

Nervous Systems & Neurotransmission

Lecture 19

Nervous Systems

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- How are nervous systems organized?
- What does each part of the human nervous system do?
- How are vertebrate brains organized?

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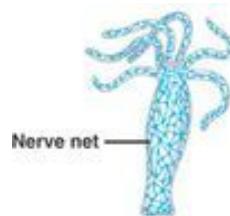
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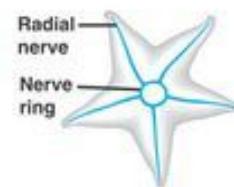
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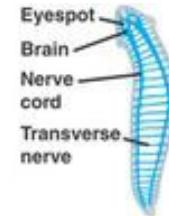
- Neurons don't act alone; they must communicate with other neurons and nerves.
- All of these neurons together form a nervous system.
- Nervous systems can be arranged in a variety of ways



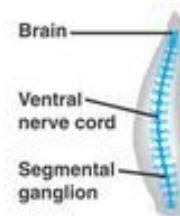
(a) Hydra (cnidarian)



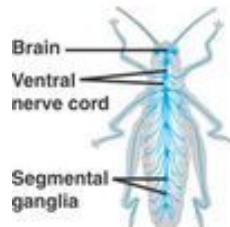
(b) Sea star (echinoderm)



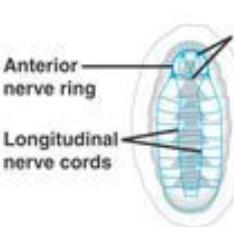
(c) Planarian (flatworm)



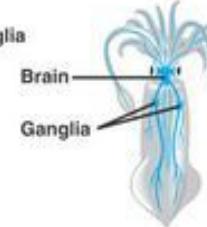
(d) Leech (annelid)



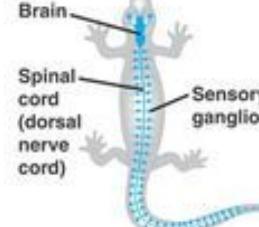
(e) Insect (arthropod)



(f) Chiton (mollusc)



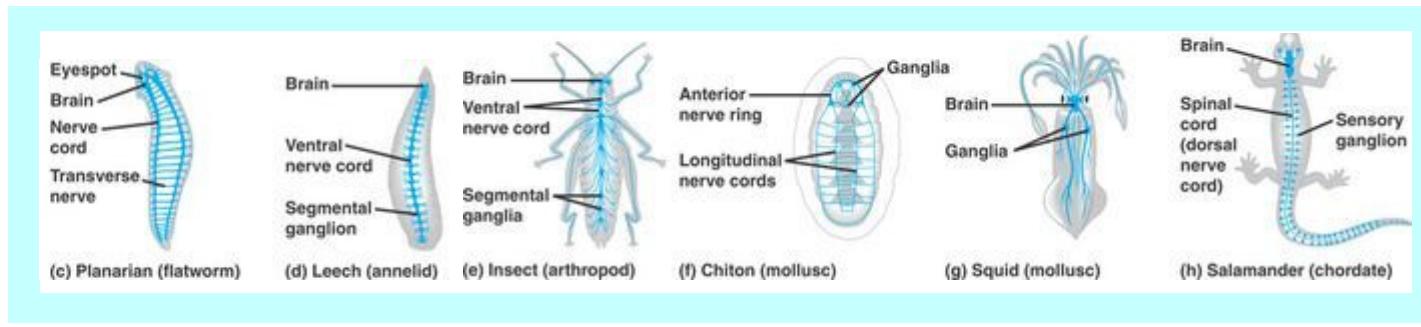
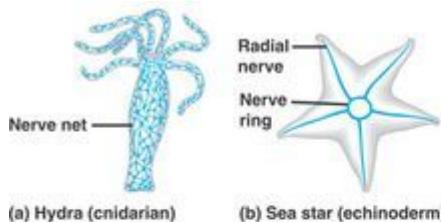
(g) Squid (mollusc)



(h) Salamander (chordate)

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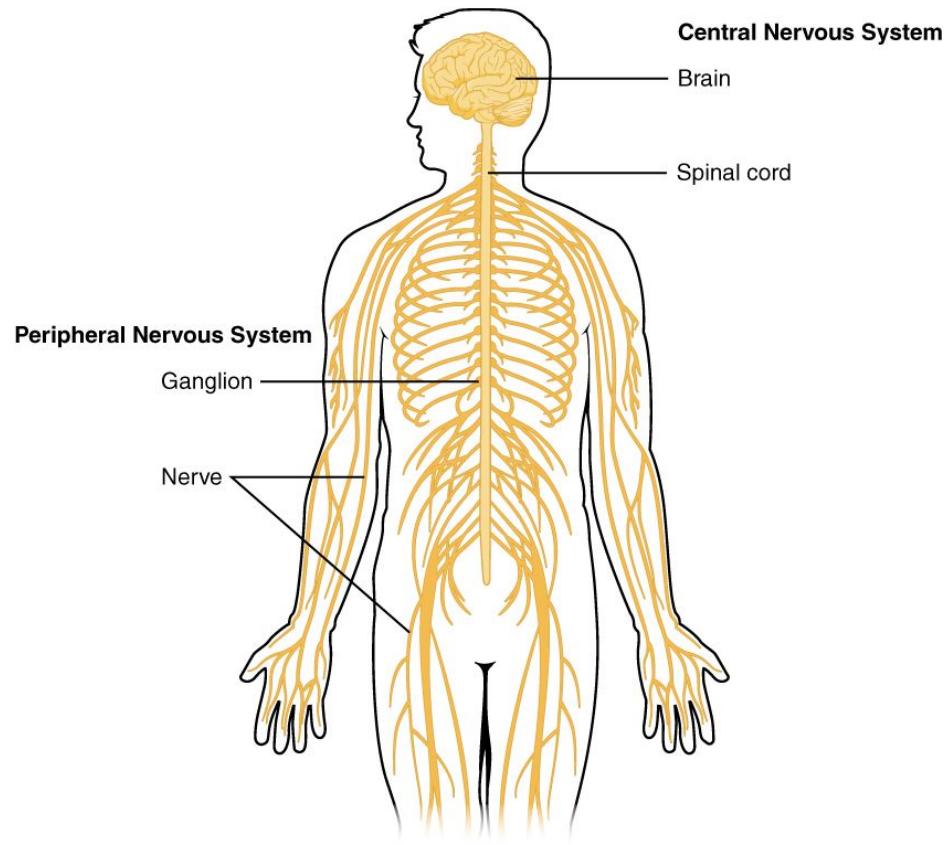
Trend of having a brain in a head

The main take-away from this, according to Dr. Selvaraj, is that as you move from basal animals like the hydra, through arthropods, into the chordates (vertebrates), there is a trend towards cephalization- organization of processing into a central **brain** in the head

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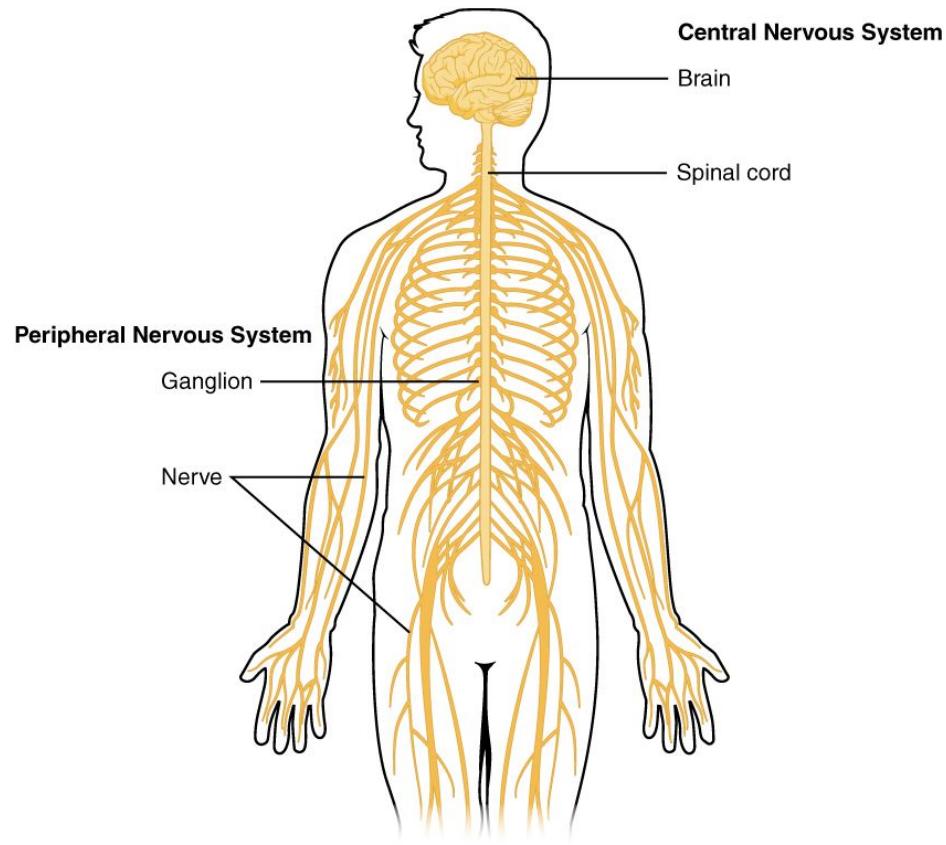
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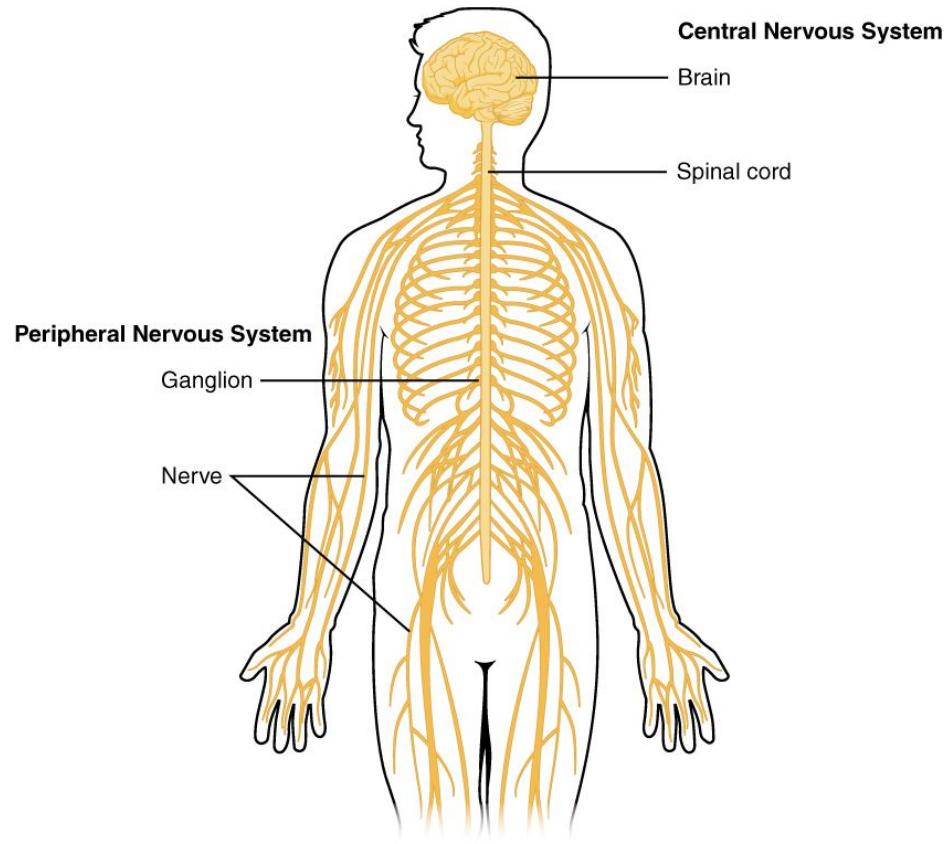
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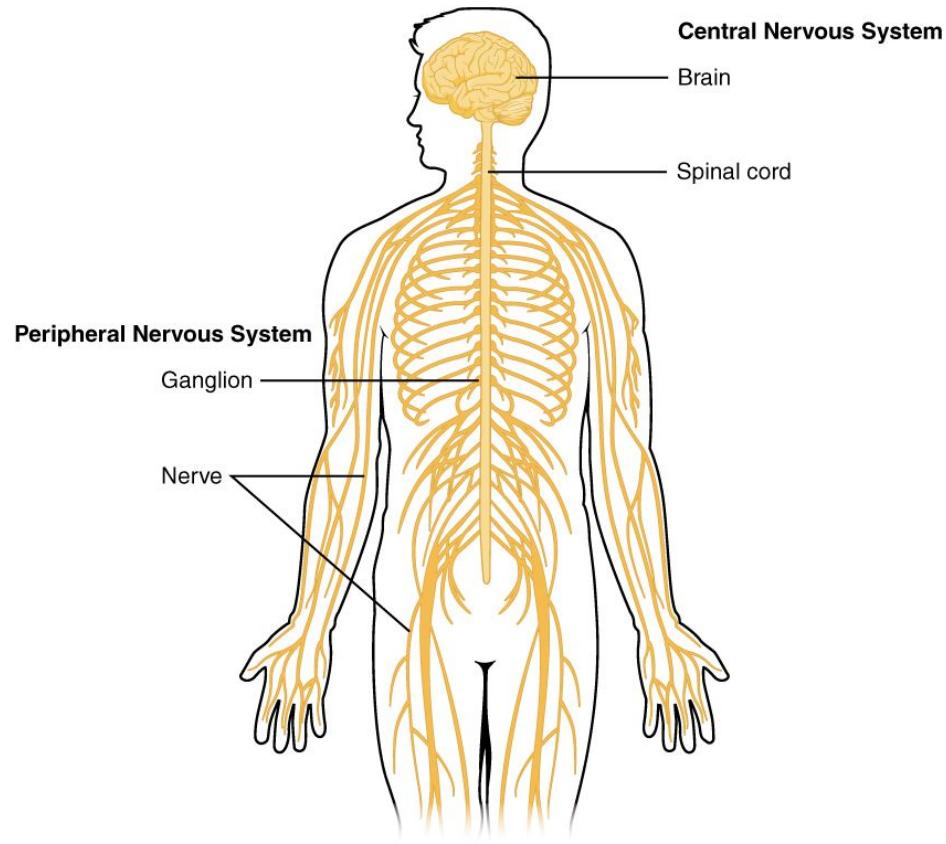
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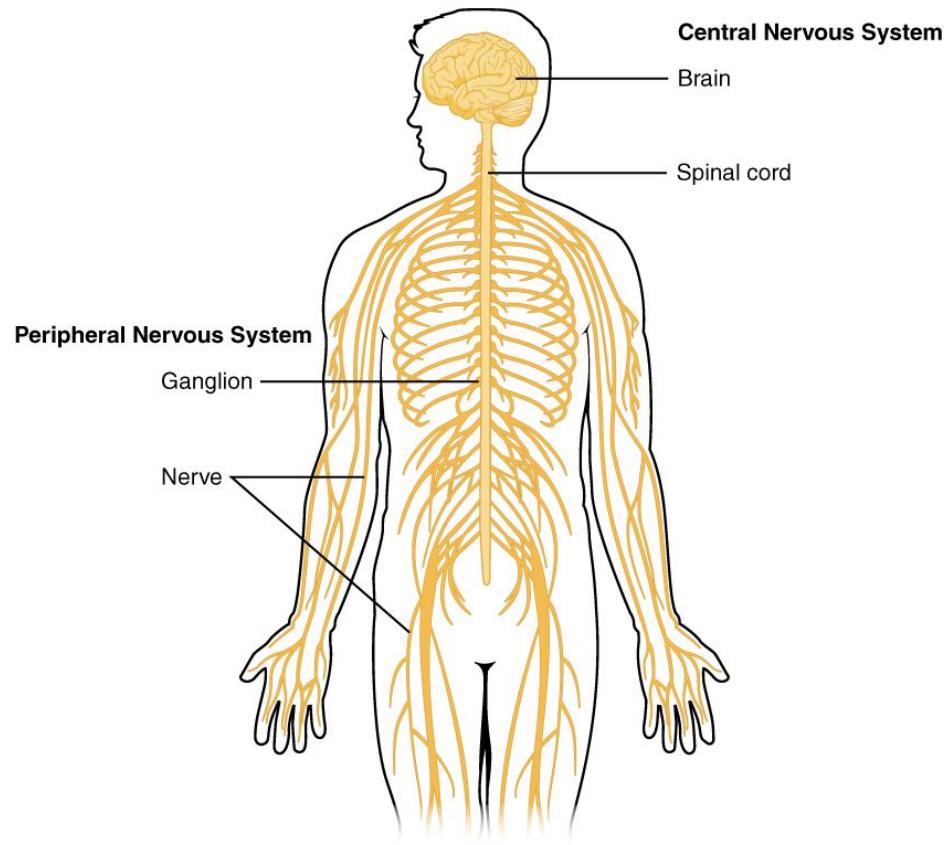
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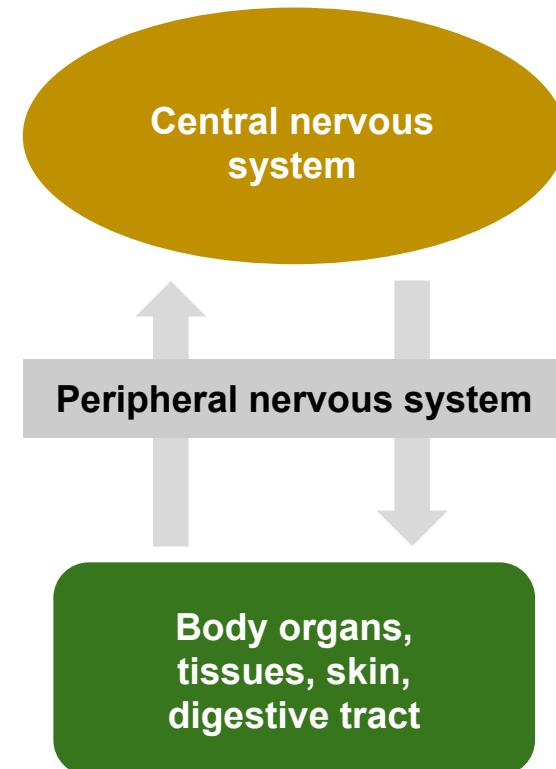
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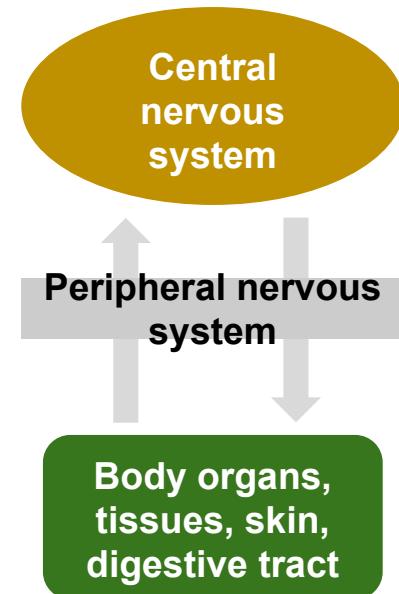
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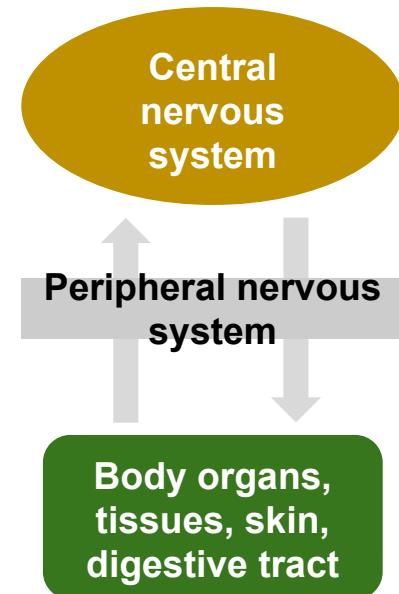
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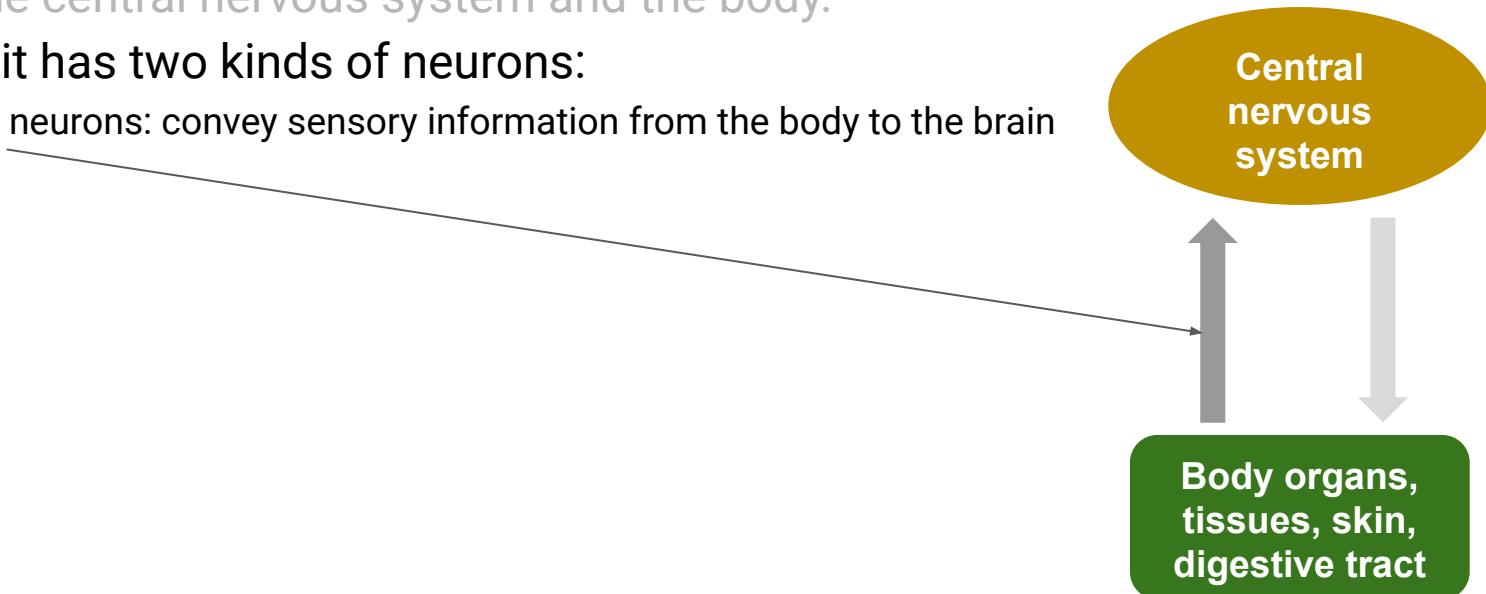
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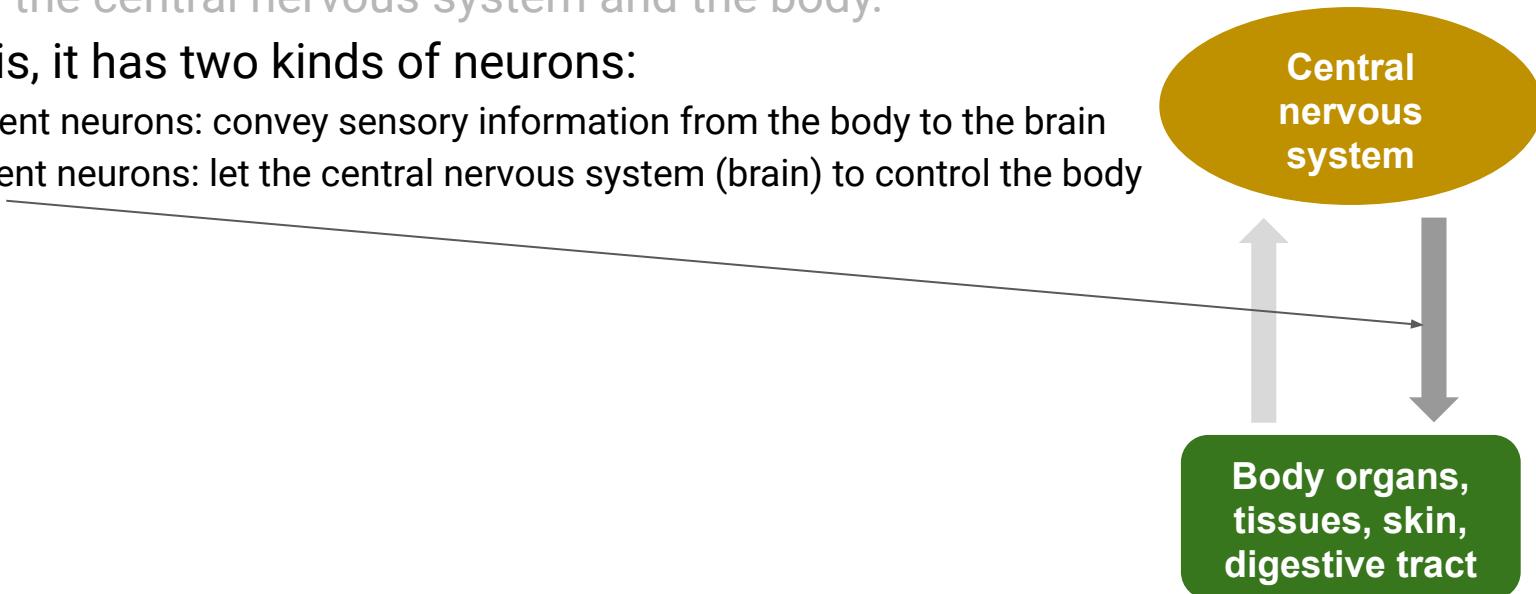
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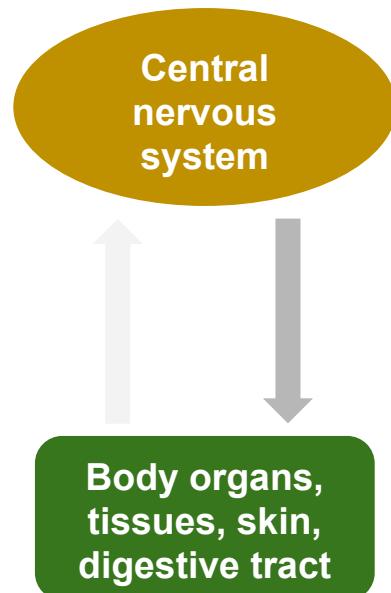
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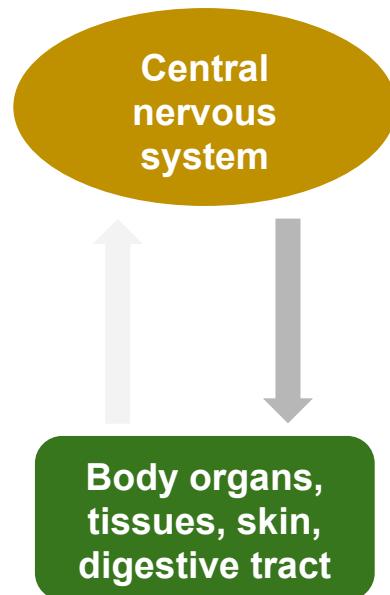
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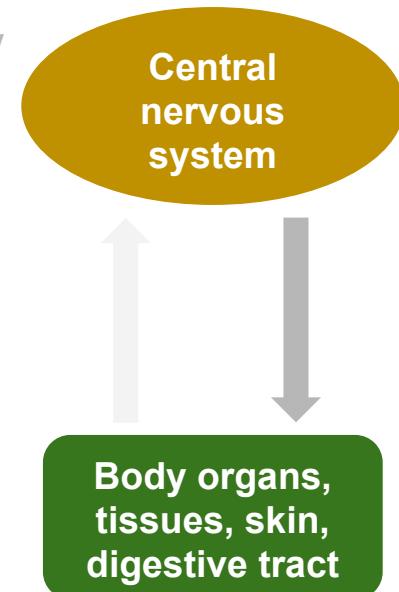
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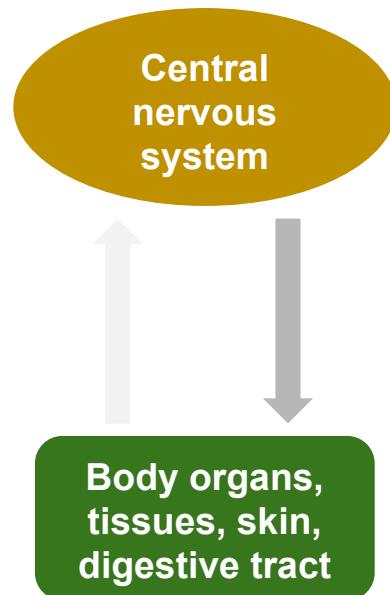
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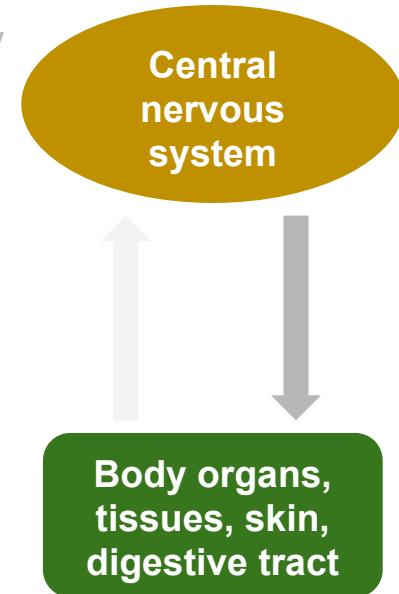
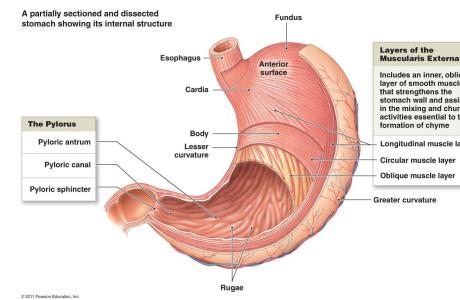
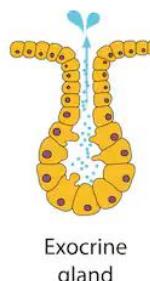
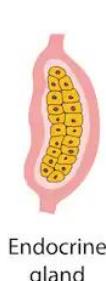
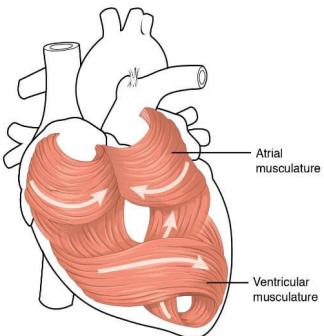
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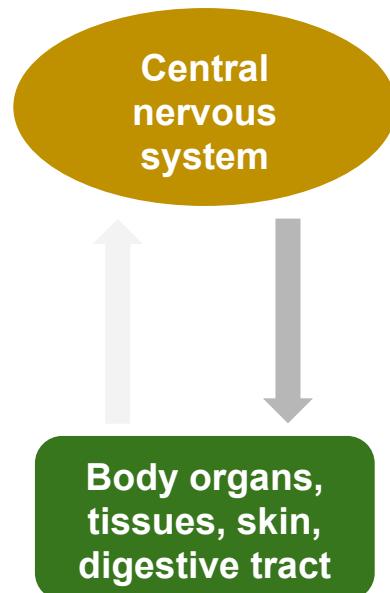
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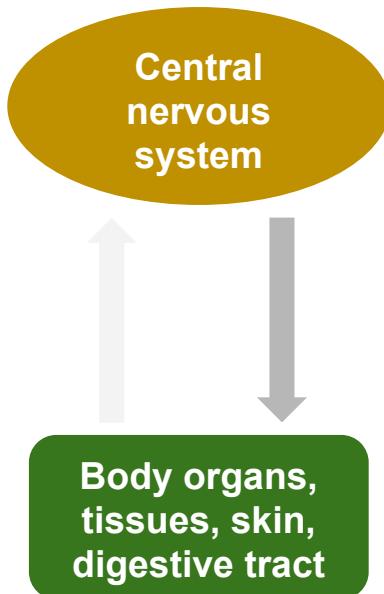
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 - This is further subdivided into three subdivisions.



