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Pavlovian learning: physiological and neural mechanisms

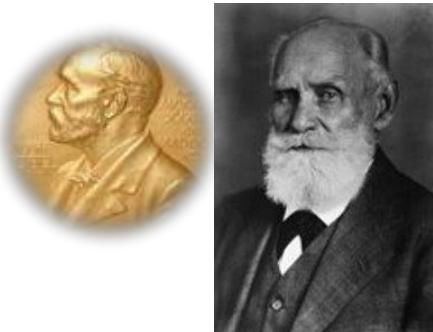
Cognition and Neuroscience
Academic year 2023/2024

Francesca Starita

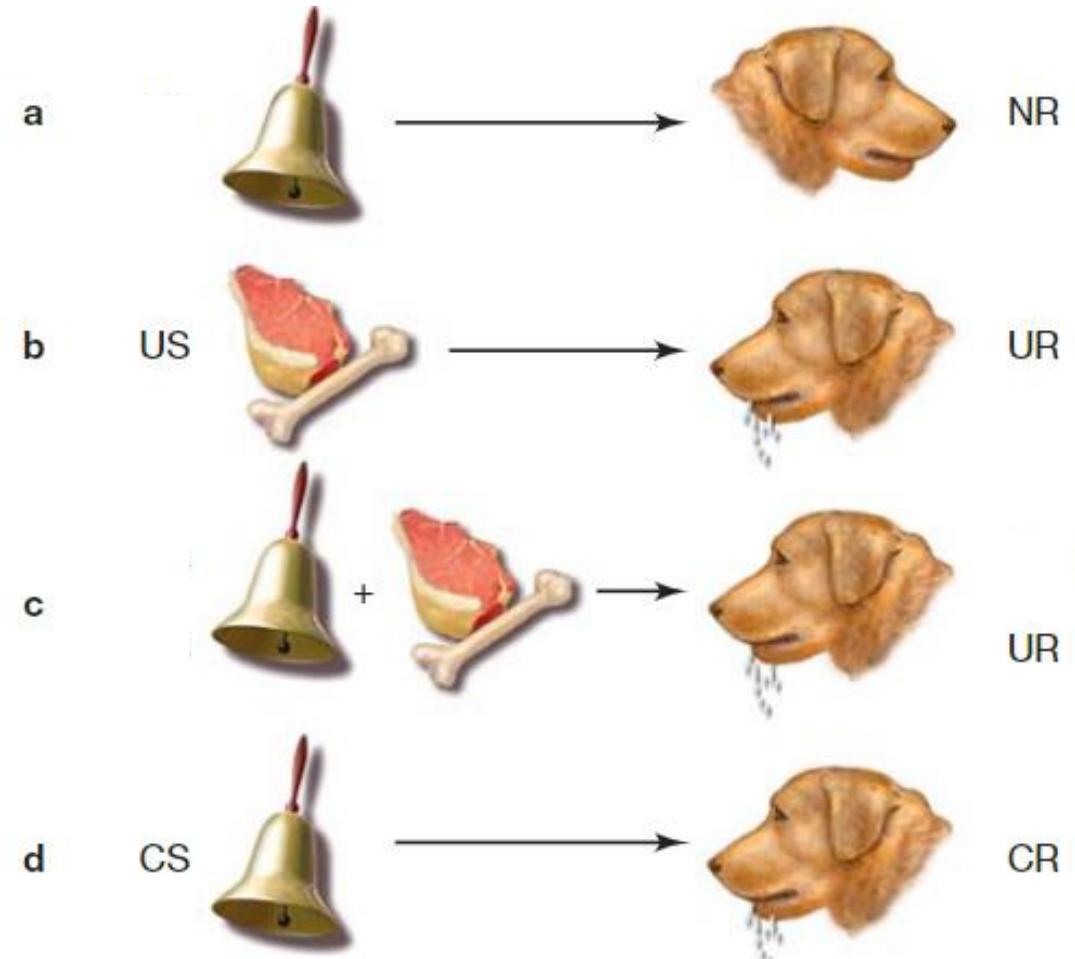
francesca.starita2@unibo.it

Pavlovian learning involves associating a stimulus with an outcome

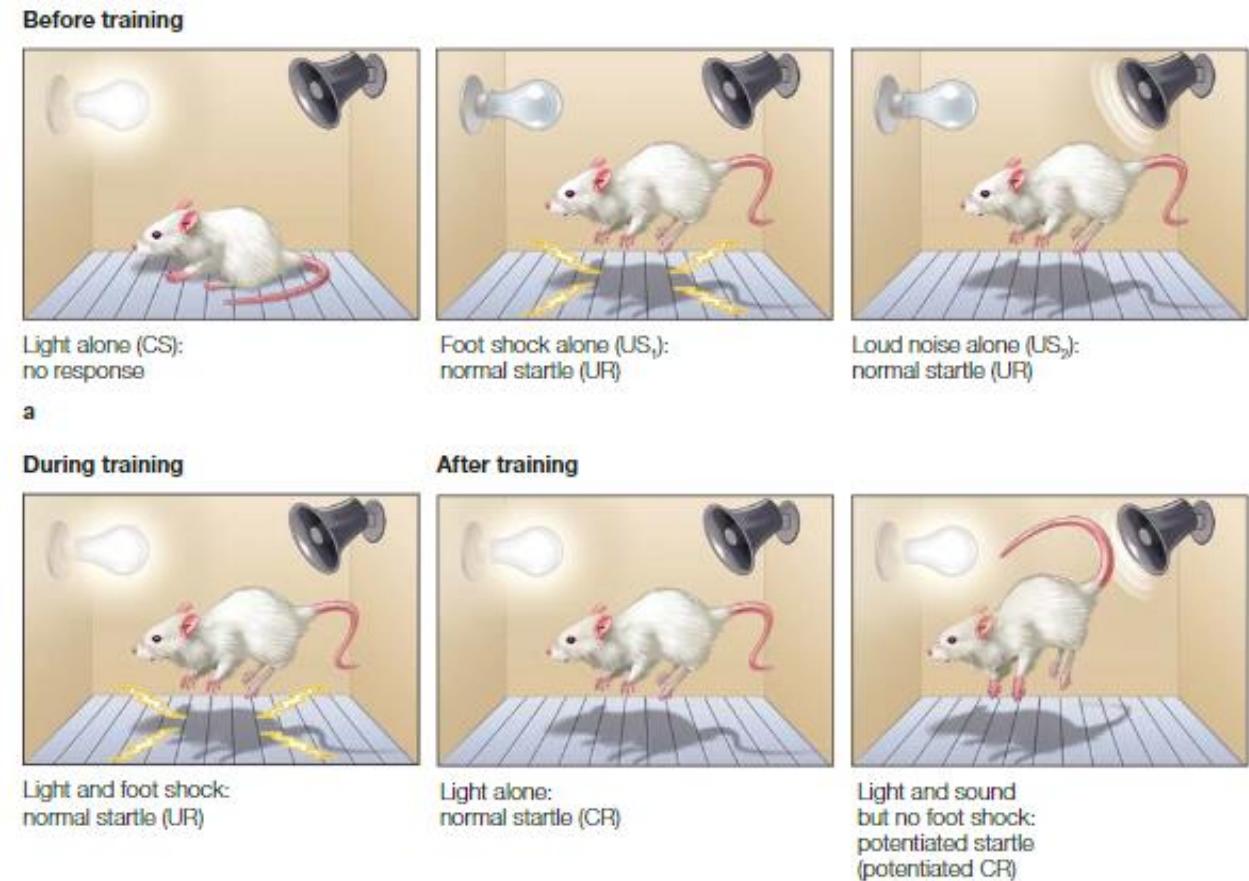
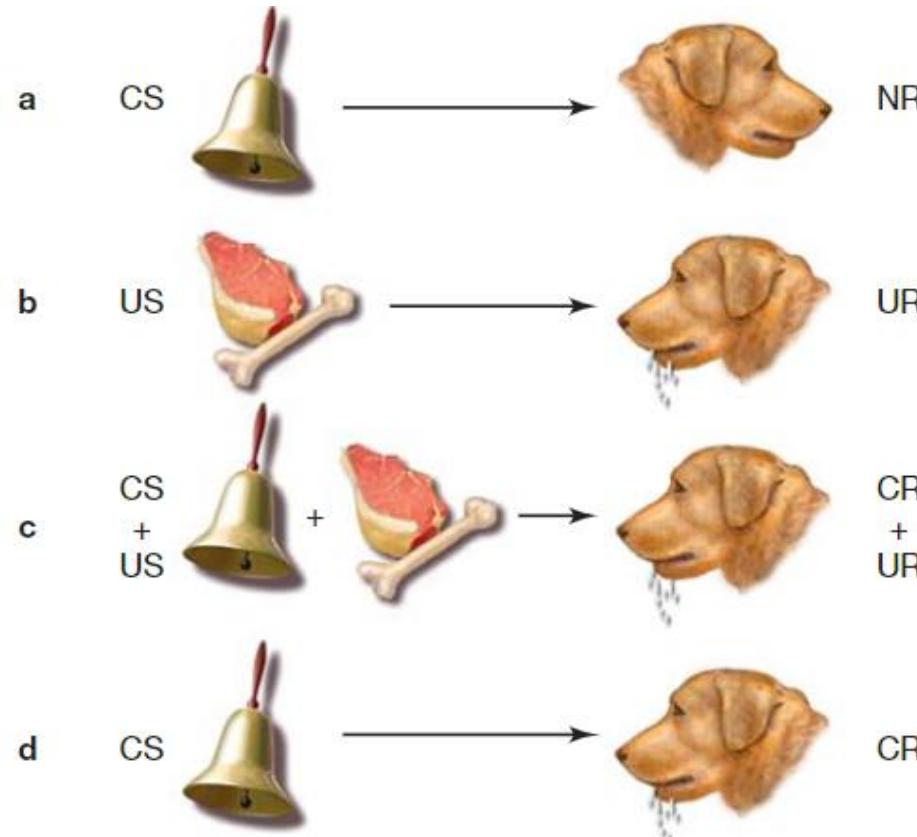
- a) A stimulus is presented that has no meaning to an animal, such as the sound of a bell, there is no response (NR)
- b) Presentation of a reinforcer like food (i.e. unconditioned stimulus, US) generates an unconditioned response (UR)
- c) When the sound is paired with the food, the animal learns the association
- d) the newly conditioned stimulus (CS) alone can elicit the response, which is now called a conditioned response (CR)



Ivan Pavlov (1849–1936) received a Nobel Prize after first demonstrating this type of learning with his dogs



Outcomes can be appetitive or aversive, triggering different responses



Different types of conditioned responses

The CR must be learned, while the UR takes place with no learning.

