Hyper-gravity Exposure Induces Alterations Of Erythrocyte Membrane And Antioxidant Potential Of Mice Housed In The MDS Facility

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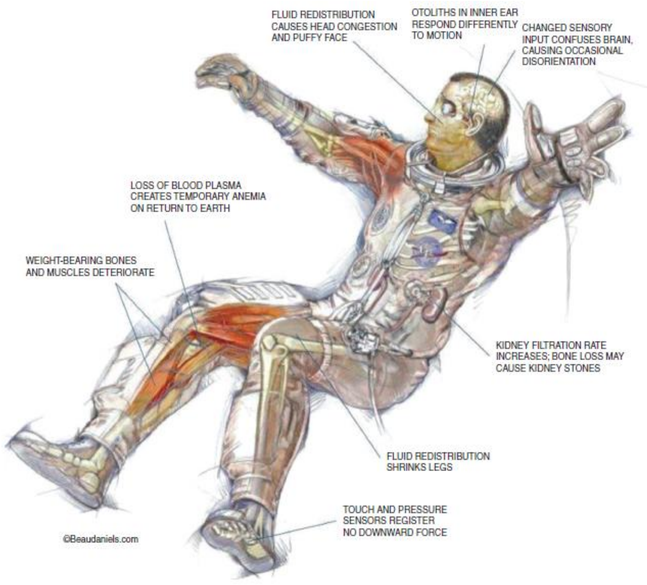
Abstract

All terrestrial organisms have evolved and adapted to live under Earth's gravitational force. Altered levels of gravity affect the physiological functions 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. Previous studies suggested that microgravity modifies the permeability of the plasma membrane and cellular metabolism in erythrocytes, modifying cholesterol and phospholipid levels. Hypergravity also affects the physiological functions of tissue and organs. The evaluation of the effects of hyper-gravity is a fundamental step toward complete knowledge of the physiological response to altered gravity



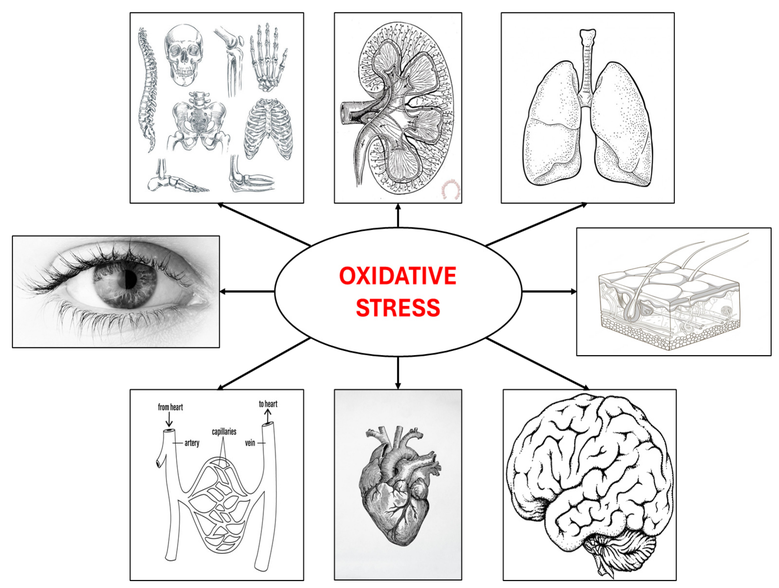


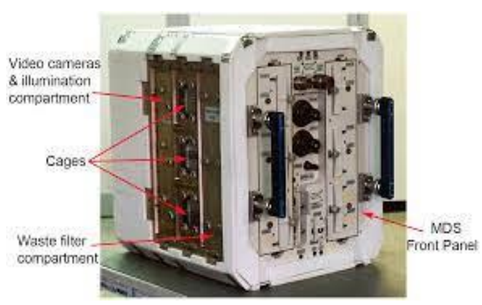
Figure 1A: effects of space flight on the human body [1] **Figure 1B:** effects of oxidative stress

