ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA
CAMPUS DI CESENA

Pavlovian learning: physiological and neural mechanisms

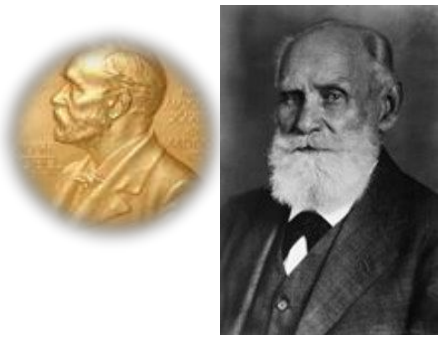
Cognition and Neuroscience
Academic year 2023/2024

Francesca Starita

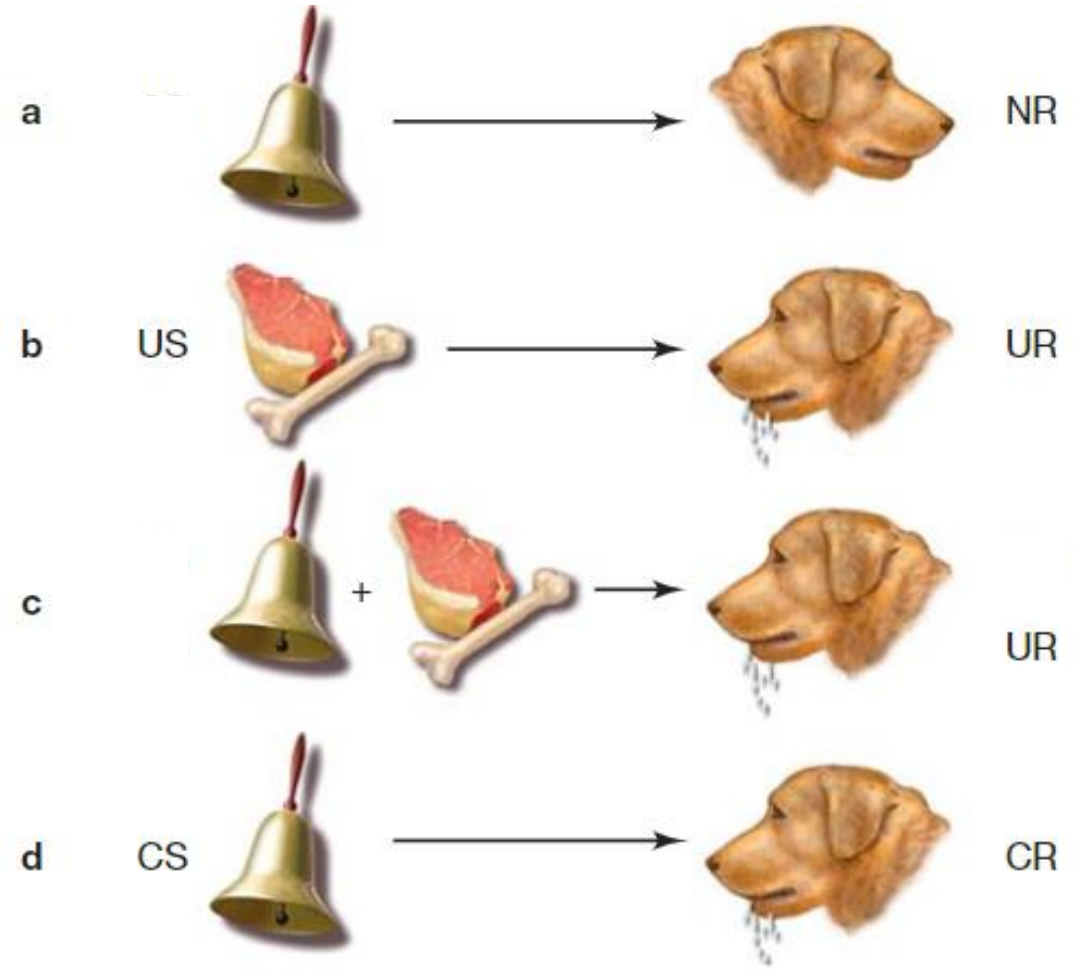
francesca.starita2@unibo.it

Pavlovian learning involves associating a stimulus with an outcome

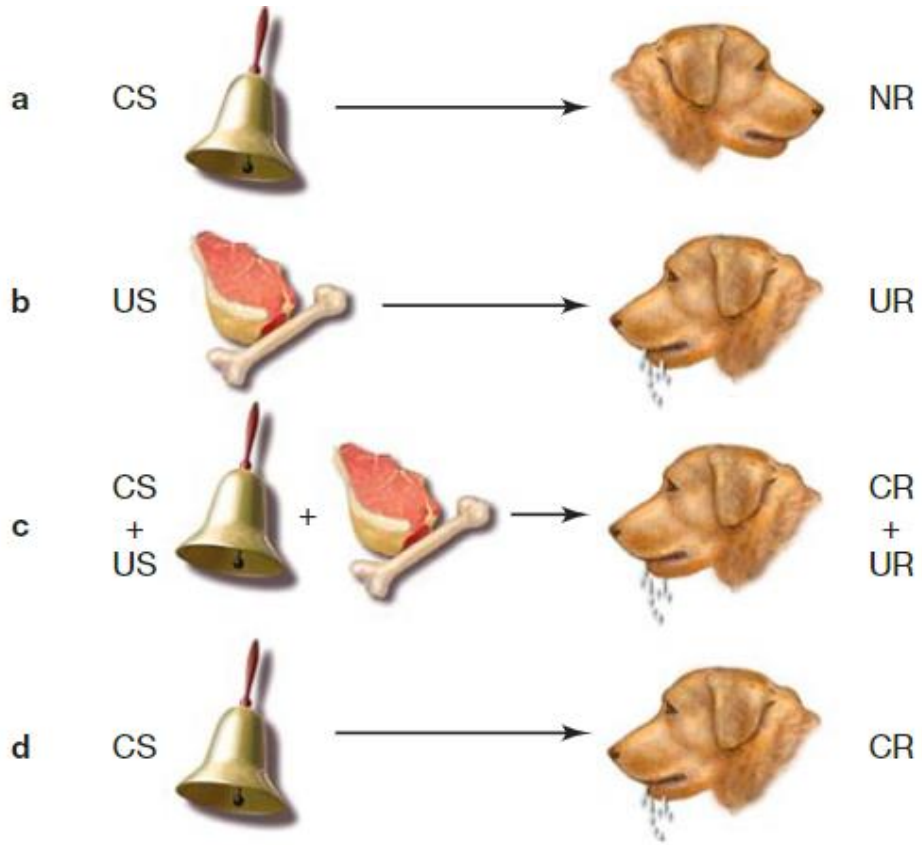
a) A stimulus is presented that has no meaning to an animal, such as the sound of a bell, there is no response (NR)
b) Presentation of a reinforcer like food (i.e. unconditioned stimulus, US) generates an unconditioned response (UR)
c) When the sound is paired with the food, the animal learns the association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

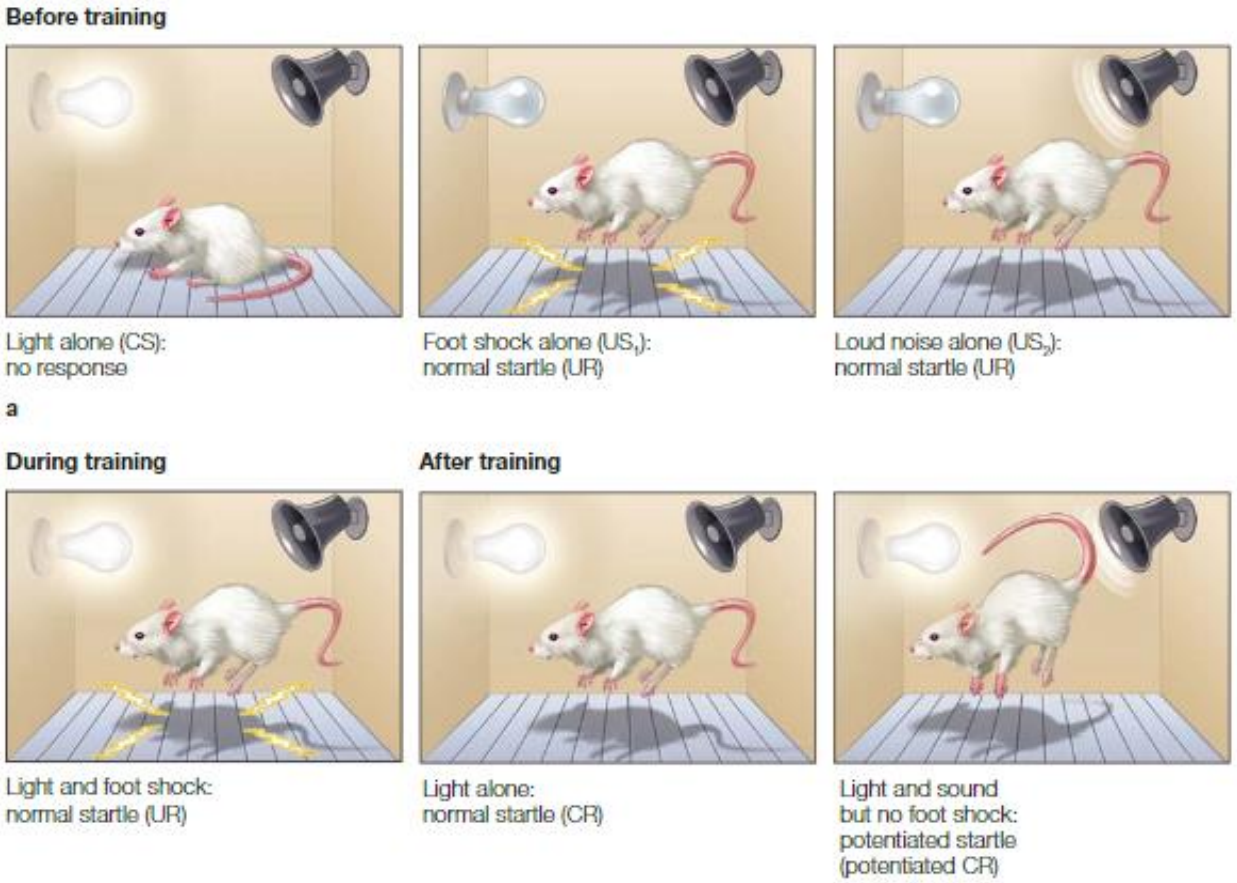


Ivan Pavlov (1849–1936) received a Nobel Prize after first demonstrating this type of learning with his dogs



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

CR are **anticipatory, predictive responses**

Unconditioned Stimulus (US)

Unconditioned response (UR)

Conditioned Stimulus (CS)

Conditioned response (CR)

