NEUROPROTECTIVE ROLE OF ADENOSINE IN THE CNS

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It is well established that in the CNS, endogenous adenosine plays a pivotal role in neurodegeneration. A low, nanomolar concentration of adenosine is normally present in the extracellular fluid, but it increases dramatically during enhanced nerve activity, hypoxia or ischemia. In these pathological conditions, adenosinergic transmission-potentiating agents, which elevate adenosine level by either inhibiting its degradation (adenosine deaminase and kinase inhibitors) or preventing its transport, offer protection against ischemic or excitotoxic neuronal damage. The directly acting adenosine A_1 receptors are known to mediate neuroprotection, mostly by the blockade of Ca^{2+} influx, which results in the inhibition of glutamate release and reduction of its excitatory effects at a postsynaptic level. More recent data have shown that antagonists of adenosine A_2A receptors markedly reduce cerebral ischemic damage in animal models of focal and global ischemia. Moreover, these compounds attenuate the neuronal loss induced by excitatory amino acids (EAA). A neuroprotective effect of adenosine A_2A receptor antagonists was also shown in animal models of Parkinson’s disease (MPTP, 6-OHDA, methamphetamine). Hence, it might be suggested that adenosine A_2A receptor antagonists may represent a novel strategy in the therapeutic approach to pathologies characterized by acute or chronic neurodegenerative events, since they not only reverse motor impairment but can act as neuroprotective compounds by promoting cell survival.

Key words: adenosine, adenosine A_1 receptors, adenosine A_2A receptors, excitotoxicity, ischemia, neuroprotection, Parkinson’s disease

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