CNS Block

1st Lecture

Physiology of Synaptic Transmission and Synaptic Receptors

Physiology Team– 430

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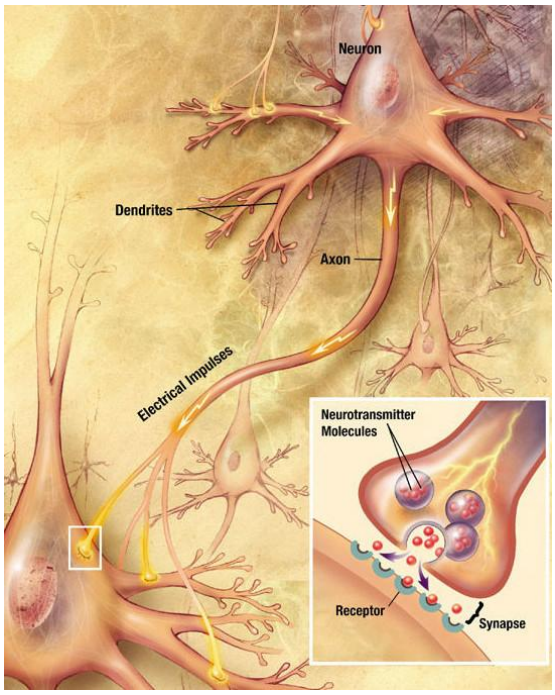
Physiology of Synaptic Transmission and Synaptic Receptors

A synapse: In the nervous system, a synapse is a structure that permits a neuron to pass an electrical or chemical signal to another cell (neural or otherwise).

At a synapse, the plasma membrane of the signal-passing neuron (the *presynaptic* neuron) comes into close apposition with the membrane of the target (*postsynaptic*) cell.



> Some neurons have only few synapses on them, but others may have as many as 10,000 synapses on their soma and dendrites.

There are two fundamentally different types of synapse:

- In a chemical synapse, the presynaptic neuron releases a chemical called a neurotransmitter that binds to receptors located in the postsynaptic cell, usually embedded in the plasma membrane. Binding of the neurotransmitter to a receptor can affect the postsynaptic cell in a wide variety of ways.

- In an electrical synapse, the presynaptic and postsynaptic cell membranes are connected by channels that are capable of passing electrical current, causing voltage changes in the presynaptic cell to induce voltage changes in the postsynaptic cell.

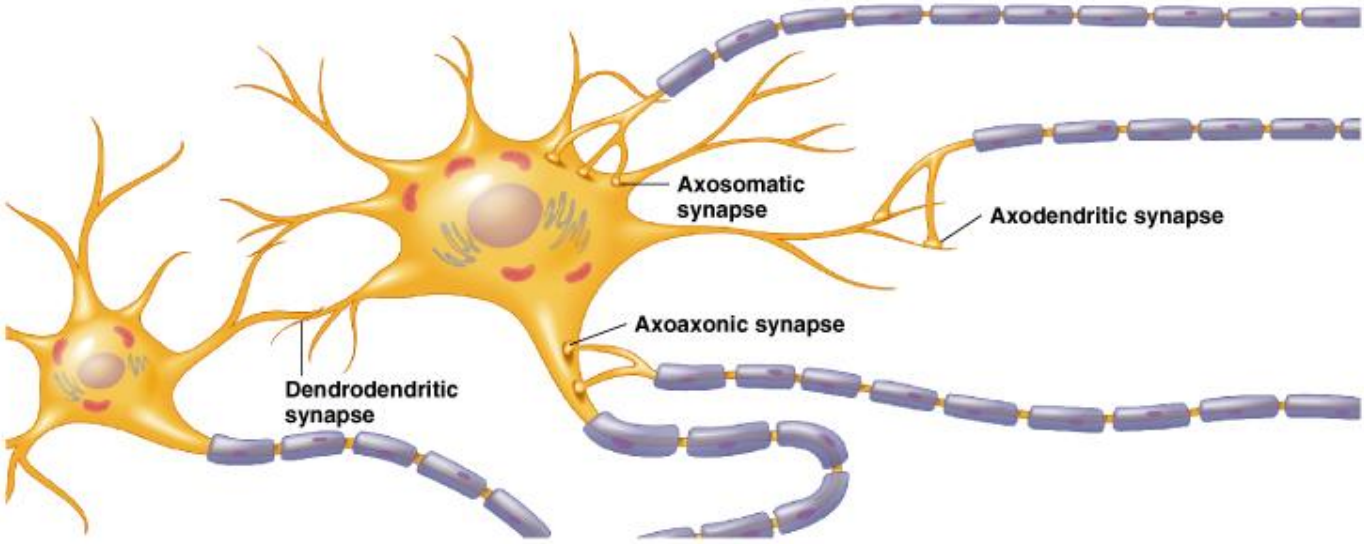
The synapse consists of

1) presynaptic membrane which is formed by the terminal button of an axon.

