

“Calcium-mediated Mechanisms Implicated in Glutamate Excitotoxicity and Mitochondrial Deregulation”

by

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Abstract

In addition to being the dominant excitatory neurotransmitter in the mammalian central nervous system, glutamate, when released under pathological conditions such as stroke or cardiac arrest, is a potent neurotoxin responsible for the resulting neuronal necrosis or apoptosis. This action, whereby the normal, excitatory action of glutamate is transformed into a neuropathological process that can rapidly kill neurons, is termed excitotoxicity. The initial event in glutamate-evoked neuronal excitotoxicity is an extensive entry of Ca^{2+} through the post-synaptic *N-methyl-D-aspartate* (NMDA) receptor, which disrupts intracellular Ca^{2+} homeostasis and initiates the activation of Ca^{2+} -dependent degradative enzymes. Altered intracellular Ca^{2+} homeostasis is also responsible for the disruption of normal mitochondrial functions, resulting in the generation of reactive oxygen species and the deregulation of cellular ATP synthesis. This seminar attempts to elucidate the route of neuronal excitotoxicity, beginning with uncontrolled glutamatergic activation, and linking it to the disruption of normal mitochondrial bioenergetics by highlighting the important role of Ca^{2+} in excitotoxic mechanisms of cell killing.