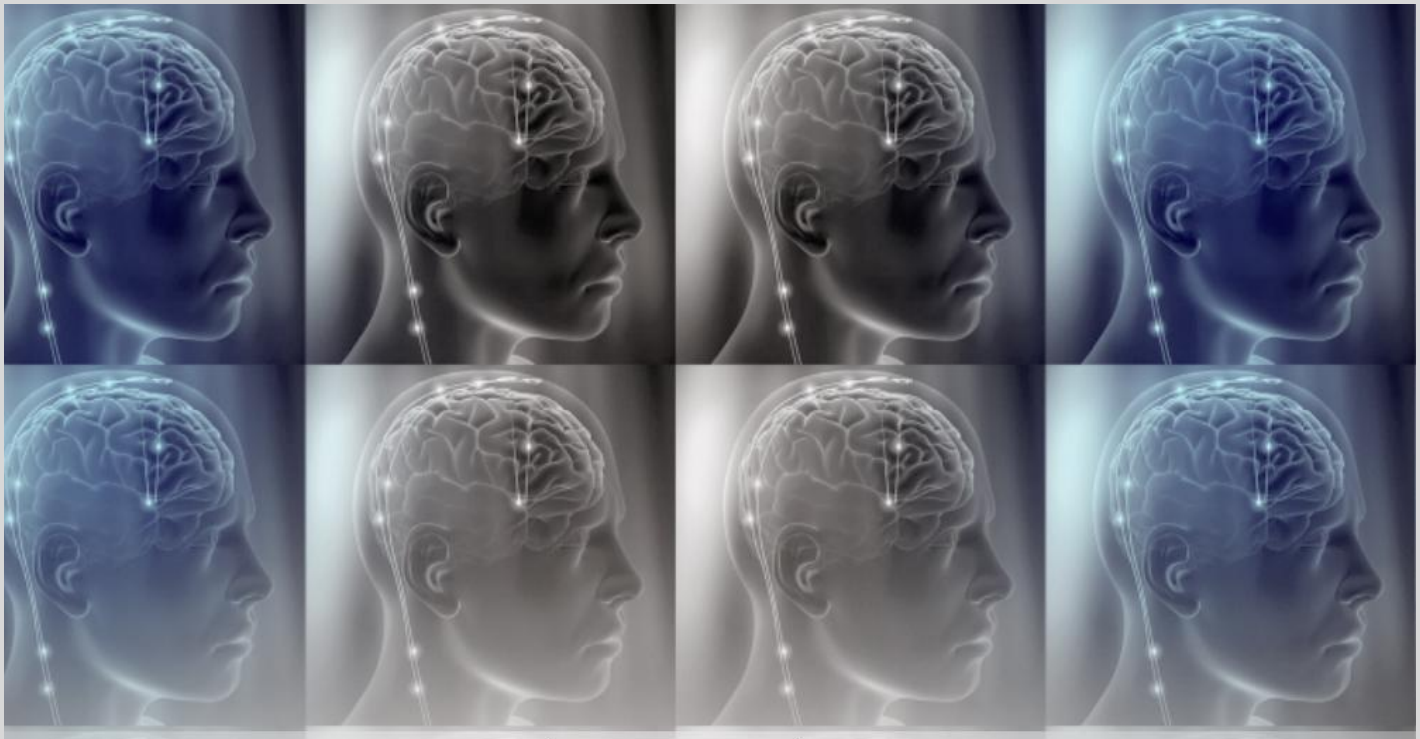


431

CNS Central Nervous System

Block

Physiology Team

	Female Side	Male side
Done By:	Najd Ben Musibeeh	Khaled Almohaimede
Revised By:	Sara Al-Anazy	Mohammed Asiri

CNS Central Nervous System

Block

Slide No.(2)

Objectives

- Define synapses
- Functions of synapses.
- Structure of synapses
- Types of synapses: anatomical & functional.
- Synaptic transmission & neurotransmitters
- Fate of neurotransmitters.
- Electrical events at synapses (EPSPs & IPSPs).
- Properties of synaptic transmission
- Factors affecting synaptic transmission

Team Notes :

Blue for Additional information

Green for information from male slides

Red for important information

CNS central Nervous System

Block

Slide No.(3)

INTRODUCTION TO SYNAPSE:

The CNS contains more than 100 billion neurons. Incoming signals enter the neuron through synapses located mostly on the neuronal dendrites, but also on the cell body.

For different types of neurons, there may be only a few hundred or as many as 200,000 such synaptic connections from input fibers.

Conversely, the output signal travels by way of a single axon leaving the neuron.

Team Notes :

Nothing else was mentioned about this slide.

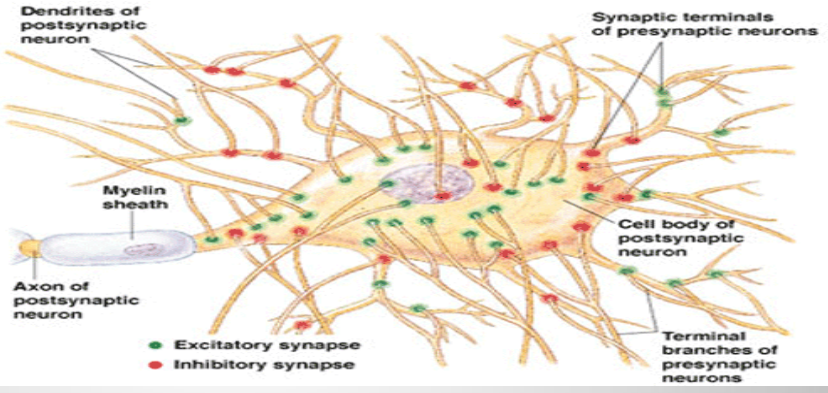
CNS central Nervous System

Block

Slide No.(4)

What is a synapse?