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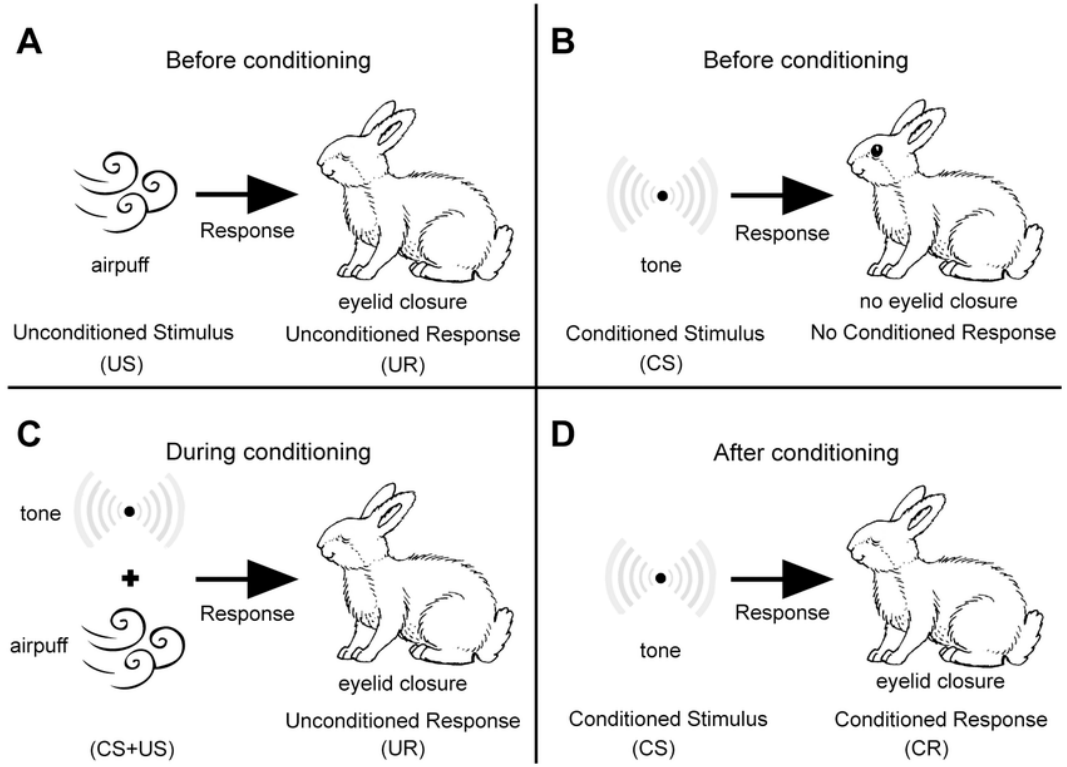

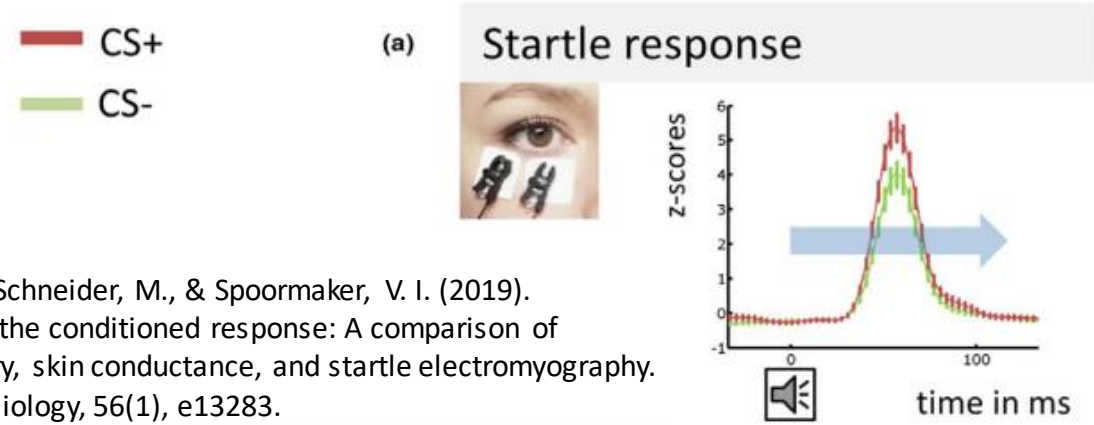

Leuchs, L., Schneider, M., & Spoormaker, V. I. (2019). Measuring the conditioned response: A comparison of pupillometry, skin conductance, and startle electromyography. Psychophysiology, 56(1), e13283. https://doi.org/10.1111/psyp.13283

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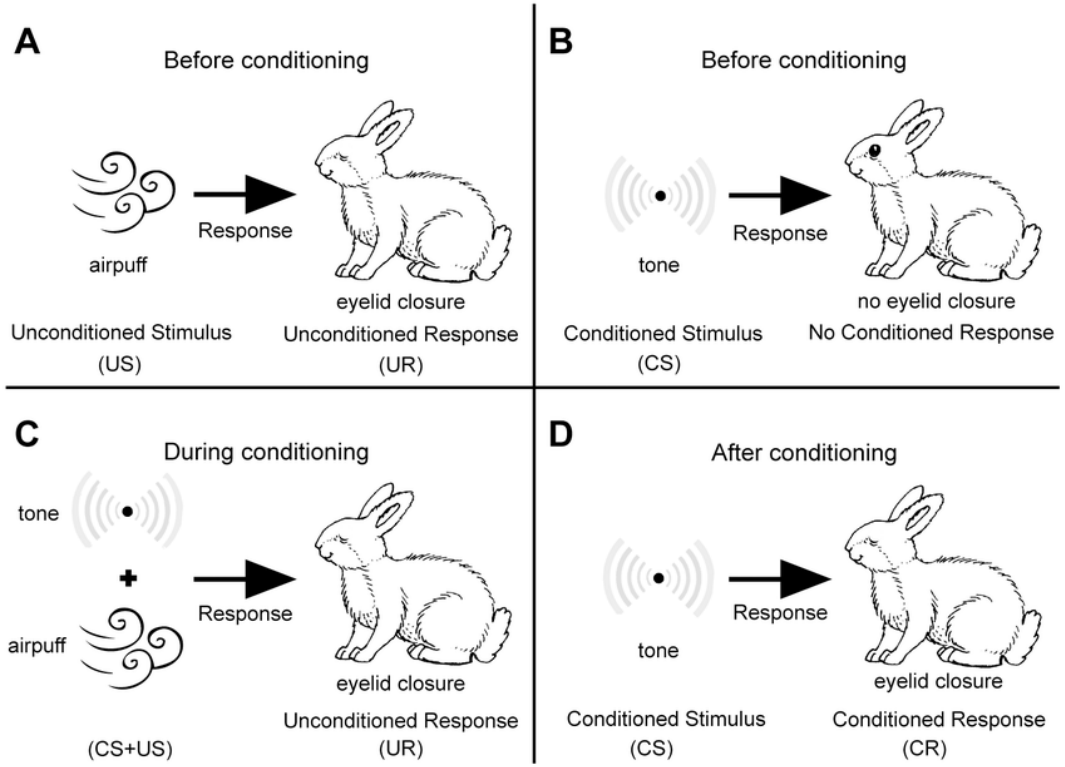

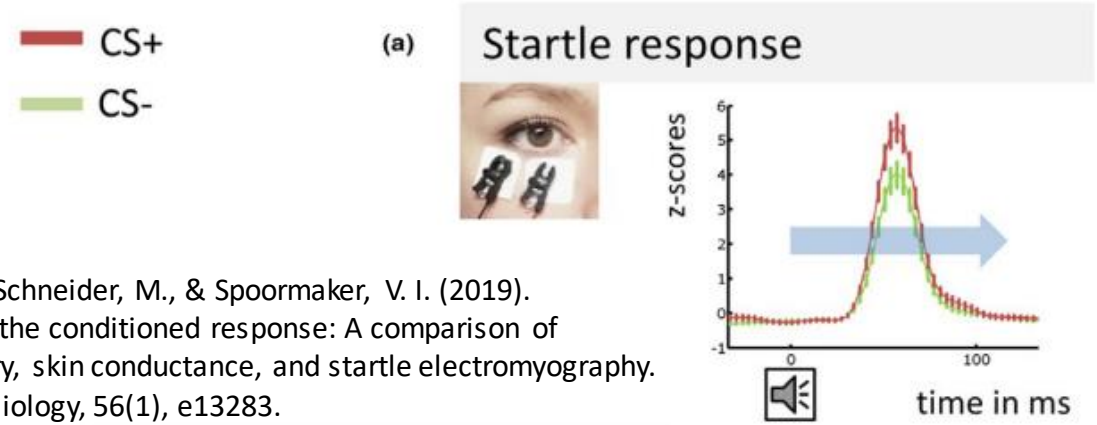

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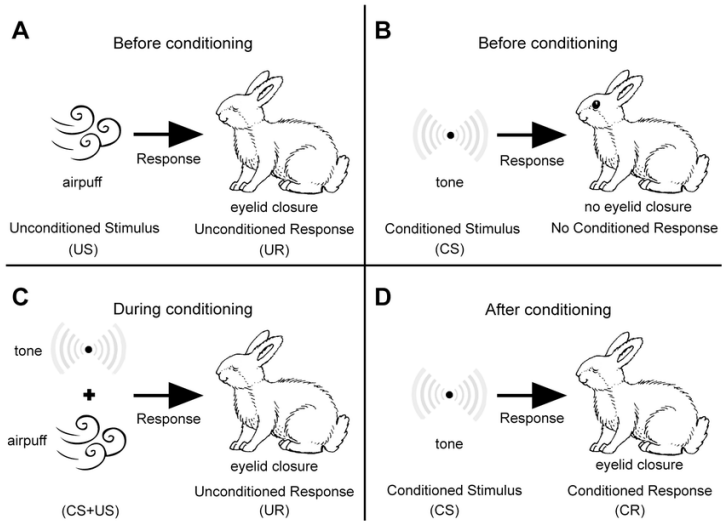
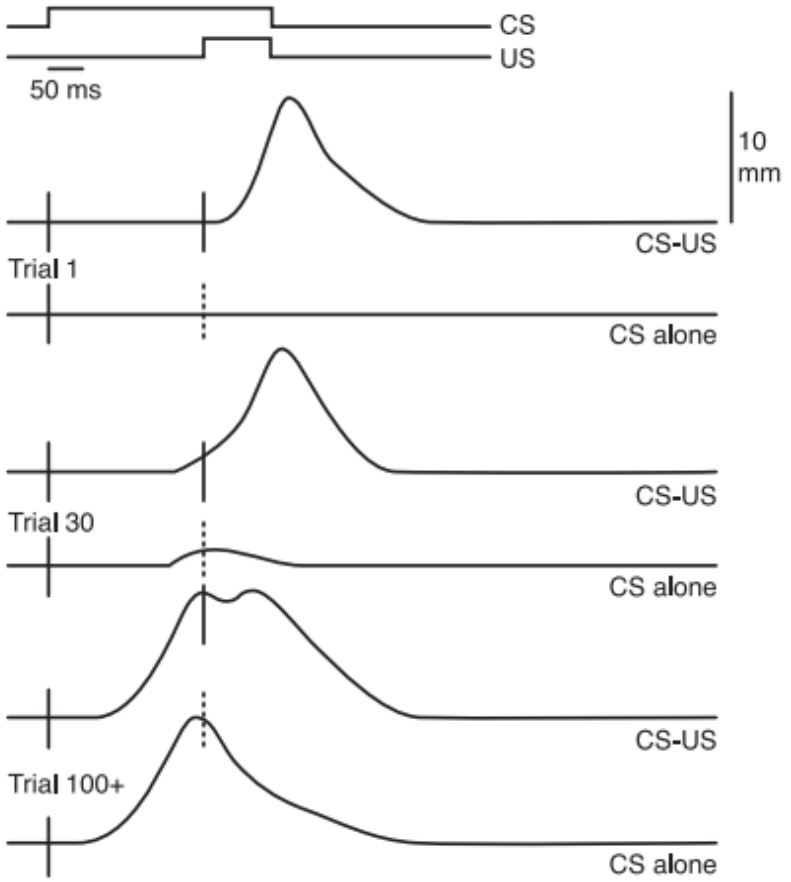
Adaptive nature of CR: predictive response

