EFFECT OF FLUOXETINE TREATMENT ON MITOCHONDRIAL BIOENERGETIC IN HIPOTHALAMUS

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Introduction: Recent investigations have focused on the mitochondrion as a direct drug target in the treatment of metabolic diseases (obesity, metabolic syndrome). There are relatively few studies, investigating whether drug therapies aimed at changing behavior by altering central nervous system function may act in part through actions on mitochondrial bioenergetics, and none exploring the effect during early neonatal development. Aim: The present study was designed to study the effects of chronic treatment of newborn male rats with the selective serotonin re-uptake inhibitor (fluoxetine) on the mitochondrial bioenergetics of the hypothalamus during the critical nursing period of development. Methods: Male Wistar rat pups received either fluoxetine (Fx-group) or vehicle solution (Ct-group) from the day of birth until 21 days of life. At 60 days of age mitochondrial bioenergetics were evaluated. The procedures followed the recommendations of the Brazilian Committee of Animal Experimentation and approval of the Research Ethics Committee of the Center of Biological Sciences-UFPE (Number of the process: 23076.015276/2012-56). Results: The Fx-group showed an increase in oxygen consumption (Basal respiration rate-V2, Fx: 10.8 ± 0.64 nmol O2/min/mg prot, N=7; Ct: 5.1 ± 0.44 nmol/min/mg prot, N=7; p<0.01). We also observed an increasing after adding an uncoupling protonophore (Fx: 45.0 ± 2.5 nmol O2/min/mg prot, N=7; Ct: 25.7 ± 2.9 nmol/min/mg prot, N=7; p<0.0001). A reduction in the production of reactive oxygen species (42% decrease in comparison to Ct; p<0.05). No change in mitochondrial permeability transition pore opening or in oxidative stress was observed in the hypothalamus. Conclusion: Taken together our results suggest that chronic exposure to fluoxetine during the nursing phase of early rat development results in a positive modulation of mitochondrial respiration in the hypothalamus persisting into adulthood. Such long-lasting alterations in mitochondrial activity in the CNS, especially in areas regulating appetite, may contribute to permanent changes in energy balance in the treated animals. Keywords: serotonin, mitochondria, hipothalamus