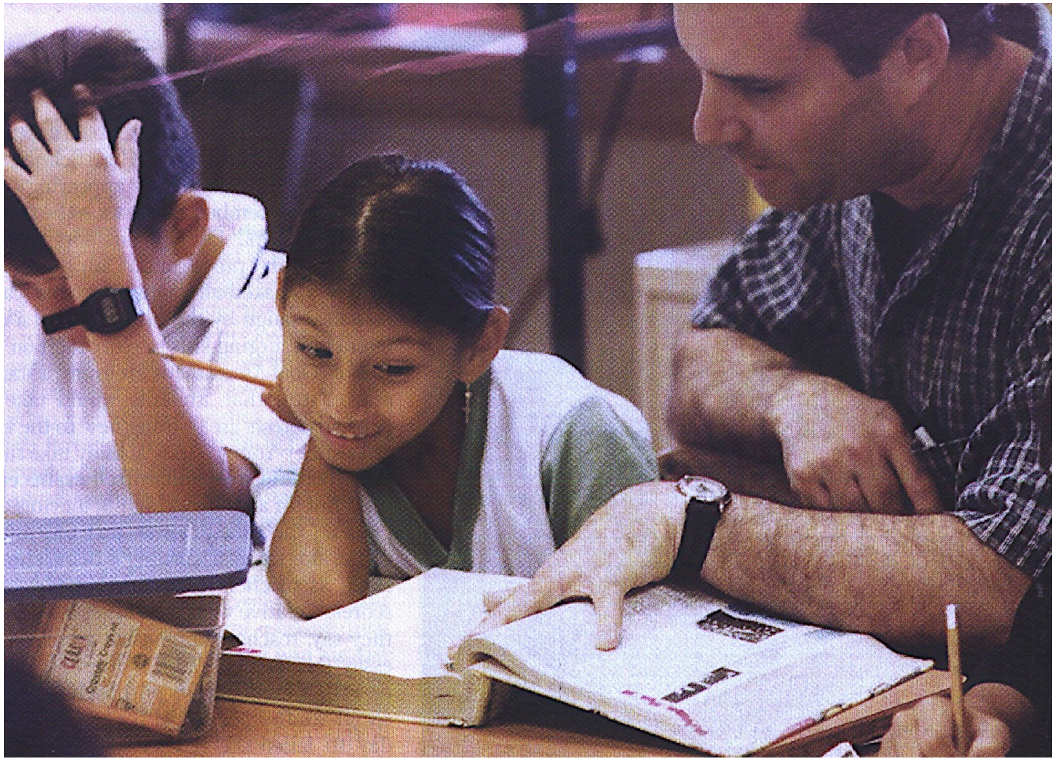
Lecture 11

Learning & Memory

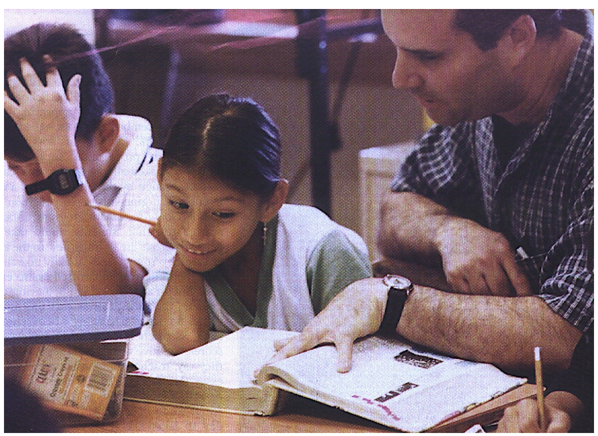


Cogs17 * UCSD

Learning & Memory

RECALL

The brain is VERY plastic!
Continues to change
- make new connections –
throughout life!



Learning =

Development of a permanent change in behavior based on experience

"Law of Effect"

Any stimulus/action/context associated with positive reinforcement will tend to be repeated

"Conditioning"

Classical Conditioning – develop association between stimuli

Operant Conditioning – develop association between stimulus and response

Classical Conditioning

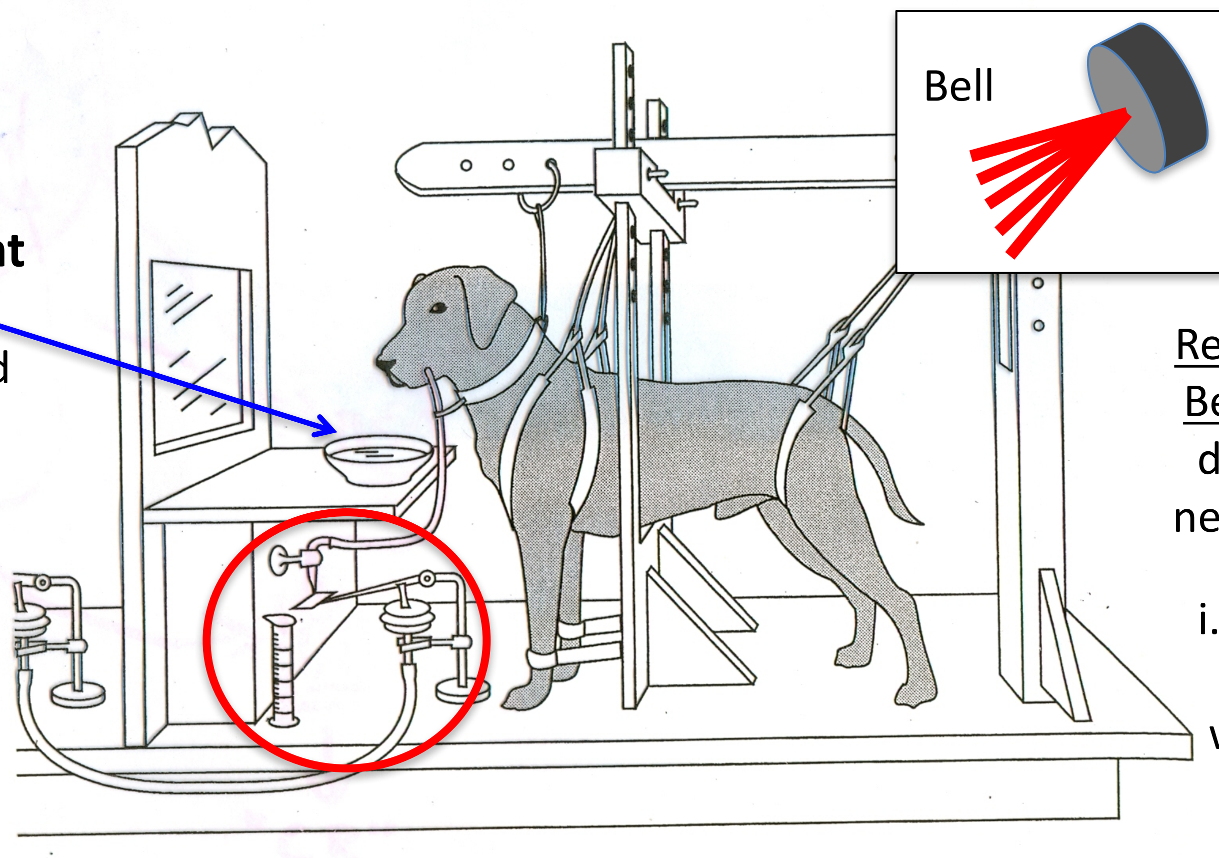
Develop, through repeated experience, an association between stimuli

e.g. **Pavlov's Dog**

Apparatus designed to collect drops of saliva to measure dog's response to stimuli

Positive Reinforcement
(Food) =
"Unconditioned Stimulus"

Present food, dog will salivate without training



"Conditioned Stimulus"

Repeatedly **pair** Bell with Food, dog will learn new association

i.e. Bell alone (no food) will produce salivation

CRITICAL: Bell and Food must be contiguous – i.e. must **co-occur in time** – for this conditioning to succeed

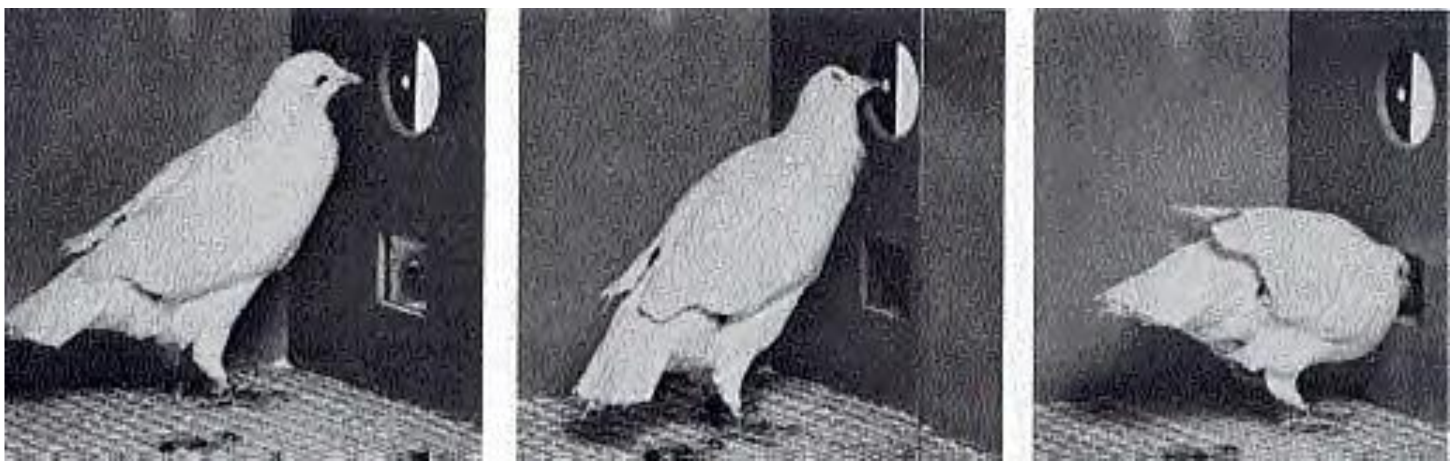
Operant Conditioning

Develop, through repeated experience, an association between stimulus & response

Pigeon presented with dot (stimulus)

Pecks dot (response)

Receives food (positive reinforcement)



Soon learns association: Predicts food when pecks dot

Again, CRITICAL: Food must **co-occur** with peck for animal to learn this association

Temporal Contiguity

The co-occurrence of events is required to learn their association
(with a few exceptions)

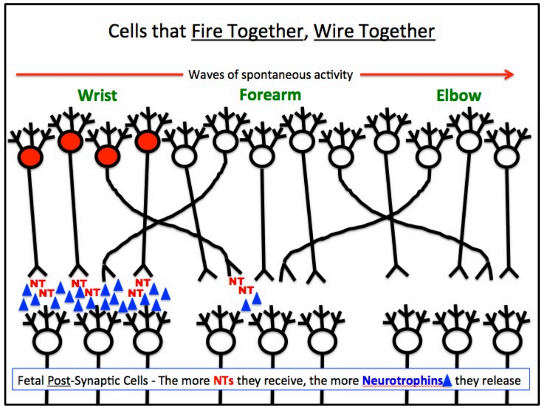
Because it is the co-occurrence of the pertinent neural activity
that leads to the development of an "association"

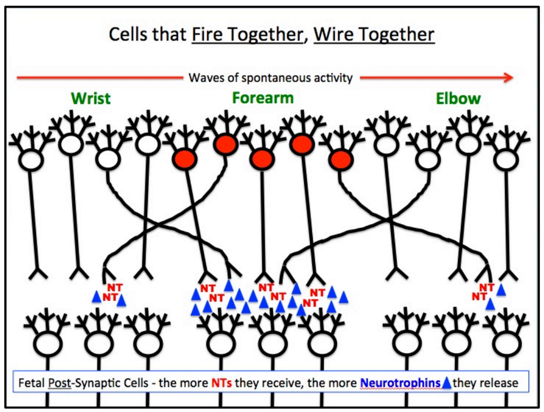
That is, the **repeated co-activation** of circuits
increases the likelihood that,
if one of those circuits is activated (e.g. hear bell),
the other one will also activate (e.g. salivate)

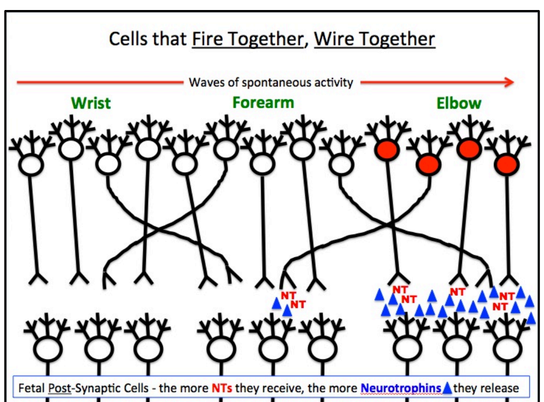
That is, the circuits that

Fire Together – Wire Together!

Fire Together – Wire Together

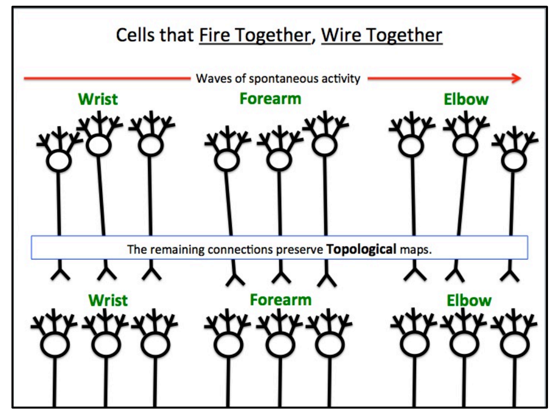






RECALL

During brain development,
co-activation of pre and post-synaptic cells
leads to formation of
topological maps



During **Learning**
repeated neural co-activity
also changes patterns of activation,
increasingly likelihood of circuits co-firing

"Hebbian Synapse"

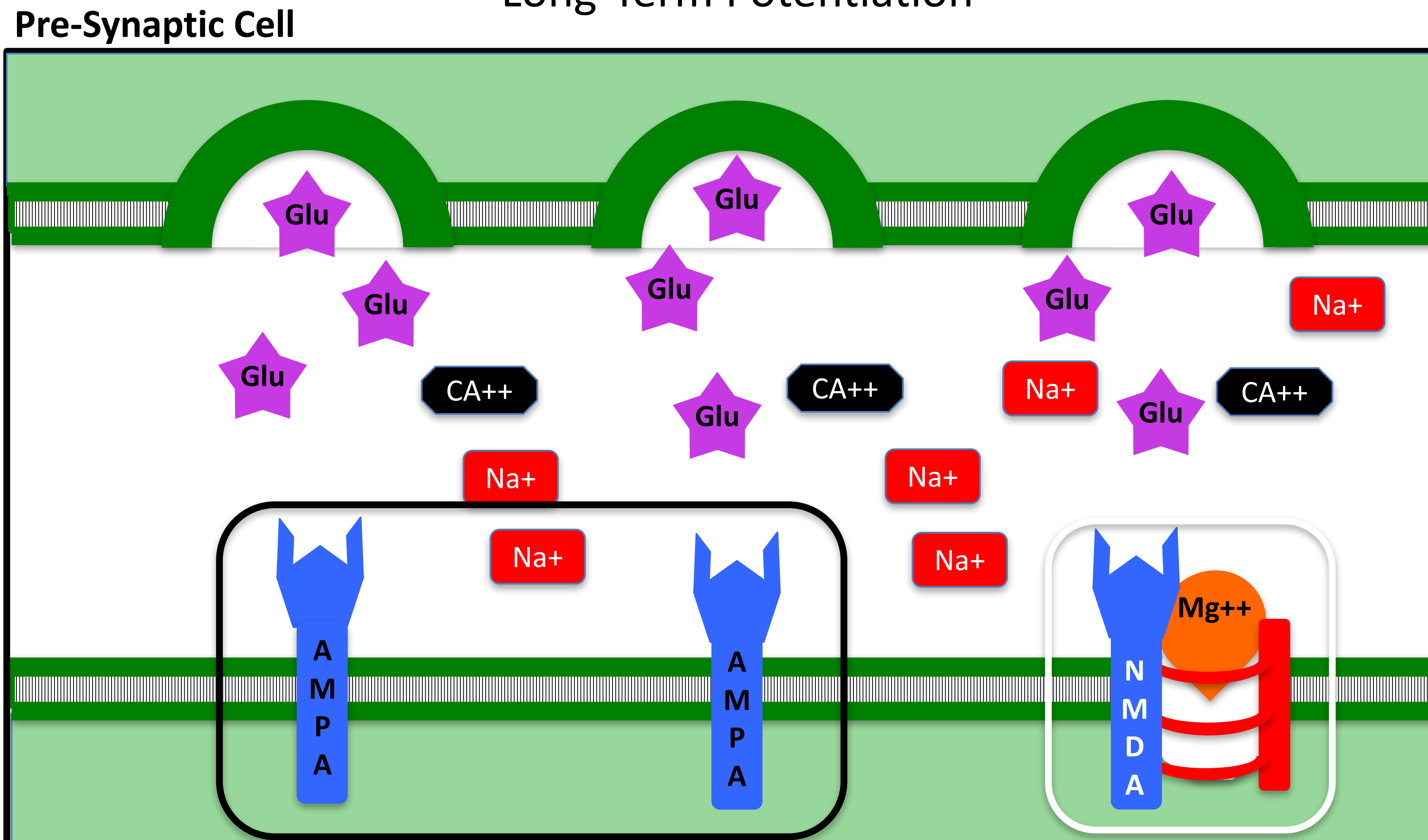
Long-Term Potentiation (LTP)

