Synapses and Synaptic Transmission

Objectives :

- Definition and Functions of synapses.
- Structure and Types of synapses: anatomical & functional.
- Synaptic transmission & neurotransmitters.
- What neurotransmitters are, and how they are released and act on their receptors.
- Fate of neurotransmitters.
- Differentiate between neurotransmitter receptors (ionotropic and metabotropic).
- Electrical events at synapses (EPSPs & IPSPs) and the differentiation.
- Properties of synaptic transmission.
- Factors affecting synaptic transmission.

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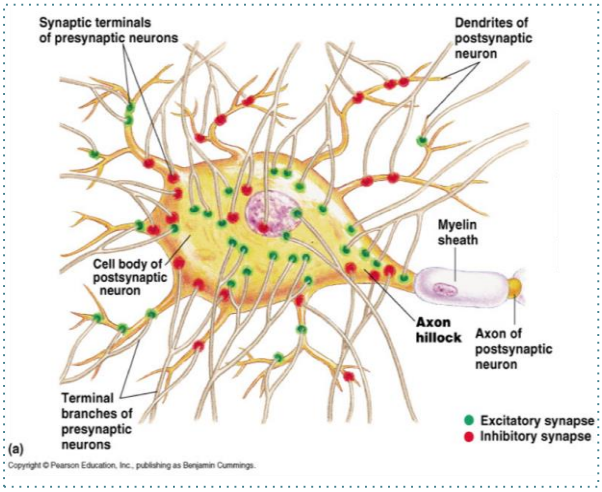
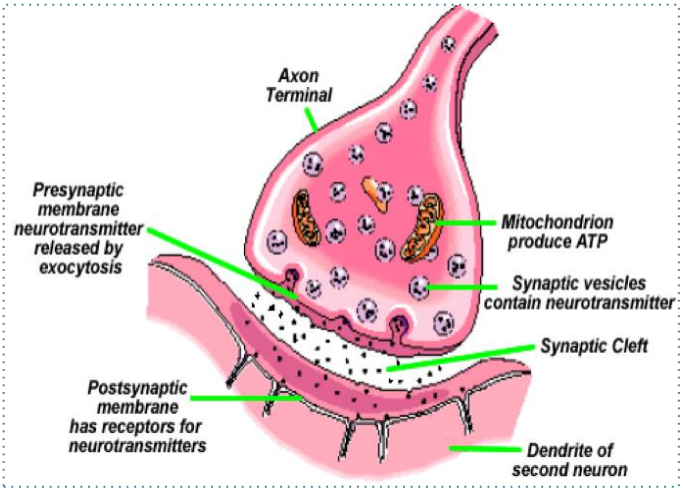
Terminology	Definition
Chemical synapses	A one direction transmission of signals where a chemical substance (neurotransmitter) is secreted by the first neuron to act on receptors on the membrane of the next neuron.
Electrical synapses	A bidirectional transmission of signals where the cytoplasms of adjacent cells are connected by ion channels called gap junctions allowing movement of ions.
Neurotransmitters	A chemical transmitter substance secreted at the end of a nerve fiber that acts on receptor proteins in the membrane of the next neuron.
Presynaptic inhibition	A synaptic inhibition occurring when an inhibitory synaptic knob laying on the termination of a presynaptic excitatory fiber releases a transmitter which inhibits the release of excitatory transmitters.
Postsynaptic inhibition	A synaptic inhibition occurring when an inhibitory neuron (releasing inhibitory substances) acts on a postsynaptic neuron leading to hyperpolarization.
Temporal summation	The type of summation where the frequency of stimulation from the same presynaptic fiber is increased.
Spatial summation	Eliciting an action potential in a neuron with input from multiple presynaptic cells.
Synaptic vesicles	Vesicles that store various neurotransmitters that are released at the synapse.
Excitatory neurotransmitters	Neurotransmitters that increase the rate or likelihood of a neuron firing by depolarizing the neuron.
Inhibitory neurotransmitters	Neurotransmitters that decrease the rate or likelihood of a neuron firing by hyperpolarizing the neuron.
Ionotropic receptors	Neurotransmitter receptors that directly open gate ion channels.
Metabotropic receptors	Receptors that act through second messenger systems.