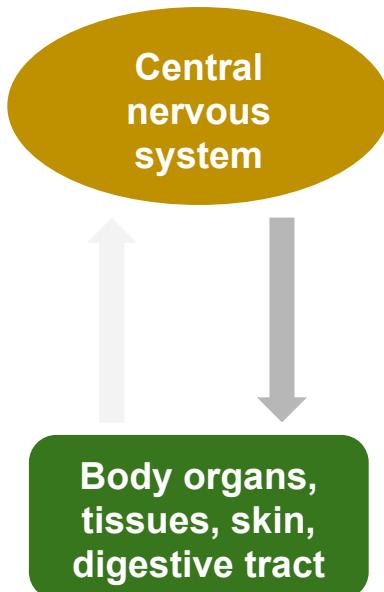
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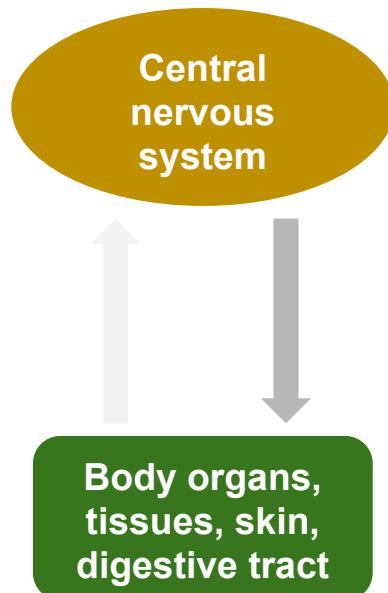
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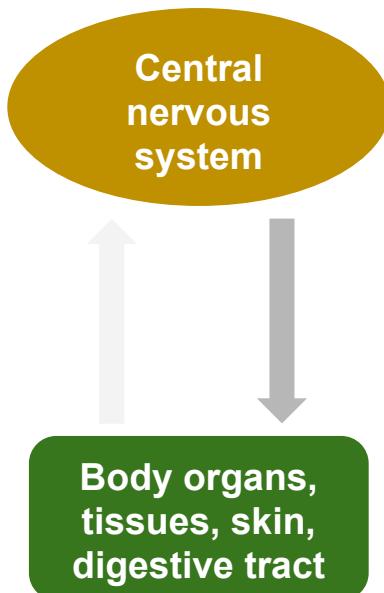
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 - Slows heart rate
 - Stimulates digestive and excretory activity



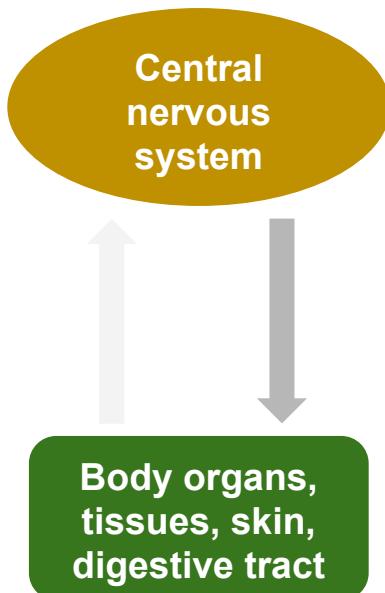
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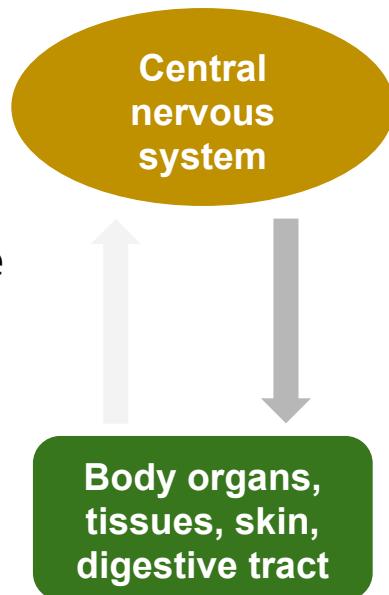
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 - Increases heart rate
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 - Causes glucose release from liver



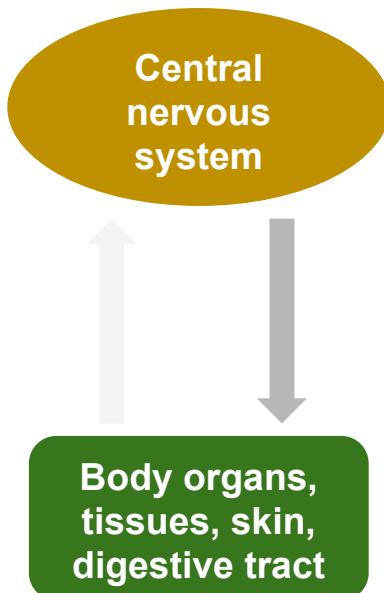
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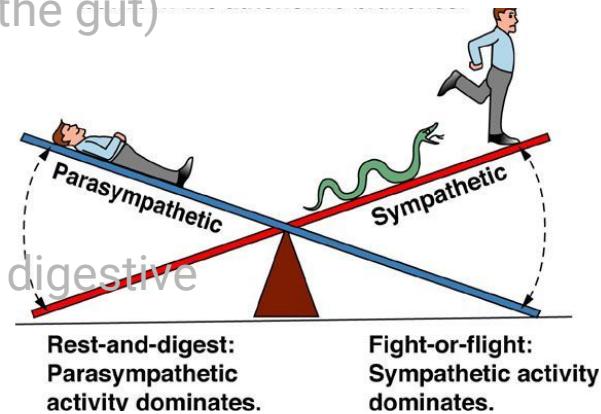
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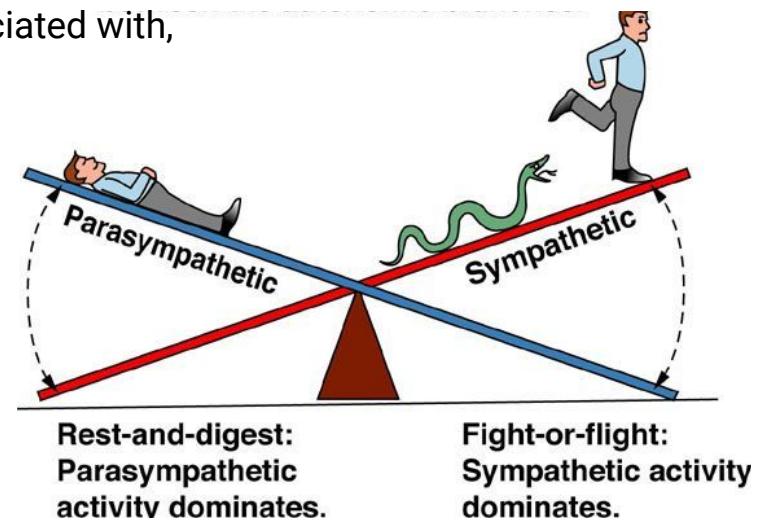
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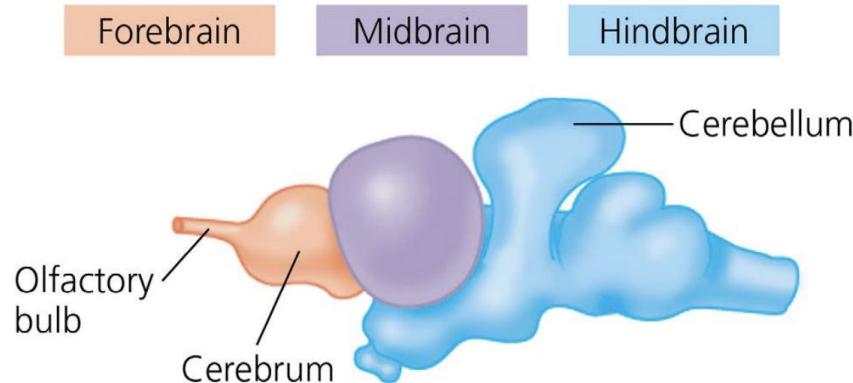
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- You should understand that the **parasympathetic** and **sympathetic** branches act together to create a balance in the body
 - When studying each **hormone** and **neurotransmitter**, think about which of the two branches it might be associated with, based on what effect it has in the body



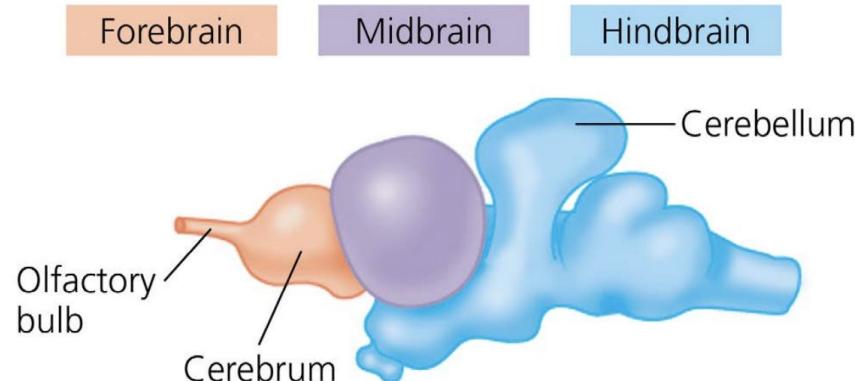
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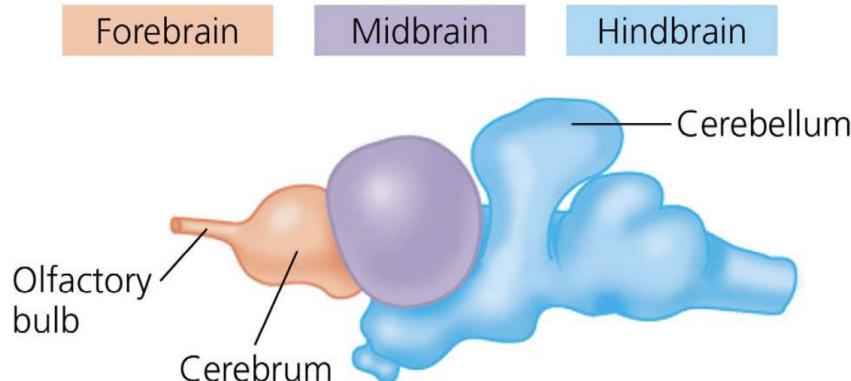
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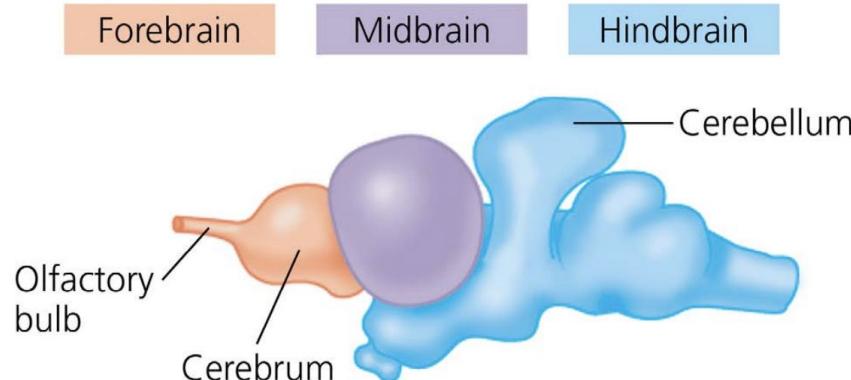
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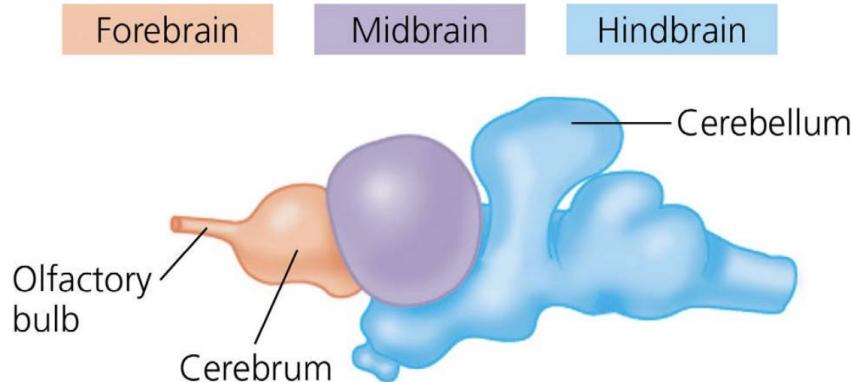
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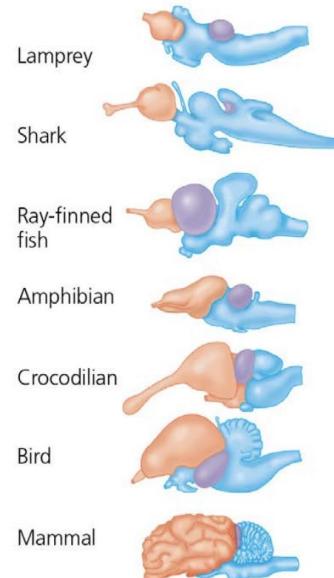
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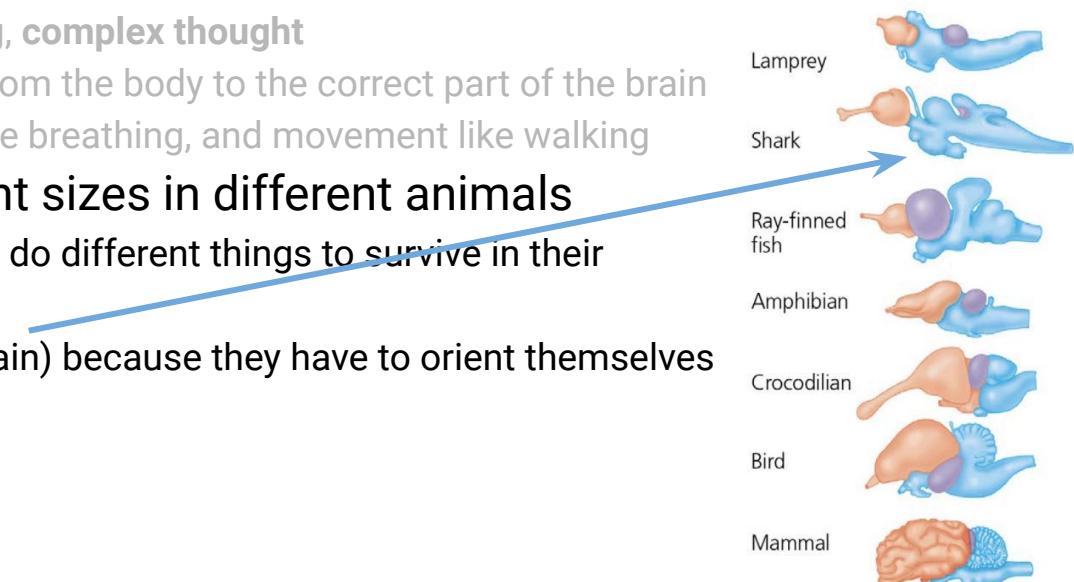
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- **These brain regions are different sizes in different animals**
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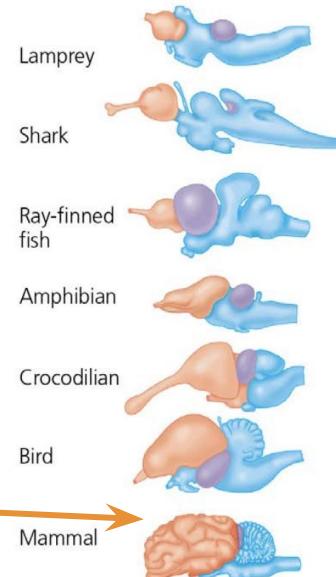
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 - Mammals and birds have bigger forebrains to allow communicate and social interaction



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- Often, **no** you don't (depending on what kind of animal you are)
- Basic, life-supporting processes can go on with just the **hindbrain**, or sometimes just the **spinal cord**.

Neurotransmission

Neurotransmission

- How are signals sent between two neurons?
- How does a neuron integrate input from multiple neighbors?
- How do neurotransmitters work?

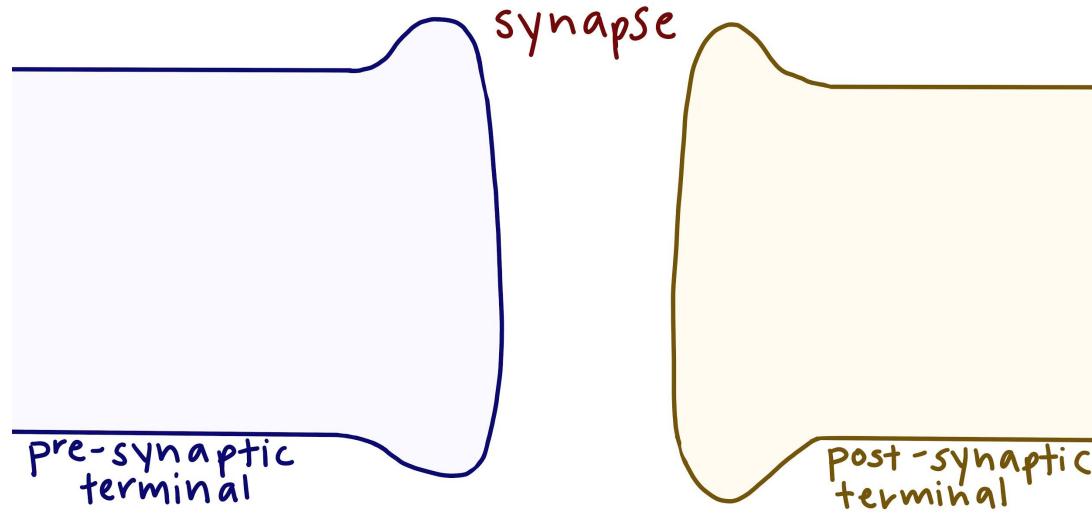
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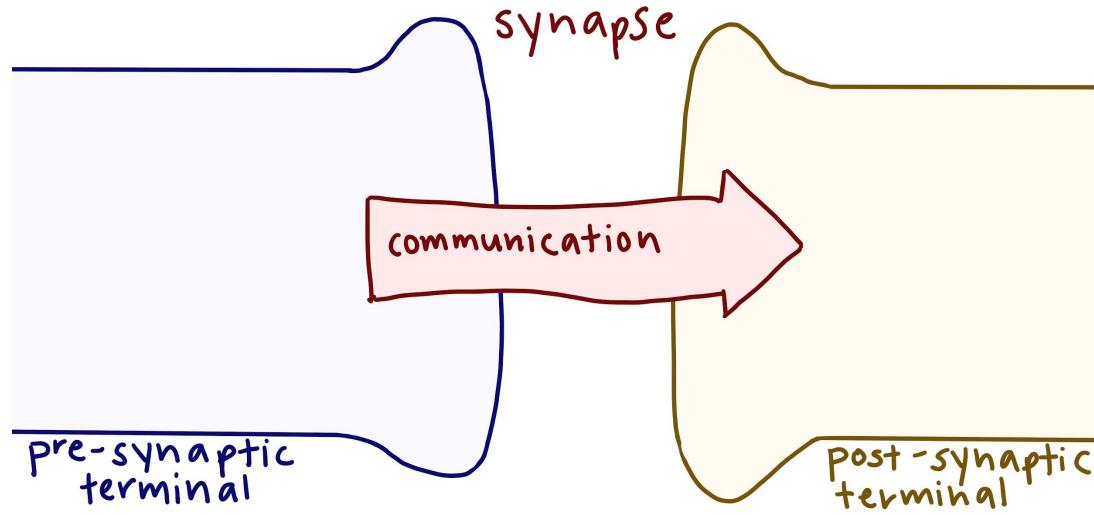
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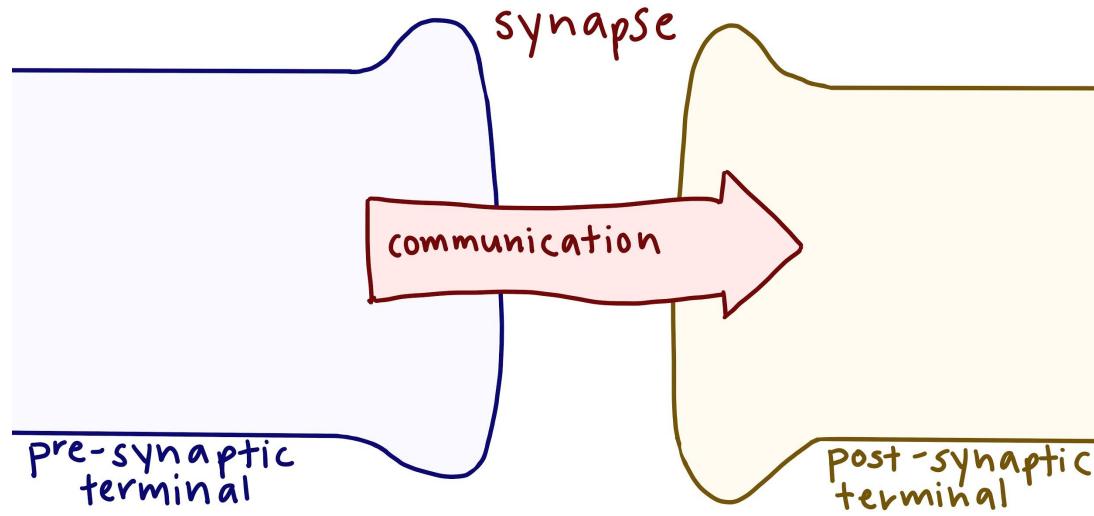
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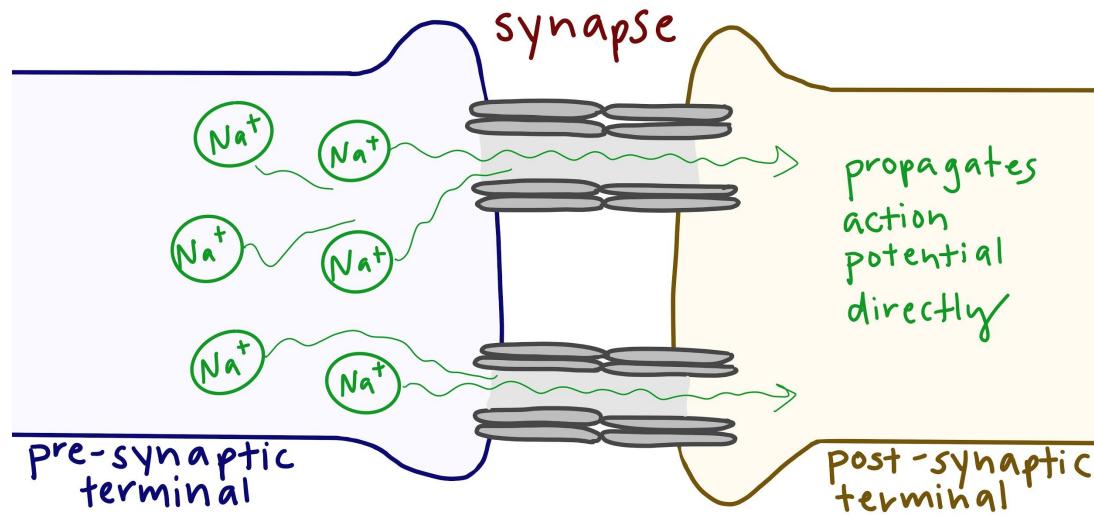
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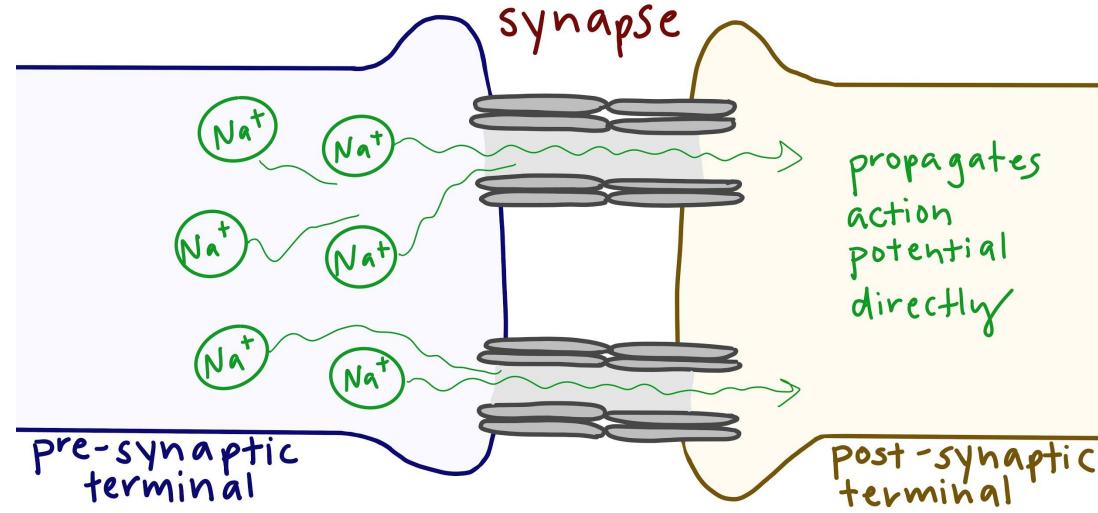
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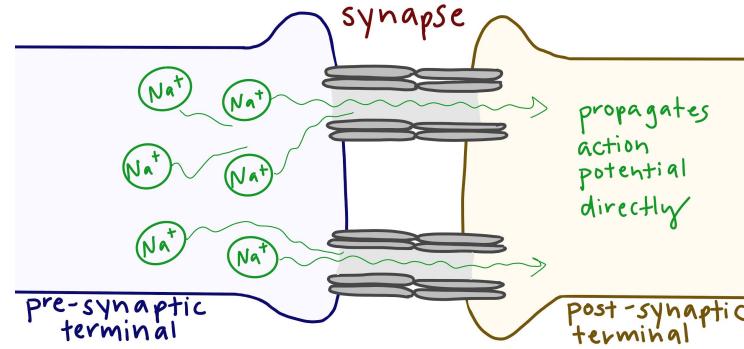
The protein channels that make those gap junctions are called **connexins**. Six connexins come together to make each neuron's half of the channel.



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 - Electrical synapses allow really fast transmission of the signal, so they are used to control behaviors that need to happen **quickly**, like escape reflexes.

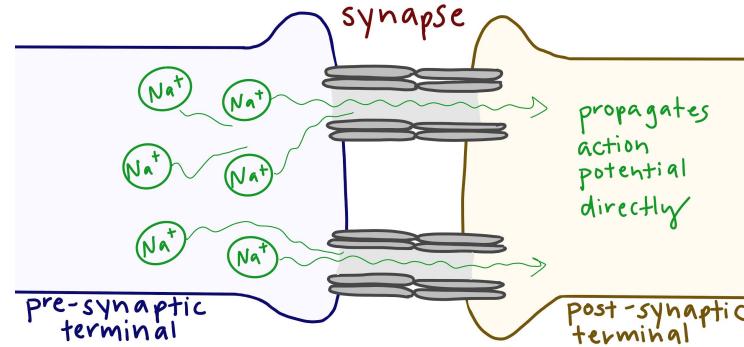
The protein channels that make those gap junctions are called **connexins**. Six connexins come together to make each neuron's half of the channel.



How do neurons communicate?

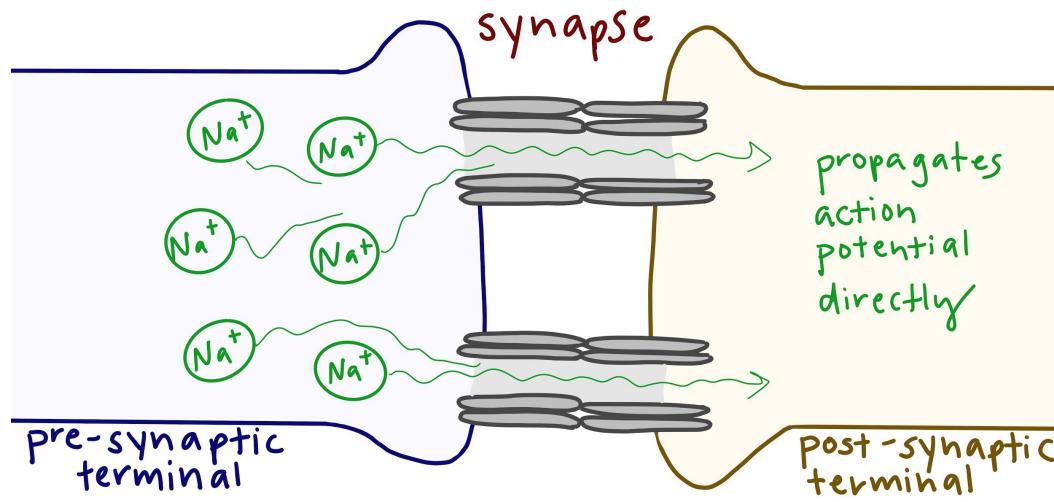
- There are two kinds of synapse:
 - **Electrical:** the communication is a direct, electrical signal between each neuron.
 - There are protein channels (**gap junctions**) between the neurons that allow the action potential to move directly between cells.
 - Electrical synapses allow really fast transmission of the signal, so they are used to control behaviors that need to happen **quickly**, like escape reflexes.
 - However, they send **all-or-nothing signals**, so they aren't as **flexible and controllable** as chemical synapses.

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Electrical synapses: take-aways

- You should know:
 - What form the message is sent in (electrical, via ion diffusion through channels)
 - What proteins make the channels (connexins)
 - The benefit of electrical synapses (very fast transmission)
 - The downside of electrical synapses (all-or-nothing signalling is not flexible)



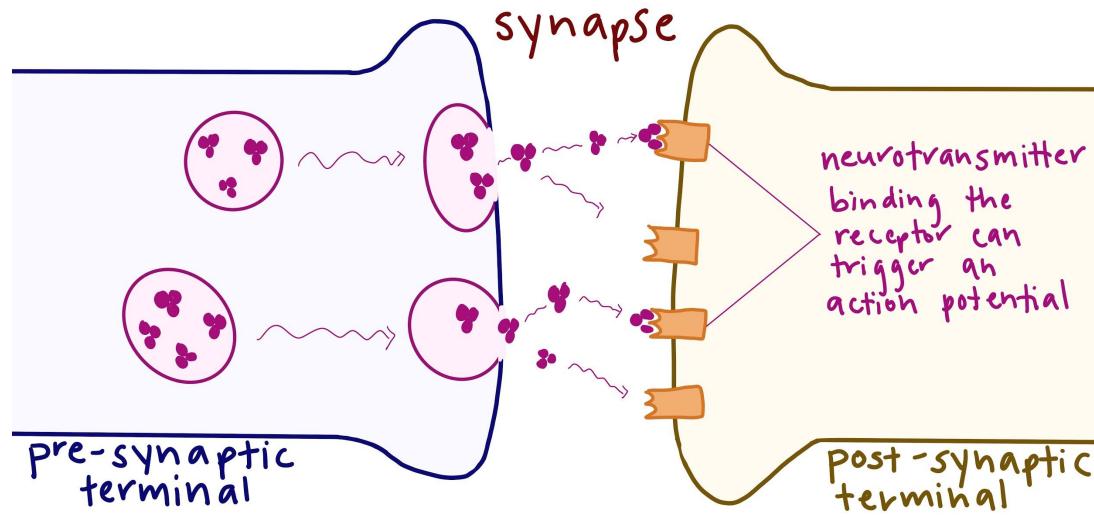
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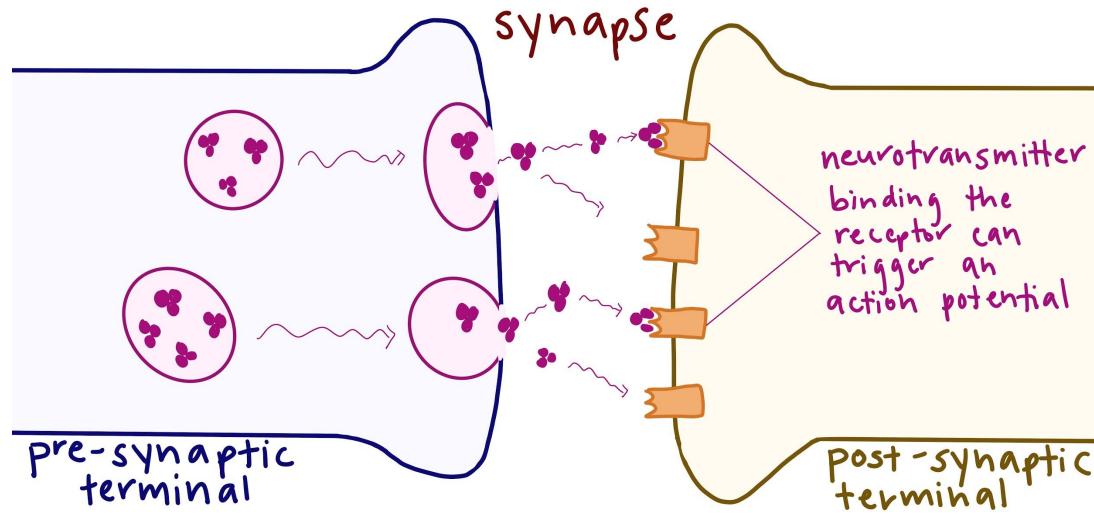
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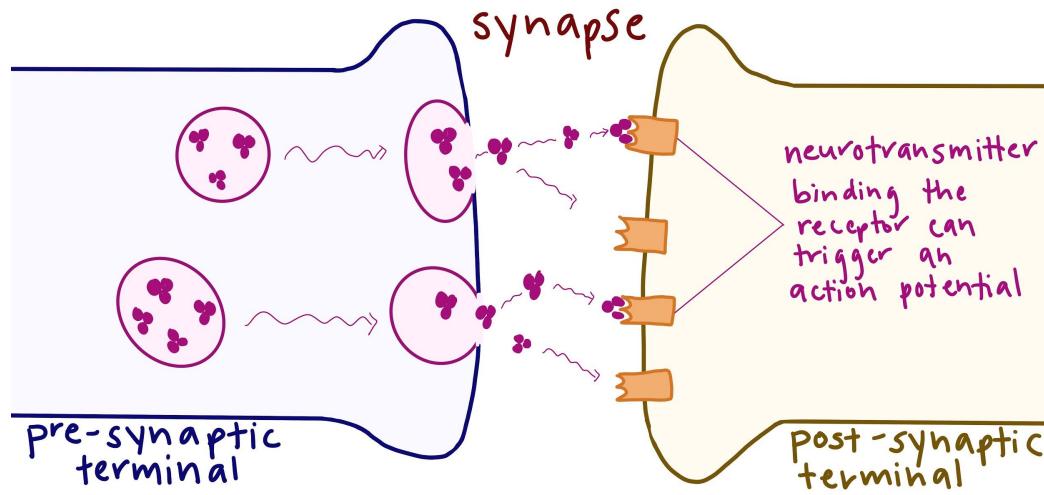
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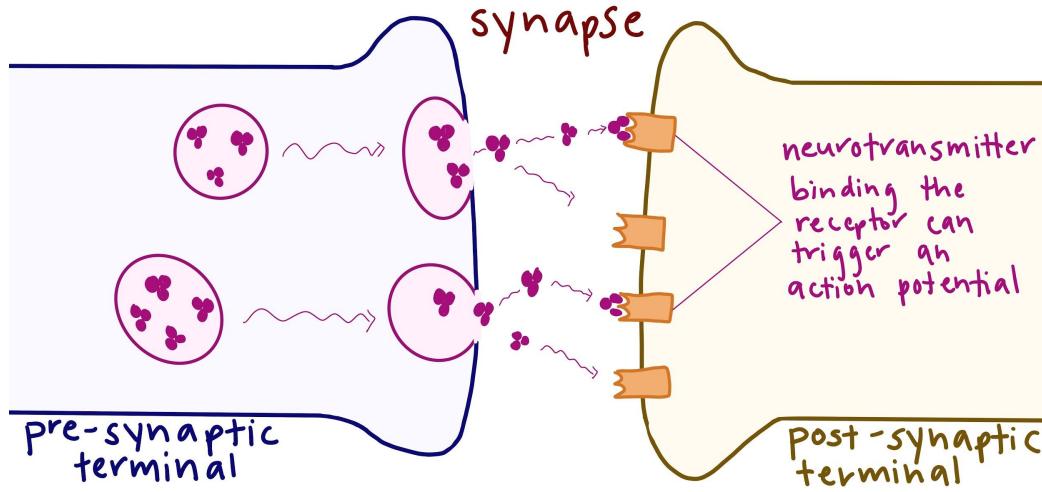
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Chemical synapses: general take-aways

- You should know:
 - **What form the message is sent in** (chemical, via neurotransmitter diffusion)
 - **How the message is received** (neurotransmitter binding receptor proteins)
 - **The benefit of chemical synapses** (flexible transmission of different signals)
 - **The downside of chemical synapses** (slower than electrical synapses)



Chemical synapses: general take-aways

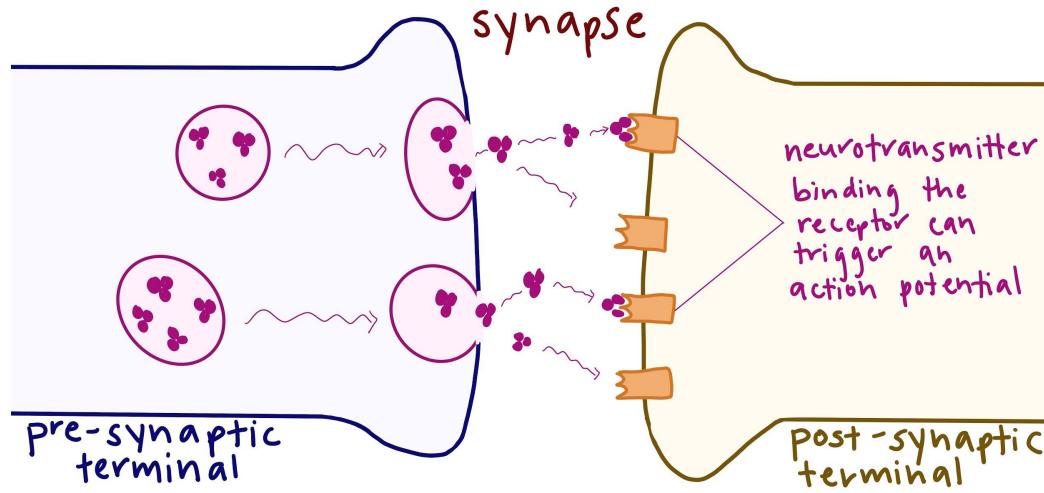
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What are the different kinds of neurotransmitter receptors?

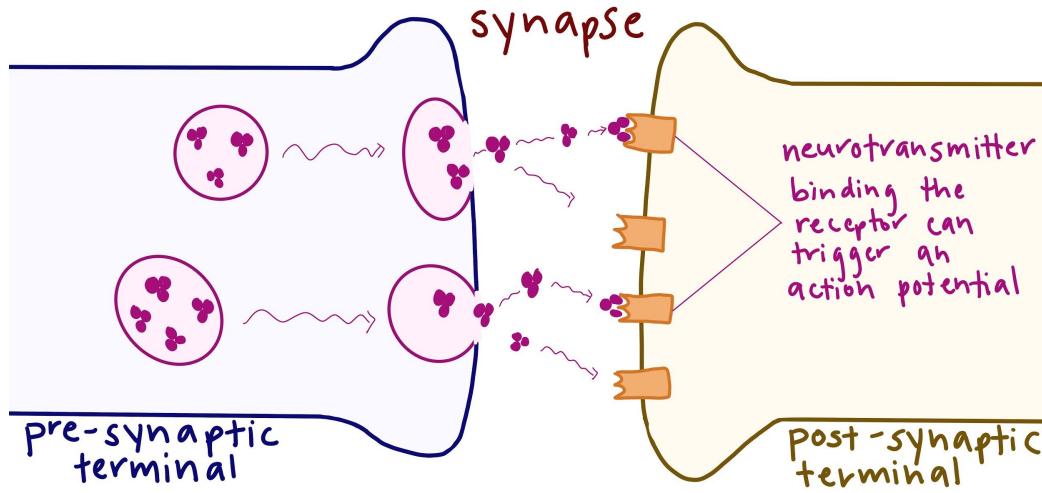
What are the different kinds of neurotransmitter receptors?

- There are many different neurotransmitters.



