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| **Fiscal Year:** | FY 2009 | **Task Last Updated:** | FY 05/08/2009 |
| **PI Name:** | Hienz, Robert D. Ph.D. | | |
| **Project Title:** | Detection & Prevention of Neurobehavioral Vulnerability 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 | | |
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| **PI Organization Type:** | UNIVERSITY | **Phone:** | 410-550-2788 |
| **Organization Name:** | The Johns Hopkins University School of Medicine | | |
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| **Zip Code:** | 21224-6823 | **Congressional District:** | 7 |
| **Comments:** | | | |
| **Project Type:** | GROUND | **Solicitation / Funding Source:** | 2007 Crew Health NNJ07ZSA002N |
| **Start Date:** | 05/01/2008 | **End Date:** | 04/30/2012 |
| **No. of Post Docs:** | 1 | **No. of PhD Degrees:** | 0 |
| **No. of PhD Candidates:** | 1 | **No. of Master' Degrees:** | 0 |
| **No. of Master's Candidates:** | 0 | **No. of Bachelor's Degrees:** | 0 |
| **No. of Bachelor's Candidates:** | 1 | **Monitoring Center:** | NSBRI |
| **Contact Monitor:** | | **Contact Phone:** | |
| **Contact Email:** | | | |
| **Flight Program:** | | | |
| **Flight Assignment:** | | | |
| **Key Personnel Changes/Previous PI:** | | | |
| **COI Name (Institution):** | Weed, Michael ( The Johns Hopkins University School of Medicine ) | | |
| **Grant/Contract No.:** | NCC 9-58-NBPF01604 | | |
| **Performance Goal No.:** | | | |
| **Performance Goal Text:** | | | |

(1) Original Aims of the Project
Aim #1: To assess the effects of space radiation across a range of cognitive/behavioral functions in rodents. Performance measures include assessments of general motor function and speed, fine motor control, inhibitory control ('impulsivity'), timing, short-term memory, spatial working memory, learning and selective attention, motivation, and basic sensory function. Groups of animals are separately trained on different tasks, exposed at Brookhaven National Laboratory to high-energy radiation at levels that astronauts would likely experience during lunar or planetary surface activities, and then immediately re-tested.

Aim #2: To assess the long-term effects of radiation across a range of cognitive/behavioral functions via extended post-exposure testing for potential performance deficits.

Aim #3: To assess both the acute and long-term effects of radiation on the neurochemical mechanisms underlying

