Behavioral Neuroscience: Fear thou not

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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></th>
<th>Decreases behavior</th>
<th>Increases behavior</th>
<th>Taking drugs?</th>
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<tbody>
<tr>
<td>Presented</td>
<td>Positive punishment</td>
<td>Positive reinforcer</td>
<td>More fun, less withdrawal</td>
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<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)
Contingency: co-occurrence

Schedules of reinforcement: Variable/fixed interval/ratio
More than contingency: 
Surprise / added information

Aversive conditioning

Blocking

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
Suggests common brain mechanisms
Amygdala
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
- Most cortical projections of the amygdala originate from BLA (none from CEA)
Fear circuit

CS Pathway

US Pathway

Auditory Cortex → Auditory Thalamus

Somatosensory Cortex → Somatosensory Thalamus

AMYGDALA

LA

B

CE

CG

LH

PVN

Periaqueductal lateral Gray hypothalamus (midbrain)

Paraventricular nucleus (hypothalamus)

FREEZING

ANS

HORMONES

Ledoux, Mcgaugh, Davis
Neurons acquire tone responses after conditioning.
LTP in the LA is required

NMDA (N-methyl-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
Long-term potentiation (LTP)

• Lomo, Bliss, Andersen, 1966, Hippocampus.
• Induced artificially by tetanic stimulation
• Long-lasting enhancement in signal transmission between two neurons that results from stimulating them synchronously.
• Increase in synaptic strength
• A cellular mechanism for learning and memory.
• Requires protein synthesis
• **Hebbian LTP** requires simultaneous pre- and postsynaptic depolarization for its induction ("fire together – wire together")
  -- Specificity: to synapse
  -- Associativity: associates a weak with a strong input
  -- Cooperativity: weak stimulation of many

Spike timing dependent plasticity
LA encodes memory independent of fear behavior
Amygdala modulation of memory

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

Morris water maze

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.
• Why is trace hippocampal-dependent?
• Maintaining the CS? Timing the trace? Harder?
• Eyelid requires ~0.3sec, and hippocampus is required when 0.5-1sec.
• 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

SOUND

ELECTRICITY

Graph showing percent freezing over habituation, conditioning, and extinction phases.
Extinction: a new learning

A. Extinction is not the same as forgetting

B. Spontaneous recovery

C. Renewal

D. Reinstatement

Faster re-learning
Extinction: brain mechanisms

a) Prefrontal cortex (safety memory)

b) Lateral amygdala (fear memory)

Nature Reviews Neuroscience
Partial reinforcement extinction effect

- Partial reinforcement
  - Fixed/variable ratio
  - Fixed/variable schedule

- Results in longer extinction learning

- Why?
  - 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

- Bad for behavior flexibility
- Good for education
Conditioned Taste Aversion

- One-trial learning
- Long-delay learning (few hours)
  - A [lack of] interference effect?
  - Still a problem for neuroscientists
- Hedonic shift: changes the CS, not its predictions
CTA

• Compound potentiation: odor + taste increase response to odor

• Preparedness:

Figure 6.5 Potentiation of odor conditioning by taste. (A) A rat is given a taste in drinking water that also contains an odor. (In many experiments, the odor comes from a cup near the spout instead of being mixed in the drink.) (b) When odor is paired with illness on its own and then tested (O-O), it does not suppress consumption much. But if it has been combined with a taste on the conditioning trial (OT-O), strong odor conditioning is obtained. (A, after Inui, Shimura, & Yamamoto, 2006; B, after Palmerino et al., 1980.)
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.
Reconsolidation

No effect on STM

Nader, Ledoux, 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)
PTSD (post-traumatic-stress-disorder)

- Extinction failure
Reconsolidation and extinction: What Freud always knew
Context Generalization / specificity
Generalization

• In 1920, Watson and Rayner showed that one-year old Albert feared a rat that was previously paired with banging of steel rail. They then showed that he was afraid of other white furry objects as well.

• Pavlov, 1927: drooling to similar sounds

• Stimulus generalization: the behavioral fact that a conditioned response formed to one stimulus may also be elicited by other stimuli which have not been used in the course of conditioning.
Categorization

Monet

Cezanne / Renoir

Picasso

Matisse / Braque

Watanabe, 95
Context generalization

• In fear conditioning, usually performed by training in one chamber, then testing in another.
• Mainly used with extinction: training in one chamber, extinguished in another.
• Implications for PTSD.
• Involves interactions between the amygdala and the hippocampus
Stimulus generalization

- Stimulus generalization on a physical dimension
- Neurons in many brain areas have tuning curves to a physical dimension
- Is generalization merely a result of discrimination?
- Earlier ideas: “subjects will generalize to the extent that they cannot discriminate”
What are emotions?

Do we run from a bear because we are afraid, or are we afraid because we run?

James proposed that the obvious answer, that we run because we are afraid, was wrong, and instead argued that we are afraid because we run.

Perception=>bodily changes=>feeling

William James
1842-1910
Stay safe, be fearless