Fiscal Year:	FY 2013	**Task Last Updated:**	FY 07/12/2013
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:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	07/01/2012	**End Date:**	06/30/2015
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: Sensorimotor Risk added per IRP Rev E (Ed., 3/19/14) NOTE: change in period of performance per July 2013 NSBRI report submission (Ed., 7/12/13) NOTE: End date change to 5/31/2015 per NSBRI (Ed., 8/23/2012)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Roma, Peter (Institutes for Behavior Resources, Inc.)		
Grant/Contract No.:	NCC 9-58-NBPF02802		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Assessing the biological consequences of living in the space radiation environment represents one of the highest priority areas of NASA research. Of critical importance is the need for an assessment of the vulnerabilities of the central nervous system (CNS) leading to functional neurobehavioral changes during long-term space missions, and the development of effective countermeasures to such risks. The present research addresses this need via the application of an innovative animal model to determine 1) the short- and long-term effects of radiation exposure on cognitive neurobehavioral function; and 2) the likely mechanisms of damage to the CNS following radiation exposure. Cognitive neurobehavioral functions relevant to astronaut mission performance effectiveness are being assessed with a rodent analog of the human Psychomotor Vigilance Test (PVT) currently used in space analog environments and by astronauts aboard ISS, which includes assessments of general motor function and speed, vigilance, inhibitory control ('impulsivity'), timing, motivation, and basic sensory function. Animals trained on the rodent version of the PVT (the rPVT) are subsequently exposed to protons and high-energy particle radiation and then tested for up to 12 months post-exposure to assess potential short- and long-term performance deficits. Likely mechanisms of damage to the CNS following radiation exposure are examined via pre-radiation behavioral pharmacology studies as well as post-radiation behavioral pharmacology studies and neurochemical assessments of CNS proteins relevant to neurotransmitter function and inflammation. Key aims of the study are to determine 1) whether pre-existing individual differences in neurotransmitter function may be predictive of the observed differential neurobehavioral susceptibility of individuals following proton radiation; 2) whether the observed neurotransmitter changes are restricted to specific brain regions, and 3) whether differential neurobehavioral susceptibility occurs following exposure to other ion species. Key Findings: Results from the project have demonstrated the reliability and validity of the neurobehavioral procedures in detecting behavioral changes following radiation over extended intervals following radiation exposure. Head-only exposure to radiation (protons, 56Fe, 28Si) has been shown to significantly impair neurobehavioral function (e.g., decrease accuracy, increase impulsivity, increase 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 exposure to 28Si ions produces highly specific effects on vigilance that are similar to the effects previously observed with both proton and 56Fe exposures, and include an individual differences effect in that only a subset of irradiated animals show neurobehavioral deficits (i.e., are radiation sensitive). In contrast to both proton and 56Fe radiation, 28Si radiation produced deficits in only about 9% of the exposed animals, suggesting a lower level of CNS-related dysfunction associated with 28Si radiation exposure. 2. Determining the degree to which behavioral responses to dopaminergic drugs differ as a function of radiation sensitivity. Radiation-sensitive and –insensitive rats were pharmacologically challenged with quinpirole (a D2 receptor agonist) and amisulpride (D2 receptor antagonist), with their behavior assessed via rate-decreasing effects of the drugs on fixed-ratio responding (a widely-used in vivo method for determining possible neurochemical differences). Results indicate 1) a likely increase in D2 receptor availability in insensitive rats, suggestive of a possible protective mechanism following radiation exposure, 2) that radiation-sensitive rats likely have decreased DA neurotransmission, and 3) that amisulpride administration may be a possible mitigation strategy to alleviate radiation-induced deficits on rPVT performance in sensitive rats. 3. Determining the radioprotective effects of a 10% flax seed diet for mitigating proton-induced neurobehavioral deficits (part of Dr. Catherine Davis' NSBRI Postdoctoral Fellowship PF02602). While the flax seed did not affect the proportion of animals developing neurocognitive deficits, there was a trend indicating that the animals receiving flax seed may show signs of early recovery from these deficits, a trend not evident in the irradiated