CNS –Neuron and Neurotransmitters

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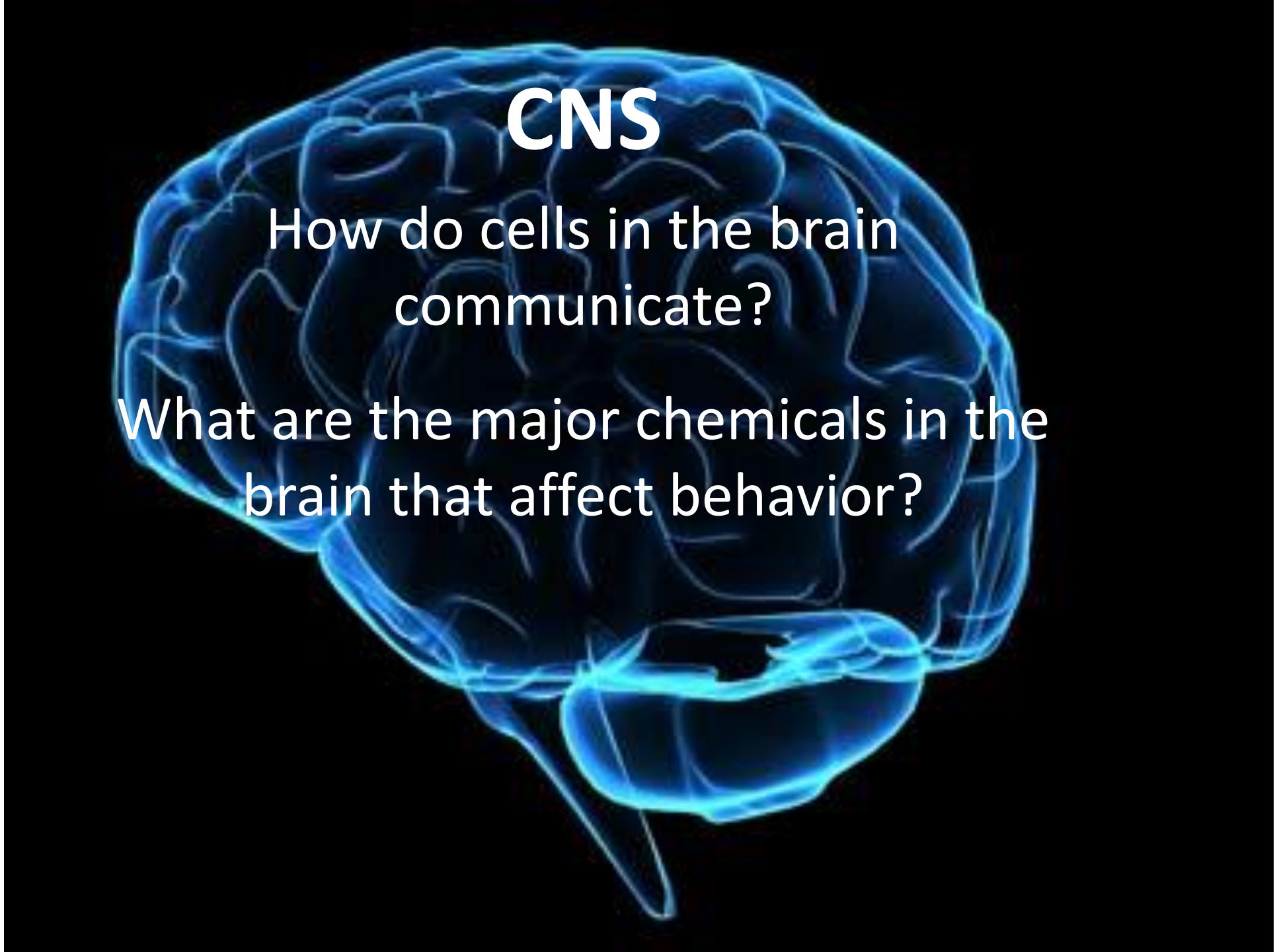
