# Lecture 18. Learning 3- Synaptic Plasticity and Learning

*Professor Christiane Linster*

## Pre-lecture preparation

(1) Watch pre-lecture video on fear conditioning
(2) Review lecture 18
(3) Read pages 633-635; Figure 18.10

## Learning Objectives

To understand the nature of long term potentiation (LTP) and long term depression (LTD)

(1) Be able to understand how LTP/LTD could be involved in learning
(2) Be able to suggest experiments to test if LTP/LTD are involved in a specific behavioral learning task
(3) Be able to relate experimental evidence to brain circuits underlying learning
(4) Be able to understand original literature
(5) Understand how classical conditioning and plasticity are present in our daily life

## Lecture Outline

(1) Experiments to study learning in animals use a number of different approaches to investigate how neural processes and learning processes interact and influence each other. Classical fear conditioning is one of these paradigms. Because it is relatively simple, the circuitry involved has been well worked out and we can use it to illustrate the neural processes underlying learning (Figure 18.10 and associated text).
(2) Investigating learning at the neural level can be done in a number of ways including lesioning of brain areas, activation of pathways, recording of neural activity and more. We will discuss a number of experimental approaches converging on a clear model of how fear conditioning in the amygdale works.
(3) Learning processes such as fear conditioning affect our daily life; we will discuss several aspects of this

## Study Questions

(1) How can experiments in brain slices shed light on behavioral observations such as fear learning?

(2) What type of evidence could you collect to demonstrate the role of synaptic plasticity in a behavior?
(3) How could stress hormones for example affect learning?

# Lecture 17: Learning at the synaptic level: LTP and LTD

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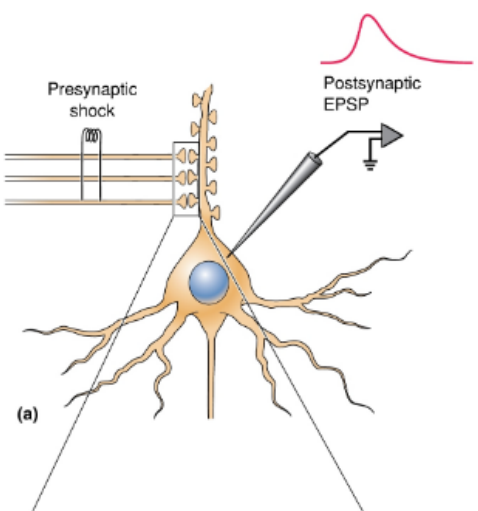
Office hours Wed. 1:30-2:30 or by appointment



# Lectures 16-21: Learning and memory

**Lecture 16** NMDA receptor allows to “associate” two events at the level of a synapse

**Lecture 17** Learning at the synaptic level: LTP and LTD

**Lecture 18** **Learning at the network level: how are LTP and LTD involved in changing networks ?**

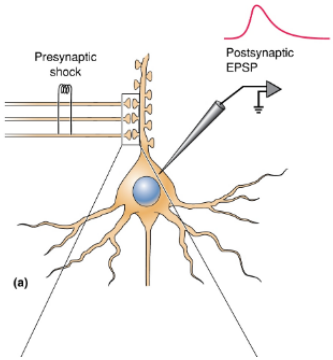
**Lecture 19** Learning while behaving: sequences of events and STDP

**Lecture 20** Remembering: Consolidation of what has been learned

**Lecture 21** What is a memory?

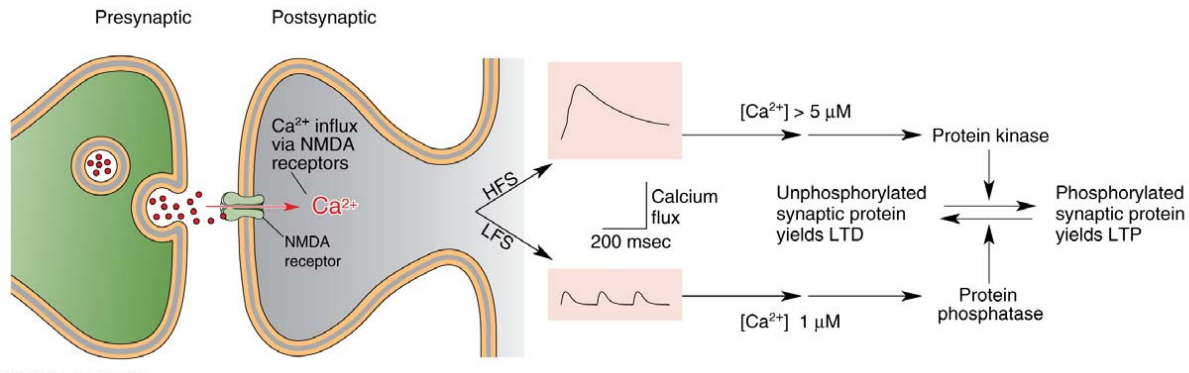
# Lecture 18: Learning 3

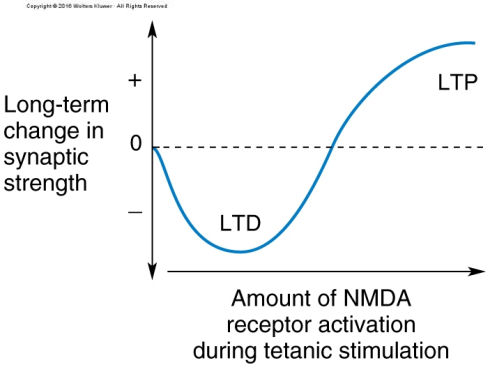
## Synaptic plasticity and learning



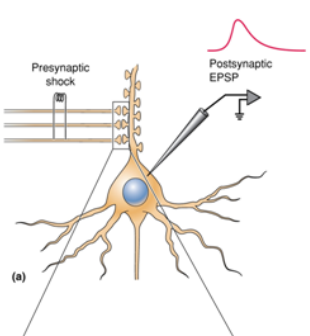

(1) Be able to understand how LTP/LTD could be involved in learning
(2) Be able to suggest experiments to test if LTP/LTD are involved in a specific behavioral learning task
(3) Be able to relate experimental evidence to brain circuits underlying learning
(4) Be able to understand original literature

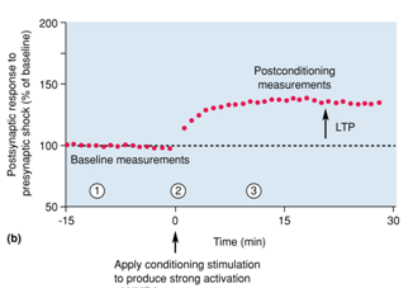
# Review

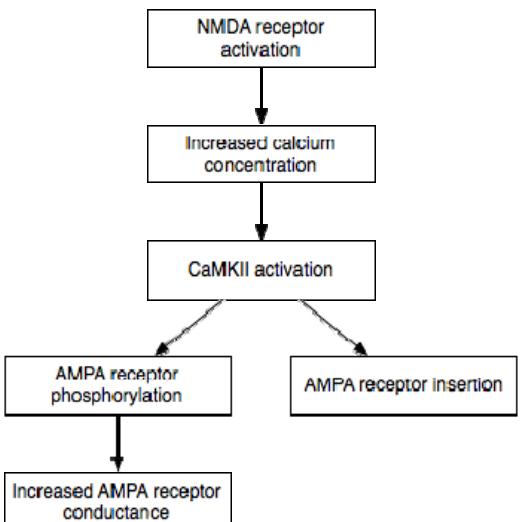



or stimulation frequency




NMDA receptor activation
Increased calcium concentration
CaMKII activation
AMPA receptor phosphorylation
AMPA receptor insertion
Increased AMPA receptor conductance

