Regarding Article “Receptor Activity-Modifying Protein-1 Augments Cerebrovascular Responses to Calcitonin Gene-Related Peptide and Inhibits Angiotensin II-Induced Vascular Dysfunction”

To the Editor:

We read with great interest the recent article by Dr Chrissobolis and colleagues1 dealing with the cerebrovascular responses in the transgenic mice with overexpression of the receptor activity-modifying protein-1 (RAMP1) for calcitonin gene-related peptide (CGRP) receptors. The results of their study demonstrated that the responses to CGRP in carotid and basilar arteries in vitro as well as cerebral arterioles in vivo were selectively enhanced in human RAMP1 transgenic mice compared with controls. In addition, the authors presented that angiotensin II-induced oxidative stress and endothelial dysfunction was prevented after expression of RAMP1. The authors propose the hypothesis that RAMP1 may be an important mediator of vascular protection and a new therapeutic target in vascular disease.

Several studies have reported that enhanced activity of the sympathetic nervous system might actively participate in the pathogenesis of vascular dysfunction. In a study we presented previously, the changes in norepinephrine release induced by CGRP was investigated in the rat central nervous system.2 In an in vitro study, we showed that CGRP inhibited the stimulation-evoked norepinephrine release in a dose-dependent manner. It was also demonstrated that a dihydropyridine-sensitive calcium channel agonist, Bay K 8644, significantly reversed the inhibitory effect of CGRP on norepinephrine release, indicating that CGRP might partially interact with dihydropyridine-sensitive calcium channels and modulate intracellular calcium mobilization. Furthermore, we showed that the inhibitory action on CGRP on norepinephrine release was significantly attenuated in spontaneously hypertensive rats compared with normotensive rats.3 In the peripheral tissues, Ohhashi and Jacobowitz4 observed that CGRP might have reduced the electric stimulation-induced contraction of rat vas deferens, suggesting that CGRP might inhibit norepinephrine release during adrenergic nerve stimulation. It can be speculated that the sympatholytic action of CGRP might be a defense against vascular dysfunction. Because angiotensin II may stimulate the sympathetic neurotransmission in the central nervous system,5 we would like to know whether changes in sympathetic nervous activity might be associated with the magnitude of the RAMP1 overexpression or whether CGRP might suppress the angiotensin II-induced sympathetic hyperactivity in the study of Dr Chrissobolis and colleagues. Further studies should be performed to assess more thoroughly the interactions between CGRP and the sympathetic nervous system and their role in the protective effect against the angiotensin II-induced vascular dysfunction in the RAMP1 transgenic mice.

Disclosures

None.

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