Expression of Glutamate Transporters in Cerebral Cortex and Striatum of Wild and Gcdh−/− Mice along Development

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Introduction: Glutaric aciduria type I (GA-I) is an autosomal recessive disease caused by deficiency of glutaryl-CoA dehydrogenase enzyme (GCDH). This deficiency alters L-lysine, hydroxyl-L-lysine and tryptophan catabolism causing the accumulation of glutaric acid (GA) and 3-hydroxy glutaric acid (3-HGA) in tissues and body fluids of affected patients. We determined the expression of glutamate transporters in the cerebral cortex and striatum of wild type and knockout mice with the GCDH enzyme deficiency (mice model of glutaric acidemia type I - GA-I) at distinct periods of postnatal development in the hopes to elucidate the pathogenesis of the brain abnormalities of GA I.

Materials and Methods: The RNA was extracted from striatum and cerebral cortex of animals with 7, 15, 30 and 60 days of age and measured by qPCR using gene-specific TaqMan FAM/MGB invetoried assays for the transporters (GLAST and GLT-1).

Results and Discussion: In striatum of knockout mice we observed highly increased expression of GLAST at 7, 30 and 60 days of age, while GLT-1 expression was higher only at 30 and 60 days of life. In cerebral cortex, GLAST and GLT-1 were more expressed in knockout mice at 30 and 60 days of life. Furthermore, no difference in the expression of glutamate transporters between knockout animals that received lysine diet and normal diet was detectable in cerebral cortex. However, in striatum, GLAST was 1.7-fold more expressed in knockout animals supplied with lysine as compared with normal diet. We also submitted the animals to a normal diet (0.9 % lysine) or a diet containing 4.7% lysine. No alterations on transporter expression were observed. Conclusion: The differential expression of glutamate transporters in the knockout animals may be possibly involved in the cortical and striatal abnormalities observed in GA-I patients.

Key words: Cerebral Cortex, Glutaric aciduria type I, Glutamate Transporters, Striatum.

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