A junction where the axon or some other portion of one cell (= presynaptic cell) terminates on the dendrites, soma, or axon of another neuron (post synaptic cell).
The term was introduced in nineteenth century by the British neurophysiologist Charles Sherrington



Team Notes :

Remember that: In the synapses **the membranes of adjacent cells are <u>in close apposition</u> (contiguity=contact, not continuity).**

CNS Central Nervous System

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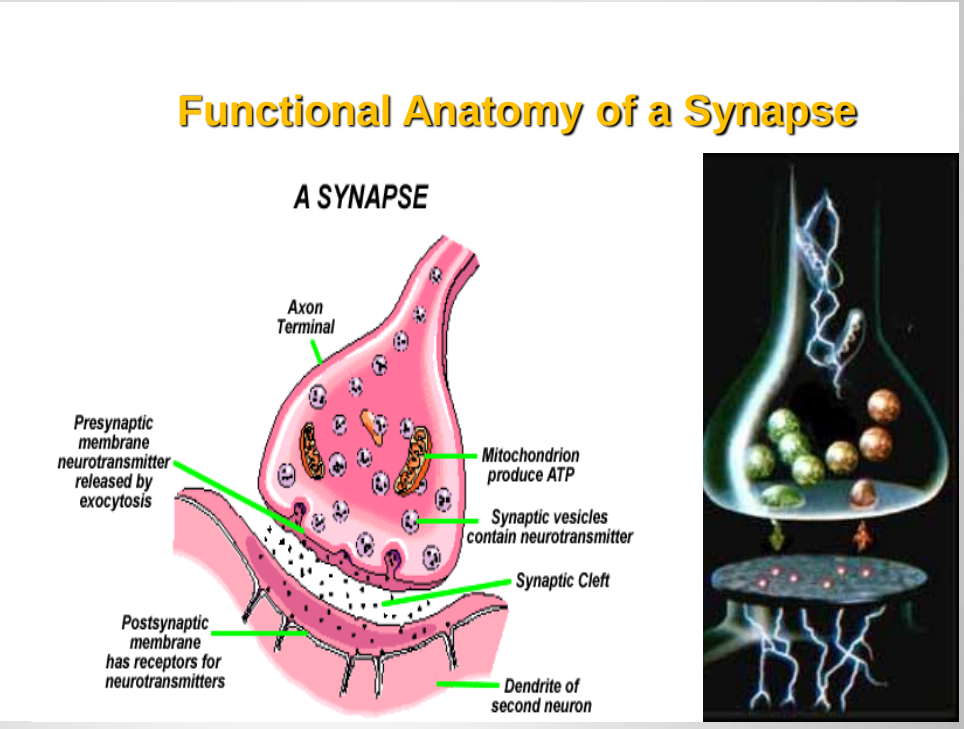
Slide No.(5)



Team Notes :

* **It is important to know that the neurotransmitter in the synapses is released by a process called *Exocytosis*.**

What is Exocytosis? (EXTRA INFORMATION)

➔ **the release of cellular substances (as secretory products) contained in cell vesicles by fusion of the vesicular membrane with the plasma membrane and subsequent release of the contents to the exterior of the cell.**

CNS Central Nervous System

Block

Slide No.(6)

Anatomical Types of Synapses

- Axodendritic – synapses between the axon of one neuron and the dendrite of another
- Axosomatic – synapses between the axon of one neuron and the soma of another
- Other types of synapses include:
  - Axoaxonic (axon to axon)
  - Dendrodendritic (dendrite to dendrite)
  - Dendrosomatic (dendrites to soma)

Team Notes :

(5) Somato-somatic

CNS Central Nervous System

Block

The Neurotransmitters

Neurotransmitter is a chemical substance 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

What are the 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.

(1) **Glutamate**: Produces EPSP by opening of C2+ channel.

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

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

In what location the neurotransmitter synthesized?

All the neurotransmitters which are peptides are synthesized in the cell body, but all those which have small molecular weight are synthesized in the nerve ending (e.g ACH)

In what location the transmitter vesicle synthesized?

Neuron cell body.

