Fiscal Year:	FY 2014	**Task Last Updated:**	FY 12/24/2013
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		
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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:**	10/31/2014
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: New end date per NSBRI December 2013 report (Ed., 12/24/13)		
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 Original Aims/Objectives 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 Fischer and Lewis rats and in radioprotectant-treated (FS) rats. To assess the likelihood of space radiation producing 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, and motivation. Groups of PVT-trained animals with inherent differences in dopamine system function were exposed to radiation and then re-tested for up to 5 months post-exposure. In an additional study, separate groups of animals were given an experimental diet supplemented with flaxseed and underwent 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. Key Findings • Radiation-induced changes in rPVT performance in the Fischer 344 and Lewis rat strains was accompanied by differential cytokine expression in the frontal cortex. Interestingly, two of the cytokines elevated in the Lewis rats, the strain that did not display any radiation-induced rPVT deficits, are cytokines reported to decrease cognitive impairments in animal models of Alzheimer's disease and ischemic injury, suggesting CNTF and GM-CSF as possible future candidates for treatments of radiation-induced cognitive deficits. • Radiation-induced changes in rPVT performance were evident in rats supplemented with a 10% flaxseed diet. However, these rats recovered from the radiation-induced rPVT deficits by the end of post-radiation testing period, whereas irradiated rats receiving a control diet had rPVT deficits that remained throughout the post-radiation test period. • Quinpirole, a D2/3 receptor agonist, and amisuplride, a D2 receptor antagonist, had differing effects on behavioral performances of rats exposed to 56Fe that were related to their performances on the rPVT following exposure. Rats displaying no rPVT deficits following exposure were more sensitive to the behavior-decreasing effects of quinpirole; rats displaying rPVT deficits were more sensitive to the behavior-increasing effects of amisulpride. These data demonstrate the importance of the dopamine system in individual behavioral differences following irradiation. Impact The key findings during this funding period support the stated hypothesis that differences in brain-region specific cytokine differences would be related to the degree of deficit on the rPVT following radiation exposure. Further, a flaxseed-containing diet appears to aid in recovery of behavioral performance following proton exposure. Proposed research for the coming year Western blot analyses will be completed on the brain tissue from rats in the flaxseed study. Relevant brain regions will be excised and subjected to Western blot analysis and mRNA detection. Proteins of interest include the dopamine D2 receptor, the dopamine transporter, cell survival proteins, and cytokines (e.g., CNTF, GM-CSF). Additional behavioral pharmacology studies assessing the effects dopamine receptor agonists in rats pre- and post-exposure will also be conducted.
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:	Radiation-induced changes in rPVT performance in the Fischer 344 and Lewis rat strains was accompanied by differential cytokine expression in the frontal cortex. Interestingly, two of the cytokines elevated in the Lewis rats, the strain that did not display any radiation-induced rPVT deficits, are cytokines reported to decrease cognitive impairments in animal models of Alzheimer's disease and ischemic injury. Given these results, CNTF and GM-CSF could be possible candidates for treatments for radiation-induced cognitive deficits in future studies. Radiation-induced changes in rPVT performance were evident in rats supplemented with a 10% flaxseed diet. However, these rats recovered from the radiation-induced rPVT deficits by the end of post-radiation testing period, whereas irradiated rats receiving a control diet had rPVT deficits that remained throughout the post-radiation test period. Quinpirole, a D2/3 receptor agonist, and amisuplride, a D2 receptor antagonist, had differing effects on behavioral performances of rats exposed to 56Fe that were related to their performances on the rPVT following exposure. Rats displaying no rPVT deficits following exposure were more sensitive to the behavior-decreasing effects of quinpirole; rats displaying rPVT deficits were more sensitive to the behavior-increasing effects of amisulpride. These data demonstrate the importance of the dopamine system in individual behavioral differences following irradiation.

Bibliography Type:	Description: (Last Updated: 11/29/2024)
Abstracts for Journals and Proceedings	Davis CM, Hienz RD. "Assessing neurobehavioral function with the rat psychomotor vigilance task." Experimental Biology 2012, San Diego, CA, April 21-25, 2012. FASEB Journal 2012 Apr;26(Meeting Abstract Supplement):1042.2. Search: http://www.fasebj.org/content/vol26/1_MeetingAbstracts , Apr-2012
Abstracts for Journals and Proceedings	Davis CM, Hienz RD. "Behavioral effects of quinpirole on schedule-controlled responding in radiation sensitive and insensitive rats." Experimental Biology 2013 meeting, Boston, MA, April 20-24, 2013. FASEB J. 2013 Apr;27(Meeting Abstract Supplement):1098.15. See also http://www.fasebj.org/content/vol27/1_MeetingAbstracts for searching. , Apr-2013
Articles in Peer-reviewed Journals	Davis CM, DeCicco-Skinner KL, Roma PG, Hienz RD. "Individual differences in attentional deficits and dopaminergic protein levels following exposure to proton radiation." Radiation Research. Resubmitted August 30th, 2013. Currently under review as of December 2013. , Dec-2013
Articles in Peer-reviewed Journals	Davis CM, Roma PG, Hienz RD. "A rodent model of the human psychomotor vigilance test: Performance comparisons." Behavioral Brain Research. Submitted in January 2012. Currently under revision as of October 2012. (Ed. note 12/2013: No update since then) , Oct-2012
Awards	Davis CM. "1st Place Postdoctoral Poster Contest HRP Investigators' Meeting, February 2013." Feb-2013
Awards	Davis CM. "American Society for Pharmacology and Experimental Therapeutics (ASPET) Washington Policy Fellow, November 2012." Nov-2012
Awards	Davis CM. "American Society for Pharmacology and Experimental Therapeutics (ASPET) Young Investigator Travel Award, April 2013." Apr-2013
Books/Book Chapters	Davis CM. "Chapter 28–Animal Models of Drug Abuse: Place and Taste Conditioning." in "Animal Models for the Study of Human Disease." Ed. P.M. Conn. London ; Waltham, MA : Elsevier, 2013. p. 681-707. http://dx.doi.org/10.1016/B978-0-12-415894-8.00028-2 , Aug-2013