Behavioral Neuroscience: Fear thou not

Neural mechanisms of Behavior

The Neuropsychological approach

Behavior – a bidirectional process

Thoughts

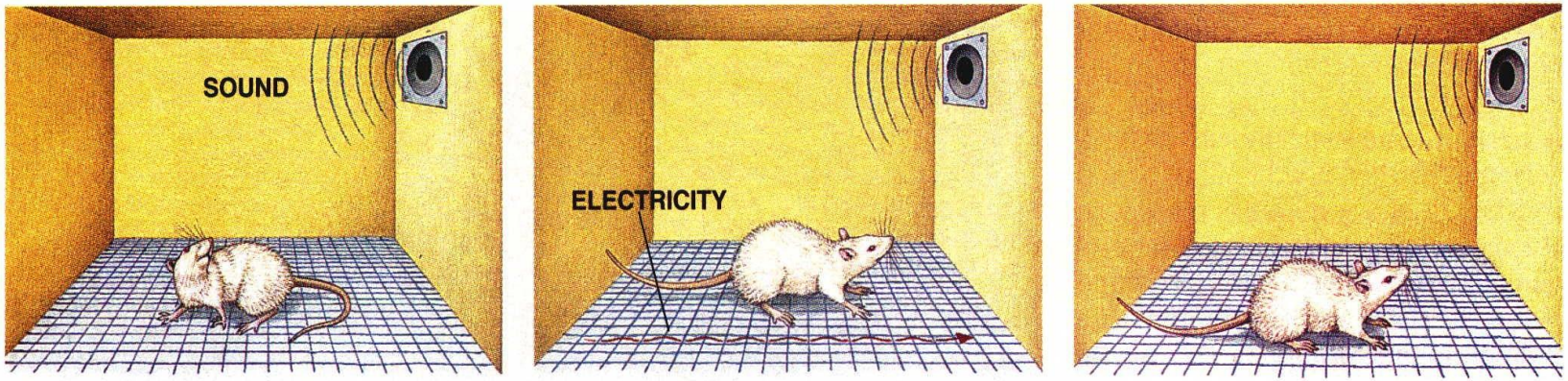
- What is a “reward”?
- Learning is best motivated by threats to survival?
- Threats are much better reinforcers?
- Fear is a prime motivator

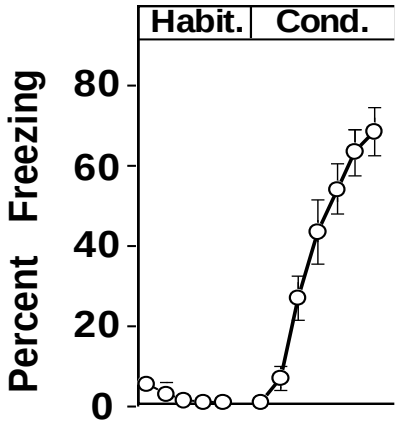
	Decreases behavior	Increases behavior
Presented	Positive punishment	Positive reinforcer
Taken away	Negative punishment	Negative reinforcer

Taking drugs?

More fun,
less withdrawal

Classical fear conditioning

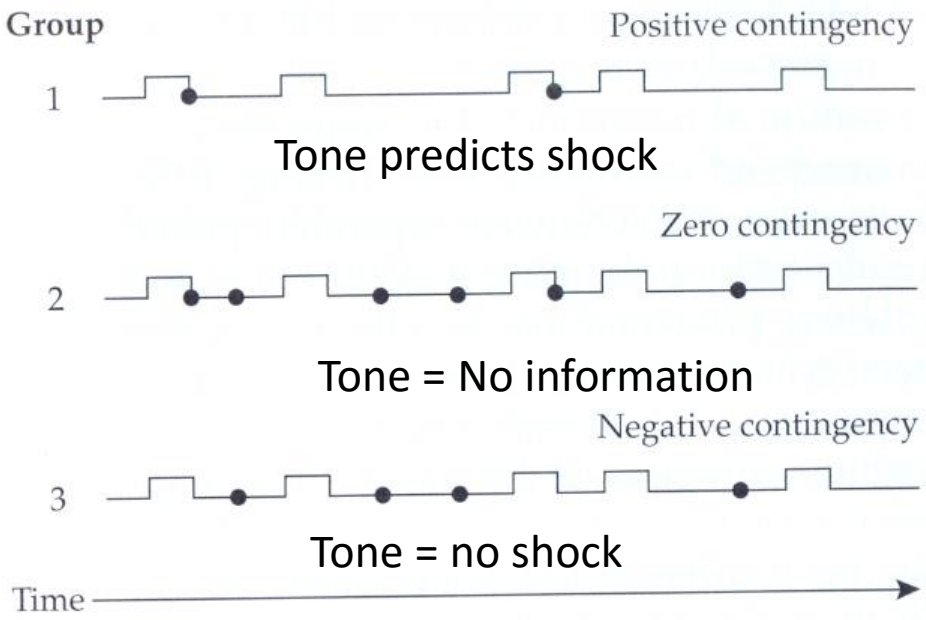


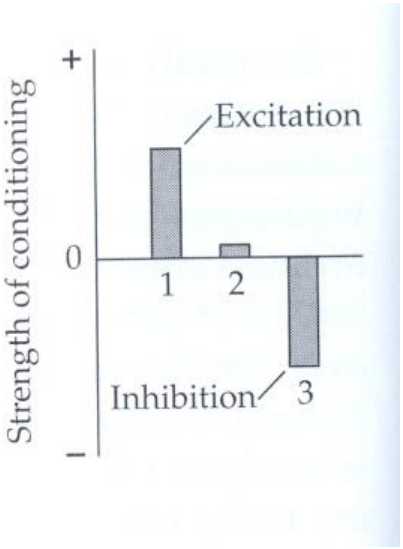


CS-US pairing
Tone = conditioned stimulus (CS)
Foot-shock = unconditioned stimulus (US)
Freezing = conditioned response (CR-UR)

The CS predicts the US → CR

Contingency: co-occurence

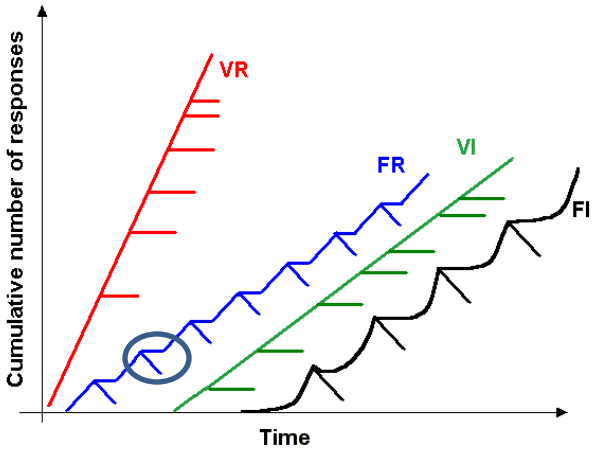




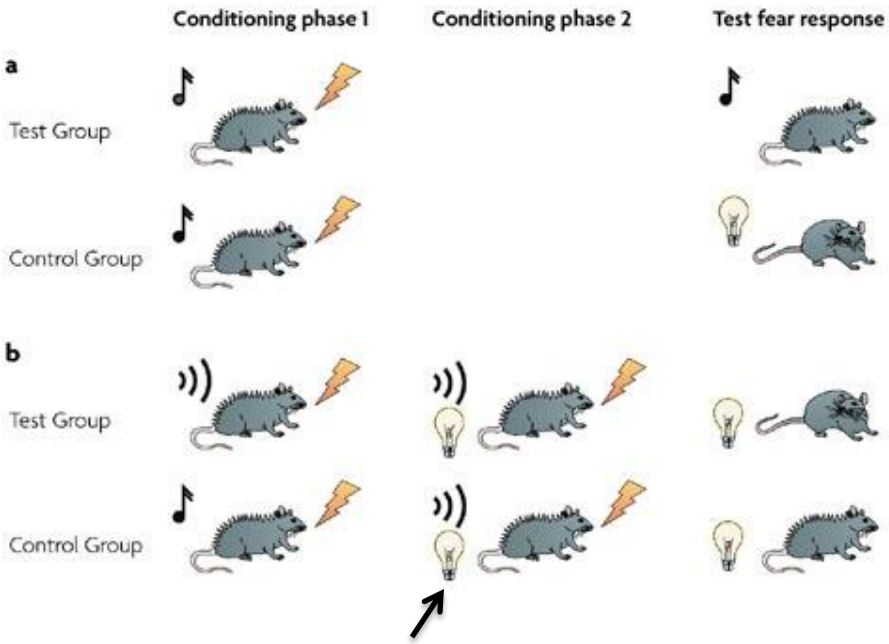
Schedules of reinforcement:
Variable/fixed interval/ratio

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



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

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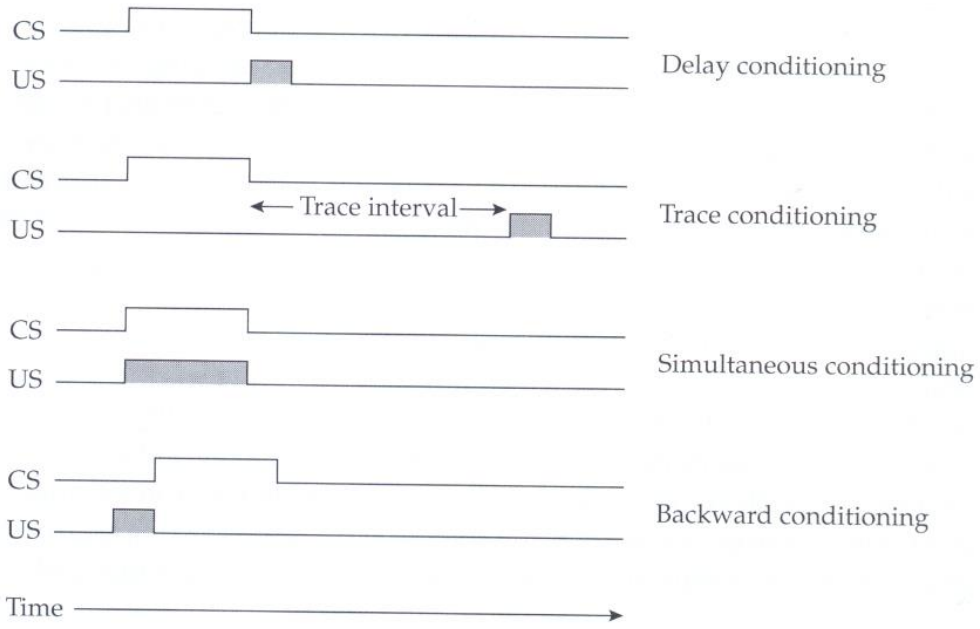
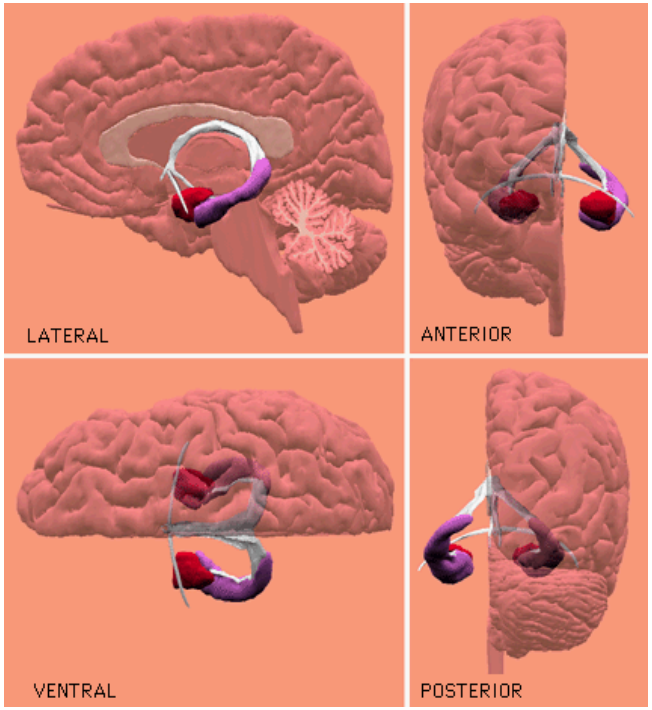
Rules of thumb for conditioning strength



