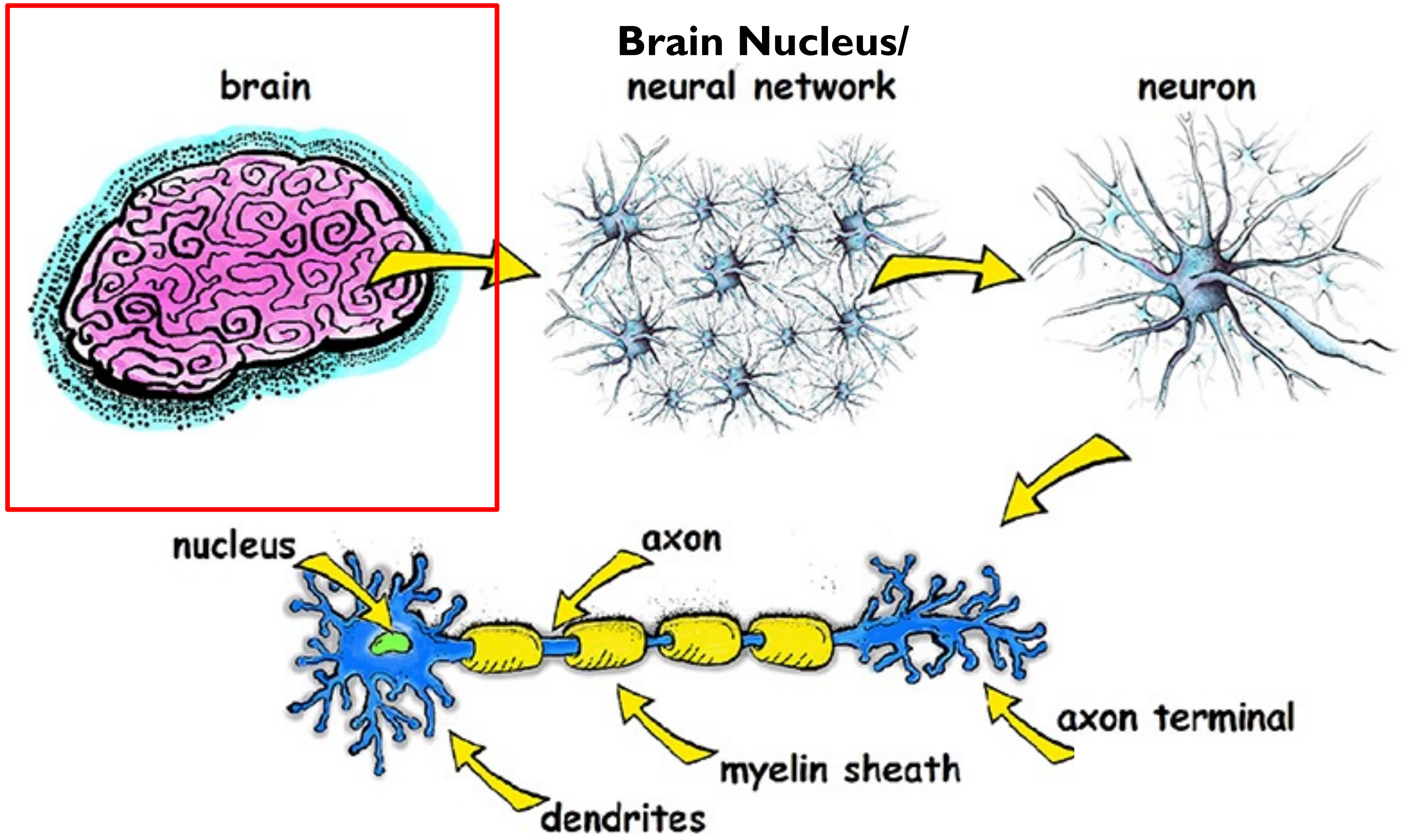
LECTURE 3

INTRODUCTION TO NEUROSCIENCE

NEUROANATOMY



PSYCHOACTIVE DRUGS ALTER BRAIN CHEMISTRY AND SIGNALING

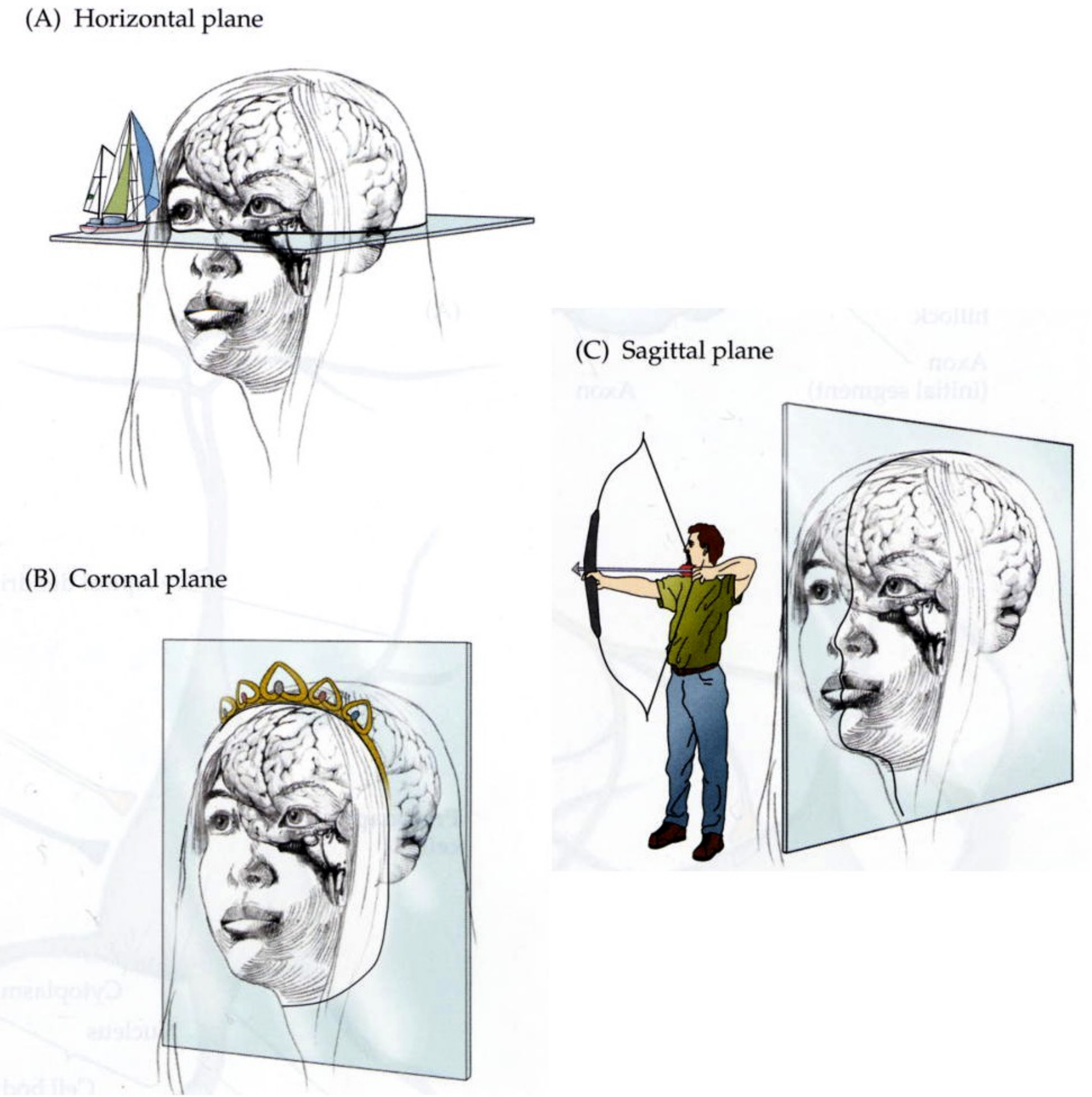
- Acute: hijack the normal brain circuitry to "activate" or "inhibit" brain cells
- Chronic: influence homeostasis
  - Both effects can ultimately change behaviour… but how does this happen?

COMMON PLANES OF BRAIN SECTIONS:

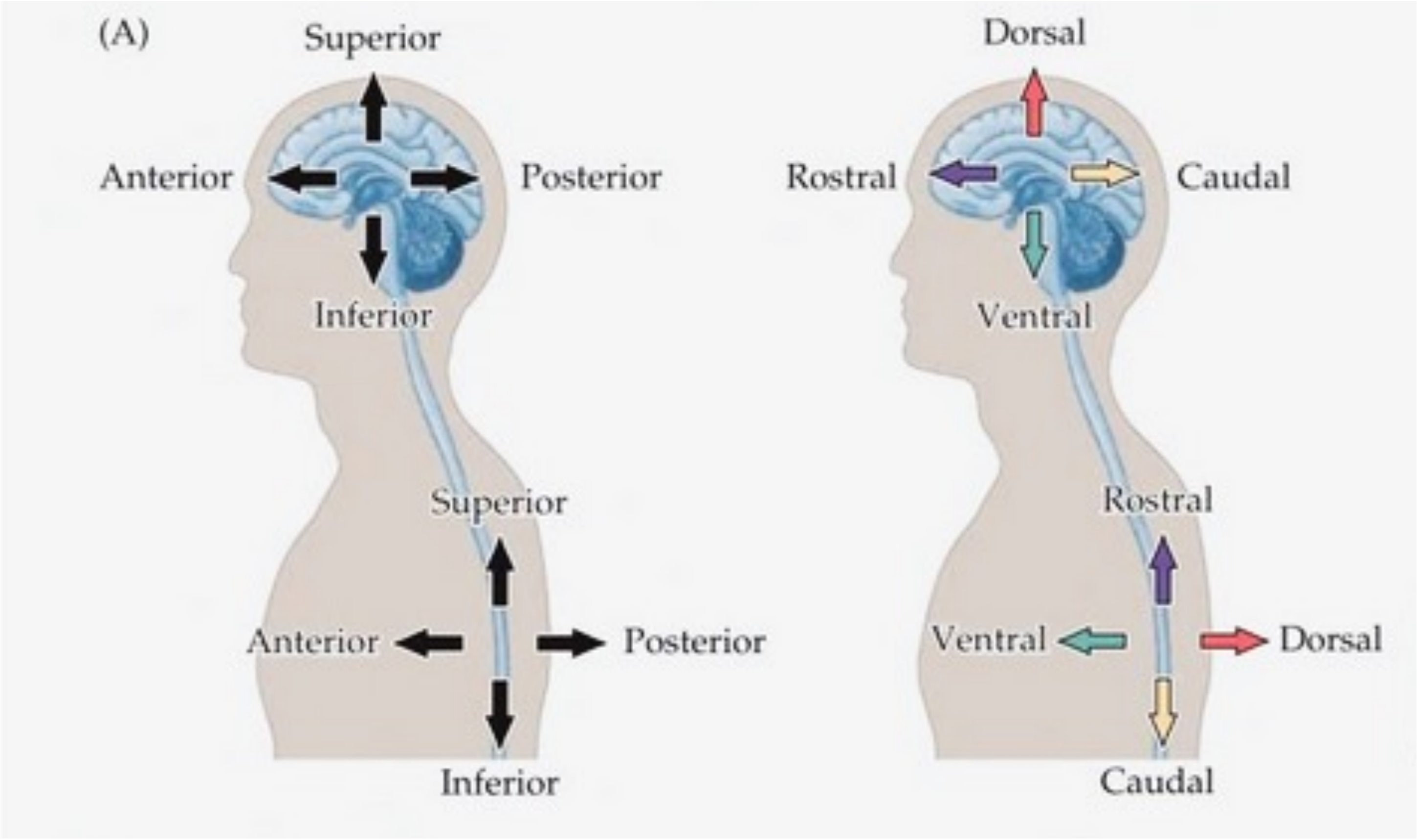
A) HORIZONTAL

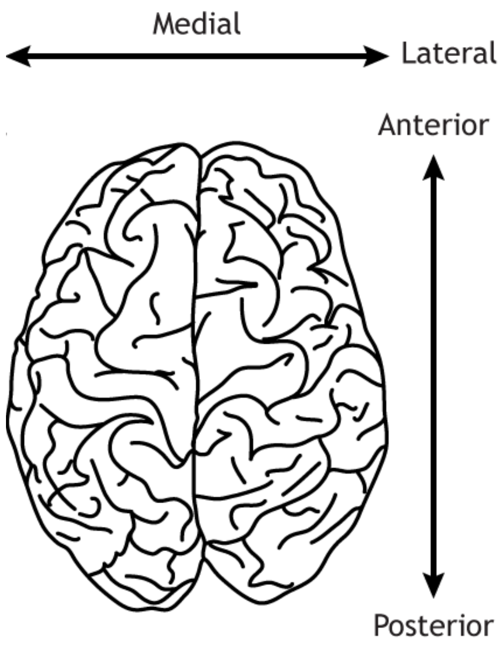
B) CORONAL

C) SAGITTAL

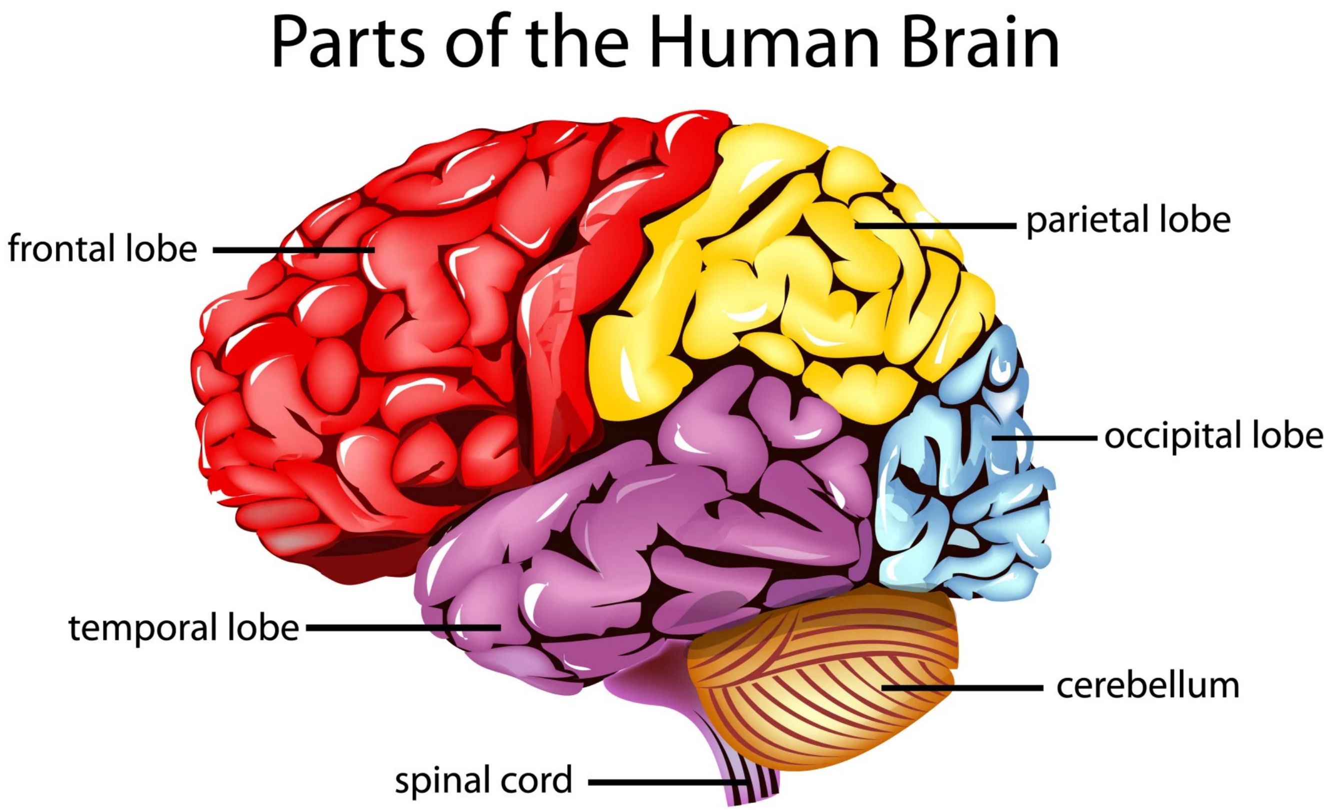


ANATOMICAL TERMS OF DIRECTION





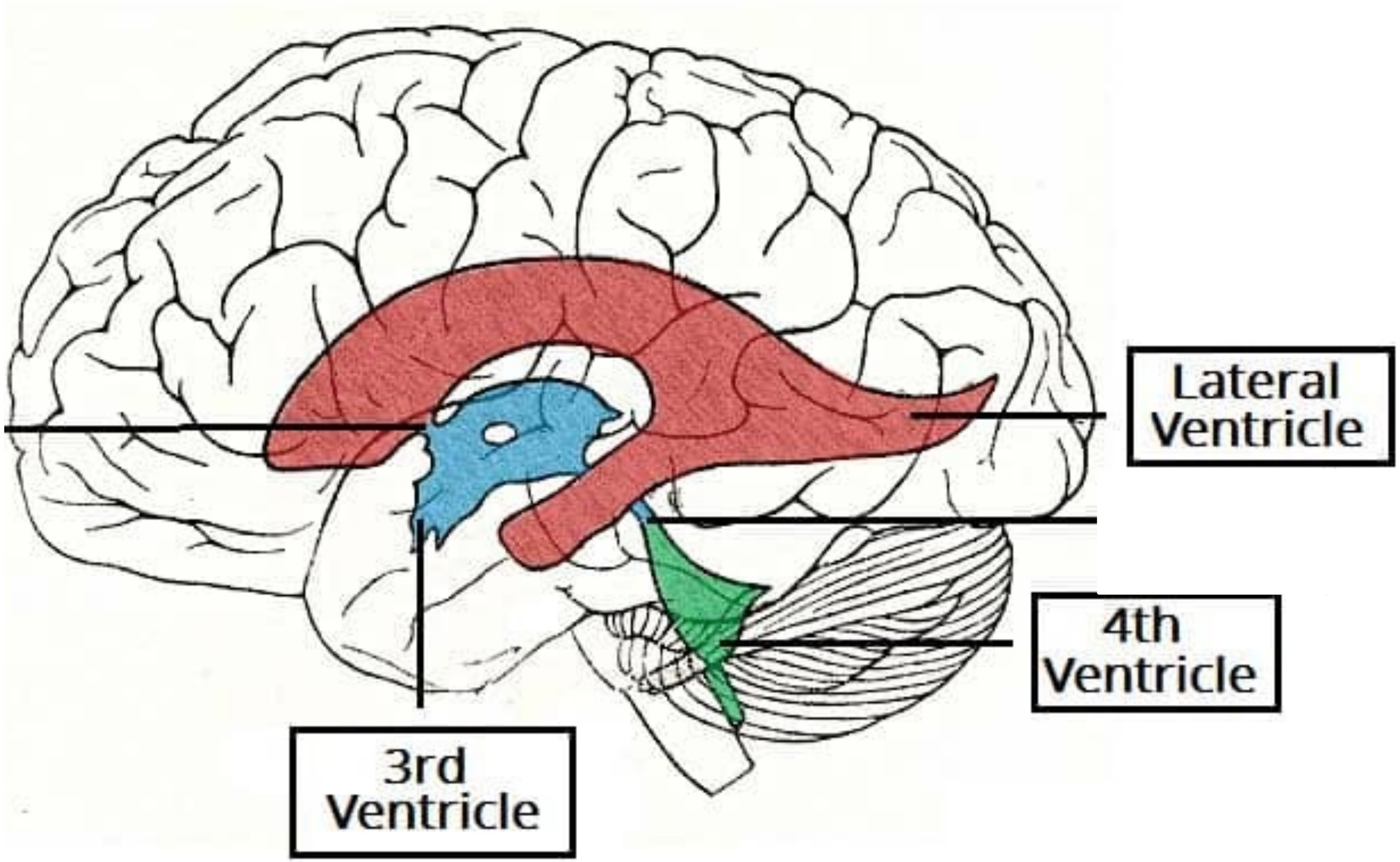
LOBES OF THE HUMAN BRAIN



The cortex has 4 primary lobes

Let's Review:
https://www.youtube.com/watch?v=LQ4DIE1Xyd4

VENTRICLES



Def: a hollow part or <u>cavity</u>

four connected fluid-filled <u>cavities</u> in the brain through which cerebrospinal fluid circulates

