Fiscal Year:	FY 2023	**Task Last Updated:**	FY 06/18/2023
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Project Title:	Circadian Rhythm Disruption and Gravitational Disturbance in a Lunar Mission Analog: Consequences for Muscle Function During and After the Mission		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Musculoskeletal Biology		
Space Biology Special Category:	None		
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Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2021 Space Biology NNH21ZDA001N-SBAS E.11: Animal Studies
Start Date:	06/01/2023	**End Date:**	05/31/2024
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA ARC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	80NSSC23K1016		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Mechanical loading is the primary stimulus required for the maintenance and health of the musculoskeletal system. Exposure to microgravity or reduced gravity results in rapid bone loss and muscle atrophy, especially in the lower limbs. In recent years, the clock system in the skeletal muscle has been recognized to play a critical role in key aspects of muscle physiology, ranging from structural maintenance to functional regulation. On Earth, perturbations of the circadian rhythm affect muscle function and are associated with the development of sarcopenia. Reciprocally, studies have demonstrated that muscle activity can directly modulate the expression of muscle clock genes in a time-dependent fashion, and recent data suggest that the circadian clock could influence skeletal muscle adaptation in response to exercise training. Since Artemis astronauts will experience alterations in muscle condition and circadian rhythm simultaneously, it is critical to develop ground-based studies that will closely mimic this situation. While these stressors will occur temporarily, their effects may linger, and negatively influence muscle recovery after return from the mission. In this ground-based Early Career Investigator (ECI) proposal, I hypothesize that light cycle disturbances induced by a model of Chronic Jet Lag (CJL) will severely impact the peripheral muscle clock and, combined with altered gravity, will lead to additive negative effects during the disuse period. Moreover, I hypothesize that circadian disruption will have long-lasting effects that will significantly impair muscle recovery during the reloading period. SA1: To characterize the impact of circadian disturbance and partial gravity in a lunar analog in male and female rats. 60 adult outbred rats (30/sex) will undergo 7 days of exposure to partial weight-bearing at 20% of normal loading (PWB20) to simulate lunar gravity. 1 group will be exposed to a regular light cycle (LD), 1 group will be kept in constant light to induce circadian free-running (LL), and the experimental group will be exposed to CJL using a 6h phase advance every other day. SA2: To determine and compare the long-term effects of circadian disturbance and altered gravity during muscle recovery in males and females. 20 animals (10/sex) will be exposed to the same PWB20+CJL paradigm as in Aim 1. Animals will be allowed to recover for 7 days at normal loading (1g) and under a standard light cycle (LD). For this work, I plan on first assessing muscle health and function through regular testing including grip strength, fatigue resistance, force production, and muscle quality. I will also monitor circadian parameters and rest/activity over several 24h periods. Finally, I will perform biomolecular assays in the suprachiasmatic nucleus and soleus muscle, targeting specific genes involved in circadian rhythm entrainment, muscle function, and inflammation. This promising pilot study will help assess the additive effects of circadian disturbance in animals exposed to partial gravity and will help determine the existence of sex-based differences in response to spaceflight stressors. Moreover, I will determine sex-based differences during muscle recovery following disuse, and the long-term impact of circadian disturbance on muscle health and function. This study, which includes phenotypical and molecular outcomes, will assess the contribution of muscle clock genes and pathways to muscle health. Finally, targeted molecular assessment will help me use my diverse background (metabolism, neuromuscular, circadian) to explore other systems of interest that may be linked to muscle health and function (e.g., metabolic signaling pathways), and help characterize the key players that could be targeted with pharmacological approaches to provide new and effective countermeasures in future studies.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2023.
Bibliography Type:	Description: (Last Updated:)