Variable Expression of Glutamate Receptors in Cerebral Cortex and Striatum of Gcdh^-/- Mice along Development

Martell, R.W.¹, Lagranha, V.L.¹, Fernandes, C.G.¹, Ritter, L.¹, Matte, U.²,³, Wajner, M.¹,²

¹Departamento de Bioquímica, ICBS, UFRGS, Porto Alegre, RS.
²Serviço de Genética Médica, Hospital de Clínicas de Porto Alegre, Porto Alegre, RS.
³Centro de Terapia Gênica, Centro de Pesquisas Experimental, Hospital de Clínicas de Porto Alegre, RS

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 evaluated the mRNA expression profile of glutamate receptors in the cerebral cortex and striatum of wild and knockout mice of glutaric aciduria type I (GA-I) along postnatal development in order to clarify the pathophysiology of the brain abnormalities in this disease.

Materials and Methods: The RNA was extracted from cerebral cortex and striatum of animals with 7, 15, 30 and 60 days of age and measured by qPCR using gene-specific TaqMan probes for the NDMA (NR1, NR2A and NR2B) and non-NMDA (GluR2 and GluR6) receptors.

Results: We observed increased expression of NR2A and NR2B at 7, 30 and 60 days of age in striatum of knockout mice, as compared to wild animals. Moreover, all subunits of glutamate receptors were more expressed at 60 days. On the other hand, all NMDA subunits had higher expression in cerebral cortex of 30- and 60-day-old knockout mice, whereas non-NMDA receptors were more expressed at 7 and 60 days. We also submitted the animals to a normal diet (0.9 % lysine) or a diet containing 4.7% lysine for 60h. We found a higher expression of NR2A and NR2B only in the striatum, whereas the GluR2 and GluR6 receptors were more expressed in both striatum and cerebral cortex from knockout animals supplemented with high lysine diet.

Conclusion: The higher expression of glutamate receptors in cerebral cortex and particularly striatum from this genetic mice model of GA-I may be involved with the abnormalities of these structures in the affected patients.

Key words: Cerebral Cortex, Gcdh^-/- Mice, Glutamate Receptors, Striatum

Financial Support: FIPE-HCPA, CNPq, CAPES