Rodent Behavioral Learning and Memory Models

From *Mechanisms of Memory, 2nd Edition* by J. David Sweatt, Ph.D.
Hippocampal Pyramidal Neuron
“of Mice and Rats”
Open Field Apparatus
Open Field Behavior

A. Center/Total Distance

B. Total Distance

C. Vertical Activity
Elevated Plus Maze
Roto Rod

Figure 4
Rotating Rod Behavior

Figure 5
Acoustic Startle and Prepulse Inhibition

Figure 6
Nociception Behavior

Figure 7

Hot Plate Test

Hind Paw Lick Latency (s)

-/+ n=26
-/- n=20

Shock Threshold

Stimulus Intensity (mA)

-/- n=6
+/- n=6

Flinching        Jumping        Vocalizing

Shock Threshold

Stimulus Intensity (mA)

-/- n=6
+/- n=6

Flinching        Jumping        Vocalizing
Visual Cliff
Ivan Pavlov
with his canine subjects

Image courtesy of Johns Hopkins Medical Institute
Pavlovian Associative Conditioning

Conditioned Stimulus → Unconditioned Response

Unconditioned Stimulus → Conditioned Response
Categories of Associative Conditioning

Delay Conditioning

[Diagram showing CS and US with Time]

Trace Conditioning

[Diagram showing CS and US with Time]
Fear Conditioning Chamber

Figure 9
Fear Conditioning

**TRAINING**
- Animal is placed in novel context
- Hears a tone
- Receives foot shock

**CONTEXTUAL TEST**
- Animal is returned to same context
- Test for freezing behavior

**CUED TEST**
- Animal is placed in modified context
- Hears a tone
- Test for freezing behavior
Fear Conditioning Paradigm

Train

What's that noise?
Fear Conditioning Paradigm

Train

Yow..!!!
Fear Conditioning Paradigm

Train

What's going on?
Fear Conditioning Paradigm

Train

What's going on?

Contextual

Test

Help!
Fear Conditioning Paradigm
Fear Conditioning

**TRAINING**

- Animal is placed in novel context
- Hears a tone
- Receives foot shock

**CONTEXTUAL TEST**

- Animal is returned to same context
- Test for freezing behavior

**CUED TEST**

- Animal is placed in modified context
- Hears a tone
- Test for freezing behavior
Variations of Fear Conditioning

A. Cue-plus-contextual Fear Conditioning
   - TRAINING
   - CONTEXTUAL TEST
   - CUED TEST

B. Context Alone Conditioning
   - TRAINING
   - CONTEXTUAL TEST

C. Context Discrimination
   - TRAINING
   - TEST
   - Context 1
   - Context 2
Fear Conditioning in Angelman Syndrome Mice
Control Experiments for Fear Conditioning
"Control" Experiments

Performance:
- Open Field Activity
- Coordination

Perception:
- Nociception
- Hearing
- Vision
- Anxiety
Latent Inhibition

Train
Context + Shock → Freezing Behavior

Test
Oh No!

Pre-exposure
Latent Inhibition → Shock → Freezing Behavior

Train
Test
Contextual Fear Conditioning

Freezing Behavior (Percent of Time)

Context + Shock  Latent Inhibition

Treatment

Freezing Behavior (Percent of Time)

MK-801 Treatment

Saline  100 µg/kg  300 µg/kg

**  ***
Memory Reconsolidation

**Figure 25**
Passive Avoidance Paradigm

Step-Through Passive Avoidance

Train

Test: measure time to step through

Step-Down Passive Avoidance

Train

Test: measure time to step down
Passive Avoidance

![Graph showing latency over different days for two groups (+/+ n=14 and +/- n=17).]
Active Avoidance Paradigm

Shuttle Box
Active Avoidance

Train

Test:
Can the animal avoid the shock?
Eye-Blink Conditioning in Rabbits

- Corneal Air Puff Elicits Eyeblink Response
- Corneal Air Puff Given with Tone
- Tone Given Alone Elicits Eyeblink Response
“Higher-order” Learning
Types of Rodent Mazes

- Lashley Maze
- 4 Arm Radial (Plus) Maze
- 8 Arm Radial Maze
- Triangle Maze
- “T” Maze
- “Y” Maze
Spatial Learning
The Morris Water Maze

- Camera
- Distal Visual Cues
- Platform
SL327 Impairs Performance in the Morris Water Maze

**Hidden Platform**

- **Escape Latency (sec)**
- **Training Block** (4 trials each)

- **Control**
- **SL327**
Morris Water Maze
No Effect of SL327 in the Visible Platform Version of the Morris Water Maze

Visible Platform

<table>
<thead>
<tr>
<th>Training Block (4 trials each)</th>
<th>Escape Latency (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
</tr>
</tbody>
</table>

- Control
- SL327
Morris Water Maze
The ERK/MAPK Cascade Is Required For Spatial Learning

---

### Quadrant Search Time (% of total time)

- **Control**
- **30 mg/kg SL327**

---

### Platform Crossings

- **Control**
- **30 mg/kg SL327**
Vehicle

30 mg/kg SL327
ERK Is **Not** Required for Maintenance of Spatial Memories

**Quadrant Search Time (% of total time)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Quadrant Search Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (1-5)</td>
<td>40 ± 5</td>
</tr>
<tr>
<td>SL327 (1-5)</td>
<td>30 ± 5</td>
</tr>
<tr>
<td>SL327 (6)</td>
<td>45 ± 5</td>
</tr>
</tbody>
</table>

