Learning and memory

Definitions of Learning and Memory

"***Memory*** is a gift of nature, the ability of living organisms to retain and to utilize acquired information or knowledge."

Endel Tulving

"***Learning*** is the name given to the process by which new information is acquired by the nervous system and is observable through changes in behavior."

"***Memory*** refers to the encoding, storage, and retrieval of learned information."

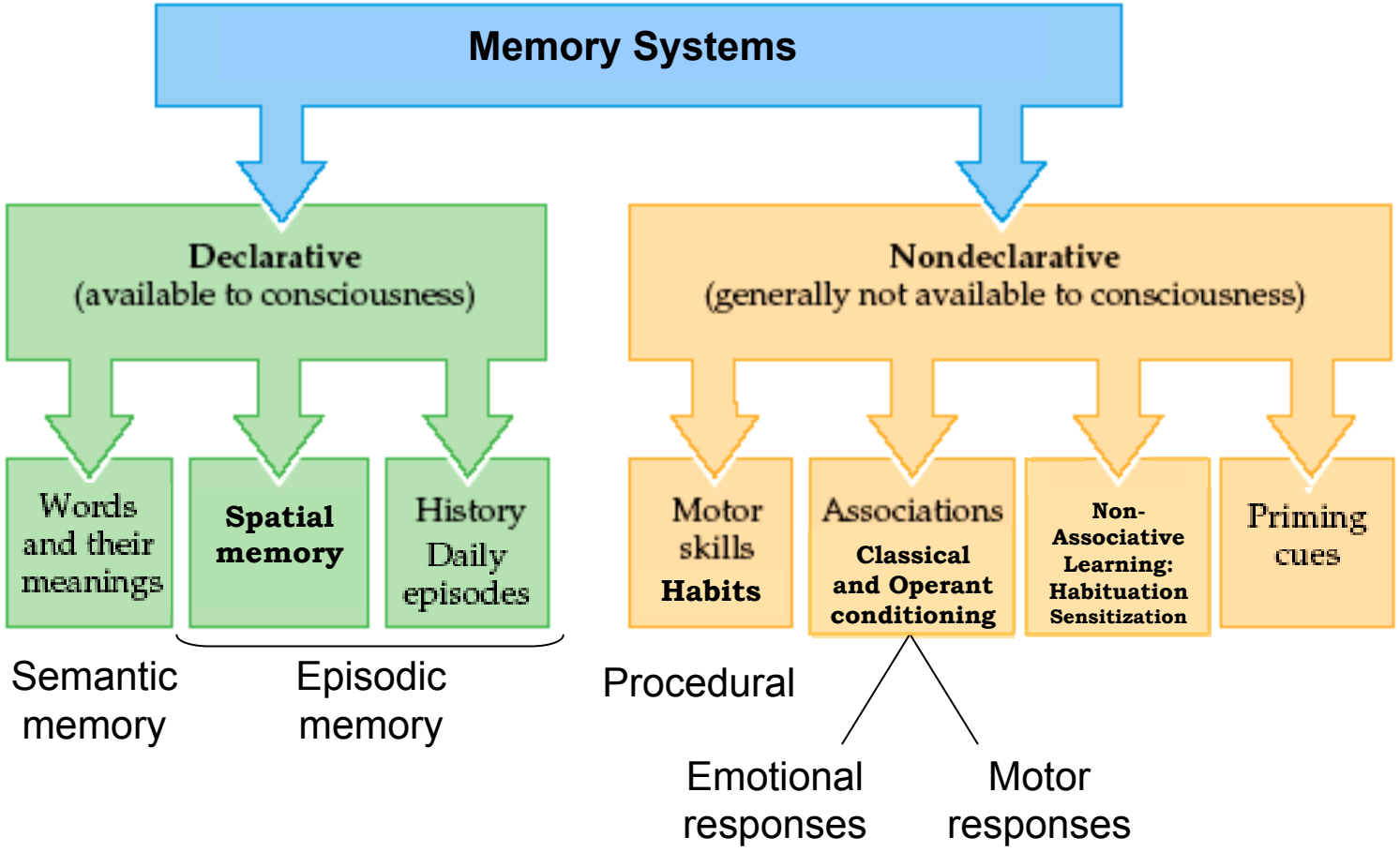
Dale Purves et al.

General principles

1. Multiple memory systems are present in the brain.
2. Each memory system uses different brain structures.
3. Acquisition and storage of information does not need to happen in the same anatomical locations.
4. Learning and memory results in changes in neural circuits (molecular, electrophysiological, anatomical).
5. Short-term forms of learning and memory require changes in existing neural circuits.
6. Long-term forms of memory require new protein synthesis and morphological changes (e.g. growth of new connections).

Qualitative categories of Memory

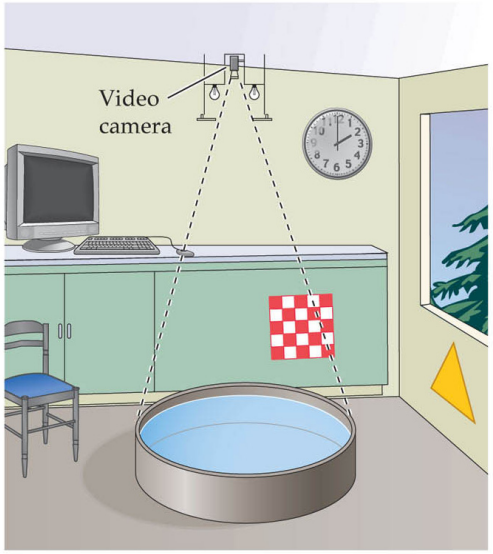
Type of information
Form of acquisition – Form of retrieval

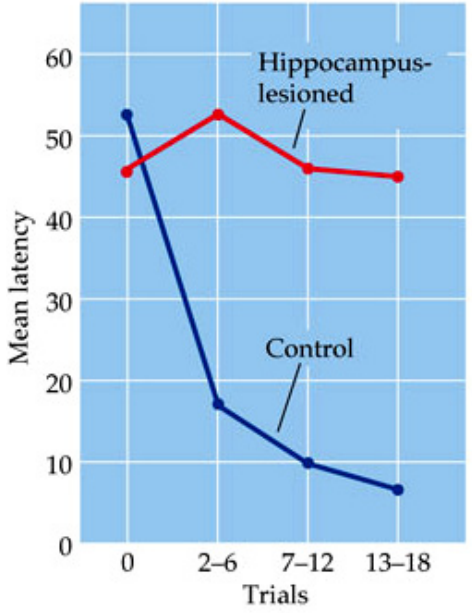


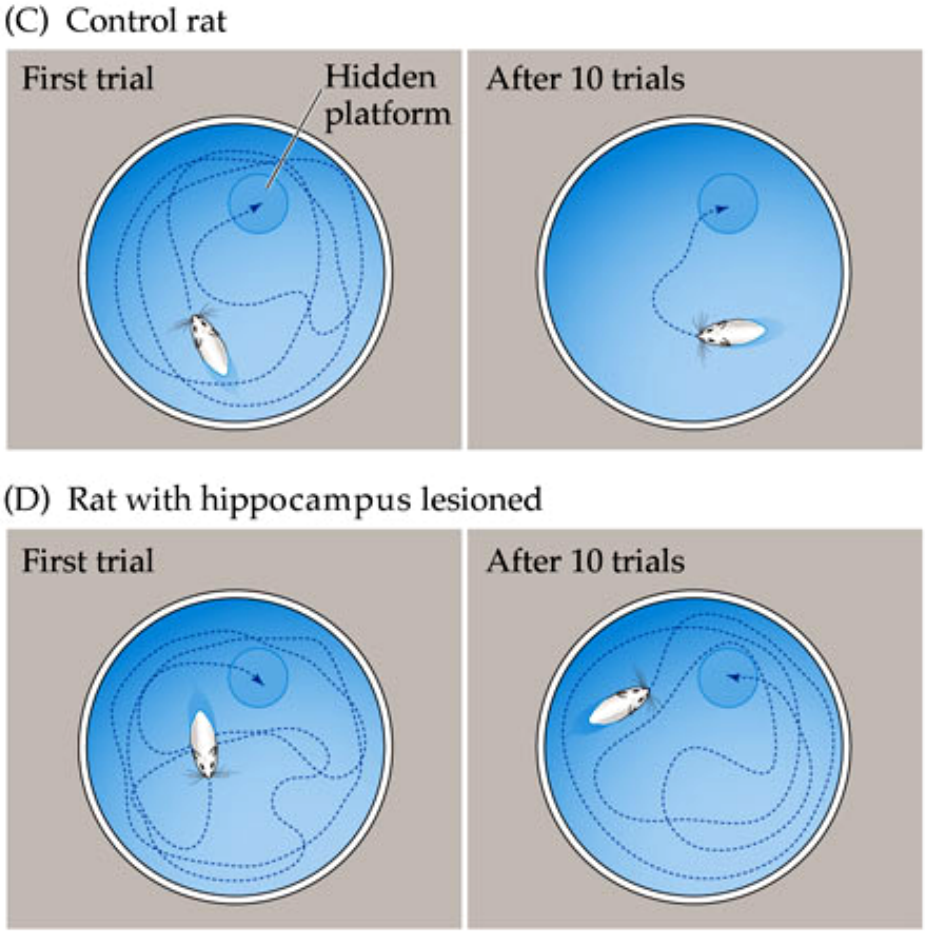
Categories are not mutually exclusive!

