Reply to Zhang

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TO THE EDITOR: We appreciate the opportunity to further discuss the effects of spaceflight on the cerebral circulation. Dr. Zhang’s letter (6) emanates from the multiple observations that in head-down hindlimb-unloaded (HU) rats, an animal model used to simulate microgravity exposure, the cerebral arteries demonstrate greater vasoconstrictor responsiveness and hypertrophic remodeling (e.g., 5) that result in lower brain blood flow and higher cerebral vascular resistance (5). In contrast, two studies have now shown that cerebral artery vasoconstrictor responsiveness is decreased in mice flown on the Space Shuttle (4) and Bion-M1 Biosatellite (3). Dr. Zhang suggests this discrepancy is based on an increase in cerebral artery transmural pressure in HU rats, which is also assumed to occur in astronauts and cosmonauts, but not in space-flown mice. This suggestion implies that the HU rat may be a better animal model for elucidating microgravity-induced cerebrovascular adaptations in humans than space-flown mice.

Although we understand Dr. Zhang’s reasoning and agree that the lack of a fluid shift in mice is a clear limitation of the model, we disagree that the findings of cerebral artery adaptations in space-flown mice are not directly applicable to humans for several reasons. First, the microgravity-induced cephalic fluid shift in humans will undoubtedly elevate intravascular pressure in cerebral arteries. However, the extent to which cephalic fluid shifts increase extravascular intracranial pressure remains unknown. If intracranial pressure is elevated to the same extent as intravascular pressure, then cerebral artery transmural pressure will remain unchanged, similar to what is presumed to occur in space-flown mice. Second, although the human spaceflight literature is mixed, the preponderance of evidence indicates that cerebral perfusion is elevated in cosmonauts and astronauts, but not in space-flown mice. Such findings lead us to believe that multiple factors are acting on the cerebral circulation in space, and although current ground-based animal and human models are useful for developing hypotheses, they are not a substitute for flight studies.

We are a long way from fully elucidating the effects of spaceflight on the cerebral circulation, but these two flight studies with mice (3, 4) provide a valuable glimpse into these effects. Continued international cooperation is vital for this effort to be successful, including the valuable contributions Dr. Zhang has made in expanding our understanding of the effects of microgravity on cerebrovascular adaptations.

DISCLOSURES
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REFERENCES