To the Editor:

We read with great interest the article by Dr Peña-Silva and colleagues1 dealing with the relationship between angiotensin-converting enzyme type 2 (ACE2) and cerebrovascular function in mice. The results of their study demonstrated that vasodilation of cerebral arteries to acetylcholine was significantly reduced in adult ACE2 knock-out (KO) mice compared with wild-type (WT) mice, indicating that genetic deficiency of ACE2 impaired endothelial function in the cerebral arteries. The cerebrovascular dysfunction during aging was greater in ACE2 KO mice than in WT mice. In addition, because tempol significantly improved endothelial function in adult and old ACE KO and WT mice, it is suggested that oxidative stress might play a key role in cerebrovascular dysfunction with ACE2 deficiency and during aging. The authors proposed that by modulating the effects of angiotensin II (Ang-II), ACE2 might play an important role in the maintenance of vascular function and prevention of cerebrovascular disease.

Evidence indicates that ACE2–Ang-(1–7)–Mas receptor axis might have an opposite effect against classical ACE–Ang-II–Ang type 1 (AT1) receptor pathway and actively participate in the mechanisms of cardiovascular protection.2 In a study presented previously, it was demonstrated that Ang-(1–7) and bradykinin can interact to modulate cardiovascular responses, such as baroreflex control of the heart rate, suggesting that the centrally modulatory effect of Ang-(1–7) might be mediated, at least in part, by the release of kinins.3 Gironacci et al4 demonstrated that Ang-(1–7) decreased K+-induced norepinephrine release in the hypothalamus of spontaneously hypertensive rats by the nitric oxide and bradykinin B2 receptor–dependent mechanisms. It can be speculated that the interactions among Ang-(1–7), nitric oxide, and bradykinin might have a crucial role in the regulation of cerebrovascular functions. Recently, it was demonstrated that both Ang-(1–7)- and bradykinin-induced relaxations of rat mesenteric arteries were augmented by the renin–angiotensin system–related vascular effect of casein-derived tripeptide.5 Therefore, we would like to know whether bradykinin-induced vasodilatory effect might be altered in ACE KO mice in the study of Peña-Silva et al. It would be important to assess more precisely the links between Ang-(1–7) and bradykinin, and their role in the preventive effects against vascular damage in ACE2 deficiency.

Disclosures

None.

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Letter by Tsuda Regarding Article, "Impact of ACE2 Deficiency and Oxidative Stress on Cerebrovascular Function With Aging"
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