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SPACEFLIGHT IMPACTS ON NEUROVASCULAR REMODELING AND BARRIER FUNCTION

Abstract

The health risk from spaceflight-induced neuronal damage and potential adverse neurovascular effects are a chief concern. The goal of the present study was to characterize the effects of spaceflight on the structure and function of the mouse brain and blood-brain barrier (BBB) integrity. To investigate possible mechanisms, changes in protein expression profiles were examined in mouse brain tissue after spaceflight. Metabolic changes associated with physiological response to spaceflight exposure were also characterized. Ten week old male C57BL/6 mice were launched to the International Space Station (ISS) on Space-X 12 at the Kennedy Space Center (KSC) on August, 2017. After a 35-day mission, mice were returned to Earth alive. Within 38+/-4 hours of splashdown, mice were euthanized and brain tissues were collected for analysis. Ground control (GC) and vivarium control mice were maintained on Earth in flight hardware or normal vivarium cages respectively. Quantitative assessment of brain tissue demonstrated that the flight group had significant apoptosis in the brain and hippocampal vascular endothelial cells compared to control groups ($p < 0.05$). Immunohistochemical analysis of the brain revealed that an increased expression of aquaporin-4 (AQP-4) in the flight mice compared to controls gave strong indication of disturbance of BBB integrity. There were also a significant increase in the expression of platelet endothelial cell adhesion molecule-1 (PECAM-1) and a decrease in the expression of the BBB-related tight junction protein, Zonula occludens-1 (ZO-1). Levels of 4-hydroxynonenal (4-HNE) protein, an oxidative specific marker for lipid peroxidation were significantly elevated in the brain after spaceflight compared to controls. Quantitative proteomic analysis showed that many proteins and pathways responsible for mitochondrial function, nervous system development, behavior, protein/organelle transport and metabolism were significantly altered after spaceflight in the brain. Pathways associated with adhesion molecular remodeling was also significantly altered. Our data demonstrate that exposure to the spaceflight environment induces significant changes in protein expression related to neuronal structure, neurovascular integrity and metabolic function.