Fiscal Year:	FY 2013	**Task Last Updated:**	FY 12/19/2012
PI Name:	Davis, Catherine M. Ph.D.		
Project Title:	Mitigating Neurobehavioral Vulnerabilities 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:	catherine.davis-takacs@usuhs.edu	**Fax:**	FY 301-400-4023
PI Organization Type:	NON-PROFIT	**Phone:**	301-400-4596
Organization Name:	Henry M. Jackson Foundation		
PI Address 1:	6720-A Rockledge Dr.		
PI Address 2:			
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City:	Bethesda	**State:**	MD
Zip Code:	20817-1891	**Congressional District:**	8
Comments:	Campus address (Jan 2022): Department of Pharmacology and Molecular Therapeutics, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814. NOTE: PI formerly at Johns Hopkins University; moved to Henry M. Jackson Foundation for the Advancement of Military Medicine in fall 2020.		
Project Type:	Ground	**Solicitation / Funding Source:**	2011 NSBRI-RFA-11-01 Postdoctoral Fellowships
Start Date:	11/01/2011	**End Date:**	10/31/2013
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:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Hienz, Robert (MENTOR/ Johns Hopkins University)		
Grant/Contract No.:	NCC 9-58-PF02602		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	POSTDOCTORAL FELLOWSHIP (1) Original Aims Aim 1: To determine the degree to which radiation-induced deficits in neurobehavioral function differ as a function of basal dopaminergic tone. Aim 2: To determine the radioprotective effectiveness of dietary flaxseed (FS) to mitigate the deleterious effects of low-dose proton radiation on neurobehavioral function. Aim 3: To determine DAergic and inflammatory protein levels in radiation-induced, neurobehaviorally-impaired rats and in radioprotectant-treated rats. To assess the likelihood of space radiation producing long-term functional changes in the CNS, neurobehavioral functions are being measured in rodents via an animal test analogous to 'vigilance' tests in humans. Cognitive neurobehavioral functions relevant to astronaut mission performance effectiveness are assessed with a rodent analog of the Psychomotor Vigilance Test (PVT) currently used in space analog environments and by astronauts aboard ISS. Neurobehavioral functions examined include assessments of general motor function and speed, vigilance, memory, inhibitory control ('impulsivity'), timing, motivation, and basic sensory function. Groups of animals with inherent differences in dopamine system function were trained on the rodent version of the PVT, following which they were exposed to radiation and then re-tested periodically for up to 5 months post-exposure to assess potential performance deficits. In an upcoming study, separate groups of animals will be given an experimental diet supplemented with flaxseed and will undergo the same behavioral testing using the rPVT. Likely mechanisms of damage to the CNS following radiation exposure and flaxseed treatment are being examined using Western blotting of proteins relevant to neurotransmitter function and inflammation. (2) Key Findings • 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. • Data showing that radiation-induced deficits in neurobehavioral function differ as a function of basal dopaminergic tone 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. (3) Impact of key findings. The key findings during this funding period support the stated hypothesis that basal differences in dopaminergic tone would influence the extent of neurobehavioral deficits following irradiation. (4) Proposed research plan for the coming year. Western blot analyses will be completed on the brain tissue from the Fischer 344 and Lewis rats from the previous funding year. More specifically, brain regions implicated in attentional performance will be subjected to Western blot analysis and mRNA detection. Proteins of interest include, but are not limited to, the dopamine D2 receptor, the dopamine transporter, cell survival proteins, and inflammatory cytokines. In addition, separate groups of rats will be maintained on a diet containing 10% flax seed or a control diet, trained on the rPVT, and exposed to proton radiation. Follow-up behavioral testing will occur for at least 5 months after irradiation to determine if dietary flax seed mitigates the neurobehavioral deficits following proton exposure. Once the behavioral testing period has ended, brain tissue will be removed and analyzed as described above.
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. Moreover, 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 first year include: • 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. • 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. • Data 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: 11/29/2024)
Abstracts for Journals and Proceedings	Davis CM, Guida PM, Hienz RD. "Individual Differences in Neurobehavioral Deficits Following Proton Irradiation are Related to Basal Dopamine Function." 23rd Annual NASA Space Radiation Investigators' Workshop, Durham, NC, July 8-11, 2012. 23rd Annual NASA Space Radiation Investigators' Workshop, Durham, NC, July 8-11, 2012. , Jul-2012
Awards	Davis CM. "2nd Place, Best Abstract Competition (Postdoc), Behavioral Pharmacology Division of the American Society for Pharmacology and Experimental Therapeutics (ASPET), April 2012." Apr-2012
Awards	Davis CM. "3rd Place, Postdoctoral Fellow Poster Contest, for 'Individual Differences in Neurobehavioral Deficits Following Proton Irradiation are Related to Basal Dopamine Function," 23rd Annual NASA Space Radiation Investigators' Workshop, July 2012." Jul-2012
Awards	Davis CM. "ASPET Young Scientist Travel Award to attend Annual Experimental Biology Meeting in San Diego, CA, April 2012." Apr-2012
Awards	Davis CM. "Honorable Mention, Postdoctoral Fellow Poster Contest for 'Neurobehavioral Effects of Space Radiation on Psychomotor Vigilance,' 22nd Annual NASA Space Radiation Investigators' Workshop, September 2011." Sep-2011
Awards	Davis CM. "Student (competitive enrollment), NASA Space Radiation Summer School at Brookhaven National Laboratory, May 2012." May-2012
Books/Book Chapters	Davis CM. "Animal Models of Drug Abuse: Place and Taste Conditioning." in "Animal Models for the Study of Human Disease." Ed. P.M. Conn. New York : Elsevier, in press as of December 2012., Dec-2012