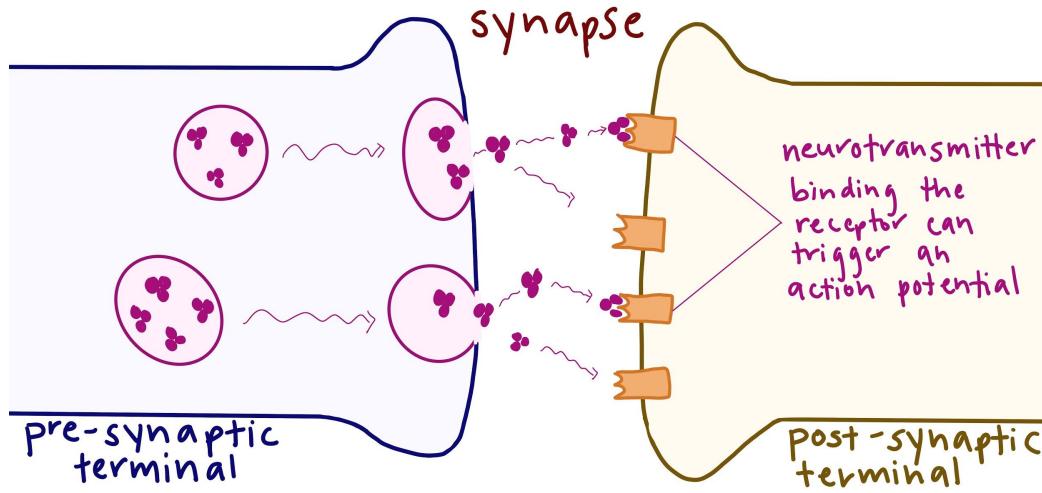
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- There are even more different receptors, because most neurotransmitters can bind several different receptors.



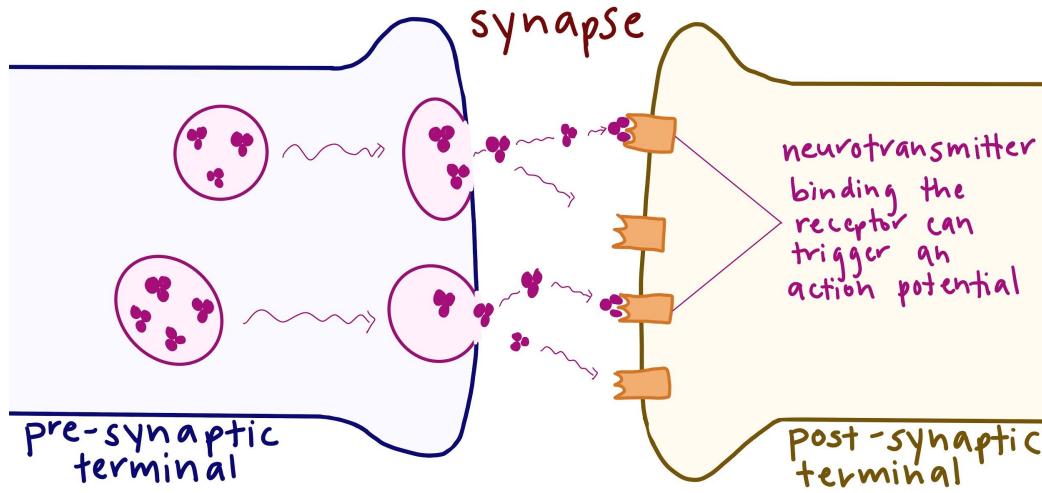
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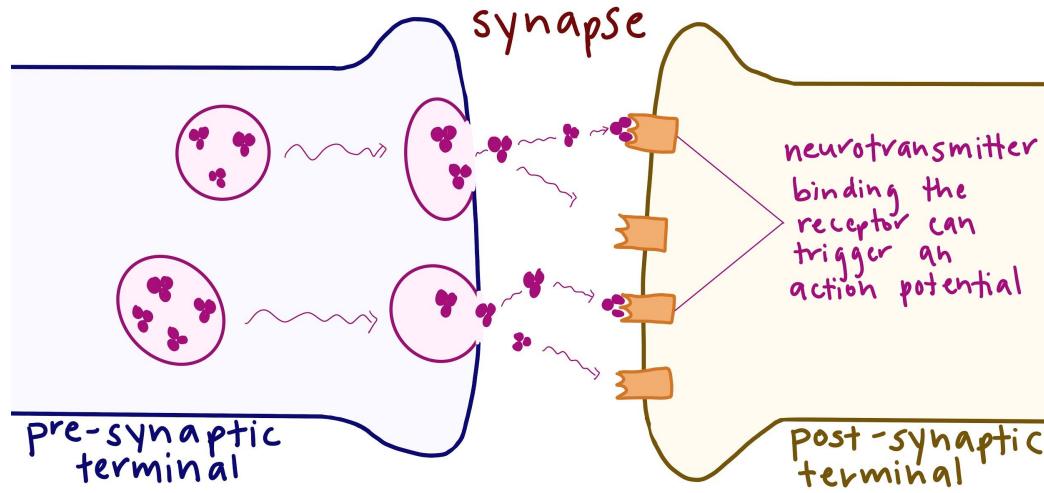
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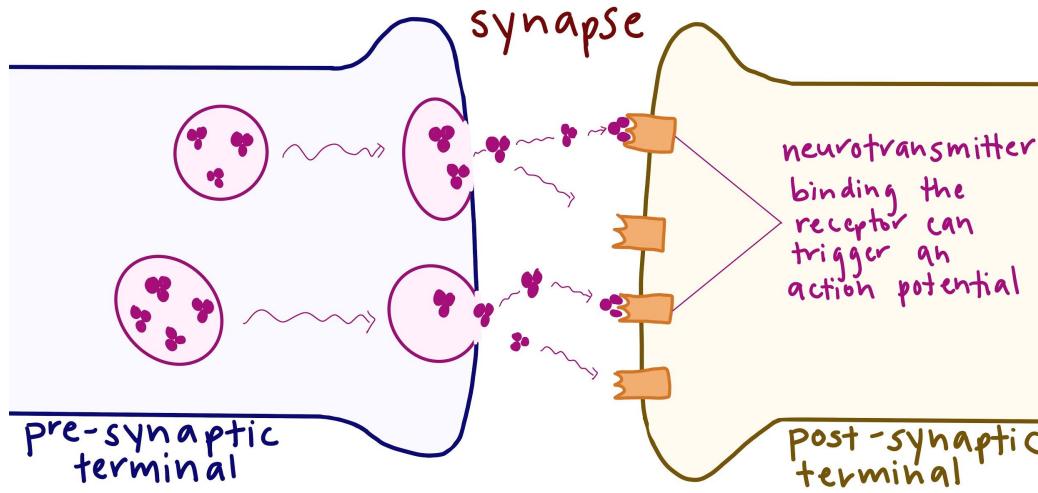
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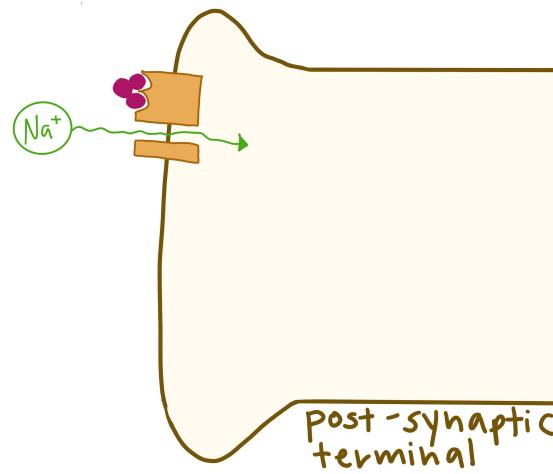
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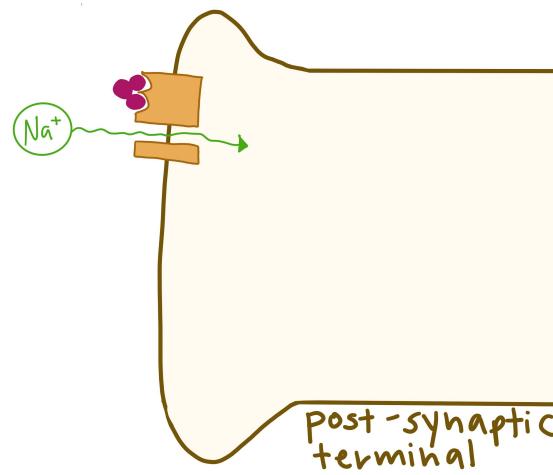
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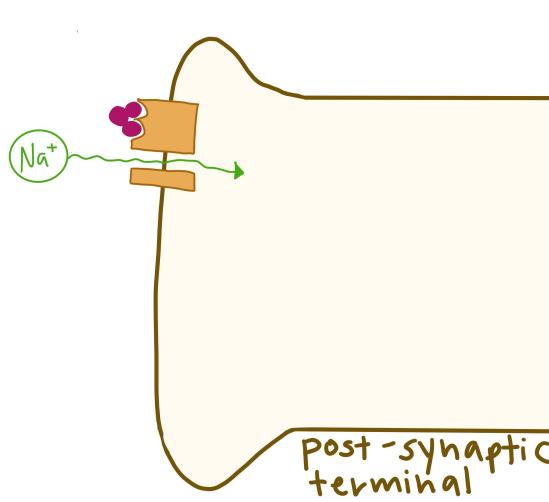
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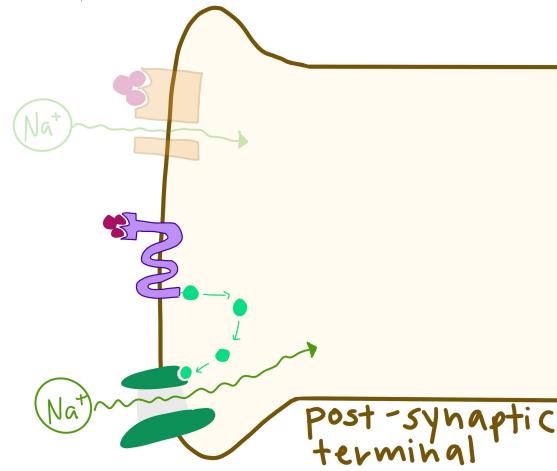
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Keep this in mind later when we go over **excitatory postsynaptic potentials** and **inhibitory postsynaptic potentials**. We will also connect this concept to **graded potentials**.

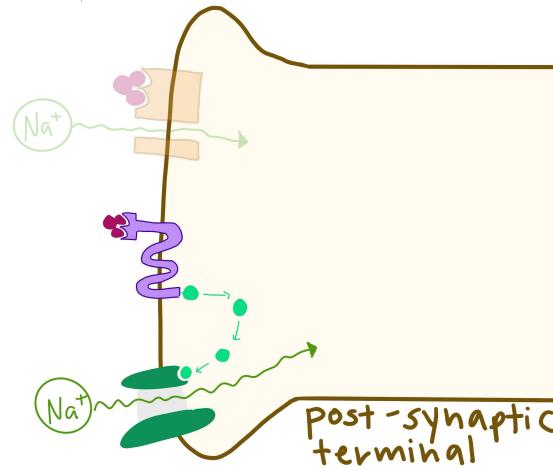
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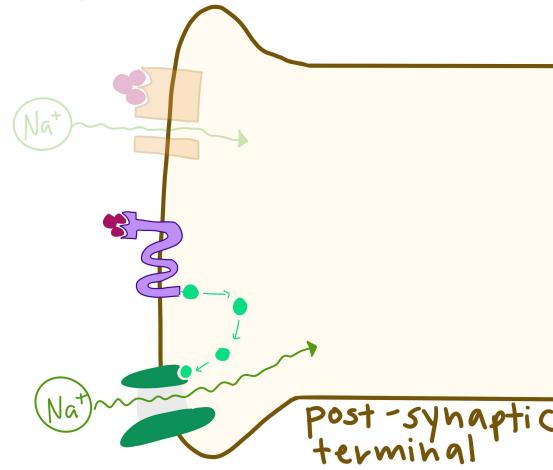
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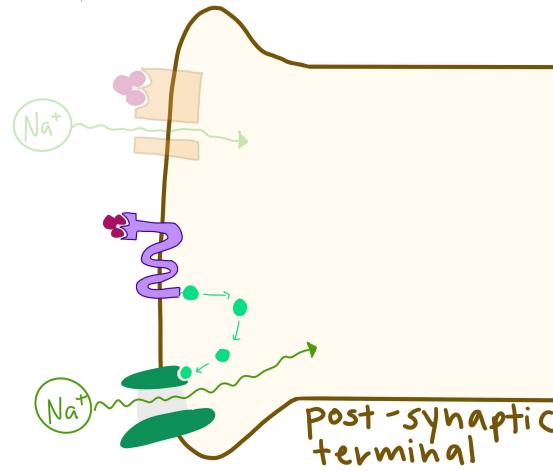
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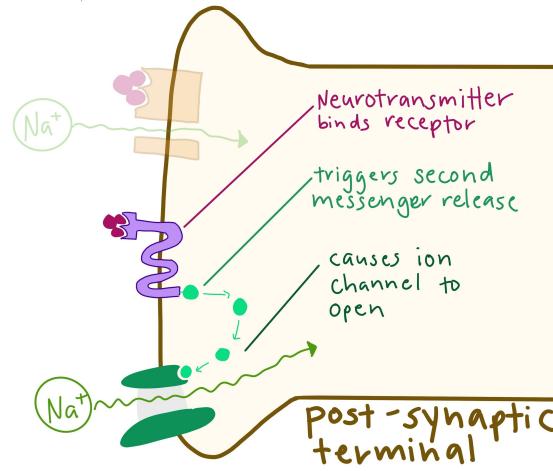
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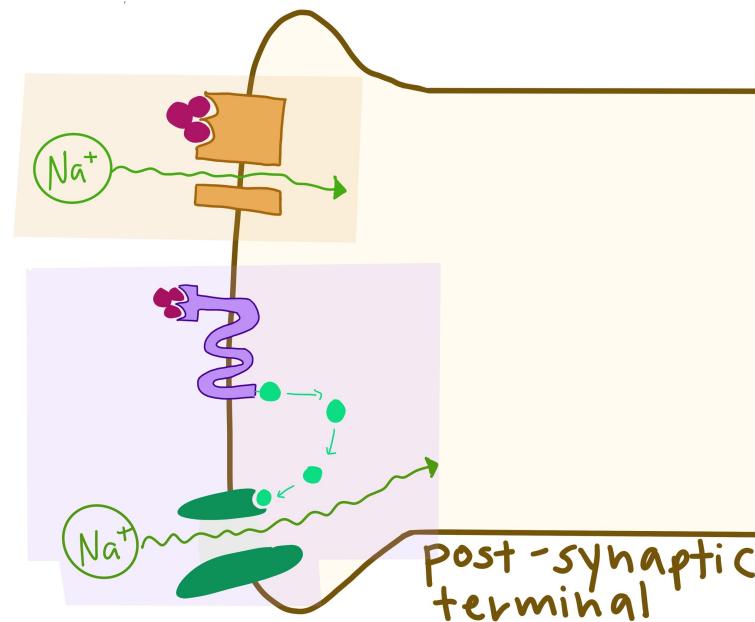
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Receptor types: general take-aways

- You should know:
 - The two kinds of receptor
 - Result of neurotransmitter binding in each type
 - (ionotropic and metabotropic)
 - (ion channel opens, second messenger release)
 - Be able to diagram those processes



Receptor types: general take-aways

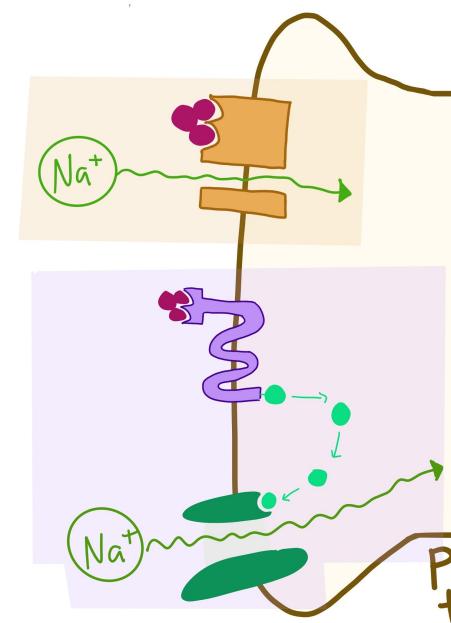
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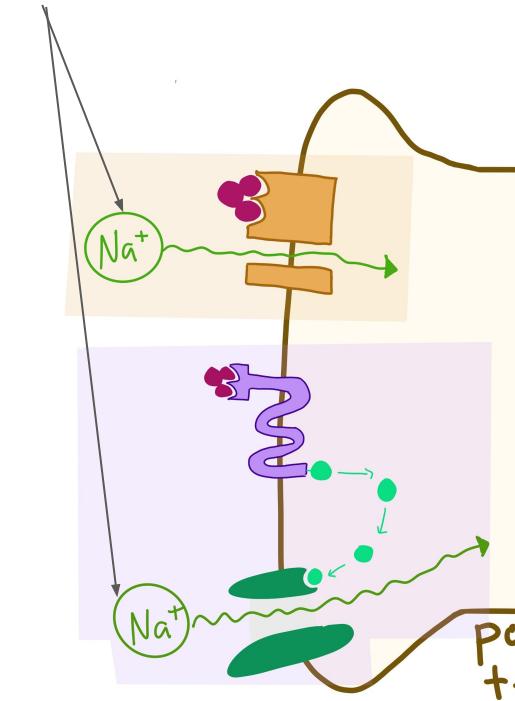
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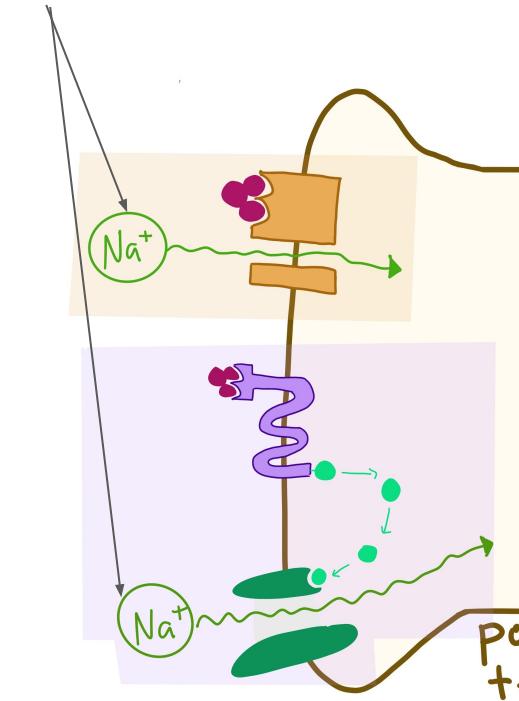
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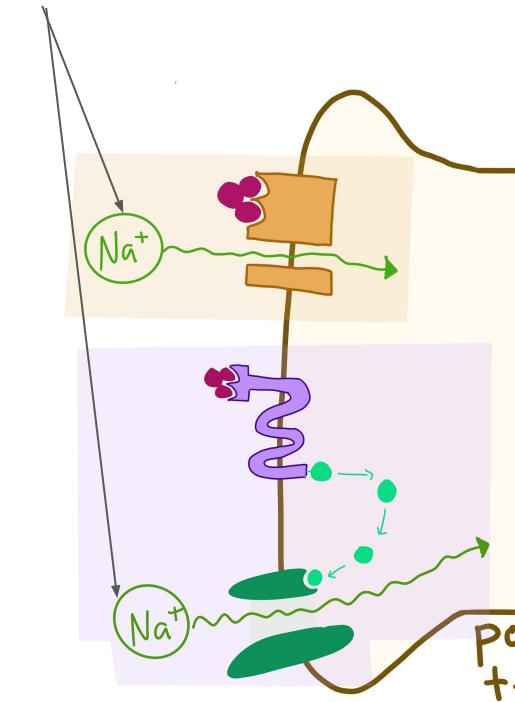
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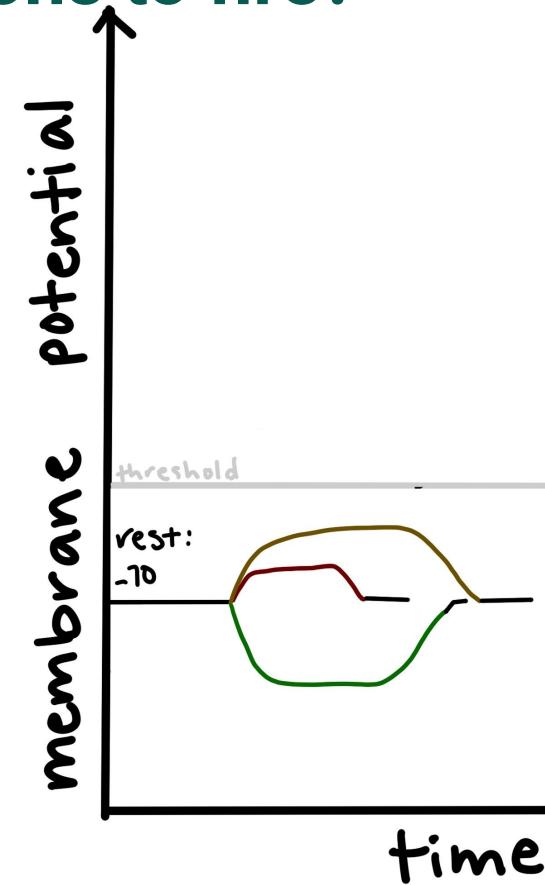
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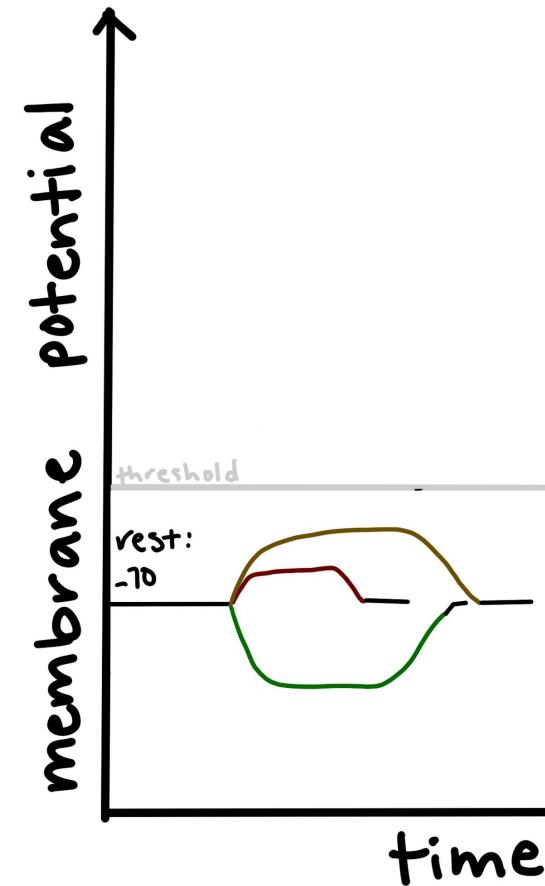
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- This means they can cause different **graded potentials**



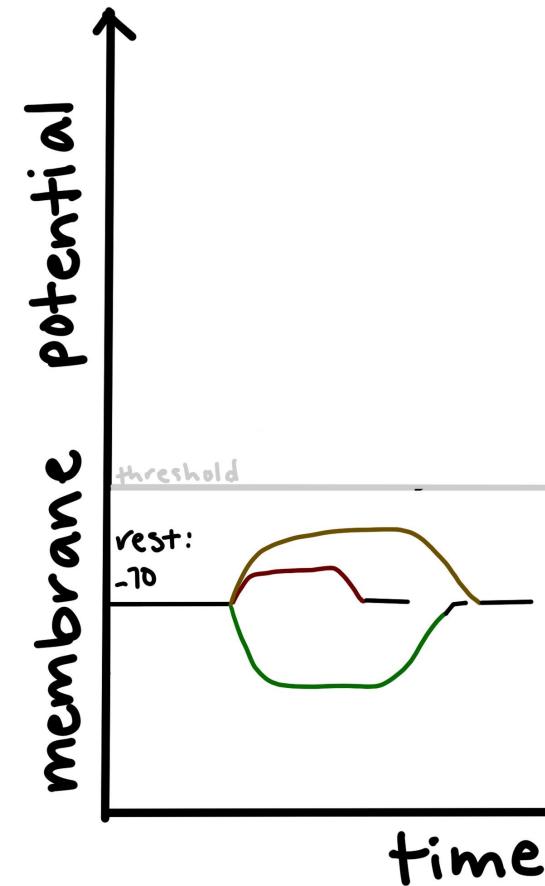
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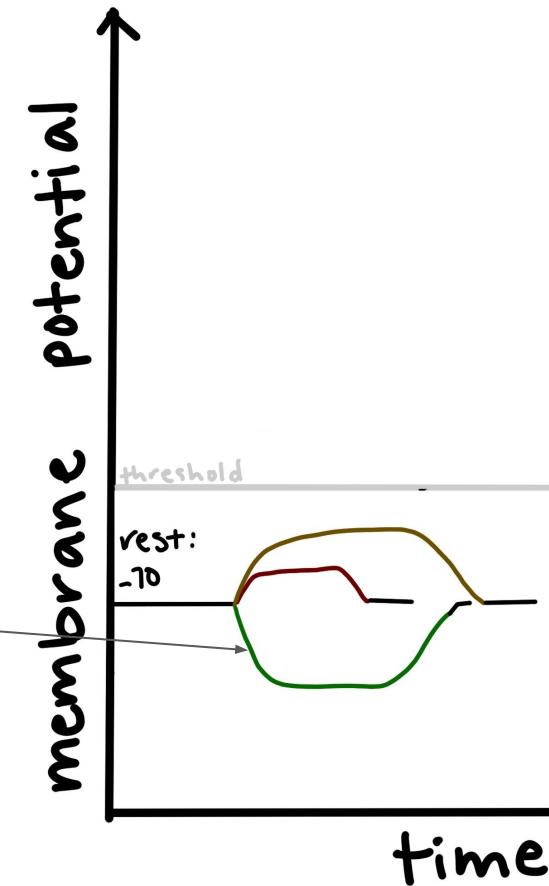
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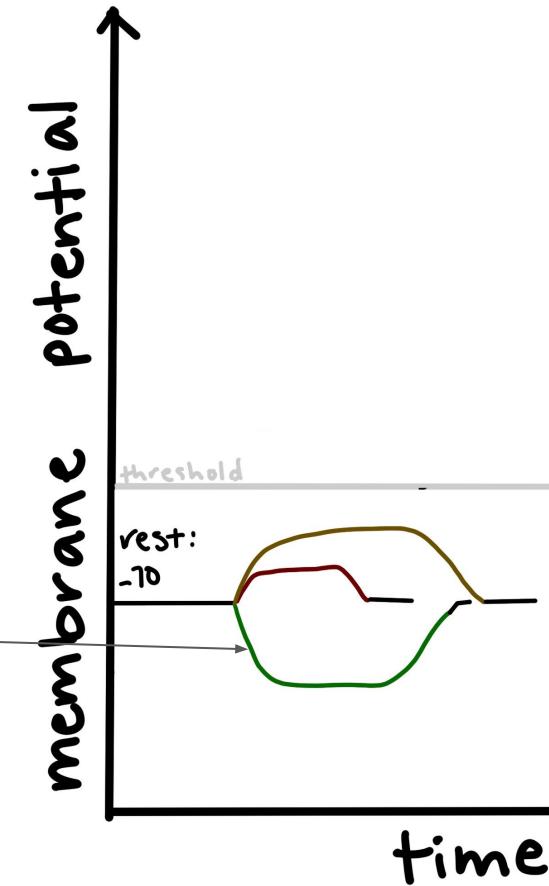
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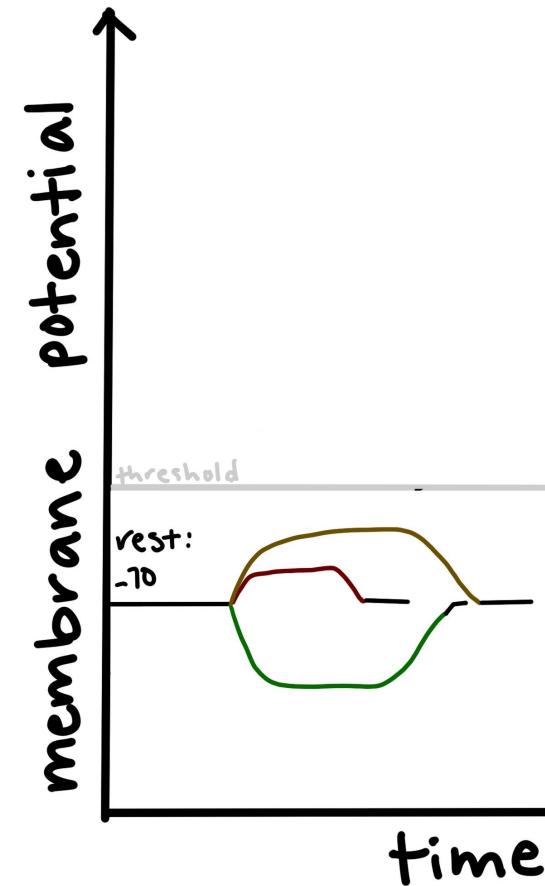
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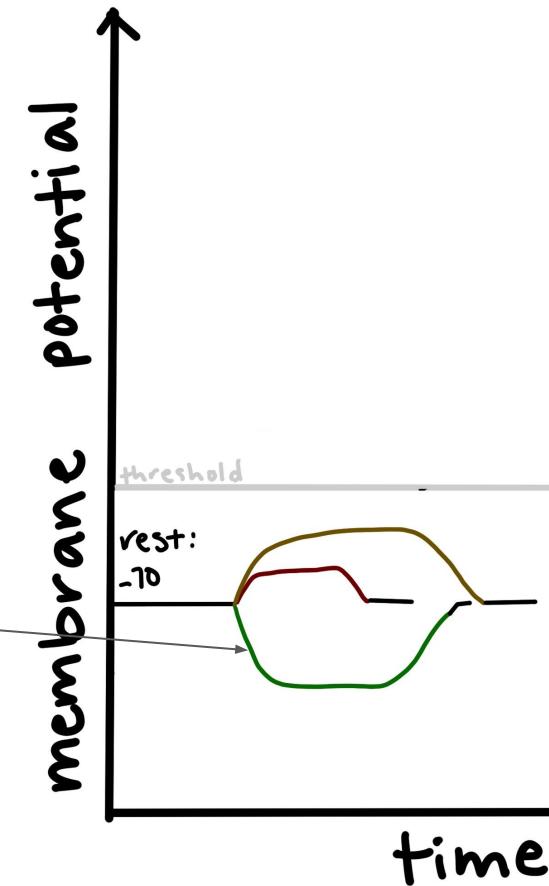
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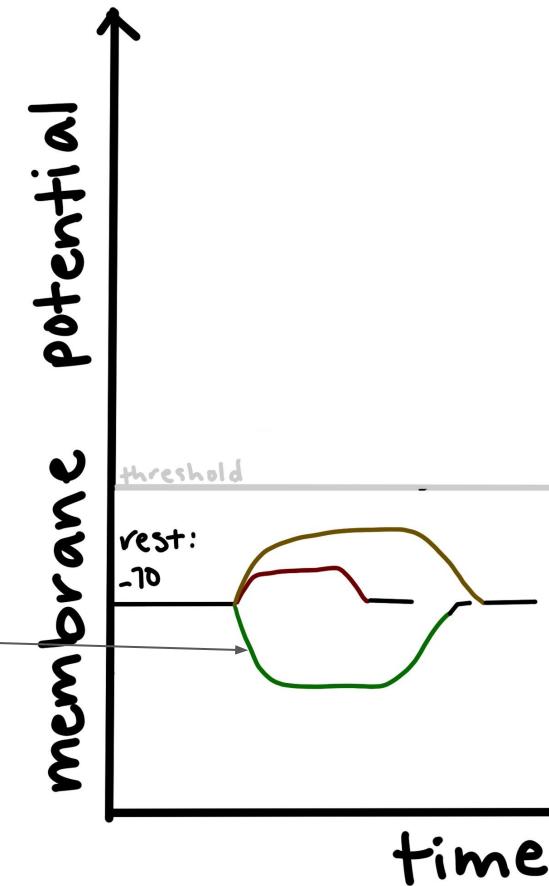
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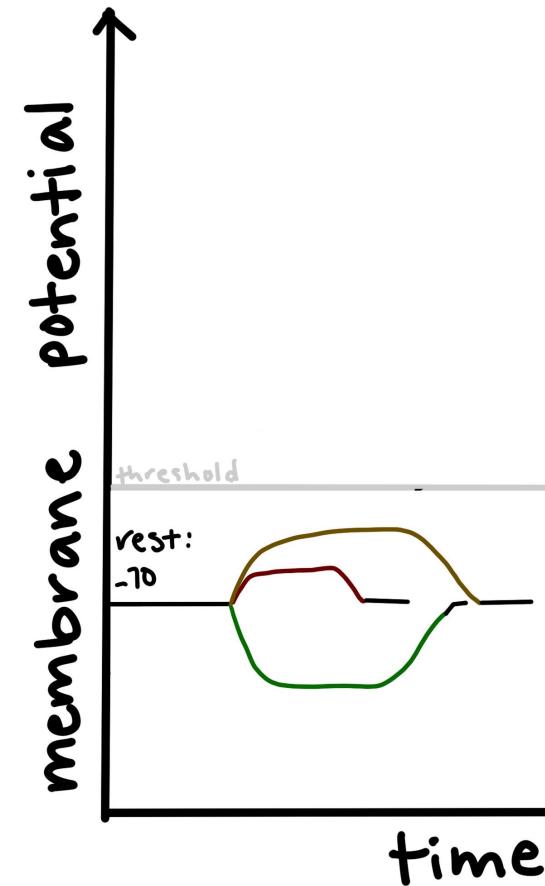
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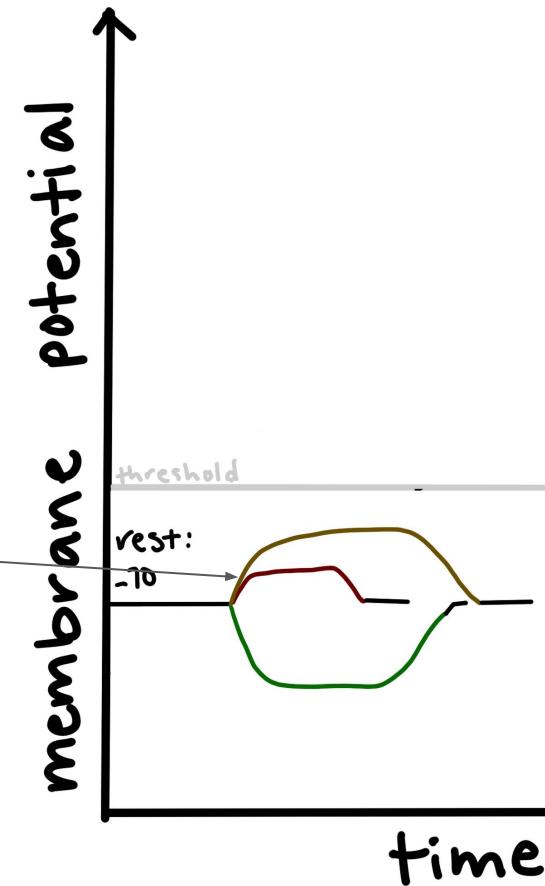
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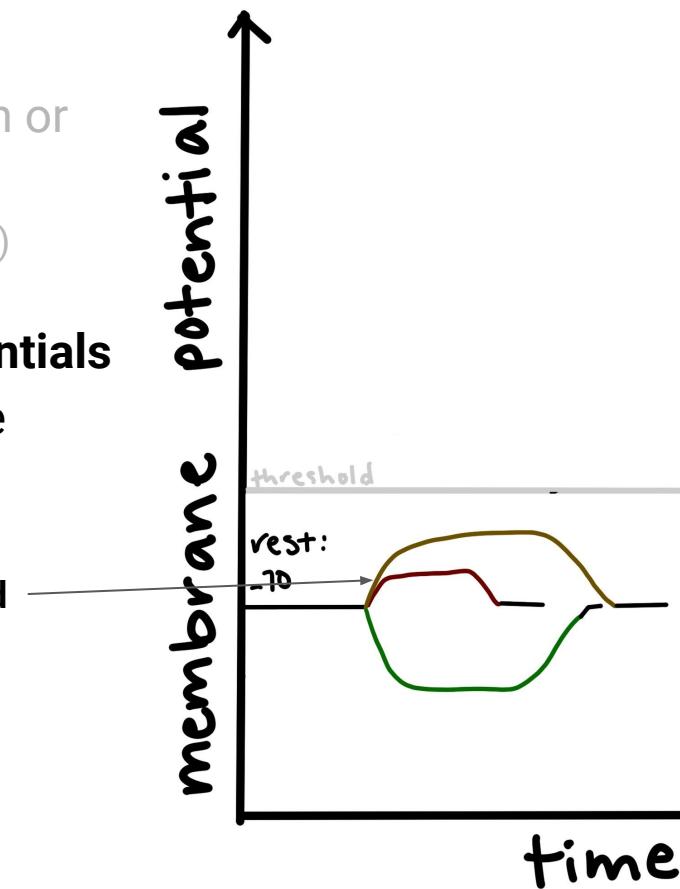
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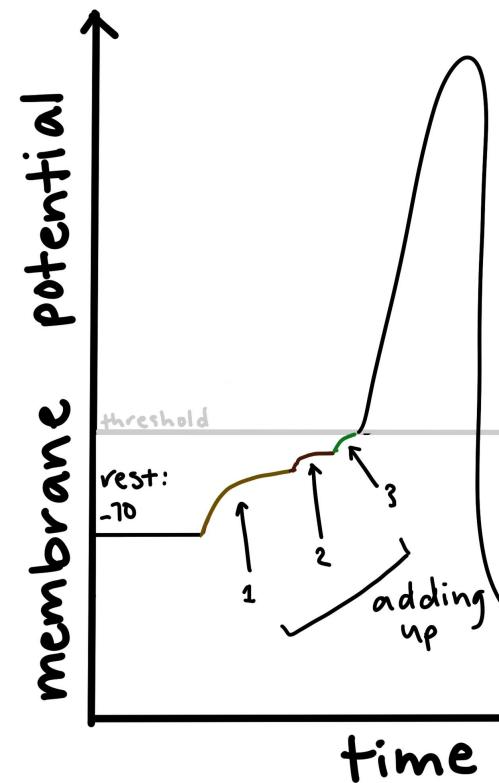
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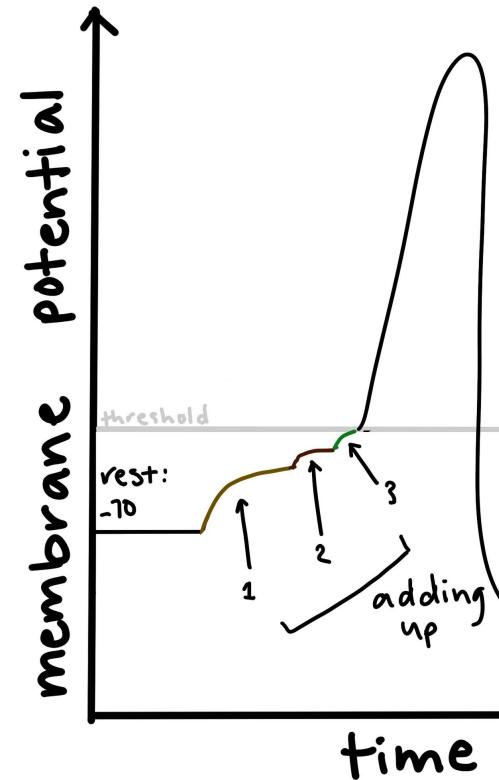
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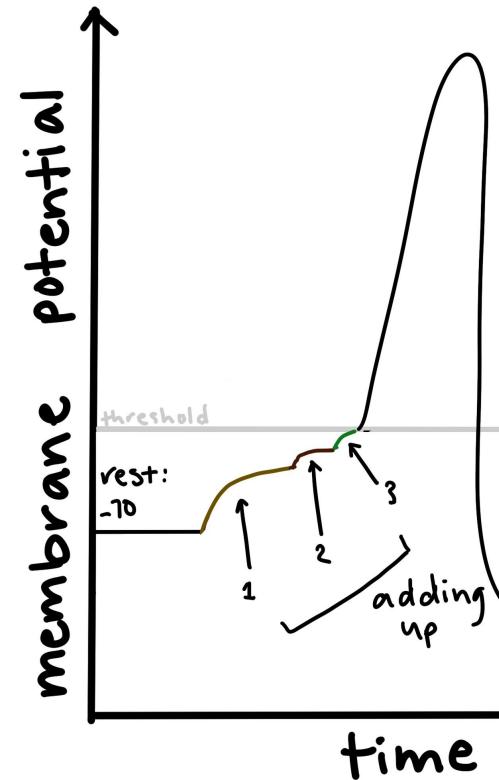
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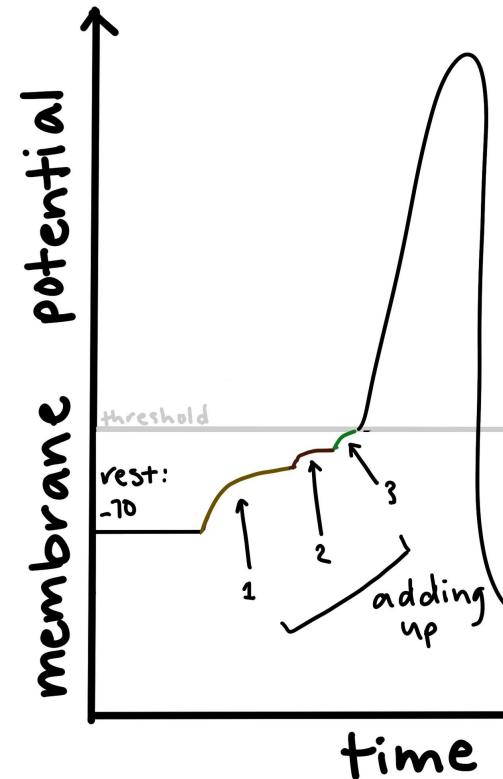
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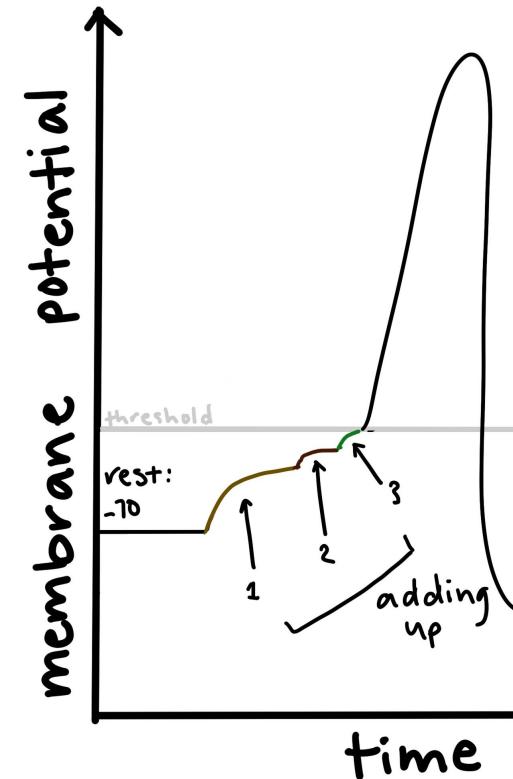
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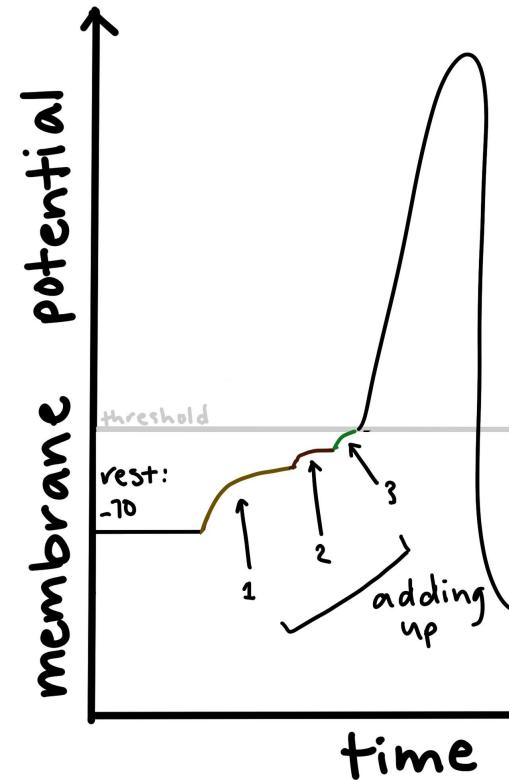
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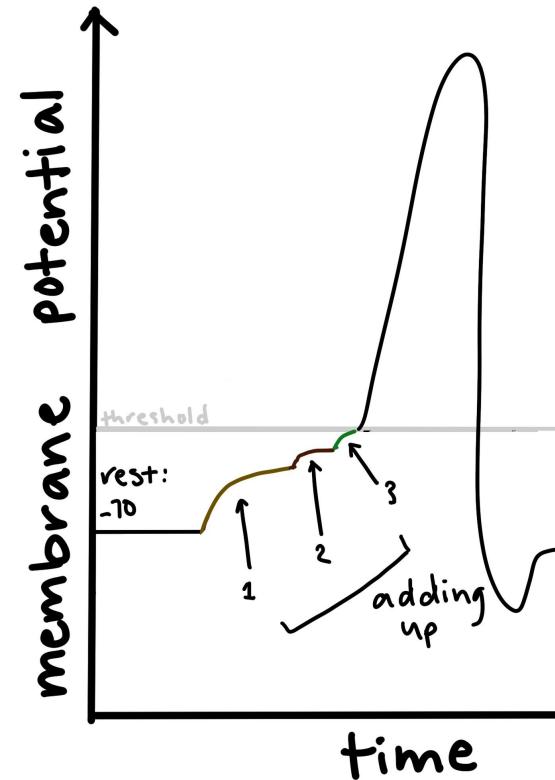
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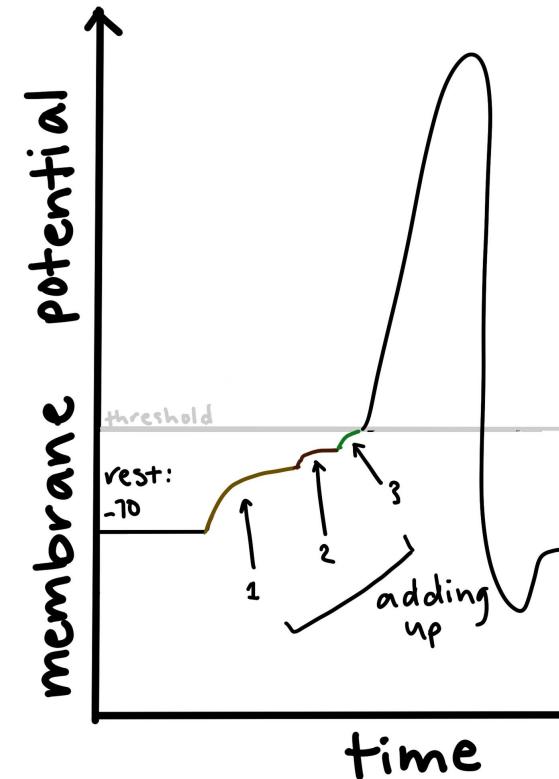
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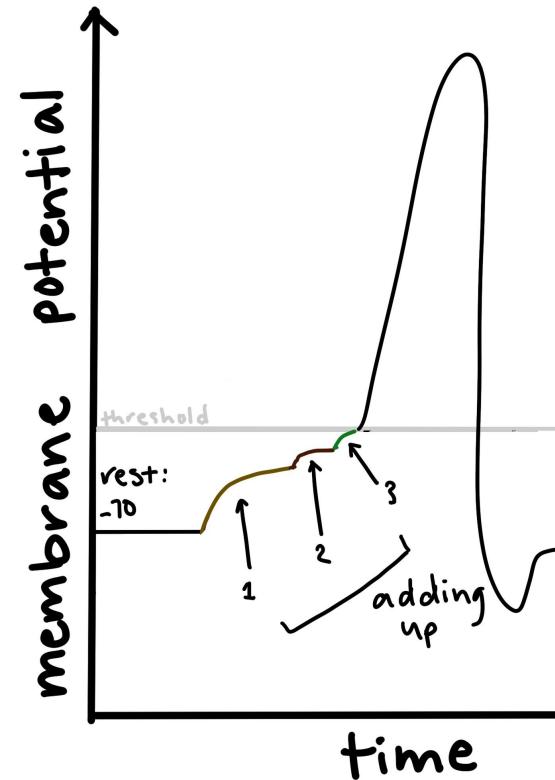
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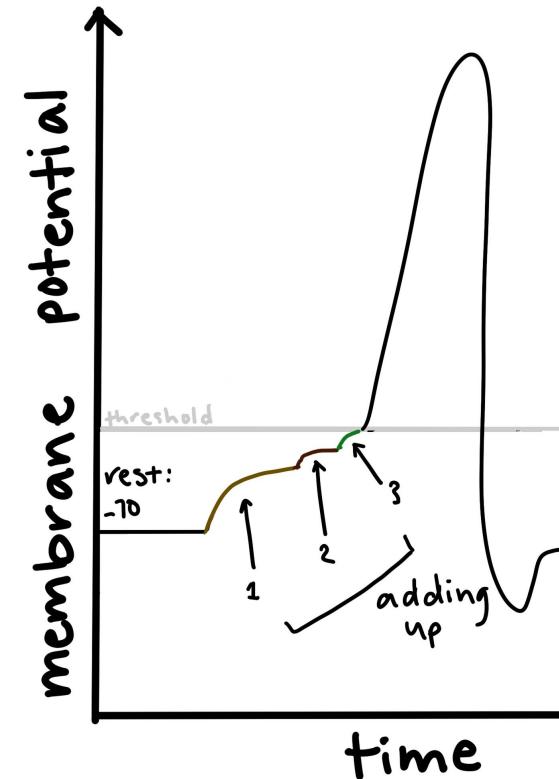
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 - So you ask a bunch of friends what they thought about the class
 - This corresponds to all the different neurotransmitter inputs
 - Some say it's a great class, some say it's terrible
 - This corresponds to graded depolarizations and hyperpolarizations
 - You weigh all the advice and decide to take BIOEE 1780



