Low Dose Radiation Stimulates Antioxidant Capacity in the Brain and Lessens Behavioral Symptoms in a 6-OHDA-Induced Rat Model of Parkinson's Disease.

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Background: Progressive degeneration of dopaminergic neurons in the substantia nigra (SN) pars compacta results in motor deficits in Parkinson's disease (PD) patients. Oxidative damage to the nigral dopaminergic neurons has been implicated in the pathogenesis of Parkinson's disease. Our hypothesis is that low dose radiation induces the production of antioxidants in the brain, which could provide protection to the dopaminergic neurons, potentially leading to prevention or stabilization of PD. The purpose of the study is (1) to determine the effect of low dose radiation on the total antioxidant capacity in SN in normal rats, (2) to determine if the higher level of antioxidants stimulated by low dose radiation can reduce the oxidative damage caused by high dose radiation, and (3) to determine the effect of low dose radiation on the behavioral symptoms in the 6-OHDA-induced rat model of PD. 6-OHDA, which produces radical oxygen species and induces neurotoxic death of dopaminergic neurons, is used to produce an experimental model of Parkinson's disease in rats.

Methods: (1) Sprague-Dawley (SD) rats were exposed to radiation applied to the brain in the dose range of 0 to 90 cGy at the rate of ~9 cGy/minute. The animals were sacrificed at various time points after the irradiation and total antioxidant capacity was measured in substantia nigra. (2) SD rats were exposed to 45 cGy radiation to the brain or sham radiation. Two days later, their brains were subjected to 12 Gy of radiation. The animals were sacrificed four weeks later, and the amount of oxidative damage in the SN was assessed. (3) Behavioral rotations were evaluated in 6-OHDA unilaterally lesioned rats exposed to the dose range of 0-45 cGy to the brain. Complete 360° turns were counted in 45 min periods and measured at weekly intervals during the period of 3 to 7 weeks after the induction of the disease.

Results: (1) Results showed that low dose radiation induced increases in the total antioxidant capacity in substantia nigra as a function of dose when rat brains were irradiated in the dose range of 0 to 63 cGy and decreased as a function of exposure to higher doses. The elevated antioxidant capacity was maintained for at least 3 weeks. (2) Low dose radiation at 45 cGy was found to reduce oxidative damage in rat brains, when the animals were subsequently subjected to a 12 Gy radiation dose to the brains. (3) The evaluation of the effects of low dose radiation on behavioral rotations in Parkinsonian rats showed that the number of rotations in 6-OHDA-lesioned rats was decreased after the treatment with low dose radiation in groups of animals exposed to 10 and 45 cGy compared to controls that were sham radiated. The reduction in the number of rotations was greater for the rats exposed to 45 cGy compared to those exposed to 10 cGy.

Discussion: Our data suggest that exposure to low dose radiation stimulates antioxidant capacity in the brain and may reduce behavioral symptoms in the 6-OHDA-induced rat model of PD. These are preliminary findings following behavioral symptoms of this PD rat model. Further experimentation with additional animal groups is needed to determine the extent of these observed protective effects of low dose radiation on symptoms of PD and its statistical significance. The results of our study appear to be consistent with our hypothesis that low dose radiation stimulates the production of antioxidants providing protection to dopaminergic neurons, potentially leading to prevention or stabilization of PD. If further testing confirms the observations of the protective effect of low dose radiation, translation of the concept to human studies may be considered as a means to slow down the progression of PD.

Acknowledgements: This research was supported by the Office of Science (BER), U.S. Department of Energy, under Award No. DE-SC0001196.