Impairment Of Brain Redox Homeostasis In Rats Injected With D-2-Hydroxyglutaric Acid

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Introduction: D-2-hydroxyglutaric aciduria (DHGA) is an inborn error of metabolism biochemically characterized by tissue accumulation and elevated urinary excretion of D-2-hydroxyglutaric acid (D-2-HG). Affected patients usually present neurological symptoms, such as epilepsy, hypotonia and retarded psychomotor development. However, the mechanisms of tissue damage in this disorder are poorly known. Material e methods: We investigated the ex vivo effects of intrastriatal administration of D-2-HG on oxidative stress parameters, namely thiobarbituric acid-reactive substances (TBA-RS, lipid peroxidation), carbonyl formation (protein oxidative damage), reduced glutathione (GSH) levels and the activities of the antioxidant enzymes glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT) (antioxidant defenses) in striatum from 30-day-old rats. Results and discussion: D-2-HG induced lipid peroxidation (TBA-RS increase), but did not change carbonyl formation, suggesting absence of protein oxidative damage. D-2-HG also decreased GSH levels, the most important brain antioxidant, and the activities of GPx and SOD, but did not alter CAT activity. Moreover, D-2-HG-induced increase of TBA-RS, decrease GSH levels and GPx activity were fully prevented by the NMDA-receptor antagonist MK-801, indicating the involvement of the NMDA glutamate receptor in these effects. Conclusions: Our results suggest that the oxidative stress induced by D-2-HG administration may be involved in the pathophysiology of the brain injury observed in individual affected by DHGA.

Keywords: D-2-hydroxyglutaric aciduria, oxidative stress, striatum.

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