Postsynaptic potentials

- Graded potentials from different neurotransmitter inputs add to cause an action potential to fire (or not fire)
- I like to imagine this with the following scenario:
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 - This corresponds to the neuron trying to decide whether to fire an action potential
 - So you ask a bunch of friends what they thought about the class
 - This corresponds to all the different neurotransmitter inputs
 - Some say it's a great class, some say it's terrible
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 - You weigh all the advice and decide to take BIOEE 1780
 - This corresponds to reaching threshold and firing an AP



How do neurons “add up” their inputs?

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- I said that weighing advice when deciding to take a class is like a neuron weighing input when deciding whether to fire

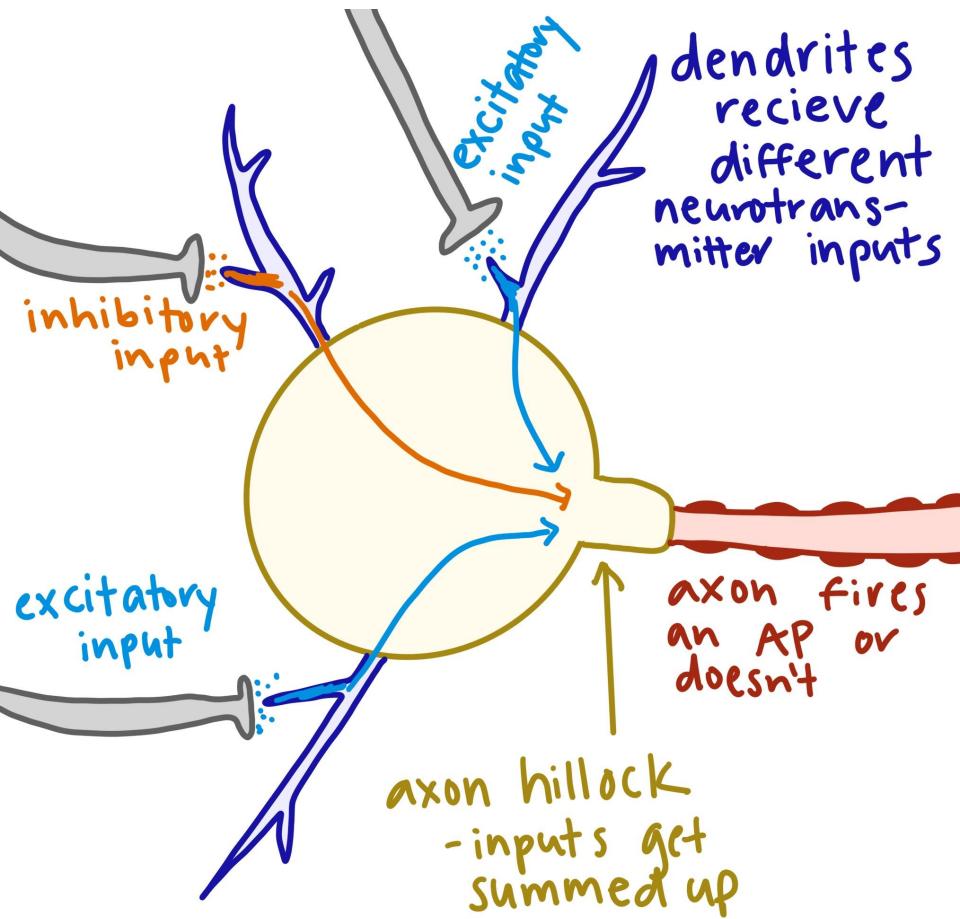
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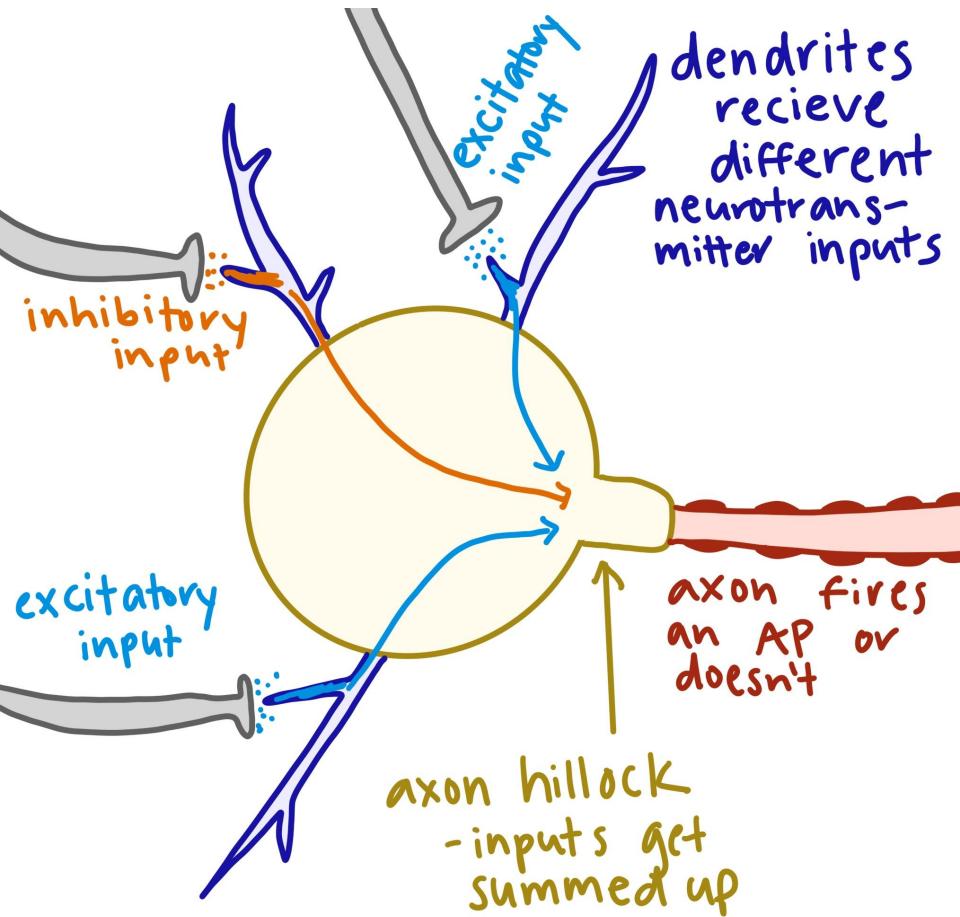
- I said that weighing advice when deciding to take a class is like a neuron weighing input when deciding whether to fire
- How do neurons weigh their inputs?
 - Via **spatial** and/or **temporal summation**

How do neurons “add up” their inputs?



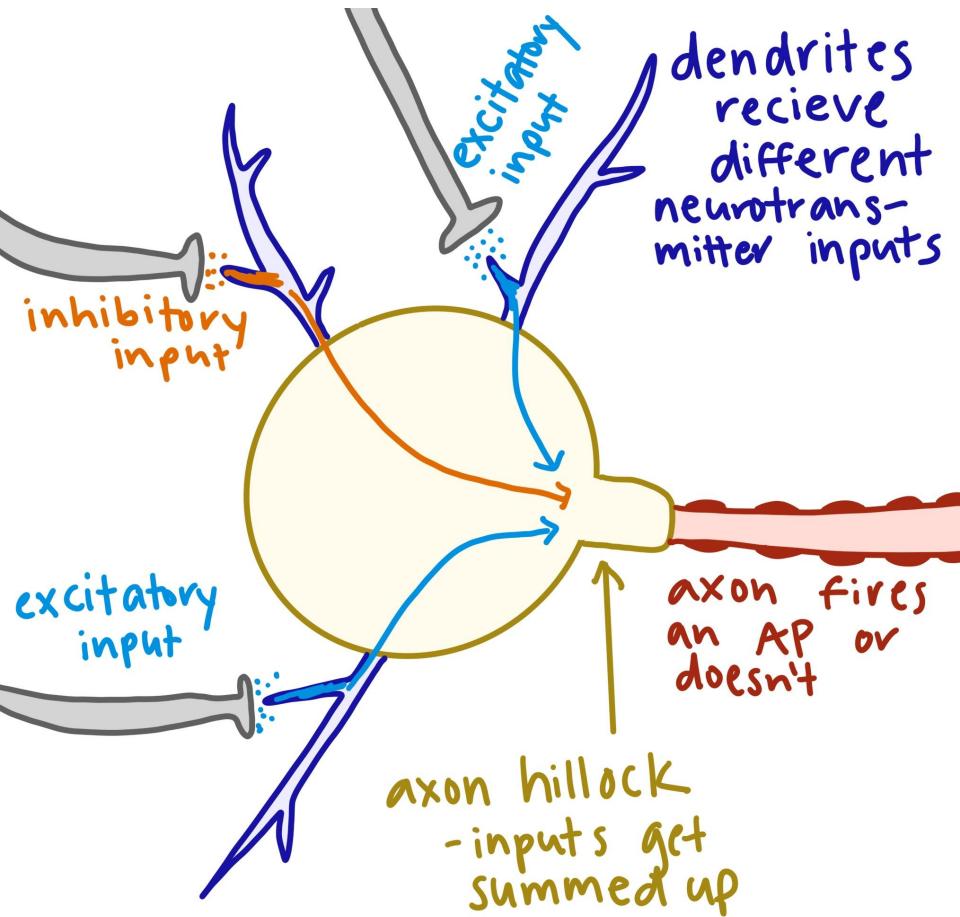
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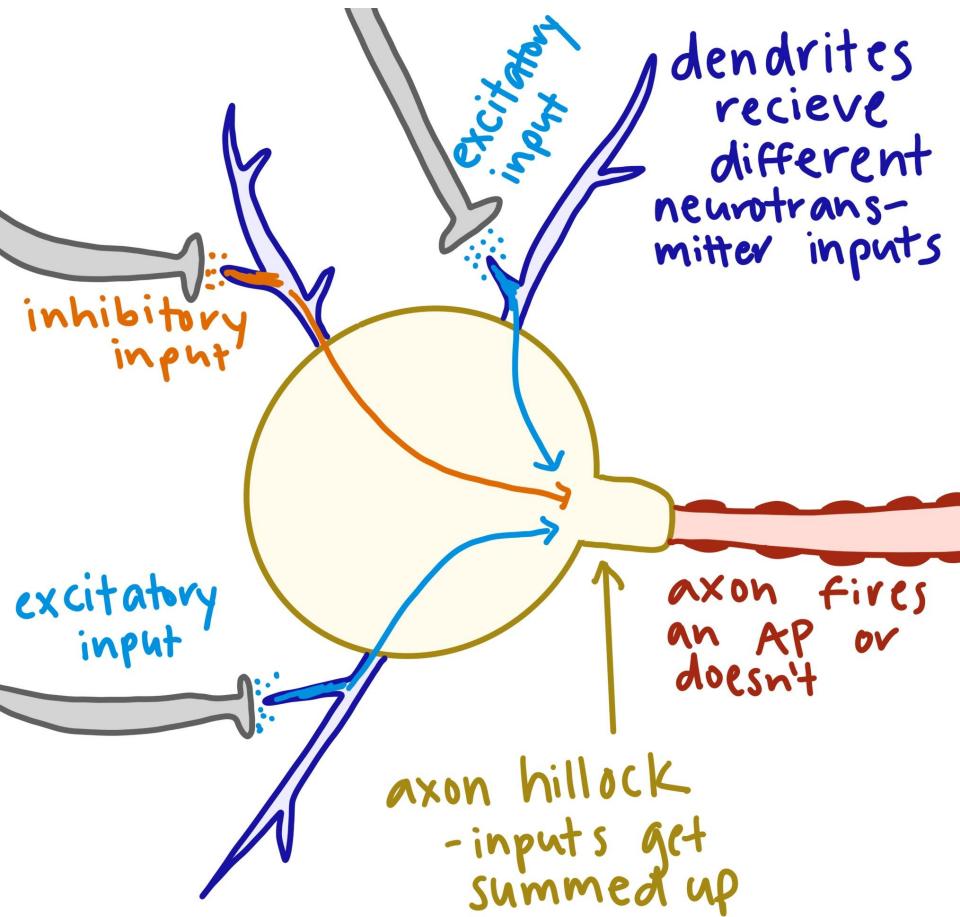
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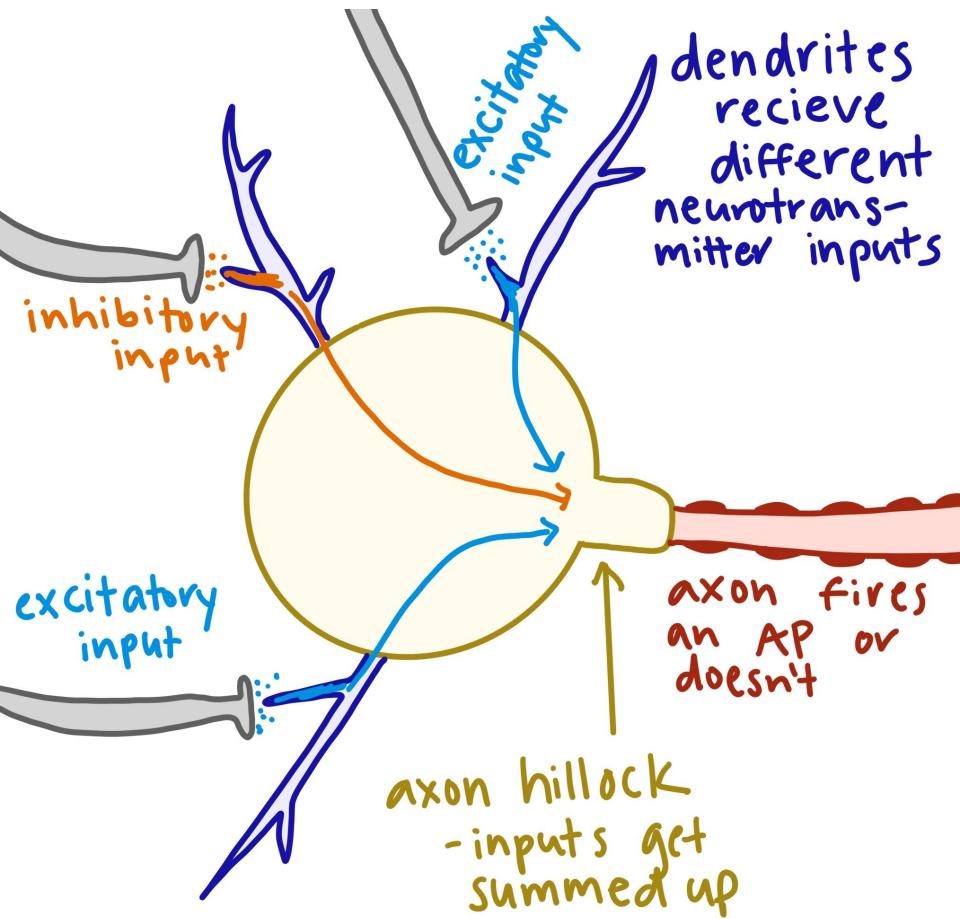
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- The result of that addition determines if an **action potential** is produced or not

How do neurons “add up” their inputs?

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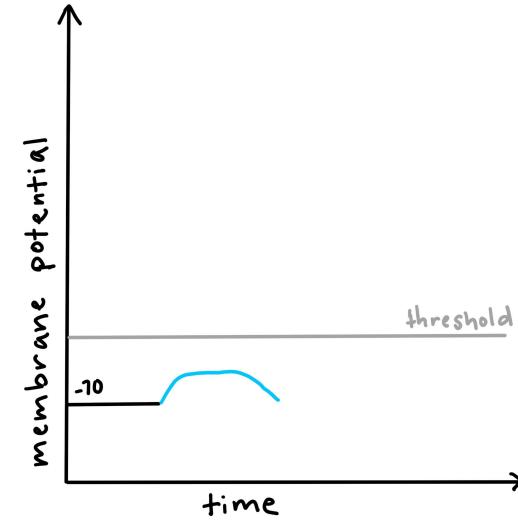
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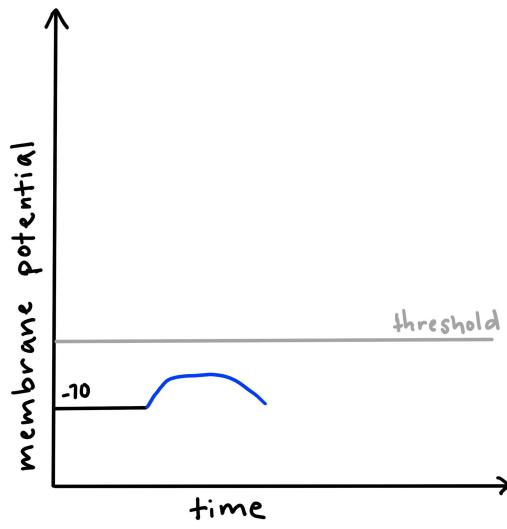
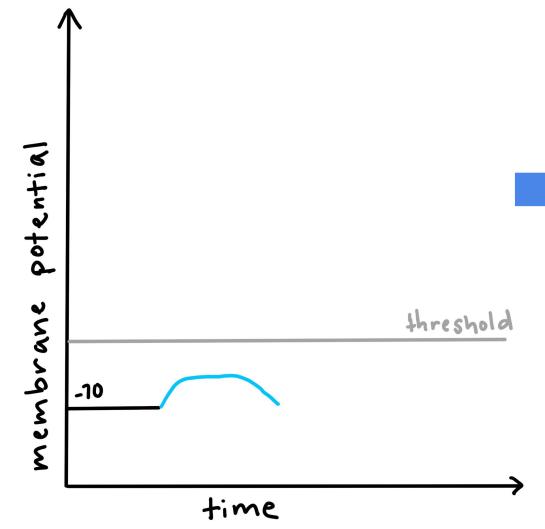
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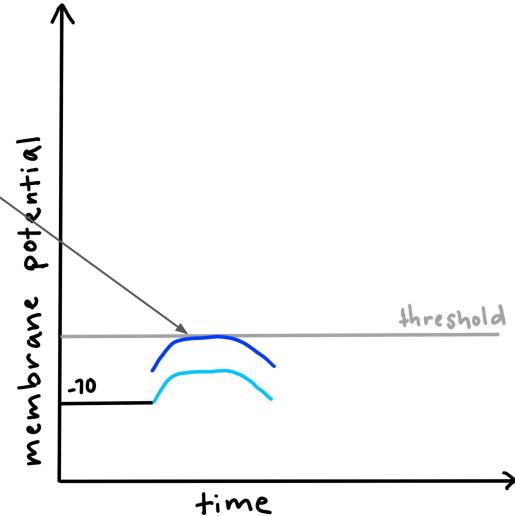
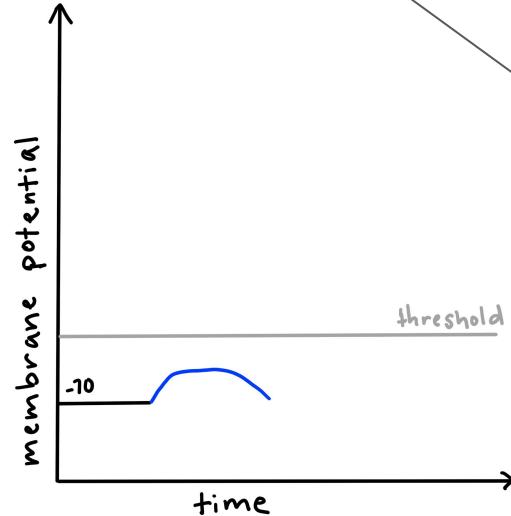
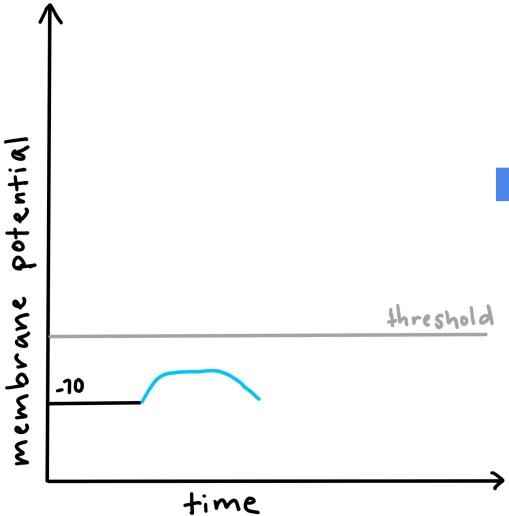
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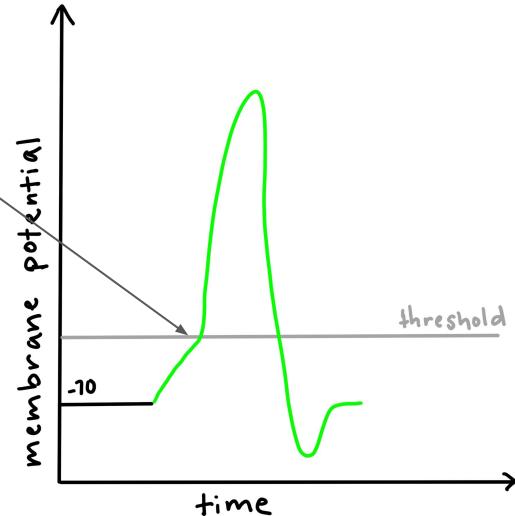
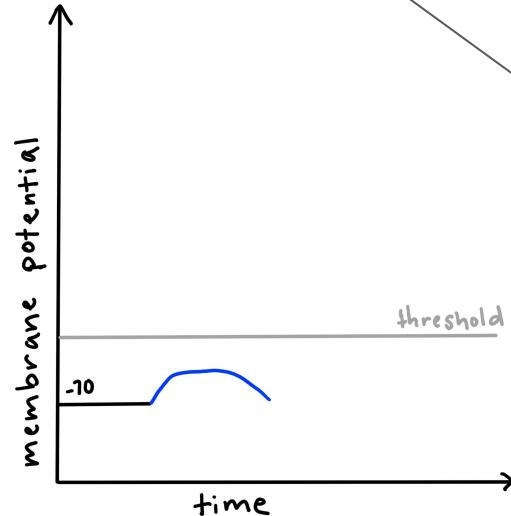
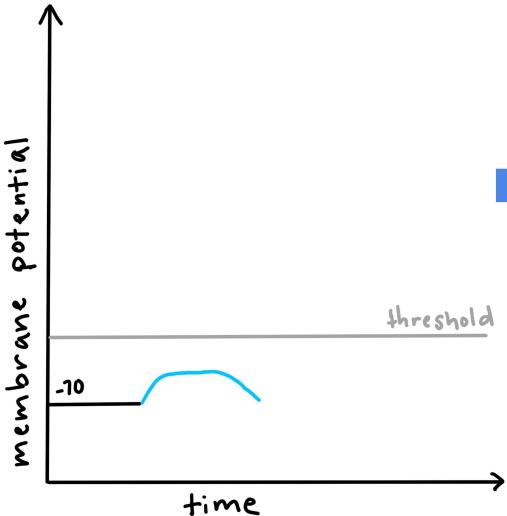
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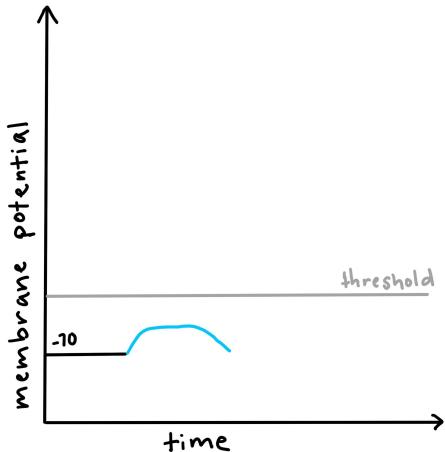
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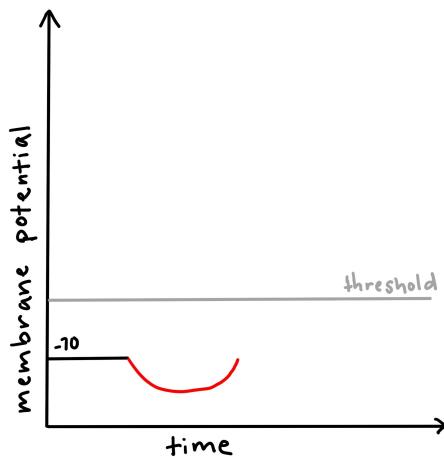
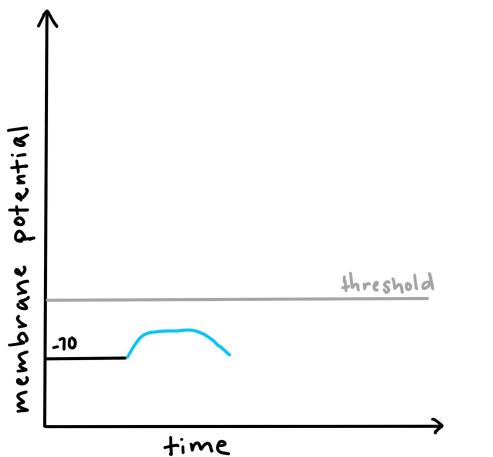
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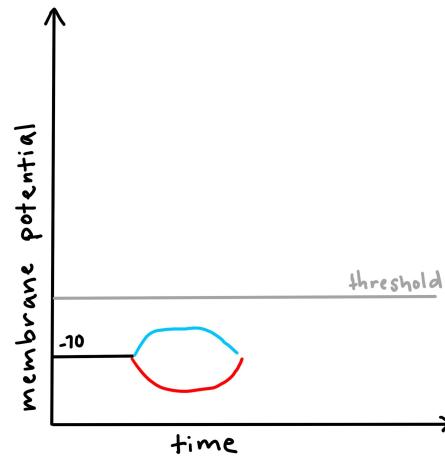
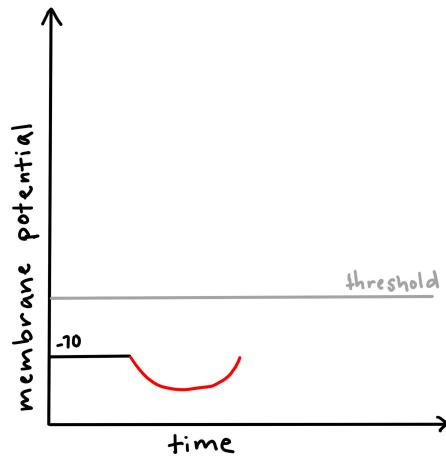
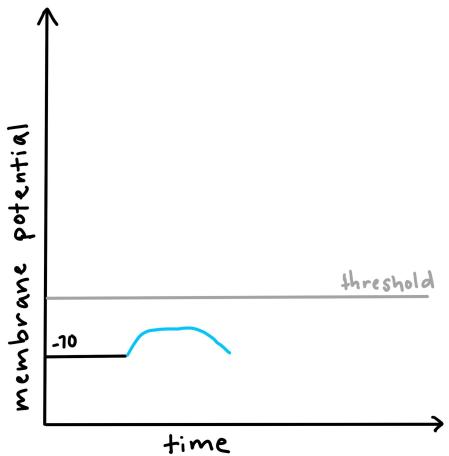
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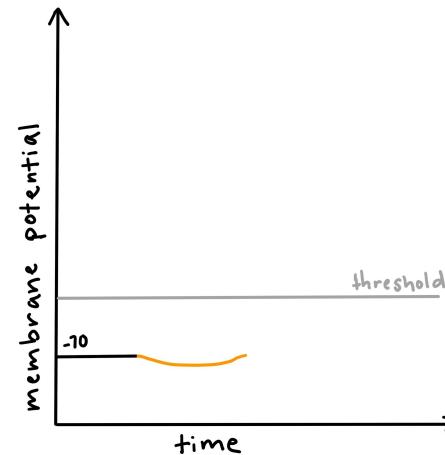
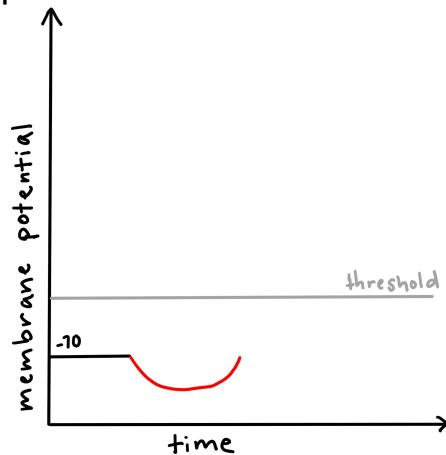
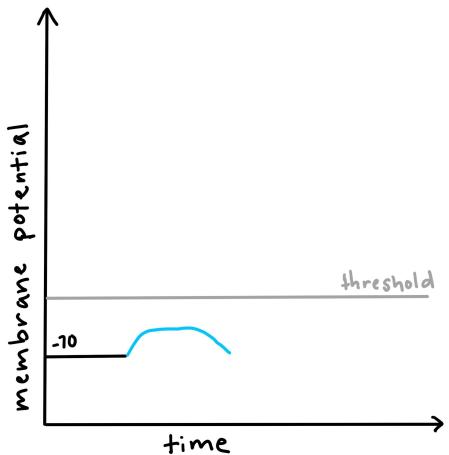
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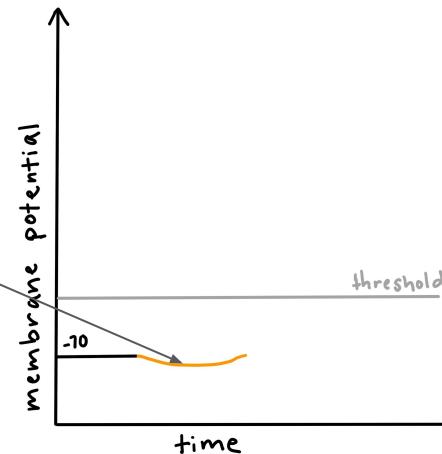
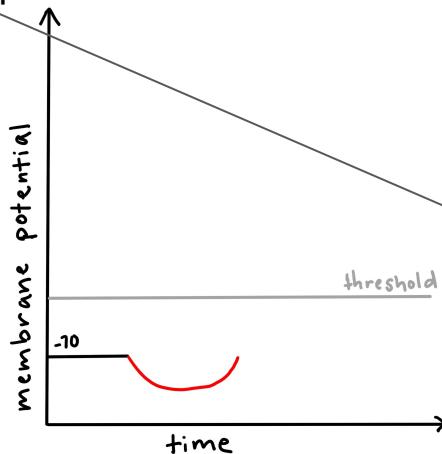
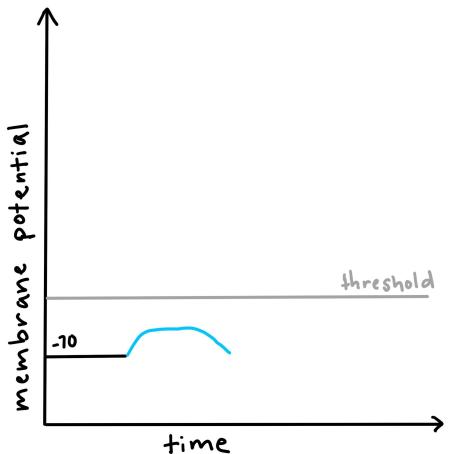
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- You should understand all these concepts, and connect them back to the idea that chemical synapses allow more **flexible** control of neural signalling