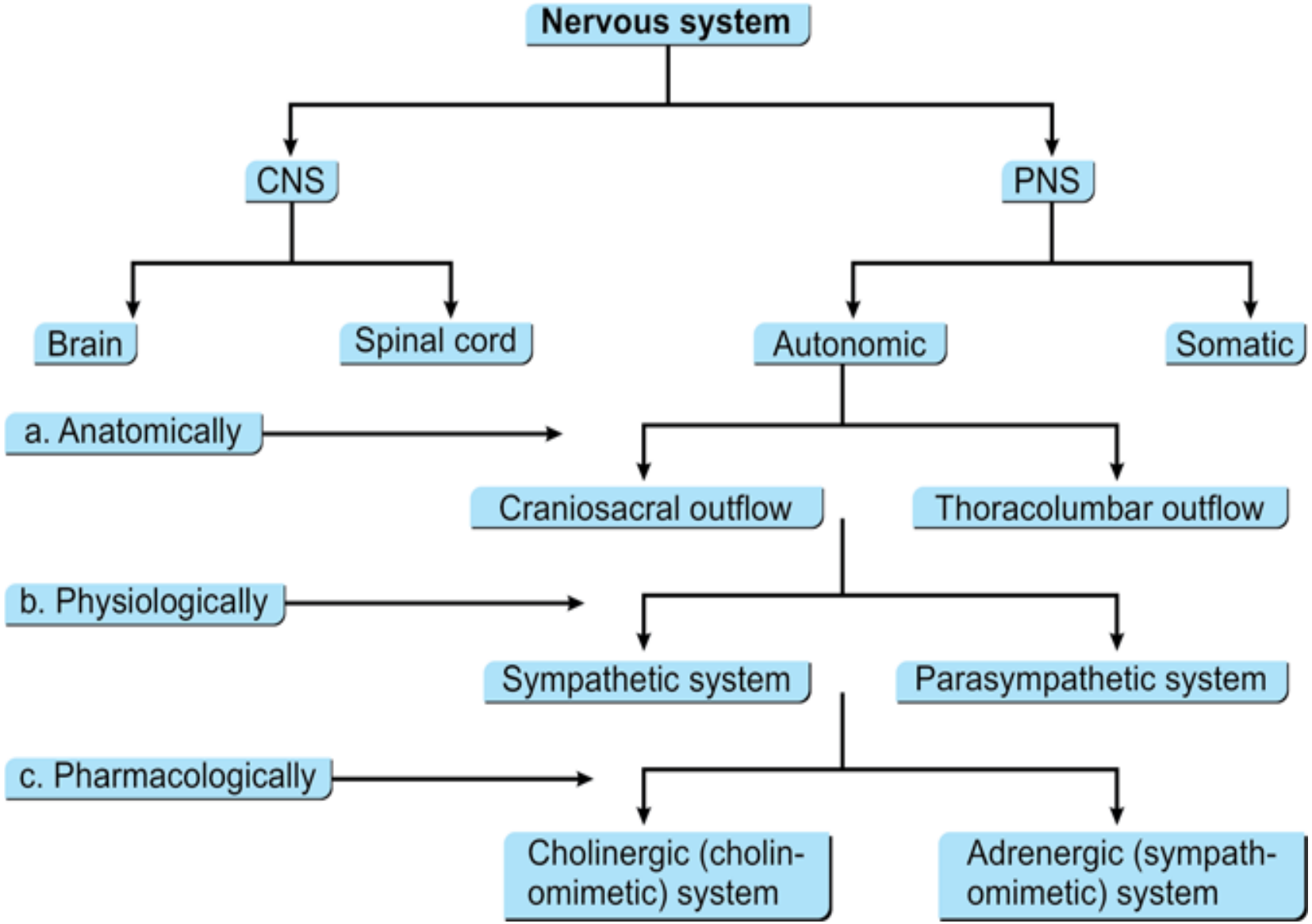
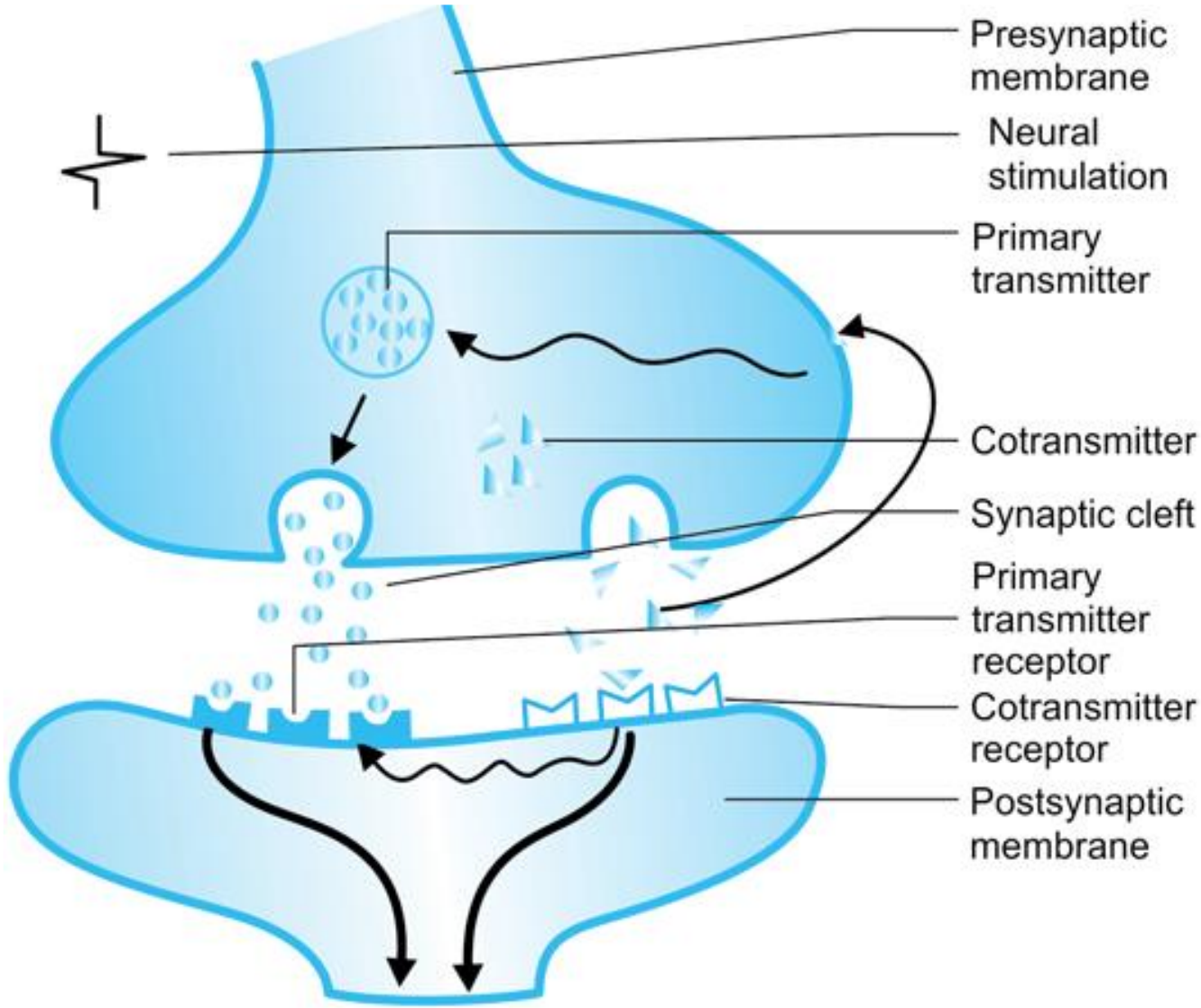
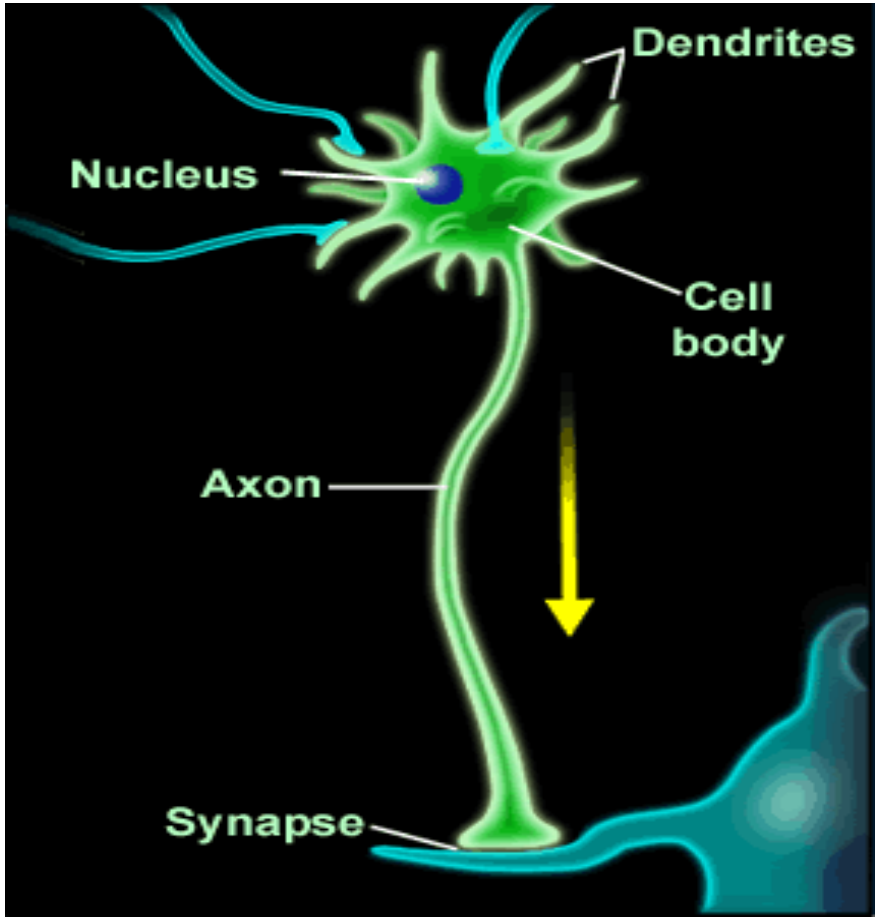