CNS Central Nervous System

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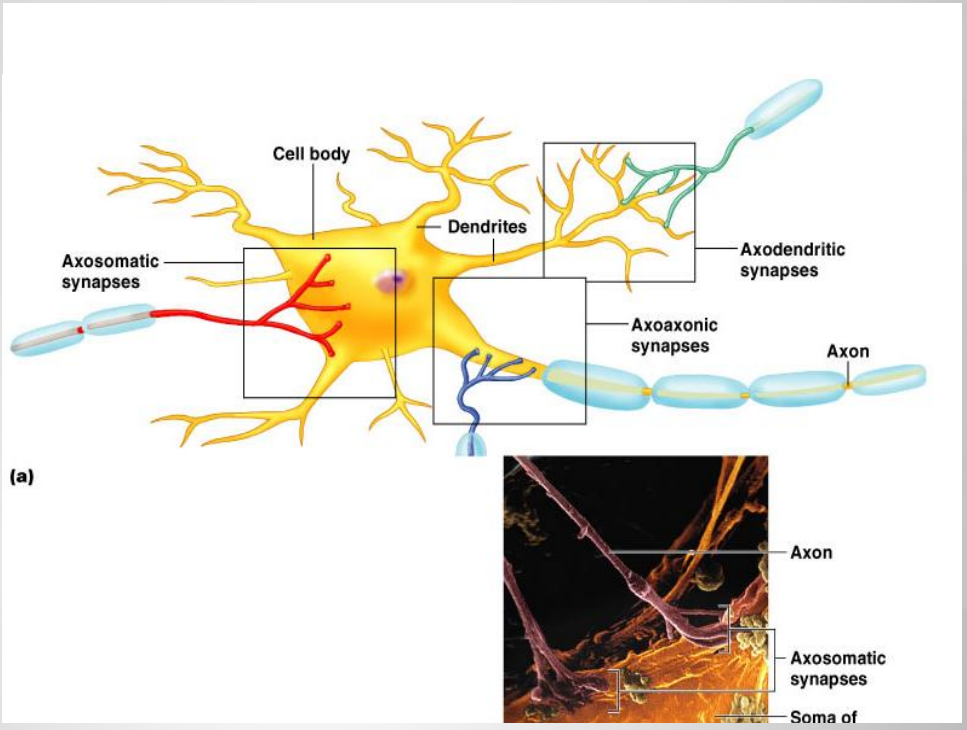
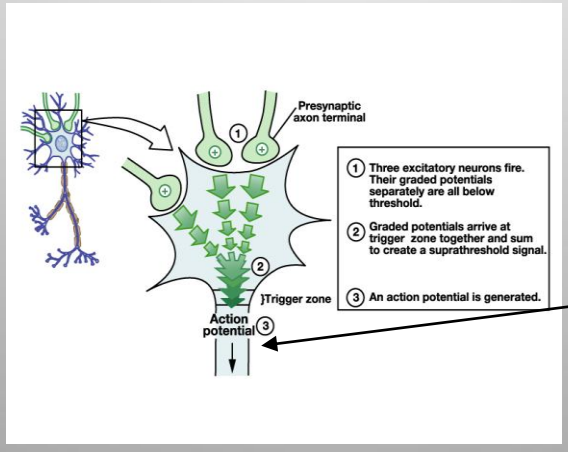
Slide No.(7)



Team Notes :

What is the Trigger zone ?



Trigger zone (functional term) is at the anatomical Axon Hillockn (Beginning of the Axon as it comes out of the Soma)

An area where Action potential is formed

CNS Central Nervous System

Block

Slide No.(8)

Functional types of synapses

A. Chemical synapse

Almost all synapses used for signal transmission in the CNS of human being are chemical synapses.

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.

Team Notes :

Notice in this slide that:

- Chemical synapses is the MOST COMMON type of synapses in the CNS

- In this type of synapses, there is One-way conduction → since that the neurotransmitter is released by the presynaptic neuron to act on the postsynaptic neuron, and cannot be in the opposite way.

- Slower than electrical synapses in conduction of nerve Impulses.

CNS Central Nervous System

Block

Slide No.(9)

B. Electrical Synapses

Membranes of the pre- and post-synaptic 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
– Are important in the CNS in:

Arousal from sleep

- Mental attention
- Emotions and memory
- Ion and water homeostasis

Team Notes :

Notice in this slide that:

- Gap junctions are formed in the cell membranes of the two neurons in the synapse (why?) → to allow the easy passage of ions across the membranes, which explains why the electrical synapses are much more faster in conduction of nerve impulses, compared to the chemical synapses. Therefore, it is required in process such as mental attention and arousal from sleep.

- Less common than the chemical synapses.

CNS Central Nervous System

Block

Slide No.(10)

C. Conjoint synapse

Both electrical and chemical.
Examples → neurons in lateral vestibular nucleus.

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(11)

What happens at the synapse?

Information is transmitted in the CNS mainly in the form of APs "=nerve impulse", which pass from one neuron to another.

Each impulse through its way from one neuron to another may be:-

1. **blocked** in its transmission from one neuron to another
2. changed from single impulse to **repetitive impulses.**

∴ Synaptic transmission is a complex process that permits grading and adjustment of neural activity necessary for normal function.

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(12)

Examples of synapses outside CNS

1. NMJ

2. Contact between:
   autonomic neurons and
   smooth , cardiac muscles,
   and other effector cells.

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(13)

SYNAPSE: STRUCTURE & FUNCTIONS

Synaptic cleft: This the space between the axon terminal and sarcolemma. It has a width of 200-300 angstroms.

Synaptic knobs (presynaptic terminal) cover about 40% of soma and 70% of dendritic membrane

Team Notes :

- Synaptic Knob contains neurotransmitters
- Synaptic Cleft (space) contains enzymes that destroy neurotransmitters.