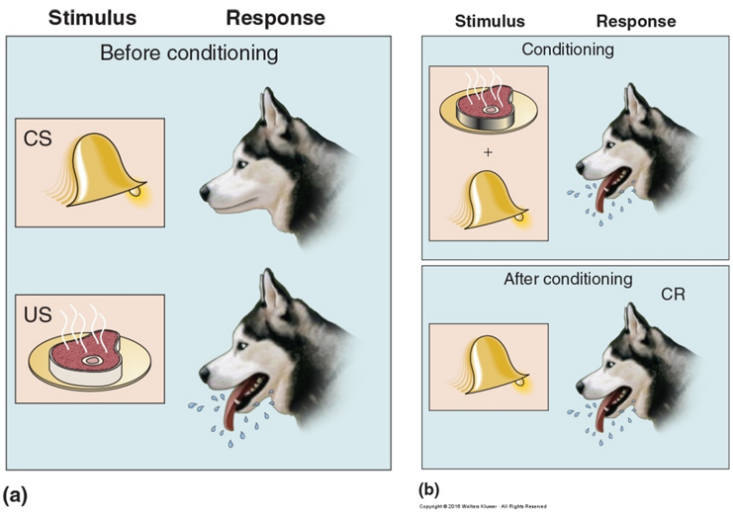
# Every day leaning

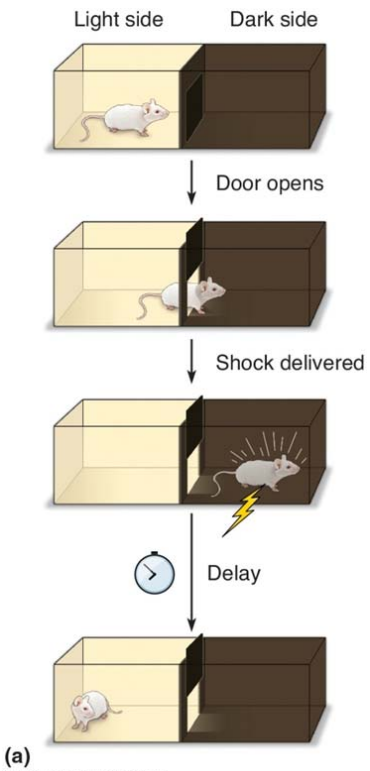


***https://slideplayer.com/slide/4282009/***

| | POSITIVE (ADDED) | NEGATIVE (SUBTRACTED) |
|---|---|---|
| **REINFORCEMENT (STRENGTHENS)** | •a coach pats you on the back after a good play<br>• a paycheck for working<br>• $10 for getting an "A" on your report card | •You leave early for school to avoid traffic<br>• You take Tylenol to remove back pain |
| **PUNISHMENT (WEAKENS)** | •Touch and hot stove and get burned<br>• Getting a ticket for speeding | • You lose your driving privileges for breaking curfew<br>• Loss of freedom to combat bad behavior |

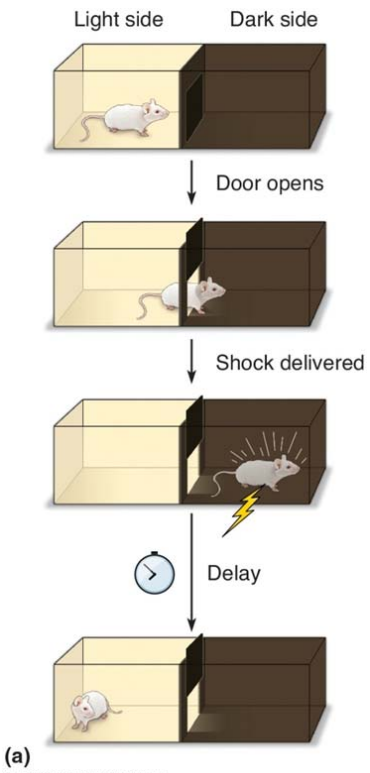
# Appetitive and aversive conditioning



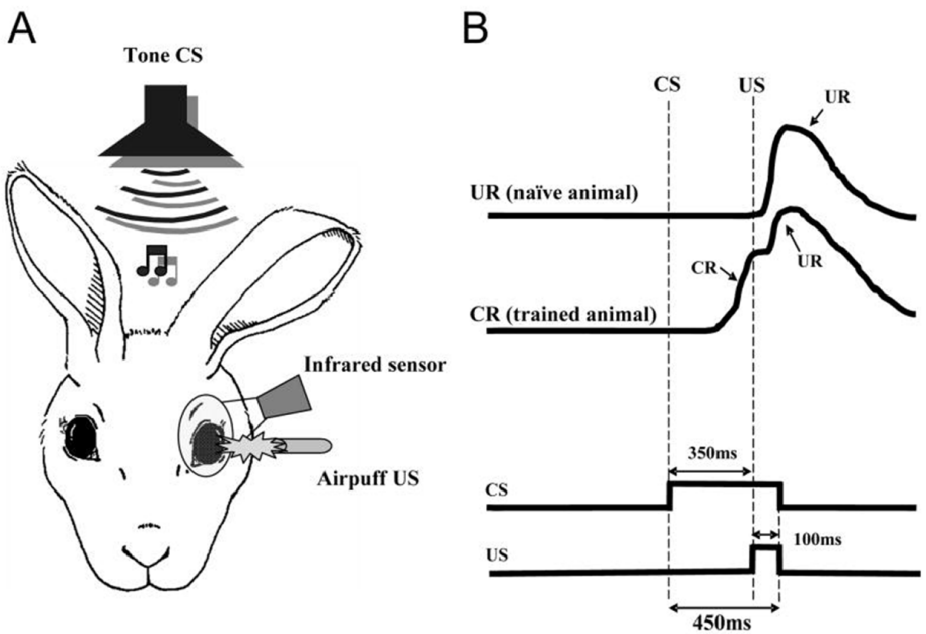
# Review

**This paradigm has been shown to involve LTP**



# How about LTD?

## Nictating membrane response and the cerebellum



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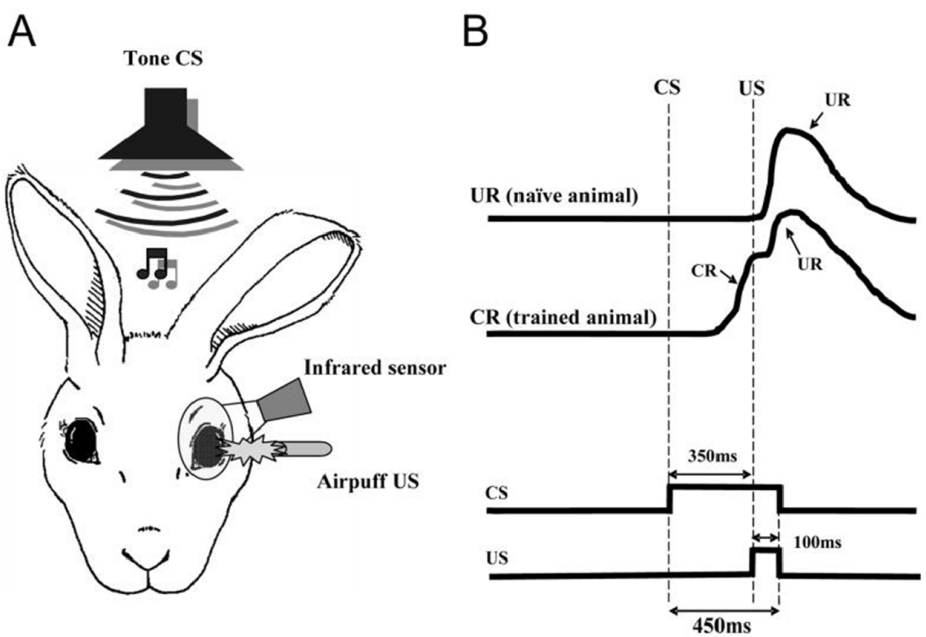


