GABA-ERGIC SYSTEM

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OUTLINE

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INTRODUCTION

- GABAergic means "pertaining to or affecting the neurotransmitter GABA". A synapse is GABAergic if it uses GABA as its neurotransmitter.

- A GABAergic or GABAergic agent is any chemical that modifies the effects of GABA in the body or brain. Some different classes of GABAergic drugs include the following:

  - GABA receptor agonists, GABA receptor antagonists, and GABA reuptake inhibitors.
GABA

- GABA stands for gamma amino butyric acid which is a zwitter ion with deprotonated carboxyl group and protonated amino group.

- GABA acts at inhibitory synapses in the brain by binding to specific transmembrane receptors in the plasma membrane of both pre and postsynaptic neuronal processes.

- It is most highly concentrated in the substantia nigra and globus pallidus nuclei of the basal ganglia, followed by the hypothalamus, the periaqueductal grey matter.

- There are two types of GABA receptors: GABA-A & GABA-B
SYNTHESIS & METABOLISM OF GABA
 STORAGE

- Newly synthesized GABA is stored in synaptic vesicle by means of vesicular transporter.
- These are stored at postsynaptic terminal until action potential release.

RELEASE

- Stored GABA releases into synaptic cleft stimulated by depolarisation of presynaptic neurons.
- GABA diffuses across the cleft to target receptors on postsynaptic surface.
- The action of GABA is terminated by reuptake of GABA by presynaptic nerve terminals & glial cells.
MECHANISM OF ACTION

- GABA open chloride receptors channels and induce the cellular hyperpolarization by increasing intracellular concentration of chloride ions.
GABA receptors:

- It has pentameric structure.
- Each GABA-A receptor contains two alpha, two beta and one gamma subunits.
- It has structural and functional similarity with ligand gated ion channel.
GABA-B

- There are two hetero dimers.

- GABA-B have been cloned to subunits B₁ and B₂.

- B₁ subunit has a GABA binding site while B₂ subunit interact with G protein.

- It has two biological actions:
  - increase K⁺ conductance
  - decrease Ca²⁺ conductance
FUNCTIONS OF GABA

- Relieving from anxiety
- Improving mood
- Regulating the release of sex hormone
- Promoting lean muscle growth
- Burning fat
- Lowering elevated blood sugar levels in diabetes
- Stabilizing the blood pressure
# DRUGS ACTING ON GABA RECEPTOR

<table>
<thead>
<tr>
<th></th>
<th>GABA A</th>
<th>GABA B</th>
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<tbody>
<tr>
<td>TYPE</td>
<td>Ionotropic</td>
<td>Metabotropic</td>
</tr>
<tr>
<td>LOCATION</td>
<td>Widespread, mainly GABAergic interneurons</td>
<td>Widespread, presynaptic and postsynaptic</td>
</tr>
<tr>
<td>SUBCELLULAR EVENT</td>
<td>Post synaptic inhibition by increase in chloride ion influx</td>
<td>Presynaptic inhibition by decrease in calcium entry</td>
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<tr>
<td></td>
<td></td>
<td>Postsynaptic inhibition by increase in potassium ion influx</td>
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<tr>
<td>AGONIST</td>
<td>GABA, Mucimol, Gabaxadol, Barbiturates, Benzodiazepines, Steroid anesthetics</td>
<td>GABA, Baclofen</td>
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<tr>
<td>ANTAGONIST</td>
<td>Flumazenil, Gabazine, Bicuculline</td>
<td>Saclofen</td>
</tr>
<tr>
<td>CHANNEL BLOCKER</td>
<td>Picrotoxin</td>
<td>NA</td>
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CONCLUSION

- GABA is an amino acid made in brain cells from glutamate. It functions as an inhibitory neurotransmitter, meaning it blocks nerve impulses.

- Without GABA, nerve cells fire too often and too easily.
THANK YOU