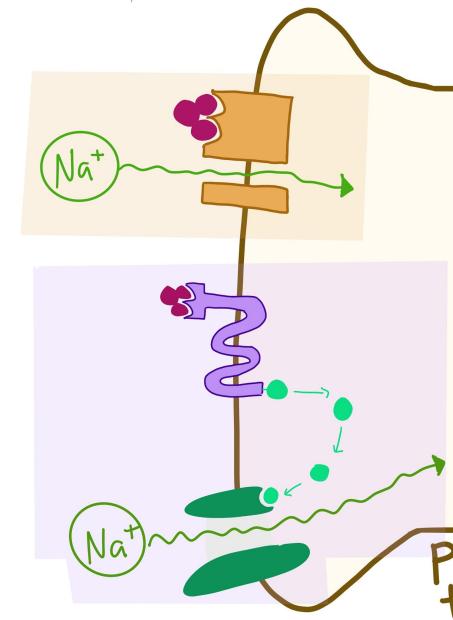
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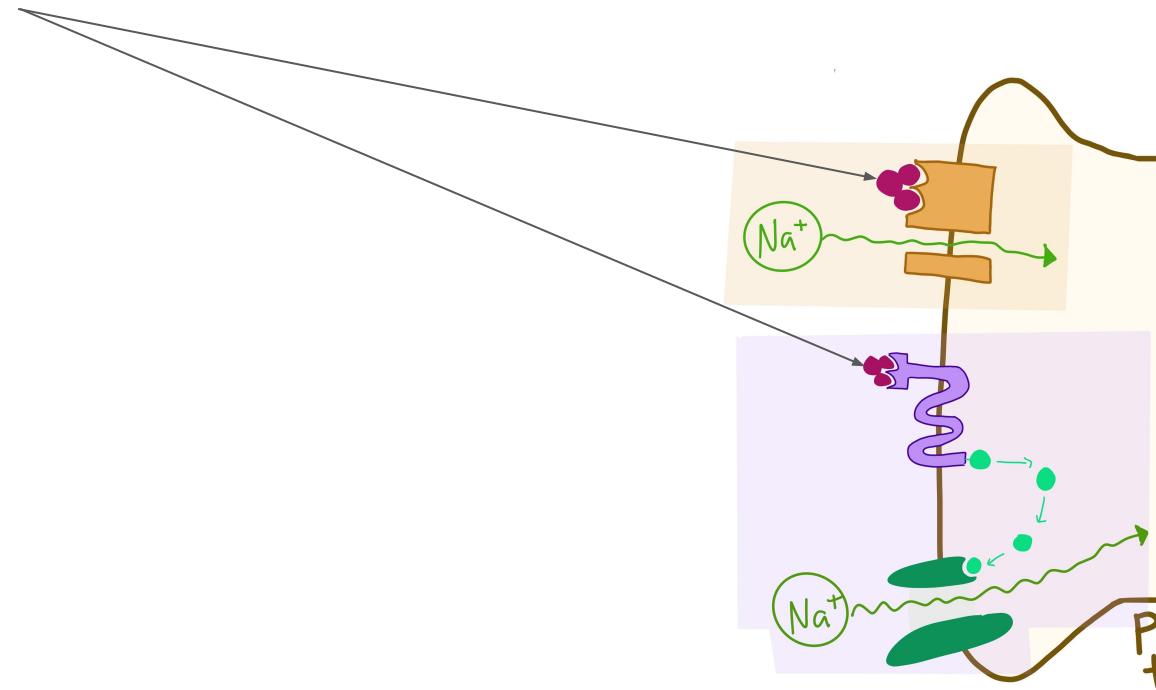
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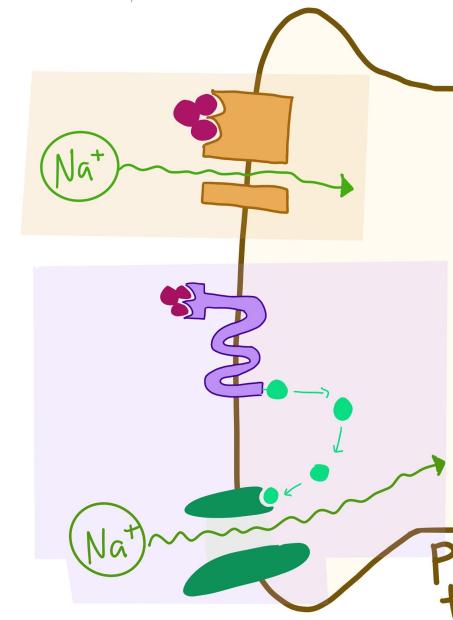
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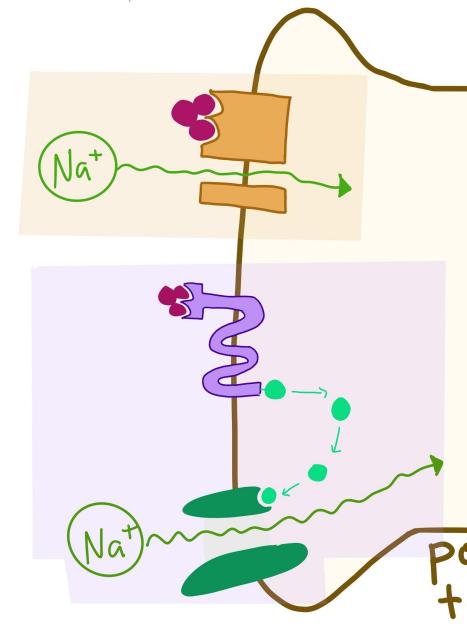
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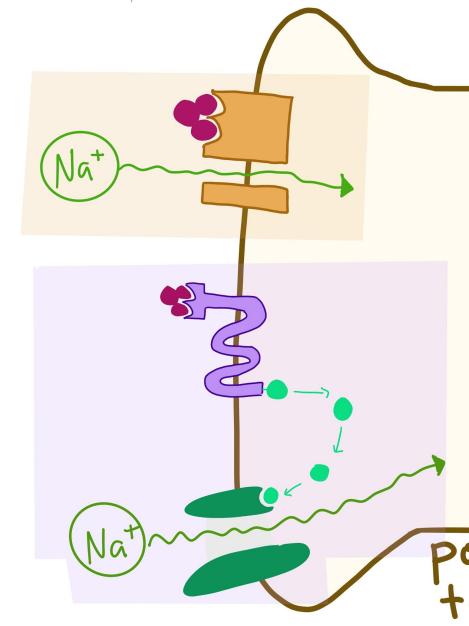
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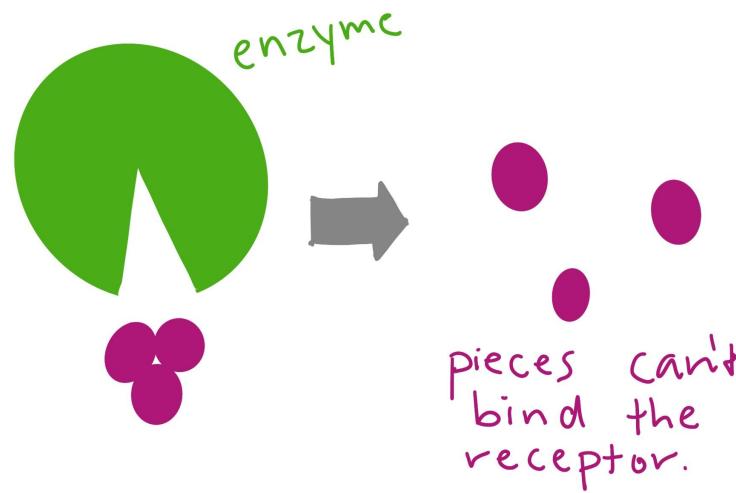
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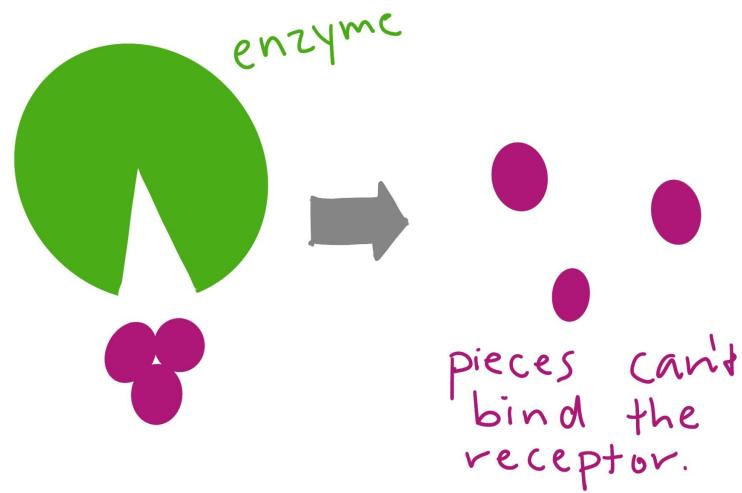
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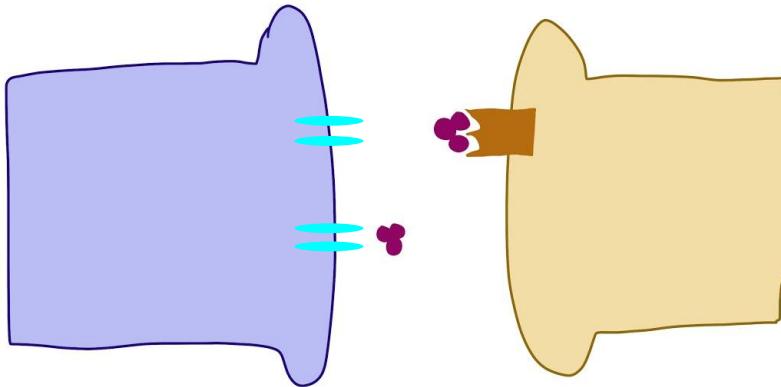
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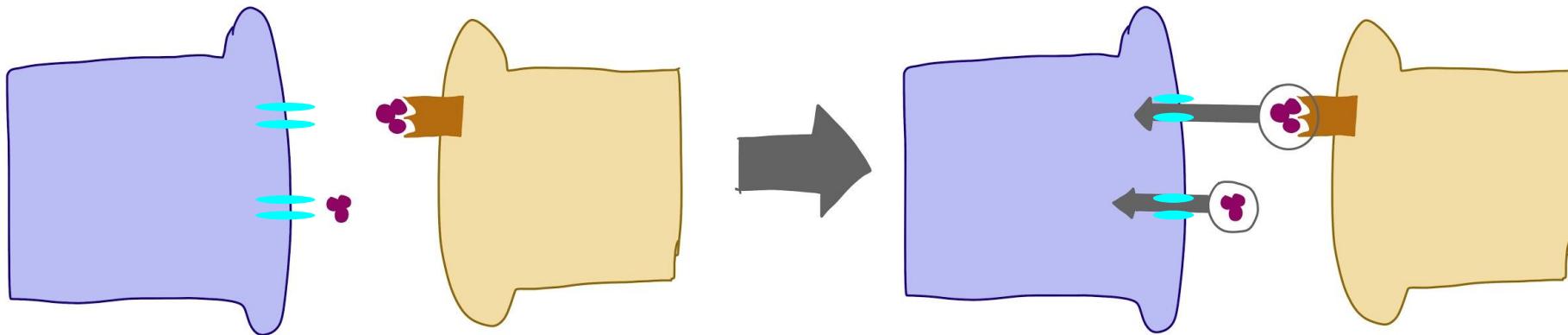
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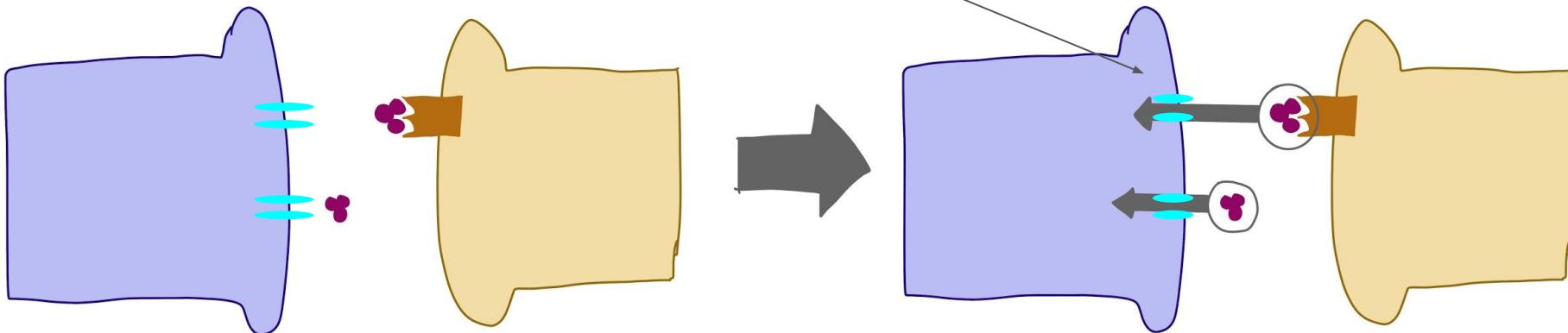
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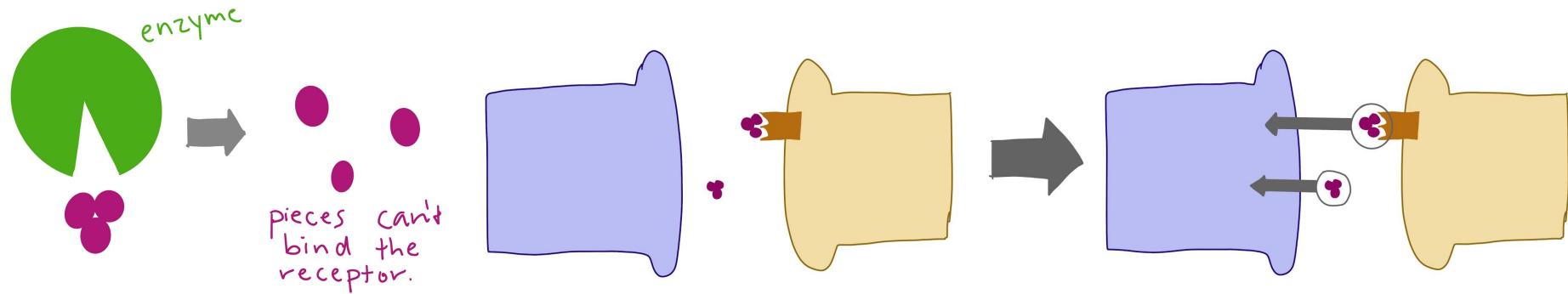
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We will see examples of both these strategies as we discuss individual neurotransmitters in more detail.



Different neurotransmitters

Different neurotransmitters

- What are some different neurotransmitters?
- What happens when they bind different receptors?
- How can different drugs interfere with normal neurotransmission?

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- Acetylcholine
- Norepinephrine
- GABA
- Glycine
- Glutamate
- Dopamine
- Serotonin
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You'll want to make a review flashcard for each of these neurotransmitters

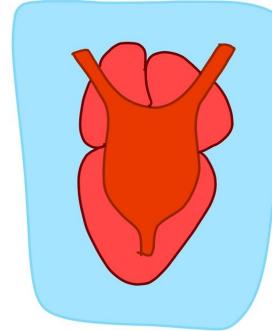
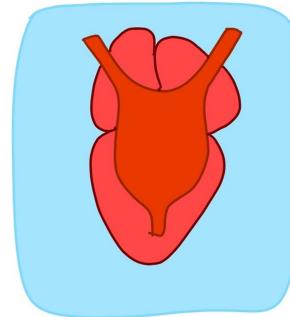
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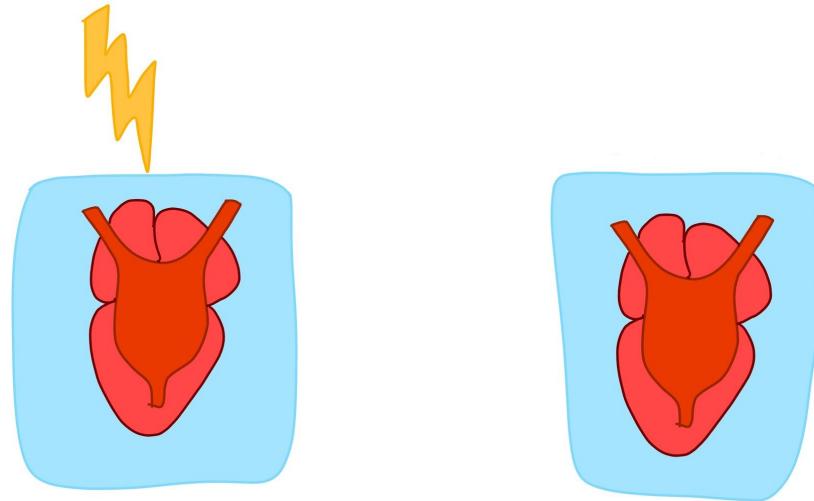
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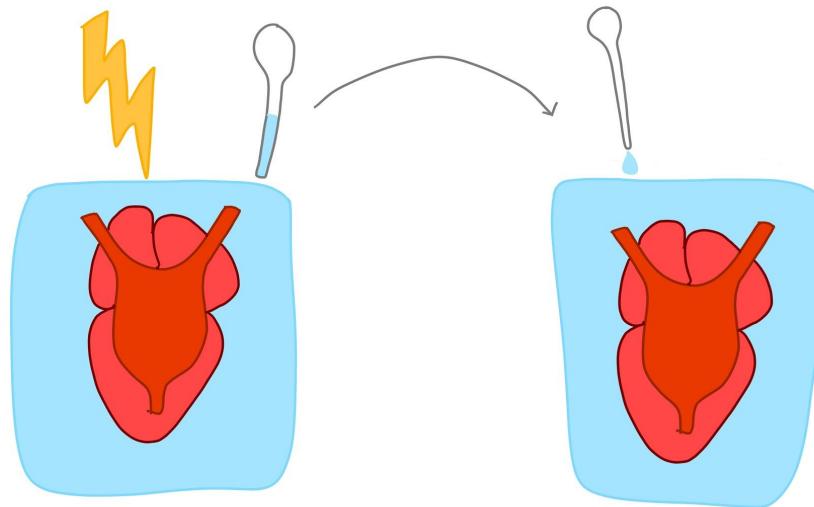
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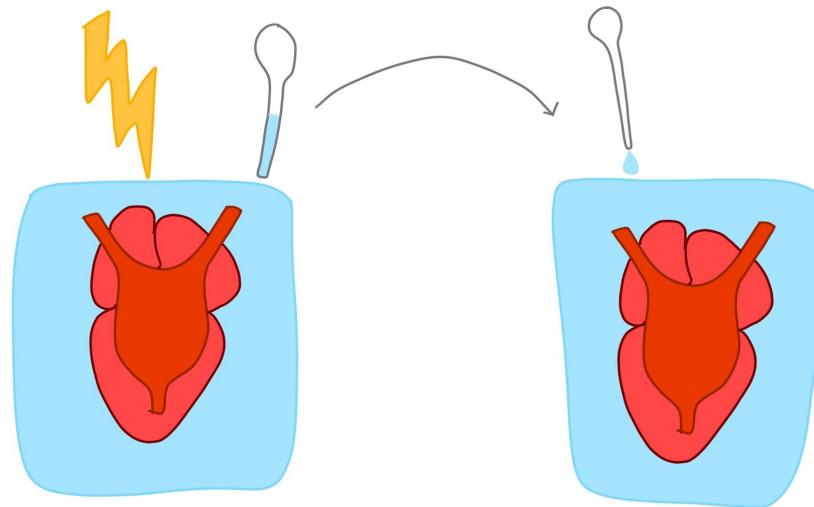
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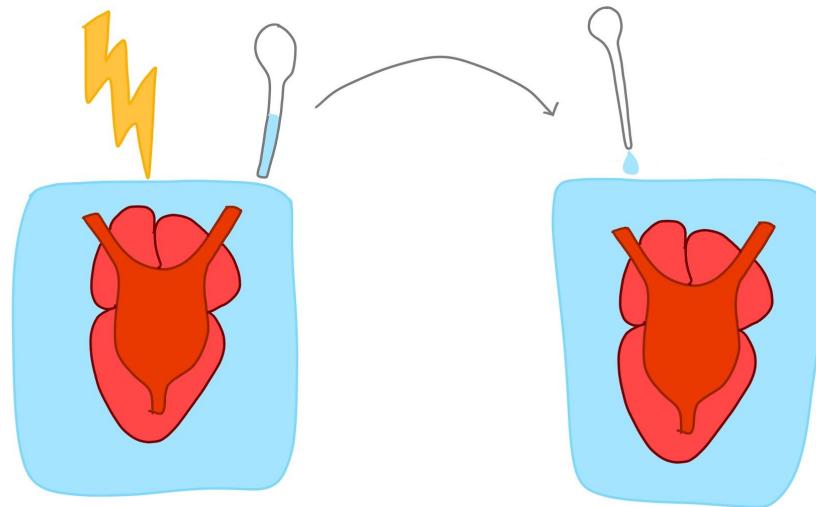
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 - And some chemical in the saline slowed the other heart: that chemical was **acetylcholine**.

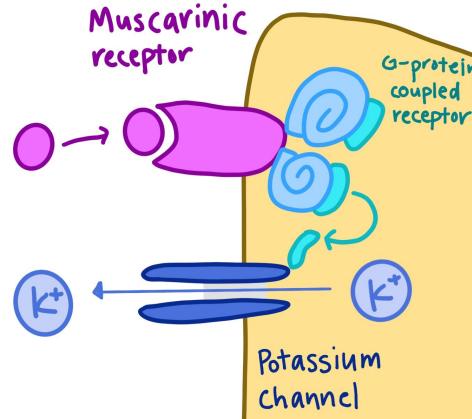


Acetylcholine

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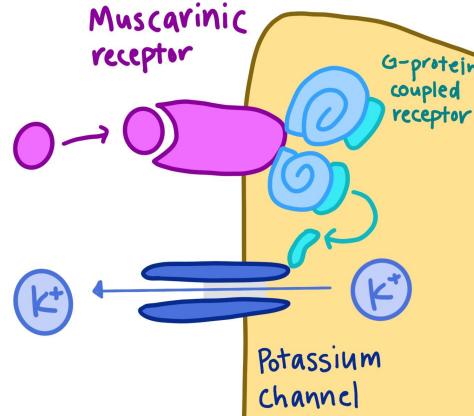
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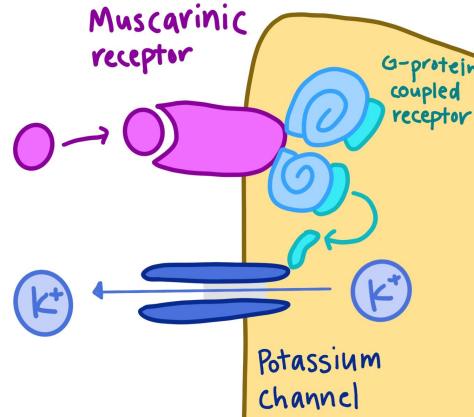
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You should be able to tell why it's inhibitory- because it lets potassium OUT of the neuron



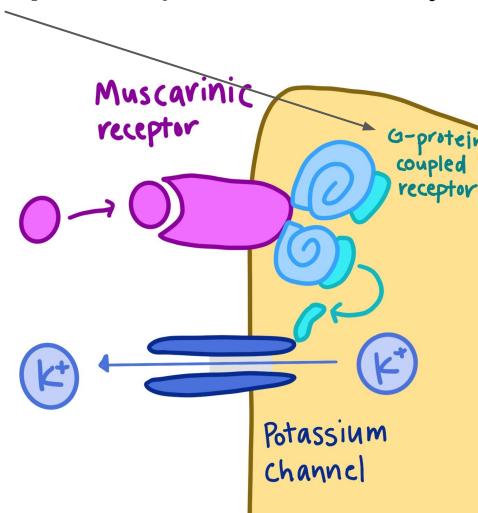
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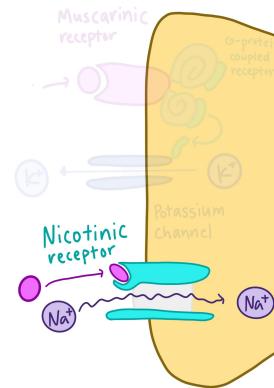


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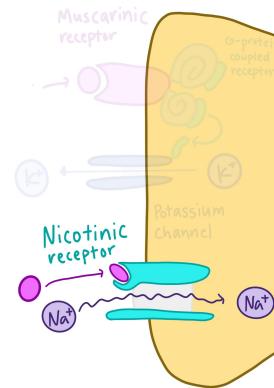
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- **Nicotinic acetylcholine receptor:** has an excitatory effect, increasing the likelihood of an action potential



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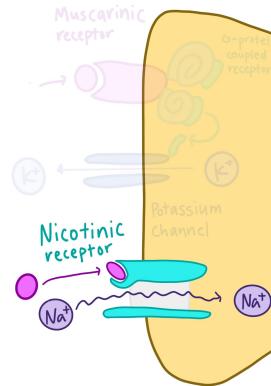
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You should be able to tell why it's excitatory because it lets sodium INTO the neuron



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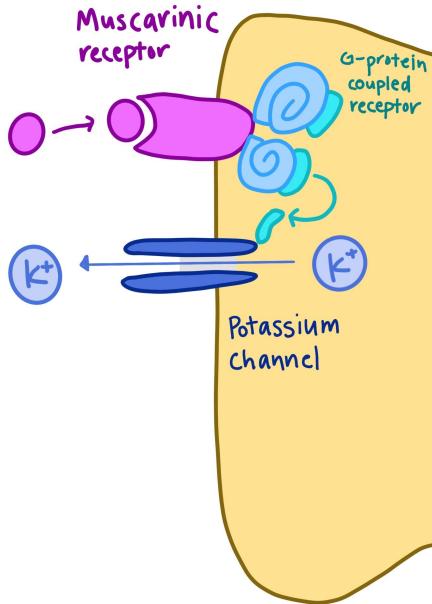
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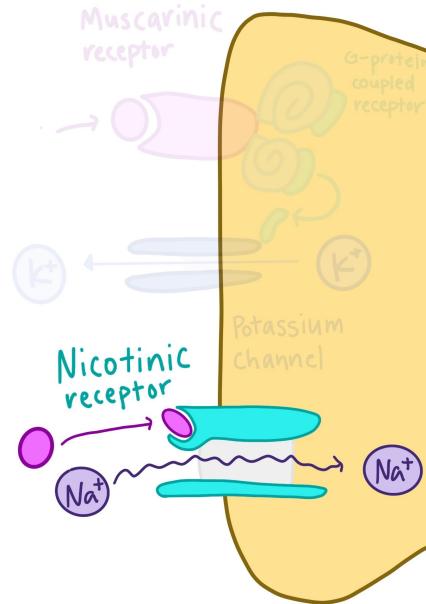
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 - **Malathion** is a pesticide that interferes with acetylcholinesterases
 - It makes it so that the insect can't move or breathe properly

Acetylcholine

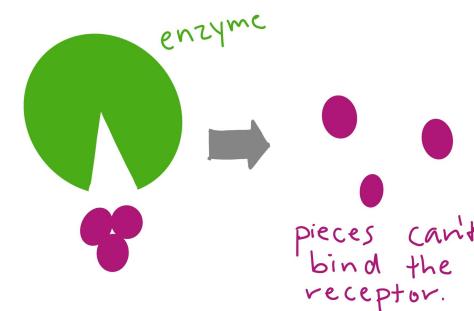
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- **Acetylcholinesterase:** breaks down acetylcholine, prevents too much signalling



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Muscarine	Atropine	Nicotine	Curare
Agonist of muscarinic receptors.	Antagonist of muscarinic receptors.	Agonist of nicotinic receptors.	Antagonist of nicotinic receptors.
Makes the neuron even less likely to fire.	Prevents the normal inhibitory effect of acetylcholine.	Makes the neuron even more likely to fire.	Prevents acetylcholine from causing its normal action potentials.
Causes sweating, flushing, high heart rate	Causes lack of sweating, pupil dilation	Agitation, muscle twitching	Paralysis, inability to breathe

Acetylcholine: agonists and antagonists

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And know these effects for
acetylcholinesterase inhibitors like
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Muscarine	Atrone	Acetylcholinesterase	Malathion
Agonist Causes sweating, flushing, high heart rate	Antagonist Causes lack of sweating, pupil dilation	Prevents acetylcholine from causing its normal action potentials . Overexposure can cause muscle spasms, even death. It's very likely to fire.	Prevents acetylcholine from causing its normal action potentials .
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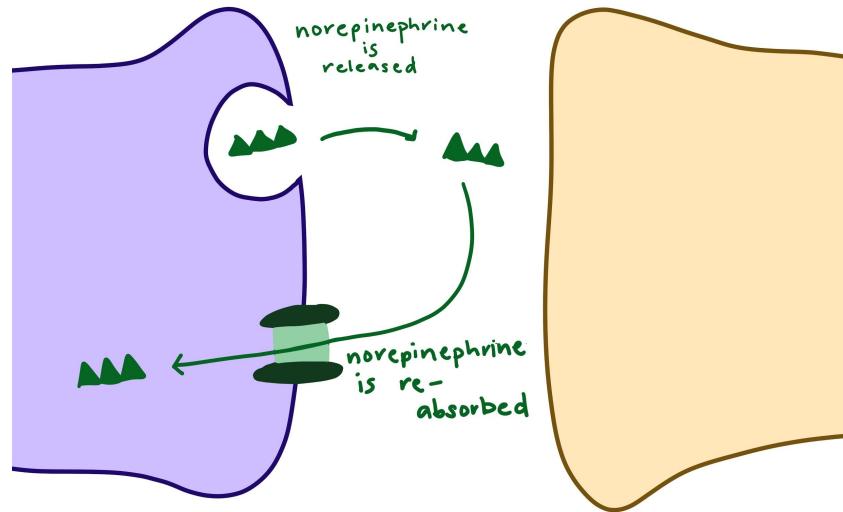
They have their effect by releasing second messenger molecules, which change gene expression and metabolism in the neuron. The effects depend on what the second messengers do.

