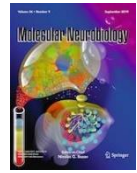
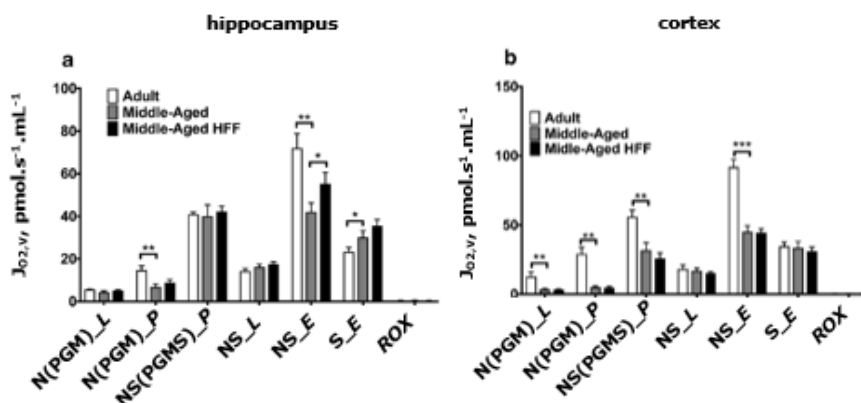


## Effect of Initial Aging and High-Fat/High-Fructose Diet on Mitochondrial Bioenergetics and Oxidative Status in Rat Brain

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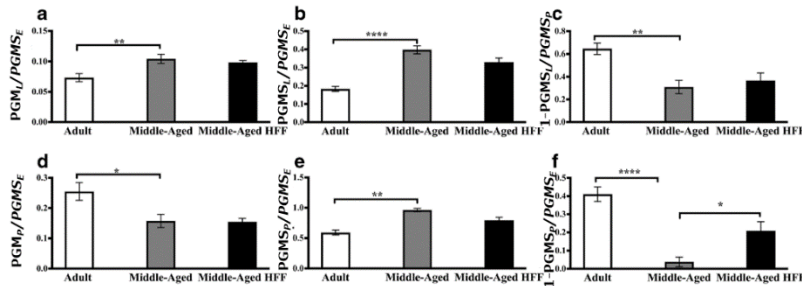
### Effect of age and/or dietary treatment on brain mitochondrial physiology



**Figure 1.** Age-induced decrease in ADP or FCCP supported respiration with N-linked substrates or NS-linked 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 age-related decrease with N- and NS-linked substrates with no respiration effect from HFF diet (**b**). Values are means  $\pm$  SEM (N = 8, \* $p$  < 0.05, \*\* $p$  < 0.01, \*\*\* $p$  < 0.001). \*

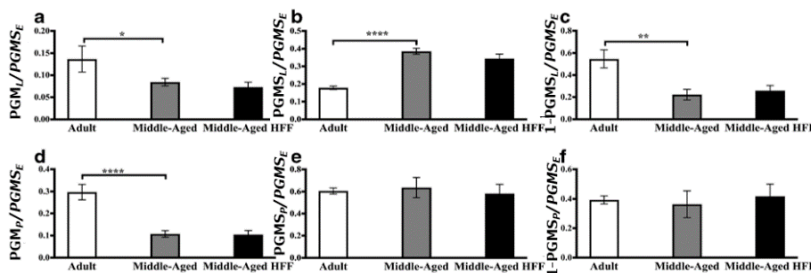
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## Impaired coupling efficiency and limitation by ATP synthase in an age-dependent manner



**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 ( $PGMS_L/PGMS_E$ ) (b), coupling efficiency of oxidative phosphorylation ( $1 - PGMS_L/PGMS_P$ ) (c), phosphorylating respiration with 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 ( $1 - PGMS_P/PGMS_E$ ) (f). Values are the means  $\pm$  SEM (N=8). \**p* < 0.05, \*\**p* < 0.01, \*\*\*\**p* < 0.0001

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



**Keywords:** Substrates added and their corresponding rates: malate + pyruvate + glutamate = N(PGM)<sub>L</sub>, ADP = N(PGM)<sub>P</sub>, succinate = NS(PGMS)<sub>P</sub>, oligomycin = NS<sub>L</sub>, FCCP = NS<sub>E</sub>, rotenone = S<sub>E</sub>, antimycin A = ROX

PGM<sub>L</sub> = LEAK respiration with complex I substrate; PGMS<sub>L</sub> = LEAK respiration with complex I and II substrates; PGM<sub>P</sub> = phosphorylating respiration with complex I substrate; PGMS<sub>P</sub> = phosphorylating respiration with complex I and II substrates; PGMS<sub>E</sub> = 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].

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