THE HUMAN BRAIN: MAJOR STRUCTURES/REGIONS

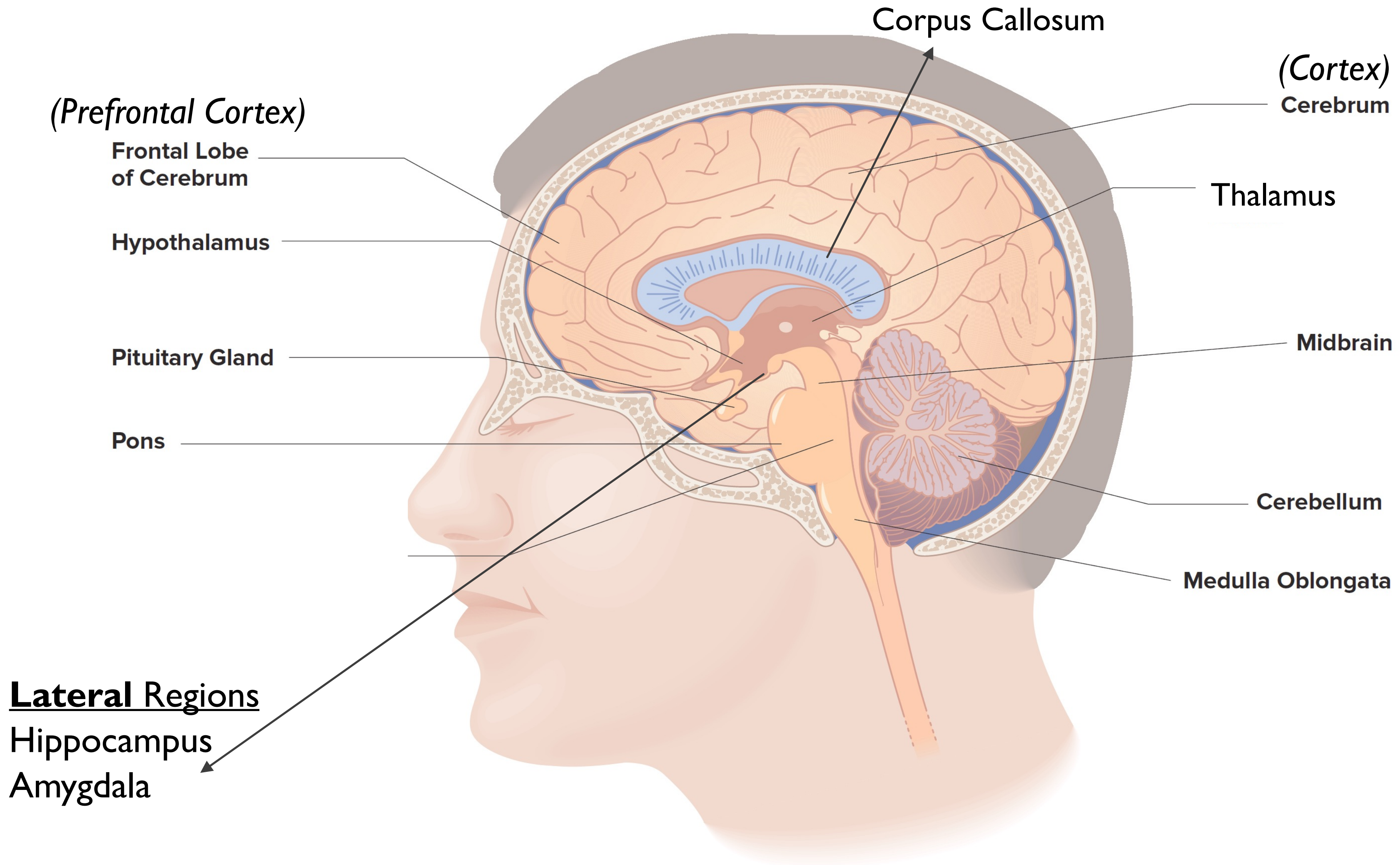
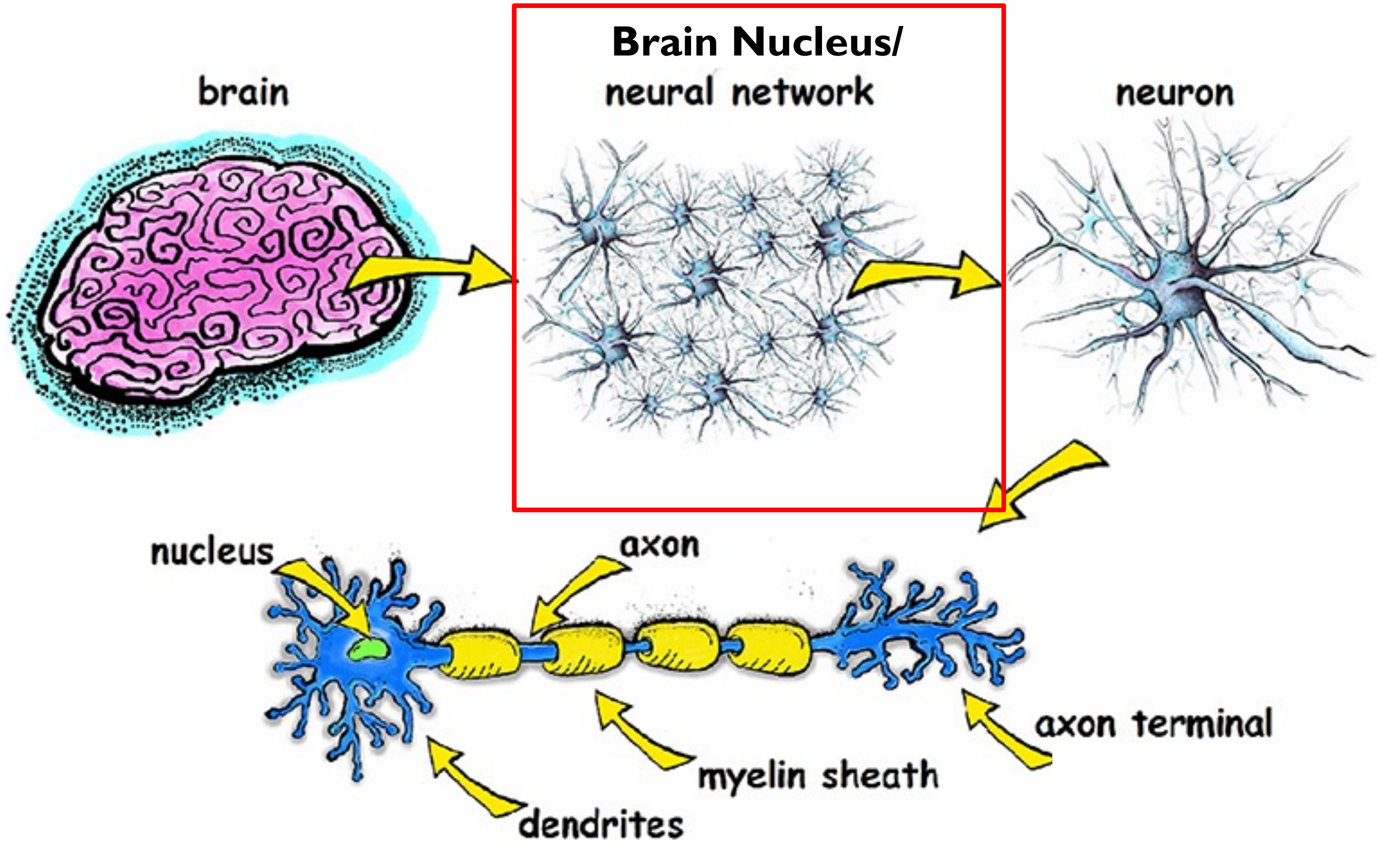


Figure 4.4

THE HUMAN BRAIN: FUNCTIONS OF MAJOR STRUCTURES/REGIONS

- Cortex –
- Cerebellum –
- Spinal cord –
- Thalamus –
- Hypothalamus –
- Pituitary gland –
- Midbrain –
- Pons –
- Medulla oblongata –
- Hippocampus –
- Amygdala –

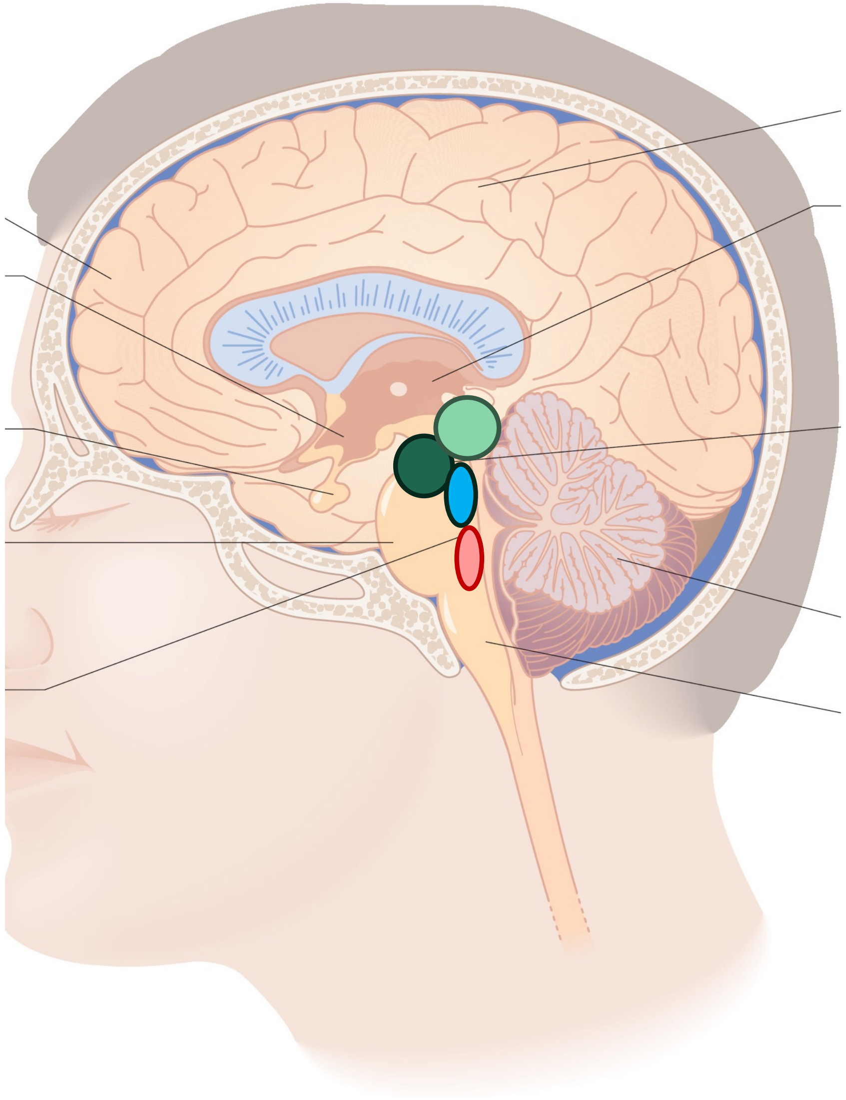
NEUROANATOMY



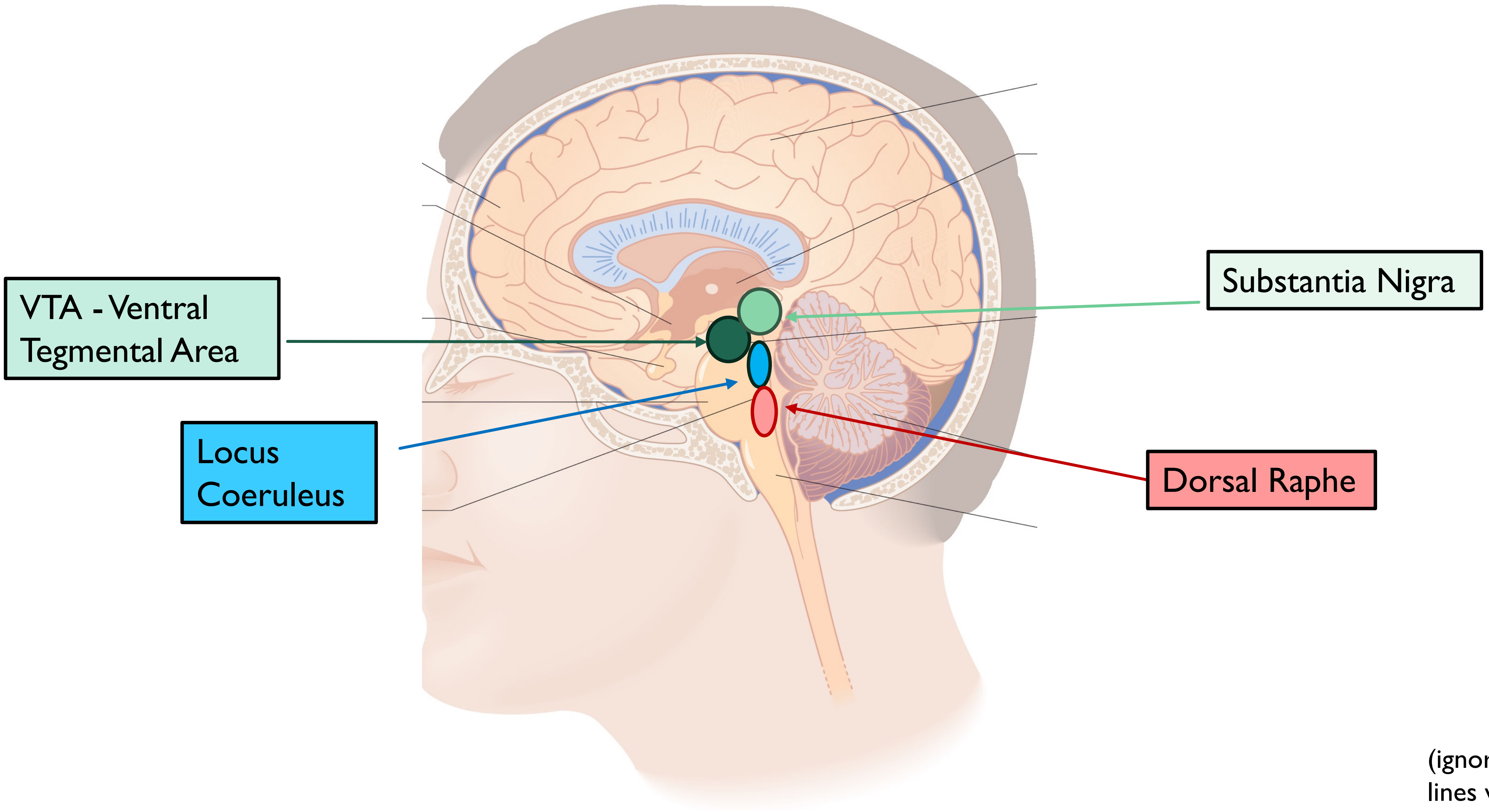
THE BRAIN: CRITICAL NUCLEI FOR DRUGS EFFECTS

In neuroanatomy, a nucleus (pl. : nuclei) is **a cluster of neurons, located deep within the cerebral cortex and brainstem**.

The neurons within one nucleus usually have roughly similar connections and functions.

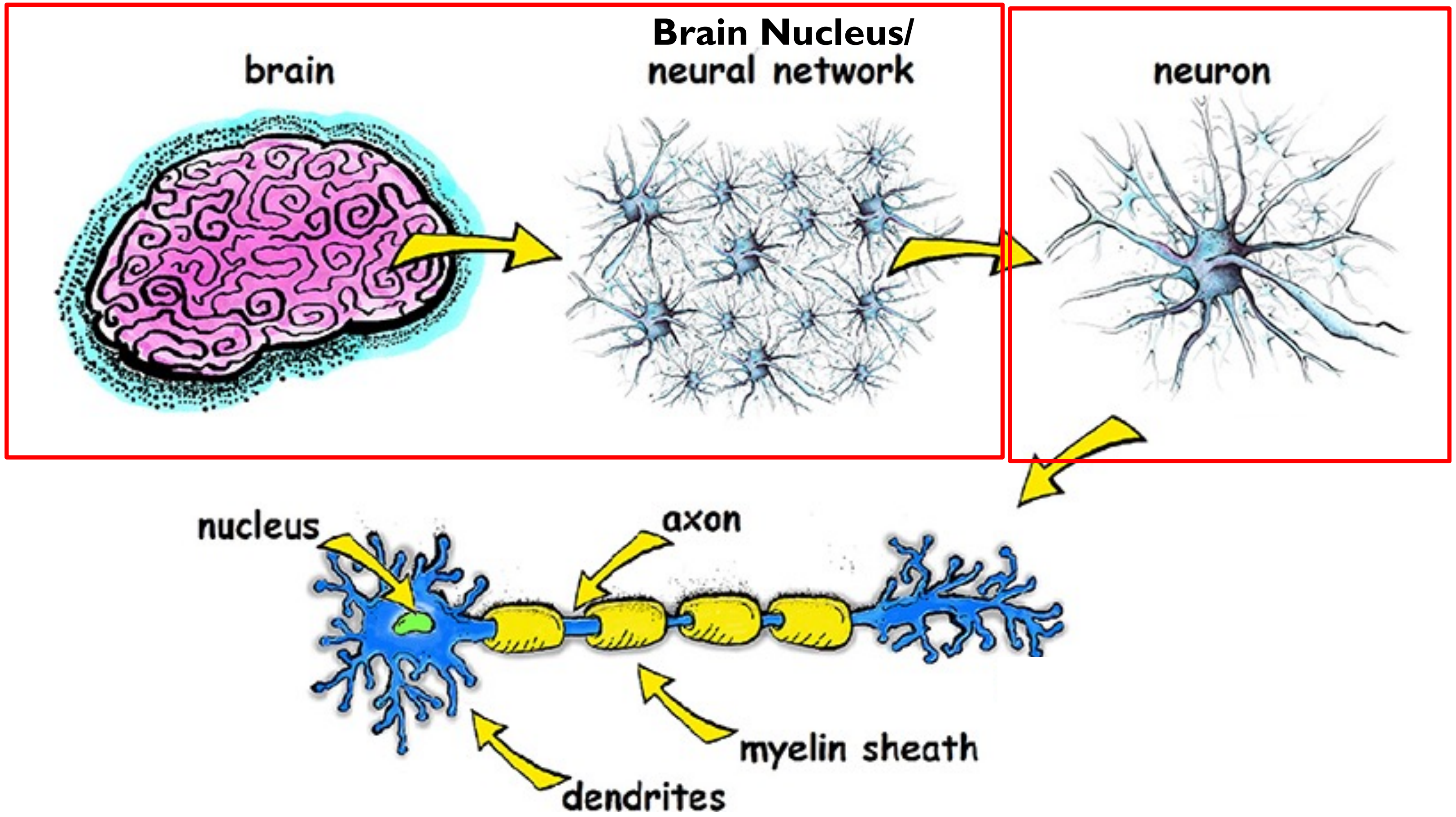


THE BRAIN: KEY NUCLEI



(ignore any black lines without →)

NEUROANATOMY



COMPONENTS OF THE BRAIN AND NERVOUS SYSTEM

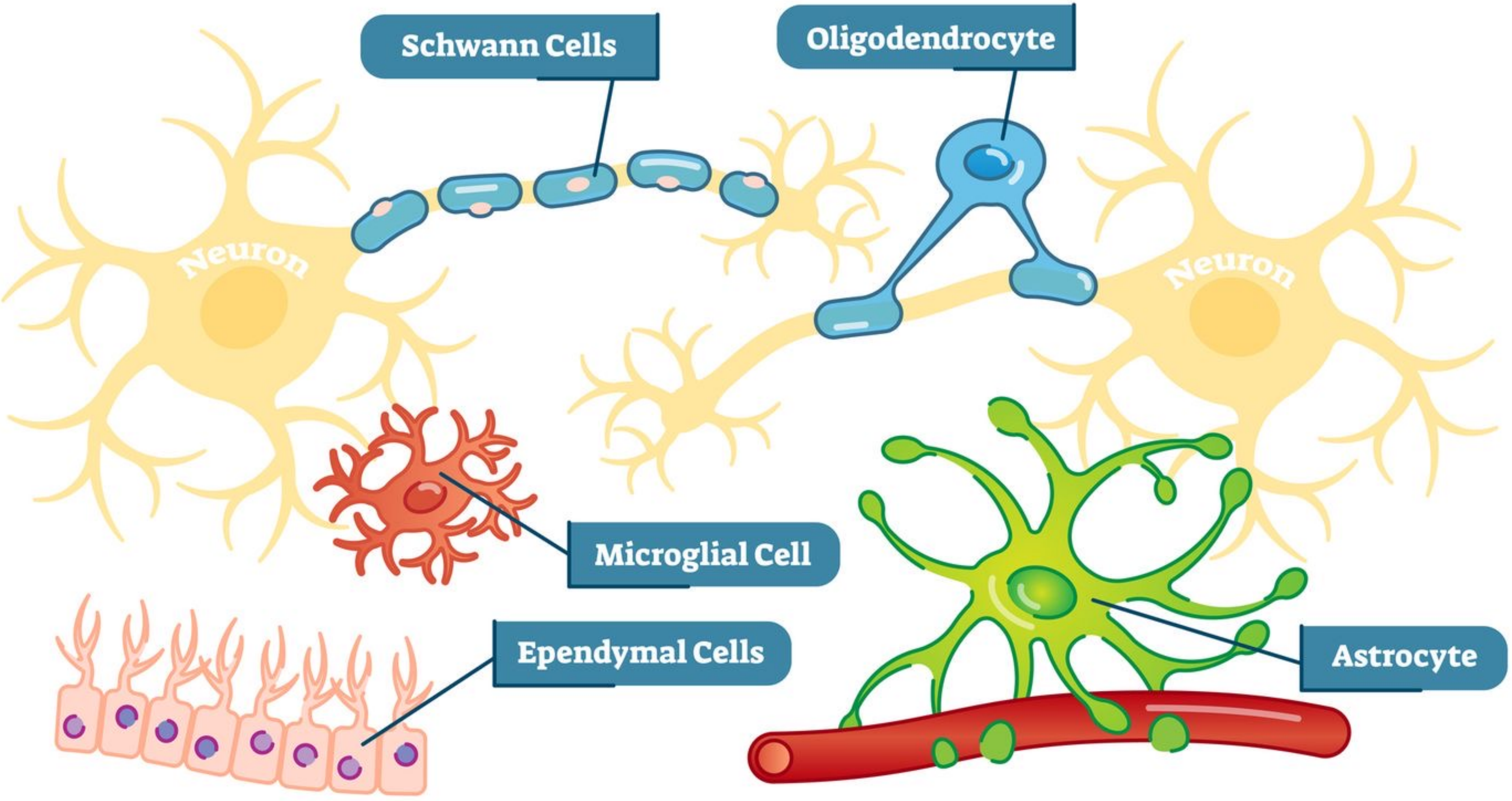
- Two major types of cells in the nervous system.
  - **1) Neurons**, or nerve cells.
  - **2) Glia**, or glial cells.