CR are **anticipatory responses**

Response can be

- Physiological
- Behavioral
- Change in subjective experience

Unconditioned Stimulus (US)



Unconditioned response (UR)

Conditioned Stimulus (CS)



Conditioned response (CR)



Different types of conditioned responses

Response can be

- **Behavioral**
- Physiological
- Change in subjective experience

Unconditioned Stimulus (US)



Unconditioned response (UR)

CR are **anticipatory, predictive responses**

Conditioned Stimulus (CS)



Conditioned response (CR)

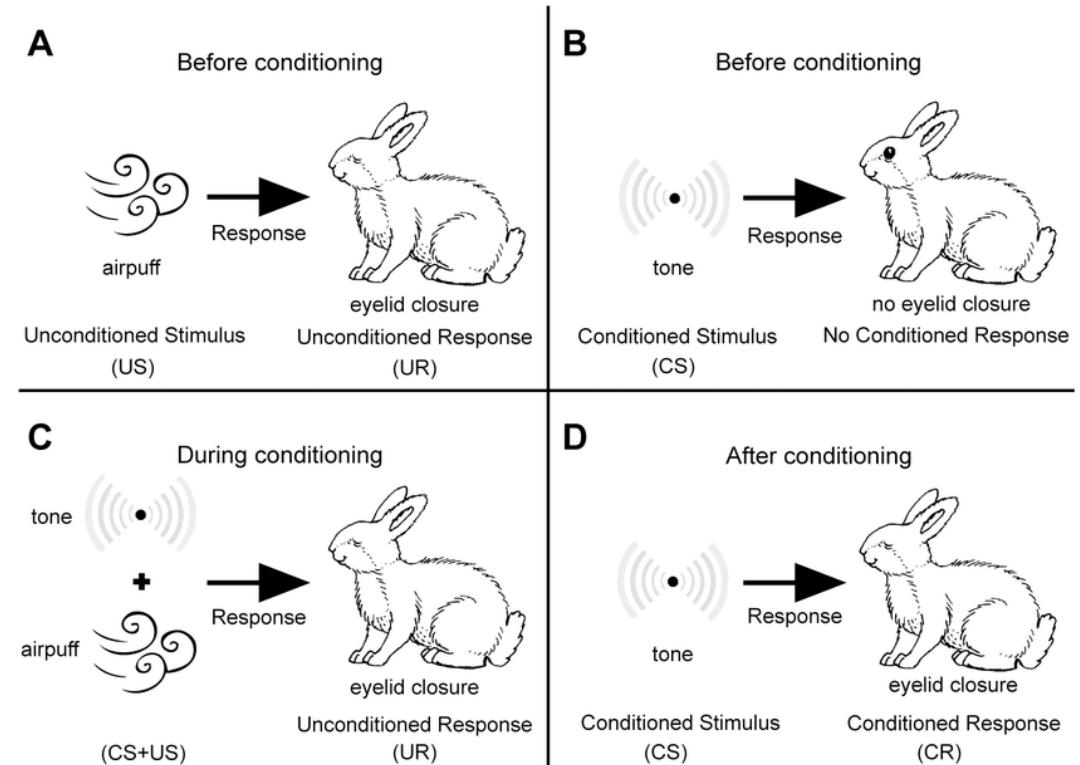


Different types of conditioned responses

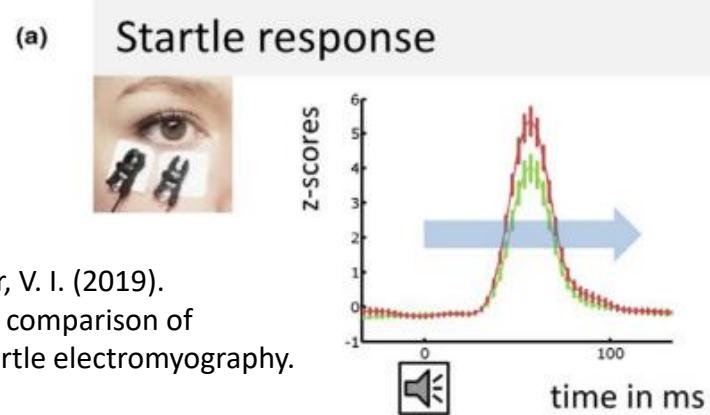
Response can be

- **Behavioral**
- Physiological
- Change in subjective experience

CR are **anticipatory, predictive responses**



— CS+
— CS-



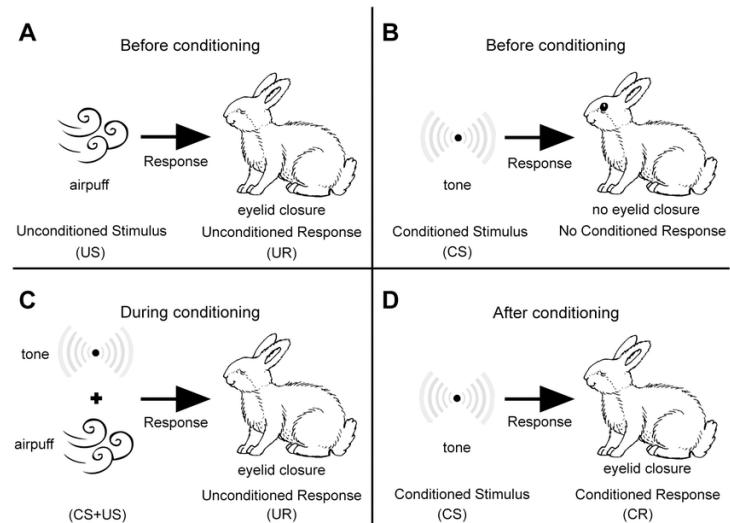
Leuchs, L., Schneider, M., & Spoormaker, V. I. (2019). Measuring the conditioned response: A comparison of pupillometry, skin conductance, and startle electromyography. *Psychophysiology*, 56(1), e13283. <https://doi.org/10.1111/psyp.13283>



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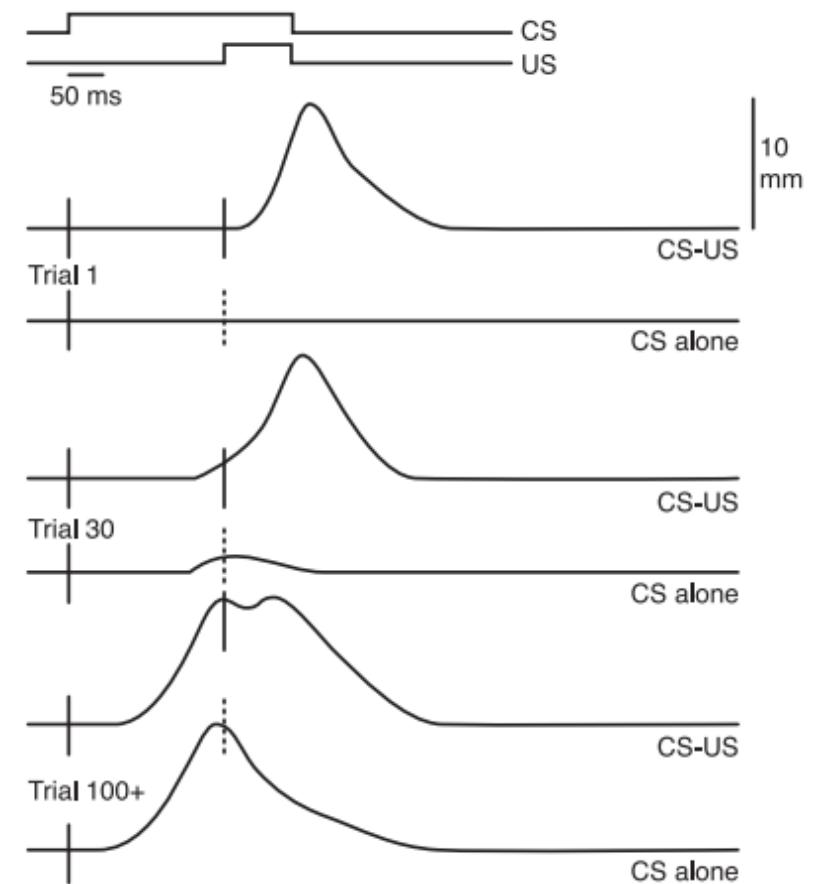
Adaptive nature of CR: predictive response

The animal respond to the CS with a CR that prepares the animal for, or protects it from, the predicted US



The tone comes to trigger a CR consisting of the nictitating membrane closure that begins before the air puff and eventually **becomes timed** so that peak closure occurs just when the air puff is likely to occur. This CR, being **initiated in anticipation of** the air puff and appropriately timed, offers better protection than simply initiating closure as a reaction to the irritating US.

development of the conditioned eyelid response



Sutton, R. S., & Barto, A. G. (2018). Reinforcement learning: An introduction. MIT press.



