

# GLUTAMATERGIC SYSTEM



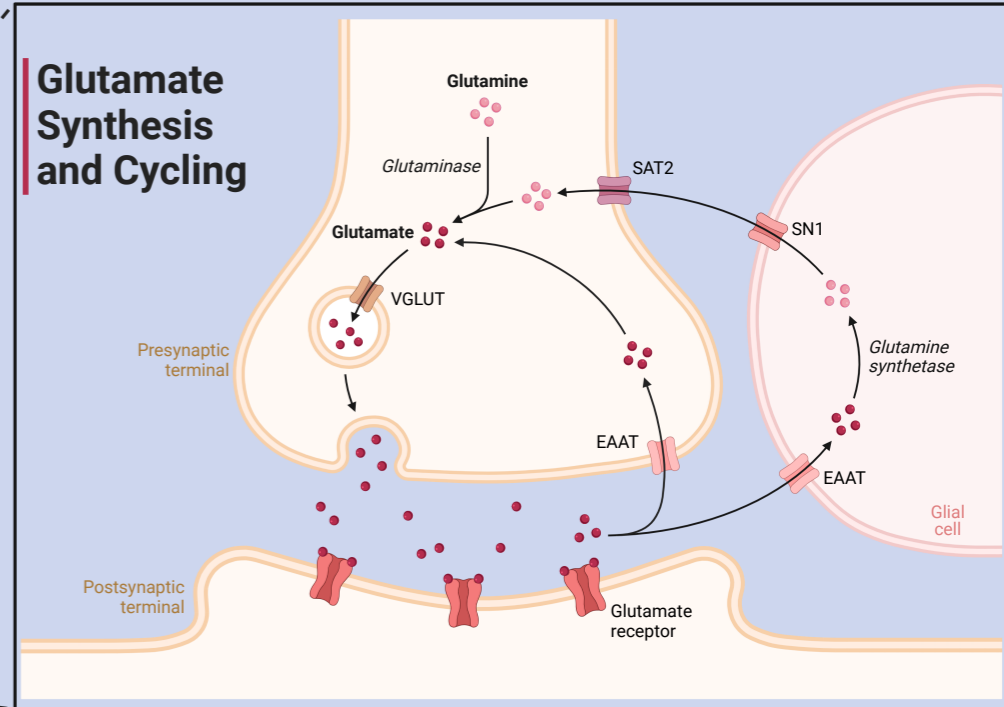
The conformation of the receptor varies according to the tissue in which it is located

Brain regions

Glutamate  
 $C_5H_9NO_4$

Glutamate is an excitatory amino acid neurotransmitter that is highly distributed

Glutamate and aspartate are charged amino acids and therefore do not cross the blood-brain barrier. They are synthesized in the brain from glucose and a variety of other precursors. Glutamate, which is the reduced form of glutamic acid, is found in a metabolic group with  $\alpha$ -oxoglutaric acid and glutamine.