- There are ~100,000,000,000 of each type of these brain cells!

GLIA

- Major functions: (generally)
  - Providing structure and support to the brain.
  - Getting nutrients into the system.
  - Eliminating waste.
  - Forming **myelin**.
  - Communicating with other glia.
  - **Maintaining the blood–brain barrier**

GLIA (5 "TYPES"*)



Schwann Cells
Oligodendrocyte
Neuron
Neuron
Microglial Cell
Ependymal Cells
Astrocyte

ASTROCYTES CREATE THE BLOOD BRAIN-BARRIER

- **The blood–brain barrier** – a semi-permeable membrane protecting the brain from toxic chemicals.
    - A drug molecule must be able to pass through the barrier to be psychoactive.

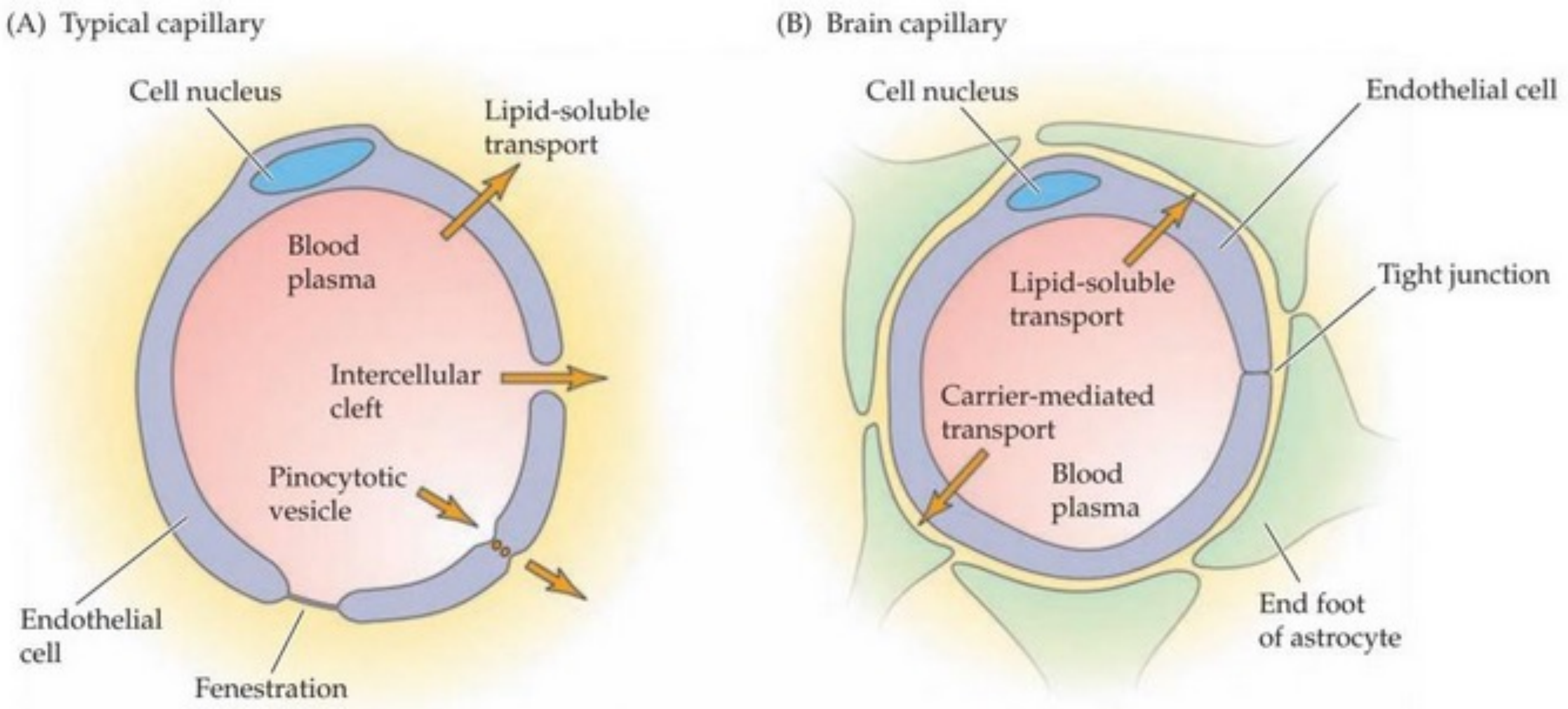


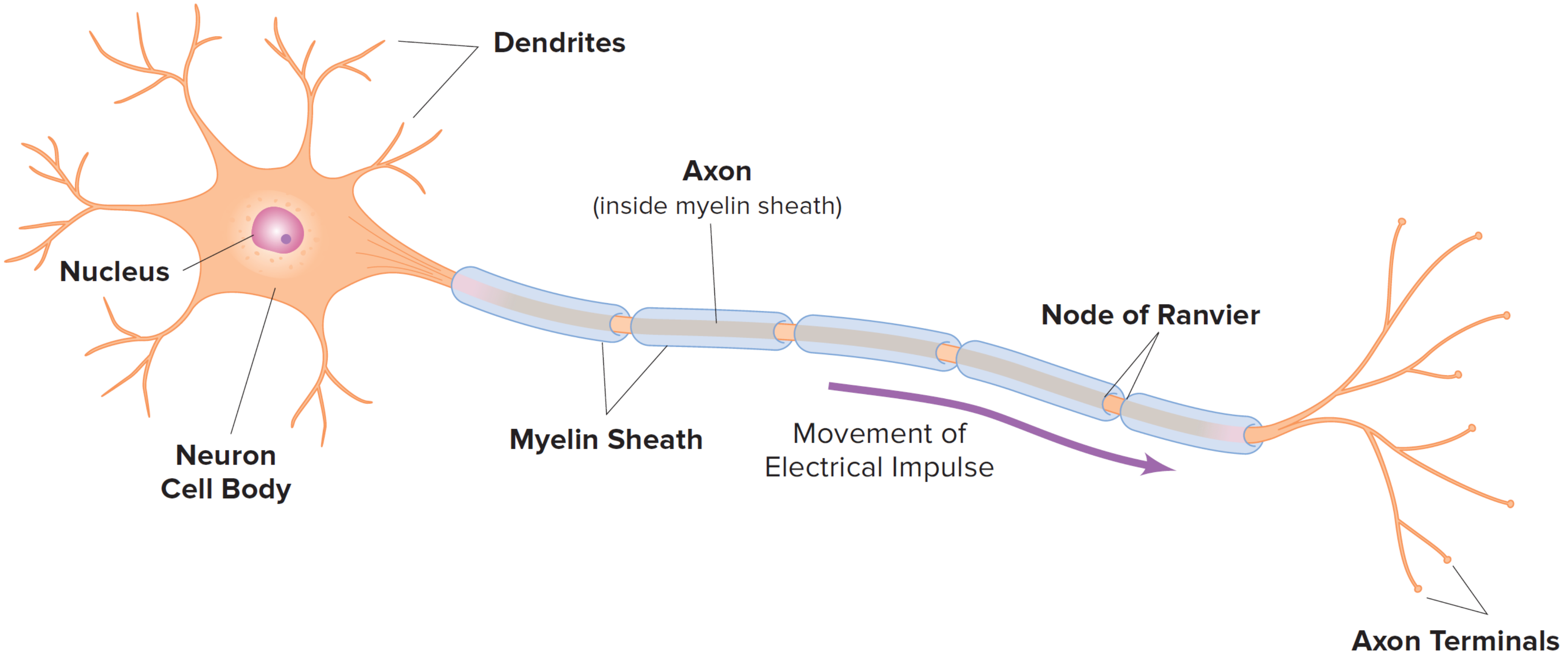
FIGURE 1.8 Cross-section of typical capillaries and brain capillaries (A) Capillaries found throughout the body have characteristics that encourage movement of materials between the blood and surrounding cells. (B) Brain capillaries minimize movement of water-soluble molecules through the blood vessel wall because there are essentially no large or small clefts or pinocytotic sites. (After W. H. Oldendorf. 1977. *Exp Eye Res* 25: 177–190. © 1977. Reprinted with permission from Elsevier.)

NEURONS

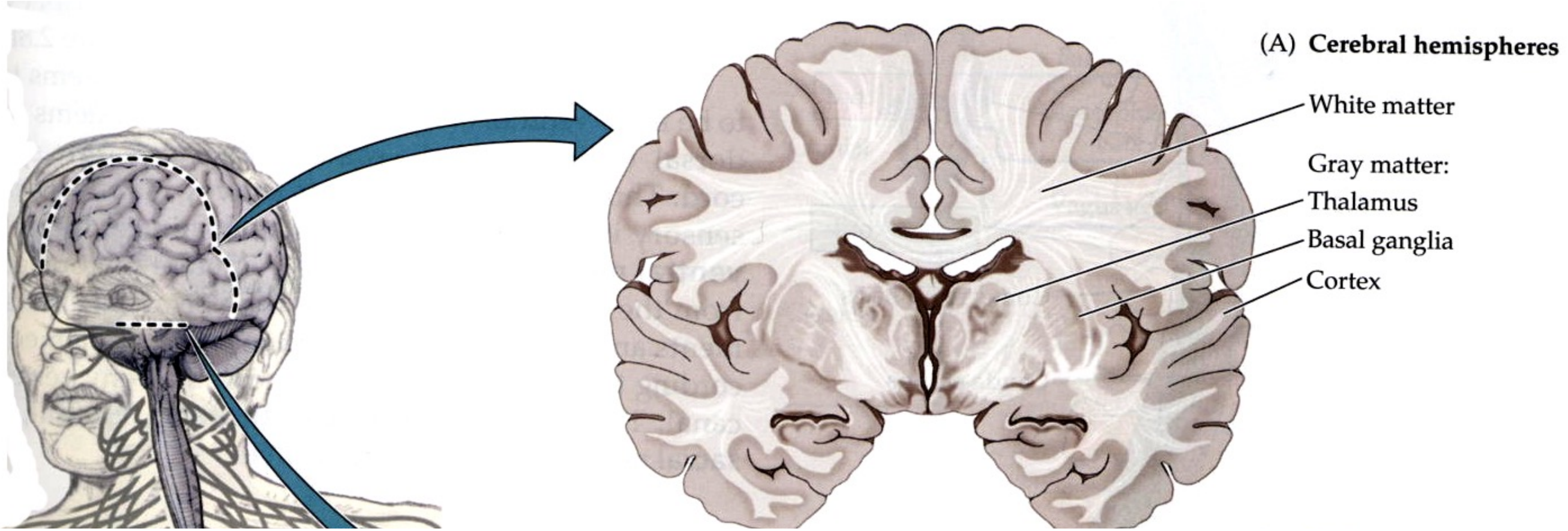
- Primary cells of the nervous system that analyze and transmit information.

- Defined regions:
  - **Cell body**.
    - Contains the processes that maintain the life of the neuron, including the nucleus.
  - **Dendrite**.
    - Contains **receptors** that respond to chemical signals.
  - **Axon**.
    - Specializes in transmitting signals to other neurons.
  - **Axon terminal**.
    - Contains **synaptic vesicles** that store **neurotransmitters**.

FIGURE 4.1: NEURONS HAVE:
CELL BODY, DENDRITES, AXON, AND AXON TERMINALS

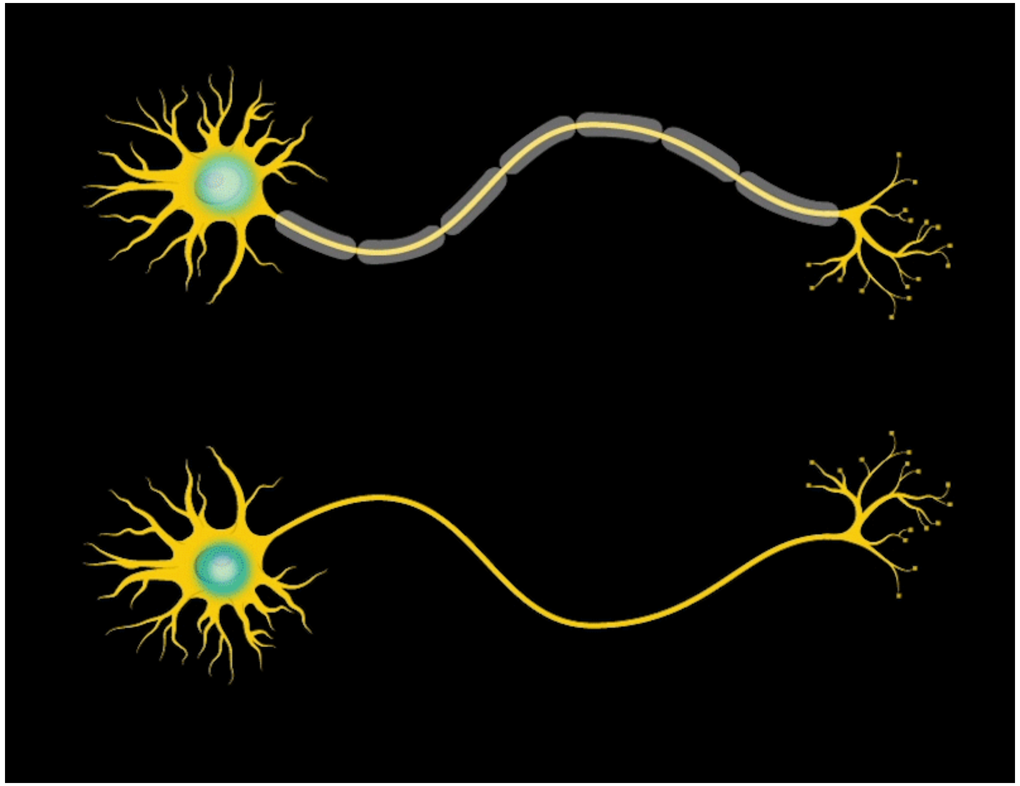


WHITE MATTER (AXONS, MYELIN) AND GRAY MATTER (CELLS)



NEURONS HAVE ACTION POTENTIALS

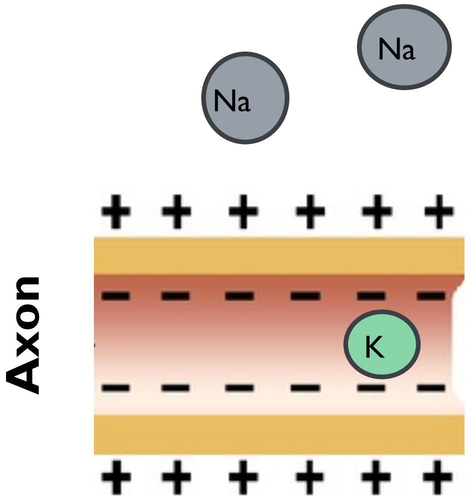
- An **Action potential** is, put most simply, a neuron "firing"
  - What is actually happening is a brief, very fast **electrical signal** is transmitted along the axon.
  - This signal is considered "all-or-none" – aka the neuron fires or it doesn't



How does an Action Potential, or neural firing occur?

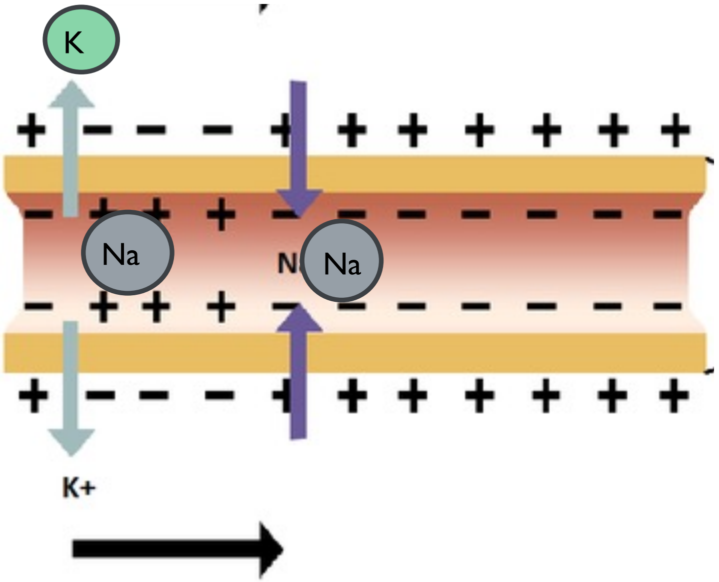
NEURONS ARE POLARIZED!

- This is caused by an uneven distribution of charged Na^+ and K^+ ions between the outside and inside of a neuron

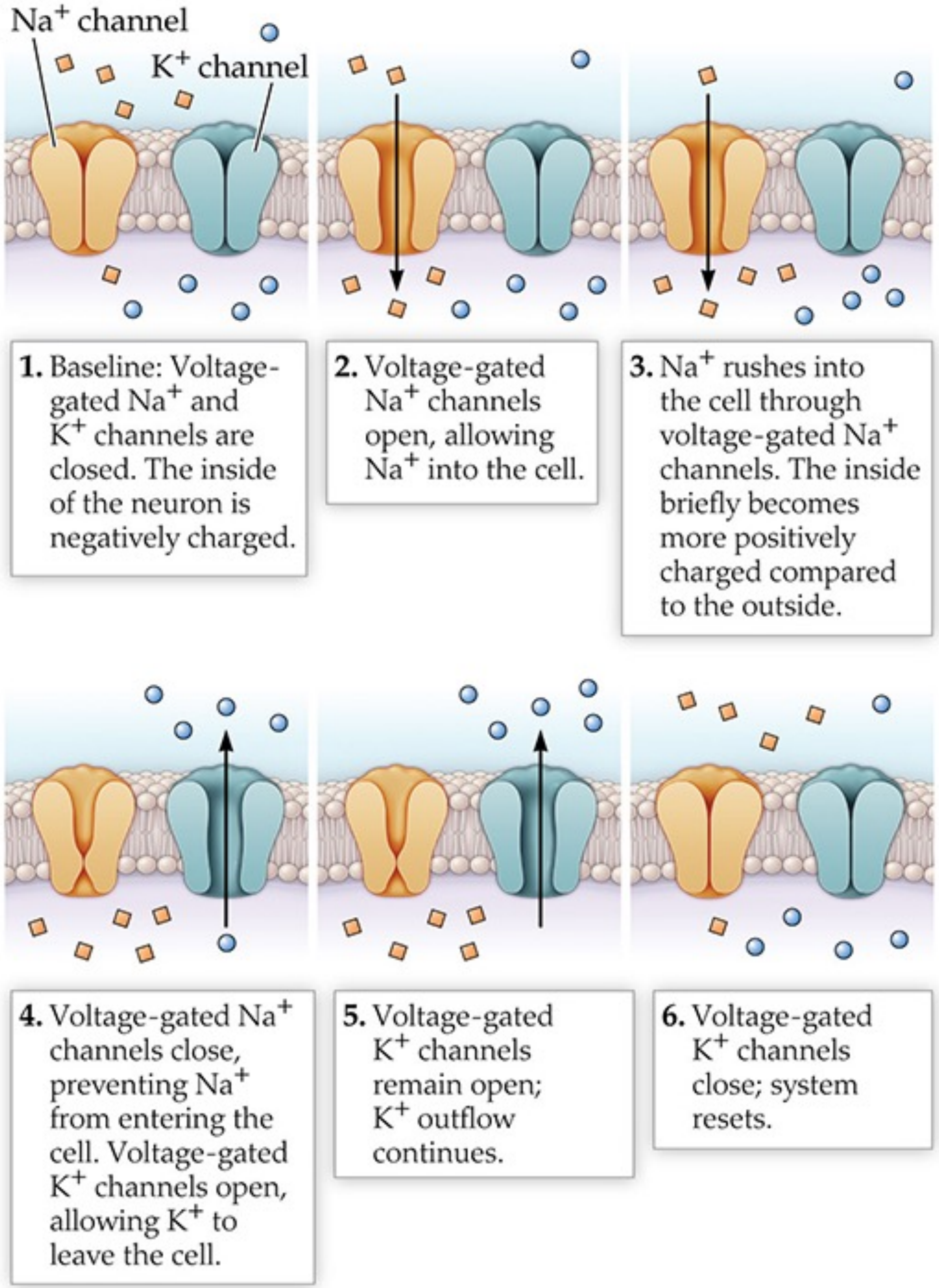


- Before a neuron fires, it is simply "resting" in a **hyperpolarized** state (aka there is a greater negative charge on the inside of the neuron than the outside.)
  - We call this "**Resting potential**"