General Facts about Synapses

- ★ It is a **junction** where the axon or some other portion of one cell (presynaptic cell) terminates on the dendrites, soma, or axon of another neuron (postsynaptic cell).
- ★ The CNS contains more than 100 billion neurons. The brain has 86 billion neurons
- ★ Some CNS neurons receive 20,000 synapses.
- ★ Synaptic input is converted to a nerve impulse (AP) at the **AXON HILLOCK**
- ★ The output signal (AP) travels by way of a single axon leaving the neuron.





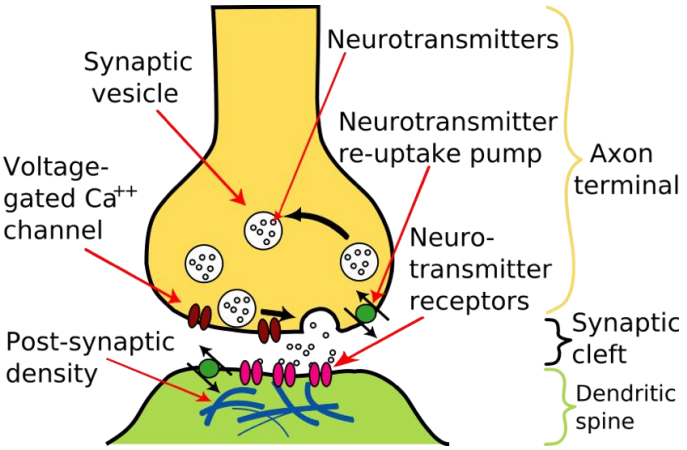
How brain functions?

1. Collecting of sensory input
2. Central integration
3. Motor output

Functions of synapse

- In the CNS, this other cell is also a neuron.
- In the PNS, the other cell may be either a neuron or an effector cell eg; gland or muscle.
- The synapses determine the directions that the nervous signals will spread through the nervous system.
- The synapses perform a selective action, often blocking weak signals while allowing strong signals to pass.

Structure of synapse



1. **Synaptic knobs** (presynaptic terminal): It has synaptic vesicles (neurotransmitters).
2. **Synaptic cleft**: It is the space between the axon terminal and sarcolemma. It has a width of 200-300 angstroms.

Looks like a button because of dilatation which helps to increase the surface area, thus, increase the efficiency

1. **Postsynaptic membrane** It has receptors for neurotransmitters or ion channels.

Anatomical Types of Synapses

Axodendritic synapses between the axon of one neuron and the dendrite of another

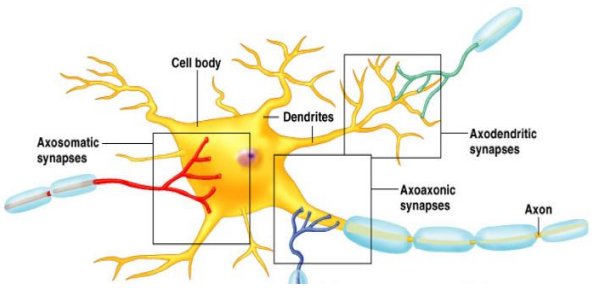
Other types of synapses include:

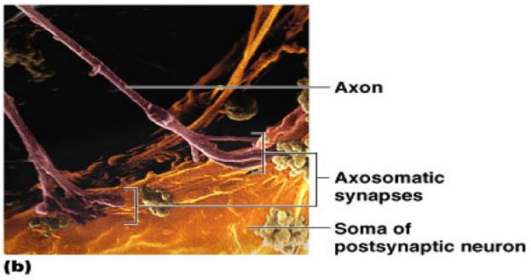
Axosomatic synapses between the axon of one neuron and the soma of another

Axoaxonic (axon to axon)

Dendrodendritic (dendrite to dendrite)

Dendrosomatic (dendrites to soma)





Functional Types of Synapses

A. Chemical synapse

Almost all synapses in the CNS. (I.e. first neuron secretes a chemical substance called **neurotransmitter** at the synapse to act on receptor on the next neuron to excite it, inhibit or modify its sensitivity). **One direction** transmission*.

