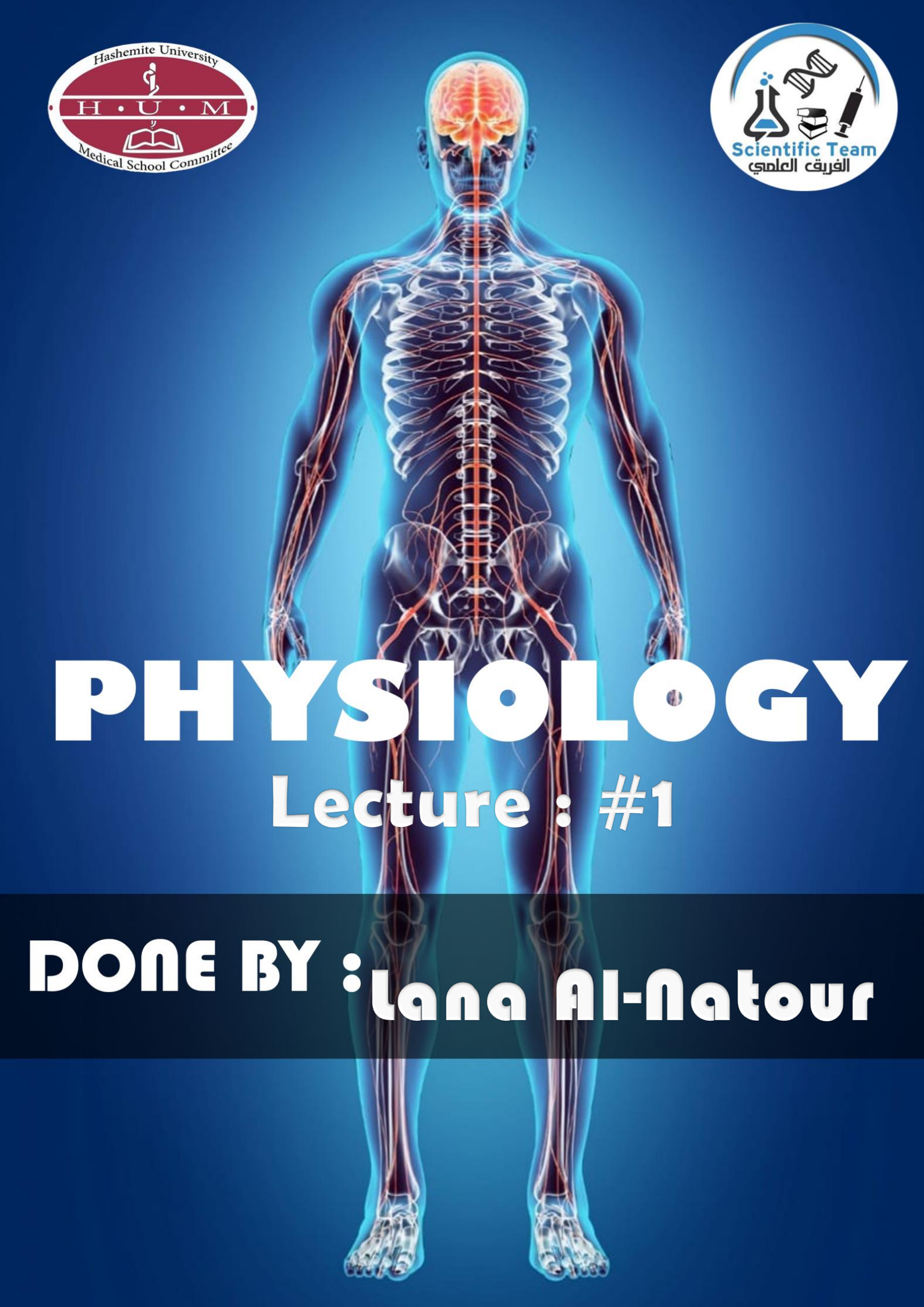
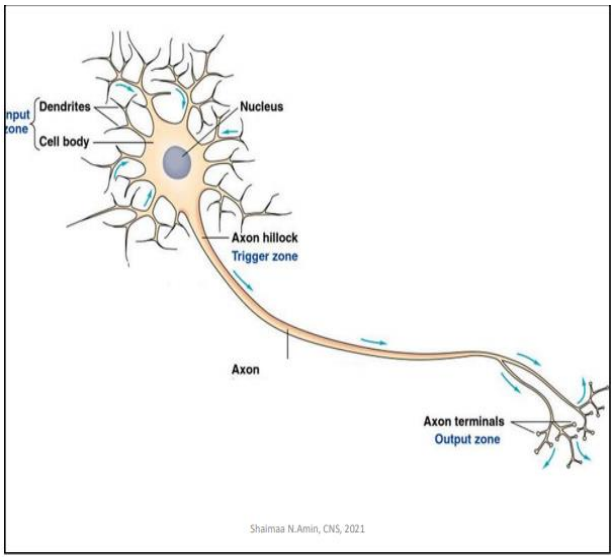