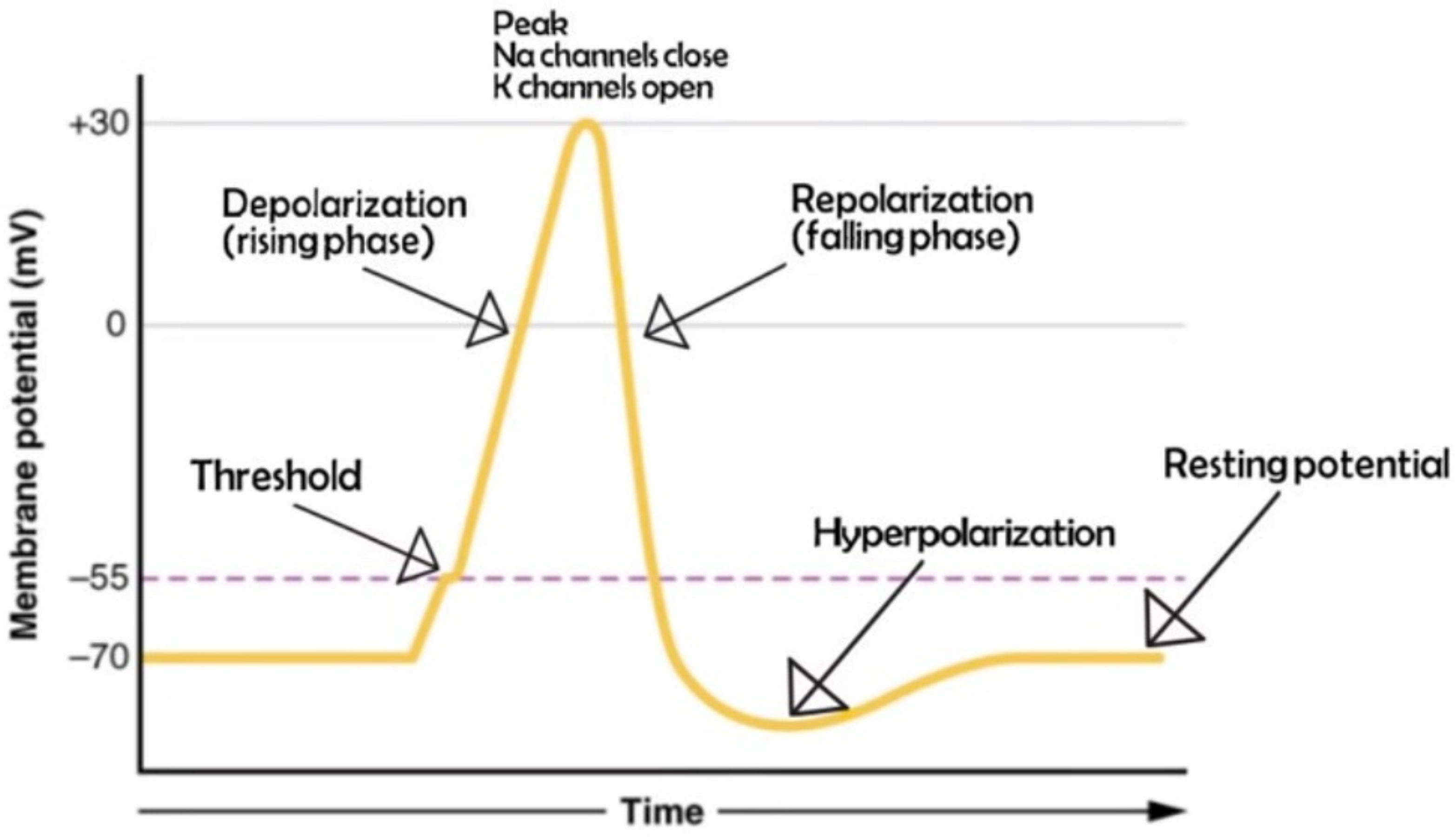
HOW DOES AN ACTION POTENTIAL HAPPEN? (AKA, HOW DOES A NEURON "FIRE"?)



- **Na+ Ion channels** on the neuron open.
  - Allows ions to move inside the cell, causing it to **depolarize**.
  - If the cell is depolarized to a **threshold** of excitation, an action potential occurs and the neuron fires!


Na$^+$ channel
K$^+$ channel
1. Baseline: Voltage-gated Na$^+$ and K$^+$ channels are closed. The inside of the neuron is negatively charged.
2. Voltage-gated Na$^+$ channels open, allowing Na$^+$ into the cell.
3. Na$^+$ rushes into the cell through voltage-gated Na$^+$ channels. The inside briefly becomes more positively charged compared to the outside.
4. Voltage-gated Na$^+$ channels close, preventing Na$^+$ from entering the cell. Voltage-gated K$^+$ channels open, allowing K$^+$ to leave the cell.
5. Voltage-gated K$^+$ channels remain open; K$^+$ outflow continues.
6. Voltage-gated K$^+$ channels close; system resets.

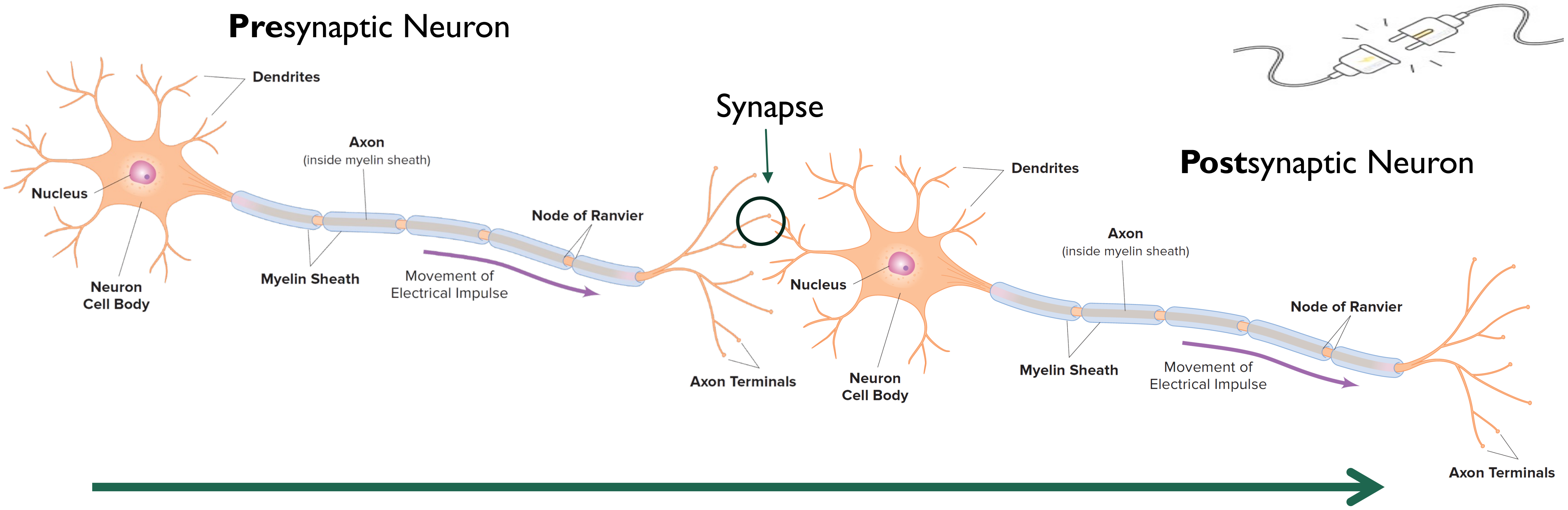
IONIC MOVEMENT AND MEMBRANE POTENTIALS



- We can chart these changes in membrane potentials during neural firing as a measure of time vs. voltage!

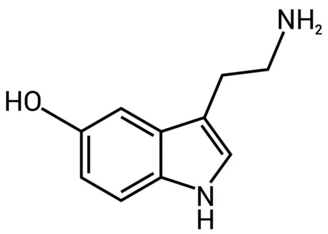
THE SYNAPSE AND NEUROTRANSMISSION

- **Neurotransmission -** transferring information from one neuron to another at a synapse
  - Occurs via an action potential causing the <u>release</u> **neurotransmitter** into the synapse.

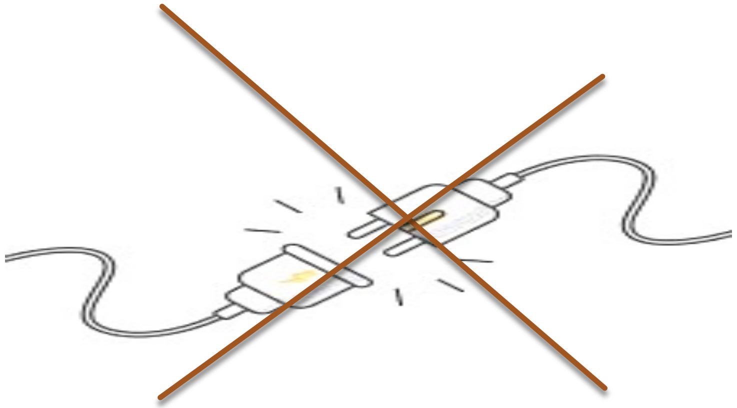


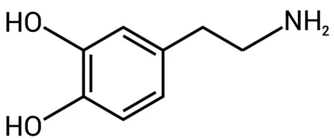
WHAT IS A NEUROTRANSMITTER?

- **Neurotransmitters** are endogenous chemicals that allow neurons to communicate with each other throughout the body.
- Critical/major ones to know are:
  - 1) Dopamine (DA)
  - 2) Norepinephrine (NE)
  - 3) Serotonin (5-HT)
  - 4) Acetylcholine (ACh)
  - 5) GABA
  - 6) Glutamate (Glut)
  - 7) Peptide hormones (incl. endogenous opioids)
  - 8) Endocannabinoids



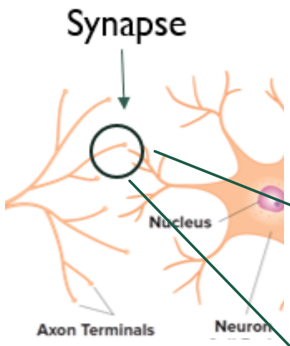
Serotonin



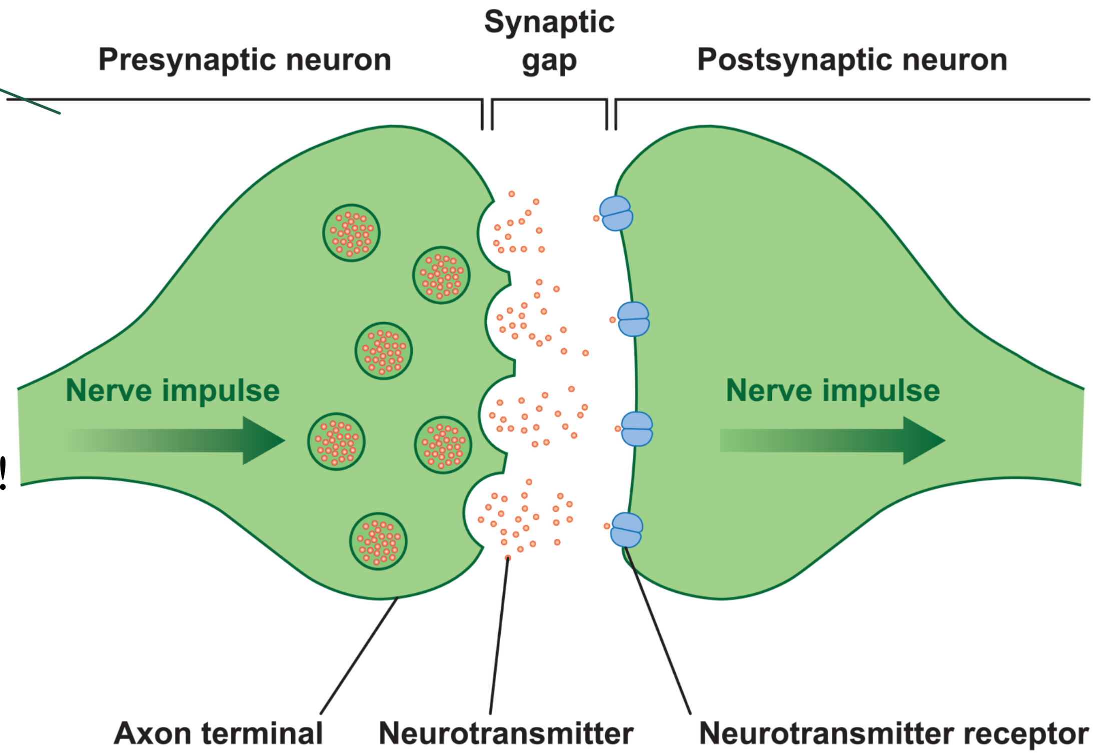


Dopamine

- Ultimately the action potential results in release of neurotransmitter into the **synapse**
  - **= a chemical signal**
  - Think of the whole action potential process as one that converts an electrical signal (the action potential) into a chemical signal (neurotransmitter release)



Synaptic Transmission



Action potential!

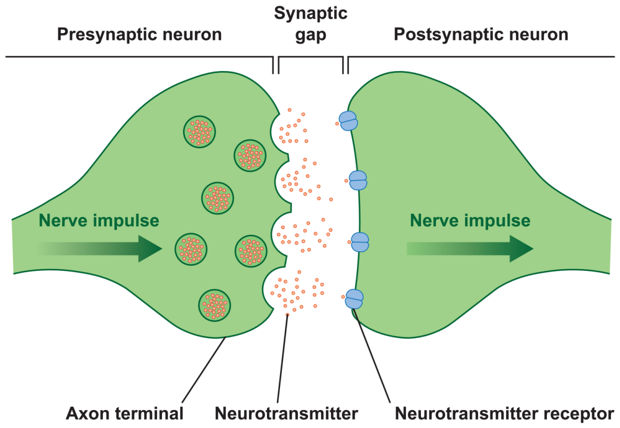
…Action potential?

…maybe…

EXCITATORY VS. INHIBITORY NEURAL SIGNALING

- When neurotransmitter is released by one neuron, that neurotransmitter can make the *next* neuron either <u>more</u> or <u>less</u> likely to have an action potential.
  - <u>Excitatory postsynaptic potential (EPSP)</u>: neurotransmitter causes next neuron to **be more likely** to fire
    - Also known as a **depolarization**
  - <u>Inhibitory postsynaptic potential (IPSP)</u>: neurotransmitter causes the next neuron to be **less likely** to fire
    - Also known as a **hyperpolarization**

- **When a neurotransmitter binds its receptor, this ends the process of the chemical signal.**



NEUROTRANSMISSION

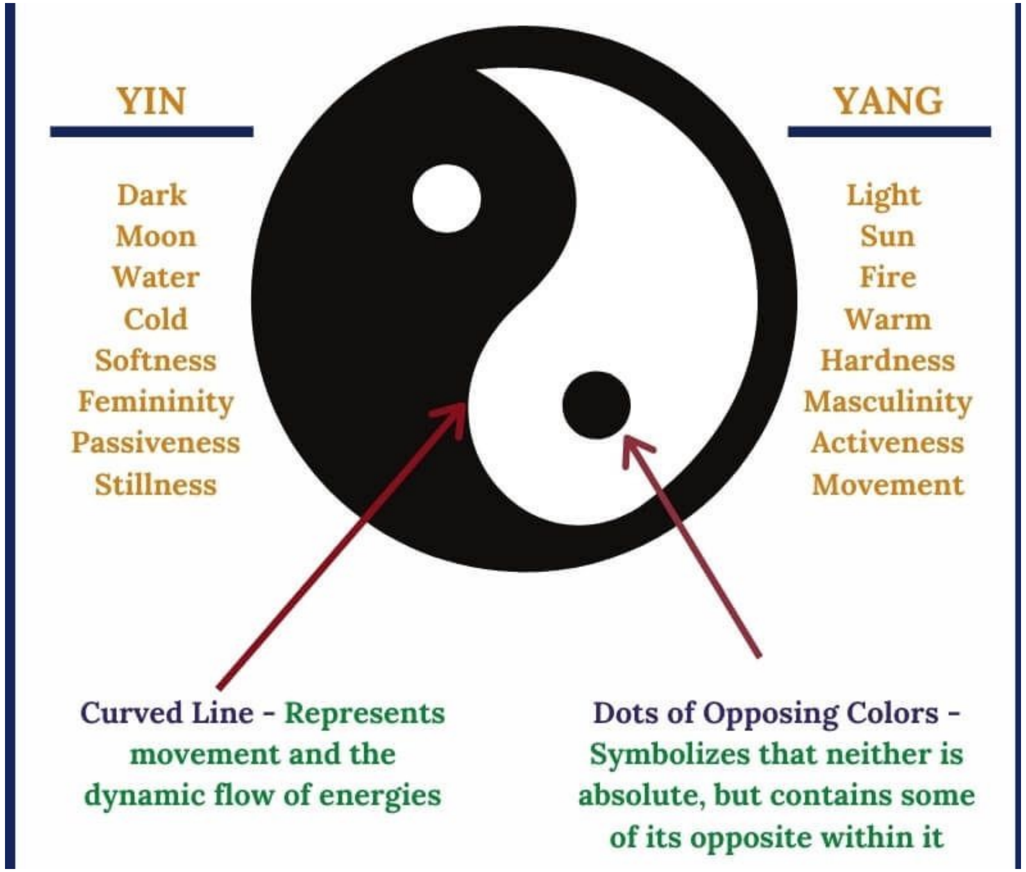
CHEMICAL THEORIES OF BEHAVIOR HISTORICALLY

- Many attempts have been made to explain normal variations in behavior in terms of changes in brain and body chemistries.