"Learning", in neurological terms, = LTP

(Semi-) Permanent structural & connectivity changes among neurons

Increase likelihood of activity along (repeated) circuit/s

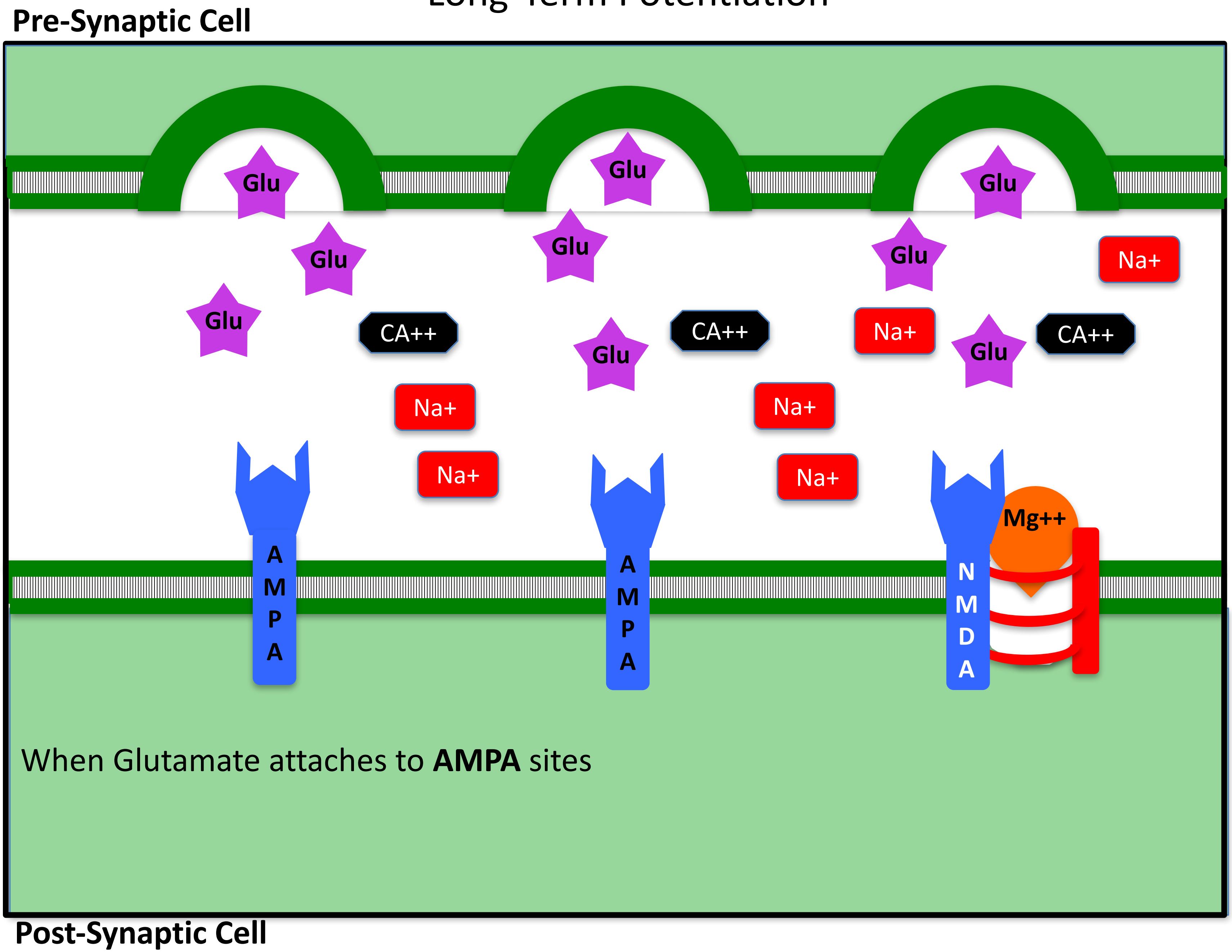
Long-Term Potentiation



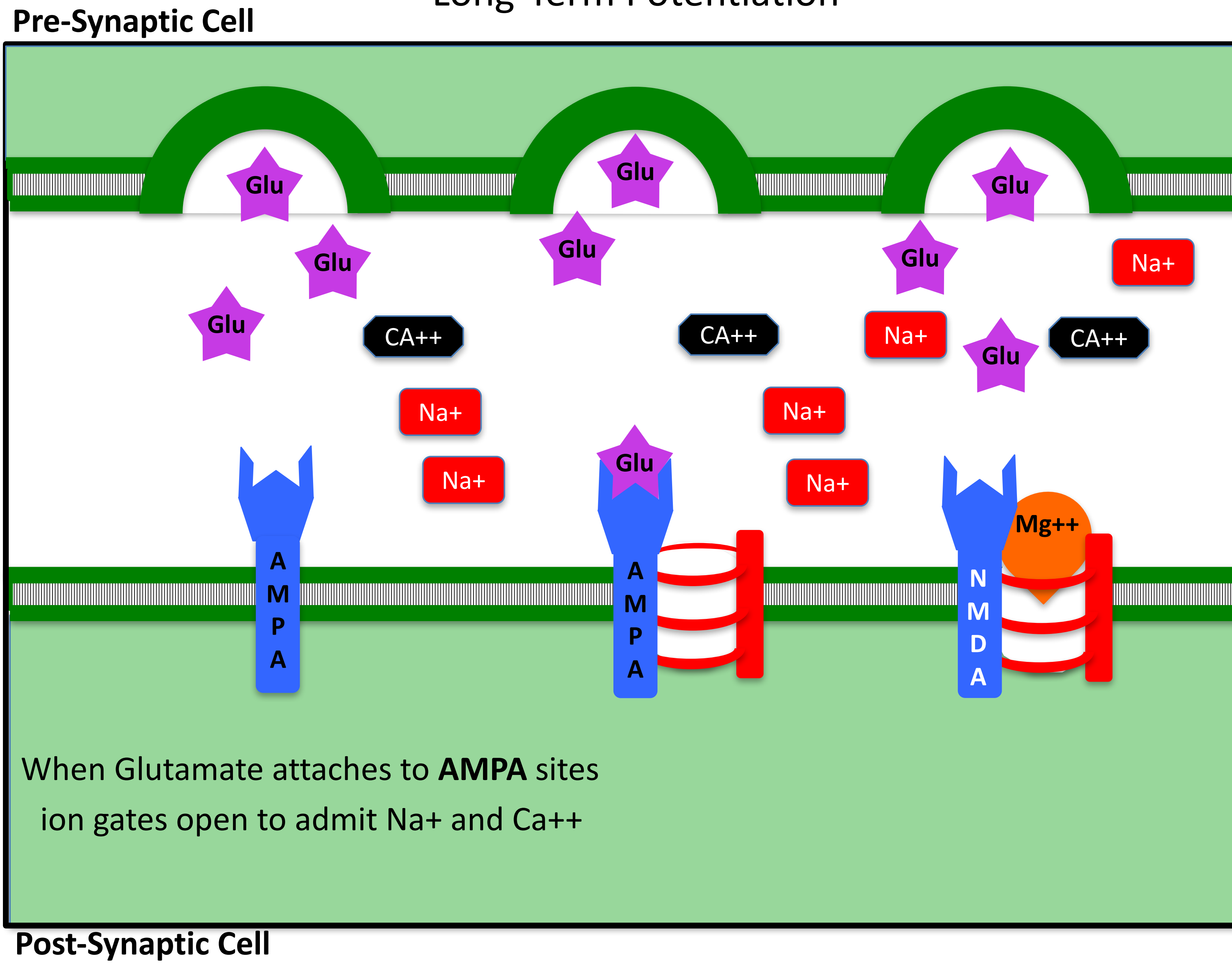
Glutamate is principal NT implicated in Learning