- **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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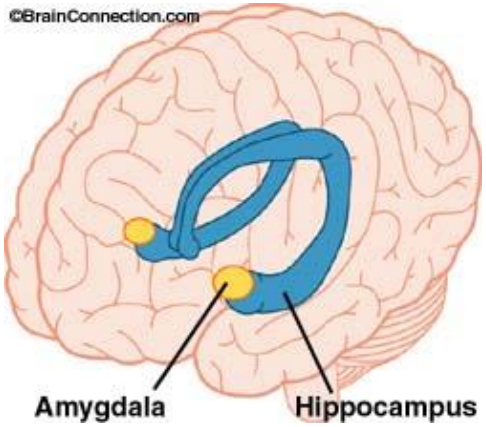
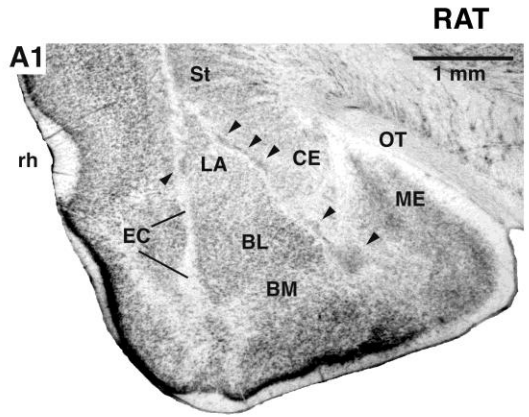
ANTERIOR
VENTRAL
POSTERIOR


©BrainConnection.com
Amygdala
Hippocampus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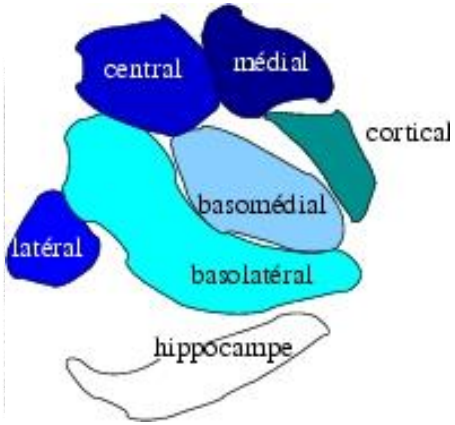
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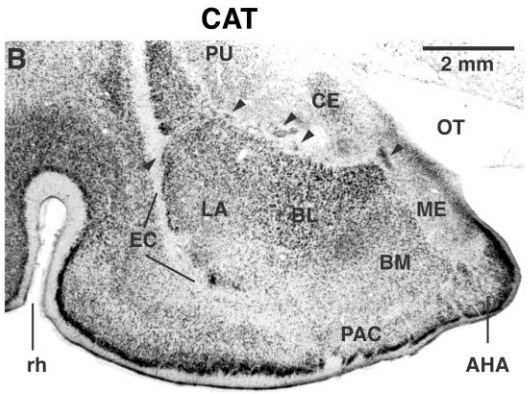
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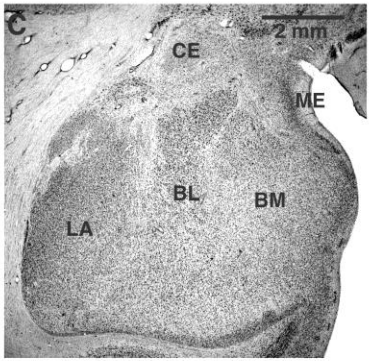
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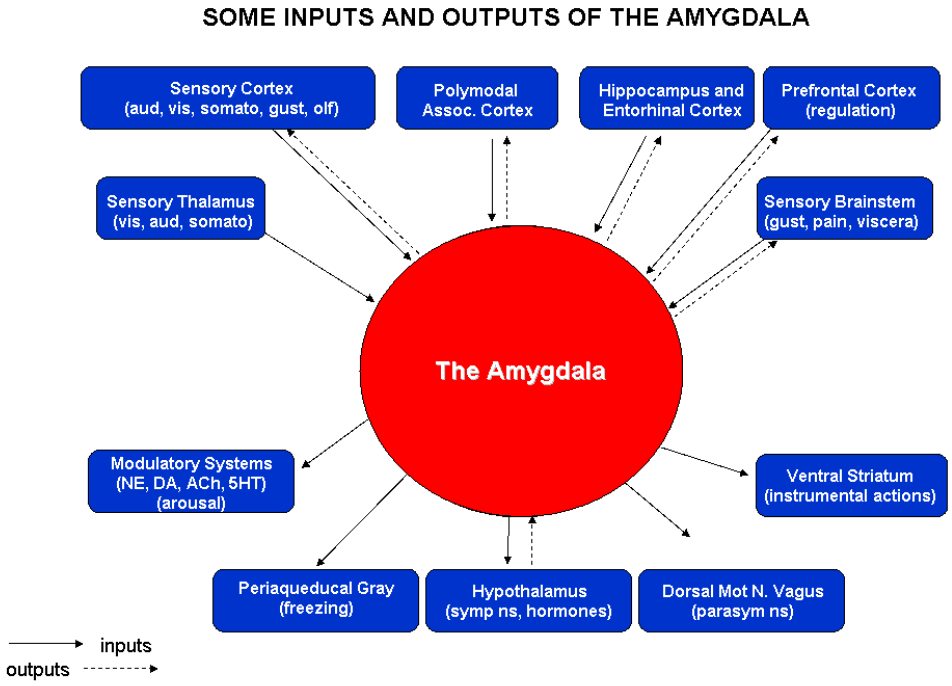
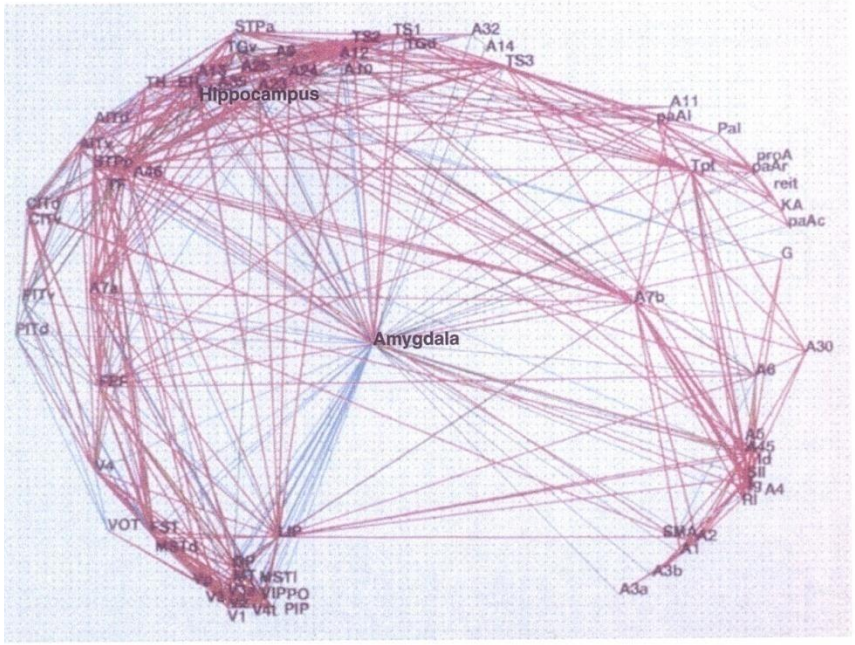
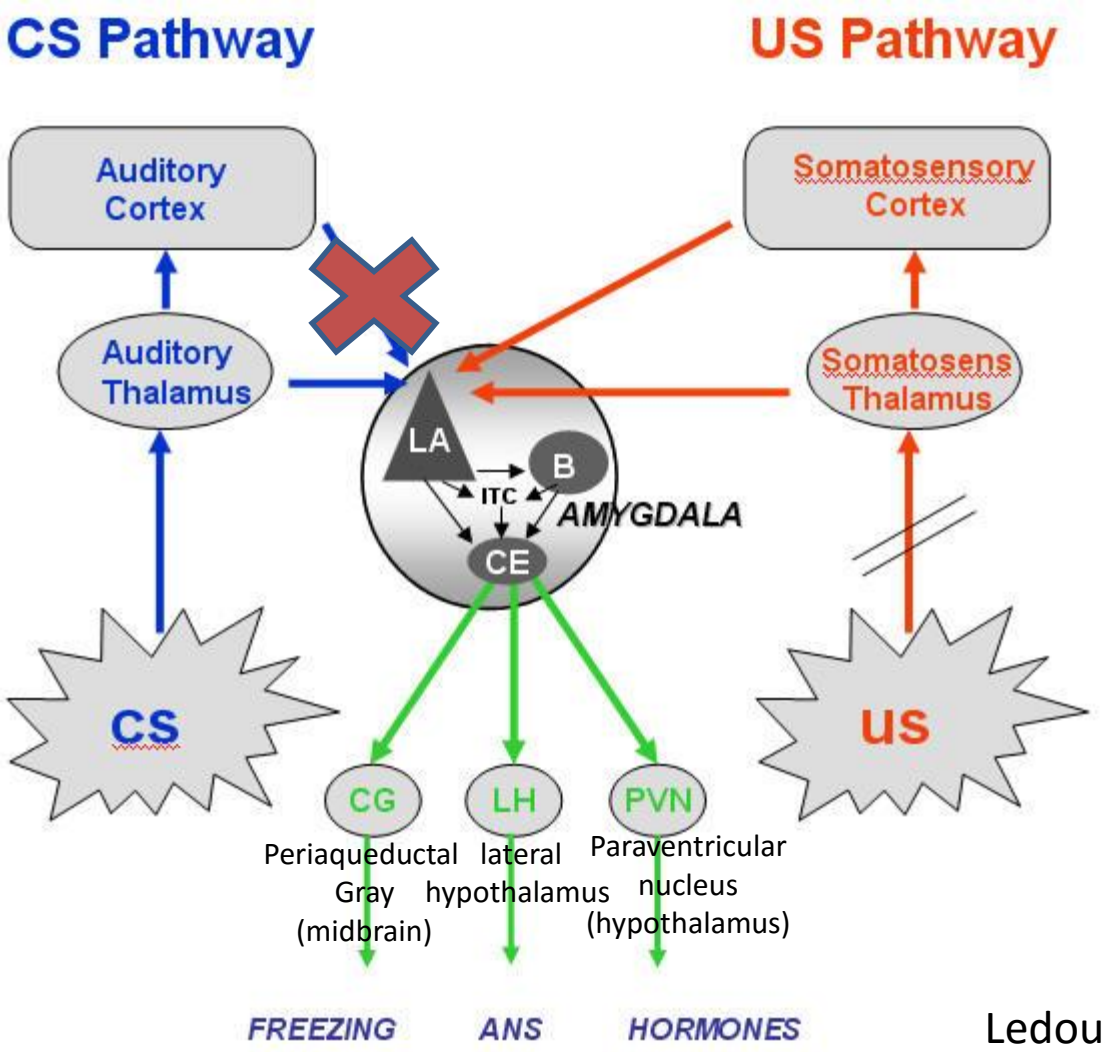
Amygdala and its basolateral complex (BLA)

