

Behavioral Neuroscience: Fear thou not

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Thoughts

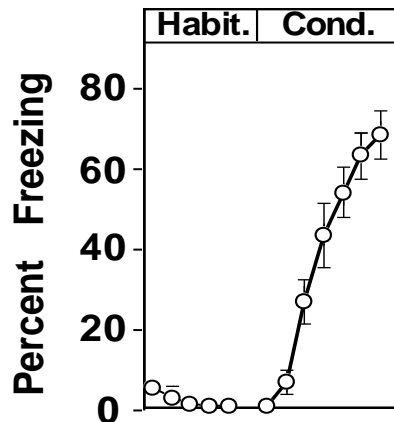
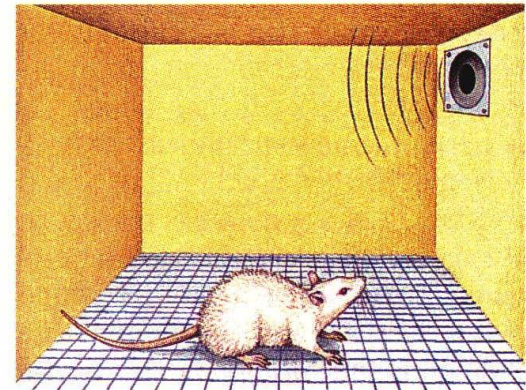
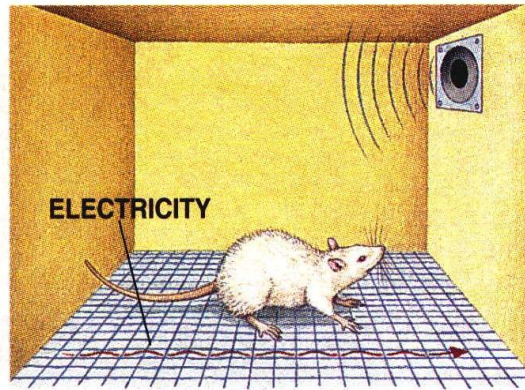
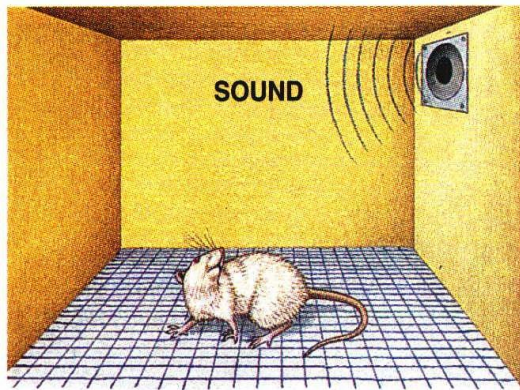
- What is a “reward”?
- Learning is best motivated by threats to survival?
- Threats are much better reinforcers?
- Fear is a prime motivator

	Decreases behavior	Increases behavior
Presented	Positive punishment	Positive reinforcer
Taken away	Negative punishment	Negative reinforcer

Taking drugs?

More fun,
less withdrawal

Classical fear conditioning



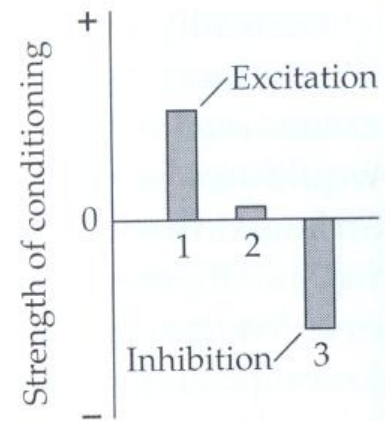
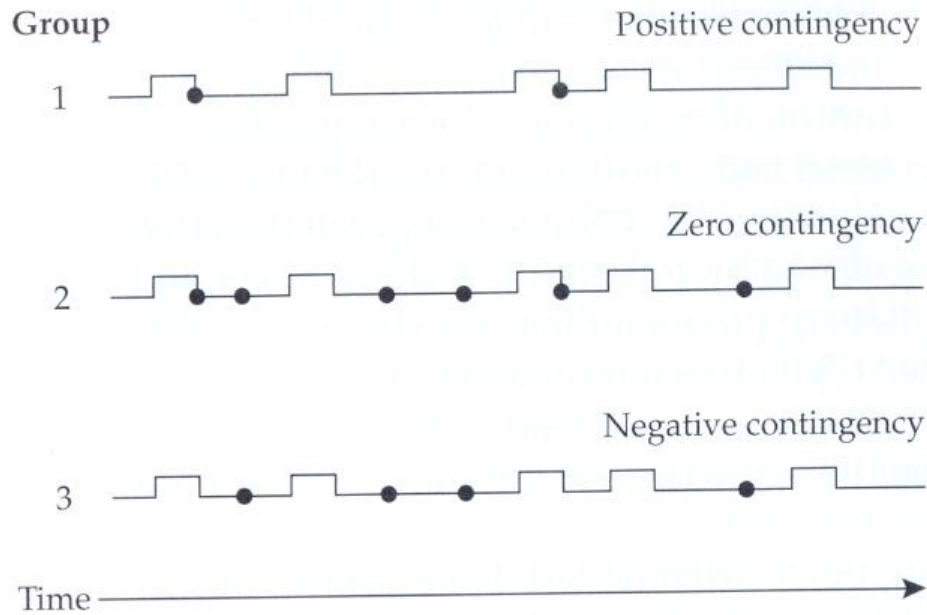
CS-US pairing

Tone = conditioned stimulus (CS)

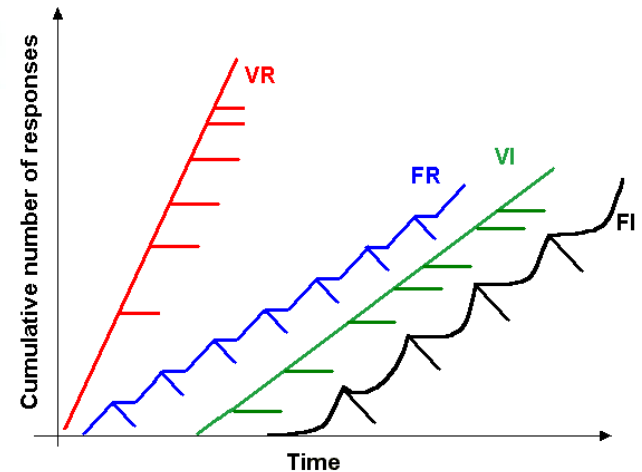
Foot-shock = unconditioned stimulus (US)

Freezing = conditioned response (CR-UR)

