SARCOSINE PRECONDITIONING INDUCES ISCHEMIC TOLERANCE AGAINST GLOBAL CEREBRAL ISCHEMIA

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ABSTRACT

Brain ischemic tolerance is an endogenous protective mechanism activated by a preconditioning stimulus that is closely related to N-methyl-D-aspartate receptor (NMDAR). Glycine transporter type 1 (GlyT-1) inhibitors potentiate NMDAR and suggest an alternative strategy for brain preconditioning. The aim of this work was to evaluate the effects of brain preconditioning induced by sarcosine, a GlyT-1 inhibitor, against global cerebral ischemia and its relation to NMDAR. Sarcosine was administered over 7 days (300 or 500 mg/kg/day, ip) before the induction of a global cerebral ischemia model in Wistar rats (male, 8-week-old). It was observed that sarcosine preconditioning reduced cell death in rat hippocampi submitted to cerebral ischemia. Hippocampal levels of glycine were decreased in sarcosine-treated animals, which was associated with a reduction of [3H] glycine uptake and a decrease in glycine transporter expression (GlyT-1 and GlyT-2). The expression of glycine receptors and the NR1 and NR2A subunits of NMDAR were not affected by sarcosine preconditioning. However, sarcosine preconditioning reduced the expression of the NR2B subunits of NMDAR. In conclusion, these data demonstrate that sarcosine preconditioning induces ischemic tolerance against global cerebral ischemia and this neuroprotective state is associated with changes in glycine transport and reduction of NR2B-containing NMDAR expression.