CNS
How do cells in the brain communicate?
What are the major chemicals in the brain that affect behavior?


Nervous system
CNS
PNS
Brain
Spinal cord
Autonomic
Somatic
a. Anatomically
Craniosacral outflow
Thoracolumbar outflow
b. Physiologically
Sympathetic system
Parasympathetic system
c. Pharmacologically
Cholinergic (cholin-omimetic) system
Adrenergic (sympath-omimetic) system

Points of difference	Sympathetic system	Parasympathetic system
Origin (other name)	Thoracolumbar	Craniosacral
Distribution	($T_1 \rightarrow L_3$)	(III, VII, IX, X S2 → S4)
Distribution ganglia	Wide	Limited to head and neck
Length of postganglionic fiber	Long, away from organs	Short on or close to the organ
Fiber ratio (pre: postganglionic fiber ratio	1:20 → l :100	1: 1 → 1:2
Released transmitter	NA (major), ACh (minor)	ACh
Transmitter stability	NA stable, diffuses for wider action	ACh rapidly destroyed locally by cholinesterase
Purpose	Tackling stress and emergency	Assimilation of food and conservation of energy

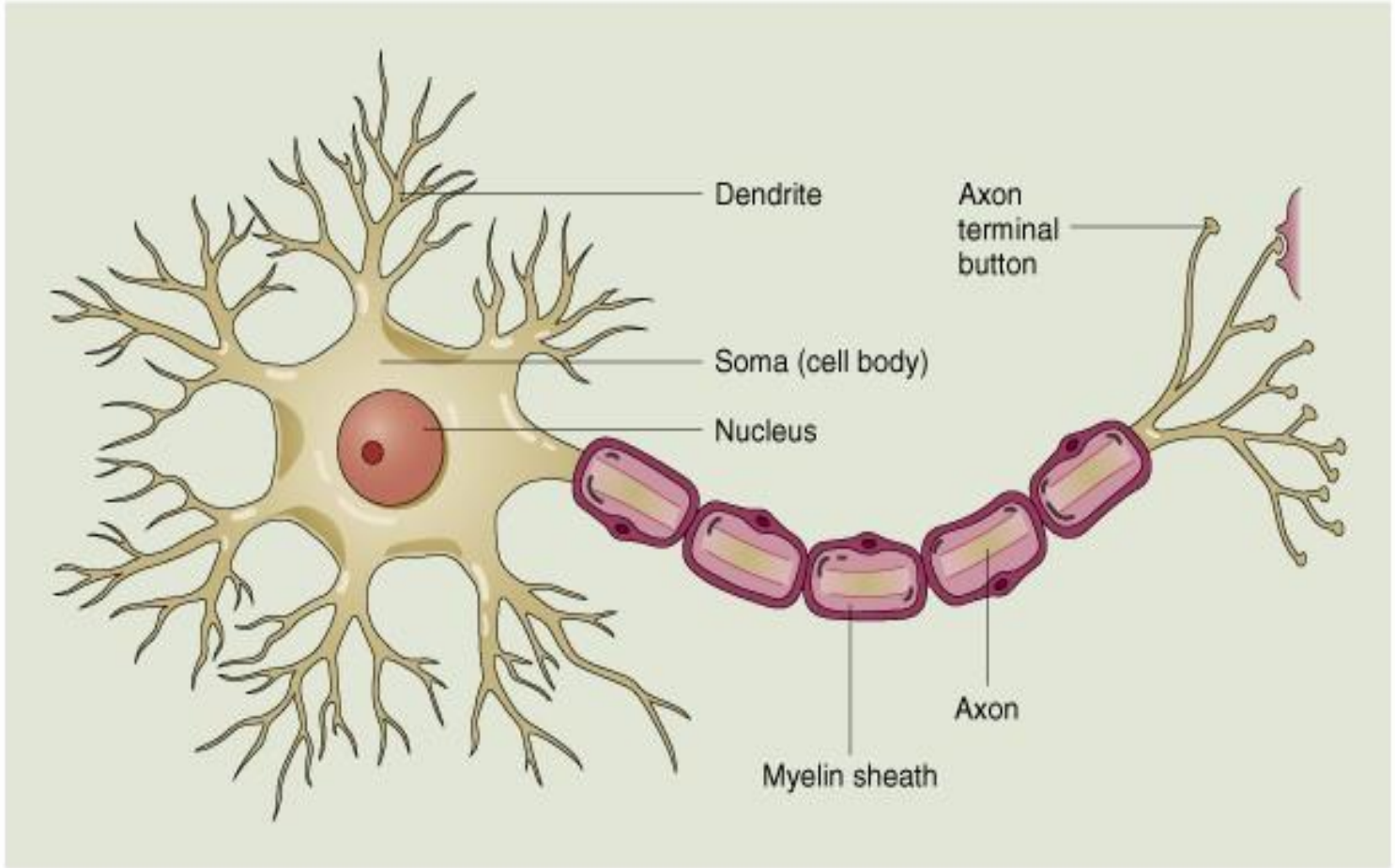

Presynaptic membrane
Neural stimulation
Primary transmitter
Cotransmitter
Synaptic cleft
Primary transmitter receptor
Cotransmitter receptor
Postsynaptic membrane

