◉Sheet ○Slides

Number

20

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Notes from review questions:

1- Adaptation means that the stimulus is existing but action potential isn't generated.
2- The question was if the generator potential reaches its highest point (+30 mV) we can't increase the Action potential, is this considered adaptation ? The answer is **No.**
3- The whole pathway from the receptor to the cerebral cortex is SPECFIC for certain stimulus, NOT the neuron pathway.
4- Every sensory receptor is sensitive to certain stimulus, like: In a burn case, the patient feels pain and heat, because thermoreceptors and pain receptors both are stimulated.
5- The receptor might be stimulated by other modalities, but what ever the stimulus there is one kind of sense (You will feel pain from pain receptors even if the real stimulus was the heat itself).
6- Sensory Receptors are organs that convert any type of energy into Electrical energy but the pathway of sensation from PNS to CNS contains proteins receptors found in the postsynaptic membrane, where NT binds and that causes EPSP or IPSP (excitatory/inhibitory postsynaptic potential).

Neuronal processing

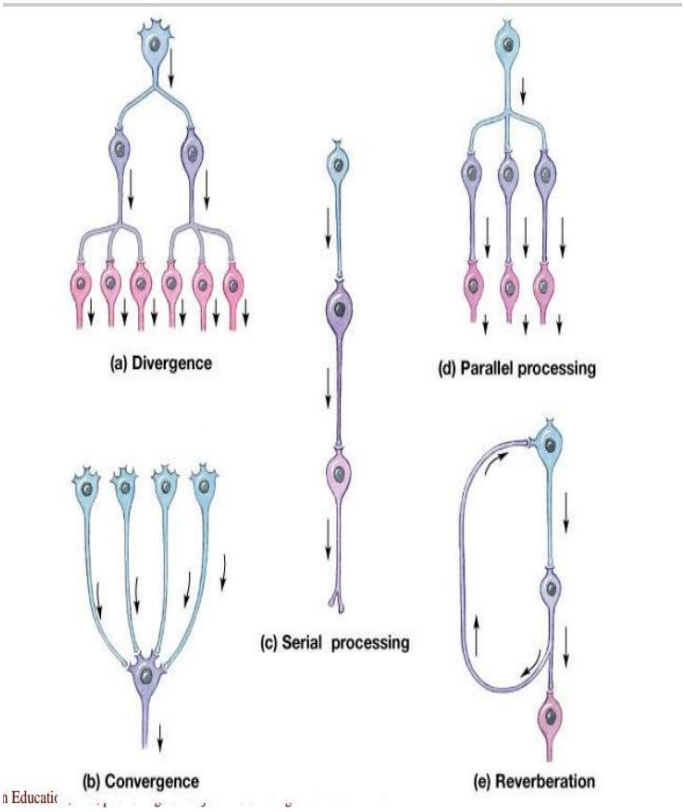
- ✓ Neuronal pool is a group of neurons with special organization comprising different types of neuronal circuits, and they have the same function, and also has:

1. Central region called Discharge zone: It's usually stimulated and generates AP.
2. Peripheral region called Facilitation zone: While the generation of action potential in the discharge zone, the membranes of facilitated neurons become less negative and nearer to the threshold. **Only if the stimulus is strong enough, facilitated neurons reach the threshold and generate AP (so it could be a discharge zone).**

Types of Neuronal Circuits

1. *Diverging circuit :*

- One presynaptic neuron synapses with many postsynaptic neurons.
- An impulse (signal) from a single neuron causes the stimulation of increasing numbers of neurons.
- You feel that a large area is stimulated because AP is transmitted to a large area in the cerebral cortex.
- Poorly localized, so it causes Crude touch (not being able to determine the stimulated area specifically).



2. *Converging circuit :*

- Several presynaptic neurons synapse with one post synaptic neuron.
- Many signals from multiple inputs converging to a single neuron.
- The inputs could be from one source or multiple sources.
- EPSP and IPSP are summated at the output, if they reach the threshold, the neuron generates action potential.
- Causes loss of localization, it stimulates large area and that is transmitted to small area on the cerebral cortex (again you feel the stimulated area is smaller than it really is).

3. *Reverberating circuit*

- Terminals of the later neurons synapse with earlier neurons (backwards direction)
- Causes a positive feedback, the output neuron can re-excite the input neuron of the same circuit by sending signal back to it.
- A neuron could re-stimulate itself.
- The reverberation can't continue forever due to the inactivation of the neurons.
- Can have facilitation & inhibition neurons.

4. *Parallel circuit :*

- It can be One presynaptic neuron synapsing with many postsynaptic neurons in such a way they the impulses prolong in the same direction.
- Or it can be many presynaptic neurons synapsing with one post synaptic neuron in such a way that impulses prolong in the same direction.
- Causes prolongation to the response time.