Historical precedents included…

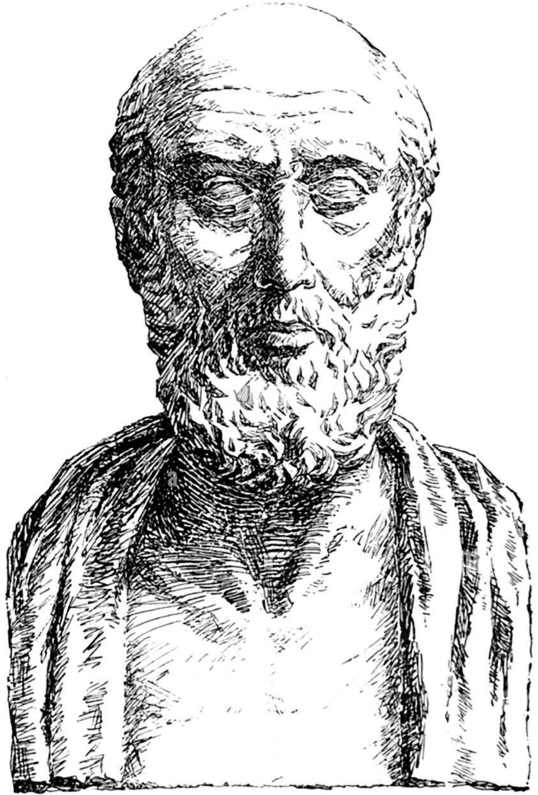
CHEMICAL THEORIES OF BEHAVIOR

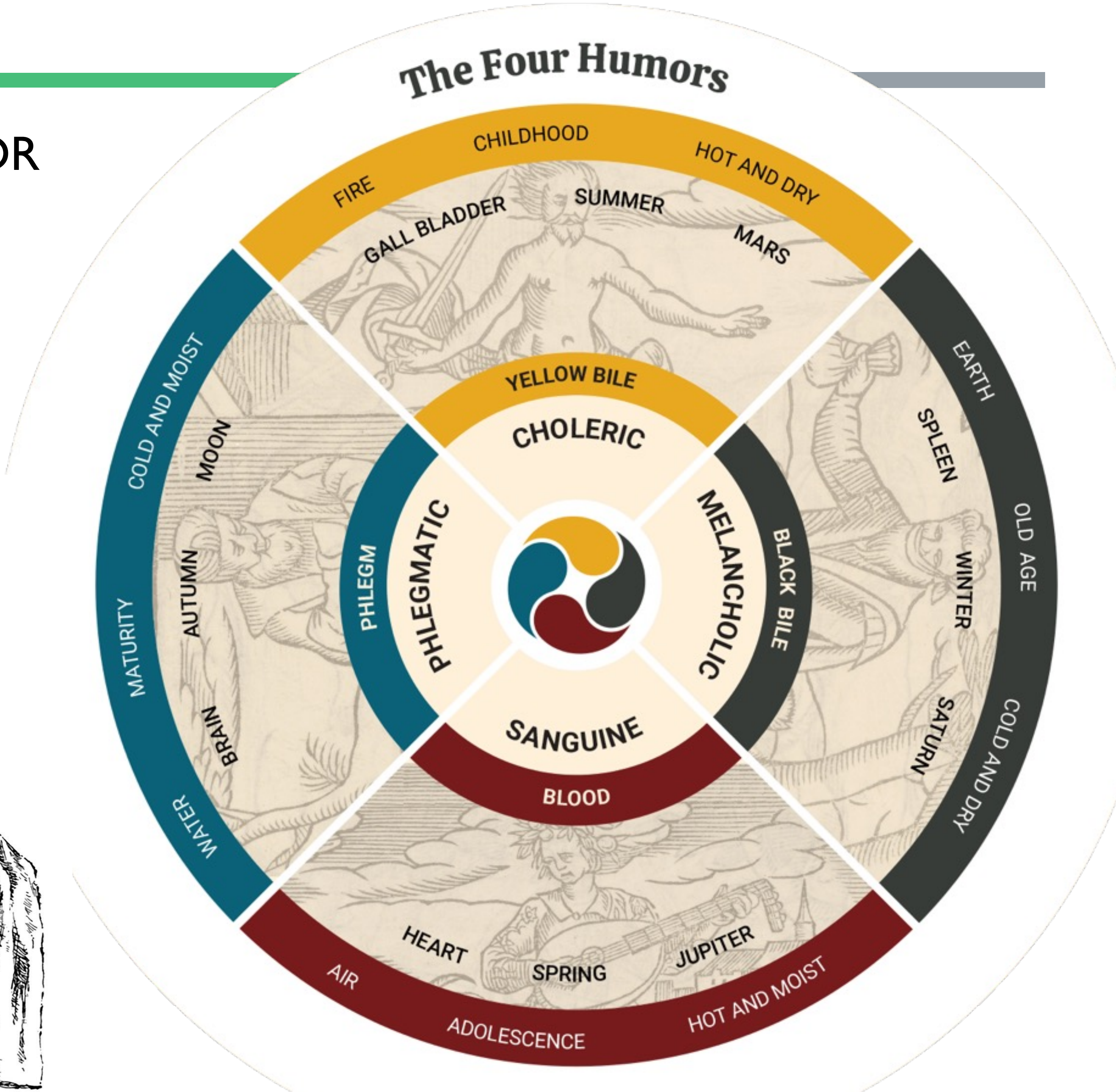
Chinese philosophy of *yin* and *yang*.



CHEMICAL THEORIES OF BEHAVIOR

Greek physician Hippocrates and the four humors: blood, phlegm, yellow bile, and black bile.





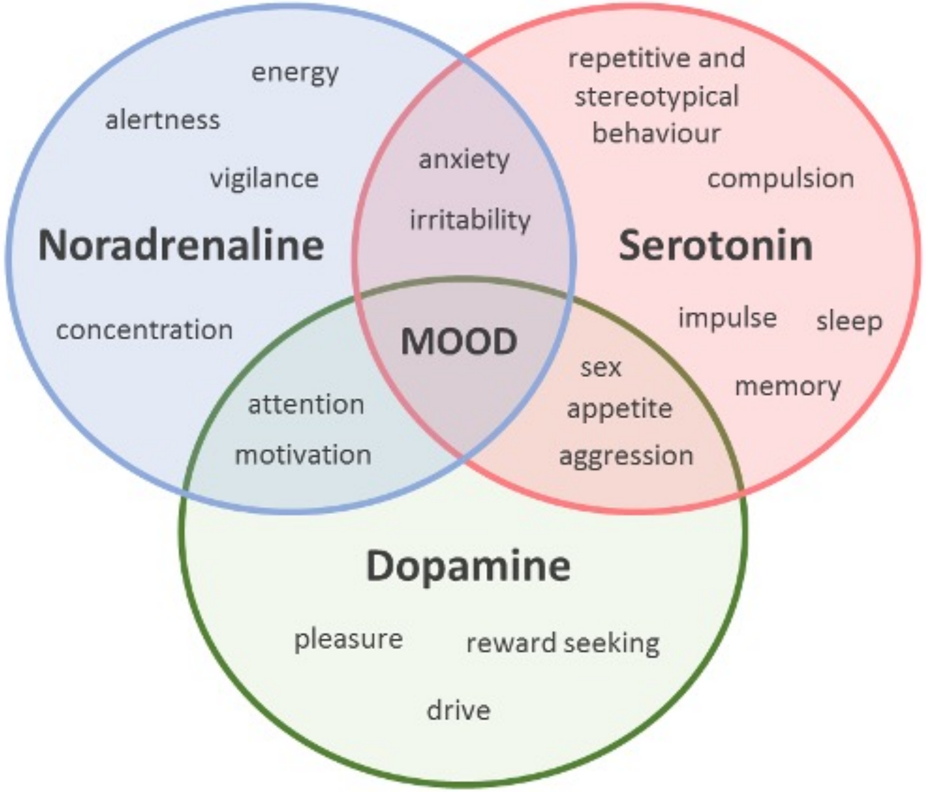
CHEMICAL THEORIES OF BEHAVIOR – MODERN DAY

Neuropharmacology

- What is pharmacology?
  - "The science of drugs"
  - Greek words
    - *pharmakos*, refers to a poisoner, a magician, or a sorcerer
      - Evolved to later mean "a magical substance"
    - *logos*, 'to study'
- Why neuropharmacology?

CHEMICAL THEORIES OF BEHAVIOR

The major theory guiding the clinical treatment of neuropsychological disorders hinges upon the fact that disruptions or dysregulation of neural activity in the monoamine neurotransmitters can alter mood and behavior.



CHEMICAL THEORIES OF BEHAVIOR – MODERN DAY

- 1) Dopamine (DA)
- 2) Norepinephrine (NE)
- 3) Serotonin (5-HT)
- 4) Glutamate (Glut)
- 5) GABA
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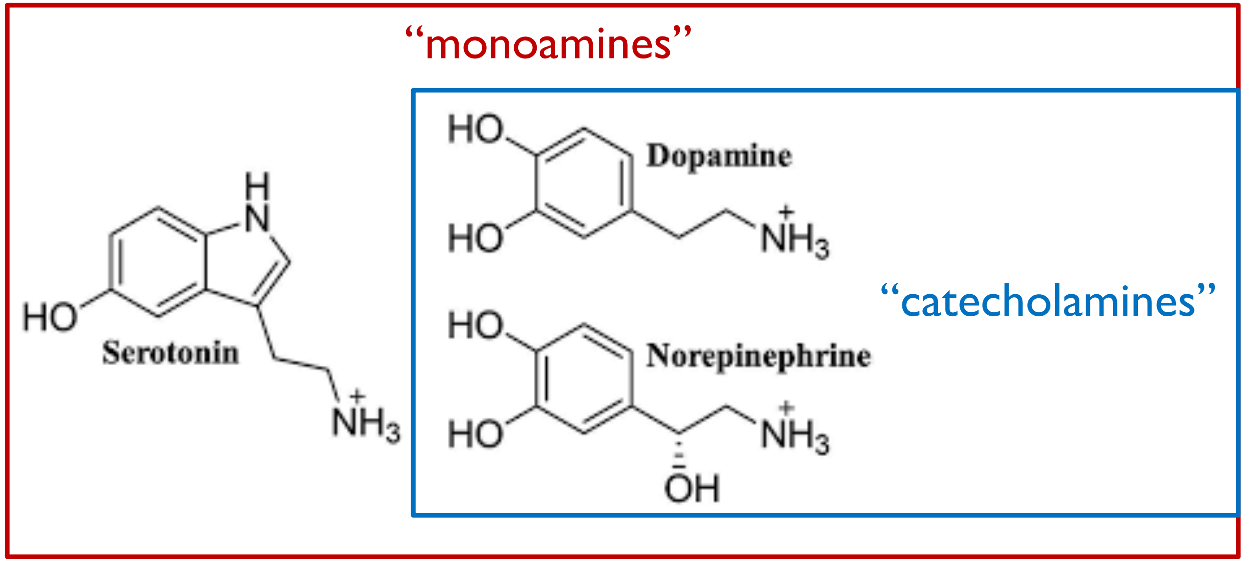
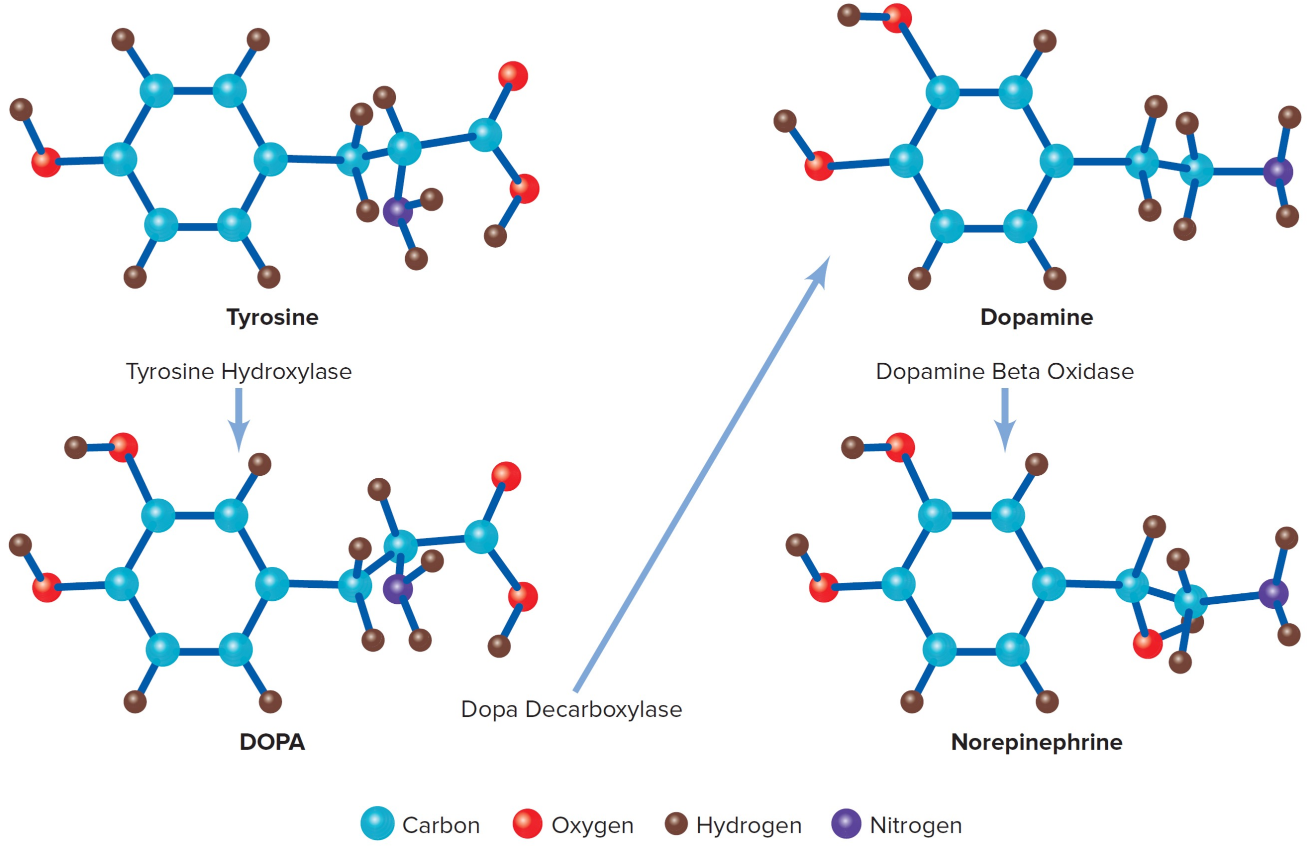


GENERATION OF NEUROTRANSMITTERS

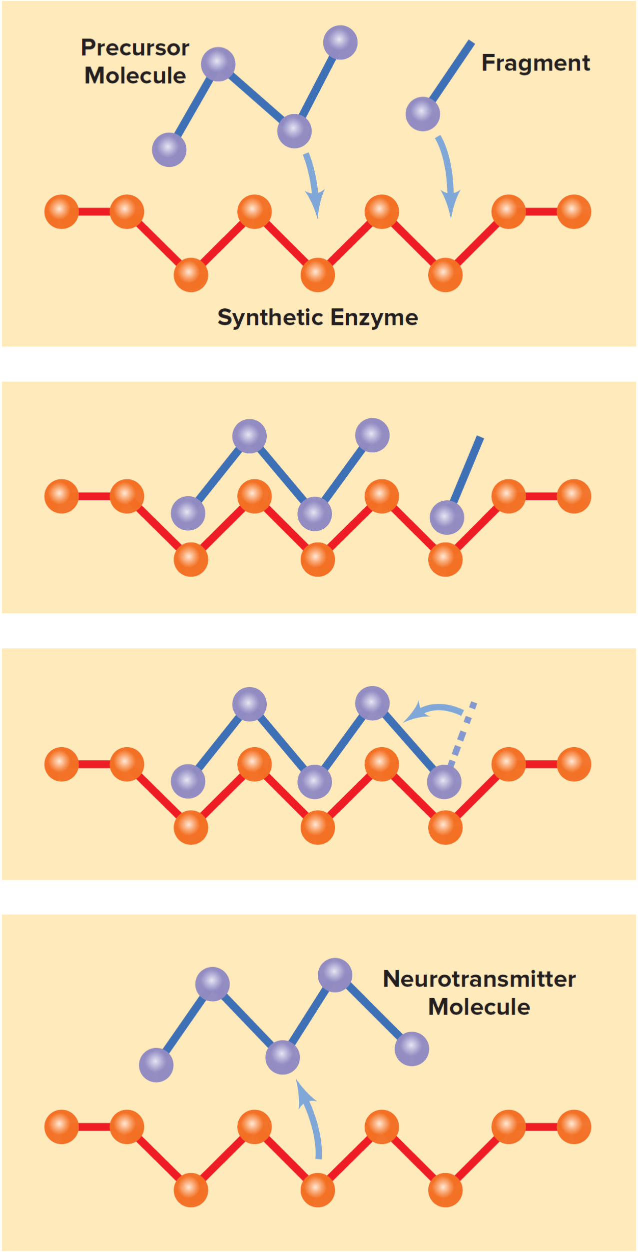
- Neurotransmitter precursors are found circulating in the blood supply and in the brain.
  - certain selected precursors are taken up by neurons, then stored in **synaptic vesicles**.



Catecholamine synthesis of the neurotransmitters Dopamine and Norepinephrine

LIFE CYCLE OF A NEUROTRANSMITTER

- Step 1: Uptake/**Synthesis**.
  - Precursors are synthesized into neurotransmitters through the actions of **enzymes**.
- Step 2: **Storage**.
  - Neurotransmitters are stored in synaptic vesicles near the terminal from which they will be released.
  - For monoamines, done via the "vesicular monoamine transporter" or "**VMAT**" enzyme

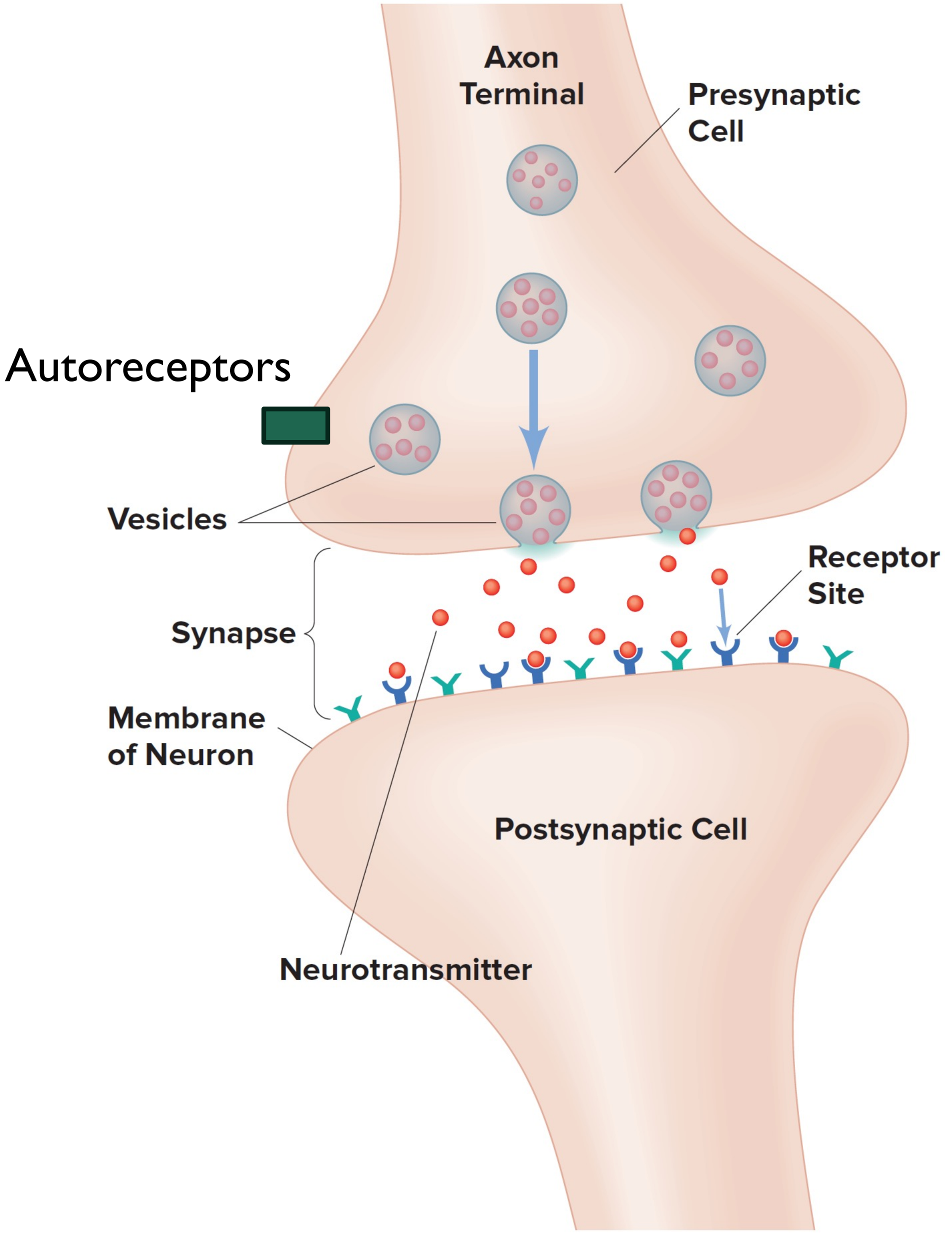


LIFE CYCLE OF A NEUROTRANSMITTER

- Step 3: **Release**.
  - When the action potential arrives, neurotransmitters are released into the **synapse**.

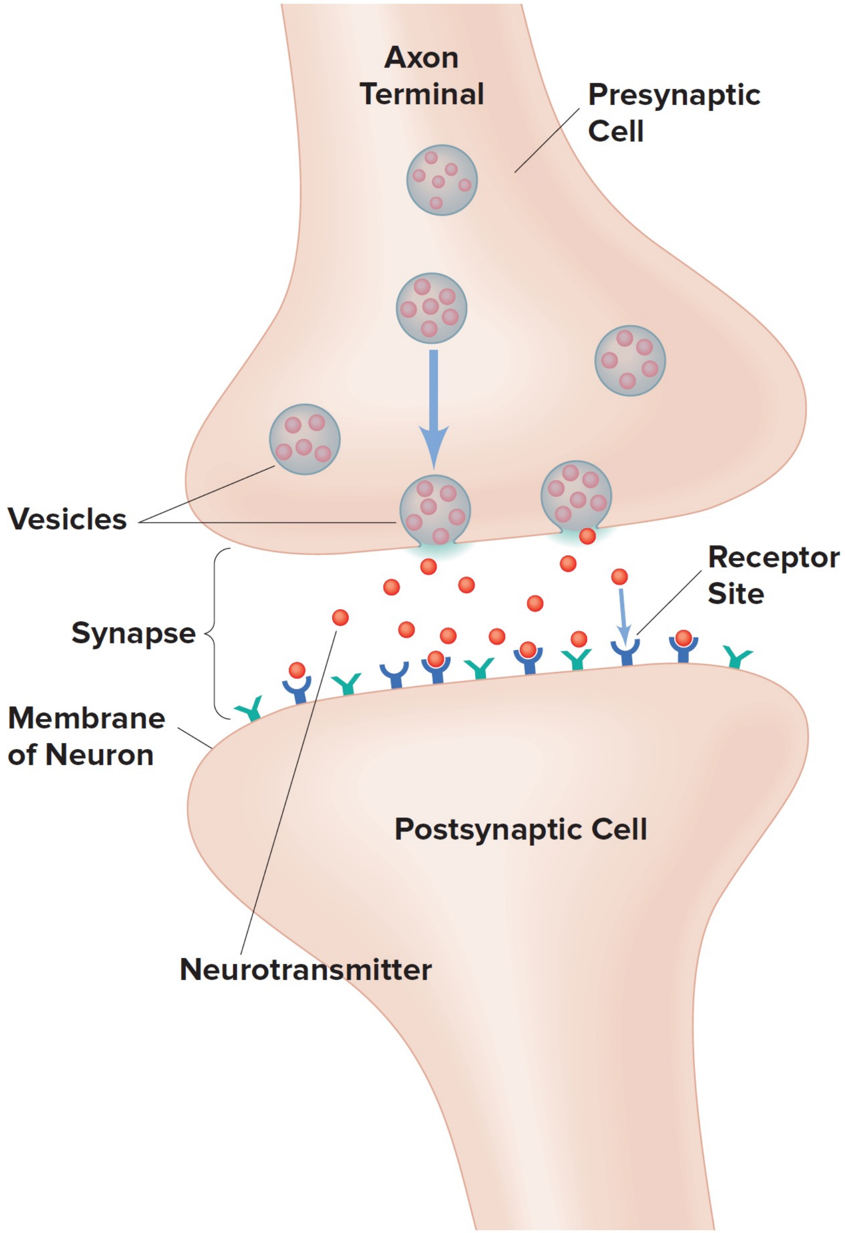
Autoreceptor – (presynaptic) help to self regulate the amount of neurotransmitter released

Binding to the autoreceptors tells the neuron to halt synthesis and release – a homeostatic feedback loop!



