# CENTRAL NERVOUS SYSTEM

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- ○ Anatomy
- ● Physiology
- ○ Pathology
- ○ Biochemistry
- ○ Microbiology
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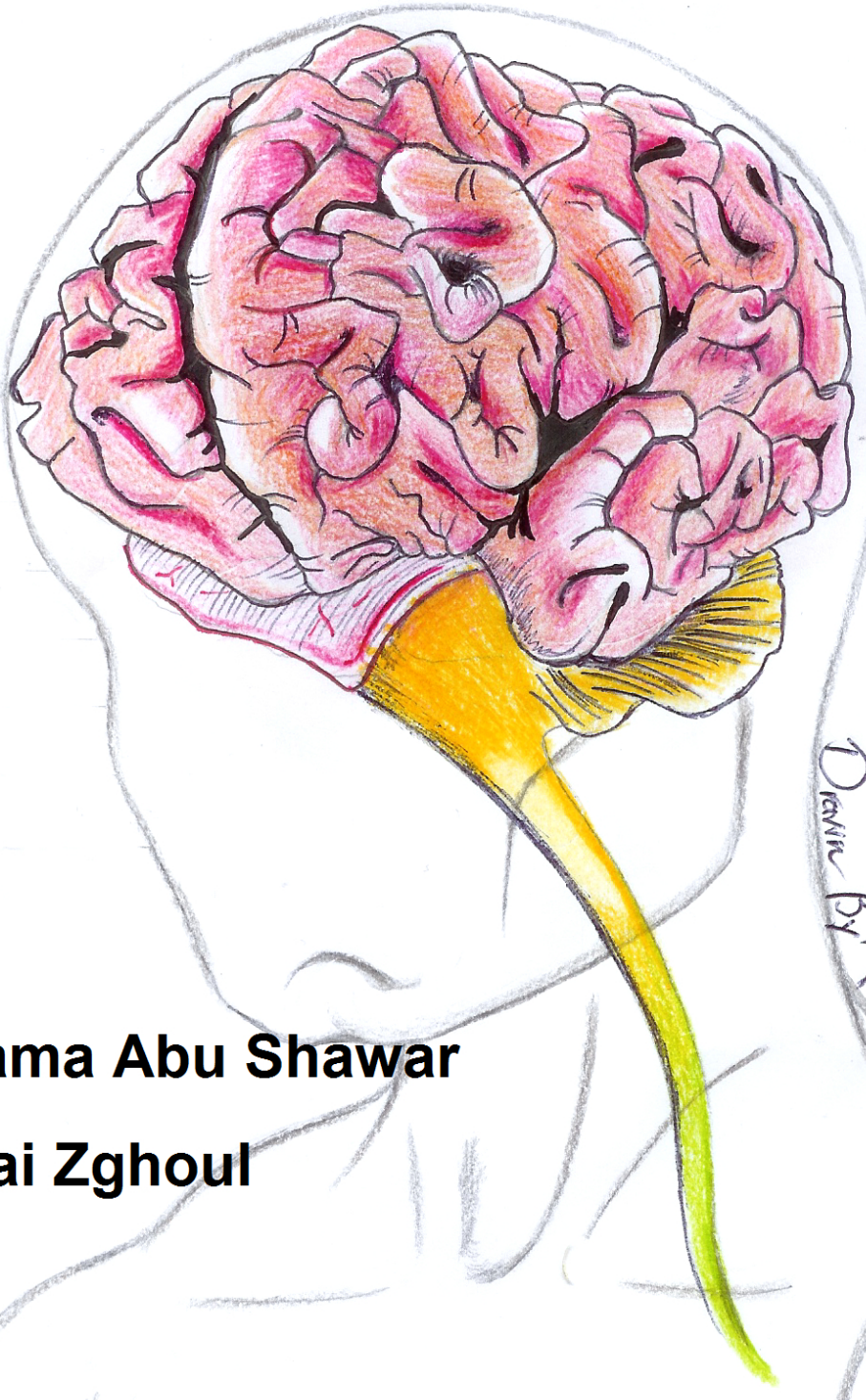