Norepinephrine

- The body uses the second strategy to end norepinephrine signalling-**reuptake.**

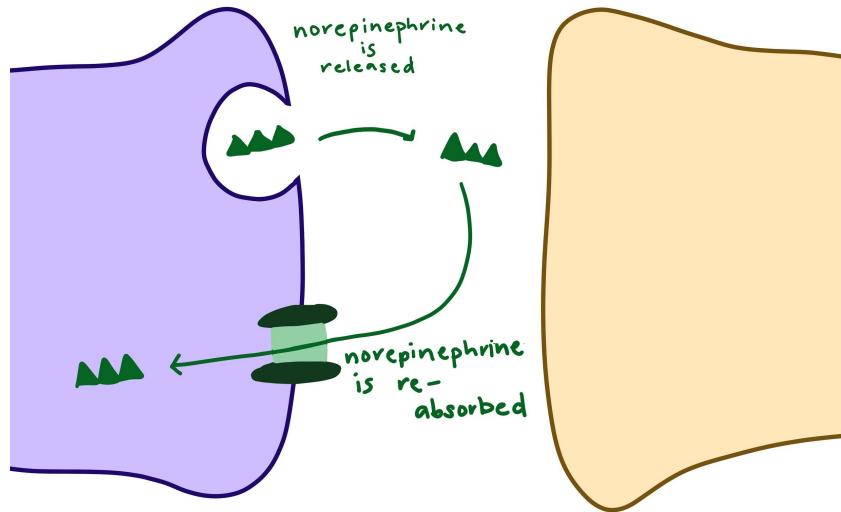
Norepinephrine

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- **Norepinephrine transporters** re-absorb the norepinephrine back into the presynaptic neuron.



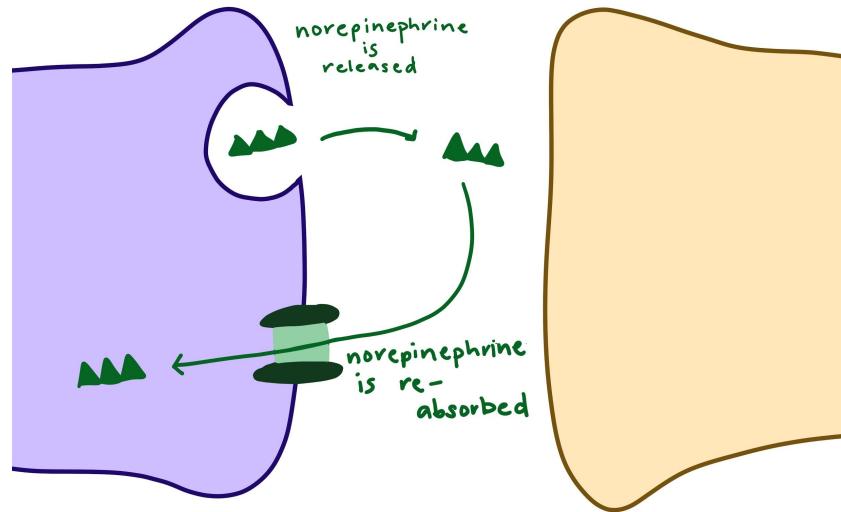
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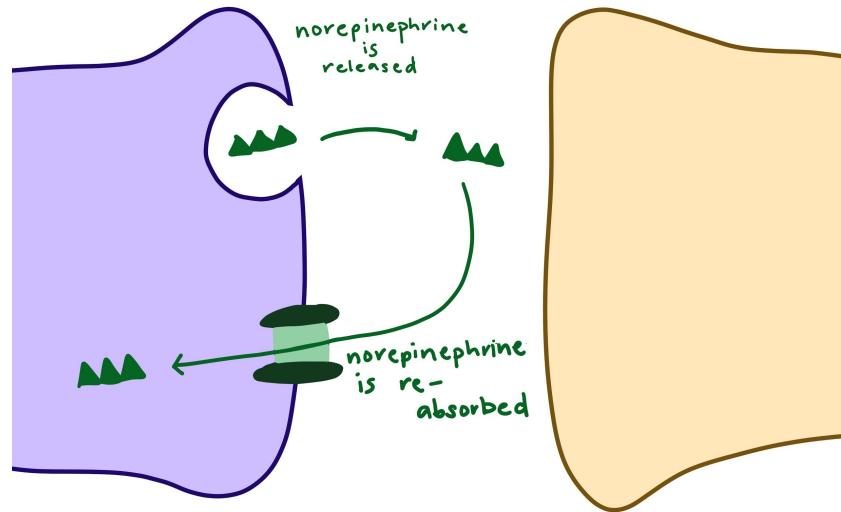
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- What would happen if **norepinephrine transporters** were blocked?
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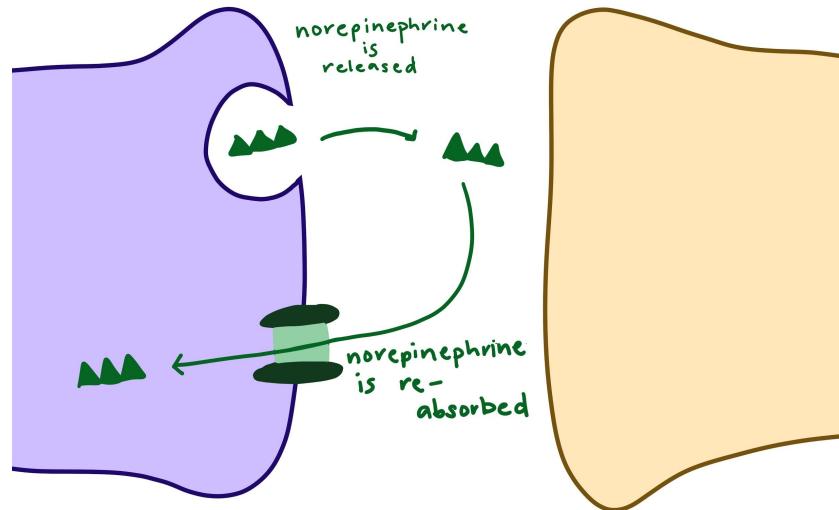
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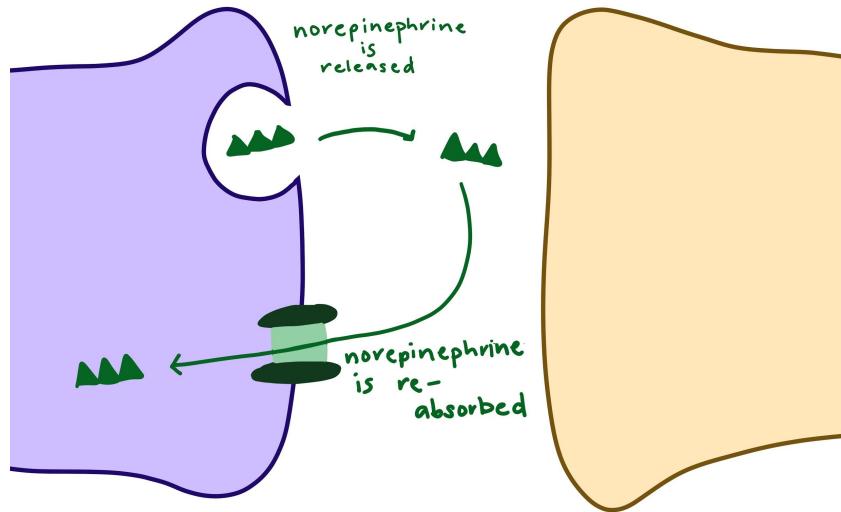
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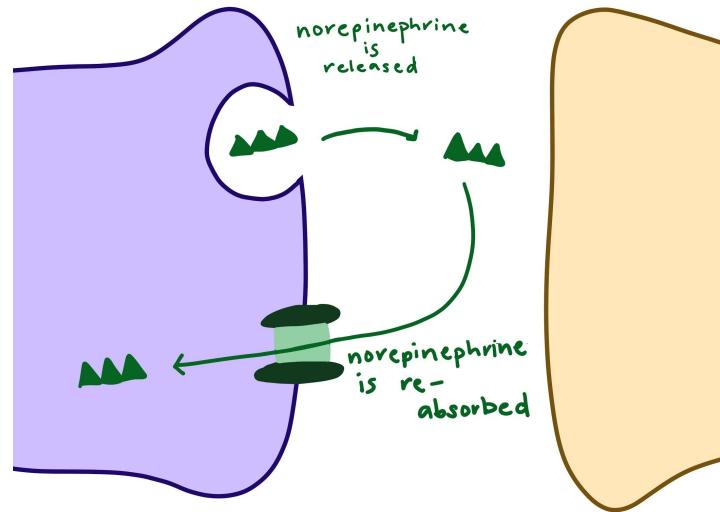
- Why would you care if norepinephrine transporters were blocked?
 - This is one kind of question you should be able to answer for the prelim, whether multiple choice or short answer.
 - So do some drugs like cocaine.



Norepinephrine

Example questions:

1. If you were designing a drug to increase alertness, that drug might have which of the following effects?
 - a. Agonist of Alpha 2 norepinephrine receptors
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 - c. Antagonist of norepinephrine transporters
 - d. b and c
2. A patient comes to you complaining of narcolepsy (uncontrollable sleep). Explain what kind of drug you might prescribe, specifying what neurotransmitter receptor, transporter or enzyme it would target, and how it would change neurotransmitter signalling and post-synaptic potentials.

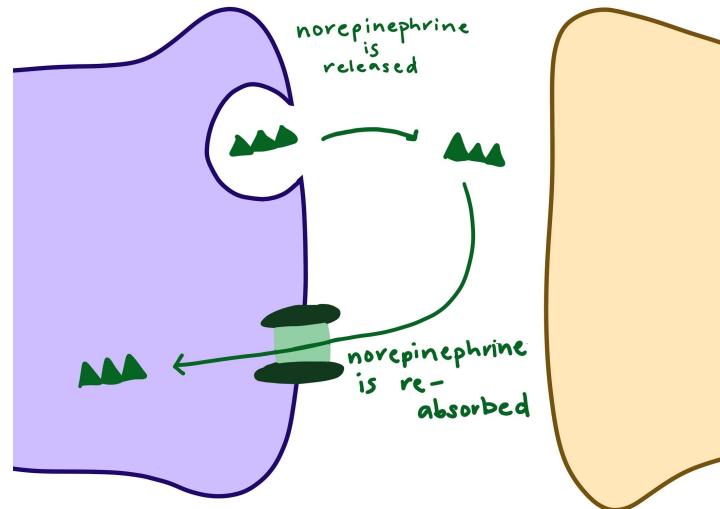


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Norepinephrine transporter inhibitor; increase norepinephrine in synaptic cleft; increase excitatory postsynaptic potentials and action potential firing



GABA- Gamma Aminobutyric Acid

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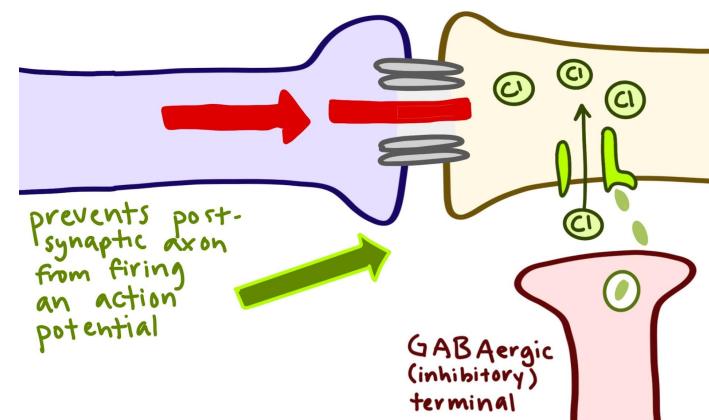
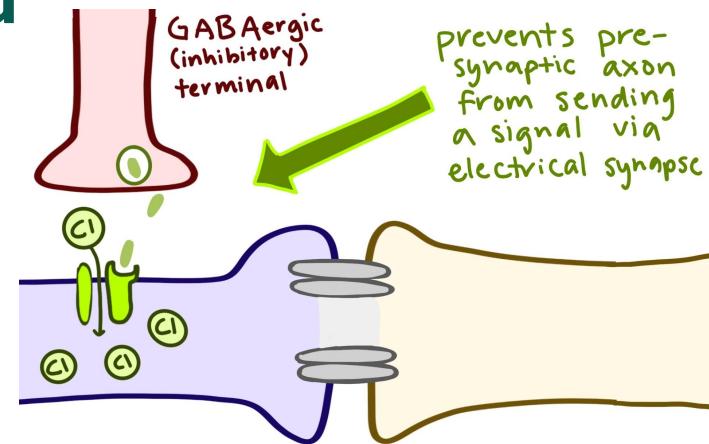
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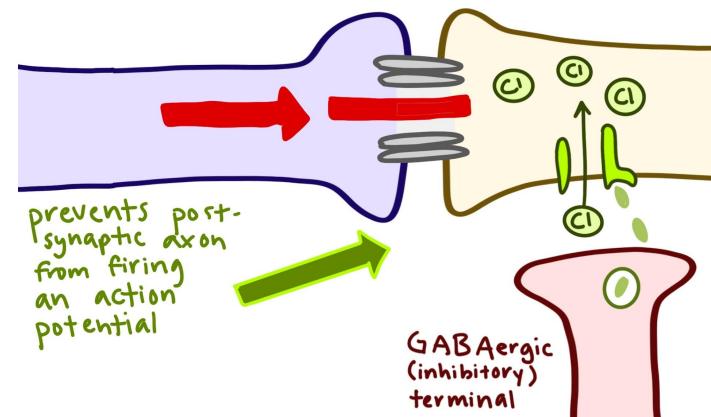
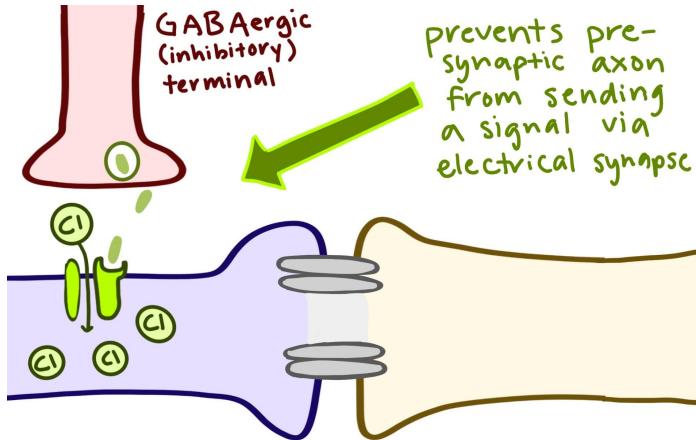


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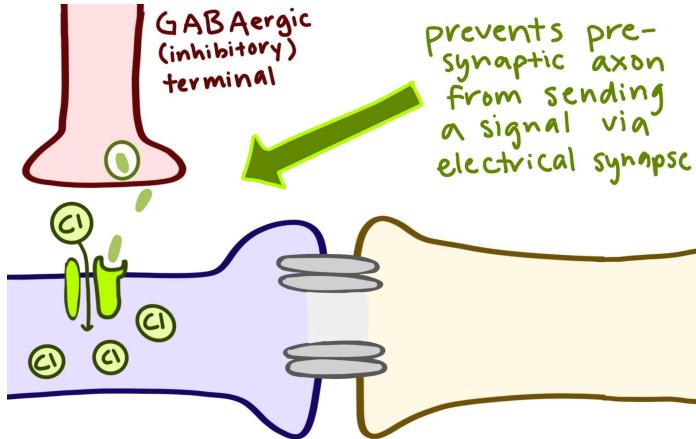
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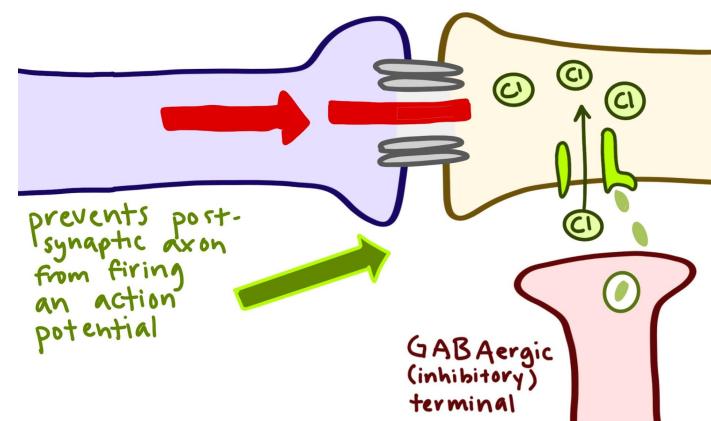
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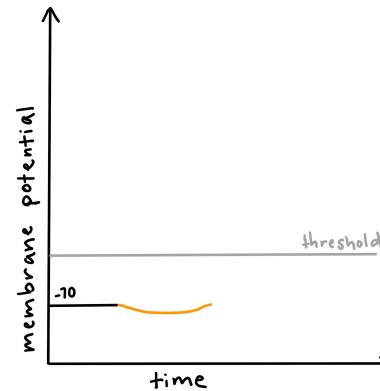
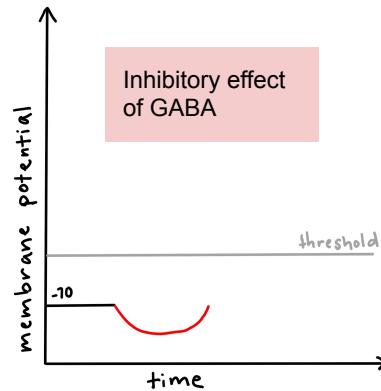
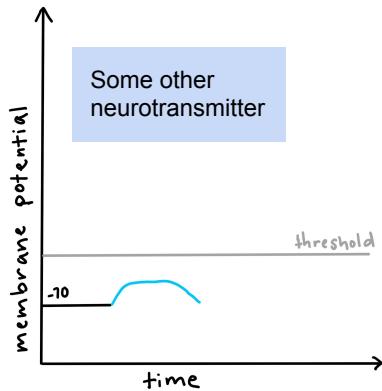


Can kill the action potential when it gets to the postsynaptic neuron so it doesn't propagate along.



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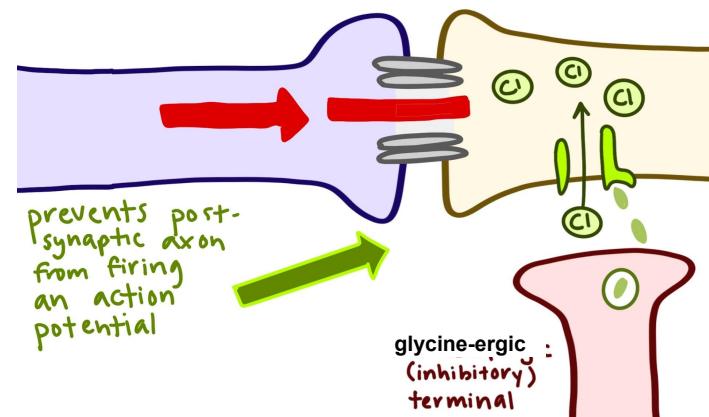
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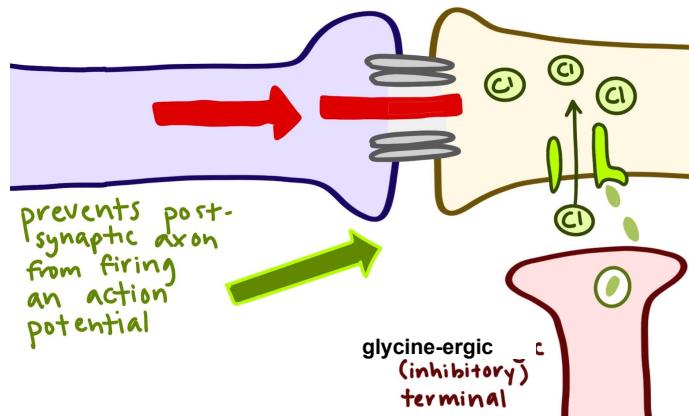


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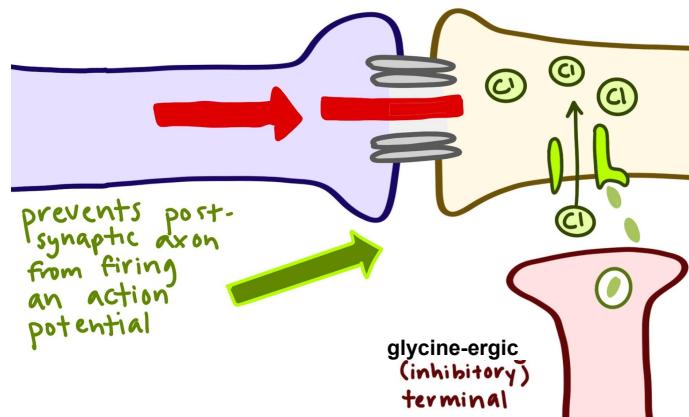
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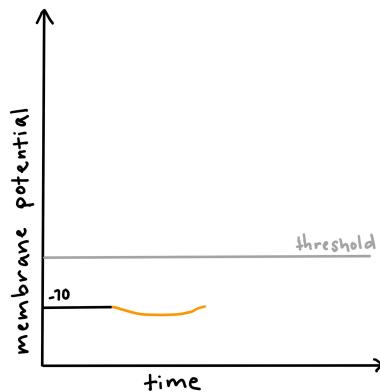
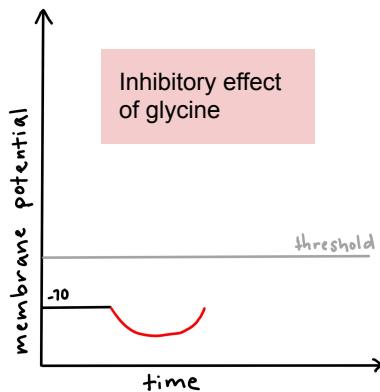
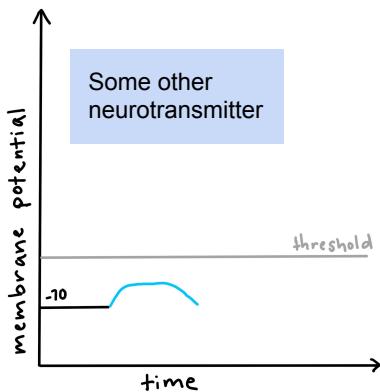
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 - **Caffeine** also has this effect, albeit much more mildly. That's why it makes you less relaxed.

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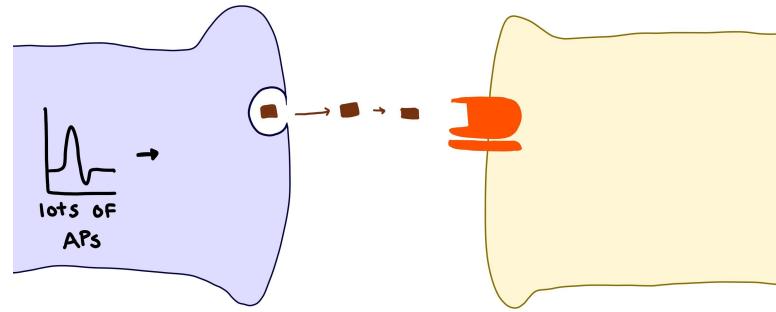
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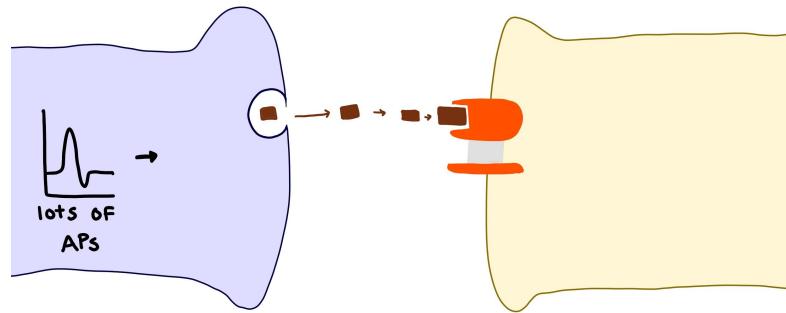
Glutamate: long term potentiation

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 - **Rapid, intense** stimulation of presynaptic neurons causes them to release glutamate into the synapse



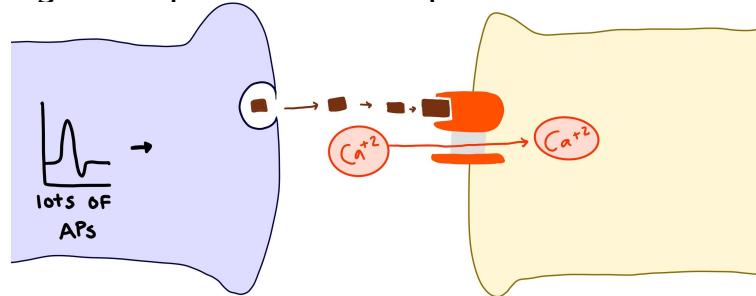
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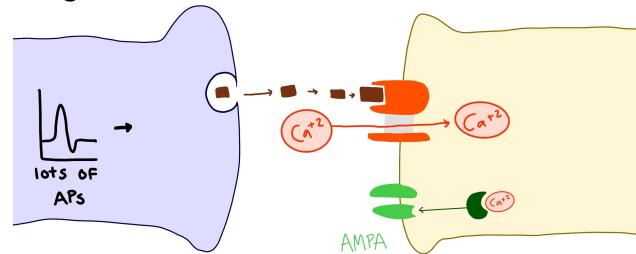
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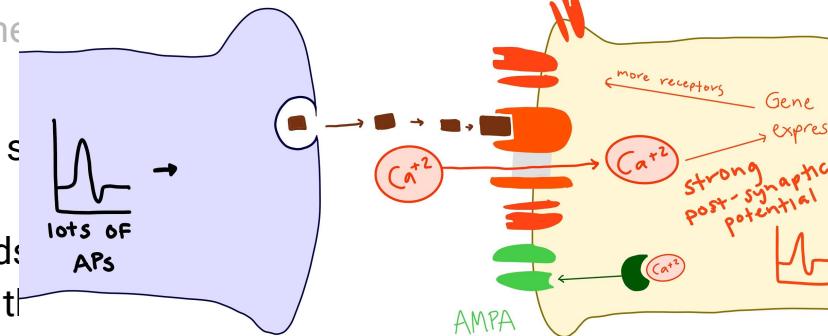
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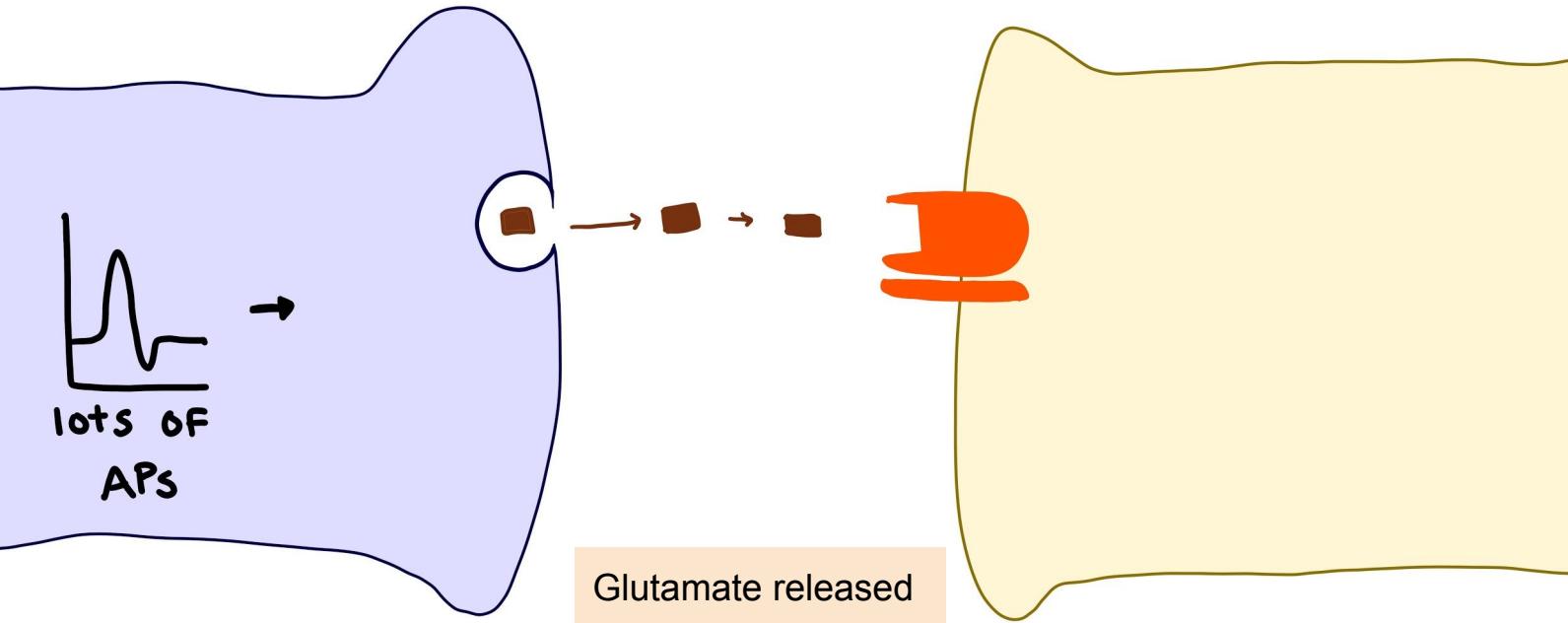
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 - Glutamate binds to receptors
 - Calcium flows through channels
 - Calcium binds a protein
 - Calcium binds a protein **more easily**
 - Gene expression changes so that **more NMDA receptors** are made and put into the membrane, making it fire a stronger signal when glutamate binds in the future