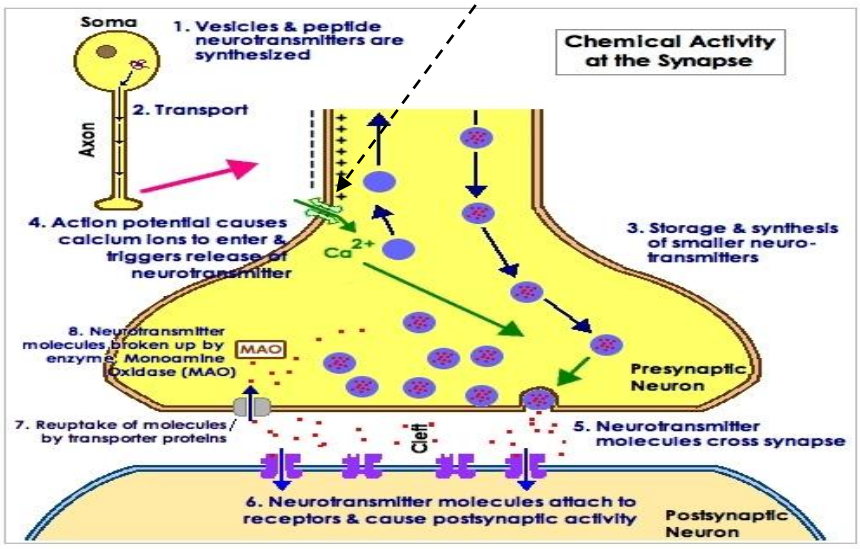
CNS Central Nervous System Block

IMPORTANT:

Calcium is the ion that causes the release of neurotransmitter from the presynaptic axon terminal, and it enters to the axon terminal by Voltage-gated calcium Channels

Slide No.(14)

Mechanism of Synaptic Transmission:



Team Notes :

* The story of Synaptic Neurotransmission:

1. Synthesis of Neurotransmitter peptides and the vesicles in the cell body, and then they will be transferred to the Axon terminal.
2. In the Axon terminal, the neurotransmitter will be stored in those small vesicles.
3. Action potential will be traveling along the axon until it reaches the axon terminal where it causes the opening of Voltage-gated Calcium channel, allowing the influx of the Ca++.
4. The entry of Ca++ will cause the release of neurotransmitter in the synaptic cleft.
5. Neurotransmitter will act on the postsynaptic cell receptors and cause an activity there (according to the type of neurotransmitter)
6. After acting on the receptors, the neurotransmitter will be either: diffused to the fluid outside the synaptic cleft, undergone enzymatic destruction, or uptaken by Active transport to the presynaptic axon terminal where it will be stored again in vesicles.

CNS Central Nervous System

Block

Slide No.(15)

Action of the transmitter substance on post-synaptic neuron:

At the synapse, the membrane of post-synaptic neuron contains large number of receptor proteins. Binding of the neurotransmitter to its receptor will result in **inhibition** or **excitation** of the post-synaptic membrane depending on the type of the neurotransmitter i.e. excitatory or inhibitory.

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(16)

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

Ion channels

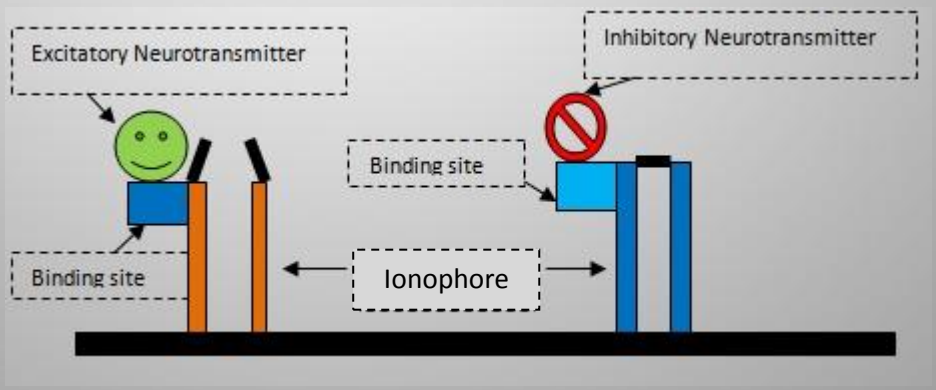
Cation channels
Na+ (most common)
K+
Ca++
Opening of Na+ channels → ↑ membrane potential in positive direction toward threshold level of excitation → (+) neuron

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

2nd messenger system in the post-synaptic membrane.
This mechanism is important where prolonged post-synaptic changes are needed to stay for days, months . . Years (memory).
Effects: intracellular enzymes activation, gene transcription, etc…

Team Notes :

Nothing else was mentioned about this slide.



CNS Central Nervous System

Block

Slide No.(17)

Fate of a neurotransmitter

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 pre-synaptic terminal itself e.g. norepinephrine

Team Notes :

Q: What happens to the transmitter after it has combined with its postsynaptic receptors and produced its effect?

