Zinc translocation accelerates infarction after mild transient focal ischemia.

許重義
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Abstract

Excess release of chelatable zinc (Zn(2+)) from central synaptic vesicles may contribute to the pathogenesis of selective neuronal cell death following transient forebrain ischemia, but a role in neurodegeneration after focal ischemia has not been defined. Adult male Long-Evans rats subjected to middle cerebral artery occlusion (MCAO) for 30 min followed by reperfusion developed delayed cerebral infarction reaching completion 3 days after the insult. One day after the insult, many degenerating cerebral neurons exhibited increased intracellular Zn(2+), and some labeled with the antibody against activated caspase-3. I.c.v. administration of the Zn(2+) chelator, EDTA saturated with equimolar Ca(2+) (CaEDTA), 15 min prior to ischemia attenuated subsequent Zn(2+) translocation into cortical neurons, and reduced infarct volume measured 3 days after ischemia. Although the protective effect of CaEDTA at this endpoint was substantial (about 70% infarct reduction), it was lost when insult severity was increased (from 30 to 60 min MCAO), or when infarct volume was measured at a much later time point (14 days instead of 3 days after ischemia).These data suggest that toxic Zn(2+) translocation, from presynaptic terminals to post-synaptic cell bodies, may accelerate the development of cerebral infarction following mild transient focal ischemia