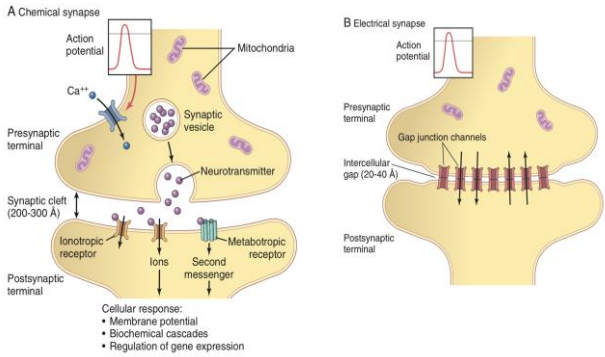
B. Electrical Synapses

*The transmission can occur in both directions. Which allows it to control the activities of large groups of interconnected neurons, and allow the synchronized firing.

Membranes of the pre- and postsynaptic neurons come close together and **gap junctions** forms → low membrane borders which allow passage of ions.

- Are less common than chemical synapses
- Correspond to gap junctions found in other cell types.
- Each gap junction is composed of 12 connexin proteins.
- Are important in the CNS in:
  - Mental attention
  - Emotions and memory
  - Arousal from sleep

Thus, if one cell is excited the other cells will be excited too. (Like the cardiac muscles)



C. Conjoint synapse

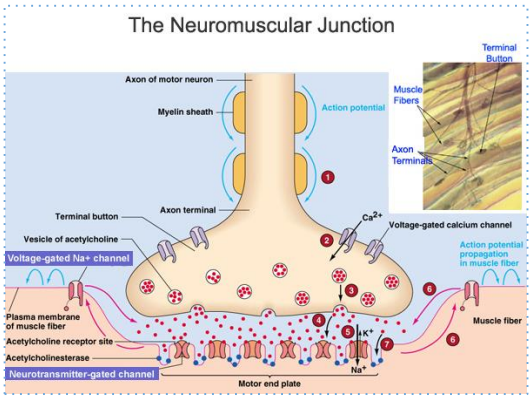
Relates to balance and equilibrium, and those are connected to sight, hearing, and muscle tone.

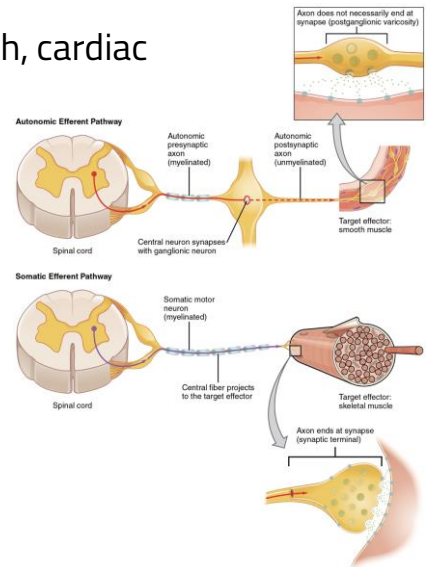
Both electrical and chemical.

Examples: neurons in lateral vestibular nucleus.

Examples of synapse outside the CNS

- Neuromuscular junction
- Contact between: autonomic neurons & smooth, cardiac muscles, & other effector cells.

