



Biological Psychology

M5X00908 Brain, Behaviour, and Cognition (BBC)

Lecture 2: Neural Conduction and Synaptic transmission

Dr Kate Williams

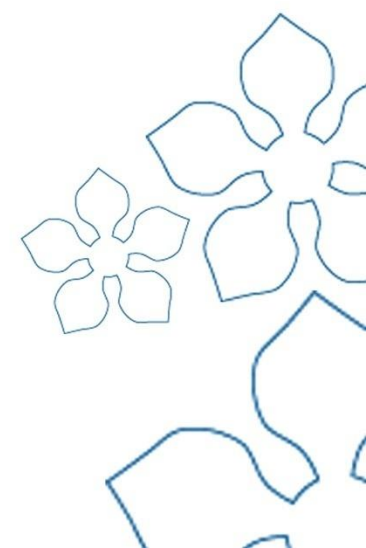


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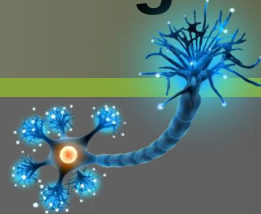
Neural Conduction and Synaptic transmission

- Last week discussed anatomy of the nervous system and the structure of neurons.
- This week we will discuss how neurons function:
 - Process of how neurons conduct and transmit electrochemical signals through the nervous system.
 - Focus on axon conduction, how a resting membrane turns to an action potential, and what the steps are to neurotransmitter activation.
 - Discussion of the genetic and neural mechanisms involved in developmental disorders.

Resting Membrane Potential



- First we must understand how signals are made in a neuron.
- Neurons work through Membrane potential:
 - Difference in electrical charge between inside and outside of the cell.
- Record the membrane potential with electrodes (electrical conductors: intra and extra cellular).
- Inside neuron is negative compared to outside
- Resting membrane potential is about -70mV
- Membrane is said to be *polarized*: carries a charge



Ions Contributing to Resting Potential



- Neuron is polarized because particles in neural tissue are separated into +ve & -ve charged particles called ions – the 4 ions that contribute are:

- 1 Sodium (Na^+)
- 2 Chloride (Cl^-)
- 3 Potassium (K^+)
- 4 Negatively charged proteins (A^-)
Synthesized within the neuron, found primarily within the neuron

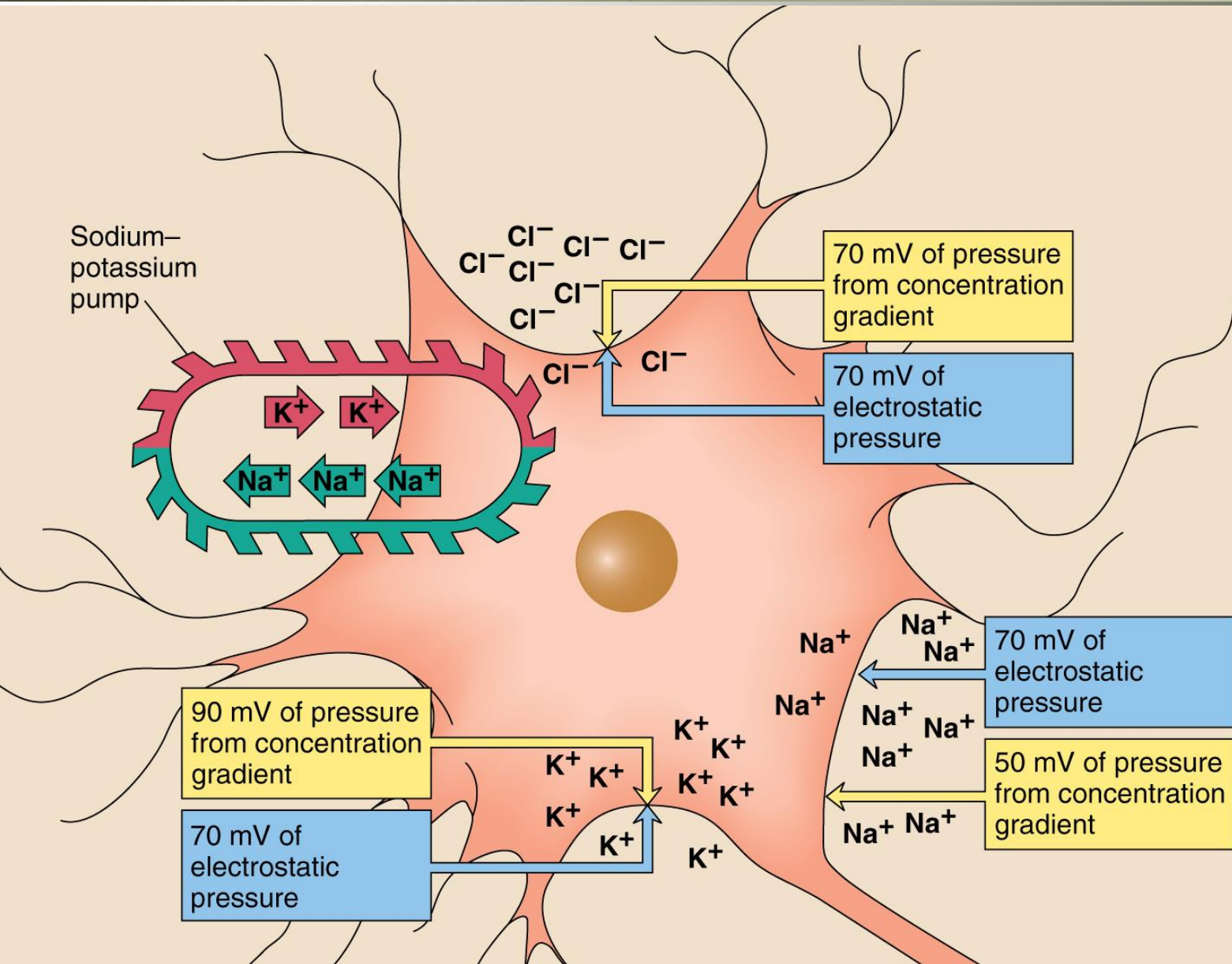
- Unequal balance of charges due to interaction of 4 factors.
 1. Homogenizing (equalizing) factor of random motion.
 2. Electrostatic pressure: + or – charges dispersed by other like charges & attract opposite charges (like magnets).
 3. Differences in permeability of ions (ability to pass membrane).
 4. Equilibrium Potential: active, energy-consuming process involved in maintenance of resting potential.

Hodgkin-Huxley model

The cycle for a Neuron at Rest



The Neural Membrane



The passive and active factors that influence the distribution of Na^+ , K^+ , and Cl^- ions across the neural membrane

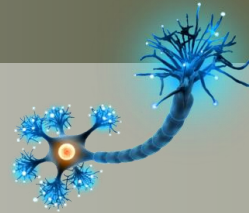
Hodgkin-Huxley model

Generation and Conduction of Postsynaptic Potentials (PSPs)



