SULFITE IMPAIRS GLUTAMATERGIC NEUROTRANSMISSION AND ANTIOXIDANT DEFENSES IN VITRO IN RAT CEREBRAL CORTEX SLICES

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INTRODUCTION AND OBJECTIVE: Sulfite oxidase (SOX) is a mitochondrial enzyme that catalyzes the degradation of sulfite derived from exogenous sources and sulfur-containing amino acids. SOX deficiency is an inherited disorder caused either by mutations in the gene encoding SOX or by defects in the synthesis of the molybdopterin cofactor. This pathology is biochemically characterized by tissue accumulation of sulfite and thiosulfate. Affected patients present neurological dysfunction and brain abnormalities that include encephalopathy, marked neuronal loss, demyelination, gliosis and diffuse spongiosis. In the present study we evaluated the in vitro effects of sulfite and thiosulfate on parameters of glutamatergic neurotransmission and oxidative stress in rat cerebral cortex slices, a system with preserved cell machinery and structure.

MATERIAL AND METHODS: Slices were exposed for 1 or 3 h to sulfite and thiosulfate (10-500µM) and used to determine glutamate uptake, glutamine synthetase (GS) activity, thiobarbituric acid-reactive substances (TBA-RS) levels, glutathione (GSH) concentrations, and the activities of glutathione peroxidase (GPx), glutathione reductase (GR), glutathione S-transferase (GST) and glucose-6-phosphate dehydrogenase (G6PDH).

RESULTS AND CONCLUSIONS: After 1 h incubation, sulfite decreased glutamate uptake, and tended toward inhibiting GS activity, while thiosulfate inhibited GS activity, but did not affect glutamate uptake. We also verified that 10µM sulfite decreased GSH concentrations and increased TBA-RS levels, whereas thiosulfate did not alter these parameters. Regarding the antioxidant enzymes, sulfite and thiosulfate did not alter the activity of GPx, GR, GST and G6PDH after an incubation of 1 h. However, when the slices were exposed for 3 h to 500µM sulfite, this metabolite decreased GPx, GST and G6PDH activities. Taken together, these data suggest that impairment of glutamatergic neurotransmission and redox homeostasis may play an important role in the neuropathophysiology of SOX deficiency.

ACKNOWLEDGEMENTS: CNPq, PROPESq/UFRGS, FAPERGS, PRONEX, FINEP, IBN-Net and INCT-EN. Keywords: Sulfite oxidase deficiency, glutamatergic neurotransmission, redox homeostasis.