Alterations on Cytoskeletal Proteins and Behavioral Parameters in the Rat Quinolinic Acid Model of Huntington’s Disease

Pierozan, P.1; Heimfarth, L.1; Loureiro, S. O.1; Reis, K. P.1; de Lima, B. O.1; Ferreira, F.1; Fernandes, C. G.1; Carvalho, R. V.1; Lisboa, N.G.1; Pandolfo, P.1; Espinosa, J.1; Porciúncula, L.1; Pessoa-Pureur, R.1; Wajner, M1,2.

1Departamento de Bioquímica, UFRGS, PoA - RS, Brazil; 2Serviço de Genética Médica, HCPA, PoA - RS, Brazil.

Quinolinic acid (QUIN) is an agonist of the N-methyl-D-aspartate (NMDA) receptor and has been demonstrated to be involved in many disorders. Intermediate filaments (IF) are important cytoskeletal proteins and phosphorylation of their subunits is one of the main regulatory mechanisms of cellular function. In the present study, we investigated alterations of IFs in the excitotoxic model of Huntington disease (HD) and we related these alterations to the onset of behavioral changes. A single intrastriatal injection of QUIN (150 nmol/0,5 µL) was administered in rats and 7, 14 and 21 days afterwards the effects on cytoskeletal proteins and behavioral changes were evaluated. Results showed that at day 7 after the insult the phosphorylation level of glial fibrillary acidic protein-GFAP and neurofilament subunits-NF were not altered in the striatum and in the cerebral cortex. We observed hypophosphorylation of IFs from cerebral cortex 14 and 21 days after the insult. Open-field and Y-maze tasks in QUIN-treated rats showed no alterations in the locomotor activity and in the spatial memory until day 21. The object recognition task showed that QUIN-injected animals had a short term memory deficit. Since we have recently described that acute intrastriatal administration of QUIN provokes IF hyperphosphorylation in the striatum 30 min after injection, the present results suggest that QUIN lesion progressively attained the signaling pathways targeting the cytoskeletal proteins in the cerebral cortex and probably these findings could be related to the cognitive impairment we observed in the QUIN model.

Words Keys: quinolinic acid, cytoskeletal proteins, behavioral alterations
Supported by: CNPq, Fapergs