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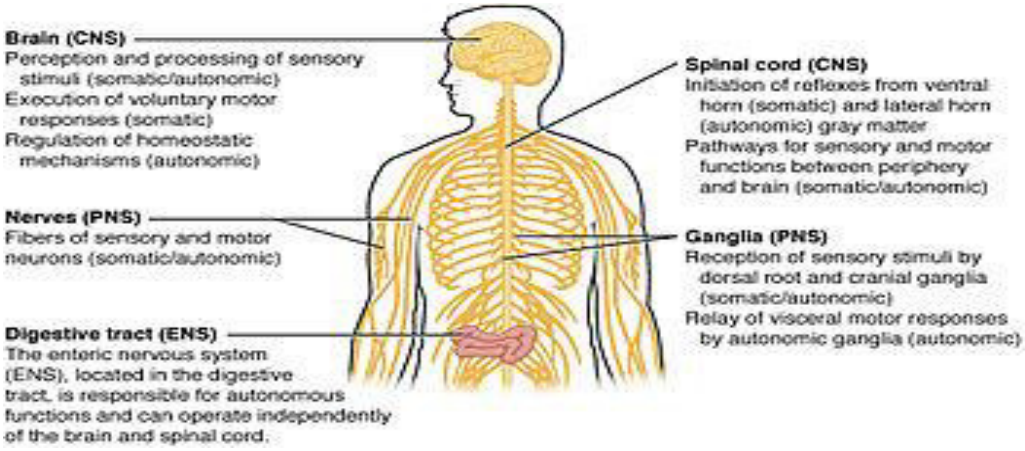
بسم الله الرحمن الرحيم

The nervous system consists of two main parts:

1. Central nervous system (CNS): Brain (cerebral cortex and sub-cortex) and spinal cord.
2. Peripheral nervous system (PNS): spinal and cranial nerves.

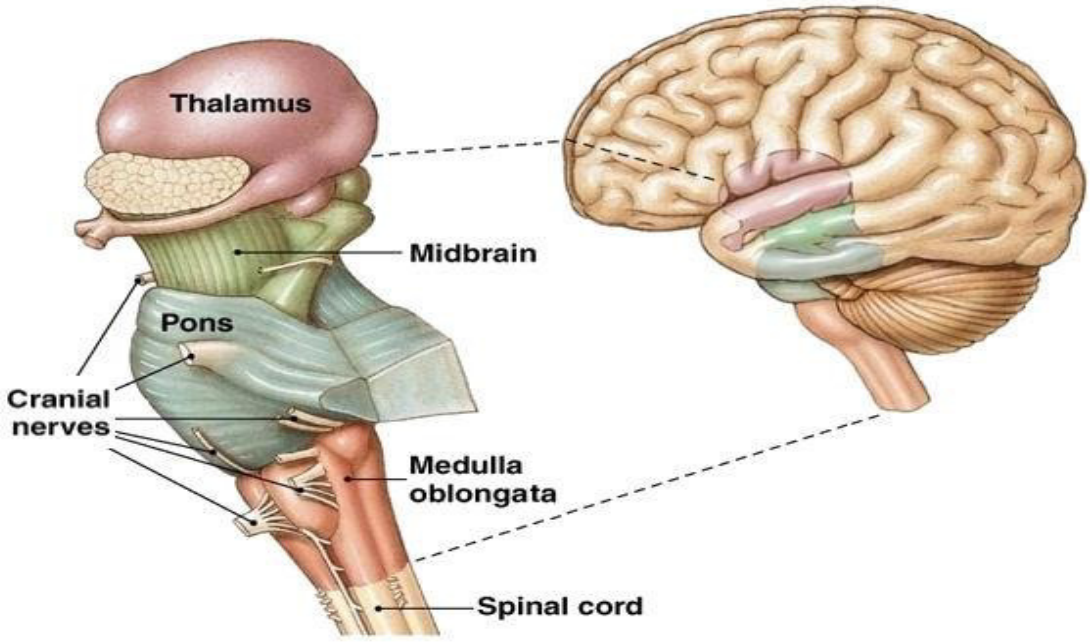
We also have the enteric nervous system in the GIT.