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| **Task Description:** | changes in cognitive/behavioral functions by examining the integrity of the neurotransmitter systems known to mediate those neurobehavioral functions found impaired.<br><br>(2) Key Findings of the Project<br><br>Results from the project thus far demonstrate the ability to establish an automated training and testing facility for assessing cognitive and behavioral function in the rodent model, and indicate that rodents are readily trainable in the cognitive/behavioral testing procedures, and readily learn to perform simple reaction time procedures, delayed-estimation/motor preparation tasks, and complex visual discriminations. Data obtained on changes in cognitive/behavioral performances following 5-Gy gamma radiation demonstrated the reliability and validity of the procedures in detecting behavioral changes following radiation, that an analog of a human psychomotor performance assessment procedure can be employed with rodents to automatically assess neurobehavioral function on a daily basis, and that such a procedure can be used to effectively track changes in neurobehavioral function over extended intervals following radiation exposure. Specifically, the results showed that head-only radiation produces discrete neurobehavioral changes by significantly decreasing discrimination accuracy and increasing false alarms in the reaction time procedure, with the latter result being indicative of a decrease in inhibitory control. These findings support the likely success of the rodent model for studying the risks from living in the space radiation environment in terms of damage to the CNS and changes in cognitive/behavioral function.<br><br>During the current reporting year, rats were trained to perform an intradimensional/extradimensional (ID-ED) task that is a computerized analog of the Wisconsin card sort task used to test category abstraction, and is similar in function to non-automated tests of set shifting in rats that use odor, texture or color as stimulus dimensions. Set shifting tasks measure learning, reversal learning, perseverative responding, and the ability to switch attentional sets between categories. Following training, experimental rats were exposed to head-only x-ray irradiation (2.3 Gy), while control rats were sham-exposed using the same anesthesia protocol. Initial data with this procedure indicates that the procedure can clearly detect radiation-induced changes in standard discrimination and discrimination learning reversal in rats. Additionally, differences in error rates of the rats' also differentiated between different discrimination conditions, thus indicating that the ID-ED procedure can track a rat's ability to shift attention between different stimulus dimensions. The results of these experiments confirm the feasibility of an animal model approach for assessing neurobehavioral risks associated with living in a space radiation environment, and demonstrate the sensitivity of differing neurobehavioral test measures to the effects of radiation that produce highly specific effects on neurobehavioral function.<br><br>(3) Impact of these Findings<br><br>Very little is known about the brain's response to HZE particle radiation encountered in space. The present research addresses several important questions of relevance to NASA's mission (Risk Number 29, Acute and Late CNS Risks, as described in the Bioastronautics Roadmap). To address these questions, the work is providing for the development and application of the acquisition and long-term performance of a number of neurobehavioral tasks in a cognitive/behavioral animal test battery in rodents, and additionally for the demonstration of the validity and reliability of the procedures to measure critical cognitive/behavioral functions following specific interventions (e.g., pharmacologic disruptions). The research will provide critically needed dose-response data on the effects of high-energy (HZE) radiation (protons, GCR's, SPE's) on a range of cognitive/behavioral functions.<br><br>(4) Proposed Research Plan for the Coming Year<br><br>Animals are currently being trained in selected neurobehavioral tasks for subsequent transport and exposure at Brookhaven National Laboratory to protons. Within the next year, approximately 120 rats will undergo this training/exposure/post-testing protocol, covering a dose range of 0 - 200 cGy. |
| **Rationale for HRP Directed Research:** | |
| **Research Impact/Earth Benefits:** | Research conducted on the effects of ionizing radiation on cognitive/behavioral function will provide the basis for extrapolating the effects of the space radiation environment on human cognitive function and performance. The Earth-based applications of this research will extend to providing a means for generalizing these effects to numerous types of radiation exposures (e.g., workplace, medical) on earth. Thus the outcomes of these studies are expected to have an important impact on safety and the quality of life in many Earth-based applied settings, and the society at large will further benefit from the resulting methodological advances that effectively provide quantitative risk assessments for radiation exposure on cognitive function. |
| **Task Progress:** | An automated, computerized training and testing facility for measuring long-term effects of radiation exposure on a range of cognitive/behavioral functions in rodents has been established at the Johns Hopkins Medical Institutions. Initial establishment of the laboratory has been completed, and includes 14 experimental testing chambers and associated equipment for assessing neurobehavioral function in rodents, and provide for the daily automated, computerized training and testing of a range of cognitive and behavioral functions in test subjects.<br>The rodent training and testing facility has been developed to provide for automated, computerized assessments of cognitive, behavioral, sensory, and motor function in research subjects on a daily basis. The facility supports both the exportation of groups of well-trained subjects to NASA-related radiation exposure testing facilities (e.g., Brookhaven National Laboratory, the Department of Radiation Oncology of the Johns Hopkins Hospital) as well as the importation of radiation-exposed rodents from such facilities for detailed, long-term neurobehavioral risk assessments at the testing facility.<br><br>Initial data with an intradimensional-extradimensional (ID-ED) set shifting procedure indicates that the procedure can clearly detect changes in standard discrimination and discrimination learning reversal in rats. Additionally, differences in error rates of the rats' performances also differentiate between different discrimination conditions, thus indicating that the ID-ED procedure can track a rat's ability to shift attention between different stimulus dimensions. During this initial year of funding, 16 experimental rats were exposed to head-only x-ray irradiation (2.3 Gy), while control rats were sham-exposed using the same anesthesia protocol. Initial data with this procedure indicates that the procedure can clearly detect radiation-induced changes in standard discrimination and discrimination learning reversal in rats. Additionally, differences in error rates of the rats' performances also differentiated between different discrimination conditions, thus indicating that the ID-ED procedure can track a rat's ability to shift attention between different stimulus dimensions. |

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| | The results of these experiments confirm the feasibility of an animal model approach for assessing neurobehavioral risks associated with living in a space radiation environment, and demonstrate the sensitivity of cognitive/behavioral test measures to the effects of head-only radiation that produce highly specific effects on neurobehavioral function. |
| **Bibliography Type:** | Description: (Last Updated: 01/12/2021) |
| **Articles in Peer-reviewed Journals** | Hienz RD, Brady JV, Gooden VL, Vazquez ME, Weed MR. "Neurobehavioral effects of head-only gamma-radiation exposure in rats." Radiat Res. 2008 Sep;170(3):292-8. PMID: 18763858 , Sep-2008 |
| **Awards** | Brady JV. "Brady, J.V.: 2008 Mentorship Award of the College on Problems of Drug Dependence (CPDD), San Juan, PR, June 2008." Jun-2008 |
| **Awards** | Hienz RD. "Robert D. Hienz: Invited to join scientific advisory committee for the 2010 COSPAR Meeting, Bremen, Germany, January 2009." Jan-2009 |