PHYSIOLOGY

Lecture : #1

DONE BY : Lana Al-Natour

Lecture 1: synaptic transmission and neuronal pool



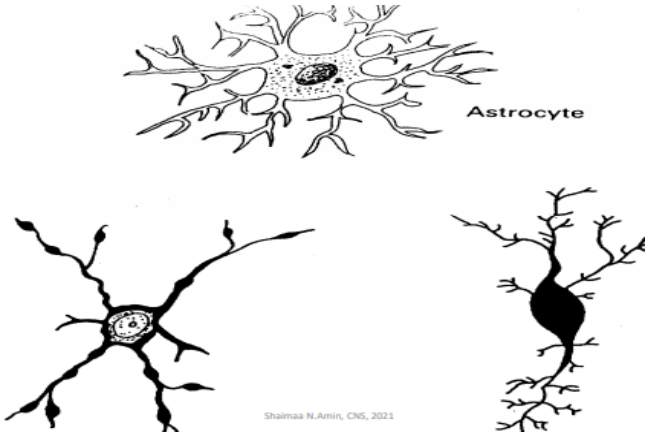
We can see here the anatomical structure of the neuron

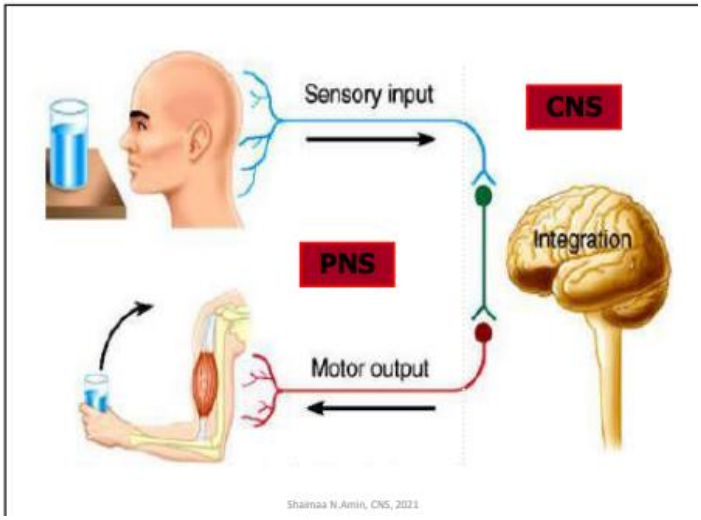
Axon hillock هو اكثر جزء بيتهيج في العصبون طيب ايش يلي عمله most excitable؟؟ لانه اكثر جزء فيو sodium voltage gated channels يلي بتساعد في depolarization

The central excitatory state favours firing of action potentials from the postsynaptic neurons. The portion in these neurons with the lowest threshold for production of action potentials is the *initial segment of the axon* (at and just beyond the axon hillock). For this reason, *the most rapid transmission of signals normally occurs at the axo-axonic synapses.*

فيه خلايا بتسوي supporting لل neurons اسمها glial cells وبتعمل

maintains hemostasis of the electrolytes and neurotransmitters around the neurons





Nervous system is classified anatomically to: central nervous system and peripheral nervous system

Classified functionally to : voluntary and involuntary (autonomic)

ويمكن اصنفه على حسب اتجاه signal فاذا كان من sensory: منسميه periphery to the central

واذا كان الاتجاه من central to the periphery منسميه: motor

مثال :بشوف ايشي من بعيد بيهجم (vision (sensation وردة الفعل اني اضربه مثلا (motor)

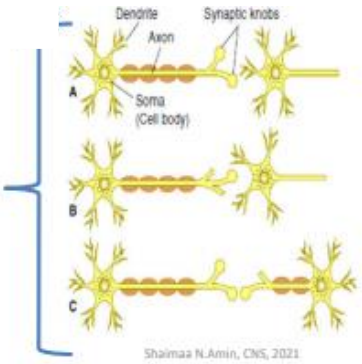
What is synapse? It is a junction between an axon terminal of one neuron (presynaptic neuron) and a second neuron (postsynaptic)

It can be axo-axonic synapse

axo-somatic synapse

axo-dendritic synapse

Anatomical Classification



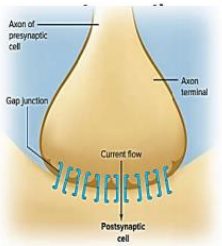
Synaptic transmission: transmission of one neuron to another ..physiological types are :

1-electric transmission

هو الاسرع ويتصف بوجود gap junctions بتنقل فيه electrolytes

(2) Electrotonic (or gap junction) synapses : These are *few* but more rapid. The membranes of the pre and post-synaptic neurons come close to each other and *gap junctions form between them*. Such junctions constitute *low-resistance bridges* through which ions can pass easily, allowing transmission of the depolarization waves directly from one neuron to the other.

