SYNAPSES AND SYNAPTIC TRANSMISSION

○ 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 single axon leaving the neuron.

❖ *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).

- [in brief : it is the communication between presynaptic and postsynaptic neuron]

❖ *WHAT HAPPENS AT THE SYNAPSE?*

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

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

1- Blocked in its transmission from one neuron to another , i.e from pre to post- synaptic
2- (stimulation) Changed from single impulse to repetitive impulses to cause AP.

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

○ Anatomical Types of Synapses:-

1. Axodendritic: synapses between the axon of one neuron and dendrite of another.
2. Axosomatic: synapses between the axon of one neuron and soma of another.
3. Other types synapses include:
   a) Axoaxonic (axon to axon)
   b) Dendrodendritic (dendrite to dendrite)
   c) Dendrosomatic (dendrite to soma)

Types of synapses (functional classification or types of communication):

1. *Chemical Synapse*: [between two neurons]

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

     ✓ i.e. first neuron secrets a chemical substance called neurotransmitter at the synapse to act on receptor on the next neuron to excite it, inhibit or modify its sensitivity.

     - e.g. in autonomic + nerve + muscle.

2. *Electrical Synapse* : [maybe between two neuron or between neuron and tissue]

   ✓ membranes of 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 [wake up]
     - Mental attention.
     - Emotions and memory
     - Ion and water homeostasis.

3. *Conjoint Synapse*: [Both electrical and chemical]

   ✓ Examples for electrical and conjoint → neurons in lateral vestibularnucleus.

- **Examples of Synapse Outside CNS:**

1- NMJ (neuromuscular junction)
2- Contact between Autonomic neurons and smooth and cardiac muscles.

- **Functional Anatomy of a Synapse:** (Structure and Functions)

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

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

- **Properties of synapses:**

1. One way conduction:-MCQ-

- Synapses generally permit conduction of impulses in one way i.e. from pre to post synaptic neurons. (chemical mediator at the junction at presynaptic terminal explains one way conduction).

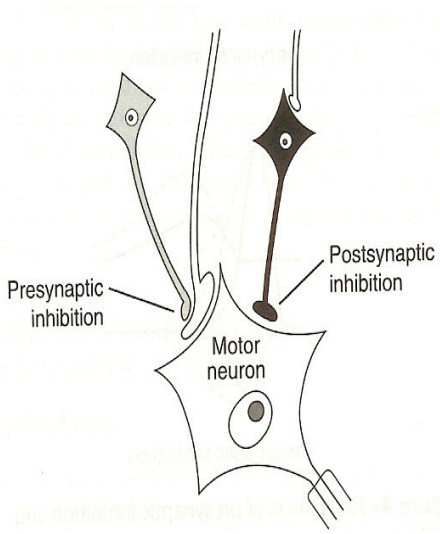
2. Synaptic delay: -MCQ-

- is the minimum time required from transmission a cross the synapse (0.5 ms).
- Most of the time is spent in:
    1. release of transmitter substance by presynaptic terminals.
    2. Diffusion of transmitter substance to post synaptic membrane.
    3. Action of transmitter on its receptor.
    4. Action of transmitter substance to increased membrane permeability.
    5. increase diffusion of Na to increased post synaptic potential.

3. Inhibition of the synapse:

A. Direct inhibition: -MCQ-

- it is called post-synaptic inhibition or IPSP.
- Example: some interneuron in the spinal cord that inhibit antagonist muscle.
- Glysine is the neurotransmitter.
- Occurs when an inhibitory neuron (releasing inhibitory substance) act on post-synaptic neuron => leading to hyperpolarization due to opening of Cl^- channels (influx) and k+ (efflux).



B. Indirect inhibition:-MCQ-

- it is called as pre-synaptic inhibition.
- This happens when an inhibitory synaptic knob lie directly on the termination of a pre-synaptic excitatory fibers.
- The inhibitory synaptic knob releases a transmitter from the pre-synaptic fiber (the inhibition produced by increased Cl^- & k^+).
- Example: GABA (gamma-aminobutyric acid), which open Cl^- channels.
- Occurs in dorsal horn => pain gating.

