Commentary

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Study of GABA Receptors and their Clinical Significance

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Description

Gamma Amino-Butyric Acid (GABA) receptors are the major inhibitory neurotransmitter in the central nervous system. GABA is thought to be present in the majority of neurons in the brain and spinal cord. Because of the enormous number of receptor subtypes and the diversity of ligands that bind with particular places on the receptors, they appear to be the most complex of the ligand-gated ion channel superfamily.

Types of GABA Receptors

There are two distinct classes of GABA receptors, GABAA and GABAB. They differ from each other in their pharmacological, electrophysiological and biochemical properties.

GABAA receptors

A rise in membrane conductance is mediated by the GABAA-receptor. This increase in conductance is frequently accompanied by membrane hyperpolarization, resulting in a rise in the firing threshold and, as a result, a decrease in the probability of action potential initiation, resulting in neural inhibition. The GABA-dependent acceleration of Cl- ion inflow through a receptor-associated channel accomplishes this decrease in membrane resistance. Increased Cl- permeability, on the other hand, might depolarize the target cell under certain circumstances of high intracellular Cl-.

GABAB receptors

The GABAA-receptor mediates a rise in membrane conductance. This increase in conductance is typically accompanied by membrane hyperpolarization, which increases the firing threshold and, as a result, a decrease in the frequency of action potential initiation, leading to neural inhibition. The GABA-dependent enhancement of Cl- ion inflow through a receptor-associated channel achieves this decrease in membrane resistance. Increased Cl- permeability, might depolarize the target cell under certain conditions of high intracellular Cl-

Clinical Significance

Low GABA levels have been linked to a variety of illnesses. Low GABA concentrations have been associated to a variety of mental diseases. One example is generalized anxiousness. Because GABA is an inhibitory neurotransmitter, a reduction in its concentration would cause anxiety. It's also been linked to schizophrenia, autistic spectrum disease, and significant depression. Although GABA concentrations may be changed in various psychiatric illnesses, treatment with GABAA receptor agonists are not recommended as first-line therapy due to the significant addiction potential and potentially deadly side effects. Valproic acid, a GABA analog, can be used to treat mood instability by increasing GABA concentrations.

Low GABA levels are linked to seizures and epilepsy. Cells in the cerebral cortex get depolarized when inhibition levels fall, resulting in seizure activity. Seizures are treated with GABA agonists such as Valproic acid. Seizures can result with abrupt discontinuation from drugs such as benzodiazepines, a GABAA positive allosteric modulator. GABA antagonists are also pro-convulsant.

Inherited abnormalities of GABA metabolism are rare, requiring a rise in clinical suspension. GABA-transaminase insufficiency, uccinic semialdehyde dehydrogenase deficiency and homocarnosinosis are the most frequent disorders. The most prevalent neurotransmitter deficiency is SSADH. It has a hazy phenotypic, varied neurological symptoms, and psychological disease. Because GABA cannot be converted to succinic acid, Gamma-Hydroxy-Butyrate (GHB) accumulates. GABA and GHB concentrations are elevated in serum and urine. GABA excretion in the urine and enhanced signaling in the globus pallidus on MRI can be used to make the diagnosis. Characteristics include expressive language impairment, hypotonia, and seizures. Sleep disruption is the most prevalent neuropsychiatric condition; additional concerns include inattention, hyperactivity, and Obsessive-Compulsive Disorder (OCD). There is no conventional therapy for SSADH deficiency at the moment. GABA-transaminase deficiency and homocarnosinosis are more rare. GABA-transaminase deficiency is a recessive autosomal disease. Seizures can occur in the newborn period, and additional symptoms include hypotonia, hyperreflexia, significantly delayed psychomotor development, and a high-pitched scream. Serum and cerebrospinal fluid have high levels of GABA. Only one family has been known to have homocarnosinosis. Progressive spastic diplegia, intellectual impairment, and retinitis pigmentosa are all symptoms.

GABA agonistic drugs

- GABAA receptor agonists: Alcohol (ethanol), barbiturates, and benzodiazepine.

- GABAB receptor agonists: Baclofen, sodium oxybate (GHB), propofol. GABAB agonists increase CNS depression.
- GABA analogs: Valproic acid, pregabalin, gabapentin.

GABA antagonistic drugs

Antagonistic drugs bind to GABA receptors but do not raise the quantity of GABA. Picrotoxin and bicuculline methiodide are two examples. Both are mostly utilized for research purposes. GABA antagonists are both anticonvulsants and stimulants.