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 **to the**

***Decadal Survey on Biological and Physical Sciences (BPS) Research in Space 2023-2032***

**Topical:**

**NASA Biological and Physical Sciences – The Study of Partial Gravity Effects on Animal Physiology**

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1. **Executive Summary**

We review the major achievements and gaps of existing Biological and Physical Sciences (BPS) with respect to partial gravity studies on animal physiology in the context of our space exploration efforts. We provide recommendations for the expansion of this subject for the future, as well as focus areas for development of new initiatives relevant to the interdisciplinary field of space biology and physical sciences.

1. **Rationale**

In the 2010 Decadal Survey on Biological and Physical Sciences in Space, studies of the effect of lunar gravity was described as a knowledge gap, while also highlighting that a lunar outpost could provide the opportunity for an important research platform for ongoing studies in partial gravity. Indeed, in the near future, space agencies plan to send the first crew for extended stays on and around the Moon and Mars, where gravity is significantly reduced compared to Earth (0.16 g and 0.38 g, respectively). However, the long-term effects of partial gravity have not yet been elucidated, and ensuring astronauts’ health and performance is critical to the success of these missions. We have extremely limited human physiology data from Apollo lunar missions, the only crew experiencing lunar gravity effects, with no data available on women. Furthemore, as crew travel to the Moon and Mars, they will experience long-term exposure to microgravity, as well as transitions between gravitational states, of which we have limited knowledge (1). Long-term studies are particularly rare and longitudinal assessments to date are minimal.

Furthermore, despite numerous science experiments being conducted in space, the detailed mechanisms of physiological adaptation are not yet fully understood. We have also entered a new space era with commercial space travel set to become the next normal. The rapid transition from the high-G acceleration followed by a high-G deceleration of entry, is a quintessential component of suborbital space flights. The amount and orientation of the acceleration and gravitational load imposed on participants depends upon the flight profile and vehicle configuration (2). Indeed, the neuro-vestibular, cardiovascular, kidney, pulmonary, immune, musculoskeletal issues are some of the major health concerns associated with long term exposure to microgravity.

Finally, if we plan on living long-term on the Moon or Mars, we should understand if partial gravity will counteract the detrimental effects of weightlessness on human physiology and eliminate the need for certain countermeasures. This is not currently predictable from microgravity and 1g data, and animal models present a unique opportunity for exploring integrated physiological responses in ways that cannot be as easily interrogated in cell or tissue cultures, nor thorough investigations that can be done with astronauts.

1. **Findings from Recent Studies and Research Issues Investigating Partial Gravity**

In terms of research areas, we propose two primary questions related to partial gravity exposure: 1) What will be the main physiological effects of partial gravity and changes to loading regimens on the body? and 2) Are there key g-thresholds for different physiological systems?

We have extensive knowledge from our research experiments of microgravity exposure (whether from spaceflight or simulated) on the effects of weightlessness, as a comparison to partial gravity effects. Conducting microgravity research on- orbit is costly with limited resources and crew-time availability. Microgravity simulators specific to cellular studies include strong magnetic field-induced levitation, two-dimensional and three-dimensional clinostats, rotating wall vessels and random positioning machines. These simulation techniques have generated data that is similar to those observed in spaceflight studies. (3-5)

**With respect to simulated Partial Gravity experiments, our current knowledge of partial gravity effects is focused in the areas of musculoskeletal deconditioning and behavior (1, 6). However, there exist many additional topics and research questions unaddressed, some of which include:** reproduction & development, cardiovascular, gastrointestinal, neurological & sensorimotor, immune, circadian rhythms, multi-organ interaction and adaptations, and sex differences, etc. On a related note, we lack a current understanding of the cellular, physiological, and biochemical intra-cellular adaptations. Thus, there is a significant gap of knowledge of Lunar and Martian gravity adaptations across disciplines.

1. **Research Priorities and Platforms**

Given these research gaps, we suggest these recommendations of how to approach these gaps of knowledge, including:

* Programmatic: promoting interdisciplinary research and multi-team projects that simulate crew operations of missions to the Moon and Mars
* Technological: does the current technology and animal housing equipment simulates partial gravity conditions appropriately?
* Countermeasures: are novel countermeasures required to mitigate any negative physiological effects from an altered gravitational state, and/or does partial gravity mitigate the effects of microgravity exposure?
1. **Overarching and Programmatic Issues**

Finally, there exist overarching areas to consider and programmatic issues that we should consider in moving forward for the next decade in addressing the gaps of knowledge mentioned in this topical paper. We propose the following recommendations:

* + Reference and validation flights on mice on ISS leveraging centrifugation (lunar-g and martian-g) following a consortia-based approach with multiple investigators to maximize utilization of resources (and multiple physiological systems of focus).
	+ We recommend the more widespread use of artificial gravity in-flight for animals onboard the ISS (or other spacecrafts)
	+ We recommend studying the long-term physiological effects of reduced mechanical loading on an animal's physiology.
	+ We recommend incorporating several spaceflight stressors (such as partial gravity and radiation, circadian alterations) to better understand the overall impact of the lunar or martian environments.
	+ Use of short duration partial-gravity studies (suborbital, short orbital) to identify acute effects and mechanisms of g-transitions and g-sensing.
	+ Use of short duration partial-gravity studies (suborbital, short orbital) to fine tune instrumentation and other supporting technologies for LEO and Lunar studies.
	+ Using ground-based partial-gravity in combination with exercise interventions to understand nuances of musculoskeletal and cardiovascular adaptations to resistance and aerobic exercise.
	+ We recommend the use of studies assessing the adaptations to partial gravity in both sexes.

**Summary**

Our physiological systems have evolved on Earth and in the presence of a specific gravitational environment. The next ten years requires more research to determine how space affects our physiology in specific altered gravitational environment (i.e. Lunar and Martian). We need the development of equipment and methodologies to facilitate these studies. This work will help in the development of safe and effective inflight medical practice and will also have Earth-life benefits related to extreme environments.

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