Role of Hyperglycemia and Glutamate Receptors in Ischemic Injury in Acute Cerebral Infarction

To the Editor:

We read with great interest the recent article by Dr Martin and colleagues1 dealing with the relationship between hyperglycemia and ischemic injury in acute cerebral infarction. The results of their study demonstrated that acute hyperglycemia intrinsically aggravated ischemic damage in transient middle cerebral artery occlusion in rats. The authors also indicated that the hyperglycemia-exacerbated brain damage cannot be fully explained by the negative effects of plasma corticosteroids or neutrophil infiltration. They proposed that the contribution of other intrinsic effects of high glucose, such as brain protein O-glycosylation, might be addressed.

Evidence indicates that hyperglycemia may actively participate in the regulation of cellular Ca-kinetics. Barbagallo et al.2 showed that hyperglycemia elevated cytosolic free Ca both in myocardial and vascular smooth muscle cells, suggesting that glucose-related excess intracellular Ca might be a fundamental lesion in diabetes that would contribute to the cellular dysfunction. Recent studies have shown that the glutamate-induced excitation and neurotoxicity might be involved in the mechanisms of neural cell damage.3 In a study presented earlier, we showed that glutamate increased the release of acetylcholine from rat central nervous system, which was inhibited by the N-methyl-D-aspartate type of glutamate receptor antagonist MK-801.4 Furthermore, it was demonstrated that the Ca channel blocker significantly reduced the glutamate-evoked acetylcholine release and that the inhibitory effect was more pronounced in the presence of magnesium.5 It was also shown that the Ca channel blocker inhibited the glutamate-evoked intracellular Ca increase and prevented the glutamate-induced apoptosis in purified retinal ganglion cells.6 Bomont et al.7 demonstrated that administration of MK-801 significantly reduced the volume of ischemic damage of the brain after middle cerebral artery occlusion in hyperglycemic and diabetic rat models. In this context, we speculate that the glutamate receptor-mediated Ca conductance might have a crucial role in the hyperglycemia-induced neurotoxic disorders in the brain. Because the O-glycosylation of the proteins might partially be related to the cellular Ca-handling,8 we would like to know whether the O-glycosylation in the brain might be associated with the alterations in glutamate receptor functions or intracellular Ca-kinetics. Further studies should be performed to assess more precisely the mechanisms underlying the harmful effects of hyperglycemia in acute cerebral infarction.

Disclosures

None.

Kazushi Tsuda, MD, FAHA
Department of Cardiology
Wakayama Medical University
Wakayama, Japan

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Kazushi Tsuda

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