Fiscal Year:	FY 2018	**Task Last Updated:**	FY 09/26/2017
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
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No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
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Flight Program:			
Flight Assignment:	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. (Easterm Virginia Medical School)		
Grant/Contract No.:	NNX16AC40G		
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Task Description:	The proposed studies will address multiple issues of concern to NASA. These studies will determine the relative potencies of mission-relevant doses of two HZE (high energy) particles (with Z<14) to impair Attentional Set Shifting (ATSET). This data can be used to address central nervous system (CNS) Gap 2, and determine the likelihood of Astronauts being able to successfully conduct neurocognitive (problem-solving) tasks. The data generated on the inter-individual susceptibility to develop Hadron-induced Impairment of Executive Function (HIIEF) could be used (by others) to determine whether the dichotomous (all-or-none) induction of HIIEF requires reconsideration of the use of population Threshold Dose for dose risk estimations (CNS Gap 3). This study will establish the impact that SlpDep/SlpFrag has on the severity of HIIEF (CNS 8), and whether Hadron exposure will result in a diminished ability to restore SlpDep decrements in Executive Function (CNS Gap 8). The proposed studies will thus 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). Aim 1: Studies to determine the Impact of sleep-fragmentation on Attentional Set Shifting performance. Aim 2: Studies to determine the Impact of sleep fragmentation occurring at pre- or post-HZE exposure on Attentional Set Shifting performance. Aim 3: Studies to determine the Impact of HZE exposure on sleep related electroencephalogram (EEG), and sleep homeostasis.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	Astronauts on the mission to Mars will be exposed to Galactic Cosmic Radiation (GCR) and most will experience problems with their sleep patterns. Inadequate sleep is well known to adversely impact performance in multiple cognitive tasks, including problem solving. Data from our laboratory, and others, have shown that mission-relevant GCR doses reduces problem solving ability in 30-50% of rats. This project will determine whether sleep perturbation alters the severity of the GCR-induced impairment of problem solving performance. The GCR ion primarily used in these studies was 600 MeV/n 28Si (400 MeV/n 4He ions have also been used but the data from those studies is too preliminary to report at present). This study will also determine the relative severity of the GCR-induced and sleep-perturbation-induced decrements in problem solving ability. Over the last year, studies were conducted that determined whether GCR-irradiated rats differ in their problem solving ability following sleep perturbation compared to non-irradiated rats subjected to the same sleep stress. Irradiated rats with apparently normal problem solving performance (in the attentional set shifting (ATSET) assay), and unirradiated rats, were subjected to sleep perturbation and reassessed for ATSET performance the following day. Sleep perturbation resulted in 10% of the sham rats performing badly in all stages of the ATSET test, with the exception of the IDS stage where 30% of the sham rats performed badly. In contrast, sleep perturbation resulted in 40-50% of the irradiated rats under-performing in the IDS, IDR, EDS, and EDR stages of the test, despite them previously having good performance when not sleep deprived. Sleep perturbation appears to have a bigger impact on ATSET performance in irradiated rats than in unirradiated rats. Thus, the true impact of GCR cognitive impairment may not be fully evident in normally rested rats. Inadequate sleep leads to marked levels of inflammation within the brain. Such changes could change the response of the brain to GCR irradiation. Another series of experiments were conducted to determine whether the frequency and/or severity of GCR-induced cognitive impairment differs in rats that have been fully rested to prior irradiation, or have been subjected to sleep perturbation. With respect to ATSET performance, the only measureable impact of sleep perturbation prior to GCR exposure was a decrease in the speed with which the irradiated rats completed IDS, a task regulated by the anterior and posterior cingulate cortex. We also investigated the impact that prior sleep perturbation had on insightful (creative) problem solving as assessed by the Unconstrained Cognitive Flexibility (UCFlex) test. Exposure to 1, 5, and 10 cGy 600 MeV/n 28Si resulted in a significant reduction in the number of rats that could solve the UCFlex task, and increased the time it took the rats to solve the UCFlex task. In contrast, the UCFlex performance of the rats that were sleep perturbed prior to irradiation was indistinguishable from the shams. We observed a similar protection by prior sleep perturbation in rats exposed to 10 cGy 400 MeV/n 4He, although we have insufficient numbers to include in this report according to NASA guidelines. We plan to repeat both the Si and He studies in the next grant reporting period. We are currently investigating whether the sleep perturbation has altered the composition of the proteome of the temporal lobe, perhaps invoking some free radical scavengers, or activating glial cells and astrocytes. The other possibility we are exploring is that the rats that have been sleep perturbed prior to irradiation, rapidly fall asleep after being irradiated, while the non-sleep perturbed rats remain awake and active in their cages for 12 hours. It is possible that the reduced EEG and metabolic activity within the temporal lobe of the rats that fall immediately asleep, may reduce the deleterious effects of the GCR exposure. During the next reporting period we will establish whether keeping the sleep-perturbed rats awake after irradiation changes the UCFlex performance. The final aspect of our studies will determine how GCR-exposure impacts EEG activity (delta and theta wave activity), and the sleep homeostatic response. The first batch of rats are scheduled to be irradiated in October 2017.
Bibliography Type:	Description: (Last Updated: 05/16/2025)