

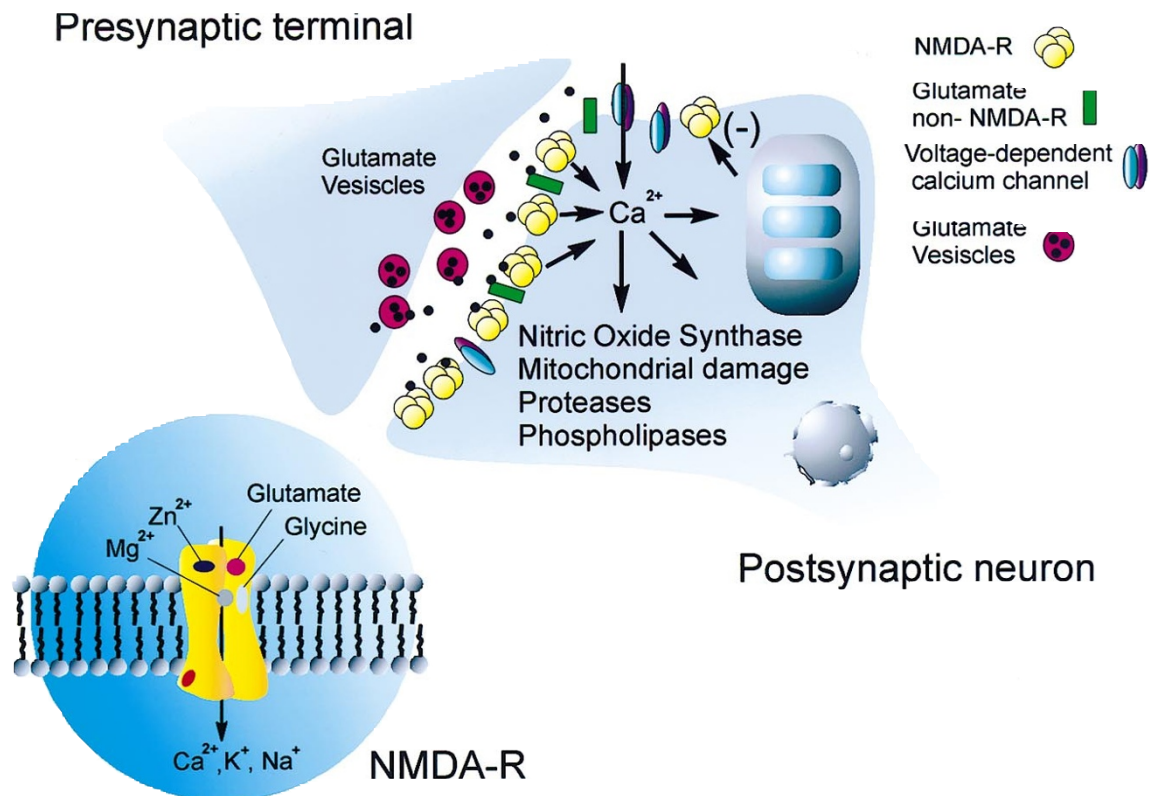


Educational Corner

Excitotoxicity

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The term excitotoxicity describes the supra-physiological stimulation of excitable cells by excitatory amino acids. The N-methyl-D-aspartate receptor (NMDA-R) is a heteromeric molecule belonging to the class of ionotropic glutamate receptors and it is probably the most important for neuron death. Upon agonist stimulation, this ligand-gated channel opens to Ca^{2+} and Na^+ when a potential-controlled Mg^{2+} - block is removed. Other classes of ionotropic glutamate receptors (i.e., kainate or quisqualate) open primarily to Na^+ and facilitate NMDA-R activation. In acute neurologic diseases, such as stroke and head trauma, excitotoxicity may be related to excessive glutamate release and/or lack of clearance from synaptic clefts, resulting in excessive stimulation of ionotropic glutamate receptors. Due to the prolonged opening of NMDA-Rs, intracellular Ca^{2+} overload triggers downstream processes resulting in cell death.

These include mitochondrial damage and the activation of phospholipases, proteases and the Ca^{2+} - calmodulin-dependent, nitric oxide synthase (NOS), which generates NO.

Further Reading

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