It can be destroyed

For example:

Acetylcholine→ Acetyl cholinesterase (Ach-esterase)

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

CNS Central Nervous System

Block

Slide No.(18)

Electrical events in post-synaptic neurons:

1. RMP of neuronal soma:

~ –65mV i.e. less than sk. ms. [–70 to –90mV]

- If the voltage is less negative → the neuron is excitable

Causes of RMP:

1. Leakage of K+ (high K+ permeability)
2. Large number of negative ions inside: proteins, phosphate
3. Excess pumping of Na+ out by Na+-K+ pump

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

- **What are EPSP and IPSP?**

They are local responses

- **What is their bioelectric nature?**

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

- **In what way do they affect the excitability of the postsynaptic membrane?**

EPSP makes the postsynaptic membrane more excitable(thus more liable to fire AP;& IPSP makes it less excitable)

- **In what ways do they differ from action potentials?**

(1) They are proportional to the strength of the stimulus (i.e., do not obey All-or-None Law)

(2) They can summate (addup)

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

CNS central Nervous System

Block

Slide No.(19)

2. Effect of synaptic excitation on post-synaptic membrane:

= Excitatory post-synaptic potential [EPSPs]

When **excitatory** neurotransmitter binds to its receptor on post-synaptic membrane →
partial depolarization [↑ Na influx] of post-synaptic cell membrane immediately under presynaptic ending, i.e. EPSPs
If this potential rises enough to threshold level → AP will develop and excite the neuron (via central or neuronal summation)

Team Notes :

What happens if the neurotransmitter is excitatory in action?

1. The neurotransmitter will bind to its binding site, which will cause opening of Na+ channels.

2. There will be increase in the positivity inside the cell due to influx of sodium → causing partial depolarization immediately under presynaptic ending, i.e. EPSP (and we said "immediately under the presynaptic endings" because EPSP is not propagated)

3. If this change in potential rises to the threshold level, AP will develop and excite the neuron.

CNS Central Nervous System

Block

Slide No.(20)

This summation will cause the membrane potential to increase from –65mV to –45mV.

∴ EPSPs = +20mV which makes the membrane reach the firing level → AP develops at axon hillock.

N.B. Discharge of a single pre-synaptic terminal can never increase the neuronal potential from –65mV to –45mV.

Team Notes :

* **The discharge of only one presynaptic neuron can NEVER increase the neuronal potential form resting to the firing level, so to raise it up to the threshold level; it requires the process of summation.**

CNS Central Nervous System

Block

Slide No.(21)

EPSPs are characterized by:

- Graded, unpropagated response.
- Proportionate to the strength of the stimulus
- Can be summated
- If large enough to reach firing level → AP is produced
  Post-synaptic potential of +10 to +20mV is needed to produce AP

Team Notes :

So, we can say that EPSP is the step before developing AP.

***Summary:**

RMP → EPSP by Na+ influx, if it reaches the firing level → AP will develop → Nerve is excited.

CNS Central Nervous System Block

Slide No.(22)

3. Inhibitory post-synaptic potentials (IPSPs):

When an **inhibitory** neurotransmitter binds to its receptor on post-synaptic membrane, it causes hyperpolarization of the post-synaptic memb. which is the IPSP.

Causes:

An increase in membrane permeability to Cl^- of post-synaptic memb. (produced by inhibitory neurotransmitter) → ↓ excitability and memb. potential becomes away from firing level.

Also IPSP can be produced by:-

-Opening of K+ channels → outward movement of K+

-Closure of Na+ or Ca++ channels

-IPSP = –5mV

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

What is long-term-potentiation (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.**

What transmitter is involved in it?

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

What is the physiologicalfunction of LTP?

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

CNS Central Nervous System

Block

Slide No.(23)

Synaptic properties

1. One-way conduction

Synapses generally permit conduction of impulses in one-way i.e. from pre-synaptic to post-synaptic neuron.

Team Notes :

One-way conduction especially seen in the Chemical Synapses .

CNS Central Nervous System

Block

Slide No.(24)

Properties of synapses (con…)

2. Synaptic delay

Is the minimum time required for transmission across the synapse.

This time is taken by

- 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 ↑ membrane permeability
- Increased diffusion of Na+ to ↑ post-synaptic potential

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(25)

Properties of synapses (con…)

3. Synaptic inhibition

Types:

A. Direct inhibition
B. Indirect inhibition
C. Reciprocal inhibition
D. Inhibitory interneuron

Team Notes :

Inhibitions:

A/ Presynaptic Inhibition (indirect)
B/ Postsynaptic Inhibition (also called Direct Inhibition)
C/ Feedback Inhibition (Renshaw Cell Inhibition)
D/Lateral (Surround) Inhibition

CNS Central Nervous System

Block

Slide No.(26)

Properties of synapses (con...)

A. Direct inhibition

Occurs when an inhibitory neuron (releasing inhibitory substance) acts on a post-synaptic neuron leading to → its hyperpolarization due to opening of Cl^- [IPSPs] and/or K+ channels.

Example : Glycine at the level of the spinal cord to block pain impulses.

Team Notes :

* So , Glycine is an inhibitory neurotransmitter

CNS Central Nervous System

Block

Slide No.(27)

Properties of synapses (con…)

B. Indirect inhibition

(=Pre-synaptic inhibition).

This happens when an inhibitory synaptic knob lie directly on the termination of a pre-synaptic excitatory fiber.

The inhibitory synaptic knob release a transmitter which inhibits the release of excitatory transmitter from the pre-synaptic fiber.

The transmitter released at the inhibitory knob is GABA.

The inhibition is produced by ↑ Cl^- and ↑ K+. e.g. occurs in dorsal horn → pain gating.