○ **This study aims to investigate the *in vivo* effects of hypergravity on lipid phenotype and metabolism in mice erythrocytes.**

Materials and Methods

Exposition of mice within the MDS module to a hypergravity condition using the LDC centrifuge for 27 days

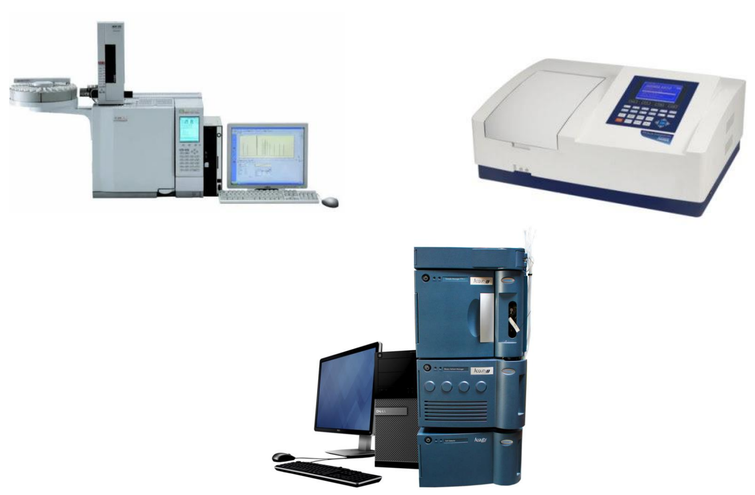
The LDC centrifuge (ESA)



The MDS facility (ASI-Thales)

Collection of blood and plasma samples from mice under study during the tissue sharing phase performed in Leiden (NL), March 2023.

Lab Analyses of the anti-oxidant enzyme activity and the alteration of cell membrane lipid composition induced by gravity field variations (GC- UPLC, etc.).



Results:

V = Vivarium; GC = Ground Control; 3xg = Mice exposed to Hyper-gravity condition.

Table 1: Fatty acids distribution of red blood cell membranes purified from mice of the MDS experiment.

Fatty Acid	V	GC	3xg	P.value	
				3xg / V	3xg / GC
C16:0	26.2 ± 0.40	26.1 ± 0.29	25.4 ± 0.32	***	****
C16:1	0.92 ± 0.10	1.00 ± 0.055	0.77 ± 0.075	***	****
C18:0	11.9 ± 0.59	12.0 ± 0.52	12.6 ± 1.07	NS	NS
C18:1	11.0 ± 0.28	11.2 ± 0.21	10.2 ± 0.27	***	****
C18:2 n-6	12.6 ± 0.58	12.0 ± 0.41	13.2 ± 0.95	NS	**
C18:3 n-3	0.18 ± 0.022	0.19 ± 0.027	0.17 ± 0.021	NS	NS
C18:3 n-6	0.57 ± 0.052	0.58 ± 0.064	0.58 ± 0.058	NS	NS
C20:3 n-6	1.86 ± 0.11	1.92 ± 0.11	1.62 ± 0.11	***	****
C20:4 n-6	22.6 ± 0.53	22.4 ± 0.44	22.5 ± 0.61	NS	NS
C20:5 n-3	0.73 ± 0.063	0.74 ± 0.03	0.80 ± 0.058	*	*
C22:5 n-3	1.20 ± 0.085	1.21 ± 0.10	1.28 ± 0.062	*	NS
C22:6 n-3	10.0 ± 0.18	10.3 ± 0.29	10.5 ± 0.26	***	NS
MUFA	11.9 ± 0.35	12.2 ± 0.21	11.0 ± 0.31	****	****
Omega-6	37.2 ± 0.49	36.6 ± 0.46	37.6 ± 1.31	NS	*
Omega-3	12.5 ± 0.21	12.8 ± 0.32	13.2 ± 0.28	****	*