2) postsynaptic membrane which is composed of a segment of dendrite or cell body.

3) the space between these two structures which is called the synaptic cleft.

Classification of Synapses according to their location



(b) Locations of neuron-to-neuron synapses

They could be:

(1) Axo-dendritic, (2) Axo-axonal (axo-axonic), (3) Axo-somatic

& less commonly: (4) Dendro-somatic, (5) Somato-somatic

The Neurotransmitter

The neurotransmitter is released by a neuron (called presynaptic cell), crosses the synaptic cleft, and binds to a receptor located on the membrane (postsynaptic membrane) of another cell

A neurotransmitter is a chemical substance

Types of transmitters:

• Excitatory neurotransmitter:
It's a transmitter that produces excitatory postsynaptic potential (EPSP) on the **postsynaptic neuron**.

• Inhibitory neurotransmitter:
It's a transmitter that produces inhibitory postsynaptic potential (IPSP) on the **postsynaptic neuron**.

* Examples of excitatory transmitter:

(1) Acetylcholine: Opens sodium channels in the Postsynaptic Cell Membrane →depolarization → EPSP.

(2) Glutamate: Produces EPSP by opening of C^{2+} channel.

(3) Serotonin (5-Hydroxytryptamine) Present in high concentration in brain Raphe Nuclei. It is involved in sleep production.

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* Examples of inhibitory transmitter:

(1) GABA (which in some places opens chloride channels, and in others opens potassium channels).

(2) Enkephalin: Inhibitory transmitter. Found in the GIT and spinal cord. In the spinal cord it exerts analgesic activity, reducing the feeling of pain.

(3) Glycine : in the spinal cord

Comparison of Graded Potentials and Action Potentials

(just so to be reminded) (very easily useful)

Characteristics	Graded Potentials	Action Potentials
Origin	Arise mainly in dendrites and cell bodies	Arise at trigger zones and propagate along axon
Types of channel	Chemical, mechanical, or light	Voltage gated ion channels
Conduction	Not propagated, localized, thus permit communication over a few mm	Propagated, thus permit communication over long distances
Polarity	May be hyperpolarizing (inhibitory to generation of action potential) or depolarizing (excitatory to generation of action potential)	Always consist of depolarizing phase followed by repolarizing phase and then return to resting membrane potential
Refractory Period	No, thus exhibit temporal and spatial summation	Yes, therefore not subject to summation

These are graded potentials NOT action potentials.

Examples of Factors that Affect Neurotransmission:
- Alkalosis: Increases transmission.
- Hypoxia: Decreases transmission.
- Acidosis: Decreases transmission.

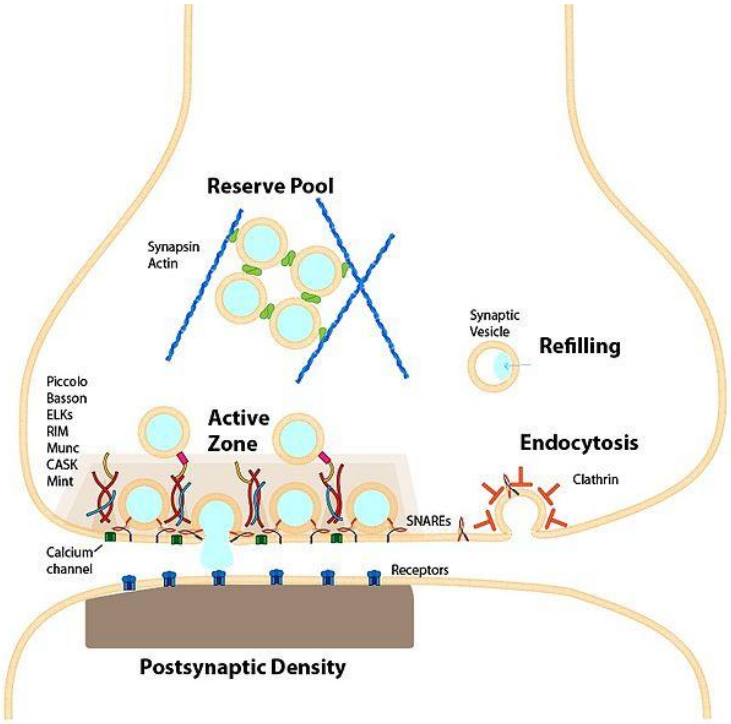
Q: What happens to the transmitter after it has combined with its postsynaptic receptors and produced it effect?
In the synaptic cleft there are enzymes that will then destroy the receptor:
In case of:

