Fiscal Year:	FY 2012	**Task Last Updated:**	FY 07/12/2012
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		
PI Email:	bhienz@jhmi.edu	**Fax:**	FY 410-550-2780
PI Organization Type:	UNIVERSITY	**Phone:**	410-550-2788
Organization Name:	The Johns Hopkins University School of Medicine		
PI Address 1:	Department of Psychiatry & Behavioral Sciences		
PI Address 2:	5510 Nathan Shock Drive		
PI Web Page:			
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:**	06/30/2012
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:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date change to 6/30/2012 per NSBRI report submission (Ed., 7/12/2012) 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:			

Task Description:	(1) Original Aims Aim #1: To assess the effects of space radiation across a range of neurobehavioral functions in rodents, including assessments of general motor function and speed, inhibitory control (impulsivity), timing, learning, selective attention, and motivation. 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 changes in neurobehavioral functions by examining the integrity of the neurotransmitter systems known to mediate those neurobehavioral functions found impaired. (2) Key Findings 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. Using a version of the human Psychomotor Vigilance Test (PVT) adapted for use in rats (the rodent PVT, or rPVT), head-only exposure to radiation (including both protons and 56Fe particles) has been shown to significantly impair neurobehavioral function (e.g., decreased accuracy, increased impulsivity, increased lapses in attention) and slow motor function. These findings support the success of the rPVT as a rodent model for studying the risks of living in the space radiation environment due to changes in neurobehavioral function. Specific findings from the past year include: 1. Demonstrating that individual differences in susceptibility to the effects of radiation exist, with 56% of rats exposed to proton radiation showing a radiation sensitivity as indicated by marked neurobehavioral deficits, with these deficits being independent of dose (i.e., 25 cGy produced effects similar to 50 – 200 cGy). Importantly, only radiation-sensitive animals showed significant changes in proteins associated with the levels of dopamine (DA) D2 receptors as well as dopamine transporter (DAT) in the brain, suggesting that DA level differences may play an important role in how an organism responds to radiation neurobehaviorally, and have important implications for possible screening of radiation sensitivity and future development of radioprotectants. 2. Demonstrating that exposure to 56Fe ions at 10, 25, and 50 cGy produces highly specific effects on vigilance. Similar to the effects of proton radiation, 56Fe ion exposures produced an "individual differences" effect in that only a subset of irradiated animals showed neurobehavioral deficits (i.e., were "radiation sensitive"), with these deficits also being independent of dose. In contrast to proton radiation, 56Fe radiation did not produce deficits in inattention or motor function, and 56Fe radiation produced deficits in only 15% of the exposed animals. 3. Assessing the initial inflammatory response in the brain following proton irradiation by examining the expression of translocator protein 18 kDa (TSPO), a sensitive marker of reactive gliosis in proton-exposed rats. TSPO levels were significantly elevated in the forebrain, cerebellum, and whole brain tissue following proton exposure up to 14 days post-exposure, suggesting that proton radiation causes immediate damage to the brain via inflammation and reactive gliosis, and that the immediate inflammatory response and likely subsequent glial cell death and extended brain inflammation could underlie such neurobehavioral changes following proton exposure and impact an individual's sensitivity to proton radiation. 4. Studies supported by this grant were conducted by Dr. Catherine Davis as part of her newly-funded NSBRI Postdoctoral Fellowship to determine the degree to which radiation-induced deficits in neurobehavioral function differ as a function of basal dopaminergic function. Using inbred rats with inherent differences in dopamine (DA) function (Fischer 344 and Lewis rats), radiation-sensitive rats were found in the inbred Fischer rats, a strain with greater functioning DA system compared to Lewis rats but not yet in the Lewis strain, indicating again a possible involvement of the dopaminergic system in an individual's susceptibility to radiation-induced neurobehavioral damage to the CNS. (3) Impact of 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) Plan for the Coming Year Plans for the first year of this newly-funded project (will be a new project with the same title, "Detection and Prevention of Neurobehavioral Vulnerability to Space Radiation," with new period of performance) include 1) starting new behavioral pharmacology studies to determine the degree to which pre-existing individual differences in neurotransmitter function may be predictive of the observed differential neurobehavioral susceptibility of individuals following radiation, and 2) neurotransmitter protein level studies to determine the degree to which the observed neurotransmitter changes are restricted to specific brain regions. Additionally, this project will support Dr. Catherine Davis' NSBRI Postdoctoral Fellowship studies designed to determine the radioprotective effectiveness of dietary flaxseed to mitigate the deleterious effects of low-dose proton radiation on neurobehavioral function.
