processes. Long lasting production of ROS results in the accumulation of DNA damage both in nucleous and mitochondria. Although caloric restriction has been shown to retard aging processes and increase lifespan of various organisms, the underlying mechanism remains unknown. To clarify the relationship between mitochondrial energy transduction and ROS generation, properties of liver mitochondria from young and aged male Wistar rats were analyzed with and without giving starvation. Kinetic analysis using a high sensitive chemiluminescence probe L012 revealed that ROS generation associated with succinate oxidation of mitochondria differed significantly with their respiratory states; ROS production by mitochondria was higher with young (19-week-old) than with aged (two-year-old) rats. Mitochondrial generation of ROS decreased significantly after starvation of both animal groups. Similar results were also obtained with gulutamate oxidation. Recent studies demonstrate that cellular generation of ROS increased prior to the onset of mitochondrial permeability transition and DNA fragmentation. Thus, we analyzed the ROS generation by Ca^{2+}-loaded mitochondria and its relationship with their swelling and cytochrome c release. We found that the ROS generation by control rat liver mitochondria was greater than that by caloric restriction group. These results suggest that caloric restriction affects mitochondrial generation of ROS and sequence of events leading to apoptosis in the liver of young and aged subjects. Effects of dietary ubiquinone and related compounds on mitochondrial ROS generation and cytochrome c release will be discussed.

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LIPID, GENOMIC AND MITOCHONDRIAL DNA OXIDATIVE DAMAGE CAUSED BY THE ALTERATIONS OF HYPOTHALAMIC-PITUITARY-GONADAL AXIS IN THE BRAIN OF MALE AND FEMALE RATS

B. Marzani,[1] *S. Giardina,*[1] *M. Tonini,*[1] *and F. Marzatico*[1]

[1]***Department of Physiological-Pharmacological Sciences, Section of Pharmacology and Pharmacological Biotechnologies, University of Pavia, Piazza Botta 11-27100 Pavia, Italy***

During aging neuroendocrine functions undergo changes, particularly to the hypothalamic-pituitary-gonadal (HPG) axis. The aim of this study was to analyse whether HPG axis alterations were associated with changes of brain oxidative status. Basal and stimulated lipid peroxide (LPO) levels, genomic and mitochondrial 8-hydroxy-2′-deoxyguanosine (8-OHdG) content, were detected in the hippocampus and the cortex of sham-operated controls and gonadectomized Wistar rats of both sexes. In the hippocampus, castration increased basal LPO levels, while in stimulated LPO levels were unaffected. Both these parameters remained unchanged in the hippocampus of ovariectomized female rats. In the cortex, castration did not modify basal and stimulated LPO levels. In the cortex of ovariectomized female rats basal LPO content was enhanced, whereas no change was found after stimulation. In the hippocampus, castration reduced while ovariectomy increased 8-OHdG content in genomic DNA; no changes were observed in mitochondrial DNA. In the cortex, gonadectomy increased 8-OHdG content in both genomic and mitochondrial DNA. To conclude, HPG axis alterations were associated with lipid and DNA oxidative changes in the rat hippocampus and cortex. A different response of the two brain areas and the two sexes to modifications of gonadal hormone levels was observed.

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MODERATE EXERCISE RETARDS NEUROLOGICAL IMPAIRMENT, OXIDATIVE STRESS AND DECREASED MITOCHONDRIAL ELECTRON TRANSFER ASSOCIATED TO AGE

A. Navarro,[1] *N. Escudero,*[1] *J. Fernández-Carrión,*[1] *C. Piñuela,*[1] *and A. Boveris*[2]

[1]***Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Cadiz, Spain,*** [2]***School of Pharmacy and Biochemistry, University of Buenos Aires, Argentina***

Moderate exercise training in a treadmill, from 28 wk to 78 wk of age, extended male and female mice survival with medium lifespan increases of 19 % and 9 % respectively, accompanied by increased performance in behavioural tests (tightrope and T-maze tests) at 52 wk of age, in males and females. In brain, heart, liver and kidney at 52 wk of age, moderate exercise significantly decreased the aging-associated development of oxidative stress by preventing: 1) the increase in protein carbonyls and TBARS contents of submitochondrial membranes; 2) the decrease in antioxidant enzyme activities (mitochondrial and cytosolic superoxide dismutase, Mn-SOD and Cu, Zn-SOD, and catalase) and 3) the decrease in mitochondrial NADH-cytochrome c reductase and cytochrome oxidase activities. These effects were no longer significant at 78 wk of age. Moderate exercise increased lifespan and increased neuromuscular function and exploratory performance, likely by decreasing oxidative stress and by protecting mitochondrial functions from the age-associated decrease in mitochondrial enzyme activities.

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HISTOLOGICAL MITOCHONDRIAL MARKERS OF TO AGING IN MICE HIPPOCAMPUS

A. Navarro[1] *and C. Piñuela*[1]

[1]***Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Cadiz, Spain***

Mitochondrial markers were determined by histochemical and inmunohistochemical techniques in the hippocampus of aging rats with the aim of establishing an association between the markers and both normal aging and age-related neurodegenerative disorders. Nitric oxide synthase activity (mtNOS and nNOS) was determined by staining for NADPH-diaphorase (NADPH-d), and mitochondrial