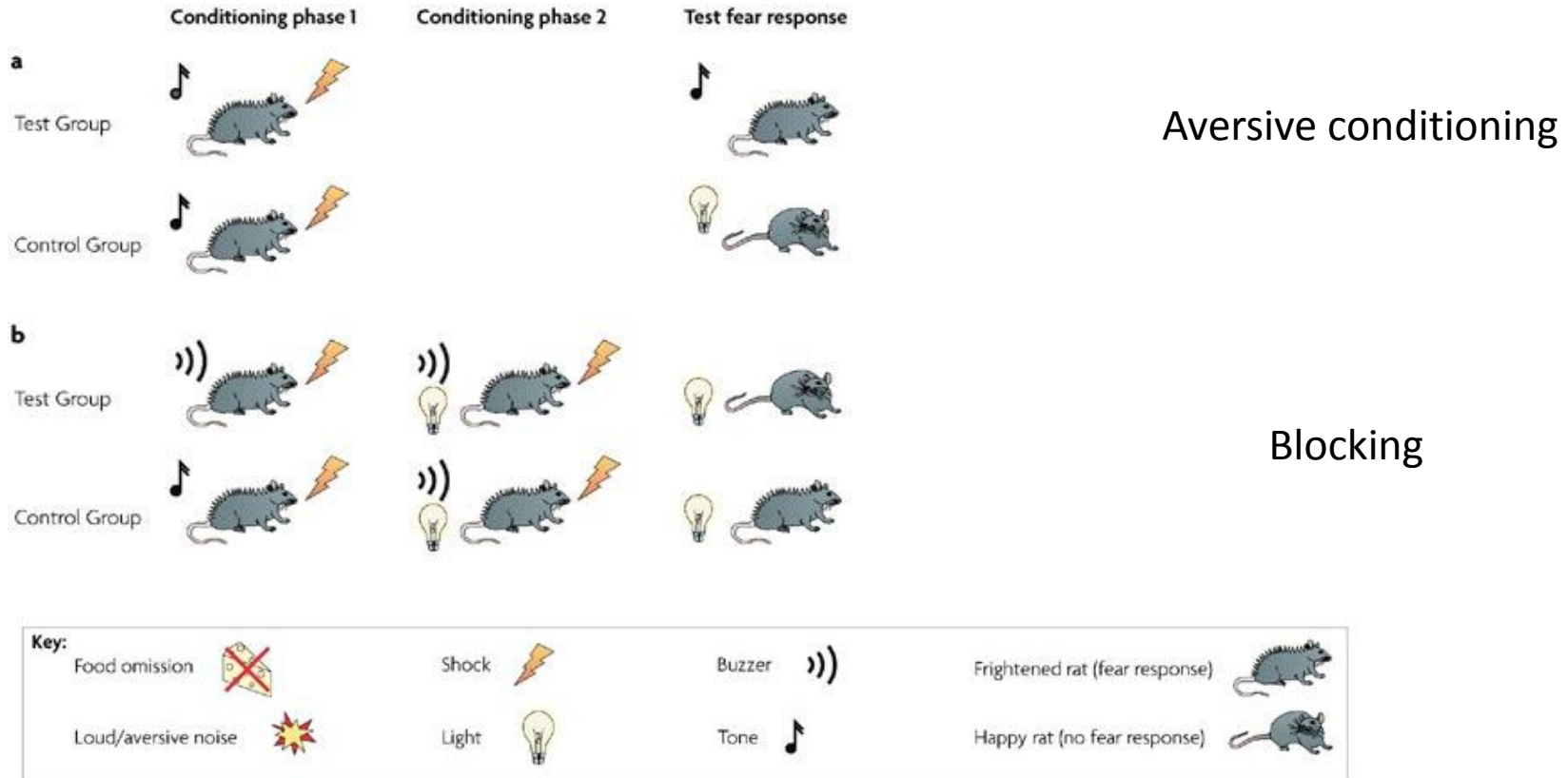
Contingency: co-occurrence



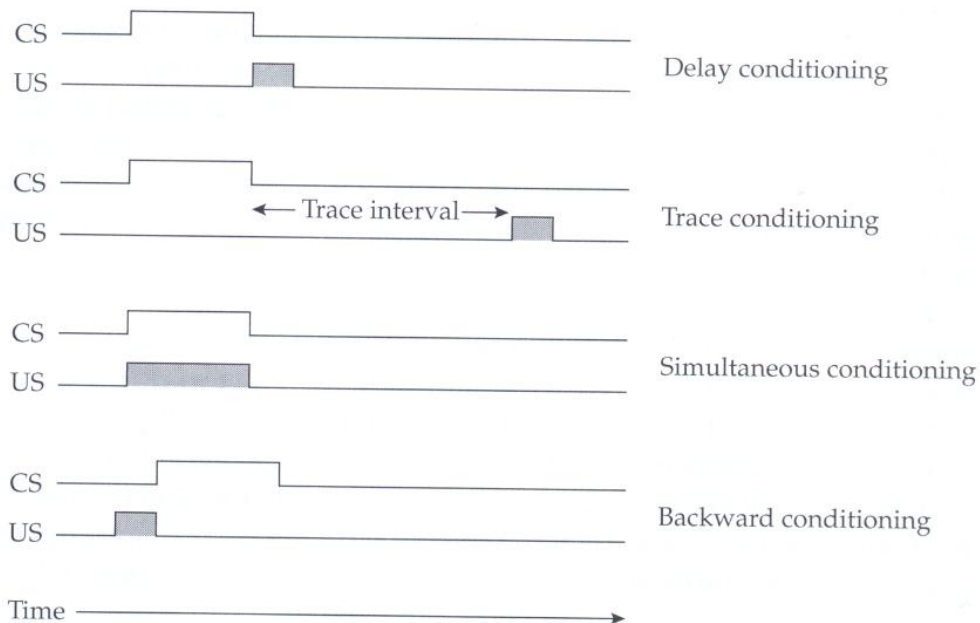
Schedules of reinforcement:
Variable/fixed interval/ratio



More than contingency: Surprise / added information

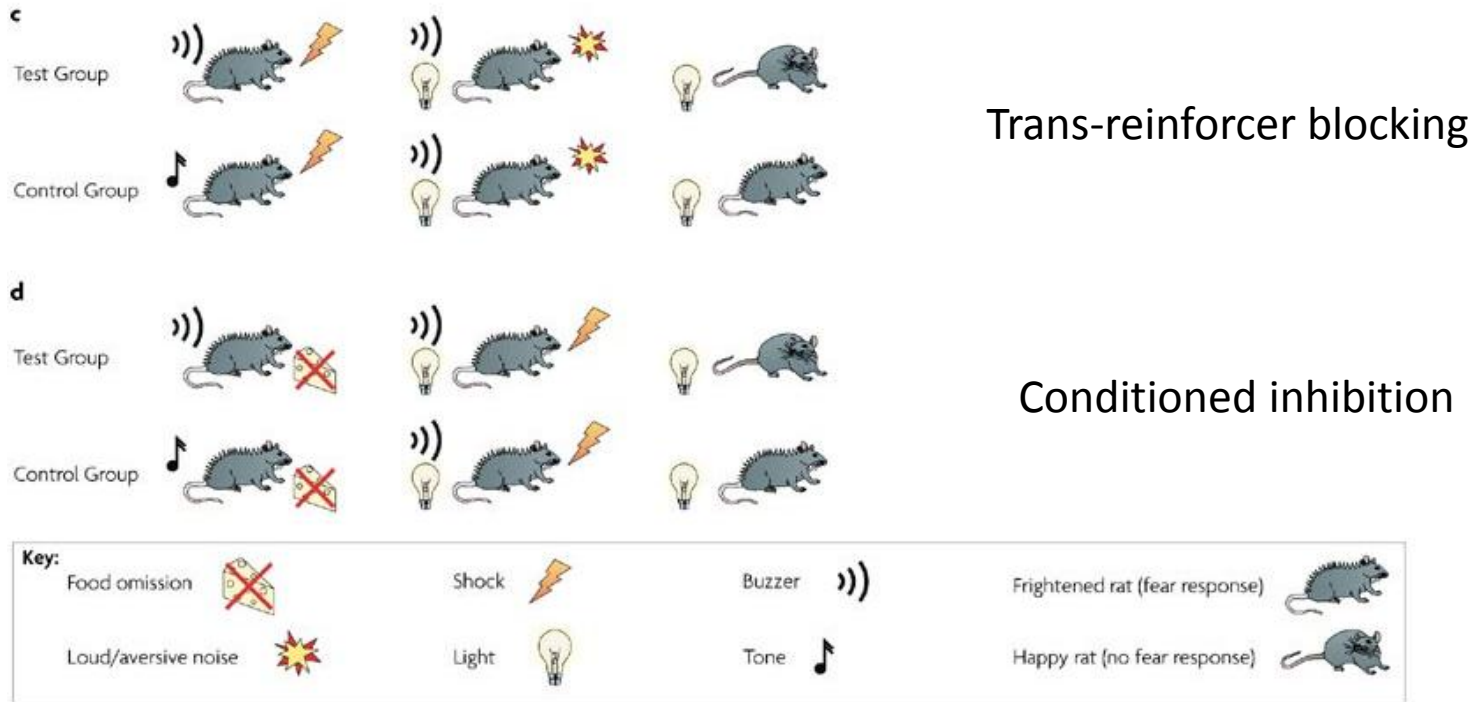


Rules of thumb for conditioning strength



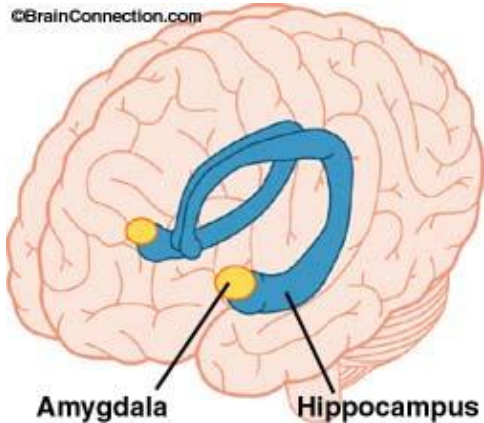
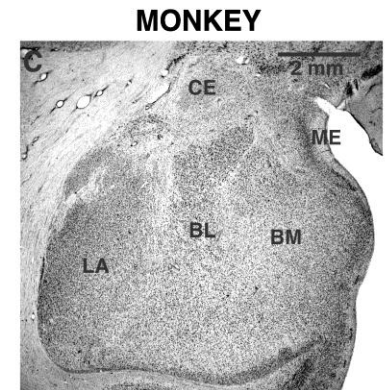
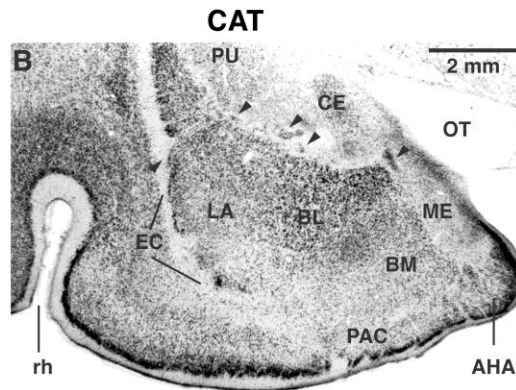
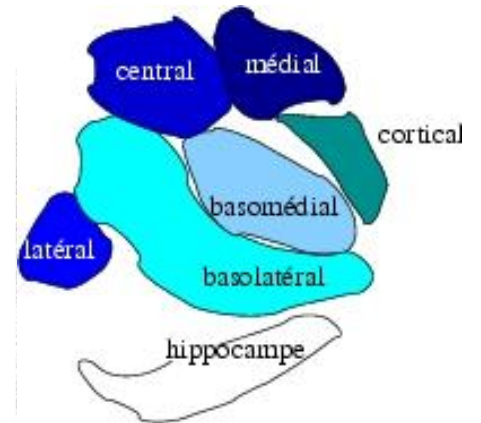
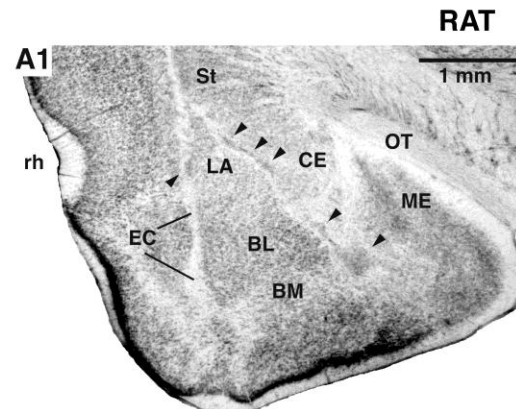
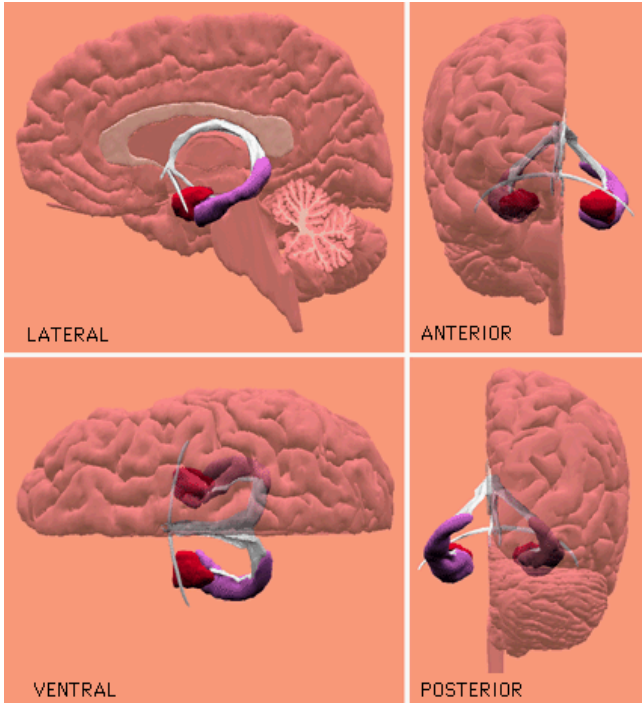
- Backward < simultaneous < trace < delay
- In trace: short interval > long interval
- In delay: short CS > long CS
- Salience of the CS
- Strength of the US
- Spaced trials is better than massed trials (the ratio between inter-trial-interval and the CS)