5. *Serial circuit :*

- Each neuron in the circuit synapses only with one postsynaptic neuron.

Lateral Inhibition

1) Inhibitory neurons are found in some circuits in the sensory pathways and in the CNS.
2) Causes Localization and Discrimination the point of the stimulus.
3) Keeps ***Central Sensation***: Causes the sharpening of sensation, such as when a blunt object touches your skin, you feel a single touch.
4) Enables you to demarcate (distinguish) between two points on your skin.
5) The pathway of **fine touch** uses lateral inhibition.

✓ The circuit can be stopped by many ways :

- Neurotransmitter Removing Mechanisms.
- Synaptic Fatigue.
- Neural Inhibition.
- Downregulation.

Stabilization of neuronal discharge

1. Synaptic fatigue:

- short term and acute adjustment of sensitivity.
- The process of Recycling and Synthesis of NT IS NOT enough, So it runs out of Neurotransmitters due to Continuous Impulses in the neuron.

2. Neuronal inhibitory circuits:

a) Gross inhibition: Basal ganglia inhibits muscle tone "mentioned in the slide".

b) Feedback Inhibition-Cortico-fugal fibers:

- A negative feedback from the cerebral cortex descending fibers to control the intensity and sharpness of the signals.
- It decreases the receptor potential, so increases the sensitivity.

3. Downregulation and Upregulation: Long term stabilization through modification of the receptor availability (internalization or externalization).

- **Downregulation** usually occurs when the circuits is very active, the protein receptors in the postsynaptic membranes are internalized: enters the intracellular part of the membrane, so The NT cannot bind to its receptor, that decreases the activity of the circuit. It happens to *beta receptors.*
- In **Upregulation** increasing the receptor numbers in the extracellular part of the membrane, that increases the sensitivity of the pathway, and is called Externalization.

Mechanisms for prolongation of time response

1) *Synaptic after-discharge:*

✓ It occurs when a stimulus causes an EPSP higher than the threshold.

✓ This EPSP lasts for 15-20 msec, at this time, it continuously generates action potential until it becomes lower than the threshold.

✓ since the time of EPSP (15-20 msec) is longer than the time of AP (0.1 – 10 msec) then then we have multiple APs per one EPSP.

✓ We can notice that when we close our eyes and still see light or blotch, because EPSP is generating action potential even the stimulus stopped.

2) *Parallel circuits.*

Signal transduction

- Signaling: Cell to Cell communication via signals.
- Signal transduction: Process of converting extracellular signals into intracellular responses.
- Ligand: The signaling molecule, hormone or neurotransmitter, the first Messenger.
- Receptors:

i. Specific proteins bind to specific ligands.
ii. Transmit signals to intracellular targets.
iii. Different receptors can respond differently to the same ligand.
iv. A ligand doesn't work without its receptor.
v. According to the type of ligand, Receptors can be found in cells membrane, Cytoplasm or Nucleus.

- Target cell : the cell that has the receptor of the ligand.
- Components involved in signaling: Ligands, Receptors, Intracellular Signaling Proteins, Intermediary Proteins, Enzymes, Second Messengers, Target Proteins, and Inactivating Proteins.

I. It's not necessary to include all of them in every signal transduction.
II. Target proteins can be:

Cytoskeletal proteins: results in a change in the movement or shape of the cell.

Gene regulatory proteins: results in a change in gene expression.

Metabolic enzymes: results in a change in metabolism.

Intercellular Communication

A. *Endocrine Communication:* a non-neuronal cell releases/secretes hormone into blood. This hormone affects the target cell which is so far from the endocrine cell.

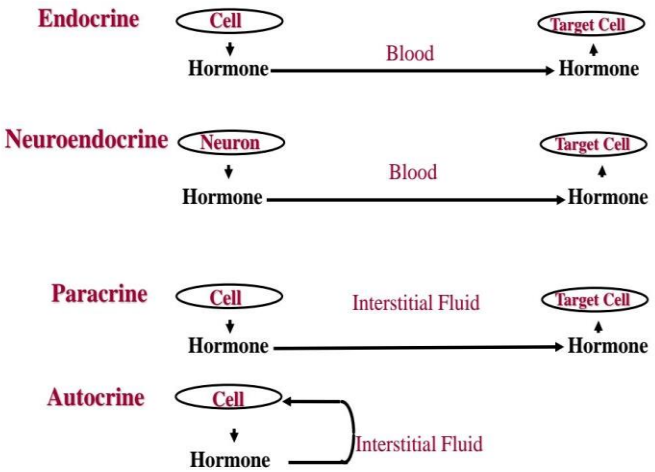
B. *Neuroendocrine Communication:* a neuron secretes a hormone into blood. This hormone affects the target cell.

