Fiscal Year:	FY 2014	**Task Last Updated:**	FY 03/26/2014
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Project Title:	Changes in the Neuroproteome Associated with HZE-Induced Impairment of Cognition		
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:	(1) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (2) **Sensorimotor**:Risk of Altered Sensorimotor/Vestibular Function Impacting Critical Mission Tasks		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:			
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Flight Program:			
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COI Name (Institution):	Dutta, Sucharita (Eastern Virginia Medical School) Semmes, Oliver (Eastern Virginia Medical School)		
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Task Description:	One of NASA's biggest concerns about the long-term health of astronauts who go on deep space missions is the impact that High Z, High Energy (HZE) particles have on brain function (neurocognition). Data from our laboratory and others suggests that there is significant impairment of certain neurocognitive tasks (spatial memory and Executive function-attentional set shifting) following exposure to low HZE doses. The goal of this application is to determine the Threshold dose for the induction of HZE-induced spatial memory impairments (HISMI) or Attentional Set Shifting Impairments (HIASSI) following exposure to 56Fe, 48Ti, and 28Si particles. The proposed studies will also identify the changes in the proteome of the brain (neuroproteome) of rats that differ in their susceptibility to HISMI and HIASSI, which will provide further insight into the factors that lead to HISMI/HIASSI and perhaps more importantly, that prevent its emergence. Our underlying hypothesis is that HISMI and HIASSI arise as the direct result of HZE-induced changes in the neuroproteome. We also hypothesize that exposure to HZE species that have different track structures will result in different mechanisms of HZE-induced cognitive impairment (HICI). Collectively, these studies will give some insight into the underlying cause for HISMI and HIASSI. Our studies will thus address CNS Gaps 1, 2, and 6, and we shall specifically focus on the following aims: Aim 1. Determine the Threshold dose for the induction of HISMI and HIASSI following exposure to 56Fe, 48Ti, and 28Si particles when delivered as a single dose. Aim 2. Determine the Threshold dose for the induction of HISMI and HIASSI following exposure to 56Fe, 48Ti, and 28Si particles when delivered in three fractions over a 5-day period. Aim 3. Identify changes in the neuroproteome that are associated with susceptibility or resistance to developing HISMI and HIASSI following exposure to 56Fe particles. Aim 4. Determine the mechanism of HISMI and HIASSI induced by HZE particles of differing LET. In Aim 1, socially mature (~6 month old) male Wistar rats will be irradiated with 56Fe, 48Ti, and 28Si particles (with incident energies of 600 and 1000 MeV/nucleon). Rats will receive whole body HZE irradiation (2.5, 5, 10, 15, and 20 cGy), and HISMI and HIASSI will be assessed at 3 months post irradiation. In Aim 2, 6-month old male Wistar rats will be exposed to the 56Fe, 48Ti, and 28Si particle beams using a 5 day, 3 x 5 cGy fraction irradiation scheme with a 48 h. inter-fraction time. HISMI and HIASSI will be assessed at 3 months post irradiation and the severity of HISMI and HIASSI compared to that induced when 15 cGy was delivered as a single dose. These studies can be iteratively modified (change in fraction size, number, and inter-fraction time) if warranted so that modelers can extrapolate our findings to a more realistic HZE exposure pattern. In Aims 3 and 4, the composition of the neuroproteome (hippocampus and selected regions of the prefrontal cortex) of irradiated rats that have “normal” cognitive performance or have developed HISMI or HIASSI will be established using an unbiased proteomic profiling approach. We shall use a label free differential protein profiling workflow on the Q-Exactive Orbitrap mass spectrometer. These studies will give considerable insight into the underlying cause for HZE-induced neurocognitive failure. The proposed studies will continue to define the minimum dose of HZE particles that will induce HISMI and HIASSI. Moreover, our studies will provide considerable insight into the underlying mechanism of HICI, and will identify prognostic biomarkers that could be translated to human studies to monitor the emergence of HICI. These studies may also help to develop appropriate countermeasures and help identify sensitive individuals, so that NASA’s medical staff can implement appropriate countermeasures to protect these at risk individuals.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2014.
Bibliography Type:	Description: (Last Updated: 02/21/2024)