Reply to “Letter to the editor: ‘Targeting cerebrovascular myogenic dysfunction in stroke’”

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REPLY: We thank Dr. Jiménez-Altayó and colleagues (4) for providing feedback to our article published in the American Journal of Physiology-Heart and Circulatory Physiology, entitled “Protein nitration impairs the myogenic tone of rat middle cerebral arteries in both ischemic and nonischemic hemispheres after ischemic stroke” (3).

We set our experiments to determine if ischemia-reperfusion injury has a global effect on both hemispheres and to identify the possible mechanisms underlying this effect. To answer these questions, middle cerebral arteries were isolated from ischemic and nonischemic hemispheres after 30 min ischemia and 45 min reperfusion, and their myogenic behaviors were determined. Our results showed that ischemia-reperfusion injury impaired myogenic function in both hemispheres, which was restored by scavenging peroxynitrite or inhibiting nitration. Therefore, our study design specifically the short-term effect of ischemia-reperfusion injury on the vascular function of both hemispheres.

The question raised by Jiménez-Altayó et al. (4) about the impact of these treatments on stroke outcomes is highly significant but was out of the scope of the mentioned study (3). However, we recently showed that contralateral myogenic dysfunction was exacerbated in conditions characterized with poor stroke outcomes as acute hyperglycemic stroke. Moreover, we found that augmented contralateral myogenic dysfunction was associated with infarct size, edema expansion together with poor behavioral outcomes (1). Currently, we are investigating, 1) the impact of depleting one of the parent radicals of peroxynitrite on myogenic tone impairment after short term of acute hyperglycemic stroke and 2) the impact of improving myogenic dysfunction on neurovascular outcomes. Part of this work was presented at the International Stroke Conference 2014 (2).

The second question raised by Jiménez-Altayó et al. (4) was about the possibility of preventing/reversing myogenic impairment within a reasonable time window. Our laboratory previously studied the effect of scavenging peroxynitrite on vascular injury and functional outcomes in a diabetic model of acute ischemic stroke. Diabetic rats were subjected to 3 h ischemia, followed by 21 h of reperfusion, and acute treatment with 5,10,15,20-tetrakis-(4-sulfonatophenyl)porphyrinato iron (III) (FeTPPs), a peroxynitrite scavenger, was administered at reperfusion. We found that scavenging peroxynitrite at reperfusion reduced stroke-mediated micro- and macroscopic bleeding together with functional impairment in diabetes (6). Although we did not measure myogenic behavior in those rats, in another ex vivo study we showed that hypoxia led to myogenic tone impairment in diabetic rats. Acute treatment with FeTPPs at reoxygenation prevented that loss of tone (5). The findings of both studies suggested that scavenging peroxynitrite in diabetic stroked rats decreased bleeding and edema via preventing the peroxynitrite-mediated loss of myogenic reactivity. Further studies need to be done to confirm long-term myogenic impairment on stroke outcomes and to identify the reasonable time window for restoring myogenic behavior.

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AUTHOR CONTRIBUTIONS
M.C. drafted manuscript; M.C. and A.E. edited and revised manuscript; M.C., W.L., M.J., S.C.F., and A.E. approved final version of manuscript.

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