Two types of Receptor Sites for Glutamate – **AMPA** and NMDA

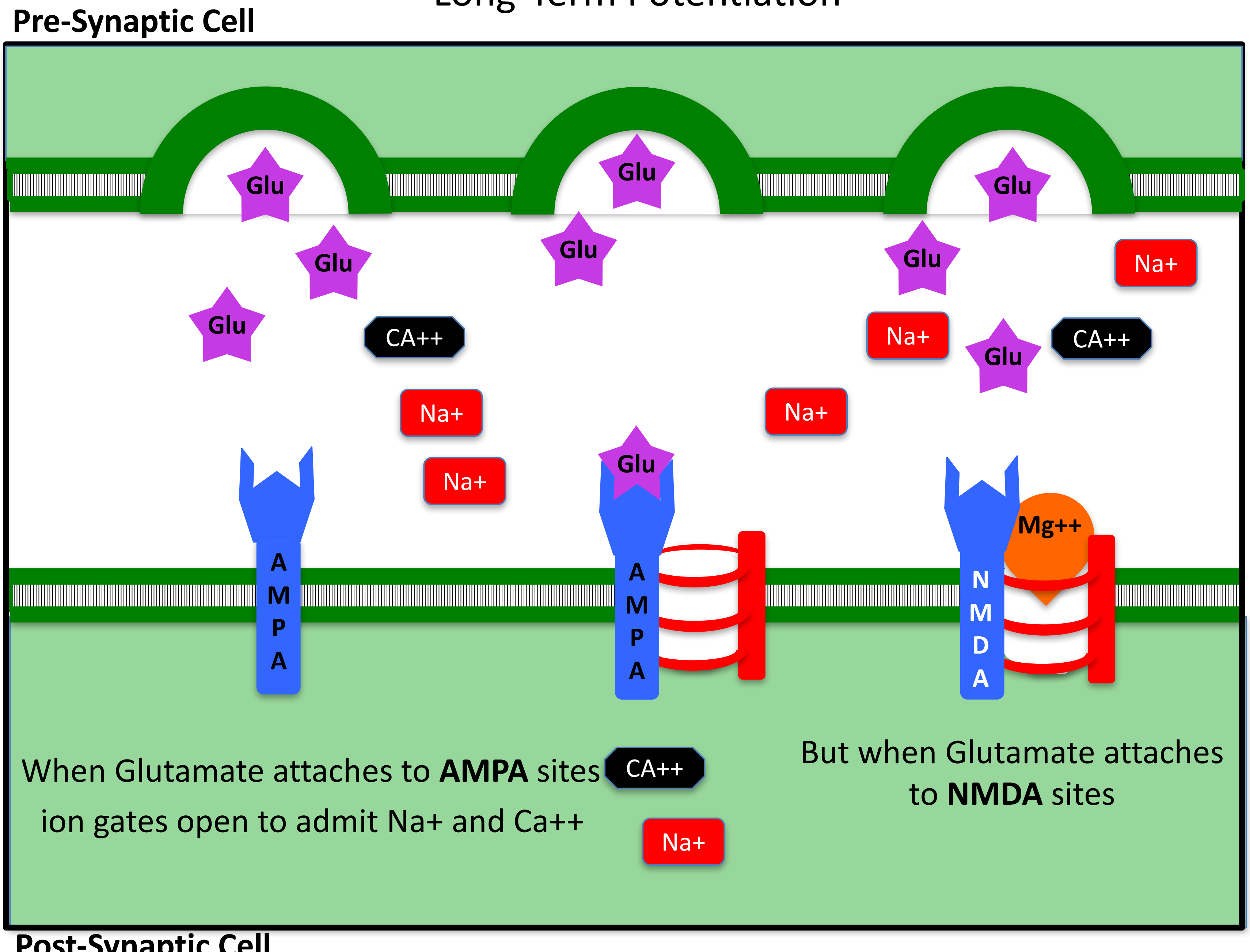
Long-Term Potentiation



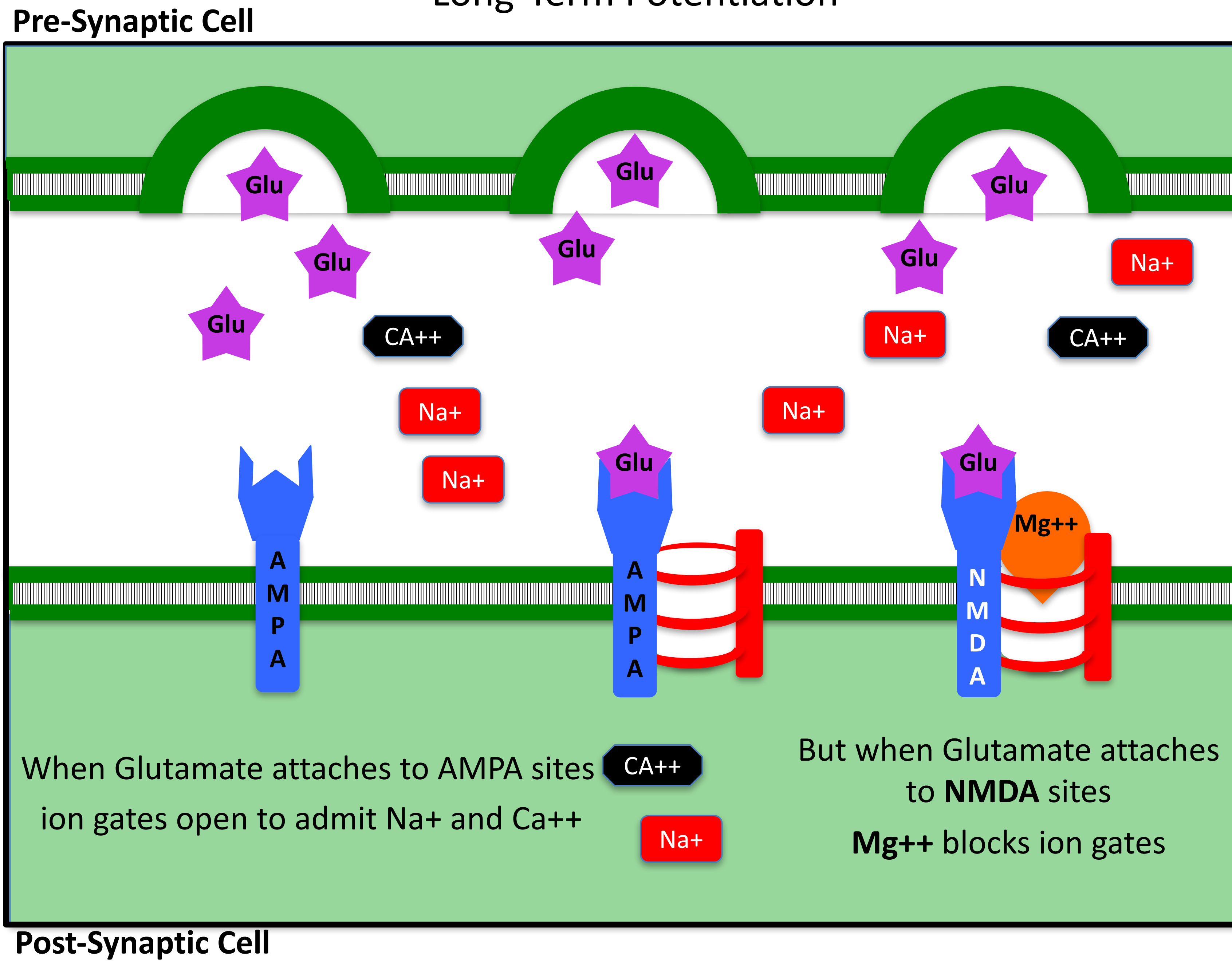
Long-Term Potentiation



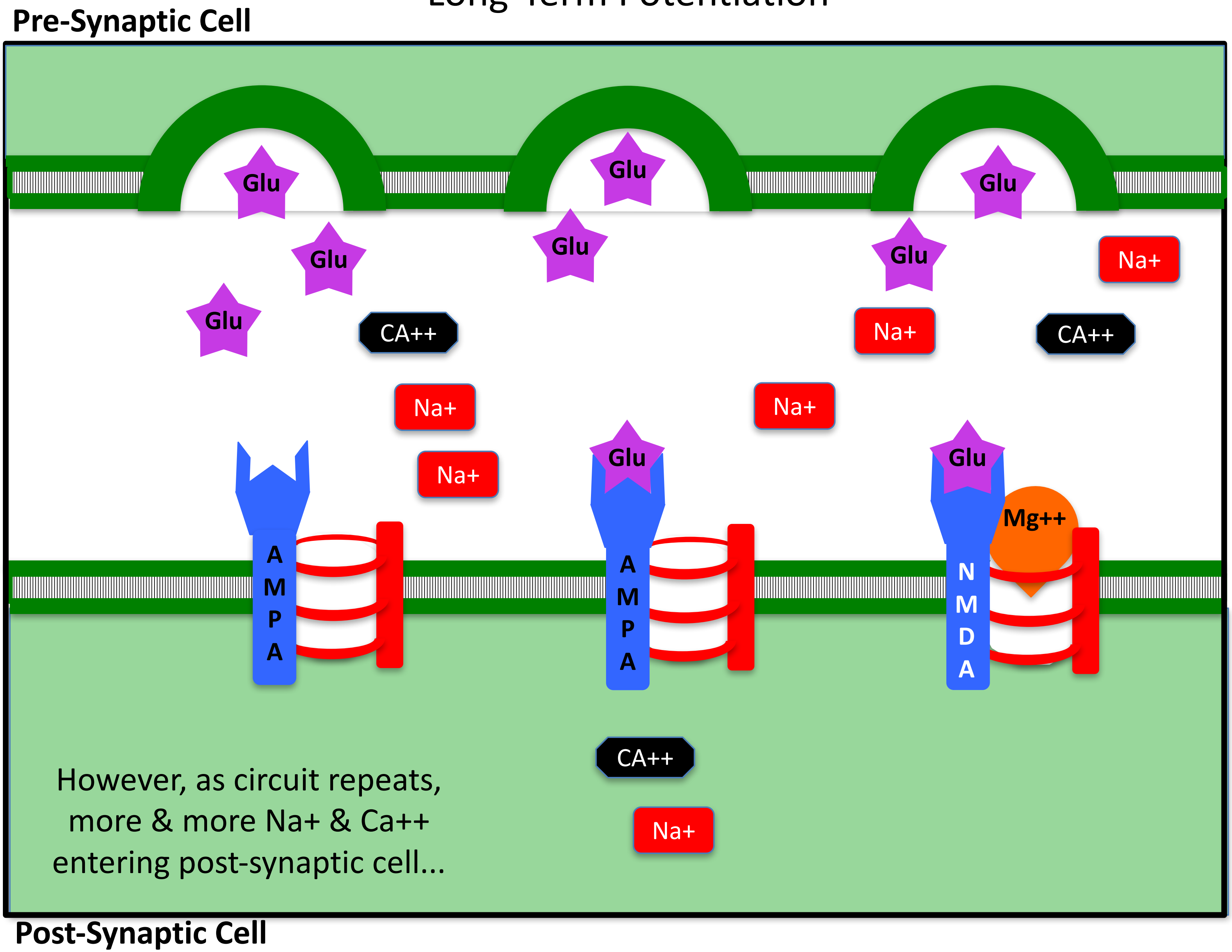
Long-Term Potentiation



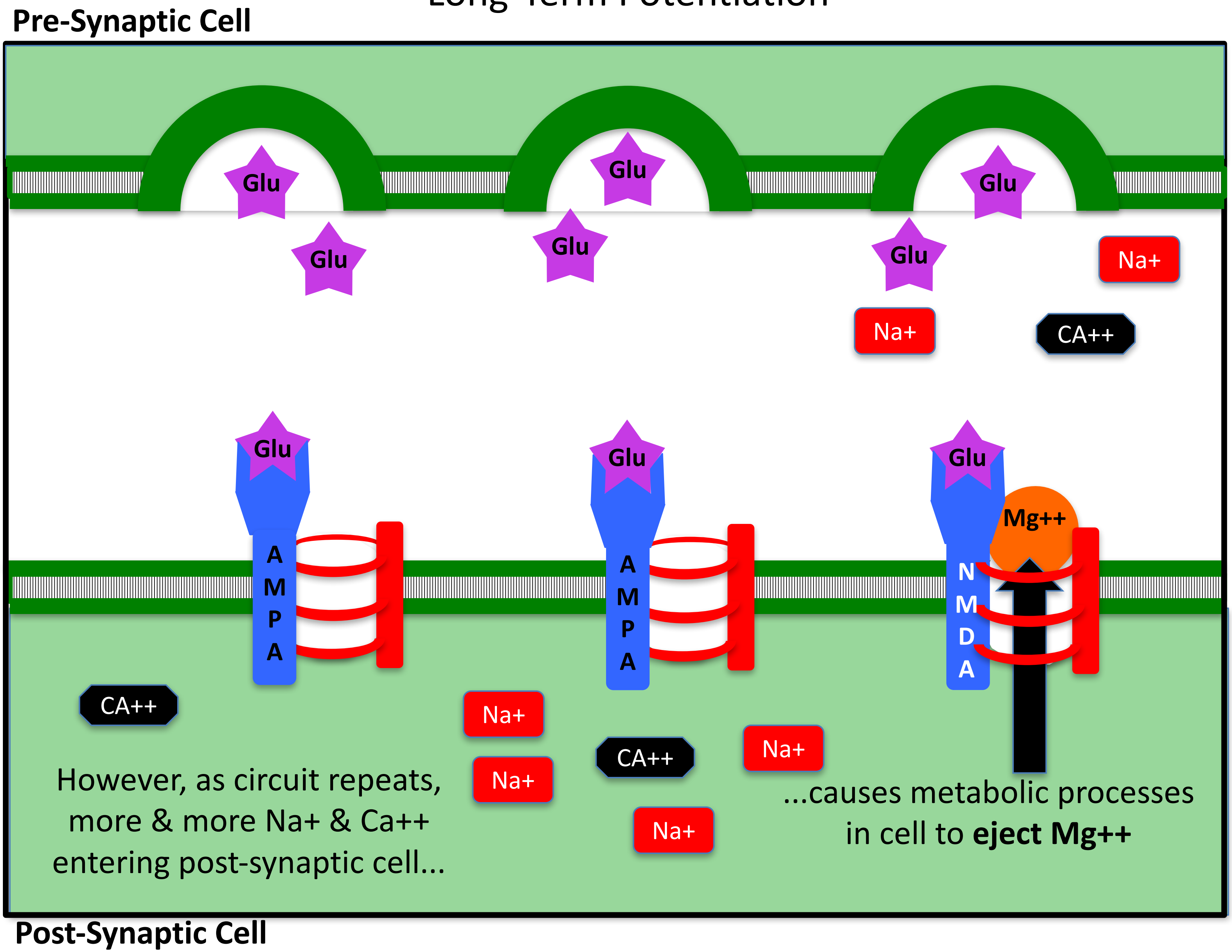
Long-Term Potentiation



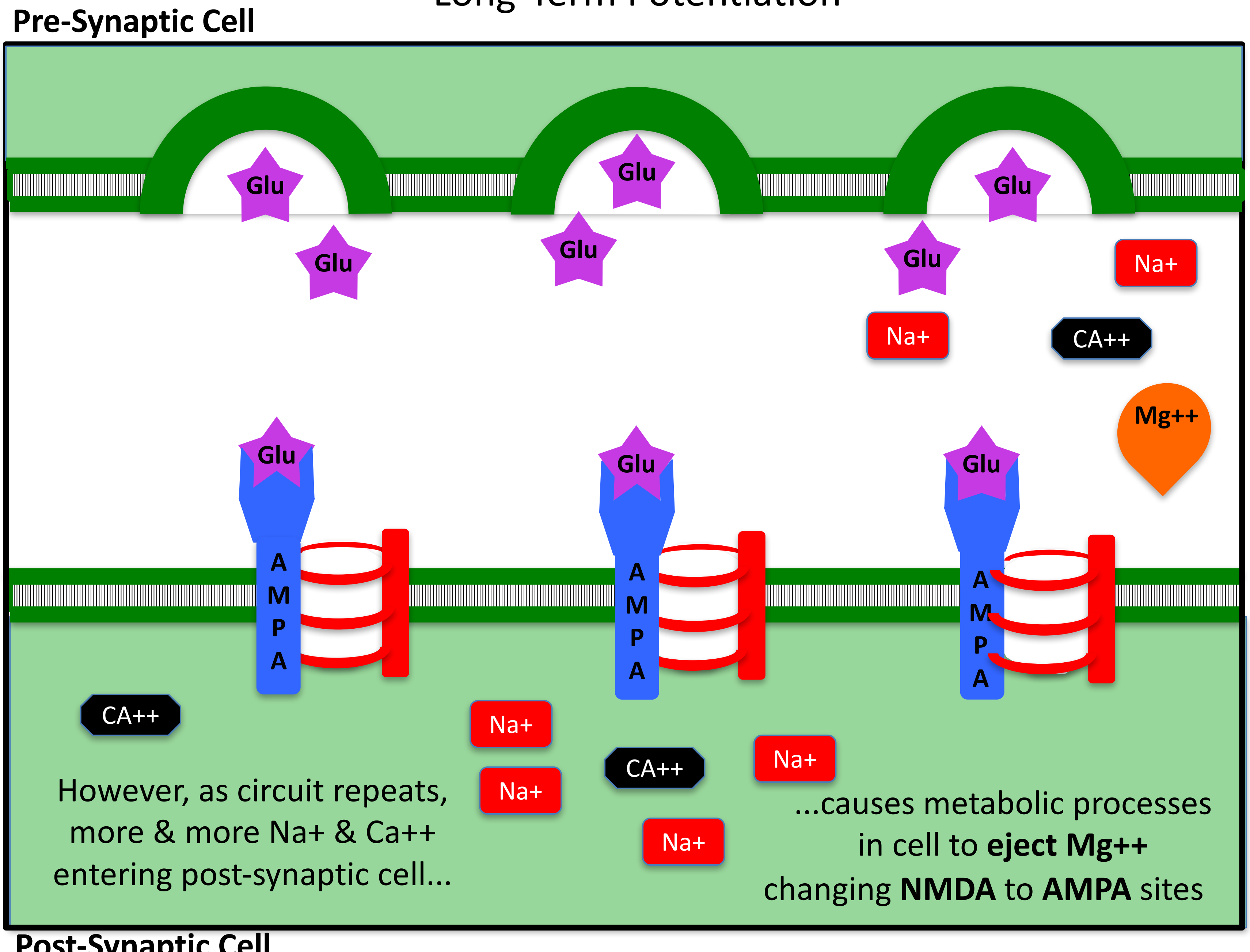
Long-Term Potentiation



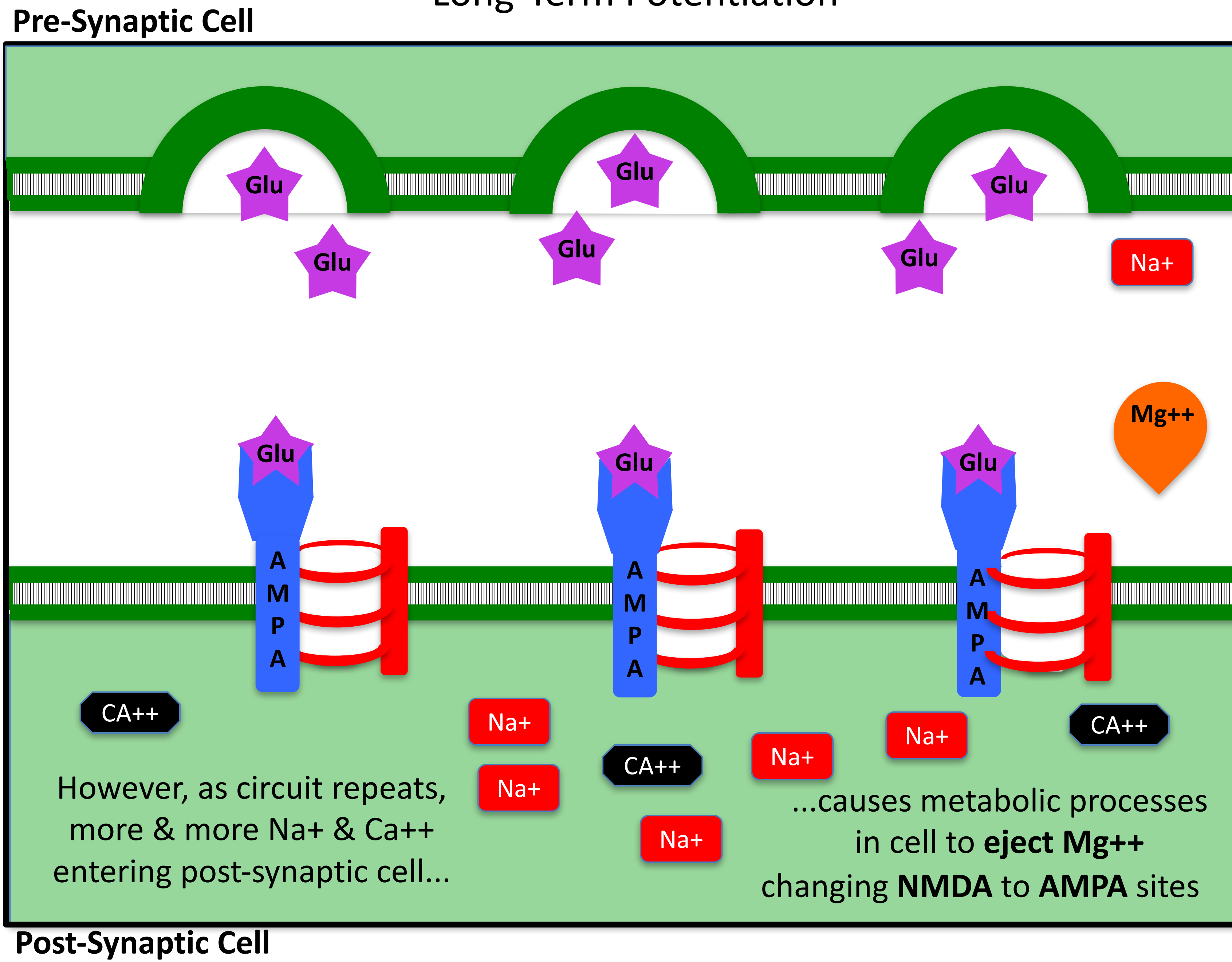
Long-Term Potentiation



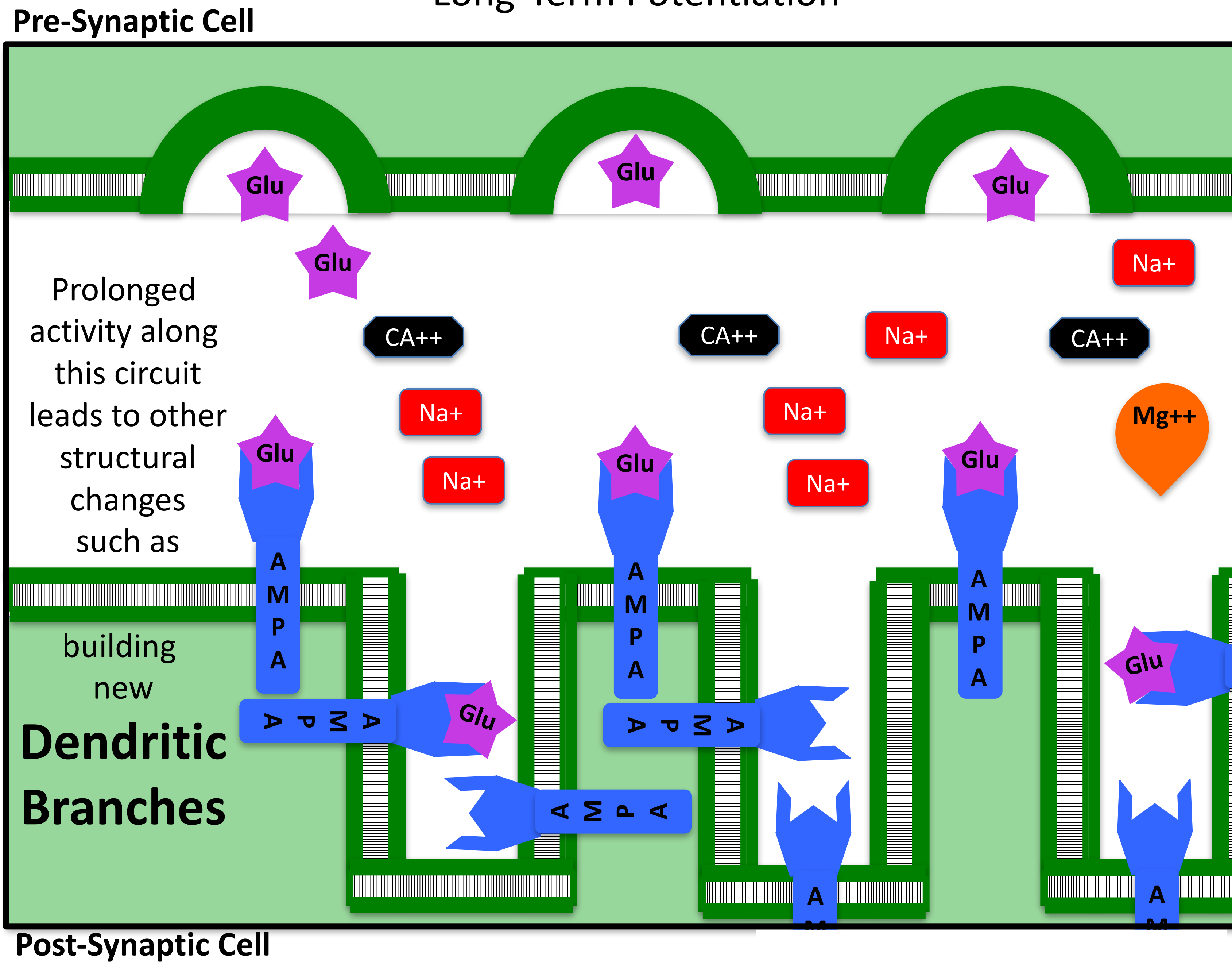
Long-Term Potentiation



Long-Term Potentiation

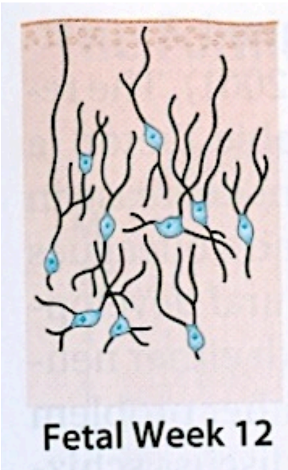


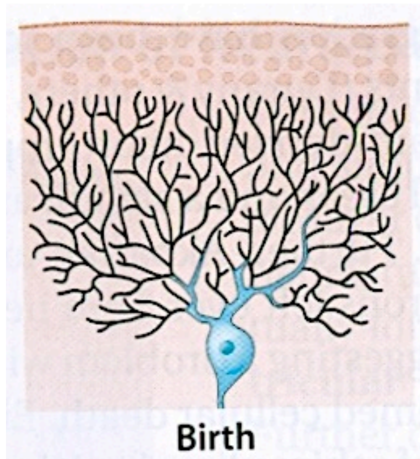
Long-Term Potentiation

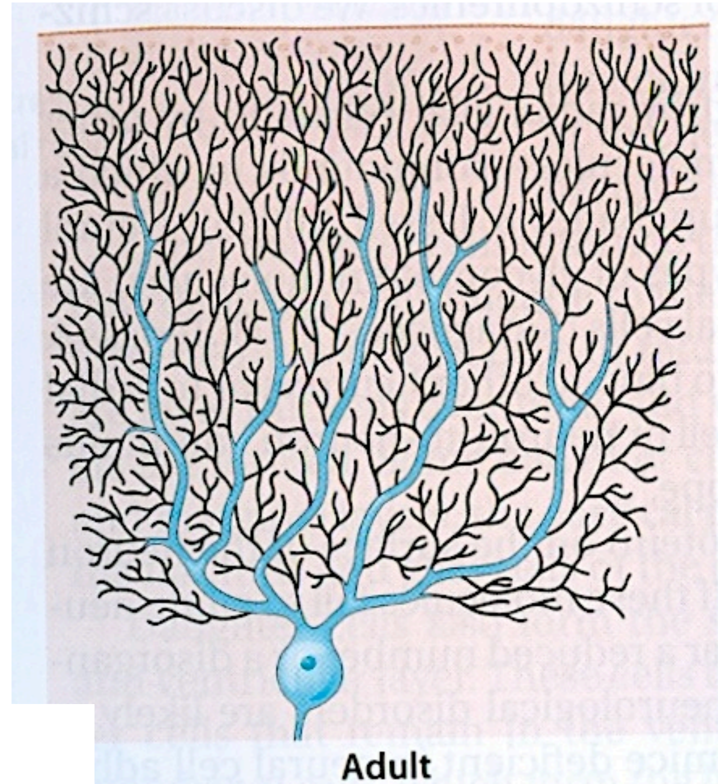


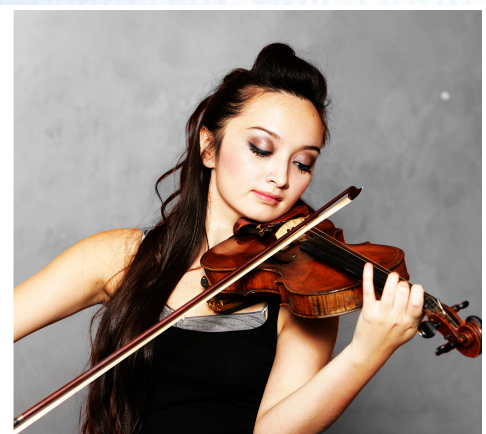
Dendritization: Increase in # of branches & thus in # of receptor sites

RECALL


Fetal Week 12


Birth

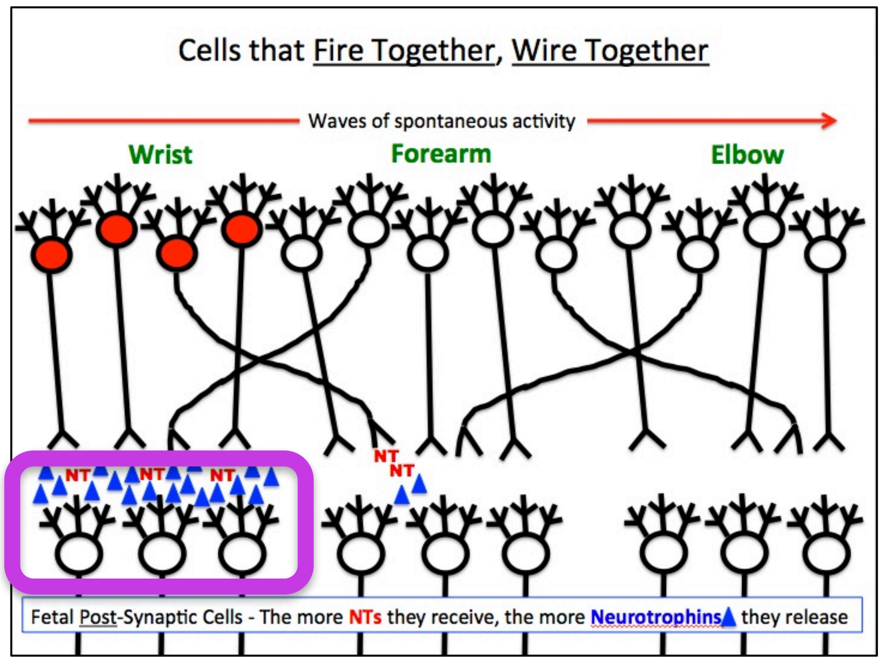

Adult



Long-Term Potentiation

RECALL

During brain development,
post-synaptic cells
release chemical feedback,
promoting further pre-synaptic activity



While common during
fetal development,
after birth, in most circuits,
chemicals (NTs) are only released
by **pre**-synaptic cells.