Mean±DS (n=12 GC and V; n=11 3xg). *p<0.05, **p<0.01, ***p<0.001 ****p<0.0001

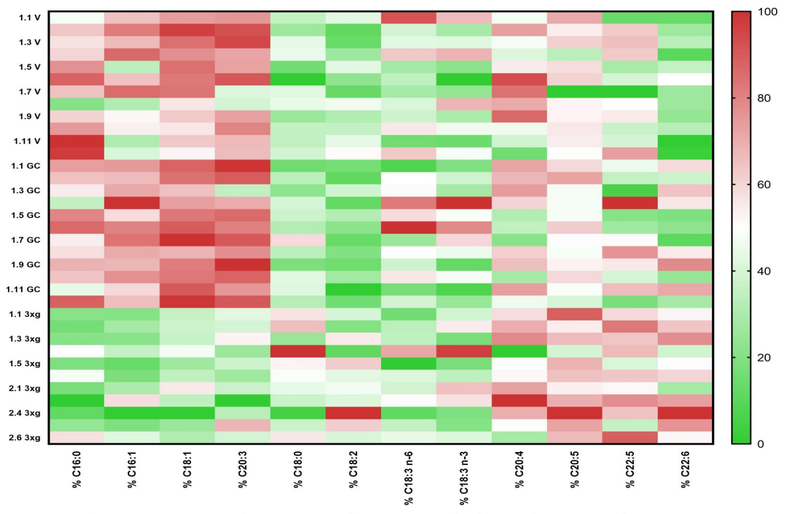


Figure 2: Erythrocyte fatty acid distribution heat map

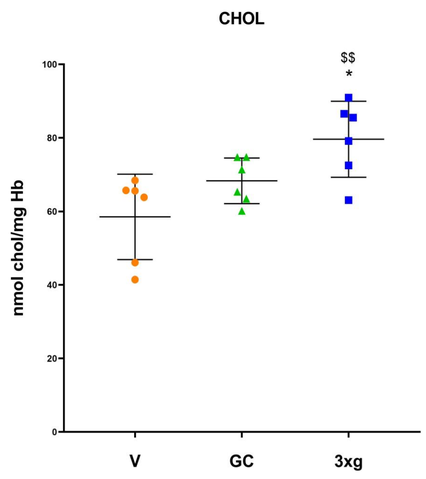


Figure 3: Cholesterol content.

