Neurotoxicity of human neural cells induced by space radiation: in vitro risk assessment and countermeasure

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As the duration of space missions increases, the potential for neurological damage to astronauts resulting from exposure to radiation also increases. To explore the cytotoxic effects of low and high LET radiation on cells of the central nervous system, we utilized a model in vitro system consisting of a human neuronal progenitor cell line (NT2) and its terminally differentiated derivative (hNT neurons). We found that exposure to numerous forms of ionizing radiation induced cell detachment, necrosis and apoptosis in time, dose and LET dependent manners. From the slopes of the dose-response curves, we calculated RBE values for each form of heavy ion radiation. A sequential field of 1 GeV/n protons and iron ions induced apoptosis to a greater extent than either ion alone, and the time between "hits" was also an important determining factor. In addition, cycling neuronal progenitor cells underwent a dramatic, G2 phase specific cell cycle delay within 6 hours following exposure to either low or high LET radiation. The molecular effects of HZE radiation were also investigated, with an emphasis on the cell stress response protein p53. Heavy ion radiation induced expression of p53 in a time and dose dependent manner in both neuronal progenitor and mature neuronal cells. Furthermore, several post-translational modifications to the p53 protein were detected 2 hours after exposure to gamma rays. Experiments incorporating pifithrin-α, a small molecule inhibitor of p53, suggest that induction of both apoptosis and the cell cycle delay in human NT2 cells is p53 independent. To test for a potential ability to counteract the cytotoxic effects of radiation on neuronal progenitor and post-mitotic neuronal cells, several compounds were utilized such as melatonin, TGF-β, lipoic acid, selenomethionine, strawberry and blueberry extracts. Results showed that only TGF-β and lipoic acid were effective in protecting neurons and progenitor cells in culture, respectively.