Fiscal Year:	FY 2011	**Task Last Updated:**	FY 05/04/2011
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:**	09/30/2012
No. of Post Docs:	1	**No. of PhD Degrees:**	0
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:	1	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date change to 9/30/2012 (from 4/30/2012) per NSBRI (Ed., 1/24/2012)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Weed, Michael (The Johns Hopkins University School of Medicine) Guilarte, Tomas (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 neurobehavioral 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, and motivation. 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		

Task Description:	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 changes in neurobehavioral 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 have demonstrated the reliability and validity of the neurobehavioral procedures in detecting behavioral changes following radiation, 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 proton radiation produces discrete neurobehavioral changes by significantly impairing aspects of sustained attention (e.g., decreased accuracy, increased impulsivity, increased lapses in attention) and motor function (i.e., a slowing in reaction times). 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 neurobehavioral function. During the current year studies continued to track daily performances on the rat psychomotor vigilance test (rPVT), which is an animal analog of the Psychomotor Vigilance Test (PVT) used to study sustained attention in humans. Following irradiation, performances on the rPVT were disrupted at all exposure levels studied (i.e., 25, 50, 100, and 200 cGy protons). Changes in motor function were manifested as consistent, significant increases (i.e., a slowing) in reaction times, indicative of a decrease in sustained attention. Other changes in sustained attention included decreases in accuracy, increases in performance lapses, and increases in impulsivity. New pilot studies of the effects of additional circadian disruptions on these rodent PVT performances have been conducted to determine the degree to which the observed radiation effects on neurobehavioral function may be compounded when disruptions in sleep/wake schedules occur (i.e., as under conditions of heavy workload and/or extended-duration exploration missions). Initial data indicates that disruptions in circadian rhythms has the potential to exacerbate ongoing radiation-induced neurobehavioral impairments, with radiation-exposed animals showing pronounced increases in sustained attention greater than those observed with radiation alone. Additionally, in a new study designed to measure impulsive choice behaviors in rodents, exposure to 200 cGy produced an increase in impulsivity compared to controls, indicating this may be an additional fruitful model for investigating biological consequences of radiation exposure as well as pharmacotherapy and other countermeasures aimed at preventing these radiation-induced brain and behavioral changes. To summarize, the data obtained during the current year demonstrate that significant changes in sustained attention, impulsivity, and motor function can be shown to occur following proton exposures as low as 25 cGy for the exposure groups as a whole. Importantly, significant variations in responding to these proton doses occurred among animals within groups that indicate that these "average" effects of proton irradiation may not be indicative of all animals. In animals that respond significantly to proton irradiations, all exposure doses produced similar effects on accuracy, lapses, and reaction times. Finally, the changes in sustained attention were tracked over time for up to 1 year post-exposure and found to persist over this extended time period. (3) Impact of these Findings The present results demonstrate the sensitivity of tests such as the rPVT for assessing the effects of head-only space radiation on cognitive neurobehavioral function. Such deficits could significantly impact routine performances in operational environments during long-duration exploratory missions, and also negatively affect post-mission adjustment upon return to Earth. 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 while providing an innovative experimental platform for exploring the bases of individual vulnerability to radiation-induced impairments and evaluating potential prophylactics, countermeasures, and treatments. (4) Proposed Research Plan for the Coming Year Animals are currently being trained in the rodent version of the PVT. Once training is completed, they will be transported and exposed in May 2011 at Brookhaven National Laboratory to iron ions over a dose range of 0 - 150 cGy, and then returned for extensive post-radiation testing. Studies of the effects of circadian disruptions as well as the effects of both stimulants and depressants, in combination with irradiations, will be completed. Additional data will be obtained via neuropathological imaging of the tissue with the translocator protein TSPO (Dr. Guilarte), as well as data on the integrity of the dopaminergic (DA) system using Western blot analyses (in collaboration with Dr. De Cicco-Skinner).
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Research conducted on the effects of ionizing radiation on cognitive/behavioral function provides the basis for extrapolating the effects of the space radiation environment on human cognitive function and performance. The Earth-based applications of this research extend to providing a means for generalizing these effects to numerous types of radiation exposures on earth (e.g., workplace, medical). 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. In addition, the development of a comprehensive and experimentally flexible animal model of neurobehavioral performance provides a useful tool for preclinical research and development in other domains such as sleep/chronobiology, neuropsychiatric disorders, aging, and cognitive enhancement. Moreover, the human Psychomotor Vigilance Test (PVT) is a standardized and widely validated objective measure of neurobehavioral status not only employed by NASA, but also utilized in a variety of settings such as clinical neuropsychiatric assessment, military, shiftwork, and aviation. As such, the present rodent analog of the PVT provides a direct translational link to performance capacity on Earth. Once validated, the rPVT model developed here may be used as a basic and translational research tool to predict performance deficits induced by radiation or other CNS insults while providing an innovative experimental platform for exploring the bases of individual vulnerability to performance impairments and evaluating potential prophylactics, countermeasures, and treatments.

