Mild Hyperhomocysteinemia Promotes Changes in Cytokines Levels and Immunocontent of NF-κB in Brain of Rats


INTRODUCTION: Homocysteine is a sulfur amino acid that is metabolized by remethylation to methionine or transsulfuration to cysteine by the route of cystathionine. In plasma, homocysteine levels less than 15 µM are considered normal. Nevertheless, when there is an increase in these levels occurs hyperhomocysteinemia, which can be characterized as mild (15-30 µM), moderate (31-100 µM) or severe (> 100 µM). Studies have shown an association between mild hyperhomocysteinemia and cerebral diseases, but the mechanisms by which the homocysteine promotes such changes are still poorly understood. In the present study we evaluated some inflammatory parameters in cerebral cortex and hippocampus of hyperhomocysteinemic rats, such as interleukin 1-beta (IL-1β), tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), monocyte chemotactic protein-1 (MCP-1) and the immunocontent of the cytosolic and nuclear fractions of the nuclear factor-kappaB (NF-κB).

MATERIALS AND METHODS: Wistar rats received two daily subcutaneous injections of homocysteine (0.03 µM/g body weight) or saline (control), from the 30th to the 60th day of life. Twelve hours after the last injection, the animals were decapitated and the cerebral cortex and hippocampus were dissected. The cytokines levels were determined by Enzyme-Linked Immunosorbent Assay (ELISA) and the immunocontent of NF-κB were measured by Western Blotting.

RESULTS AND DISCUSSION: Results showed that homocysteine promoted an increase in IL-1β levels and nuclear fraction of NF-κB, while other parameters were not altered in cerebral cortex and hippocampus. On the other hand, in the hippocampus were observed an increase in IL-1β, TNF-α and IL-6 levels and a decrease in MCP-1 levels, cytosolic and nuclear fractions of NF-κB.

CONCLUSION: These findings suggest that the mild hyperhomocysteinemia promotes neuroinflammation that might be related, at least in part, with the pathophysiology of cerebral diseases.

Keywords: Mild hyperhomocysteinemia, cytokines, chemokine, NF-κB and neuroinflammation.

Supported by: CNPq, FAPERGS and PROPESQ/UFRGS.