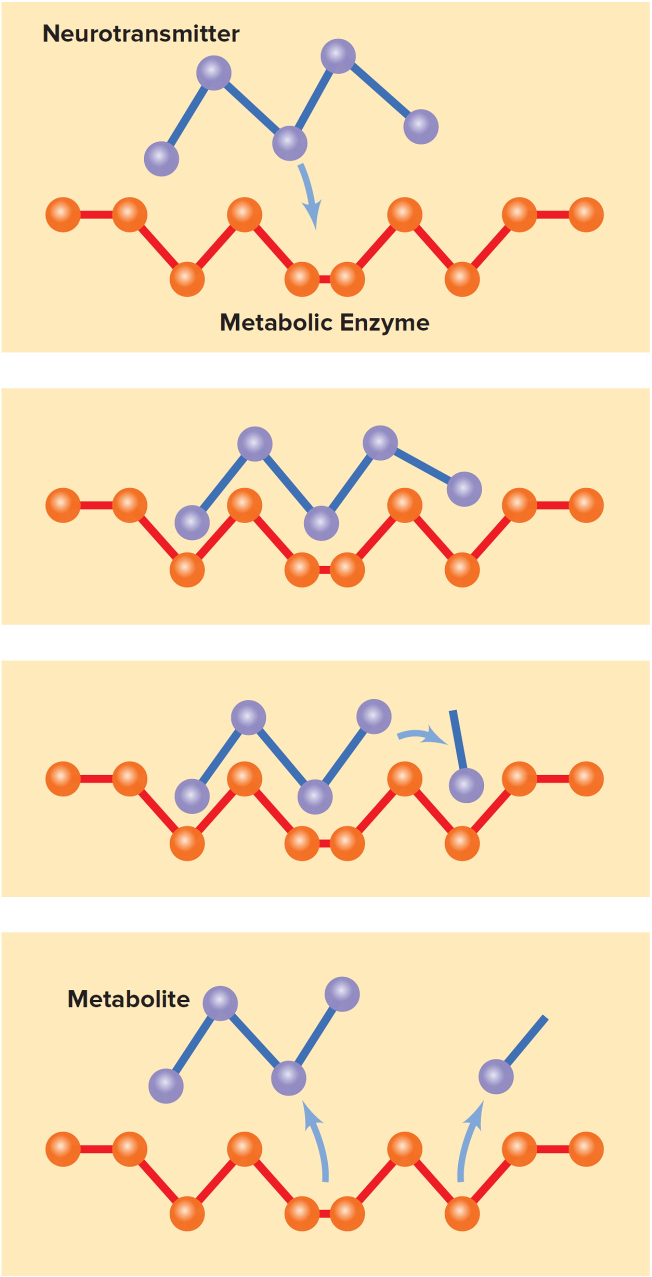
LIFE CYCLE OF A NEUROTRANSMITTER

- Step 4: **Binding**.
  - Released neurotransmitters bind with receptors on the membrane of the **postsynaptic cell**.
  - Neurotransmitters may have excitatory or inhibitory effects depending on the type of receptor.



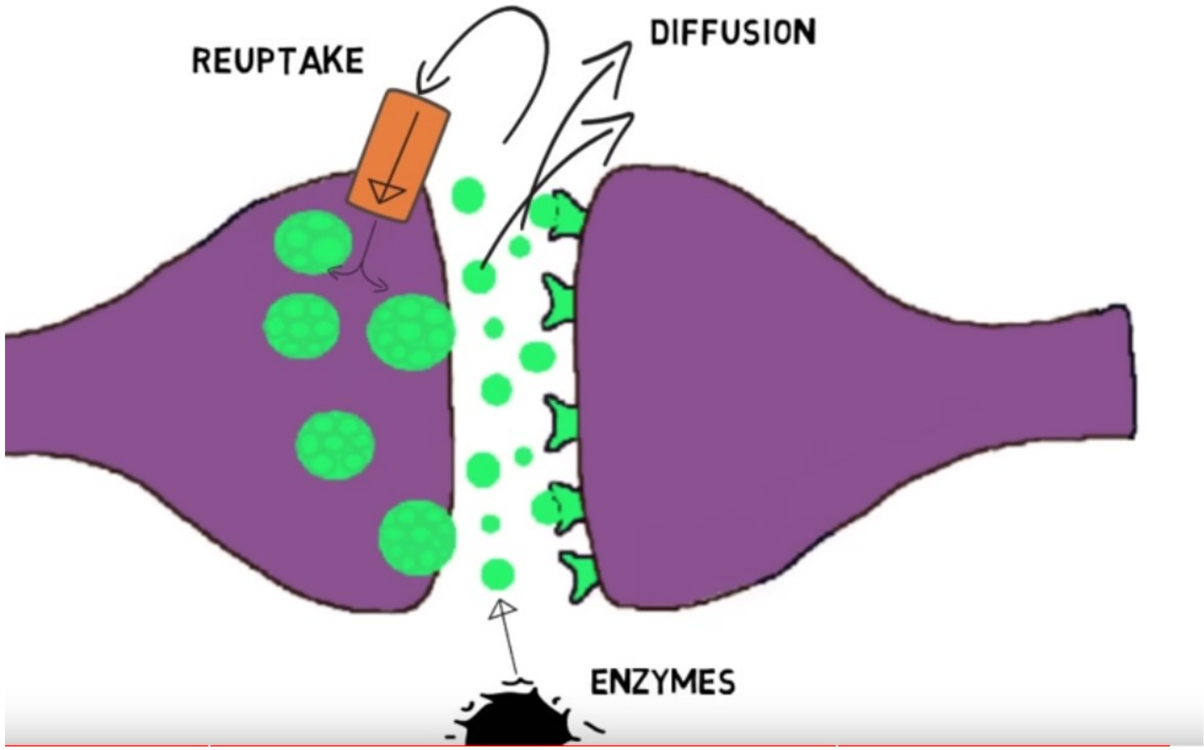
LIFE CYCLE OF A NEUROTRANSMITTER

- Step 5: **Metabolism**.
  - Once a signal has been sent, neurotransmitters are removed from the synapse.
  - Two major enzymes to know in this breakdown process:
    - MAO – monoamine oxidase
    - COMT – Catechol-O-methyltransferase



NEUROTRANSMITTER DEGRADATION AND REUPTAKE

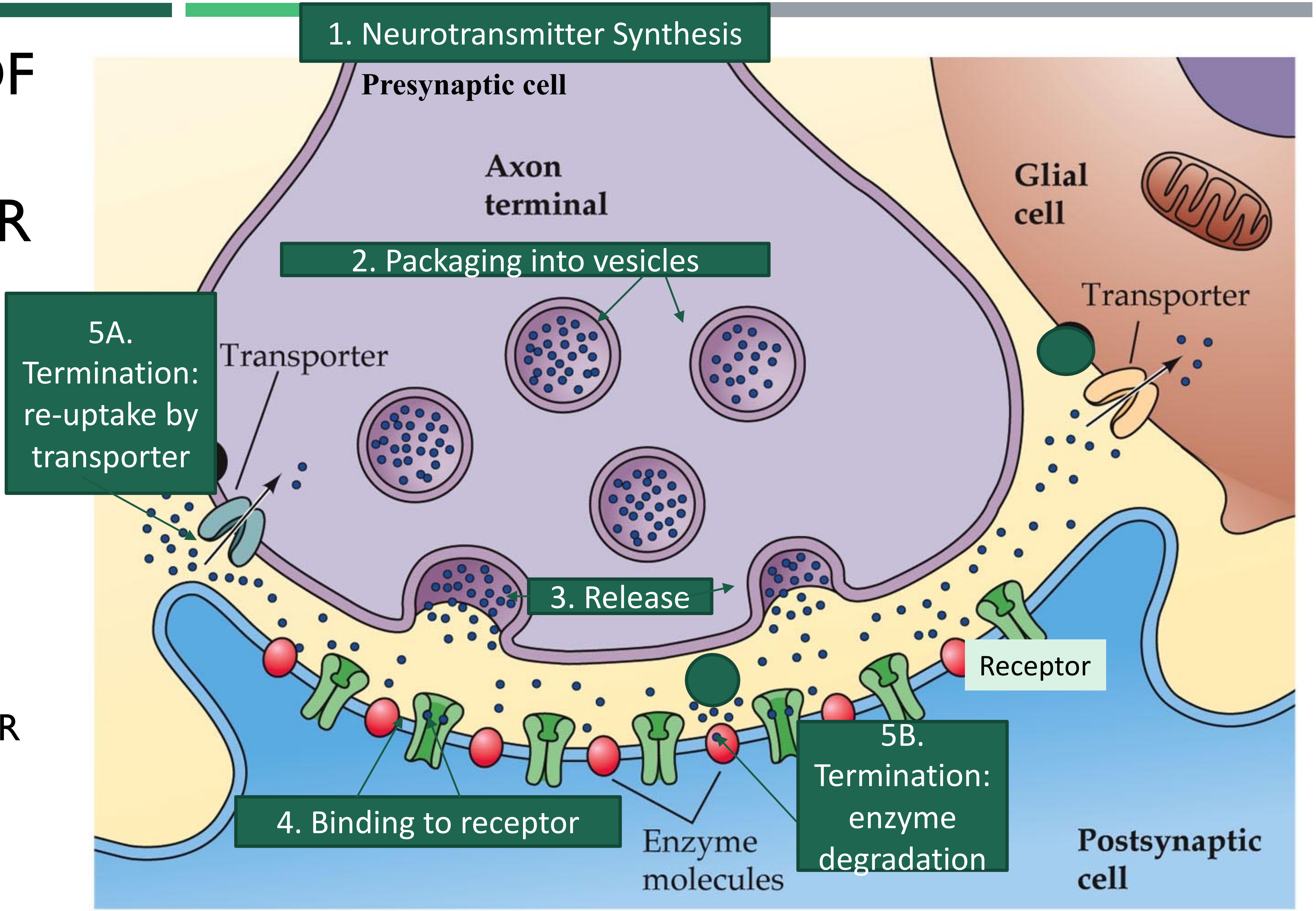
- https://www.youtube.com/watch?v=WhowH0kb7n0



LIFE CYCLE OF A NEURO-TRANSMITTER

5 MAJOR "STEPS"

FOR NEUROTRANSMITTER SIGNALING AT A SYNAPSE…



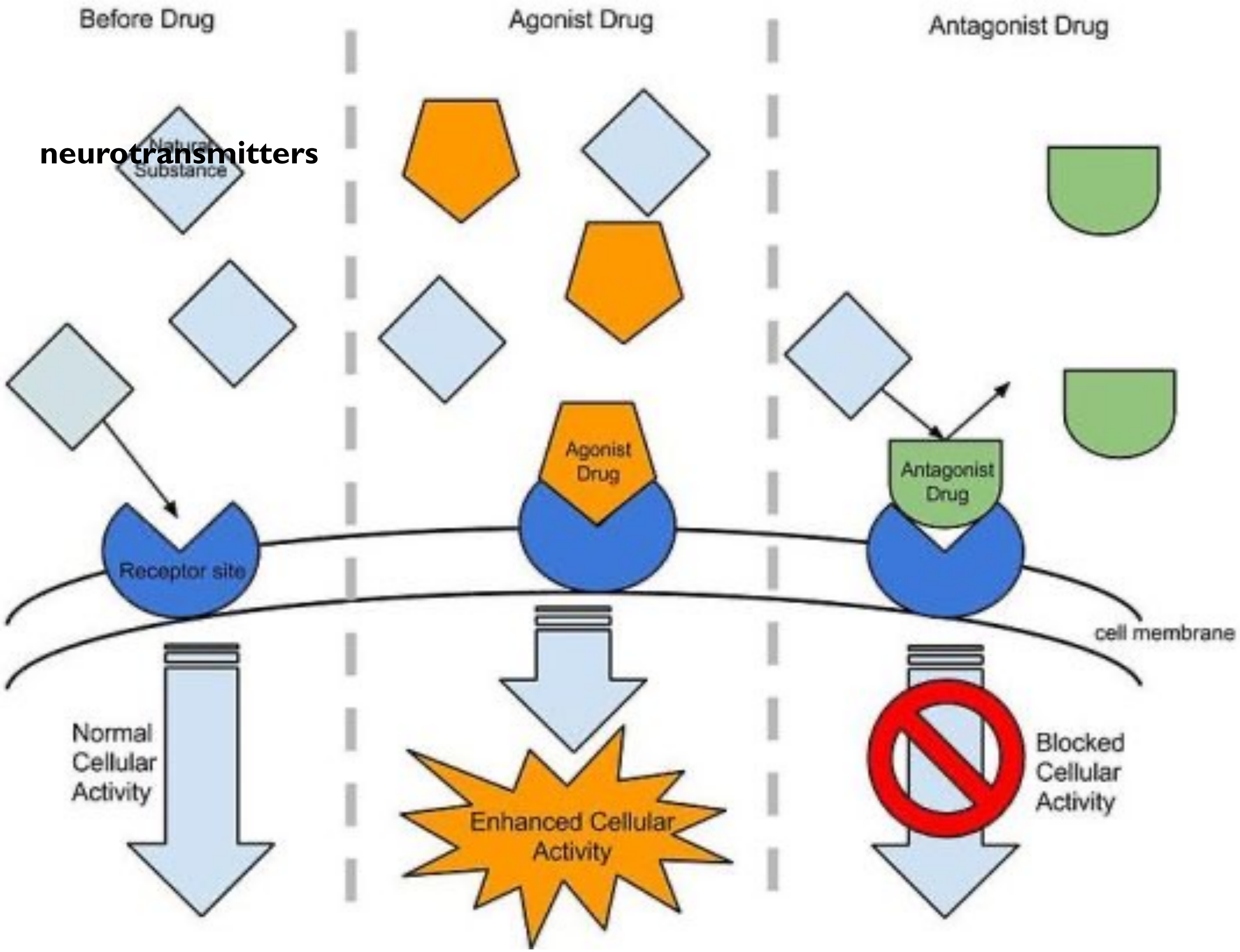
Zoomed in at the synapse…

Why do *we* care so much about neurotransmitters?

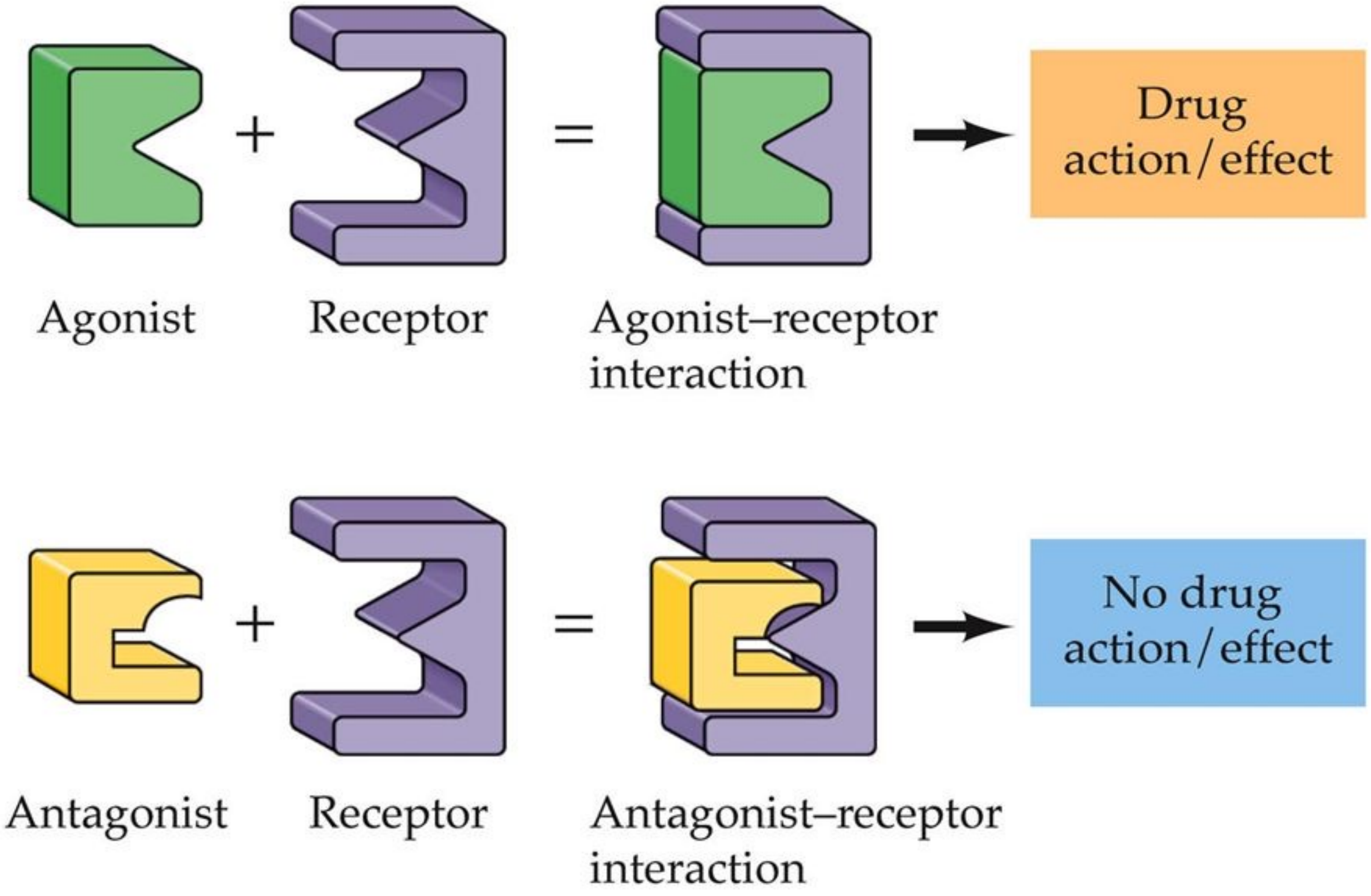
MOST drugs act (i.e., exert their function) at sites where neurotransmitters act!

