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LETTER

The effect of long-duration spaceflight on perivascular spaces within the brain

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We read with great interest and enthusiasm the article by Barisano et al. (1) entitled "The effect of prolonged spaceflight on cerebrospinal fluid and perivascular spaces of astronauts and cosmonauts" published recently in PNAS. We would like to congratulate the authors for performing this MRI study with findings of great importance for future long-duration human space missions, and would appreciate the opportunity to make a comment.

In this MRI study, Barisano et al. (1) assess the preflight to postflight alterations in multiple cerebrospinal fluid (CSF) compartments, including perivascular spaces (PVS), across space crews from different space agencies. The authors analyzed brain MRI scans acquired before and within the first 2 wk after long-duration spaceflight on the International Space Station in 24 NASA astronauts, 13 Roscosmos (ROS) cosmonauts, and a small group of European Space Agency astronauts. White matter (WM) and basal ganglia PVS volumes were found to be significantly increased after long-duration spaceflight, with significantly greater percentage enlargements in NASA astronauts compared to ROS cosmonauts. WM-PVS enlargement was significantly correlated with reduction of the subarachnoid space at the vertex. Further, changes in WM-PVS were significantly correlated with mission duration.

PVS are key anatomical components of the recently discovered glymphatic system (2), and some studies have speculated that enlarged PVS may be a manifestation of dysfunction of this perivascular pathway (3). In a very recent article, we speculated that the enlargement of PVS observed in long-duration space travelers may result from impaired cerebral venous outflow and compromised CSF resorption, leading to obstruction of glymphatic perivenous outflow and increased periarterial CSF inflow, respectively (4). We hypothesized that the cephalad venous fluid shift experienced during spaceflight may increase the hydraulic resistance of perivenous spaces. Indeed, blood volume in cerebral veins may increase as a result of a microgravity-induced decrease in cerebral venous outflow (5), which, in turn, may lead to closure of the perivenous spaces. This may compromise the glymphatic CSF-interstitial fluid (ISF) outflow from the interstitial tissue, resulting in CSF-ISF stagnation. As a consequence, the CSF may stagnate and accumulate at the periarterial site with simultaneous dilation of the periarterial spaces. Furthermore, given that the venous and lymphatic CSF outflow pathways may be compromised due to the microgravity-induced headward fluid shifts (6), and given the chronic, mildly elevated intracranial pressure in space (7), the question is whether these factors could further drive CSF into the periarterial spaces, causing further fluid accumulation and enlargement of periarterial spaces. From this point of view, it can be anticipated that, especially, the periarterial spaces become enlarged under prolonged microgravity conditions. With regard to this hypothesis, it would be interesting to know whether the enlarged PVS observed in space crews were arteriolar, venular, or both. We therefore wonder whether Barisano et al. (1) were able to distinguish whether the dilated PVS were periarteriolar and/or perivenular, and whether the authors have such data for review.

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The authors declare no competing interest.

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