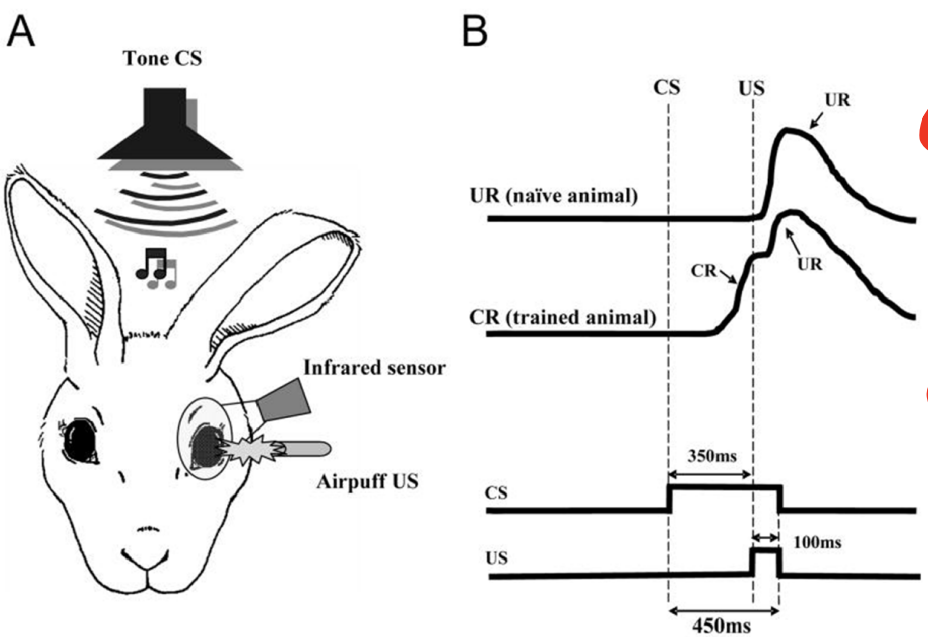

**Clicker question**

A. The air puff is the CS and the tone the US

B. The air puff is the US and the tone to CS

# How about LTD?

## Nictating membrane response and the cerebellum




**Clicker question**

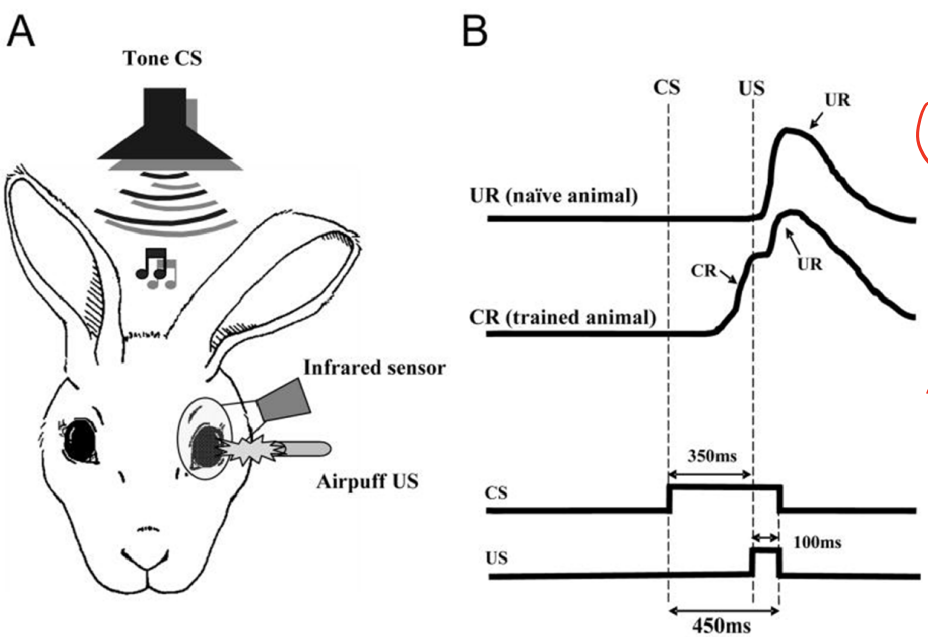
A. The air puff is the CS and the tone the US
B. The air puff is the US and the tone to CS

**You are recording from a neuron triggering the membrane response. Before conditioning you expect it to**

A. Spike in response to the tone
B. Spike in response to the air puff
C. Spike in response to both

# How about LTD?

## Nictating membrane response and the cerebellum

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# How about LTD?

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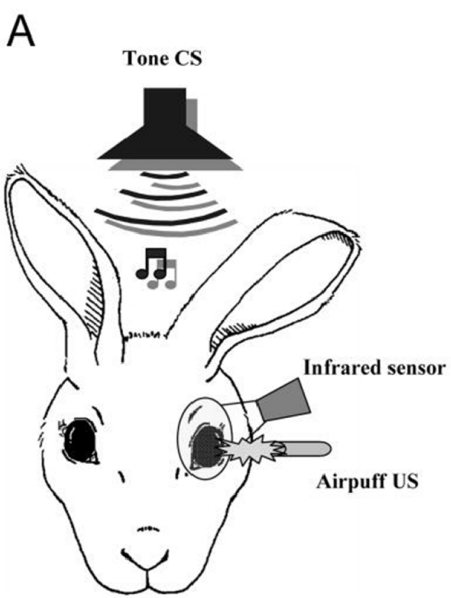


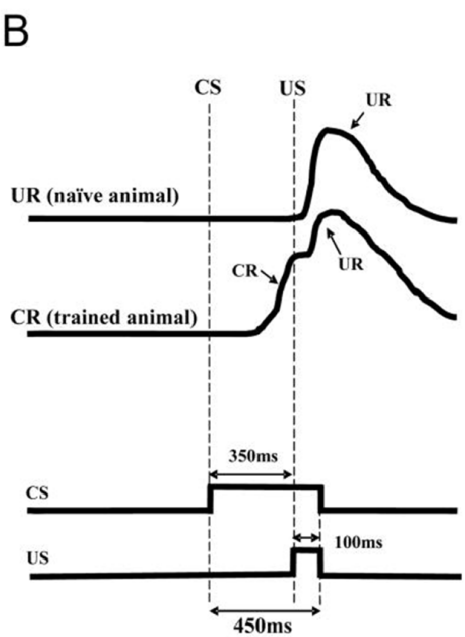


**Clicker question**

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B. The air puff is the US and the tone to CS

**You are recording from a neuron triggering the membrane response. BEFORE conditioning you expect it to**

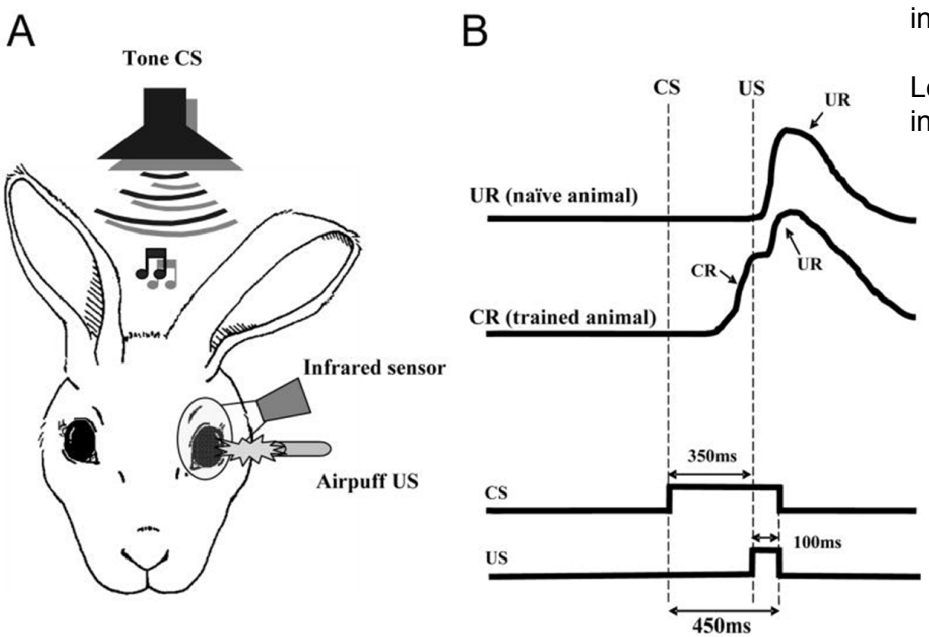
A. Spike in response to the tone
B. Spike in response to the air puff
C. Spike in response to both

**You are recording from a neuron triggering the membrane response. AFTER conditioning you expect it to**

Spike in response to the tone
Spike in response to the air puff
Spike in response to both

# How about LTD?

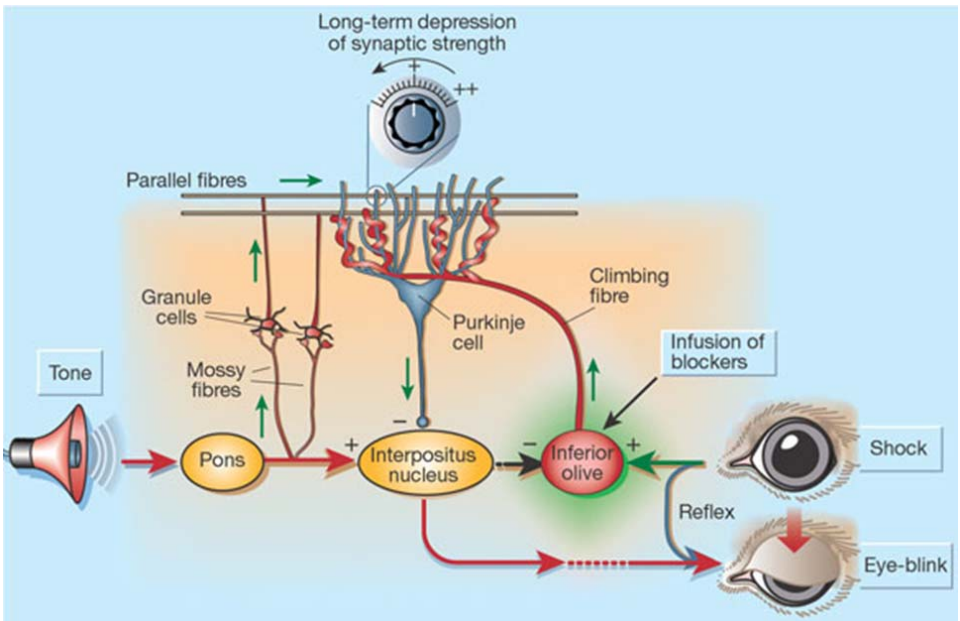
## Nictating membrane response and the cerebellum