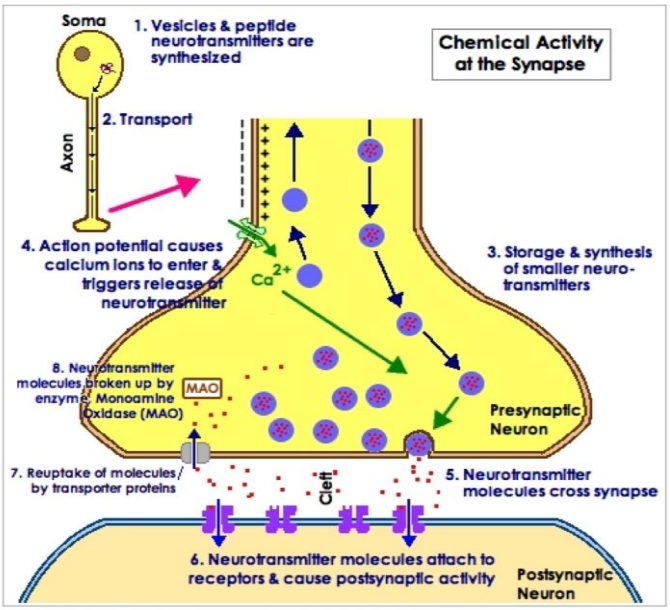


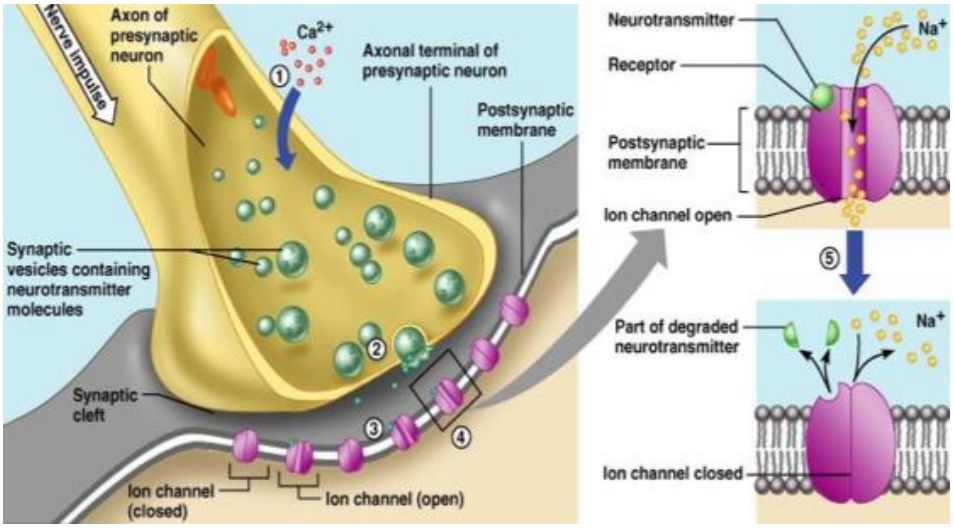


Mechanism of Synaptic Transmission

AP → Open of ca channel > NT release at docking site > Binding to postsynaptic receptors (**inhibition** or **excitation**) of the postsynaptic membrane (Depending on the type of the neurotransmitter, i.e. excitatory or inhibitory).

- ➔ Ca activates calmodulin which activates (PK) protein kinase.
- ➔ Information is transmitted in the central nervous system mainly in the form of nerve action potentials, called NERVE IMPULSES, through a succession of neurons, one after another.





Fate of Neurotransmitters

After a transmitter substance is released at a synapse, it must be removed by :

- ➢ **Diffusion** out of synaptic cleft into surrounding fluid.
- ➢ **Enzymatic destruction** e.g Ach esterase for Ach.
- ➢ **Active transport** back into presynaptic terminal itself e.g norepinephrine.

These receptors have two components

1- **Binding site** that face the cleft to bind the neurotransmitter.

2- **Ionophore** : It passes all the way through the membrane to the interior. It is of two types :

2nd messenger system in the postsynaptic neuron. This mechanism is important where **prolonged** postsynaptic changes are needed to stay for days, months.. years (memory).
Effects : intracellular Enzymes activation, gene transcription, etc...

Ion channel

Cation channels

Na^+ (most common)
K^+
Ca^{++}
Opening of Na^+ channels → ↑membrane potential in positive direction toward threshold level of excitation → (+) neuron

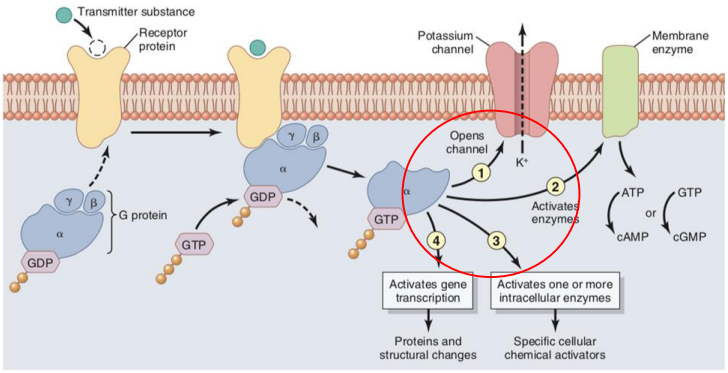
Anion channels

Cl^- mainly
Opening of Cl^- channels → diffusion of negative charges into the membrane → ↓membrane potential making it more negative → away from threshold level → (-) neuron

Neurotransmitter receptors that directly gate ion channels are often called ionotropic receptors, whereas those that act through second messenger systems are called metabotropic receptors.

