Learning & Memory (Ch.17) III

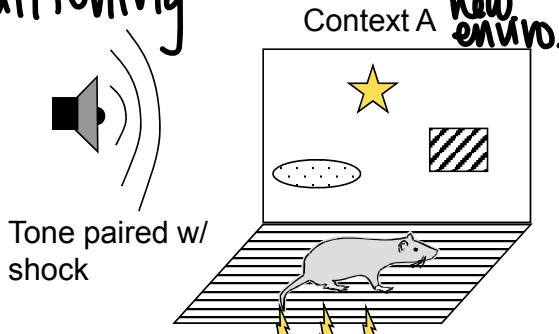
- The hippocampus and contextual memory
- A theory of how the hippocampus mediates episodic memory
- Multiple Memory Systems in the Brain
  - Dissociations, Interactions and Cooperation Among Systems
- Synaptic Plasticity
  - Synaptic changes that may be related to long term memory
  - **Long term potentiation**: A cellular model for long term memory

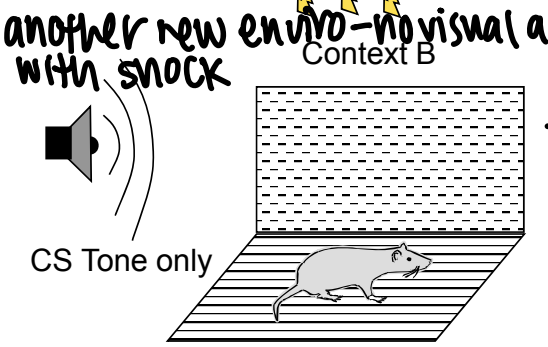
when I hear tone, I get

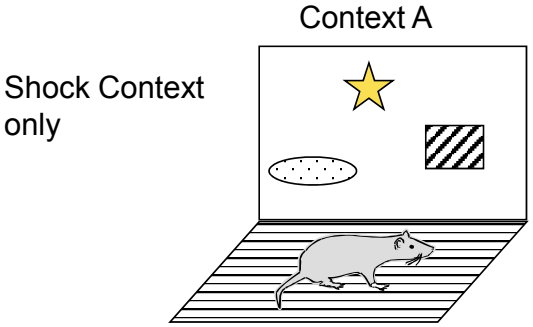
learning 2 things: shocked; when I'm in this enviro, I get shocked

Hippocampus and Contextual Memory

standard fear conditioning







➢ **Contextual** Fear Conditioning

– Give CS tone-shock pairings in one distinct context → cued-single tone shock

- Give CS tone in ***separate*** context (B) =
  - Normal rats show fear freezing
  - Hipp. lesioned rats show ***normal fear to tone***
    - Implicit/procedural learning intact

Just walking around & recognizing

- Put rat in ***shock context (A)*** with no CS tone =
  - Normal rats show fear freezing
  - Hippocampal lesioned rats ***do not*** show contextual fear conditioning

