

THE ROLE OF OXIDATIVE STRESS AND INFLAMMATION IN SYNAPTIC FUNCTION AFTER SPACE RADIATION

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Space irradiation at low doses affects cognition. Altered cognition in turn may be related to the activation of the innate immune response and its effects on neuronal function. The underlying mechanisms for radiation-induced deficits in synaptic function are unknown, but likely are multifaceted, involving inflammation and chronic oxidative stress. Our recently published data suggest that the lack of CCR2 is protective against low doses of ⁵⁶Fe and gamma irradiation. These data offer new insights into the mechanism(s) of radiation-injury and suggest that activation of the innate immune system is a potential mediator of hippocampal neuronal dysfunction and hippocampal cognitive impairments after irradiation. Recent evidence indicates that the activation of myeloid cells is a polarized process leading to a potentially neurotoxic M1 "classical activation" or potentially neuroprotective M2 "alternative activation" phenotypes. We reported that gamma irradiation induced polarization of macrophages. The regulation of this functional polarization after space radiation is still unknown and will be determined in the proposed studies. We hypothesize that space radiation, even at low doses, impairs synaptic functions and that these effects are mediated by oxidative stress and neuroinflammation. We are examining a series of endpoints to determine: 1) how low doses of protons and ⁵⁶Fe affect homeostatic synaptic function, 2) if these changes are regulated by oxidative stress, and 3) if these changes are associated with activation of the innate immune system, polarization of myeloid cells, and release of cytokines.

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