Neurotransmitters(cont)

4) Histamine:

- It is Excitatory NT.
- It is formed from Histidine in the hypothalamus, *gastric mucosa and stomach.*
- There are 3 receptors of Histamine:
  - H1 ,H2 ,H3
    - ✓ These receptors can be found in peripheral tissues & the brain.
      *Like H3 in the stomach may causes vomiting.

5) GABA (gama amino butyric acid):

- It is an inhibitory NT.
- Synthesis :

1) krebs cycle→α-ketoglutarate→→glutamate←←glutamine (2
↓
↓ GAD (decarboxilation)
↓
GABA

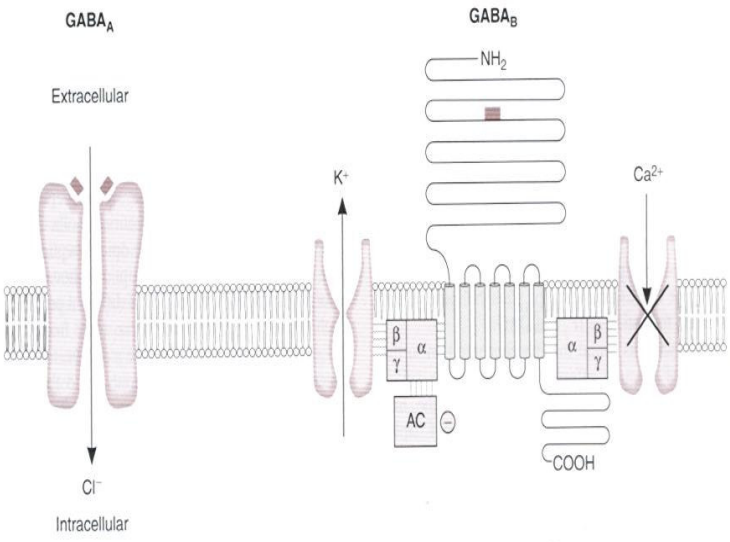
- It is formed in the CNS and works in the brain.
- Then GABA is broken down by (GABA transferase).
- If GAD enzyme is absent GABA will not be formed , thus there will be no inhibition And the muscle will be contracted , is addition to the accumulation of glutamate which is excitatory NT .a condition called Stiff man's syndrome.

- **Receptors of GABA :(3 TYPES)**
- GABA – A increases the Cl^- conductance into the cell *which is ENHARNCE by Benzodiazipine*

- GABA – B is metabotropic works with G – protein GABA transaminase catalyzes:
  - It causes hyperpolarization by increasing (K^+) outflow.

N.B both A&B are found in the brain

- GABA – C found exclusively in the retina. Stimulate the visual activity by <u>hyperpolarization</u>



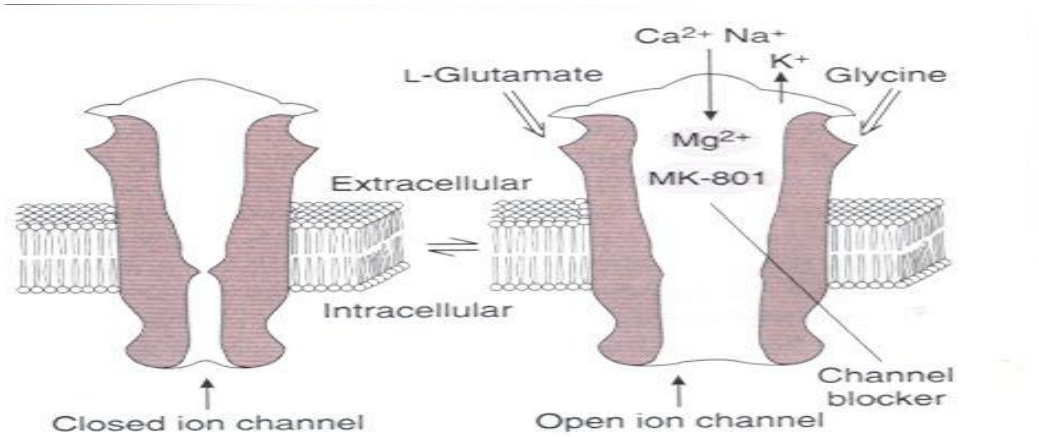
Clinical information :

- epilepsy: is a condition in which there is abnormal excessive neural discharge .
    - this disease sometimes can be controlled by controlling GABA by blocking the transferase , so GABA will inhibit the excessive discharge.

6) Glutamate:

- It is an Excitatory NT .
- *Most commonly found NT in the brain*
- It is formed by krebs cycle in the brain & spinal cord .
- It is very neurotoxic substance .

- Glutamate has Ionotropic (AMPA) and metabotropic (MNDA) receptors .
- MNDA works via G-protein Coz it a metabotropic
- The most important function of glutamate throught MNDA is (Long term potentiation) involved in memory and learning by causing Ca^{++} influx.



- When glutamate bind to the receptors , the closed ion channels (**LEFT)** opens, but at resting membrane potential, the channel is blocked by Mg^{++} **(right)** this Mg^{++} is removed after partial depolarization that means we need to activate (**left**) to get the (**right**) activated

- After glutamate perform its function it is broken down it is convert into glutamine , this happen inside the neuroglial cells (Astrocytes).

- Ischemic cells release glutamate which cause cell death .
- Glutamate is also important in perception of pain .

7) glycine :

- It is an inhibitory NT .
- It is formed from the amino acid (**serine**) in the spinal cord .
- It works on the anterior horn of the spinal cord .
- *Strychnine is a glycin antagonist*

♦ There are several types of cells in the Anterior horn :

- (**α – motorneuron**) : responsible for skeletal muscle contraction .also gives a branch to Renshaw cells.
- (**Renshaw cells**) : when α –motor neuron are discharging (to make the muscle contract) , a message will go to Renshaw cells which will inhibit α cells to terminate to movement . Renshaw cells perform this inhibitory function thru **Glycine** .

N.B. : in some cases of spasm (continuous muscle contraction) we enhance Renshaw cells to relax the muscle .by secreting glycine.

- (γ –receptor) work as receptor in the muscle spindle which is a receptor (sensory receptor) inside the muscle and works as an α-motor nuormone receptors.
- paraplegia may be treated by Glycine. To reduce spasm

RECEPTORS DYSFUNCTION

1. Effects at Presynaptic level

i) Botulinum toxin:

- It's an exotoxin that binds to the presynaptic membrane, and prevents the release of Ach resulting in weakness and reduction of tone.
- It is used to control dystonia in which body shows overactive muscular activity.
- It is used to control hemifascail spasms.

ii) Lumbert – Eaton syndrome:

- Antibodies directed against Ca++ channels located in presynaptic terminals and interfere with transmitter release causing weakness.

  ✓ In this case the beginning of movement is weak, but after a while it gets better.

iii) Neuromyotonia :

- Patient complains of muscle spasm and stiffness resulting in continuous motor activity in the muscle.

- It is caused by antibody directed against the presynaptic voltage gated K^+ channel so that the nerve terminal is always in a state of depolarization .

2. Effects at Postsynaptic level

i) Curare :

- This substance binds to the acetylcholine receptor (AchR) and prevents Ach from acting on it ,and so that it induces paralysis.

ii) Myasthenia gravis :

- Is caused by an antibody against the Ach receptors.

  ✓ Ach receptors are reduced in number , so the Ach released has few receptor available to work , and patients complain of weakness that increases with exercise.