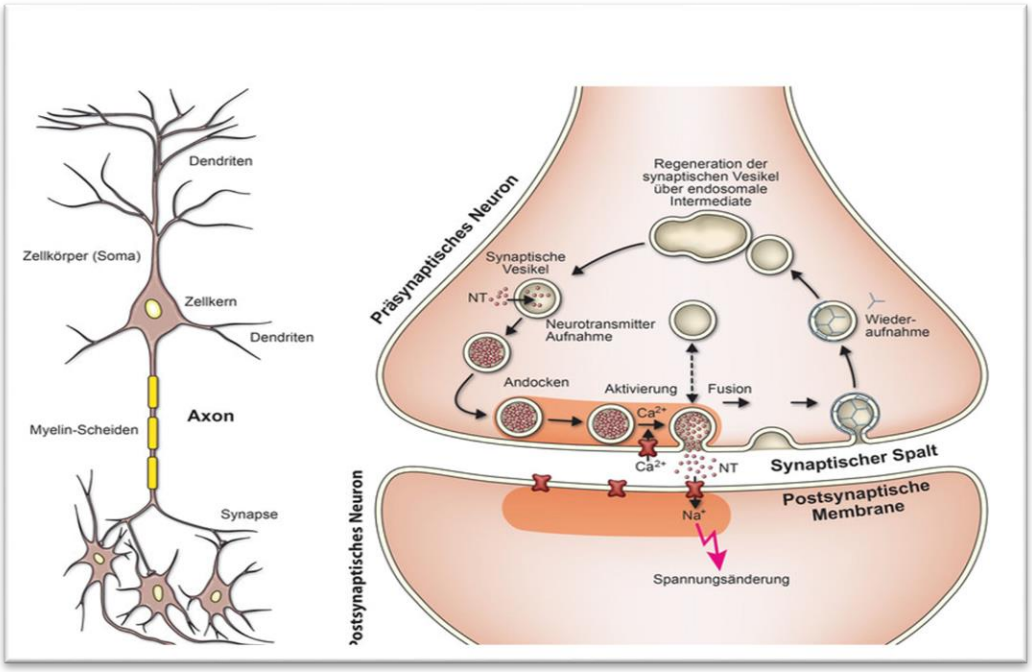
Department of Anesthesia Techniques
Title of the lecture:-Physiology of Neurotransmission
Dr.Sura A. Awadh
sura.abdailahalek@mustaqbal-college.edu.iq

Physiology of Neurotransmission

Nervous System Communication via Synapses

- Synapses: Junctions that allow neurons to communicate with each other.

Neurotransmitters : Chemicals that released from pre-synaptic neuron into synaptic cleft and received by post synaptic neuron.