C. Receprocal inhibition :

- inhibition of antagonist activity is initiated in the spindle in the agonist muscle
- impulses pass directly to motor neurons supplying the same muscle and via branches to inhibitory interneurons that end on motor neurons of antagonist muscle

D. inhibitory interneurons (Renshaw cells) :

- negative feedback inhibitory of interneurons of a spinal motor neuron , this feedback inhibition also occurs in :

    a) cerebral cortex
    b) limbic system
    c) note that Renshaw cells are in spinal cord

E. feed forward inhibition :

- occurs in cerebellum to limit duration of excitation

F. Lateral inhibition :

- because of lateral inhibition, the lateral pathways are inhibited more strongly
- this happens in pathways utilizing most accurate localization

✓ e.g. movement of skin hair can be well located, temperature and pain are poorly located

Neurotransmitters

- **Definitions:**

  - *Synapse*: It is the junction between a neuron and another neuron or an effector organ.

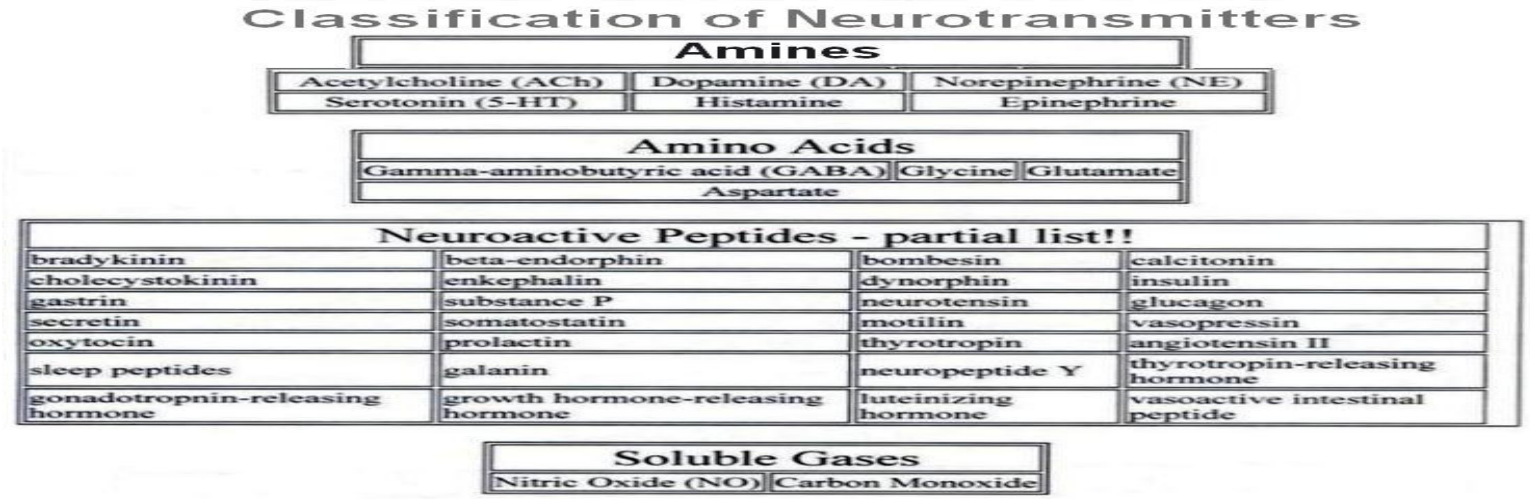
  - *Neurotransmitter (NT):* It is a chemical transducer released by electrical impulses into the synaptic cleft and has a role in changing chemical activity to electrical activity.

- **When do we call a chemical a neurotransmitter:-**

  1) It must be produced stored and released by the neuron.
  2) It must act on the postsynaptic membrane.
  3) It must be inactivated after it performs its action.

- **Classification of neurotransmitters:**

  - They can be classified into:
    a. Amines.
    b. Amino acids (small molecules).
    c. Neuroactive peptides.
    d. Soluble gases (this is an exception from the previous ones which are all solid).



