Fiscal Year:	FY 2023	**Task Last Updated:**	FY 10/15/2022
PI Name:	Davis, Catherine M. Ph.D.		
Project Title:	VNSCOR: Mechanisms of Radiation-Induced Changes in Sustained Attention and Social Processing (80NSSC22K0022)		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HFBP**:Human Factors & Behavioral Performance (IRP Rev H)		
Human Research Program Risks:	None		
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:			
PI Web Page:			
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:**	2016-2017 HERO NNJ16ZSA001N-SRHHC. Appendix E: Space Radiobiology and Human Health Countermeasures Topics
Start Date:	12/14/2021	**End Date:**	12/13/2023
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	1	**No. of Master' Degrees:**	0
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:	3	**Monitoring Center:**	NASA JSC
Contact Monitor:	Whitmire, Alexandra	**Contact Phone:**	
Contact Email:	alexandra.m.whitmire@nasa.gov		
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Hienz, Robert Ph.D. (Johns Hopkins University) Robinson, Siobhan Ph.D. (Hamilton College)		
Grant/Contract No.:	80NSSC22K0022		
Performance Goal No.:			
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Task Description:	[Ed. note Jan 2022: Continuation with same Principal Investigator (PI) Dr. Catherine Davis, of "VNSCOR: Mechanisms of Radiation-Induced Changes in Sustained Attention and Social Processing," grant #80NSSC18K1080 when PI was at Johns Hopkins University. See also project, "VNSCOR: Responses of the Nervous System to Chronic, Low Dose Charged Particle Irradiation" (Principal Investigator (PI): Greg Nelson)] NELSON/DAVIS VIRTUAL NASA Specialized Center of Research (NSCOR): The project is organized as 5 large experimental campaigns to quantify responses for an interrelated set of central nervous system (CNS) outcome measures in mice to acute and protracted exposures to protons at a dose of 0.5 Gy and sham controls; acute and protracted exposures to 0.25 and 0.5 Gy of charged particles; and acute and protracted exposures to 0.5 and 1.5 Gy of gamma rays. This research builds on previous studies that demonstrated that proton and HZE (high charge energy) exposures result in individual differences in deficits in sustained attention, but more general deficits in recognition memory. This current project is combined with "Responses to the Nervous System to Chronic, Low Dosed Charged Particle Irradiation" (PI: Nelson) in order to explore if these effects are LET (linear energy transfer)-dependent for 16O ions, add a relatively understudied, but important, ion (4He), and examine CNS effects in whole animals following fractionated exposures, and the interaction of other space flight factors (e.g., sleep fragmentation). Revised Specific Aims: Aim 1a: Effects of protracted exposure to five-ion GCR [galactic cosmic rays] sim (1H, 4He, 28Si, 16O, 56Fe) Aim 1b: Effects of protracted exposure to GCR sim without protons (4He, 28Si, 16O, 56Fe) Aim 1c: Effects of protracted exposure to protons only Aim 1d: Acute exposure to 4He (250 MeV/n) Aim 2a: Neuronal activation and molecular markers following radiation Aim 2b: Chemogenetic silencing of mPFC subregions Specific Aims: 1) Determine the effects of acute, single 16O and 4He ion exposures on sustained attention, social odor recognition memory, and social dominance. (This aim has been modified in order to integrate with Nelson project); 2) Determine the effects of a fractionated exposure on sustained attention and recognition memory in comparison to the effects of single ion exposures on these measures; 3) Determine the effects of circadian disruptions and sleep fragmentation on sustained attention and recognition memory following radiation exposure (This aim has been modified in order to integrate with Nelson project); 4) Examine the underlying mechanisms of these deficits using immunohistochemical and pharmacogenetic procedures. ORIGINAL PROPOSAL 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 proposal addresses this need via the application of an animal model to 1) determine the effects of acute, single 16O and 4He ion exposures on sustained attention, social odor recognition memory, and social dominance; 2) determine the effects of a fractionated exposure on sustained attention and recognition memory in comparison to the effects of single ion exposures on these measures; 3) determine the effects of circadian disruptions and sleep fragmentation on sustained attention and recognition memory following radiation exposure; and 4) examine the underlying mechanisms of these deficits using immunohistochemical and pharmacogenetic procedures. Prior research has 1) identified rats that are sensitive to radiation-induced deficits in sustained attention and 2) shown that acute, single ion exposures alter social motivation and social odor recognition memory. The current proposal will determine how the immediate effects of irradiation impact subsequent neurobehavioral deficits by assessing various behavioral, physiological, and neurobiological markers of radiation exposure at early and later time points post-exposure. Groups of animals will be trained on a rodent version of the human psychomotor vigilance test, exposed to radiation, and then tested for both social processing and sustained attention deficits following exposure; subsets of rats will be implanted with biotelemetry devices to measure fluctuations in spontaneous locomotor activity and body temperatures following radiation exposure and changes in sleep or circadian disruptions. Individual variations in these behavioral, physiological, or neurobiological responses following radiation will be assessed. Likely mechanisms of damage to the CNS following radiation exposure will be examined using brain tissue, in addition to a pharmacogenetic technique to determine the severity of radiation-induced neurobehavioral deficits.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The results of the current project will be used to understand how radiation exposure affects the central nervous system to induce deficits in neurobehavioral function.