Declarative memory in non-human animals?

Mazes: **Spatial representation – Spatial memory**

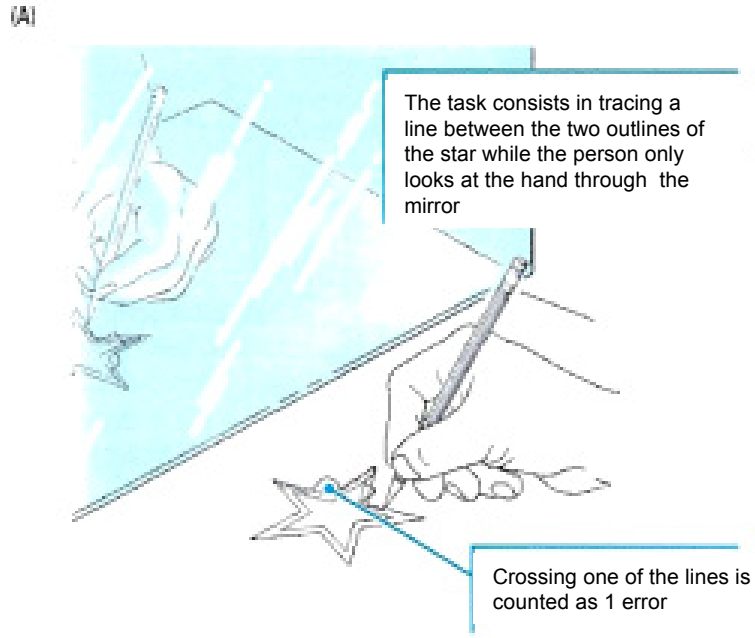






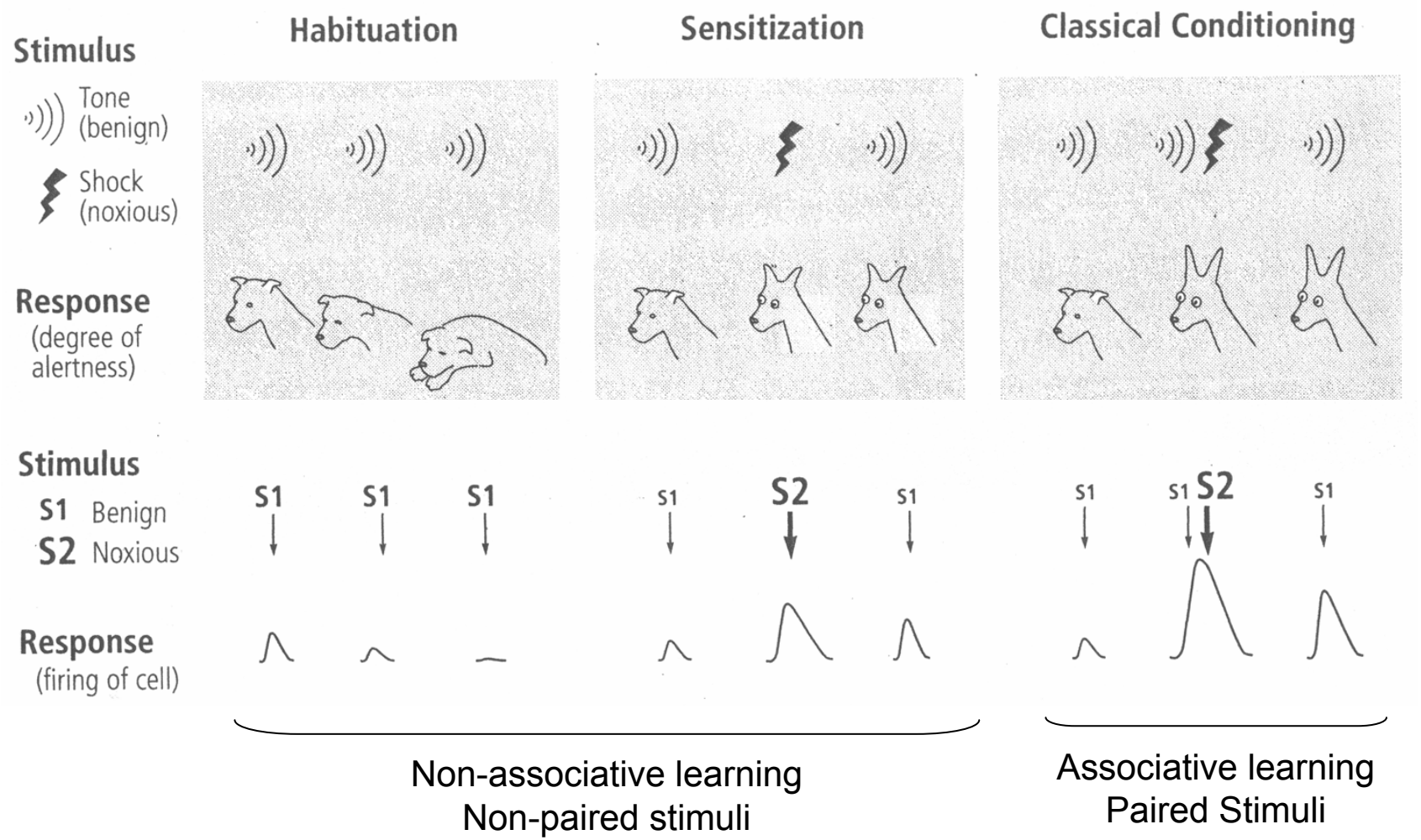
Non-declarative memory systems

Motor skills



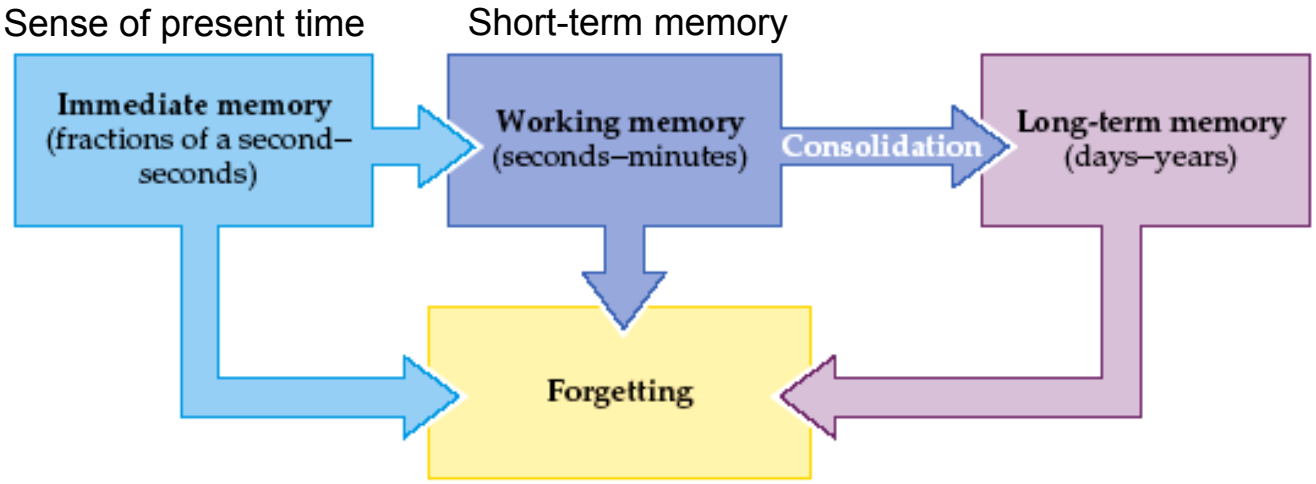
Non-declarative memory systems

Non-associative vs. Associative learning



Example of conditioning: ***Fear conditioning*** → ***Emotional Memory***

Temporal categories of Memory



Forgetting the stored information

Normal forgetting: VERY important!