**Neurons pass messages through “firing”:
releasing neurotransmitter chemicals.**

**Neurotransmitters bind at postsynaptic
receptors and cause electrical changes**

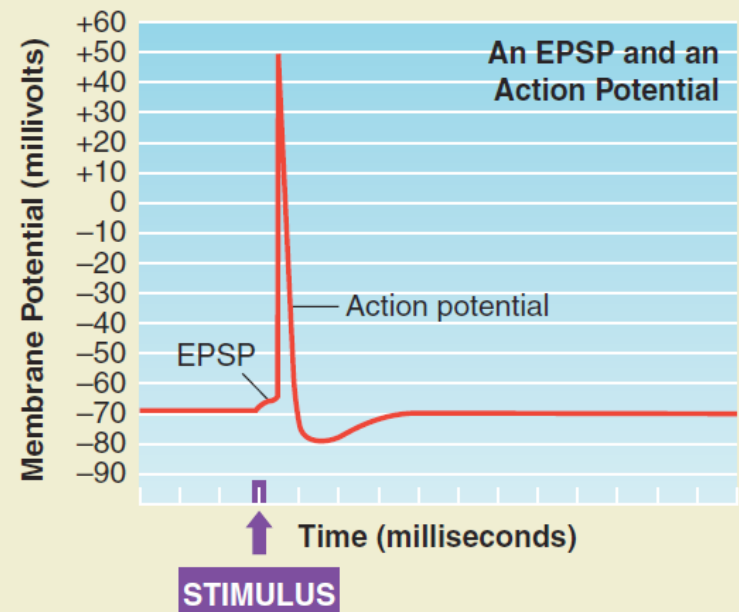
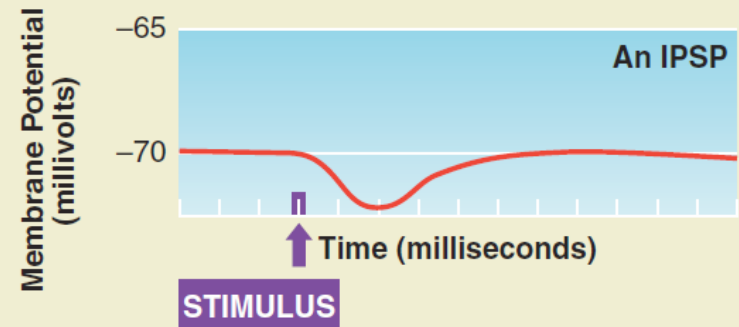
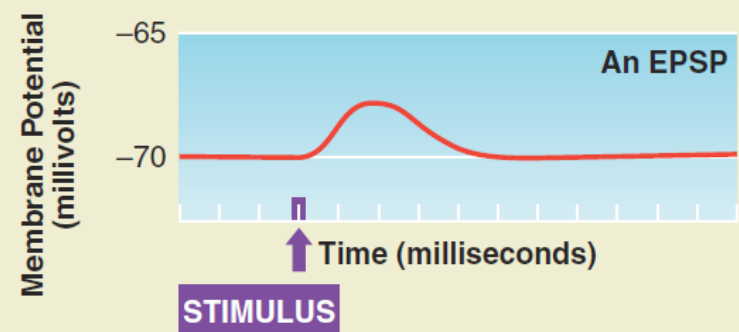


- **Depolarizations: make membrane potential less negative – Excitatory (EPSPs: increase neuron fire)**
- **Hyperpolarization: make membrane potential more negative – Inhibitory (IPSPs decrease neuron fire)**
- **Both are graded responses: the amplitude is the same as the intensity of the signal that elicits them**
 - **Weak signal = small potential; strong = large.**

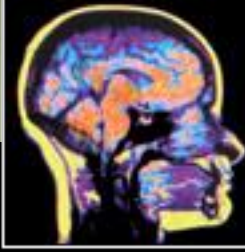
Integration of Postsynaptic Potential and Generation of Action Potentials

EPSPs and IPSPs

- Travel passively from site of origination
- Decremental (graded): get smaller as they travel
- One EPSP not sufficient to cause neuron to “fire” and release neurotransmitter – summation is needed
- To generate an AP (or “fire”), the threshold of activation must be reached near the axon hillock
- Integration of IPSPs and EPSPs must result in a potential of about -65mV in order to generate an AP.



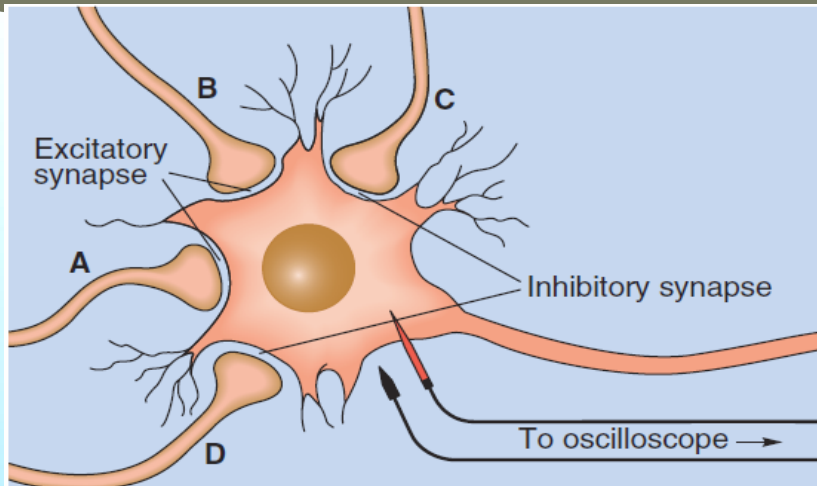
Integration



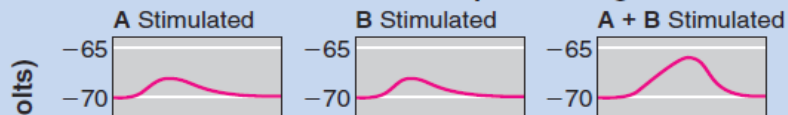
- Adding or combining a number of individual signals into one overall signal is called integration.
- Spatial summation – integration of events happening at different places
- Temporal summation – integration of events happening at different times

Integration

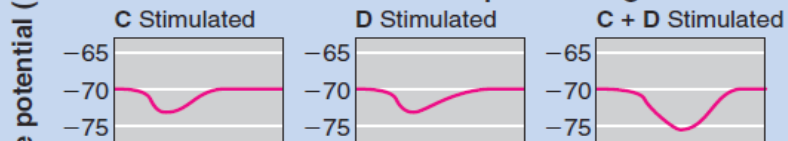
The three possible combinations of spatial summation



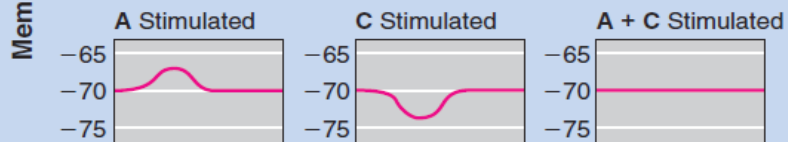
Two simultaneous EPSPs sum to produce a greater EPSP



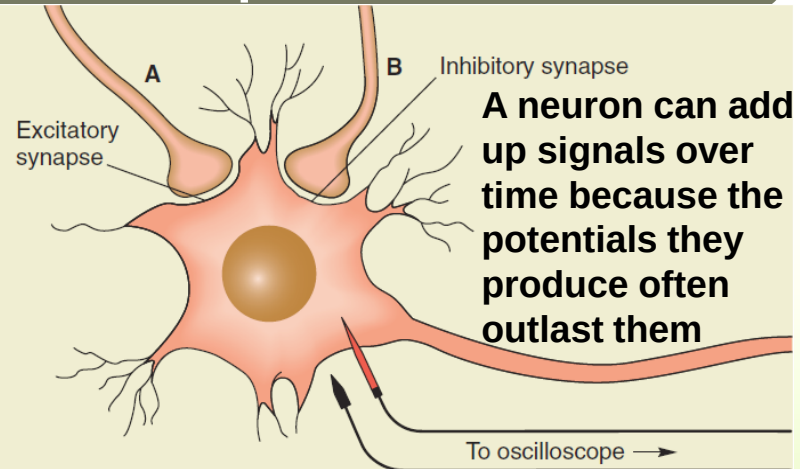
Two simultaneous IPSPs sum to produce a greater IPSP



A simultaneous IPSP and EPSP cancel each other out

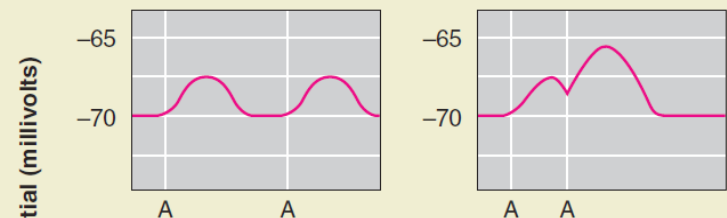


The two possible combinations of temporal summation.