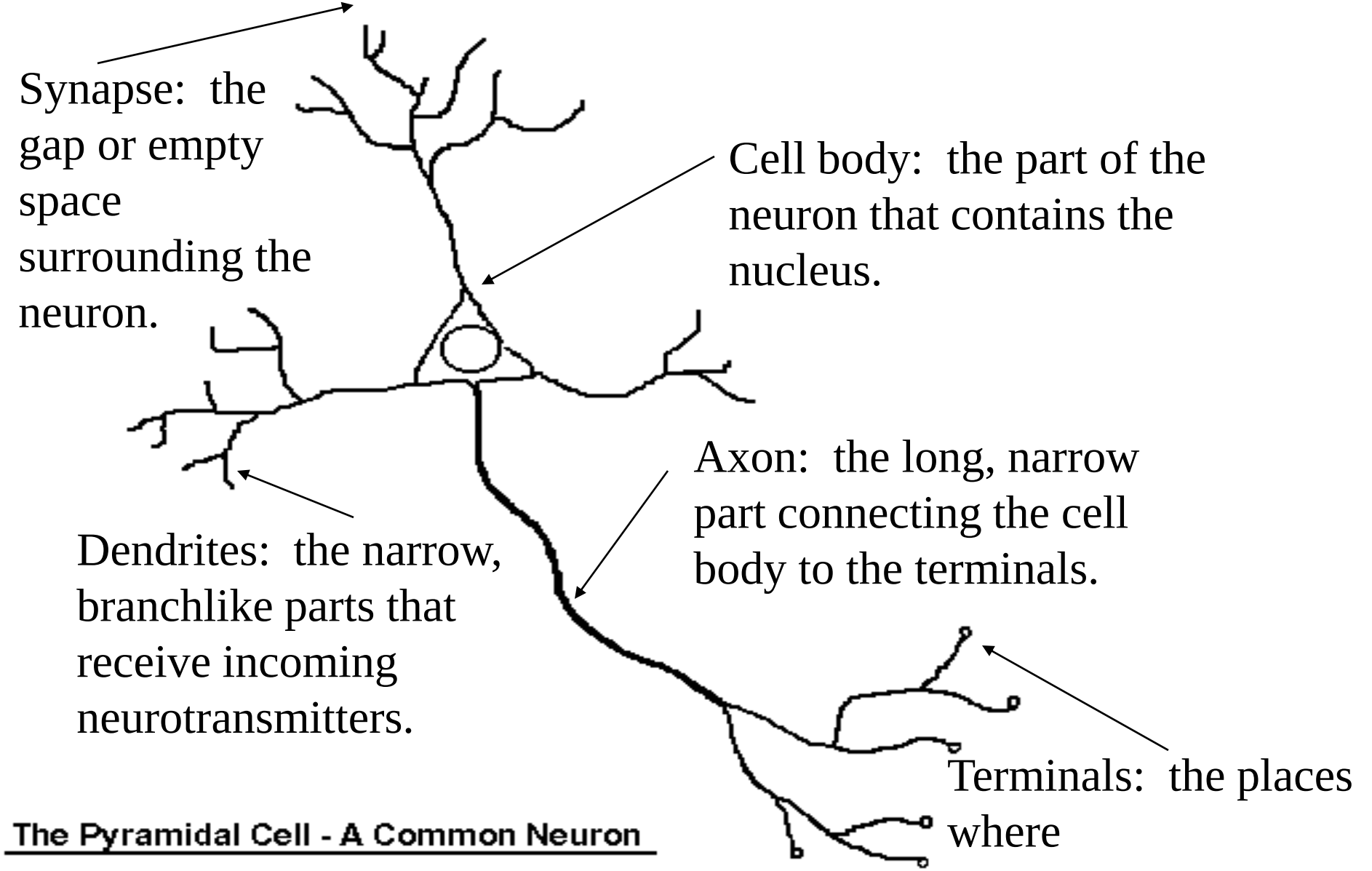
Neurons



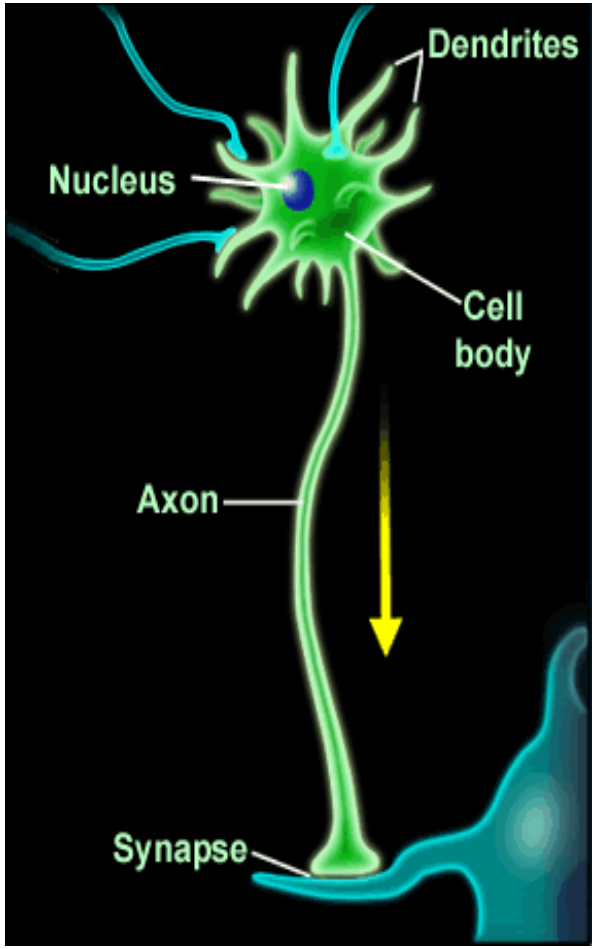
Cells in the brain that carry messages through signals to other parts of the brain.

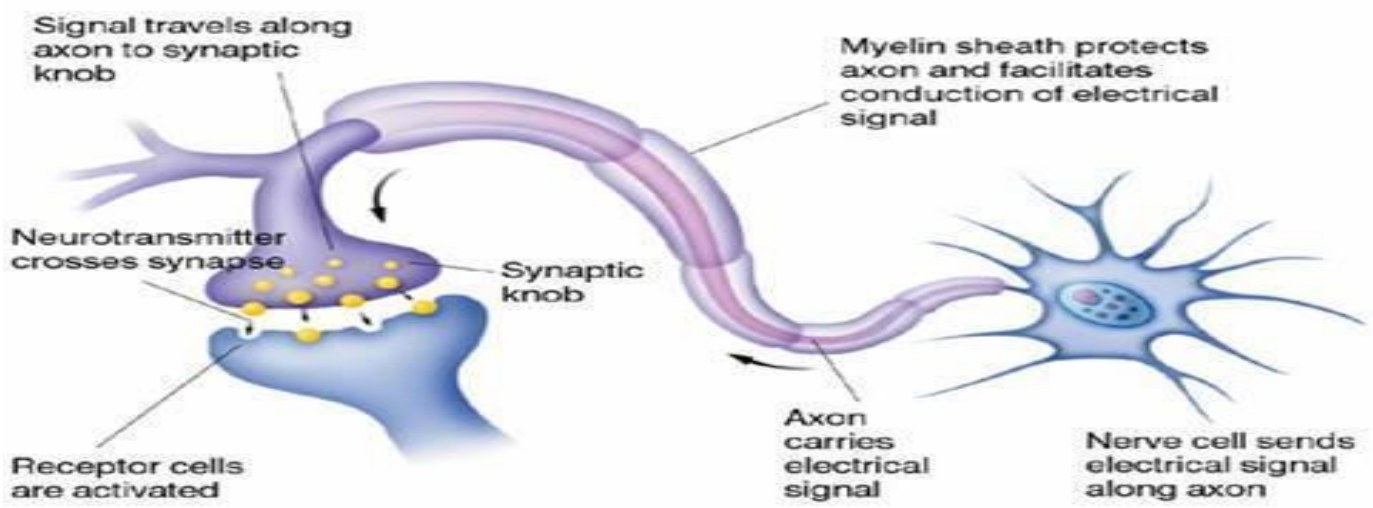
Parts of the neuron




Synapse: the gap or empty space surrounding the neuron.
Cell body: the part of the neuron that contains the nucleus.
Axon: the long, narrow part connecting the cell body to the terminals.
Dendrites: the narrow, branchlike parts that receive incoming neurotransmitters.
Terminals: the places where neurotransmitters wait to cross the synapse.
The Pyramidal Cell - A Common Neuron

How does the brain work?





Connections between neurons

Dendrites = *Take in information*

Axon = *Send out information*

Neurotransmitters

- Neurotransmitter and neurotransmission chemical substances which transmit impulses from one neuron to another neuron or from neuron to effector organ is called **neurotransmitter** and the process is known as **neurotransmission.**
- There are dozens of different **neurotransmitters** (NT) in the neurons of the body.
- NTs can be either **excitatory** or **inhibitory**
- Each neuron generally synthesizes and releases a **single type of neurotransmitter**
- The **major neurotransmitters** are indicated on the **next slide**.