Ionotropic	Metabotropic
Mediate rapid PSPs	Mediate slower PSPs
Duration of PSPs is 10-30 ms or less	Duration from 100's ms to minutes or longer
PSPs (EPSP or IPSP) develop within 1-2 ms after an AP reaching the presynaptic terminal	This is slowness is due to activation of second messengers leading to opening Ion channels.
A NT may activate both Ionotropic and Metabotropic receptors to produce both fast and slow postsynaptic potentials as the same synapse.	

2nd messenger system in the postsynaptic neuron acts in :
*** focus on the 4 ways



Electrical Events in Post-synaptic Neurons

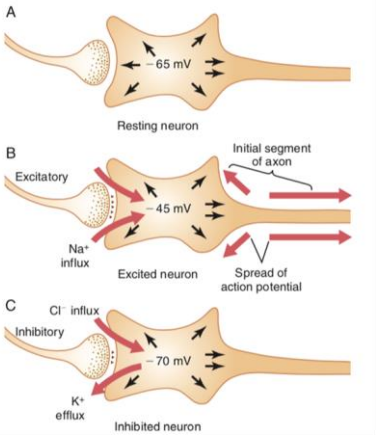
There will be a question about this part

1- RMP of Neuronal Soma

- -65 mV i.e. less than skeletal muscles (-70 to -90 mV).
- If the voltage is less negative→ the neurons is excitable.

2- Excitatory Post-synaptic Potential (EPSPs)

- When excitatory neurotransmitters binds to its receptor on post-synaptic membrane > partial depolarization (increase Na influx) of post-synaptic cell membrane immediately under presynaptic ending, i.e. EPSPs.
- This summation will cause the membrane potential to increase from -65 mV to -45mV.
- EPSPs = +20mV which makes the membrane reach the firing level → AP develops at **axon hillock.**



- How EPSPs differs from Action Potential ?
  - Proportionate to the strength of the stimulus
  - Can be summated
  - If large enough to reach firing level > AP is produced

3- Inhibitory Post-synaptic Potentials (IPSPs)

- When an inhibitory NT binds to its receptor on post-synaptic membrane, it causes hyperpolarization of the post-synaptic membrane.
- Increase membrane permeability to Cl^- of post-synaptic membrane (produced by inhibitory neurotransmitter)→ ↓excitability and membrane potential (more negative).

Synaptic Properties

"Chemical Synapses"

1. One-way conduction synapses generally permit conduction of impulses in one-way i.e. from pre-synapstic to post-synaptic neuron.

2. Synaptic delay is the minimum time required for transmission across the synapse. It is 0.5 ms for transmission across one synapse.

This time is taken by: (why there is a delay?) it could come as MCQ

- Discharge of transmitter substance by pre-synaptic terminal.
- Diffusion of transmitter to post-synaptic membrane.
- Action of transmitter on its receptor.
- Action of transmitter to increase membrane permeability.
- Increased diffusion of Na^+ to increase post-synaptic potential.

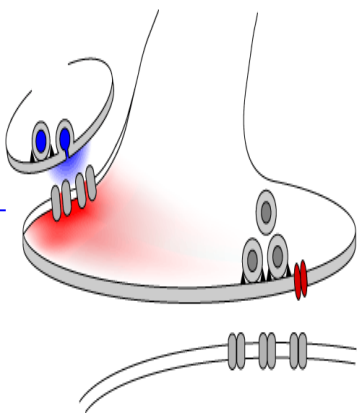
Clinical Importance : We can know how many synapses are involved in the pathway by the time lag.