But notice it is hard to estimate backwards learning

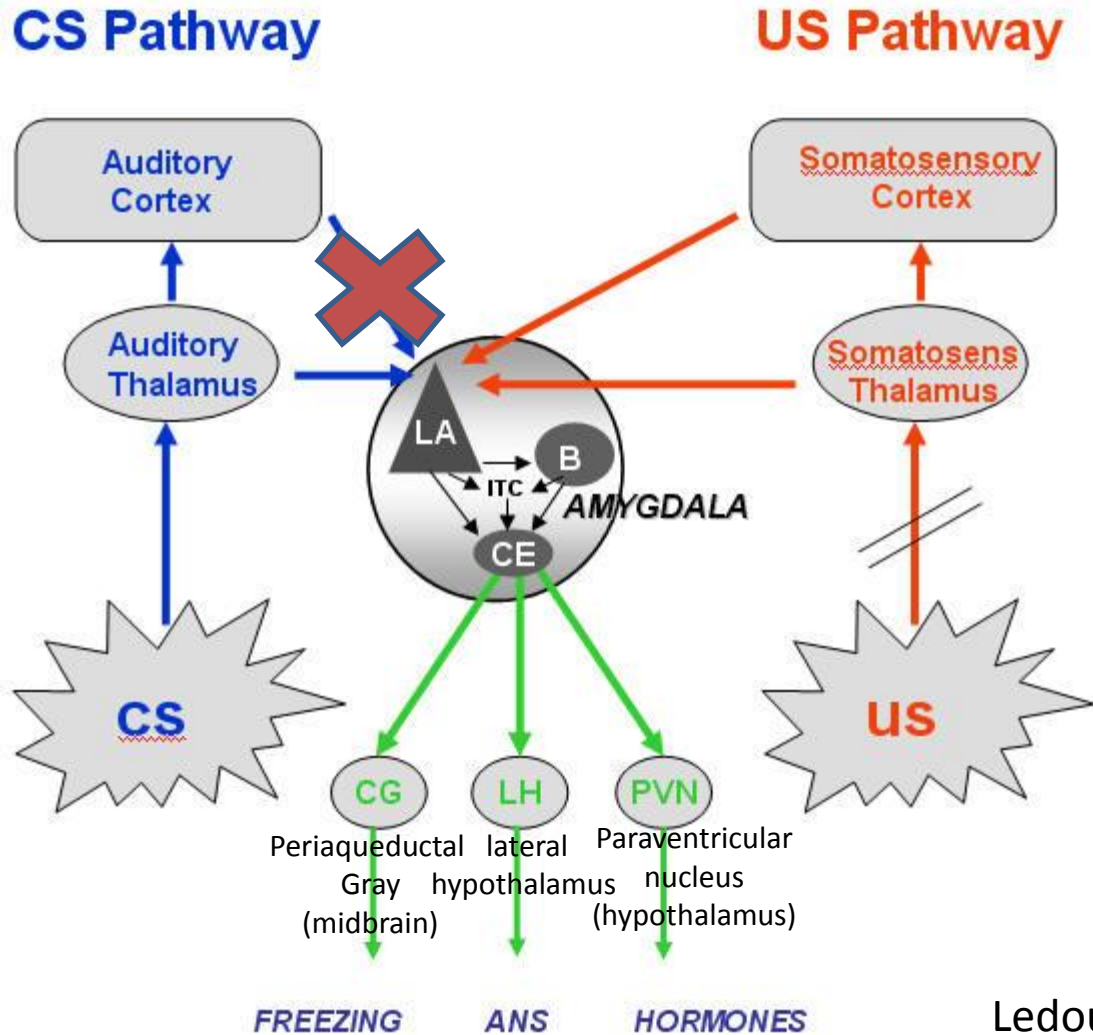


Suggests common brain mechanisms

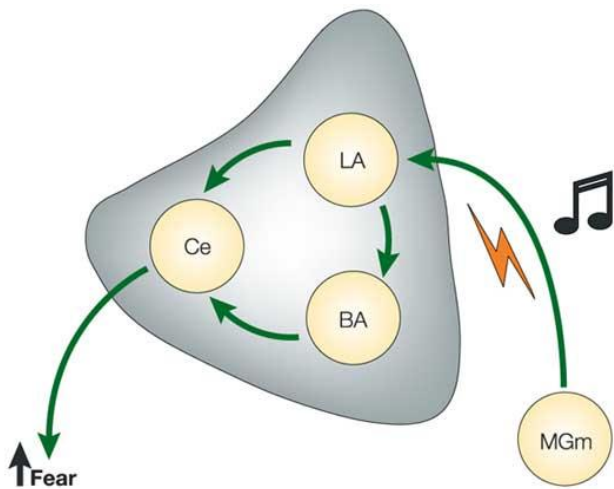
Amygdala



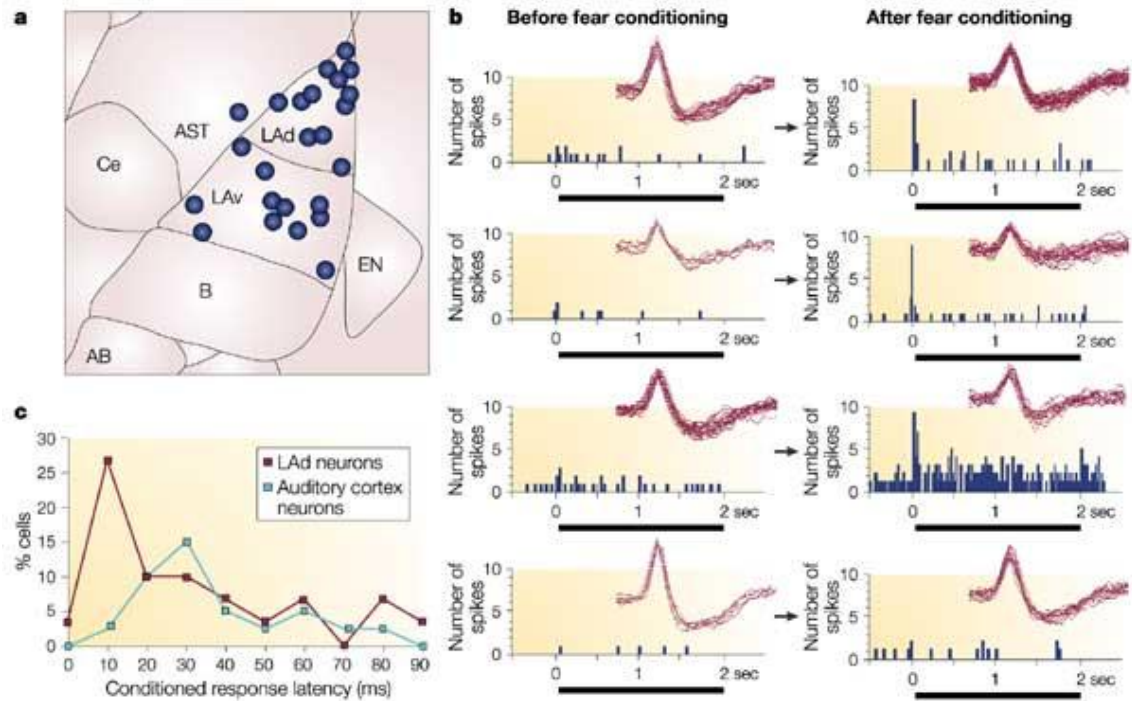
Fear circuit



Neurons acquire tone responses after conditioning



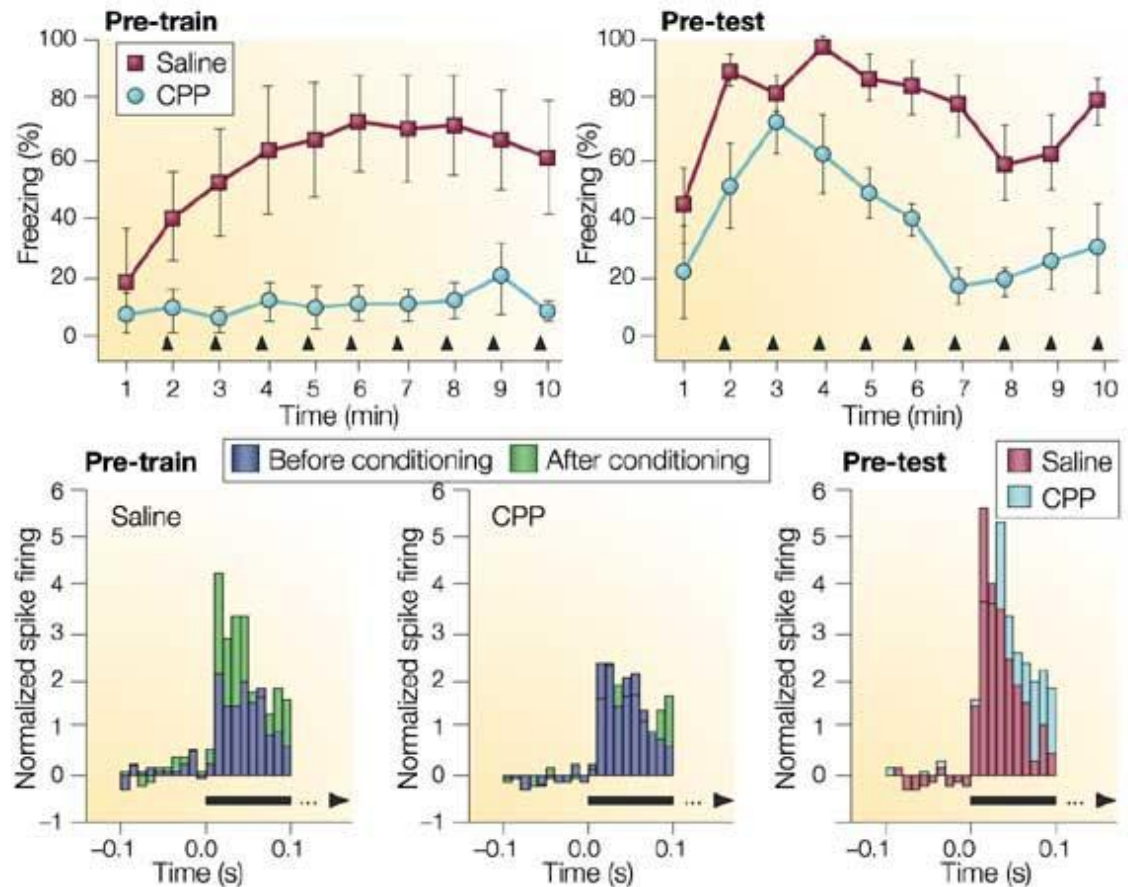
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LTP in the LA is required

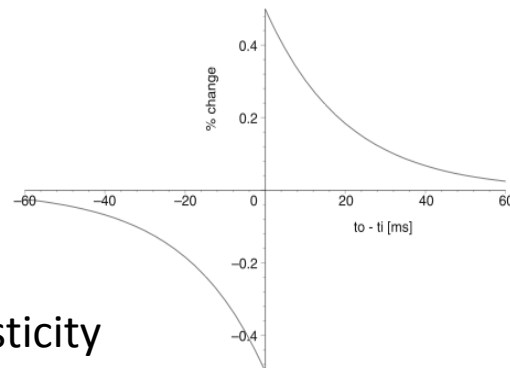
NMDA (*N*-methyl-*D*-aspartate, glutamate receptor) is involved in both the acquisition of fear memory and the induction of long-term potentiation (LTP) in the amygdala.