Glutamate Synthesis and Cycling



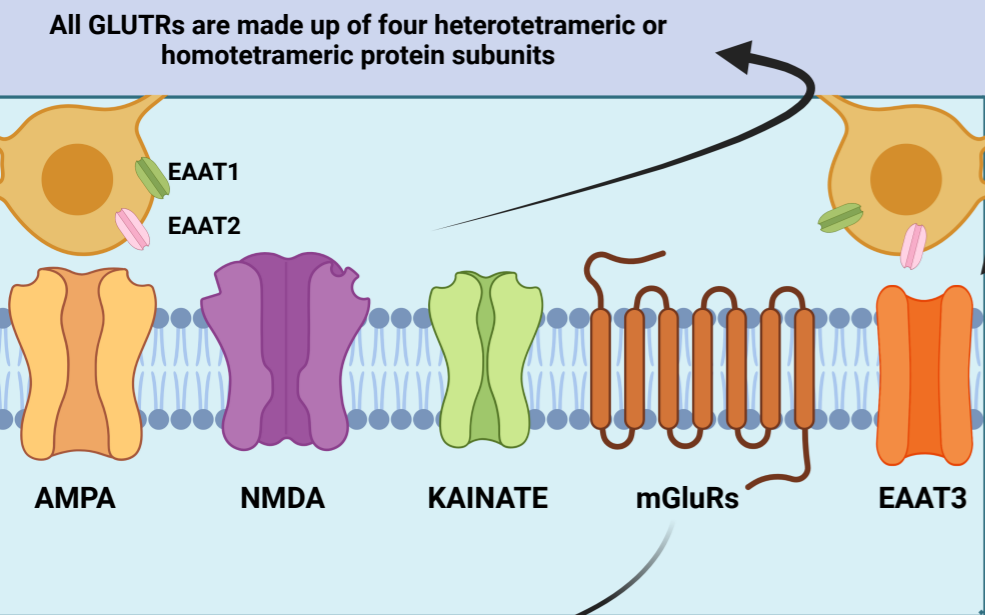
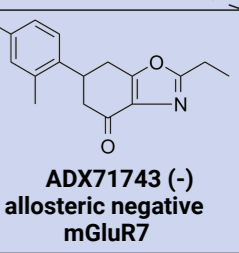
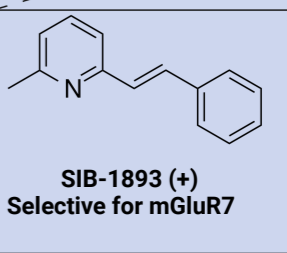
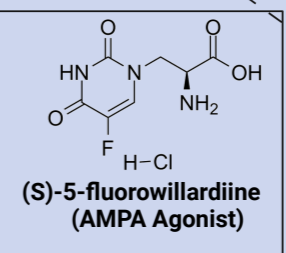
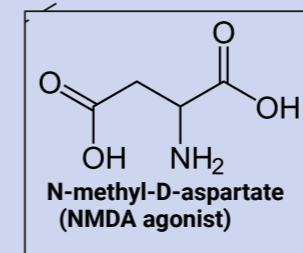
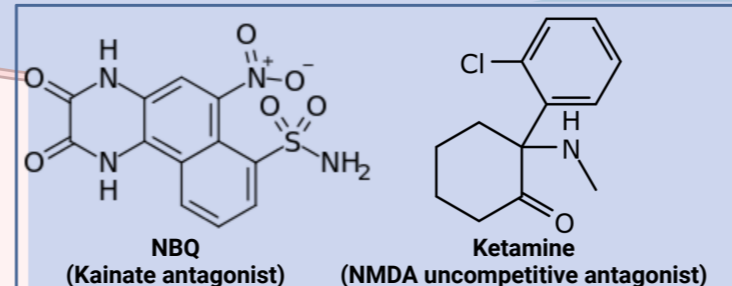
- Excitotoxicity
- Huntington disease
- Progressive loss of memory
- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Stroke
- Epilepsy

