Enlargement of Perivascular Spaces as a Downstream Consequence of Spaceflight Analog-Induced Alterations in Cerebral Venous Hemodynamics

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We read with great interest the article by Tidwell and colleagues[1] entitled "Longitudinal Changes in Cerebral Perfusion, Perivascular Space Volume, and Ventricular Volume in a Healthy Cohort Undergoing a Spaceflight Analog" published recently in the *American Journal of Neuroradiology*. We would like to congratulate the authors for performing this MR imaging study in a spaceflight analog with findings of great importance for future human space missions, and would appreciate the opportunity to make a comment.

The authors evaluated the relationship among changes in cerebral perfusion, ventricular volume, and perivascular space (PVS) volume in healthy participants before, during, and after a spaceflight analog comprising 30 days of 6° head-down tilt (HDT) bed rest combined with 0.5% atmospheric CO_2.[1] Global perfusion decreased during the analog period, whereas ventricular volume and PVS volume increased. This was followed by a reversal of these patterns during the 2-week recovery period. The authors correctly state that an increase in PVS volume may reflect obstruction or inefficiency in the exchange of CSF and interstitial fluid (ISF) that occurs in the perivascular channels. Given the negative correlation between cerebral perfusion and PVS volume seen in their study and given that CSF is driven through PVS by arterial pulsations, they propose that decreased perfusion could reduce the ability to circulate CSF, causing the observed PVS dilation.

Here, we propose an additional alternate mechanism to explain how altered hemodynamics in real and simulated microgravity may contribute to PVS dilation. In a recent article, we speculated that altered venous hemodynamics during spaceflight may cause disruption of the glymphatic system.[2] Microgravity has been demonstrated to cause stagnation and even reversal of the cerebral venous outflow in the internal jugular veins of a long-duration International Space Station crew.[3] This finding suggests that spaceflight may cause venous congestion and even some degree of retrograde blood flow from the central veins through the internal jugular vein into the brain. Signs of cerebral venous congestion have also been demonstrated in an HDT microgravity analog setting.[4] Cerebral vein distention could then increase the hydraulic resistance of perivenous spaces, given that increased blood volume in the cerebral veins may result in closure of the perivenous spaces.[2] This outcome could compromise the glymphatic outflow and drainage, resulting in CSF-ISF stagnation. As a consequence, the CSF may stagnate and accumulate at the periarterial site, with resultant periarterial dilation.[2] We propose that this could provide an additional alternate explanation for the observed PVS enlargement during the analog period.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

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