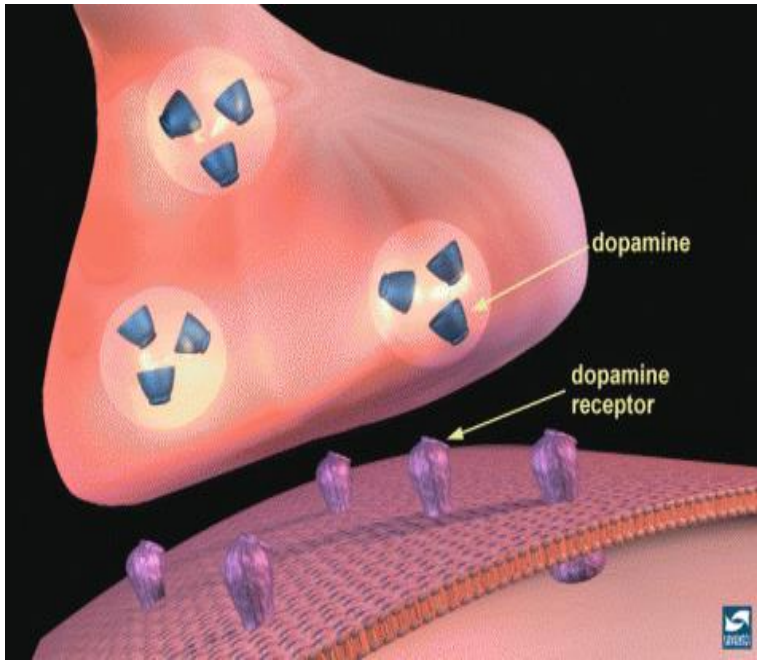
Major Neurotransmitters in the Body

Neurotransmitter	Role in the Body
Acetylcholine	A neurotransmitter used by the spinal cord neurons to control muscles and by many neurons in the brain to regulate memory. In most instances, acetylcholine is excitatory and inhibitory
Dopamine	The neurotransmitter that produces feelings of pleasure when released by the brain reward system. Dopamine has multiple functions depending on where in the brain it acts. It is usually inhibitory.
GABA (gamma-aminobutyric acid)	The major inhibitory neurotransmitter in the brain.
Glutamate	The most common excitatory neurotransmitter in the brain.
Glycine	A neurotransmitter used mainly by neurons in the spinal cord. It probably always acts as an inhibitory neurotransmitter.
Norepinephrine	Norepinephrine acts as a neurotransmitter and a hormone. In the peripheral nervous system, it is part of the flight-or-flight response. In the brain, it acts as a neurotransmitter regulating normal brain processes. Norepinephrine is usually excitatory, but is inhibitory in a few brain areas.
Serotonin	A neurotransmitter involved in many functions including mood, appetite, and sensory perception. In the spinal cord, serotonin is inhibitory in pain pathways.

NIH Publication No. 00-4871

Neurotransmission

- What's happening at a synapse?



- Chemical release from one neuron to another
- Packages of chemicals (vesicles of neurotransmitters) are released from one neuron
- Another neuron receives the chemicals (receptors)

What is Synapse and Ganglia

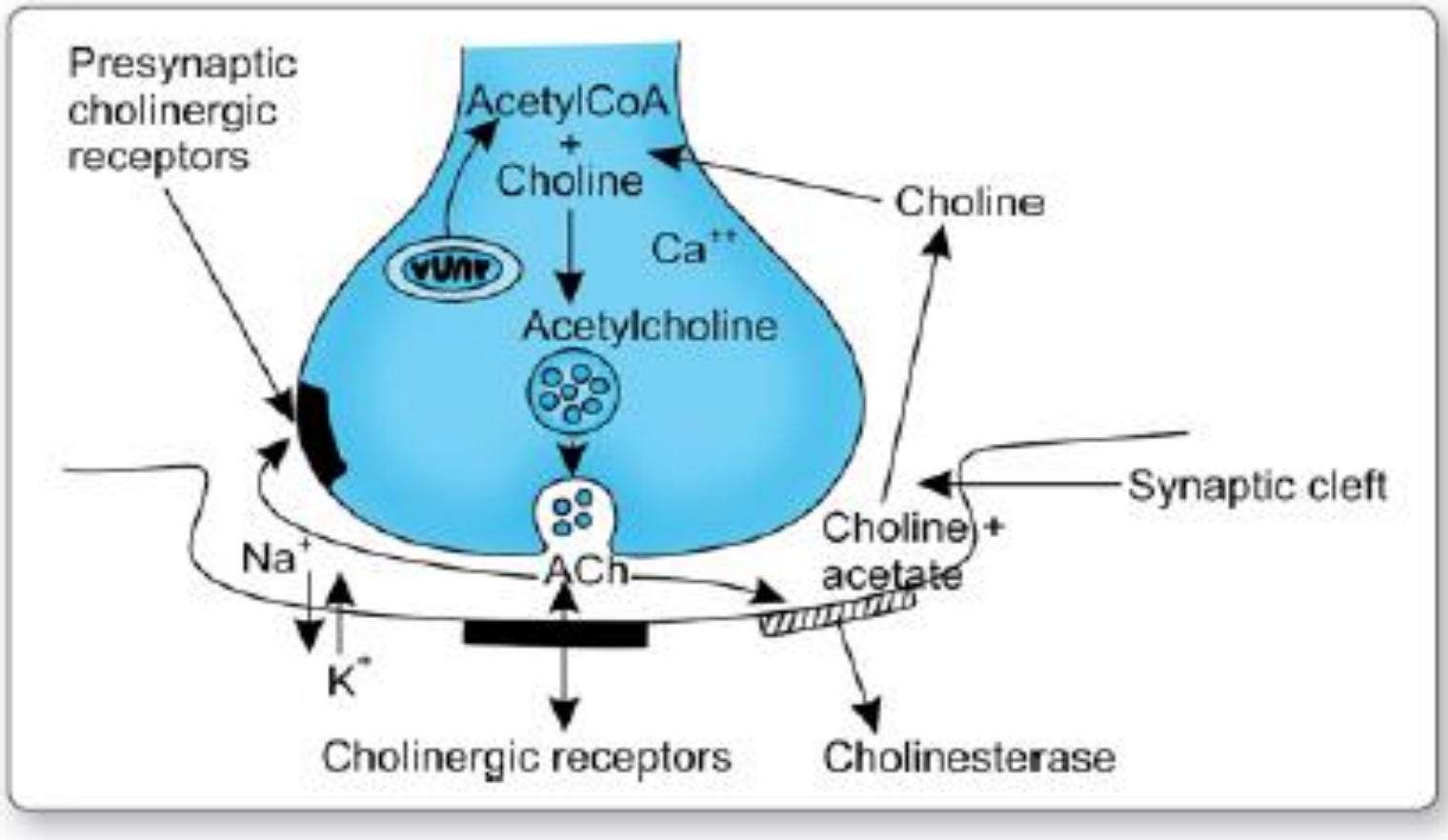
- **Synapse** is the junctional region between two neurons where one neuron relays the impulse to other so that the impulse is transmitted.
- **Ganglion**—It is the site where the axons of the preganglionic fibers make synapse with the neurons of the postganglionic fibers.

