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Hypergravity Exposure Induces Alterations Of Erythrocyte Membrane And Antioxidant Potential Of Mice Housed In The MDS Facility

All living organisms have evolved and adapted to live under Earth's gravitational force. To sustain safe human space exploration, it is important to understand how the different effectors, including gravitational force, influence organisms. Altered levels of gravity affect the physiological function of multiple tissues, cells, and organs in living organisms. Many adverse conditions present in Space, such as hypoxia, hypothermia, and microgravity, cause integrated alterations in the lipid membrane composition, inducing greater sensitivity to oxidative stress. Indeed, previous studies, also from our laboratory, suggested that microgravity modifies the permeability of the plasma membrane and cellular metabolism in erythrocyte, modifying cholesterol and phospholipid levels. In addition, hypergravity also affects the physiological functions of tissues and organs; furthermore, the evaluation of the effects of the hypergravity is a fundamental step towards complete knowledge of the physiological response to altered gravity. Aim of this study was to investigate in vivo the effects of hypergravity on lipid phenotype and metabolism in mice erythrocytes. Animals were housed in the Italian Space Agency's Mice Drawer System (MDS), a facility designed to house rodents on the ISS and adapted by Thales Alenia Space to the Large Diameter Centrifuge (LDC-ESA), to expose mice to a 3xg environment. Vivarium animals and MDS-like cage animals were compared as controls. After 30 days of experiment a tissue sharing protocol was performed among international researchers, to analyze all the tissue specimens. We purified and analyzed the red blood cells from whole blood. The membrane lipid phenotype was assessed by gas-chromatography and liquid-chromatography. Finally, to analyze the impact on oxidative homeostasis, the hemolyzed fractions were used to test antioxidant enzyme activities. Our results show that the exposure of mice to an altered gravity induced a modification in the fatty acid composition of 3xg mice compared to control mice, indicating a direct effect of the increased level of gravity. The cholesterol content in membranes was significantly increased. To evaluate the effect of hyper-gravity conditions on the animal's inflammatory and metabolic processes, the ratio between inflammatory eicosanoids and anti-inflammatory eicosanoid precursors was calculated, and a slight reduction in the inflammation index given by arachidonic acid/eicosapentaenoic acid ratio was observed. These findings could be due to a process of metabolic compensation during long-term exposure that leads to a resolution of inflammation. To evaluate the impact of fatty acid composition on the potential level of oxidative stress, we calculated the peroxidability index (PI), which measures the sensitivity of fatty acids to peroxidation; PI was significantly increased under 3xg conditions. Furthermore, we have analyzed the endogenous antioxidant activity in the hemolysate of scavenging enzymes, and the amount of glutathione content in the red blood cells. The enzyme activity of GSH peroxidase shows a significant increase in 3xg mice compared to control mice. This study demonstrates that hypergravity induces changes in both lipid composition and antioxidant system of erythrocytes. Our results will be integrated with other tissue and metabolic data obtained by other researchers of the team. Further studies will be necessary to identify possible countermeasures to ensure an adequate level of crew health and safety during long-duration space missions.

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