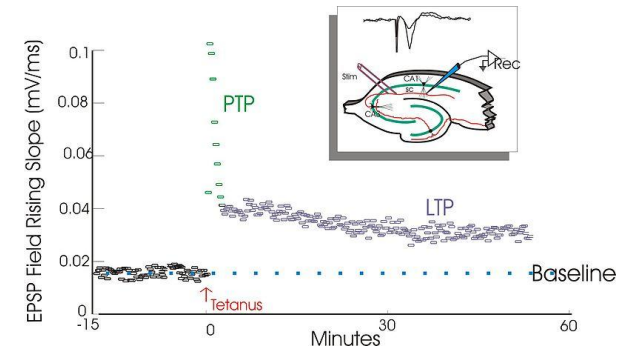
CPP (3-(2-carboxypiperazin-4-yl) propyl-1-phosphonic acid), a competitive NMDA-receptor antagonist

Long-term potentiation (LTP)

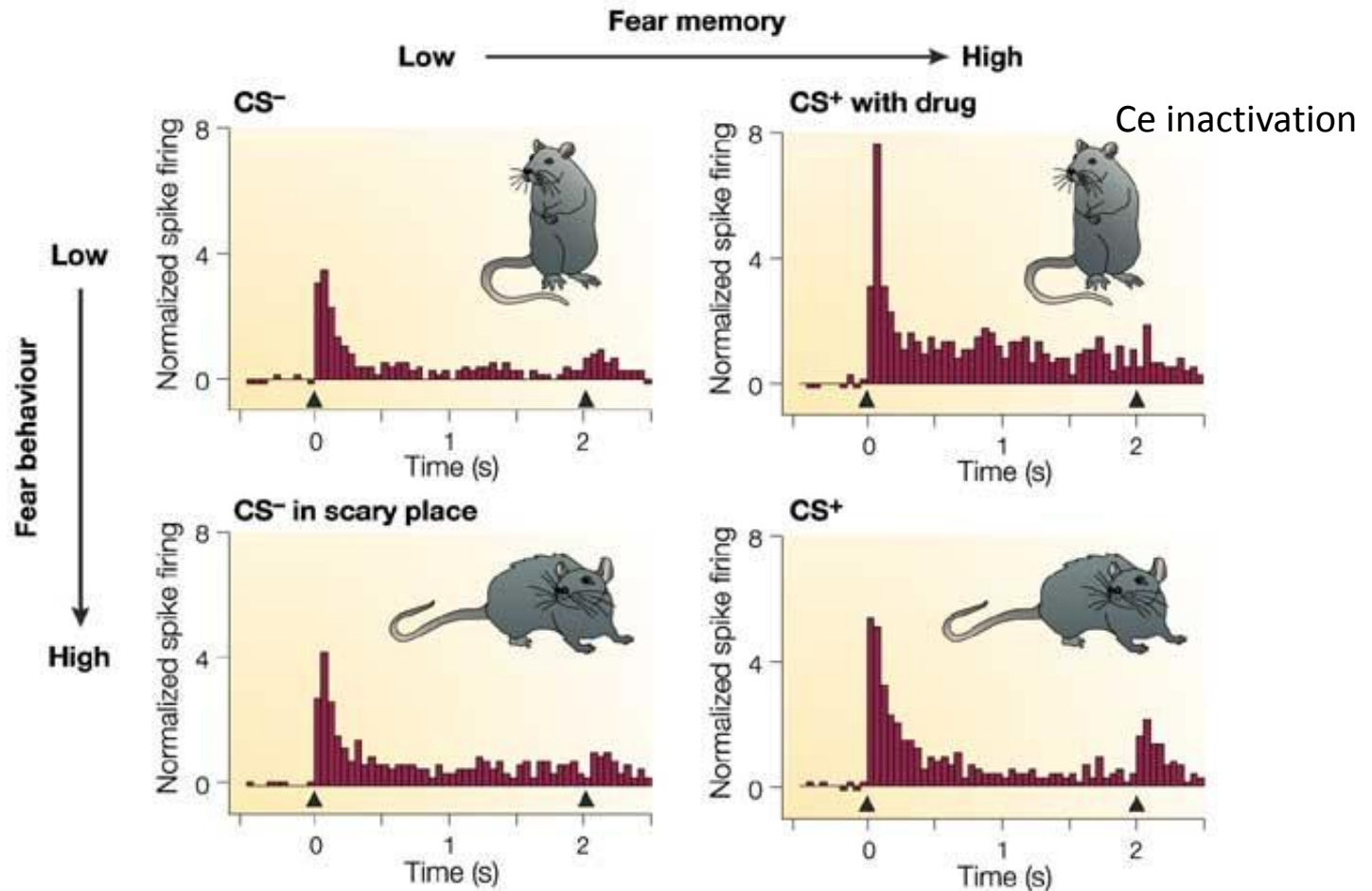
- Lomo, Bliss, Andersen, 1966, Hippocampus.
- Induced artificially by tetanic stimulation
- Long-lasting enhancement in signal transmission between two neurons that results from stimulating them synchronously.
- Increase in synaptic strength
- A cellular mechanism for learning and memory.
- Requires 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
 - Coopertaivity: weak stimulation of many



Spike timing dependent plasticity



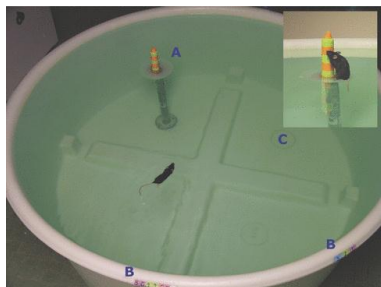
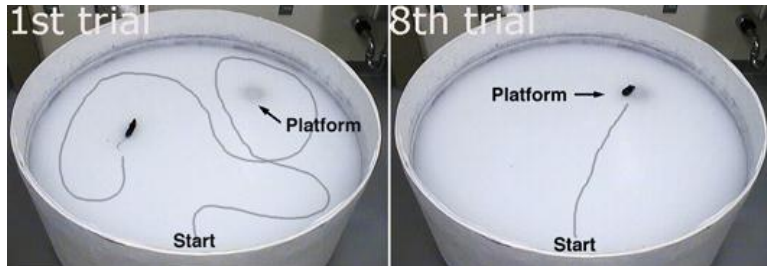
LA encodes memory independent of fear behavior



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

Neurobiology: Packard *et al.*

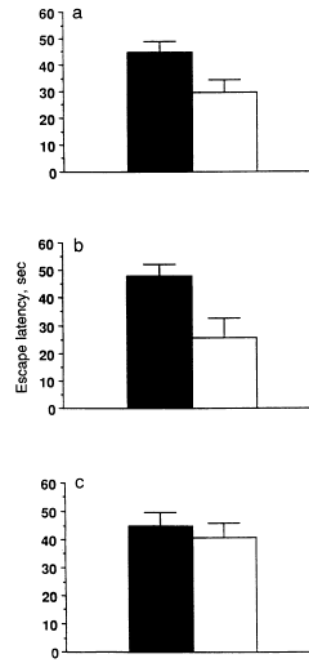


FIG. 1. Mean (\pm SE) escape latencies of *d*-amphetamine (10 μ g) (\square) and saline-treated (\blacksquare) rats on the retention test trial in the spatial task. (a) Hippocampal injections. (b) Amygdala injections. (c) Caudate nucleus injections.

posttraining intracaudate and intrahippocampal injections of *d*-amphetamine on retention of cued and spatial learning in

Proc. Natl. Acad. Sci. USA 91 (1994) 8479

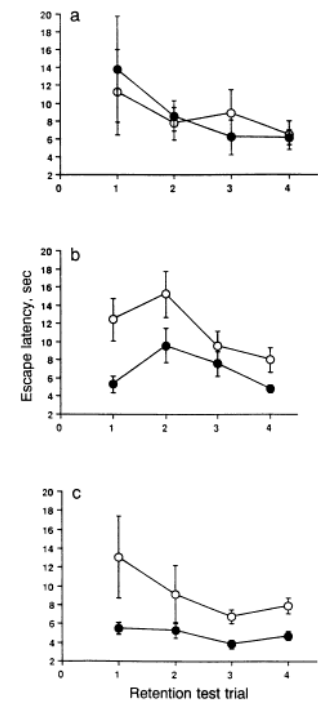


FIG. 2. Mean (\pm SE) escape latencies of *d*-amphetamine (10 μ g) (\bullet) and saline-treated (\circ) rats on the retention test trial in the cued task. (a) Hippocampal injections. (b) Amygdala injections. (c) Caudate nucleus injections.

