

HEPATIC OXIDATIVE STRESS DURING AGING: THE EFFECTS OF LIFE-LONG CALORIE RESTRICTION AND WHEEL RUNNING

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Effects of life-long calorie restriction and life-long exercise on hepatic oxidative stress were investigated in male Fisher-344 rats. Four groups were compared: young controls (6 mo), old controls (24 mo), old calorie restricted (8% CR, 24 mo) and old calorie restricted with daily voluntary wheel running (8% CR, 24 mo). The old ad libitum fed group displayed significantly higher levels of reactive oxygen species (ROS), nitric oxide (NO[•]) and peroxynitrite (ONOO⁻) compared to the young group. Also, the old control group had a significantly reduced sulfhydryl group (-SH) content and glutathione (GSH) content tended to be lower as well. A significant increase in RNA oxidation in livers of the old ad libitum fed rats was detected using the biomarker 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxoGuo) using HPLC coupled to electrochemical detection (HPLC-EC-UV). Also, 8-oxodGuo (DNA oxidation) tended to be increased with age. Further, Western blotting immunodetection showed that hepatic tissues from old rats had significantly increased nuclear presence of the transcription factor NF- κ B (assessed by the subunits p50 and p65) and in connection, increased levels of regulatory cytosolic phosphorylated I- κ B (active form) and decreased cytosolic dephosphorylated I- κ B (inactive) suggesting an increased inflammatory response. The age-associated increase in parameters of oxidative stress was attenuated in the livers from both the 8% CR and the wheel running (with 8% CR) groups. All together, the data shows that hepatic oxidative stress is increased in aging and that a life-long reduced calorie intake as well as increased exercise can attenuate the age-associated increases in parameters of oxidative stress.