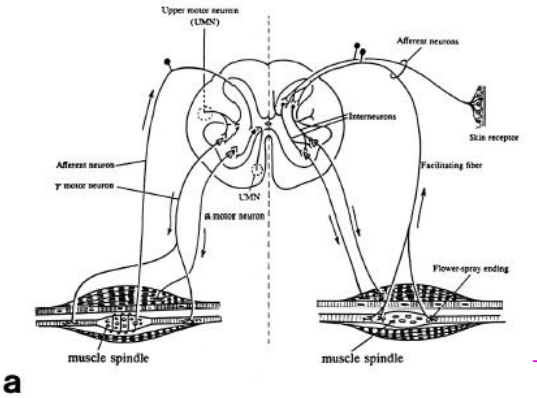
3. Synaptic inhibition:

Types: Direct inhibition, Indirect inhibition, Reciprocal inhibition & Inhibitory interneuron

A. Direct inhibition: Occurs when an inhibitory neuron (releasing inhibitory substances) acts on a postsynaptic neuron leading to hyperpolarization due to opening of Cl^- [IPSPs] and/or K+ channels. Example: Glycine at the level of the spinal cord to block pain impulses.

B. Indirect Inhibition (Presynaptic inhibition): This happens when an inhibitory synaptic knob lie directly on the termination of a pre-synaptic excitatory fiber. The inhibitory synaptic knob releases a transmitter which inhibits the release of excitatory transmitters from the pre-synaptic fiber. e. g. GABA (Pain modification).





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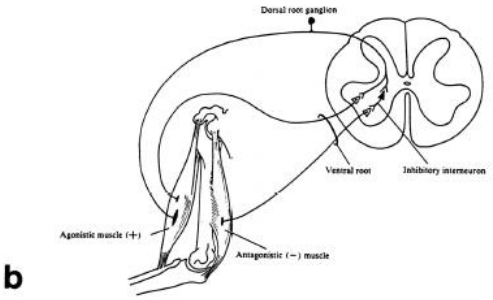
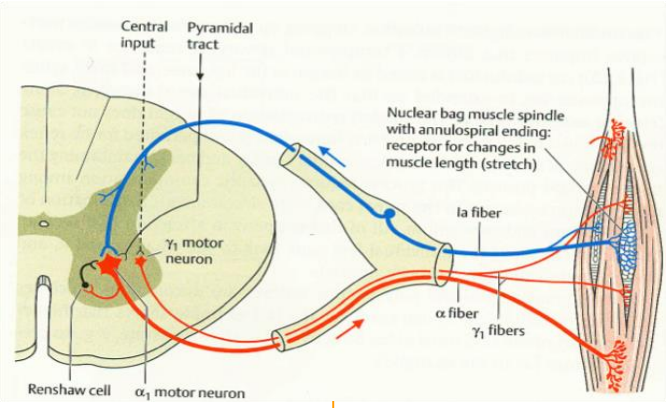


b

C. Reciprocal inhibition: Inhibition of antagonist activity is initiated in the agonist muscle. Impulses pass directly to the motor neurons supplying the same muscle and via branches to inhibitory interneurons that end on motor neurons of antagonist muscle.



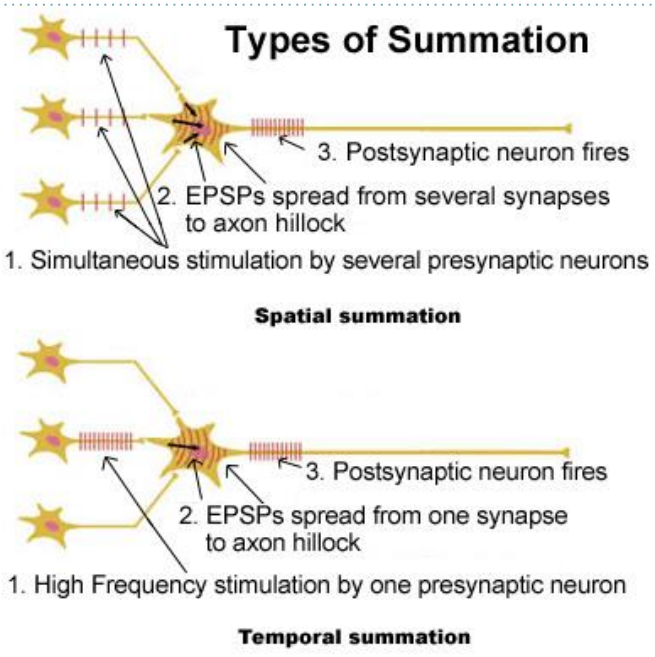
D. Inhibitory interneuron (Renshaw cells) Negative feedback inhibitory interneuron of a spinal motor neuron (Control the strength of contraction)

4. Summation:

Increase the efficiency of AP developed by the postsynaptic neuron

A. Spatial summation.
Eliciting an action potential in a neuron with input from multiple presynaptic cells. (Greater number of fibers)

B. Temporal summation.
When the frequency of stimulation increased from the same presynaptic fiber. (Increase number of frequency of nerve impulses in each fibers).