rats not on flax seed. 4. Determining the degree to which radiation-induced deficits in neurobehavioral function differ as a function of basal dopaminergic function (supported by this grant and part of Dr. Catherine Davis's NSBRI Postdoctoral Fellowship PF02602). Brain tissue of both F344 and LEW rats displaying long-term deficits in rPVT performance were examined to determine if chronic inflammatory changes were evident. Significant changes in frontal cortex cytokine levels were found only in those F344 rats displaying a radiation-induced behavioral deficit in the rPVT, suggesting a chronic inflammatory state in the brain could damage numerous areas important for sustained attention and impulsive behavior. Plans for the Coming Year: Plans include 1) 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, 2) neurotransmitter protein level studies to determine the degree to which the observed neurotransmitter changes are restricted to specific brain regions, and 3) continued support of Dr. Catherine Davis' NSBRI Postdoctoral Fellowship studies designed to assess neurochemical changes in the brain following radiation.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	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 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:	During this year, 110 rats were trained in the rodent version of the PVT (the rPVT) for studies designed to examine the effects of protons and Silicon ions on the neuropharmacology and neurochemistry underlying those neurobehavioral functions previously shown susceptibility to low-dose irradiation from our prior experiments. 1. One study (N=60) examined the effects of 28Si radiation (0, 10, 25, and 50 cGy, 300 MeV/n) on rPVT performance, and showed that 28Si ions produce highly specific effects on vigilance that are similar to the effects previously observed with both proton and 56Fe radiation. 28Si also produces an individual differences effect in that only a subset of irradiated animals show neurobehavioral deficits, with these deficits also being independent of dose. 28Si radiation produced deficits in only about 9% of the exposed animals, suggesting a lower level of CNS-related dysfunction associated with exposure to this ion species. 2. A second study (N=50, part of Dr. Catherine Davis' NSBRI Postdoctoral Fellowship) determined the radioprotective effects of a 10% flax seed diet for mitigating proton-induced neurobehavioral deficits. While the flax seed did not affect the proportion of animals developing neurocognitive deficits, there was a trend indicating that the animals receiving flax seed may show signs of early recovery from these deficits, a trend not evident in the irradiated rats not on flax seed. 3. A third study determined the degree to which behavioral responses to dopaminergic drugs differ as a function of radiation sensitivity on the rPVT. Radiation-sensitive and -insensitive rats were pharmacologically challenged with quinpirole (a D2 receptor agonist) and amisulpride (D2 receptor antagonist), with their behavior assessed via rate-decreasing effects of the drugs on fixed-ratio responding (a widely-used in vivo method for determining possible neurochemical differences). Results indicate 1) a likely increase in D2 receptor availability in insensitive rats, suggestive of a possible protective mechanism following radiation exposure, 2) that radiation-sensitive rats likely have decreased DA neurotransmission, and 3) that amisulpride administration may be a possible mitigation strategy to alleviate radiation-induced deficits on rPVT performance in sensitive rats. 4. A fourth study (part of Catherine Davis' NSBRI Postdoctoral Fellowship) determined the degree to which radiation-induced deficits in neurobehavioral function differ as a function of basal dopaminergic function. Brain tissue of both F344 and LEW rats displaying long-term deficits in rPVT performance were examined to determine if chronic inflammatory changes were evident. Significant changes in frontal cortex cytokine levels were found only in those F344 rats displaying a radiation-induced behavioral deficit in the rPVT, suggesting a chronic inflammatory state in the brain could damage numerous areas important for sustained attention and impulsive behavior.
Bibliography Type:	Description: (Last Updated: 01/12/2021)
Abstracts for Journals and Proceedings	Davis CM, Guida PM, Hienz RD. " Neurobehavioral and neurochemical changes following head-only radiation exposure in the inbred Fischer 344 and Lewis rats." 19th IAA Humans in Space Symposium, Cologne, Germany, July 7-13, 2013. 19th IAA Humans in Space Symposium, Cologne, Germany, July 7-13, 2013. Abstract #359. , Jul-2013
Awards	Davis CM. "1st Place Postdoctoral Competition, HRP Meeting, Houston, TX, February 2013." Feb-2013
Awards	Davis CM. "3rd Place, Postdoctoral Poster Competition, NASA Space Radiation Investigators' Workshop, July 2012." Jul-2012
Awards	Davis CM. "ASPET Washington Fellow Travel Award, April 2013." Apr-2013