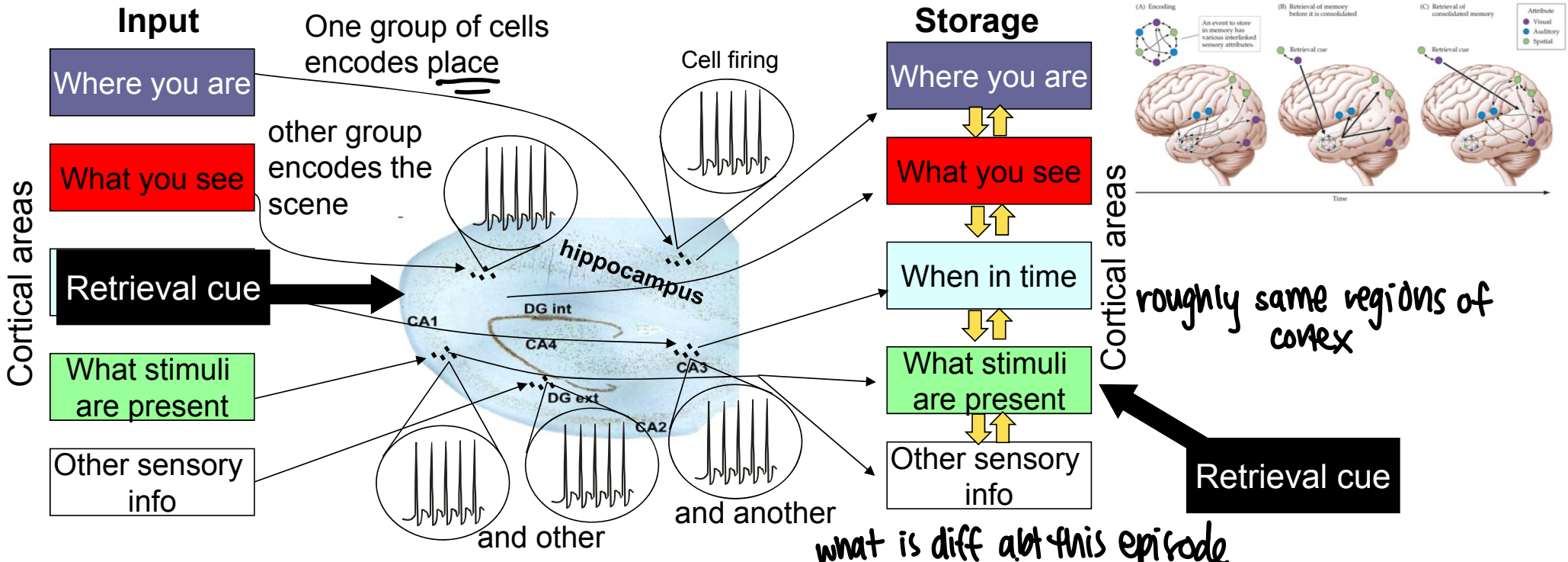
don't remember the context

- Hippocampus involved in remembering **relations** between contexts and what events that occurred in those contexts
  - Note: **amygdala** lesions impair fear learning about ***both*** the tone ***and*** the context → important for both

Don't need hippocampus to learn 1 tone, but need it to learn more (enviro/context)

* he said he prob wont test us on the details of this

The Hippocampus and Episodic Memory



roughly same regions of cortex

what is diff abt this episode

-Hippocampus records multiple bits of info about episode and relation to each other: encodes as distinct patterns of activity

-Helps consolidate different bits of information linked to a particular memory in the same cortical regions that originally processed that aspect of the memory like how when you recall a mem, can almost see it

-When you remember an episode, similar pattern of activation in hippocampus can activate similar regions of cortex to trigger recall same patterns

-Over time, a retrieval cue may be able to activate cortex to retrieve the memory without the hippocampus

relation to bunch of stimulus = hippocampus

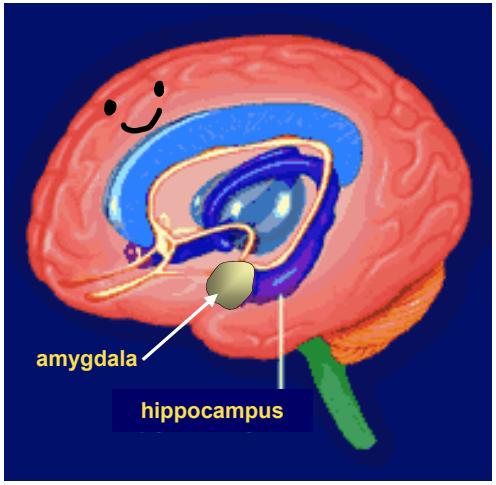
↳ x just one tone

remember unusual memories better → bc easier retrieval cues

Summary of Some Anatomically-Dissociable Memory Systems

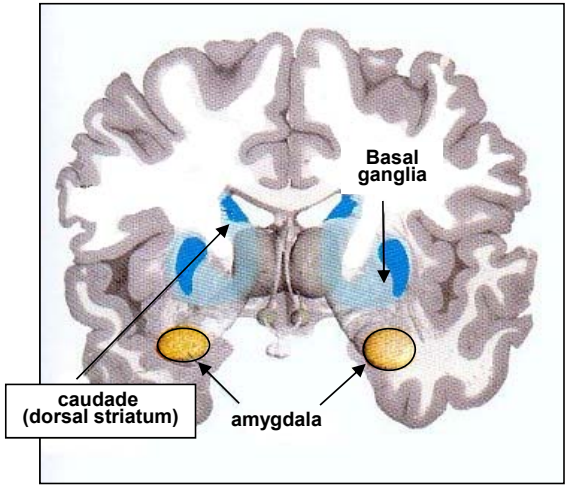
- **Hippocampus**
  - Declarative Memory (**Humans**), Spatial/ Relational Memory (**Rats**)
- **Striatum** (a.k.a. Caudate Nucleus, Basal Ganglia)
  - Procedural memory/skill/habit learning (**Humans**); Instrumental conditioning (**Rats**)
- **Amygdala**
  - Pavlovian conditioning for appetitive or aversive events (**Humans and Rats)**

learn: if I move in this way, smth happens



- Multiple brain regions can interact to regulate a particular type of memory
- However, different brain regions can participate in separate forms of learning & memory, independent of each other
  - Different learning systems can encode different aspects of the environment in parallel, i.e.: each system learning something different
- When 2 or more brain regions are independently involved in separate forms of learning (i.e.: lesions to one area impair on one task but not others) this is referred to as a ***dissociation*** of memory systems