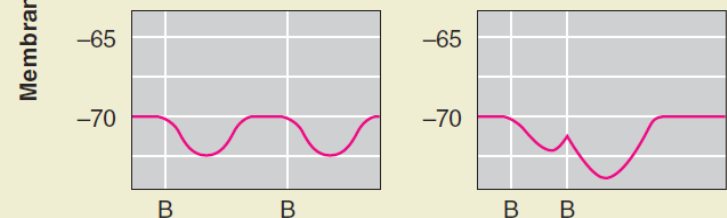


A neuron can add up signals over time because the potentials they produce often outlast them

Two EPSPs elicited in rapid succession sum to produce a larger EPSP



Two IPSPs elicited in rapid succession sum to produce a larger IPSP



Conduction of Action Potentials

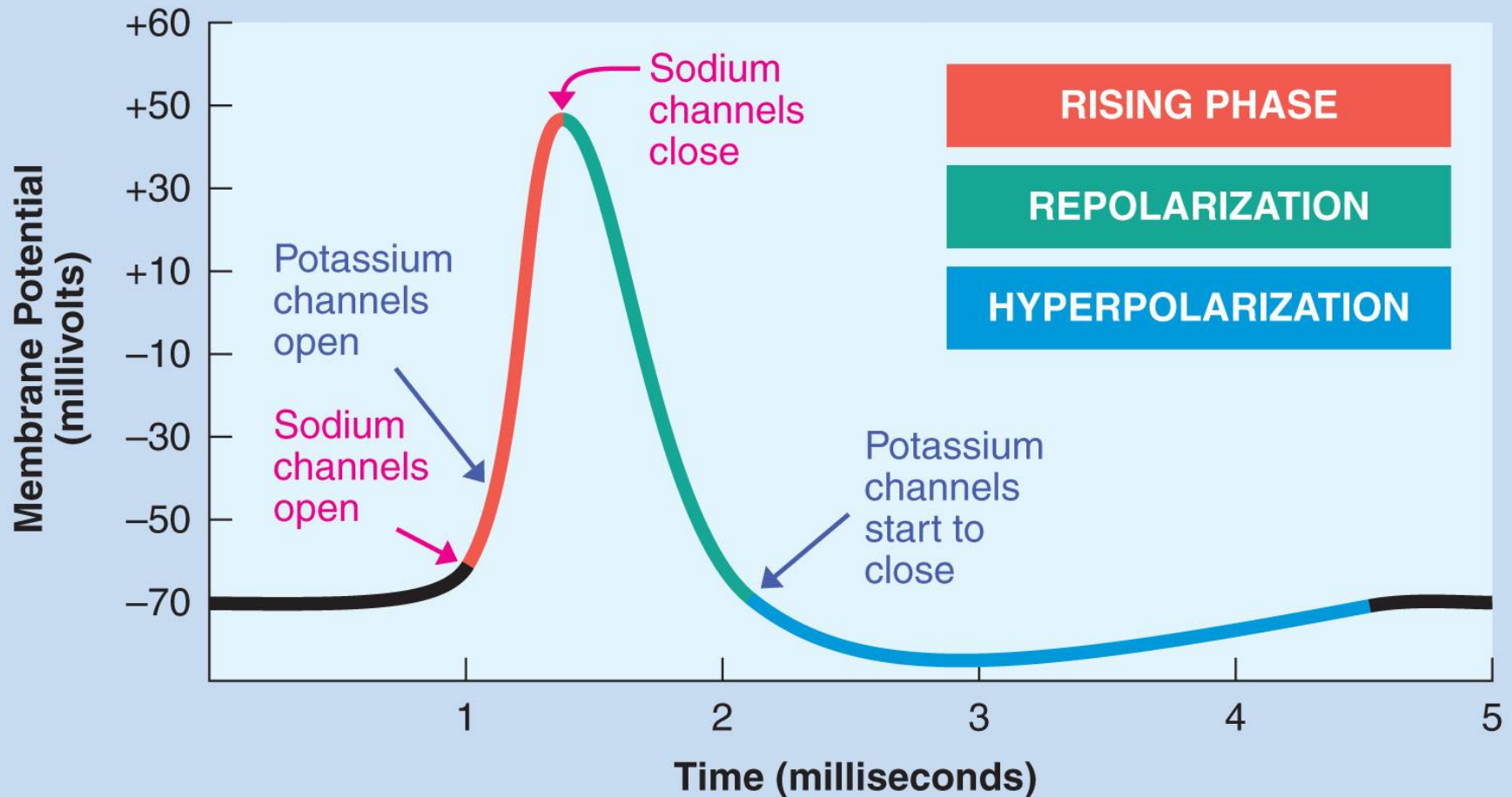


- **All-or-none – when threshold is reached the neuron “fires” and the action potential either occurs or it does not**
- **When threshold is reached, voltage-activated ion channels are opened**

Sodium and Potassium Channels



The opening and closing of voltage-activated sodium and potassium channels during the three phases of the action potential: rising phase, repolarization, and hyperpolarization.



Refractory Periods



After action potential starts there is 1 to 2 milliseconds where another cannot be started called the absolute refractory period.



**This is followed by the relative refractory period:
Time when it is possible for a neuron to fire again but at a more difficult rate and which requires above normal levels of stimulation.**

The refractory period is important because it prevents backwards movement of APs and limits the rate of firing.

Post Synaptic Potential vs. Action Potential



PSPs

EPSPs/IPSPs

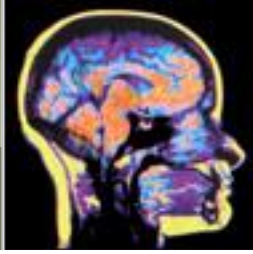
- **Decremental**
- **Fast**
- **Passive (energy is not used)**

APs

Action Potentials

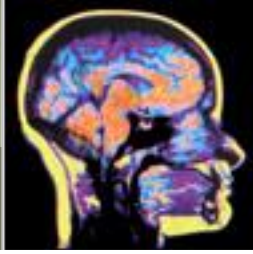
- **Nondecremental**
- **Conducted more slowly than PSPs**
- **Passive and active**

Axonal Conduction of Action Potentials



- Once AP is generated it travels passively along axonal membrane to next voltage-activated sodium channel.
- Arrival of this signal opens the channel and sodium rushes in to the neuron to generate an AP.
- The signal is then carried passively to the next sodium channel where another AP is activated.
- This keeps happening until a full-blown AP is triggered in all terminal buttons.
- It is a single wave spreading at constant speed along the axon.

Axonal Conduction of Action Potentials



- Once AP reaches Terminal buttons it triggers exocytosis.
- Axons of some neurons are insulated with myelin, so ions can pass through the axonal membrane at the nodes of Ranvier, the gaps in-between adjacent myelin segments.
- When an AP is generated in a myelinated axon, the signal is conducted passively, its instant and does so in a decremented manner along the first segment of myelin to the next node of Ranvier.
- This signal diminishes as it moves along but is strong enough to open the voltage-activated sodium channels at the next node in order to generate the next AP.