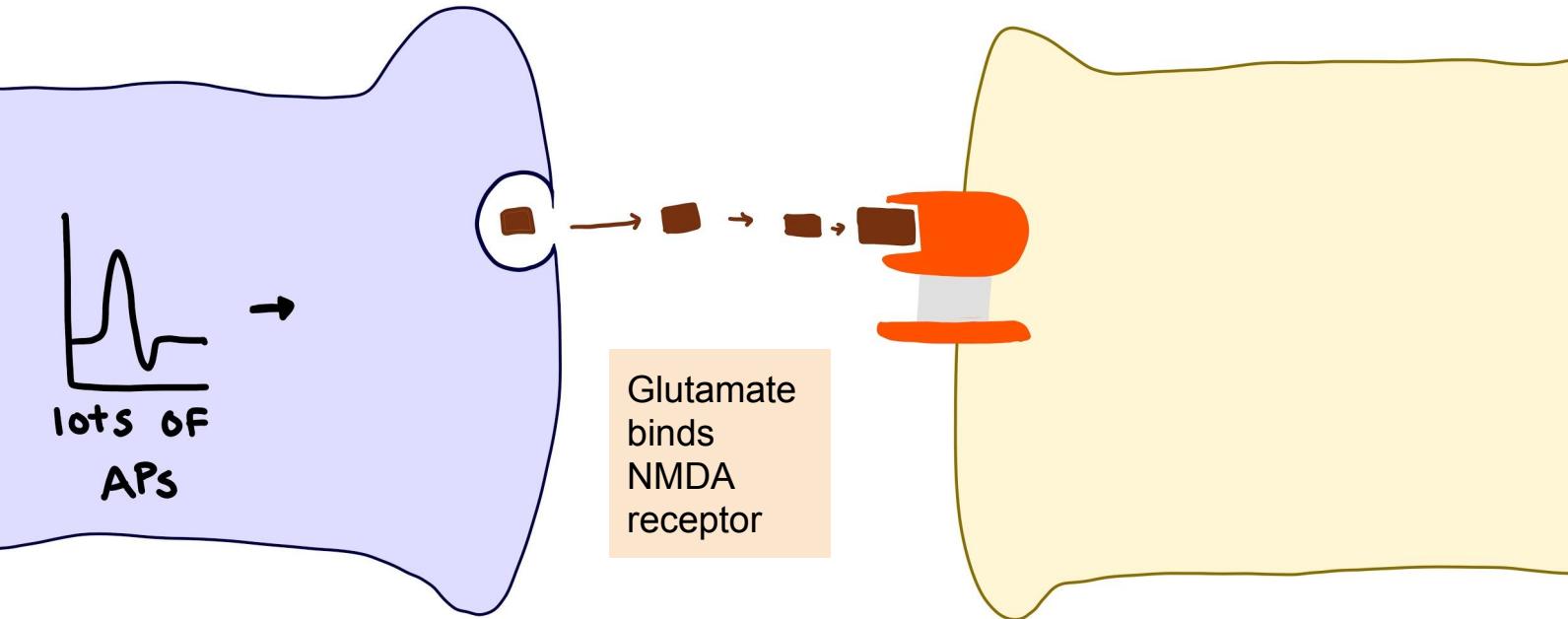
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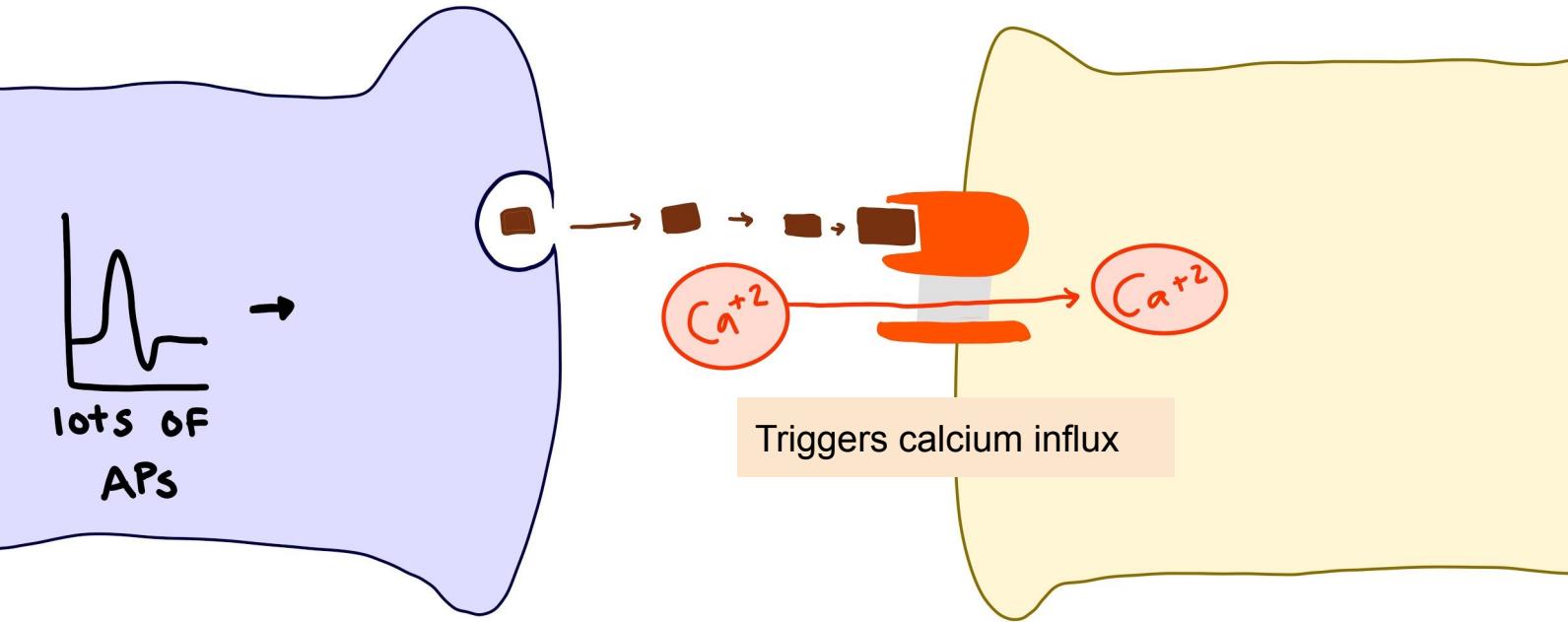
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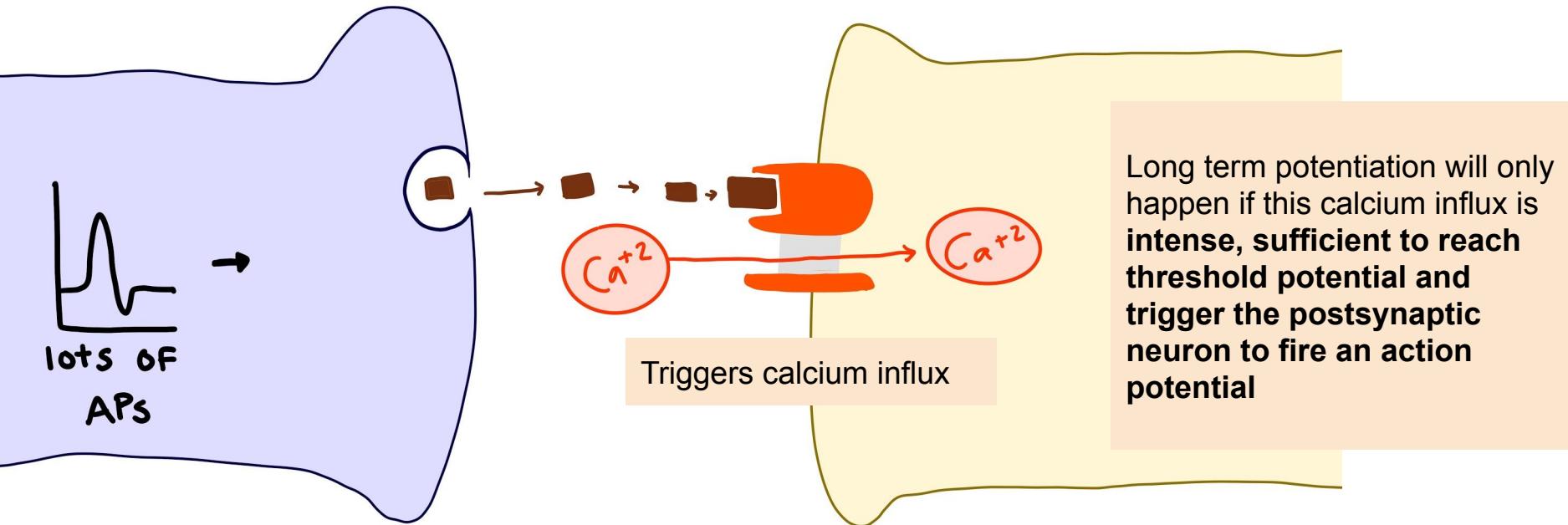
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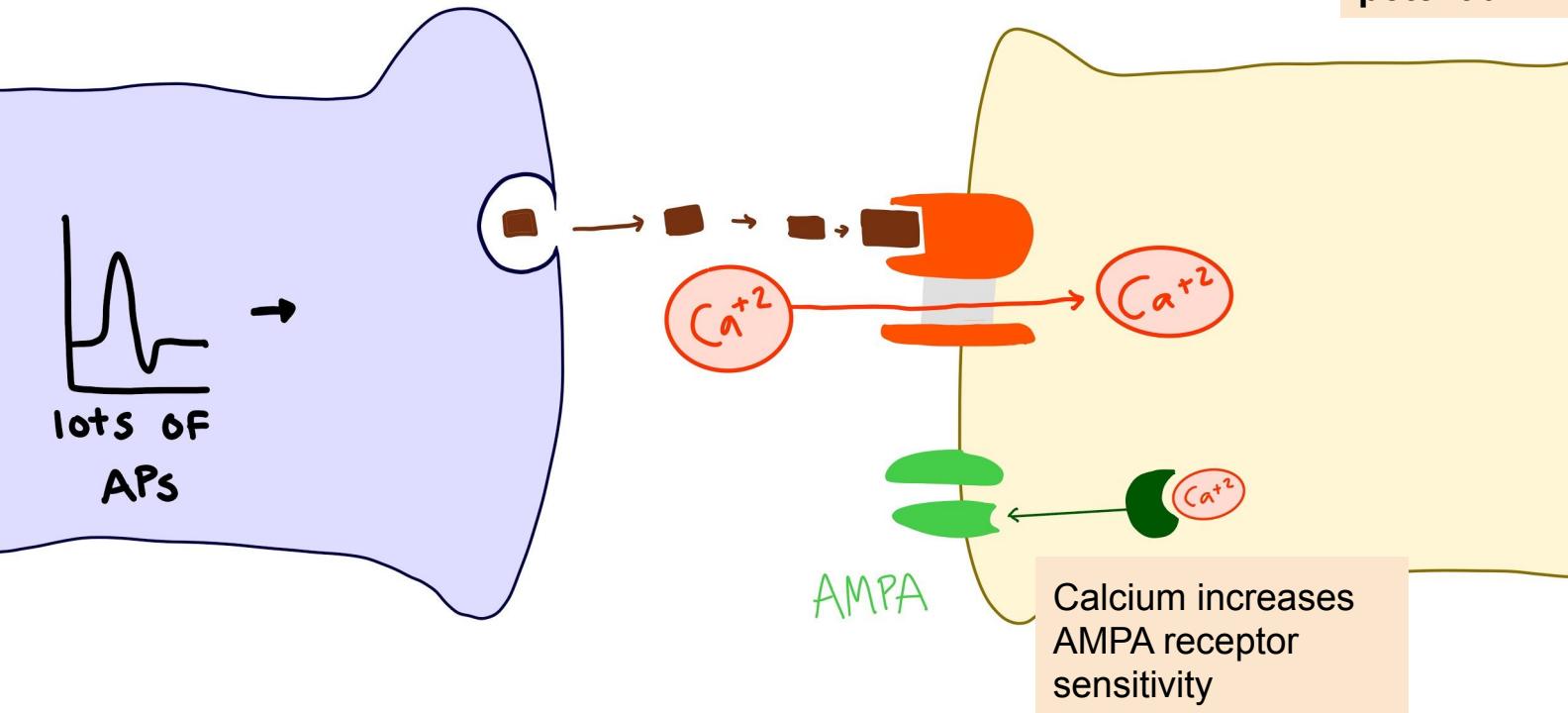


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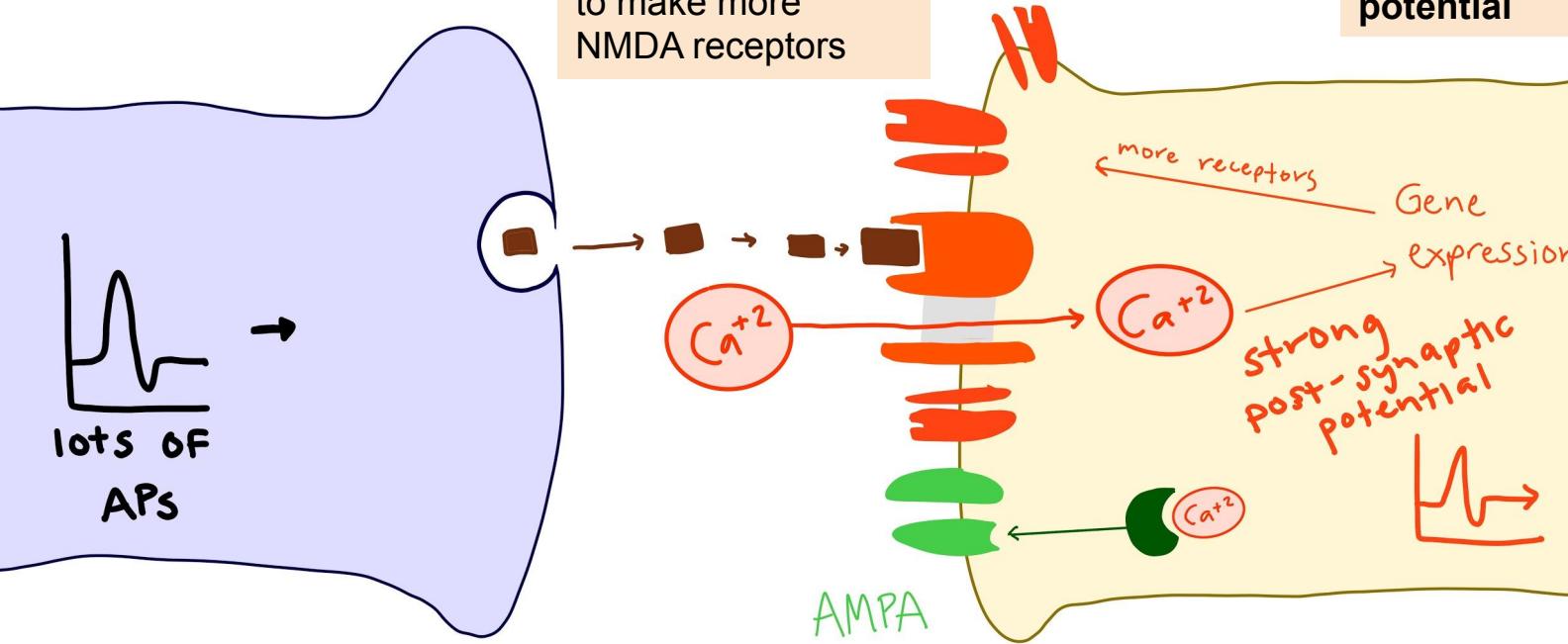
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Long term potentiation will only happen if calcium influx is intense, sufficient to reach threshold potential and trigger the postsynaptic neuron to fire an action potential



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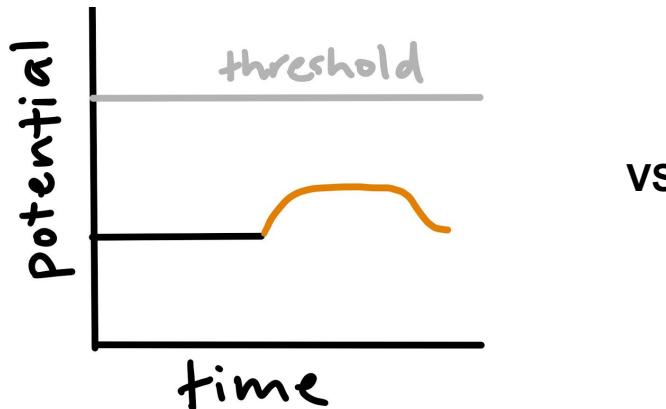
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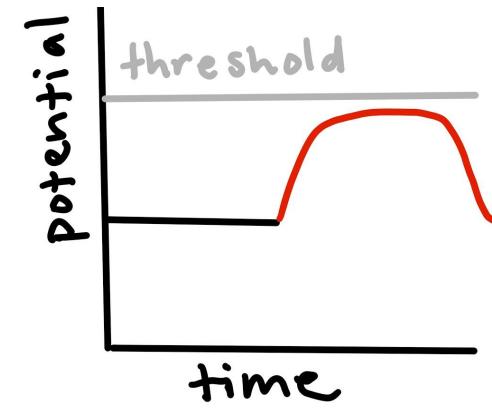
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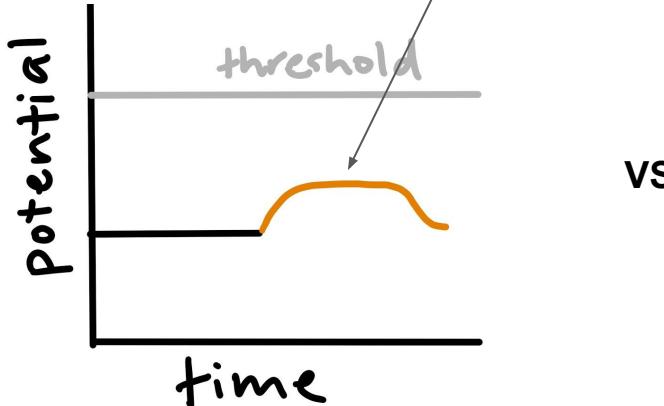


vs.

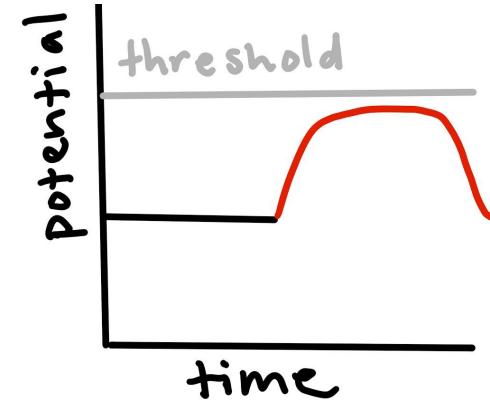


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 - That smaller postsynaptic depolarization causes the postsynaptic neuron to **remove AMPA receptors from the membrane**
 - That means that when the same neuron is stimulated in the future, **it won't fire as strongly**

Glutamate: take-aways

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- According to Dr. Selvaraj, you should know the three ionotropic glutamate receptors and that they are all excitatory
 - You should be able to interpret what would happen if, for example, an agonist or antagonist bound to a receptor.

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- According to Dr. Selvaraj, you should know the three ionotropic glutamate receptors and that they are all excitatory
 - You should be able to interpret what would happen if, for example, an agonist or antagonist bound to a receptor.
- You should have a solid understanding of the steps of **long-term potentiation** and **long-term depression**
 - If given an example of how a neuron is firing and associated changes in postsynaptic potential or postsynaptic receptors, you should be able to identify if the scenario is LTP or LTD

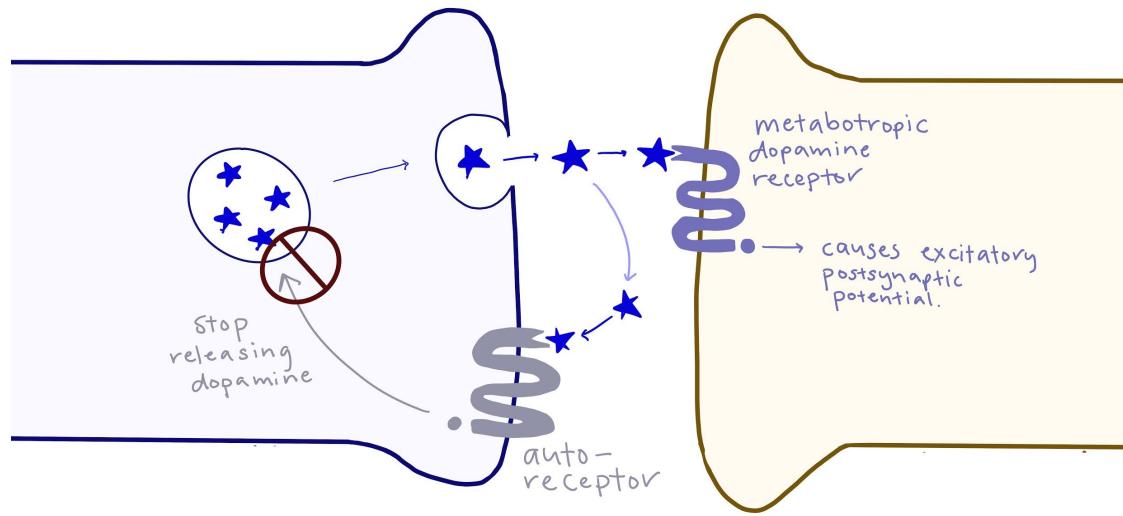
Dopamine

Dopamine

- Creates feelings of reward and anticipation of reward

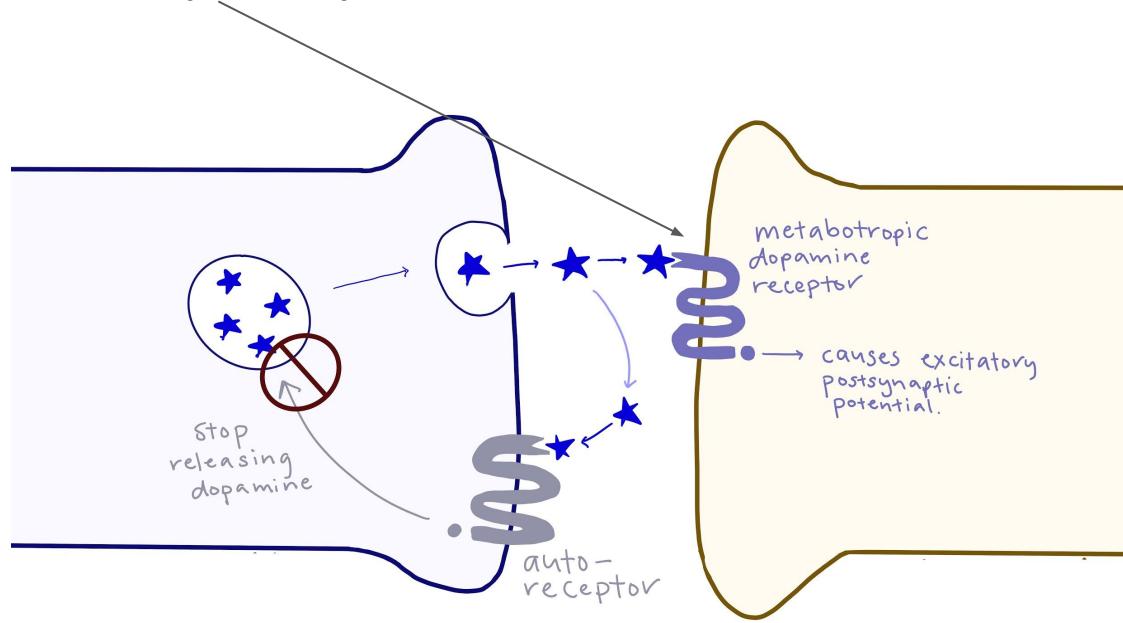
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- Binds to **metabotropic dopamine receptors** (a g-coupled protein receptor) to cause an excitatory postsynaptic potential



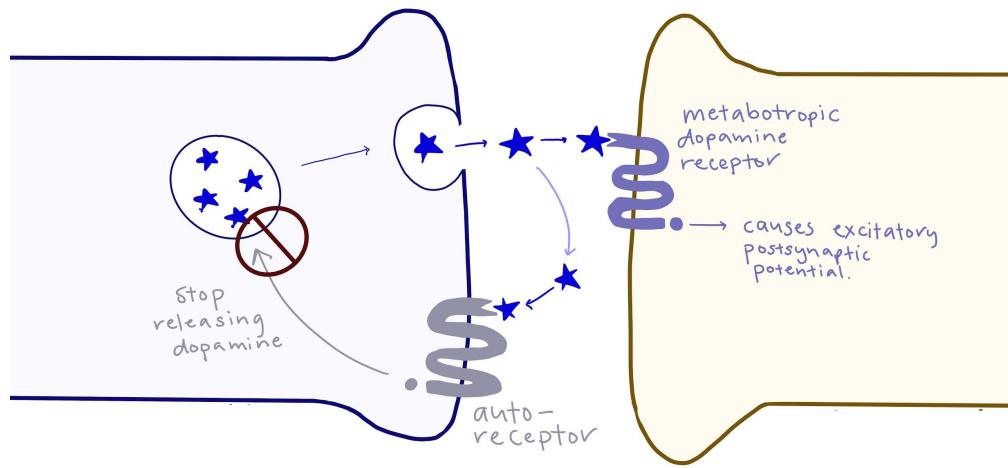
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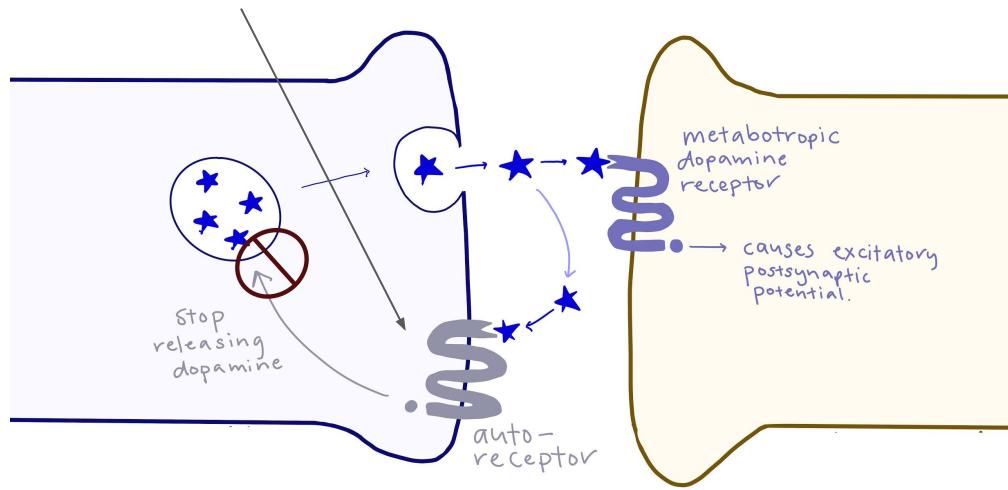
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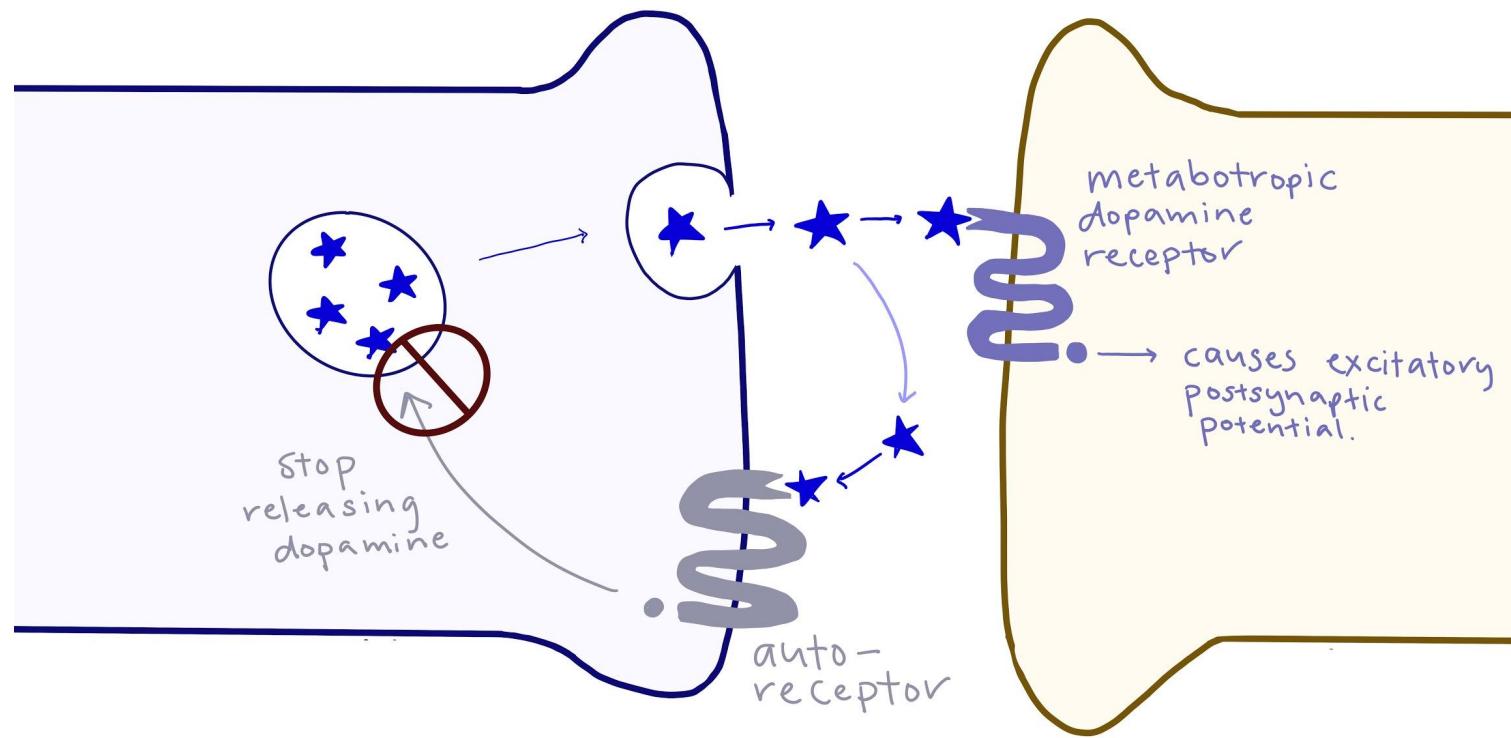
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Dopamine

Autoreceptors sense when there is too much dopamine and stop the neuron from releasing any more.



Dopamine

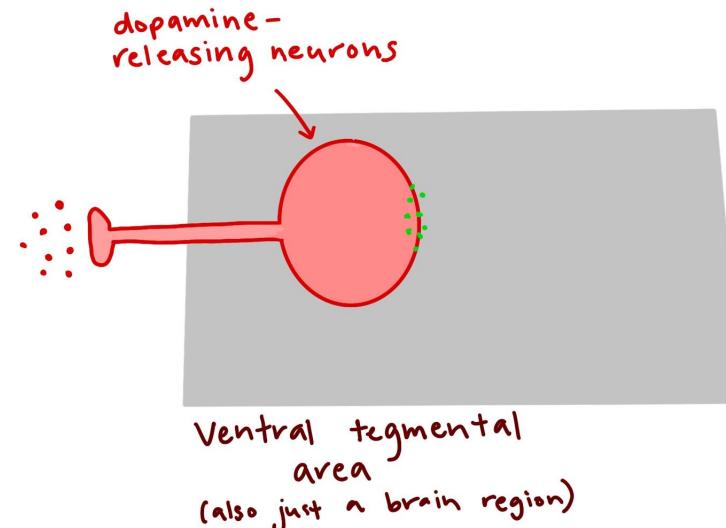
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Dopamine: reward regulation

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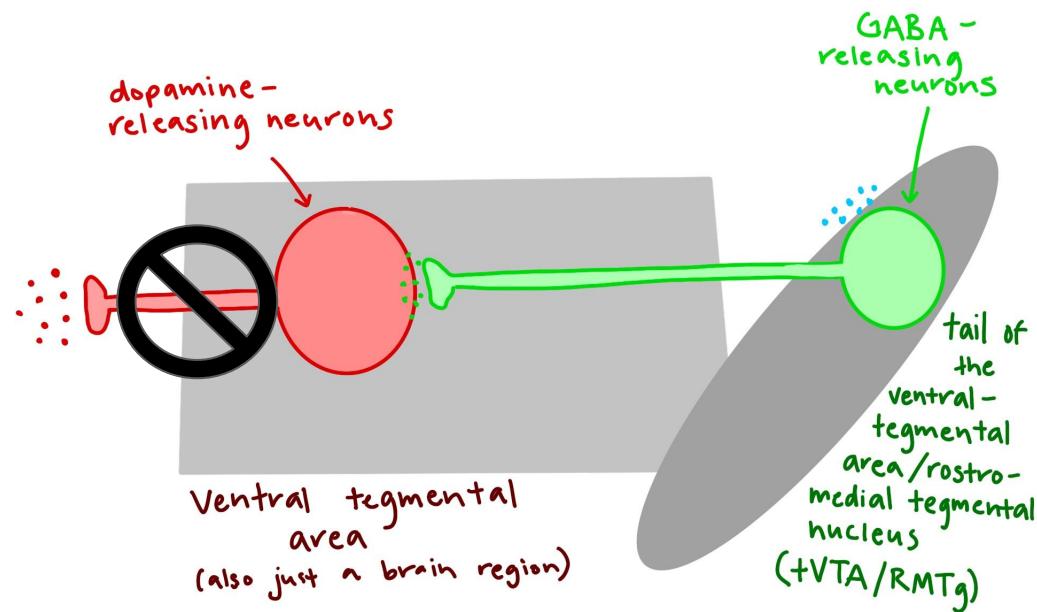
Dopamine: reward regulation

- There are dopamine-releasing neurons in the reward circuit of the ventral tegmental area



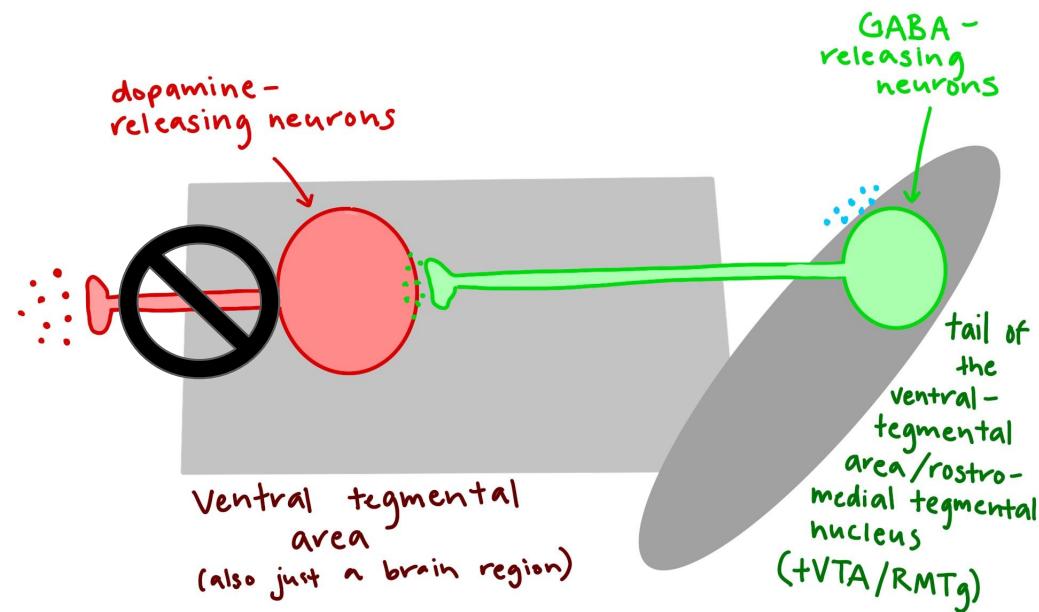
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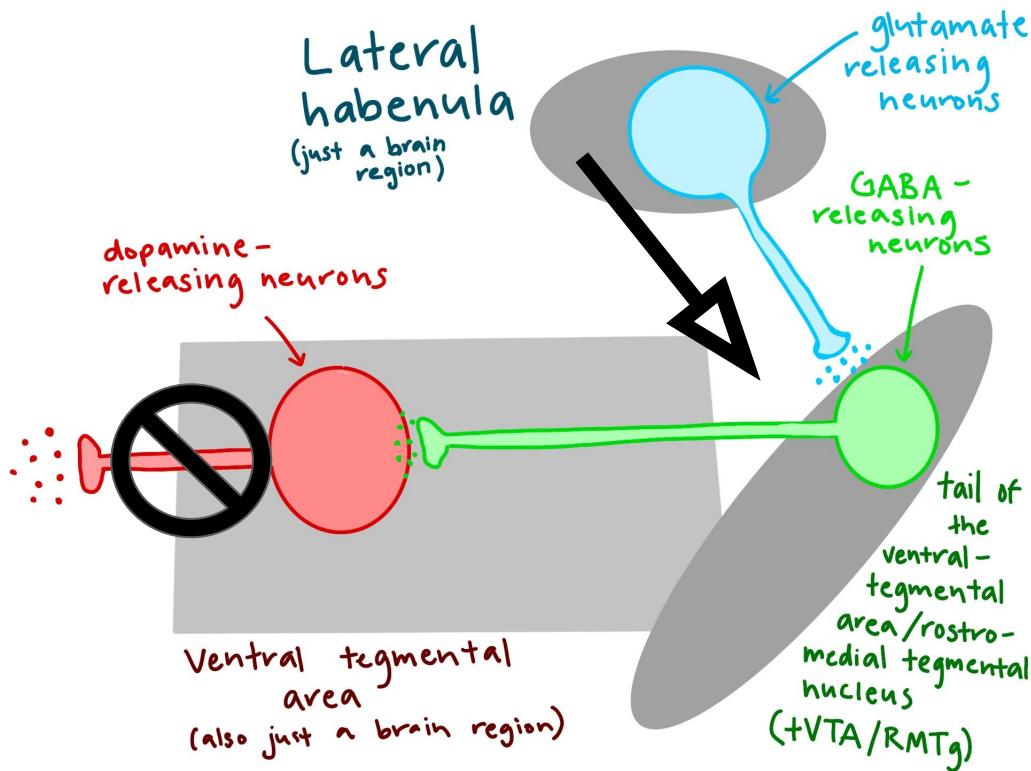
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 - This should make sense since we know that GABA is an inhibitory neurotransmitter



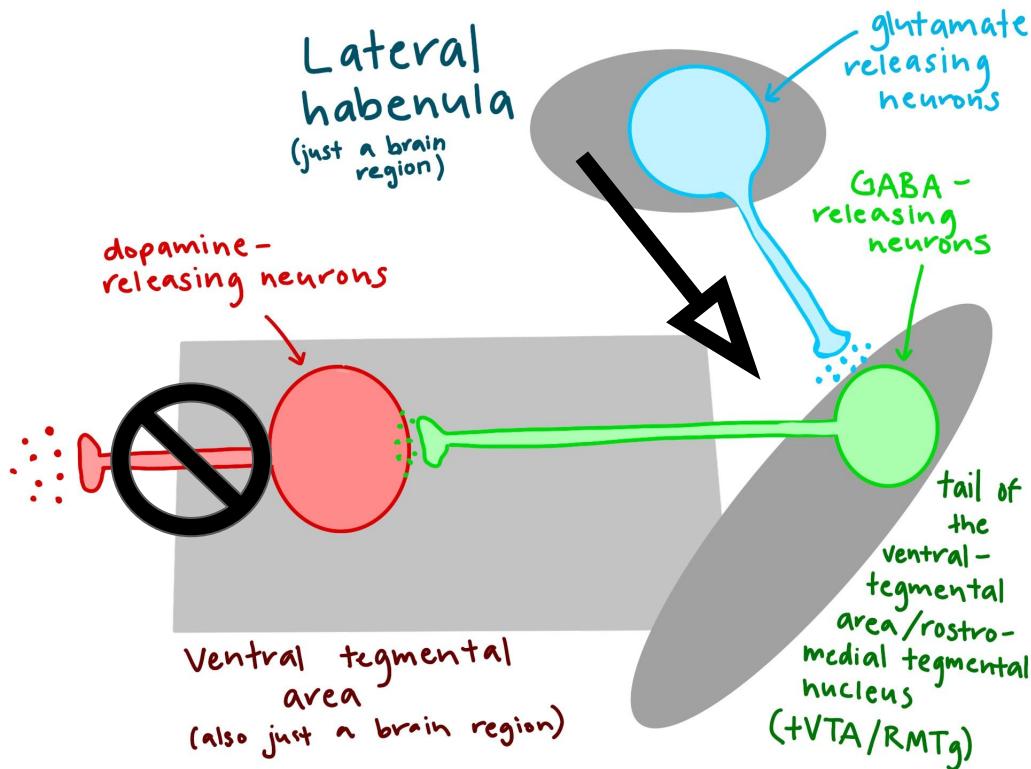
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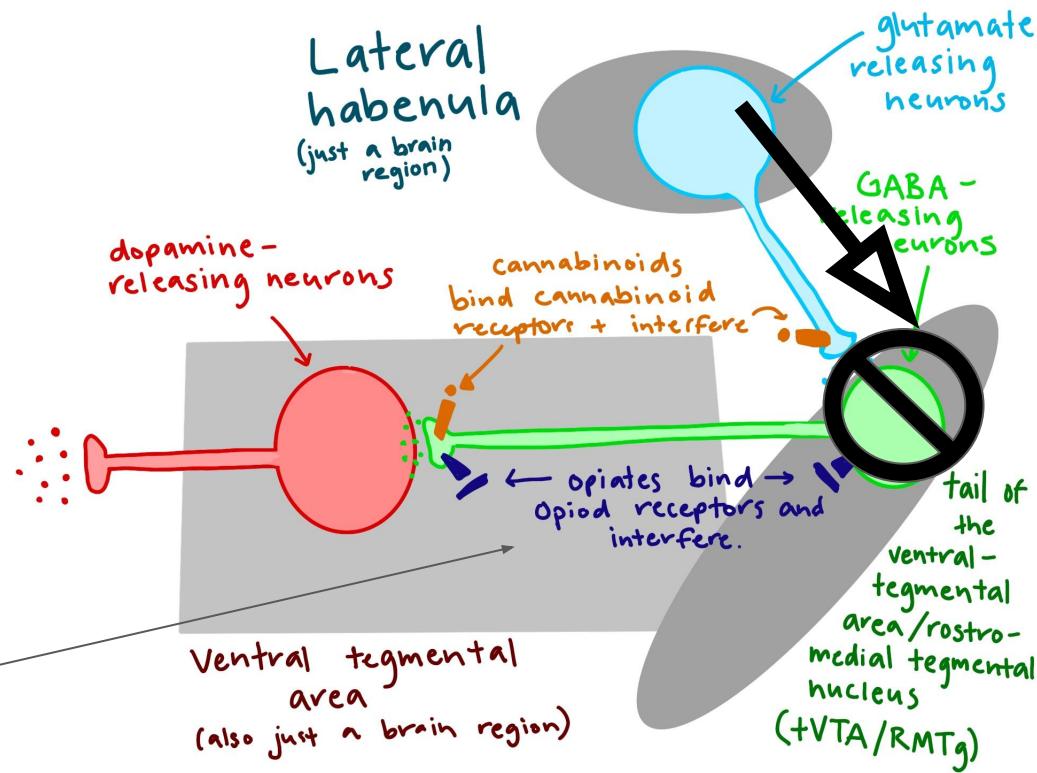
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 - Again, this should make sense, since we know glutamate is **excitatory** and in this case it is exciting an **inhibitory system**.

