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RETINAL HAEMODYNAMICS IN RESPONSE TO SIMULATED SPACE STRESSORS: HEAT, EXERCISE AND EMULATED MICROGRAVITY

Abstract

The etiology of space-associated neuro-ocular syndrome (SANS) remains unclear. Recent mouse studies indicate there may be a link between changes in the mechanical environment during microgravity exposure and retinal endothelial dysfunction. In concert, documented increases in core temperature during spaceflight may have implications for thermoregulatory and cerebrovascular function in humans. Ground-based inter-species experiments of responses to lower body elevation, heat and exercise, coupled with fluid simulation, may help to inform these impacts.

We investigated endothelial dysfunction and haemodynamics in control (n=4) and tail suspended (TS) (n=4) mice eye samples stained for apoptotic regions co-located with the vessel plexus using confocal imaging and three-dimensional (3D) computational fluid dynamics simulation (CFD). Separately, we exposed young healthy human participants (n=12) to passive heating (PH) and heated exercise (HE) in a climate-controlled chamber (50 mins, 40°C). We measured blood flow responses in the common carotid (CCA), internal carotid (ICA) and central retinal (CRA) arteries using ultrasound, as well as microvascular blood flow responses in the skin using optical coherence tomography angiography and in the retinal arterioles using 3D CFD.

In mice, structural changes were found in TS samples compared to controls, and wall shear stress (WSS) and pressure were higher in the TS cohort, particularly in smaller vessels ($<10\mu$m, WSS: P=0.034, pressure: P=0.004). Apoptosis was variable in TS mice compared to controls, and WSS and pressure were generally higher in these regions, but significance was variable and limited to small to medium sized vessels ($<20\mu$m). In human participants, PH responses demonstrated increased skin blood flow (P<0.001), while CRA flow decreased (P=0.038) despite unchanging ICA flow. HE further exacerbated these differences, with increased CCA flow (P=0.007), unchanging ICA flow, decreased CRA flow (P<0.001), and interactions between vascular (CCA vs. ICA P=0.018; CCA vs. CRA P=0.004) and microvascular (skin vs. retinal arteriolar P<0.001) territories. Furthermore, simulations revealed uniform patterns of decreased retinal WSS following HE.

Our murine findings suggest a link may exist between emulated microgravity and retinal endothelial dysfunction. In concert, our human findings indicate different responses occur in distinct vascular territories under challenging conditions – with blood flow distribution favouring systemic thermoregulation while flow may redistribute within the brain. Together these findings suggest there may be haemodynamic changes that occur during spaceflight, which may have implications for SANS development.