Role of Bradykinin and Catecholamines in Cerebral Infarction and Brain Edema

To the Editor:

We read with great interest the article by Dr Austinat and colleagues dealing with the effect of the bradykinin B1 receptor (B1R) blockade on cerebral infarction and brain edema in mice. The results of their study demonstrated that B1R knockout mice developed significantly smaller brain infarctions and less neurological deficits evoked by transient middle cerebral artery occlusion compared to wild-type controls, although B2R deficiency did not confer neuroprotection and had no effect on the development of tissue edema. Pharmacological blockade of B1R likewise salvaged ischemic tissues. The authors propose that blockade of B1R receptors can diminish brain edema and cerebral infarction in mice and may open new avenues for acute stroke treatment in humans.

Several studies have reported the mechanisms for the neuronal effects of BK in the central nervous system. In a study we presented earlier, the change in norepinephrine (NE) release induced by BK was investigated in the hypothalamus of normotensive and spontaneously hypertensive rats. In an in vitro study using rat brain slices, we showed that BK increased the stimulation-evoked NE release in a dose-dependent manner. It was also shown that a dihydropyridine-sensitive Ca channel agonist, Bay K 8644, significantly potentiated the facilitatory effect of BK on NE release. In contrast, a dihydropyridine-sensitive Ca channel blocker, nicardipine, inhibited the increase in NE release evoked by BK and Bay K 8644. The finding might suggest that BK might stimulate NE release by increasing transmembrane Ca-influx in the central nervous system. On the other hand, Kamiya et al showed that BK levels in plasma and tissues corresponded to cerebral edema progression and that BK suppression decreased edema formation in spontaneously hypertensive rats with bilateral common carotid artery occlusion. It was also demonstrated that, in the ischemic neuronal models, ischemia significantly increased NE release in rat spinal cord. These observations might propose that BK as well as catecholamines might have a crucial role in the pathophysiology of ischemia and edema of neuronal tissues. Therefore, we would like to know whether the contents of BK and catecholamines in the injured regions might be changed in the B1R knockout mice compared with wild-type mice in the study of Dr Austinat and colleagues. Further studies should be performed to assess more precisely the relationships between BK and catecholamines, and their contribution to the pathogenesis of cerebral infarction and brain edema.

Disclosures

None.

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Stroke. 2009;40:e103; originally published online March 5, 2009;
doi: 10.1161/STRK.109.547752
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

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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