diff types of systems designed to solve specific problems



looks same as control- can't remember where they've been

stan ♡'s this study

central hub w/ 8 arms coming out

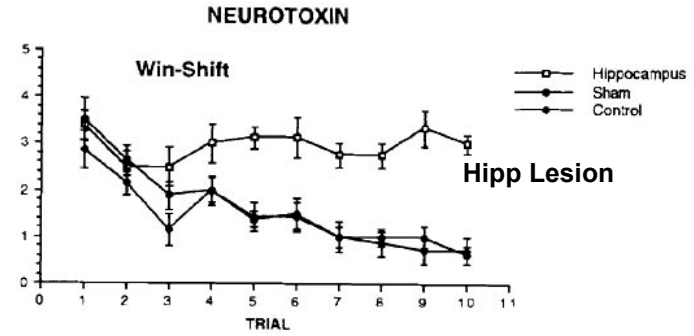
A Triple Dissociation of Memory Systems

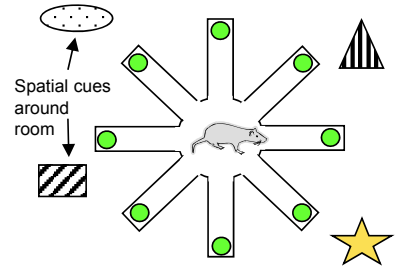
all rat has to do is go to arm, get food, don't go back to same arm

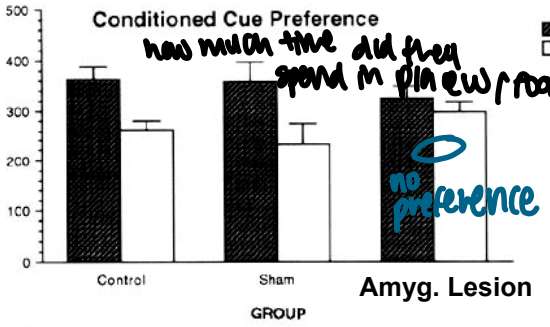
Three radial arm maze tasks:

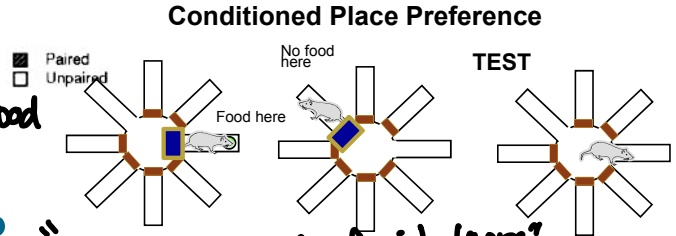
- **Spatial Radial Maze**
  - Don't go back to previously entered arm (spatial/relational learning)
  - **Hippocampal lesion = Impairment**
  - Amygdala lesion = no impairment
  - Dorsal Striatum lesion =no impairment
- **Conditioned Place Preference**
  - Go back to arm where you got food before (Pavlovian Learning)
  - Hippocampal lesion = no impairment
  - **Amygdala lesion = Impairment**
  - Dorsal Striatum lesion =no impairment - acts like controls
- **Locally Cued-Radial Arm Maze**
  - NO SPATIAL CUES (curtains around the maze)
  - Go to arms where a light is on (Stimulus-Response)
    - Once rat eats food from arm, light turns off
  - Hippocampal lesion = no impairment
  - Amygdala lesion = no impairment
  - **Dorsal Striatum lesion =Impairment**

McDonald and White (1993)

