Fiscal Year:	FY 2024	**Task Last Updated:**	FY 10/03/2023
PI Name:	Britten, Richard Ph.D.		
Project Title:	Hadron-induced Impairment of Executive Function: Role of Perturbed Neurotransmission and the Exacerbating Impact of Sleep Deprivation		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	23507-1607	**Congressional District:**	3
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2013-14 HERO NNJ13ZSA002N-NSCOR Radiation
Start Date:	12/02/2015	**End Date:**	12/31/2024
No. of Post Docs:	1	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:	Elgart, Robin	**Contact Phone:**	281-244-0596 (o)/832-221-4576 (m)
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 12/31/2024 per NASA JSC Grants Office (Ed., 11/27/23). NOTE: End date changed to 12/31/2023 per NSSC info (Ed., 6/9/22). NOTE: End date changed to 5/01/2022 per NSSC info (Ed., 11/30/20) NOTE: End date changed to 12/31/2020 per NSSC info (Ed., 11/12/19) Ed. NOTE (April 2016): Proposal modified from original NSCOR proposal, per Space Radiation Element; not an NSCOR project		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Sanford, Larry Ph.D. (Eastern Virginia Medical School) Wellman, Laurie Ph.D. (Eastern Virginia Medical School) Yoon, Hargsoon Ph.D. (Norfolk State University) Blackwell, Ashley Ph.D. (Eastern Virginia Medical School)		
Grant/Contract No.:	NNX16AC40G		
Performance Goal No.:			

Performance Goal Text:	
Task Description:	The proposed studies will address multiple issues of concern to NASA. The proposed studies will generate data on the likelihood that GCR (galactic cosmic radiation) exposure will result in the impairment of neurocognitive (Executive Function) tasks that will be absolutely vital for the successful completion of a deep-space mission, under conditions that are more representative of the actual mission (when individuals are suffering from perturbed sleep). These studies will be conducted in a rat model that is relatively unique in that the rats are exercised regularly, and are preselected for a high level of executive function performance (high cognitive reserved) prior to space radiation exposure. Such a model system more closely resembles the physical and cognitive reserve of astronauts, and addresses a key operational issue of whether space radiation exposure will impact previously imprinted cognitive skills. Specifically, these studies will determine the impact that mission-relevant doses of space radiation (Z<15 single ion exposures, in addition to the multi-ion GCRSim) have on advanced executive functions, specifically Attentional Set Shifting (ATSET) and creative problem solving, or unconstrained cognitive flexibility (UCFlex). This data can be used to address Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders Bmed Gap 102 [previously central nervous system (CNS) Gap 2], and determine the likelihood of astronauts being able to successfully conduct neurocognitive (problem-solving) tasks. This study will also determine whether the incidence and/or severity of executive function impairments would be altered by exposure to another frequent flight stressor, insufficient sleep [Bmed-107 and Bmed-108, formerly CNS Gap 8]. A key component of these studies is an assessment of inter-individual susceptibility to develop deficits in these two cognitive processes following space radiation exposure (with or without the additional sleep stressor). Such data can be used (by others) to determine the best approach to develop a population Threshold Dose for dose risk estimations [Bmed-102 and Bmed-107, formerly CNS Gap 3]. [Ed. note October 2020: Human Research Program (HRP) gaps have changed with Integrated Research Plan Rev L such that gaps listed previously have been merged into newer gaps, as noted] Initially, three hypotheses were tested by the studies covered by this grant. 1. Sleep perturbation reduces the ability of rats to perform executive functions, and will be especially pronounced in space radiation (SR)-irradiated rats. 2. Sleep perturbation alters the sensitivity of the brain to develop SR-induced cognitive impairment. 3. SR irradiation alters Delta and Theta wave activity (EEG), and that these SR-induced changes in EEG activity are the underlying cause of the impairment of executive function performance. In 2019, we received supplemental funding (an HRP-IWS Graduate Fellowship) to develop the technical capability to simultaneously assess neural activity in multiple brain regions (neural network activity) of rats that are actively engaged in cognitive flexibility tasks, and how sleep fragmentation impacts neural network cohesiveness. In 2020, we received further supplemental funding (an HRP-IWS Graduate Fellowship) to establish whether sleep fragmentation exacerbates SR-induced deficits in fine motor skills.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The newly developed capability of measuring neural network functionality when rodents are under cognitive loading will allow more detailed work on establishing the basis for chemo- and beamo-brain in cancer patients, and to help understand how task switching is impaired in age-related cognitive impairment.
