NMDA receptor

The N-methyl-D-aspartate receptor (also known as the NMDA receptor or NMDAR), is a glutamate receptor and ion channel protein found in nerve cells. The NMDA receptor is one of three types of ionotropic glutamate receptors. The other receptors are the AMPA and kainate receptors. It is activated when glutamate and glycine (or D-serine) bind to it, and when activated it allows positively charged ions to flow through the cell membrane.

The NMDA receptor is very important for controlling synaptic plasticity and memory function.

The endogenous neurotrophic peptides pituitary adenylate cyclase-activating polypeptides (PACAP-27/38) protect against stroke, but the molecular mechanism remains unknown.

Primary rat neural cells were exposed to PACAP-27 or PACAP-38 before induction of experimental acute ischemic stroke via oxygen-glucose deprivation-reperfusion (OGD/R) injury. To reveal PACAP's role in neuroprotection, Kaneko et al. from the University of South Florida and Xuanwu Hospital employed fluorescent live/dead cell viability and caspase 3 assays, optical densitometry of mitochondrial dehydrogenase and cell growth, glutathione disulfide luciferase activity, ELISA for high mobility group box1 extracellular concentration, ATP bioluminescence, Western blot analysis of PACAP, NMDA subunits, apoptosis regulator Bcl-2, social interaction hormone oxytocin, and trophic factor BDNF, and immunocytochemical analysis of PACAP.

Both PACAP-27 and PACAP-38 (PACAP-27/38) increased cell viability, decreased oxidative stress-induced cell damage, maintained mitochondrial activity, prevented the release of high mobility group box1, and reduced cytochrome c/caspase 3-induced apoptosis. PACAP-27/38 increased the protein expression levels of BDNF, Bcl-2, oxytocin, and precursor PACAP. N-methyl-D-aspartate receptor (NMDA receptor)-induced excitotoxicity contributes to the cell death associated with stroke. PACAP-27/38 modulated the protein expression levels of NMDAR subunits. PACAP-27/38 increased the protein expression levels of the GluN1 subunit, and decreased that of the GluN2B and GluN2D subunits. PACAP-27, but not PACAP-38, increased the expression level of the GluN2C subunit.

This study provides evidence that PACAP regulated NMDAR subunits, affording neuroprotection after OGD/R injury [1].

1)
Kaneko Y, Tuazon JP, Ji X, Borlongan CV. Pituitary Adenylate Cyclase Activating Polypeptide Elicits Neuroprotection Against Acute Ischemic Neuronal Cell Death Associated with NMDA Receptors. Cell Physiol Biochem. 2018 Dec 4;51(4):1982-1995. doi: 10.1159/000495722. [Epub ahead of print] PubMed PMID: 30513524.