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EFFECTS OF SIMULATED MICROGRAVITY AND ARTIFICIAL GRAVITY ON ENDOTHELIAL  
CELLS: CHANGES IN INFLAMMATION AND ADHESION MOLECULE EXPRESSION**Abstract**

**Objectives:** Microgravity (MG) is known to lead, at the physiological level to cardiovascular deconditioning. Prior investigations have also demonstrated that MG is also likely to affect cellular function and regulation, including those of endothelial cells (ECs). At the present time, it is unclear if microgravity could bring on changes potentially impacting pathophysiological processes such as atherosclerosis, and if those could be reversed by application of artificial gravity (AG). The goal of this study was to investigate the impact of simulated MG and AG on ECs, with the hypothesis that MG alters baseline expression of inflammatory and adhesion molecule gene expression, and these changes are reversed by AG.

**Methods:** Human umbilical vascular endothelial cells (HUVECs) grown to confluency were used as a cellular model. A desktop random positioning apparatus and a gravitational cell-loading apparatus provided MG and AG conditions, respectively. The experimental conditions included: 1) control exposed to 1-gravity environment for 24 h (CL), 2) MG for 24 hours, 3) MG for 24 hours with three 30-minute periods of AG of 12-gravity (MG/AG). Gene expression was studied with qRT-PCR and surface cell adhesion molecule with flow cytometry.

**Results:** MG led to a significant decrease in gene expression of the adhesion molecules ICAM-1 ( $p=0.0001$ , 97% fold decrease), VCAM-1 ( $p=0.0001$ , 99% fold decrease), E-Selectin ( $p=0.0001$ , 99% fold decrease), IL-6 ( $p=0.0003$ , 96% fold decrease), TNF- $\alpha$  ( $p=0.0001$ , 99% decrease) and VEGF ( $p=0.0001$ , 70% decrease). NOS-3, Caveolin-1 and -2 were significantly increased with MG ( $p=0.0001$ , 0.0111, 0.0001, with 5, 1.5, and 2 fold increase, respectively). There was also a significant decrease in cell surface proteins ICAM-1, VCAM-1 and E-Selectin with MG seen on flow cytometry. The changes observed in gene expression with MG were reversed by AG (MG/AG).

**Conclusions:** Simulated MG decreases inflammatory and adhesion molecule gene expression, and these changes are reversed by short periods of AG. These findings underline the importance of gravitational loading in cellular function. Although some of these changes (i.e. NOS-3) support physiological conditions associated with cardiovascular deconditioning, more studies are needed to understand the impact adhesion molecule expression and inflammatory changes with simulated MG on processes such as atherosclerosis.