Velocity and Conduction



**Conduction in
Neurons
without Axons**

**Velocity of
Axonal
Conduction**

**Conduction in
interneurons is
typically
passive and
decremental**

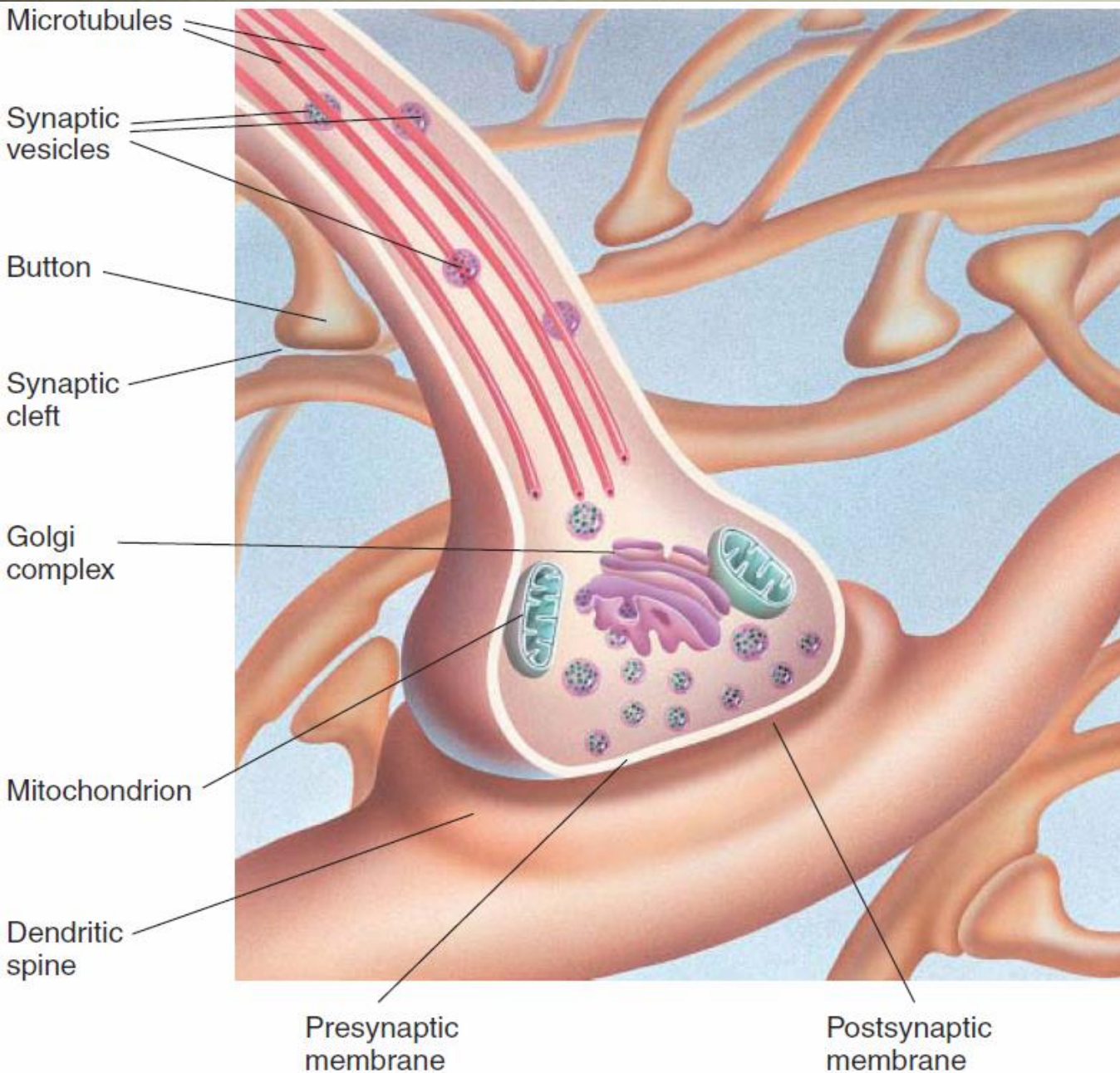
**Maximum velocity
of conduction in
human motor neurons
is about 60 meters
per second**

The Hodgkin-Huxley Model in Perspective



- **The Hodgkin-Huxley model was based on motor neurons of squids**
- **So, considered as more of a theory.**
- **It gives a simple and effective explanation of the ways neurons conduct signals.**
- **However, it is not representative of the variety and complexity, and plasticity of many of the neurons seen in the brains of a mammal.**
 - **E.g., cerebral neurons fire continually without any input, do not have axons and do not display action potentials.**

Synaptic Transmission: Structure of Synapses



Axodendritic are most common; axons synapse onto dendritic spines

Directed synapse: site of release and contact are in close proximity

Non-directed synapse: site of release and contact are separated by some distance

The anatomy of the typical synapse.

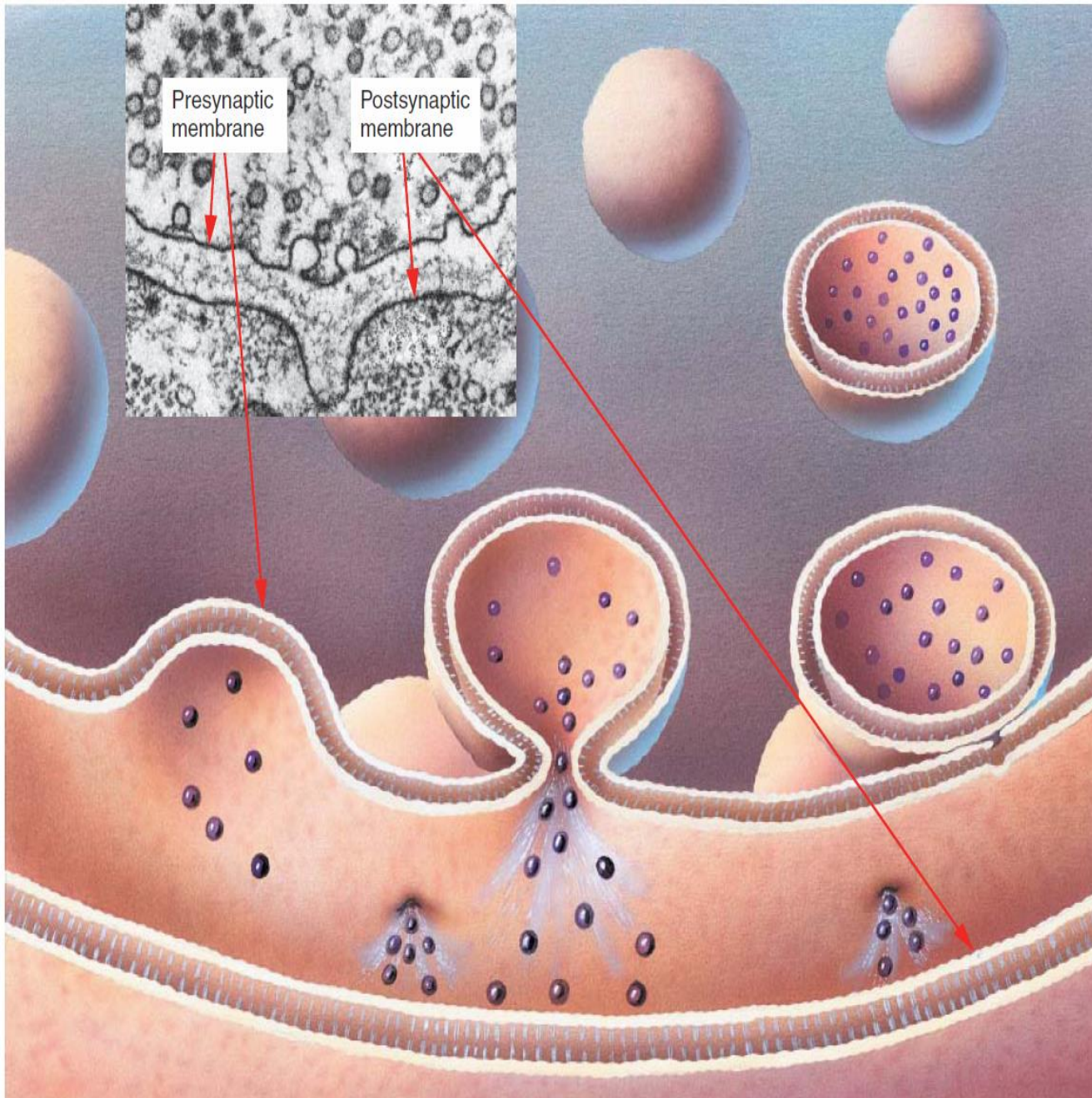
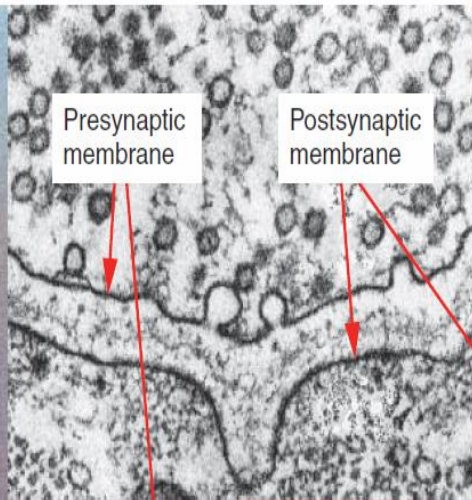
Synthesis, Packaging, and Transport of Neurotransmitter Molecules



Neurotransmitter Molecules are either:

- **Small: synthesized in terminal button & packaged in synaptic vesicles by golgi complex.**
- **Large: assembled in cell body on ribosomes, packaged in vesicles by golgi complex, and transported in microtubules to axon terminal.**
- **Many neurons contain 2 neurotransmitters (coexistence)**

Release of Neurotransmitter (NT) Molecules



Exocytosis – the process of NT release

The arrival of an AP at the terminal opens voltage-activated Ca^{2+} channels

The entry of Ca^{2+} causes vesicles to fuse with the terminal membrane and release their contents

Schematic and photographic illustrations of exocytosis.

