677.13

STRONG DOWNREGULATION OF NUCLEAR FACTOR KAPPA B ACTIVATION IN GLIAL CELLS AFTER TRIFLUSAL TREATMENT. L. Acarin*, B. Gonzalez and B. Castellano. Unit of Histology, Faculty of Medicine, Autonomous University of Barcelona, Spain.

Two of the most important transcription factors related with early gene activation in glial reactivity are the Signal Transducer and Activator of Transcription 3 (STAT-3) and the Nuclear Factor kappa B (NFkB). The upregulation of NFkB and STAT-3 activation in astrocytes and microglial cells has been implicated in the production of inflammatory products and, in this regard, in the regulation of neuronal cell death. The aim of the present work was to analyze the capacity of Triflusal (2-acetoxy-4-trifluoromethyl-benzoic acid), a compound structurally related to the salicylate group, to downregulate the activation of NFkB and STAT-3 in glial cells and, therefore, to evaluate its eficacy as a putative neuroprotective drug. Triflusal was supplied by gastric probe to postnatal rats from day seven to nine in 3 doses (30 mg/Kg) every 24 hours. Glial reactivity was induced by intracortical injection of N-methyl-D-aspartate at postnatal day nine, one hour after the last drug dose administration. After survival times ranging from 2 to 24 hours, brains were cut in a cryostat and sections processed for NFkB and STAT-3 immunocytochemistry. Astrocytes were demonstrated by glial fibrillary acidic protein immunocytochemistry and microglial cells by tomato lectin histochemistry.

In control animals, cortical neurons but not glial cells showed constitutively activated NFkB, which is downregulated following triflusal administration. On the other hand, the constitutive neuronal activation of STAT-3 was not affected by Triflusal treatment. When an excitotoxic lesion was performed, we observed a rapid activation of both transcription factors NFkB and STAT-3 in glial cells. However, if lesioned rats received Triflusal, activation of NFkB was completely inhibited, both in the astroglial and microglial populations. In contrast, a rapid glial activation of STAT-3 was observed from 2 hours post-lesion.

These results indicate that Triflusal could be a good therapeutic expectative in pathological situations where the regulation of glial NFkB activation is an important step in the evolution of neurodegenerative processes.