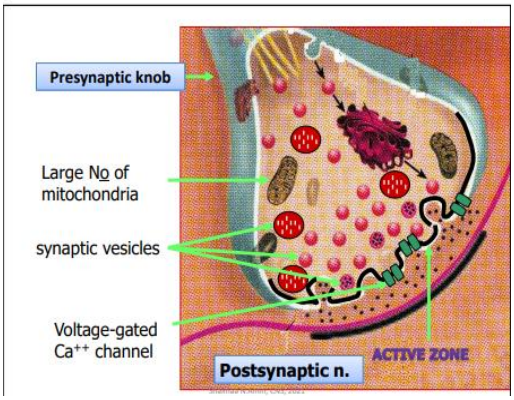
Electrical Transmission (Gap



2-chemical transmission

هو الذي يحفز عن طريق neurotransmitters

(1) Chemical synapses : These are the *majority* in the CNS. The synaptic knobs contain *vesicles in which neurotransmitters are synthesized*, and are rich in *mitochondria* that provide the required energy. Stimulation of the presynaptic neurons leads to release of the neurotransmitters from these knobs which affect the excitability of the postsynaptic neurons (see below).



Functional anatomy of the synapse:

1-presynaptic terminal (presynaptic knob)

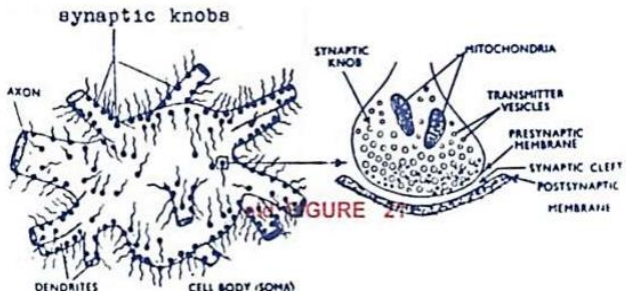
منشوف فيه ميتوكندريا ومنلاقي فيه vesicles ومنلاقي كمان بروتينات على wall يلي بتعمل interaction مع البروتينات يلي موجودة على سطح vesicle ومنسميها active zone و حتى يصير release of the neurotransmitters

2-synaptic cleft :a space between presynaptic and postsynaptic neurons and contains extracellular fluid

فيو extracellular fluid وبالتالي هو rich in sodium and have less potassium

3-post synaptic membrane contains the receptors of the neurotransmitters for example: acetylcholine>>> cholinergic receptors

The synapses are the sites of junction between neurons. The axon of the *presynaptic neuron* divides into about 2000 branches on the average, each of which ends by a knob called the ***synaptic knob***. A large number of these knobs terminate on the ***dendrites, soma and axon of the postsynaptic neuron*** (e.g. about 10000 knobs terminate on each spinal motor neuron), and at the sites of contact, the knobs are separated from the postsynaptic membranes by gaps filled with ECF called the ***synaptic clefts*** (figure 21).



Mechanism of synaptic transmission:

هلا v-snare موجود على vesicles و T-snare موجود عند سطح presynaptic neuron

فهلا لو ما حصل عنا signal for releasing neurotransmitters رح تضلها vesicles in storage zone ولكن لما توصل signal رح تتحرك عن طريق vesicles

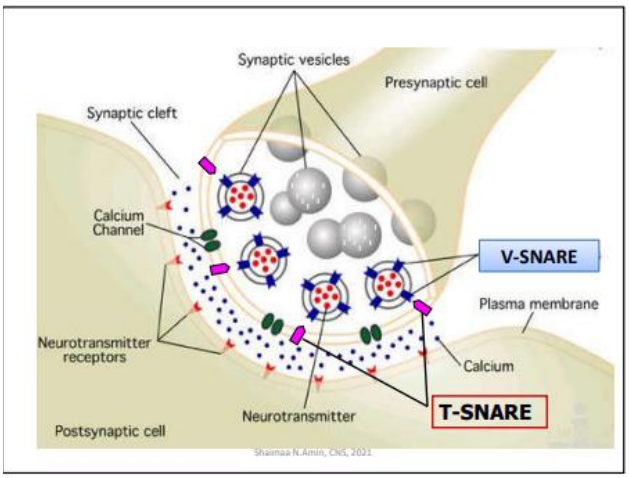
Molecular motor ((needs ATP, calcium))

ورح تتحرك من storage zone الى releasing zone بحيث بتقرب من جدار presynaptic terminal وبصير

Interaction between V-snare and T-snare

بحيث لما يوصل signal رح يصير depolarization وتفتح calcium voltage gated channels ((بيدخل كالسيوم من extracellular الى nerve terminal))

و neurotransmitters حتعدي synaptic cleft ويصير interaction بينها وبين receptors



Mechanism of impulse transmission in chemical synapses

(1) Release of transmitters : Depolarization of the knobs leads to opening of voltage-gated Ca^{2+} channels, which allows ***Ca^{2+} influx*** into the knobs. *Ca^{2+} causes fusion of the vesicles with the knob's membrane* at specific ***active zones***, which then rupture leading to release of the transmitter by ***exocytosis*** into the synaptic clefts. The process of fusion involves interaction between 2 proteins, one in the vesicle membrane (= ***synaptobrevin***) and the other in the knob's membrane (= ***syntaxin***). Recently, it was also found that certain proteins called **neurexins** bind the membranes of the presynaptic and postsynaptic neurons together.

