

EFFECTS OF DIETARY IRON AND GAMMA RADIATION ON THE RAT RETINA

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A health risk of concern for NASA relates to radiation exposure and its synergistic effects with other space environmental factors, including nutritional status of the crew. Astronauts consume almost three times the recommended daily allowance of iron due to the use of fortified foods aboard the International Space Station, with iron intake occasionally exceeding six times the recommended values. Recently, NASA has become concerned with visual changes associated with spaceflight, and research is being conducted to elucidate the etiology of eye structure alterations in the spaceflight environment. Terrestrially, iron overload is also associated with certain optic neuropathies. In addition, due to its role in Fenton reactions, iron can potentiate oxidative stress, which is a recognized cause of cataract formation. As part of a study investigating the combined effects of radiation exposure and iron overload on multiple physiological systems, we focused on defining the effects of both treatments on eye biology. In this study, 12-week-old Sprague-Dawley rats were assigned to one of four experimental groups: normal iron/no radiation (Control/Sham), high iron/no radiation (Fe/Sham), normal iron/gamma radiation (3 Gy cumulative dose, fractionated at 0.375 Gy/d every other day for 16 d) (Control/Rad), and high iron/gamma radiation (Fe/Rad). Oxidative stress-induced DNA damage, measured as concentration of the marker 8-hydroxy-2'-deoxyguanosine (8OHdG) in eye retinal tissue by enzyme-immunoanalysis did not show significant changes among treatments. However, there was an overall increase in 8OHdG immunostaining density in retina sections due to radiation exposure ($P = 0.05$). Increased dietary iron and radiation exposure had an interactive effect ($P = 0.02$) on 8OHdG immunostaining of the retinal ganglion cell layer with iron diet increasing the signal in the group not exposed to radiation ($P = 0.05$). qPCR gene expression profiling of relevant target genes indicated upregulation of ferritin light chain ($P = 0.09$) as a result of dietary iron but no change in expression of the gene for ferritin heavy chain. Immunolocalization of light chain and heavy chain of the iron storage protein ferritin showed the expected distribution in the choroid, photoreceptor layer, inner nuclear layer and in the inner plexiform layer that corresponded to the synaptic terminals of bipolar cells. Evidence of stress and damage in the retina was also suggested by a decrease in expression of the survival marker Bcl2 ($P = 0.01$) and the protective proteins clusterin ($P = 0.04$) and heat shock factor 1 (Hsf1, $P < 0.001$), as a result of increased dietary iron. The effect of increased iron on expression of the antioxidant enzyme heme oxygenase 1 (Hmox1) had a significant interaction with the effect of radiation ($P < 0.001$). In summary, the results of this study indicate that both gamma radiation exposure and a moderate increase in dietary iron can contribute to deleterious changes in retinal health and physiology.