- BLA evolution parallels that of the prefrontal cortex
- BLA cell types reminiscent of cortex
- Cortical projections are much more extensive in primates



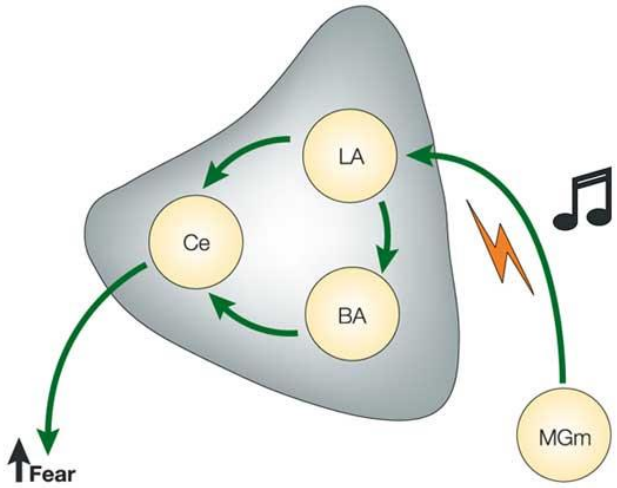


Fear circuit



Ledoux, Mcgaugh, Davis

Neurons acquire tone responses after conditioning



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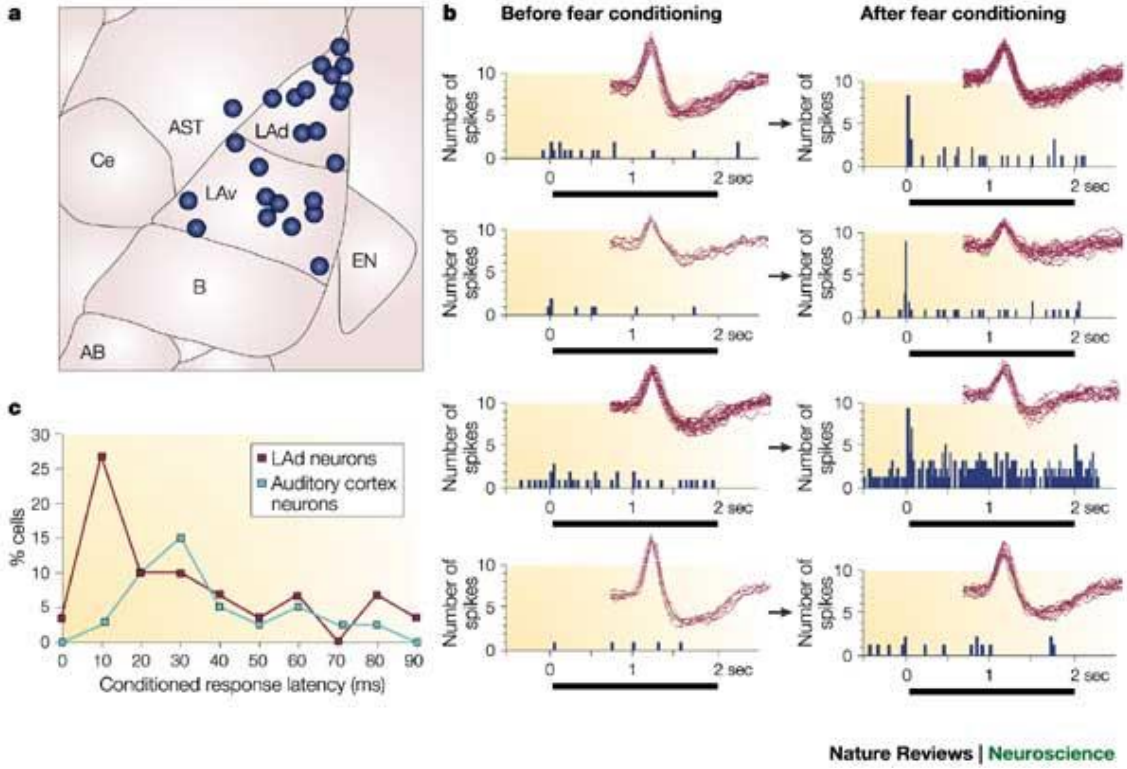

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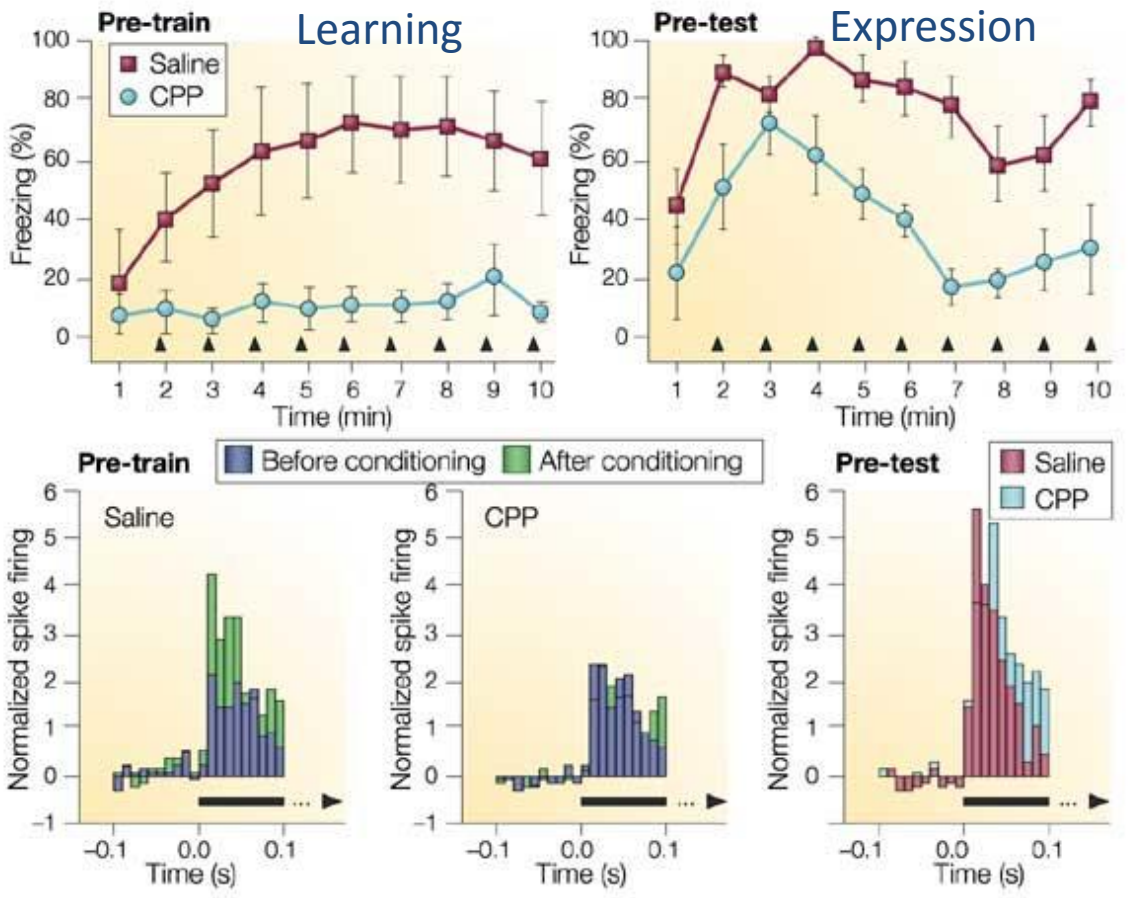
LTP in the LA is required

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.



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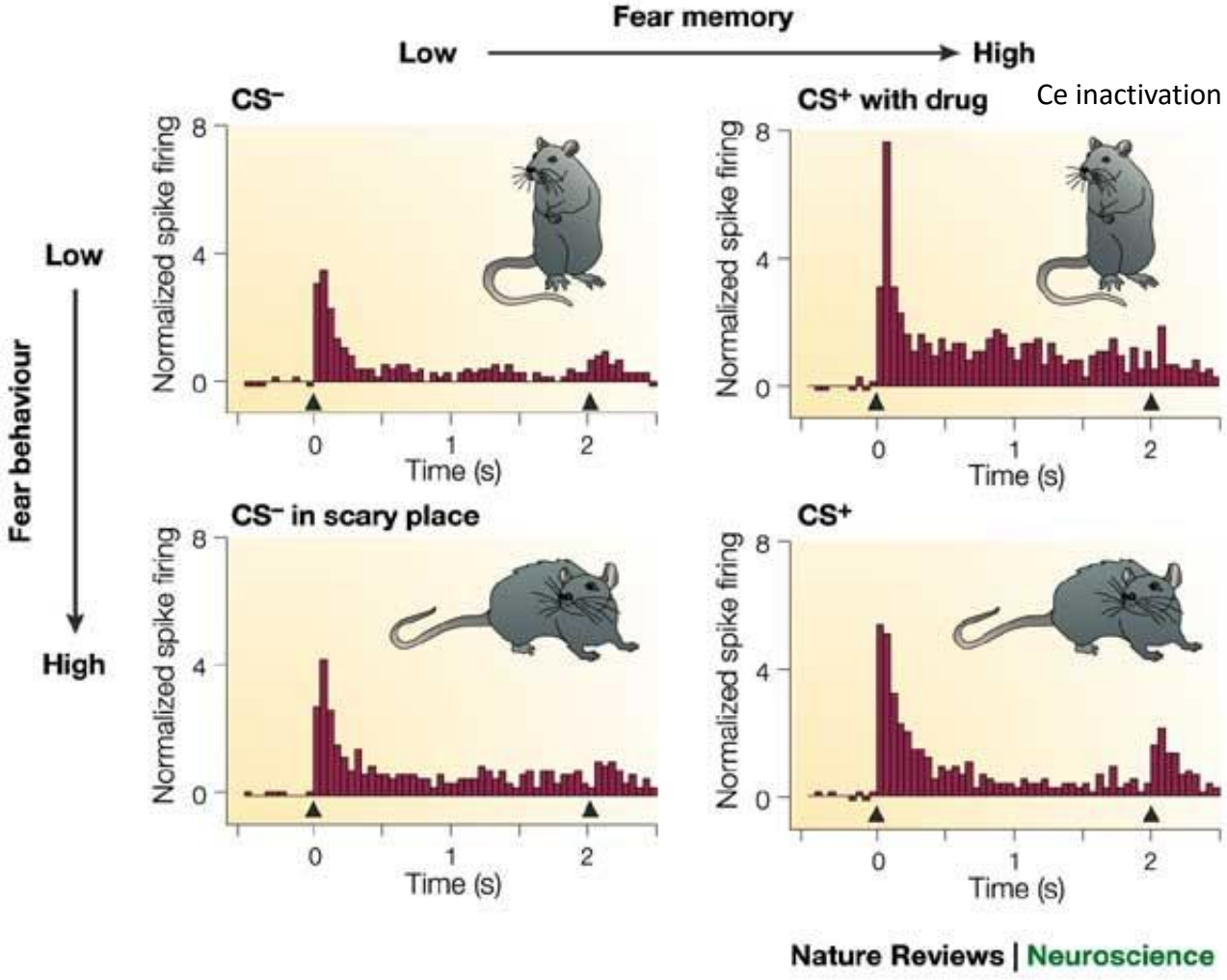
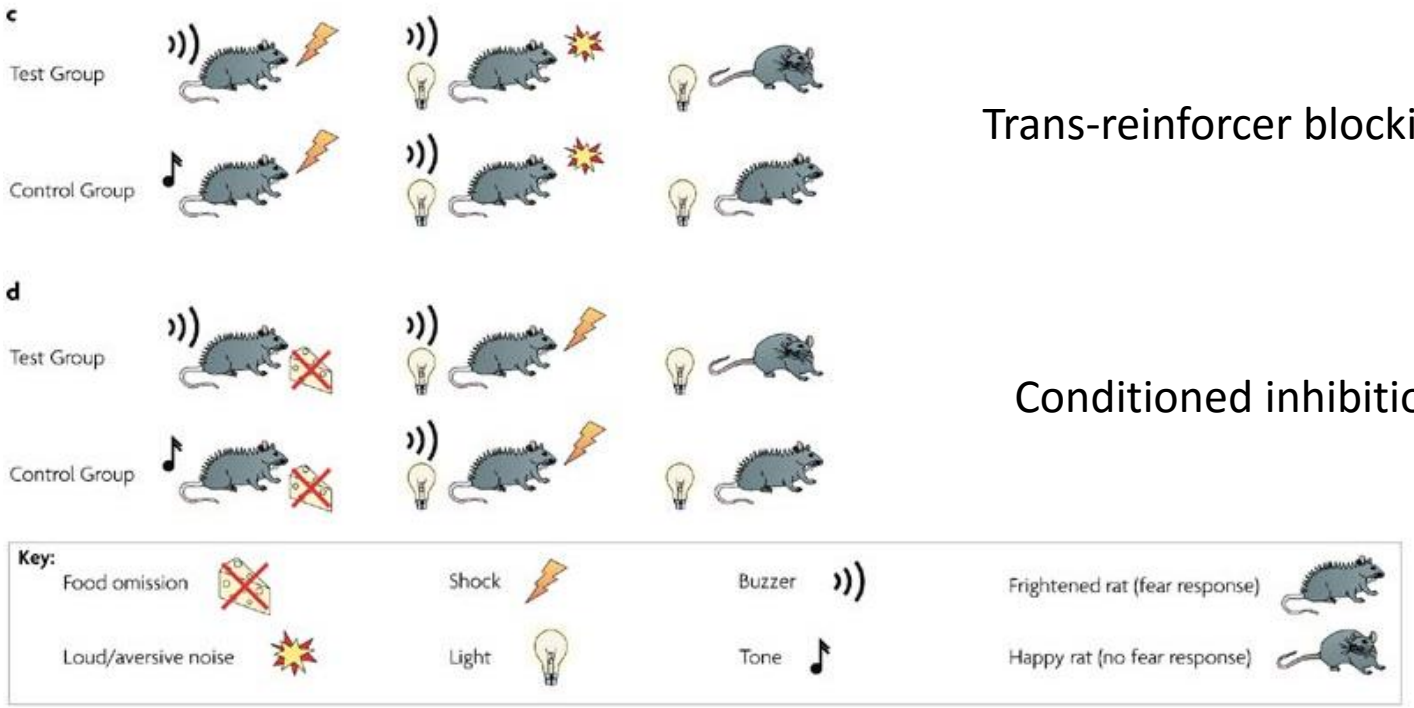
CPP (3-(2-carboxypiperazin-4-yl) propyl-1-phosphonic acid), a competitive NMDA-receptor antagonist

