead, but could be paralyzed in a way. You could make the incision just right, and then a little deviation, might be a leg or an arm, or maybe an eye too; on one side in fact.

Q: Do you remember when you had your operation?
A: No I don’t

Q: What do you think happened there?
A: Well I think I was ah – well, I’m having an argument with myself right away. I’m the third or forth person who had it, and I think that they. Well, possibly did not make the right movement at the right time, themselves then. But they learned something.

Q: They did indeed.
A: That would help other people around the world too.

Q: They never did it again.
A: They never did it again because by knowing it - [pause] – and a funny part, I always thought of being a brain surgeon myself.

Q: Did you?

A: Yeah. And I said “no” to myself.

Q: Why was that?

A: Because I said that an attendant might mop your brow and might move your glasses over a little bit, and you would make the wrong movement.

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**PICTURE RECOGNITION TASK**
FREED AND CORKIN, 1988

- 120 Target slides
- 120 Distractor slides
- Yes-No recognition tested 10 min and 6 Months later
- H.M. and normals are closely matched after 10 min
- H.M. impaired at 6 mos

![Graph showing percent correct recognition over time]

± S.D.
**FAMOUS FACES TEST: SEMANTIC INFORMATION**
Kensinger and Corkin, 2000

- Seven test sessions over 26 years
- Equal (or better) than control from 1920s-40s
- Better than controls for faces before 1950s
- Surgery in 1953
  - Lack of retroactive interference?

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**H.M. HAS ABILITY TO STORE SOME INFORMATION: IMPLICIT LEARNING WITHOUT EXPLICIT KNOWLEDGE?**

- Wheelchair
- Solitaire
- Priming tasks (limited)
  - Shown word “DEFINE” and later given the stem DEF and asked to complete it with the first word that comes to mind
  - But unable to pick out word just seen from a list of words
WORD STEM COMPLETION TASK (PRIMING TASK) WITH PRE-1965 WORDS
(POSTLE & CORKIN, 1998)

- Study session: Ss read 20 words aloud as presented on computer for 5 sec each
- 1 Min later, Ss viewed 40, 3-letter stems (1/2 were “studied” words, other ½ not studied)
- Asked to complete stem with “first word that came to mind”

H.M. shows normal performance on pre-1965 words

WORD STEM COMPLETION TASK WITH POST-1965 WORDS
(POSTLE & CORKIN, 1998)

Compared to normals, H.M. does poorly on priming task involving post-1965 words
**SUMMARY: PATIENT H.M.**

- Patient H.M. exhibited:
  - Severe anterograde amnesia
  - Normal STM
  - Normal LTM for events prior to the surgery
  - Normal perceptual learning
  - Normal sensory-response learning
  - Normal motor learning
- H.M.’s problem was transfer from STM to LTM
CONCLUSIONS

- The experiments done on H.M. and other amnesic patients suggest that the Hippocampus and amygdala (and other temporal lobe structures):
  - Are required to move STM into LTM
  - Are required for explicit learning (“Knowing that”: Declarative memories = Episodic or Semantic)
  - Are not required for implicit learning (“Knowing how” Procedural memories/skills; Priming)

H.M.

http://www.youtube.com/watch?v=jKQrOcV14iE

http://www.nytimes.com/2008/12/05/us/05hm.html?_r=1&hp
AJ – THEOPPOSITE OF HM?


TIME ESTIMATION

- Ogden, 1991 anecdote:
  - H.M. told he would be left alone for a period and he would be asked to estimate the elapsed time
  - Left at 2:05 and returned at 2:17
  - Response: “12 minutes. Got you there!”
  - Clock on wall. H.M. rehearsed beginning time and then subtracted from current time.
  - Shows intellect: ability to estimate time without memories
IMMEDIATE MEMORY

- Borderline *normal* memory span for digits: 5-6
  - H.M. given 5 digits
  - Experimenter called away
  - Returned over an hour later to find H.M accurately repeating the 5 digits
  - Little awareness of time since time is measured by memories laid down as it passes?

DEFICITS IN ESTABLISHING NEW MEMORIES

- H.M.’s Deficits in…
  - Story learning
  - Paired associate learning
  - Song/drawing learning
  - Learning new vocabulary words
  - Learning digit strings
  - Learning object names/locations