Pathological forgetting (amnesias)
- Anterograde amnesia
- Retrograde amnesia

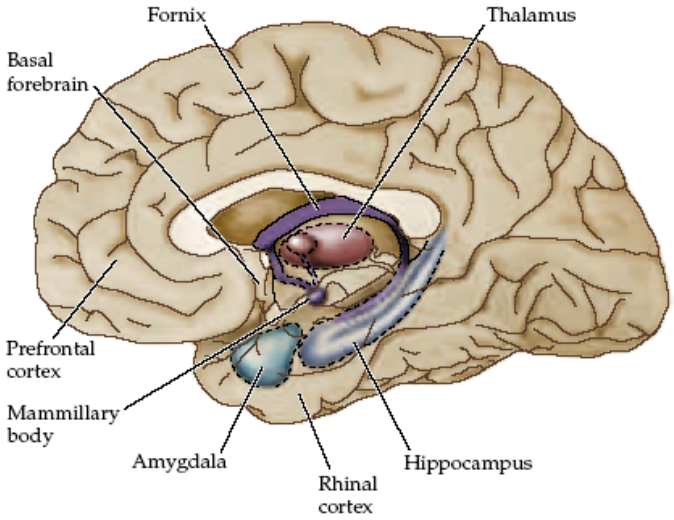
Processes Involved

1. Encoding (acquisition = Learning)
2. Consolidation
3. Storage
4. Retrieval
5. Loss (= Forgetting)
   - → Physiological forgetting
   - → Pathological forgetting (amnesias)

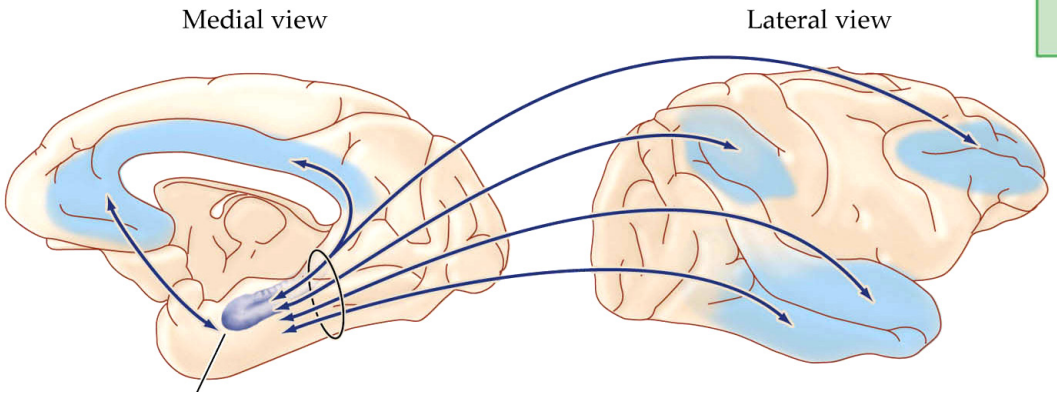
Age dependent changes in these processes
- → Physiological aging
- → Pathological aging (memory deficits in neurodegenerative diseases)

Brain systems underlying declarative memories

1. Hippocampus and medial diencephalic structures: *Formation and short-term storage of declarative memories*



2. Specialized areas of cerebral cortex: *Long-term storage of declarative memories*



Acquisition and storage of declarative information

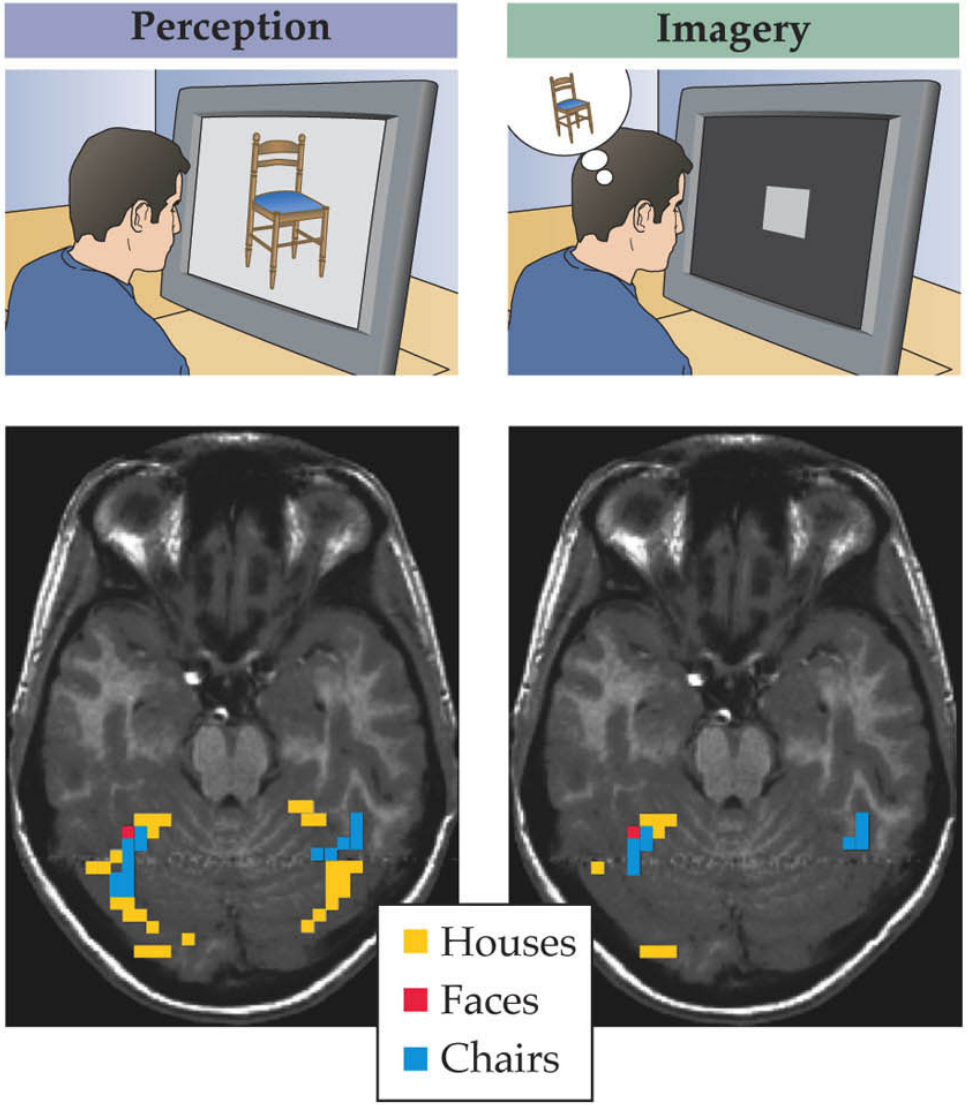
Long-term storage
(a variety of cortical sites: Wernicke's area for the meanings of words, temporal cortex for the memories of objects and faces, etc.)

Short-term memory storage
(hippocampus and related structures)

The retrieval process

3. Frontal cortical areas: *Retrieve declarative information from long-term storage*

Retrieval of information activates the same regions involved in perception.



Retrieval of memory ↔ Perception

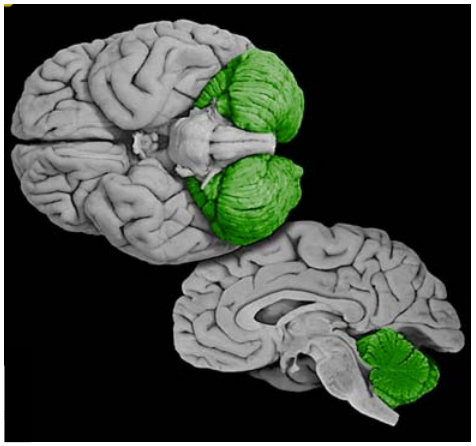
Constructive Process

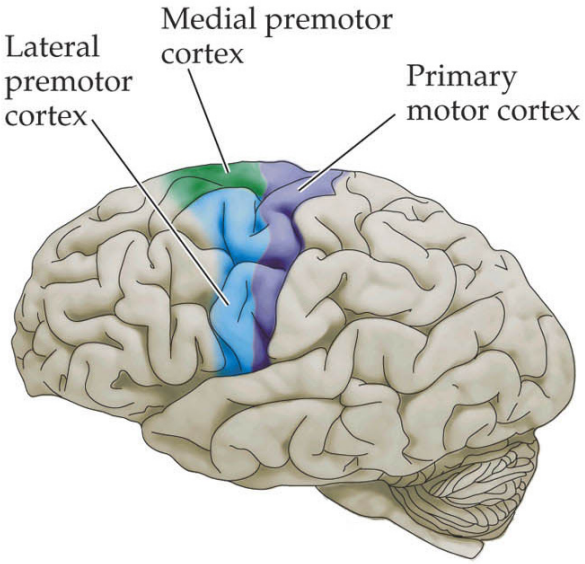
(a model of reality)

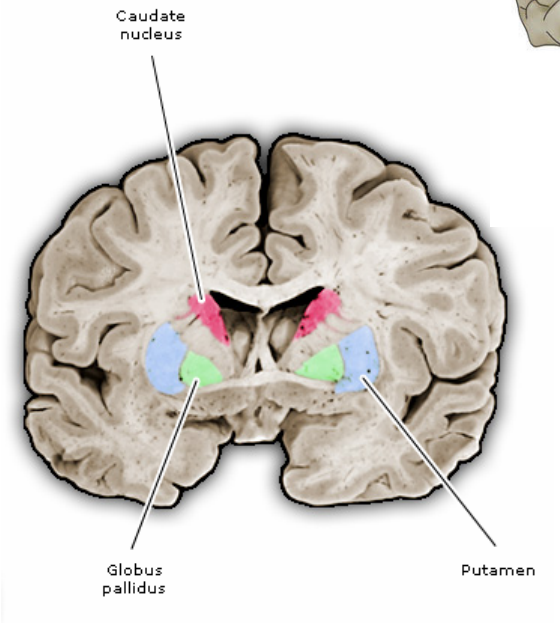
Memory → distortion

Perception → illusions

Brain systems underlying non-declarative memories







Acquisition and storage of nondeclarative information

Long-term storage
(cerebellum, basal ganglia, premotor cortex, and other sites related to motor behavior)

Short-term memory storage
(sites unknown but presumably widespread)

What changes do occur in our brain when we Learn, Retain, Retrieve or Forget information with our multiple Memory Systems?