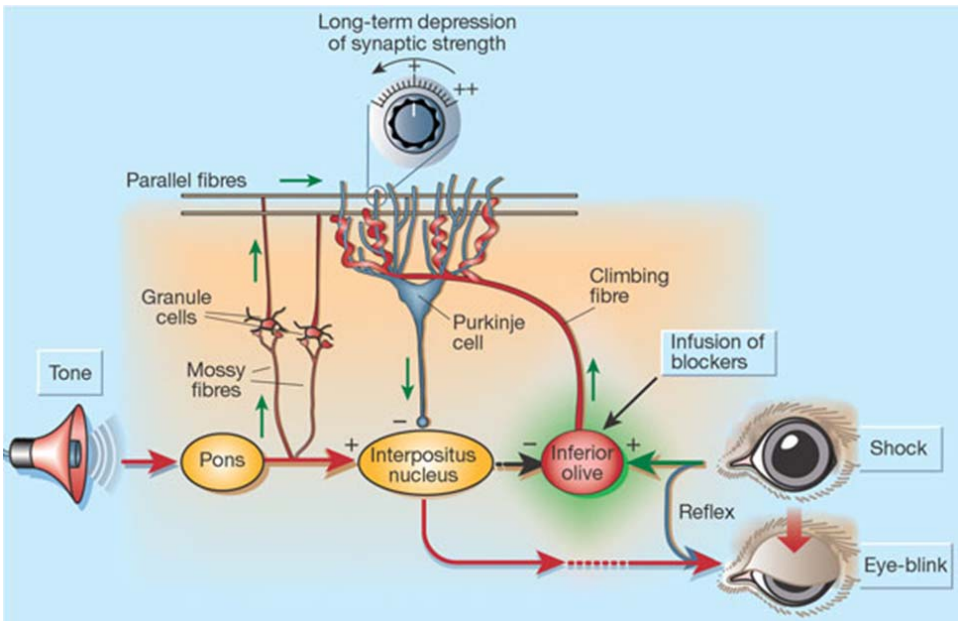

We are looking for an area in the brain in which somatosensory and auditory information converges.

Learning in this brain area should NOT interfere with the reflex response

# Cerebellum

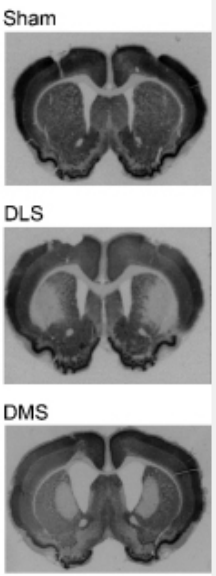

Long-term depression
of synaptic strength
+
++
Parallel fibres
Granule
cells
Mossy
fibres
Tone
Pons
Purkinje
cell
Climbing
fibre
Infusion of
blockers
Interpositus
nucleus
Inferior
olive
Shock
Reflex
Eye-blink

# Cerebellum




What type of evidence can we collect to show that cerebellum is involved in this learning process?

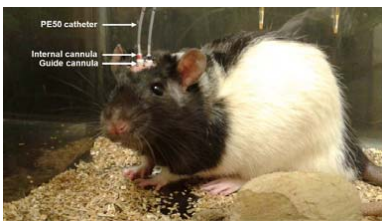
## (1) Lesions




*https://openi.nlm.nih.gov*

Electrical
Chemical
Mechanical

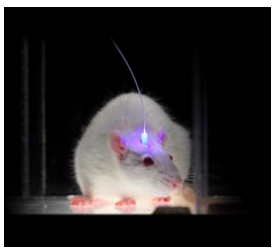
## (2) Pharmacology




*Researchgate.net*

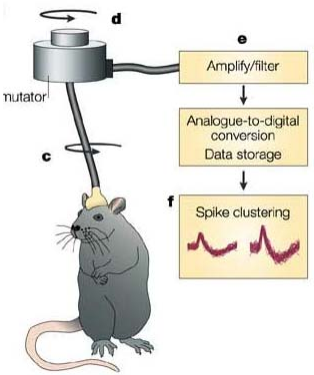
Agonists
Antagonists
Temporary inactivation
Neuromodulation

## (3) Optogenetics

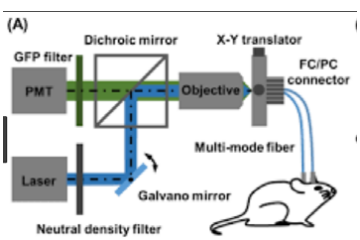


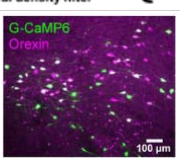
Fast time scale activation
or inactivation of
specific neural populations

## (4) Recordings

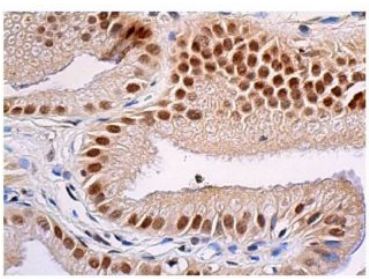



## (5) Imaging

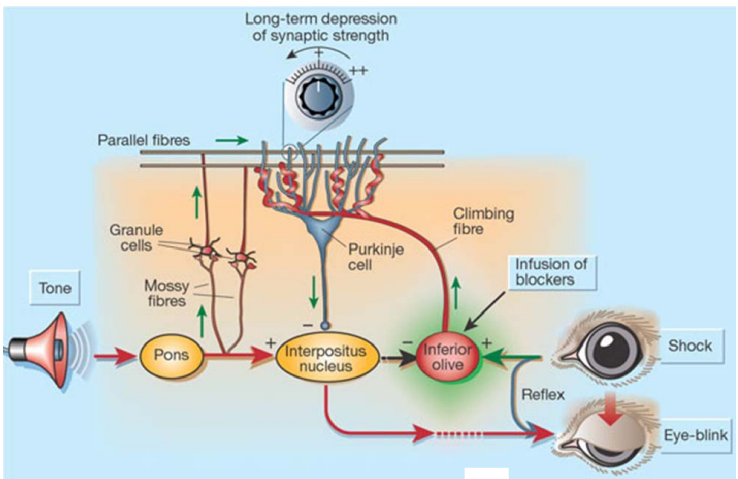



## (6) Mapping



# Cerebellar LTD mediates learning



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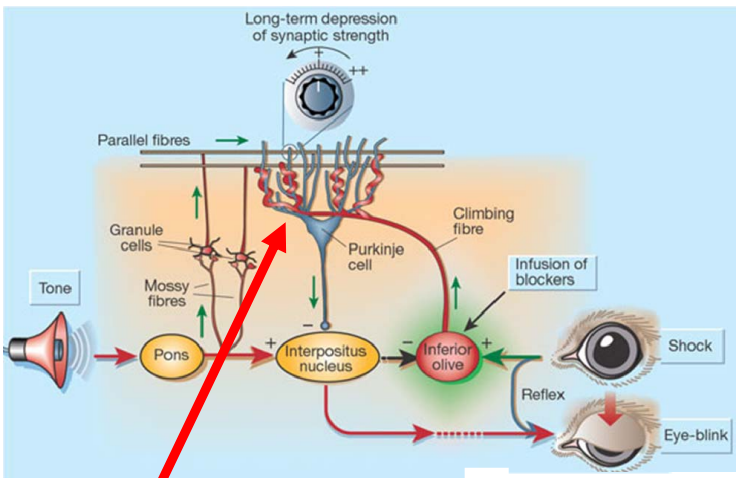