Neurotransmission -Acetylcholine

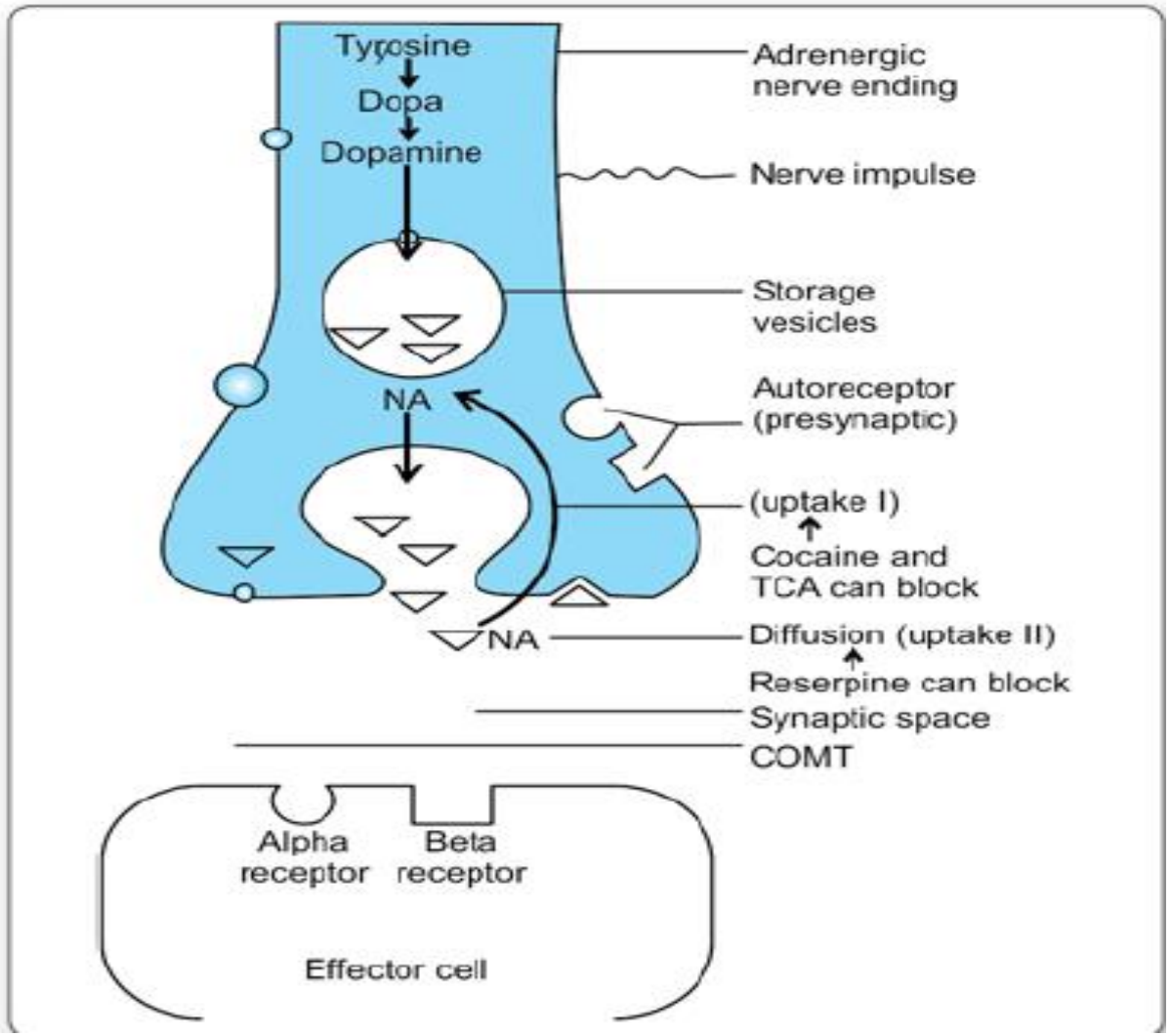
- Neurotransmission in **cholinergic neurons involves six steps.**
- **The first four step**—synthesis, storage, release and binding of the acetylcholine—to a receptor, are followed by the **fifth step**, degradation of the neurotransmitter in the synaptic gap (that is, the space between the nerve endings and adjacent receptors located on nerves or effect or organs) and the sixth step, the recycling of choline.

Cholinergic transmission

ACh is a major neurohumoral transmitter at cholinergic nerves.



Adrenergic transmission



Properties - Neurotransmitters

- ***Properties***
- They have—
- 1. Precursor(s)
- 2. Synthesizing enzymes
- 3. Storage vesicles
- 4. Release by neural stimulation
- 5. Postsynaptic receptors
- 6. Specific antagonists
- 7. Degrading enzymes.

Properties - Neurotransmitters

Points	Cholinergic NTs	Adrenergic NTs
Precursor (s)	Acetate and choline	Phenylalanine
Enzyme for synthesis	Acetyltransferase	Tyrosine hydroxylase → Methyltransferase
Storage	With ACh+ATP+ Chromo-granin	With NA + ATP + proteoglycan
Release	By exocytosis	By exocytosis
Postsynaptic receptors	Either nicotinic on muscarinic receptor	Either α or β
Specific antagonists	• Atropine on muscarinic receptors • d-tubocurarine on nicotinic receptors	• Prazosin on α-receptors • Propranolol on β-receptors
Degrading enzymes	Cholinesterases • True • Pseudo	• Monoamine oxidase • Catechol–O– methyl-transferase

Neurotransmitters function in your body

- Glutamate – excites neurons to fire, involved in memory
- GABA – inhibits (stops) other neurons from firing
- Serotonin – affects mood
- Dopamine – involved with feeling reward, learning, & emotion
- Acetylcholine – involved with memory & attention &muscle action
- Norepinephrine – involved with alertness

What do you predict happens when these neurotransmitters are out of balance?

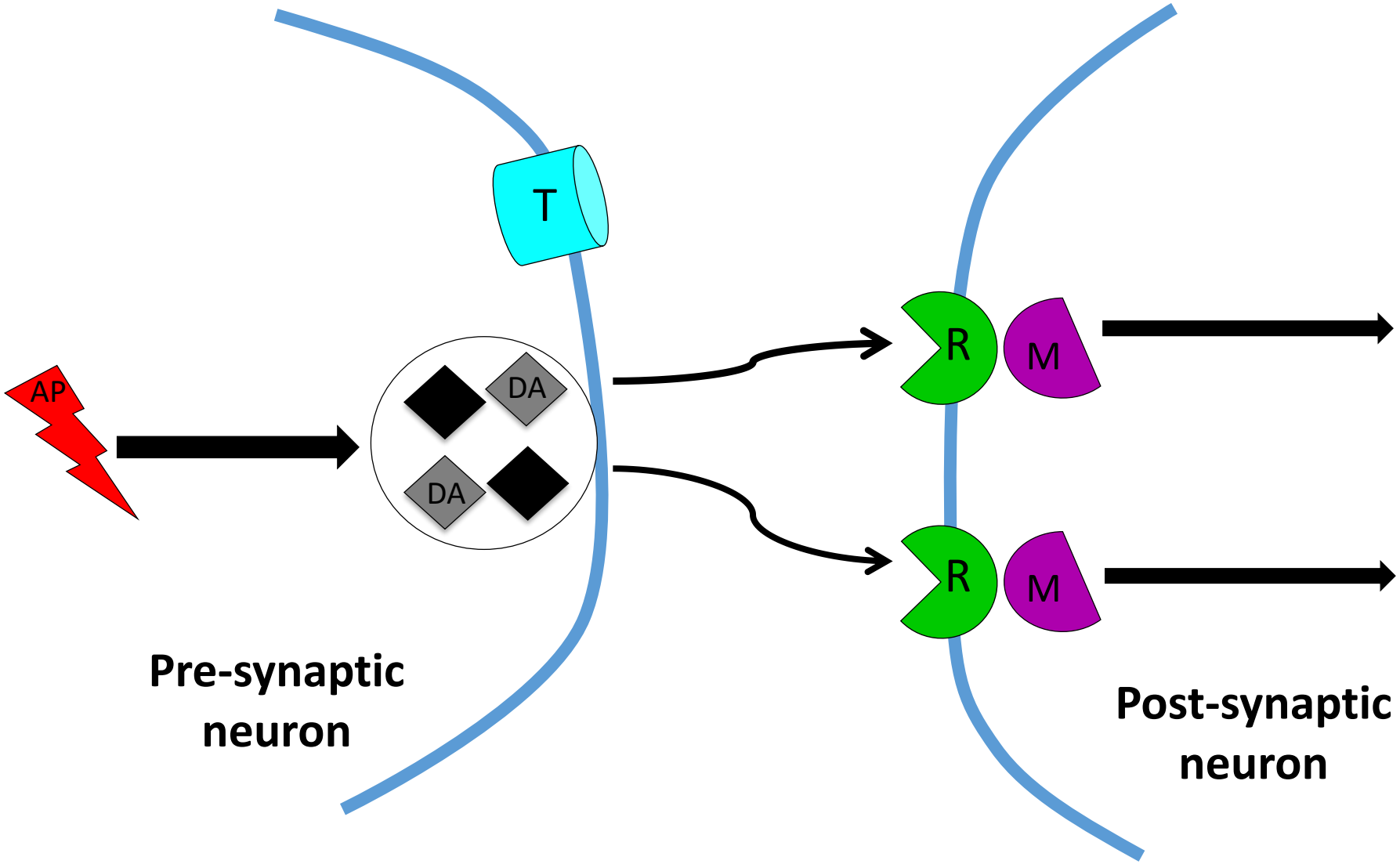
Neurotransmitter	Normal Function	Imbalance
Glutamate	Excites neurons, memory	**TOO MUCH** leads to migraines or seizures
GABA	Inhibits (stops) neurons	**TOO LITTLE** leads to seizures, tremors, & insomnia
Serotonin	Affects mood, hunger, & sleep	**TOO LITTLE** leads to depression
Dopamine	Involved in reward, learning, emotion	**TOO MUCH** leads to schizophrenia. TOO LITTLE leads to tremors and decreased mobility in Parkinson's & ADHD
Acetylcholine	Enables muscles, learning, & memory	Alzheimer's decreases the amount of this
Norepinephrine	Helps control alertness	**TOO LITTLE** can cause depressed mood and cause attention deficit problems