1) Intrinsic properties of cells (neurons or glia) ?

2) Properties of the connection between them (synapses) ?

Synaptic Plasticity =

Patterns of electrical activity

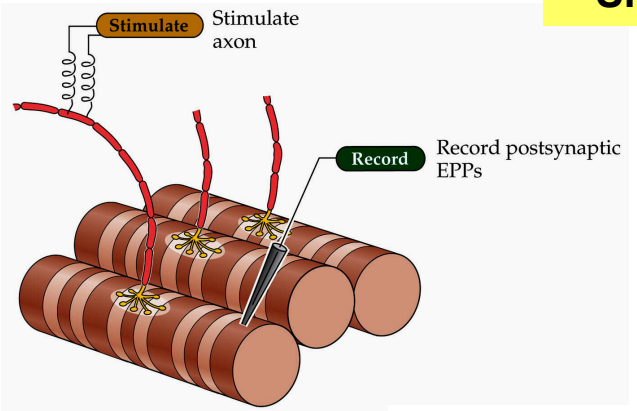
↓

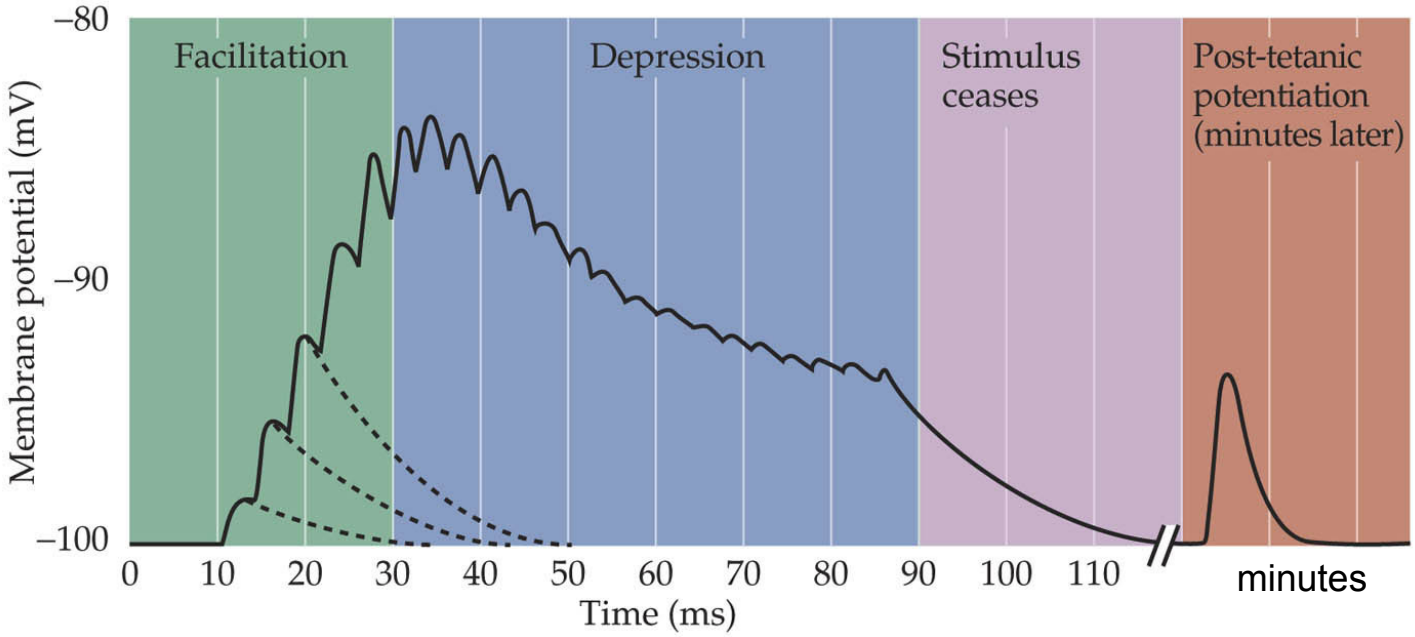
Changes in synaptic strength ↑↓

↓

Behavior changes

Short-term plasticity at the neuromuscular synapse



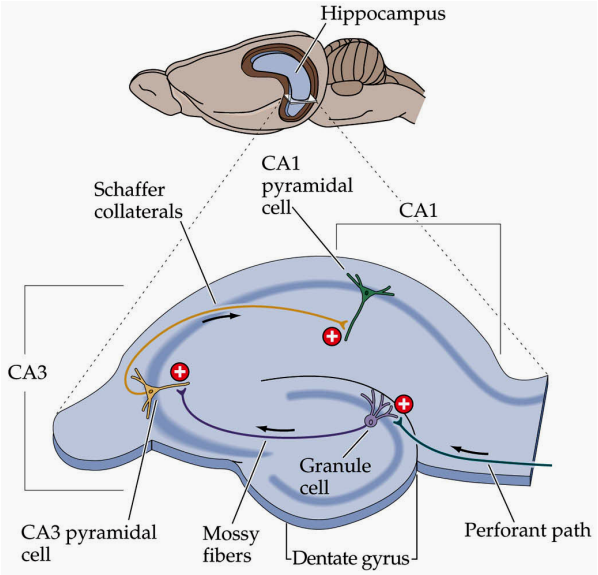


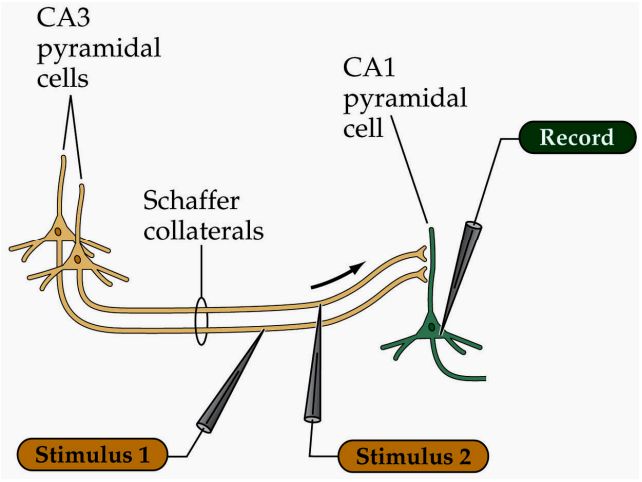
These forms of plasticity → **in all chemical synapses!**

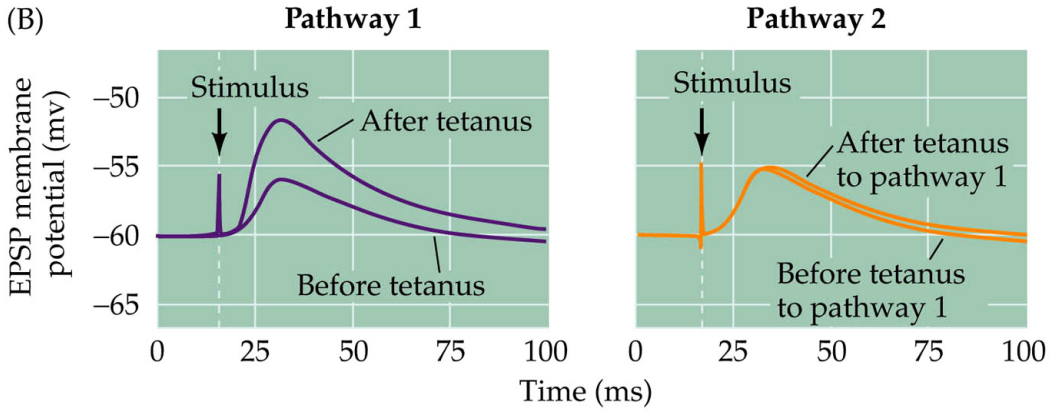
The strength of a synapse changes dynamically, **depending on recent activity history**.

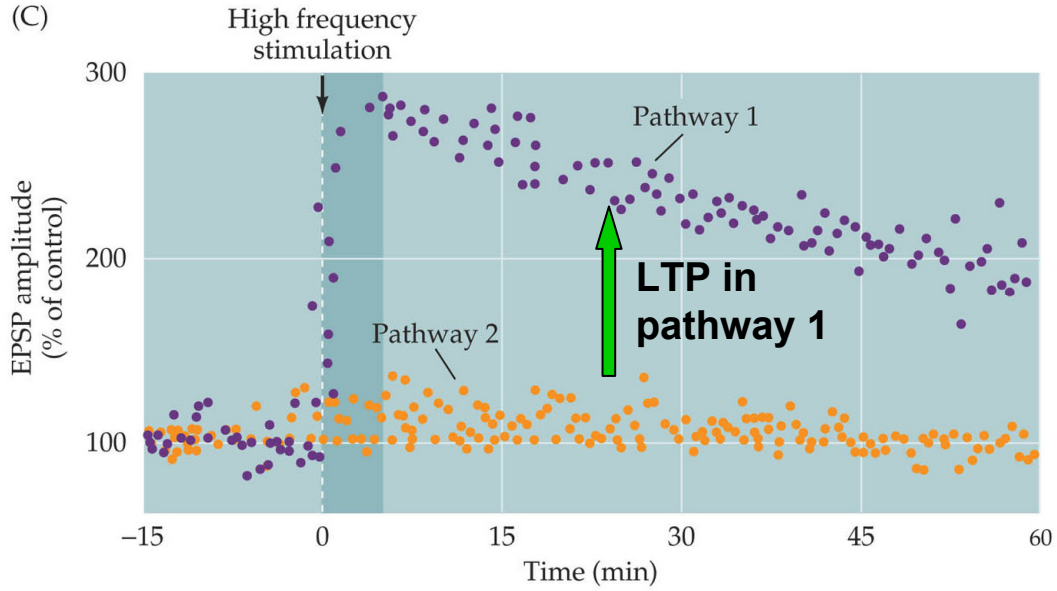
Long-term plasticity in the hippocampus

Long-term potentiation (LTP)





