Letters to the Editor

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Neuroprotective Effect of Isoflurane and N-Methyl-d-Aspartate Receptors in Ischemic Brain Injury

To the Editor:

We read with great interest the article by Dr Zhou and colleagues1 dealing with the effect of isoflurane, one of the volatile anesthetics, on the neonatal hypoxic-ischemic brain injury in rats. The results of their study demonstrated that 2% isoflurane, given immediately after hypoxic ischemia, reduced brain infarct volume in the short-term as well as brain atrophy and neurobehavioral deficits in the long-term. Moreover, the authors indicated that blocking the sphingosine-1-phosphate (S1P)-receptor with VCP23019 or inhibiting phosphatidylinositol-3-kinase (PI3K) by wortmannin attenuated the isoflurane-mediated beneficial effects. In addition, administration of VCP23019 and wortmannin also blocked the isoflurane-induced recovery of Akt activity and decrease in cleaved caspase-3 expression, a marker of apoptotic cell death. The authors propose that isoflurane provided neuroprotection against neonatal hypoxic-ischemic brain injury, which might depend on S1P/PI3K/Akt signaling.

Evidence indicates that the glutamate-induced excitation and neurotoxicity might also be involved in the mechanisms of neural cell damage and that inhibition of N-methyl-D-aspartate (NMDA) receptors by anesthetic gases and vapors might play an important role in anesthesia and neuroprotection. Dickinson et al2 showed that isoflurane could inhibit NMDA receptors by binding at the same site as the coagonist glycine. Recently, several studies have reported the mechanisms for the neuroprotective effects of the noncompetitive NMDA receptor antagonist, MK-801, in the central nervous system. Bômont et al3 demonstrated that administration of MK-801 significantly reduced the volume of ischemic damage of the brain after middle cerebral artery occlusion.

On the other hand, in the ischemic neuronal models, Nakai et al4 showed that ischemia significantly increased noradrenaline (NA) release in rat spinal cord. They also demonstrated that MK-801 suppressed the release of NA and glutamate produced by ischemia. In a study presented earlier, the changes in NA release evoked by l-glutamate were investigated in the central nervous system of rats.5 In an in vitro study, we showed that l-glutamate increased the release of NA from rat medulla oblongata, and further observed that the facilitative effect of l-glutamate on NA release was significantly counteracted by MK-801.5 It would be possible that the sympatholytic action might partially explain the neuroprotective effects of MK-801 against the ischemic injury in the brain. We would like to know, therefore, whether isoflurane could reverse the changes in the contents or release of catecholamines and glutamate in the injured regions, and whether isoflurane might synergistically act with MK-801 against the hypoxic-ischemic brain injury in the study of Dr Zhou and colleagues. It would be important to assess more precisely the relationships between isoflurane-effects and the NMDA-receptor functions, and their roles in the prevention of hypoxic-ischemic brain damages.

Disclosures

None.

Kazushi Tsuda, MD, FAHA
Cardiovascular and Metabolic Research Center
Kansai University of Health Sciences
Osaka, Japan


(Stroke. 2010;41:e578.)
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Stroke is available at http://stroke.ahajournals.org

DOI: 10.1161/STROKEAHA.110.595033
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Stroke. 2010;41:e578; originally published online September 2, 2010;
doi: 10.1161/STROKEAHA.110.595033
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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