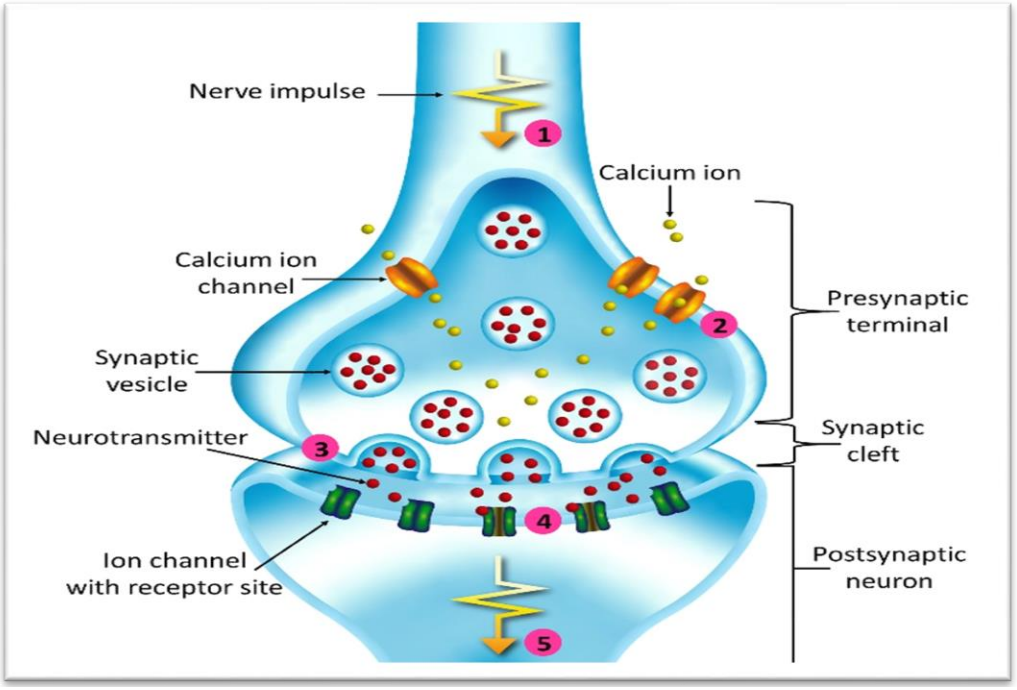


Pre-synaptic Response

A nerve impulse which begins as an electrical signal in the presynaptic neuron, will be translated chemically across the synaptic cleft by a neurotransmitter.

Post-synaptic Response

Once the neurotransmitter binds to receptors on the postsynaptic neuron, the message becomes electrical once again. This can result in either an excitatory postsynaptic potential or an inhibitory postsynaptic potential.



Mechanism of Neurotransmitter Release (Role of Calcium Ions)

- The presynaptic terminal contains large number of voltage-gated calcium channels. When an action potential depolarizes the presynaptic membrane, these Ca++ channels open and allow large number of calcium ions to flow into the terminal.
- Quantity of neurotransmitter substance is directly related to number of calcium ions that inter.
- When calcium ion, they bind with special protein molecules on release sites allowing vesicles to release their transmitter.

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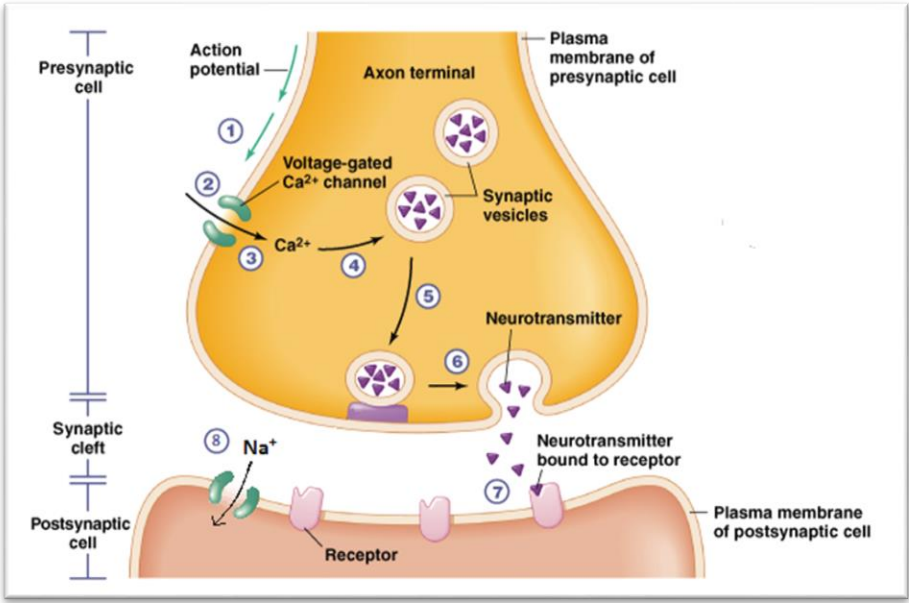
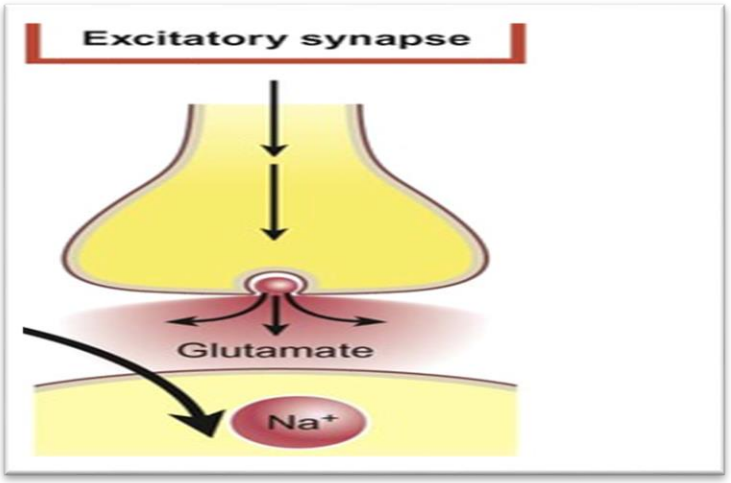
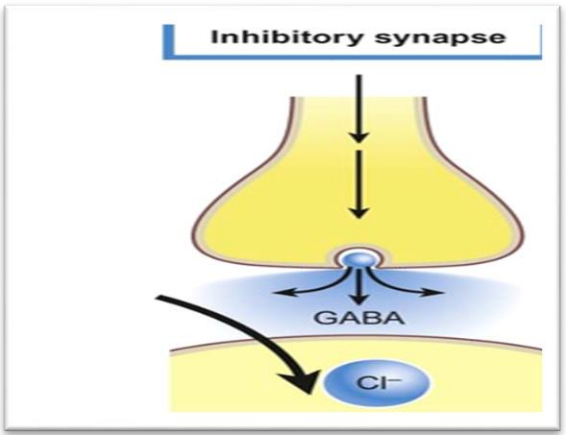