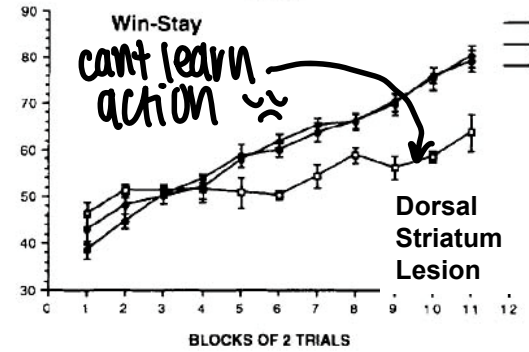


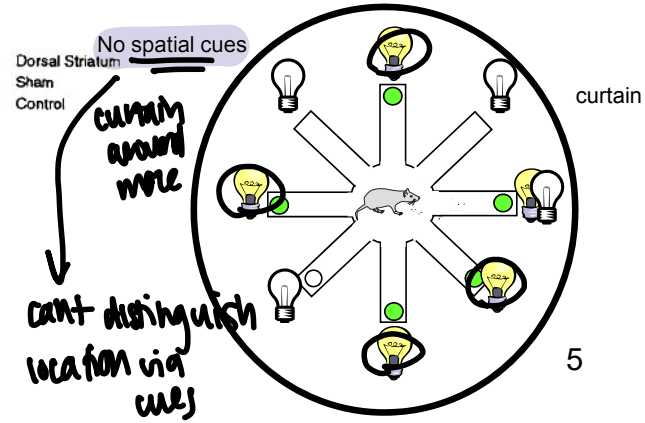






"nom nom nom fruit loops" -stan





HDR they have their special role - work indep. of each other

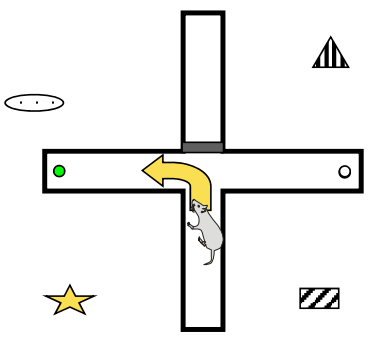
I see an arm w/ a light → get food & light goes off
* just need to learn action

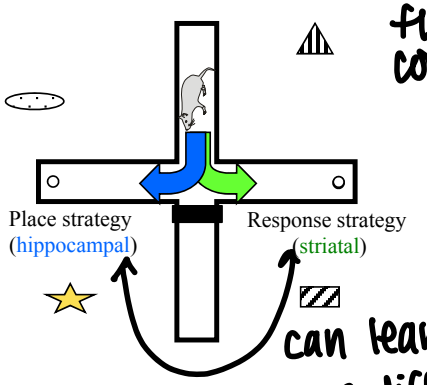
Parallel and independent processing by different memory systems

- Train to always enter one maze arm
  - Rats can use either a place (hippocampal) or response (striatal) strategy
- On probes, release from new start point, see where rats go
- **Early in training:** Most control rats use hippocampal strategy
  - **Inactivate hippocampus = many rats shift to using striatal strategy**
- **Late in training:** Most rats use striatal strategy
  - **Inactivate striatum = most rats shift to using hippocampal strategy**

➢ ***Training:*** Always turn left/west

➢ ***Probe:*** *Release from different start point*





flip config of maze

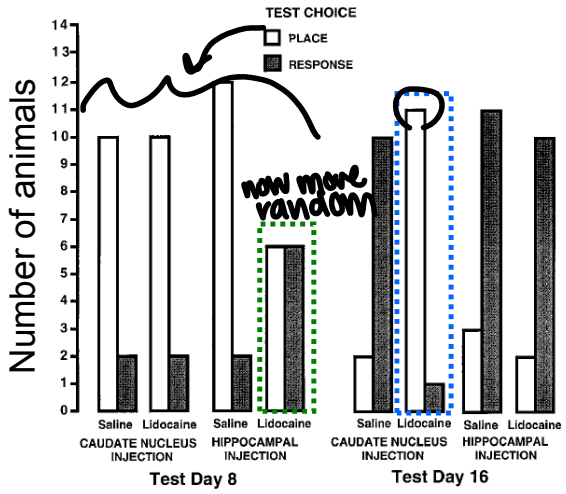
can learn in 2 diff ways

other form of learning took over

➢ **This shows:**

- **1) different memory systems can learn independently and in parallel to each other**
- **2) Suppression of one system allows behaviours driven by another to emerge**
- **3) Different systems learn at different rates (hippocampal = rapid, striatal = more gradual)**