- PNS: detection and conduction of impulses from the periphery to the CNS.
- CNS: integration, execution and processing. It consists of the brain and the spinal cord as its main gross anatomical divisions.
  From a physiological perspective the CNS is further divided into 3 functional levels; firstly the spinal cord and the third would be the cerebral cortex (outer foldings of the brain) and between them we have sub cortical division which includes many structures including cerebellum, brain stem, medulla, thalamus, basal ganglia and hypothalamus…

1. **Spinal Cord**: conduction of impulses from CNS to the PNS and vice versa. Also, an additional function is analysis and execution of reflexes which are controlled by the cerebral cortex or the sub cortical division when the situation needs a fast response. It may give orders without returning to higher levels.
   You can compare this to a company with many levels, so an employee can carry out certain tasks individually but is also taking orders from higher levels of management (in our case sub cortical division and cerebral cortex). He occasionally needs to make a decision as fast as possible without the orders from his manager!

2. **Brain stem and sub cortical level**: contains medulla, pons, hypothalamus, thalamus, cerebellum and basal ganglia. It's responsible for internal reflexes (which are unconscious) that maintain proper constant internal environment, for example regulating respiration, heart rate, blood pressure, feeding, thirst, feelings, and emotions.



**3. Cerebral Cortex**: responsible for any conscious processing; memory, thinking, decision-making, speech, language, personality and UNDERSTANDING of sensation. In other words, higher complex levels of human functions which are difficult to define. Analysis and thinking are two of the most important functions which will shape one's personality and thoughts. Analysis, processing and thinking cannot be carried out without memory (previous knowledge); hence the cerebral cortex is the main storehouse for memory. The memory needed for thinking and decision making is stored in the frontal lobe, spatial memory is stored in the parietal, that of hearing is in the temporal lobe and vision in the occipital. So the memory is stored in each part of cerebral cortex.

* There's no processing without memory and there's no memory without processing.

**>> ما زال العقل البشري عاجزا عن إدراك ذاته!!**

❖ Functional organization of the nervous system:

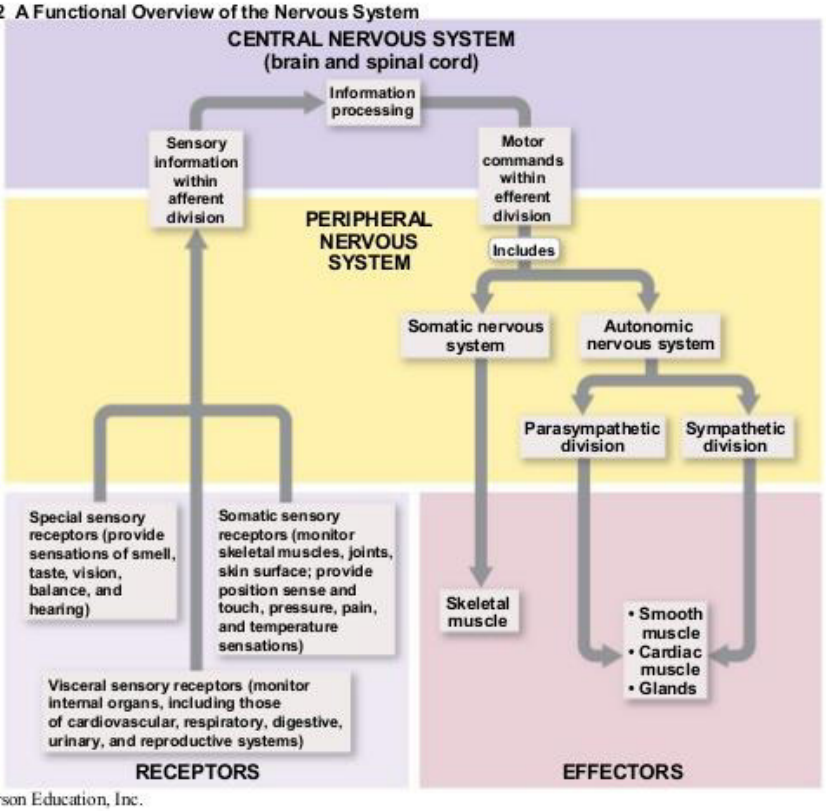
1. Sensory: input (sensation).
2. Motor: output (executive function, movement/secretion).
3. Integrative: processing, analyzing and integrating between the sensory and the motor.