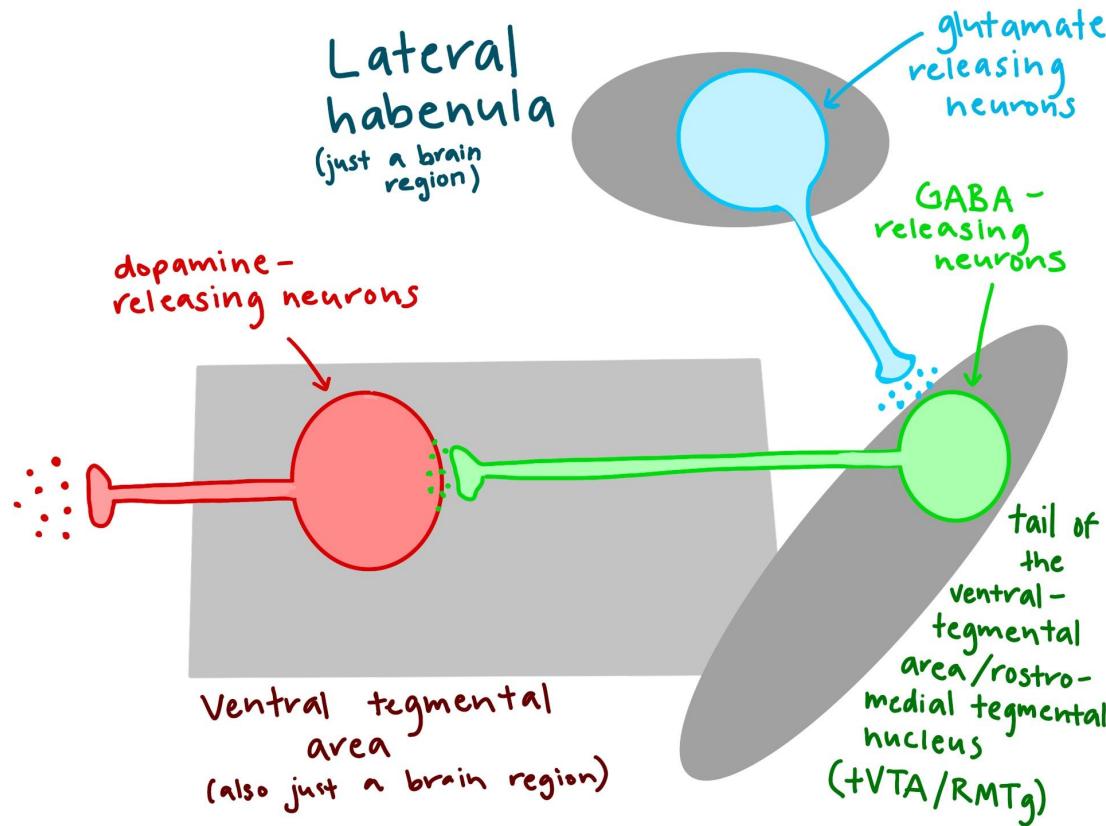


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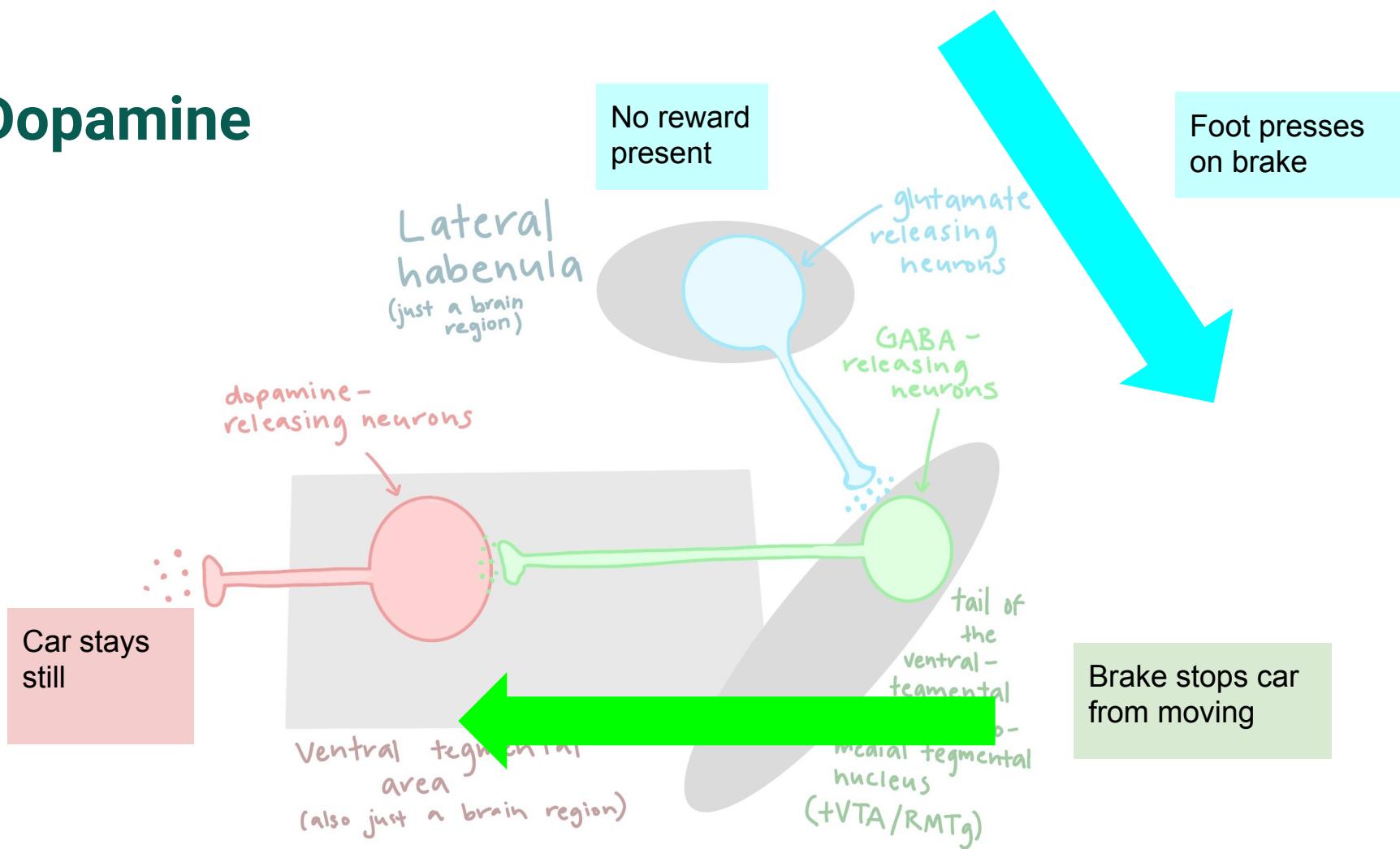
- GABA-releasing neurons in the tVTA/RMTg act as a **brake** on this release of dopamine
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- Part of why opiates and cannabinoids feel good to use is because they **turn off the brakes** on the dopamine reward system



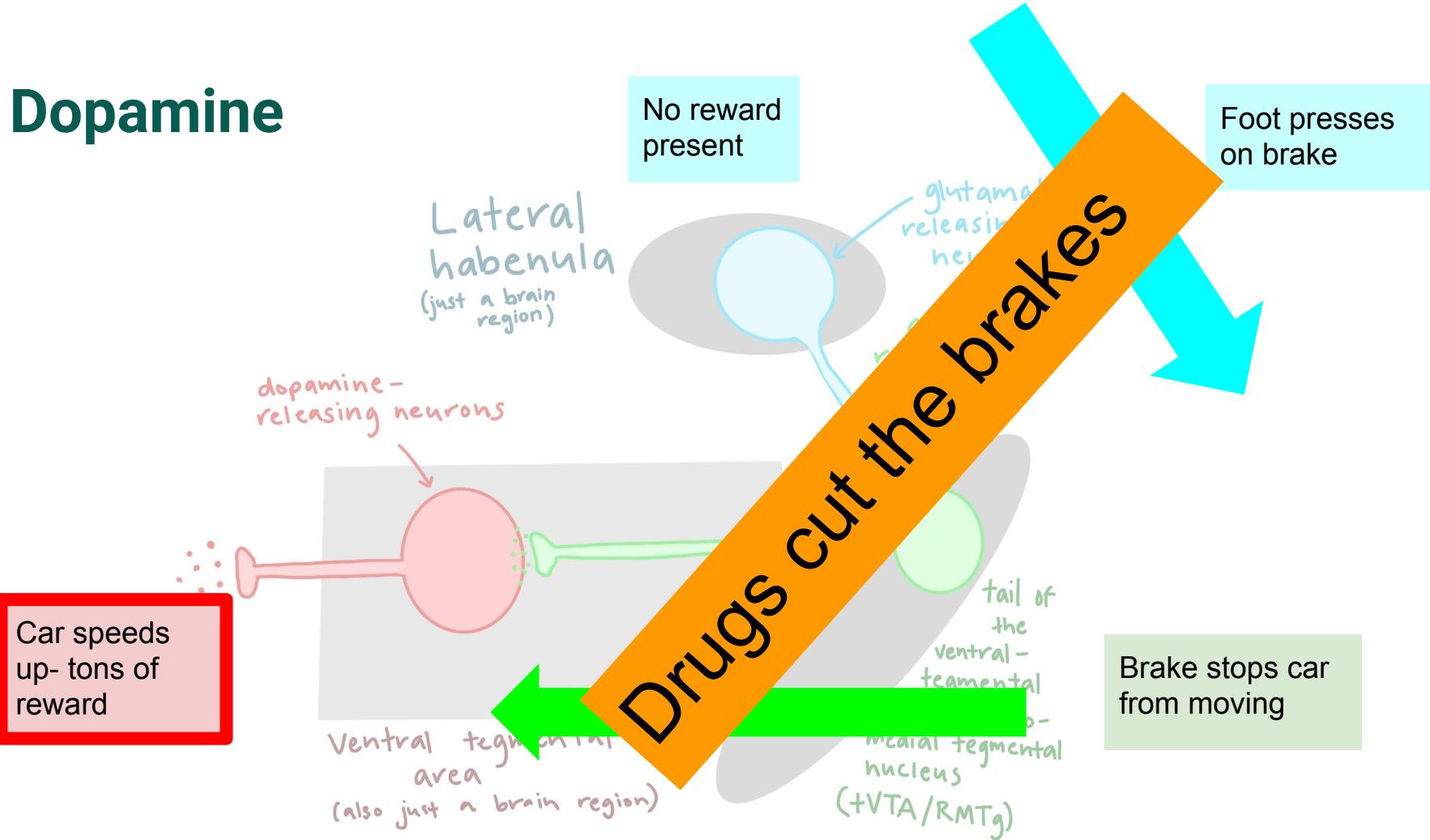
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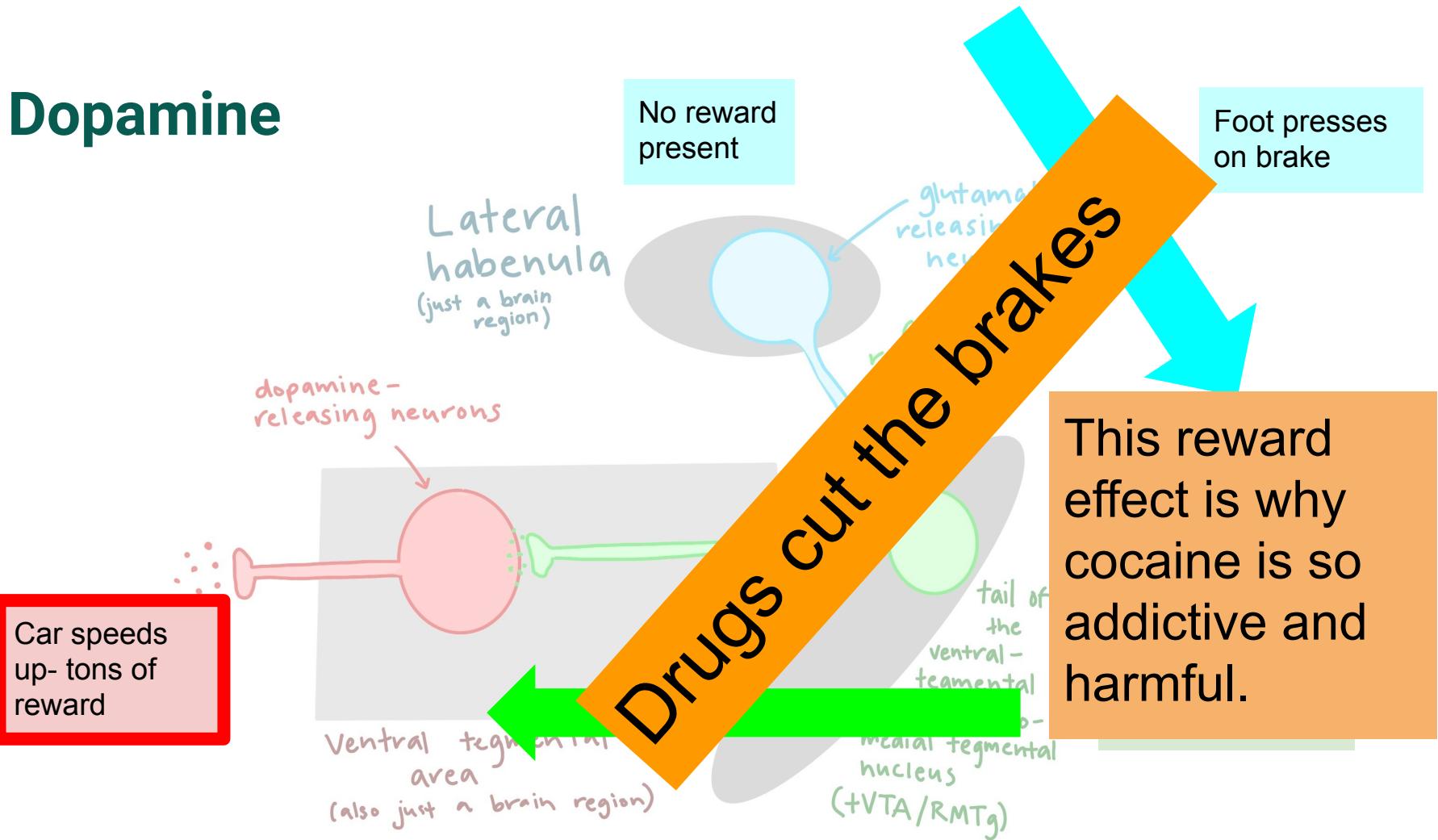
Dopamine



Dopamine



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Dopamine and reward regulation

- You should have a conceptual understanding of **how dopamine binding causes reward feelings** (because it is an excitatory neurotransmitter binding metabotropic receptors that cause postsynaptic depolarization)
- You should be able to **roughly diagram the brake-system concept of dopamine regulation**, and **be able to explain how drugs hijack this system.**

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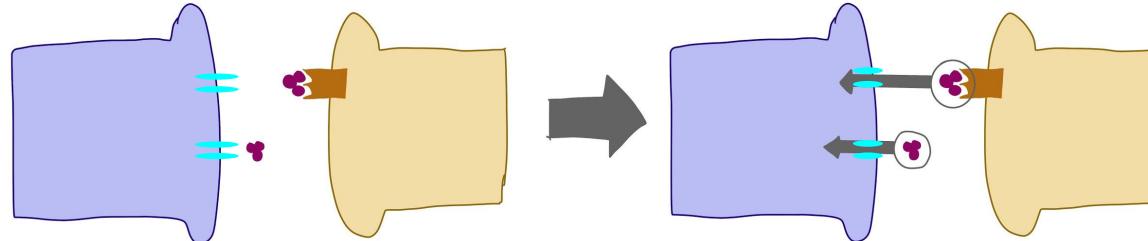
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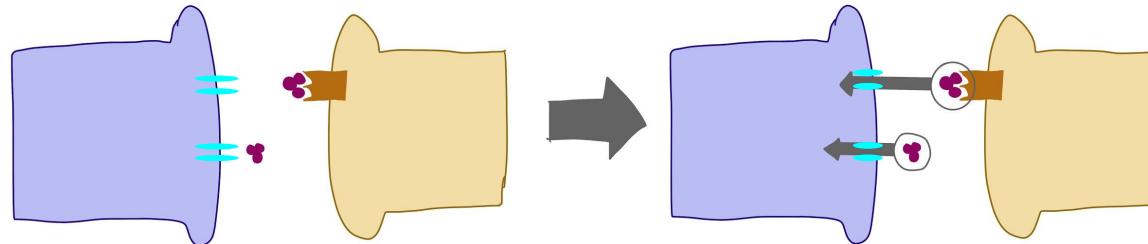
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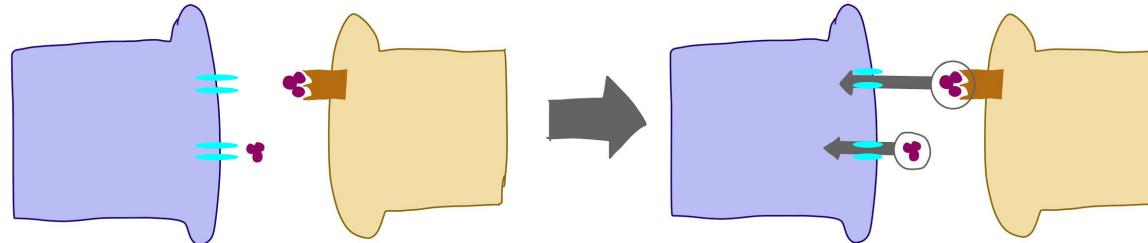
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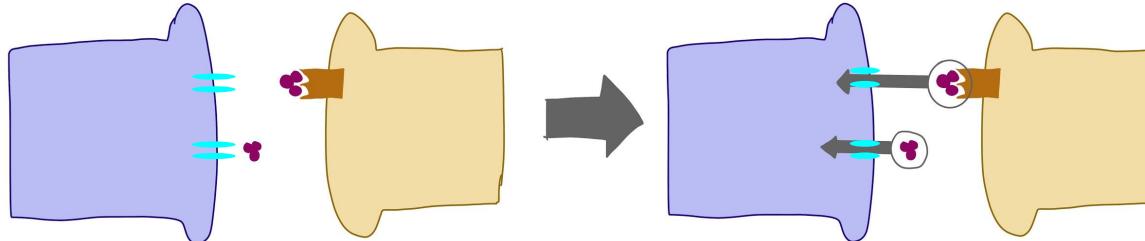
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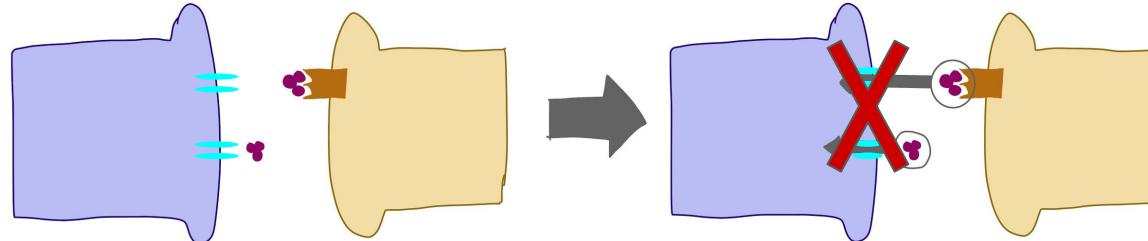
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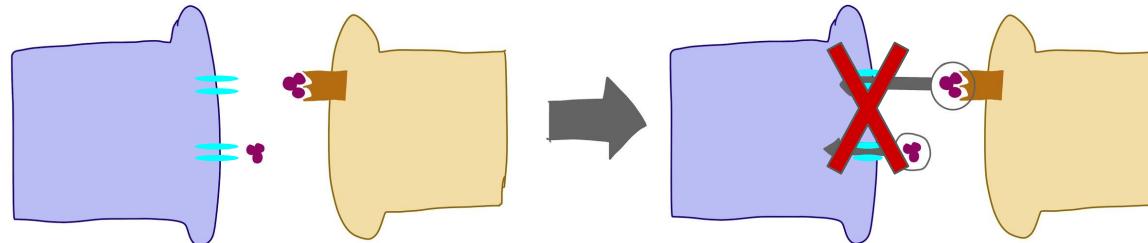
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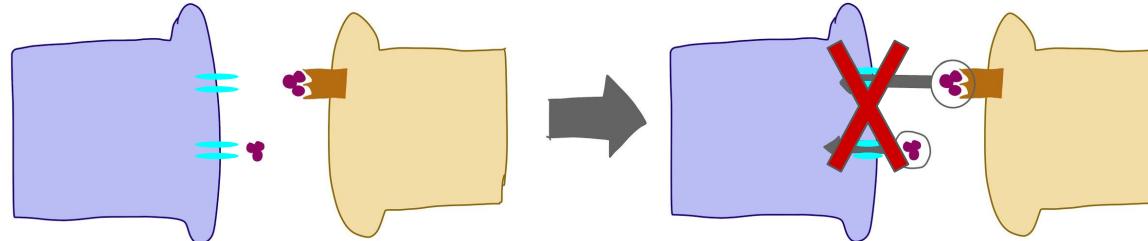
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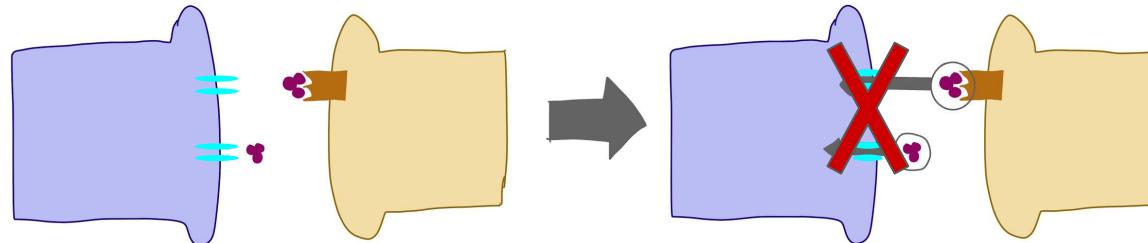
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- **Selective serotonin reuptake inhibitors (SSRIs)** are drugs that block the serotonin transporters
 - This increases the amount of serotonin in the synapse
 - It can be useful for treating depression in some folks



Serotonin: take-aways

- You should understand the general effect of serotonin on the body
- You should know the two types of serotonin receptor and their effects on the postsynaptic neuron
- You should understand what an SSRI is and how it works
 - You should also understand what would happen if someone was treated with a reuptake inhibitor for any of the other neurotransmitters we have learned about.



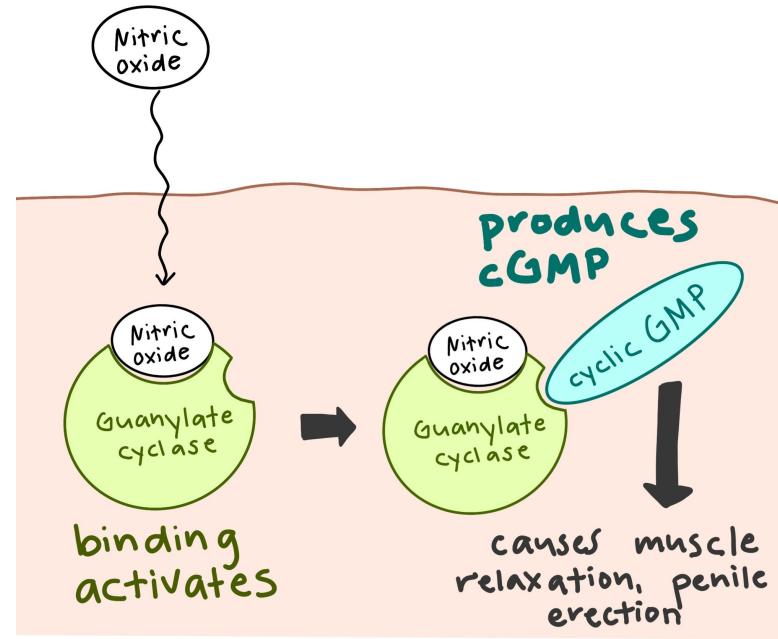
Nitric oxide

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- Nitric oxide relaxes vascular smooth muscle throughout the body

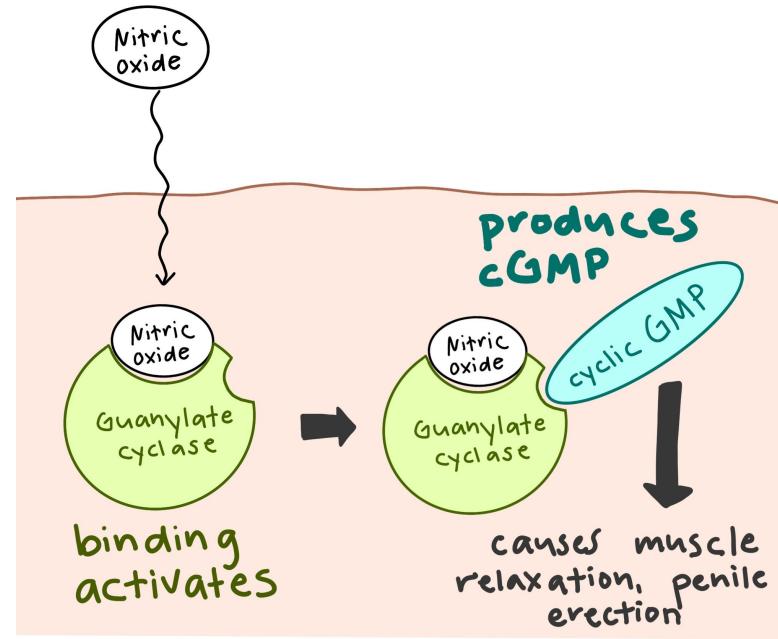
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- Nitric oxide relaxes vascular smooth muscle throughout the body
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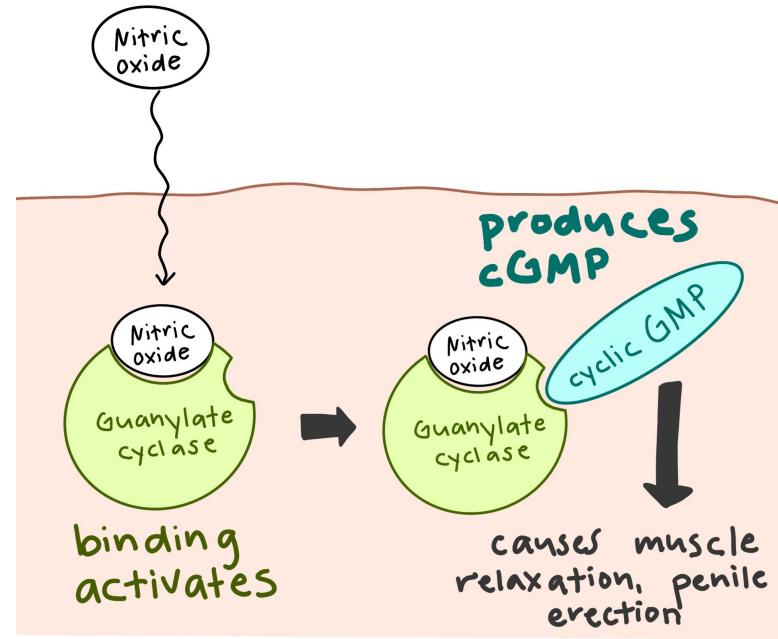
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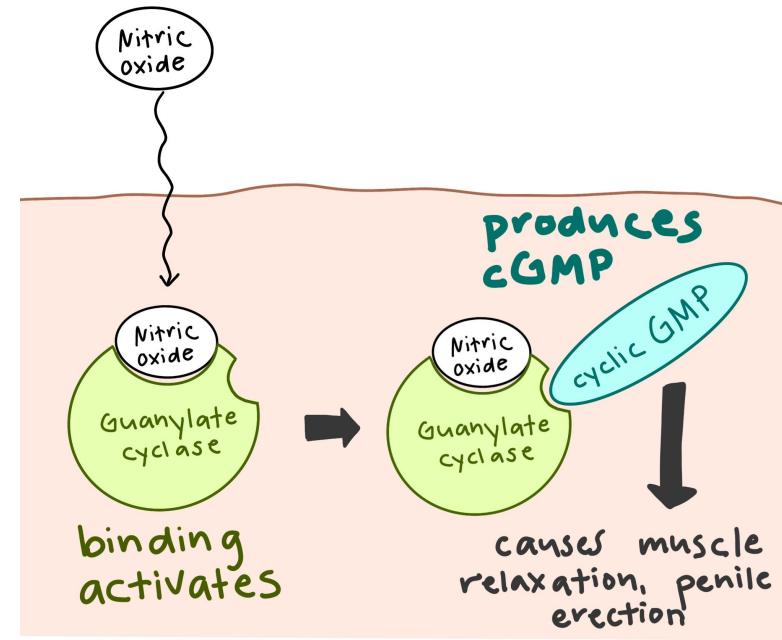
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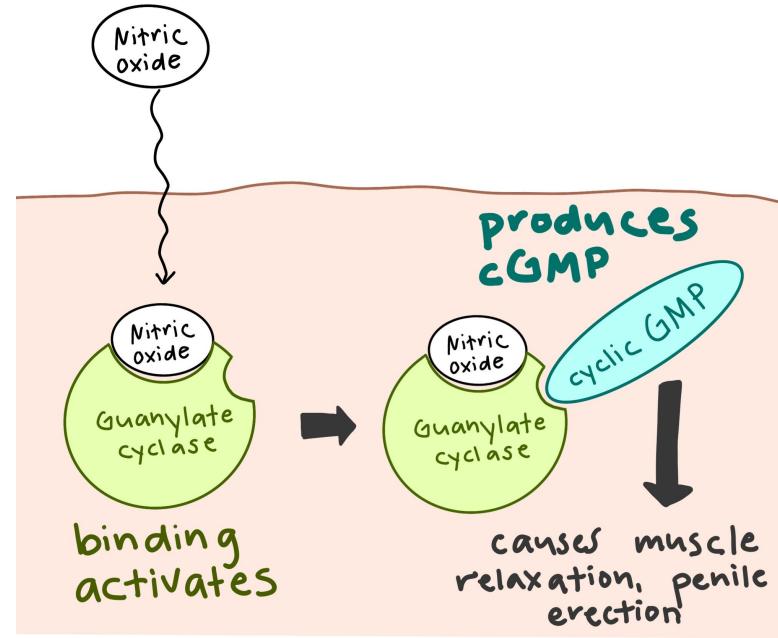
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 - This lowers blood pressure
 - It also causes penile erection by allowing blood to fill the corpus cavernosum



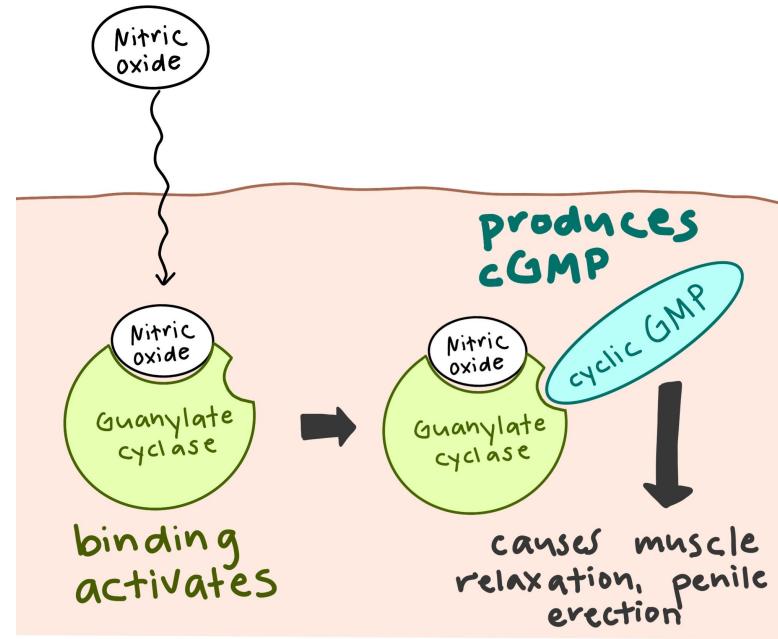
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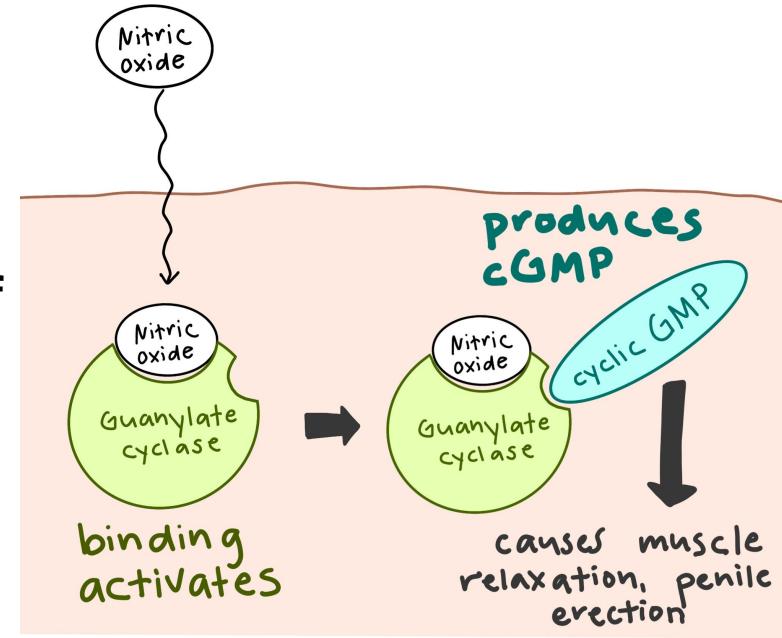
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- Cyclic GMP is broken down by phosphodiesterase 5, which ends the nitric oxide signalling.



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 - This causes penile erection by allowing blood to fill the corpus cavernosum
- Cyclic GMP is broken down by phosphodiesterase 5, which ends the nitric oxide signalling.
- Viagra works by **inhibiting this breakdown enzyme**, therefore **increasing the intensity of nitric oxide signalling and prolonging erection**.



Lecture 19 Take-aways

From Dr. Selvaraj:

"students should have a rough framework of what the different brain regions do. Know the core aspects of sympathetic and parasympathetic nervous system (we will be talking more about the CNS in Lecture 21). Be able to explain the two different synaptic transmissions with examples. EPSP and IPSP; LTP and LTD (students should be able to identify and interpret these effects/changes when provided examples). The topic of neurotransmitters might certainly be complicated for them. But if we were to provide a circuit and the receptors involved [and possible treatment with compounds] (those covered in class), students should be able to come up with an interpretation of effect/response. So they should have sufficient understanding of the core neurotransmitters and their select receptors covered in class."