Task Progress:	Post-COVID pandemic supply chain and staff recruiting issues significantly impacted progress in some aspects of this study. However, despite these issues we have made some significant progress in this project, most notably expanding our studies to assess the effect of sleep perturbation in female rats. During this reporting period, we have established that: 1. Both male and female rats exposed to 10 cGy GCRSsim exhibit significant impairments in Attentional Set Shifting (ATSET) performance. However, there are sex-dependent differences in the ATSET stage where performance decrements are observed, and in the nature of the deficits (males require more attempts to solve, while females exhibit slower processing speed). 2. Sleep perturbation revealed latent ATSET performance deficits (i.e., not observed in normally rested rats) in both male and female rats. However, there are sex dependent differences in the ATSET stage where latent performance decrements are unveiled. Increased processing time was a common performance decrement observed in both sexes. 3. These data suggest that the true impact of space radiation (SR)-induced cognitive impairment may not be fully evident in normally rested rats. 4. This is an impairment of fine motor skills in both male and female rats exposed to 10 cGy GCRSsim, and sleep perturbation has both independent and synergistic effects on fine motor skills. There is an ongoing effort to acquire and analyze local field potential (LFP) readings (a direct measure of activity) from multiple brain regions as rats perform tasks that have high or load cognitive loading. On-going analyses are now correlating these observed changes in LFP signal output to specific events/responses in the various tasks and will determine how LFP outputs are synchronized as the rats perform in the various tasks when normally rested and when they have had their sleep perturbed.
Bibliography Type:	Description: (Last Updated: 02/21/2024)
Abstracts for Journals and Proceedings	Britten RA, A.A. Blackwell, L.D. Sanford, H. Yoon. "An approach to assess neural network signaling in rodents under task loading conditions." Society for Brain Mapping & Therapeutics, Los Angeles, California, February 16-19, 2023. Abstracts. Society for Brain Mapping & Therapeutics, Los Angeles, California, February 16-19, 2023. , Feb-2023
Abstracts for Journals and Proceedings	Blackwell AA, Britten RA. "Acute Effects of low-dose space radiation on neural activity." Society for Brain Mapping & Therapeutics, Los Angeles, California, February 16-19, 2023. Abstracts. Society for Brain Mapping & Therapeutics, Los Angeles, California, February 16-19, 2023. , Feb-2023

Abstracts for Journals and Proceedings	Blackwell AA, Dunn K, Tran H, Pham V, Fesshaye A, Yoon H, Le T, Maharathi B, Britten RA. "Impact of low dose single ion (4He) exposure on neural activity." NASA Human Research Program Investigators' workshop, Galveston, Texas, February 7-9, 2023. Abstracts. NASA Human Research Program Investigators' workshop, Galveston, Texas, February 7-9, 2023. , Feb-2023
Abstracts for Journals and Proceedings	Blackwell AA, Tracz JA, Kim C, Fesshaye A, Britten RA. "Acute and protracted effects of deep space radiation on fine motor control in female rats." Human Research Program Investigators' workshop, Galveston, Texas, February 7-9, 2023. Abstracts. Human Research Program Investigators' workshop, Galveston, Texas, February 7-9, 2023. , Feb-2023
Articles in Peer-reviewed Journals	Huff JL, Poignant F, Rahmanian S, Khan N, Blakely EA, Britten RA, Chang P, Fornace AJ, Hada M, Kronenberg A, Norman RB, Patel ZS, Shay JW, Weil MM, Simonsen LC, Slaba TC. "Galactic cosmic ray simulation at the NASA Space Radiation Laboratory–Progress, challenges and recommendations on mixed-field effects." Life Sci Space Res (Amst). 2023 Feb:36:90-104. https://doi.org/10.1016/j.lssr.2022.09.001 ; PubMed PMID: 36682835 , Feb-2023
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Articles in Peer-reviewed Journals	Britten RA, Fesshaye A, Tidmore A, Blackwell AA. "Similar loss of executive function performance after exposure to low (10 cGy) doses of single (4He) ions and the multi-ion GCRSim beam." Radiat Res. 2022 Jul 20. https://doi.org/10.1667/RADE-22-00022.1 ; PubMed PMID: 35857423 , Jul-2022
Books/Book Chapters	Wellman LL, Adkins AM, Yoon H, Britten RA, Sanford LD. "Telemetry in rats and mice: Methodological considerations and example studies of stress and anxiety in ground-based spaceflight analogs." in "Psychiatric Vulnerability, Mood, and Anxiety Disorders: Tests and Models in Mice and Rats." Ed. Harro J. New York, NY: Humana, 2023. p. 201-22. https://doi.org/10.1007/978-1-0716-2748-8_11 , Jan-2024