Activation of Receptors by NT Molecules



- Released NT molecules produce signals in postsynaptic neurons by binding to receptors
- Each site receiving neurotransmitters is a specialized protein that will only receive one type of NT.
- A NT is a ligand of its receptor
- Ligand = a molecule that binds to another

Receptors



- Most NTs can bind to several types of receptors.
- Advantage = that one NT can transmit different messages throughout many different parts of the brain.
- Once NT has bound to a receptor subtype, it can influence the postsynaptic neuron in 1 of 2 ways depending on whether the receptor is....
- Ionotropic: associated with ligand-activated ion channels
- Metabotropic: associated with signal proteins and G proteins

Reuptake, Enzymatic Degradation, & Recycling

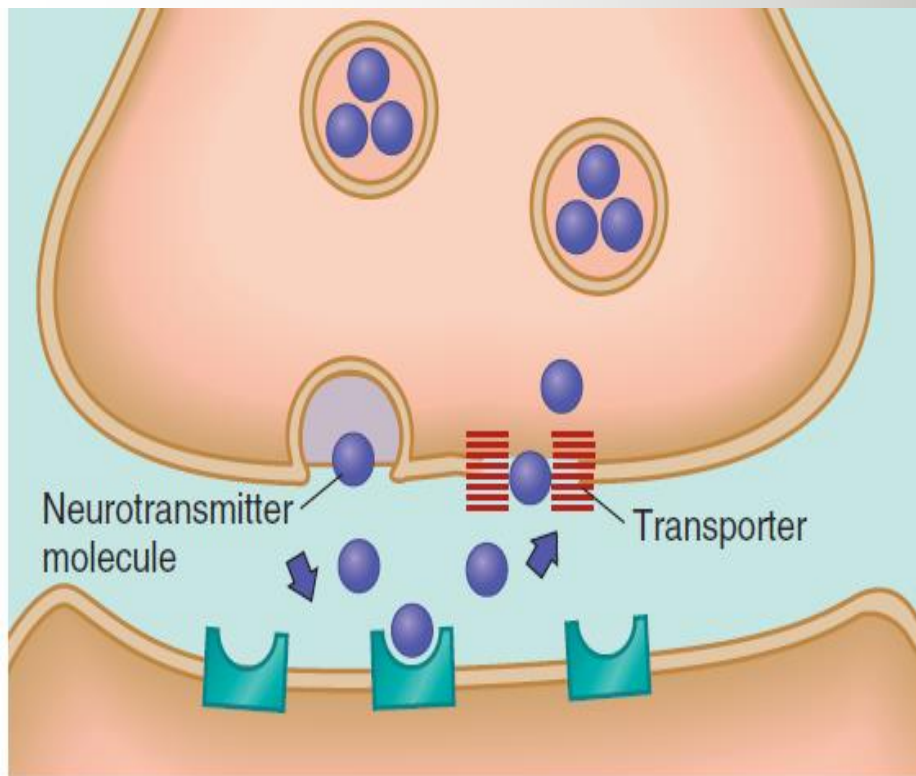


As long as NT is in the synapse, it is “active”.

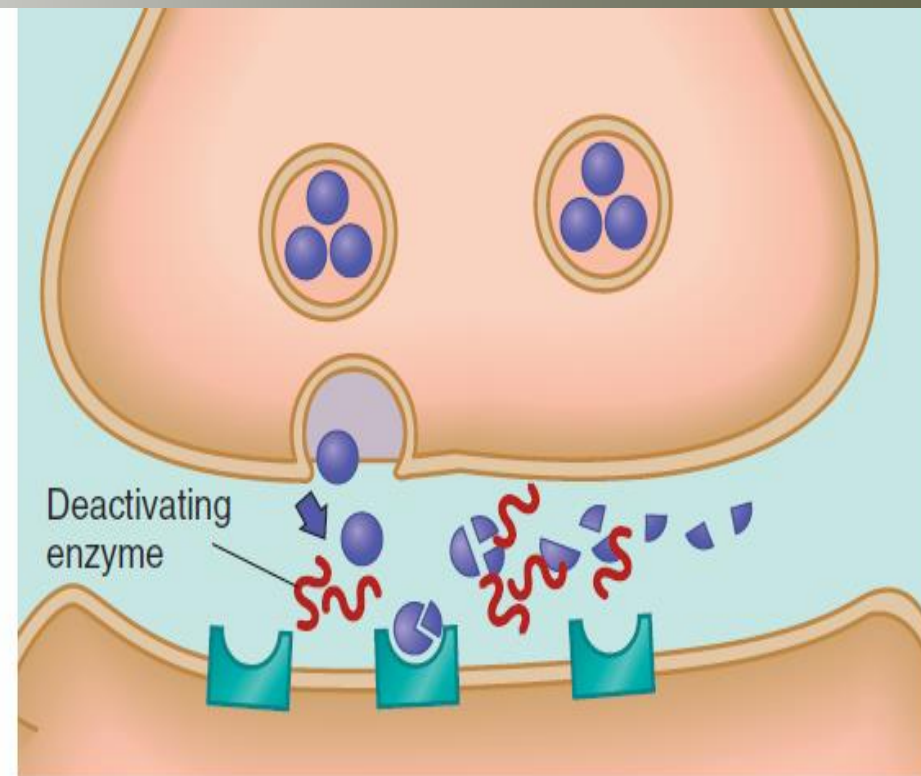
Activity must be turned off to avoid clogging-up channel of communication

Reuptake – scoop up and recycle NT

Enzymatic degradation – a NT is broken down by enzymes



Reuptake



Enzymatic Degradation

Glial Function & Synaptic Transmission



Role of glial cells in this process, with astrocytes performing many functions, e.g., releasing chemical transmitters, conduct signals, and are involved in reuptake.

Some communication in the brain appears to be happening through gap junctions.