Different types of conditioned responses

Response can be

- Behavioral
- **Physiological**
- Change in subjective experience

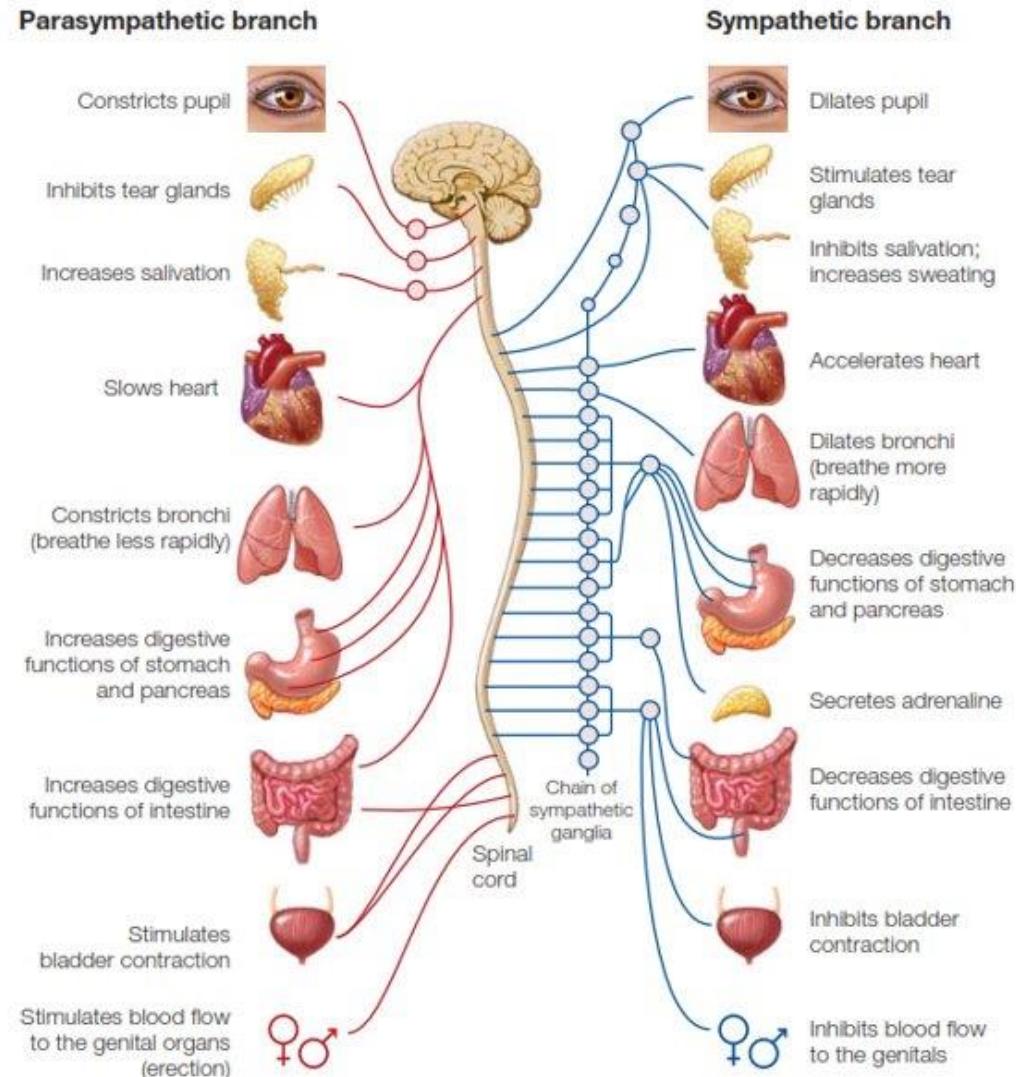
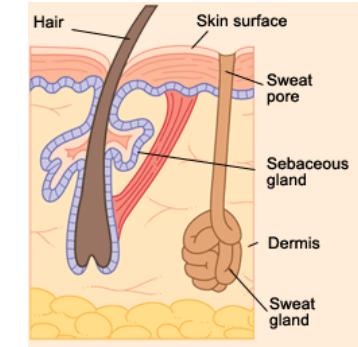


FIGURE 2.17 Organization of the autonomic nervous system, showing sympathetic and parasympathetic branches.



Different types of conditioned responses

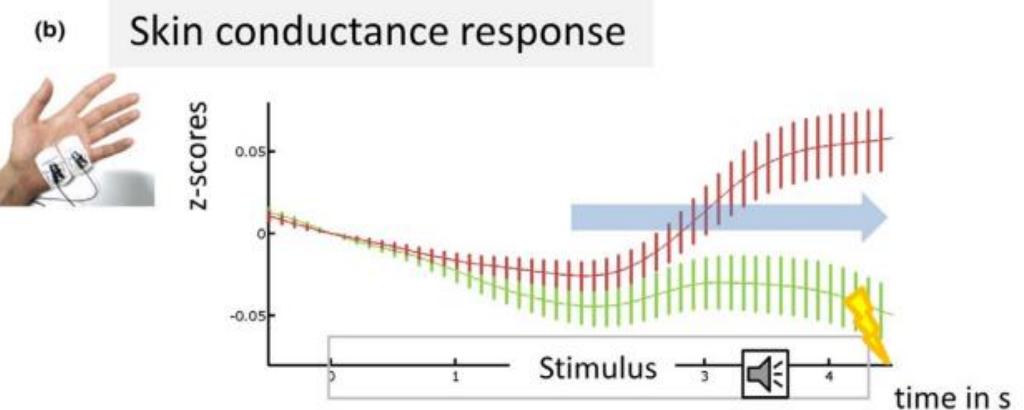
Response can be

- Behavioral
- **Physiological**
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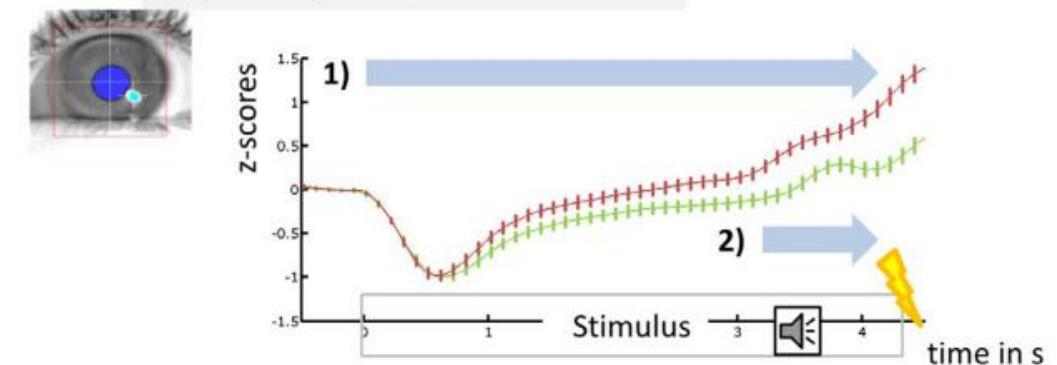
CR are **anticipatory, predictive responses**

— CS+
— CS-

(a)



(c) Pupil response



Leuchs, L., Schneider, M., & Spoormaker, V. I. (2019). Measuring the conditioned response: A comparison of pupillometry, skin conductance, and startle electromyography. *Psychophysiology*, 56(1), e13283. <https://doi.org/10.1111/psyp.13283>

Pavlovian learning is a flexible process

FORGET
IT

IT'S IMPORTANT TO BE ABLE TO EXTINCTION A LEARNING AS QUICK AS WE ACQUISITE IT. FOR EXAMPLE IF WE LEARNED IT IN A SHORT TIME IN WHICH IT WAS VALUABLE WHILE NOW IT ISN'T ANYMORE.

Acquisition

- The probability of occurrence of a conditioned response increases if the CS is repeatedly presented with the US.
- Adaptive because...

Extinction

- The probability of occurrence of a conditioned response decreases if the CS is repeatedly presented without the US.
- Adaptive because...

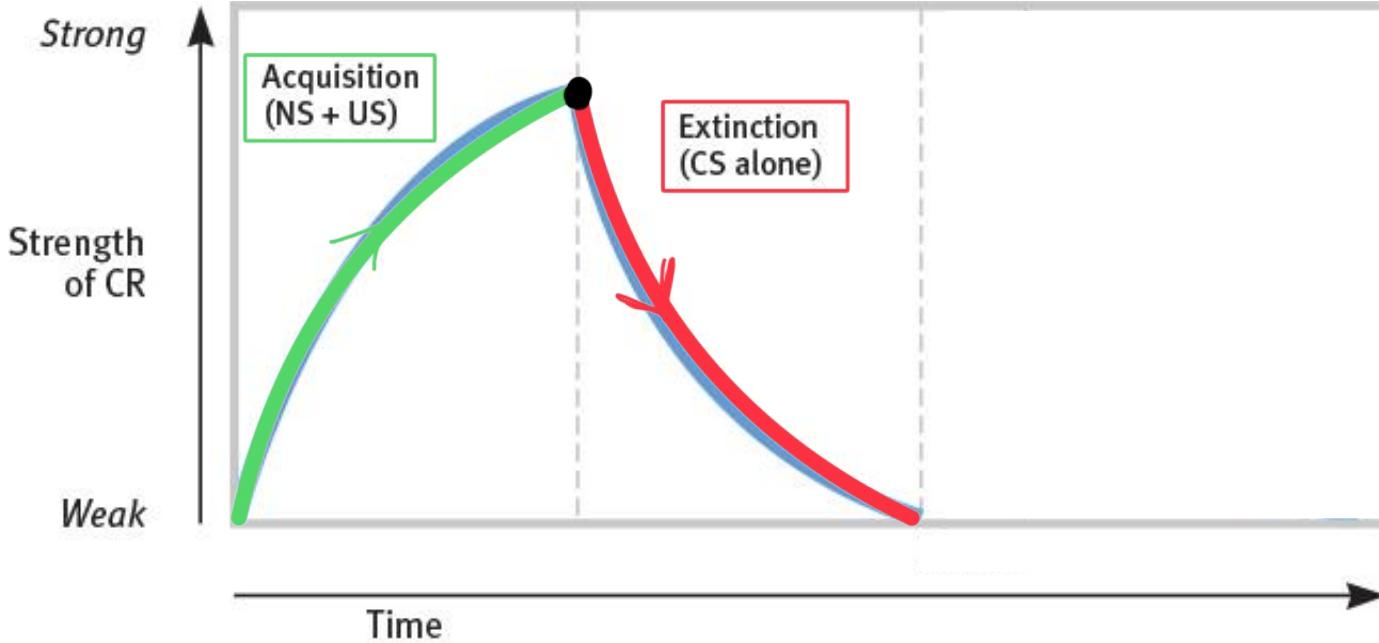


Figure 6.5

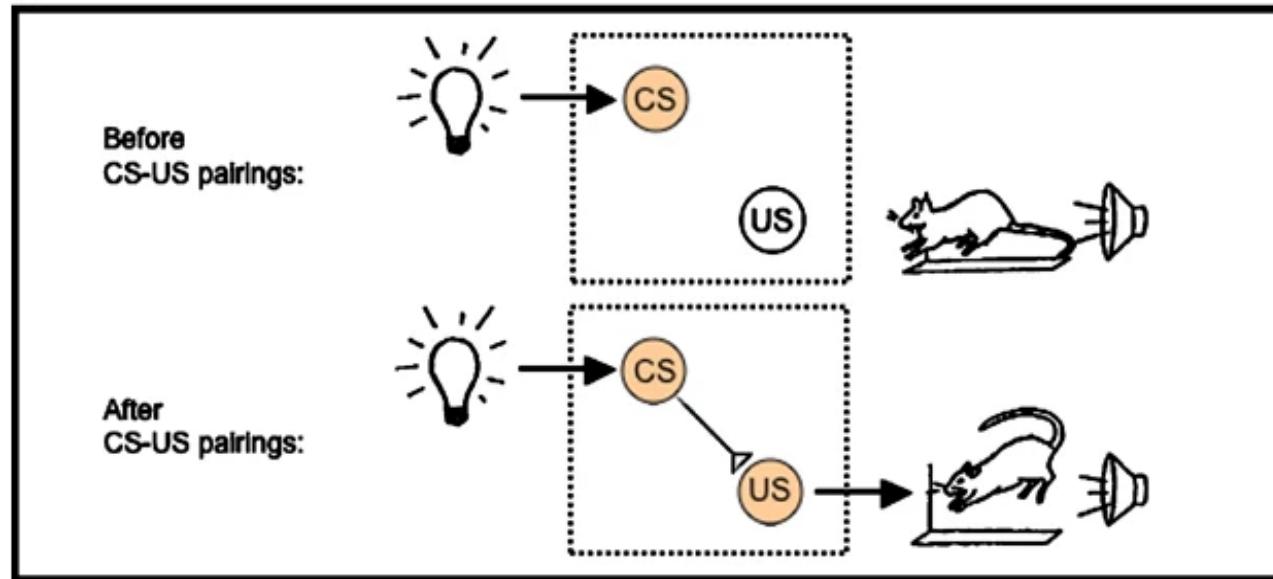
Myers/DeWall, *Psychology in Everyday Life*, 4e, © 2017 Worth Publishers