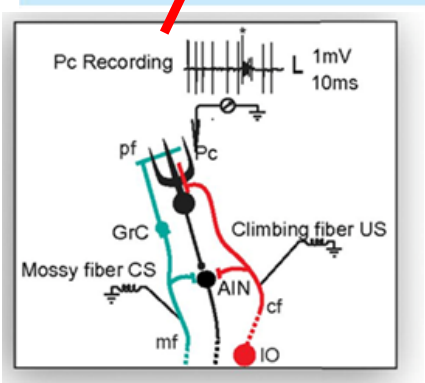


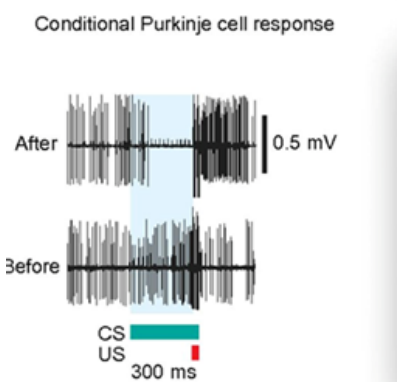

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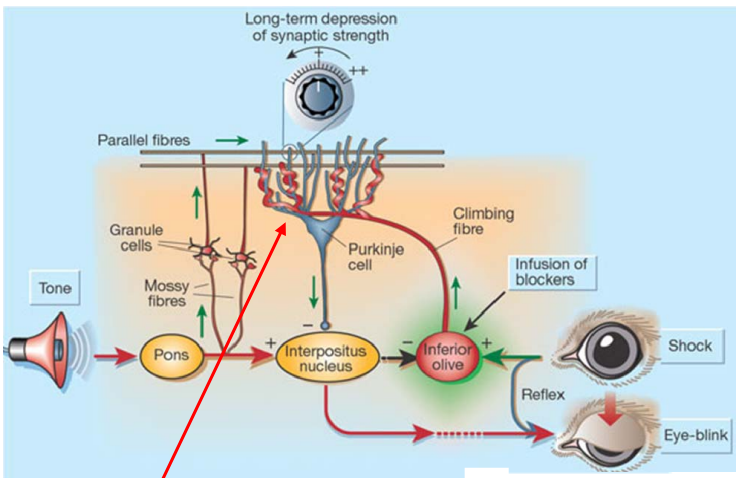


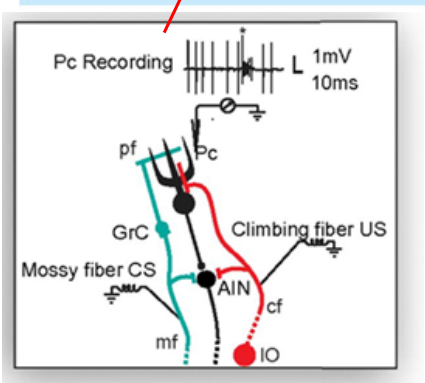


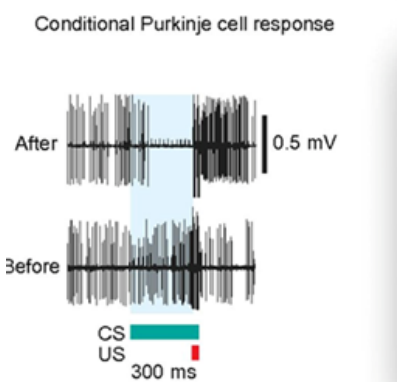


**Clicker question**

**Purkinje cell is**

A. Excited by CS after learning
B. Inhibited by CS after learning

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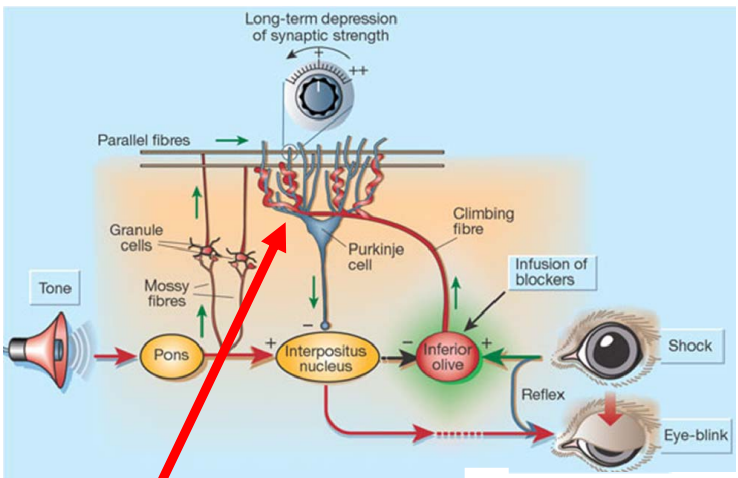


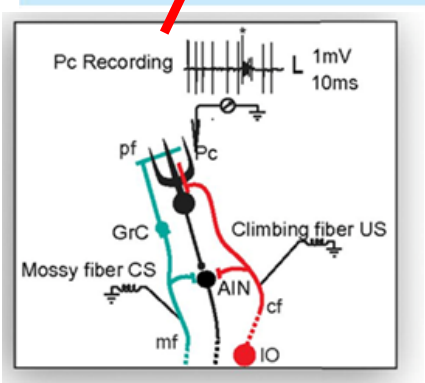


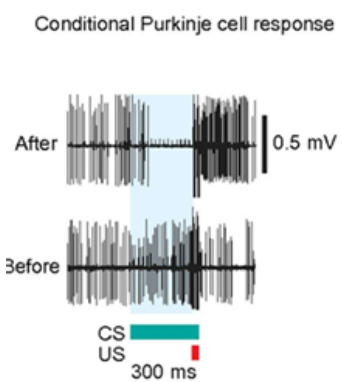


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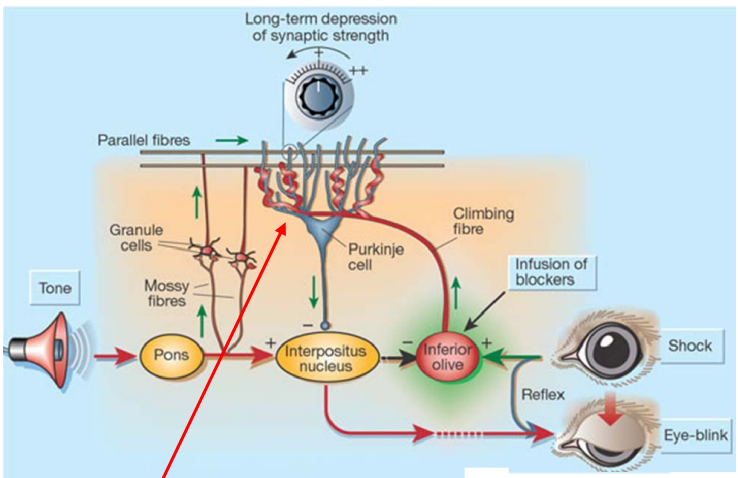
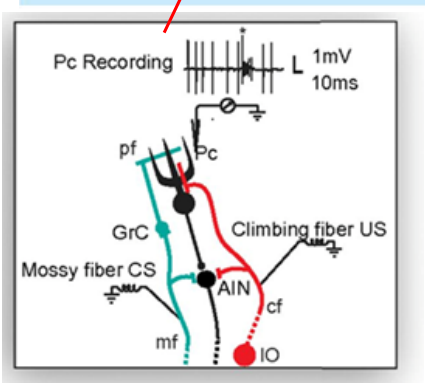
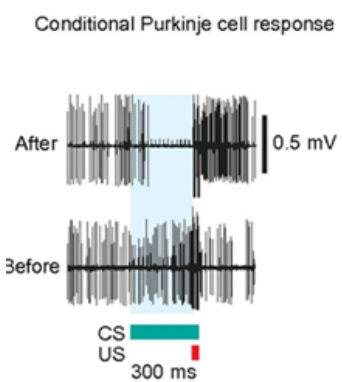
**The change of response from inhibited to responsive points to**

