AMPA

AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) is a compound that is a specific agonist for the AMPA receptor, where it mimics the effects of the neurotransmitter glutamate.

There are several types of glutamatergic ion channels in the central nervous system including AMPA, kainic acid and N-methyl-D-aspartic acid (NMDA) channels. In the synapse, these receptors serve very different purposes. AMPA can be used experimentally to distinguish the activity of one receptor from the other in order to understand their differing functions.

Activation

AMPA generates fast excitatory postsynaptic potentials (EPSP).

AMPA activates AMPA receptors that are non-selective cationic channels allowing the passage of Na+ and K+ and therefore have an equilibrium potential near 0 mV.

Activation of α-amino-3-hydroxy-5-methyl-4-isoxazole propionate receptor (AMPAR) is thought to cause acute brain injury, but the role remains poorly understood in subarachnoid hemorrhage (SAH).

A study was conducted to evaluate if AMPAR activation induces acute blood-brain barrier disruption after SAH. C57BL/6 male adult mice (n = 117) underwent sham or filament perforation SAH modeling, followed by a random intraperitoneal injection of vehicle or two dosages (1 mg/kg or 3 mg/kg) of a selective non-competitive AMPAR antagonist perampanel (PER) at 30 min post-modeling. The effects were evaluated by mortality, neurological scores, and brain water content at 24-48 h and video electroencephalogram monitoring, immunostaining, and Western blotting at 24 h post-SAH. PER significantly suppressed post-SAH neurological impairments, brain edema, and BBB disruption. SAH developed epileptiform spikes without obvious convulsion, which were also inhibited by PER. Western blotting showed that the expression of AMPAR subunits GluA1 and GluA2 was unchanged after SAH, but they were significantly activated after SAH. PER prevented post-SAH activation of GluA1/2, associated with the suppression of post-SAH induction of tenascin-C, a causative mediator of post-SAH BBB disruption. Meanwhile, intracerebroventricular injection of a subtype-selective GluA1/2 agonist augmented the activation of GluA1/2 and the induction of tenascin-C in brain capillary endothelial cells and aggravated post-SAH BBB disruption without increases in epileptiform spikes. Neurological impairments and brain edema were not correlated with the occurrence of epileptiform spikes. This study first showed that AMPAR plays an important role in the development of post-SAH BBB disruption and can be a novel therapeutic target against it [1)].

Abe et al. found that facilitated experience-driven synaptic glutamate AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic-acid) receptor delivery and resulted in the acceleration of motor function recovery after motor cortex cryoinjury in mice in a training-dependent manner through cortical reorganization. Edonerpic maleate bound to Collapsin response mediator protein family 2 (CRMP2) and failed to augment recovery in CRMP2-deficient mice. Edonerpic maleate enhanced motor function recovery from internal capsule hemorrhage in nonhuman primates. Thus, edonerpic maleate, a

Neuroplasticity enhancer, could be a clinically potent small compound with which to accelerate rehabilitation after brain damage [2].

1)
Kawakita F, Kanamaru H, Asada R, Imanaka-Yoshida K, Yoshida T, Suzuki H. Inhibition of AMPA (α-Amino-3-Hydroxy-5-Methyl-4-Isoxazole Propionate) Receptor Reduces Acute Blood-Brain Barrier Disruption After Subarachnoid Hemorrhage in Mice. Transl Stroke Res. 2021 Aug 3. doi: 10.1007/s12975-021-00934-0. Epub ahead of print. PMID: 34342874.
2)
Abe H, Jitsuki S, Nakajima W, Murata Y, Jitsuki-Takahashi A, Katsuno Y, Tada H, Sano A, Suyama K, Mochizuki N, Komori T, Masuyama H, Okuda T, Goshima Y, Higo N, Takahashi T. CRMP2-binding compound, edonerpic maleate, accelerates motor function recovery from brain damage. Science. 2018 Apr 6;360(6384):50-57. doi: 10.1126/science.aao2300. PubMed PMID: 29622647.