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***Reply:***

D.R. Roberts, D. Asemani, P.J. Nietert, M.A. Eckert, D.C. Inglesby, J.J. Bloomberg, M.S. George and T.R. Brown

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**REPLY:**

**W**e thank Drs Bevelacqua, Welsh, and Mortazavi for their interest in our article, “Prolonged Microgravity Affects Human Brain Structure and Function.” We disagree, however, that we have ignored the multiple unique features of the spaceflight environment to which astronauts are exposed and that “this omission has possibly affected the validity of the findings.”

As we stated in the article, many factors affect individual astronaut performance. These factors include psychological stress, gravitational changes, and radiation exposure as highlighted in the letter of Drs Bevelacqua, Welsh, and Mortazavi. Other unique characteristics of the spaceflight environment include elevated carbon dioxide levels, cephalad fluid shifts, and unique microbial habitats among others. Any of these factors may act individually or in synergy to result in the changes in brain structure and cognitive function that we have documented in astronauts after spaceflight.

Our study highlights the need for further investigations of human brain adaptation to spaceflight to disentangle the relative contribution that each factor, including radiation exposure, may

have on brain health. This work will be important in guiding the development of effective countermeasures protecting brain function in support of future human spaceflight.


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