A. LTD
B. LTP

# Cerebellar LTD mediates learning

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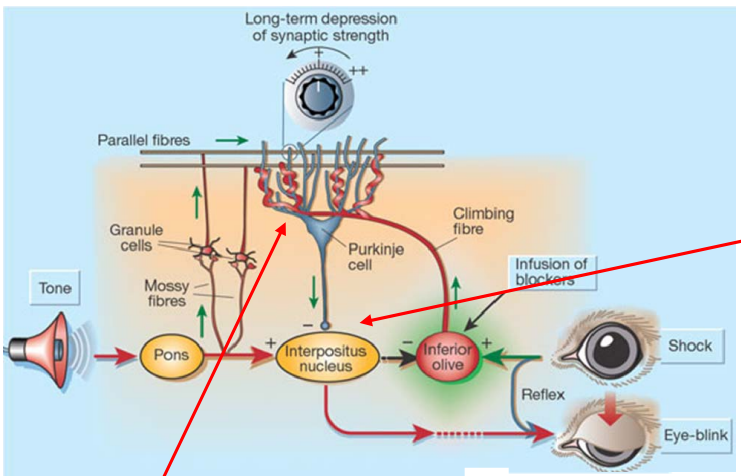
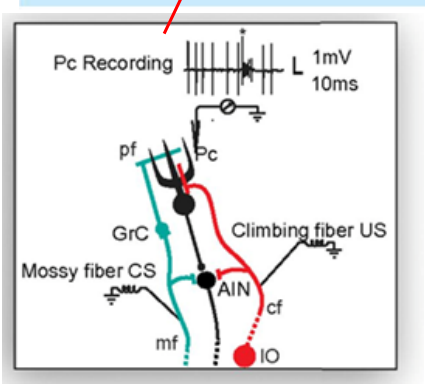
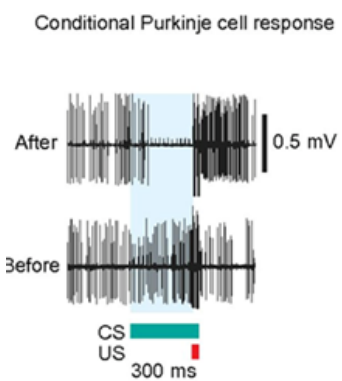
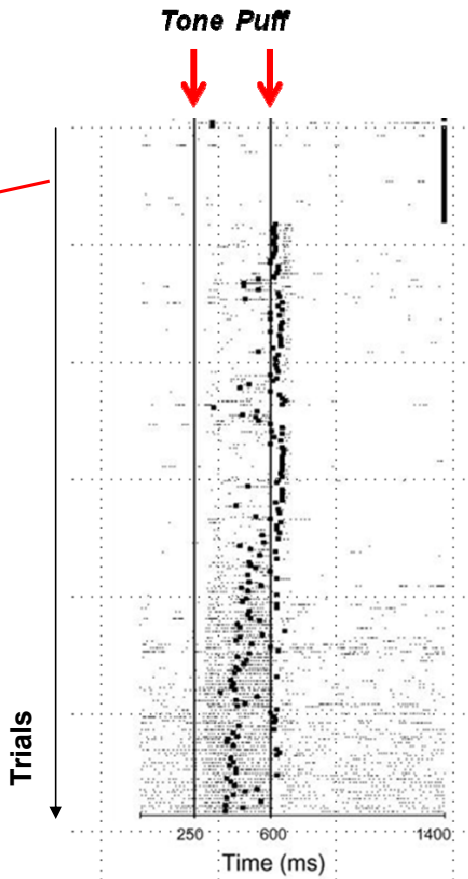
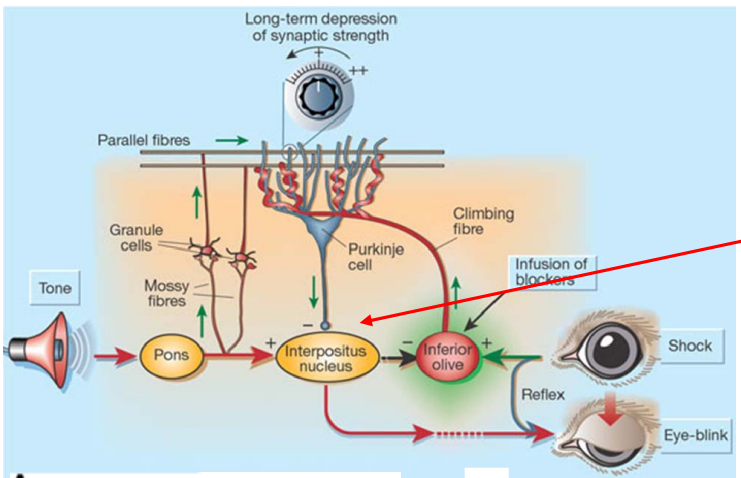