Rationale for HRP Directed Research:	
	The critically-needed research on the effects of ionizing radiation on cognitive/behavioral functions will provide the basis for extrapolating the effects of the space radiation environment on human cognitive function and performance. Earth-based applications of this research will extend to comparing the effects of other types of radiation exposures (e.g., from the workplace, medical environment, home) on neurobehavioral functions. Knowledge of those neurobehavioral functions and related brain areas affected by acute exposure to space radiation is extremely important in not only the development of a biobehavioral risk assessment model of radiation-induced deficits that could compromise operational performance during long-duration space exploration missions, but also in the development of mitigation strategies, countermeasures, as well as appropriate self-administered tests that astronauts can use to gauge their performance readiness for critical tasks. In addition, the development of a comprehensive and experimentally flexible animal model

Research Impact/Earth Benefits:	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 last funded year include: • Determinations of Individual differences in susceptibility to the effects of radiation exist, with 56% of rats exposed to proton radiation showing a radiation sensitivity as indicated by marked behavioral deficits in rPVT performance measures, with these deficits being relatively independent of dose. • Findings of radiation-sensitive animals showing significantly higher levels of dopamine D2 receptors as well as dopamine transporter (DAT) in the brain, with non-sensitive-but-exposed rats as well as control rats showing no such changes in DA protein levels, suggesting that DA level differences may play an important role in how an organism responds to radiation neurobehaviorally, and may have important implications for possible screening of radiation sensitivity and future development of radioprotectants. • Findings showing that exposure to 56Fe ions at 10, 25, and 50 cGy also produce highly specific effects on vigilance, including impairments in accuracy and impulsivity, and that a subset of the irradiated animals showed strong neurobehavioral deficits, and thus appeared to be quite "radiation sensitive." • Discovery that the initial inflammatory response in the brain is elevated in the forebrain, cerebellum, and whole brain tissue following proton exposure immediately following and up to 14 days post-exposure. This inflammatory response continues for a significant amount of time following irradiation and that could possibly lead to cellular changes and negatively impact neurobehavioral function, and suggests that the immediate inflammatory response and likely subsequent glial cell death and extended brain inflammation could underlie such neurobehavioral changes following proton exposure and impact an individual's sensitivity to proton radiation. • Dr. Catherine Davis' NSBRI Postdoctoral Fellowship study showing that radiation-induced deficits in neurobehavioral function differ as a function of basal dopaminergic function when examined in Inbred strains of rats with inherent differences in dopamine (DA) function, and indicating a likely involvement of the dopaminergic system in determining an individual's susceptibility to radiation-induced neurobehavioral damage to the CNS.
Bibliography Type:	Description: (Last Updated: 01/12/2021)
Articles in Peer-reviewed Journals	Davis CM, DeCicco-Skinner KL, Roma PG, Hienz RD. "Changes in Neurobehavioral Performance and Dopaminergic Function Associated with Exposure to Space Radiation." Submitted, May 2011. , May-2011
Articles in Peer-reviewed Journals	Davis CM, Roma PG, Hienz RD. "A Rodent Model of the Human Psychomotor Vigilance Test: Performance Comparisons." Submitted, May 2011. , May-2011
Awards	Davis C. "Honorable mention in the NASA Radiation Investigators' Workshop postdoctoral poster contest, Houston, Texas, September 2011." Sep-2011
Awards	Davis C. "Second place in the Experimental Biology meeting postdoctoral poster contest, San Diego, CA, April 2012." Apr-2012