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

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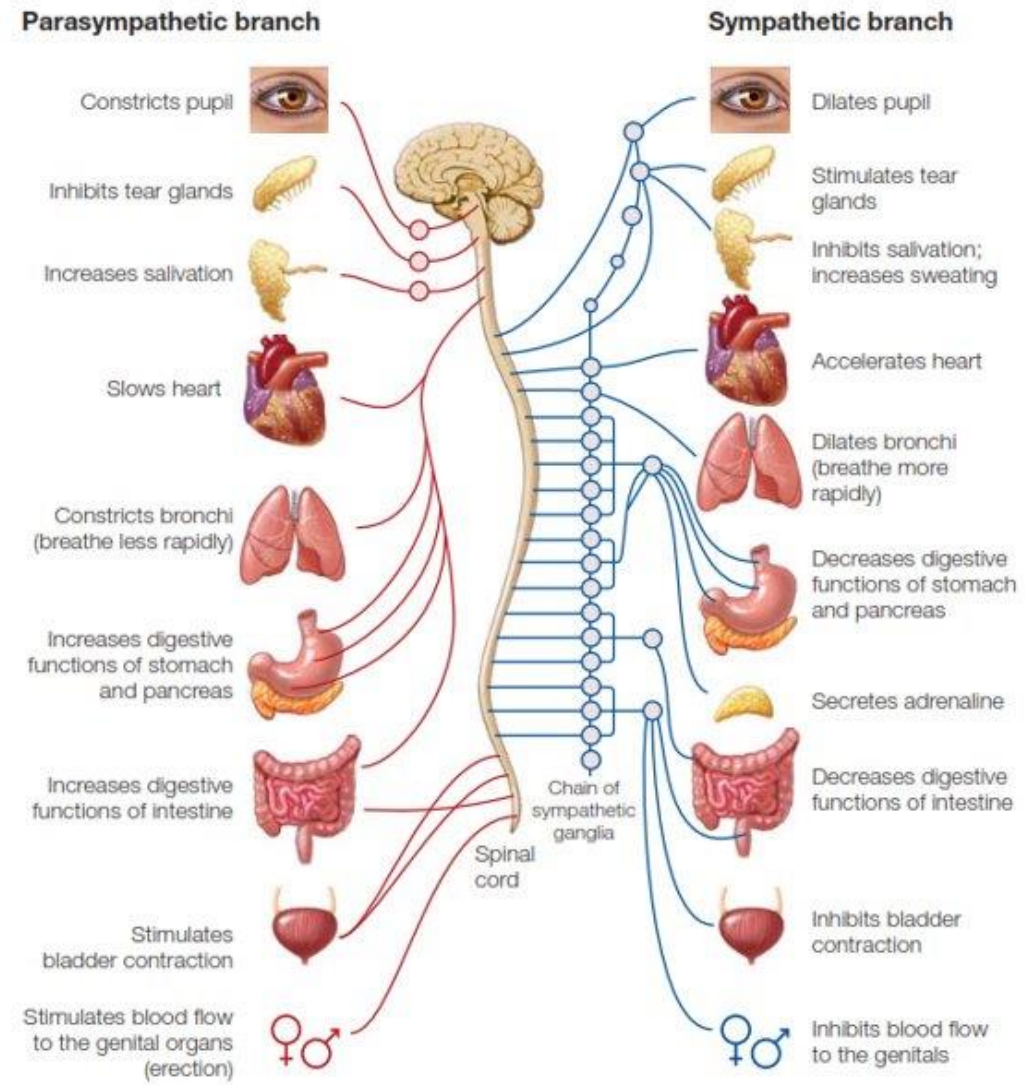
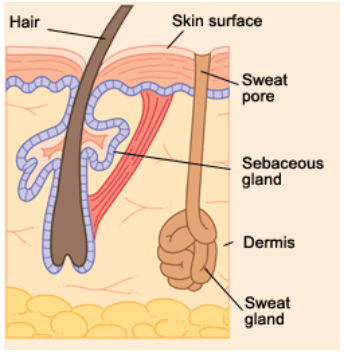


FIGURE 2.17 Organization of the autonomic nervous system, showing sympathetic and parasympathetic branches.



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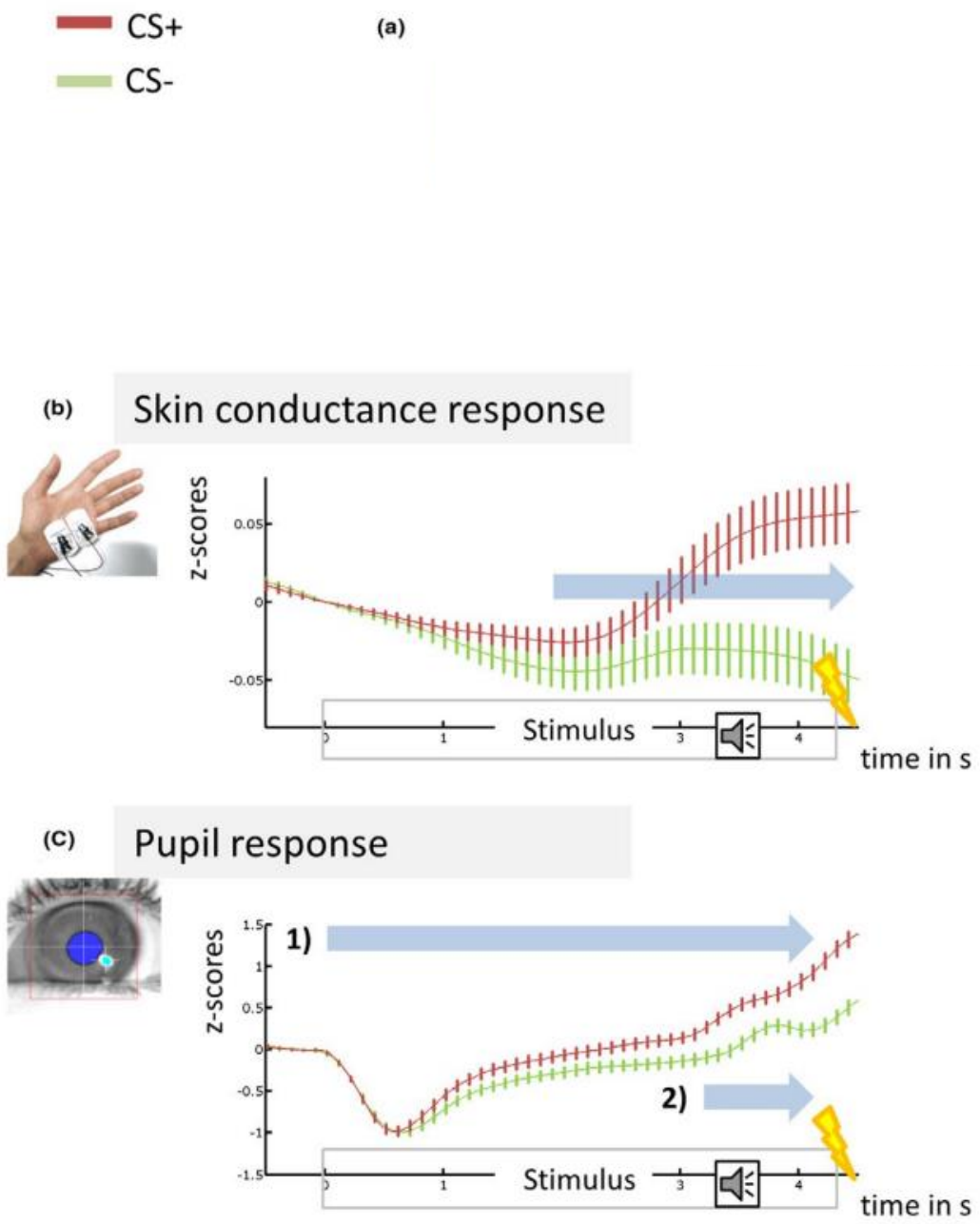

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Pavlovian learning is a flexible process

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…

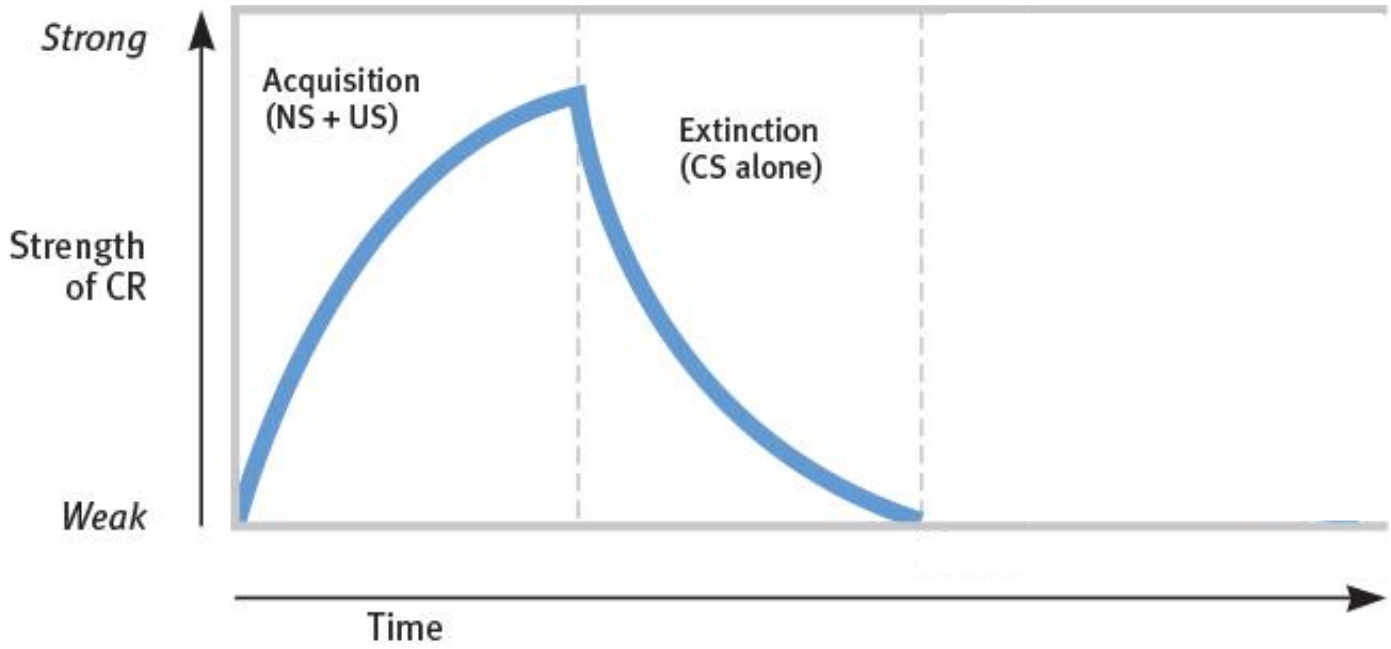


Figure 6.5
Myers/DeWall, *Psychology in Everyday Life*, 4e, © 2017 Worth Publishers