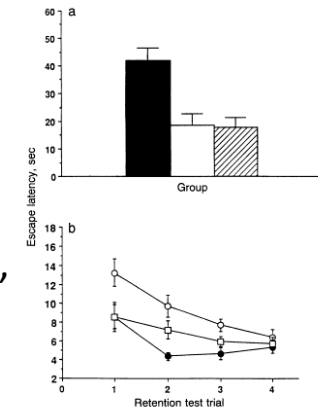


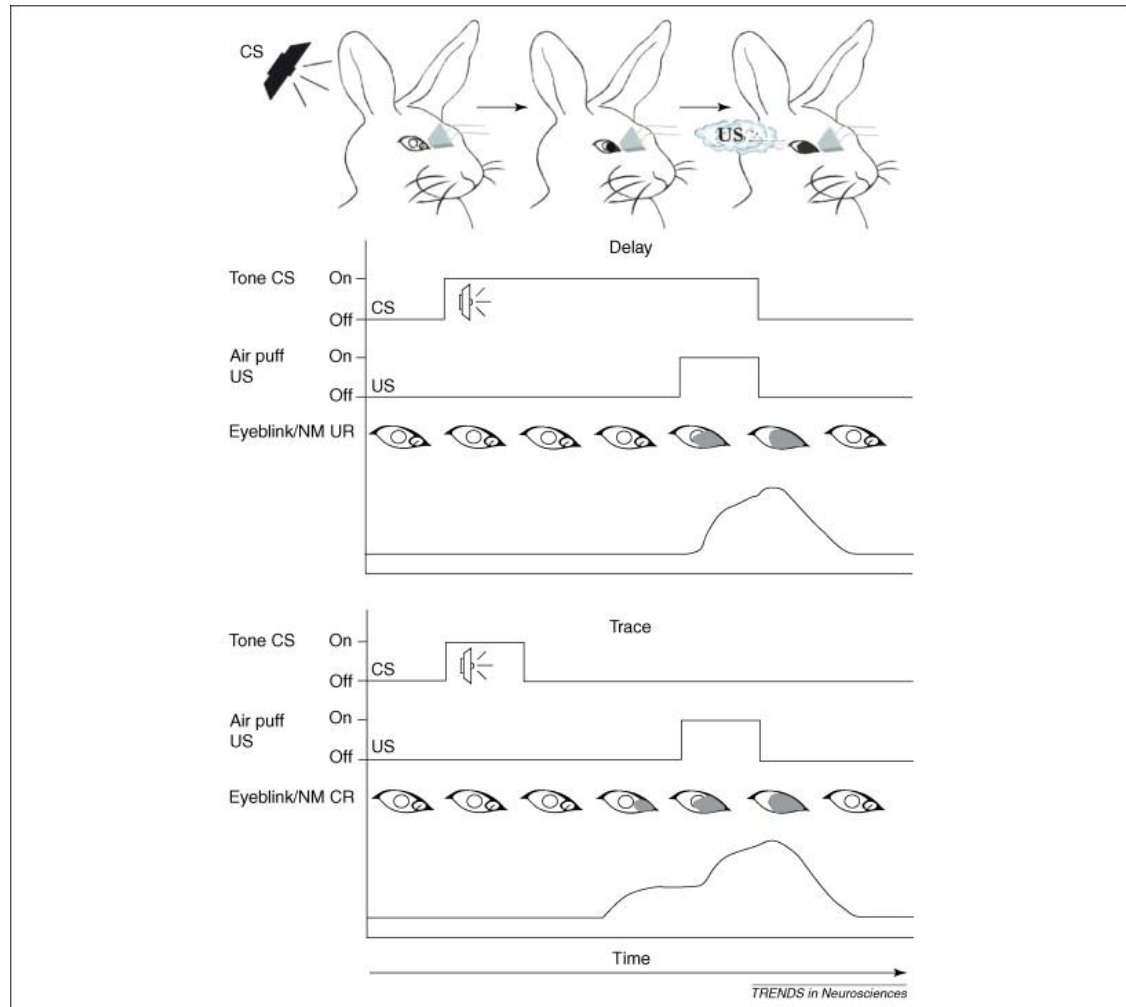
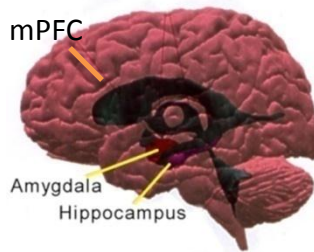
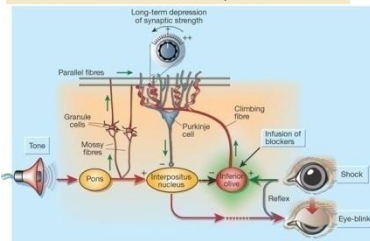
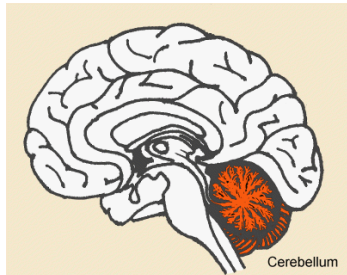
FIG. 3. Mean (\pm SE) escape latencies of rats receiving intra-amygdala posttraining *d*-amphetamine or saline and rats receiving pretraining test lidocaine or saline on the retention test trial(s) in the spatial task (a) and cued task (b). Posttraining/pretraining: \bullet (a) and \circ (b), saline/saline; \square (a) and \blacksquare (b), *d*-amphetamine/saline; \square (a) and \square (b), *d*-amphetamine/lidocaine.

Packard, Mcgaugh

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

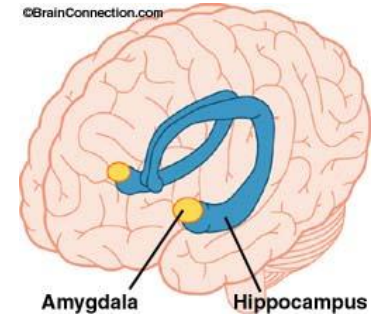
- **It depends.**

Eyelid (blink) reflex conditioning

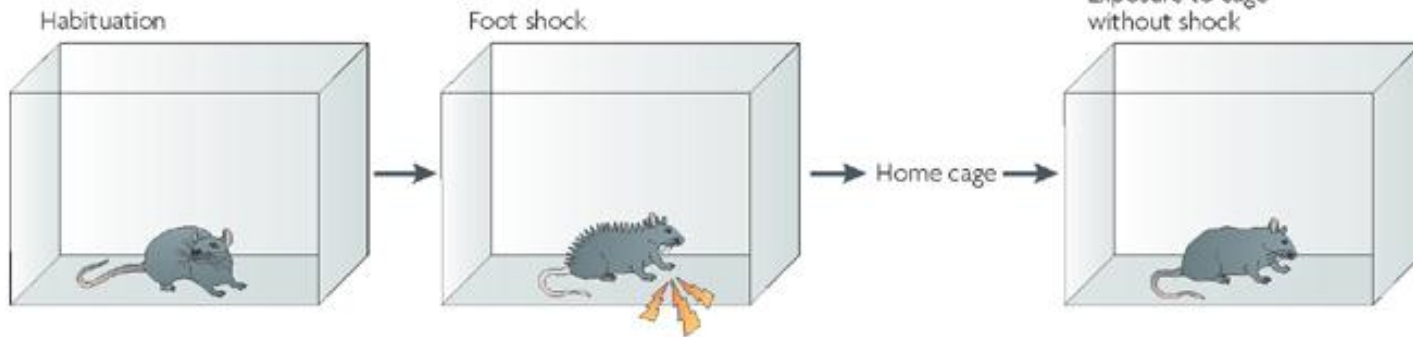


- Why is trace hippocampal-dependent?
- Maintaining the CS? Timing the trace? Harder?
- Eyelid requires ~0.3sec, and hippocampus is required when 0.5-1sec.
- In tone-shock, trace can be 3sec, and hippocampus is required for ~20sec
- This suggest context-conditioning

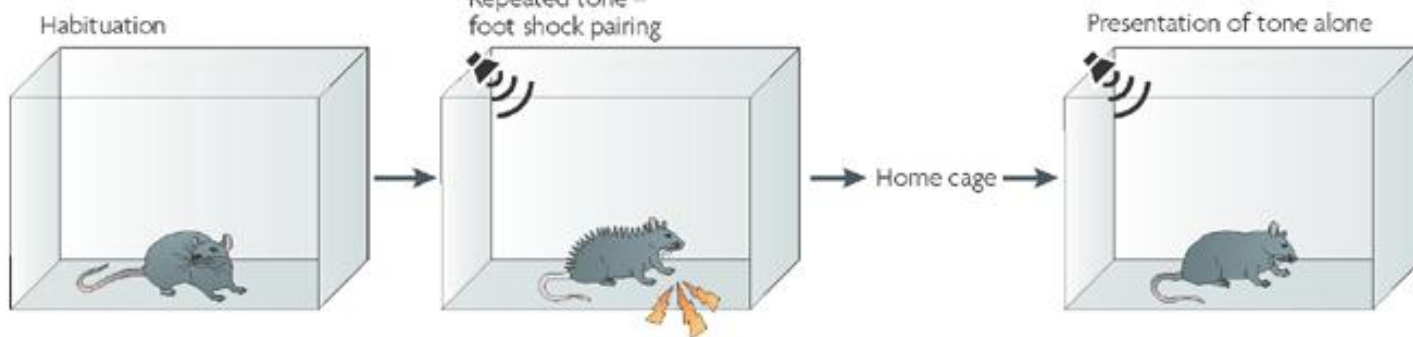
Contextual fear



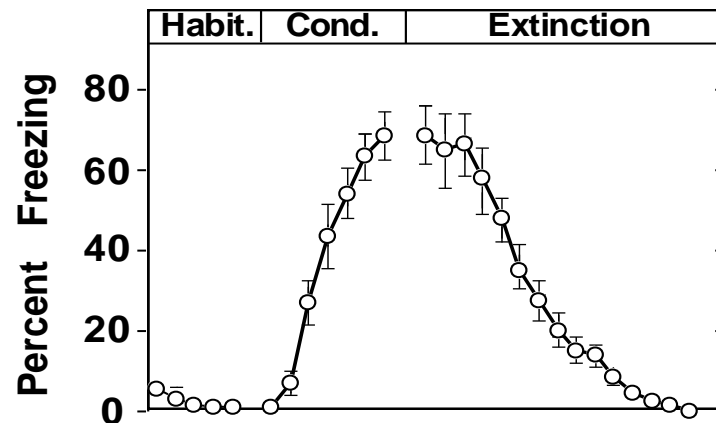
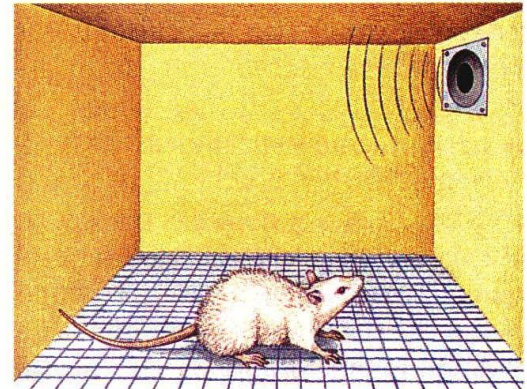
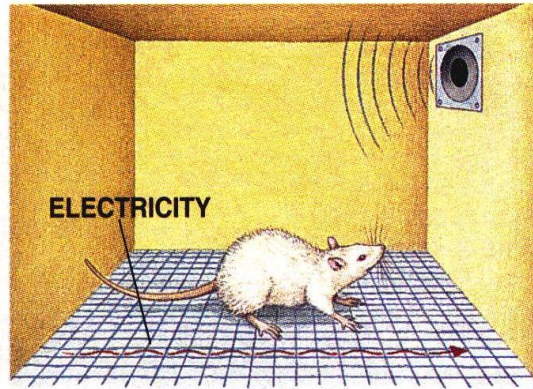
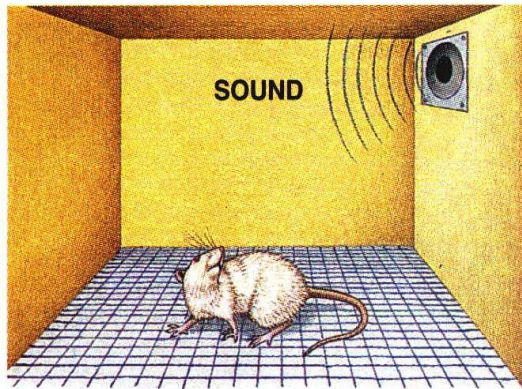
a Contextual fear conditioning