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Pavlovian learning is a flexible process

a

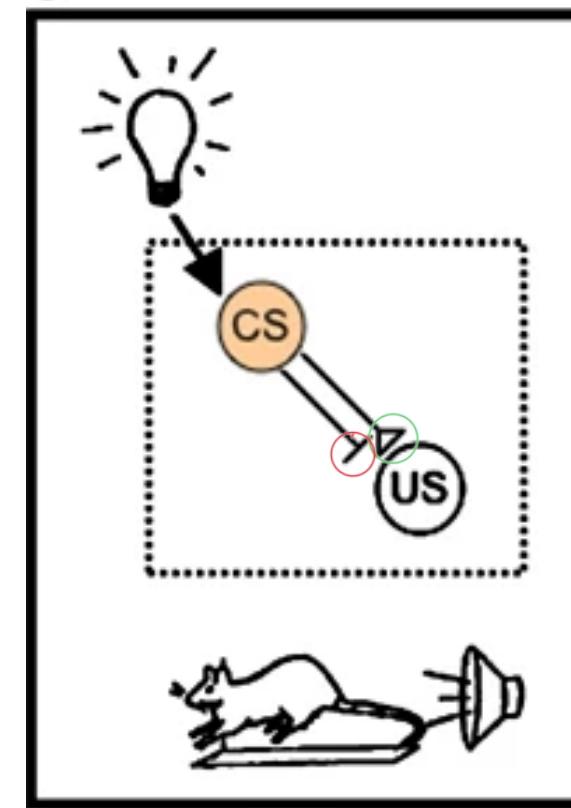


Conditioned fear is acquired as the animal forms representations of the cues involved (conditioned stimulus, CS; unconditioned stimulus, US) and develops an excitatory association (line terminating in triangle) between them. When this occurs, physical presentation of the light CS activates the CS representation (indicated by gray), which in turn activates the US representation and triggers a fear response (illustrated as potentiated startle, i.e., a greater amplitude startle response when startle is elicited in the presence of the CS relative to when it is elicited in the absence of the CS)

Myers, K., Davis, M. Mechanisms of fear extinction. *Mol Psychiatry* **12**, 120–150 (2007).
<https://doi.org/10.1038/sj.mp.4001939>

Extinction is not the same as forgetting,
BUT it is new learning.

c



Extinction involves the formation of a second, inhibitory association whose effect is opposite that of the excitatory association. When this occurs, the CS representation no longer activates the US representation and no fear is triggered.

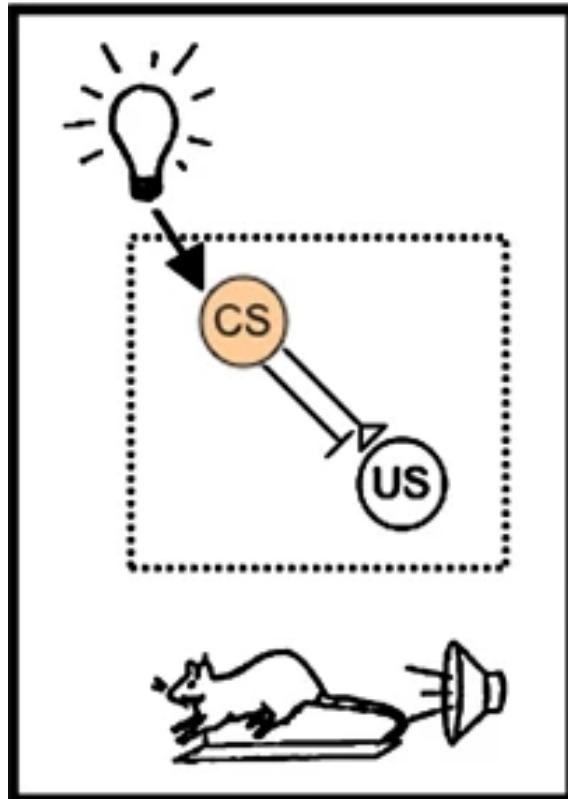
BUT HOW WOULD YOU SHOW THIS?



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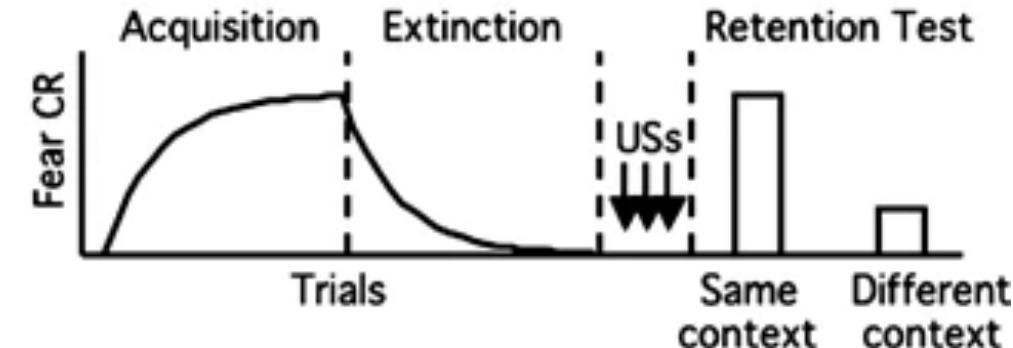
**Extinction is not the same as forgetting,
BUT it is new learning!**

c

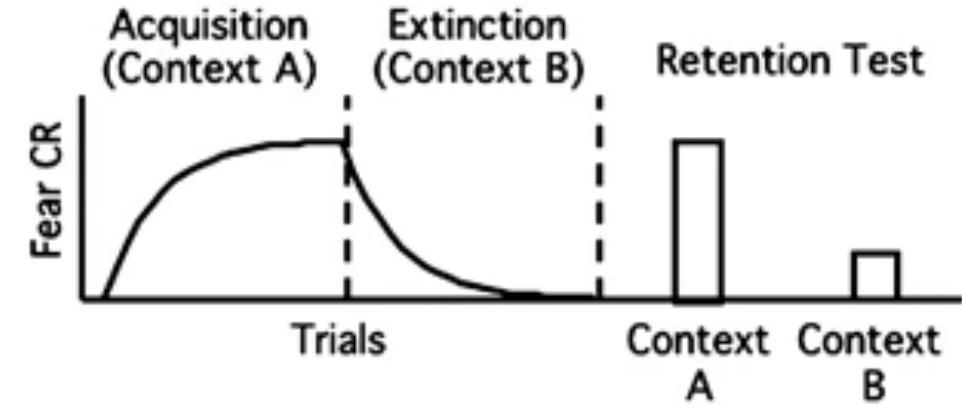


BUT HOW WOULD YOU SHOW THIS?

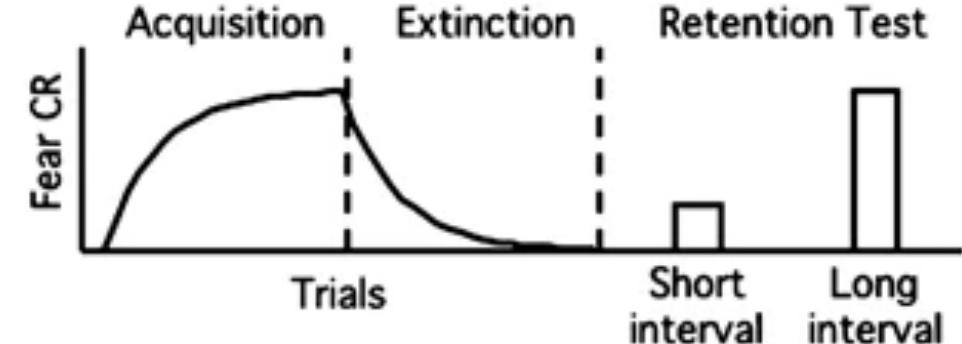
a Reinstatement



b Renewal



c Spontaneous recovery



Pavlovian learning is a flexible process

Generalization: Other stimuli that are not involved in the initial learning process and that resemble the original CS come to elicit a CR

- Generalization vs discrimination → BETTER
SAFE THAN
SORRY
- Adaptive or maladaptive?

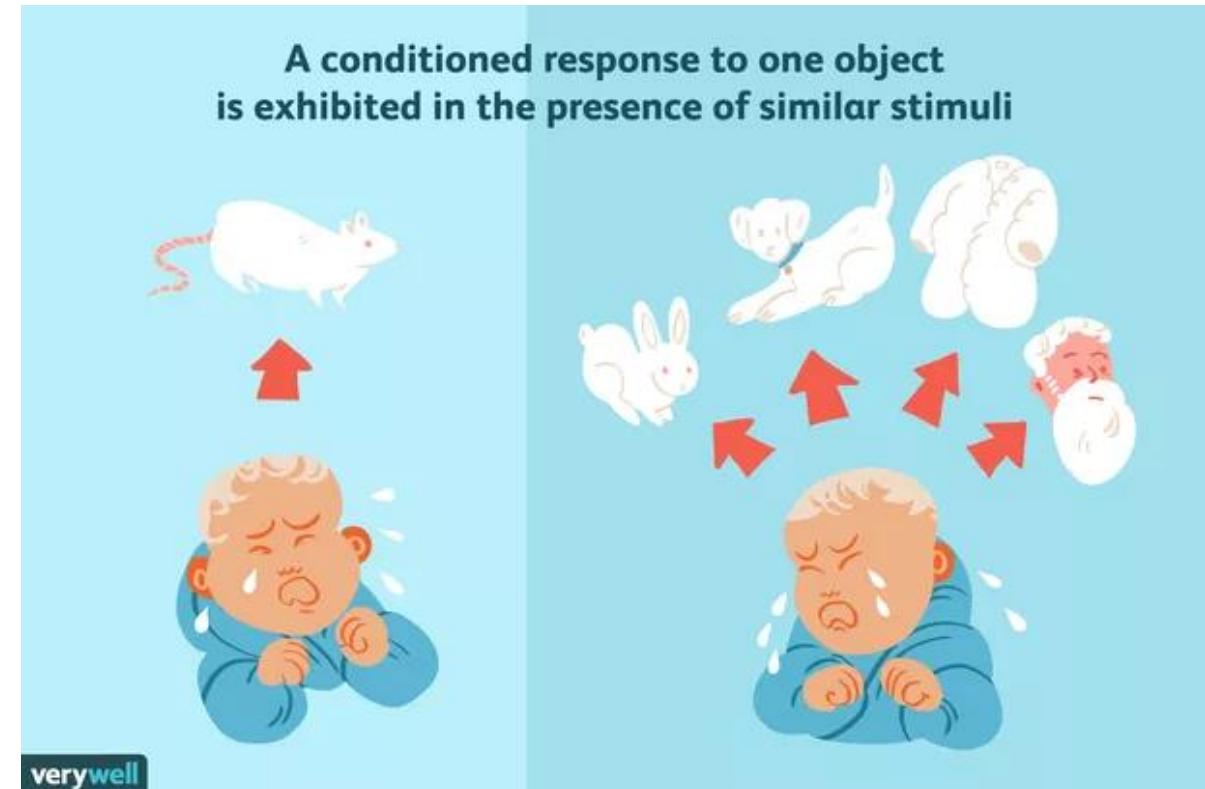


Illustration by Emily Roberts, Verywell



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In the past, it was often assumed
that the difference between normal, healthy fear

<https://youtu.be/G5QAKnMf4Xc>





**GO TO THE
NEXT ONE**

Measuring learning in human classical threat conditioning: Translational, cognitive and methodological considerations



Karita E. Ojala^{a,b}, Dominik R. Bach^{a,b,c,*}

Table 1
Summary of the reviewed findings for each conditioned response.

