072.5 *Poster p42 - Mon 15, 11:00*

NEUROPROTECTION AND DOWNREGULATION OF THE GLIAL RESPONSE AND INFLAMMATORY MOLECULES BY TRIFLUSAL POST-TREATMENT AFTER EXCITOTOXIC DAMAGE TO THE POSTNATAL BRAIN.

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Triflusal (2-acetoxy-4-trifluoromethyl-benzoic acid) is a compound structurally related to the salicylates that downregulates activation of the transcription factor Nuclear Factor kappa B (NF-kB), which is involved in the expression of genes participating in stress, inflammation and the glial response. In this study we have evaluated the capacity of Triflusal to dowregulate injury-induced glial NF-kB and its involvement in excitotoxic lesion outcome. Postnatal day nine rat pups received an intracortical injection of NMDA and an oral administration of Triflusal (30mg/kg) 8 hours later. After different survival times, pups were sacrificed and brains were processed for demonstration of specific glial cell types, NF-kB, pro-inflammatory cytokines and some inflammation-related enzymes.

Lesioned animals without Triflusal show early glial activation of NF-kB preceeding the microglial and astroglial response. Reactive microglial cells express IL-1beta and COX-2 within the first hours, displaying ameboid and pseudopodic morphologies. Reactive astrocytes express IL-1beta and TNFalpha and show GFAP overexpression and cell hypertrophy. In addition, some glial cells surrounding blood vessels express iNOS. Triflusal postreated animals present significative inhibition of glial NF-kB, accompanied by a downregulation of the glial response: reactive microglial cells are mainly pseudopodic/ramified and reactive astrocytes show decreased GFAP labelling and hypertrophy. Triflusal administration also induces a decrease in the glial expression of IL-1beta, TNFalpha, COX-2 and iNOS. Downregulation of the glial response and inflammatory molecules correlates with a strong reduction in the lesion volume (49% decrease). This study suggest that Triflusal administration may be a therapeutic strategy in neuropathological conditions where inflammation and glial response have a relevant role. Supported by DGES PB98-0892, 'la Caixa'00/074-00 and Uriach & Cia.