EXCEPT
in some memory circuits,
Retrograde Messengers
(e.g. Nitrous oxide)
are released, throughout life,
by **post**-synaptic cells

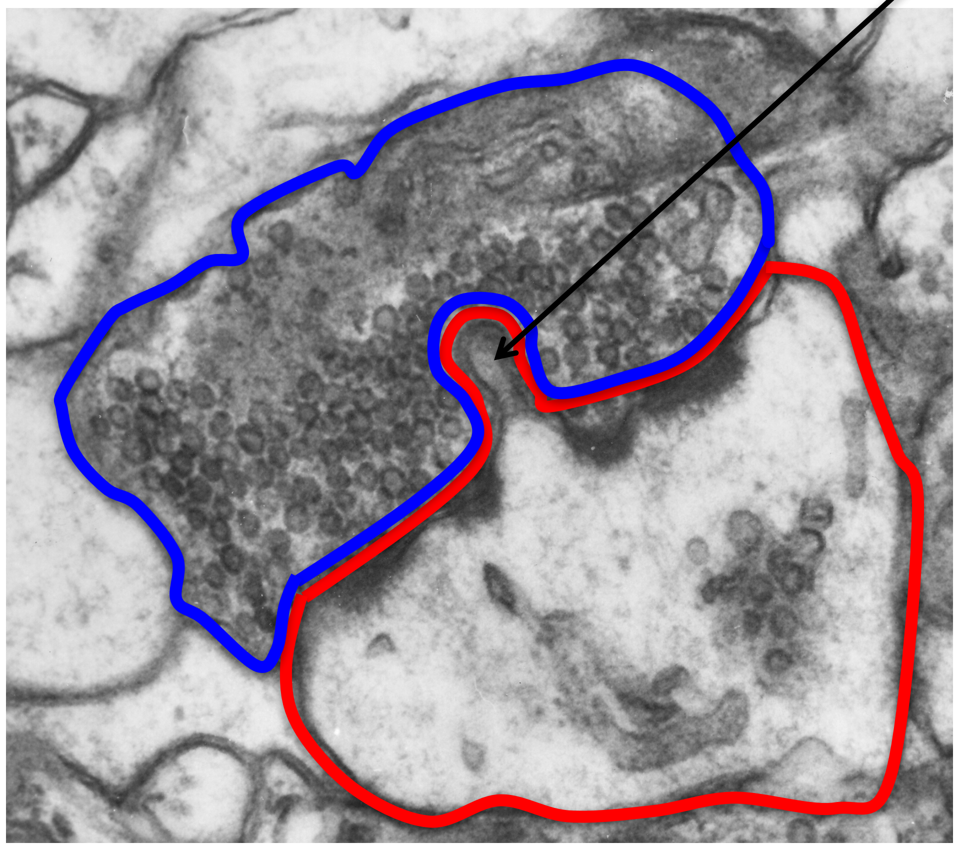
These prolong release of
neurotransmitters
by **pre**-synaptic cells

Long-Term Potentiation: **Perforation**

Post-Synaptic cell builds a temporary protuberance that deforms Pre-Synaptic terminal

Pre-Synaptic Terminal

("perforated" – membrane stretched, not broken)

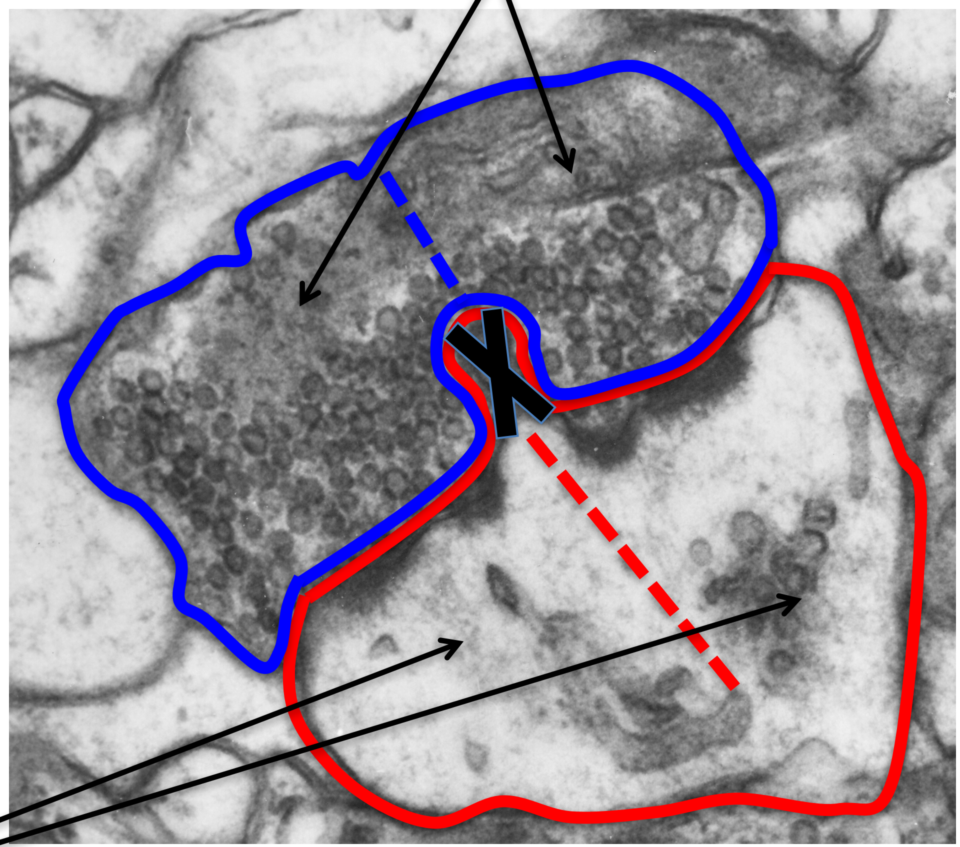


Post-Synaptic dendritic spine

(with protuberance that "perforates" pre-synaptic terminal)

Long-Term Potentiation: **Perforation**

This "perforation" promotes the division of the Pre-Synaptic terminal into two terminal buttons

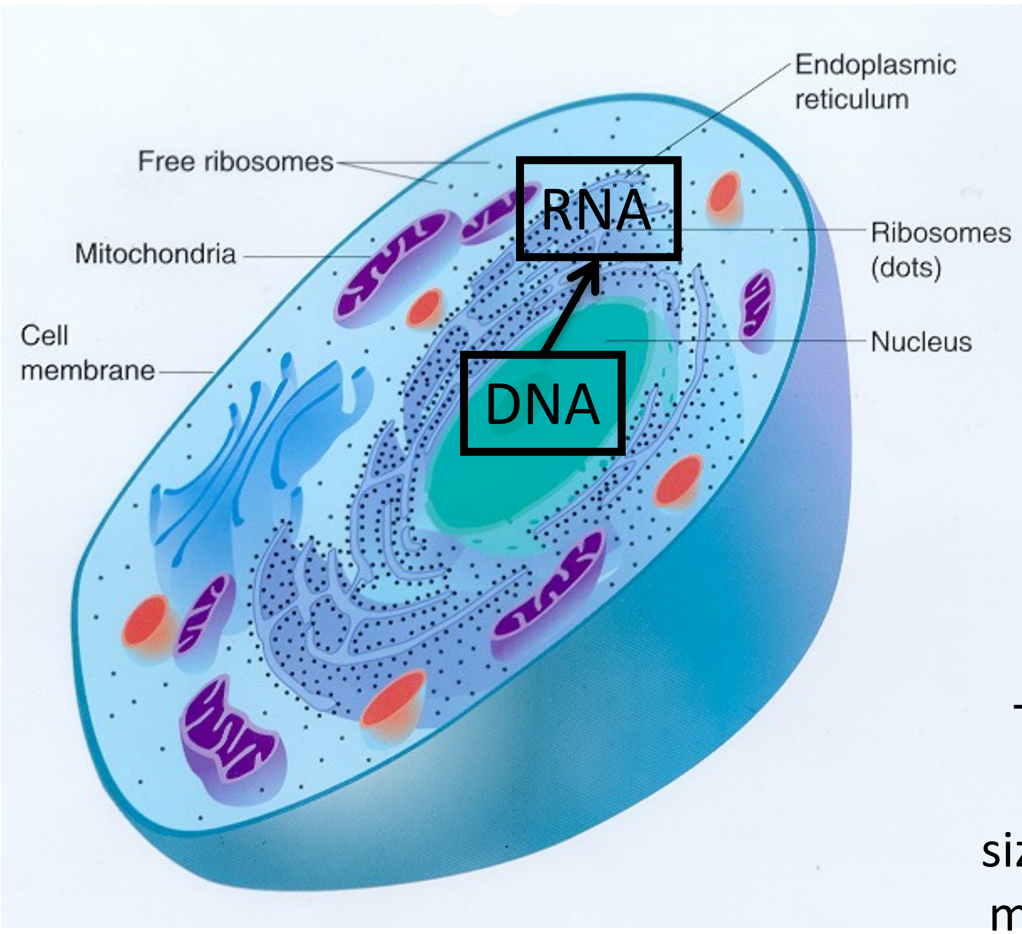


Pre-Synaptic Terminal

Post-Synaptic dendritic spine

Then dendrite dismantles protuberance, and divides into two dendritic spines, each receiving NT from one of the new terminal buttons

Other Factors that Modify Function based on Experience



RECALL

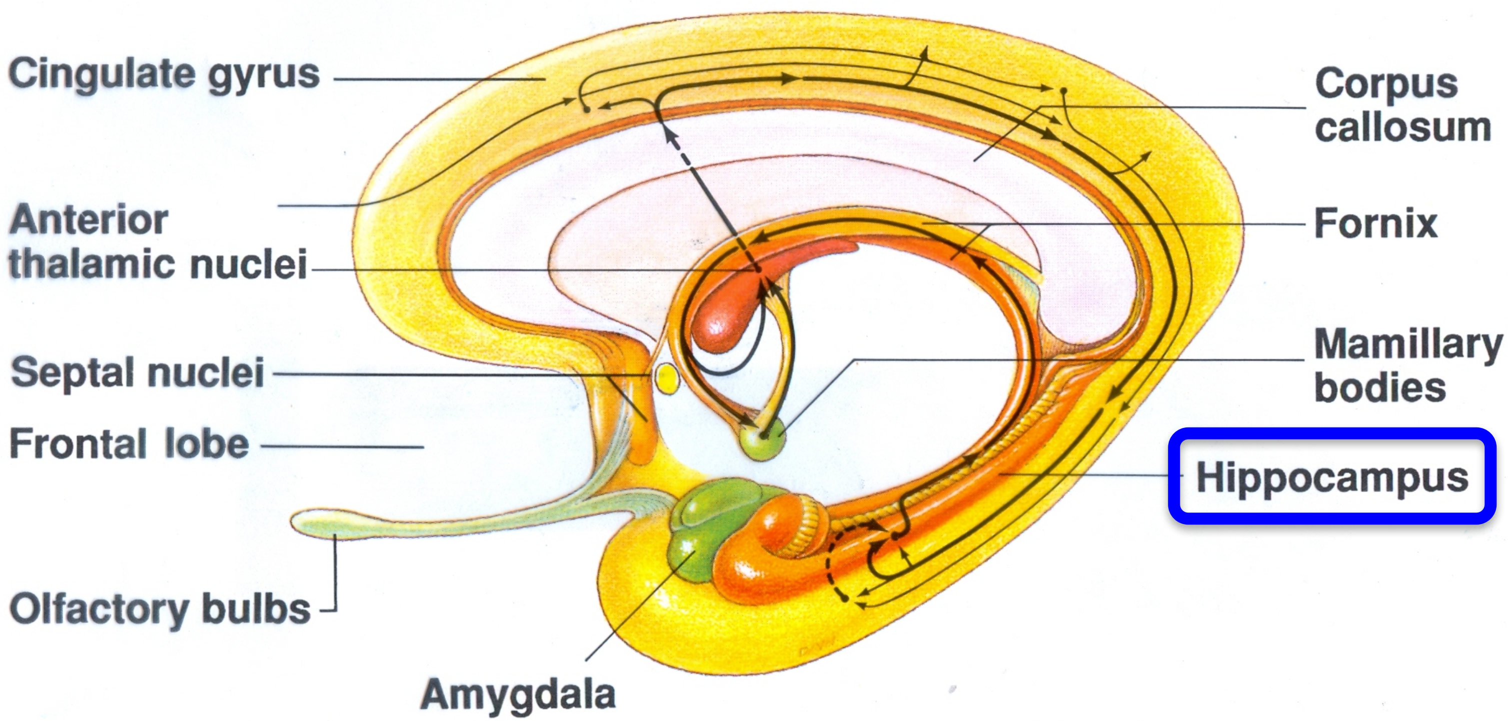
GENE TRANSCRIPTION

Copies of segments of DNA (= RNA) are made, to code for protein production

These proteins can change # of NTs available, size & distribution of vesicles, metabolic processes in cells, etc etc etc!

Neurogenesis (Rare)

In a few brain areas – such as <u>Hippocampus</u> – can see **NEW CELL** growth



Especially re: Temporal-based and Spatial learning
(more below)

Memory

Often divided into 3 classes, per areas of brain most critical to each

- Spatial
  - Hippocampus

Where is it?

How do you get there?

- Procedural
  - Cerebellum & Basal Ganglia

How do you do X?

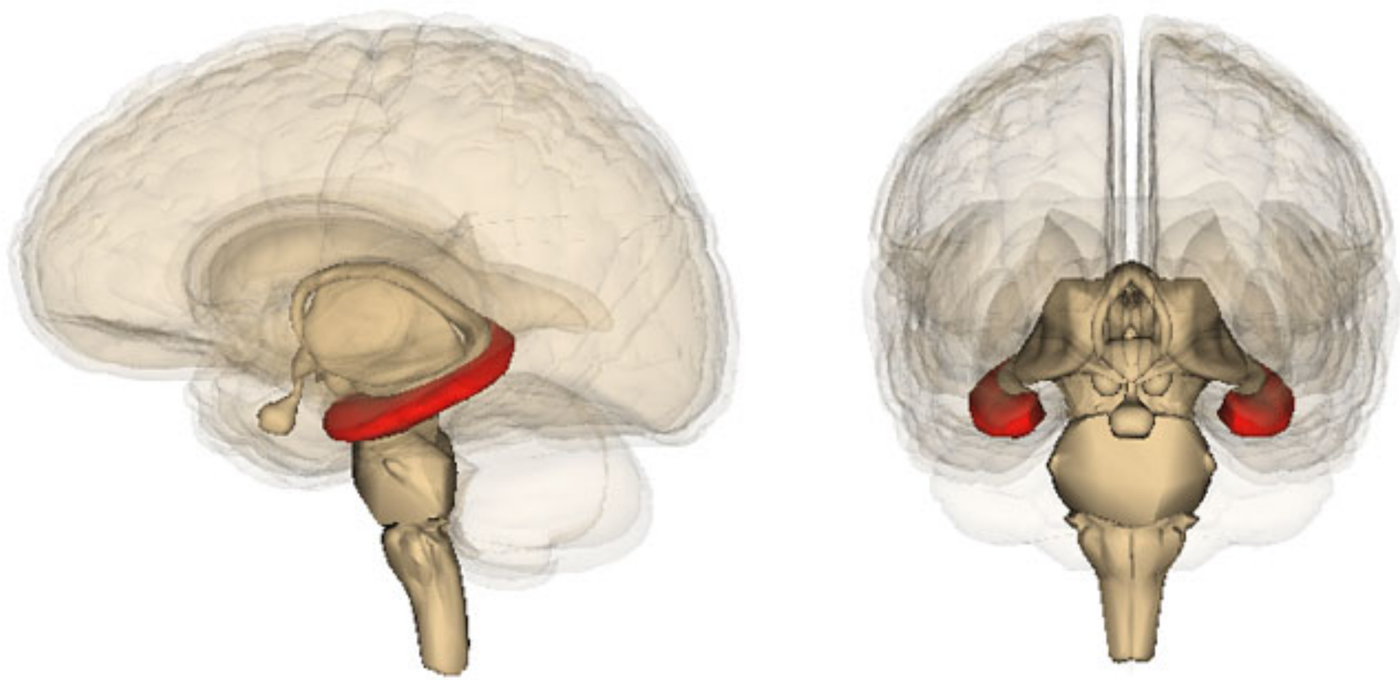
How do you do Y?

- Declarative
  - Hippocampus, MDN (Thalamus) & Prefrontal Cortex

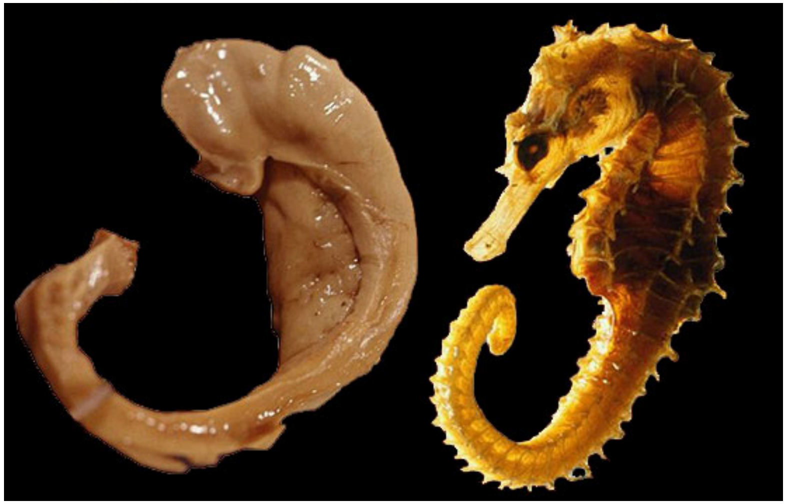
Who is this?

What are the rules?

Hippocampus



"Hippocampus"
- Latin for
"Seahorse"



MNEMONIC:
If I you saw a
hippo on campus,
you'd never forget!

