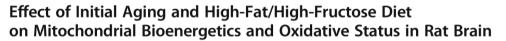


http://wiki.oroboros.at/index.php/O2k-Publications: Aging, senescence

High-resolution respirometry and aging



Raffaella Crescenzo<sup>1</sup> · Maria Stefania Spagnuolo<sup>2</sup> · Rosa Cancelliere<sup>1</sup> · Lucia Iannotta<sup>1</sup> · Arianna Mazzoli<sup>1</sup> · Cristina Gatto 1 · Susanna Iossa 1 [ D · Luisa Cigliano 1





## Effect of age and/or dietary treatment on brain mitochondrial physiology

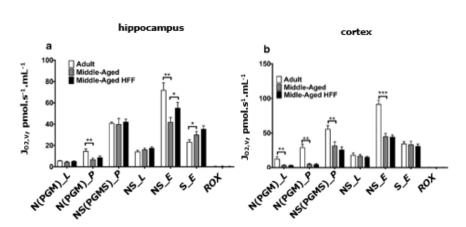
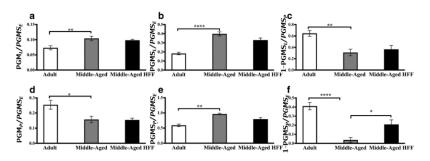
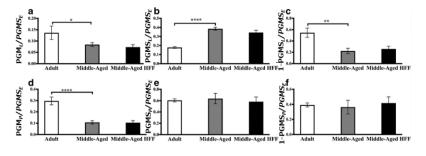


Figure 1. Age-induced decrease in ADP or FCCP supported respiration with N-linked substrates or NSlinked substrates, respectively. High-Fat/High Fructose (HFF) diet increases respiration with N- and NS-linked substrates in the hippocampus mitochondria (a). Mitochondria from the frontal cortex suffer a significant agerelated decrease with N- and NSsubstrates with respiration effect from HFF diet (b). Values are means  $\pm$  SEM (N = 8, \*p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001). \*

## Impaired coupling efficiency and limitation by ATP synthase in an age-dependent manner



## **Functional impairment of Complex I** with age in the cortex



Figures 2 and 3. Respiratory flux control ratios and coupling control factors in hippocampus (2) and frontal cortex (3). Leak respiration with electron provision from complex I  $(PGM_L/PGMS_E)$  (a) and complexes I and II (PGM $S_L/PGMS_E$ ) **(b)**, coupling efficiency of oxidative phosphorylation (1 PGMS<sub>L</sub>/PGMSP) phosphorylating respiration electron provision from complex I  $(PGM_P/PGMS_E)$  (d), and complexes I and II ( $PGMS_P/PGMS_E$ ) (e), apparent excess capacity of the electron transport chain  $(1 - PGM_P/PGMS_E)$  (f) Values are the means  $\pm$  SEM (N=8). \*p < 0.05, \*\* p < 0.01, \*\*\*\* p < 0.0001

Substrates added corresponding rates: malate + glutamate =  $N(PGM)_L$ , pyruvate +

 $ADP = N(PGM)_P$ , succinate =  $NS(PGMS)_P$ , oligomycin =  $NS_L$ , FCCP =  $NS_E$ , rotenone =  $S_E$ , antimycin A = ROX

 $PGM_L$  = LEAK respiration with complex I substrate;  $PGMS_L$  = LEAK respiration with complex I and II substrates;  $PGM_P = phosphorylating respiration with$ complex I substrate; PGMS $_P$  = phosphorylating respiration with complex I and II substrates; PGMS $_E$ = maximum capacity of the electron transfer pathway with complex I and II substrates

Reference: Crescenzo R, Spagnuolo MS, Cancelliere R, Iannotta L, Mazzoli A, Gatto C, Iossa S, Cigliano L (2019) Effect of initial aging and high-fat/high-fructose diet on mitochondrial bioenergetics and oxidative status in rat brain. Mol Neurobiol [Epub ahead of print].

 $\textbf{Text and figures slightly modified based on the recommendations of the COST Action MitoEAGLE CA15203. \underline{Doi:10.26124/mitofit:190001.v6}$