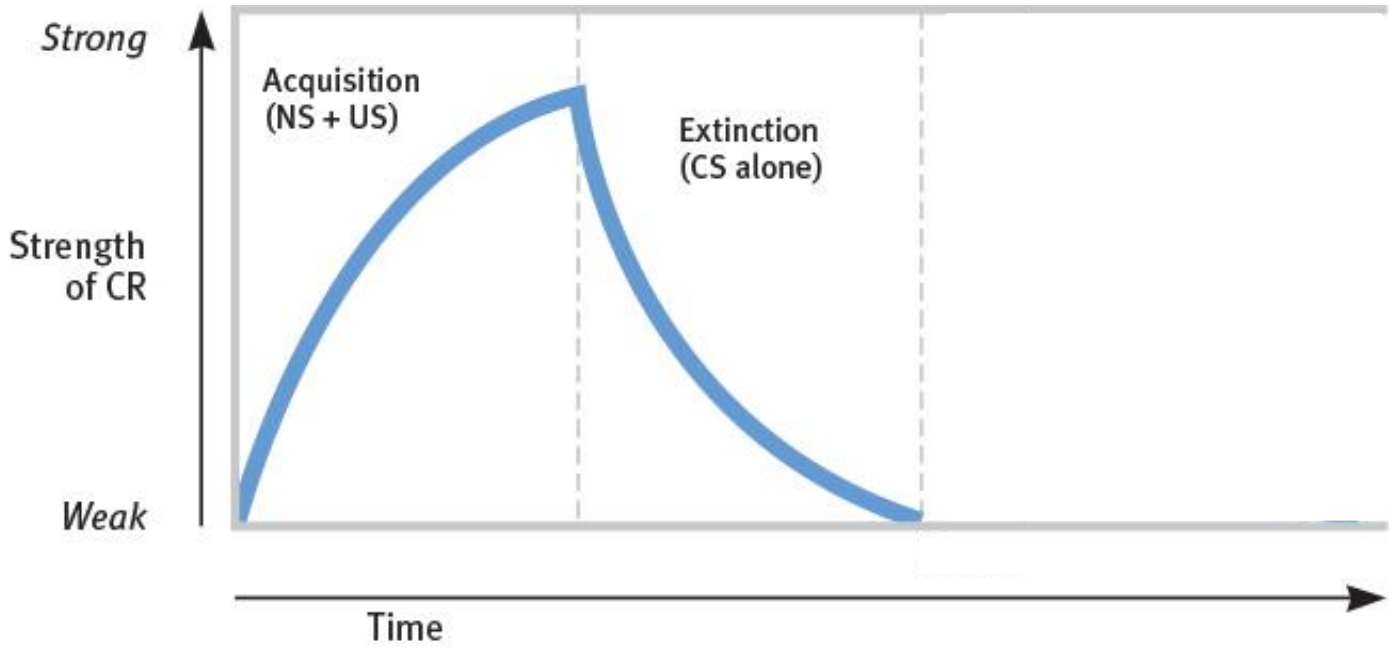
Pavlovian learning is a flexible process

Acquisition

- The probability of occurrence of a conditioned response increases if the CS is repeatedly presented with the US.
- Adaptive mechanism ensures that an animal responds to cues that are meaningful to survival

Extinction

- The probability of occurrence of a conditioned response decreases if the CS is repeatedly presented without the US.
- Adaptive mechanism ensures that an animal stops responding to cues that are no longer meaningful to it



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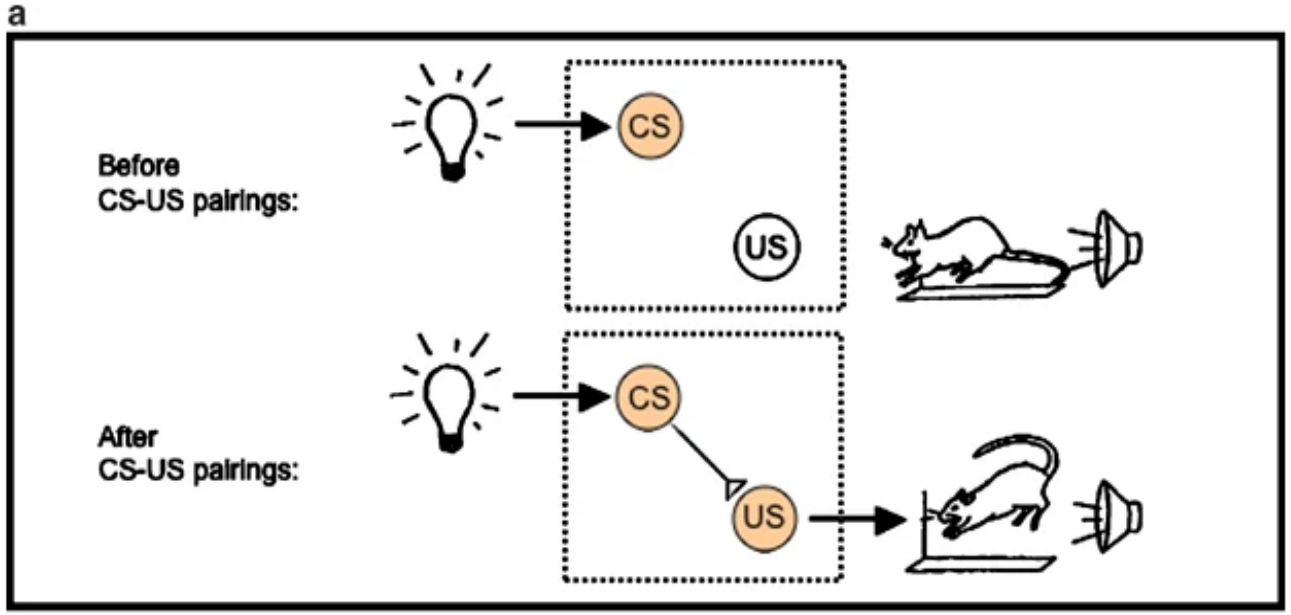
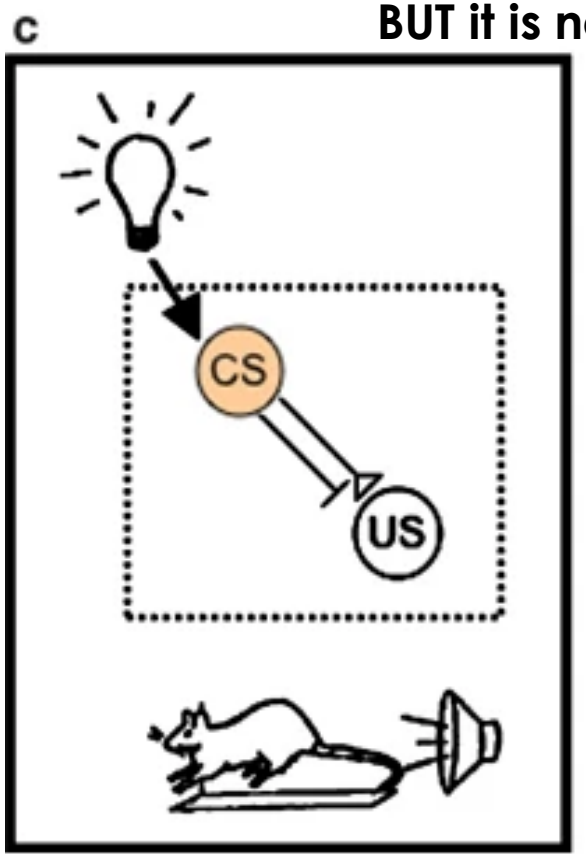


Conditioned fear is acquired as the animal forms representations of the cues involved (conditioned stimulus, CS; unconditioned stimulus, US) and develops an excitatory association (line terminating in triangle) between them. When this occurs, physical presentation of the light CS activates the CS representation (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)

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



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?

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

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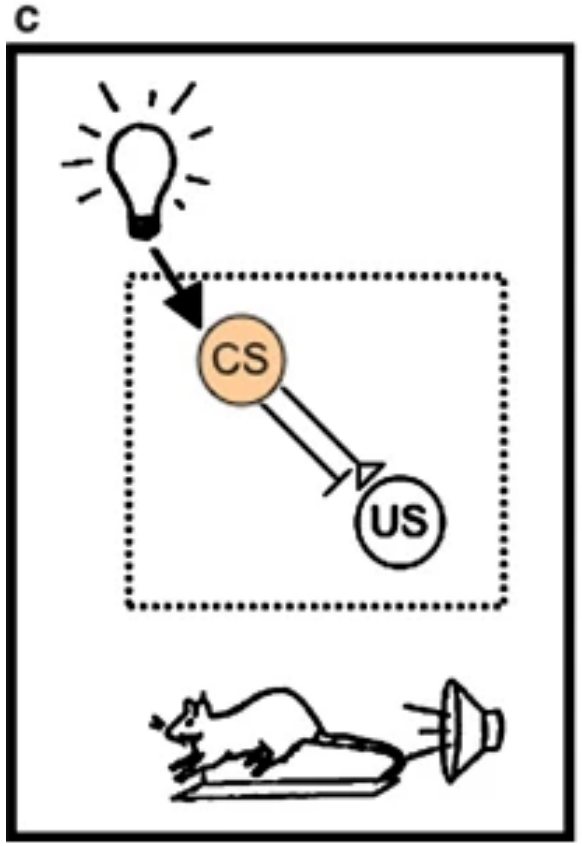