Task Progress:	Highlights for this year include: - With a rodent version of the human psychomotor vigilance test (PVT), proton radiation exposures of 25 cGy and higher result in increased reaction times. Recently, the effects of additional circadian disruptions on these PVT performances have been shown to exacerbate these effects, with radiation-exposed animals (200 cGy) showing pronounced decreases in sustained greater than those observed with radiation alone. - Studies of the effects of stimulant and sedative compounds were begun, with the effects of amphetamine currently being examined on rodent PVT performances for irradiated and non-irradiated subjects. Once complete, these studies will be combined with the circadian disruption protocol to determine the interactive effects of stimulants and sedatives on PVT performances in irradiated rats before and after circadian disruptions. - Continued study of the effects of radiation exposure on choice impulsivity as measured by a "delayed discounting" procedure have demonstrated that 200 cGy proton exposures produce deficits in choice impulsivity as well, vis-à-vis the "motor impulsivity" effects previously shown with the rodent PVT procedure. - A collaboration with Drs. Strangman and Zeffiro of MGH was established to assess the effects of radiation on CNS structural changes through advanced neuroimaging. The imaging of these brains is currently underway. - During the quarter an additional 30 animals were transported to Brookhaven National Laboratory for proton radiation exposure, with subgroups being euthanized at 1, 3, 5, 7, and 14 days post-exposure. Brain tissue was sent to Dr. Tomas Guilarte (Columbia Univ.) who is employing the translocator protein TSPO, a sensitive biomarker of reactive gliosis and inflammation, for neuropathological imaging of the tissue. Preliminary analyses of the images indicate that there are definite areas that have increased TSPO expression. These analyses are continuing. - A new collaboration with Dr. Kathleen DiCicco-Skinner (American University) has been established to assess neurotransmitter function in rodent brain tissue for both irradiated and non-irradiated control animals. During this quarter tissue samples have been prepared in the laboratory and sent to Dr. De Cicco-Skinner's laboratory, where she is now examining the integrity of the dopaminergic (DA) system using Western blot analyses to quantify levels of DA proteins (e.g., receptors, DA tranporter) and the extent of degradation of DA terminals and upregulation of other proteins, including stress and inflammatory markers commonly active following brain trauma.
Bibliography Type:	Description: (Last Updated: 01/12/2021)
Abstracts for Journals and Proceedings	Davis CM, Guida PM, Brady JV, Hienz RD. "Neurobehavioral Effects of Space Radiation on Choice Impulsivity." 18th IAA Humans in Space Symposium, Houston, TX, April 11-15, 2011. 18th IAA Humans in Space Symposium, Houston, TX, April 11-15, 2011. , Apr-2011
Abstracts for Journals and Proceedings	Hienz RD, Davis CM, Weed MR, Roma PG, Guida PM, Gooden VL, Brady JV. "Neurobehavioral Effects of Space Radiation on Psychomotor Vigilance and Reaction Time Tests." 18th IAA Humans in Space Symposium, Houston, TX, April 11-15, 2011. 18th IAA Humans in Space Symposium, Houston, TX, April 11-15, 2011. , Apr-2011
Abstracts for Journals and Proceedings	Hienz RD, Davis CM, Weed MR, Guida PM, Gooden VL, Brady JV, Roma PG. "Neurobehavioral effects of space radiation on psychomotor vigilance tests." Committee on Space Research (COSPAR) 2010 38th Scientific Assembly, Bremen, Germany, July 18-25, 2010. COSPAR Abstract Book. Committee on Space Research (COSPAR) 2010 38th Scientific Assembly, Bremen, Germany, July 18-25, 2010. Abstract F23-0007-10. https://www.cospar-assembly.org/abstractcd/COSPAR-10/ ; go to Commission F to search for abstract. , Jul-2010
Awards	Hienz RD. "Robert D. Hienz: New Associate Team Lead for NSBRI NBPF Team, December 2010." Dec-2010
Awards	Roma PG. "Peter G. Roma, Ph.D.: Bank Austria Visiting Scientists Program, September 2010." Sep-2010