b Acoustic-cued fear conditioning

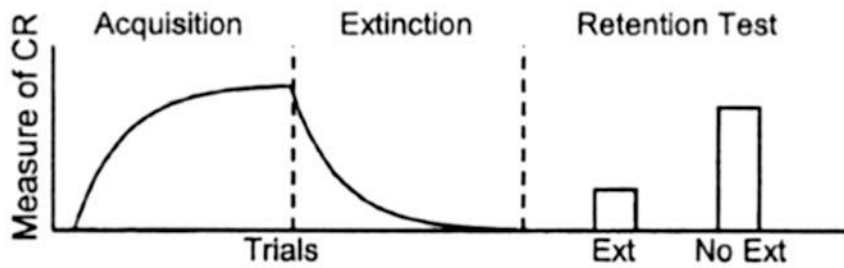


Extinction of fear-conditioning

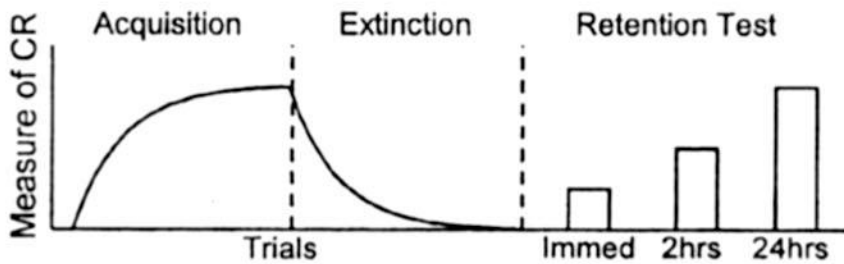


Extinction: a new learning

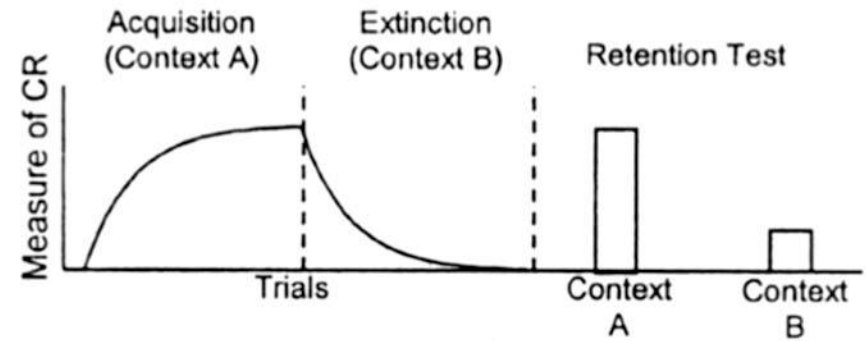
A Extinction is not the same as forgetting



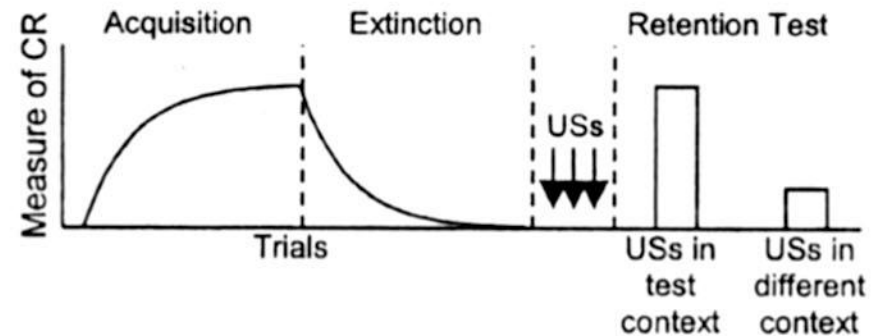
B Spontaneous recovery



C Renewal



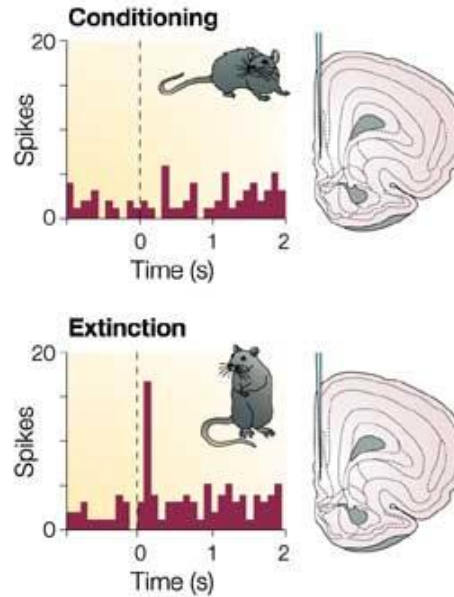
D Reinstatement



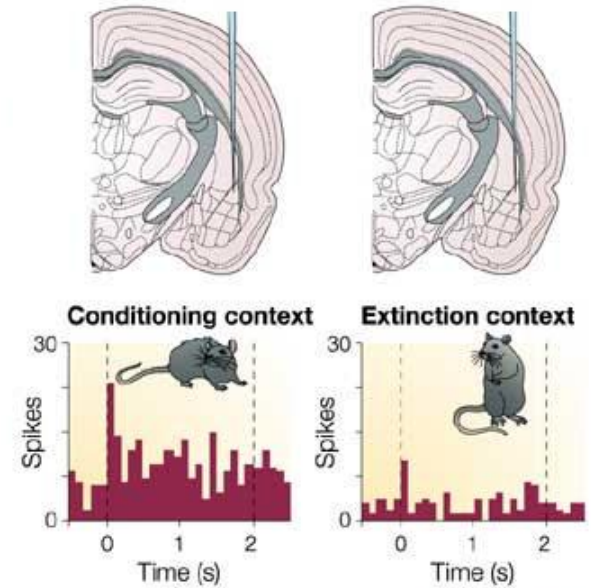
Faster re-learning

Extinction: brain mechanisms

a Prefrontal cortex (safety memory)

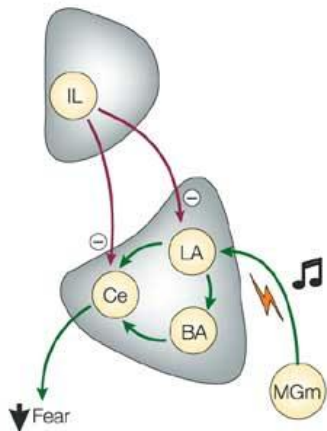


b Lateral amygdala (fear memory)

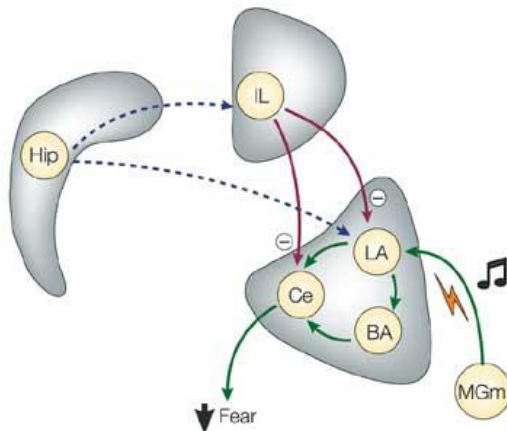


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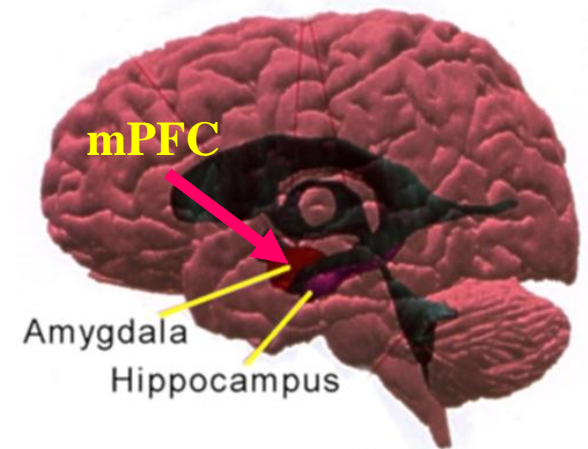
a Expression of extinction



b Modulation of extinction

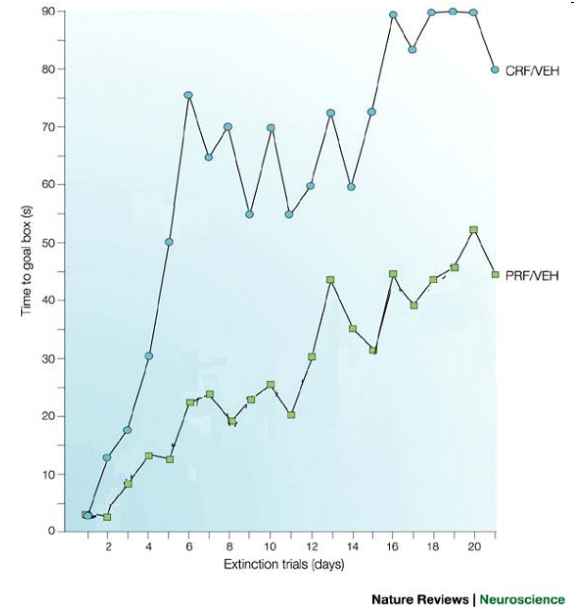


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Partial reinforcement extinction effect

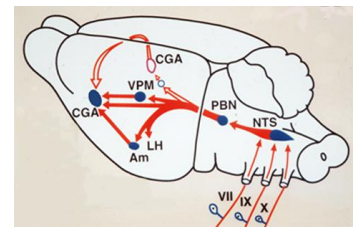
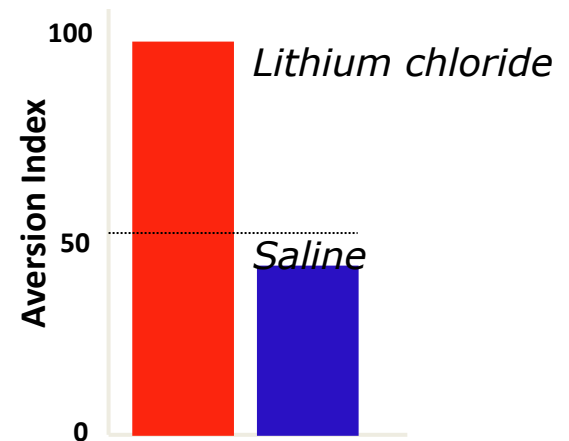
- Partial reinforcement
 - Fixed/variable ratio
 - Fixed/variable schedule
- Results in longer extinction learning
- Why?
 - Frustration theory (Amsel): The omission of the US induces frustration. Therefore, during extinction, the frustration predicts the US.
 - Sequential theory (Capaldi): conditioning to strings of NNNRNNNR
- Bad for behavior flexibility
- Good for education