Is it fear memory or just fear behavior?

LA encodes memory independent of fear behavior



Ce inactivation = No Behavioral CR



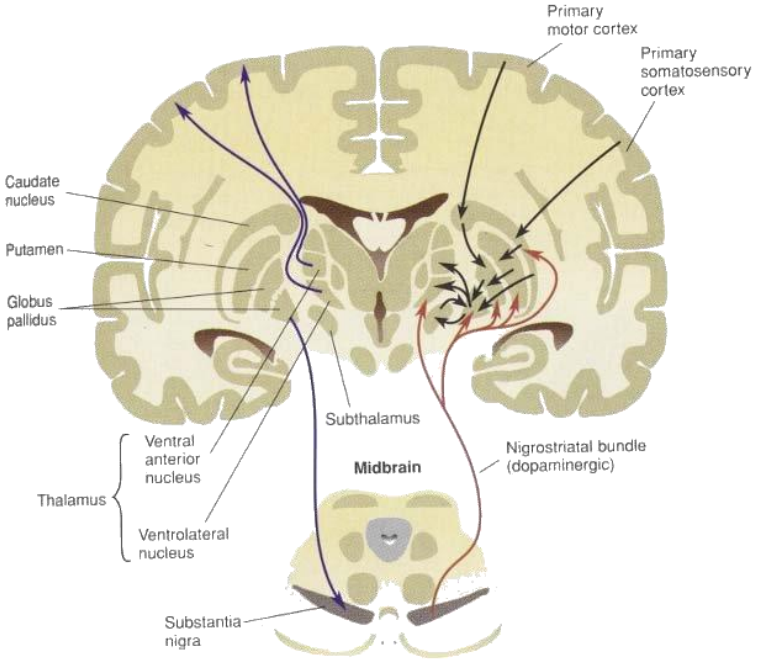
Trans-reinforcer blocking

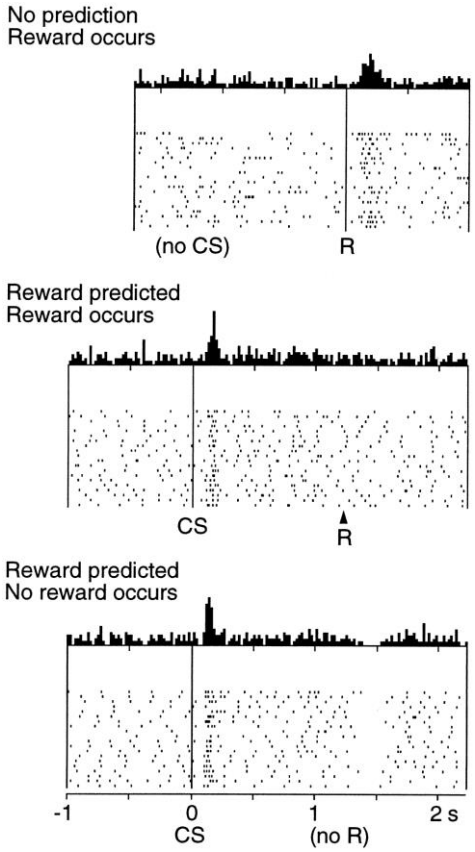
Conditioned inhibition

Suggests common brain mechanisms

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

Rescorla-Wagner and Pearce-Hall

the change (Δ) in the associative strength (symbolized V) of a CS

$$\Delta V = \alpha\,\beta(\lambda - \Sigma V)$$

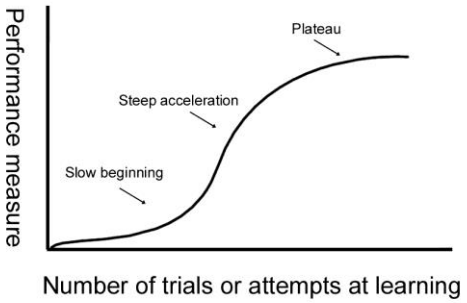
Learning rate

saliency of the CS

individual learning ability

US

Expectation



What does it take for a tone to become a CS?

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

S is intensity of the CS and λ of the US

α represents the associability of the CS (high for a novel CS)

The associability parameter is modified by experience:

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

Associability value on trial n

US

sum of the associative strengths of all stimuli present on trial n-1

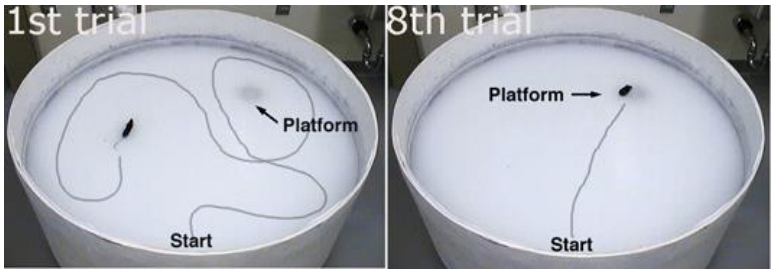
Blocking

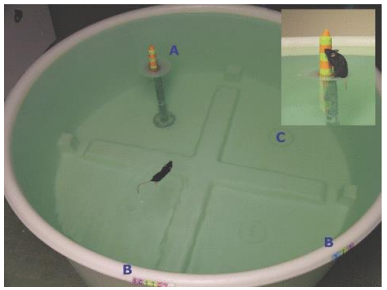
Phase 1: new CS → *α is high*

Phase 2: same CS → *α is low = no learning*

Amygdala modulation of memory

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





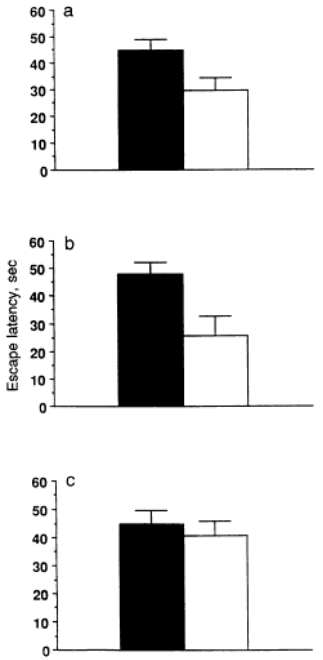


FIG. 1. Mean (±SE) escape latencies of *d*-amphetamine (10 μg) (□) and saline-treated (■) rats on the retention test trial in the spatial task. (*a*) Hippocampal injections. (*b*) Amygdala injections. (*c*) Caudate nucleus injections.

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

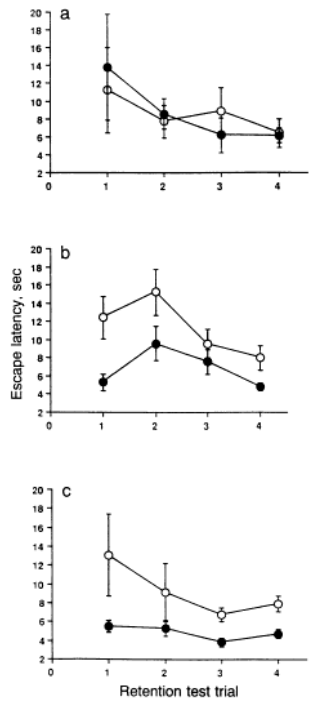


FIG. 2. Mean (±SE) escape latencies of *d*-amphetamine (10 μg) (●) and saline-treated (○) rats on the retention test trial in the cued task. (*a*) Hippocampal injections. (*b*) Amygdala injections. (*c*) Caudate nucleus injections.