diff things @ same time

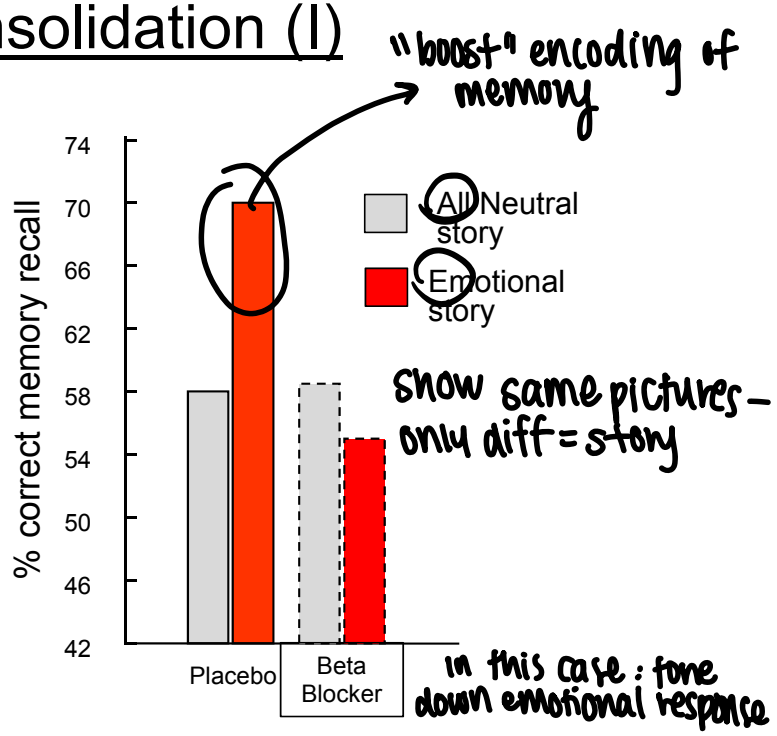


caudate nucleus = striadum

Packard and McGaugh, 1996

Emotions and Memory Consolidation (I)

- Strong emotional states can enhance memory consolidation; may be mediated in part by noradrenaline
  - Normal subjects show better memory for "emotional" vs neutral stories attributed to the same pictures

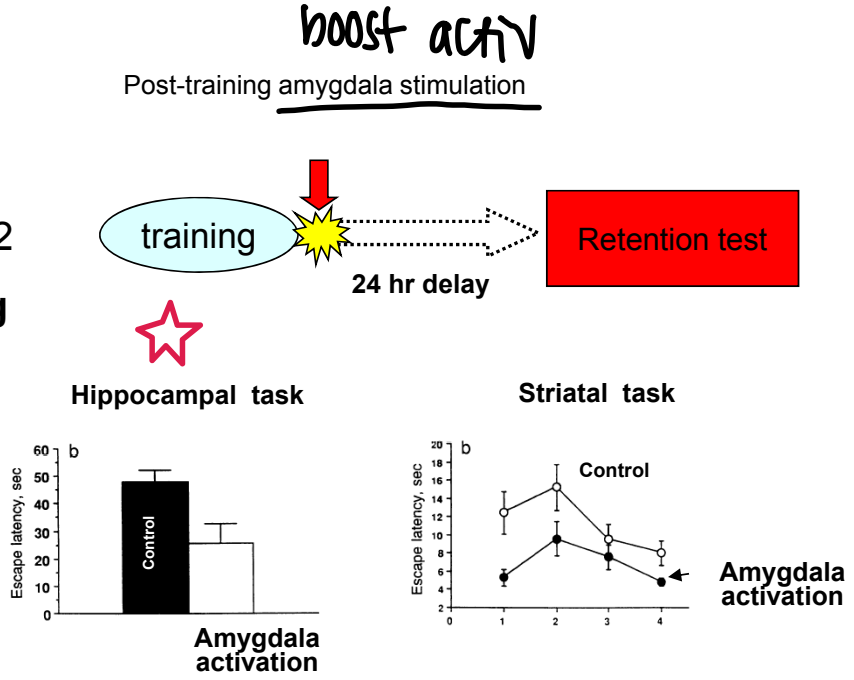


  - **Noradrenaline Beta-receptor antagonists** = selectively reduces better memory for emotional part of story (not other parts) even though they still report emotional response to story
  - An exaggerated type of memory modulation like this may underlie Post-Traumatic Stress Disorder

give Beta Blockers right after traumatic event - ↓PTSD rate

Emotions and Memory Consolidation (II)

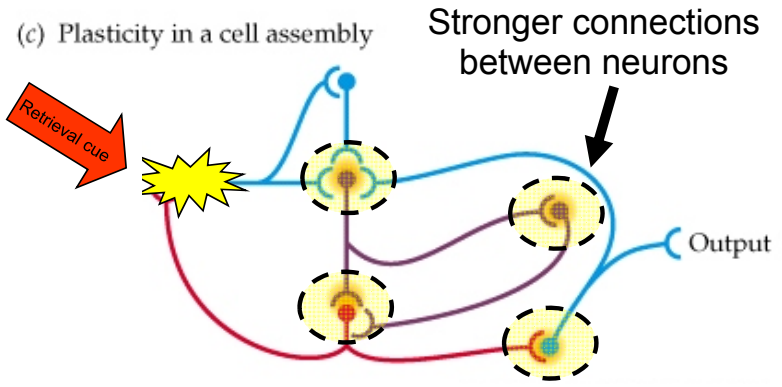
- Emotional enhancement of memory consolidation is mediated by the amygdala
  - Train rats on memory task on Day 1, test memory on Day 2
  - Stimulate amygdala with drugs **immediately post-training** on Day 1 = improved memory consolidation tested on Day 2 on tasks such as:
    - Spatial (hippocampal) learning
    - Instrumental (striatal) learning
    - Aversive (amygdala) learning



