Fiscal Year:	FY 2010	**Task Last Updated:**	FY 05/21/2010
PI Name:	Hienz, Robert D. Ph.D.		
Project Title:	Detection & Prevention of Neurobehavioral Vulnerability to Space Radiation		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Neurobehavioral and Psychosocial Factors Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **BHP**:Behavioral Health & Performance (archival in 2017)		
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:	Baltimore	**State:**	MD
Zip Code:	21224-6823	**Congressional District:**	7
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2007 Crew Health NNJ07ZSA002N
Start Date:	05/01/2008	**End Date:**	04/30/2012
No. of Post Docs:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:	1	**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:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Weed, Michael (The Johns Hopkins University School of Medicine)		
Grant/Contract No.:	NCC 9-58-NBPF01604		
Performance Goal No.:			
Performance Goal Text:			

(1) Original Aims of the Project
Aim #1: To assess the effects of space radiation across a range of cognitive/behavioral functions in rodents. Performance measures include assessments of general motor function and speed, fine motor control, inhibitory control ("impulsivity"), timing, short-term memory, spatial working memory, learning and selective attention, motivation, and basic sensory function. Groups of animals are separately trained on different tasks, exposed at Brookhaven National Laboratory to high-energy radiation at levels that astronauts would likely experience during lunar or planetary surface activities, and then immediately re-tested.

Aim #2: To assess the long-term effects of radiation across a range of cognitive/behavioral functions via extended post-exposure testing for potential performance deficits.

Aim #3: To assess both the acute and long-term effects of radiation on the neurochemical mechanisms underlying