N.B that neuropeptides function mostly as neuralmodorators (work on 2nd messenger)

- **Mechanism of conducting action potentials (AP):**

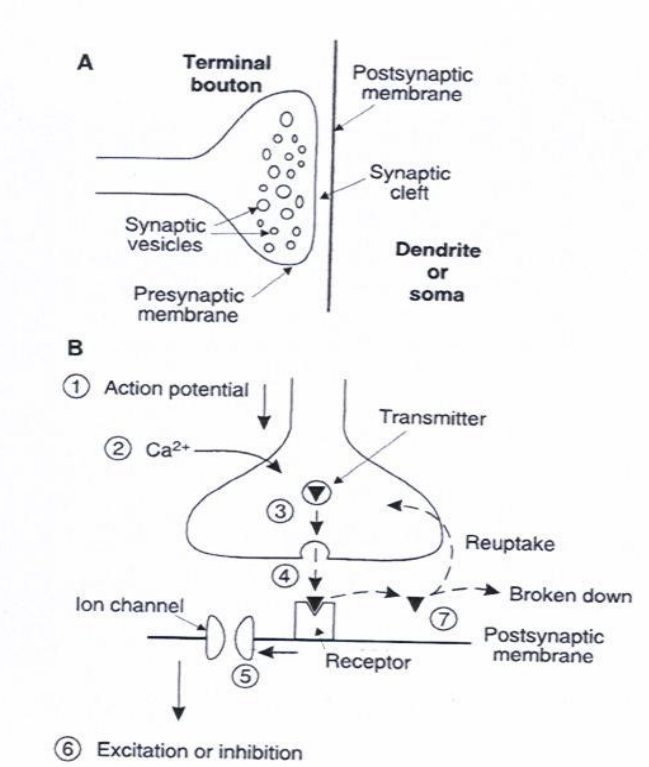
1) When the AP reaches the end of the conducting axon, the voltage-gated Ca+ channels opens.

2) Ca+ will enter the presynaptic end of the neuron.

3) Ca+ will aid the synaptic vesicles which stores the NTs to fuse with the membrane to release the NT by exocytosis .

4) The NT will combine with a receptor in the postsynaptic membrane and cause the channels to open and conduct the AP.

5) After it finishes its action, it will take one of two routes:
   - It is reuptaked by the presynaptic neuron.
   - It is degraded by enzymes.



- **Receptors:**

- They are found on the postsynaptic membrane .
- They are classified into:

I. Ionotropic (ligand-gated) receptors:

- They are the simplest, easiest and the fastest.
- It composed of 2 types:

  - ***Excitatory**: by allowing the entry of Na^+ and the exit of K^+ and causing depolarazition.*

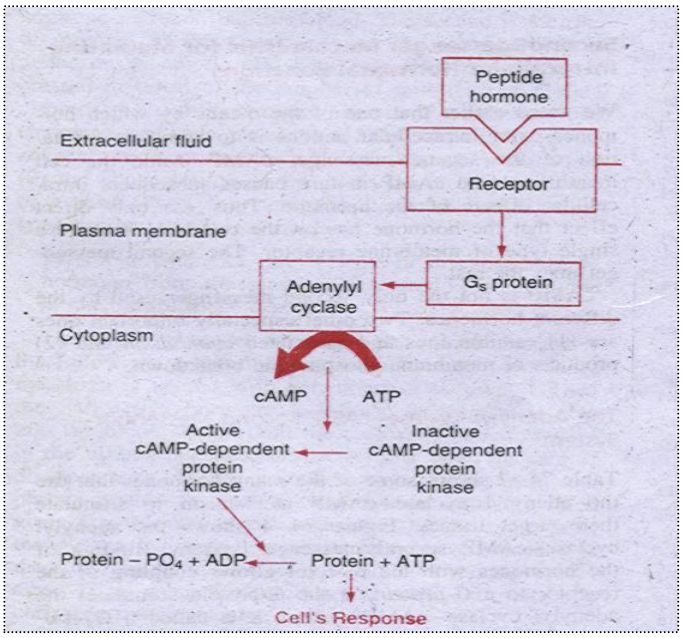
  - ***Inhibitory**: by allowing the entry of Cl^- and causing hyperpolarazition(more negativity inside the cell).*

