Positive Allosteric Modulators that Treat Central Nervous System Disorders

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Technology description

Impaired NMDA receptor function has been suggested in a wide range of neurological conditions including schizophrenia, psychoses, bipolar disorder, depression, epilepsy and Parkinson’ s disease. Due to their suspected involvement in pathology and wide disbursement throughout the central nervous system, NMDA receptors are valuable therapeutic targets. Past therapeutic approaches resulted in drugs that globally antagonized NMDA receptors and, while these drugs have therapeutic benefits, they also result in adverse side effects. Identifying drugs that target specific subunits of NMDA receptors is therapeutically useful. By affecting only the targeted brain regions that express the desired receptor subunit, deleterious effects like dissociative feelings and hallucinations can possibly be avoided.

Researchers at Emory University have identified a family of small molecules that potentiate NMDA receptor subunits GluN2C and GluN2D. GluN2C/D subunits anatomically are located in brain regions most impacted by pathology. The tetrahydroisoquinoline class of NMDA receptor positive allosteric modulators act on the GluN2C and GluN2D subunits. Because these small molecules act only in brain regions with GluN2C/D subunits, they will likely have fewer side effects than non-selective potentiators. Potential indications for use of the molecules include schizophrenia, psychoses, bipolar disorder and depression, epilepsy and Parkinson’ s disease.

Application area

Small molecules that selectively potentiate N-methyl-D-aspartate (NMDA) receptor subunits GluN2C/ GluN2D for the treatment of neurological conditions.

Advantages

Selective potentiation of only NMDA receptor that contain GluN2C or GluN2D subunits will likely reduce adverse side effects.

Selective potentiation of only NMDA receptor that contain GluN2C or GluN2D subunits may yield better pharmacological and pharmacokinetic properties versus global NMDA receptor antagonists.

Institution

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