longer periods of aortic clamping and diminished spinal cord blood flow.

Despite these limitations, Mukai and colleagues are to be congratulated in performing an elegant series of experiments to increase our knowledge of the pathophysiology of neuronal “excitotoxicity.” Their observations of the detrimental effects of excessive NMDA expression may lead to the development of NMDA antagonists that can be directly infused into the CSF during periods of aortic clamping followed by the current practice of CSF drainage for 24 to 48 hours postoperatively. This may lead to better spinal cord protection during both open and TEVAR procedures

and minimize the devastating effects of SCI during thoracic aortic surgery.

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Commentary: Building the bigger picture from patchwork-like research pieces

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Many seemingly small details determine outcomes after major aortic surgery. Spinal cord injury is a devastating complication after both open and endovascular aortic surgery.^{1,2} Decreased blood flow of the spinal cord increases the risk for spinal cord ischemia and may lead to excessive accumulation of glutamate and N-methyl-D-aspartate receptor activation, as reported earlier following cerebral ischemia.³ Would it be possible to intervene on a molecular pathway to secure spinal cord vitality?

In a well-performed experimental study, Mukai and colleagues⁴ investigated the effect of remote ischemic preconditioning after spinal cord ischemia–reperfusion injury in rats. The study included explanatory figures. Spinal cord ischemia was induced using an obstructing vessel clamp to prevent blood flow into the descending thoracic

Research results are like details in a patchwork.

CENTRAL MESSAGE

Detailed experimental research on glutamate builds a patchwork-like picture of spinal cord protection against ischemia–reperfusion injury.

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aorta for 12 minutes. Remote ischemic preconditioning was included using 4 cycles of ischemia–reperfusion maneuvers by filling an elastic tourniquet around the limb of the animal for ischemia and subsequently releasing it after 5 minutes for reperfusion. Microdialysis, motor-evoked potentials, and evaluation of motor function were investigated. Histopathology and immunofluorescence studies confirmed neuronal injury after ischemia–reperfusion injury that was associated with excessive extracellular glutamate and N-methyl-D-aspartate receptor activation. Remote ischemic preconditioning down-regulated these parameters, and it was concluded that remote ischemic

preconditioning had a protective effect after spinal cord ischemia.

Each rat did not undergo all experiments included in this study. Instead of using absolute values, glutamate concentration, motor-evoked potentials, and the amount of hydroperoxides were analyzed as the percentage changes from baseline. Some other parameters, such as lactate, which describes the metabolic state after spinal cord ischemia, could have also been measured using microdialysis.⁵

The down-regulation of glutamate alone may not always signify protection; many other molecules are also candidates for protection, such as adenosine.⁶ Several molecular pathways, including cytokines, proteases, and free radicals, participate in the induction of neuronal cell death. Many other receptors, such as glutamate transporters, regulate cellular uptake; blocking of the N-methyl-D-aspartate receptor does not suffice to control cellular glutamate, and glutamate itself does not harm the neurons.⁷ Cardioplegia with glutamate secures myocardial energy supply and provides myocardial protection during cardiac arrest,⁸ but as a neurotransmitter, excessive glutamate induces N-methyl-D-aspartate receptor activation, destabilizes calcium homeostasis, and leads to free radical production.³

Although decreased glutamate may lead to decreased N-methyl-D-aspartate receptor activation, the mechanisms associated with remote ischemic preconditioning may be multifactorial even during spinal cord protection. Reporting on temporal molecular changes cannot compensate for a chronic model based on histology. Remote ischemic preconditioning remains clinically yet unjustified during induced spinal cord ischemia,⁹ and novel means necessitate intensive experimentation.¹⁰

The value of this study seems not to be the simulation of a clinical setup; the purpose of using several research methods, including applying remote ischemic preconditioning, complete clamping of the aorta to induce ischemia, using a

N-methyl-D-aspartate receptor antagonist, and different anesthetic agents depending on experimental details, was to reveal the role of glutamate and N-methyl-D-aspartate receptor during spinal cord ischemia–reperfusion injury. Gathering patchwork-like research results suggests that antagonism of N-methyl-D-aspartate receptor activation may mitigate spinal cord ischemia–reperfusion injury.

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