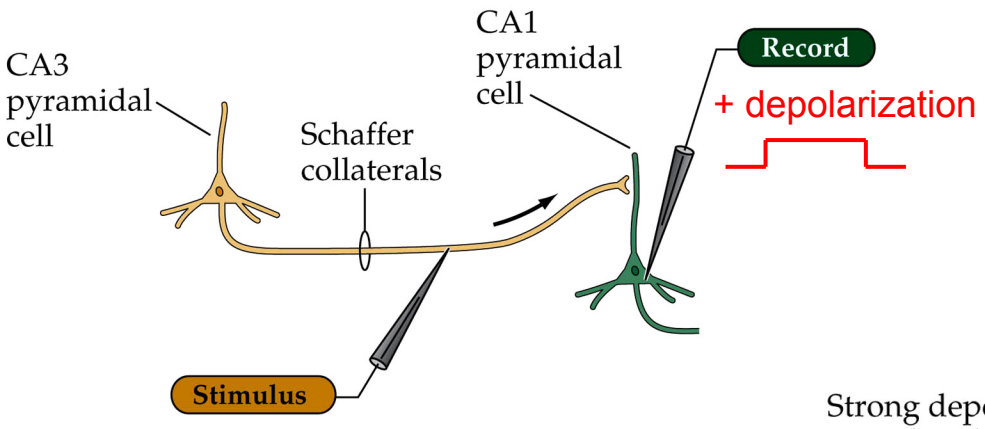


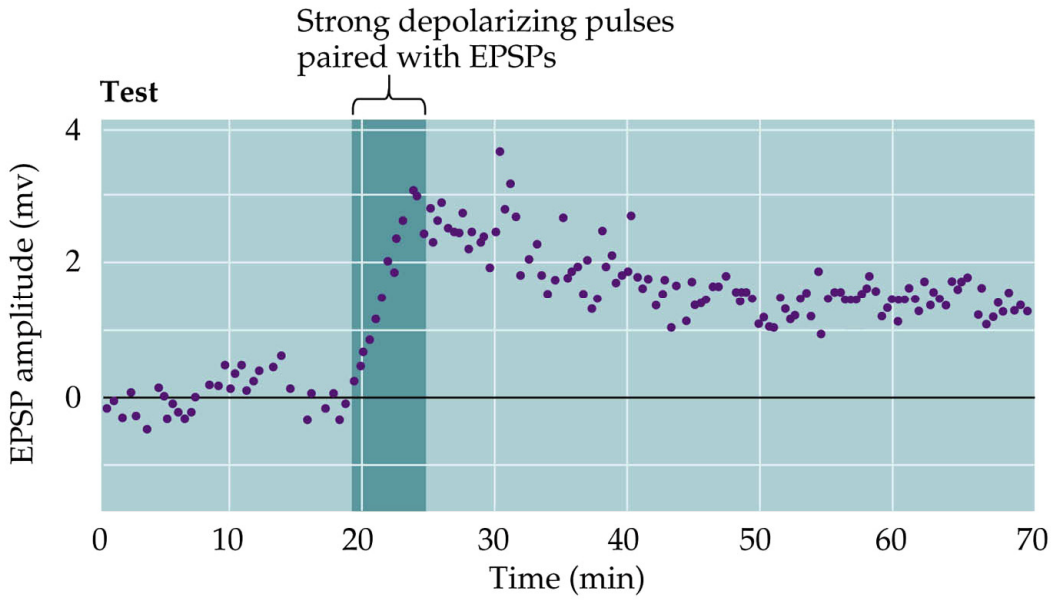


A brief + high frequency stimulus in Pathway 1 → **LTP** (only in Pathway 1)

Long-term plasticity in the hippocampus

Long-term potentiation (LTP)

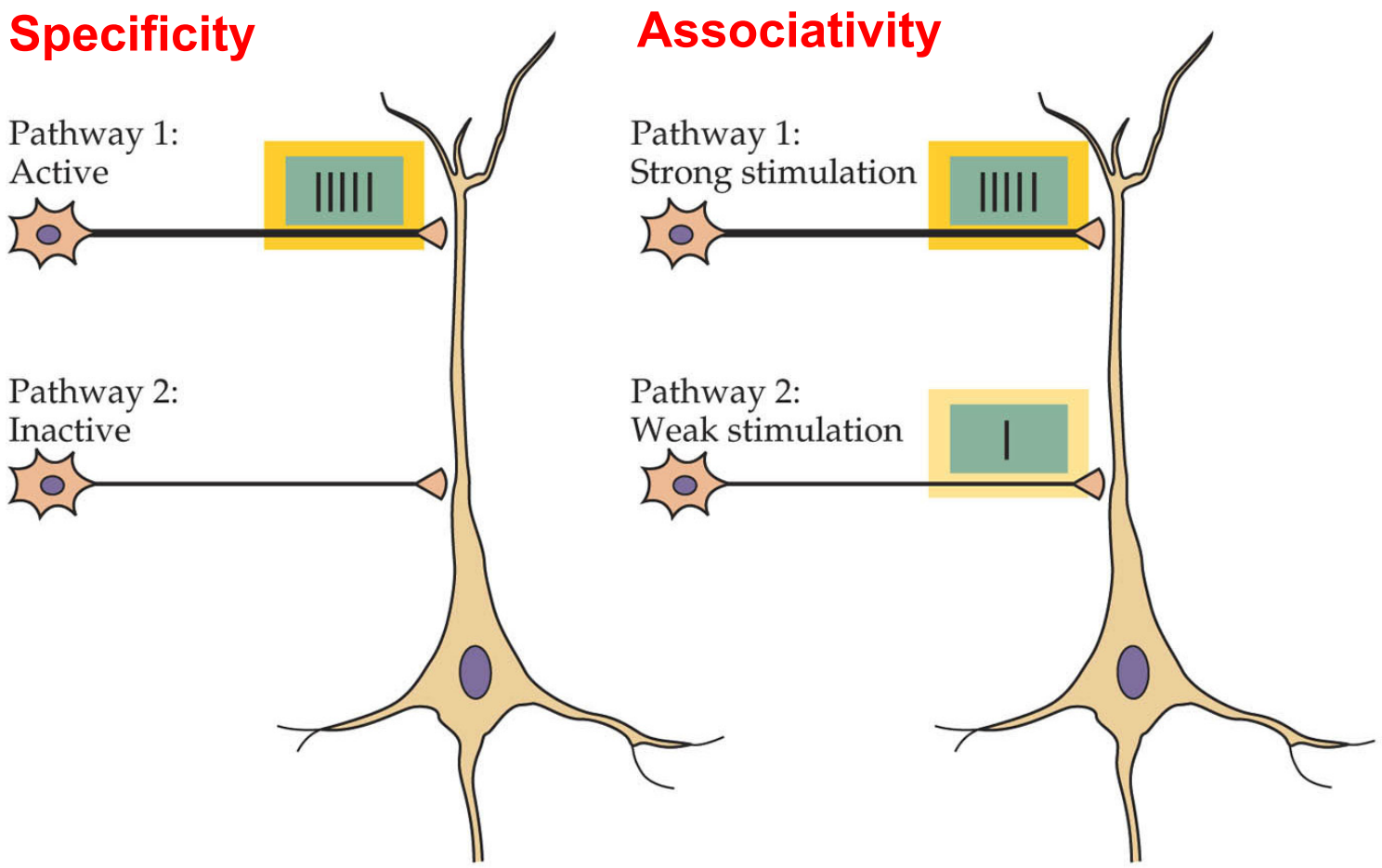




Pairing post-synaptic and presynaptic activity in a single pathway also produces **LTP**