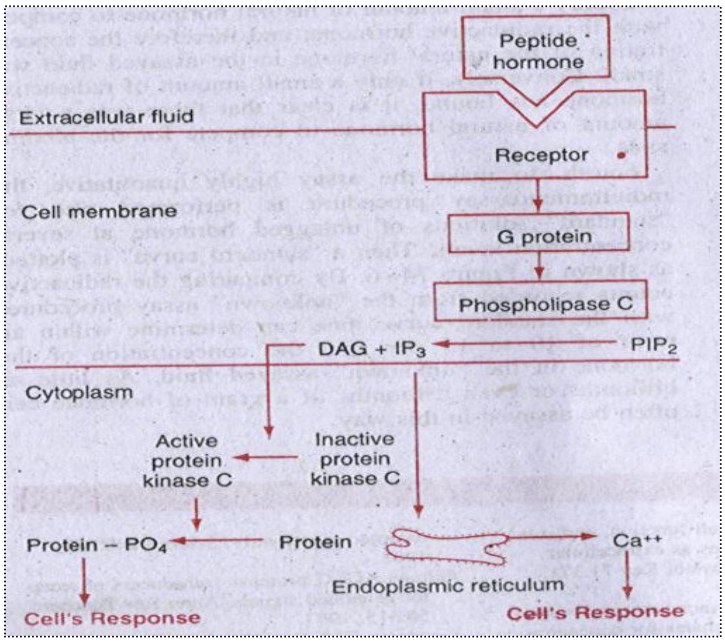
II. Metabotropic receptors:

- It is so named because it affects the metabolism of the cell.

- Usually these receptors combine with G-protein which in turn activate adenyl-cyclase or phospholipase to transmit the action.see next page

- Examples of these receptors are:
    a) Hormonal receptors.
    b) Polypeptide receptors.
    c) Sensory receptors.





- **<u>fate of neurotransmitter:</u>** **MCQ-**

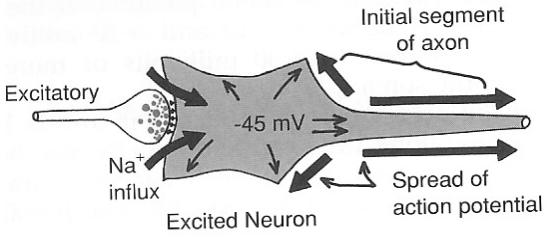
    - neurotransmitter bond to a postsynaptic neuron producing a continues postsynaptic effect blocks reception of additional (messenger)

    - after a transmitter substance is released at a synapse , it must be removed by

        1- diffusion out of synaptic cleft into surrounding fluid

        2- <u>enzymatic destruction</u> e.g . Ach esterase for Ach.
        <u>Active transport back into presynaptic</u> terminals itself.
        E.g. norepinephrine.

- **Types of responses on postsynaptic membrane:**



❖ *Excitatory postsynaptic potential (EPSPs):-*

- It is caused by depolarization.

  ✓ when excitatory neurotransmitter binds to its receptor on the post synaptic membrane => partial depolarization (increase Na+ influx) of post synaptic cell membrane immediately under presynaptic ending i.e. EPSP,s.

  ✓ If this potential rise enough to threshold level => AP will develop + excite the neuron (central or neuronal summation).

  ✓ This summation will cause the membrane potential to increase from -65mv to -45mv (firing level).

  ✓ So EPSP = +20mv which reach the membrane to firing level => AP develops at axon hillock.

N.B.

- discharge of single presynaptic terminal can never increase the neural potential from -65mv to -45mv.-MCQ-

- EPSP is produced by the action of an excitatory neurotransmitter => depolarization of post synaptic membrane.

REMEMBER:

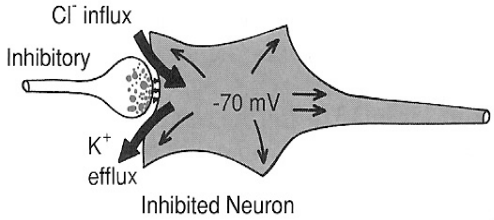
- The excitatory neurotransmitter => open Na or Ca channels => depolarization of the area under the presynaptic membrane (local response).

EPSP,s:-MCQ-

1- local or graded response.
2- Proportionate to the strength of the stimulus.
3- Can be summated.
4- If large enough to reach firing level => AP is produced

- post synaptic potential of +10 to +20mv is needed to produce AP

❖ *Inhibitory Postsynaptic potential (IPSPs):- MCQ*



- It is caused by hyperpolarization.
- IPSP = -5 mv

- Stimulation of some input presynaptic terminal => hyperpolarization of the postsynaptic membrane which is IPSP.

  - Causes:

    - ➢ It is produced by localized increase in membrane permeability to Cl^- of post synaptic membrane (produced by inhibitory neurotransmitter) => decrease excitability + membrane potential become away from firing level.

    - ➢ Also IPSP can be produced by: opening of K channel (outward movement of K) & closure of Na or Ca channels.