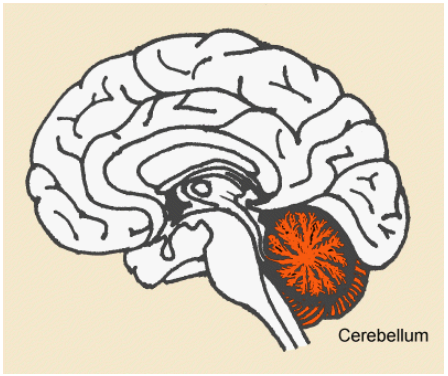
Injection of d-amphetamine into the Amygdala affects both if right after training, but not if pre-testing

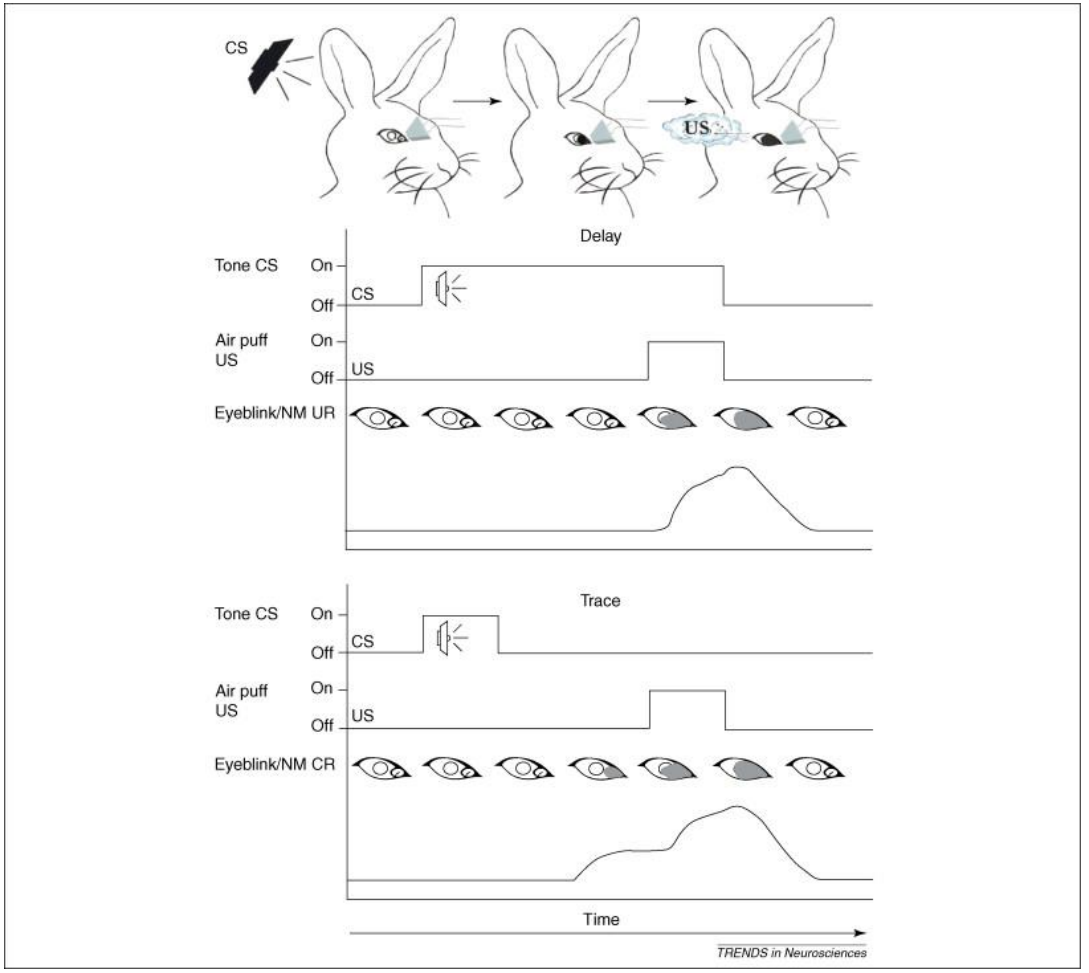
Packard, Mcgaugh

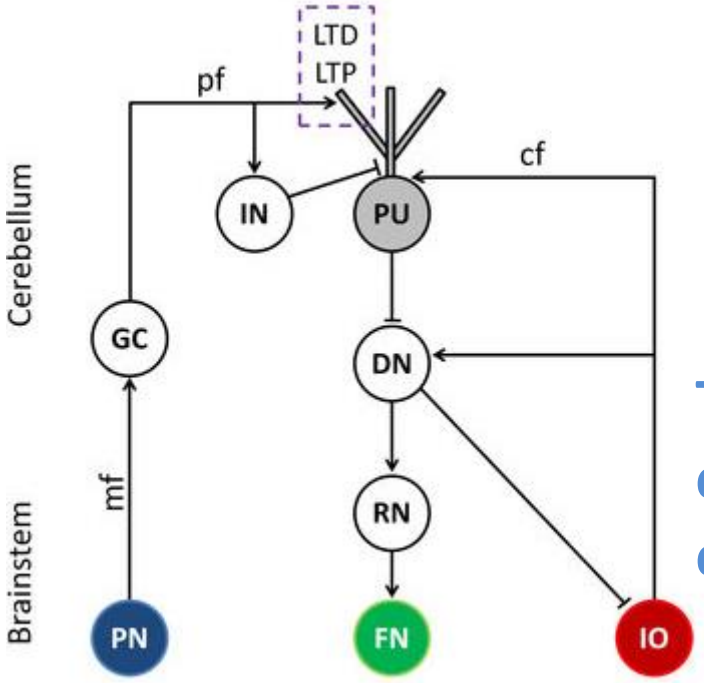
So, does it encode the memory or just modulates it?

It depends.