Role of neurotransmitters in some diseases

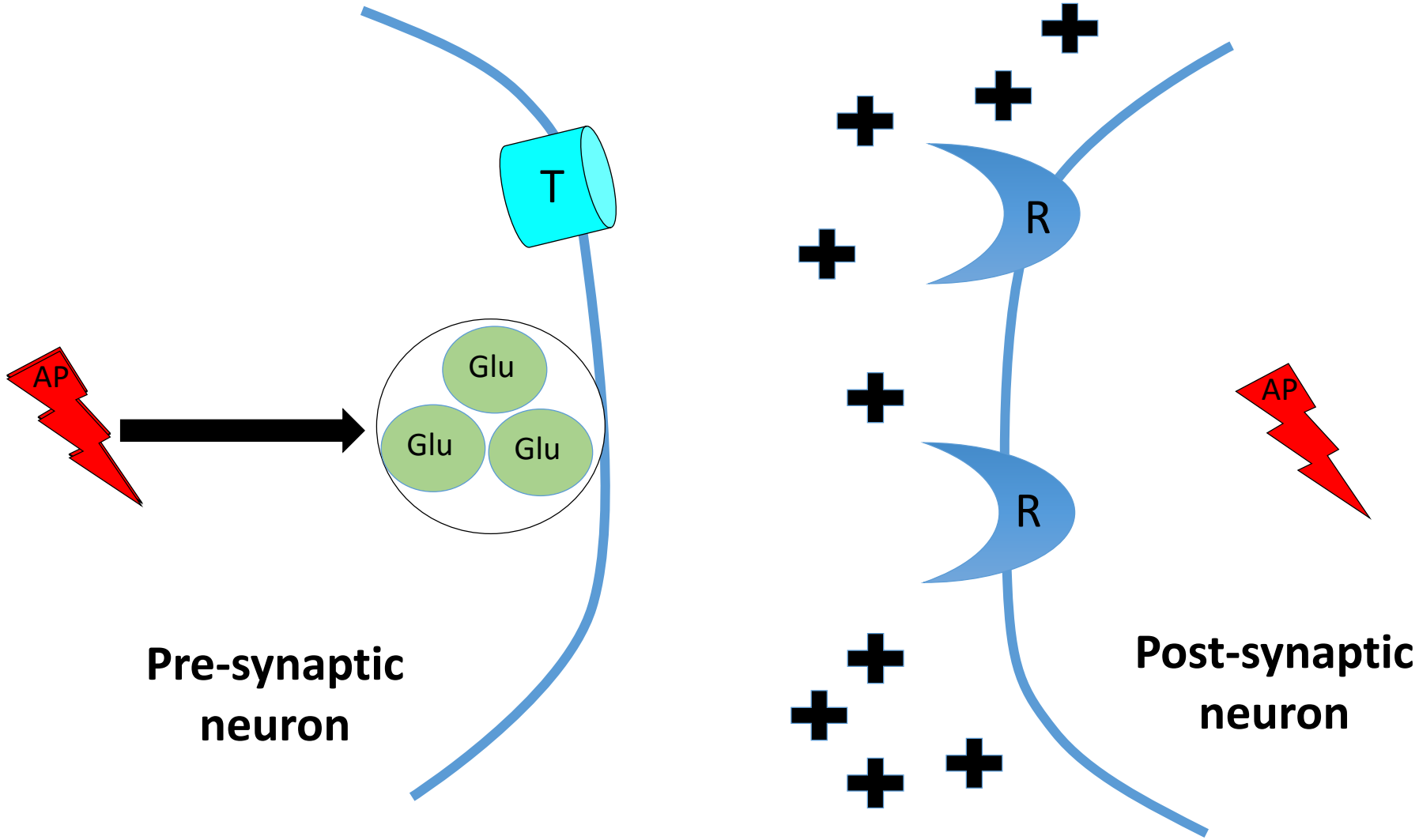
- All the NTs combine with their concern receptors and in normal cases, produce the (physiological) desired effects. Deficiency or excess of activity of these NTs may occur in many diseases, e.g.
- 1. Overactivity of dopamine is seen in schizophrenia.
- 2. Either cholinergic overactivity or dopaminergic deficiency occur in
- parkinsonism.
- 3. In depression, there is deficiency of serotonin and/or noradrenaline.
- 4. In epilepsy, NMDA mediated overactivity or GABA underactivity is seen.
- 5. Loss of cholinergic neuron may be the cause of Alzheimer's diseases.

Normal **Neurotransmission**

(Dopamine signals)