- Acetylcholine→
Acetyl cholinesterase (Ach-esterase)

- Noradrenalin →
Monoamine Oxidase (MAO) intracellularly; or Catechol-O-Methyl Transferase (COMT) extracellularly.

Vesicle Recycling

Vesicles of small molecule transmitters are recycled by invaginating back into the presynaptic terminal and pinching off.



Long – Term Potentiating (LTP)

Repetitive stimulation makes the postsynaptic membrane more excitable for a longer than normal period of time.

For example:
It potentiates (facilitates) transfer of information across that synapse → making it easier & longer lasting.

---**Glutamate Receptors** play important role in this process of LTP---

---This LTP is a is essential for formation of **memories** in the brain---

Properties of Synapses & Synaptic Transmission

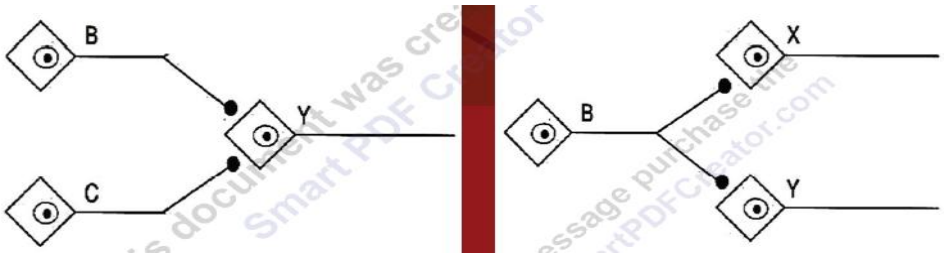
1/ One Way Conduction

2/ Synaptic Delay

It's the time taken between stimulation of the pre-synaptic ending and elicitation of the post-synaptic response.

****Average synaptic delay in one synapse= 0.5 ms****
Therefore, in 2 synapses = 1.0 ms --- in 3 synapses = 1.5 ms --- etc.

3/ Convergence and Divergence



Advantages of DIVERGENCE
(1) Spread of information.
(2) Amplification of the postsynaptic responses.

Example: in the sympathetic system one pre-ganglionic neuron can innervate up to 20 post-ganglionic neurons

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Advantage of CONVERGENCE
(1) Spatial Summation
(2) Integration and modulation of information.

Example: the spinal motor neuron (anterior horn cell, AHC) receives between 1000 – 110, 000 synaptic inputs: Some of these terminals are excitatory (produce EPSPs). And others are inhibitory (produce IPSPs) on the soma or dendrite of the post-synaptic cell.

4/ Summation: Spatial & Temporal

Spatial summation: due to adding up of EPSPs produced by more than one synaptic knob. Thus activity in one synaptic knob facilitates activity in another.

Temporal summation: Repeated afferent stimuli (even if from a single synaptic knob) cause new EPSPs before previous EPSPs have decayed.

5/ Inhibition

A/ Presynaptic Inhibition

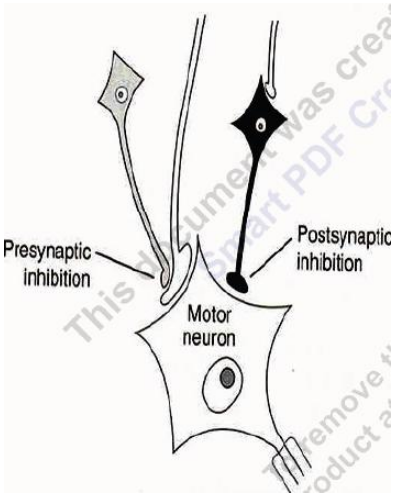
B/ Postsynaptic Inhibition (also called Direct Inhibition)

C/ Feedback Inhibition (Renshaw Cell Inhibition)