	Observed in non-human species	Amygdala-dependent learning in humans (quality of evidence)	Conditioned learning in non-human species (quality of evidence)	Declarative memory modulation	Effect size to distinguish CS+/CS- *	Retention	Extinction
Skin conductance	Yes	Yes (single case study)	Yes (two monkey studies)	Possible	Moderate	Yes	Yes
Pupil size	Yes	NA	NA	NA	High	Yes	Yes
Heart period	Yes	NA	Yes (several studies)	Possible	Moderate	Yes	Yes
Respiration	Yes	NA	NA	NA	Low	Yes	NA
Startle eye-blink	Yes	NA (conflicting results)	Yes (several studies)	Possible	High	Yes	Yes
Limb withdrawal	Yes	No (circumstantial)	No (circumstantial)	NA	NA	NA	Yes
Gaze direction	NA	NA	NA	NA	Moderate/high	Yes	NA
Reaction time	NA	NA	NA	Possible	NA	NA	Yes
PIT	NA	NA	Yes (several studies)	NA	Low	Yes	NA
Explicit memory	NA	No (single case study)	NA	-	High	Yes	Yes

NA = Not Available, i.e. no published studies identified. PIT = Pavlovian-to-instrumental transfer.

* However, different CR may reflect different underlying learning quantities, and therefore, effect size to distinguish CS+/CS- can depend on the specific experimental paradigm.

Lesional method

Study of the consequences resulting from brain lesions

- Natural occurring (e.g. tumor, stroke, degenerative disease)
- Surgically induced to treat epilepsy
- Experimentally caused (only done in animals)

Causal evidence: which region is necessary for a given behavior or response

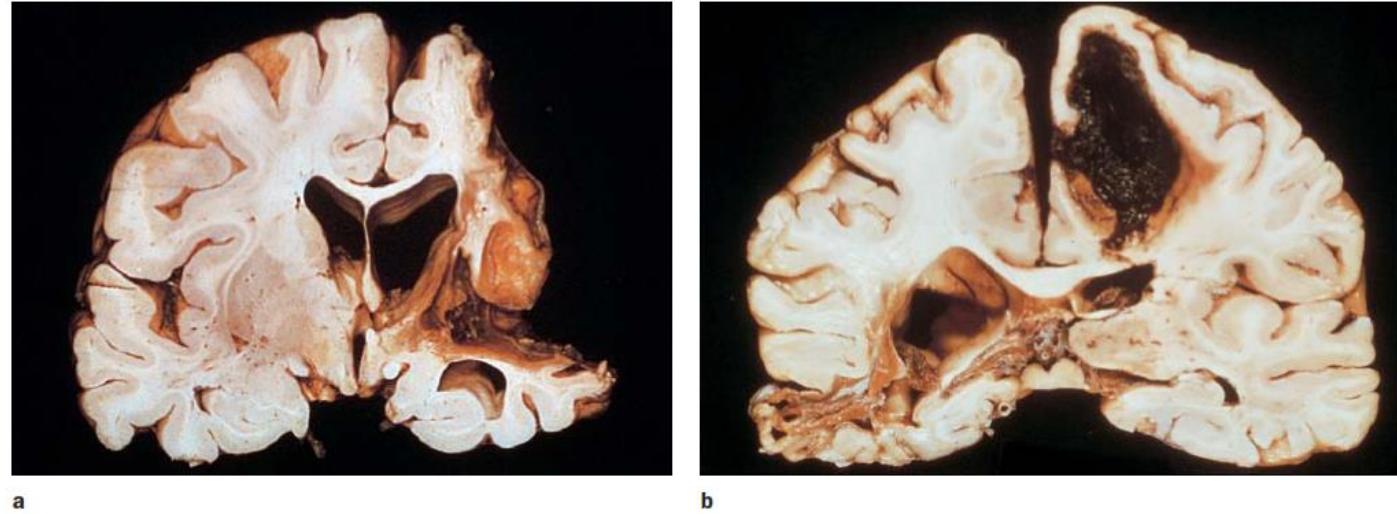


FIGURE 3.7 Vascular disorders of the brain.

(a) Strokes occur when blood flow to the brain is disrupted. This brain is from a person who had an occlusion of the middle cerebral artery. The person survived the stroke. After death, a postmortem analysis shows that almost all of the tissue supplied by this artery had died and been absorbed. (b) Coronal section of a brain from a person who died following a cerebral hemorrhage. The hemorrhage destroyed the dorsomedial region of the left hemisphere. The effects of a cerebrovascular accident 2 years before death can be seen in the temporal region of the right hemisphere.

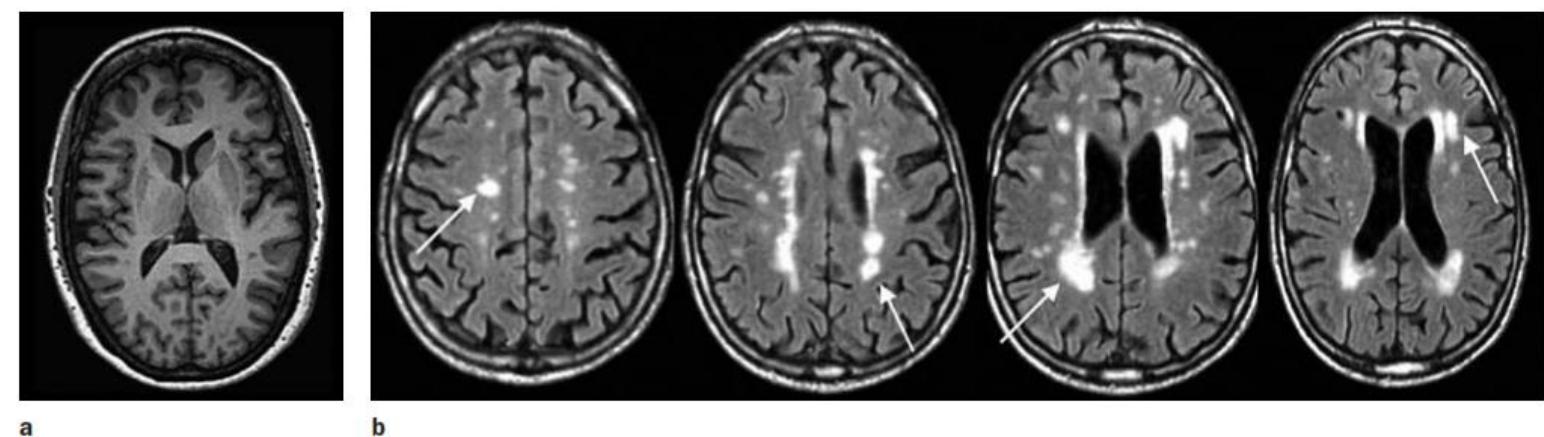


FIGURE 3.8 Degenerative disorders of the brain.

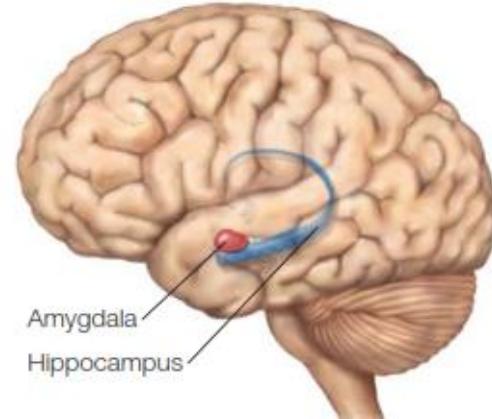
(a) Normal brain of a 60-year-old male. (b) Axial slices at four sections of the brain in a 79-year-old male with Alzheimer's disease. Arrows show growth of white matter lesions.