Conditioned Taste Aversion



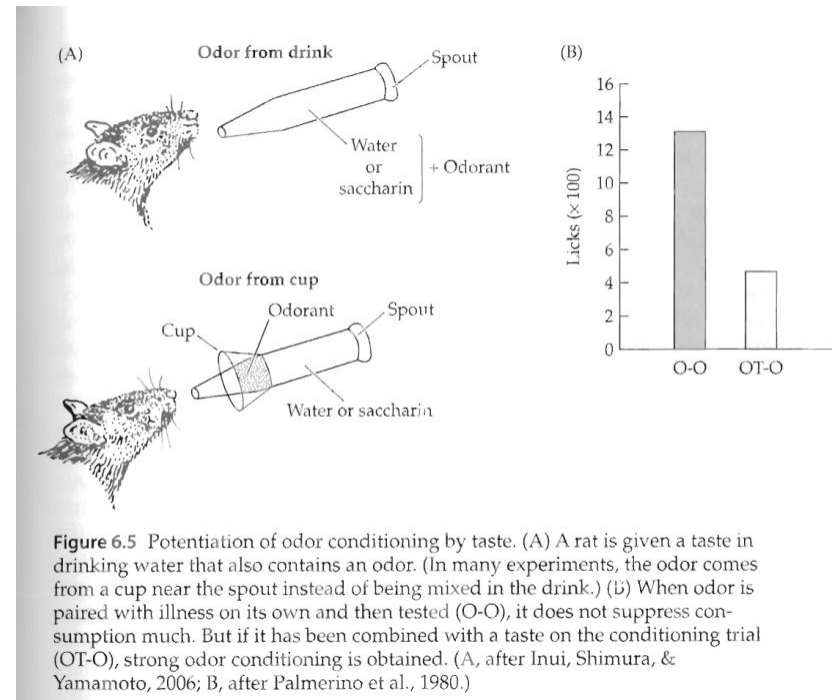
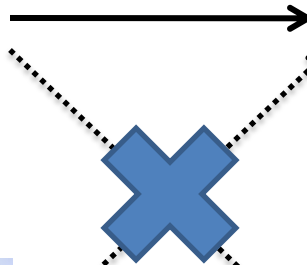
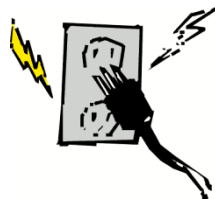
- One-trial learning
- Long-delay learning (few hours)
 - A [lack of] interference effect?
 - Still a problem for neuroscientists
- Hedonic shift: changes the CS, not its predictions



CTA

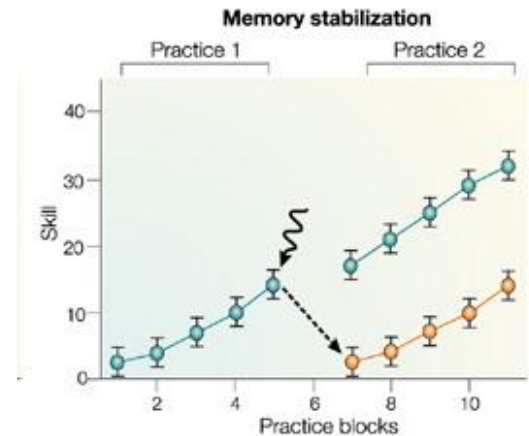
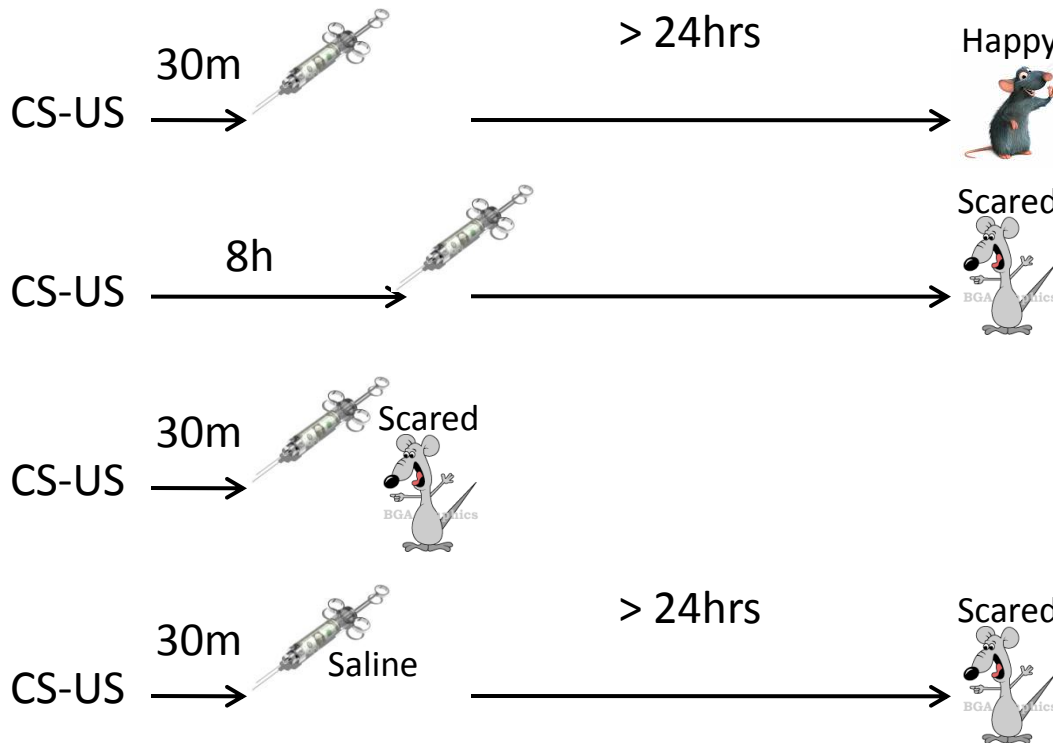
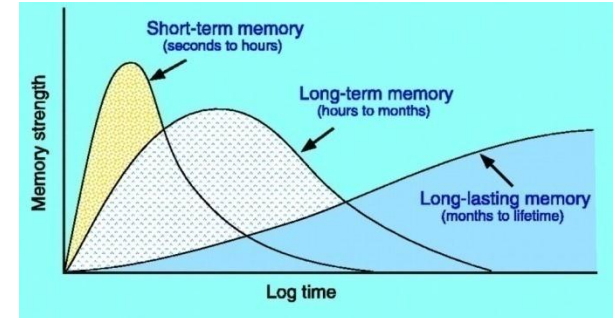
- Compound potentiation: odor + taste increase response to odor

- Preparedness:

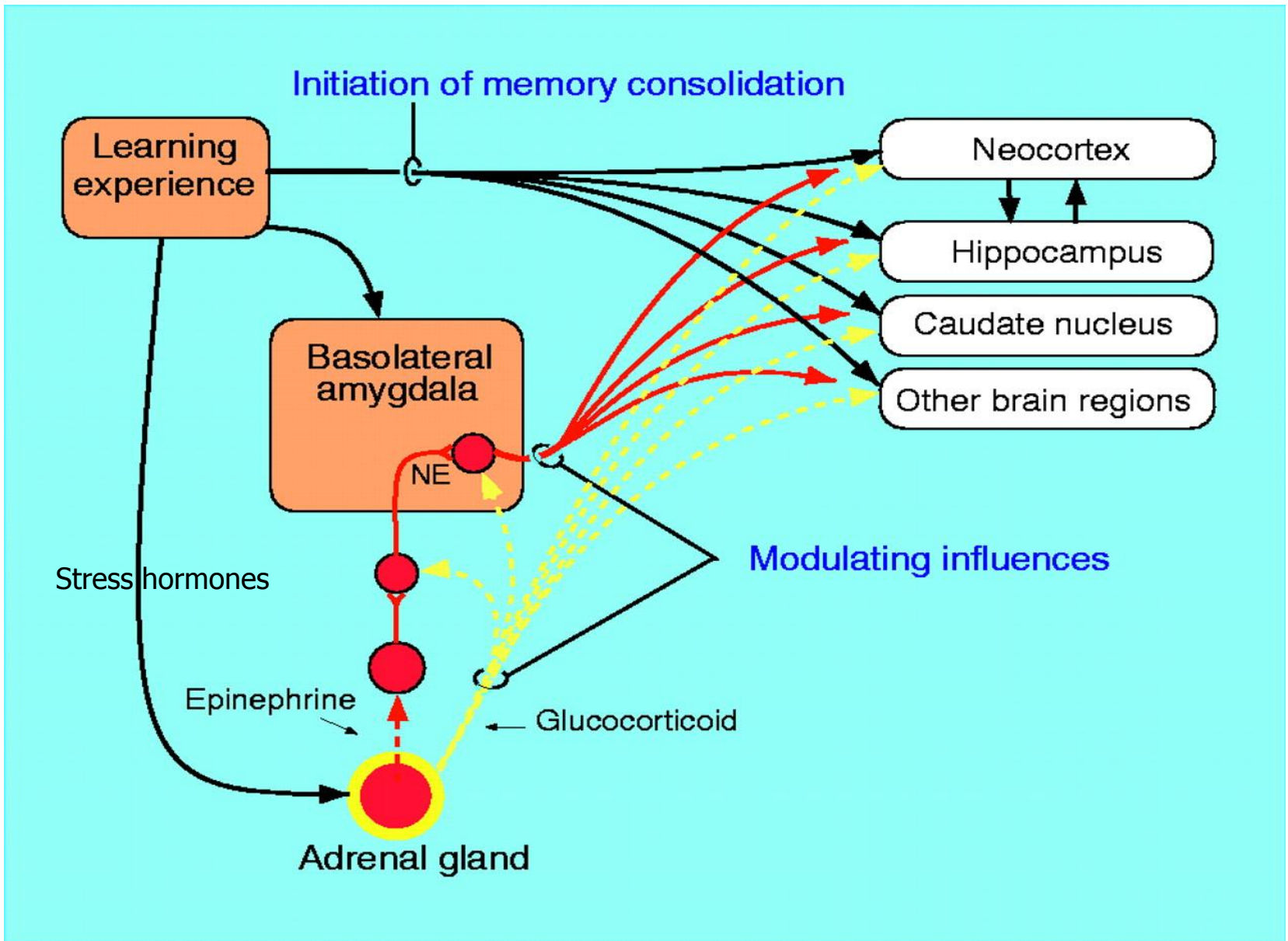


Consolidation

- 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.