- Amygdala can modulate consolidation of memories by other memory systems
- Emotional events activate amygdala, which in turn can enhance consolidation of memories (possibly via stress response mechanisms)

Synaptic Plasticity

- The brain is plastic (i.e.: it changes); every time you learn/encode a memory changes occur in neurons in brain
  - Short term memory can be carried out by **cell assemblies,** groups of interconnected neurons
  - Activity driven by an input can start a chain of activation that can continue for some time (**reverberatory circuit)** that encodes a particular memory

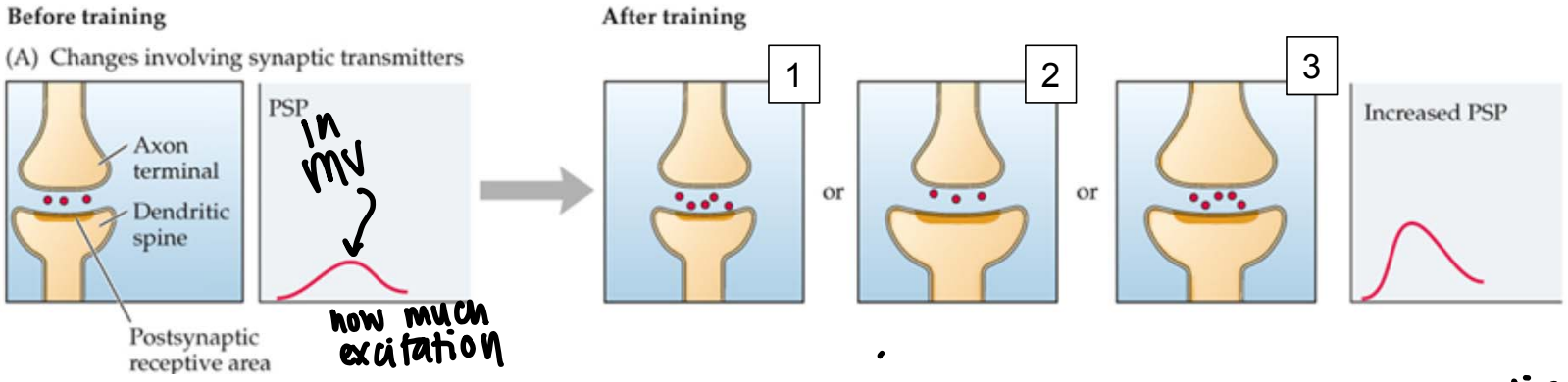


  - If activity in circuit is **strong enough/last long enough**, long term alterations can occur at synapses to make memories more permanent (i.e. same neurons can be activated in the same pattern at later time)
  - These alterations are referred to changes in **synaptic strength**

sorry i almost fell asleep >.< idont think he said anyming not on the slide tho

Mechanisms of Changes in Synaptic Strength

- **Synaptic strength** are typically measured by changes in excitatory post synaptic potential (EPSP) evoked by an input how much depolarization we get
  - ↑ strength = larger EPSPs evoked in postsynaptic neuron



ability of presynaptic neuron to Δ / effect post synaptic neuron

1) Increase in presynaptic transmitter release
2) Increase # of postsynaptic receptors or their sensitivity -or-
3) Both 1 and 2

Other types of physical changes in neurons can also occur (change in shape, # of dendrites etc) that can affect the way the post-synaptic neuron responds to input

- **Note:** opposite changes can occur too, decreasing synaptic strength

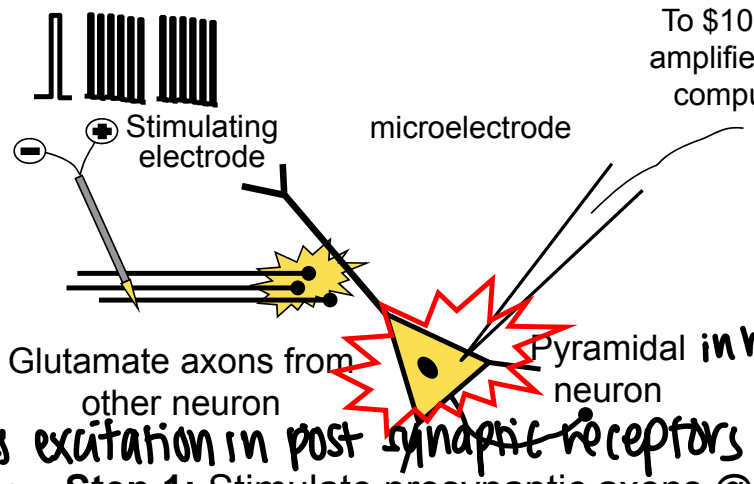
obv 1 neuron doesn't change much BUT mult. by 1000s of neurons - big change

can occur anywhere in brain where you use glutamate / have glutamate synapses

not "memory"