Sensory information (inputs) starts first at a receptor (converts the signal from one type of energy to impulses- electrical energy for instance, chemical energy as in -taste, olfaction and pain-, mechanical energy such as -touching, pressure and hearing- and electromagnetic energy/photons in vision) then this impulse is transmitted by peripheral nerves (afferent neurons) to CNS.

The signal may be transmitted directly to cortex or could stop at any level and give a branch to the spinal cord or subcortex then continue to the cortex. So the sensory pathway can stop at any level and even if it stops at the spinal cord level it'll continue to the cortex.

Motor (otputs) starts from higher order, even though there is a motor function of the spinal cord and the subcortex but initiation of motor function starts from the cerebral cortex then reaching the effectors (muscle/gland) by efferent neurons.

Figure 13.2 A Functional Overview of the Nervous System



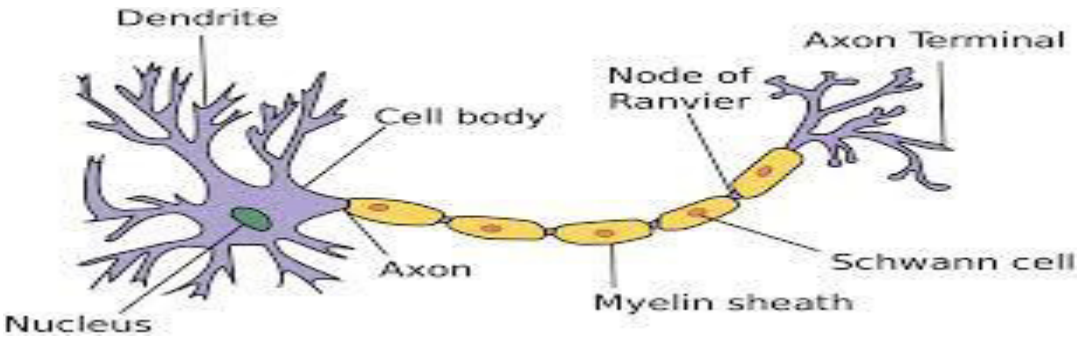



If the information was:

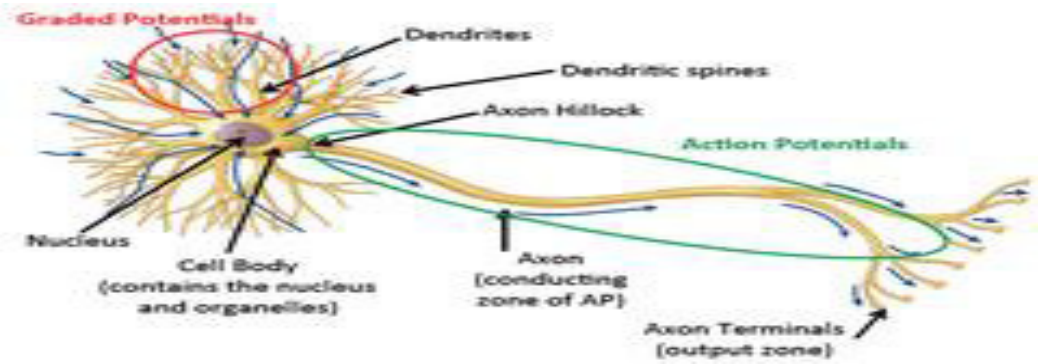
- Understanding of sensation: the target will be the cortex.
- Emotion: the target will be (mainly) the subcortex.
- Regulation of internal environment: the target will be the subcortex.
- Situation that needs a fast response (quick reflex): the target will be the spinal cord.
- Mixed information that needs a quick reflex, contains emotion and must be understood (e.g. when you put your hand on a hot surface): the target will be more than one level → the spinal cord (quick reflex), subcortex (feeling/emotion), and cortex (understanding of sensation).