Team Notes :

* **GABA is Also an inhibitory Neurotransmitter**

Also called 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:

***GABAa receptors:** increase chloride conductance—decreasing calcium entry into the excitatory synaptic knob

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

CNS Central Nervous System

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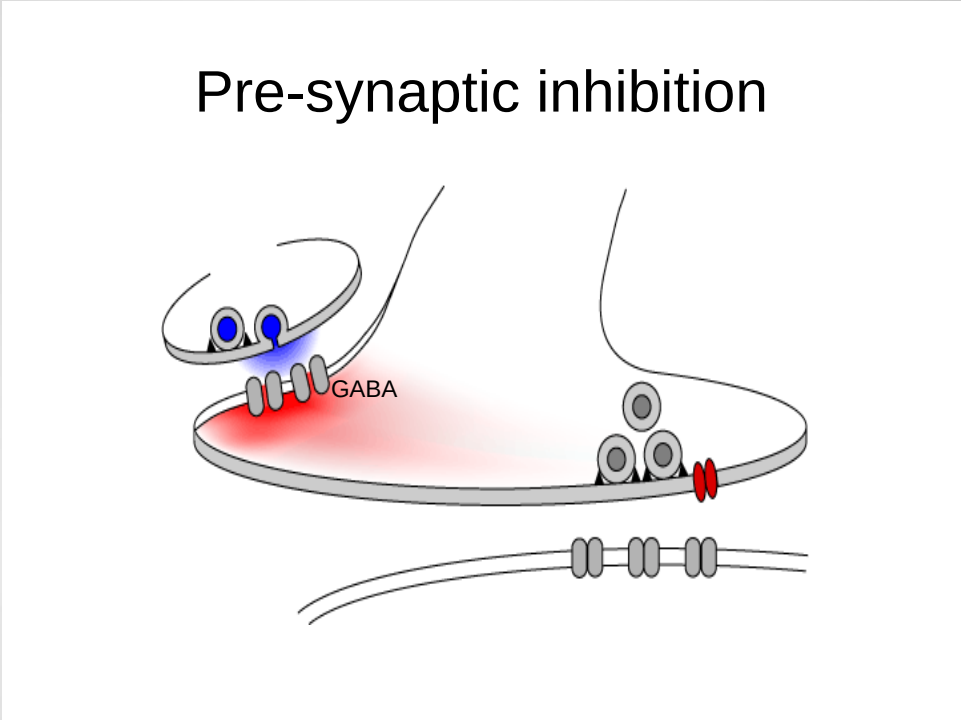
Slide No.(28)



Team Notes :

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CNS Central Nervous System

Block

Slide No.(29)

Properties of synapses (con…)

C. Reciprocal inhibition

Inhibition of antagonist activity is initiated in the spindle in the agonist muscle.

Impulses pass directly to the motor neurons supplying the same muscle and via branches to inhibitory interneurones that end on motor neurones of antagonist muscle.

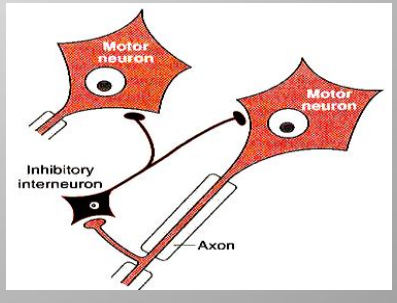
Team Notes :

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 Renshawcell 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.



CNS central Nervous System

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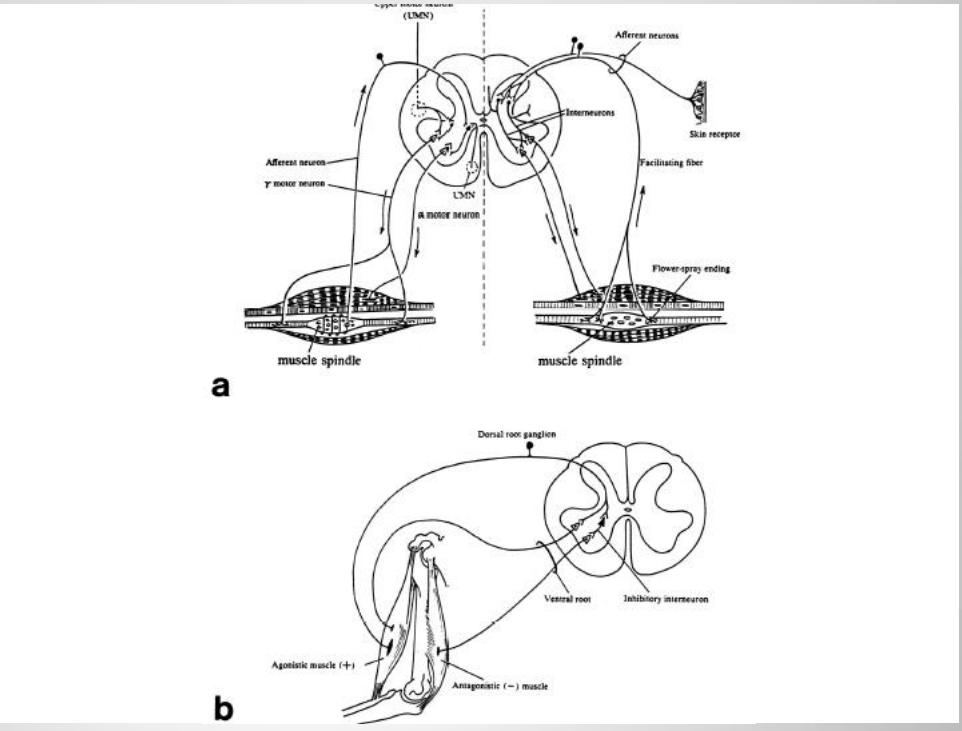
Slide No.(30)



Team Notes :

Nothing else was mentioned about this slide.

