

EFFECTS OF PROLACTIN AND THYROXINE REPLACEMENT ON ANTIOXIDANT EXPRESSION AND GLUTATHIONE METABOLISM IN LONG-LIVING AMES DWARF MICE

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Ames dwarf mice live significantly longer than their wild type siblings and exhibit elevated antioxidative defenses and reduced oxidative damage. This study was undertaken to determine the effects of prolactin (PRL) or thyroxine (T4) replacement, two hormones lacking in Ames mice, on components of glutathione (GSH) metabolism and antioxidative enzyme expression. Three and 12 month old dwarf mice (n=7/treatment/age) were treated twice daily with saline or PRL for seven days or T4 three times over a seven day period followed by tissue collection. Prolactin treatment elevated body and liver weights of 3 and 12 month old mice ($p < 0.0001$) while no effect of T4 was observed. Liver catalase activity was not affected by hormone treatment whereas protein levels decreased in PRL-treated 3 month old mice compared to age-matched saline treated mice ($p = 0.0284$). Kidney catalase protein levels were significantly decreased by both PRL and T4 at both ages tested. Significant age x treatment interactions were detected in the GSH/GSSG ratios in liver, kidney, heart and skeletal muscle tissues. Levels of the rate limiting protein in GSH biosynthesis, gamma-glutamylcysteine synthetase, were decreased by PRL treatment in livers and by T4 in kidneys of 12 month old mice. An increase in the activity of the GSH degrading enzyme, gamma-glutamyltranspeptidase, was observed in livers from young, PRL treated dwarf mice and in brain tissue of 3 and 12 month old mice. Liver and kidney GST activity was suppressed by PRL and T4 in 12 month old mice ($p < 0.05$). The effects of short-term hormone replacement on GSH metabolism and antioxidant enzyme expression were tissue- and age-dependent. Results of these experiments coupled with previous growth hormone replacement data suggest that these hormones play a role in the stress resistance, delayed aging and longevity exhibited by the Ames dwarf mouse.