(2) Action of transmitters : The transmitter binds to specific receptors in the postsynaptic membrane. This triggers either opening or closure of specific ***ligand gated ion channels*** in that membrane, resulting in electric changes called ***postsynaptic potentials*** (= ***PSPs***) which lead to either excitation or inhibition of the postsynaptic neuron, depending on the nature of the released transmitter (see below).

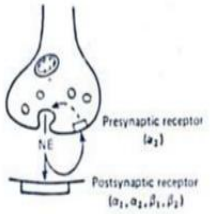
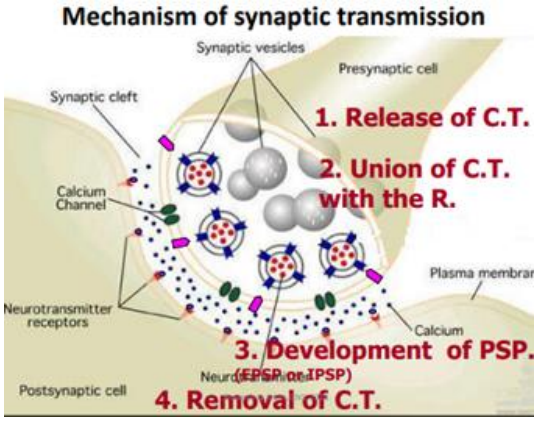


Figure 22 : Presynaptic and postsynaptic receptors at a noradrenergic nerve ending (NE = noradrenaline).

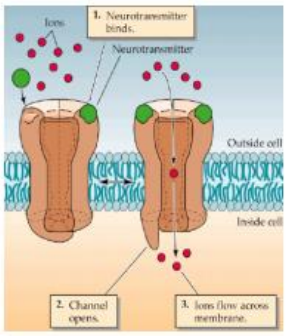
هلا بعد ما يمسك NT بال receptor لازم يصير فيه response
اما انه يكون excitatory or inhibitory على حسب نوع NT

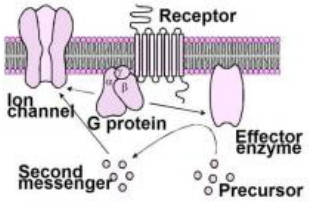
فمثلا GLUTUMATE عبارة عن excitatory ولكن GABA عبارة عن inhibitory

و epinephrine /norepinephrine ممكن تكون excitatory او inhibitory على حسب نوع event يلي حصل بعد binding سواء depolarization or hyperpolarization ونوع receptor يلي حصله activation



Types of receptors





We have 2 types of receptors that can the neurotransmitters bind:

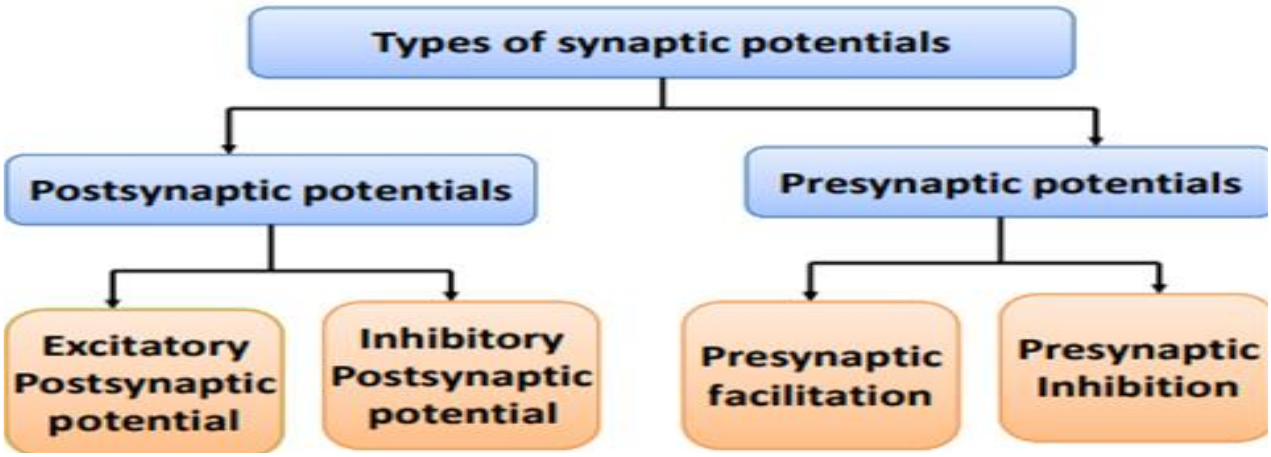
1-ionotropic receptors

((Channels))

2-G-protien coupled receptor

For example:

1. Acetylcholine has 2 types of receptors : Nicotinic and Muscarinic (the latter are 5 types termed M_1 to M_5 receptors).
2. Noradrenaline has 2 types of alpha receptors (1 and 2, each of which has 3 types) and 3 types of beta receptors (1, 2 and 3).
3. Dopamine has 5 types of receptors (called D_1 to D_5 receptors).