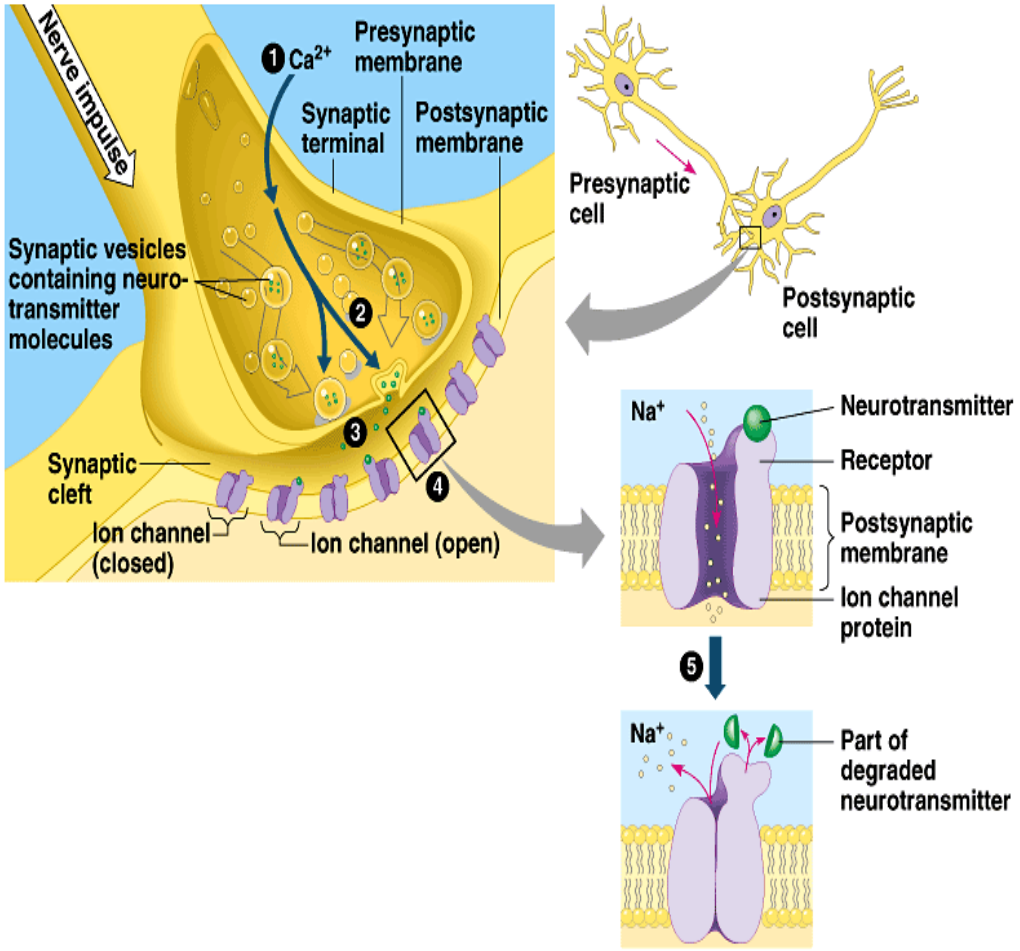
An example –
Glutamate & Epilepsy



An example – Glutamate & Epilepsy

- Glutamate **excites** neurons and make them more likely to fire action potentials.
- Epileptic seizures are an electrical storm in the brain caused by an impaired balance of excitation (glutamate) and inhibition (GABA).
- One cause of seizures may be over-activation of glutamate neurons.
- This causes the release of high levels of glutamate into the synapse.
- This glutamate binds to glutamate receptors and causes positive ions to cross through the channels into the post-synaptic neurons.
- This influx of positive ions makes these neurons more excitable and more likely to fire action potentials as well, causing overactivation across the brain and resulting in that “electrical storm”.

- Neurotransmitters – Action Potential (AP)



1. Impulse from **action potential** opens ion channels for **Ca^{++}**
2. The increased **Ca^{++}** concentration in the axon terminal initiates the release of the **neurotransmitter (NT)**
3. **NT** is released from its vesicle and crosses the “gap” or **synaptic cleft** and attaches to a protein receptor on the **dendrite**
4. Interaction of **NT** and protein receptor open **post-synaptic membrane** ion channel for **Na^+**
5. After transmission the **NT** is either degraded by an enzyme or taken back into the **pre-synaptic membrane** by a **transporter** or **reuptake pump**

Drugs Interfere with Neurotransmission

- Drugs can affect synapses at a variety of sites and in a variety of ways, including:
  1. Increasing number of impulses
  2. Release NT from vesicles with or without impulses
  3. Block reuptake or block receptors
  4. Produce more or less NT
  5. Prevent vesicles from releasing NT

Three Drugs (of many) which affect Neurotransmission

Methamphetamine

seattlepi.nwsource.com/ methamphetamines/

Nicotine

Alcohol

science.howstuffworks.com/ alcohol.htm

Methamphetamine

- **Methamphetamine** alters **Dopamine** transmission in two ways:

1. Enters dopamine vesicles in axon terminal causing release of NT

2. Blocks dopamine transporters from pumping dopamine back into the transmitting neuron

Result: **More dopamine** in the Synaptic Cleft

This causes neurons to fire more often than normal resulting in a euphoric feeling.

1. After the drug wears off, **dopamine** levels drop, and the user "crashes". The euphoric feeling will not return until the user takes more **methamphetamine**
2. **Long-term use of methamphetamine causes dopamine axons to wither and die.**
3. Note that **cocaine** also blocks **dopamine** transporters, thus it works in a similar manner.

What about Nicotine?

- Similar to **methamphetamine** and **cocaine**, **nicotine** increases **dopamine** release in a synapse.
- However, the mechanism is slightly different.
- Nicotine binds to receptors on the **presynaptic neuron**.

•**Nicotine** binds to the **presynaptic** receptors exciting the neuron to fire more action potentials causing an **increase** in **dopamine** release.

•**Nicotine** also affects neurons by **increasing** the **number of synaptic vesicles released**.

How does alcohol affect synapses?

- Alcohol has multiple effects on neurons. It alters neuron membranes, ion channels, enzymes, and receptors.
- It **binds directly to receptors** for acetylcholine, serotonin, and gamma aminobutyric acid (GABA), and glutamate.
- We will focus on **GABA** and its receptor
- **GABA and the GABA Receptor**
- **GABA** is a **neurotransmitter** that has an **inhibitory** effect on neurons.
- When **GABA** attaches to its receptor on the **postsynaptic** membrane, it allows **Cl^-** ions to pass into the neuron.
- This **hyperpolarizes** the **postsynaptic** neuron to inhibit transmission of an impulse.

Alcohol and the GABA Receptor

- When alcohol enters the brain, it binds to **GABA** receptors and amplifies the **hyperpolarization** effect of **GABA**.
- The neuron activity is further diminished
- This accounts for some of the **sedative affects** of alcohol

The Adolescent Brain and Alcohol

- The brain goes through dynamic change during adolescence, and alcohol can seriously **damage long- and short-term growth processes**.
- **Frontal lobe development** and the refinement of pathways and connections continue until age 16, and a high rate of energy is used as the brain matures until age 20.
- **Damage from alcohol at this time can be long-term and irreversible.**
- In addition, **short-term or moderate drinking impairs learning and memory** far more in youth than adults.
- **Adolescents need only drink half as much as adults to suffer the same negative effects.**

Drugs That Influence Neurotransmitters

Change in Neurotransmission	Effect on Neurotransmitter release or availability	Drug that acts this way
increase the number of impulses	increased neurotransmitter release	nicotine, alcohol, opiates
release neurotransmitter from vesicles with or without impulses	increased neurotransmitter release	amphetamines methamphetamines
release more neurotransmitter in response to an impulse	increased neurotransmitter release	nicotine
block reuptake	more neurotransmitter present in synaptic cleft	cocaine amphetamine
produce less neurotransmitter	less neurotransmitter in synaptic cleft	probably does not work this way
prevent vesicles from releasing neurotransmitter	less neurotransmitter released	No drug example
block receptor with another molecule	no change in the amount of neurotransmitter released, or neurotransmitter cannot bind to its receptor on postsynaptic neuron	LSD caffeine

NIH Publication No. 00-4871

Possible questions:

- What is neurotransmitters? Give me some name of neurotransmitters released by our body.
- Draw the neuron and label the parts of neuron.
- What do you predict happens when these neurotransmitters are out of balance?
- What are the major Neurotransmitters and mention its role in the Body?
- What is neurotransmission?
- What are the endogenous neurotransmitter in our body?
- Write the glutamate and epilepsy relations?
- What is a synapse? Briefly explain the five key points.
- Write the Alcohol and the GABA Receptor relations?

Possible questions:

- List the name of Drugs Interfere with Neurotransmission.
- What is Methamphetamine? How it will affect the neurotransmission and its causes.
- What about Nicotine?
- How does alcohol affect synapses?
- How does Adolescent Brain by Alcohol ? Explain briefly.