A double dissociation: amygdala vs hippocampus

Bechara et al. 1995,
Science

2 experiments

1. CS visual, US sound
2. CS sound, US sound

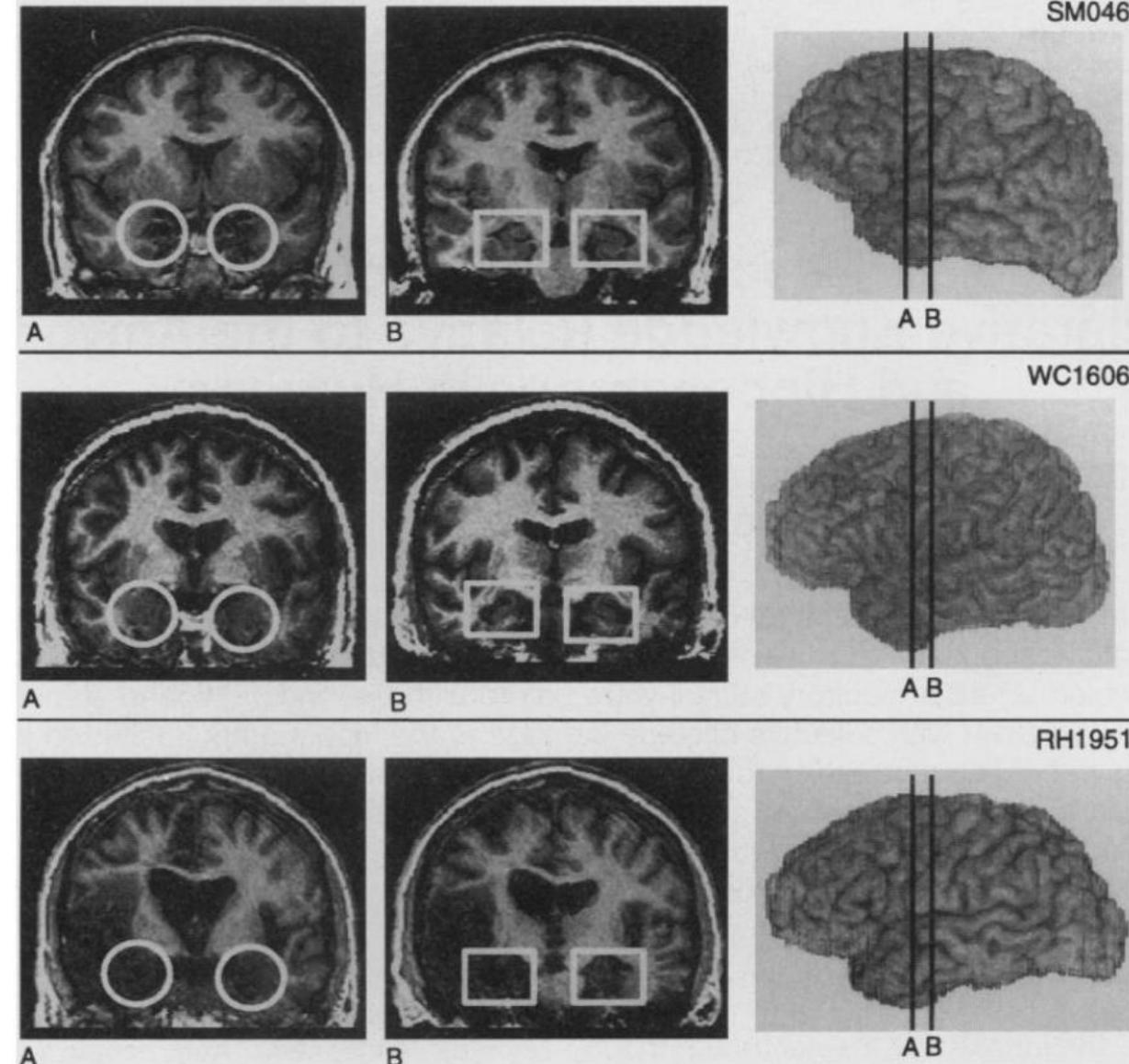


Participants

1. Patient with selective bilateral damage to the amygdala (SM046)
2. Patient with selective bilateral damage to the hippocampus (WC1606)
3. Patient with bilateral damage to both amygdala and hippocampal formation (RH1951)
4. 4 healthy control participants

Dependent measures

- SCR
- Verbal knowledge of CS-US association

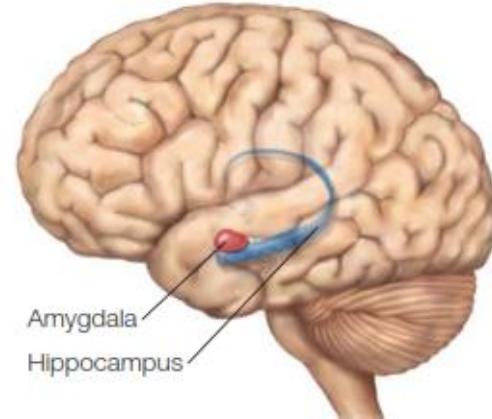


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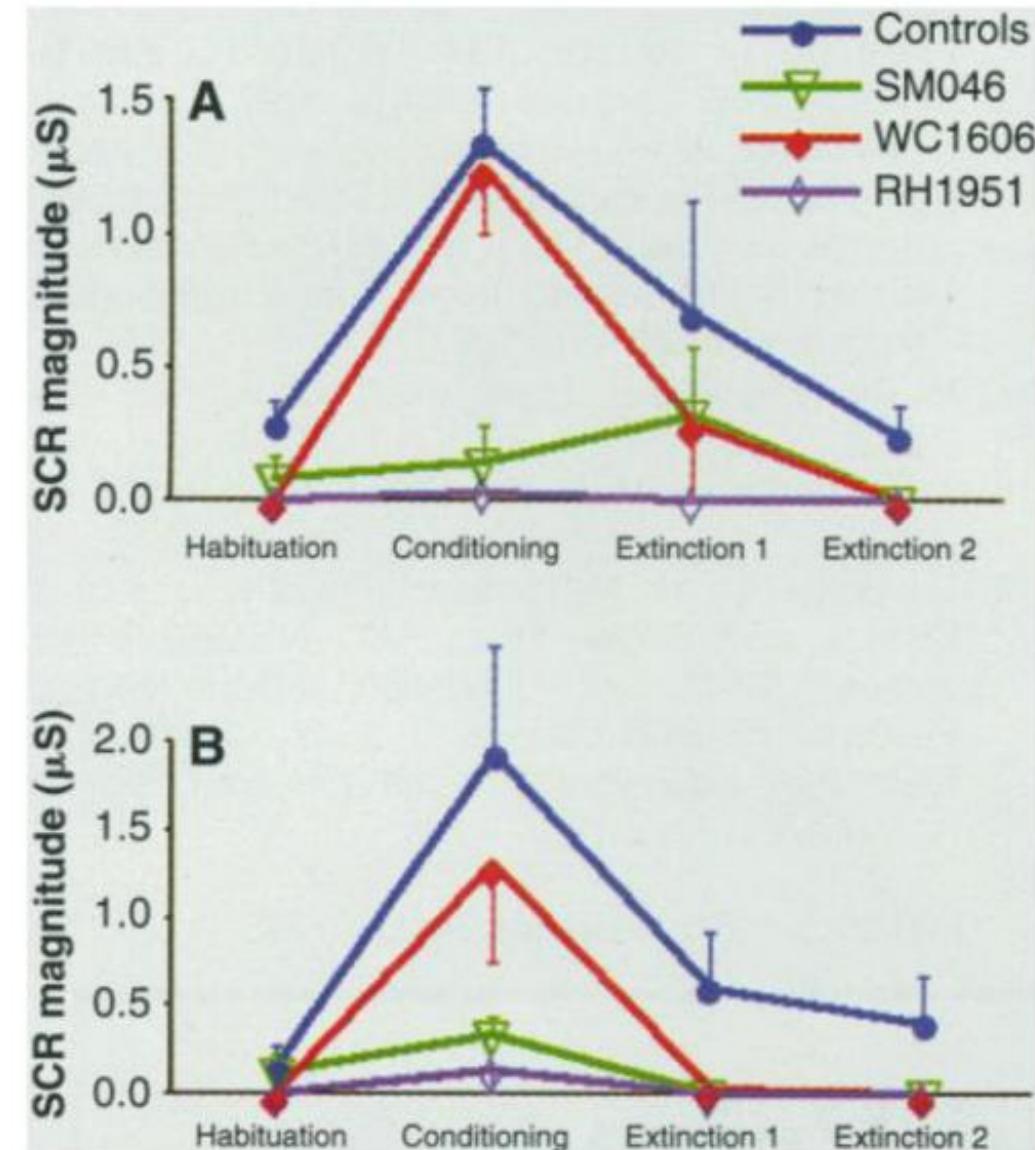


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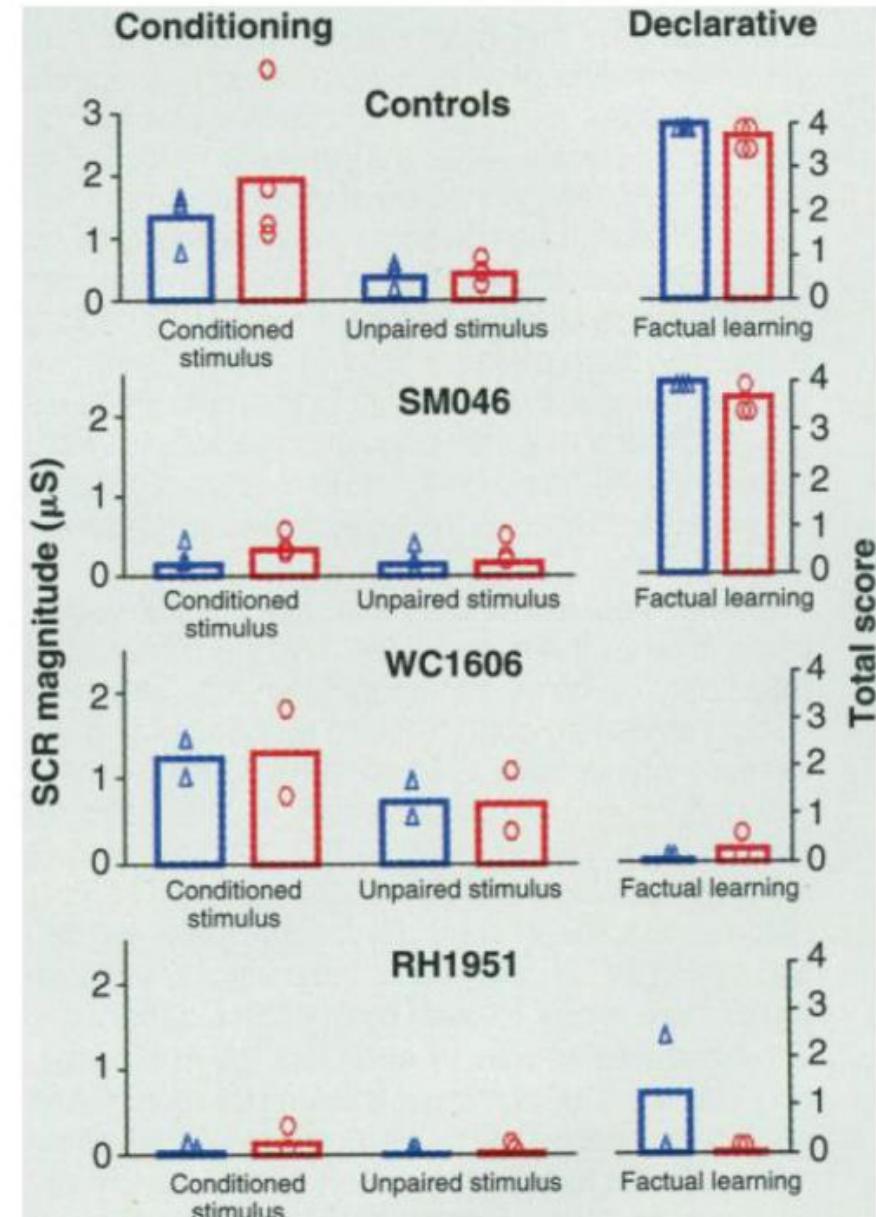
1. CS visual, US sound (blue bar)
2. CS sound, US sound (red bar)

Participants

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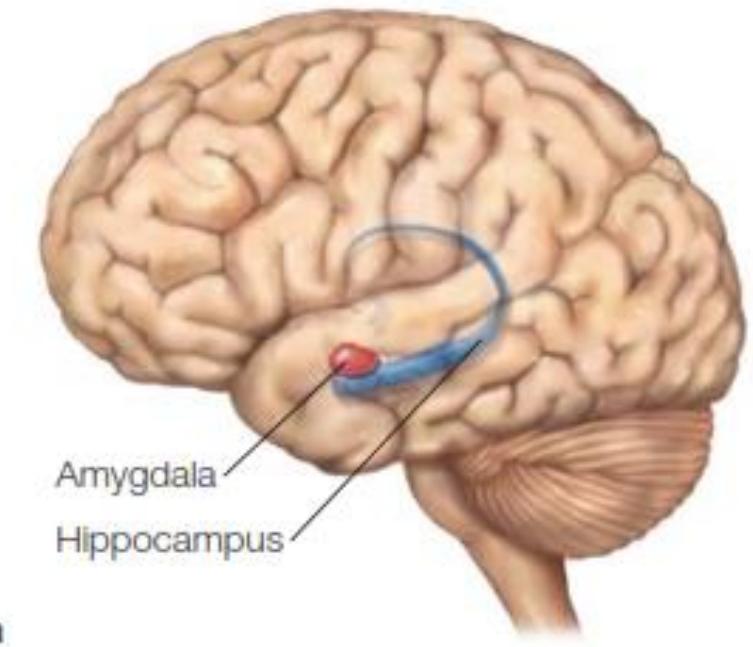


A double dissociation: amygdala vs hippocampus

Double dissociation: two related mental processes are shown to function independently of each other.