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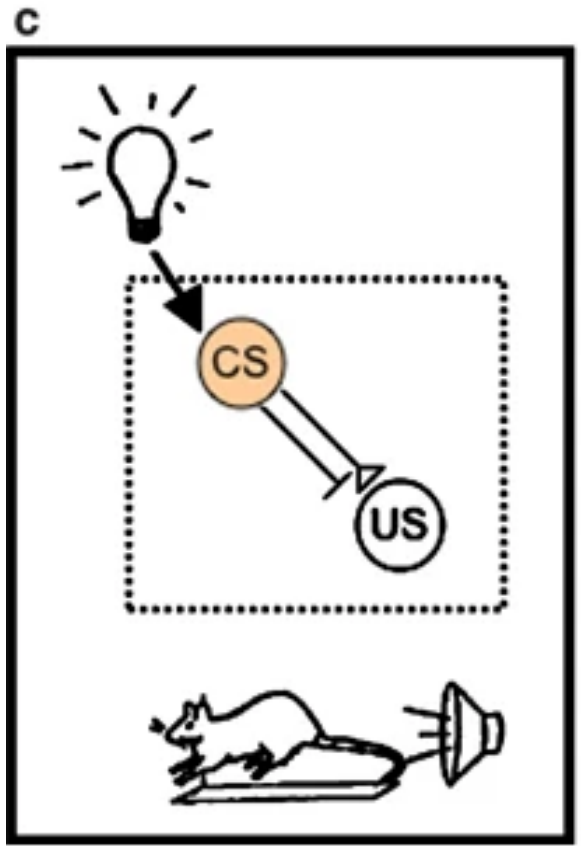
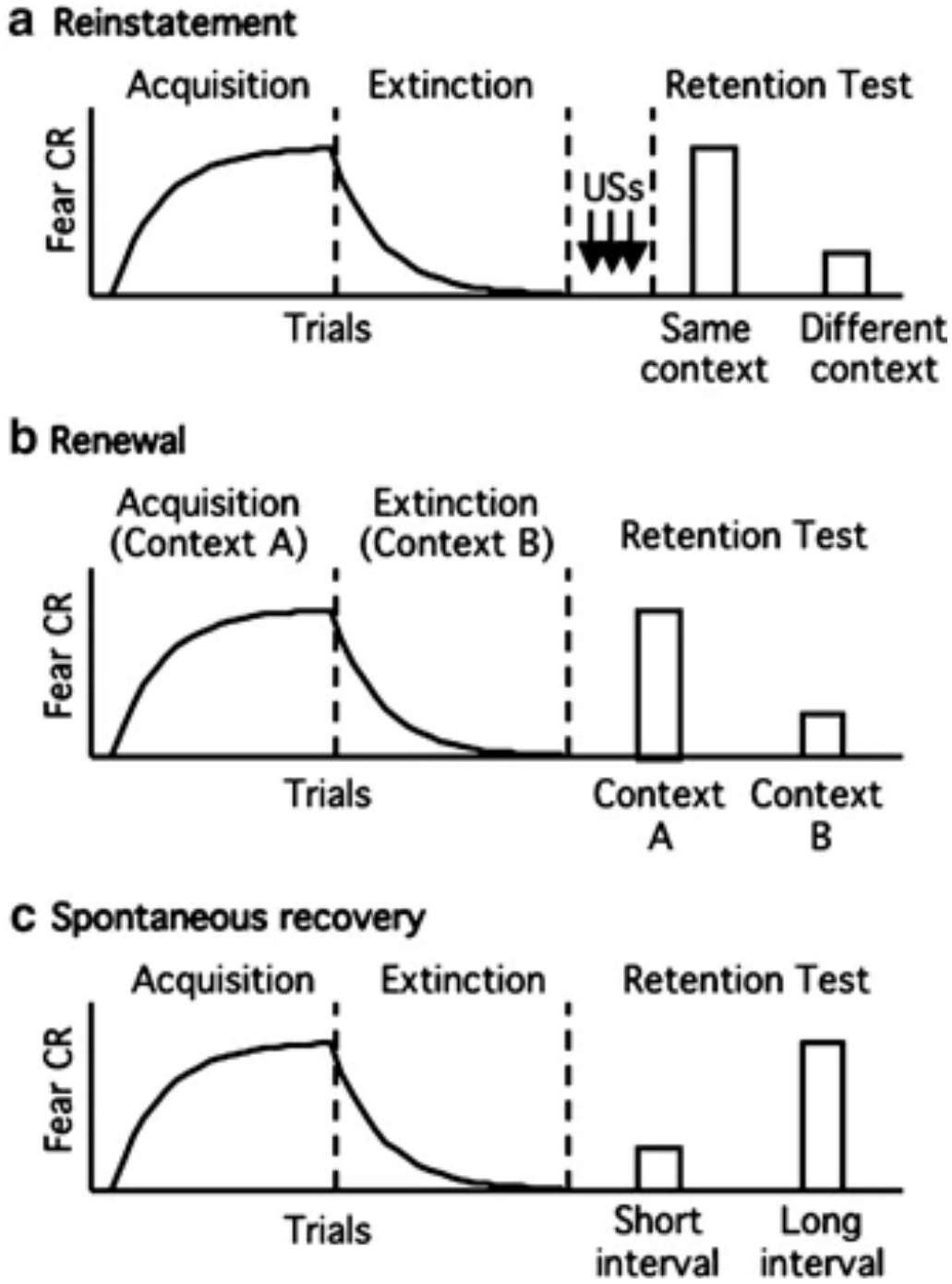


After extinction, the original CR can return under specific circumstances



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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
- Adaptive or maladaptive?

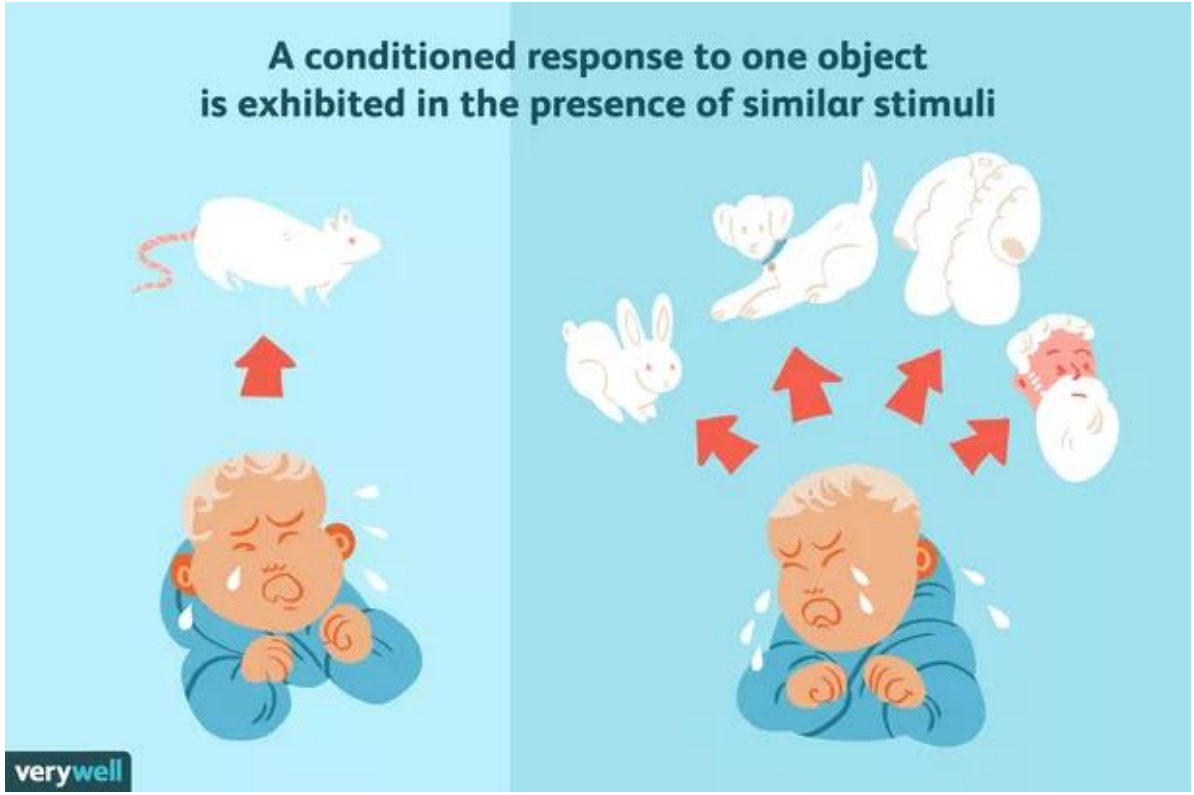


Illustration by Emily Roberts, Verywell

https://youtu.be/G5QAKnMf4Xc

Neural mechanisms of Pavlovian learning

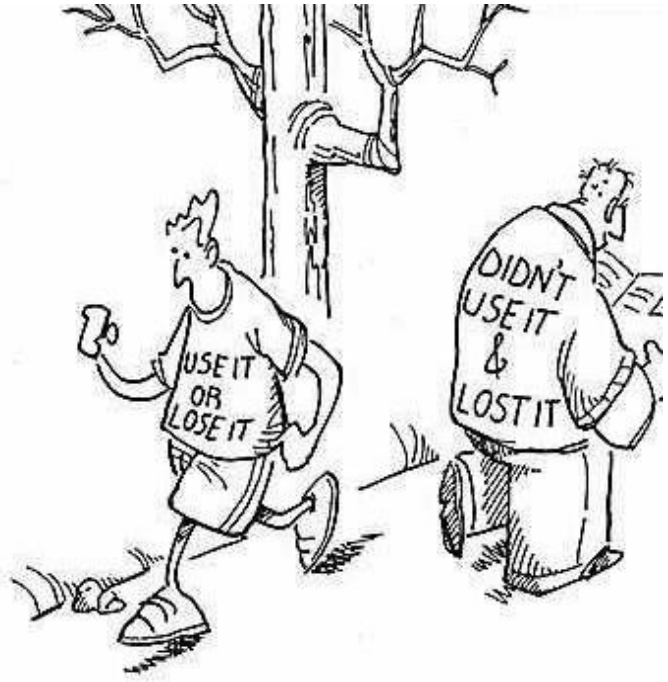
Aka

Pavlovian conditioning

Classical conditioning

Learning is the result of changes in the strength of synaptic interactions among neurons in neural networks

Plasticity: Neural connections can be modified by experience & learning



Changes in the strength of synaptic interactions can be:

- **Short-term changes:** functional physiological changes (lasting seconds to hours) that increase or decrease the effectiveness of existing synaptic connections. --> **Hebbian plasticity**

- **Long-term changes:** structural changes (lasting days) that can give rise to further physiological changes that lead to anatomical alterations, including pruning of preexisting synapses or growth of new ones.