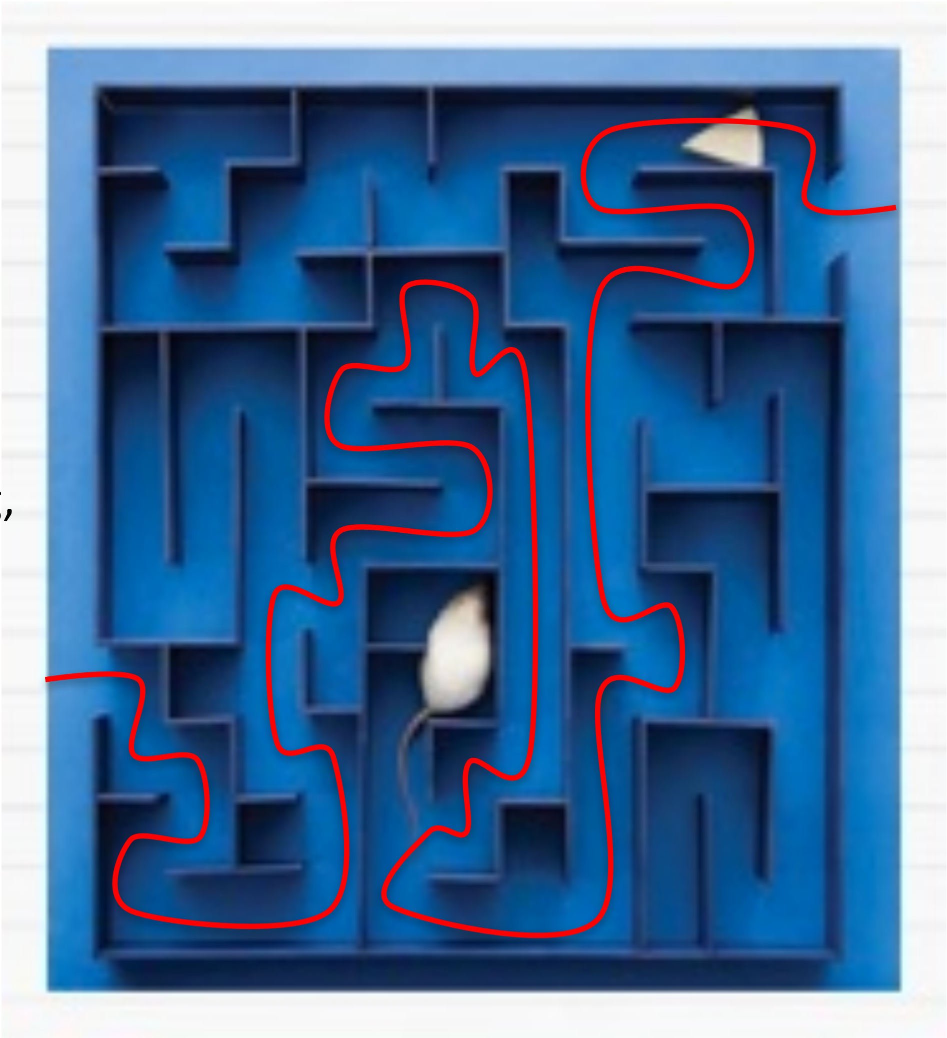
Hippocampus - Spatial Memory

Rat first explores maze,
entering all possible tunnels

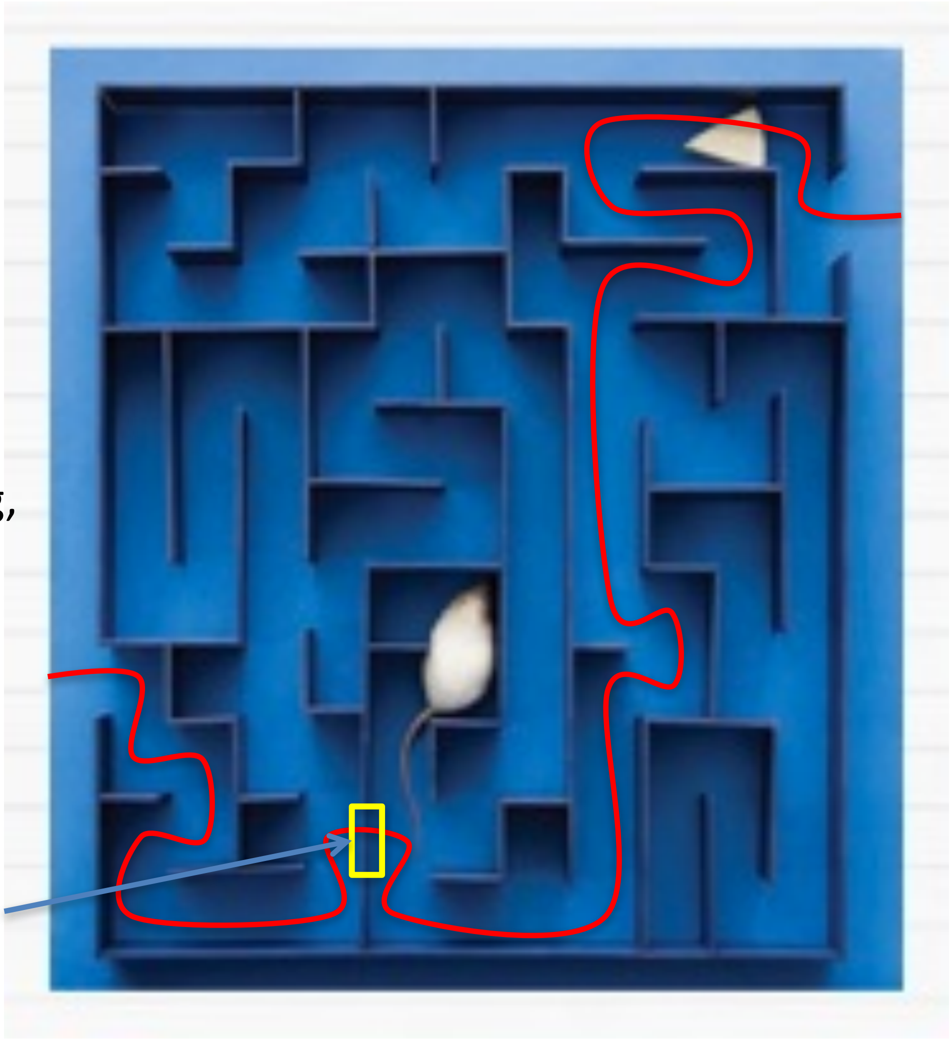
In time, develops an
efficient path through maze

Over the course of such spatial learning,
Hippocampus develops
"Place Cells"

As animal moves from
(known) place to place,
corresponding cells are active



Hippocampus - Spatial Memory



Over the course of such spatial learning, Hippocampus develops

"Place Cells"

After rat learns maze, remove this wall

Rat will take **short cut**!

Rat uses the **Cognitive Map** it developed while exploring the maze

Hippocampus - Spatial Memory

Clark's Nutcracker

Lives at high elevations (snow), must cache seeds for winter

Has much ***LARGER*** Hippocampus!

vs. closely-related

Scrub Jay

Lives at lower elevations (no snow), does little caching

Hippocampus - Spatial Memory

Clark's Nutcracker

Lives at high elevations (snow), must cache seeds for winter

Has much ***LARGER*** Hippocampus!

In the lab, has been shown to remember 1000 hiding places

Hippocampus - Spatial Memory

Clark's Nutcracker

Lives at high elevations (snow),
must cache seeds for winter

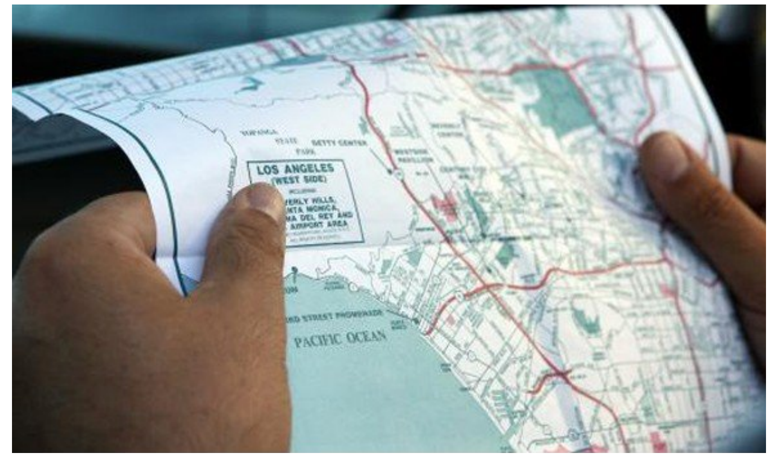
Has much ***LARGER*** Hippocampus!

Some humans have
<u>larger Hippocampi</u> than others,
per how much they <u>depend on Spatial Memory</u>

Hippocampus - Spatial Memory

Likewise, damage to human Hippocampus can impair . . .

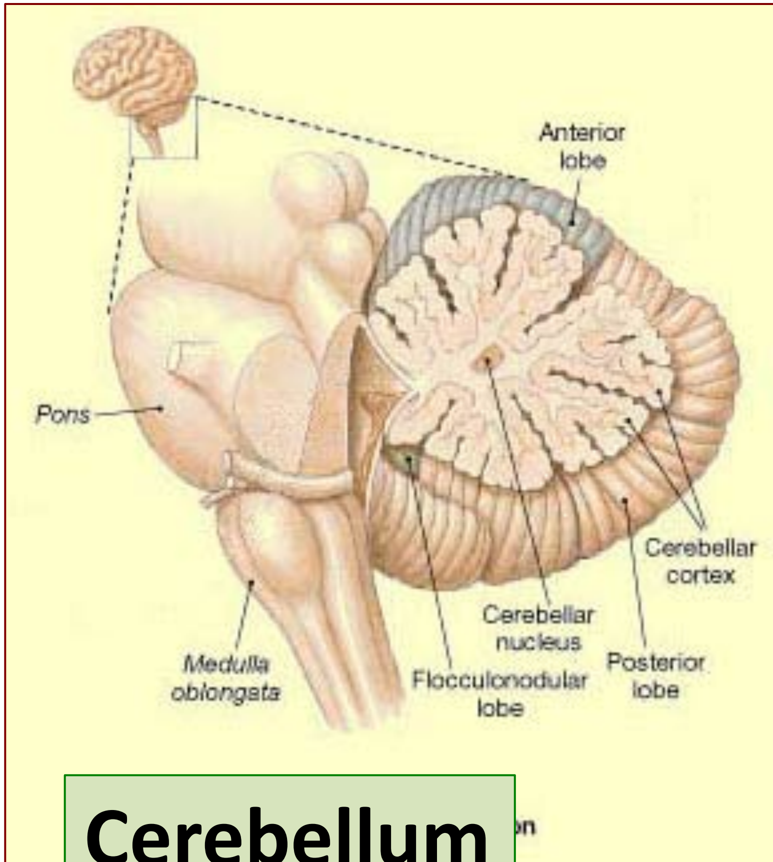
Navigation



Map Reading

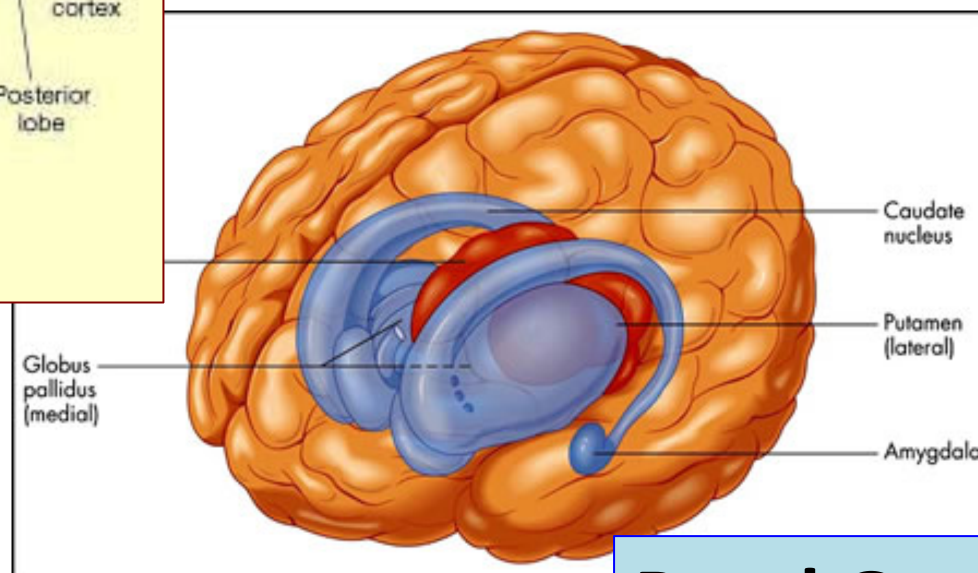
Recall of location

Procedural Memory



Cerebellum

Memory for How To...

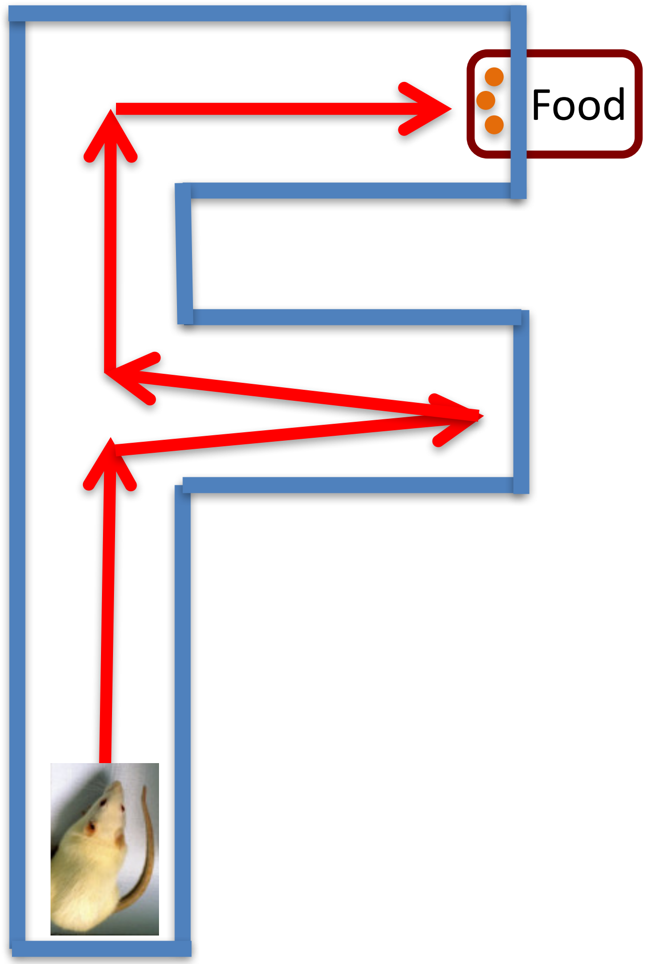


Basal Ganglia

Types of Memory...

Rat in an

"F Maze"

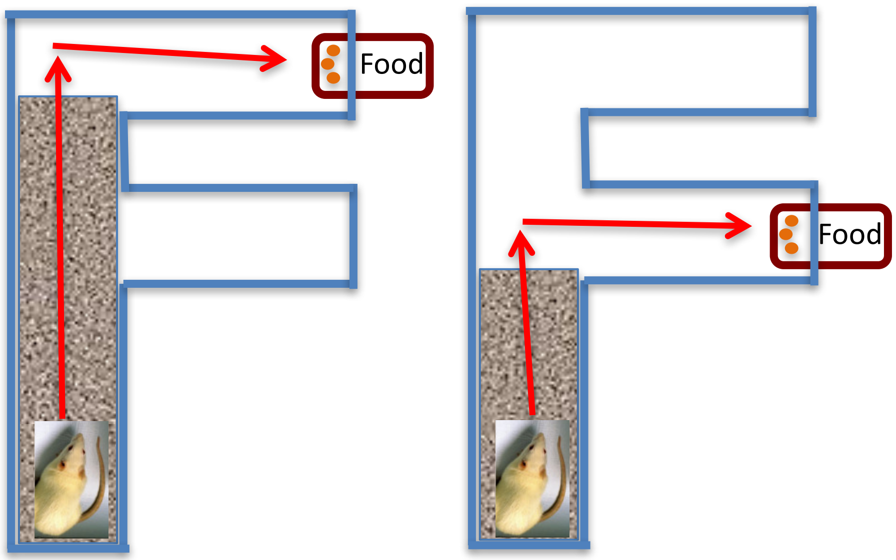


Rat will explore maze
until learns some **<u>regularity</u>**
that <u>predicts location of food</u>

Procedural vs. Declarative Memory

Condition A

As long as floor is rough,
continue forward,
then turn right



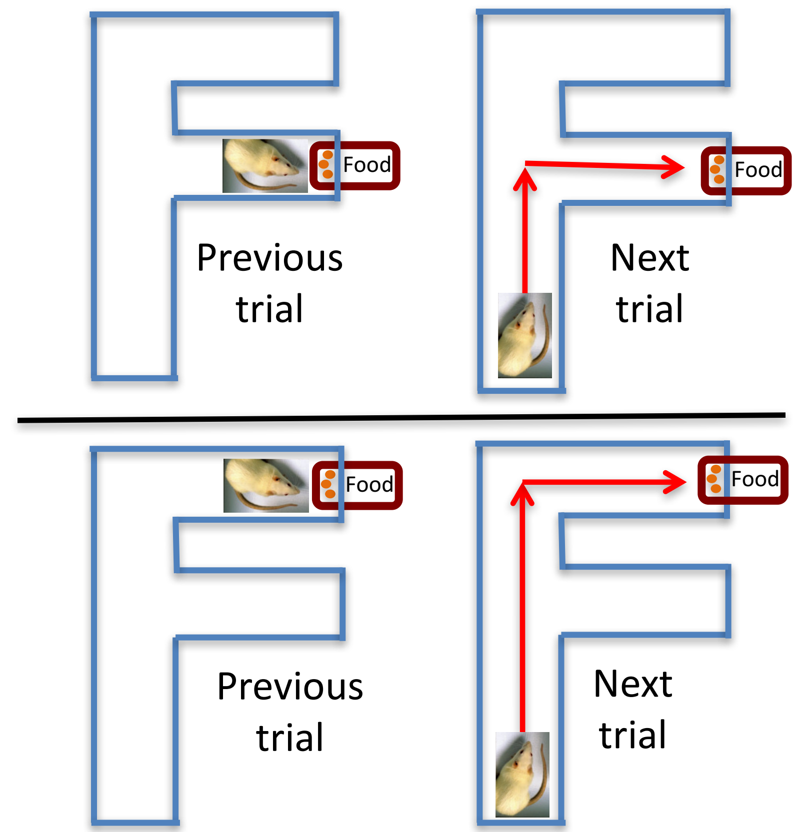
<u>Action</u> is based on <u>sensory cue</u>

<u>Procedural</u>

Damage to **Cerebellum** impairs more

Condition B

Go to same arm where
reinforced on last trial



<u>Declarative</u>

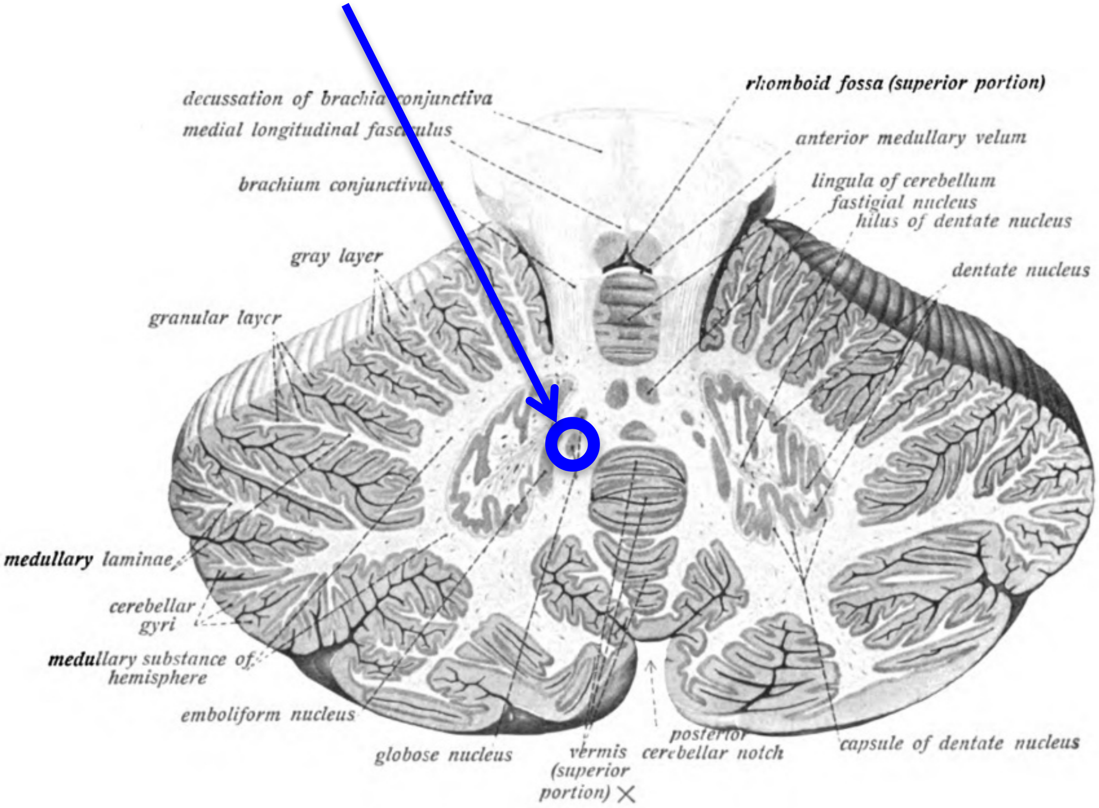
<u>Action</u> is
<u>rule-based</u>

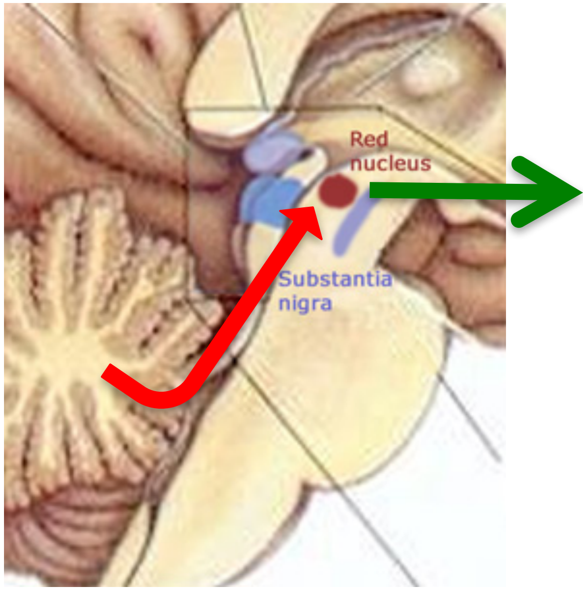
Damage to **Hippocampus** impairs more

Procedural Memory

Conditioned Eye Blink

Lateral Interpositus of Cerebellum





Sends input to **Red Nucleus** of Tegmentum

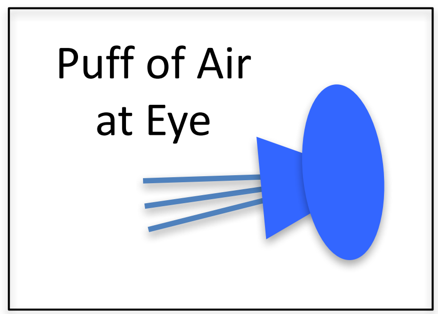
>> **Cranial Nerve** to produce Eye-Blink