Excitatory and inhibitory Synapses

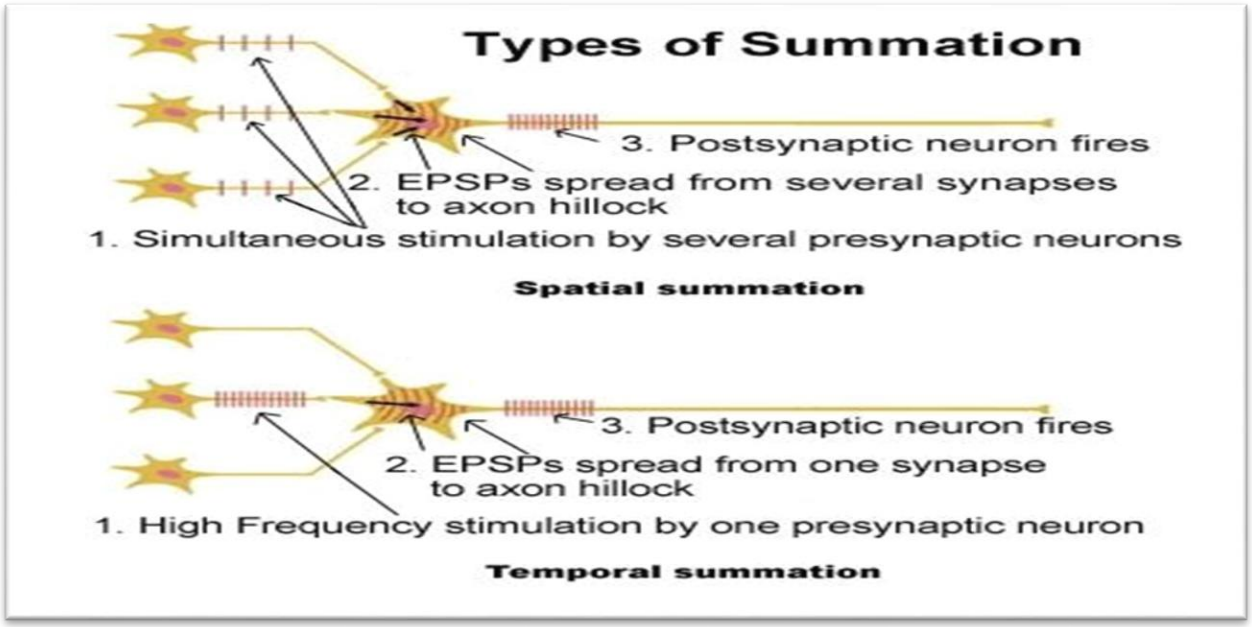
Excitatory synapse: The release of an excitatory neurotransmitter (e.g. glutamate) at the synapses will cause an inflow of positively charged sodium ions (Na+) making a localized depolarization of the membrane. The current then flows to the resting (polarized) segment of the axon.



