Fiscal Year:	FY 2020	Task Last Updated:	FY 12/04/2020
PI Name:	Eisch, Amelia Ph.D.	Ĩ	
Project Title:	HZE Particle Exposure-Induced Improvement of Pattern Separation in Mature Mice: Alterations in Mission-Relevant Behaviors and Neural Circuitry		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline Element/Subdiscipline:	HUMAN RESEARCHRadiation health		
Joint Agency Name:	Т	TechPort:	No
Human Research Program Elements:	(1) SR:Space Radiation		
Human Research Program Risks:	(1) BMed :Risk of Adverse Cognitive or B	ehavioral Conditions and	1 Psychiatric Disorders
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:	NOTE: Previously at University of Texas	Southwestern Medical C	enter at Dallas, 2000-2016
Project Type:	Ground	Solicitation / Funding Source:	2013-14 HERO NNJ13ZSA002N-RADIATION
Start Date:	08/01/2017	End Date:	02/28/2021
No. of Post Docs:	5	No. of PhD Degrees:	0
No. of PhD Candidates:	10	No. of Master' Degrees:	0
No. of Master's Candidates:	0	No. of Bachelor's Degrees:	1
No. of Bachelor's Candidates:	7	Monitoring Center:	NASA JSC
Contact Monitor:	Zawaski, Janice	Contact Phone:	
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 2/28/2021 per NSSC information (Ed., 7/31/2020)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	80NSSC17K0060		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	ED. NOTE: New grant number 80NSSC17K0060Continuation of "HZE Particle Exposure-Induced Improvement of Pattern Separation in Mature Mice: Alterations in Mission-Relevant Behaviors and Neural Circuitry," grant NNX15AE09G, with the same Principal Investigator (PI) Dr. Amelia Eisch; PI moved to Children's Hospital of Philadelphia/Univ Pennsylvania Perelman School of Medicine from University of Texas Southwestern Medical Center at Dallas. An unavoidable consequence of deep space missions is exposure to galactic cosmic radiation (GCR), which includes high (H) atomic number (Z) and energy (E) particles particles like Fe, Si, and O. Estimating radiation risks to the central nervous system (CNS) by HZE particles necountered during space missions is a high research priority. Past research has shown that rodents exposed to HZE particles have cognitive and performance deficits in numerous behavioral tasks, including those that rely on the hippocampus, a brain region involved in learning and memory. Notably, we have found that mature mice (of equivalent age to astronauts) exposed to either Si or Fe HZE particles actually show improved performance on a very difficult hippocampal task to assess the ability to discrimination two contexts that differ in discrete ways. Here we propose three aims to understand this improved context "pattern separation is linked to improved performance on related learning and memory tasks, as well as executive function tasks, in the short-term, but to decreased performance in the long-term. In Aim 2, we hypothesize that HZE particle exposure-induced improved pattern separation is linked in the short-term to diminished stress-induced emergence of anxiety and depression-like behaviors, but to greater emergence in the long-term. In Aim 3, we hypothesize that HZE particle exposure-induced improved pattern separation is lonked in the short-term to diminished stress-induced emergence of anxiety and depression-like behaviors, but to greater emergence in the long-term. In Aim 3, we hypothesize that HZE
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	An unavoidable aspect of manned space flights is exposure to galactic cosmic radiation (GCR), which is made up primarily of protons (87%), followed by helium (11%) and then high atomic number (Z) and high-energy (HZE) particles (2%) like iron, silicon, and oxygen. The energy of HZE particles can be very high (>1000 MeV/u), sufficient in many cases to penetrate the spacecraft hull and interior materials, and they have a complex track structure and high linear energy transfer (LET). Thus, while the greatest physical radiation dose of GCR comes from high-energy protons, the greatest biological radiation dose of GCR comes from HZE particles. With long-duration and exploratory space missions in the near future, we need to