- **Fast & Slow Postsynaptic potentials:**

  - Fast EPSPs & IPSPs work through ligand gated ion channels.eg. Nicotinic receptors(at the level of neuromuscular junction)

  - Slow EPSPs & IPSPs are produced by multi step process involving G protein eg. Muscarinic receptors (at the level of autonomic gangila)

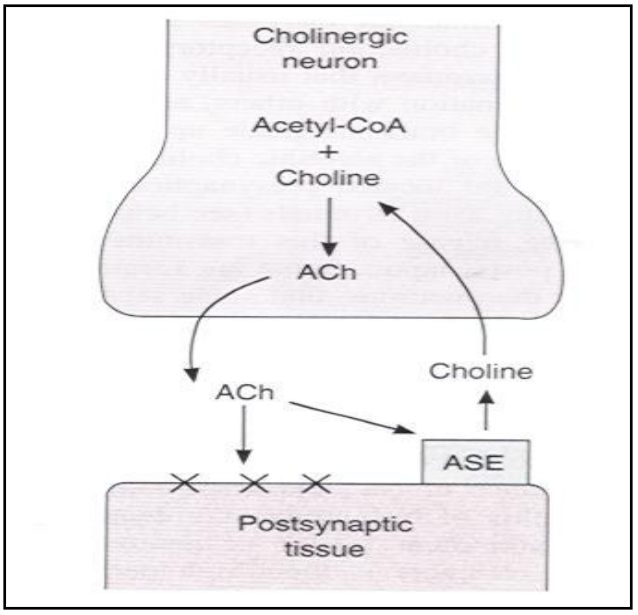
- **Major steps in neurotransmitter processing are :**

1.Synthesis 2.Storage 3.Release 4.Reception 5.Inactivation

1) Acetylcholine:

- Ach is excitatory neurotransmitter.
- Mostly found in :
  - Preganglionic sympathetic system.
  - Preganglionic & postganglionic parasympathetic system.
  - Certian area of the brain.

- **Formation** :Acetyl-coA + choline → Ach
- If we inhibit ASE→ inhibit uptake of choline so we treat mysthina gravis.
- Degradation : ACh $\xrightarrow{ASE}$ Choline + Acetate
  - Choline : will reuptaked again
  - Acetate : will remain

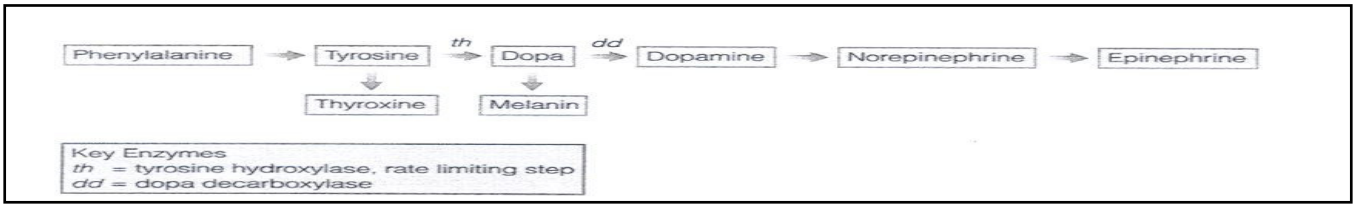


- **<u>Acetyl choline receptors:</u>**
  - Its receptors are ionotropic (legand)

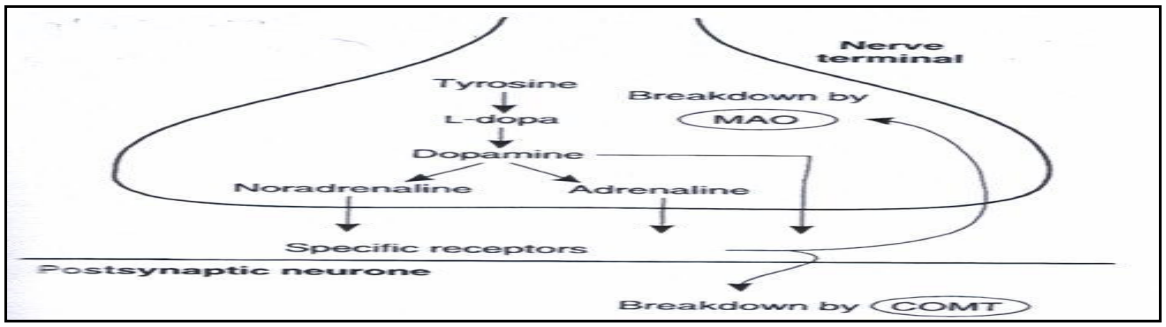
		Nicotinic	Muscarinic
1	<u>Found at:</u>	i. Neuromuscular junction of skeletal muscle ii. Postganglionic neurons of parasympathetic nervous system. iii. Ventral tegmental area.	i. Glands ii. Neuromuscular junctions of cardiac and smooth muscle. iii. Postganglionic neurons of sympathetic nervous system.
2	<u>Agonist</u>	Nicotine	Muscarine (a toxin produced by certain mushroom)
3	<u>Antagonist</u>	Curare (paralyses skeletal muscle)	Atropine