- **Inhibitory synapse**: It causes an **inflow of Cl-** or **outflow of K+** making the synaptic membrane **hyperpolarized**. This increase **prevents depolarization**, causing a **decrease** in the possibility of an **axon discharge**.
- If they are both equal to their charges, then the operation will cancel itself out.



Spatial and Temporal Summation determine whether the excitatory synapses prevail over the inhibitory synapses or vice versa

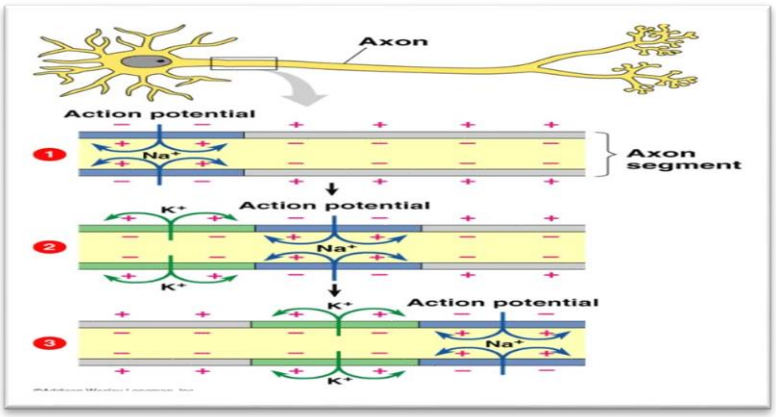


Effect of Drugs on Synaptic Transmission

- Drugs that bind to a receptor and produce a response similar to the normal activation are called **agonists**, and drug that bind to the receptor but unable to activate it are **antagonists**. They may:
  1. Altered **release** of neurotransmitter.
  2. Altered **interaction** of neurotransmitter with the **receptor**.
  3. Altered **removal** of neurotransmitter from synaptic cleft.

The Action Potential

- When a nerve is **stimulated** by pressure, electricity or chemicals, the **resting potential** changes .
- The rapid **change in polarity** that moves along the nerve fiber is called the "**action potential**.
- In order for an **action potential to occur**, it must reach **threshold**. This means that the stimulus is substantial enough to change the electrical potential of the cell membrane.
- The stimulus causes **ion channels to open**. The membrane potential of a cellular structure is determined by the **in-flow and out-flow of sodium and potassium**



Plateau in Action Potential

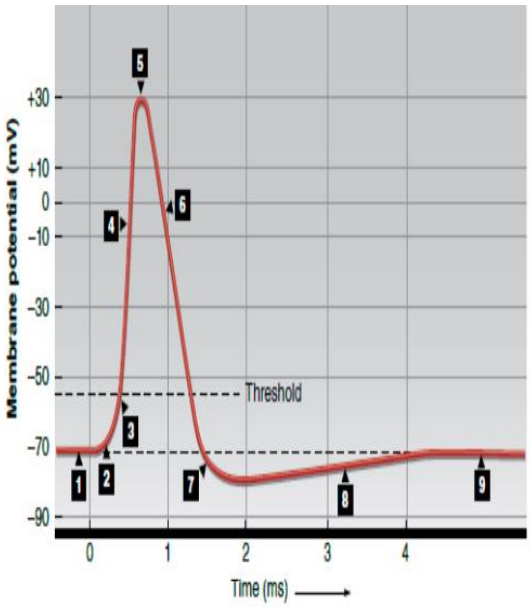
- **Depolarization**

The upswing is caused when positively charged sodium ions (Na+) suddenly rush through open sodium gates into a nerve cell. The membrane potential changes from -55 millivolts to 0. As additional sodium enters, the membrane develops a positive value (+30 millivolts).