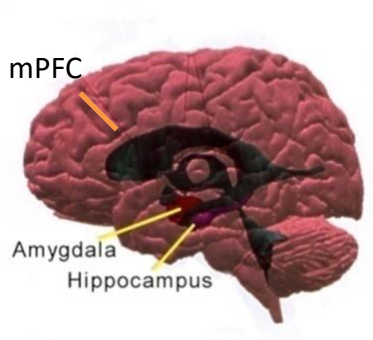
Eyelid (blink) reflex conditioning



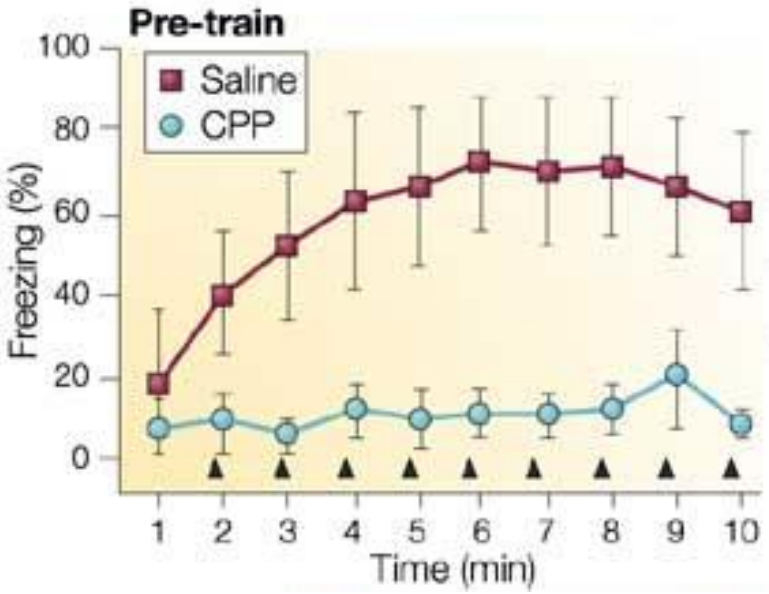




The cerebellum is essential and sufficient for eyeblink conditioning

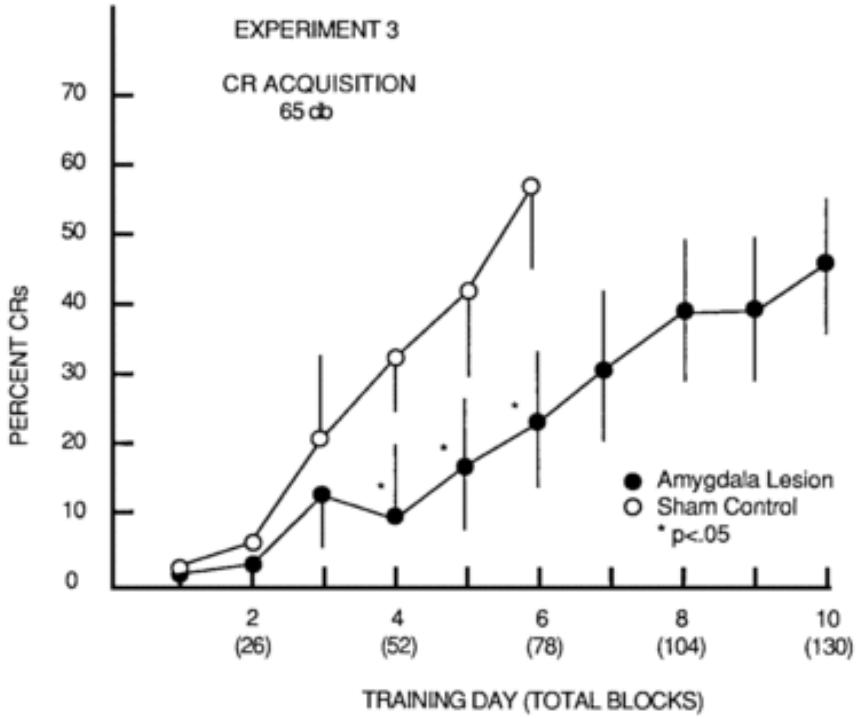


Effects of amygdala lesion on eyeblink conditioning



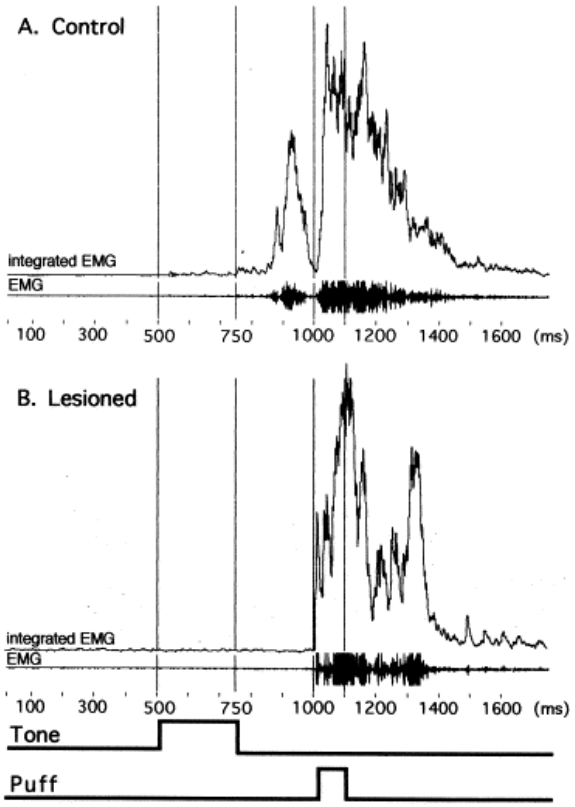
← Amygdala dependent

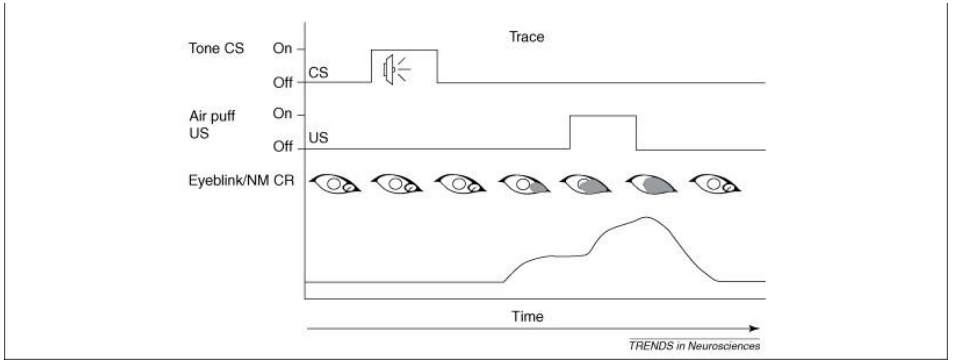
Cerebellum dependent →

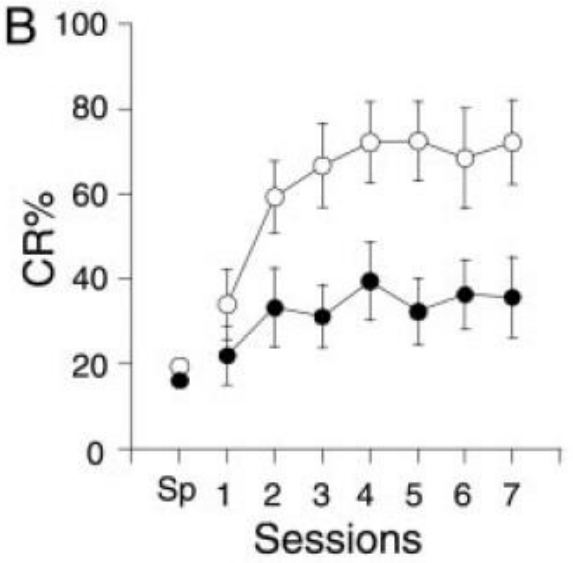


Weisz et al., 1994

Eyelid (blink) reflex conditioning – the role of the hippocampus

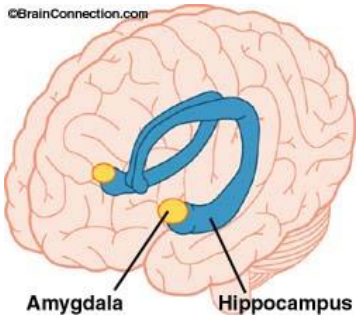


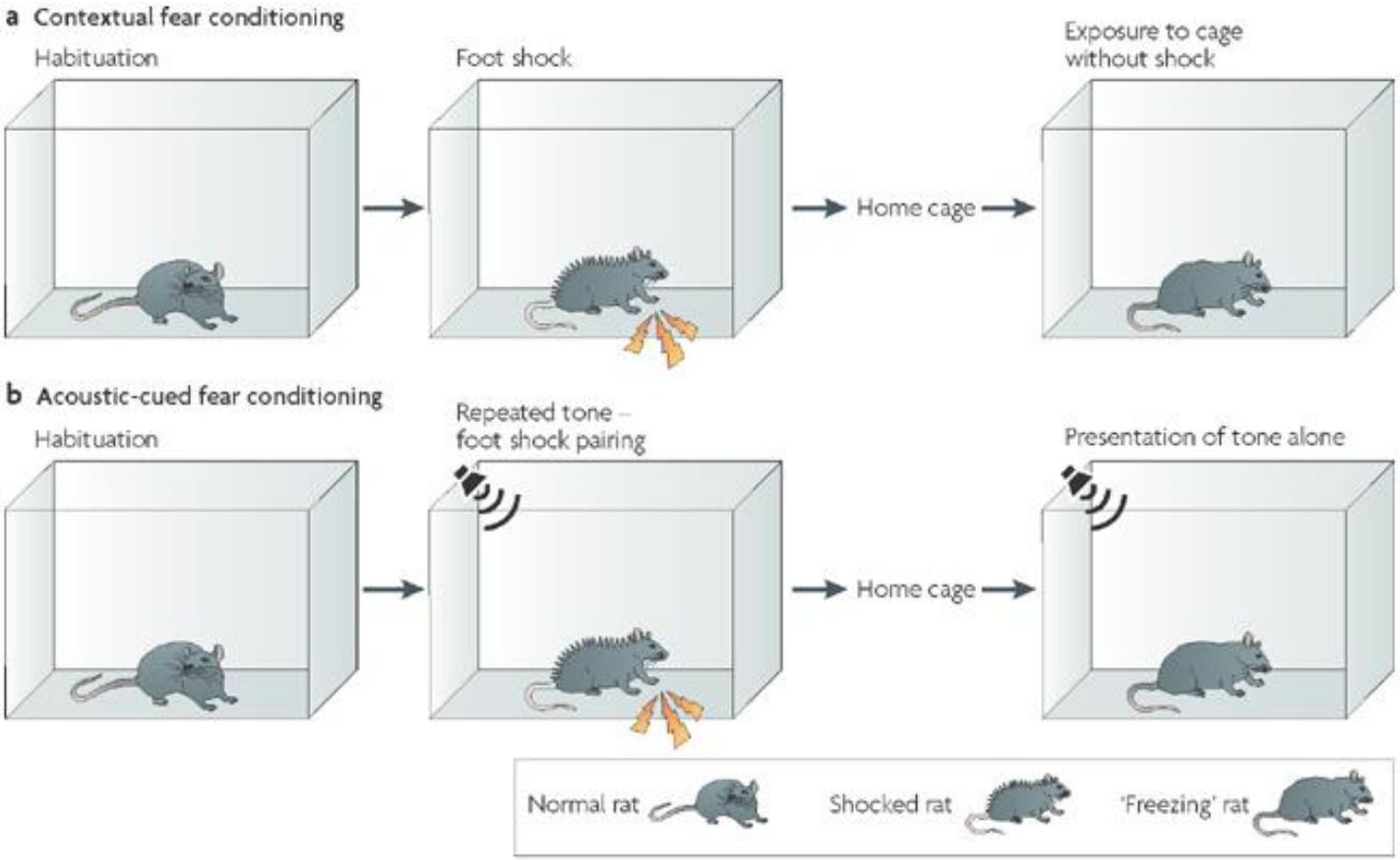




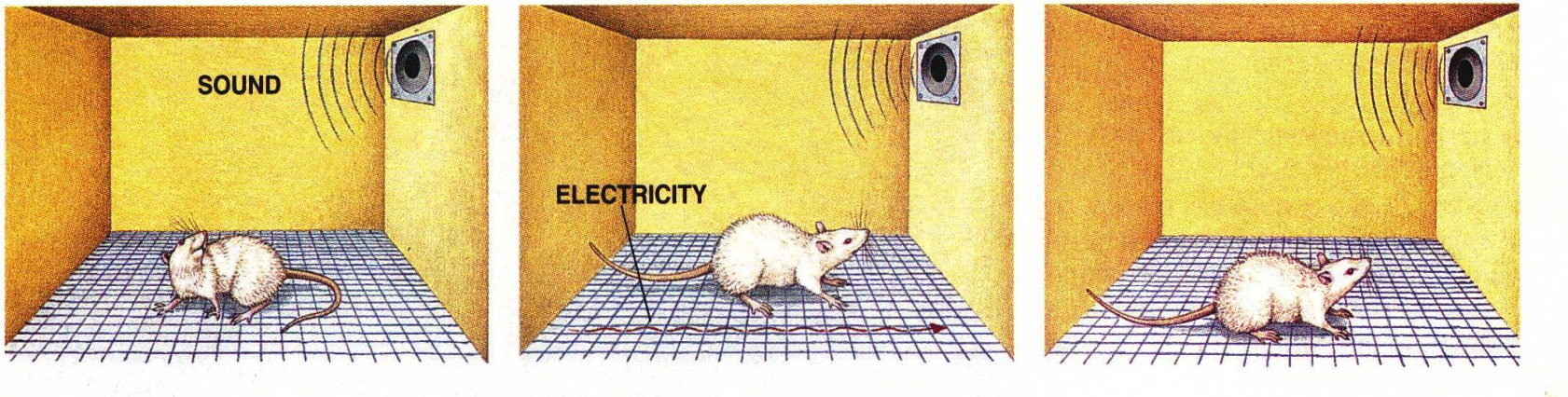
- Why is trace hippocampal-dependent?
- Maintaining the CS? Timing the trace? Harder?
- Eyelid requires ~0.2sec, and hippocampus is required when 0.4-1sec.
- In tone-shock, trace can be 3sec, and hippocampus is required for ~20sec
- This suggest context-conditioning

