

ISOVALERIC ACID REDUCES Na^+ , K^+ -ATPASE ACTIVITY IN SYNAPTIC MEMBRANES FROM CEREBRAL CORTEX OF YOUNG RATS

César A. J. Ribeiro¹, Fabrício Balestro, Vanessa Grando¹ and Moacir Wajner^{1, 2}

¹Laboratory of Inborn Errors of Metabolism, Department of Biochemistry, UFRGS, Porto Alegre; ²Universidade Luterana do Brasil, Canoas, RS, Brazil.

Patients affected by isovaleric acidemia (IVAacidemia) suffer from acute episodes of encephalopathy. However, the mechanisms underlying the neuropathology of this disease are poorly known. The objective of the present study was to investigate the *in vitro* effects of the metabolites that predominantly accumulate in IVAacidemia, namely isovaleric acid (IVA) 3-hydroxyisovaleric acid (3-OHIVA) and isovalerylglycine (IVG), on Na^+ , K^+ -ATPase activity in synaptic plasma membranes from cerebral cortex homogenates of 30-day-old rats. IVA exposition to cortical homogenates provoked a marked inhibition of Na^+ , K^+ -ATPase activity, whereas 3-OHIVA acid and IVG did not affect this activity. Furthermore, pre-treatment of cortical homogenates with α -tocopherol and creatine totally prevented IVA-induced inhibition on Na^+ , K^+ -ATPase activity from synaptic plasma membranes, whereas GSH and the NO synthase inhibitor L-NAME did not alter this inhibition. These data indicate that oxygen reactive species were probably involved in this inhibitory effect. Since Na^+ , K^+ -ATPase is a critical enzyme for normal brain functioning, it is presumed that the inhibitory effect of IVA on this activity may be involved in the pathophysiology of the neurological dysfunction of isovaleric acidemic patients.

Financial Support: CNPq, Propesq/UFRGS, FAPERGS/PRONEX.