IN VIVO ADMINISTRATION OF PHYTANIC ACID IN CEREBELLUM OF ADOLESCENT RATS PROVOKES OXIDATIVE STRESS AND ASTROGLIOSIS


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Introduction: Phytanic acid (Phyt) accumulates in various peroxisomal diseases including Refsum disease (RD) and Zellweger syndrome (ZS). The pathogenesis of the neurological symptoms and especially the cerebellar abnormalities in these disorders are poorly known. Objectives: We investigated the effects of in vivo intracerebral administration of Phyt on a large spectrum of redox homeostasis parameters in cerebellum of young rats. Material and methods: Malondialdehyde (MDA) levels, sulfhydryl oxidation, carbonyl content, nitrite and nitrate concentrations, 2',7'-dichlorofluorescein (DCFH) oxidation, total (tGS) and reduced glutathione (GSH) levels and the activities of important antioxidant enzymes were determined at different periods after Phyt administration. Immunohistochemical analysis was also carried out in cerebellum. Discussion and results: Phyt significantly increased MDA and nitric oxide (NO) production and decreased GSH levels, without altering tGS, DCFH oxidation, sulfhydryl oxidation, carbonyl content and the activities of glutathione peroxidase, superoxide dismutase, catalase, glutathione reductase and glucose 6-phosphate dehydrogenase. Furthermore, immunohistochemical analysis revealed that Phyt caused astrogliosis and protein nitrosative damage in cerebellum. It was also observed that the nitric oxide synthase inhibitor L-NAME prevented the increase of MDA and NO production as well as the decrease of GSH and the immunohistochemical alterations caused by Phyt, strongly suggesting that reactive nitrogen species (RNS) were involved in these effects. Conclusions: The present data provide in vivo solid evidence that Phyt disrupts redox homeostasis and causes astrogliosis in rat cerebellum probably mediated by RNS production. It is therefore presumed that disequilibrium of redox status may contribute at least in part to the cerebellum alterations characteristic of patients affected by RD and other disorders with Phyt accumulation.

Key words: phytanic acid, redox homeostasis, astrogliosis.

Financial support: CNPq, PROPESq/UFRGS, FAPERGS, PRONEX, FINEP IBN-Net and INCT-EN.