	During the reporting period, we exposed male and female rats to the simplified galactic cosmic radiation (GCR) simulation, either a single acute dose (50 cGy) or chronic dosing (2.08 cGy per day/6 days per week for 4 total weeks; 50 cGy total dose). This was a replicate of the same dose rate study we ran in 2019. This replicate was previously canceled due to the COVID-19 pandemic. 60 rats (30 male and 30 female) were shipped to Brookhaven National Laboratory and irradiated with the GCR simulation. Some of the rats were previously trained on the rPVT. [Ed. Note: The rPVT is a sustained attention test that requires subjects to monitor the location of a stimulus that occurs infrequently.] Following exposure, all rats were tested for social odor recognition memory (SORM) at 7 days, 30 days, 90 days, and 6 months following radiation exposure. A subset of animals completed rPVT testing following radiation, from approximately 30 days to 6 months following exposure. Following the 6-month time point, all animals were sacrificed to collect brain and blood samples. In preliminary analyses of the data, radiation exposure significantly impaired social odor recognition memory; but limited sex differences were found for the early time points. For the rPVT, results suggest that both acute and chronic GCR sim

Task Progress:	exposure can impair performance, and these effects could be more robust in female animals. We also completed statistical analysis of the rPVT data from 4He exposed male rats. Using a fully saturated ANCOVA-type linear mixed effects model, we found significant dose-dependent changes in rPVT performance parameters. More specifically, exposure to 25 cGy significantly decreased accuracy (percent correct responding), increased false alarms (impulsive responding), and increased in several different reaction time measures. Interestingly, exposure to 5 cGy only induced changes in a few reaction time measures, but had no significant effect on other measures, including accuracy, false alarms, and lapses in attention. Blood samples from both 4He-exposed and GCR sim-exposed rats are being analyzed for the presence of specific miRNAs that have previously been shown to be associated with exposure to various spaceflight factors, including radiation and microgravity. Our study seeks to determine if any of these miRNAs can be used as biomarkers of these behavioral deficits. We are currently preparing for an acute proton exposure in NASA Space Radiation Laboratory (NSRL) run 22C, where we will expose groups of male and female rats to 50 cGy protons for comparison to our GCR sim studies.
Bibliography Type:	Description: (Last Updated: 11/29/2024)
Articles in Peer-reviewed Journals	Thomas PK, Sullivan LK, Dickinson GH, Davis CM, Lau AG. "The effect of helium ion radiation on the material properties of bone." Calcif Tis Int. 2021 Jan 30;108:808-18. https://doi.org/10.1007 s00223-021-00806-7 ; PMID: 33517470 , Jan-2021
Articles in Peer-reviewed Journals	Davis CM, Allen AR, Bowles DE. "Consequences of space radiation on the brain and cardiovascular system." J Environ Sci Health C Toxicol Carcinog. 2021 Apr 27;39(2):180-218. https://doi.org/10.1080/26896583.2021.1891825 ; PMID: 33902387 , Apr-2021
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Articles in Peer-reviewed Journals	Jones CB, Peiffer LB, Davis CM, Sfanos KS. "Examining the effects of 4He exposure on the gut-brain axis." Radiat Res. 2021 Mar 1;197(3):242-52. https://doi.org/10.1667/RADE-20-00285.1 ; PMID: 34752622 , Mar-2022
Awards	Davis C. "American Society for Pharmacology and Experimental Therapeutics JH Woods Early Career Award in Behavioral Pharmacology" Apr-2022