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Discipline: None Space Biology Special Category: None PI Email: catherine davis takass@aunhs.edu Fax: FY 301-400-4023 PI Organization Type: NON-PROFIT Phone: 301-400-4023 PI Organization Type: NON-PROFIT Phone: 301-400-4023 PI Organization Type: Open Academic Category: Phone: 301-400-4023 PI Address 1: OSO-PROFIT Phone: 301-400-4023 PI Address 2: Open Academic Category: Phone: 301-400-4024 PI Veb Page: State: MD Mone City: Bedhesda State: MD Zip Code: 03817-189 Congressional District: 8 Gomments: 01817-189 Congressional District: 8 Organization Y mouse address (Jan 2022): Department of Pharmacoly and Molecular Theremyerits. 8 None States: 100 Jones Hopkins in fail 2020. Comments: Organization / Funding: 2011 NSBRERA-11-01 Source: Postocotal Fellowships State: Type: Ground Solicitation / Funding: 2011 NSBRERA-11-01 No. of Photocetic: Forganization No. of Master' Degrees: 0 No. of Photocetic: Forganization No. of Photopergees: 0 No. of Photocetic: Inteladd State: NO.0 Photopergees: 0 No. of Mo	Space Biology Element:	None		
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	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
Task Description:	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.

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