Learning is the result of changes in the strength of synaptic interactions among neurons in neural networks

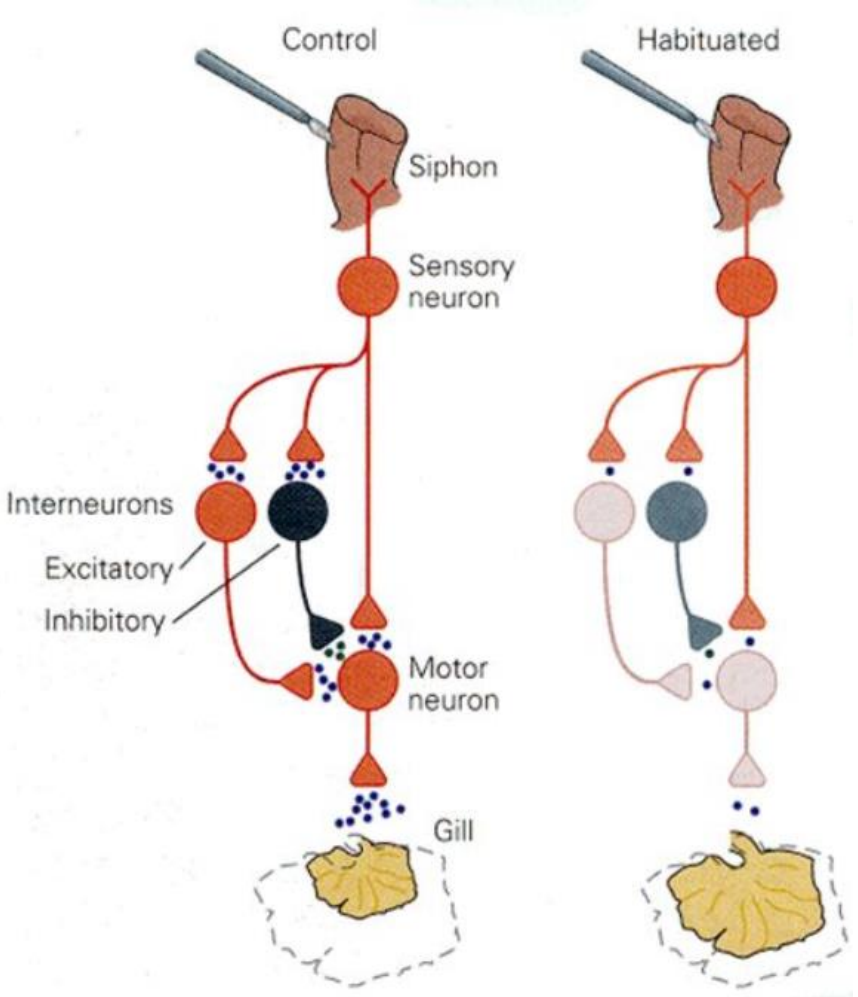
https://www.pbslearningmedia.org/resource/nvfb-sci-memhackers/wgbh-nova-memory-hackers-full-length-broadcast/

Minute 10.45-21.20: memory formation, sensitization of gill withdrawal reflex in aplysia

Learning is the result of changes in the strength of synaptic interactions among neurons in neural networks

Non-associative learning: habituation and sensitization of the gill withdrawal reflex in Aplysia Californica

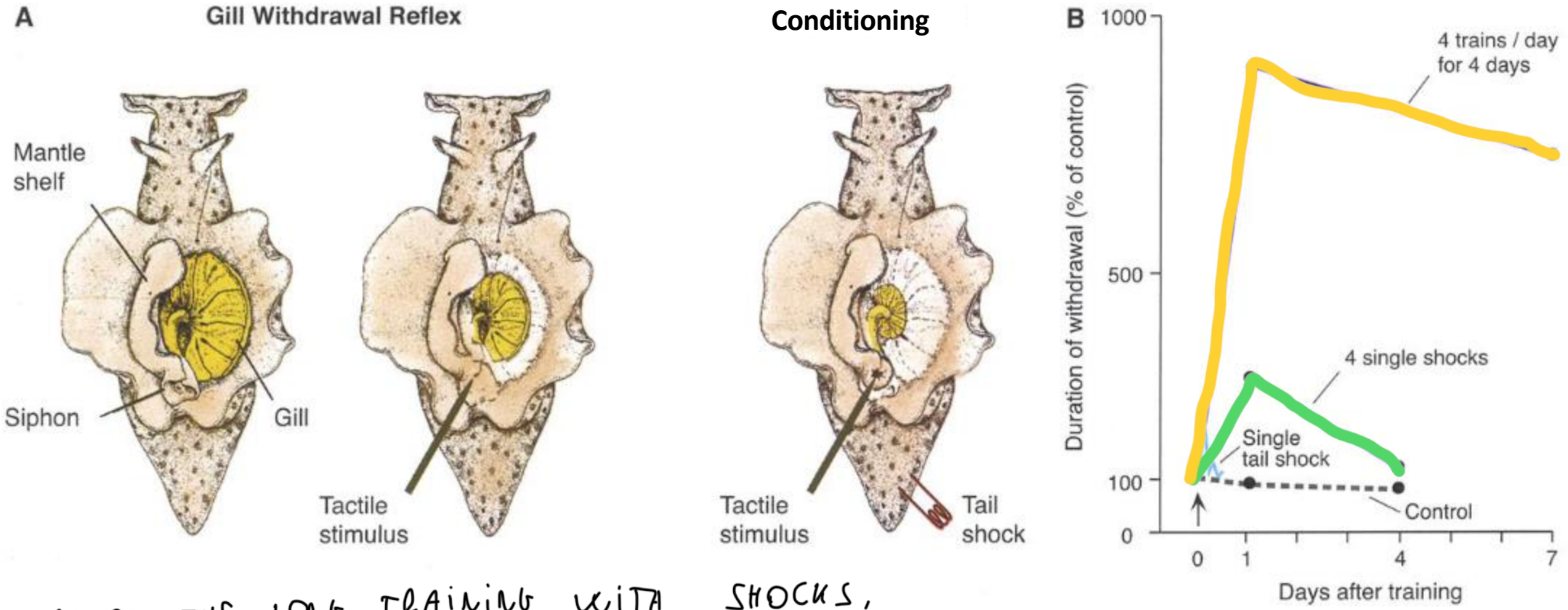
- Repeated mild stimulation of the syphon induces habituation of the reflex relative to control stimulation
- Repeated intense stimulation of the siphon induces sensitization of the reflex relative to control stimulation



Learning is the result of changes in the strength of synaptic interactions among neurons in neural networks

BEFORE LONGER TRAING
BEFORE SOME SHOCKS
THE LONGER WE PERCEIVE AND THE BETTER WE LEARN

Pavlovian conditioning of the gill withdrawal reflex in Aplysia Californica

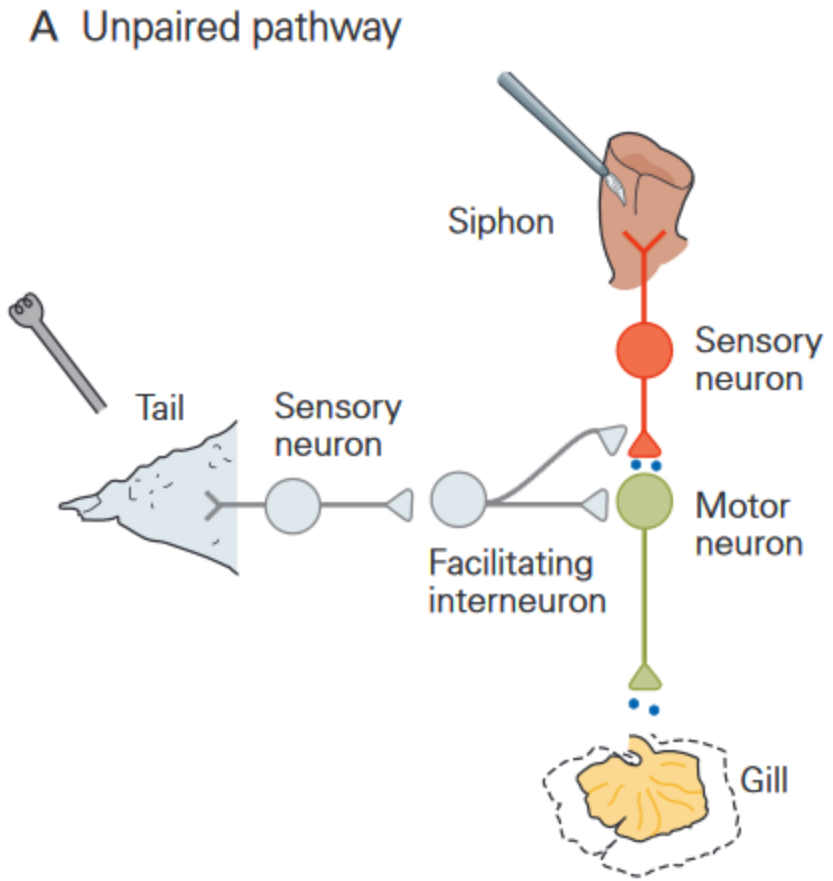


AFTER THE LONG TRAINING WITH SHOCKS, JUST A NORMAL TOUCH OF THE SIPHON CAUSES A LARGE RESPONSE ITSELF

Learning is the result of changes in the strength of synaptic interactions among neurons in neural networks

Pavlovian conditioning of the gill withdrawal reflex in Aplysia Californica

- Tactile stimulation of the syphon is paired with shock to the tail
- **Before conditioning, a weak touch to the siphon causes only a weak withdrawal reflex.**



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Pavlovian conditioning of the gill withdrawal reflex in Aplysia Californica

