MITOCHONDRIAL BIOENERGETICS IN YOUNG, ADULT, MIDDLE-AGE AND SENESCENT BROWN NORWAY RATS.

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Mitochondria are central regulators of energy homeostasis and may play a pivotal role in mechanisms of cellular senescence and age-related neurodegenerative and metabolic disorders. However, mitochondrial bioenergetic parameters have not been systematically evaluated under identical physiological conditions within multiple organ samples in diverse age-groups. In the present study, we used the Seahorse Extracellular Flux Analyzer (Seahorse Bioscience XF-24) to compare four different life-stages [i.e. 1 Month- Young (Y), 4 Month- Adult (A), 12 Month- Middle-Aged (M) and 24 Month- Old-Aged (O)] of Brown Norway rats (n=5 animals/group). Mitochondrial (15-40 µg/well) bioenergetic parameters were evaluated together from five brain regions [brain stem (BS), frontal cortex (FC), cerebellum (CER), striatum (STR), hippocampus (HIP)] and three peripheral organs [heart (HRT), liver (LVR), lung (LNG)]. In general, all the regions of the brain followed identical patterns where the maximal respiratory capacities (State V and State V_{succ}) were reduced with age (Y>A>M=O). The State III respiration in BS, CER and HIP demonstrated a similar pattern like State V (Y>A>M=O); whereas the FC and STR displayed highest State III rates in adult group (A>Y≥O≥M). The proton leak (State IV) remained unaffected. In peripheral organs, the State V and State III rates were highest in younger animals followed by gradual decline with aging as evident in both HRT (Y>A=O>M) and LNG (Y>A=O=M). In LVR, the NADH-linked bioenergetics remained unchanged whereas the FADH-linked maximal respiratory (State V_{succ}) rates increased gradually as a function of age (Y<A<M=O). In summary, the comparative data analysis of this study gives valuable insight into the metabolic status of various organs that could potentially lead to age-associated changes in neurodegenerative or metabolic disorders. Additionally, the observed changes in mitochondrial bioenergetics will serve as a basic platform to elucidate chemically-induced life-stage susceptibility mechanisms important in community health-related research. *(This abstract does not necessarily reflect USEPA policy).*