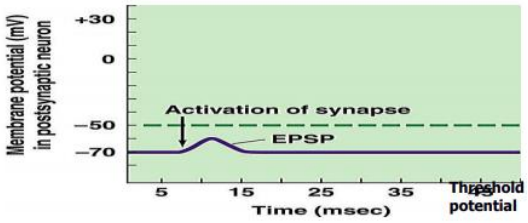


1-excitatory postsynaptic potential (EPSP)

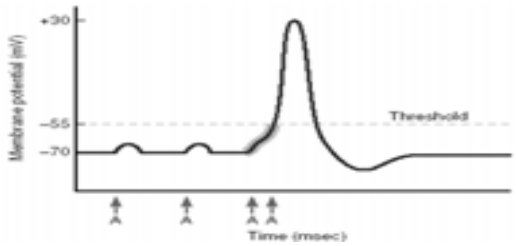
بصير عنا depolarization عن طريق excitatory neurotransmitter بحيث بيدخل الصوديوم او كالسيوم وبوصله لل level قبل threshold وبتكون بتساوي =-65 وهيك منسميه local response potential بحيث انه هيك ما بكون propagated وما بكون اسمه action potential طيب كيف بدنا نخليه يوصل threshold ويتكون action potential لازم يصير عنا summation ويحصل repeated stimulation حتى يوصل ل threshold طيب كيف يعني ؟

(A) Excitatory postsynaptic potential (EPSP)

This is a state of *transient partial depolarization in the postsynaptic membrane during which the excitability of the postsynaptic neuron to other stimuli is increased.* It occurs in excitatory synapses (at which the transmitter is excitatory e.g. acetylcholine), and is due mainly to an ***increase in*** Na^{+} ***or*** Ca^{+2} ***influx*** secondary to opening of their channels.

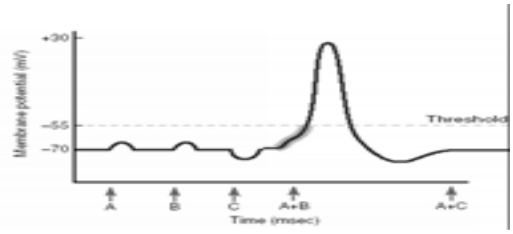


يعني لو كان عنا neuron A وصارله ESPS لازم يصيرله stimulation قبل ما decay time يخلص يلي هو تقريبا 15 ثانية حتى يوصل thresholdوبالتالي شو يعني decay time((يعني الوقت يلي لو ما اجا فيه stimulation رح يختفي ولازم يكون قبل 15 ثانية)) وهاد summation اسمه temporal summation



(2) Temporal summation : This is the summation of the PSPs produced by *repeated activation of one synaptic knob* (by continuous stimulation of a single presynaptic neuron). In this case, a new PSP must develop before the previous PSP decays (therefore, the time between successive stimuli must be *less than 15 milliseconds*, which is the time after which a single PSP decays)

وعنا نوع ثاني يلي هو spatial summation يلي مثلا neuron A +neuron B وبصيرله stimulation لحتى يوصل threshold



(1) Spatial summation : This is more common in the CNS, and is the summation of the PSPs produced by *activation of many synaptic knobs* at the same time (commonly *as a result of simultaneous excitation of multiple presynaptic neurons*).

All the note in the hand-out :

The PSP (whether excitatory or inhibitory) produced by activity in a single synaptic knob is normally very small and ineffective. However, it is ***not an all or none response*** and can be summated by 2 ways :

(1) Spatial summation : This is more common in the CNS, and is the summation of the PSPs produced by *activation of many synaptic knobs* **at the same time** (commonly *as a result of simultaneous excitation of multiple presynaptic neurons*).

(2) Temporal summation : This is the summation of the PSPs produced by *repeated activation of one synaptic knob* (by continuous stimulation of a single presynaptic neuron). In this case, a new PSP must develop before the previous PSP decays (therefore, the time between successive stimuli must be *less than 15 milliseconds*, which is the time after which a single PSP decays)

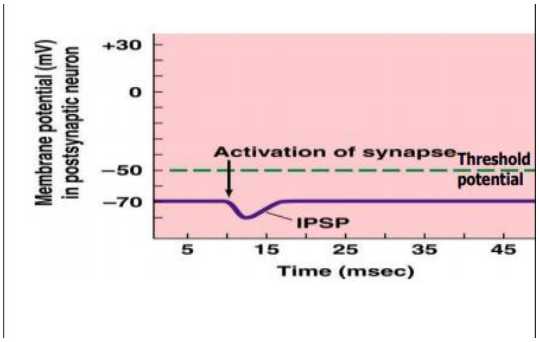
** Both types of summation may coexist (= ***temporo-spatial summation***) if several presynaptic neurons are successively stimulated rapidly one after the other at intervals not exceeding 15 milliseconds.