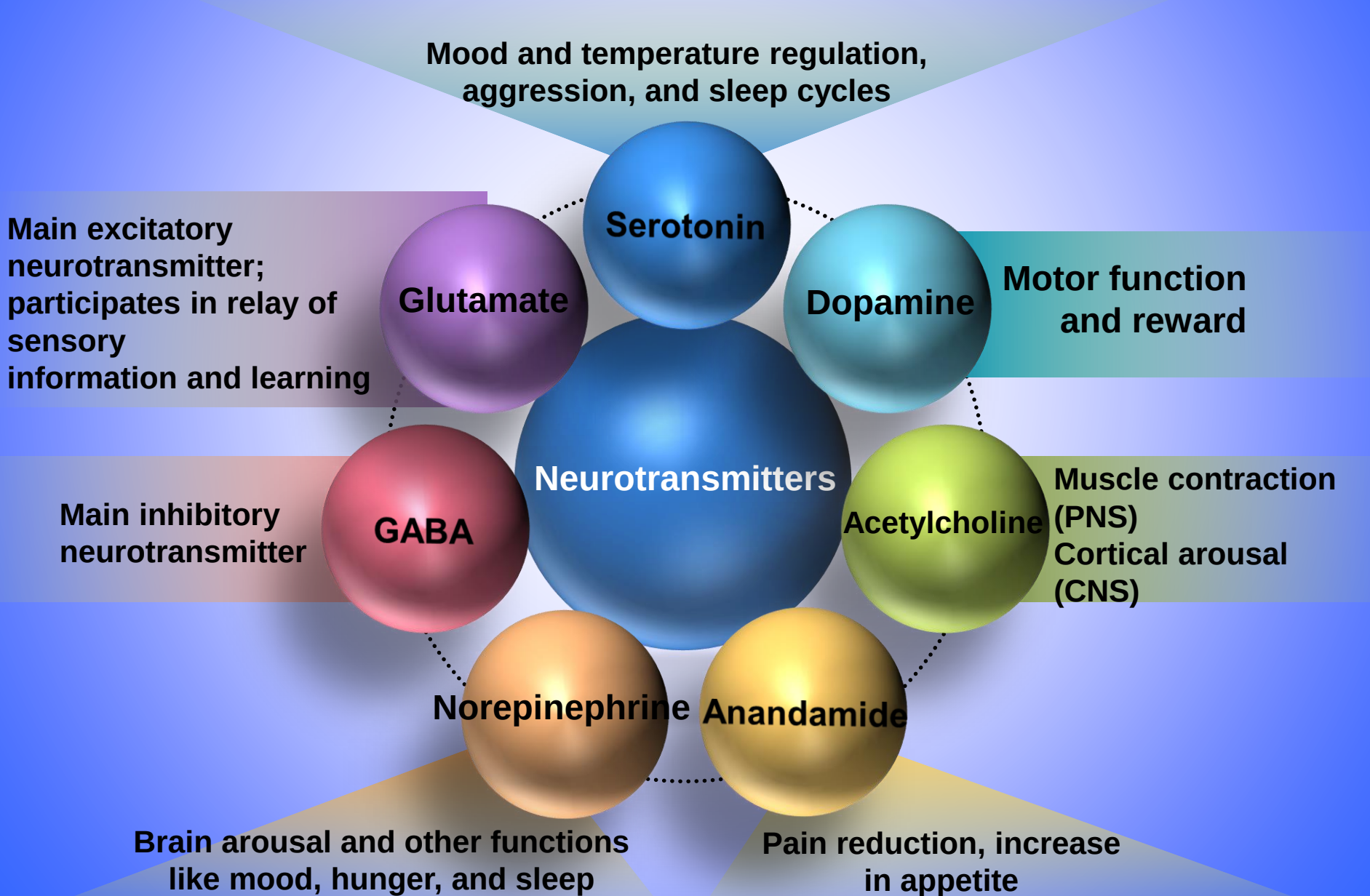
These are narrow spaces between neurons that are bridged by fine tubular channels that contain cytoplasm.

Gap junctions are referred to as electrical synapses.

So neuron to neuron connections are not the only things that make the brain work.



Over 100. These 7 are small-molecule NTs & are divided in to 3 classes: amino acids, monoamines, and acetylcholine. This figure provides information about what each are involved in/what they regulate.



Amino Acid Neurotransmitters



Usually found at fast-acting directed synapses in the CNS

Glutamate – Most prevalent excitatory neurotransmitter in the CNS



GABA

- Synthesized from glutamate
- Most prevalent inhibitory NT in the CNS



Aspartate and glycine

Monoamines and Acetylcholine



Monoamines: synthesized by single amino acid & diffused effects.

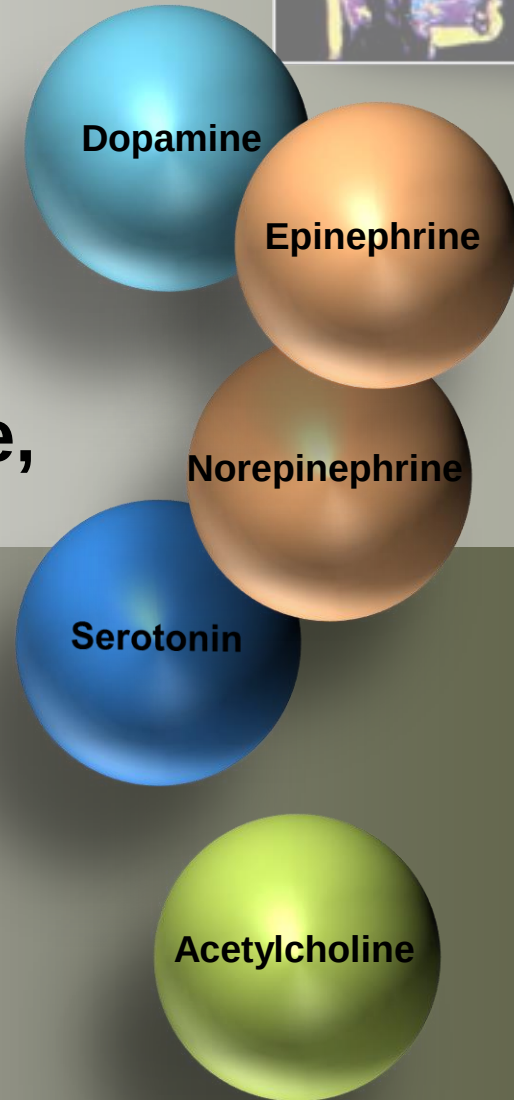
Sub-divided into 2 groups:

Catecholamines – synthesized from tyrosine (Dopamine, Norepinephrine, Epinephrine)

Indolamines – synthesized from tryptophan (Serotonin)

Acetylcholine (Ach)

- Acetyl group + choline molecule
- First identified at neuromuscular junction



Unconventional Neurotransmitters



Soluble gases – exist only briefly

- Nitric oxide and carbon monoxide
- Retrograde transmission – backwards communication

Endocannabinoids

- anandamide is one of the two known endocannabinoids.

Neuropeptides



Large molecules: Over 100 identified with actions dependent on amino acid sequence

Example – endorphins

- “Endogenous opioids”
- Produce analgesia (pain suppression)
- Receptors were identified before the natural ligand was

PAIN

Pharmacology of Synaptic Transmission & Behaviour



Seven Steps in Neurotransmitter Action

1 Neurotransmitter molecules are synthesized from precursors under the influence of enzymes.

2 Neurotransmitter molecules are stored in vesicles.

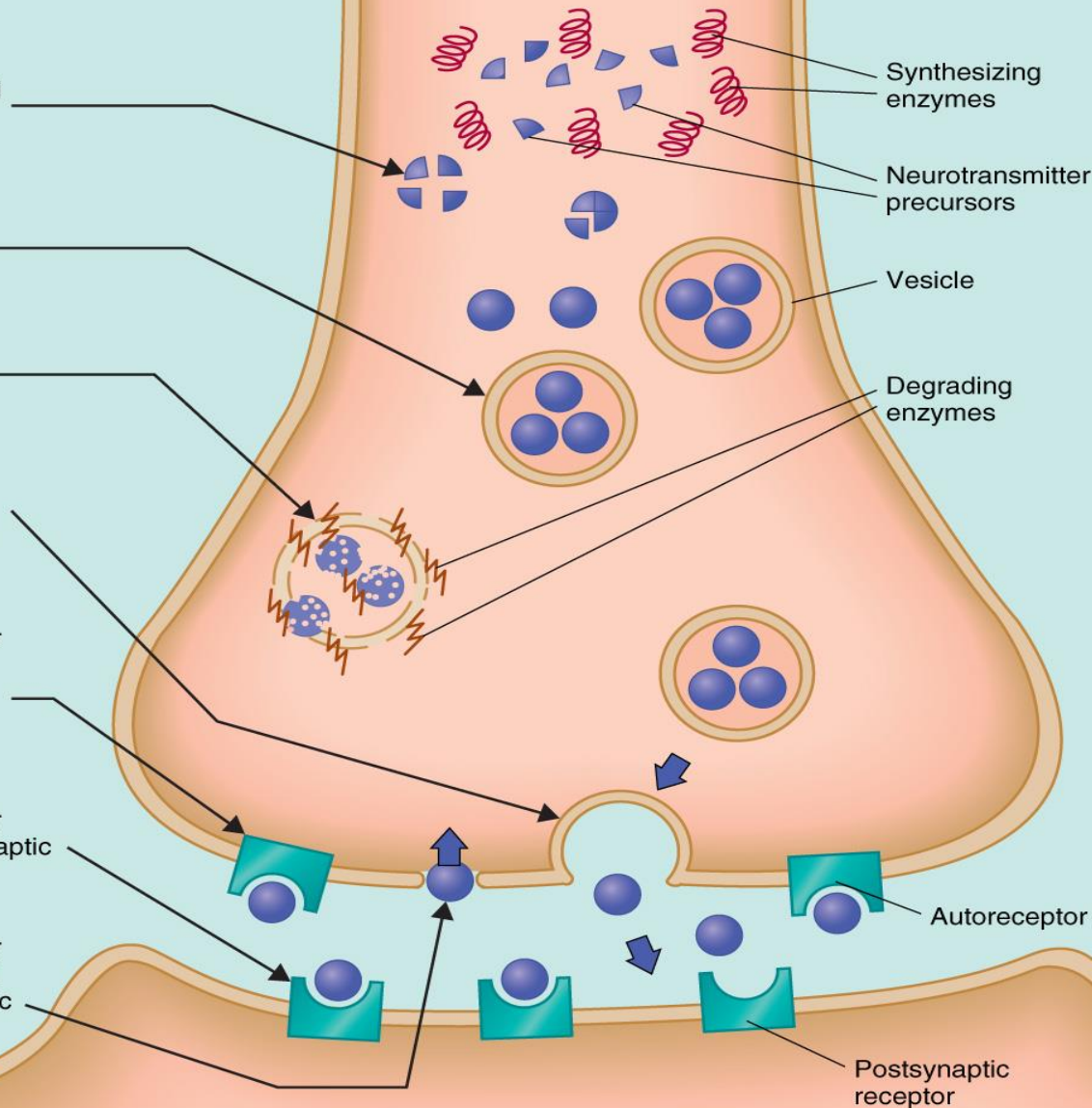
3 Neurotransmitter molecules that leak from their vesicles are destroyed by enzymes.