DRUGS AT THE SYNAPSE - KEY TERMS

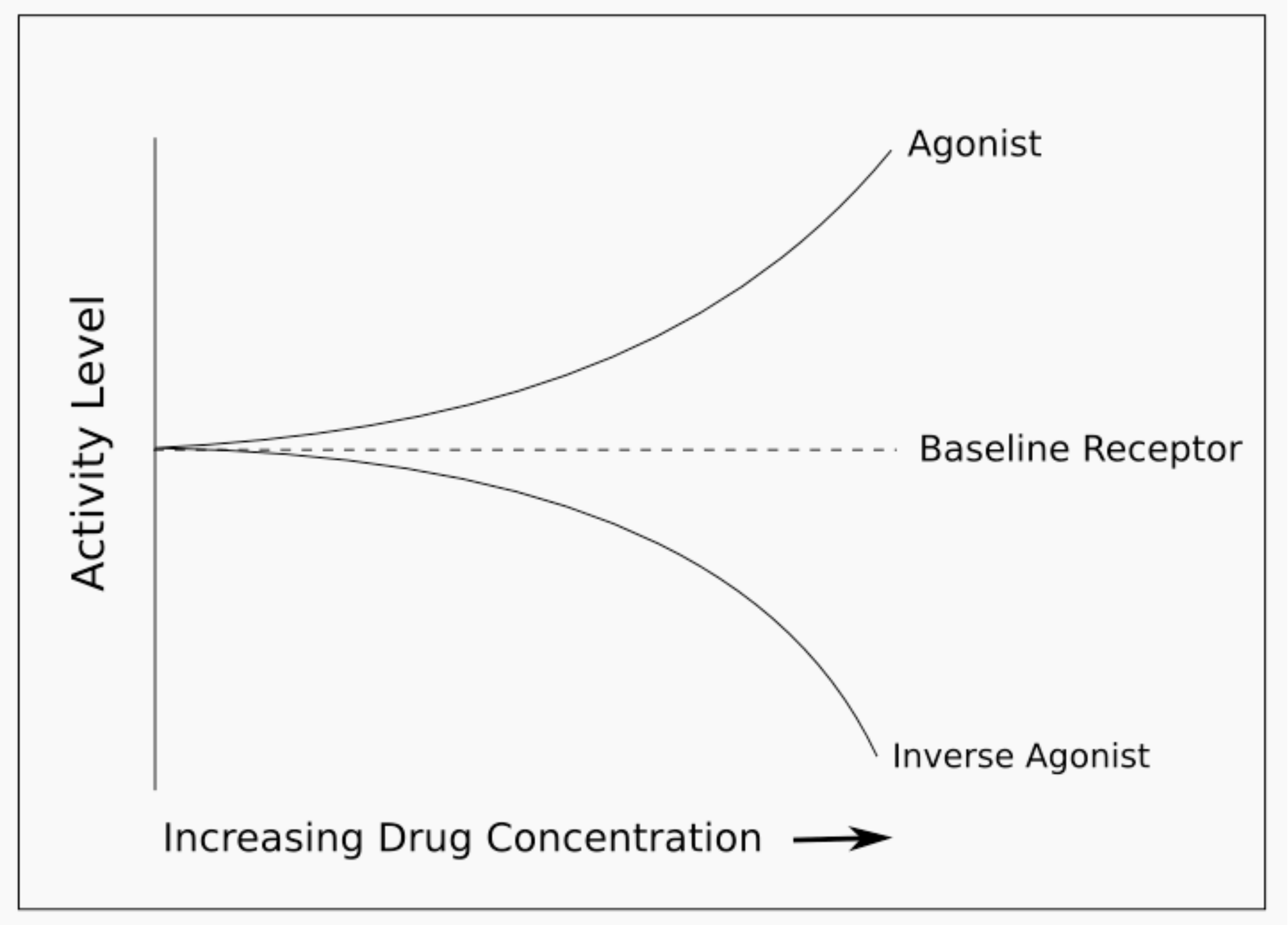
- **Ligand**: activating molecule (i.e., drug)
  - **agonist** *mimics* the action of neurotransmitters by activating the receptor.
  - **antagonist** occupies the receptor and prevents the neurotransmitter from activating it.



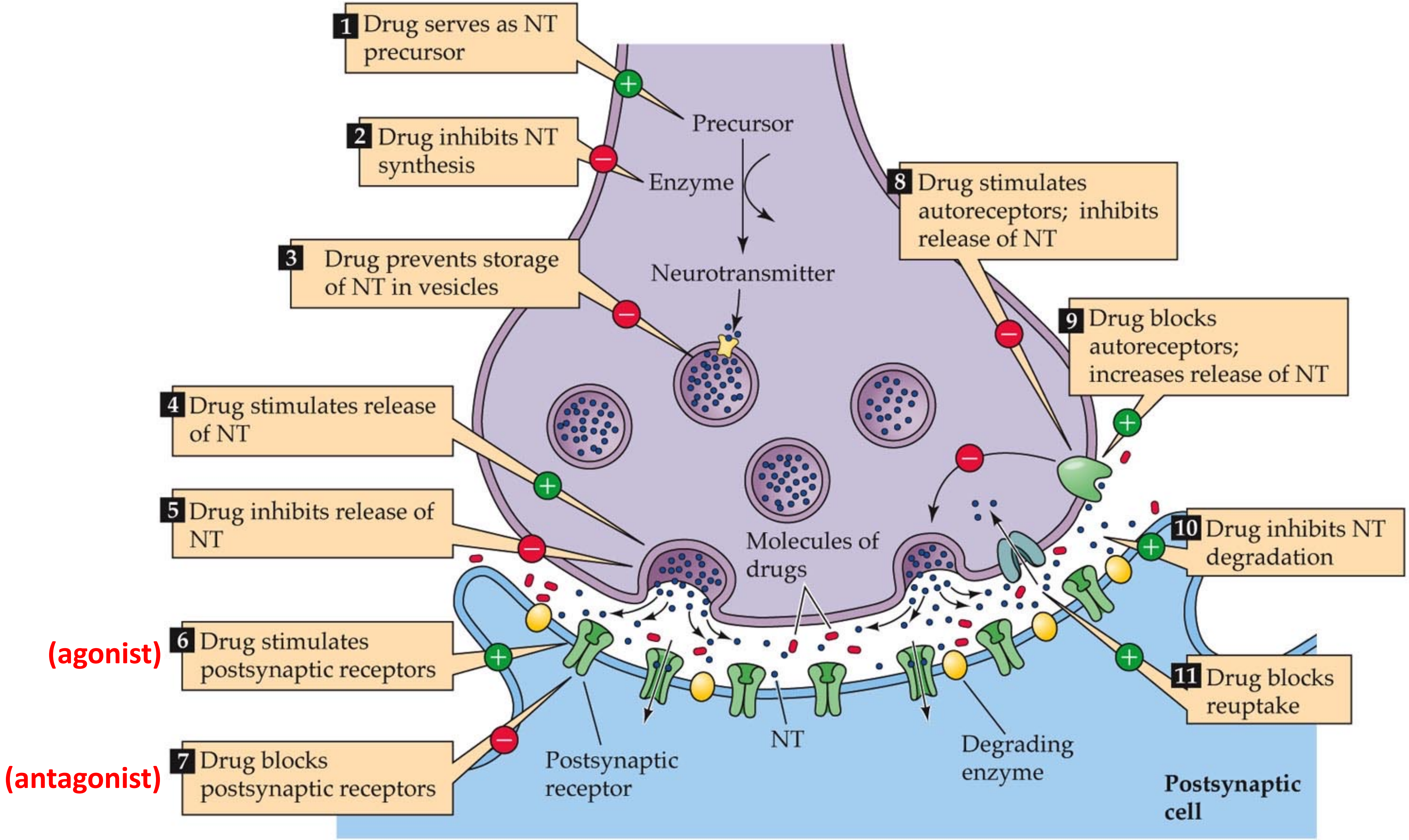
Agonist and antagonist interactions with receptors



PSYCHOPHARMACOLOGY, Figure 1.11 © 2005 Sinauer Associates, Inc.


Agonist
Activity Level
Baseline Receptor
Inverse Agonist
Increasing Drug Concentration

How drugs can alter neurotransmitter lifecycle



1) Act as neurotransmitter precursor -
2) Inhibit NT synthesis -
3) Prevent storage of NT in vesicles -
4) Stimulate release of NT -
5) Inhibit release of NT -
6) Stimulate (i.e., bind to and activate) postsynaptic receptor -
7) Block postsynaptic receptor -
8) Stimulate autoreceptor -
9) Block autoreceptor -
10) Inhibit metabolism of NT -
11) Block reuptake (transporter) -

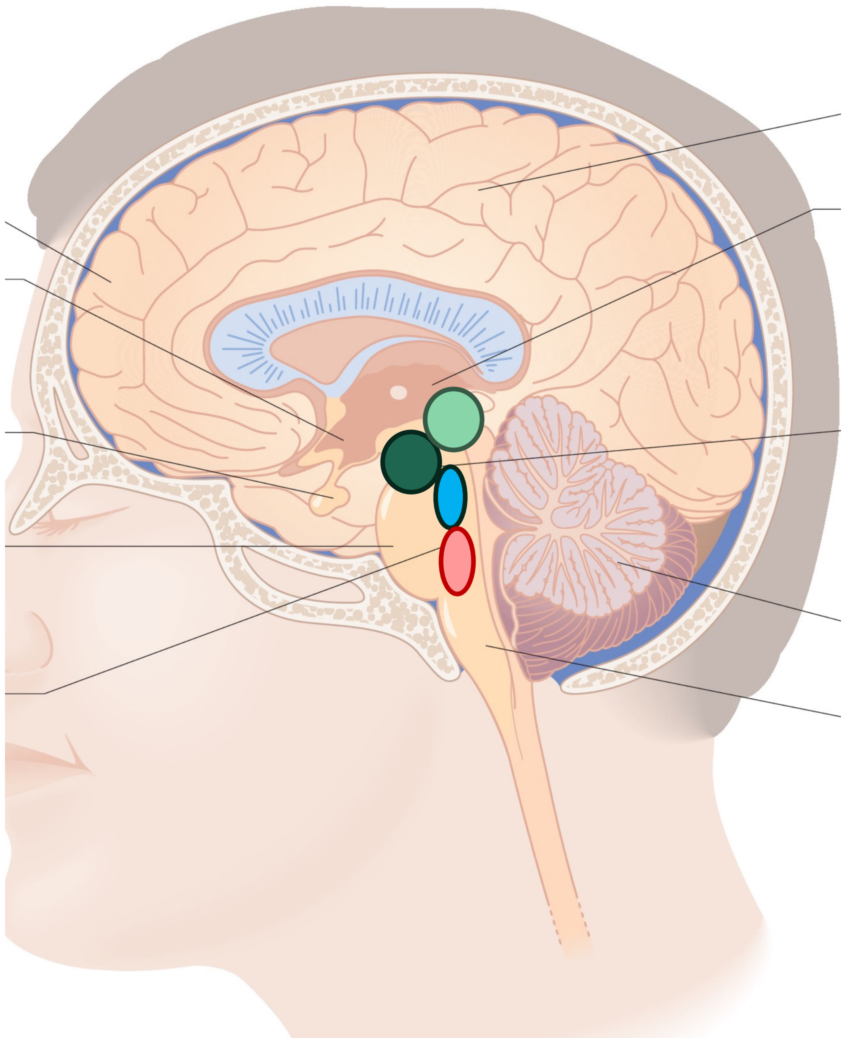
THE MAJOR NEUROTRANSMITTER SYSTEMS AND SYNTHESIS SITES

1) Dopamine (DA)
2) Norepinephrine (NE)
3) Serotonin (5-HT)

4) Glutamate
5) GABA

6) Acetylcholine (ACh)

7) Peptide hormones (incl. endogenous opioids)
8) Endocannabinoids



VTA - Ventral Tegmental Area

Substantia Nigra

Locus Coeruleus

Dorsal Raphe

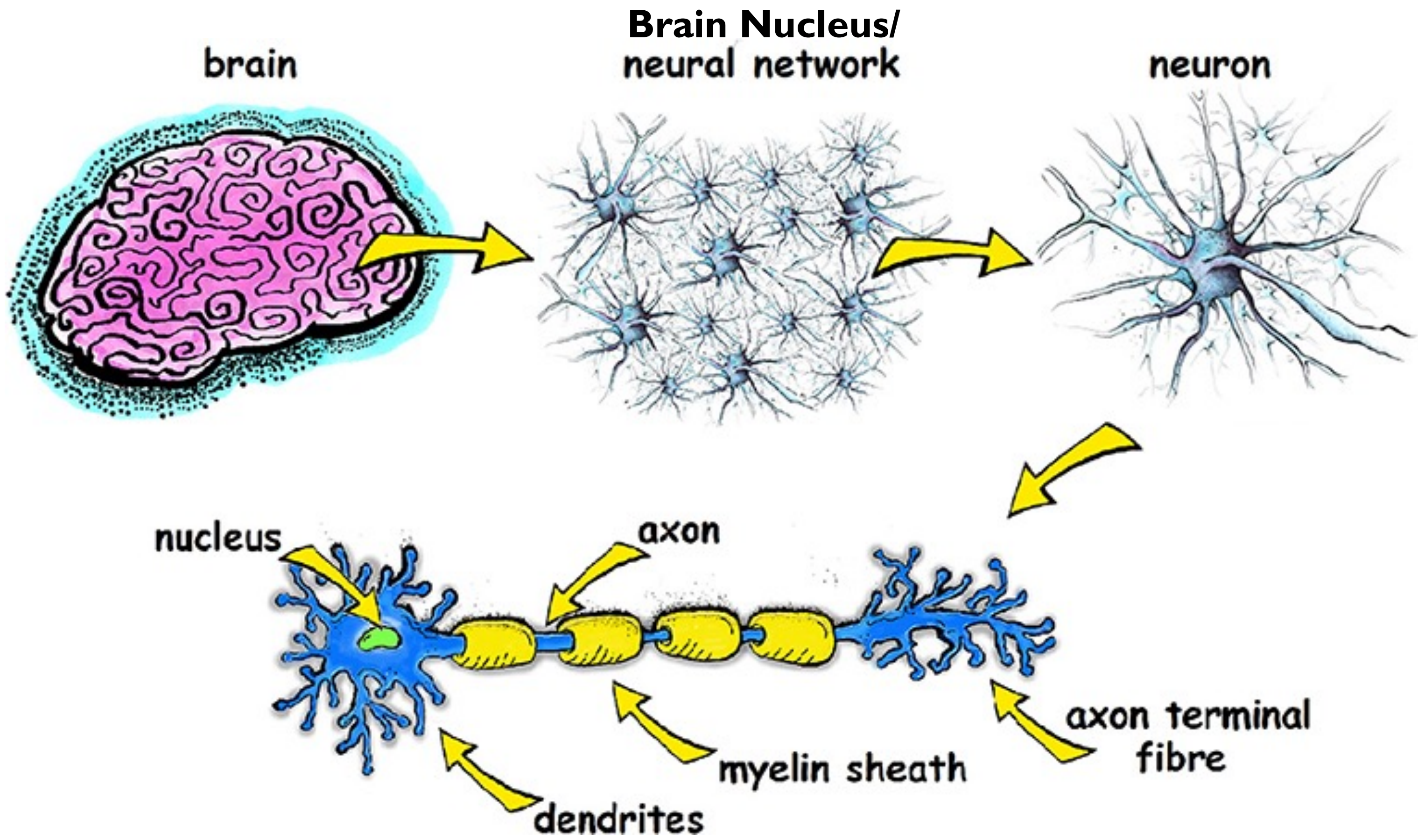
ONE NEURON … ONE NEUROTRANSMITTER? NOPE.

- Some 100 neurotransmitters and counting…
- Most, if not all neurons synthesize and release more than 1 neurotransmitter
  - Often physically separated from each other or released at different times/due to different stimulation
  - So, we are typically referring to the <u>primary</u> neurotransmitter released
- Furthermore, neurotransmitters are everywhere in your body… not just your brain!

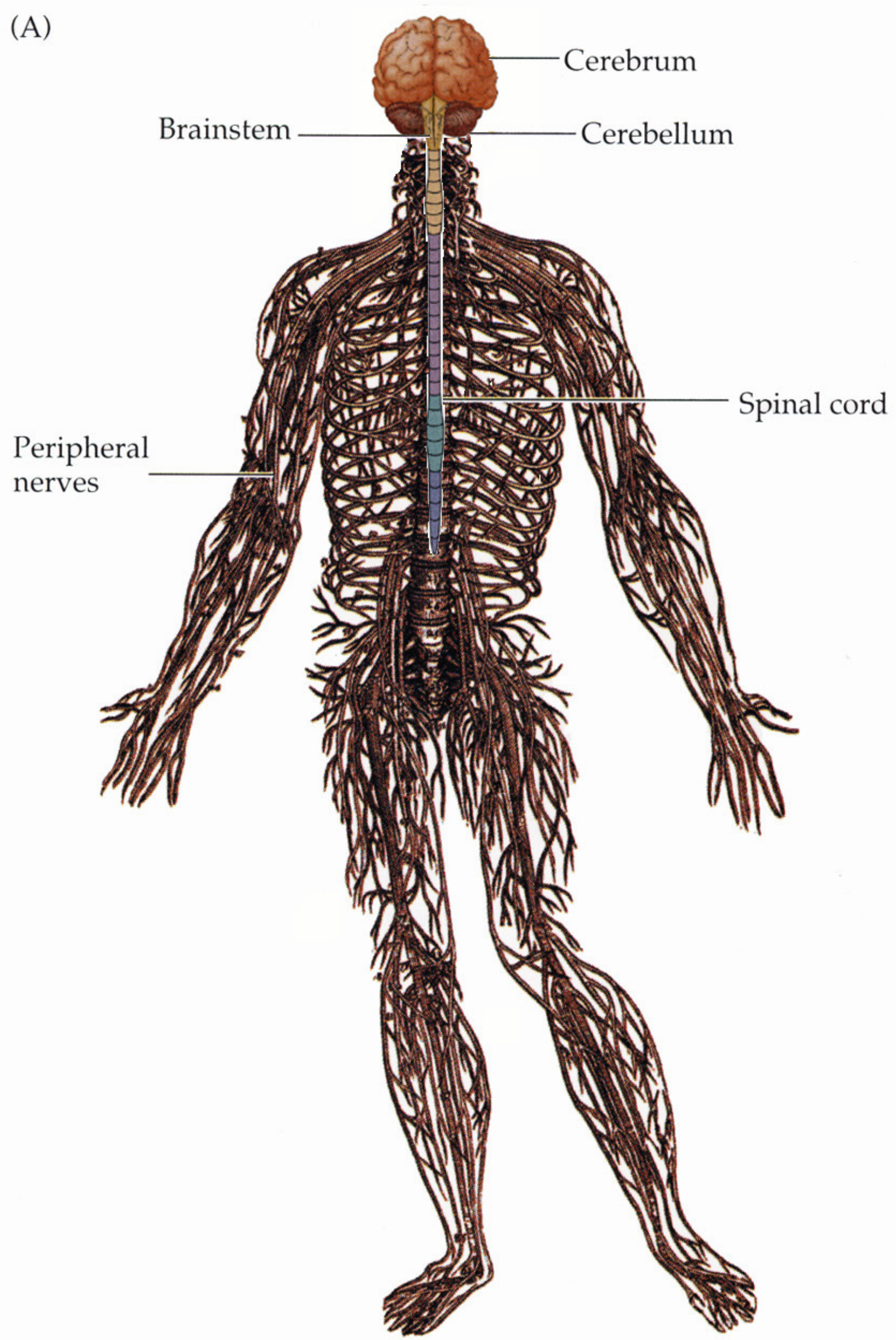
THE NERVOUS SYSTEM

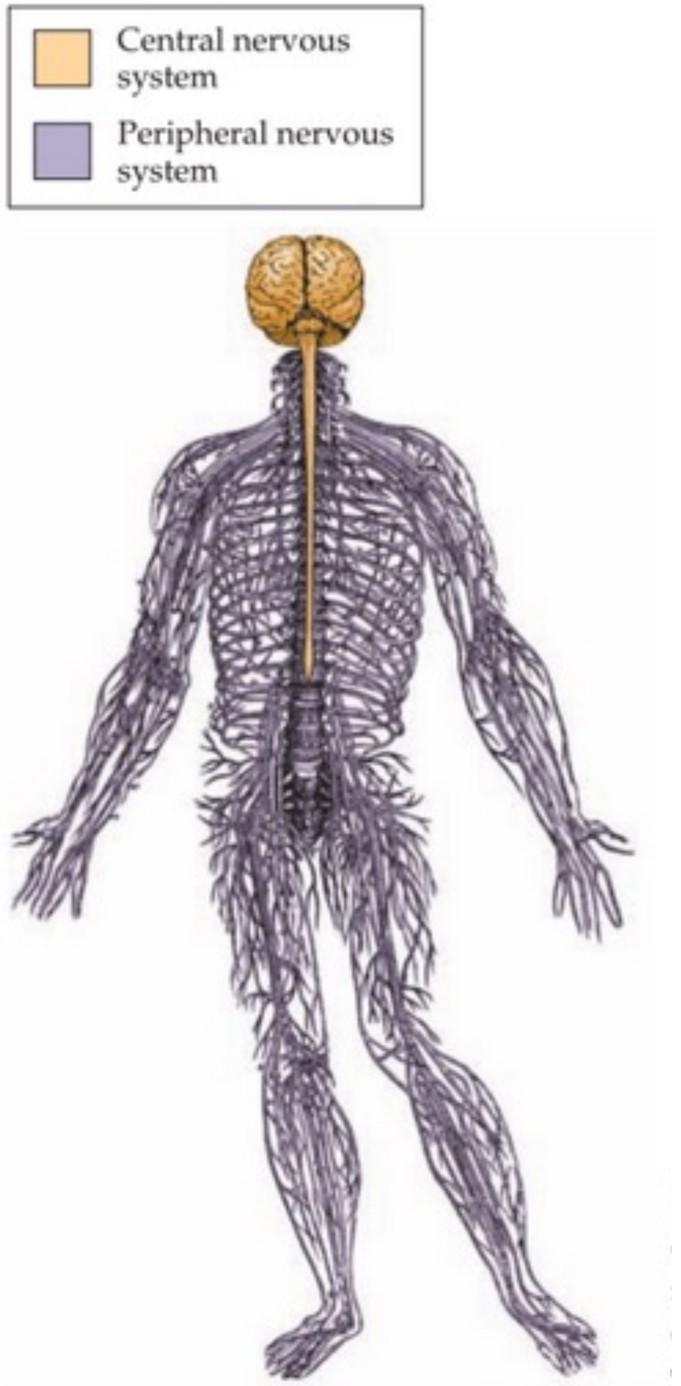
Nervous System

Body!