D/ Feed-forward Inhibition

E/ Lateral (Surround) Inhibition

A/ Presynaptic Inhibition



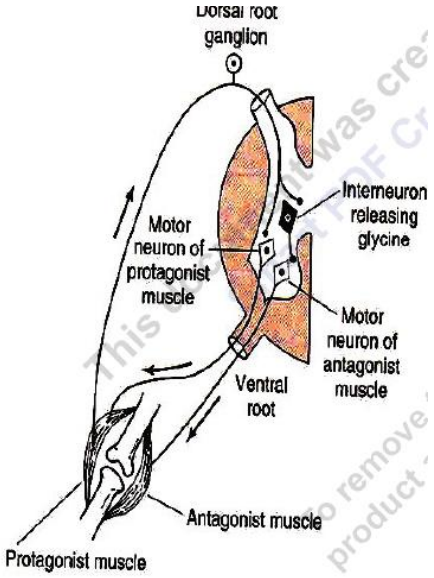
It's an inhibitory neuron, not acting directly on the target cell, but makes axo-axonal synapse on an excitatory ending that ends on the target cell. This inhibitory interneuron releases GABA which acts via either:

(1) GABAa receptors: increase chloride conductance → decreasing calcium entry into the excitatory synaptic knob

(2) GABAb receptor: through G-protein → increase potassium conductance, thereby decreasing calcium entry into the synaptic knob of the excitatory neuron.

B/ Postsynaptic Inhibition (also called Direct Inhibition)

The inhibitory interneuron acts directly on the target cell.



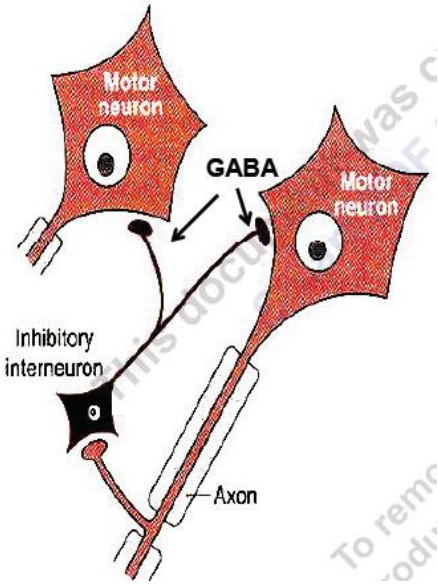
Example of this Direct Inhibition is Reciprocal Inhibition in the spinal cord , which occurs by means Reciprocal Innervations → Activity in spindle afferent , besides exciting the motoneuron supplying the agonist muscle , activates an inhibitory interneuron that → directly inhibit the motoneuron supplying the antagonist muscle .

C/ Feedback Inhibition (Renshaw Cell Inhibition)

Neurons may also inhibit themselves in a negative feedback fashion (Negative Feedback inhibition).

A spinal motoneuron gives collateral that synapses Renshaw cell which is inhibitory interneuron. Then Renshaw cell, in turn, sends back axons that inhibit the spinal motoneuron.

These axons secrete an inhibitory transmitter that produces IPSPs on cell-bodies of motoneurons and inhibit them.



The Renshaw cell

It's located in anterior horn in close association with motor neurons.

-it is an inhibitory cell excited by collaterals from an alpha motor neuron to project back and inhibit the same motor neuron

In conclusion (you should know):

- Graded Potentials (i.e., proportional to the strength of the stimulus).

- EPSP makes the postsynaptic membrane more excitable (thus more liable to produce AP), & IPSP makes it less excitable.

- Excitatory Neurotransmitter:
It's a transmitter that produces Excitatory Postsynaptic Potential (EPSP) on the postsynaptic neuron.

- The EPSP is a Local Response that decreases the membrane potential of the postsynaptic cell, bringing it closer to the Firing (Threshold) Potential

- In other words, the EPSP is a local depolarizing potential that makes the Postsynaptic Cell more liable (easier) to fire (produce) Action Potentials.

- Inhibitory Neurotransmitter: when it combines to its receptors, it produce Inhibitory Postsynaptic potential (IPSP) that hyperpolarizes the post-synaptic cell, thereby making it less excitable (more difficult to excite, more difficult to produce APs).

- Where are neurotransmitters made and how are they packaged?

Small neurotransmitters (like NO and CO) are synthesized at the presynaptic terminals of a neuron using enzymes manufactured in the cell body. Neurotransmitter precursors are pulled into the cell at the synaptic terminal and used to create neurotransmitter molecules that will be loaded into vesicles before being dumped into the synapse. See diagram below, part B.

In contrast, larger polypeptide neurotransmitters such as acetylcholine and serotonin tend to be synthesized in the cell body of the neuron by the rough endoplasmic reticulum before being packaged into vesicles by the Golgi apparatus.