4 Action potentials cause vesicles to fuse with the presynaptic membrane and release their neurotransmitter molecules into the synapse.

5 Released neurotransmitter molecules bind with autoreceptors and inhibit subsequent neurotransmitter release.

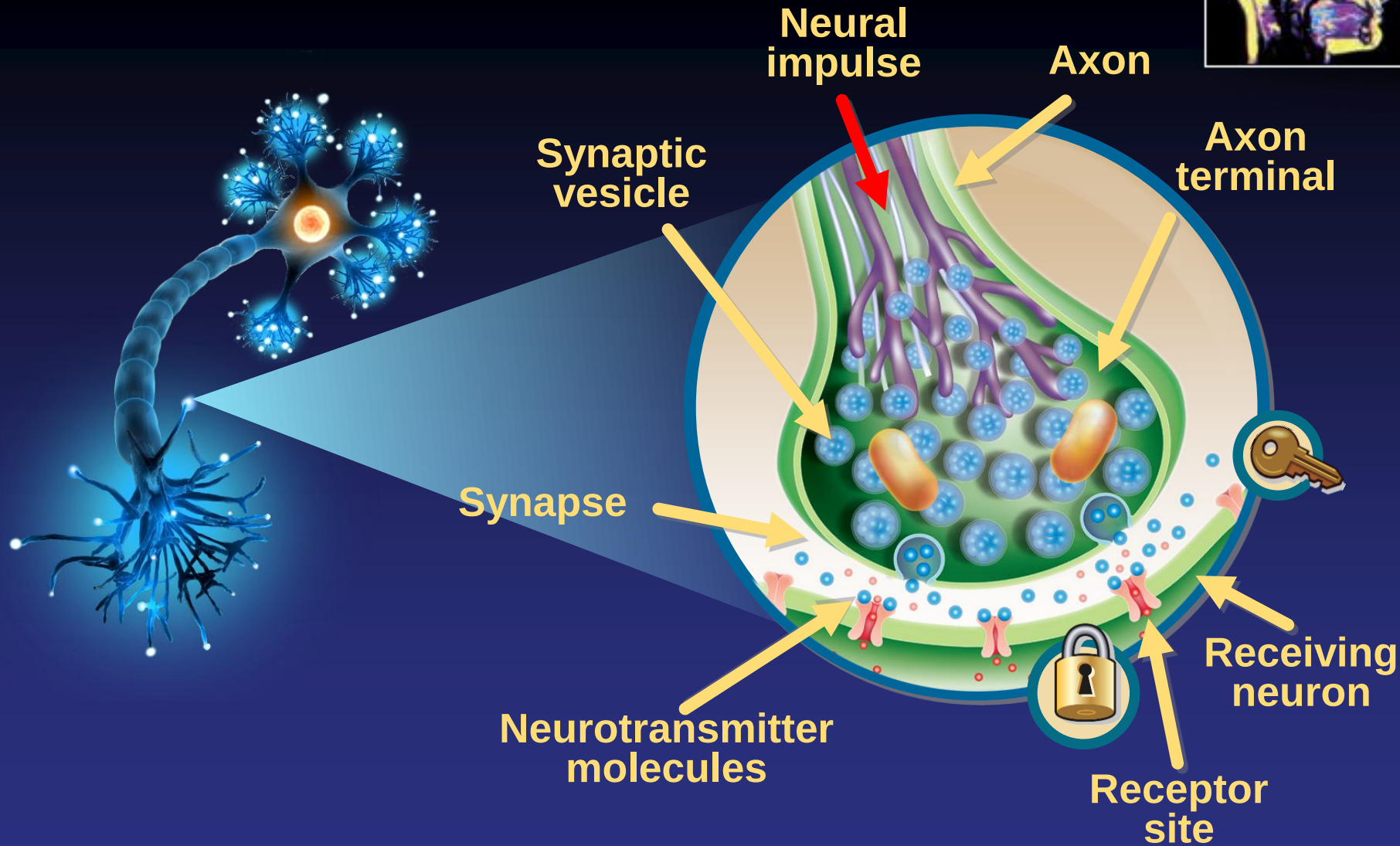
6 Released neurotransmitter molecules bind to postsynaptic receptors.

7 Released neurotransmitter molecules are deactivated by either reuptake or enzymatic degradation.



7 steps in neurotransmitter action

Axons and Axon Terminals





How drugs influence synaptic activity

- **Agonists – increase or facilitate activity**
- **Antagonists – decrease or inhibit activity**
- **A drug may act to alter neurotransmitter activity at any point in its “life cycle”**

Pharmacology examines behavioural effects of neurotransmitters.

Behavioral Pharmacology: Three Influential Lines of Research



- **Drugs selective to specific receptor subtypes may exert different effects**
 - e.g. nicotinic vs. muscarinic acetylcholine receptors
- **Discovery of the endogenous opioids provided insight into brain mechanisms of pleasure/pain**
- **Effects of dopamine agonists and antagonists on psychotic symptoms led to new treatments for schizophrenia**



Agonistic and antagonistic drug effects



Some Mechanisms of Drug Action

Agonistic Drug Effects

Drug increases the synthesis of neurotransmitter molecules (e.g., by increasing the amount of precursor).

Drug increases the number of neurotransmitter molecules by destroying degrading enzymes.

Drug increases the release of neurotransmitter molecules from terminal buttons.

Drug binds to autoreceptors and blocks their inhibitory effect on neurotransmitter release.

Drug binds to postsynaptic receptors and either activates them or increases the effect on them of neurotransmitter

Drug blocks the deactivation of neurotransmitter molecules by blocking degradation or reuptake.

Antagonistic Drug Effects

Drug blocks the synthesis of neurotransmitter molecules (e.g., by destroying synthesizing enzymes).

