Radiation-induced Parkinson's Disease: Evaluating the Level of Evidence and Recommending Future Work

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Recently, excess risks of Parkinson's disease (PD) have been seen in terrestrial occupational cohorts exposed to ionizing radiation. The result was initially observed in workers at the Mayak weapons facility [1] and then confirmed in six individual cohorts consisting of 517,000 workers within the Million Person Study (MPS) [2]. However, the subjects in these studies were exposed to primarily low Linear Energy Transfer (LET) chronic radiation, whereas space radiation is a more complex mixture of high and low LET radiation qualities. Based on the preliminary data from the MPS [2], an initial risk model was developed to project PD risks from space radiation exposure during exploration missions. The results suggest that PD risks may be high enough for concern. More specifically, for a two-year Mars flyby mission with an estimated brain radiation exposure of 0.33 Gy, the lifetime Risk of Exposure Induced Cases (REIC) of PD was estimated to be 8.75 (3.05-18.0) for 40 year-old men, and 2.44 (0.83-5.12) for 40 year-old women [4], where the confidence intervals only include statistical uncertainties from the epidemiological data. However, these estimates are highly uncertain, particularly when one considers the unquantified uncertainties such as those associated with quality factor and dose rate effects, but the large values clearly suggest a need for further evaluation. While the observational epidemiology is suggestive of a PD risk, it is currently difficult to establish causation using such data. For this reason and to develop estimates of radiation quality and dose rate effects required to scale risk estimates from the terrestrial exposures to the space radiation environment, experimental neurobiology data are important. For example, preclinical rodent models of low and high LET exposure, including studies utilizing simulated GCR, reveal evidence of neural injury, behavioral deficits, and microglia reactivation [5], all of which are commonly observed in neurodegenerative diseases, including PD. Nonetheless, little specific information, if any, is currently available that could determine a specific biological mechanism for radiation-induced PD with no available data suitable to estimate quality or dose rate effects that is directly related to PD pathogenesis. To put this information into context, an ad-hoc working group was convened to make an initial evaluation of the level of evidence of this risk according to the criteria used by the NASA Human Systems Risk Board [6] and to make specific recommendations on what research is needed to confirm this risk and better enable quantitative risk projections for exploration missions. Some of the recommendations will be addressed by epidemiological research currently underway within the context of the MPS [7] including an effort specifically focused on multiple stressors [8]. Recommendations for future studies from the ad-hoc group will focus on biology and epidemiology research beyond what is currently underway with a particular emphasis on integrating PD-related biological mechanisms with epidemiological evidence.

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