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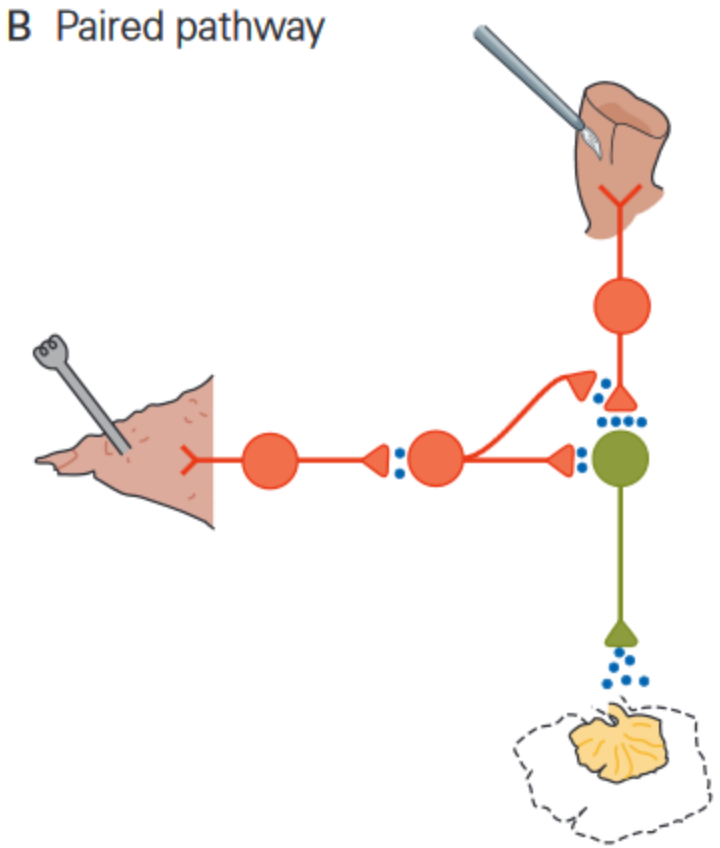
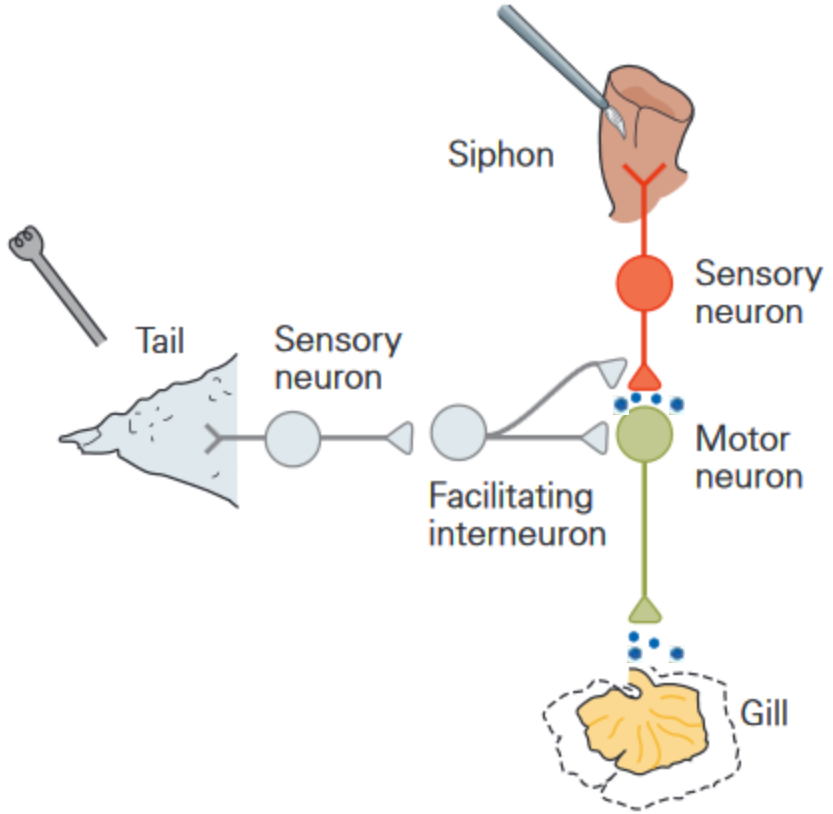
- Before conditioning, a weak touch to the siphon causes only a weak withdrawal reflex.
- **During conditioning, pairing of a noxious shock to the tail with touch to the syphon produces a much larger withdrawal response**



Learning is the result of changes in the strength of synaptic interactions among neurons in neural networks

Pavlovian conditioning of the gill withdrawal reflex in Aplysia Californica

- Tactile stimulation of the syphon is paired with shock to the tail
- Before conditioning, a weak touch to the siphon causes only a weak withdrawal reflex.
- Pairing of a noxious shock to the tail with touch to the syphon produces a much larger withdrawal response.
- **After conditioning, touch of the syphon alone, produces a much larger withdrawal response, that lasts for days**



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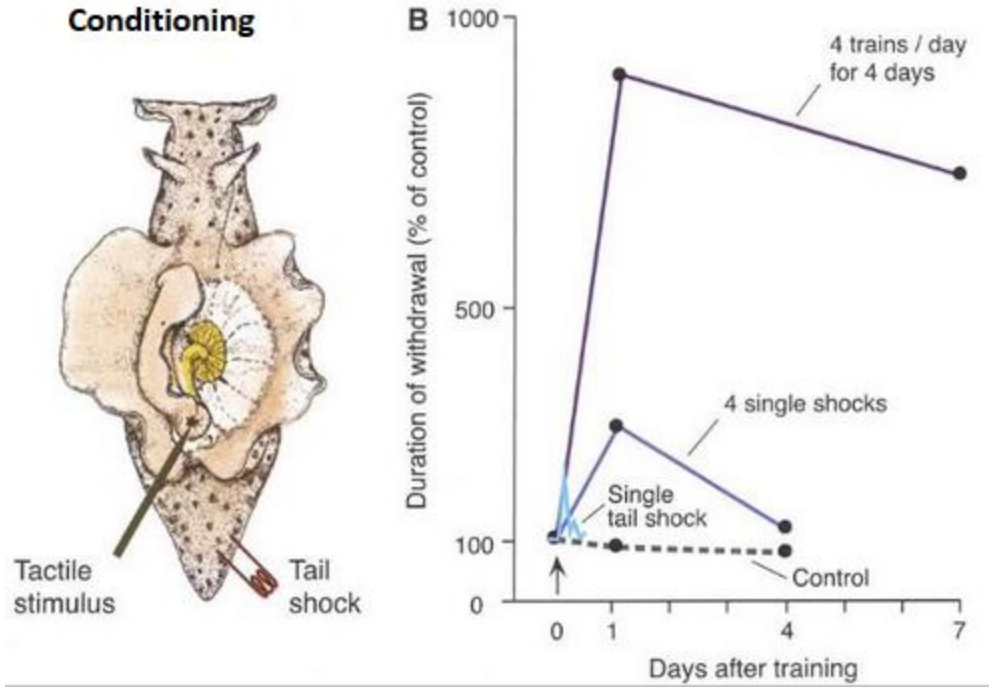

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In mammals, Pavlovian conditioning for aversive events involves the amygdala.

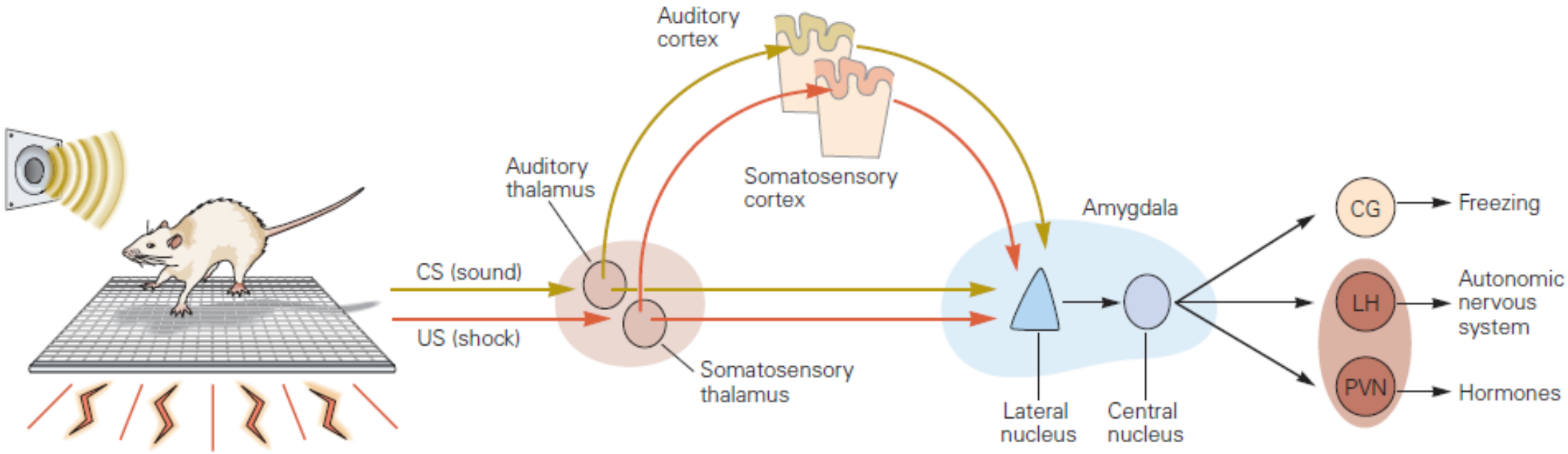

Figure 48–5 Neural circuits engaged during fear conditioning. The conditioned stimulus (**CS**) and unconditioned stimulus (**US**) are relayed to the lateral nucleus of the amygdala from the auditory and somatosensory regions of the thalamus and cerebral cortex. Convergence of the CS and US pathways in the lateral nucleus is believed to underlie the synaptic changes that mediate learning (see Figure 48–6). The lateral nucleus communicates with the central nucleus both directly and through intra-amygdala pathways (not shown) involving the basal and intercalated nuclei. The central nucleus then connects with regions that control various motor responses, including the central gray region (**CG**), which controls freezing behavior, the lateral hypothalamus (**LH**), which controls autonomic responses, and the paraventricular hypothalamus (**PVN**), which controls stress hormone secretion by the pituitary-adrenal axis. (Reproduced, with permission, from Medina et al. 2002.)

Hebbian plasticity

In "The Organization of Behaviour" (1949) Hebb proposed a mechanism to explain synaptic plasticity

Hebb's Law: **Neurons that fire together, wire together**

It describes how when a cell persistently activates another nearby cell, the connection between the two cells becomes stronger

Donald Hebb
(1904-1985)