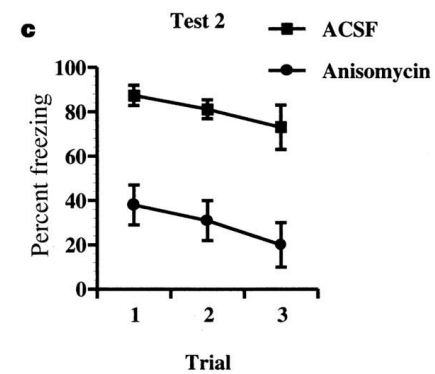
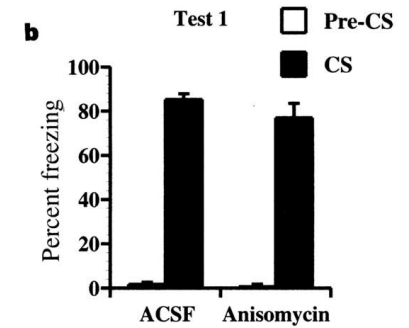
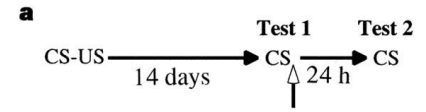
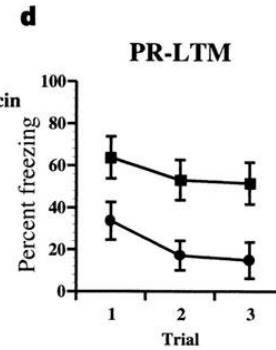
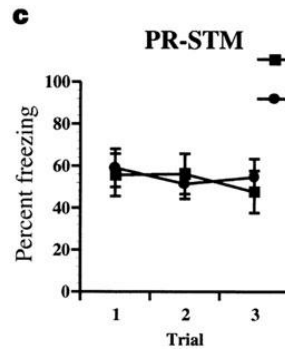
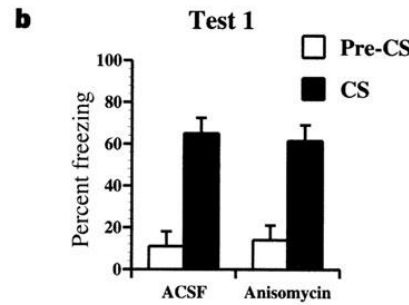
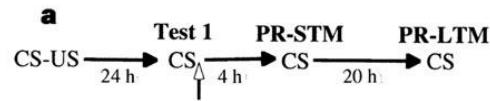
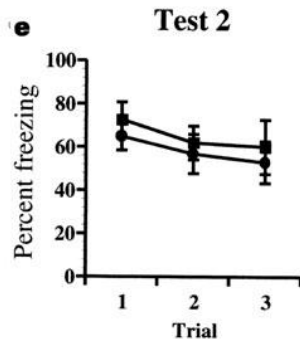
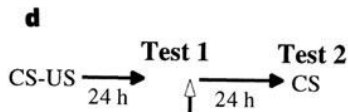
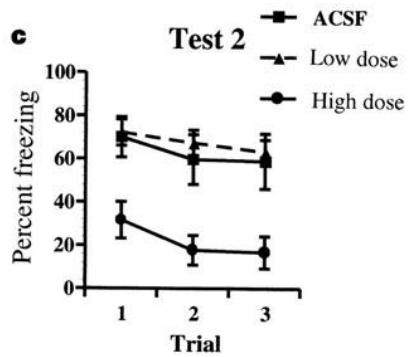
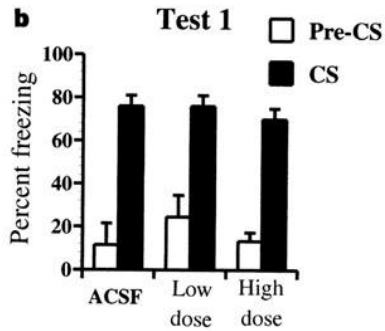
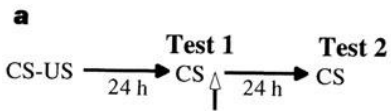


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Reconsolidation

No effect on STM



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)

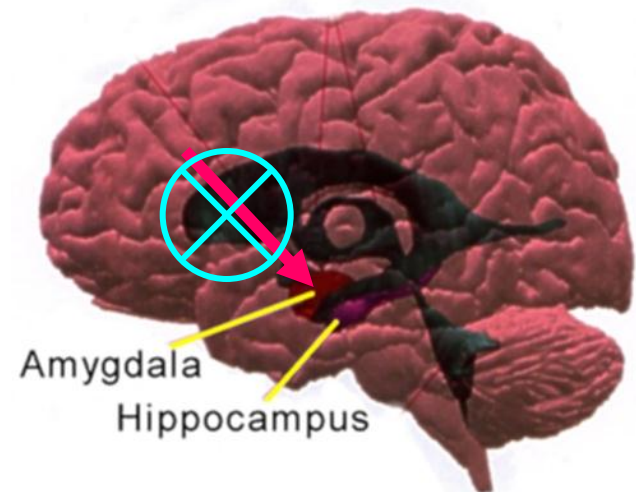
- Lasts for days to weeks
 - Inactive (insensitive to disruption)
- (Does require new RNA or protein synthesis)



PTSD (post-traumatic-stress-disorder)



- Extinction failure



Reconsolidation and extinction: What Freud always knew



Context Generalization / specificity

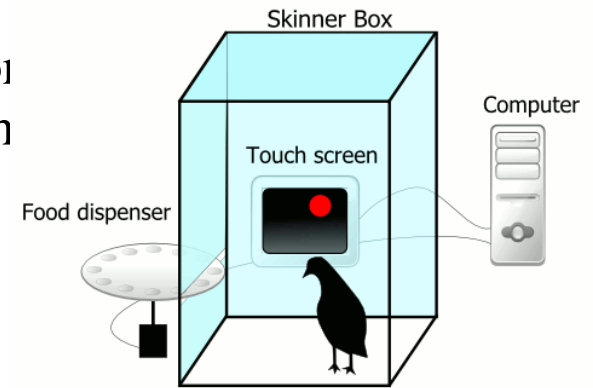


Generalization

- 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.

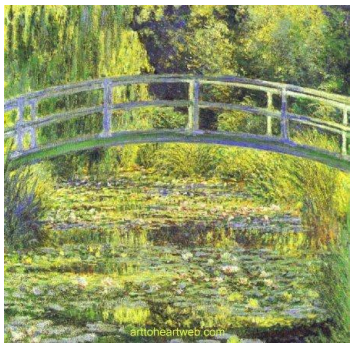
- Pavlov, 1927: drooling to similar sounds

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

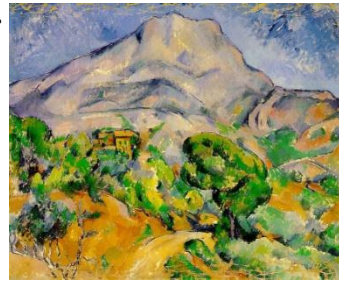


Categorization

Monet

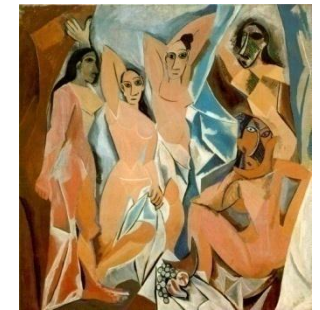


Cezanne / Renoir



Matisse / Braque

Picasso



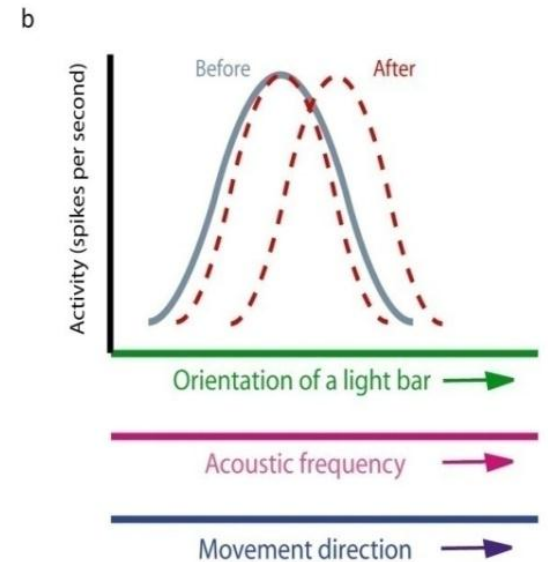
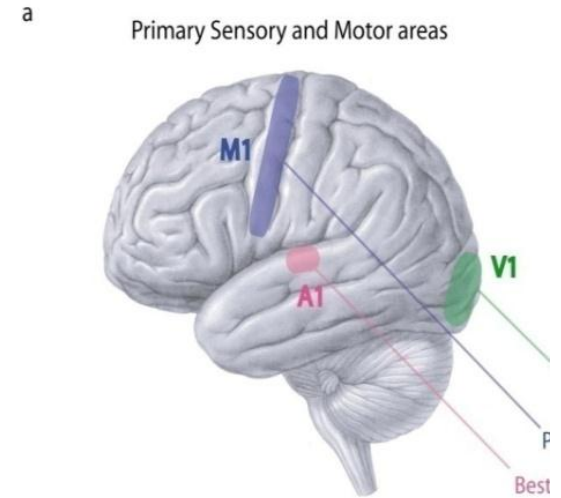
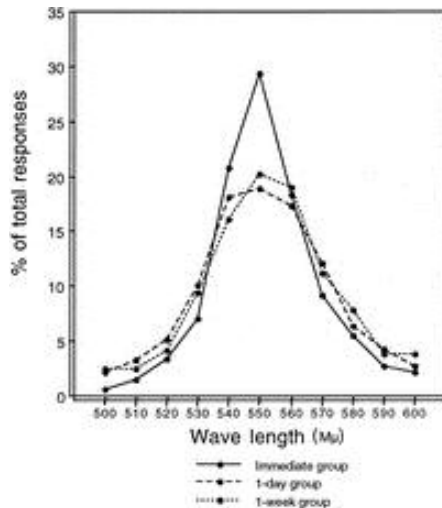
Watanabe, 95

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”

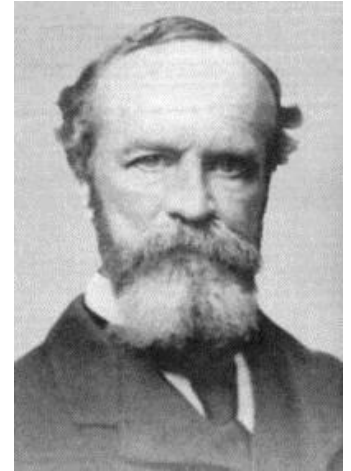


What are emotions?

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