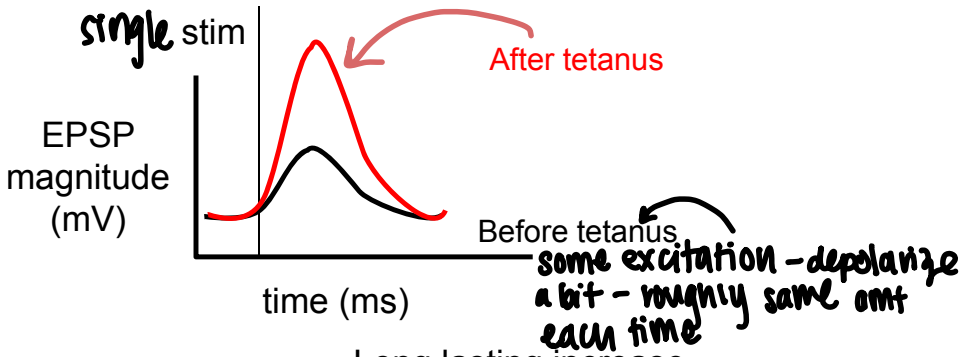
Long Term Potentiation (I)

LTP

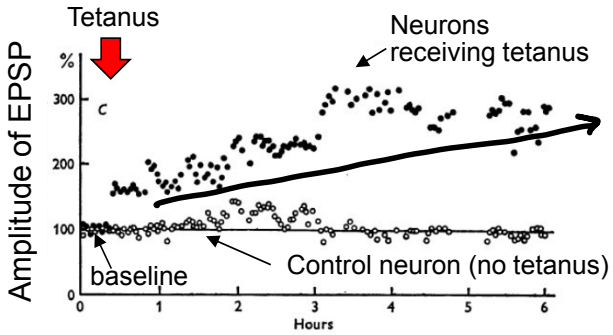


in hippocampus

causes excitation in post synaptic receptors



some excitation - depolarize a bit - roughly same amt each time



can last a huge amt of time !! ö

- **Step 1:** Stimulate presynaptic axons @ low frequency (1/15 sec) to get subthreshold EPSP (no action potentials), establish baseline
- **Step 2:** Stimulate axons at **high frequency** (i.e.: *tetanus*, e.g. 100 Hz) and get lots of action potentials in postsynaptic neuron

!!super intense!!

- **Step 3:** axons at low frequency again, same subthreshold current =

➢ **MUCH BIGGER EPSP than before**

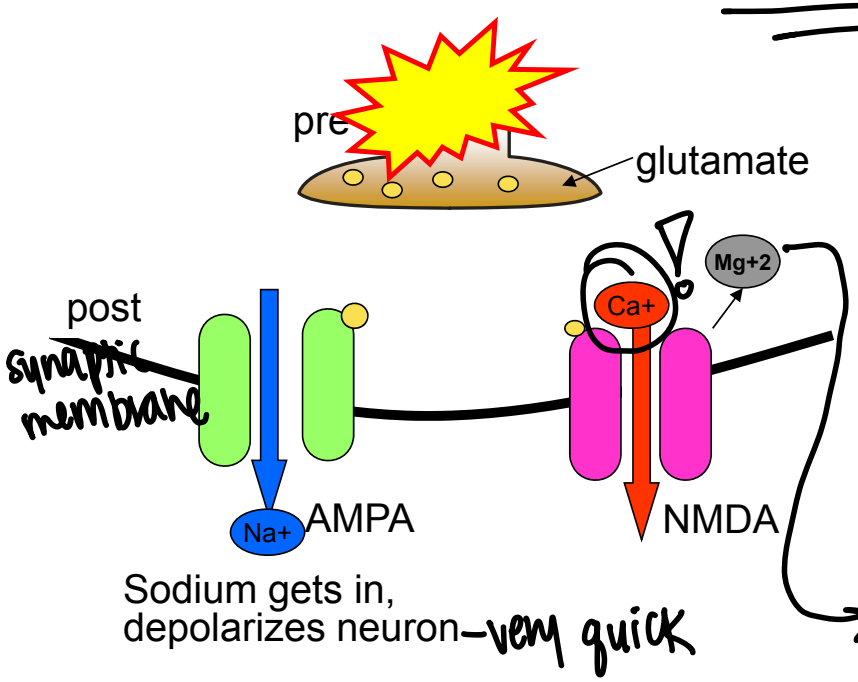
- **Input has become stronger (potentiated), larger EPSP, more likely to evoke action potential**

he will re-explain this on Thursday ♡ thanks stan :)