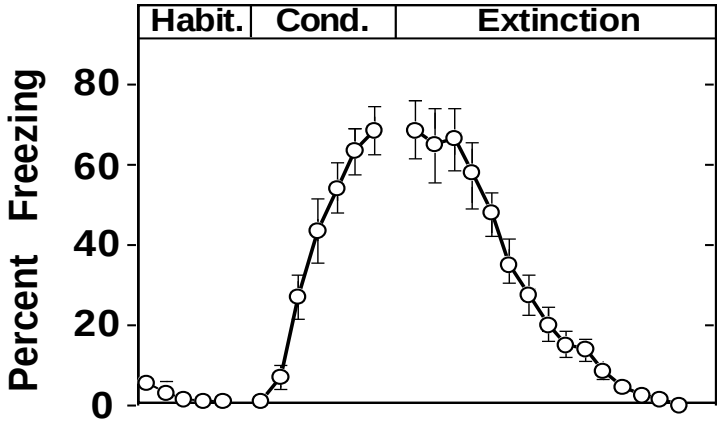
Contextual fear



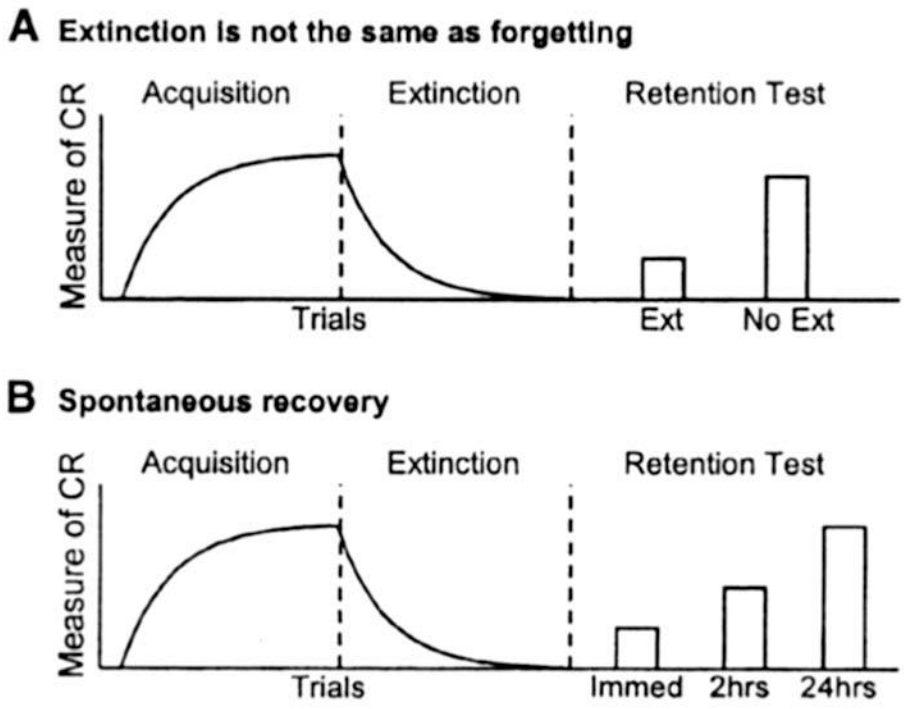


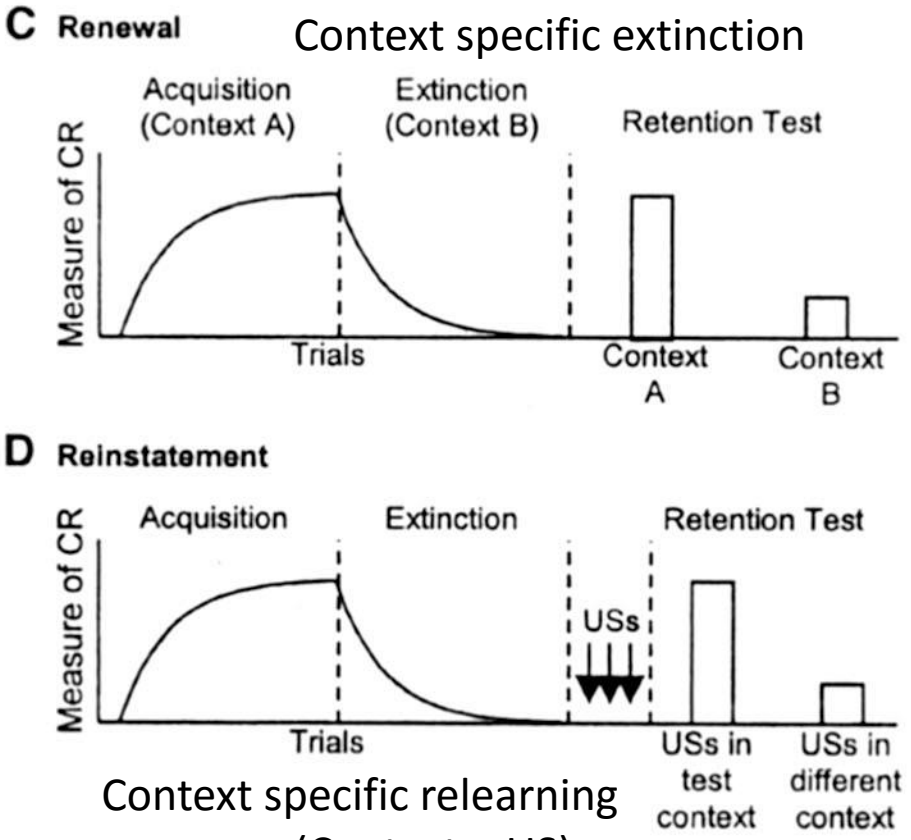
Extinction of fear-conditioning





Extinction: a new learning

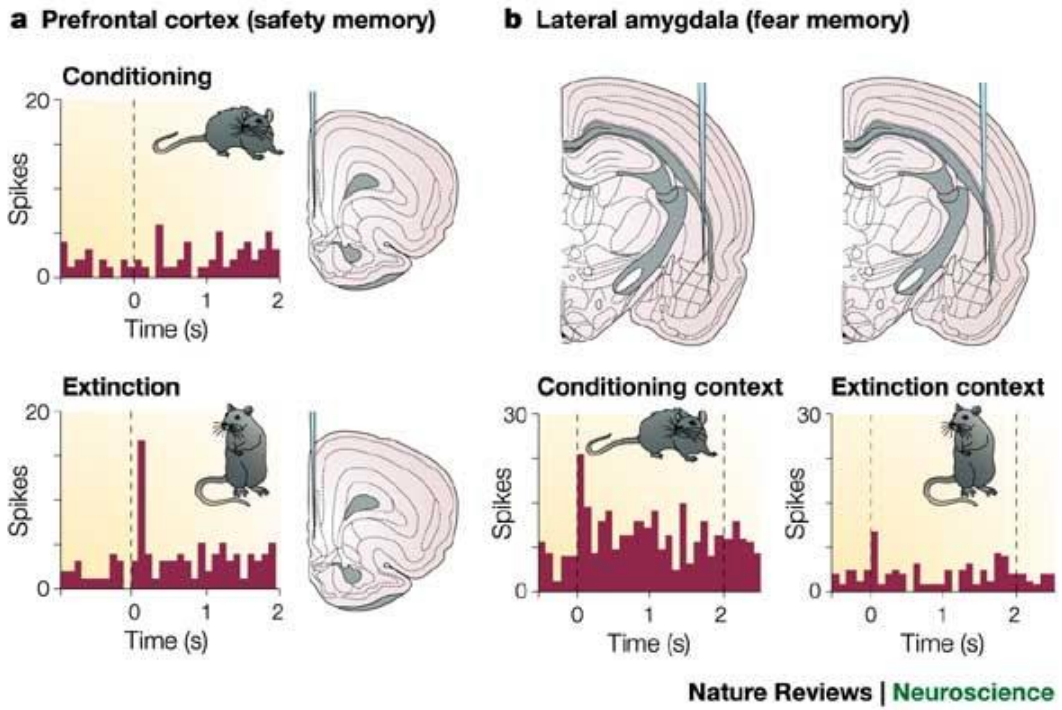


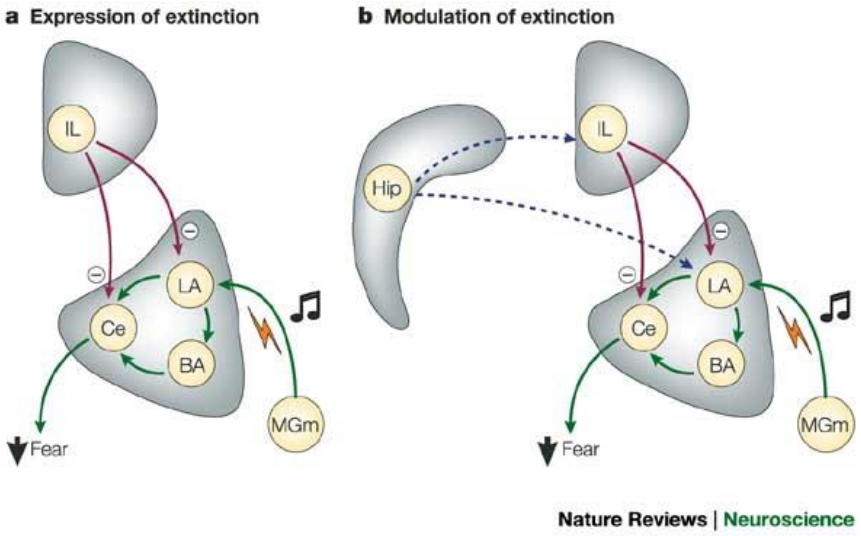


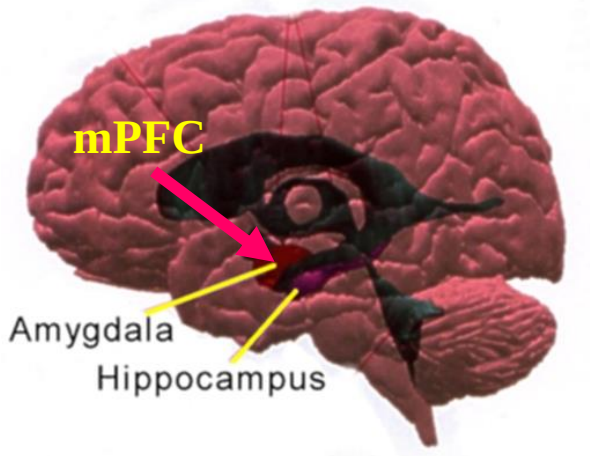
Context specific relearning
(Context + US)

Faster re-learning

Extinction: brain mechanisms

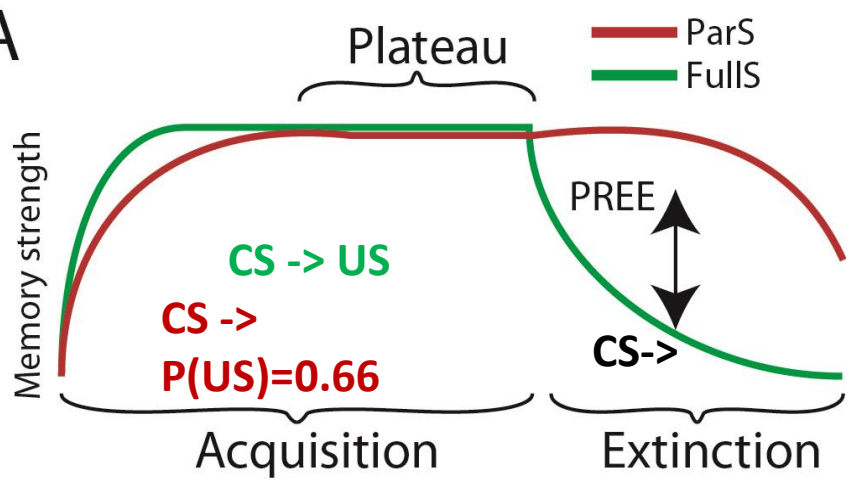






Partial reinforcement extinction effect

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



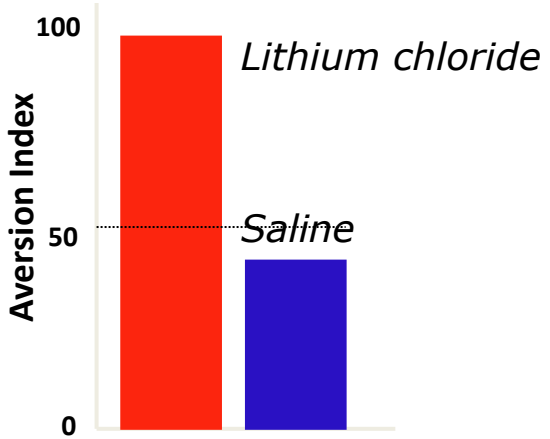
- Results in longer extinction learning

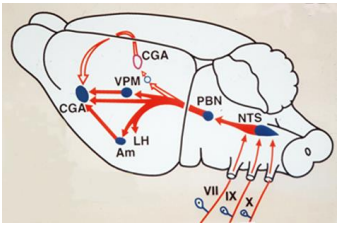
  - **Frustration theory (Amsel)**: The omission of the US induces frustration. Therefore, during extinction, the frustration predicts the US.
  - **Sequential theory (Capaldi):** conditioning to strings of NNNRNNNR

Garcia J

Conditioned Taste Aversion

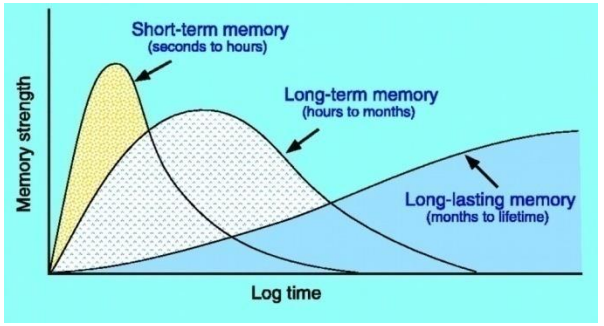
- One-trial learning
- Long-delay learning (few hours)
  - A [lack of] interference effect?
  - Still a problem for neuroscientists

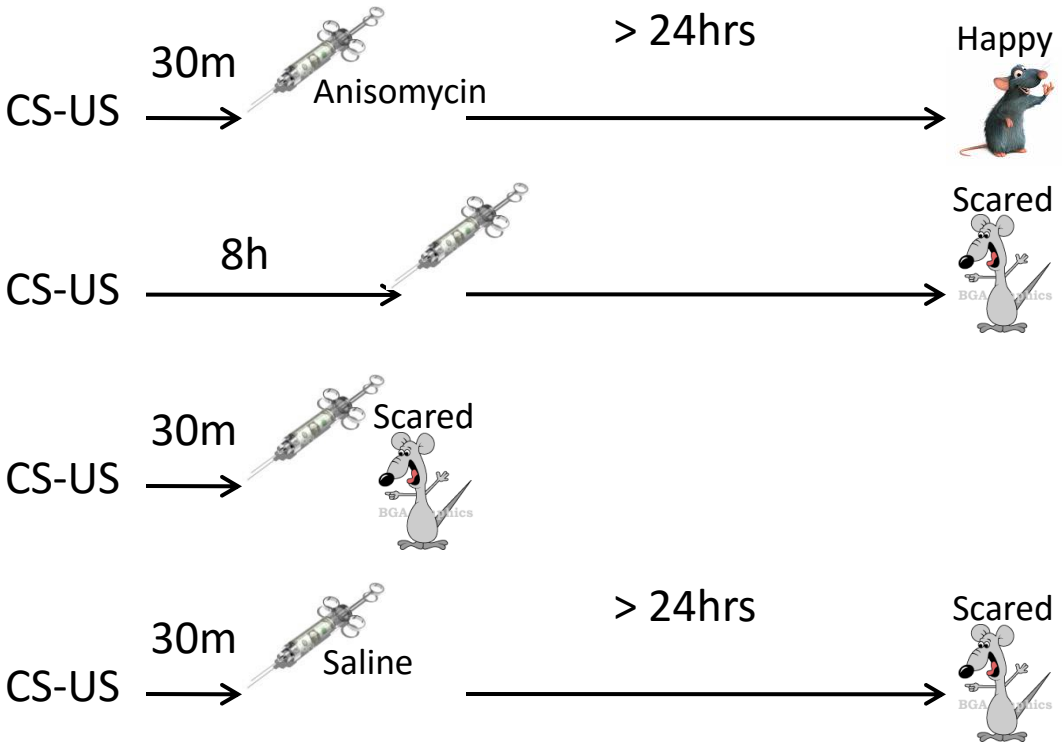


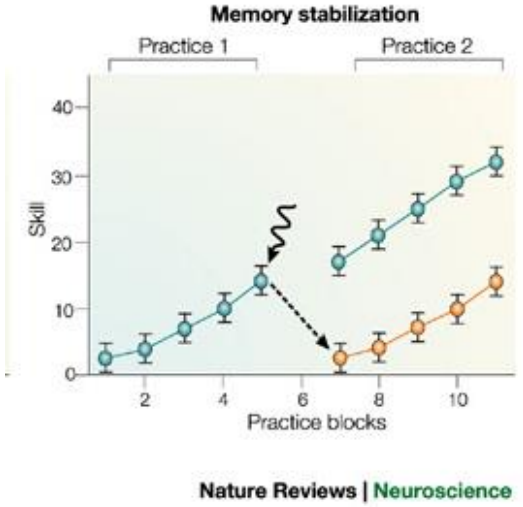


Consolidation

- 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.

