SULFITE INTRASTRIATAL ADMINISTRATION ALTERS ANTIOXIDANT DEFENSES AND DISRUPTS CELLULAR ENERGY HOMEOSTASIS IN RAT STRIATUM

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INTRODUCTION AND OBJECTIVES: Sulfite oxidase (SO) deficiency is a recessive inherited disorder that can be caused either by a defect in the enzyme protein or by the lack of functional molybdenum cofactor, resulting in accumulation of sulfite in tissues and biological fluids of patients. This disorder is characterized by severe neonatal seizures and progressive neurodegeneration with basal ganglia abnormalities, whose pathophysiology is not fully established. Thus, we investigated the ex vivo effect of sulfite administration on parameters of energy metabolism and oxidative stress in striatum of young rats. MATERIAL AND METHODS: Thirty-day-old rats received an intrastriatal injection of sulfite (2 μmol) or NaCl (2 μmol) and were euthanized 30 min after administration. The striatum was dissected, homogenized and used to examine the activities of the respiratory chain complexes I to IV, creatine kinase (CK) and antioxidant enzymes. Reduced glutathione (GSH) concentrations were also determined. Mitochondrial fractions were prepared to determine the activities of the citric acid cycle enzymes citrate synthase (CS), malate dehydrogenase (MDH) and isocitrate dehydrogenase (IDH). RESULTS AND CONCLUSIONS: Sulfite significantly decreased the activities of CS and CK, indicating an impairment of cellular energy production, transfer and buffering. In contrast, the activities of MDH, IDH and of the respiratory chain complexes were not changed. Furthermore, sulfite also decreased GSH concentrations and the activities of the antioxidant enzymes glutathione peroxidase, glutathione reductase, glutathione S-transferase and glucose-6-phosphate dehydrogenase, whereas catalase activity was increased. Superoxide dismutase activity was not altered by sulfite. These findings suggest that sulfite alters the enzymatic and non-enzymatic antioxidant defenses in striatum, mainly interfering with GSH metabolism. Therefore, it may be presumed that impairment of energy and redox homeostasis elicited by sulfite may be involved in the pathophysiology of basal ganglia injury observed in patients affected by SO deficiency. ACKNOWLEDGEMENTS: CNPq, PRONEX, FINEP, IBN-Net #01.06.0842-00, INCT-EN.

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