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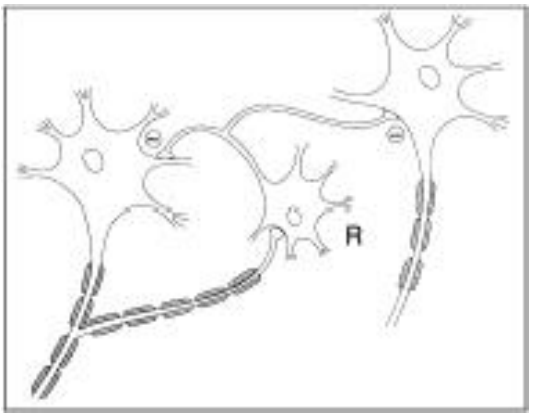
Block

Slide No.(31)

Properties of synapses (con…)

D. Inhibitory interneuron (Renshaw cells)

Negative feedback inhibitory interneuron of a spinal motor neuron .



Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(32)

Properties of synapses (con…)

4. Summation

a. Spatial summation.

When EPSP occurs in more than one synaptic knob at the same time

b. Temporal summation.

If EPSPs in a pre-synaptic knob are successively repeated without significant delay so the effect of the previous stimulus is summated to the next.

Team Notes :

Spatial summation occurs when excitatory potentials from many different presynaptic neurons cause the postsynaptic neuron to reach its threshold and fire.

Temporal summation occurs when a single presynaptic neuron fires many times in succession, causing the postsynaptic neuron to reach its threshold and fire.

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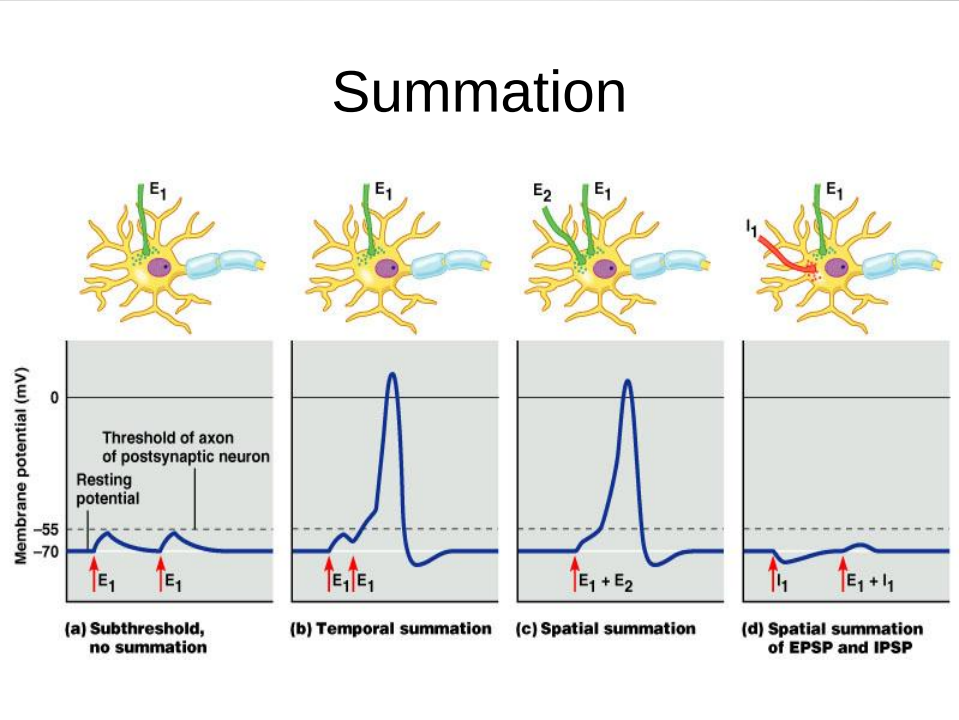
Slide No.(33)



Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(34)

Properties of synapses (con…)

5. Convergence and divergence

Convergence

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

Divergence

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

Team Notes :

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

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.

Slide No.(35)