- **Repolarization**

The downswing is caused by the closing of sodium ion channels and the opening of potassium ion channels. The expulsion of K+ acts to restore the localized negative membrane potential of the cell (about -70 mV).

1. Resting membrane potential
2. Depolarizing stimulus
3. Membrane depolarized to threshold
4. Rapid Na+ entry
5. Na+ channels close; K+ channels open
6. K+ moves into extracellular fluid
7. Hyperpolarization occurs
8. K+ channels close
9. Cell returns to resting membrane potential



Speed of Conduction

- This area of depolarization/ repolarization/recovery moves along a nerve fiber like a very fast wave.
- In myelinated fibers, conduction is hundreds of times faster because the action potential only occurs at the nodes of Ranvier by jumping from node to node. This is called "saltatory" conduction.
- Damage to the myelin sheath by the disease can cause severe impairment of nerve cell function.
- Some poisons and drugs interfere with nerve impulses by blocking sodium channels in nerves.

Effects of Local Anesthesia

- Block nerve transmission to pain centers in the CNS by binding to and inhibiting the function of an ion channel in the cell membrane of nerve cells known as the sodium channel.
- This action obstructs the movement of nerve impulses near the site of injection, but there are no changes in awareness and sense perception in other areas.

Effects of General Anesthetics

- Induce a different sort of anesthetic state, one of general insensibility to pain.
- The patient loses awareness yet his vital physiologic functions,such as breathing and maintenance of blood pressure, continue to function.

Effect of Inhalational or Volatile Anesthetics on CNS

1. Inhibit nerve transmission.
2. Cause a reduction in nerve transmission at synapses.
3. Affect the function of ion channel and neurotransmitter receptor proteins in the membranes of nerve cells.

Theories of Anesthesia

- Theories & hypotheses which explained the ability of the anesthetic agent to disrupt cellular and intercellular communication in the CNS are:

1. Expansion & fluidization of the cell membrane that result in depressed synaptic transmission.

2. Hyperpolarize neurons by increasing potassium permeability.

3. The Meyer–Overton hypothesis proposed that once a sufficient number of anaesthetic molecules were dissolved in the lipid membranes of cells within the central nervous system, anaesthesia would result by a mechanism of membrane disruption.

4. Critical volume theory: Anesthetic's direct action on ion channel proteins will lead to interruption of neurotransmission by obstructing ion flux with changes of electrical conductivity in the neurons.

5. The reticular activating system, a multi-synaptic structure, is the most important site within the CNS for anesthetic action where drugs interact with specific receptors.

Effect on Cerebral & Cranial nerve cells

1. The cells in the higher centers of the cerebral hemispheres are affected first.
2. The centers for the sensory cranial nerves subsequentlysmell, then vision, then hearing.

Mechanism

1. **Oxidation in the nerve cells**, upon which the function of the cells depends, is affected by the drug by interference with the **selective permeability** of the surface membrane of the cells.
2. 2. Anaesthetic agents do not affect the various portions of the cerebrum in quite the same order. They produce analgesia before confusion of the mind and amnesia set in, at the same time as they abolishes pain

Spinal Analgesia

By the direct application to the spinal cord of local anesthetic drugs:

1. Passage of afferent and efferent impulses along the spinal roots may be blocked.
2. Motor and sensory actions of the affected nerve tracts are abolished.
3. Thoracic region of the spinal cord is affected and extensive vasomotor paralysis ensures.
4. Fall in blood pressure may be considerable due to:
    a) Relaxation of the trunk and lower limb muscles.
    b) Stagnation of blood in the capillaries and veins.
    c) Increased exudation (diffusion) of lymph.