Parts of neuron: cell body, axon, dendrites and nerve terminals which forms synapses with other neurons. Axons conduct impulses (action potential) away from cell body, dendrites receive impulses, and cell body does processing (graded potential only).

The parts of the neuron that do processing are the dendrites and cell body. So dendrites and cell body have only graded potential not action potential.



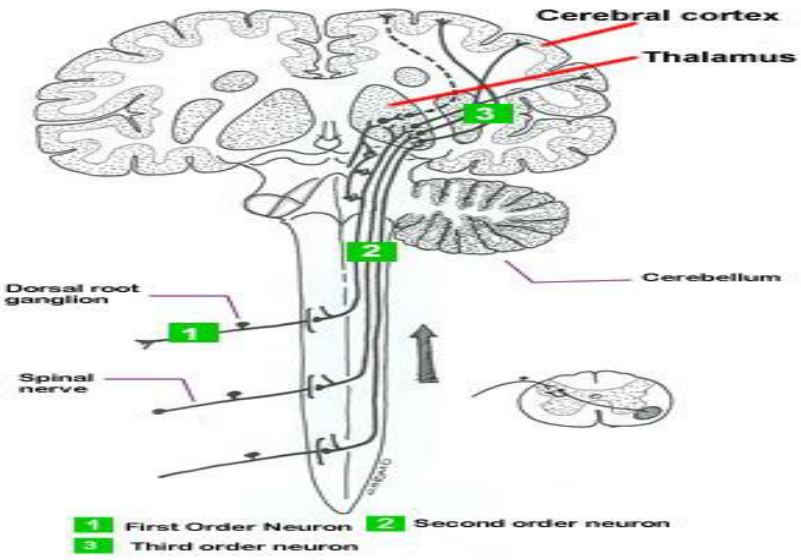

Difference between action potential and graded? Amplitude of graded potential has variable and depends on the stimulus. Also, there's summation in graded potential, but the action potential is all or none. The details about both won't discuss now.




**Pathway:** the route and the neurons which transport certain information. For e.g. somatosensory pathway. Now, the fastest way to transport an impulse would be through 1 neuron not several neurons because otherwise there'd be a delay due to the many synaptic clefts.

But why is it that we conduct the impulse through many neurons from one destination to another? This is because not all of them go to their destined site and some are used for analysis/regulation/processing.

The number of neurons involved in the pathway increases with increasing complexity of the information in the pathway.




* Motor pathway: order is sent to the muscle through it, little or no processing is needed through the transmission, so this pathway involves just 2 neurons and one synapse.

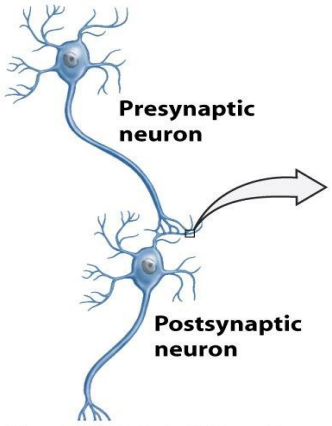
* Sensory pathway:
  - Pain, touch, pressure… etc need more processing, so 3 neurons are involved.
  - More complex sensation (e.g. vision and auditory) needs more neurons (6-7) because more and more processing is needed.

## Synapses:

Synapse: a specialized site of contact and transmission of information between a neuron and an effector cell (maybe another neuron).

There are **2 types of synapses**; **electrical** and **chemical** both are slower than action potential. In **electrical synapse**, the information is transmitted directly from one cell to another as an electrical signal (by gap junctions). Electrical synapses mostly exist in *cardiac muscle*. In the nervous system, we have some areas having electrical synapses like in the *glial cells* and *astrocytes*, but mainly the type of synapse in the *central nervous system* is **chemical synapse** (synapses that exist between neurons are almost completely chemical synapses).