5. Convergence and divergence:

a. Divergence: Axons of pre-synaptic neurons divide into many branches that diverge to end on many post-synaptic neurons.

b. Convergence: When many pre-synaptic neurons converge on any single post-synaptic neuron.

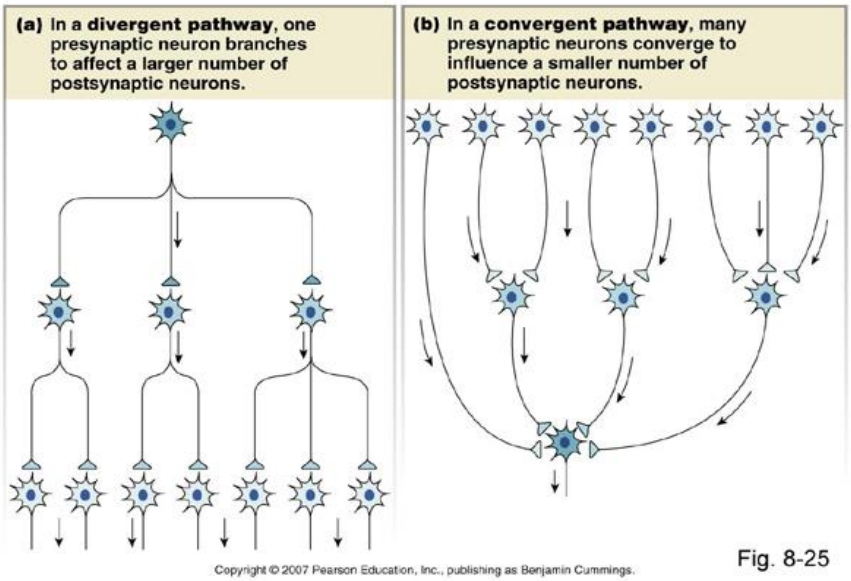


Fig. 8-25

6. Fatigue

It is due to exhaustion of neurotransmitter. If the pre-synaptic neurons are continuously stimulated there may be an exhaustion of the neurotransmitter. Resulting in stoppage of synaptic transmission. Despite giving the neuron a strong stimulus there is no AP

Factors Affecting Synaptic Transmission

Alkalosis	• Increases neuronal excitability. • Causes cerebral epileptic seizures (Increased excitability cerebral neurons). • e. g. overbreathing in person with epilepsy. The over breathing blows off carbon dioxide and therefore elevates the pH of the blood momentarily
Acidosis	• Depresses neuronal activity. • pH around 7.0 usually causes a coma. • E.g. severe diabetic or uremic acidosis.
Drugs	Caffeine found in coffee, tea, increases neuronal excitability, by reducing the threshold for excitation of neurons.
Hypoxia	Depression of neurons.

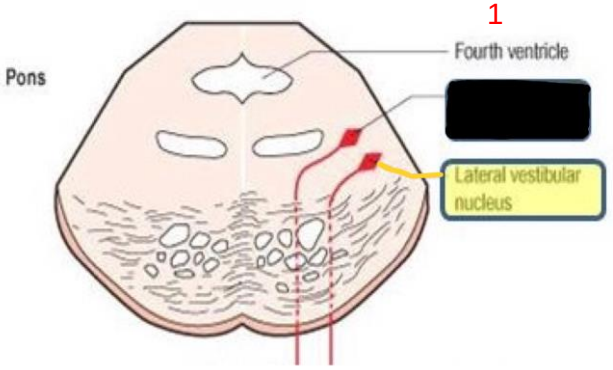
EPSPs	IPSP
1- Opening of Na channels to threshold level (Most Common).	1- Opening of Cl ion channels through the postsynaptic neuronal membrane.
2- Decrease conduction through Cl or K channels, or both.	2- Increase in conductance of K ions out of the Neuron
3- Various changes in the internal metabolism of the postsynaptic neuron to excite or, in some instances, to Increase excitatory membrane receptors or decrease inhibitory membrane receptors	3- Activation of receptor enzymes that inhibit cellular metabolic functions that increase inhibitory membrane receptors or decrease excitatory membrane receptors.