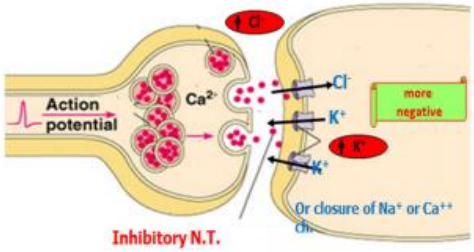
2- Inhibitory postsynaptic potential (IPSP) is a local state of slight hyperpolarization in postsynaptic membrane

طيب لو كان عنا inhibitory neurotransmitter زي GABA بيعمل hyperpolarization على post synaptic membrane اما بدخول chloride او خروج potassium وهما نفس الايشي local response وهيك صار more negative membrane

(B) Inhibitory postsynaptic potential (IPSP)

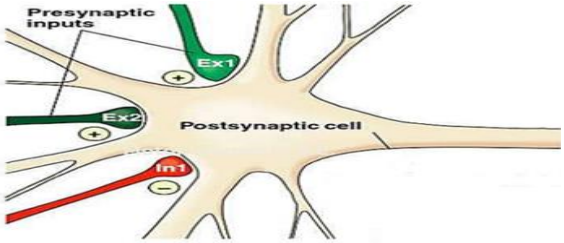
This is a state of *transient hyperpolarization in the postsynaptic membrane during which the excitability of the postsynaptic neuron to other stimuli is decreased.* It occurs in inhbitory synapses at which the transmitter is **glycine** (see below), and is due mainly to an ***increase in Cl^- influx***. However, some IPSPs are produced by ***opening of K^+ channels*** (which increases K^+ efflux) while others can be produced by *closure of Na^+ or Ca^{+2} channels.*





Grand postsynaptic potential :the sum of all EPSPs and IPSPs occurring at the same time

يعني انه neurons بيجيه excitatory or inhibitory وبناء على summation هو يلي بمشي عليه response of the neuron



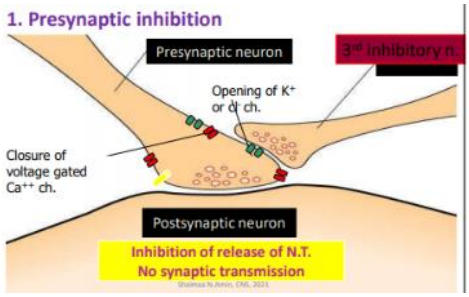
THE CENTRAL EXCITATORY & CENTRAL INHIBITORY STATES

Thousands of excitatory and inhibitory synaptic knobs normally converge on postsynaptic neurons. Therefore, both EPSPs and IPSPs commonly occur simultaneously, and the ***result depends on the algebraic sum of the*** produced ***depolarizing and hyperpolarizing effects***. Predominance of the former produces a central excitatory state (CES) while predominance of the latter produces a central inhibitory state (CIS).

The central excitatory state favours firing of action potentials from the postsynaptic neurons. The portion in these neurons with the lowest threshold for production of action potentials is the ***initial segment of the axon*** (at and just beyond the axon hillock). For this reason, ***the most rapid transmission of signals normally occurs at the axo-axonic synapses.***

3-presynaptic inhibition

بكون فيه neuron 3 بيعطي signals for presynaptic neurons وبيعمل effect على voltage بحيث ممكن يصعبها عليها وما يخلي calcium voltage gated channels تفتح



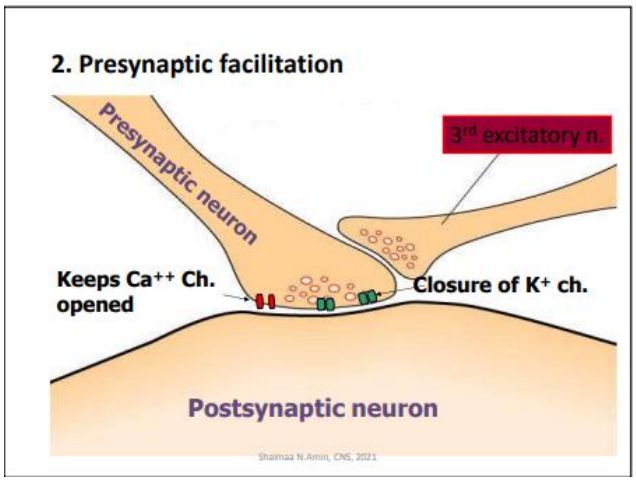
(2) Presynaptic inhibition

In this type of inhibition, the terminal knobs of the inhibitory neurons ***terminate on the excitatory nerve endings*** (= axo-axonal synapses) *and not on the postsynaptic neurons* (figure 23). It occurs ***in the dorsal horns*** where **enkephalinergic neurons** block pain transmission (refer to the ***analgesia system***, page 35) as well as in other parts in the nervous system in which the transmitter is **GABA**. These inhibitory transmitters decrease the release of the transmitter from the excitatory nerve terminals ***by either a direct effect or by decreasing Ca^{2+} influx*** (thus decreasing post-neuronal excitation).

