Response to Letter Regarding Article, “Impact of ACE2 Deficiency and Oxidative Stress on Cerebrovascular Function With Aging”

We appreciate the interest of Dr Tsuda in our study. In our article we showed that angiotensin-converting enzyme type 2 (ACE2) deficiency is associated with impaired endothelial function in cerebral arteries from adult mice and augmented endothelial dysfunction during aging. In those experiments, we used acetylcholine to gain insight into endothelial function because acetylcholine is also a neurotransmitter known to be involved in regulation of cerebral blood flow. Dr Tsuda asked whether we assessed vasodilator effects of bradykinin.

We did not test endothelium-dependent responses to bradykinin or expression of molecules of the kallikrein–kinin system in our study of ACE2-deficient mice. Previous studies suggest that interaction between these 2 systems is important for the regulation of vasomotor function in the cerebral vasculature. First, bradykinin dilates cerebral arteries in humans and in several animal models. Second, responses to angiotensin 1-7 in the cerebral circulation may be mediated in part by bradykinin. Third, angiotensin 1-7 may indirectly increase bradykinin levels. Fourth, bradykinin receptor signaling is affected by heterodimerization with other angiotensin receptors. It is possible that the angiotensin 1-7 receptor (Mas) may dimerize with bradykinin receptors and alter their signaling. Thus, responses and the impact of bradykinin in the cerebral circulation may be altered in mice genetically deficient in ACE2 or mas receptors.

Disclosures
None.

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