Ethylmalonic and methylsuccinic acids induce oxidative stress in rat cerebral cortex

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High concentrations of ethylmalonic (EMA) and methylsuccinic (MSA) acids occur in tissues and biological fluids of patients affected by short-chain acyl-CoA dehydrogenase (SCAD) deficiency, a disorder characterized by development delay with neurological and muscular symptoms. Considering that the pathomechanisms responsible for the brain damage in this disease are virtually unknown, we investigated the in vitro effects of EMA and MSA on several oxidative stress parameters in cerebral cortex from 30-day-old rats. It was observed that EMA and MSA significantly increased thiobarbituric acid-reactive substances levels (lipoperoxidation) and these effects were prevented by trolox (a-tocopherol). Moreover, it was verified a decrease in the reduced glutathione levels, the main non-enzymatic antioxidant defense in the brain, caused by both acids. In addition, EMA enhanced carbonyl formation and oxidation of sulfhydryl groups (protein oxidative damage). It was also observed that EMA effects were greater, compared to the alterations provoked by MSA. Taken together, the present results show that EMA and MSA elicit oxidative stress in rat brain, suggesting that oxidative damage may be involved in the pathophysiology of the brain injury found in SCAD-deficient patients.

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