Double dissociation between patients who have amygdala lesions and patients with hippocampal lesions

- the amygdala is necessary for the implicit expression of conditioning: psychophysiological conditioned response
- The hippocampus is necessary for the explicit or declarative expression of conditioning: awareness of CS-US association



Pavlovian learning, memory formation, consolidation and reconsolidation

<https://www.pbslearningmedia.org/resource/nvfb-sci-memhackers/wgbh-nova-memory-hackers-full-length-broadcast/>

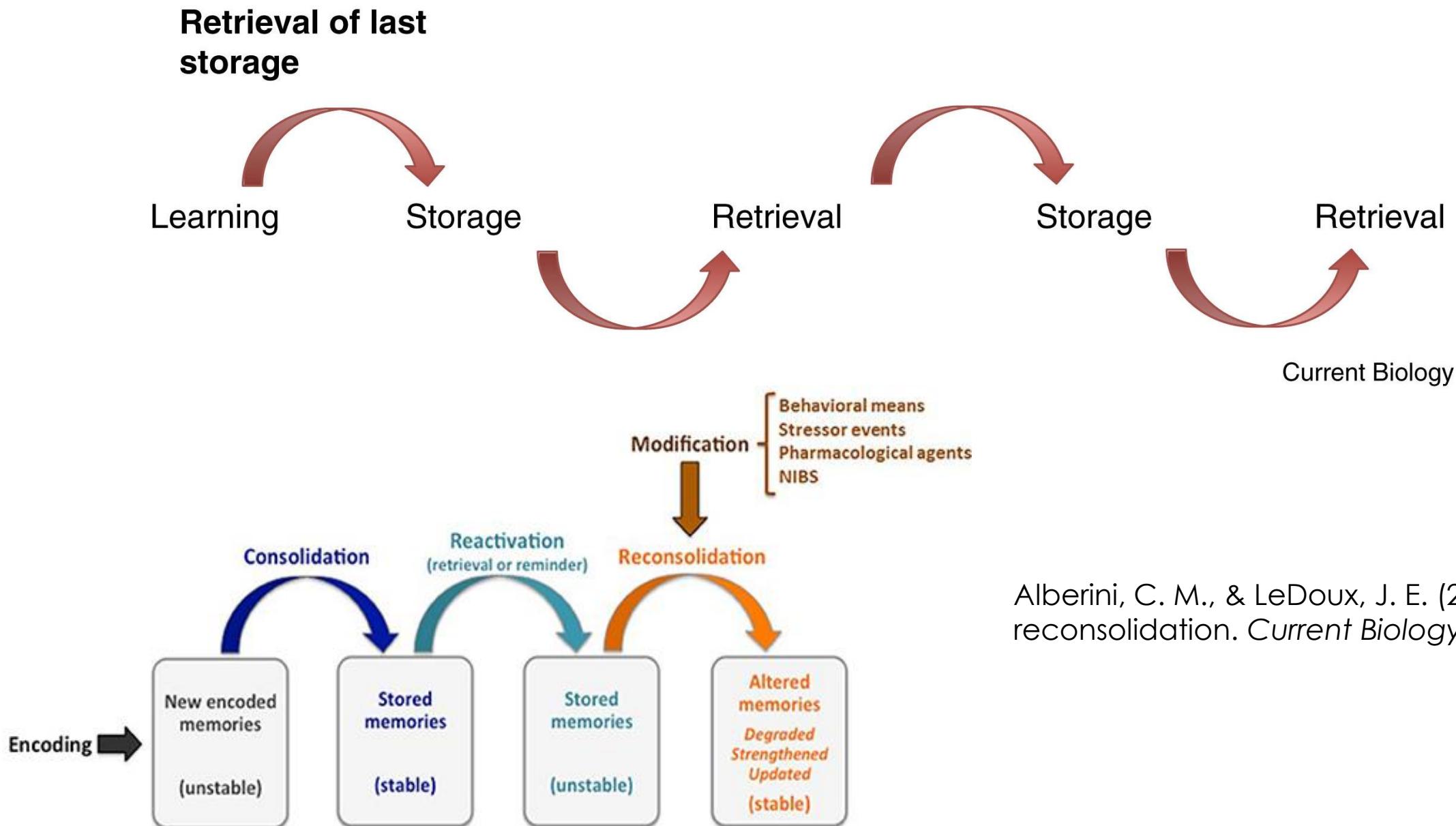
Minute 10.40-21.20: memory formation, Hebbian learning, plasticity

Minute 21.20-30.00: memory reconsolidation: animal studies

Minute 30.00 to 37.00: memory reconsolidation in humans: Kindt study



Memory reconsolidation: memories are vulnerable to alteration



Alberini, C. M., & LeDoux, J. E. (2013). Memory reconsolidation. *Current Biology*, 23(17), R746-R750.



Pavlovian learning and memory reconsolidation

VOLUME 12 | NUMBER 3 | MARCH 2009 **NATURE NEUROSCIENCE**

Beyond extinction: erasing human fear responses and preventing the return of fear

Merel Kindt, Marieke Soeter & Bram Vervliet

Animal studies have shown that fear memories can change when recalled, a process referred to as reconsolidation. We found that oral administration of the β -adrenergic receptor antagonist propranolol before memory reactivation in humans erased the behavioral expression of the fear memory 24 h later and prevented the return of fear. Disrupting the reconsolidation of fear memory opens up new avenues for providing a long-term cure for patients with emotional disorders.

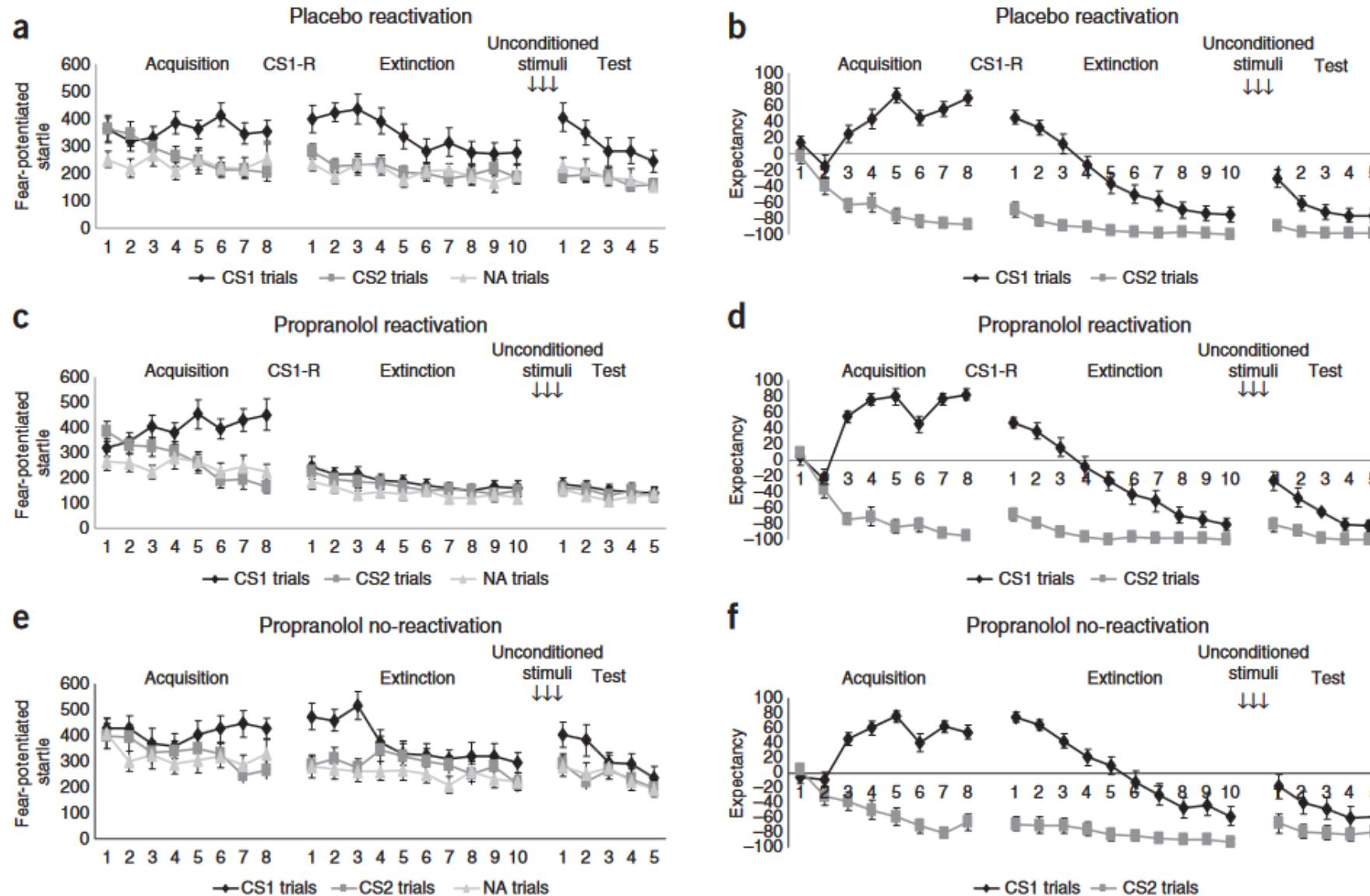
For a more technical video of Kindt study:

<https://www.jove.com/it/v/52151/disrupting-reconsolidation-fear-memory-humans-noradrenergic>

Note that what is reconsolidated is the amygdala-dependent physiological conditioned response, NOT the hippocampal-dependent declarative memory



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Note that what is reconsolidated is the amygdala-dependent physiological conditioned response, NOT the hippocampal-dependent declarative memory

Figure 1 Propranolol disrupts the reconsolidation of a fear memory, but not declarative memory. (a-f) Mean startle potentiation to the fear-conditioned stimulus (CS1), the control stimulus (CS2) and noise alone (NA) trials (left) and mean expectancy scores of the unconditioned stimulus to CS1 and CS2 trials (right) during acquisition (trial 1–8), extinction (trial 1–10) and test (trial 1–5) for the placebo ($n = 20$, a,b), propranolol reactivation ($n = 20$, c,d) and propranolol without reactivation ($n = 20$, e,f) group. CS1⁺ refers to the fear conditioned stimulus during acquisition, CS1⁻ refers to the fear conditioned stimulus during extinction and test, CS1-R refers to the reactivation of the fear conditioned stimulus and CS2⁻ refers to the control stimulus during all phases of the experiment. Error bars represent s.e.m.



