Fiscal Year:	FY 2023	**Task Last Updated:**	FY 04/10/2024
PI Name:	Gaidica, Matthew Ph.D.		
Project Title:	Manipulating Sleep Architecture as an Operational Countermeasure		
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Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	TRISH--TRISH		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	48109	**Congressional District:**	12
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2020 TRISH-RFA-2001-PD: Translational Research Institute for Space Health (TRISH) Postdoctoral Fellowships
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No. of PhD Candidates:		**No. of Master' Degrees:**	
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Contact Monitor:		**Contact Phone:**	
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Flight Assignment:	NOTE: End date changed to 7/31/2023 per TRISH (Ed., 11/7/23) NOTE: End date changed to 2/29/2024 per TRISH (Ed., 9/12/23) NOTE: End date changed to 7/31/2023 per TRISH (Ed., 8/4/22) NOTE: End date changed to 7/31/2022 (originally 7/31/2021) per TRISH (Ed., 11/2/20)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Dantzer, Ben (MENTOR: University of Michigan, Ann Arbor)		
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Task Description:	POSTDOCTORAL FELLOWSHIP Space exploration exposes humans to unique stressors that, if not addressed, compromise physical and psychological health and performance. Sleep is known to promote physiologic resilience making it paramount in challenging circumstances, but all sleep is not the same. Progressive, stereotyped sleep stages are common in mammals and form a basic structure known as “sleep architecture.” High homeostatic value has been placed on slow-wave sleep (SWS), which is the deepest state of sleep characterized synchronous 1–4 Hz brain oscillations. SWS co-occurs with important fluid rhythms and changes in neural microstructure that promote waste clearing, potentially underlying the important findings that SWS enhances memory and performance. This proposal aims to identify critical conditions for which enhancing SWS through non-invasive audio stimulation may mitigate the influence of stressors or augment performance. I propose a novel translational analog in the wild red squirrel as it is a freely behaving, tractable rodent model that exhibits human sleep patterns. The extreme northern latitude of the field site for this study provides an opportunity to investigate how a SWS countermeasure fares under varying, long-duration changes in circadian cueing. I will measure neural, cardiac, and accelerometry data to analytically describe how sleep architecture, autonomic markers of stress, and cognitive/physical performance interact. A major goal of this project is to concurrently refine the SWS countermeasure into a configurable, autonomous tool capable of being deployed towards long-duration human space missions. The perceived significance of the proposed work is to span evidence to products that bridge fundamental research towards understanding the foundations of performance and resilience while providing an operational toolset alongside empirically derived implementation strategy.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Space exploration represents an artificial environment where sleep is altered and historical data suggests sleep will be sacrificed by astronauts during missions. Since sleep is not only a physiological necessity but required to fight against physical/mental fatigue and more broadly, maintain health and performance, it is important that we understand what sleep should look like and design appropriate, well-informed countermeasures. Wild animals (i.e., those that are free-living) represent an opportunity to understand how evolution has solved many problems related to coping and thriving in austere environments. From this viewpoint, we should not only be thinking about how to maintain and improve astronaut sleep but also investigate the universe of strategies that other animals use and consider how those could be worked into sleep/rest-wake/work strategies during low earth and deep space missions. In this project, we devised an approach using the North American Red Squirrel as an analog model because they are one of the few tractable (i.e., widely available) mammal species in North America that maintains a diurnal sleep schedule and sleeps within one large, nightly bout, like humans. Unlike ground squirrels—which are the focus of other NASA and TRISH studies—red squirrels do not use torpor or hibernation to address the challenges of extreme cold, suggesting that there is much to learn about how they manage energetic resources through modifying sleep-wake behavior. Our work specifically investigates these questions from both non-invasive and invasive methodologies. Firstly, we have gathered a massive amount of accelerometer data using non-invasive collaring (>7,000 total days) from red squirrels in the Yukon, where light and temperature drastically change across seasons. Although these data provide a wealth of information across many individuals (n > 200 squirrels), inertial data alone can not sufficiently identify sleep itself, let alone specific stages of sleep and its underlying architecture (e.g., REM-NREM). Therefore, a more invasive methodology was needed, albeit only possible to deploy on a smaller scale due to the relative complexity of the surgical implant procedure and required oversight. Such that, secondly, we have used the miniature neurophysiology platform we developed to record sleep in implanted, freely behaving red squirrels at the University of Michigan. The protocols we developed solve many outstanding issues related to the use of wild animals. Namely, humane anesthesia techniques that we developed through cross-institution conversations with domain experts, as well as technological advancements in performing real-time analysis of incoming neural data on our device. In sum, all of these directions build towards constructing better approaches to understanding sleep, its evolutionary importance and design, and compiling those ideas into testable countermeasure approaches to support astronaut – and more broadly, human – health.
Task Progress:	APPROACH My project leveraged a novel translational analog in the wild red squirrel: it is a freely behaving, abundant, tractable rodent model. We recently characterized sleep-like patterns in red squirrels using accelerometry suggesting that high behavioral demands lead to more efficient sleep (unpublished). If this particular behavioral regime was better understood, it may offer a broader perspective of how sleep interplays with demanding environments and high-performing individuals. RESULTS My project aimed to characterize red squirrel sleep patterns in the wild; however, it was significantly impacted by border shutdowns at our primary field site in Canada due to COVID-19. I overcame those challenges by creating a local field site near the University of Michigan at Saginaw Forest, where I tagged, tracked, and trapped a local population of red squirrels. Although I did not collect a significant amount of field data, I was successful in a limited number of wild and lab-based neural recordings. The toolset I developed measured neural, cardiac, and accelerometry data. I demonstrated how such a device can be deployed in free-living conditions or used in a closed-loop paradigm to enhance SWS (see Gaidica & Dantzer, 2022). I also presented first-of-its-kind data that characterized red squirrel SWS periodicity, suggesting robust ~20-minute cycles. The significance of such work is threefold: (1) I refined a translational field model including new surgical methods for future use, (2) I developed a novel implantable with embedded technology that can apply to human conditions, and (3) I published convincing pilot data suggesting red squirrels are an ethologically relevant animal model who exhibits robust SWS cycles with behavioral patterns (e.g., sleep-wake) more like humans than rats or mice. YEARS 1-2 IMPACT In sum, my research worked toward a new approach and methods to reveal the foundations of performance and resilience. YEAR 3 RESEARCH PLAN The hindlimb unloading (HU) model has been used to simulate microgravity—and more broadly, disuse—for over 40 years. Since the National Aeronautics and Space Administration (NASA) confirmed similar tissue fluid shifts and musculoskeletal responses in rodents compared to subjects in the weightlessness of space, HU has become an important model to study other physiologic factors relating to metabolic, endocrine, and adrenal function. However, the current

	(and common) HU apparatus is statically calibrated, such that the hindlimbs are unloaded through tail suspension using a constant force. This weight is typically equal to a 30° incline (i.e., head-tilt down) which matches the cephalic fluid shift and pressures experienced in zero-G while providing normal weight-bearing on the forelimbs and unloading the lumbar vertebrae but not the cervical vertebrae. Since tilt-angle and weight-unloaded are co-linear, the notion that a standard unloading protocol could be implemented dynamically is possible if the unloaded weight could be monitored.
Bibliography Type:	Description: (Last Updated: 04/10/2024)
Articles in Other Journals or Periodicals	Gaidica M, Zhang M, Dantzer B. "A wireless wearable ecosystem for social network analysis in free-living animals." bioRxiv preprint server. Posted January 16, 2024. https://doi.org/10.1101/2024.01.15.575769 , Jan-2024