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EXPOSURE TO MARS GRAVITY IS NOT SUFFICIENT TO PROVIDE MITIGATING EFFECTS ON  
ORTHOSTATIC INTOLERANCE UPON RETURN TO EARTH.**Abstract**

In this study we provide results from a simulation model (NELME: Numerical Estimation of Long-term Modified-gravity effects) of the underlying changes due to the cardiovascular system deconditioning under modified gravity exposure. This model is capable to simulate the basic cardiovascular output parameters of a human person when changes in gravity and thermal exposure are applied. Fluid loading, gender differences and aerobic exercise or artificial gravity as countermeasures can also be taken into account. Orthostatic hypotension is a well-known risk that may put a human mission into jeopardy due to the effects caused by a transition from long-term hypogravity to sudden gravity exposure. This factor is mitigated when astronauts return to Earth because of external medical help is available but it may be a problem when landing on Mars or other deep space scenarios. We simulate a number of different mission scenarios at different gravity levels running on a supercomputing centre. Parameters of the model have been fit and results have been validated from available experimental data from previous experiments in parabolic flights and experiments with diverse exposure to different gravity loads. Results show that vascular resistance is not mitigated by Moon or Mars gravity from two weeks to nine-months exposure. Results of the intensive numerical simulations show a flat response of the vascular resistance when returning to the Earth gravity until  $g=0.45$  g(Earth). Then the response is nearly linear until  $g=0.78$  g(Earth) when normal values from g(Earth) are recovered. Aerobic exercise is not enough to fully compensate this decondition, with women benefitting more than men. A total risk of putting a human mission in jeopardy is then estimated, showing that a Mars mission returning to Earth is still safe to be conducted in accordance with previous studies. Thermal stress is also simulated for a number of different mission scenarios thus simulating EVA (Extravehicular activities) showing that a reduced increase in the total estimated risk is not negligible. Artificial gravity does seem to have a mitigating effect but its practical implementation poses concerns and seems unlikely to be actually undertaken. This model has been successful in estimating the risks associated with cardiovascular deconditioning in human long-term missions in space, with unprecedented and substantial variability of gravity exposure, thermal stress and mission scenarios as compared to previous studies.