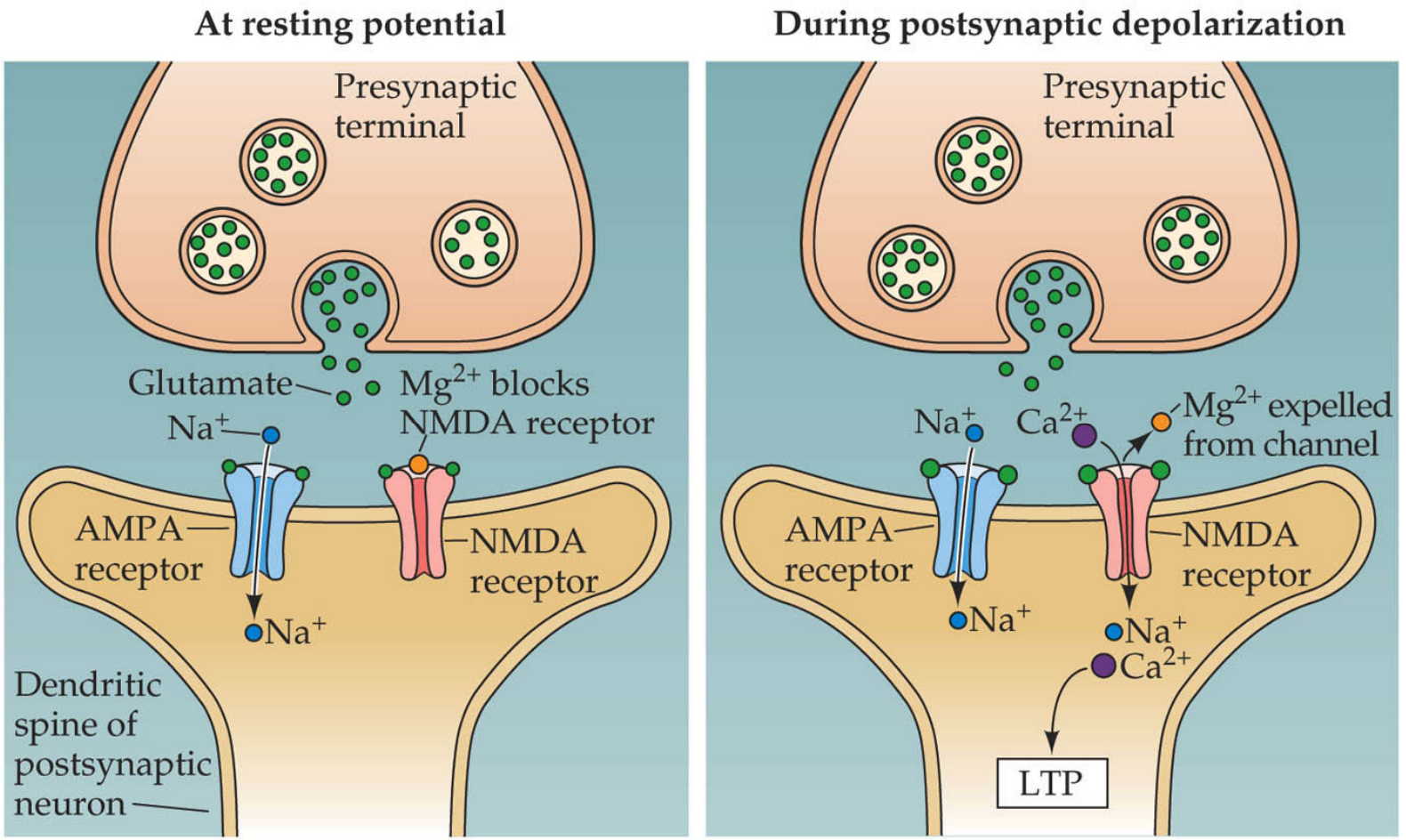
Long-term plasticity in the hippocampus

Long-term potentiation (LTP). Properties.



Long-term plasticity in the hippocampus

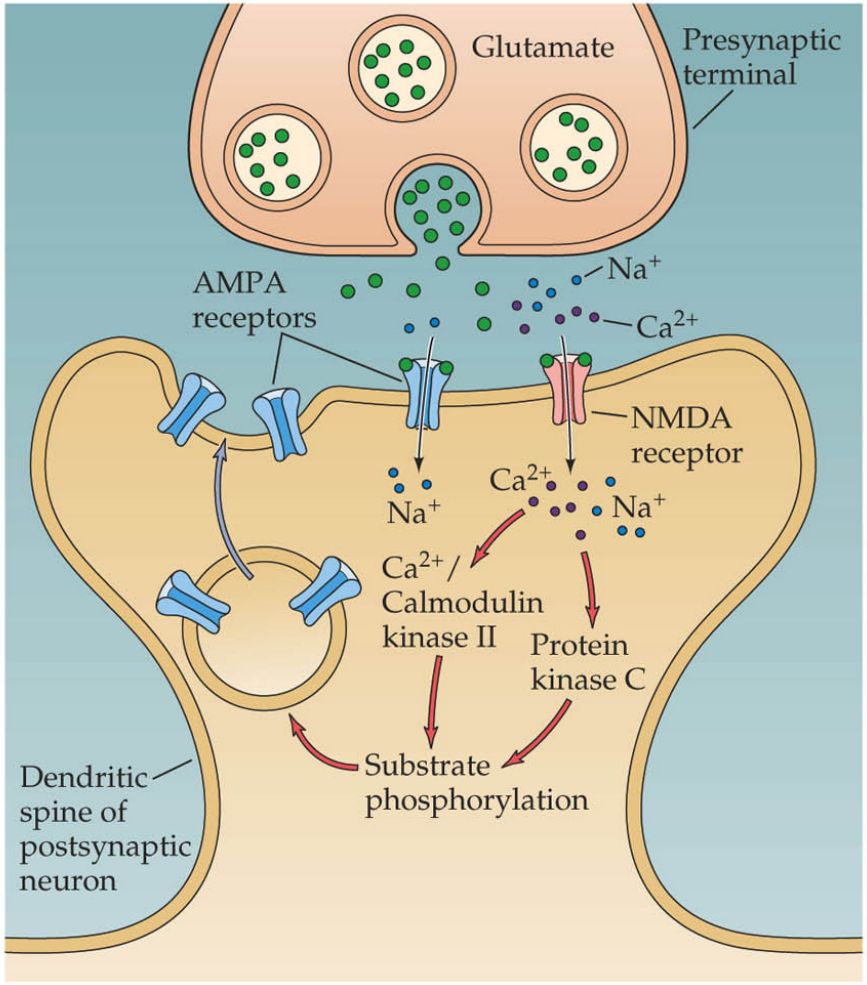
Long-term potentiation (LTP). Molecular Mechanism.



The **NMDA receptor channel** can open only during depolarization of the postsynaptic neuron

Long-term plasticity in the hippocampus

Long-term potentiation (LTP). Molecular Mechanism.



Key elements:

Coincidence of depolarizations

↓

Opening of NMDA receptors

↓

$[Ca^{2+}]_i$ increase

↓

Kinase activity (CaMKII and PKC)

↓

Phosphorylation of substrates

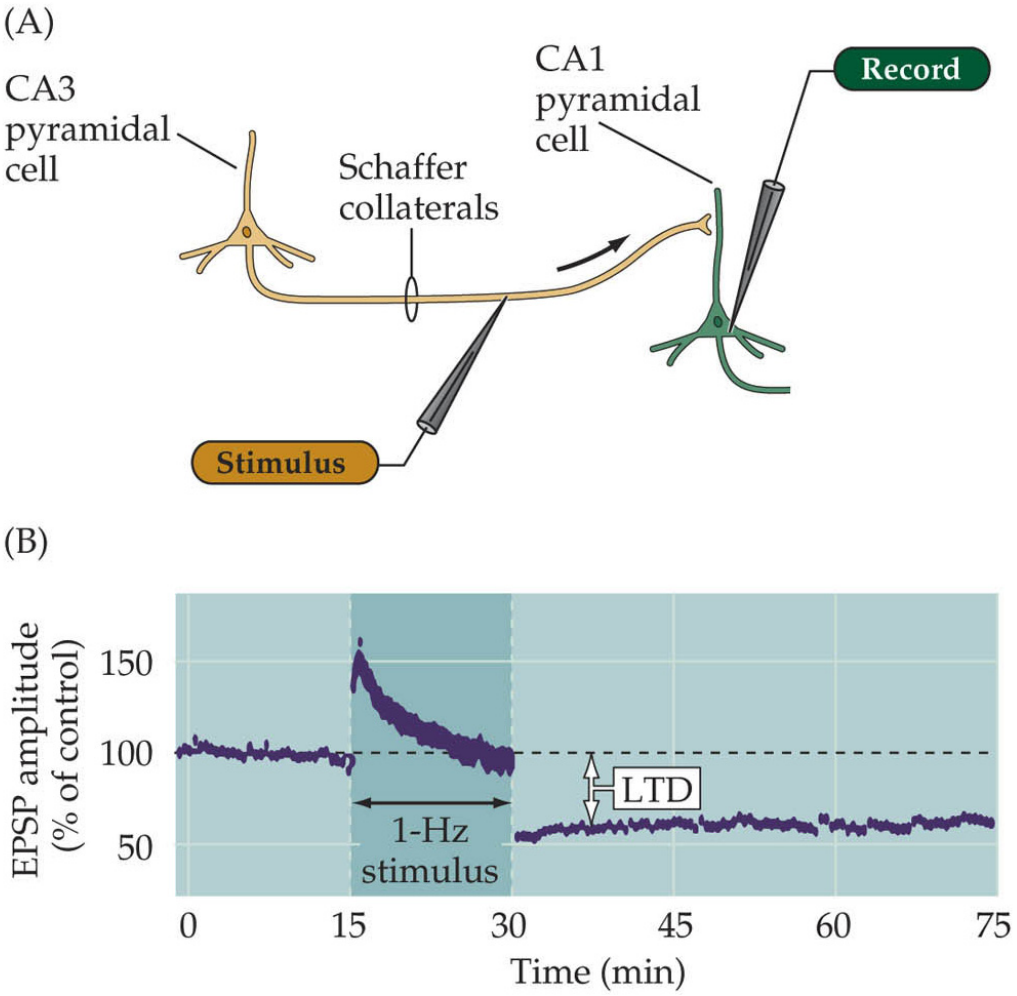
↓

More AMPA receptors in postsynaptic membrane

The **calcium** that enters through **NMDA receptor channels** triggers the long term changes

