Neuronal and inducible nitric oxide synthase expression and protein nitration in rat cerebellum after oxygen and glucose deprivation.


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A perfusion model of global cerebral ischemia was used for the immunohistochemical study of changes in the glutamate-nitric oxide (NO) system in the rat cerebellum and cerebellar nuclei during a 0-14 h reperfusion period after 30 min of oxygen and glucose deprivation, with and without administration of 1.5 mM N(omega)-nitro-L-arginine methyl ester (L-NAME). While immunostaining for N-methyl-D-aspartate receptor subunit 1 (NMDAR1) showed no marked changes during the reperfusion period, neuronal NO synthase (nNOS) immunostaining increased in stellate and basket cells, granule cells and neurons of the cerebellar nuclei. However, global cerebellar nNOS concentrations determined by Western blotting remained largely unchanged in comparison with actin expression.

Inducible NOS (iNOS) immunostaining appeared in Purkinje cells and neurons of the cerebellar nuclei after 2-4 h of reperfusion and intensified during the 6-14 h period. This was reflected by an increase in global cerebellar iNOS expression determined by Western blotting. Immunostaining for protein nitrotyrosine was seen in Purkinje cells, stellate and basket cells, neurons of the cerebellar nuclei and glial cells in controls, and showed a progressive translocation in Purkinje cells and neurons of the cerebellar nuclei from an initial perinuclear or nuclear location towards the periphery. At the end of the reperfusion period the Purkinje cell apical dendrites were notably retracted and tortuous. Prior and concurrent L-NAME administration eliminated nitrotyrosine immunostaining in controls and blocked or reduced most of the postischemic changes observed. The results suggest that while nNOS expression may be modified in certain cells, iNOS is induced after a 2-4 h period, and that changes in protein nitration may be associated with changes in cell morphology.

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