***ممكن يجي وحدة من خصائص EPSPأو خصائص الـ IPSPويلخبط بينهم

Summary

- Almost all synapses in the CNS are chemical synapses
- neurotransmitter is a chemical substance that is secreted by the first neuron at the synapse to act on receptor on the next neuron to excite it, inhibit or modify its sensitivity
- Chemical synapse is One directional in transmission while electrical synapse transmission can occur in both directions .
- Gap junction is the space between the pre- and postsynaptic neurons which allows the passage of ions
- Electrical synapses Are important in the CNS in Mental attention,Emotions, memory and Arousal from sleep.
- neurons in lateral vestibular nucleus[1] have conjoint synapse
- Ach esterase is an enzyme that destroys Ach neurotransmitter in a process called Enzymatic destruction
- Norepinephrine neurotransmitter is actively transported back into the presynaptic terminal.
- Neurotransmitter receptors that directly open gate ion channels are often called ionotropic receptors, whereas those that act through second messenger systems are called metabotropic receptors.[2]

1



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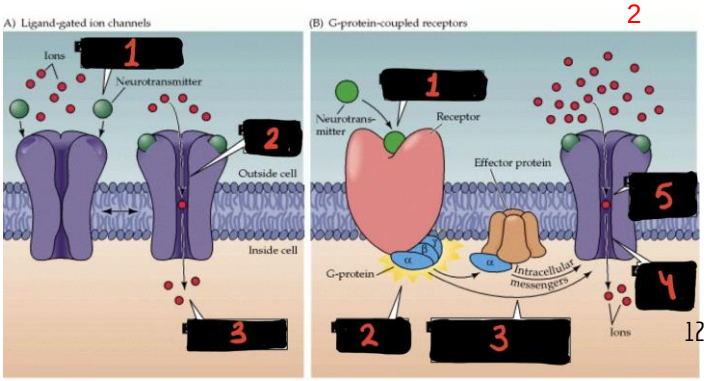

1.All synapses are junctions But not all junctions are synapses.
- A. False.
- B. True.

2.Which one of these types has one direction transmission?
- A. conjoint synapse.
- B. Chemical synapse.
- C. Electrical synapse.

3.The electrical synapse is important in:
- A. Memory.
- B. Emotions.
- C. Both A+B.

4.How many types of neurotransmitters does the synaptic vesicle contains?
- A. Each vesicle contains only one type.
- B. Each vesicle contains 3 types.
- C. Each vesicle contains 5 types.

5.Choose the correct answer:
- A. Glutamate is excitatory, GABA is inhibitory.
- B. Glutamate and GABA are excitatory.
- C. Glutamate and GABA are inhibitory.

6.Axons of pre-synaptic neurons divide into many branches called:
- A. Convergence .
- B. Divergence .
- C. None.

7.Glycine at the level of spinal cord is example for:
- A. Direct inhibition.
- B. Indirect inhibition.
- C. Reciprocal inhibition.

8.Caffeine _____ threshold and _____ neural excitability.
- A. Reduce, increase.
- B. Reduce, reduce.
- C. Increase, increase.

- what are the two types of channel activities/affect produced in the postsynaptic membrane?
  - Excitatory postsynaptic potentials EPSP
  - Inhibitory postsynaptic potentials IPSP
- What are the main two characteristics for end plate potentials EPPs?
  - Localized (they don't spread)
  - Graded (you can grade them unlike action potential)
- What are the reasons for synaptic delay?
  - Mentioned in slide 7
- What are the two mechanisms of prolongation?
  - Long acting neurotransmitter
  - Reverberating circuits

Answers:
1.B 2.B 3.C 4.A 5.A 6.B 7.A 8.A