** *GABA produces the latter effect by decreasing the size of the action potential in the excitatory endings* (which decreases opening of the Ca^{2+} channels and Ca^{2+} influx). *At the GABA $_A$ & $_C$ receptors, this occurs by increasing Cl- influx while at the GABA $_B$ receptores, it occurs by increasing K^+ efflux*

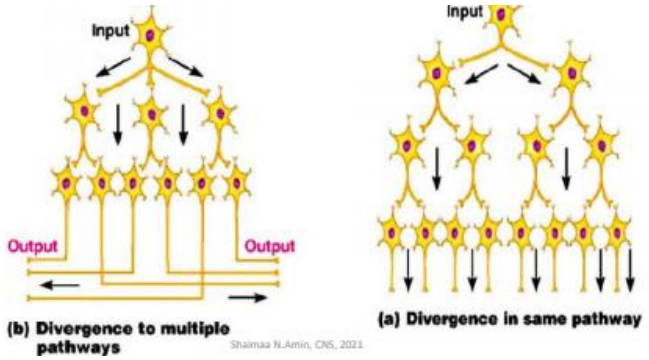
4-presynaptic facitillation

هون neuron 3 هو يلي بسهل انه يطلع NT من presynaptic neuron وبزودها عن طريق انه يخلي calcium voltage gated channels تضلها مفتوحة



Organization of neurons in different pools :

1-divergence



انه one neuron بيتوزع وبيروح على multiple neurons
اما ان يكون نفس pathway او باكثر من اتجاه

Divergence of signals in neuronal pools

This is the spread of signals from one input neuron to many output neurons, and it is 2 types :

(1) Divergence in the same tract : This is characteristic of *the cortico-spinal (= pyramidal) tract,* in which a single cerebral cortical cell can excite about 1000 muscle fibres (figure 26 A).

(2) Divergence into multiple tracts : This is spread of the input signal in 2 separate directions (figure 26 B) e.g. in the dorsal column of spinal cord, the input signals diverge into the spinocerebellar and gracile and cuneate tracts.

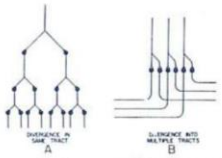
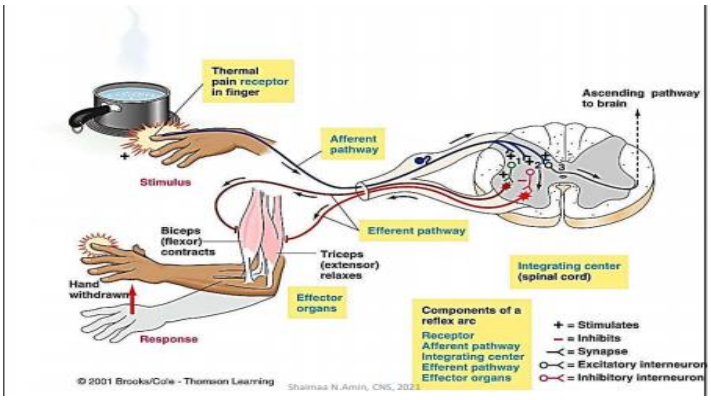


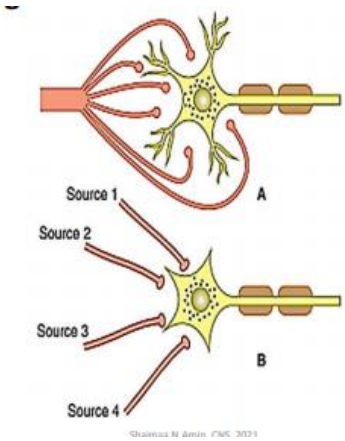
Figure 26 : Divergence in the same tract (A) and in multiple tracts (B).



هاي الرسمة بتشرح withdrawal reflex زي لما بتمسك اي مصدر ساخن و بيوصل للمراكز الدماغ وبتصير ردة فعل بأنه تبعد ايدك عن مصدر السخونة لقدام حكت الدكتورة رح ندرسه ...

2-convergence

انه multiple neurons رح يجتمعوا على output واحد يعني باكثر من synapse سواء من neuron واحد او اكثر من neuron



Convergence of signals in neuronal pools

This is the collection of signals from multiple input neurons to a single output neuron, and it is 2 types :

(1) Convergence from a single source (figure 27 A).

(2) Convergence from multiple sources (figure 27 B).

Both types lead to **summation of impulses**, which is essential for excitation of postsynaptic neurons (page 40).

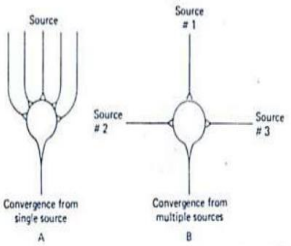
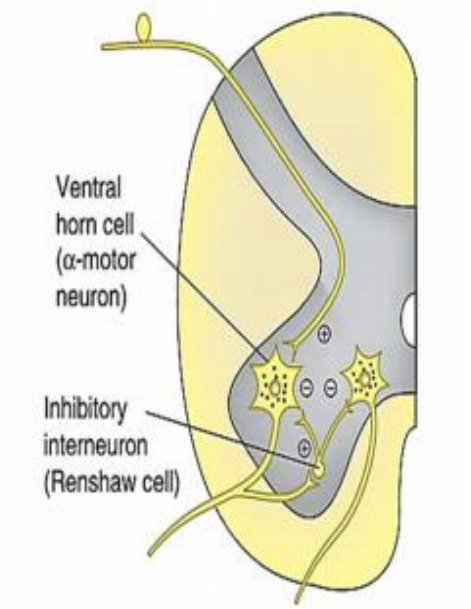


Figure 27 : Convergence from a single source (A) and multiple sources (B).

