Poster:

Triflusal prevents neuronal death by downregulating inducible NFkB activation in glial cells.

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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 analyse the capacity of 2-acetoxy-4-trifluoromethyl-benzoic acid (Triflusal), 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 efficacy as a putative neuroprotective drug. To accomplish that, Triflusal was supplied to pup rats either a) in 3 doses (30 mg/Kg) every 24 hours, before an NMDA-excitotoxic lesion (pre-treatment); or b) in an unique dose (30 mg/Kg), eight hours after the lesion (post-treatment). After survival times ranging from 2 to 24 hours, brains were cut in a cryostat and sections processed for NFkB and STAT-3 immunocytochemistry. Labelling for microglia and astroglia demonstration was performed by Tomato lectin histochemistry and GFAP immunocytochemistry. Best results were found in Triflusal post-treated animals. In these conditions, Triflusal had a potent neuroprotection effect in 42% of excitotoxically damaged animals. Our observations showed that in these animals, the extent of neuronal death was notably decreased when compared to control animals. Neuroprotection correlatedwith a strong inhibition of inducible NFkB activation in glial cells. Microglial reaction was remarkably reduced. No inhibition of STAT3 activation was noticed. In conclusion, 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.
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