EXCITATORY SYNAPTIC TRANSMISSIONS IN STRIATAL NEURONS AFTER TRANSIENT GLOBAL ISCHEMIA

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ABSTRACT

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Striatal spiny neurons are highly vulnerable to ischemia. Excitatory synaptic transmissions have been implicated in ischemia-induced excitotoxic neuronal death. Using four-vessel occlusion ischemia model and brain slices preparation, we found that excitatory postsynaptic currents (EPSCs) in spiny neurons were potentiated after ischemic insults. The potentiation in synaptic efficacy was associated with an enhancement of presynaptic release, as demonstrated by an increase in the frequency of miniature excitatory postsynaptic currents (mEPSCs) and a decrease in the paired-pulse ratio. The amplitude of inward currents evoked by exogenous application of glutamate did not show significant changes after ischemia, suggesting that postsynaptic mechanism was not involved. The ischemia-induced increase in mEPSCs frequency was not affected by blockade of voltage-gated calcium channels, but it was eliminated in the absence of extracellular calcium. Bath application of ATP P2X receptor antagonist PPADS significantly reduced mEPSCs frequency in ischemic neurons; but had no effects on the control ones. Furthermore, the inhibitory effect of PPADS on ischemic neurons was abolished in calcium-free external solution. Dopamine depressed excitatory synaptic transmission in post-ischemic spiny neurons through activation of D1 receptor (D1R). The depression was attributable to a decreased synaptic glutamate release, as demonstrated by a decrease in mEPSCs fre-

quency and an increase in paired-pulse ratio. 8-Br-cAMP, an activator of cAMP-dependent protein kinase (PKA), mimicked the depressive effects of D1R activation. Bath application of Rp-cAMP, an inhibitor of PKA, blocked the D1R-induced depression of EPSCs in post-ischemic spiny neurons, although intracellularly applied Rp-cAMP had no effects. In addition, D1Rs failed to reduce EPSCs amplitude in the presence of adenosine A1 receptors (A1Rs) antagonist. Our results suggest that enhancement of excitatory synaptic transmissions may contribute to ischemic cell death in the striatum, and that dopamine-induced A1 receptor activation may have a therapeutic potential in striatum stoke.

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