C. *Paracrine Communication:* a non-neuronal cell secretes a hormone into the interstitial fluid. This hormone affects the target cell which is near from the paracrine cell (Para=near).

D. *Autocrine Communication:* a non-neuronal cell secretes a hormone into the interstitial fluid. This hormone affects the same cell because it has the targeted specific receptor.

E. *Neuronal Communication:* a neuron secretes a NT into the synaptic cleft. This NT binds to its receptor in the target cell which is postsynaptic.

F. *Communication By Gases:* is a type of paracrine communication.



Hormones Classification

1- According to their structure :

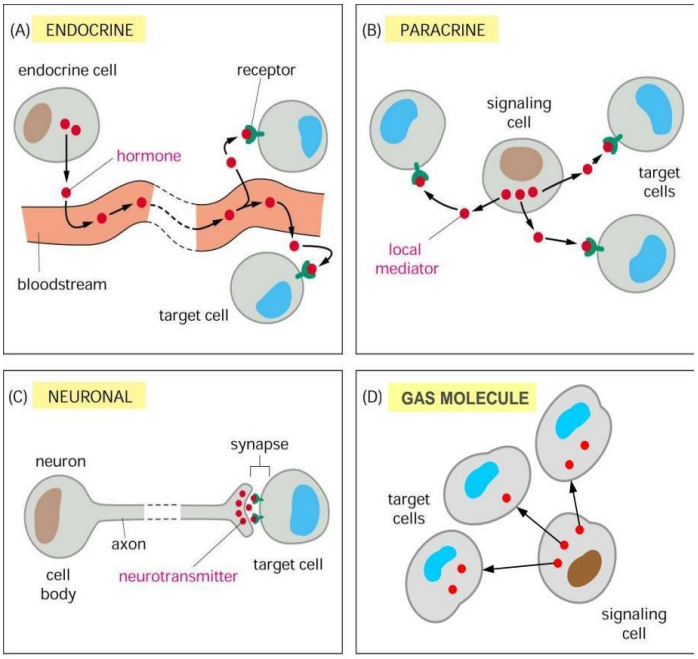
Proteins, Peptides, Amine Hormones, Steroid Hormones, Gas Molecules.

2- According to the location of their effect :

■ *Circulating Hormones :* circulate in blood throughout body and act far from the endocrine cell. (Endocrine Communication).

■ *Local Hormones :* act locally and include :

- Paracrine Hormones : act on neighboring cells.
- Autocrine Hormones : act on the same cell that secreted them.
- Gases Molecules.



3- According to their solubility :

a. ***Water-Soluble Hormones :***

I. circulate in “free” form, they are soluble in the plasma.
II. Their Receptors are membrane proteins.
III. They include :

- Amine hormones.
- Polypeptides hormones.
- Protein hormones.
- Eicosanoid (prostaglandins).

b. ***Lipid-Soluble Hormones :***

I. Use transporter (carrier) proteins in the blood, because they aren’t soluble in the plasma.
II. Their Receptors are intracellular.
III. They include:

- Steroid hormones.
- Carbon monoxide (CO).
- Thyroid hormones (T3, T4)
- Nitric oxide (NO).

*The transporter protein may be specific for one hormone or general to many types of hormones.

Peptide & Protein Hormones

1) Peptides: Polypeptide Chains of < 100 amino acids in length.

E.g. : ADH : (8 amino acids) , Adrenocorticotropin hormone: causes the growth of the adrenal gland cortex. (39 amino acids).

2) Protein hormones: Polypeptide chains with > 100 amino acids.

E.g.: Growth hormone: (181 amino acids) .

Steroid Hormones

Lipids derived from cholesterol, they are lipophilic hormones.

E.g.: Testosterone, Estradiol, Cortisol, Progesterone.

Amine Hormones

Hormones derived from **Tyrosine** and **Tryptophan**.

E.g.: NE, Epi, T4 (lipid soluble), dopamine.

Gas Molecules

E.g.: Nitric Oxide (NO), Carbon Monoxide (CO).

Eicosanoid (prostaglandins)

Hormones derived from Arachidonic Acid (a fatty acid with 12 carbon atoms and 4 double bonds).

Testicular Feminism Syndrome:

- ✓ A congenital abnormality in which the genotype of the patient is 44+ XY (the patient is male), but the phenotype is female.
- ✓ caused by **deficiency of testosterone receptors** in the target cells of the patient.
- ✓ The patient might have *high testosterone secretion* in his body due to the negative feedback, because testosterone doesn't work, there are no receptors!
- ✓ At *puberty*, the patient doesn't get in Menstrual cycle ."الدورة الشهرية"
- ✓ By Chromosome and testosterone concentration tests, the patient would be identified as male.