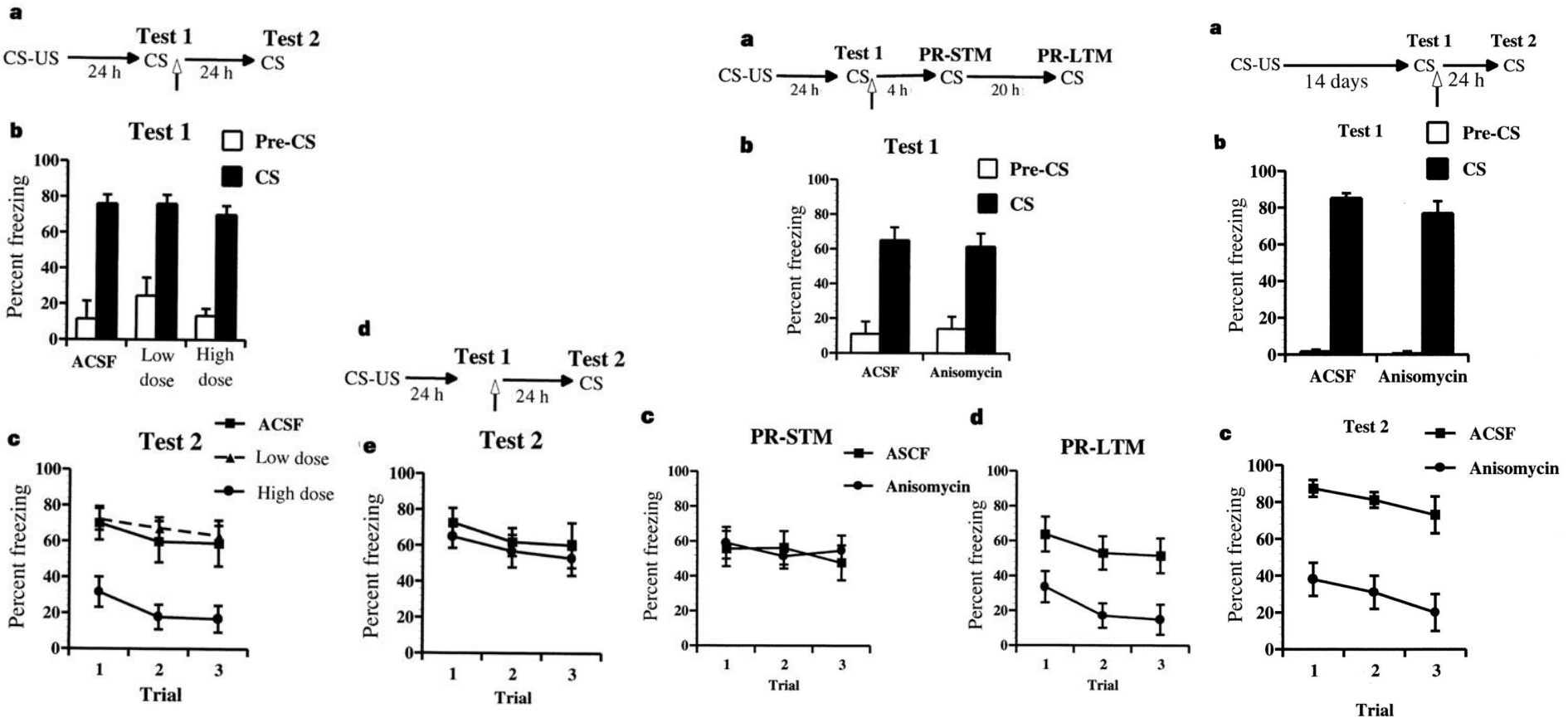






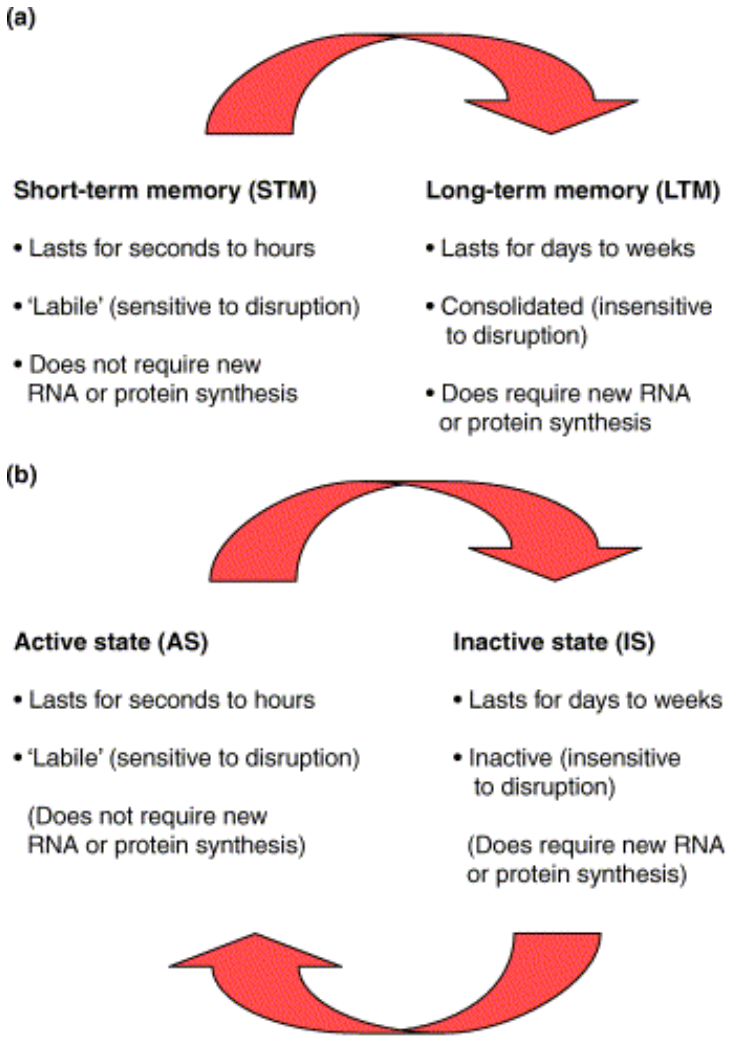
Reconsolidation

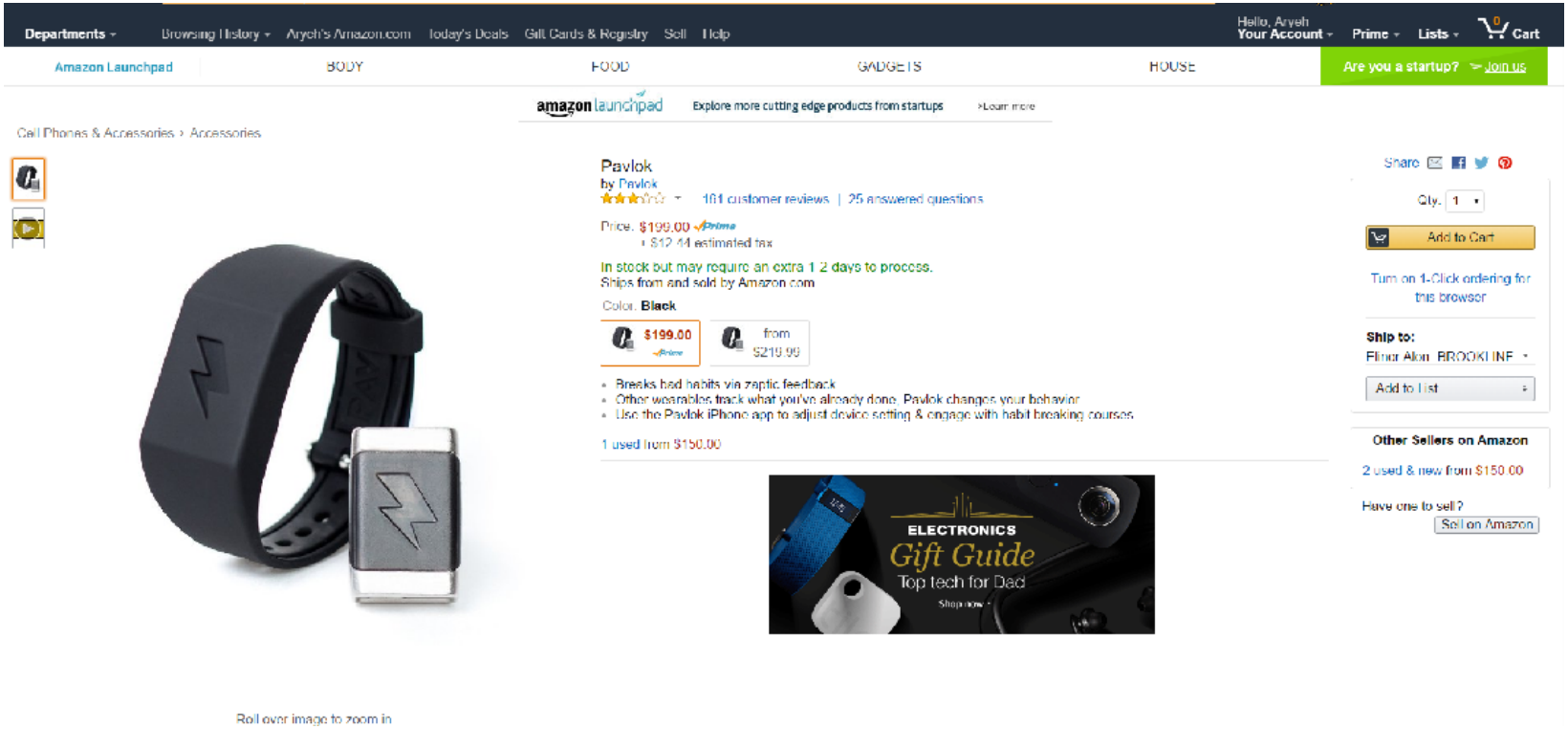
No effect on STM



Nader et al., Nature 2000

An updated view of memories





Stay safe, be fearless