**Platform Crossings**

<table>
<thead>
<tr>
<th>Group</th>
<th>Platform Crossings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (1-5)</td>
<td>2 ± 0.5</td>
</tr>
<tr>
<td>SL327 (1-5)</td>
<td>1 ± 0.5</td>
</tr>
<tr>
<td>SL327 (6)</td>
<td>1 ± 0.5</td>
</tr>
</tbody>
</table>

Significance levels: **p < 0.01; ***p < 0.001**
The Barnes Maze

Spatial Cues

Escape Chamber

Search strategy A

Search strategy B
“Higher-order” Learning
Bar Press Operant and/or Conditioned Place Preference
Novel Object Recognition
Novel Object Recognition

Figure 24
Hermissenda

Image courtesy of Mike Johnson
Lifelong Single-trial Learning
Taste Learning

**NEOPHOBIA**

- **DAY 1 10’**
  - Measure *increased* consumption as index of long-term memory of novel taste

- **DAY 2 10’**
  - Measure *increased* consumption as index of long-term memory of novel taste

**TASTE AVERSION**

- **DAY 1 10’**
  - Nutri-Grain
  - LiCl

- **DAY 2 10’**
  - Nutri-Grain

Measure *decreased* consumption as index of long-term memory of novel taste
Conditioned Taste Aversion

A

DAY 1

1\textsuperscript{st} Exposure to Food Item

Injection of LiCl or NaCl

DAY 2

2\textsuperscript{nd} Exposure to Food Item

B

Grams Ingested on 2\textsuperscript{nd} Exposure

(LiCl treated group compared to NaCl treated control)
Neophobia

DAY 1

1\textsuperscript{st} Exposure to Food Item

DAY 2

2\textsuperscript{nd} Exposure to Food Item

Grams Ingested

(1\textsuperscript{st} exposure compared to second exposure)
Imprinting – Konrad Lorenz
<table>
<thead>
<tr>
<th>Test Name</th>
<th>Measurement</th>
<th>Index Of:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open Field Analysis</td>
<td>Distance Moved Over Time</td>
<td>Activity</td>
</tr>
<tr>
<td>Elevated Plus Maze</td>
<td>Time Spent in Open Arms</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Rotating-rod</td>
<td>Time to Fall Off</td>
<td>Coordination and Motor Learning</td>
</tr>
<tr>
<td>Acoustic Startle</td>
<td>Force of Jump</td>
<td>Hearing</td>
</tr>
<tr>
<td>Pre-pulse Inhibition</td>
<td>Suppression of Startle</td>
<td>Sensorimotor Gating</td>
</tr>
<tr>
<td>Hot Plate</td>
<td>Time to Lick Paw</td>
<td>Nociception</td>
</tr>
<tr>
<td>Hargreave’s Apparatus</td>
<td>Time to Lift Paw</td>
<td>Nociception</td>
</tr>
<tr>
<td>Light-Dark Exploration</td>
<td>Time in Lit Chamber</td>
<td>Vision</td>
</tr>
<tr>
<td>Visual Cliff</td>
<td>Suppression of Movement</td>
<td>Vision</td>
</tr>
<tr>
<td>Fear Conditioning: Cued</td>
<td>Freezing or Startle</td>
<td>Auditory Associative Learning</td>
</tr>
<tr>
<td>Fear Conditioning: Contextual</td>
<td>Freezing or Startle</td>
<td>Spatial Associative Learning</td>
</tr>
<tr>
<td>Passive Avoidance</td>
<td>Time Spent in Lit Chamber</td>
<td>Spatial Associative Learning</td>
</tr>
<tr>
<td>Active Avoidance</td>
<td>Time Spent in Cued Chamber</td>
<td>Operant Conditioning</td>
</tr>
<tr>
<td>Lever Press</td>
<td>Number of Bar Presses</td>
<td>Operant Conditioning</td>
</tr>
<tr>
<td>Conditioned Place Preference</td>
<td>Time Spent in One Chamber</td>
<td>Operant Conditioning</td>
</tr>
<tr>
<td>Eye-blink Conditioning</td>
<td>Blink in Response to Cue</td>
<td>Associative Conditioning</td>
</tr>
<tr>
<td>Simple Maze Learning</td>
<td>Errors or Time to Completion</td>
<td>Spatial Learning, Working Memory</td>
</tr>
<tr>
<td>Morris Water Maze</td>
<td>Quadrant Time, Platform Crossings</td>
<td>Spatial Memory</td>
</tr>
<tr>
<td>Barnes Maze</td>
<td>Errors</td>
<td>Spatial Memory</td>
</tr>
<tr>
<td>Conditioned Taste Aversion</td>
<td>Food or Taste Avoidance</td>
<td>Taste Learning</td>
</tr>
<tr>
<td>Novel Taste Learning</td>
<td>Attenuation of Neophobia</td>
<td>Taste Learning</td>
</tr>
<tr>
<td>Novel Object Recognition</td>
<td>Time Spent with Object</td>
<td>Recognition Memory</td>
</tr>
</tbody>
</table>