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Full Length Research Paper

Co-expression of citrulline-nitric oxide cycle enzymes and decreased glutamine synthetase expression in different regions of brain in epilepsy rat model

Mummedy Swamy*, Wan Roslina Wan Yusof, Intan Nurfirdaus Mat Zin, K. N. S. Sirajudeen, Zulkarnain Mustapha and Chandran Govindasamy

Department of Chemical Pathology, School of Medical Sciences, Health campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.

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The aim of this study was to determine the mRNA expression of nitric oxide synthetase (NOS), argininosuccinate synthetase (AS), argininosuccinate lyase (AL) and glutamine synthetase (GS) in different regions of brain in rats subjected to kainic acid (KA) mediated epilepsy. The short term (acute) group animals were sacrificed after 2 h and the long term (chronic) group animals were sacrificed after 5 days of single injection of KA. After decapitation of rats, cerebral cortex (CC), cerebellum (CB) and brain stem (BS) were separated and in their homogenates, the relative amount of nNOS, iNOS, AS, AL and GS mRNA was assessed by reverse transcriptase-polymerase chain reaction (RT-PCR). Results showed an increased expression of iNOS in all brain regions tested in chronic group as compared to either control or acute group, and it indicate a favorable condition of nitric oxide production. AL expression was significantly increased only in CB in acute group whereas in chronic group it is increased in CC and CB and decreased in BS as compared to control. The aforementioned increased expression of AL may contribute effective recycling of citrulline to arginine. No change in expression of nNOS and AS in both acute and chronic groups of epilepsy. GS expression was significantly decreased only in chronic group of epilepsy in all brain regions tested when compared with control group. The decreased GS may be contributing prolonged availability of glutamate in chronic epilepsy.

Key words: Citrulline-nitric oxide cycle enzymes, glutamine synthetase, reverse transcriptase-polymerase chain reaction (RT-PCR), epilepsy.

INTRODUCTION

Generation of nitric oxide (NO), a versatile molecule in signaling processes and unspecific immune defense, is intertwined with synthesis, catabolism and transport of arginine which thus ultimately participates in the regulation of a fine-tuned balance between normal and pathophysiological consequences of NO production (Wiesinger, 2001). NO is synthesized from arginine by nitric oxide synthase (NOS; EC 1.14.13.39), and the citrulline generated as a by-product can be recycled to arginine by successive actions of argininosuccinate synthetase (AS; EC 6.3.4.5) and argininosuccinate lyase (AL; EC 4.3.2.1) via the citrulline-NO cycle (Zhang et al., 2000). In the mammalian tissue, NO is synthesized by a family of three isoenzymes, namely neuronal NOS (nNOS), inducible NOS (iNOS), endothelial NOS (eNOS) and their functioning neuronal signaling process, immune defense and vascular relaxation, respectively. Co-induction of AS, Cationic amino acid transporter-2 and NOS in activated murine microglial cells (Kawahara et al., 2001) and co-induction of inducible NOS and arginine recycling enzymes in cytokine-stimulated PC12 cells and high output production of NO were reported (Zhang et al., 2000). Kainic acid (KA), a glutamate analogue is widely used to induce exitotoxicity in experimental animals, that is, a model for temporal lobe epilepsy and a model for neurodegenerative disorders (Sperk, 1994). KA induced *status epilepticus* was associated with both apoptotic and

*Corresponding author. E-mail: mswamy@kb.usm.my or mummedys@yahoo.co.in. Fax: +609-765 3370.