Sulfite Impairs Mitochondrial Respiration by Inhibiting Glutamate and Malate Oxidation in Rat Brain

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INTRODUCTION: Sulfite and thiosulfate accumulate in tissues and biological fluids of patients affected by the deficiency of sulfite oxidase (SO), which is a mitochondrial enzyme that catalyzes the oxidation of sulfite derived from the metabolism of sulfur amino acids. Patients affected by SO deficiency present severe neurological symptoms and abnormalities in cerebral cortex and basal ganglia, whose pathophysiology is not fully established. Therefore, we investigated the in vitro effects of sulfite and thiosulfate on important parameters of energy homeostasis in rat brain. MATERIAL AND METHODS: Mitochondrial preparations from brain of thirty-day-old Wistar rats were used to examine state 3, state 4 and CCCP-stimulated state of mitochondrial respiration and the respiratory control ratio (RCR) assessed by oxygen consumption using glutamate plus malate, succinate, pyruvate plus malate and α-ketoglutarate as substrates. We also investigated the activities of glutamate, malate and α-ketoglutarate dehydrogenases. RESULTS AND DISCUSSION: It was verified that sulfite decreased state 3, CCCP-stimulated state and RCR in mitochondria respiring with glutamate plus malate, but not with succinate, pyruvate plus malate and α-ketoglutarate, suggesting that oxidation of glutamate and/or malate could be impaired. We also observed that sulfite was able to inhibit the activity of glutamate and malate dehydrogenases, but not α-ketoglutarate dehydrogenase, implying an impairment of glutamate and malate oxidation, which could explain the inhibition of the mitochondrial respiration. On the other hand, thiosulfate did not alter oxygen consumption with any of the substrates used. CONCLUSIONS: These data indicate that mitochondrial energy homeostasis impairment induced by sulfite may represent a pathomechanism of brain injury found in patients affected by SO deficiency.

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