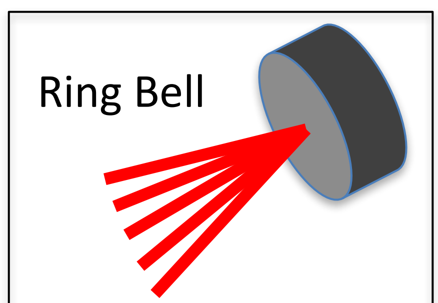
Procedural Memory

Conditioned Eye Blink

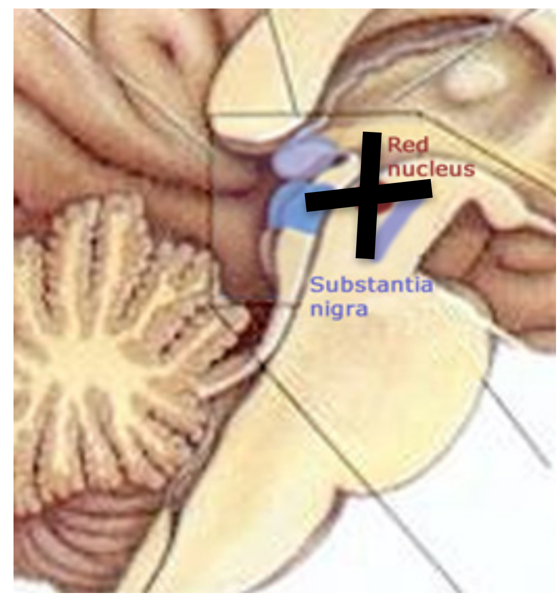
Research involves Rabbits, ...

... Stimuli
(Puff of air to eye,
&/or Ring Bell) ...



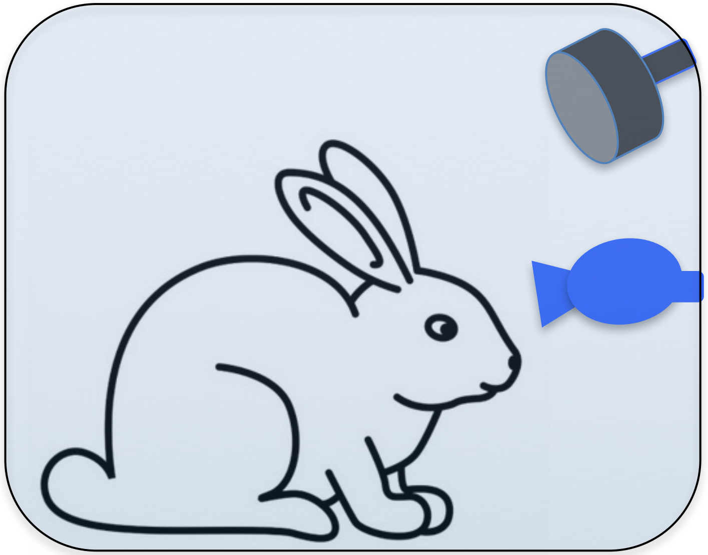


... & **<u>Targeted Cooling</u>**,
that temporarily
renders an area inactive

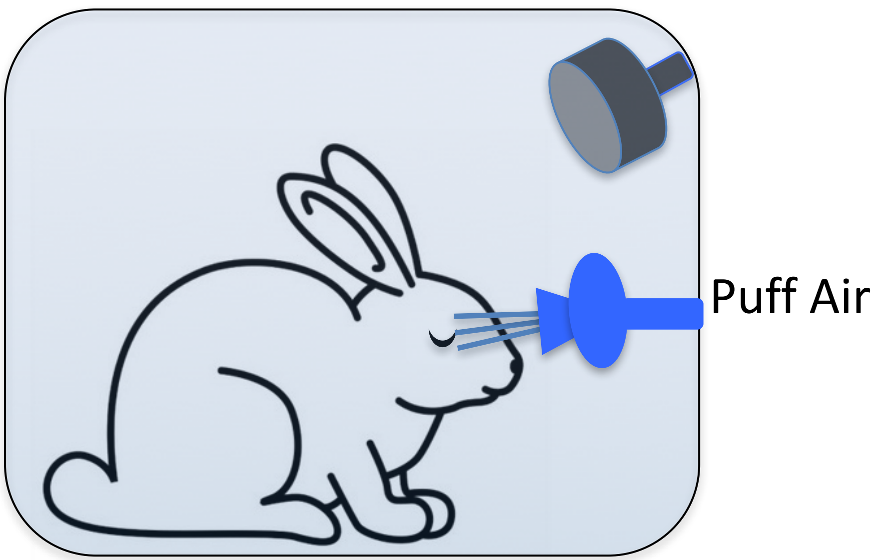


Conditioned Eye Blink

Procedural Memory



Rabbits,
like many of us,
have a "Eye Blink" Reflex

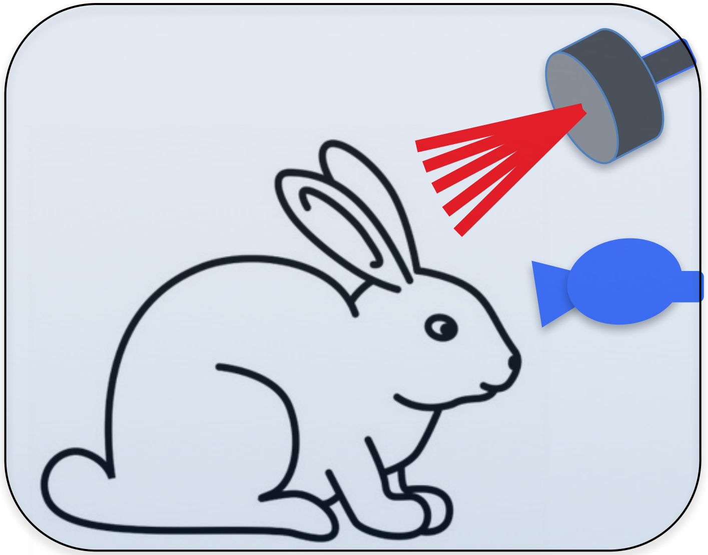


i.e. A puff of air to eye
results in a Blink

This is an
unconditioned response
(no learning required)

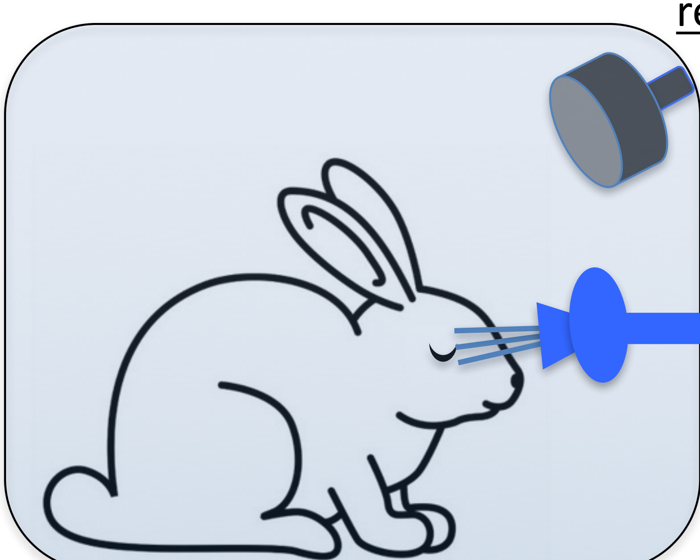
Conditioned Eye Blink

Procedural Memory



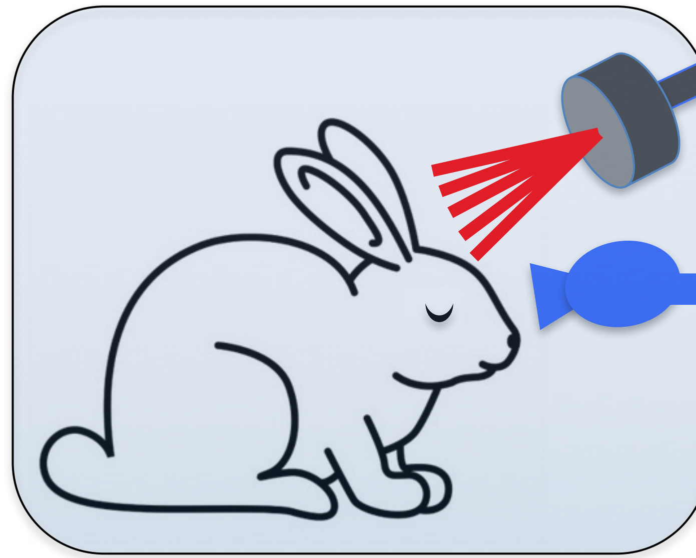
Ring Bell

Pair
these
stimuli
<u>repeatedly</u>



Puff Air

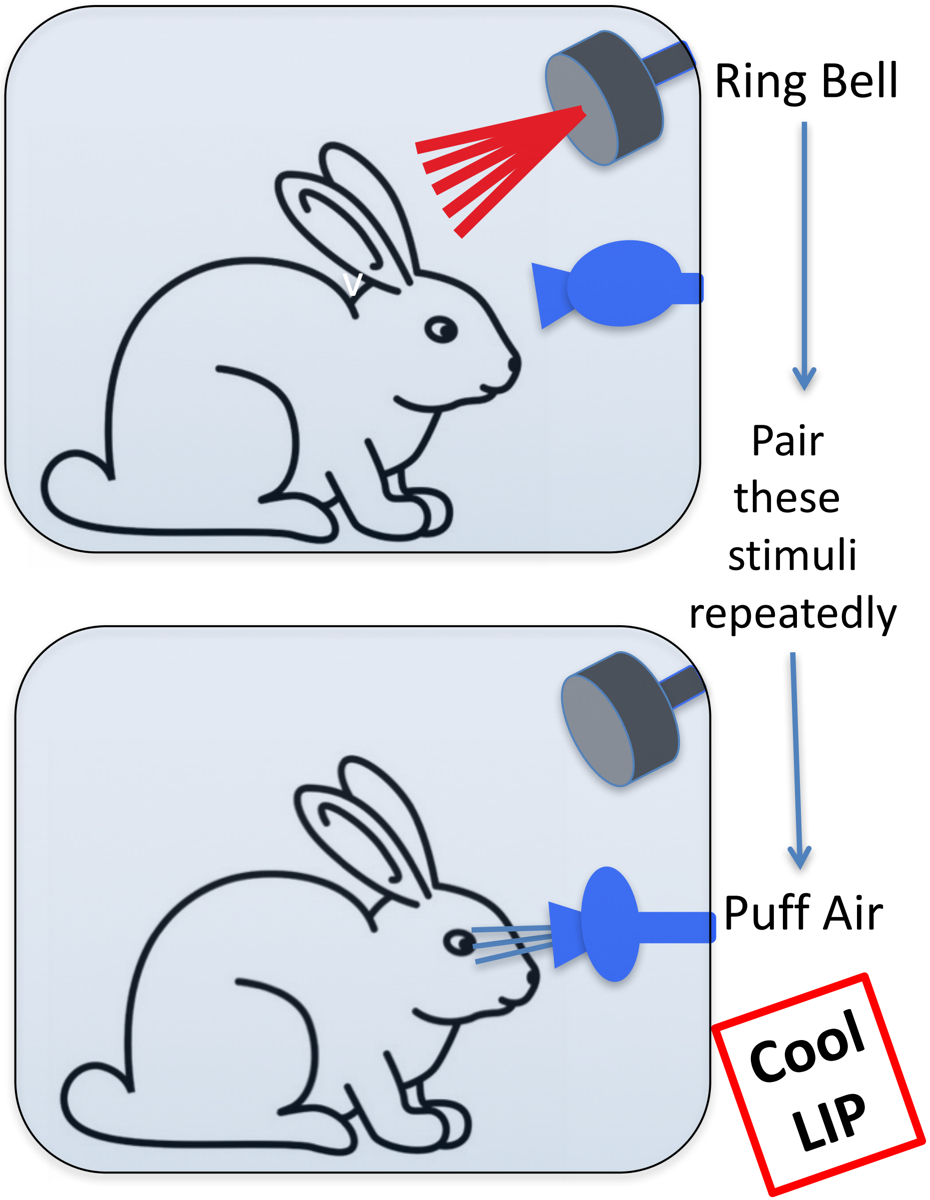
Eventually,
when <u>Rabbit hears Bell alone</u>
it will <u>close its eyes</u>
(anticipating Air Puff)



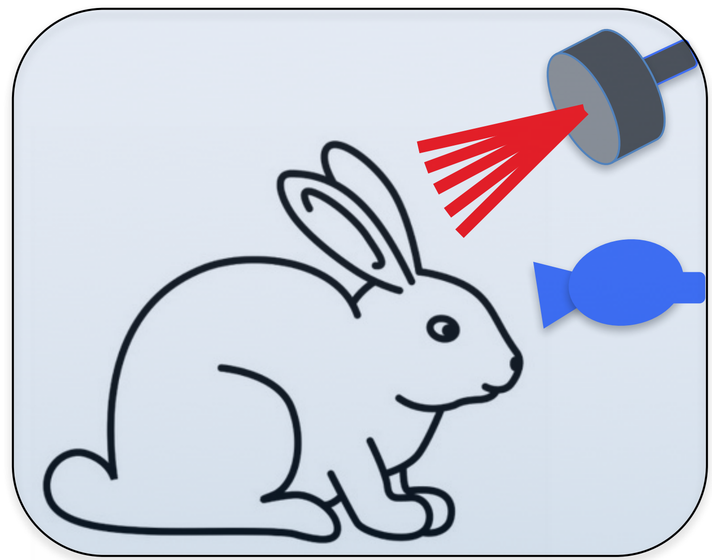
It has **Learned**
(Classical Conditioning)

Conditioned Eye Blink

Procedural Memory



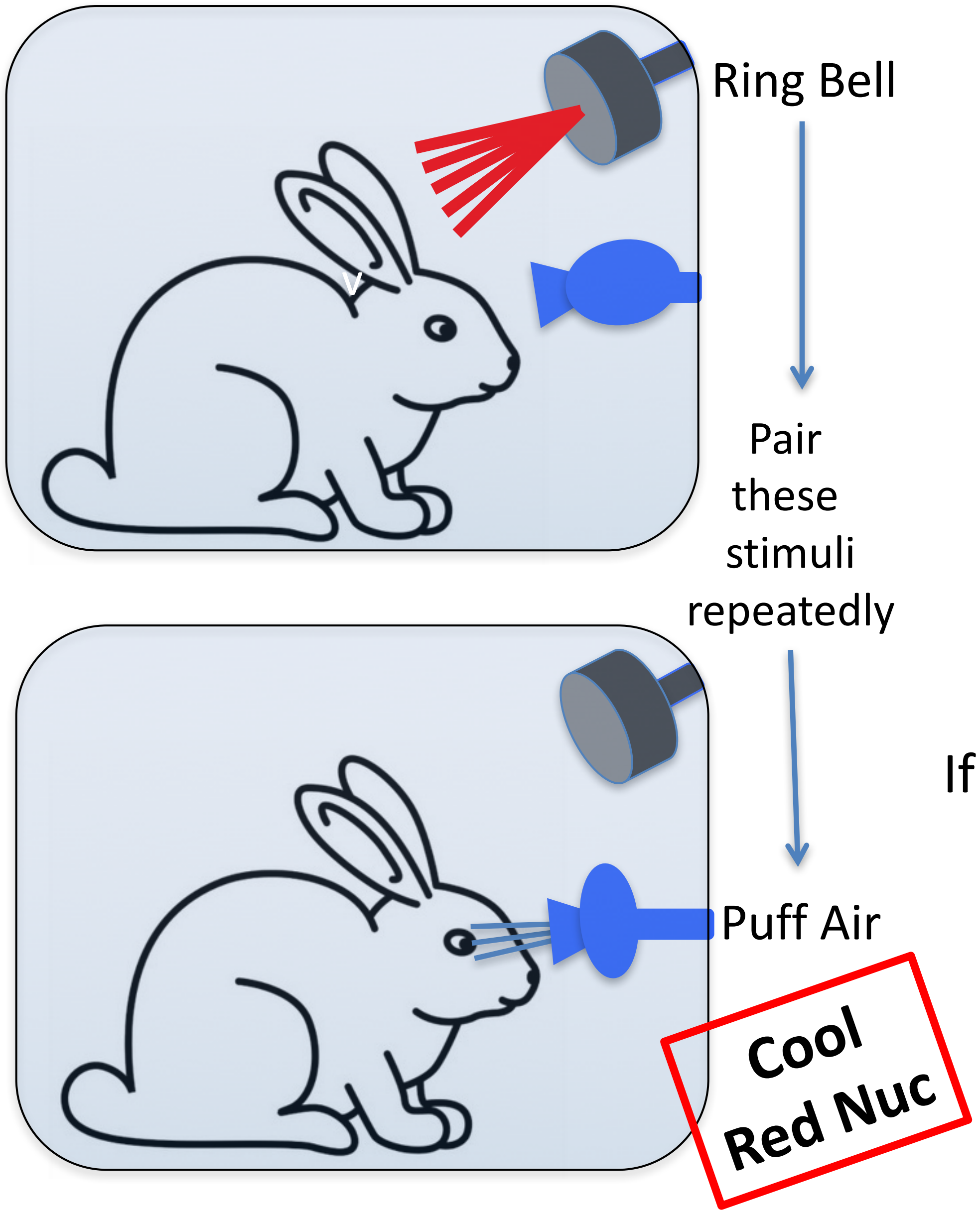
If suppress (cool) **LIP**
of Cerebellum,
subject does not blink
during training
(i.e. reflex temporarily disabled)