* P-value < 0.05 vs TC; $$ P-value <0.01 vs Vivarium

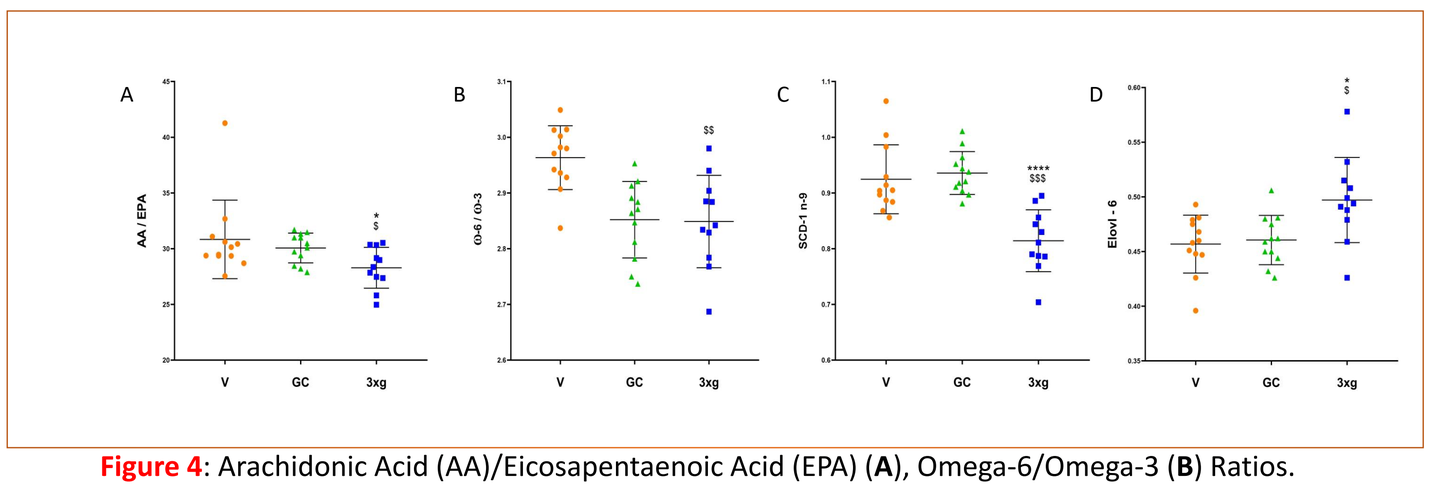


Figure 4: Arachidonic Acid (AA)/Eicosapentaenoic Acid (EPA) (**A**), Omega-6/Omega-3 (**B**) Ratios. SCD-1 n-9 (**C**), elongase Elovl-6 (**D**) estimated activities.

* P-value < 0.05; **** P-value < 0.0001 vs TC; $ P-value < 0.05; $$ P-value <0.01; $$$ P-value < 0.001 vs Vivarium

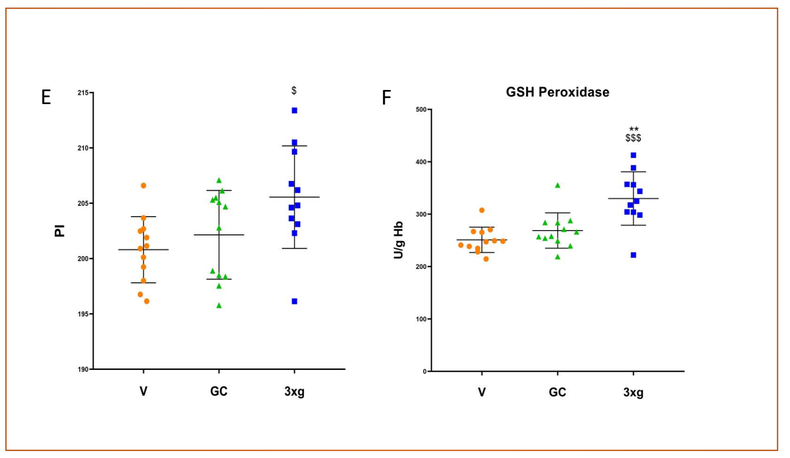


Figure 5: peroxidability index (PI) (**E**) and GSH peroxidase (**F**) antioxidant activity .

** P-value < 0.01 vs TC; $ P-value < 0.05; $$$ P-value < 0.001 vs Vivarium

- Decrease of monounsaturated fatty acid and increase of polyunsaturated fatty acid in 3xg mice compared to Ground Control and Vivarium mice.
- Slight reduction in the inflammation index given by the AA/EPA and omega-6/omega-3 ratio compared to the Ground Control mice.
- Decrease of SCD-1 desaturase activity, which plays an important role in the process of synthesis of monounsaturated fatty acids and increase of elongase Elovl-6.
- Increase in membrane cholesterol, probably related to the mice hepatic metabolism, which can partially compensate the increase in polyunsaturated fatty acids
- Increase in the peroxidability index in 3xg mice
- Enzyme activity of GSH peroxidase, shows a statistically significant increase in 3xg mice exposed to the hyper-gravity condition compared to Control and Vivarium mice, indicating a compensatory effect induced by oxidative stress.

Conclusions: Exposure to altered gravitational conditions can modify the physiological behaviours of an organism to respond to the characteristics of the new environment. To obtain a deeper understanding of the physiological response to gravity it is necessary to obtain data from experiments performed in opposite gravitational conditions. The data collected so far on exposure to the hyper-gravity condition highlight significant differences in the antioxidant enzymatic activity and membrane composition of the erythrocytes. To have a complete vision it will be important to obtain further results on the lipidomic composition and oxidative stress and to correlate our data with that obtained by the other researchers of the team in other tissues and plasma of the same mice.

REFERENCES: [1] Hodkinson PD, et al. Br J Anaesth. 2017 Dec 1 doi: 10.1093/bja/aex336.

Project selected by esa and funded by asi