Letter to the Editor

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Letter by Shang Regarding Article, “Relative Contributions of Sympathetic, Cholinergic, and Myogenic Mechanisms to Cerebral Autoregulation”

To the Editor:

The recent publication by Hamner and Tan, titled Relative Contributions of Sympathetic, Cholinergic, and Myogenic Mechanisms to Cerebral Autoregulation,1 was of great interest to our group. They analyzed the relationship between specific physiological mechanisms of autoregulation and the overall cerebral pressure–flow relationship. Using projection pursuit regression analysis and ANCOVA decomposition, they were able to analyze the relative contribution of sympathetic, cholinergic, and myogenic mechanisms to cerebral autoregulation, which accounted for 62% of the total cerebral pressure–flow relationship. However, 38% of the cerebral pressure–flow relationship was unexplained. The possible contribution of intrinsic mechanical vessel properties to the cerebral pressure–flow relationship was investigated by testing the pressure–flow relationship on human brachial artery after blockage of sympathetic control. They found that the pressure–flow relationship was mostly linear. Similar linear responses were observed in study of denervated animal middle cerebral artery. Thus, the authors concluded that the intrinsic resistance artery properties could not explain the remaining nonlinearity in the pressure–flow relationship, and therefore could not contribute the 38% of unexplained cerebral autoregulation.

The authors should be congratulated for their great effort in elucidating the complex cerebral autoregulation process. Cerebral autoregulation not only involves multiple systems, including neurogenic, myogenic, and metabolic mechanisms, but also develops segmental regulation pathways.2,3 One of the manifestations of cerebral autoregulation complexity is the varied neurogenic reactivity because cerebral vessels branch down from the pial artery to parenchymal artery.4,5 Both the pial artery and the parenchymal artery contribute almost equally to the cerebral vascular resistance system, and thus, cerebral autoregulation. However, there are fundamental differences between the pial artery and the parenchymal artery. The pial artery receives perivascular innervation from peripheral nervous system, such as superior cervical ganglion and trigeminal ganglion (extrinsic innervation). However, the parenchymal artery is innervated by nerve afferents from subcortical neurons, such as locus coeruleus and raphe nucleus (intrinsic innervation).6,7 Furthermore, there is heterogeneity in neurogenic reactivity in the pial and parenchymal arteries. The β-adrenoceptor reactivity is absent in the parenchymal artery because of a shift in the expression of α- to β-adrenoceptor receptor.4 Similar heterogeneity has been shown with the serotonin receptor.4 For example, some neurotransmitters (serotonin and norepinephrine) have a marked constrictive effect on the large cerebral pial artery but not on the parenchymal artery. In contrast, these neurotransmitters either have no effect on or dilate the parenchymal artery.4,5 Another interesting characteristic of the cerebral parenchymal artery is that it possesses greater basal tone when compared with the pial artery.2 Under this basal tone, pressure-induced myogenic reactivity in parenchymal artery is minimal when compared with corresponding changes in the pial artery.5 In sum, these findings suggest that the parenchymal artery may have additional or different mechanisms, when compared with the pial artery, in regulating cerebral autoregulation.

Considering the anatomic and functional differences between the intracranial and the extracranial artery, between the pial and the parenchymal artery, current data from human brachial artery and animal middle cerebral artery may not be readily applicable to the parenchymal artery. The nonlinear pressure–flow relationship may exist in the parenchymal artery because of its unique intrinsic property and its interaction with regulatory mechanisms. In addition to the mechanisms discussed extensively in the study, other important and recognized mechanisms in cerebral autoregulation include metabolic and monooxygenase mechanisms. Particularly, it is reasonable to postulate the critical role of a serotoninergic mechanism in cerebral autoregulation, considering the broad distribution of serotonin receptors and its potent function on vascular reactivity in intracranial arteries. Thus, it is possible that the intrinsic reactivity of the parenchymal artery could contribute to the unexplained 38% of cerebral autoregulation. More research is required for a reliable analysis of the complex mechanisms of cerebral autoregulation.

Disclosures

None.

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