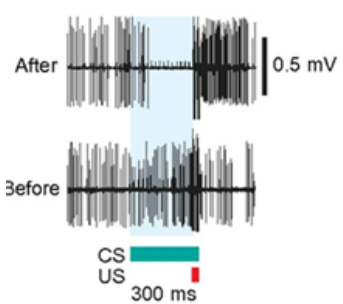



# Cerebellar LTD mediates learning

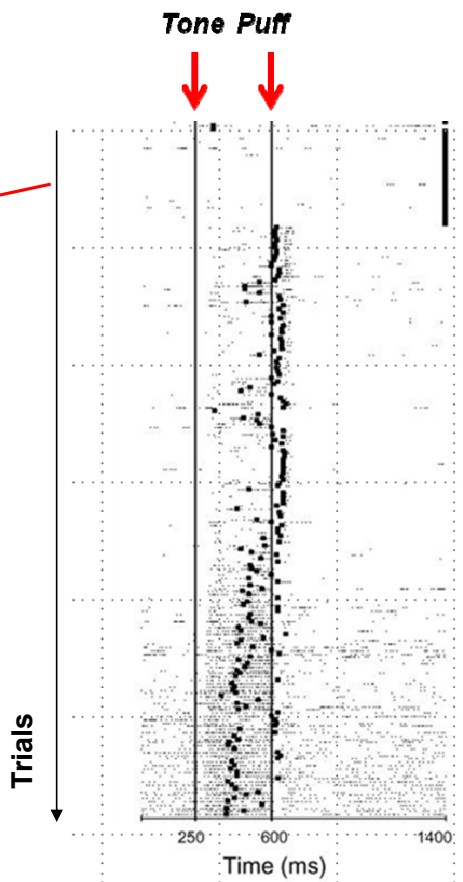



A Conditional Purkinje cell response

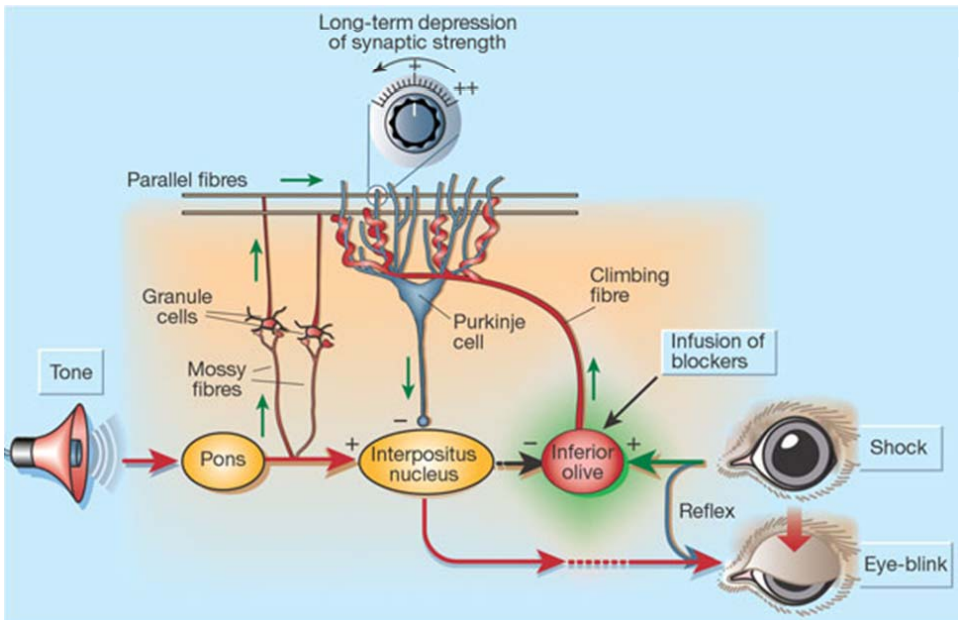



**Interpositus nucleus is excited by CS after conditioning**

**PC cell is disinhibited by CS after conditioning**

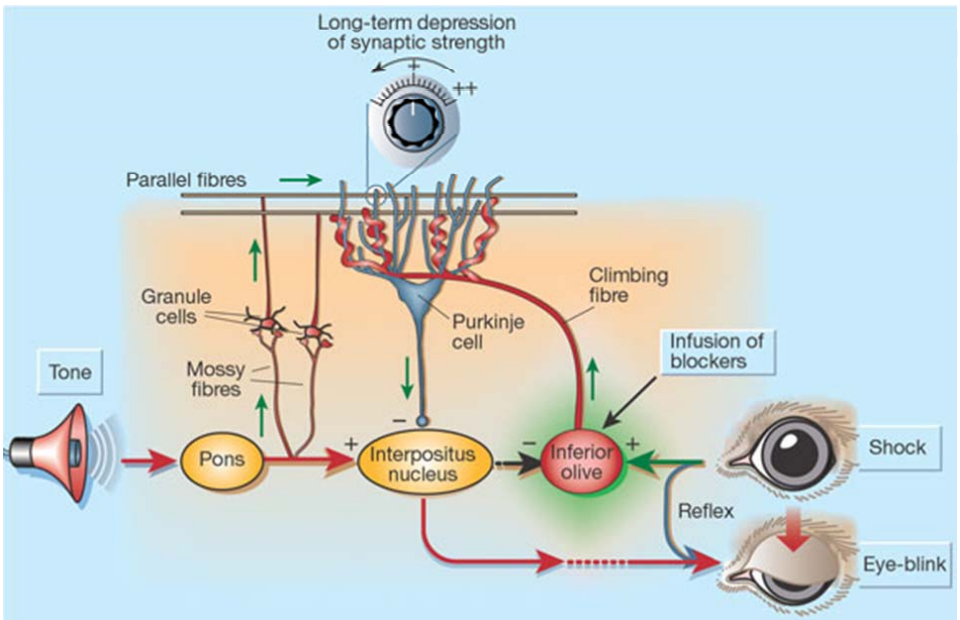


# Cerebellar LTD mediates learning




(1) Puff to eye elicits reflex response

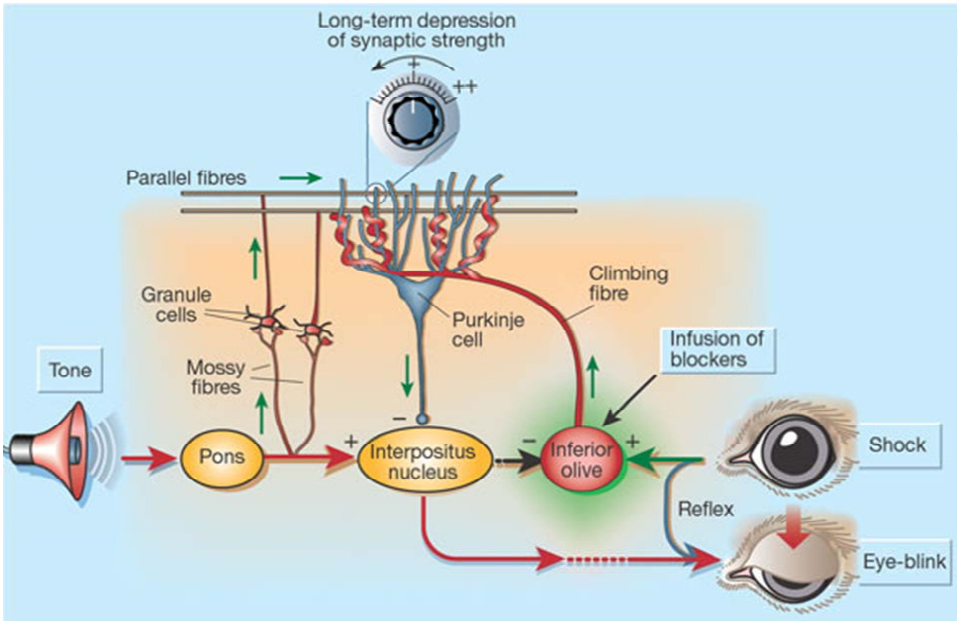
# Cerebellar LTD mediates learning




(1) Puff to eye elicits reflex response

(2) After pairing tone and puff, puff elicits conditioned response

# Cerebellar LTD mediates learning




(1) Puff to eye elicits reflex response

(2) After pairing tone and puff, puff elicits conditioned response

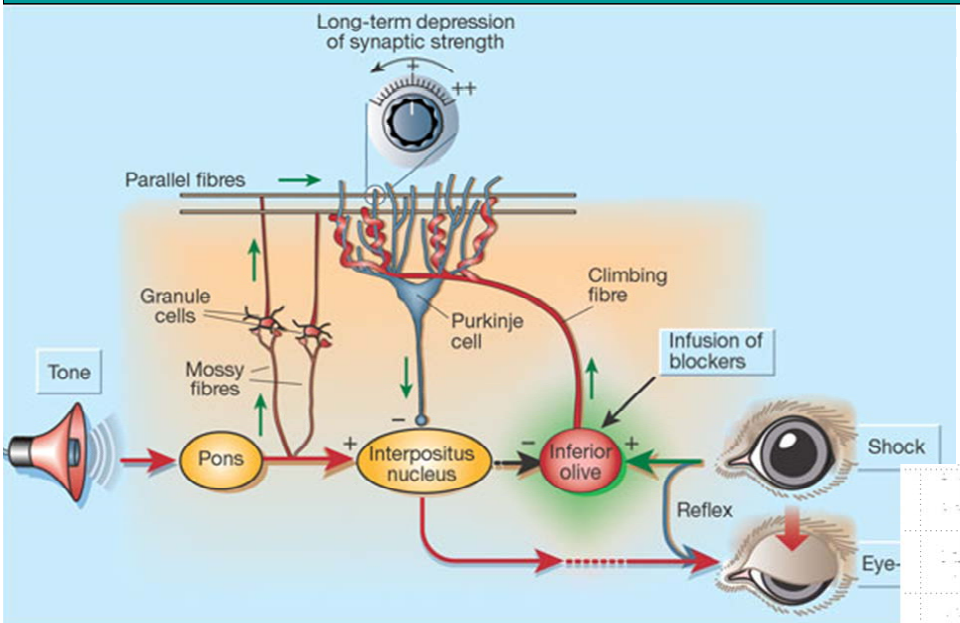
(3) Acquisition of CR:

Puff -> climbing fibers

Tone -> parallel fibers

LTD -> between parallel fibers and Purkinje cells leads to disinhibition of Interpositus nucleus and allows for CR

# Cerebellar LTD mediates learning

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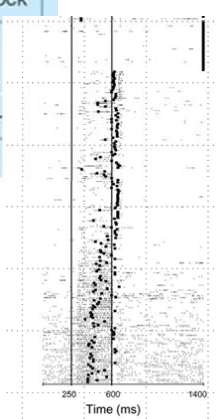



*You don't have to recall the names of brain areas*
*But you should know the pathways involved in the reflex response and in learning*

# Fear conditioning and amygdala

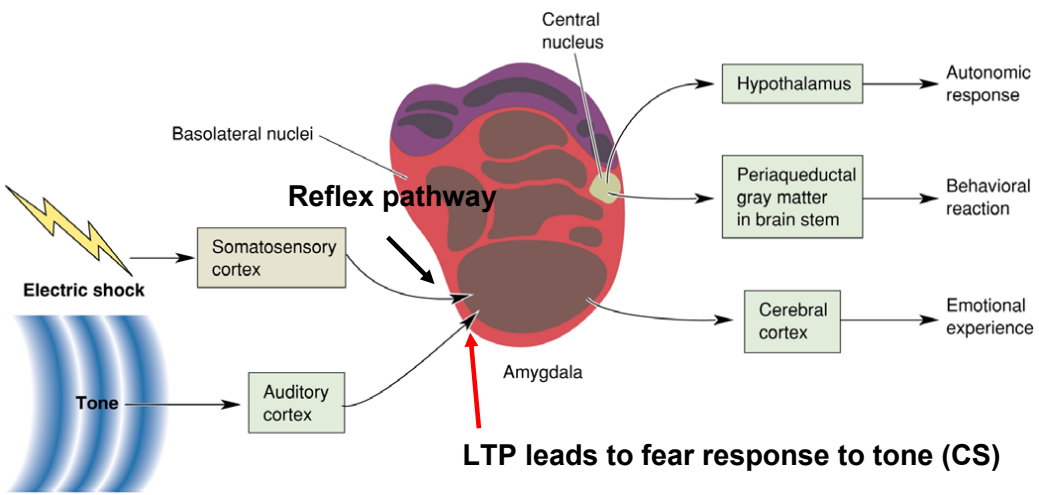
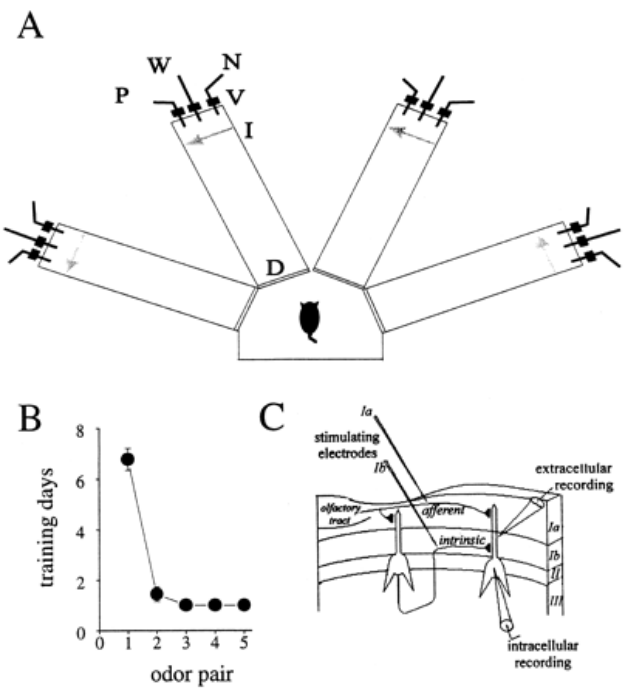