## *Chemical synapses:*



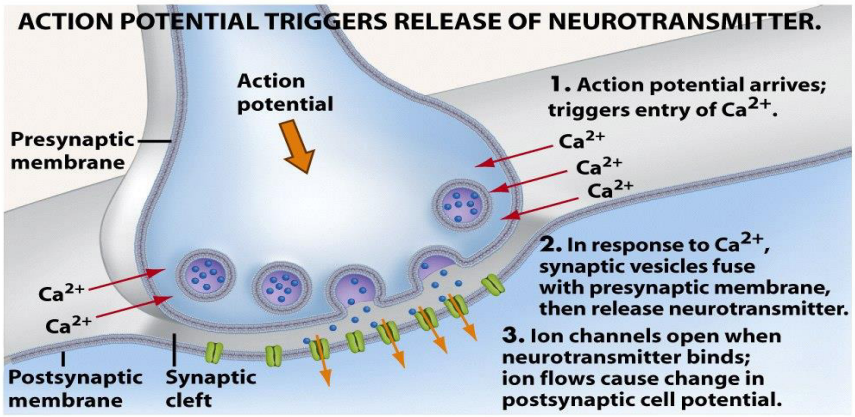




Figure 45-15 Biological Science, 2/e
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When the AP reaches the axon terminal which has voltage-gated Ca+2 channels, the Ca+2 enters the terminal through these channels. Ca+2 entry causes fusion of the vesicle with the presynaptic membrane, so the vesicle opens then releases neurotransmitter (which could be a peptide or non-peptide). Then, the neurotransmitter binds receptor protein in the postsynaptic membrane of the 2nd neuron thus causing changes in the 2nd neuron.

After release into the synaptic cleft, neurotransmitters interact with receptor proteins on the membrane of the postsynaptic cell. Usually we have 2 types of receptors: 1. Ion channels receptors 2. Second messenger receptors.

the first one, when it binds NT, it opens an **ion channel** (which could be Na+ channel, K+ channel, Cl- channel or other ion channel). When Na+ channel opens, more +ve ions flow through it to the inside of the cell causing depolarization. * Usually, anything that increases the Resting Membrane Potential (RMP) (i.e. makes RMP closer to threshold) and makes the neuron easily to be excited, we'll call it **excitatory neuron**.*

While when Cl- or K+ channels open, hyperpolarization occurs (RMP will become further away from threshold). This influx of negative ions or outflux of positive ions serves to hyperpolarize the cell thus inhibiting the firing of an action potential. * Anything that makes the RMP further away from threshold and makes the neuron harder to be excited, we'll call it **inhibitory**.*

The activity of the synapses is mostly controlled by the type of the receptor, not by NT or Ca++ channels. Any activity of the neuron increase the probability of AP called Excitatory, and any decrease is Inhibitory.

The 2nd type of receptors:

## Second messenger receptors

2nd messenger receptor is the type of receptor that when binds neurotransmitter it will activate another protein called 2nd messenger or activate one of the signaling cascades (most common 2nd messenger receptor: the G-protein coupled receptor, most common signaling cascade: cAMP cascade, DAG/IP3 cascade).

2nd messenger receptor may cause activation of protein which could be ion channel. If this protein was an ion channel, the RMP will be changed thus the neuron will be excited or inhibited. Also, this receptor can activate more than one protein, and any protein can affect the cell and change its nature by changing the energy causing the neuron to become more excited or more inhibited. The protein may also go to the DNA and affect gene transcription → all these may change the nature of the cell.

Differences between 2nd messenger receptor and ion channel receptor:

1. 2nd messenger receptor has a **long-term effect** (it's more like modulation of the neuron) not as the effect of ion channel receptor which is short-term effect.
2. **Amplification** of the signal happens in the case of 2nd messenger receptor (because here there's a cascade of signal and one receptor can activate more than one protein which can activate more than one enzyme and so on…), this amplification may cause big changes which have long-term effects.

