Behavioral Neuroscience: Fear thou not

Neural mechanisms of Behavior
The Neuropsychological approach
Behavior – a bidirectional process

Thoughts

• What is a “reward”?

• Learning is best motivated by threats to survival?

• Threats are much better reinforcers?

• Fear is a prime motivator

<table>
<thead>
<tr>
<th>Decreases behavior</th>
<th>Increases behavior</th>
<th>Taking drugs?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presented</td>
<td>Positive punishment</td>
<td>Positive reinforcer</td>
</tr>
<tr>
<td>Taken away</td>
<td>Negative punishment</td>
<td>Negative reinforcer</td>
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Classical fear conditioning

CS-US pairing
Tone = conditioned stimulus (CS)
Foot-shock = unconditioned stimulus (US)
Freezing = conditioned response (CR-UR)

The CS predicts the US $\rightarrow$ CR

Percent Freezing

Habit | Cond.
--- | ---
0 | 0
10 | 20
20 | 40
30 | 60
40 | 80
Contingency: co-occurrence

Schedules of reinforcement:
Variable/fixed interval/ratio

**Variable-ratio** - number of responses needed for a reward varies

**Variable-interval** - the subject gets the reinforcement based on varying and unpredictable amounts of time

Tone predicts shock

Zero contingency

Tone = No information

Negative contingency

Tone = no shock
More than contingency: 
Surprise / added information

Aversive conditioning
Tone + Shock = CR
Tone + Light = No CR
Tone = predictor

Blocking
No CR to the light → the outcome is well predicted

Key:
- Food omission: ❌
- Shock: ⚡
- Buzzer: 🎧
- Frightened rat (fear response): 🐁
- Loud/aversive noise: 🎈
- Light: 💡
- Tone: 🎶
- Happy rat (no fear response): 🐁
Rules of thumb for conditioning strength

- Backward < simultaneous < trace < delay
- In trace: short interval > long interval
- In delay: short CS > long CS
- Salience of the CS
- Strength of the US
- Spaced trials is better than massed trials (the ratio between inter-trial-interval and the CS)

But notice it is hard to estimate backwards learning
Amygdala and its basolateral complex (BLA)

- BLA evolution parallels that of the prefrontal cortex
- BLA cell types reminiscent of cortex
- Cortical projections are much more extensive in primates
Fear circuit
Neurons acquire tone responses after conditioning
LTP in the LA is required

NMDA (\textit{N}-methyl-\textit{D}-aspartate, glutamate receptor) is involved in both the acquisition of fear memory and the induction of long-term potentiation (LTP) in the amygdala.

CPP (3-(2-carboxypiperazin-4-yl) propyl-1-phosphonic acid), a competitive NMDA-receptor antagonist
Is it fear memory or just fear behavior?
LA encodes memory independent of fear behavior

Ce inactivation = No Behavioral CR
Suggests common brain mechanisms

Trans-reinforcer blocking

Conditioned inhibition
The dopamine system
Is learning driven by changes in the expectations about future events?

Schultz et al, Science, 1997

Changes in VTA’s dopamine neurons’ output code for an error in the prediction of appetitive events
Learning occurs not because two events co-occur, but because that co-occurrence is UNPREDICTED
What does it take for a tone to become a CS?

$$\Delta V = S \cdot \alpha \cdot \lambda$$

$S$ is intensity of the CS and $\lambda$ of the US

$\alpha$ represents the associability of the CS (high for a novel CS)

_The associability parameter is modified by experience:_

$$\alpha_n = |\lambda - \Sigma V|_{n-1}$$

# Blocking

- **Phase 1:** new CS $\rightarrow$ $\alpha$ is high
- **Phase 2:** same CS $\rightarrow$ $\alpha$ is low = no learning
Amygdala modulation of memory

- Hippocampal dependent learning: spatial
- Striatum dependent-learning: cue-related

Injection of d-amphetamine into the Amygdala affects both if right after training, but not if pre-testing

Packard, Mcgaugh
So, does it encode the memory or just modulates it?

It depends.
The cerebellum is essential and sufficient for eyeblink conditioning.
Effects of amygdala lesion on eyeblink conditioning

Weisz et al., 1994
Eyelid (blink) reflex conditioning – the role of the hippocampus

• Why is trace hippocampal-dependent?
• Maintaining the CS? Timing the trace? Harder?
• Eyelid requires ~0.2sec, and hippocampus is required when 0.4-1sec.
• In tone-shock, trace can be 3sec, and hippocampus is required for ~20sec
• This suggest context-conditioning
Contextual fear

(a) Contextual fear conditioning
- Habituation
- Foot shock
- Exposure to cage without shock

(b) Acoustic-cued fear conditioning
- Habituation
- Repeated tone–foot shock pairing
- Presentation of tone alone

Normal rat  Shocked rat  ‘Freezing’ rat
Extinction of fear-conditioning

Habit. | Cond. | Extinction

Percent Freezing
Extinction: a new learning

Context specific extinction

Faster re-learning (Context + US)
Extinction: brain mechanisms
Partial reinforcement extinction effect

- Partial reinforcement
  - Fixed/variable ratio
  - Fixed/variable schedule
- Results in longer extinction learning

- **Frustration theory (Amsel):** The omission of the US induces frustration. Therefore, during extinction, the frustration predicts the US.
- **Sequential theory (Capaldi):** conditioning to strings of NNNRNNNR
Conditioned Taste Aversion

- One-trial learning
- Long-delay learning (few hours)
  - A [lack of] interference effect?
  - Still a problem for neuroscientists
Consolidation

- Anisomycin, a protein synthesis inhibitor, into the Basolateral complex of the amygdala (BLA)
  - No effect on short-term-memory
  - No effect after XX time (rule of thumb is 6hrs)
  - But harms long-term memory below that.

![Diagram showing memory consolidation process with Anisomycin treatment]
Reconsolidation

No effect on STM

Nader et al., Nature 2000
An updated view of memories

(a)

Short-term memory (STM)
- Lasts for seconds to hours
- ‘Labile’ (sensitive to disruption)
- Does not require new RNA or protein synthesis

Long-term memory (LTM)
- Lasts for days to weeks
- Consolidated (insensitive to disruption)
- Does require new RNA or protein synthesis

(b)

Active state (AS)
- Lasts for seconds to hours
- ‘Labile’ (sensitive to disruption)
  (Does not require new RNA or protein synthesis)

Inactive state (IS)
- Lasts for days to weeks
- Inactive (insensitive to disruption)
  (Does require new RNA or protein synthesis)
Stay safe, be fearless