Divergence & convergence

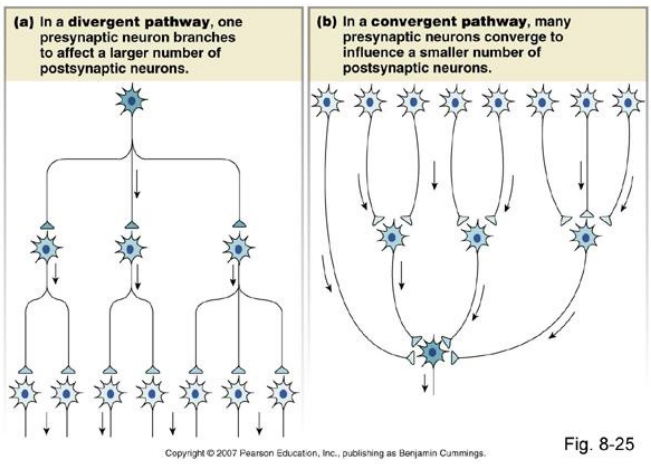


Fig. 8-25

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

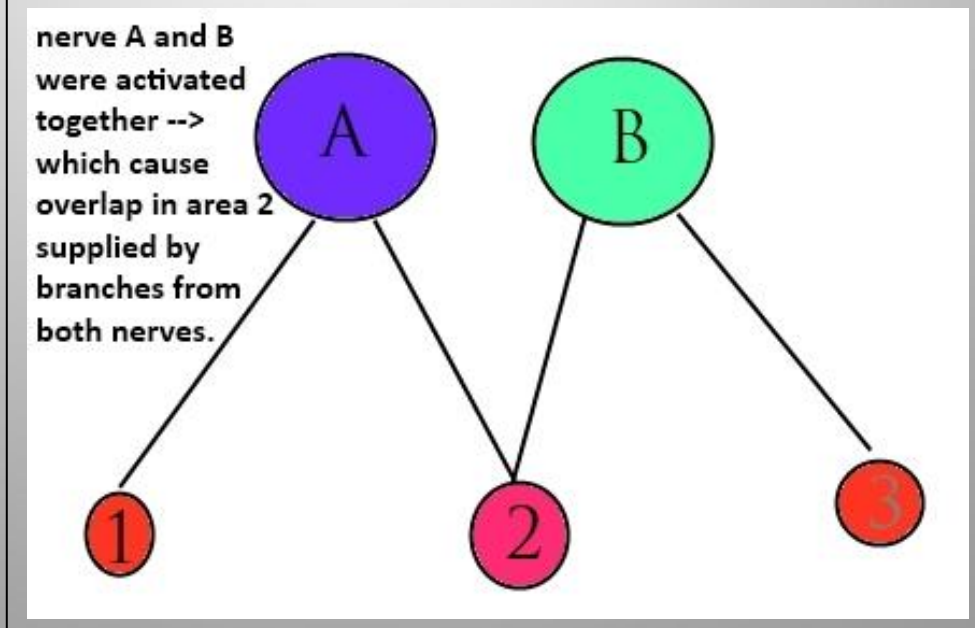
Slide No.(36)

Properties of synapses (con…)

6.Occlusion

It is a decrease in the expected response due to pre-synaptic fibers sharing post-synaptic neuron [=overlap].

Team Notes :



CNS Central Nervous System

Block

Slide No.(37)

Properties of synapses (con…)

7. 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.

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(38)

Factors affecting synaptic transmission:

Alkalosis:

Normally, alkalosis greatly increases neuronal excitability.
For instance, a rise in arterial blood pH from the 7.4 norm to 7.8 to 8.0 often causes cerebral epileptic seizures because of increased excitability of some or all of the cerebral neurons.
This can be demonstrated by asking a person who is predisposed to epileptic seizures to over breathe.
The over breathing blows off carbon dioxide and therefore elevates the pH of the blood momentarily

Team Notes :

* **Focus on those points:**

1. **Alkalosis normally causes neuronal excitation.**
2. **It causes epileptic attacks**
3. **An Example of that, is a young child who is crying all the day, which cause him to hyperventilate and more wash out of Co2, this child is predisposed to have epilepsy.**

CNS Central Nervous System

Block

Slide No.(39)

Acidosis:

Conversely, acidosis greatly depresses neuronal activity;
A fall in pH from 7.4 to below 7.0 usually causes a comatose state.
For instance, in very severe diabetic or uremic acidosis, coma virtually always develops.

Team Notes :

* **Focus on those points:**

1. **Acidosis normally causes depression of the neuronal activity.**
2. **An important example on this point is a patient with diabetic ketoacidosis, he might be comatose.**

CNS Central Nervous System

Block

Slide No.(40)

Drugs:

Many drugs are known to increase the excitability of neurons, and others are known to decrease excitability.

Caffeine found in coffee, tea, *increases* neuronal excitability, by reducing the threshold for excitation of neurons.

Team Notes :

Nothing else was mentioned about this slide.

CNS Central Nervous System

Block

Slide No.(41)

Strychnine:

Is one of the best known of all agents that increase excitability of neurons.

It *inhibits the action of some normally inhibitory transmitter substances*, especially glycine in the spinal cord.

Therefore, the effects of the excitatory transmitters become overwhelming, and the neurons become so excited that they go into rapidly repetitive discharge, resulting in severe tonic muscle spasms.

Team Notes :

Nothing else was mentioned about this slide.

Slide No.(42)

Hypoxia

- Depression of neurons

Team Notes :

So, to summarize the last points:

- Alkalosis
- Drugs such as caffeine & Strychnine

→ **Causes Neuronal Excitation**

- Acidosis
- Hypoxia

→ **Causes Neuronal depression**

Questions :-

1) Synaptic transmission is depressed by:

a. Hypertension
b. Alkalosis
c. Hypoxia
d. Hypokalemia

2) The excitatory postsynaptic potential (ESPS):

a. It is propagated through the nerve fiber
b. A single (EPSP) in one neuron can produce an AP
c. Is produced by K efflux
d. It is a local response on the cell membrane
e. Cannot be summated

3) GABA:

a. In one of the major excitatory neurotransmitters
b. Mediates synaptic facilitation
c. Acts by opening chloride channels
d. Deficiency results in muscle paralysis
e. Is secreted manly by peripheral nerves

Answers :-

1- C
2- D
3- C