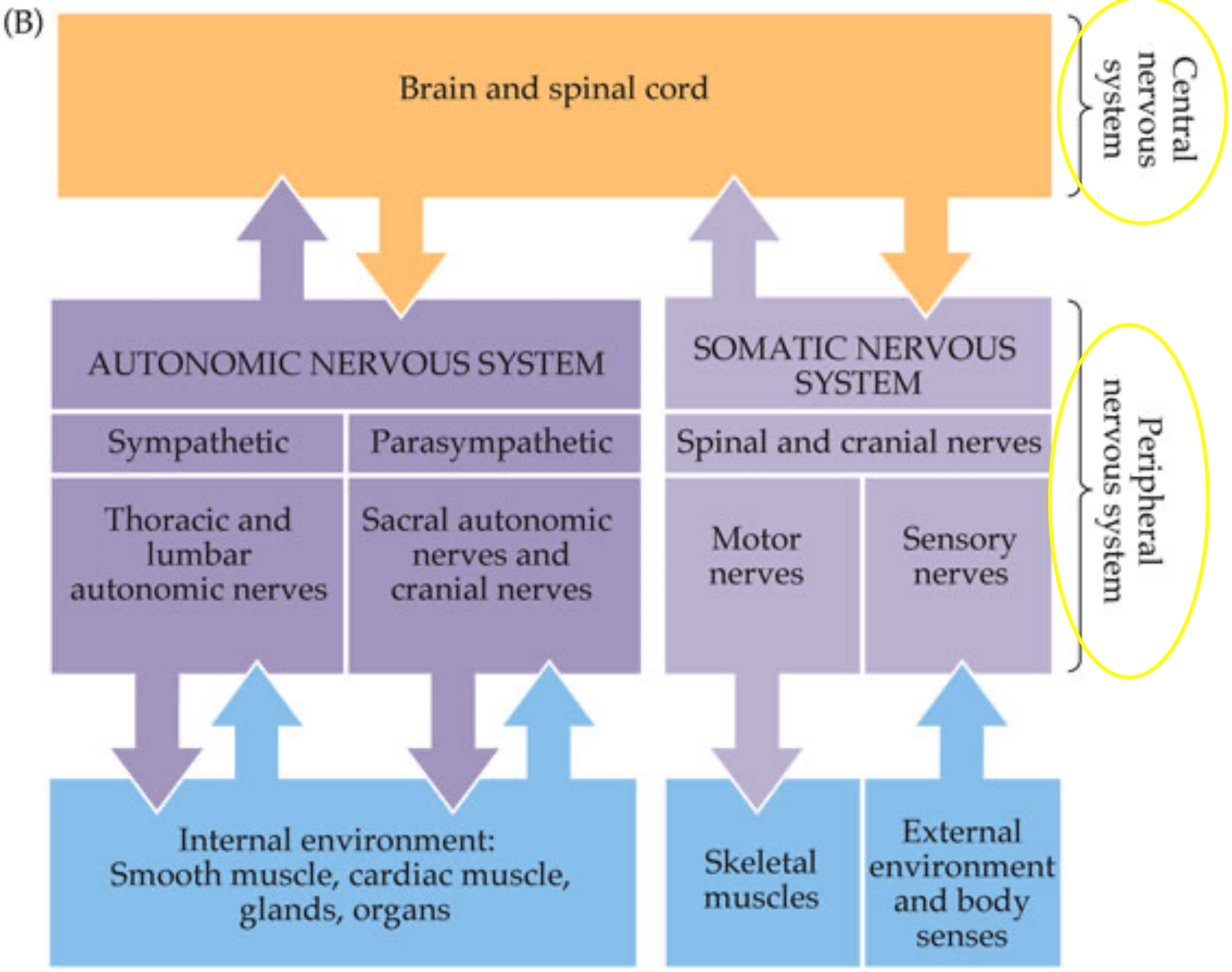


The nervous system has central and peripheral components





Major Divisions of the Nervous System



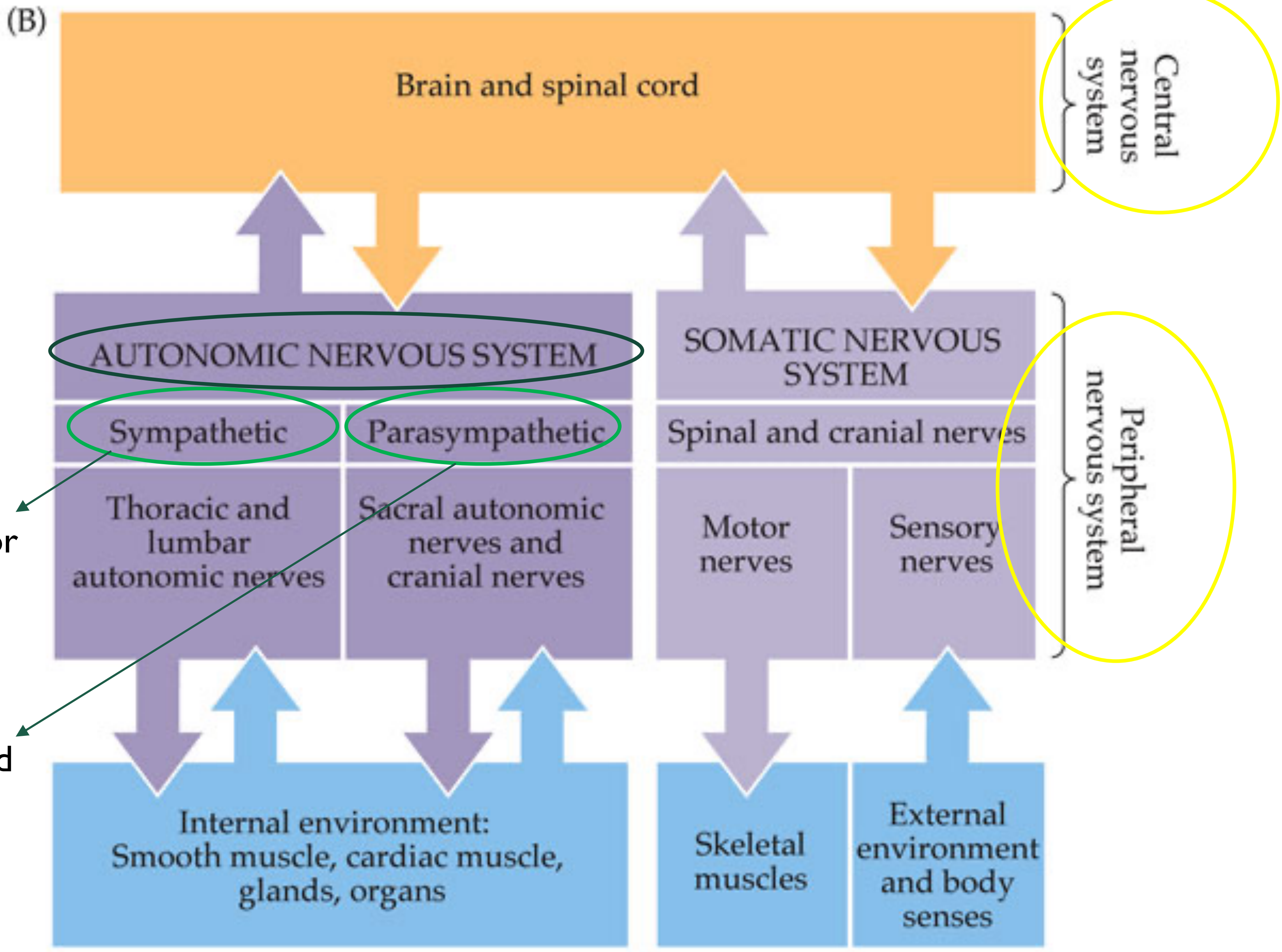
CENTRAL NERVOUS SYSTEM

- Consists of the brain and spinal cord.
- Functions.
  - Integration of information.
  - Learning and memory.
  - Coordination of activity.

PERIPHERAL NERVOUS SYSTEM

- Nerves and nuclei (i.e., ‘ganglia’) that lie outside of the brain and spinal cord.
- Functions depend on sub-system…

Major Divisions of the Nervous System



"Fight or flight" system

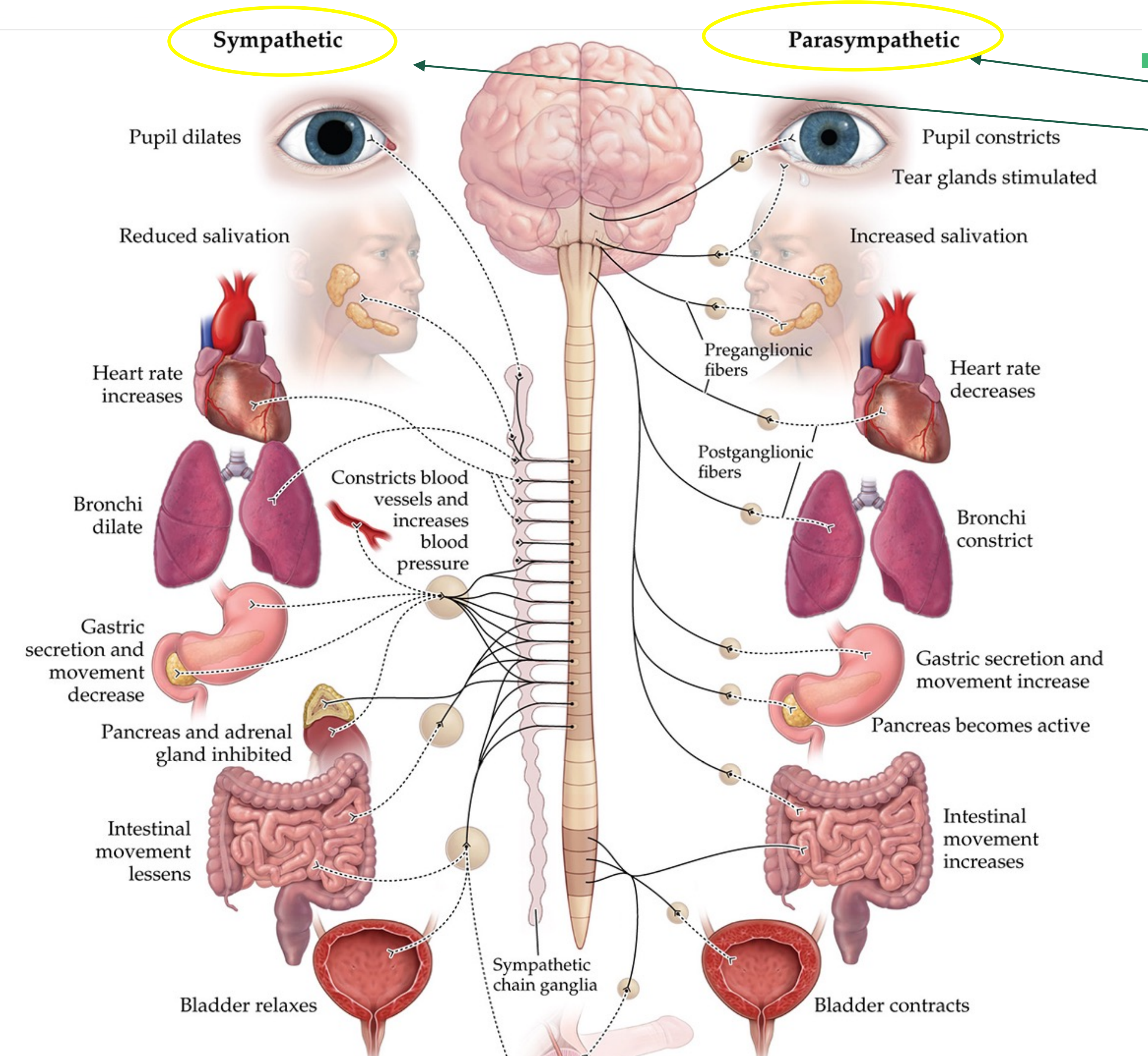
"Rest and digest" system

AUTONOMIC NERVOUS SYSTEM

- Many psychoactive drugs affect the brain and the autonomic nervous system simultaneously
- Uses feedback and feedforward loops to maintain homeostasis
  - Monitors and controls the body's internal environment and involuntary functions.
    - Heart rate and blood pressure.

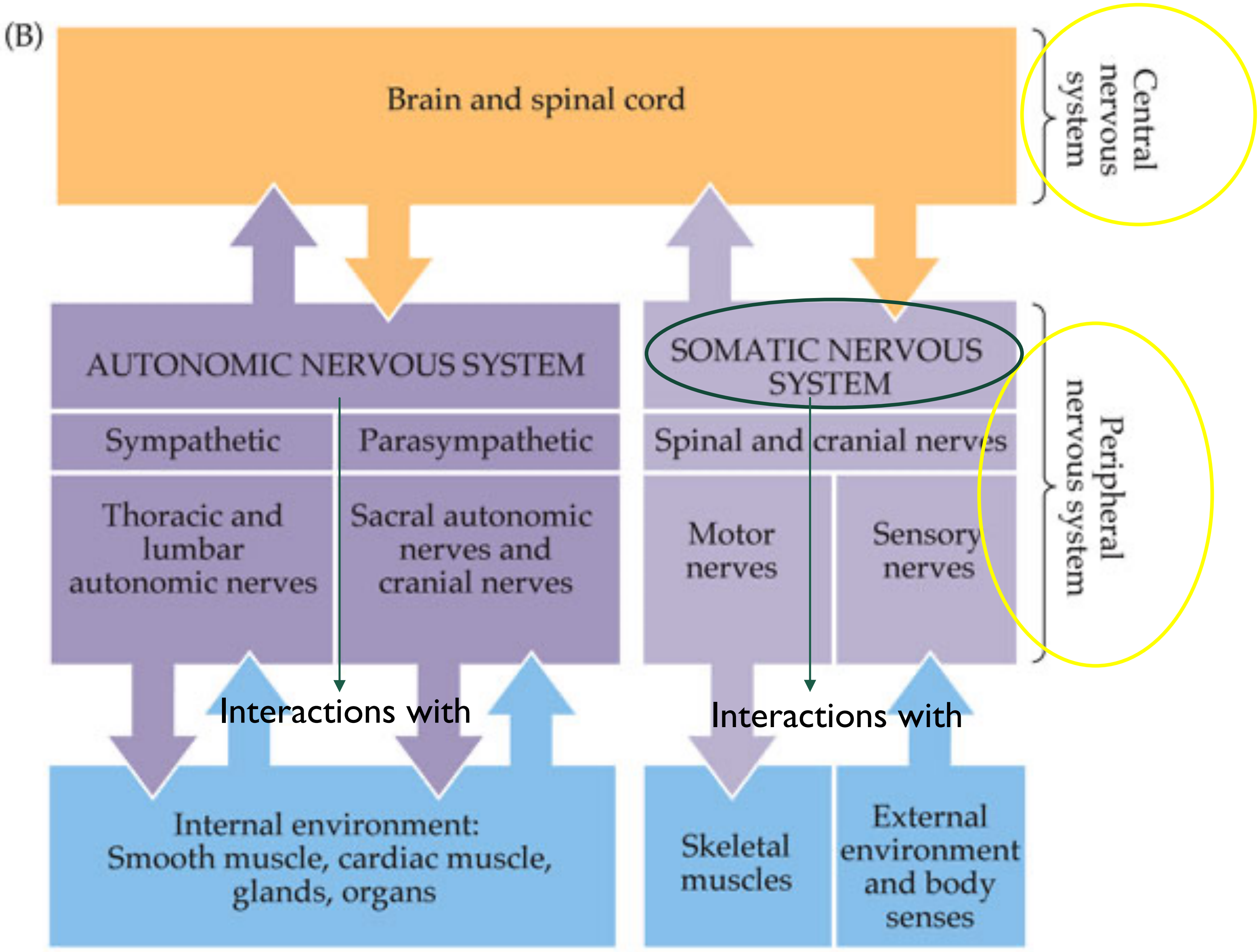
- Two branches of the Autonomic Nervous system often act in opposition:
  - **Sympathetic** branch.
    - Example: **Norepinephrine** is involved in increasing heart rate.
    - "Fight-or-flight" response.
  - **Parasympathetic** branch.
    - Example: **Acetylcholine** is involved in decreasing heart rate.

Branches of the Autonomic Nervous System



https://www.youtube.com/watch?v=q3OITaAZLNc

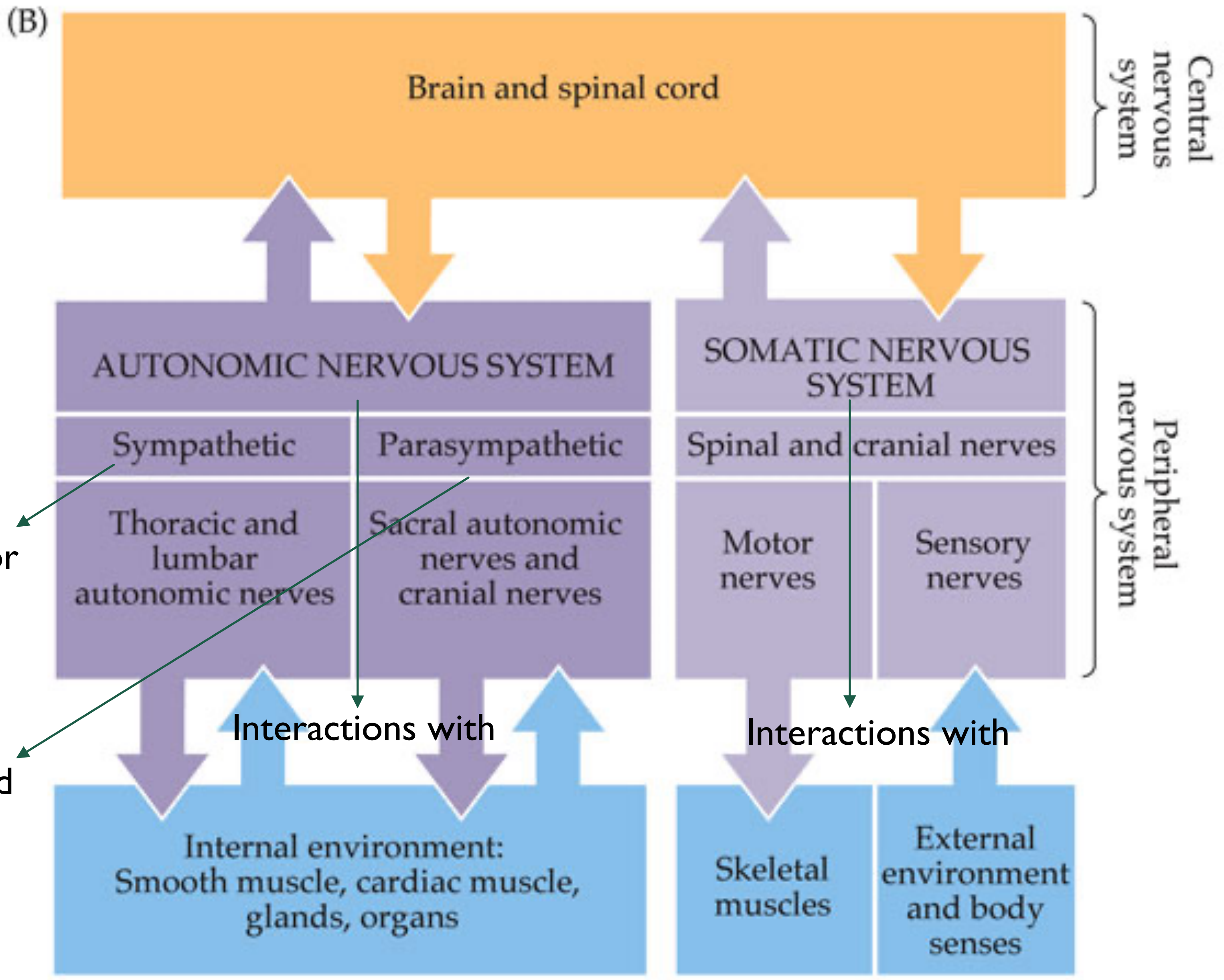
Major Divisions of the Nervous System



SOMATIC NERVOUS SYSTEM

- Nerve cells on the "front lines," interacting with the external environment.
  - Controls voluntary actions.
  - Carries sensory information into the central nervous system, or CNS.
  - Carries motor, or movement, information back out to the peripheral nerves.

Major Divisions of the Nervous System



"Fight or flight" system

"Rest and digest" system

Interactions with

Interactions with