Task Description:	changes in cognitive/behavioral functions by examining the integrity of the neurotransmitter systems known to mediate those neurobehavioral functions found impaired. (2) Key Findings of the Project Results from the project thus far demonstrate the reliability and validity of the neurobehavioral procedures in detecting behavioral changes following radiation, that analogs of human psychomotor performance assessment procedures can be employed with rodents to automatically assess neurobehavioral function on a daily basis, and that such procedures can be used to effectively track changes in neurobehavioral function over extended intervals following radiation exposure. Specifically, the results have shown that head-only radiation produces discrete neurobehavioral changes by significantly decreasing discrimination accuracy and increasing false alarms in the reaction time procedure, with the latter result being indicative of a decrease in inhibitory control. These findings support the likely success of the rodent model for studying the risks of living in the space radiation environment due to changes in cognitive/neurobehavioral function. During the current reporting year, an additional 60 rats were trained in a simple reaction time (RT) and another 60 rats trained in a line orientation discrimination (LD) task. Following training, rats were exposed to head-only radiation to isolate the possible CNS effects from whole-body effects. Rats were irradiated with high-energy (150 MeV) protons generated at the NASA Space Radiation Laboratory (NSRL) at Brookhaven National Laboratory (BNL), as this energy of protons is prevalent in the deep space environment. Control rats were sham-exposed using the same anesthesia protocol, but not brought into the beam line. The RT task required rats to depress a lever for a random (1-3 sec) time, and to release the lever within 1.5 sec of a 'reaction time' stimulus (correct trial) to receive a food pellet. Lever releases prior to the release stimulus terminated the trial and were considered errors. The LD task required rats to learn to discriminate vertical from horizontal line stimuli, and then to learn the reverse discrimination. The LD task measures basic learning, reversal learning, and perseverative responding. Additionally, a 'recognition memory' test that requires no training was used after radiation exposure test the degree to which rats explore wooden beads impregnated with either their own odors, or with the odors of novel, unfamiliar rats. Results indicated that performances following exposure to 200 cGy showed a consistent, significant increase in reaction times for the irradiated animals that has persisted and shows no signs of recovery at 11 months post-exposure. For the first 6 months post-exposure, no significant changes were observed in discrimination accuracy, vigilance, or food intake. During the last 5 months, however, decrements in both accuracy and vigilance have been observed. For animals that learned the basic line orientation discrimination and repeated the discrimination following radiation exposure, no significant differences were observed between control and radiated animals. However, the odor recognition memory tests revealed differences in recognition memory performances for irradiated vs. control groups. The results of these experiments confirm the feasibility of an animal model approach for assessing neurobehavioral risks associated with living in a space radiation environment, and demonstrate the sensitivity of cognitive/behavioral test measures to the effects of head-only radiation that produce highly specific effects on neurobehavioral function. (3) Impact of these Findings Very little is known about the brain's response to HZE particle radiation encountered in space. The present research addresses several important questions of relevance to NASA's mission (Risk Number 29, Acute and Late CNS Risks, as described in the Bioastronautics Roadmap). To address these questions, the work is providing for the development and application of the acquisition and long-term performance of a number of neurobehavioral tasks in a cognitive/behavioral animal test battery in rodents, and additionally for the demonstration of the validity and reliability of the procedures to measure critical cognitive/behavioral functions following specific interventions (e.g., pharmacologic disruptions). The research will provide critically needed dose-response data on the effects of high-energy (HZE) radiation (protons, GCRs, SPEs) on a range of cognitive/behavioral functions. (4) Proposed Research Plan for the Coming Year Animals are currently being trained in new neurobehavioral tasks that are designed to detect changes in choice impulsivity. Once completed, they will be transported and exposed in late April at Brookhaven National Laboratory to protons. Within the next year, approximately 120 rats will undergo this training/exposure/post-testing protocol, covering a dose range of 0 - 200 cGy.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Research conducted on the effects of ionizing radiation on cognitive/behavioral function will provide the basis for extrapolating the effects of the space radiation environment on human cognitive function and performance. The Earth-based applications of this research will extend to providing a means for generalizing these effects to numerous types of radiation exposures (e.g., workplace, medical) on earth. Thus the outcomes of these studies are expected to have an important impact on safety and the quality of life in many Earth-based applied settings, and the society at large will further benefit from the resulting methodological advances that effectively provide quantitative risk assessments for radiation exposure on cognitive function.
Task Progress:	During the current year, 60 rats were trained in a simple reaction time (RT) and another 60 rats trained in a line orientation discrimination (LD) task. Following training, rats were exposed to head-only radiation. Rats were irradiated with high-energy (150 MeV) protons generated at the NASA Space Radiation Laboratory (NSRL) at Brookhaven National Laboratory (BNL), as this energy of protons is prevalent in the deep space environment. Control rats were sham-exposed using the same anesthesia protocol, but not brought into the beam line. The RT task required rats to depress a lever for a random (1-3 sec) time, and to release the lever within 1.5 sec of a 'reaction time' stimulus (correct trial) to receive a food pellet. Lever releases prior to the release stimulus terminated the trial and were considered errors. The LD task required rats to learn to discriminate vertical from horizontal line stimuli, and then to learn the reverse discrimination. The LD task measures basic learning, reversal learning, and perseverative responding. Additionally, a 'recognition memory' test that requires no training was used after radiation exposure test the degree to which rats explore wooden beads impregnated with either their own odors, or with the odors of novel, unfamiliar rats. Results indicated that performances following exposure to 200 cGy showed a consistent, significant increase in reaction times for the irradiated animals that has persisted and shows no signs of recovery at 11 months post-exposure. For the first 6 months post-exposure, no significant changes were observed in discrimination accuracy, vigilance, or food intake.

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In sum, exposure to proton radiation produces discrete neurobehavioral changes in reaction time and impulsivity, with the latter result being indicative of a decrease in inhibitory control. Such effects are being successfully tracked over the life span of these animals, and suggest the occurrence of permanent changes in neurobehavioral function over extended intervals following radiation exposure. These findings support the likely continued success of the rodent model for studying the cognitive, neurobehavioral, and CNS risks associated with living in the space radiation environment.

Bibliography Type:	Description: (Last Updated: 01/12/2021)