... and **does not learn**
association

Conditioned Eye Blink

Procedural Memory



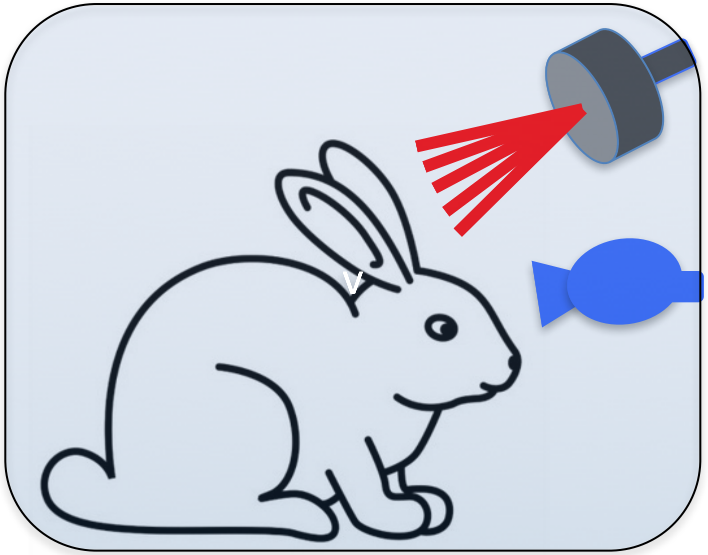
If suppress (cool) **Red Nucleus**

Rabbit **does not blink** during training

(Since Red Nucleus cannot send signal to eye muscles)

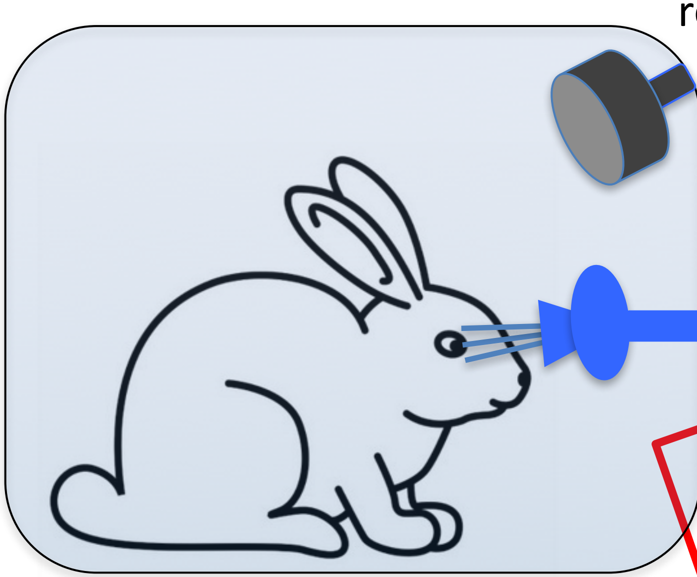
Conditioned Eye Blink

Procedural Memory



Ring Bell

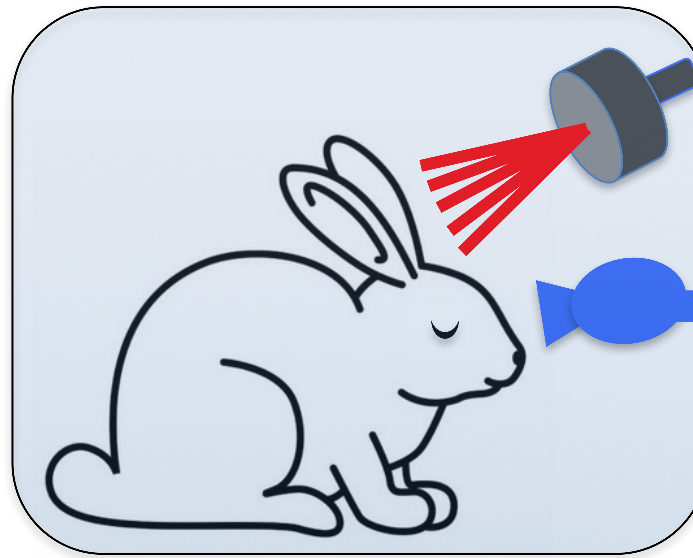
Pair these stimuli repeatedly



Puff Air

Cool Red Nuc

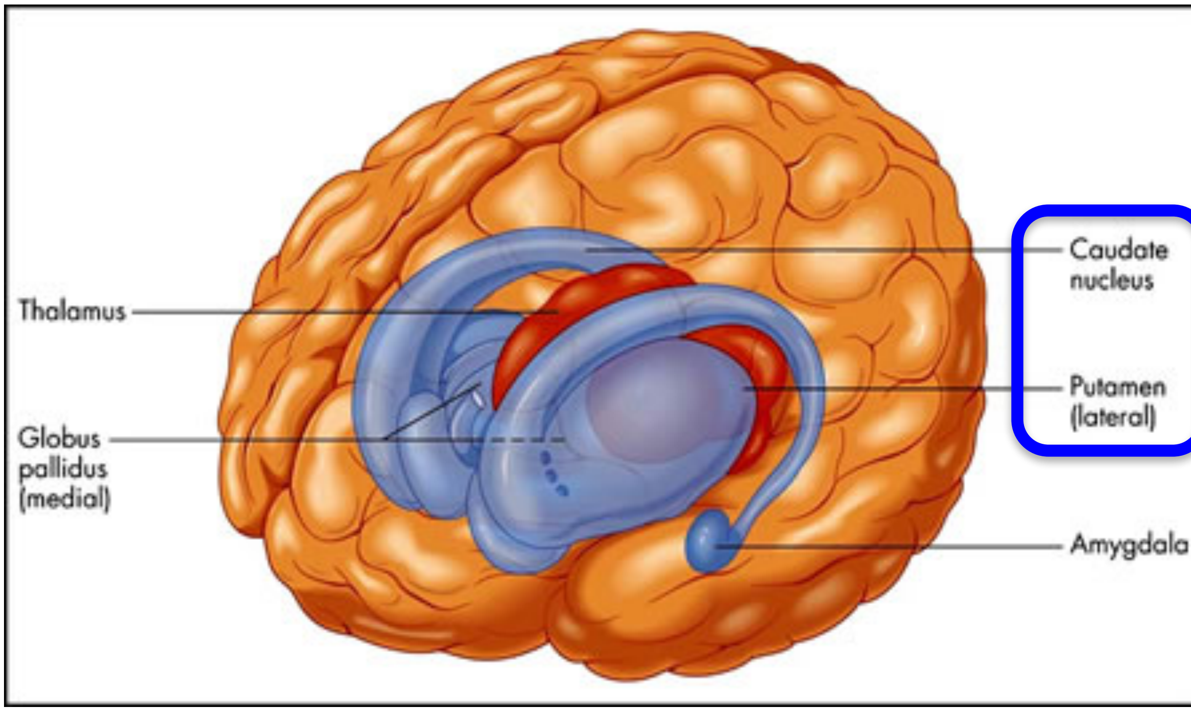
BUT
when Red Nucleus
warms again,
Rabbit blinks to Bell,
showing it HAS learned!



Thus we say it is the
Cerebellum
that is primarily responsible for such
Procedural Learning

Procedural Memory

Basal Ganglia also plays a major role in Procedural Learning
e.g. “Automating” habits



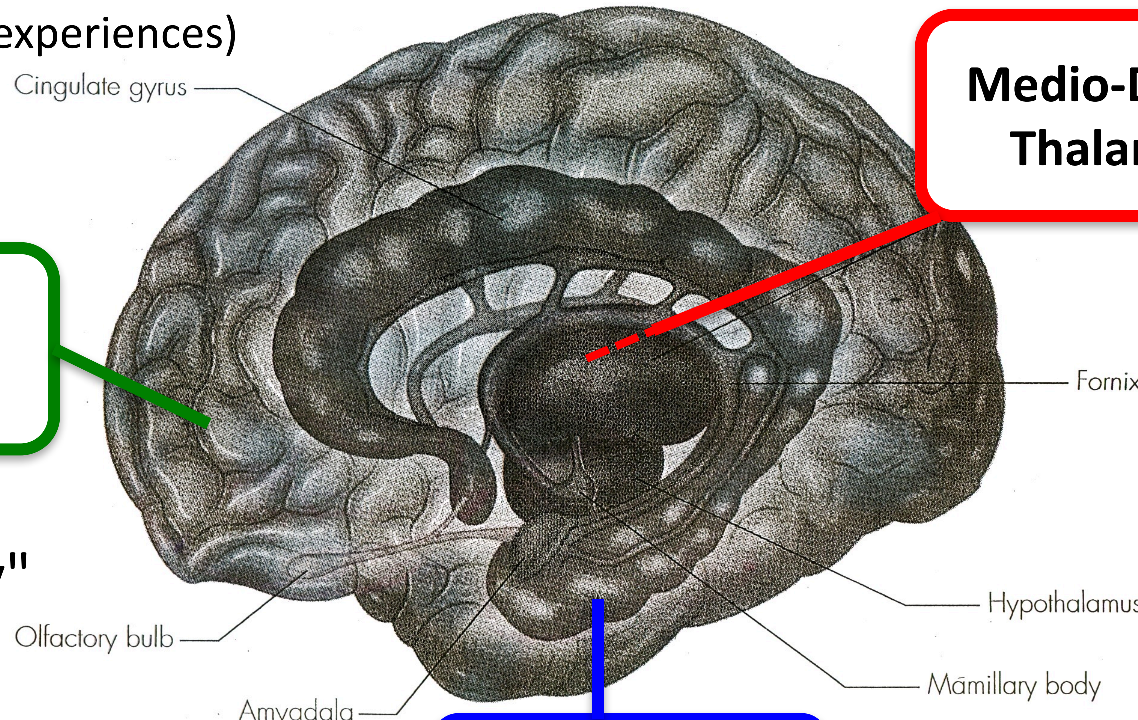
Striatum
(input)

e.g. **<u>NMDA-Antagonist</u>** injected into Striatum interferes with recall of learned, cued-procedures
(like F Maze, Cond A, above)

Declarative Memory

Memory for "Facts", abstract "Rules", "Episodic Memory"
(particular life experiences)

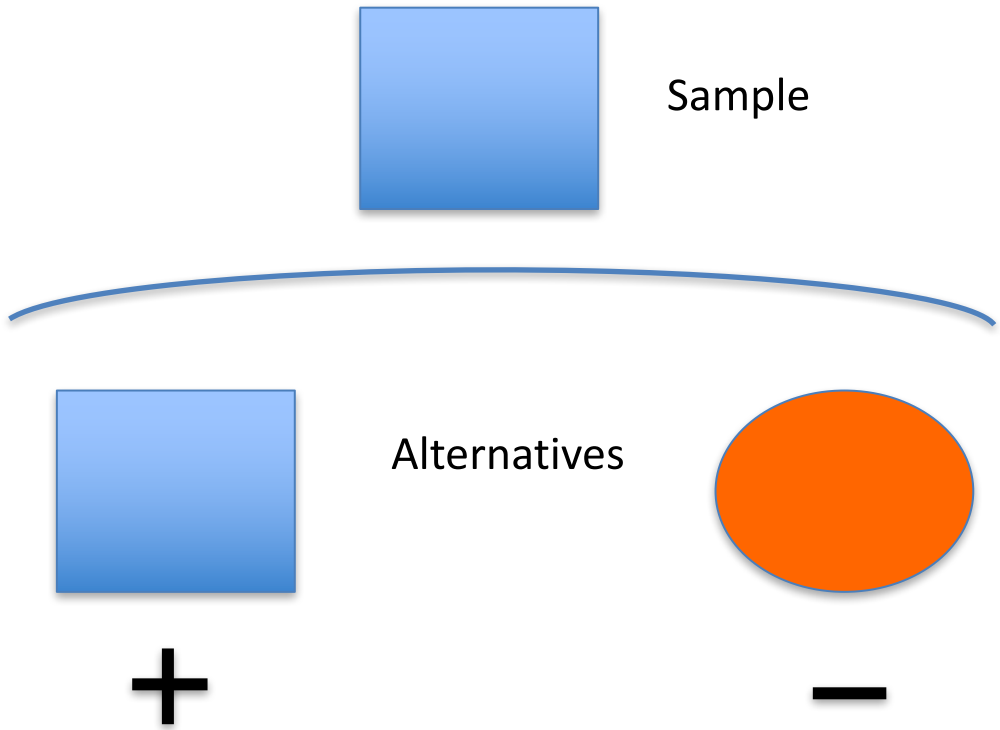
MNEMONIC:
"Memory Doctor"
<u>MD</u>N of Thalamus



"Working Memory"

Declarative Memory

Match-to-Sample

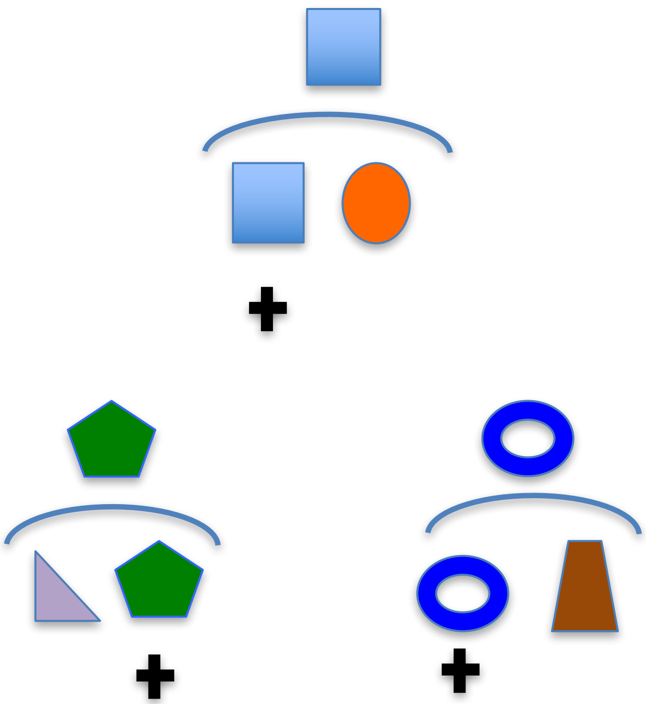


Select this alternative,
gain <u>positive</u> reinforcement

Select this alternative,
gain <u>negative</u> reinforcement

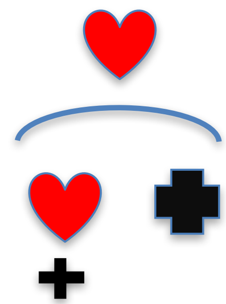
Declarative Memory

Match-to-Sample

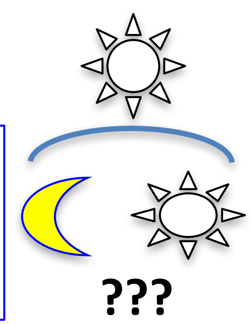


After repeated exposure to such problems...

"Learn rule" when can respond correctly to novel stimuli



If lesion **Hippocampus** after animal has learned rule, performance impaired

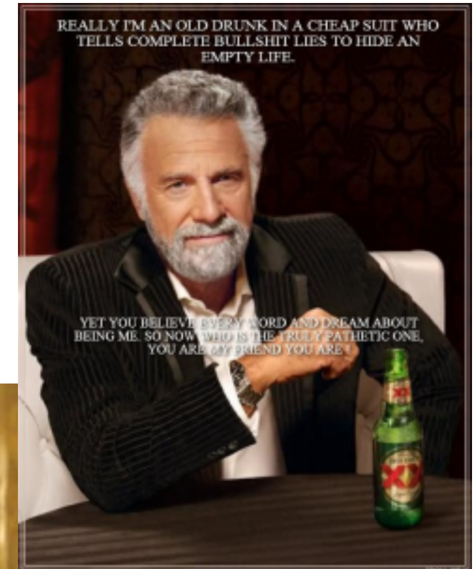


So, hippocampus plays a role both in forming AND retrieving memories

Declarative Memory

If connections from **MDN**
to **Prefrontal Cortex** damaged…

…as in B1 deficiency
(required for cells to metabolize glucose)
that develops in <u>chronic alcoholism</u>



"Korsakoff's Syndrome"

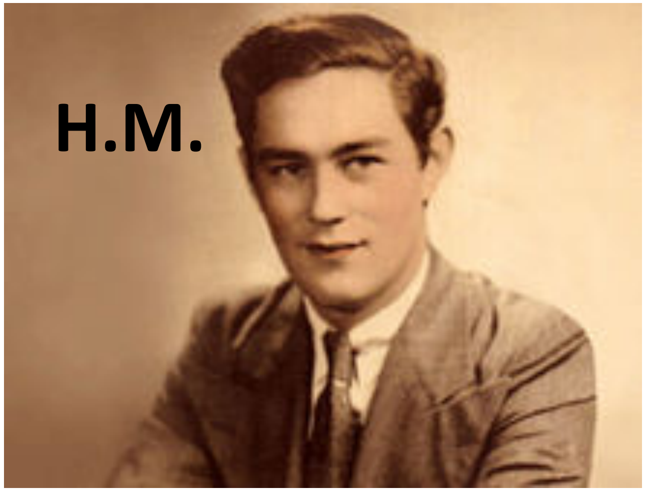
Suffer from
<u>Anterograde Amnesia</u>

Inability to form
<u>new</u> memories

And from
Confabulation

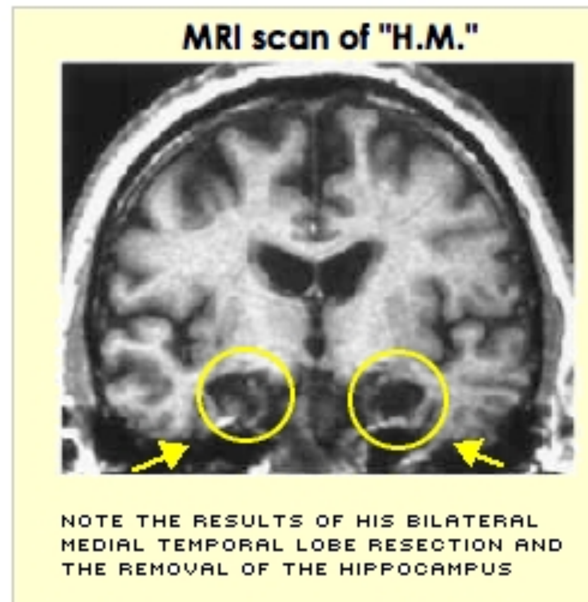
Make things up
based on
current cues

Declarative Memory



Had epilepsy, suffered from *grand mal* seizures

Had much of **Hippocampus**, plus
some amygdala & temporal cortex removed



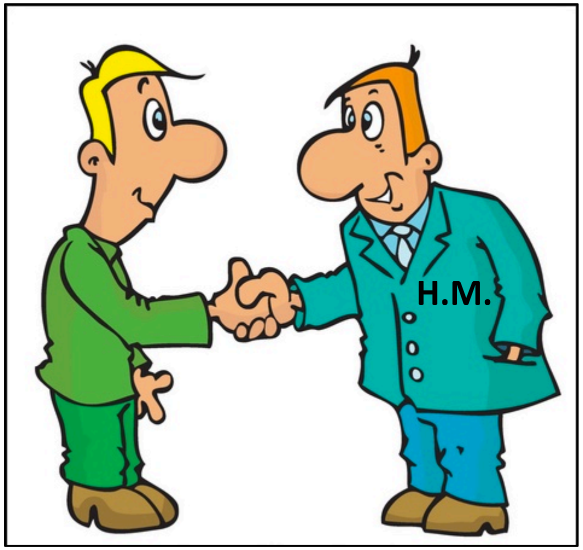
Much reduced epilepsy symptoms,
but developed other problems

IQ & personality largely intact, but had
severe **Anterograde Amnesia**

http://thebrainobservatory.ucsd.edu/hm

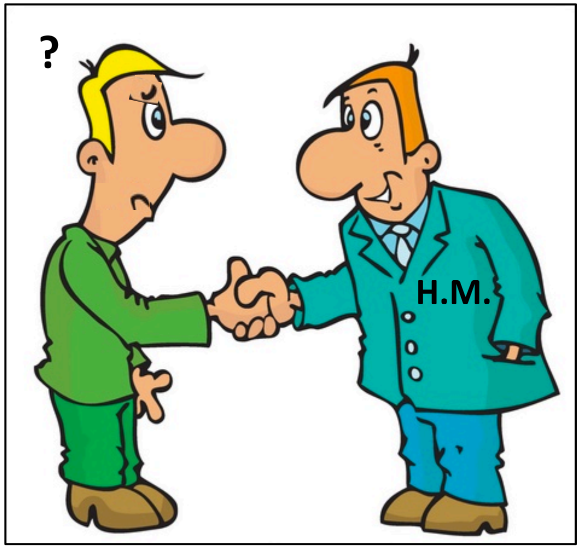
Declarative Memory

"Episodic Memory"



H.M. suffered from
Anterograde Amnesia
(inability to form
new memories)

e.g. He would meet
new people . . .