understand how GCR influences human health and behavior. Estimation of radiation risks to the central nervous system (CNS) is a high research priority according to both a National Academy of Sciences report and NASA's Radiation Health Bioastronautics Roadmap. In rodents, HZE particles induce cognitive domain deficits, including decreased hippocampal learning and memory and cortically based executive function. However, it remains unclear whether the age at irradiation (IRR) influences the outcome of behavioral tests. It is also unclear whether these cognitive decrements extend to other cognitive tests, or to other behavioral domains, such as mood and stress response. Recently, we found that mice exposed at maturity ("astronaut-aged") to 28Si or 56Fe HZE particle IRR perform better than control mice on a hippocampal-based pattern separation task (context discrimination fear conditioning, CDFC). We want to understand if this behavioral improvement in pattern separation is reflective of other changes in behavior, and whether these changes will be beneficial or detrimental to mission success. We propose a behavioral domain- and brain network-based analysis to understand the HZE particle-induced behavioral improvement shown in our pilot data. These data will have relevance for understanding the risks fac
Task Progress:	Using mice irradiated at astronaut-age and multiple time points post-irradiation, we have found that mice of astronaut age show improved pattern separation in both appetitive and aversive tasks. Our ongoing work is revealing the sex- and task-dependency of this result, which is being prepared for publications. In addition to our ongoing work on how the translationome of genetically-defined dentate gyrus granule cells is altered after radiation, we are collaborating with other investigators to determine the efficacy of key countermeasures that may prevent irradiation-induced behavioral changes.
Bibliography Type:	Description: (Last Updated: 10/09/2024)
Articles in Peer-reviewed Journals	Ortega SB*, Torres VO*, Latchney SE, Whoolery CW, Noorbhai IZ, Poinsatte K, Selvaraj UM, Benson MA, Meeuwissen AJM, Plautz EJ, Kong X, Ramirez DM, Ajay AD, Meeks JP, Goldberg MP, Monson NL, Eisch AJ, Stowe AM. *equal contribution. "B cells migrate into remote brain areas and support neurogenesis and functional recovery after focal stroke in mice." Proc Natl Acad Sci U S A. 2020 Mar 3;117(9):4983-93. https://doi.org/10.1073/pnas.1913292117; PMID: 32051245; PMCID: PMC7060723, Mar-2020
Articles in Peer-reviewed Journals	Tran FH*, Spears SL*, Ahn KJ, Eisch AJ, Yun S. *equal contribution. "Does chronic systemic injection of the DREADD agonists clozapine-N-oxide or compound 21 change behavior relevant to locomotion, exploration, anxiety, and depression in male non-DREADD-expressing mice?" Neuroscience Letters. 2020 Nov 20;20;739:135432. Epub 2020 Oct 17. <u>https://doi.org/10.1016/j.neulet.2020.135432</u> ; <u>PMID: 33080350</u> , Nov-2020
Articles in Peer-reviewed Journals	Rivera PD, Simmons SJ, Reynolds RP, Just AL, Birnbaum SG, Eisch AJ. "Image-guided cranial irradiation-induced ablation of dentate gyrus neurogenesis impairs extinction of recent morphine reward memories." Hippocampus. 2019 Aug;29(8):726-35. Epub 2019 Feb 18. <u>https://doi.org/10.1002/hipo.23071</u> ; <u>PMID: 30779299</u> ; <u>PMCID: PMC7036142</u> , Aug-2019
Articles in Peer-reviewed Journals	Snitow ME, Zanni G, Ciesielski B, Burgess-Jones P, Eisch AJ, O'Brien WT, Klein PS. "Adult hippocampal neurogenesis is not necessary for the response to lithium in the forced swim test." Neurosci Lett. 2019 Mar 30;704:67-72. https://doi.org/10.1016/j.neulet.2019.03.052 ; PMID: 30940476; PMCID: PMC6594907 , Mar-2019

Articles in Peer-reviewed Journals

Bulin SE, Simmons SJ, Richardson DR, Latchney SE, Deutsch HM, Yun S, Eisch AJ. "Indices of dentate gyrus neurogenesis are unaffected immediately after or following withdrawal from morphine self-administration compared to saline self-administering control male rats." Behav Brain Res. 2020 Mar 2;381:112448. https://doi.org/10.1016/j.bbr.2019.112448; PMID: 31870778; PMCID: PMC7036141, Mar-2020