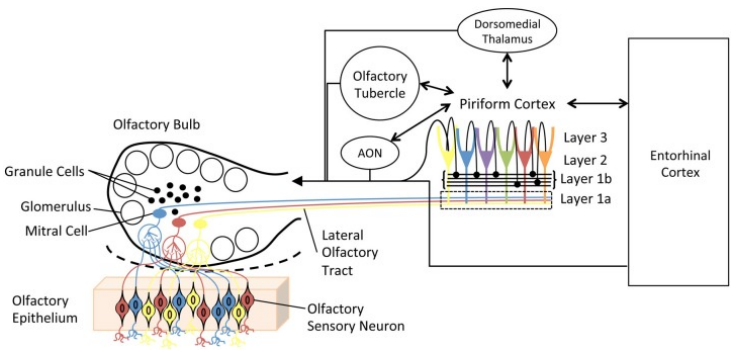

*Figure 18.10*

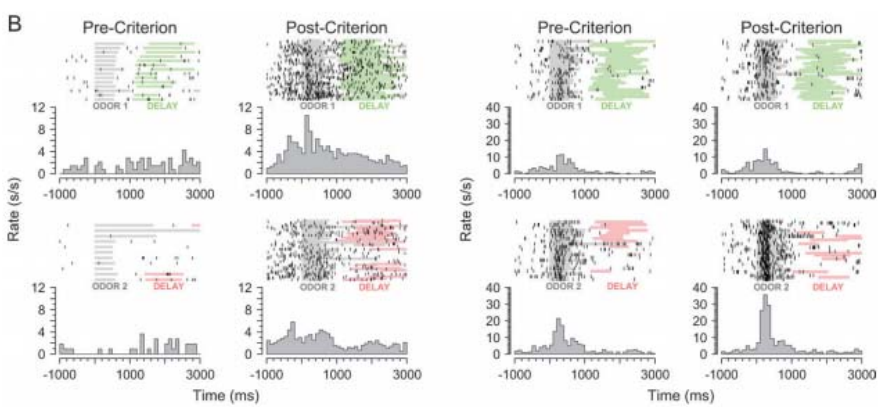
# Appetitive conditioning in olfactory cortex




*Saar et al. 1999*

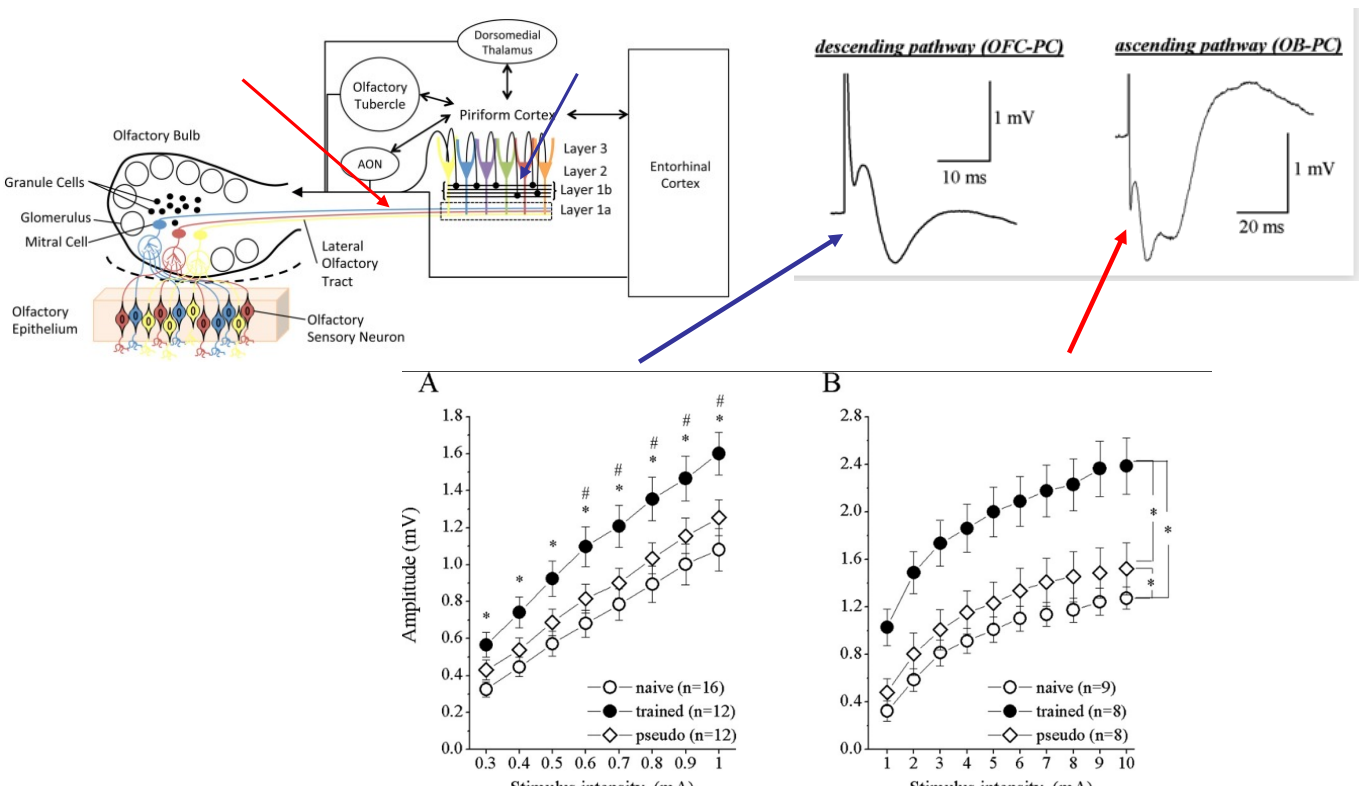
# Appetitive conditioning in olfactory cortex



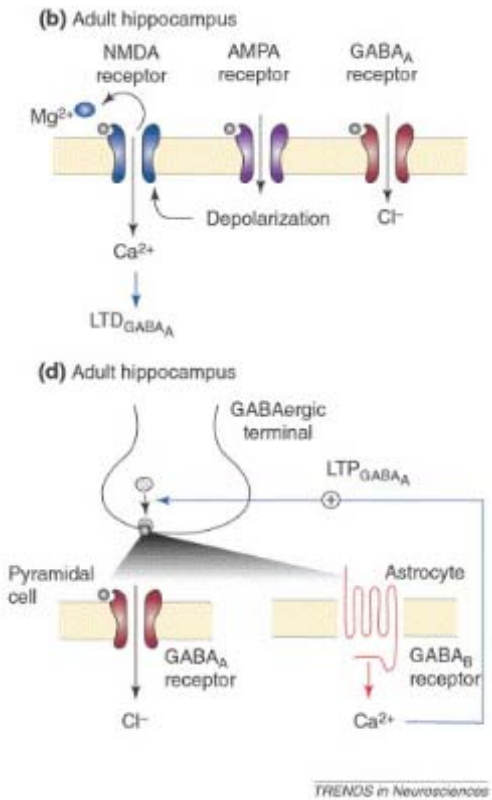




*Schoenbaum et al. 1999*

# Appetitive conditioning in olfactory cortex



# Plasticity on inhibitory synapses




(1) A postsynaptic rise in intracellular Ca2+ concentration ([Ca2+]I) is required to induce long-term plasticity at GABAergic synapses.

(2) (b) In the adult rat hippocampus, NMDA-dependent **LTD** can be induced at GABAergic synapses. At this later stage, however, activation of AMPA receptors provides the depolarization that leads to the unblocking of NMDA-receptor channels.

(3) (d) In the adult hippocampus, GABA released from GABAergic terminals activates GABAA receptors on pyramidal cells, and also GABAB receptors located on neighbouring astrocytes. Activation of these GABAB receptors leads to a postsynaptic rise in [Ca2+]i that triggers the release of a retrograde messenger, probably glutamate, leading to an increase in the probability of GABA release.

***https://doi-org.proxy.library.cornell.edu/10.1016/S0166-2236(02)02269-5***

# What you should take away from this lecture and remember

(1) Difference between appetitive and aversive learning (conditioning)
(2) Design experiments to test if LTP/LTD are involved in a learning paradigm
(3) Explain how cerebellar LTD contributes to nictating membrane response
(4) Explain how fear conditioning to a tone happens in amygdale
(5) Understand two ways for plasticity on in inhibitory synapses.