TRANSCRIPTION FACTORS NF-kB AND STAT3 ARE EXPRESSED IN GLIAL CELLS FOLLOWING AN EXCITOTOXIC LESION IN THE YOUNG BRAIN

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The expression of transcription factors such as the nuclear factor kappa B (NFkB) and the family of signal transducers and activators of transcription (STATs), may play a key role in the activation of several genes involved in the glial response to injury. Target genes of these transcriptions factors include the glial fibrillary acidic protein (GFAP) gene as well as several cytokines, adhesion molecules and major histocompatibility complexes (MHC).

In this study, excitotoxic lesions were induced by the intracortical injection of N-methyl-D-aspartate in postnatal day nine rats. After survival times ranging from 4 hours to 7 days, brains were processed for the obtention of cryostat sections. The immunocytochemical detection of NFkB and STAT3 was carried out by using rabbit polyclonal primary antibodies, anti-rabbit biotinylated secondary antibodies, avidin-peroxidase complexes and DAB as chromogen.

In the excitotoxically damaged cortex, STAT3 positive glial nuclei were already observed at 4 hours post-injection in the surroundings of the lesion core. At 10 hours post-injection, when both necrotic and apoptotic-like neurons are observed in the lesion core, there is an increase in the number of STAT3 positive glial nuclei, which are located both inside the lesion core and surrounding it. From 1 day post-injection, and until 7 days, STAT3 is observed cytoplasmatically, and the ramified morphology of positive glial cells becomes clearly distinguishable. NFkB immunoreactivity is observed in the cytoplasm of few positive reactive glial cells in the damaged cortex at 4 hours post-injection, the number of labelled glial cells increases thereafter and peaks at day 1. Positive cells are present in the lesion site until 7 days post-injection, although mildly decreased in number.

The activation of these transcription factors clearly preceeds the peak of microglial MHC expression and astroglial GFAP increase and hypertrophy, which occur at 3-5 days and 7 days post-injection respectively, in the same lesion model. These results may suggest an implication of STAT3 and NFkB in triggering the glial response in the young brain.