Pharmacological intervention can modulate the alterations

Agonist

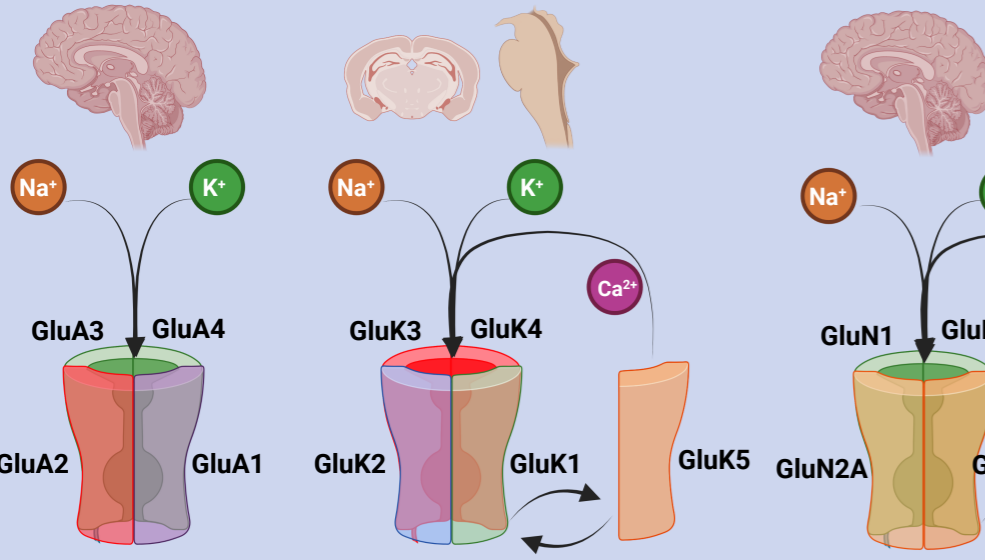
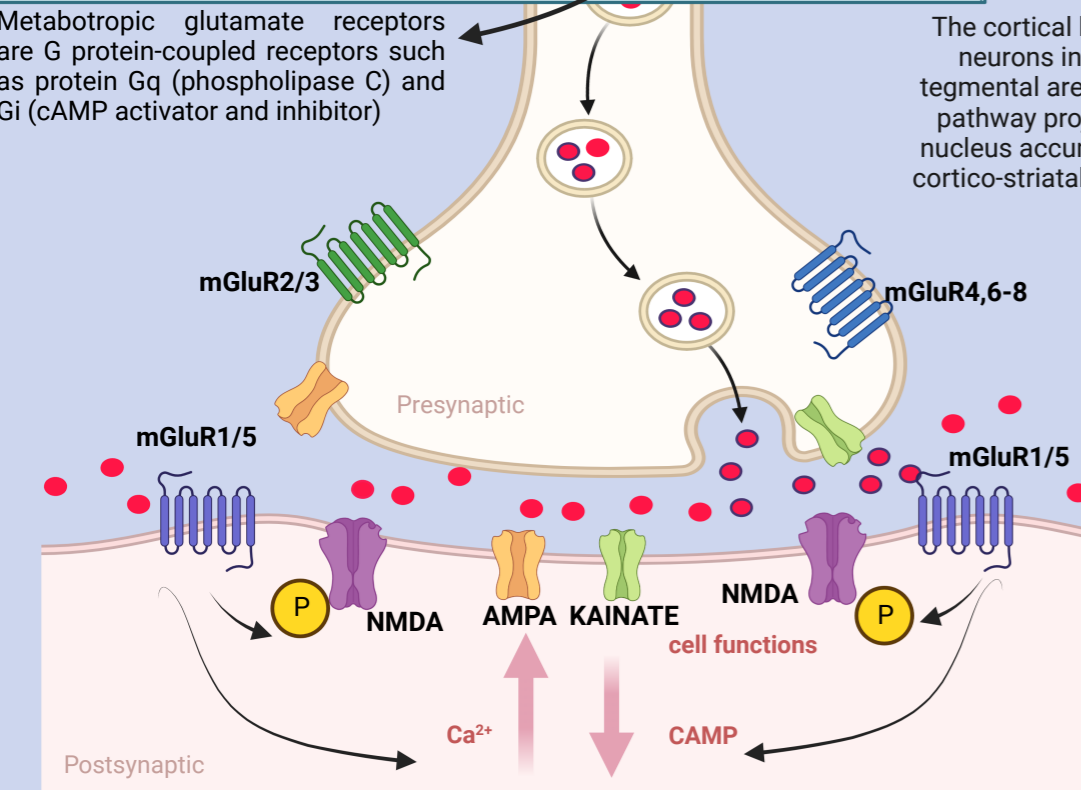
antagonist

Selectives modulators



Metabotropic glutamate receptors are G protein-coupled receptors such as protein Gq (phospholipase C) and Gi (cAMP activator and inhibitor)

The cortical brainstem glutamate projection is a descending pathway that projects from cortical pyramidal neurons in the prefrontal cortex to brainstem neurotransmitter centers (raphe, locus coeruleus, ventral tegmental area, substantia nigra) and regulates neurotransmitter release. Another descending glutamatergic pathway projects from the prefrontal cortex to the striatum (cortico-striatal-glutamate pathway) and to the nucleus accumbens (cortico-accumbens glutamate pathway), and constitutes the "cortico-striatal" portion of cortico-striatal-thalamic loops. pathways project from the frontal cortex and penetrate into deeper brain areas where they exert control over the neuroanatomic structures residing there.



All GLuTRs are made up of four heterotetrameric or homotetrameric protein subunits