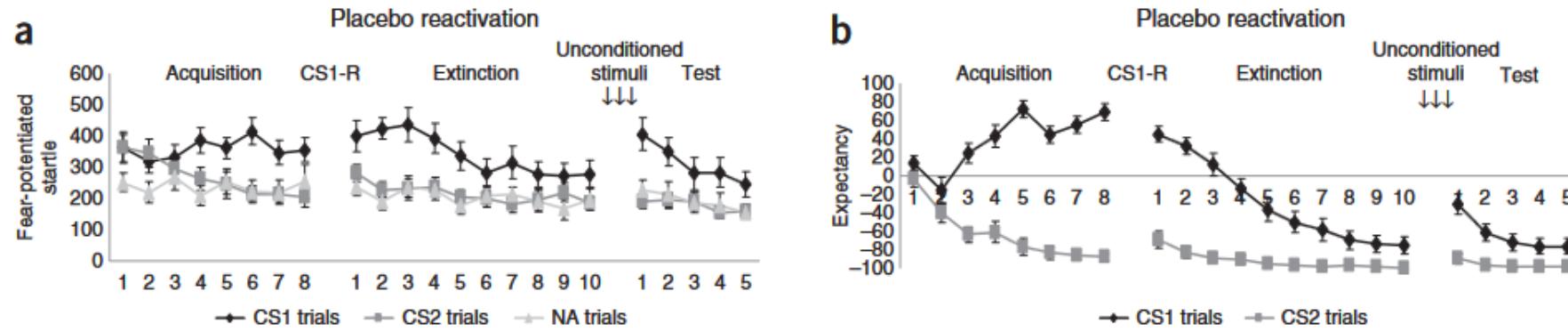


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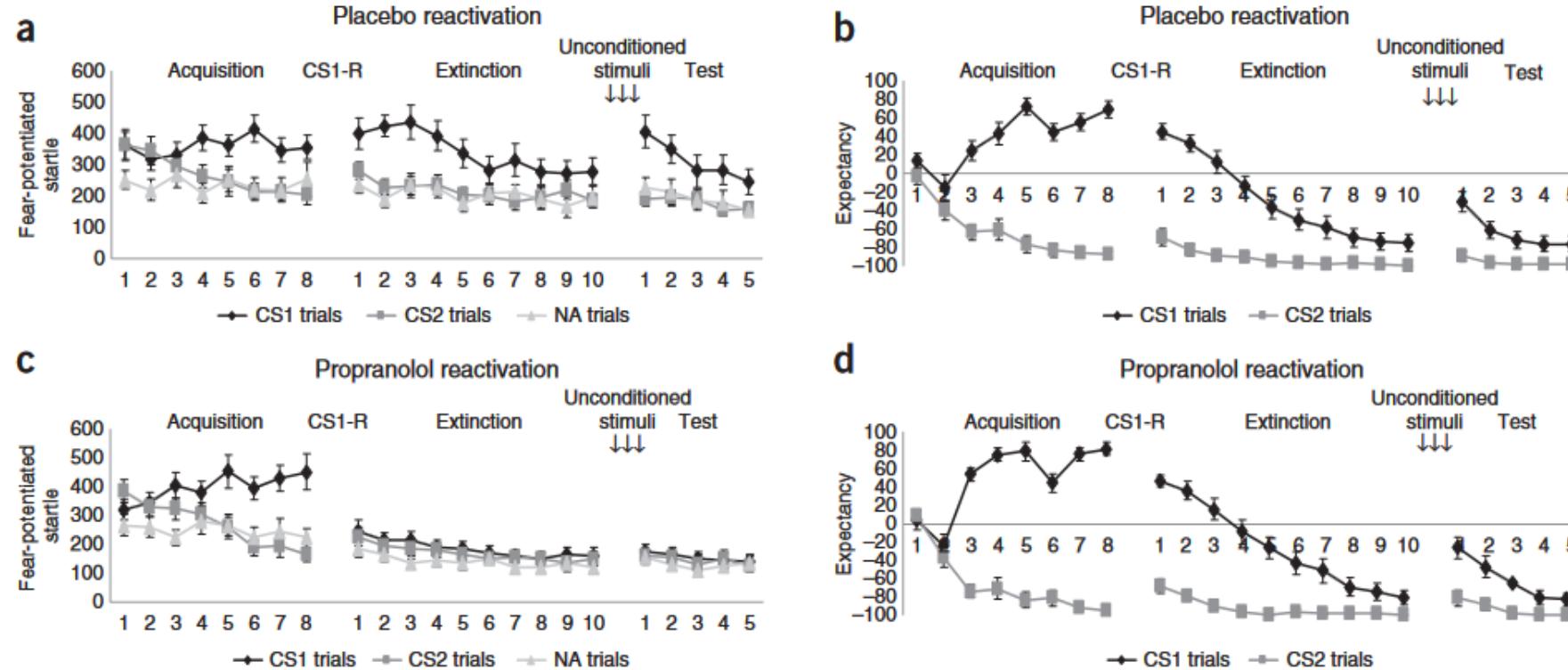


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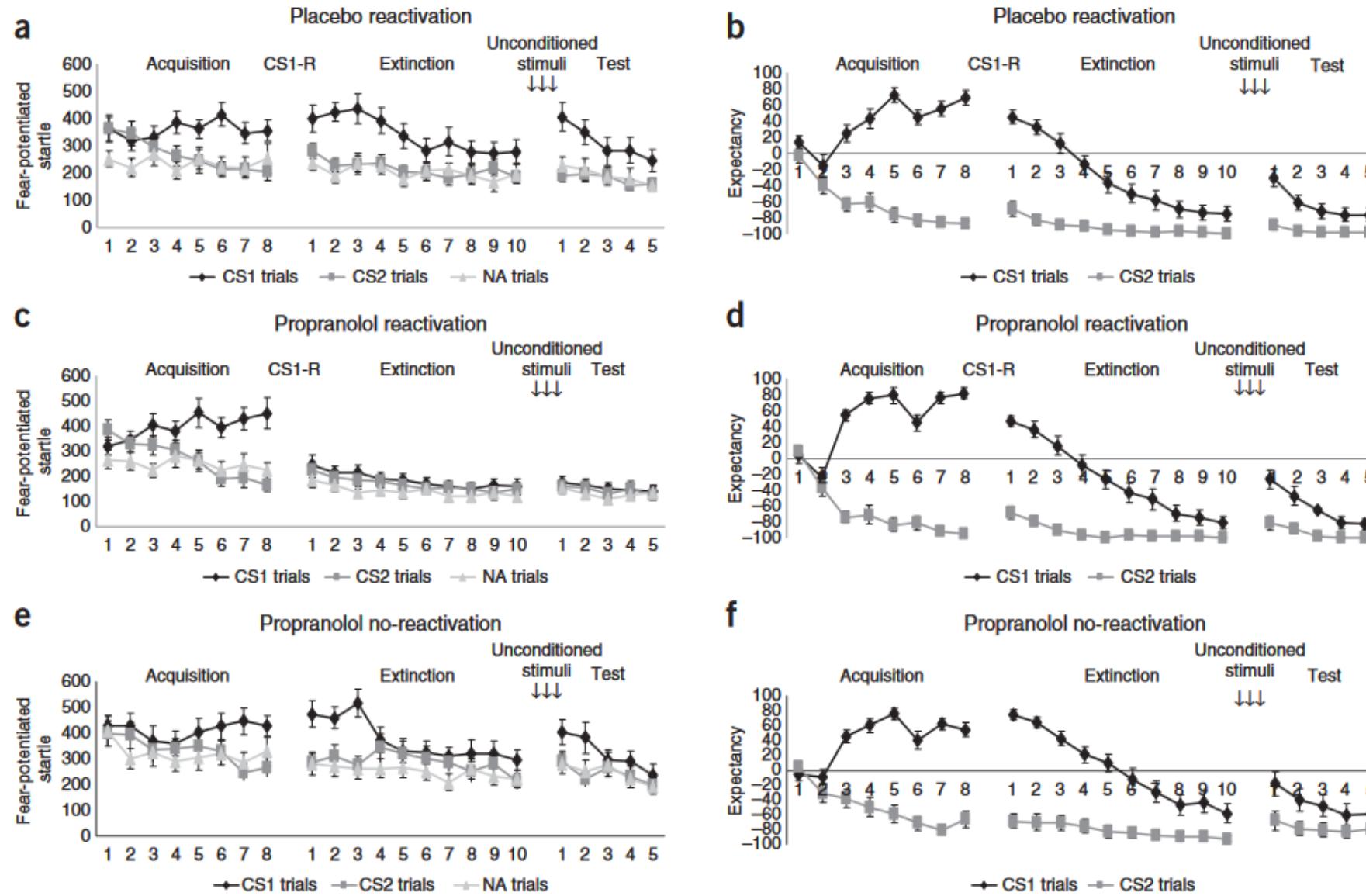


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Note that what is reconsolidated is the amygdala-dependent physiological conditioned response, NOT the hippocampal-dependent declarative memory



Recommended readings

- Daw, N. D., & O'Doherty, J. P. (2014). Multiple systems for value learning. In Neuroeconomics (Chapter 21, pp. 393-410). Academic Press.
- Gazzaniga, M. S., Ivry, R. B., & Mangun, G. R. (2014). Cognitive Neuroscience, The biology of the mind.
 - Pages 437-443
- Kandel, E. R., Schwartz, J. H., Jessell, T. M., Siegelbaum, S., Hudspeth, A. J., & Mack, S. (Eds.). (2000). Principles of neural science. New York: McGraw-hill.
 - chapter 48 sections:
 - The Amygdala Emerged as a Critical Regulatory Site in Circuits of Emotions



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