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# THE NEBULA PROJECT: EFFECT OF PREFLIGHT ENDURANCE AND RESISTANCE TRAINING AS A COUNTERMEASURE AGAINST MICROGRAVITY-INDUCED MUSCULOSKELETAL DECONDITIONING

**Abstract**

Musculoskeletal system deconditioning is a major consequence of spaceflight for astronauts, leading to a rapid decrease in muscle strength, mass, oxidative qualities and to fat infiltrations. These deconditioning impacts astronauts during and after their mission, therefore, muscle recovery becomes a critical point after a mission, requiring astronauts to go through intense rehabilitation programs to recover muscle capacity after returning to Earth. In order to mitigate it, countermeasures are being studied by space agencies, and physical exercise appears to be the most efficient method for now. However, current astronaut training programs aboard the ISS are still not fully efficient in the prevention of muscle loss. In that way, studies have investigated the effect of moderate intensity endurance training sessions carried out before the induction of microgravity, and have shown significant protective effects of these trainings, delaying the onset of muscle waste.

Our study aimed to evaluate the impact of a specific physical training program consisting of an acceleration-based endurance training and resistance training exercises during the pre-flight period (pre-conditioning) in order to delay muscle wasting. Sixty 14 weeks old males C57B6J mice were dispatched into 5 groups (n=10) performing or not a pre-conditioning training (endurance and resistance), followed by a 1 or 3 weeks hindlimb suspension (HLS) period. Throughout the experimentation, we longitudinally followed the evolution of the mice's grip force, as well as their aerobic qualities (Maximum Aerobic Velocity) and their global muscular and body fat composition through EchoMRI. Terminal data consisted of hindlimb muscle mass, myofibers typologies and cross-sectional area, as well as biomolecular insights in muscle protein (protein balance, REDOX balance, apoptosis, satellite cells, inflammation, mitochondrial dynamics), and mRNA content.

Here we expect to observe delays in muscular atrophy during the first week of HLS in group performing preconditioning, as well as a less severe deconditioning in the following HLS weeks. We expect trained mice to show a smaller strength and endurance loss after HLS, as well as a different protein and RNA content between timepoints, due to the different molecular pathways activated in the short and long term by the physical training. Trained mice should show more stable body composition throughout the protocol.

As space agencies are planning travels to the Moon and Mars involving periods of microgravity from a few days to several months or years, finding countermeasures to preserve the muscular integrity of the astronauts is a major concern.