EFFECTS OF ELEVATED CO_2 ON GLYMPHATIC FUNCTION

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The microgravity environment of the International Space Station (ISS) has several known effects on the nervous system including ventricular expansion and an upward shift of the brain within the skull. Moreover, the enclosed environment of the ISS results in elevated CO_2 levels in comparison to ambient air on Earth [1,2,3]. Research with rodent models has shown that elevated CO_2 impairs function of the glymphatic system, a perivascular fluid transport pathway responsible for facilitating metabolic waste circulation and clearance through the brain [4,5,6]. Disruption of the glymphatic system has been linked to the increased protein aggregation found in neurodegenerative diseases such as Alzheimer's and Parkinson's diseases and has been thought to potentially play a role in Spaceflight-Associated Neuro-ocular Syndrome (SANS) [6,7]. Comprehensive understanding of the effects of extreme environments on glymphatic clearance is therefore important to maintain and improve astronaut health. Here, we assessed the effect of breathing carbon dioxide mixes on glymphatic clearance in comparison to an ambient air control, using percent change in brain tissue signal intensity over time following intravenous injection of a gadolinium-based contrast tracer.

Twelve healthy adults were each randomly assigned one of three carbon dioxide gas mixes (1%, 1.5%, 2% CO_2; 4 participants per group), counterbalanced with an ambient air session. They were then injected with a gadolinium-based contrast agent and imaged at 0 (pre-injection), 90, and 360 minutes post-injection to trace the percent change in signal intensity from baseline. These timepoints were selected based on a previous pilot study we conducted with more frequent sampling over time [8]. The imaging sequences included T1, T1 Black Blood, T2 FLAIR, rapid fMRI, and intravoxel incoherent motion (IVIM) scans. Participants remained supine for the duration of the protocol (within and without the scanner) and focused on a projected cross during the rapid fMRI. Participants also completed the Defense Automated Neurobehavioral Assessment (DANA) Rapid battery and underwent ultrasound imaging of the internal jugular vein and optic nerve after each scan, as well as blood draws after their first and final scans. This protocol was repeated in full for each participant's second scanning session. Sessions were separated by at least 30 days to mitigate any confounding effects from potential gadolinium deposition.

Preliminary results suggest a difference in signal intensity percent change between the 2% CO_2 group and their ambient data in a few regions of interest, indicating that glymphatic clearance is slowed under hypercapnic conditions. This effect seems less pronounced in the 1 and 1.5% CO_2 groups, though further within-subject analyses are needed to confirm; these additional statistical analyses are currently ongoing.

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References

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