Fiscal Year:	FY 2022	**Task Last Updated:**	FY 10/04/2021
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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City:	Norfolk	**State:**	VA
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:**	12/31/2023
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 12/31/2023 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:	October 2021 report: Dr. Ashley Blackwell from Eastern Virginia Medical School was added as a Co-Investigator to help develop the neural network cohesiveness studies, and to conduct fine motor skill assessments.		
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:	The COVID pandemic significantly impacted progress in some aspects of this study. The decision by New York State to ban residents of Virginia from entering the state, and thus BNL, jeopardized the irradiation of the rats in November 2020. Fortunately, Dr. Blackwell, who was a New York resident at the time, was able to go to Brookhaven National Laboratory (BNL) and was able to irradiate the rats. Due to ongoing restrictions imposed by the Governor of Virginia, only two staff members were allowed to work in the laboratories at EVMS. Thus, the amount of rats that could be processed in the sleep/attentional set shifting (ATSET) interaction study was significantly reduced (to just 2 rats/week). Three medical students at Eastern Virginial Medical School (EVMS) volunteered in the Britten lab after hours, allowing some studies on the impact that sleep perturbations had on fine motor skills and performance in a high cognitive task load (CTL) “ARMIT” test. The ARMIT task is designed to evaluate executive functioning, working memory, cognitive flexibility, and long-term memory in the face of interference (stress loading). During this reporting period, we have demonstrated that sleep perturbation: 1. Reveals latent deficits in CDR-stage performance (ATSET) in rats exposed to 10 cGy of simulated Galactic Cosmic Radiation (GCR). 2. Leads to additional loss of string pulling (fine motor skills) performance over that observed in space radiation (10 cGy of GCR or He) exposed rats. 3. Leads to loss of performance in the C.1.3. high CTL stage of the ARMIT test (preliminary) by decreasing anterograde interference in radiation naive rats. We have also acquired local field potential (LFP) readings (a direct measure of activity) from two brain regions as rats perform in low and high CTL tasks, and determined how LFP outputs are synchronized as the rats performs in the various tasks. Ongoing analyses are now correlating these observed changes in LFP signal output to specific events/responses in the various tasks.
Bibliography Type:	Description: (Last Updated: 02/21/2024)

Abstracts for Journals and Proceedings	Britten RA, Fesshave AS, Wellman LL, Sanford LD. "Exacerbation of space radiation-induced neurocognitive impairment by sleep perturbation may be specific for Z=14 ions." 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021
Articles in Peer-reviewed Journals	Willey JS, Britten RA, Blaber E, Tahimic CGT, Chancellor J, Mortreux M, Sanford LD, Kubik AJ, Delp MD, Mao XW. "The individual and combined effects of spaceflight radiation and microgravity on biologic systems and functional outcomes." J Environ Sci Health C Toxicol Carcinog. 2021 Apr 27;39(2):129-79. Review. https://doi.org/10.1080/26896583.2021.1885283 ; PubMed PMID: 33902391; PubMed Central PMCID: PMC8274610 , Apr-2021
Articles in Peer-reviewed Journals	Britten RA, Wellman LL, Sanford LD. "Progressive increase in the complexity and translatability of rodent testing to assess space-radiation induced cognitive impairment." Neurosci Biobehav Rev. 2021 Jul;126:159-74. Review. https://doi.org/10.1016/j.neubiorev.2021.01.027 ; PubMed PMID: 33766676 , Jul-2021
Articles in Peer-reviewed Journals	Blackwell AA, Schell BD, Osterlund Oltmanns JR, Whishaw IQ, Ton ST, Adamczyk NS, Kartje GL, Britten RA, Wallace DG. "Skilled movement and posture deficits in rat string-pulling behavior following low dose space radiation (28Si) exposure." Behav Brain Res. 2021 Feb 26;400:113010. https://doi.org/10.1016/j.bbr.2020.113010 ; PubMed PMID: 33181183 , Feb-2021