Long-term plasticity in the hippocampus

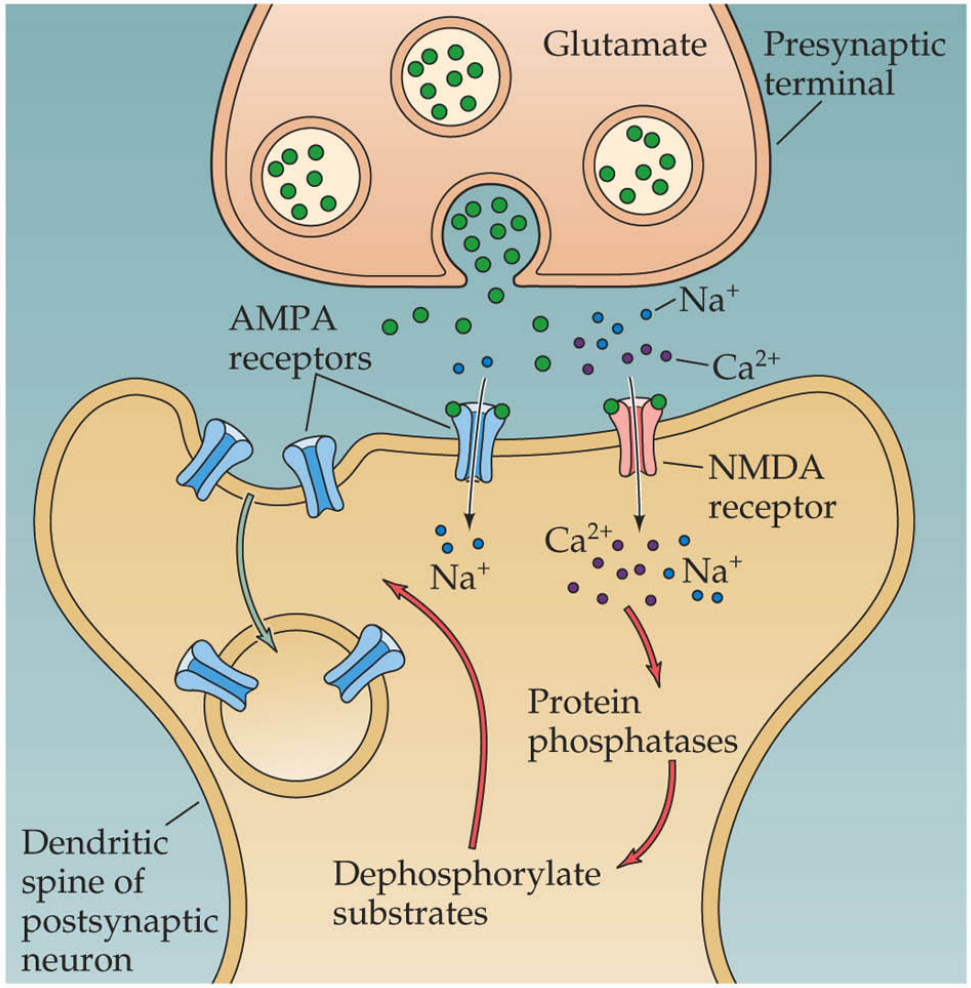
Long-term depression (LTD).



A low frequency + long stimulus → **LTD**

Long-term plasticity in the hippocampus

Long-term depression (LTD). Molecular Mechanism.



Key elements:

Coincidence of depolarizations

↓

Opening of NMDA receptors

↓

$[Ca^{2+}]_i$ increase (low but sustained)

↓

Phosphatase activity

↓

De-phosphorylation of substrates

↓

Internalization of AMPA receptors in postsynaptic membrane

The **calcium** that enters through **NMDA receptor channels** also triggers LTD

Long-term plasticity in the mammalian CNS

Long Term Plasticity =
(weeks, months, years)

- Long Term Potentiation (LTP)
- ⇕
- Long Term Depression (LTD)

STIMULUS
- short + high frequency → **LTP**
- long + low frequency → **LTD**

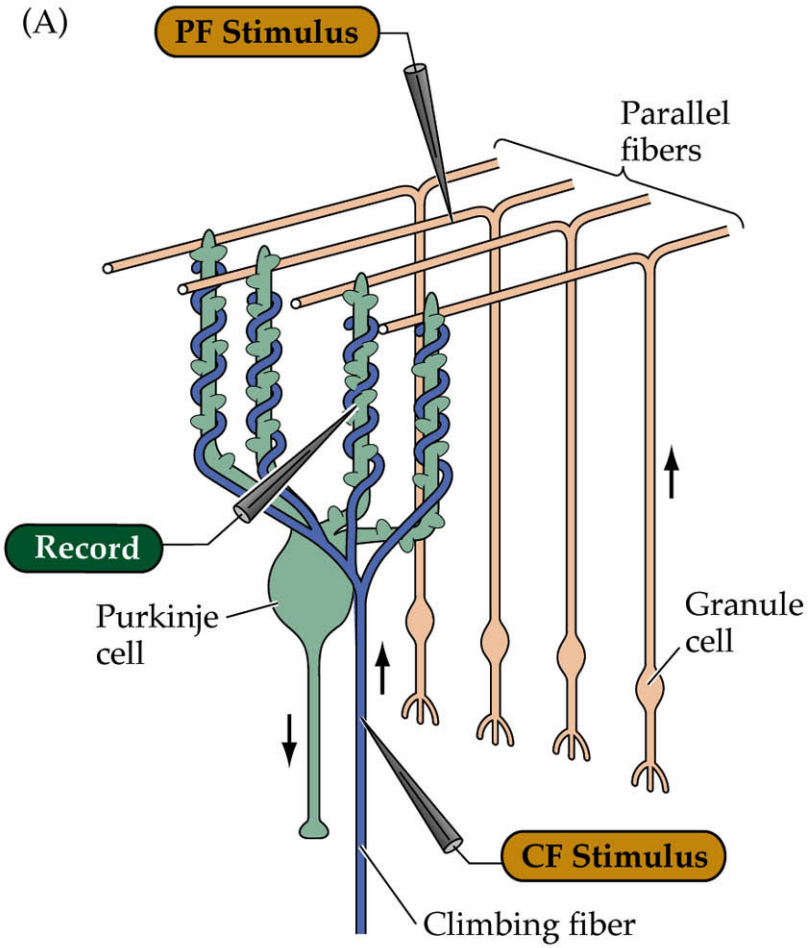
single synapse → **LTP** → **↑ strength** → **LTD** → **↓ strength**

These forms of plasticity → **hippocampus, cortex, amygdala, cerebellum**
The strength of a synapse **depends on its activity history**.

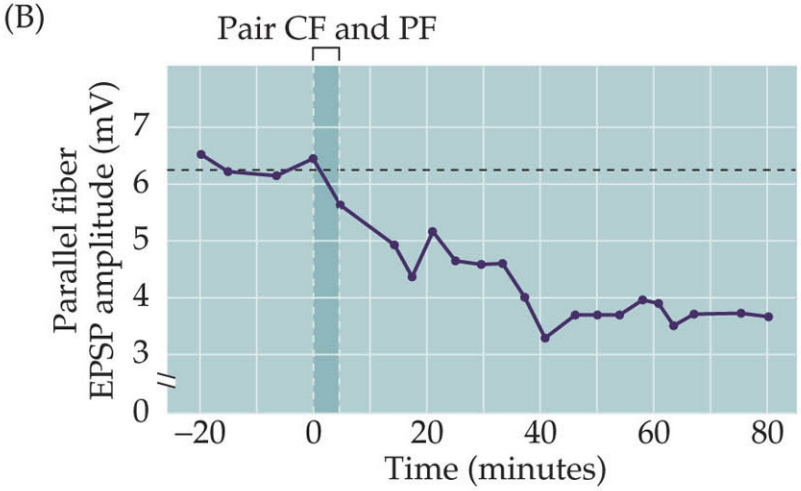
The **molecular mechanisms** to obtain LTP or LTD vary from cell to cell

