In Vitro Evidence that 2-Methylbutyrylglycine Induces Lipid Oxidative Damage and Reduces Antioxidant Defenses in Rat Cerebral Cortex

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Short/branched chain acyl-CoA dehydrogenase deficiency (SBCADD) is an autosomal recessive disorder of isoleucine metabolism biochemically characterized by accumulation of 2-methylbutyric acid (MB) and 2-methylbutyrylglycine (MBG). SBCADD-affected patients present predominantly neurological symptoms. Considering that the pathophysiology of this disease is not yet established, in this work we investigated the in vitro effects of MB and MBG on important parameters of oxidative stress in cerebral cortex of young rats. Thirty-day-old Wistar rats were sacrificed by decapitation, the cerebral cortex dissected, homogenized and used for the biochemical assays. Our results show that MBG, but not MB, increased thiobarbituric acid-reactive species (TBA-RS) (lipid oxidation). MBG also induced sulfhydryl oxidation and decreased glutathione (GSH) levels, reflecting a reduction of antioxidant defenses, whereas MB did not alter these parameters. Furthermore, MBG-induced increase of TBA-RS levels and decrease of GSH were prevented by free radical scavengers. Finally, since nitric oxide production was not altered by 2MBG and 2MB, it is presumed that reactive oxygen species possibly underlay 2MBG effects. The present study shows that MBG induces lipid oxidative damage and reduces non enzymatic antioxidant defenses in rat brain probably mediated by reactive oxygen species. Therefore, it may be concluded that oxidative stress induced by MBG is involved, at least in part, in the pathophysiology of the neurological dysfunction found in SBCADD-affected patients.

Word keys: Short/branched chain acyl-CoA dehydrogenase deficiency, 2-methylbutyrylglycine, oxidative stress, brain.

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