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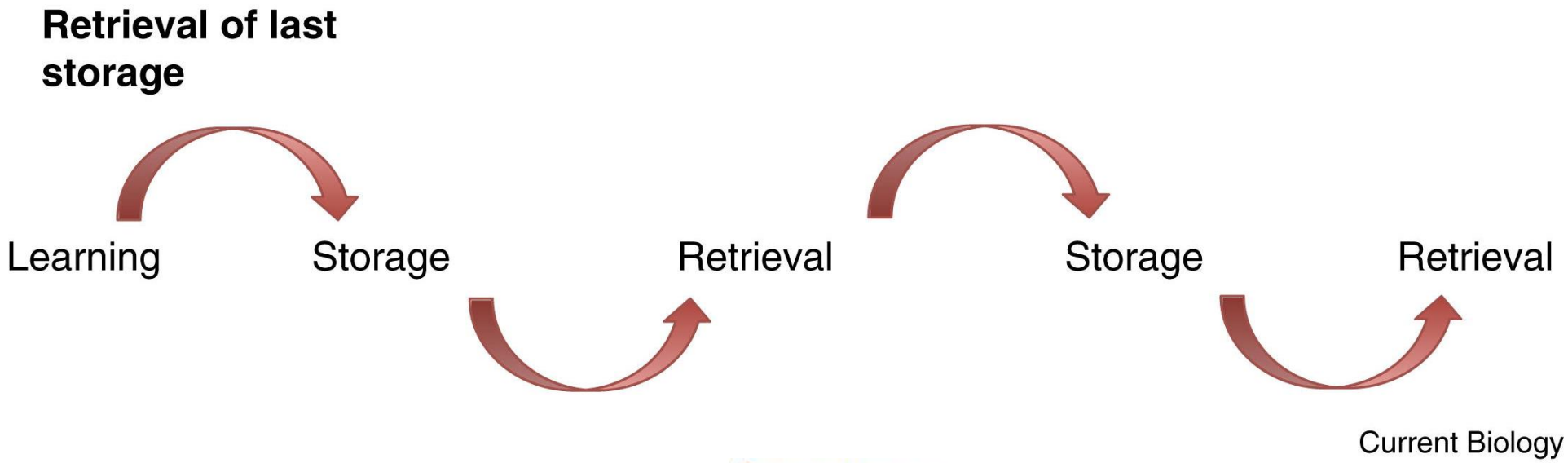
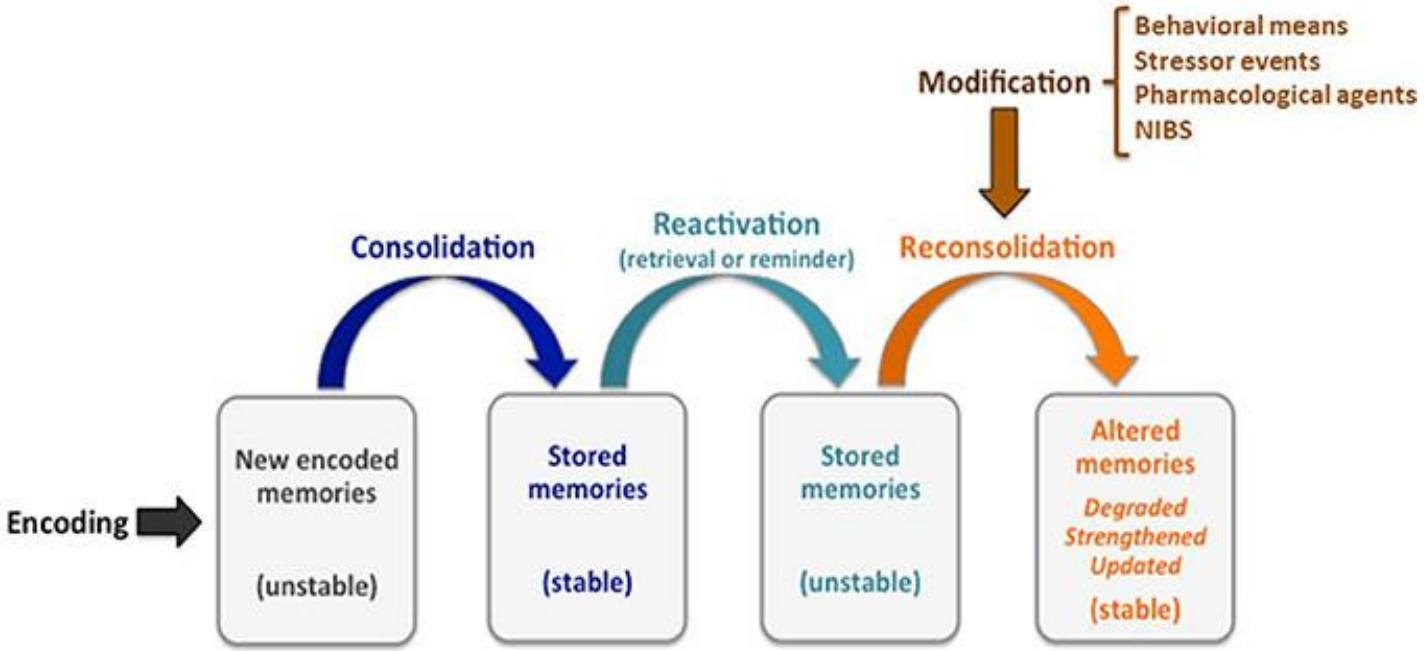
Minute 10.45-21.20: memory formation, sensitization of gill withdrawal reflex in aplysia

Minute 21.20-30.00: memory reconsolidation: animal studies

WE COULD RECONSIDER TRAUMATIC MEMORIES IN ORDER NOT TO BE PAINFUL ANYMORE

Memory reconsolidation: memories are vulnerable to alteration





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

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Minute 10.45-21.20: memory formation, sensitization of gill withdrawal reflex in aplysia

Minute 21.20-30.00: memory reconsolidation: animal studies

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

STEPS:
1) TRIGGER THE FEAR MEMORY → START RECONSOLIDATION
2) TAKE A DRUG (PROPANOLOL) THAT BLOCKS THE PRODUCTION OF SOME ORMONS → BLOCK THE NEW FEAR MEMORY TO CONSOLIDATE
3) THE FEAR SEEMS TO BE DELETED → WE CAN'T BE SURE ABOUT THAT BECAUSE WE CAN ONLY OBSERVE THE NEW BEHAVIOUR

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

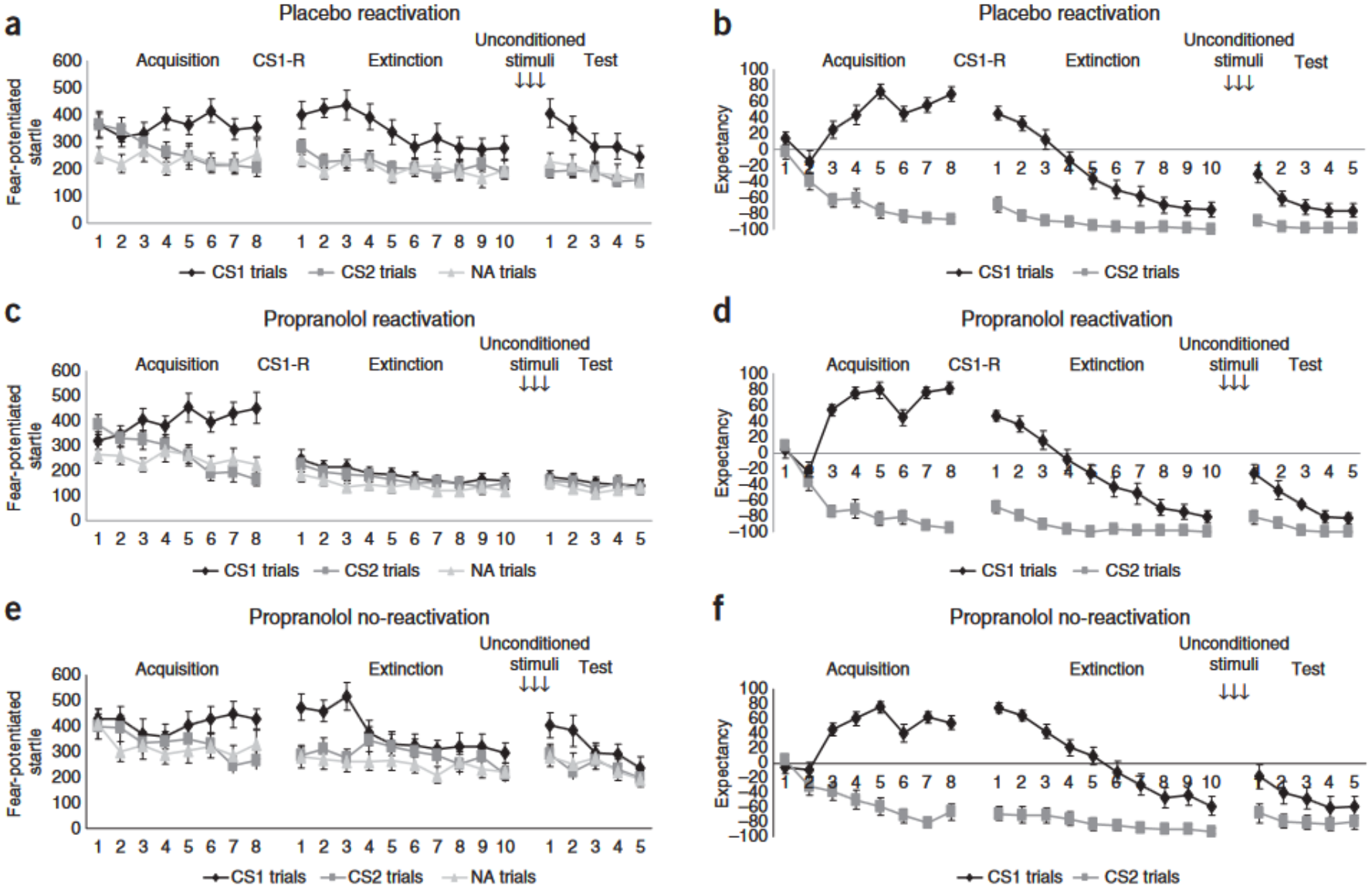

Figure 1 Propranolol disrupts the reconsolidation of a fear memory, but not declarative memory. (**a**–**f**) Mean startle potentiation to the fear-conditioned stimulus (CS1), the control stimulus (CS2) and noise alone (NA) trials (left) and mean expectancy scores of the unconditioned stimulus to CS1 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.

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

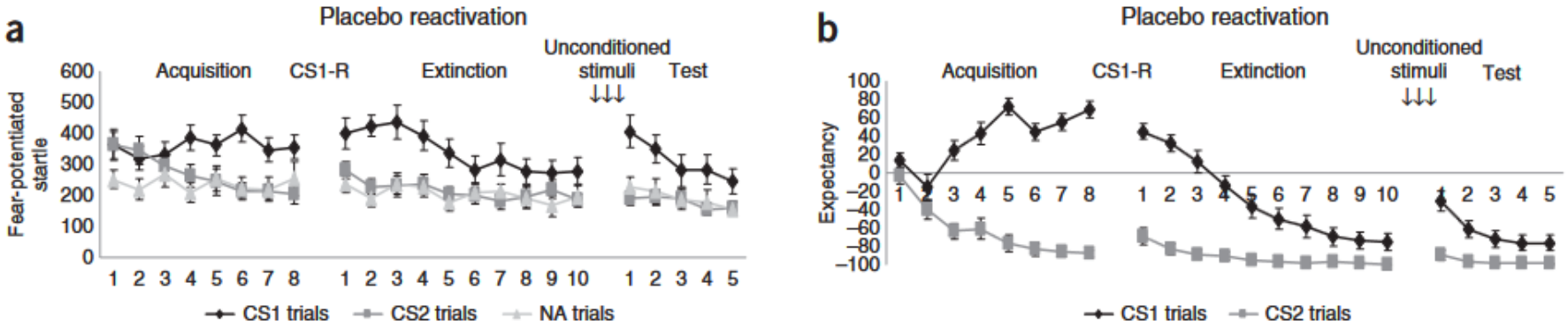

Figure 1 Propranolol disrupts the reconsolidation of a fear memory, but not declarative memory. (**a**–**f**) Mean startle potentiation to the fear-conditioned stimulus (CS1), the control stimulus (CS2) and noise alone (NA) trials (left) and mean expectancy scores of the unconditioned stimulus to CS1 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.

Recommended readings

- Daw, N. D., & O'Doherty, J. P. (2014). Multiple systems for value learning. In *Neuroeconomics* (Chapter 21, pp. 393-410). Academic Press.
- 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 66 (this chapter provides more details than what we went through)