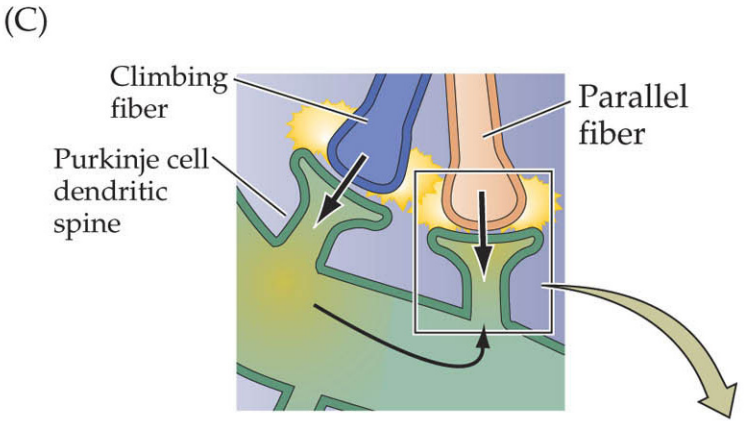
Long-term plasticity in the cerebellum

LTD in the cerebellum



coincidence

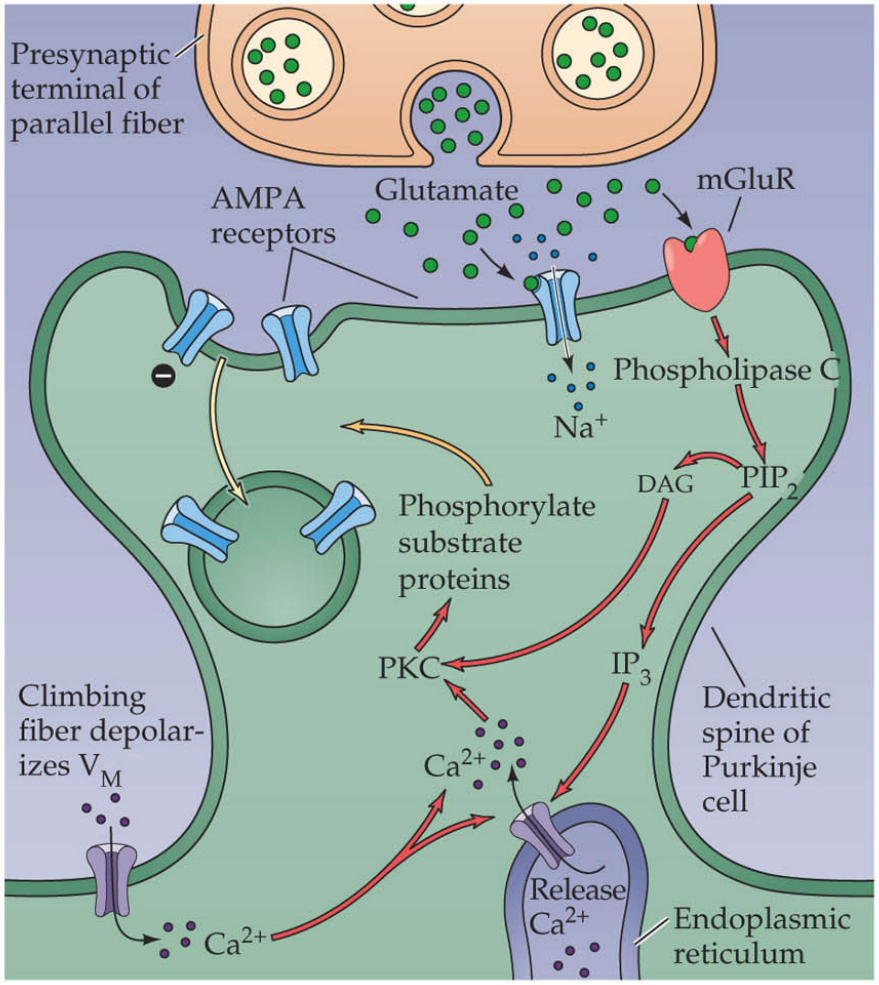




Coincidence of CF and PF activity → **LTD** in the synapse between PF and Purkinje cell

Long-term plasticity in the cerebellum

LTD in the PF-Purkinje synapse. Molecular Mechanism.



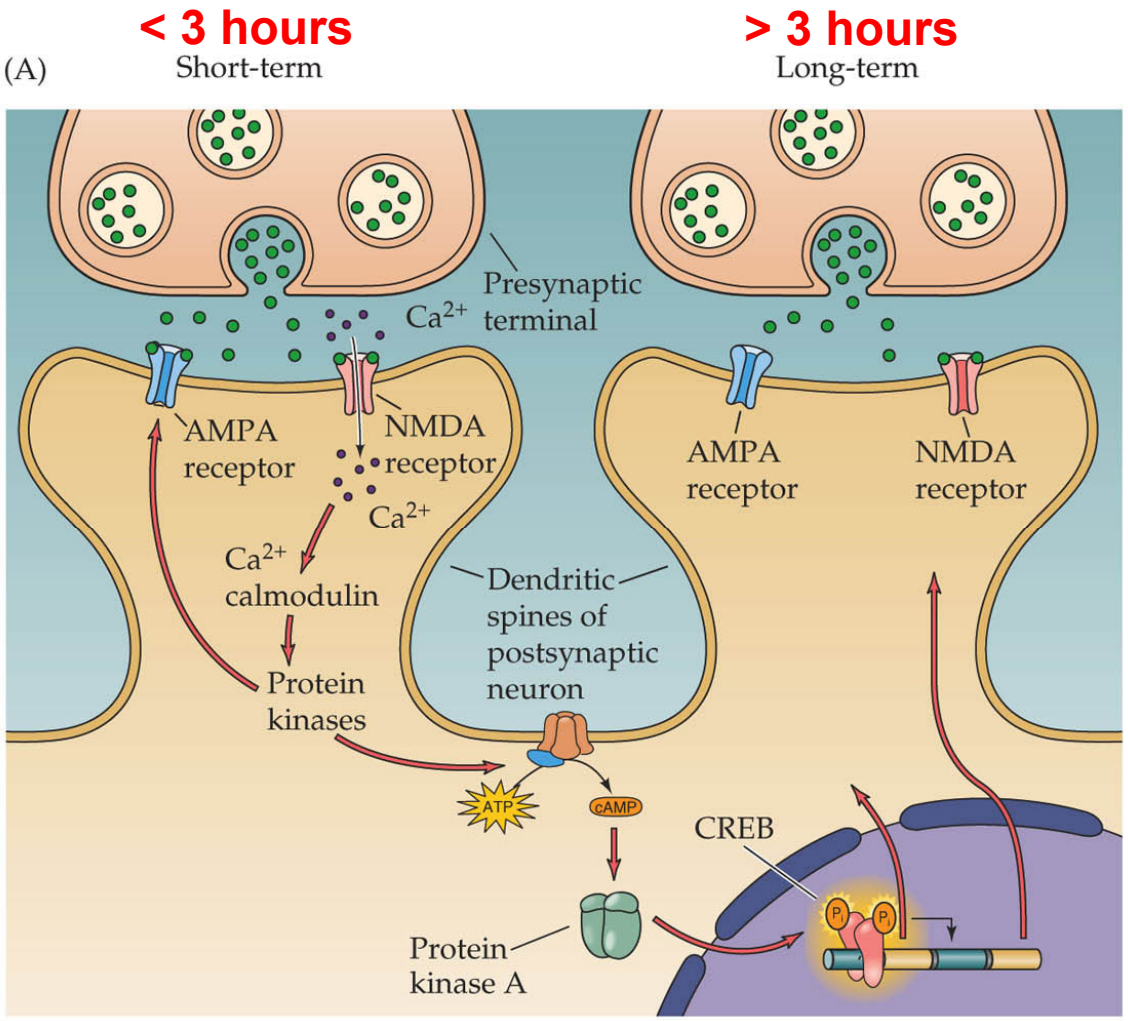
Key elements:

Coincidence of depolarizations
↓
AMPA and mGluR
↓
IP_3/DAG signaling cascade
↓
$[Ca^{2+}]_i$ increase
↓
Kinase activity (PKC)
↓
Internalization of AMPA receptors in postsynaptic membrane

This mechanism **<u>does not</u> use NMDA receptor channels,** and uses **calcium** and **kinases.**

Long-term plasticity in the cerebellum

LTD early phases vs. long-lasting changes



Key elements:

cAMP

↓

Kinase activity (PKA)

↓

Phosphorylation of CREB

↓

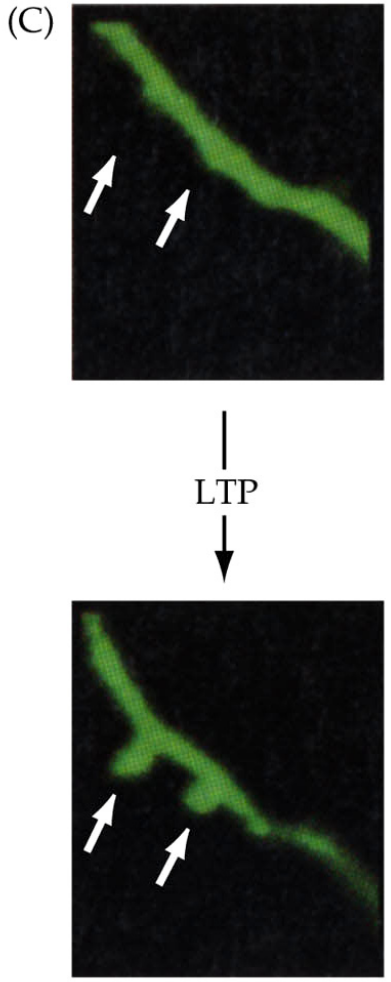
Activation of transcription of downstream genes

↙ ↓ ↘

Structural changes (addition of synapses)

Long-term plasticity in the mammalian CNS

LTP, long-lasting structural changes:



Creation of new synapses → **dendritic spines!**