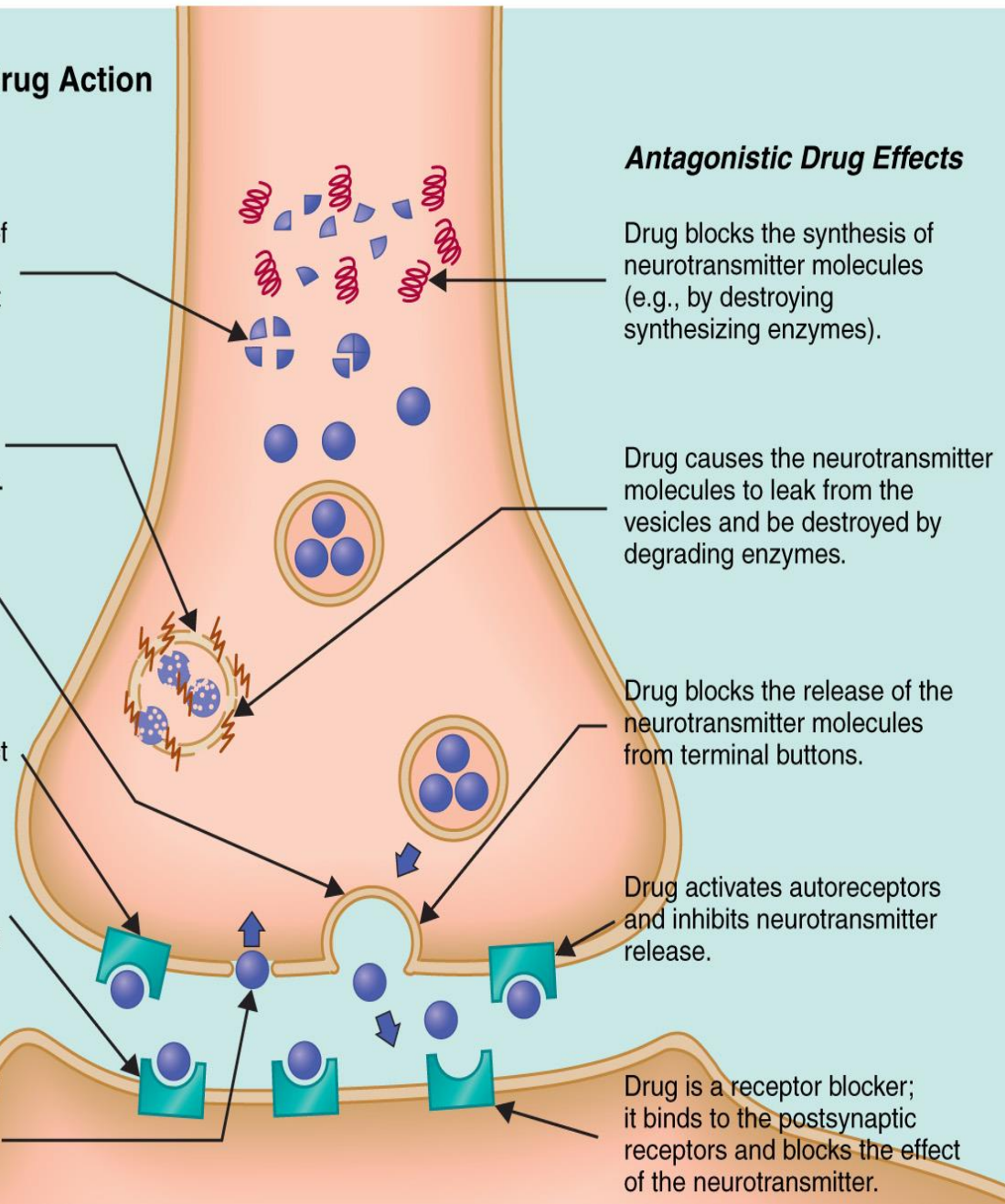
Drug causes the neurotransmitter molecules to leak from the vesicles and be destroyed by degrading enzymes.

Drug blocks the release of the neurotransmitter molecules from terminal buttons.

Drug activates autoreceptors and inhibits neurotransmitter release.

Drug is a receptor blocker; it binds to the postsynaptic receptors and blocks the effect of the neurotransmitter.

Some mechanisms of agonistic and antagonistic drug effects



Disorders of Neurodevelopment: Autism



- Issues during the development of the nervous system can have detrimental effects.
- **Three core symptoms of Autism:**
 - Reduced ability to interpret emotions
 - Reduced capacity for social interaction
 - Preoccupation with a single subject or activity
- Intensive behavioral therapy may improve function
- **It is a Heterogenous disorder** – level of brain damage and dysfunction varies
- Often considered a spectrum disorder



Disorders of Neurodevelopment: Autism



- Incidence: **6.6 per 1,000 births (or 1 in 166)**
- 80% males, 60% have mental disorders, 35% epileptic, 25% have little or no language ability
- Most have some abilities preserved – rote memory, jigsaw puzzles, musical ability, artistic ability
- **Autistic Savants** – poor intellectual abilities but display specific cognitive or artistic abilities.
 - ~1/10 autistic individuals display savant abilities
 - Perhaps a consequence of compensatory functional improvement in one area following damage to another

Genetic Basis of Autism



- **Siblings of children with autism have a 5% chance of having autism (above rate in general population)**
- **But below 50% chance expected if autism was only caused by a single dominant gene and lower than the 25% chance expected if autism was caused by a single recessive gene.**
- **60% concordance rate for monozygotic twins**
- **Several genes interacting with the environment**

Source: Bouchard & McGue, 1981

Neural Mechanisms of Autism



Understanding of brain structures involved in autism is still limited, so far implicated:

- Cerebellum
- Amygdala
- Frontal cortex

Two lines of research on cortical involvement in autism:

- Abnormal response to faces in autistic patients
 - Spend less time than non-autistic subjects looking at faces, especially eyes
 - Low fMRI activity in fusiform face area
- Possibly deficient in mirror neuron function



Disorders of Neurodevelopment: Williams Syndrome

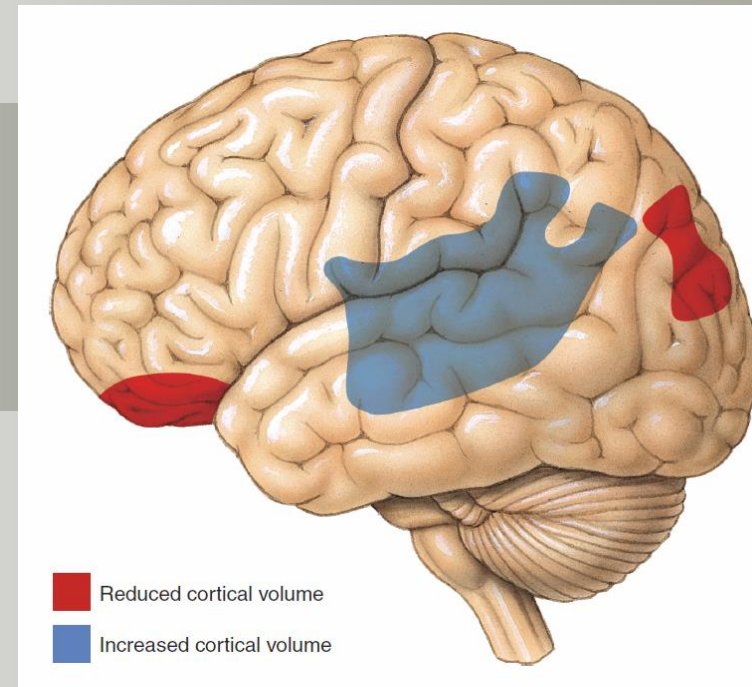


- Incidence: **1 in every 7,500 births**
- Mental disorders and an uneven pattern of abilities and disabilities
- Sociable, empathetic, and talkative– exhibit language skills, music skills, and an enhanced ability to recognize faces
- Profound impairments in spatial cognition
- Usually have heart disorders associated with a mutation in a gene on chromosome 7 – the gene (and others) is absent in 95% of those with Williams

Disorders of Neurodevelopment: Williams Syndrome



- General thinning of cortex at juncture of occipital and parietal lobes, and at the orbitofrontal cortex.
- A lack of development in these 2 areas may be related to the impairment of spatial cognition and hyper sociability
- Thickness of cortex in superior temporal gyrus is normal and has been linked to the high levels of language and music processing.
- “Elfin” appearance: short, small upturned noses, oval ears, broad mouths



Two areas of reduced cortical volume and one area of increased cortical volume observed in people with Williams syndrome.

Next Week...



The Visual System

Essential Reading...

Pinel: Biopsychology – Chapter 6