2) catecholamines
(epinephrine , norepinephrine , dopamine)

- They are all arise from phenylalanine .

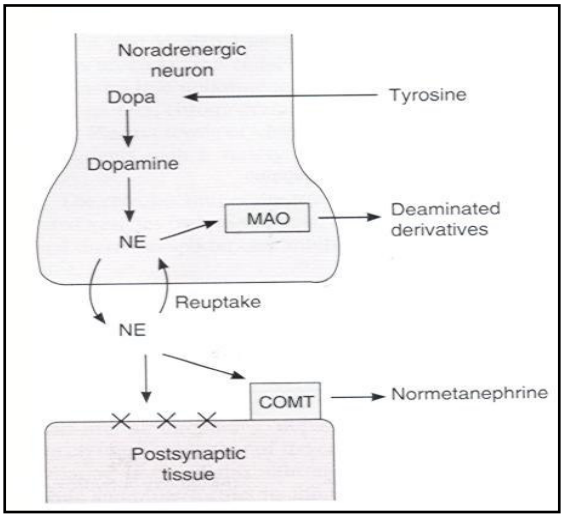


- Catecholamines & serotonin are brokendown by 2 routes :-
  - Inside neuron : in mitochondria by monoamineoxidase enzyme (MAO)
  - Outside of neuron : after they have done their work , they are broken by Catechol-O-Methyl-Transferase(COMT) in synaptic cleft.



- N.B. : if a patient have depression , he is treated by (MAO inhibitor)

- (MAO) works by deamination
- (COMT) will give normetanephrine



- In pheocromocytoma there is a tumor in adrenal medulla → there is excessive production of epinephrine

- Normetanephrine is measured in urine to indicate such case.

- N.B.: The main source of epinephrine is the Adrenal melulla.

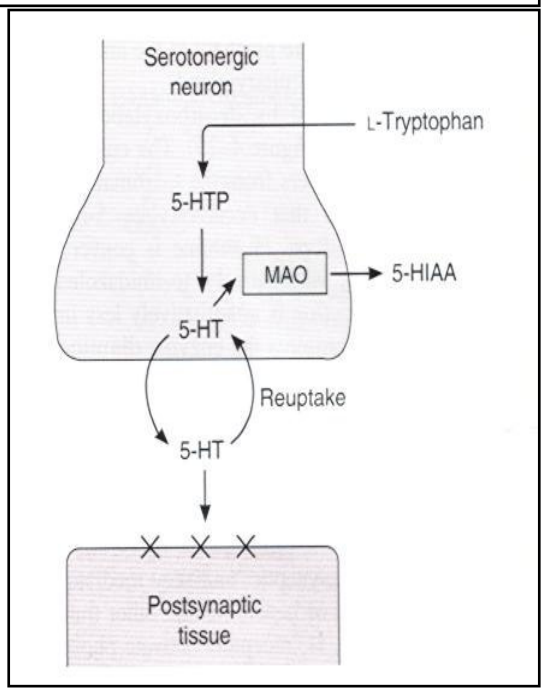
- The main source of norepinehren is Nerve Endings.

- Both epinephrine and norepinephren are important in the control of attention & Arosal .

3)serotonin

- Is found in brain & intestine.
- Is synthesized from tryptophan.

- Its other name is 5-hydroxytryptamine.
- It is produced in serotogenic neuron.
- Serotonin keeps us awake & have a role in reducing the threshold of pain .
    - ✓ If the uptake of 5-hydroxytryptamine is blocked it will make benefit in treatment of depression .



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