The following is not mentioned in the record:

"There are two types of postsynaptic receptors that recognize neurotransmitters. Ionotropic receptors, also referred to as ligand-gated ion channels, act quickly to depolarize the neuron and pass on the action potential (or hyperpolarize the neuron and inhibit additional action potentials). Depolarization usually occurs a millisecond or two after the action potential has been received and lasts only up to ten milliseconds.

G-protein linked receptors, do not work as simply as ligand-gated ion channels do. Like ionotropic receptors, G-protein linked receptors also have an extracellular neurotransmitter recognition site, yet these receptors do not form a membrane-spanning pore that can allow the direct passage of ions. Instead, when a neurotransmitter associates with the extracellular recognition site, an intermediate molecule within the postsynaptic cell, called a G-protein, is activated and, either directly or through a series of enzymatic reactions, opens or closes ion channels located at other places on the cell membrane. Because the action of G-protein linked receptors is not as direct, their action is slower. Depolarization takes longer, typically lasting up to hundreds of milliseconds, and in some cases, going on for several minutes, hours, or even days.

G-protein linked receptors also alter some enzymes that excite or inhibit the cell or activate internal cascades and activate gene transcription, the most common cascade is the c-AMP or less common the c-GMP. Also, second messenger may include the activation of phospholipase enzyme which converts PIP2 to (DAG + IP3) which induce release of Ca+.

Keep in your mind that all the 2nd messengers including the Ca++ can affect the transcription and the survival or the characteristic of the cell.
The best characteristics differ between the 2nd messenger and the voltage gated channels are signal amplification and response; the response through ion channels will directly make excitation and cause AP in the post synaptic neuron but the response of 2nd is slower."

**Do you believe in miracles??**
**Extrasensory perception!!**

https://www.youtube.com/watch?v=jqm44iQWySA&list=PLWi1Sp_6aBB-8ajbD0V_LSEUPTn6bbCqq&index=3

❖ The doctor revised some **pharmacodynamic** concepts:

We said that neurotransmitter will bind a receptor (this receptor could be ion channel receptor or second messenger receptor).

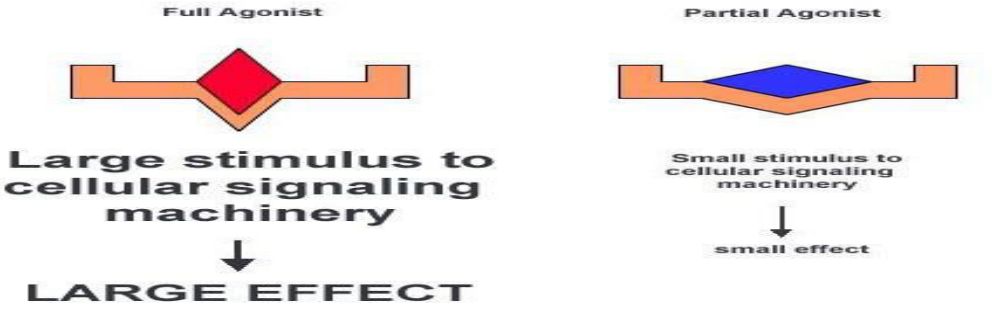
- Any drug which can bind this receptor and cause the receptor to function as if the neurotransmitter exists → will be called "**agonist**".
- Any molecule which can bind this receptor at the NT binding site and cause the receptor to stop working → will be called "**antagonist**".
  Note: antagonist *doesn't oppose* the function of the agonist or the neurotransmitter; it just prevents the neurotransmitter from binding and functioning.

* We can't be sure that blocking will happen after administration of an antagonist, or enhancement will occur after administration of an agonist. Because this depends on the kinetics of the drug, the receptor and the neurotransmitter.

The following is not mentioned in the record:

"Full Agonists: Compounds which are able to elicit a maximal response following receptor occupation and activation.

Partial Agonists: Compounds that can activate receptors but are unable to elicit the maximal response of the receptor system."