Glutamate Mechanisms of LTP

- LTP can occur anywhere in the brain where there are **glutamate synapses**
  - Hippocampus, Cortex, Amygdala, Striatum etc
- Two main types of ionotropic glutamate receptors: activation

brain doesn't release these :o
NT ?
a bit confused about this part >.<



AMPA and NMDA receptors

- Both allow Na+ to pass thru and depolarize neuron

Only NMDA receptor allows Ca2+ to get into neuron

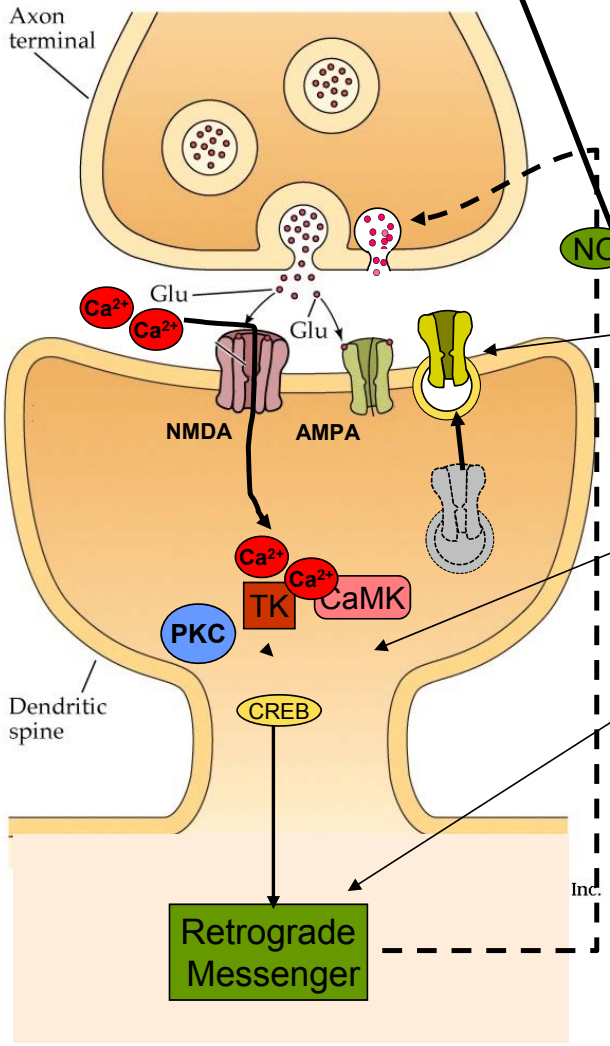
- If neuron is hyperpolarized, NMDA receptor blocked by Mg2+ ions cannot be activated by glutamate
  PLUG RECEPTOR!!!
- AMPA receptors are not blocked; can always be activated by glutamate

gets thrown off if neuron is excited

- If AMPA receptors depolarize neuron enough, Mg2+ block of NMDA receptor is removed (**voltage dependent Mg2+ block**)
- Glutamate can now activate NMDA receptor, allows Ca2+ to get into cell

stop

Cellular Mechanisms of LTP (I)



- Once Ca2+ enter cell, it activates multiple enzyme pathways (**kinases = phosphorylate other proteins)**
- Ca2+ activates **Ca**lcium-Cal**m**odulin which in turn activates other kinases
- CaM Kinase hits latent AMPA receptor (floating inside cell) and inserts in membrane = more receptors

- **P**rotein **K**inase **C** and **T**yrosine **K**inase can activate CREB = short term and long term effects
- CREB can lead to formation of retrograde messenger (molecule that goes from postsynaptic neuron to presynaptic terminal (e.g., Nitric Oxide)
  - These messengers promote more transmitter release
- ↑ synaptic strength by both pre and postsynaptic mechanisms

Cellular Mechanisms of LTP (II)

- LTP comes in two phases.
- **1st phase:** ↑ in receptors/glutamate release occur quickly (<1 hr)
  - ➢ These changes blocked by NMDA antagonists
- **2nd phase:** CREB activates **protein synthesis**, that causes longer lasting changes (>3 Hrs)
  - — Dendrite shape and size, more ion channels, more dendrites, etc
  - — These changes are processed for hours after initial memory was encoded
  - ➢ These latter of LTP phases also blocked by **protein synthesis inhibitors**
- **Both phases blocked by prevention of Ca2+ entry into the cell**
  - Ca2+ entry is localized, so only certain synapses/ dendrites on a neuron will change synaptic strength