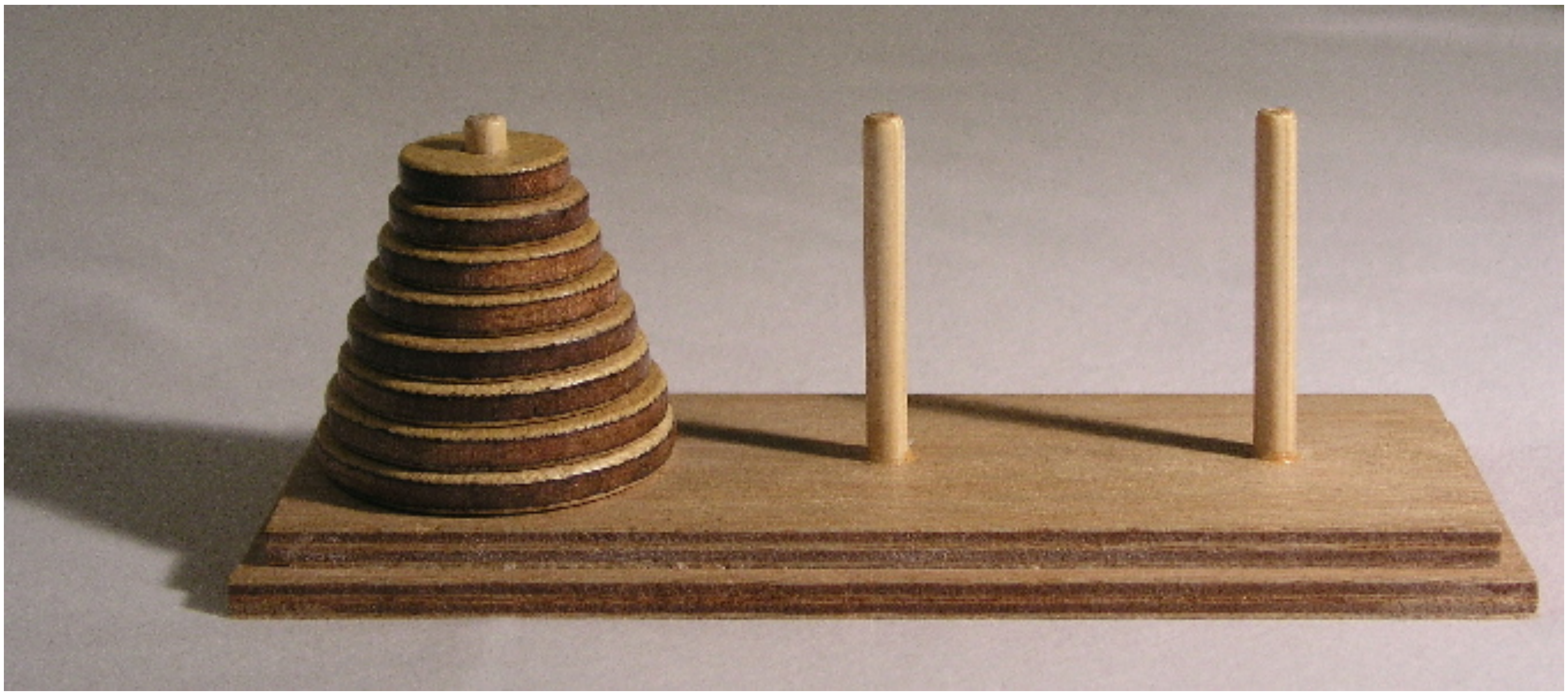


. . .but, 15 minutes later, have
no memory of
having met them.

He was unable to remember
episodes from his life,
that occurred after his operation

H.M. - Tower of Hanoi Puzzle

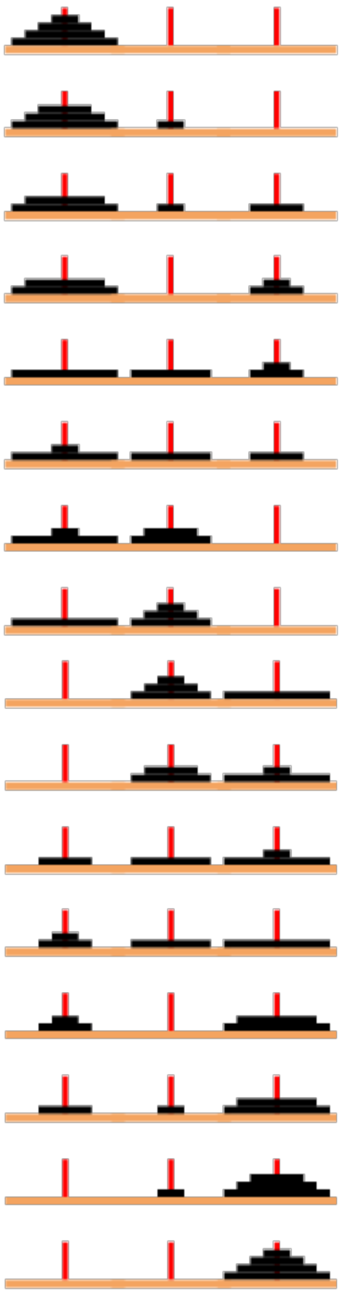
Move entire tower to the third pole,
by moving only one ring to another pole at a time,
and never putting a larger ring on top of a smaller one



H.M. was given repeated exposure to this puzzle, but
each time he was presented with it, he did not recall ever having seen it before

Nonetheless, after repeated practice, he did get very good at it!

H.M. - Tower of Hanoi Puzzle



The most efficient solution
(and one players often converge on)
is a sequence of moves -

i.e. a *Procedure!*

H.M.'s **Procedural Memory**
was largely **intact**

(Cerebellum and Basal Ganglia
little affected by surgery)

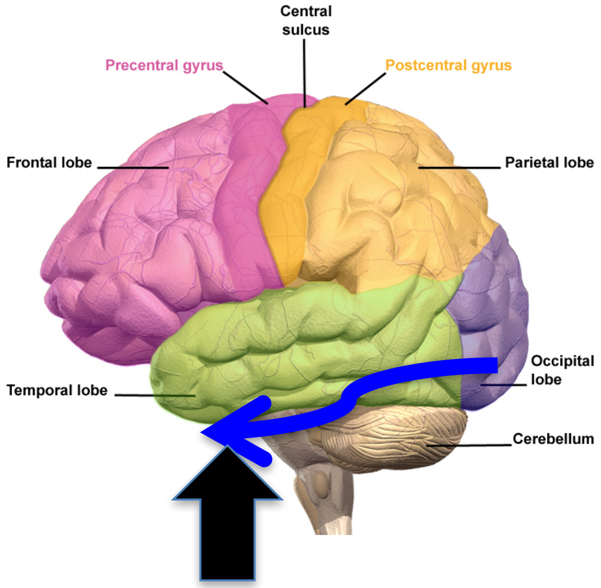
It was H.M.'s **Declarative Memory**
that was most impacted
by removal of much of Hippocampus

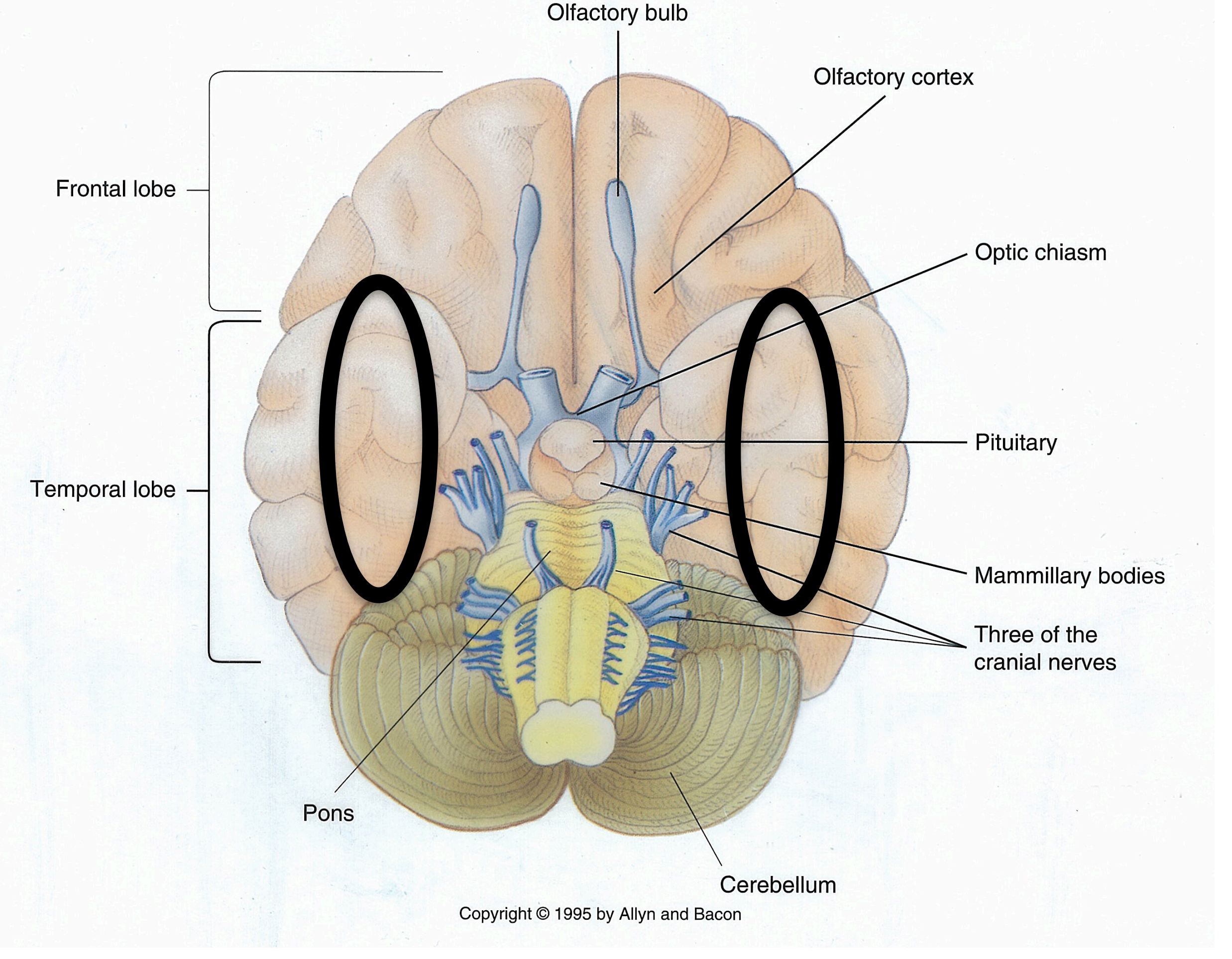
Long-Term Memory Storage

Declarative Memory not stored in Hippocampus / Thalamus / Prefrontal circuits

Those circuits required for consolidation & retrieval of information
stored elsewhere in cortex

Long-Term Memory Storage

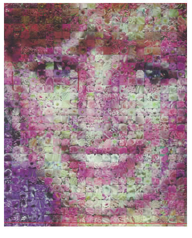




Fusiforme Gyrus

of Inferior Temporal (IT)

Higher visual cortex

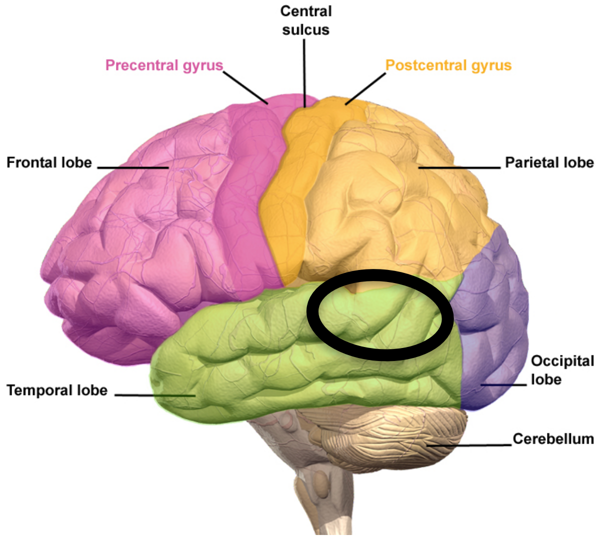


For recognizing

Faces

Damage leads to **Prosopagnosia**

Long-Term Memory Storage



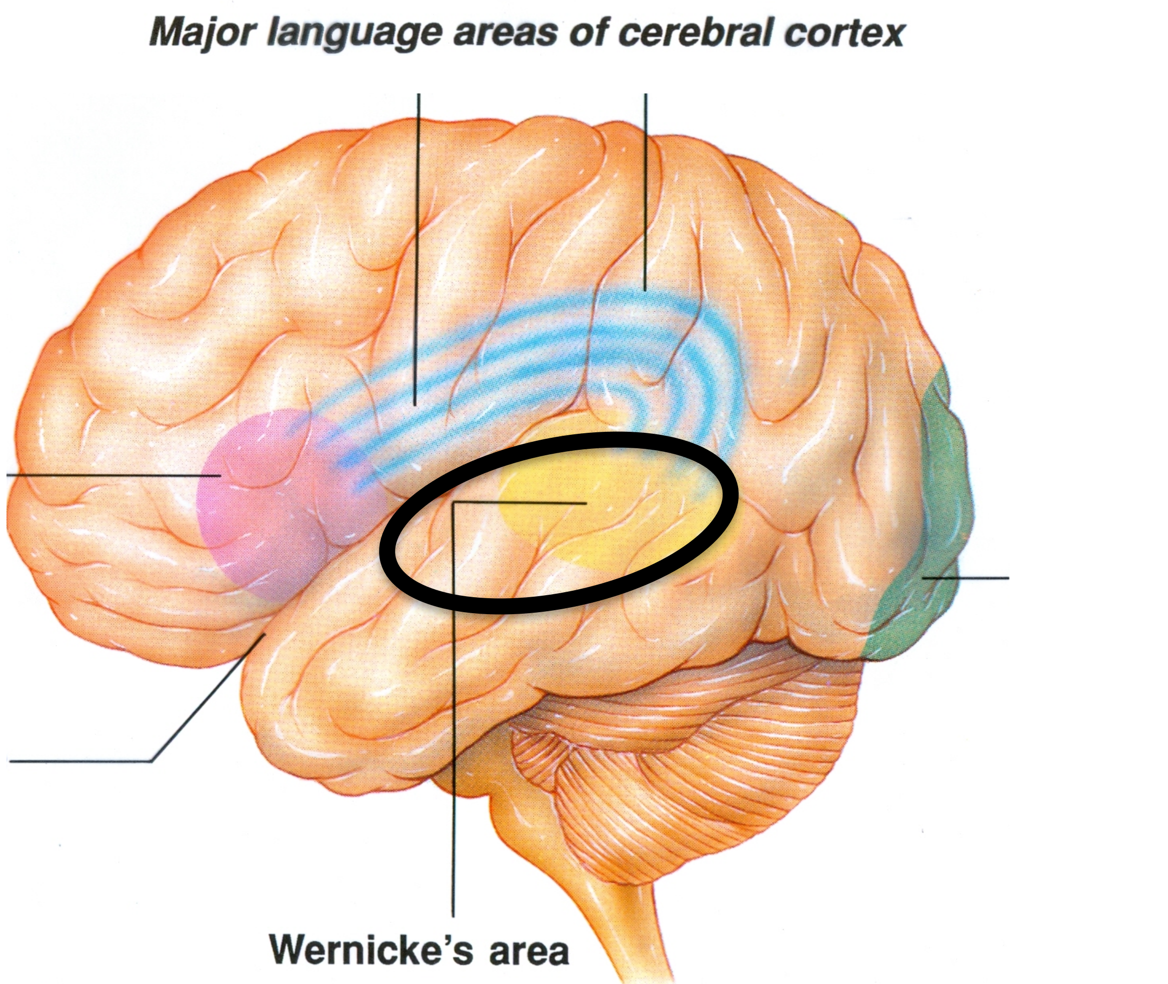
Dorsal Temporal Cortex

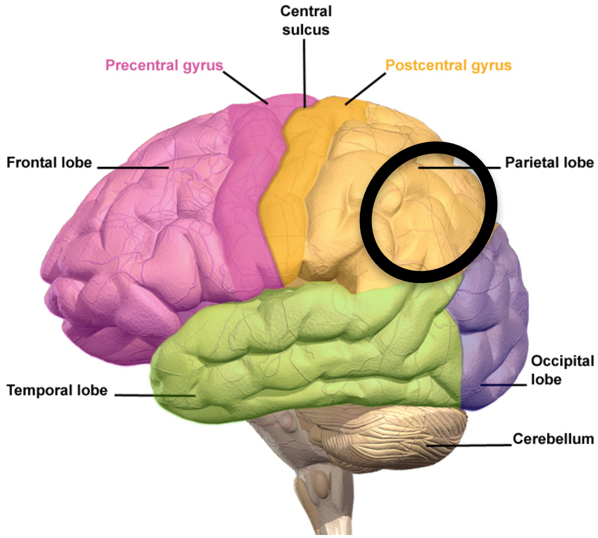
including

Wernicke's Area

for

recognizing Words, Voices





Long-Term Memory Storage

Posterior Parietal
Spatial memory for
"**Praxic**" space, from an
egocentric frame of reference

Etc...