3-inhibitory circuits

هلا في ventral horn عنا 2 motor neurons بينهم Renshaw cells (interneurons) لما يصيرلها stimulation من neuron يلي من جهة الشمال بتروح عاملة negative feedback inhibition عن طريق glycineعلى حهة الشمال وبتعمل على جهة اليمين مثلا انه تطلع lateral inhibition



stimulates a Renshaw cell, and this cell in turn sends signals that inhibit the following neurons through releasing **glycine :**

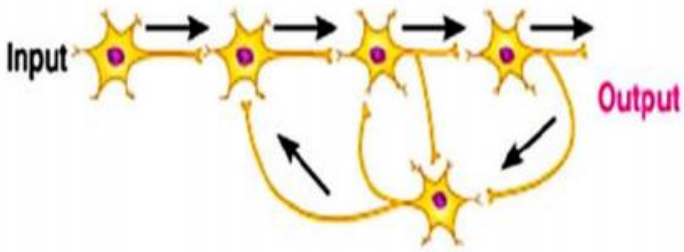
(a) The original motor neuron, leading to its inhibition (that is commonly called *negative feedback, collateral, recurrent or Renshaw inhibition*) which results in shortening of the output signals.

(b) The motor neurons in the surrounding area, leading to *lateral inhibition* of these neurons, which sharpens the output signals (see next).

** Another mechanism for shortening of signals is present in the cerebellum and is called **negative feed-forward inhibition** (page 108).

4-revrebatory circuit

هلا input بكون خلص signal تاعه يلي بده يوصل لل output وبصير collaterals interneurons وبعمل restimulation of the neuron between the input and output وطيب كيف بالاخير رح يوقف عن طريق انه يصير depletion of the NT؟



(b) Reverberatory (= oscillatory or closed-chain) circuits : In this type, the output neuron is repeatedly stimulated through closed circuits of interneurons called *reverberators* by a *positive feedback mechanism* as follows : Collaterals from the interneurons feedback by way of the reverberators to re-excite the output neuron again and again after the input signal stops (most right in figure 28), and this continues for variable periods, after which it stops due to either fatigue of the synaptic transmission or by the effect of an inhibitory input (see below).

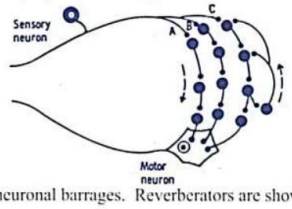


Figure 28 : Interneuronal barrages. Reverberators are shown most right.

****inhibition at synapse: post-synaptic inhibition, pre-synaptic inhibition, lateral inhibition and feedback inhibition ,feed forward inhibition**

Characters of synaptic transmission:

الدكتورة هون ما زادت ايشي عن hand out

THE PROPERTIES OF SYNAPTIC TRANSMISSION

(1) One way conduction (forward direction) : In synapses, impulses are conducted ***only from the presynaptic to the postsynaptic neurons*** (because the chemical transmitters are present only in the presynaptic knobs).

(2) Delayed conduction (synaptic delay) : There is a delay of impulse transmission in synapses of about ***0.5 millisecond*** due to the time required for release of the neurotransmitter, its diffusion through the synaptic cleft and its binding to and activation of the postsynaptic receptors.

** The **number of synapses in a reflex can be calculated as follows :** The ***total reflex time*** and the time of conduction in the ***afferent and efferent nerves*** are determined. The difference between both represents the time of conduction in the CNS, and is known as the ***central delay***. The number of synapses in the reflex = **Central delay / Synaptic delay** (e.g. if the central delay is 3 milliseconds, the number of synapses = 3 / 0.5 = 6 synapses).

(3) Synaptic fatigue : This is slowing or failure of impulse conduction across synapses that occurs after repetitive stimulation of presynaptic neurons. It may be due to depression of the postsynaptic neurons but it is believed to be primarily due to ***depletion of the neurotransmitter***.

(4) Synaptic afterdischarge : This is continuation of discharge from the postsynaptic neurons for some time ***after stopping stimulation of presynaptic neurons***. It is due to *persistence of the central excitatory state* produced by the initial stimulus, and it leads to prolongation of discharge of signals from motor neuronal pools (page 48).

(5) Summation of postsynaptic potentials : This occurs by both spatial and temporal mechanisms (page 40).

(6) High sensitivity to the following :

1- Blood pH : Alkalosis increases while acidosis decreases synaptic transmission. Thus, a rise of blood pH from 7.4 to 7.8 leads to convulsions while its fall is associated with drowsiness (or coma in severe acidosis).

2- Blood O_2 level : Hypoxia decreases synaptic transmission, so unconsciousness occurs if the cerebral circulation stops for only 3-5 seconds.

Factors affecting synaptic transmission:

Changes of composition of internal environment:

1-ph of the blood

Acidosis :inhibition of the synaptic transmission

Alkaolosis:stimulation of synaptic transmission

2-hypoxia

Inhibition of synaptic transmission

3-hypoglycemia

Inhibition of synaptic transmission

4-hypocalcemia

Increase excitability of synaptic transmission

GOOD LUCK ☺