**Allosteric modulator**: it's any molecule that when given will bind the neurotransmitter receptor at a site other than the binding site of the neurotransmitter and change the function of the receptor (increase or decrease it).

There're different types of allosteric modulators.

- Any molecule that will bind the receptor at a site other than the NT binding site and cause the receptor to function better and more efficiently will be called "**positive allosteric modulator**".
  * The difference between agonist and allosteric modulator?
  1. The site of binding: agonist binds at the NT binding site, allosteric modulator binds at a site other than the NT binding site.
  2. The agonist alone has an effect, but the allosteric modulator doesn't work (doesn't have an effect on the receptor) alone; it needs the presence of NT or an agonist to function.
- Any molecule that will bind the receptor at a site other than the NT binding site and cause the receptor to function less efficiently or block it completely will be called "**blocker**".

**Affinity**: how strong the molecule can bind the receptor.

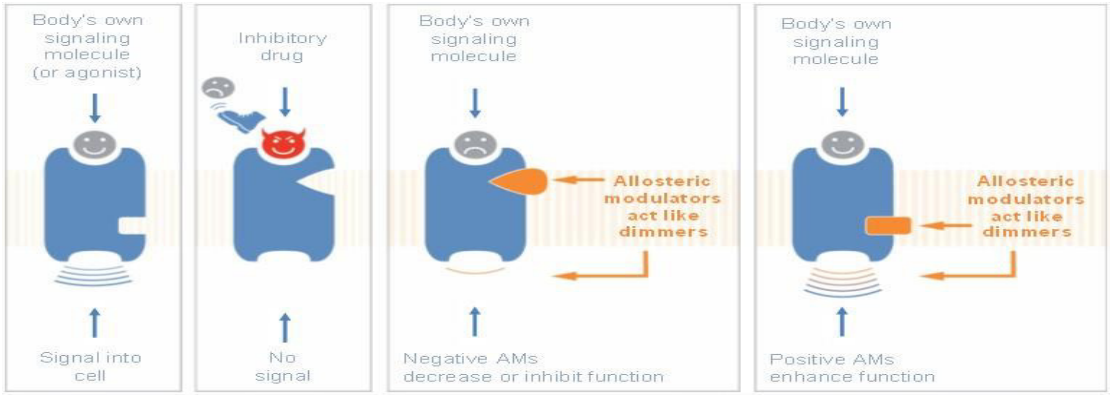
**Efficiency:** how much is the resulted effect.

If a molecule binds the NT binding site in the receptor and causes the receptor to work and produce 100 cAMP per min (if you know that NT action lead to production of 100 cAMP), then this agonist is as efficient as the NT. If it leads to production of 80 cAMP per min instead of 100, then the efficiency of the agonist is less efficient by 20%.
If a molecule binds the NT binding site in the receptor and causes the receptor to work and produce 10 cAMP per min instead of 100, this is called "**partial agonist**".
* Partial agonist can work as an antagonist.

The following is not mentioned in the record:

"A substance which indirectly influences (modulates) the effects of an agonist at a target protein, for example a receptor. Allosteric modulators bind to a site distinct from that of the agonist binding site. Usually they induce a conformational change within the protein structure. A positive allosteric modulator (PAM) or allosteric enhancer induces an amplification of the agonist's effect, either by enhancing the binding affinity or the functional efficacy of the agonist for the target protein.

A negative modulator (NAM) reduces the effects of the ligand, but is inactive in the absence of the ligand."




## How to study this amazing system (CNS) anatomy and physiology??

| Videos | Books |
|---|---|
| **A**-Medical neuroscience at "coursera" application- website (40-45 h). Highly recommended to understand from A to Z.<br><br>**B**-Kaplan neuroscience.<br><br>**C**-Dr. Najeeb (more than 80 hours!). | A. Fundamental neuroscience.<br>B. Neuroscience by Dr. Purves.<br>C. Kaplan LTN.<br>D. High yield neuroanatomy. |

**قال تعالى: (سنريهم آياتنا في الآفاق وفي أنفسهم حتى يتبين لهم أنه الحق)**