NEURONAL, ASTROGLIAL AND MICROGLIAL CYTOKINE CROSSTALK FOLLOWING AN EXCITOTOXIC LESION IN THE IMMATURE RAT BRAIN. B. González, L. Acarin, A.J. Castro* and B. Castellano. Unit Medical Histology, Autonomous University Barcelona, 08193 Spain; Cell Biology, Neurobiology and Anatomy, Loyola University Chicago, IL 60153.

Cytokines are important intercellular messengers involved in neuron-glia interactions and in the microglial-astroglial crosstalk, modulating the glial response to brain injury and the lesion outcome. In this sense, the balance between pro-inflammatory cytokines like IL-1, IL-6 and TNFα and the anti-inflammatory cytokine TGF-ß is thought to control the expression of several key genes implicated in inflammation, glial activation and scar formation. In this study, excitotoxic lesions were induced by the intracortical injection of *N*-methyl-D-aspartate in postnatal day nine rats, and analyzed at different survival times ranging from 2 hours to 14 days. Floating cryostat sections were processed for the immunocytochemical demonstration of IL-1ß, IL-6, TNFα and TGF-ß, and cytokine-expressing glial cells were identified by means of double labelling with glial fibrillary acidic protein (GFAP) or tomato lectin binding.

Both neurons and glia were capable of cytokine production and very different patterns were observed in the excitotoxically damaged area versus the non-degenerating surrounding gray matter. Excitotoxically-damaged neurons showed upregulation of IL-6 and downregulation of TNFα and TGF-ß before they degenerated. Moreover, in the surrounding gray matter an increased expression of neuronal IL-6, TNFα and TGF-ß was observed. A subpopulation of microglial cells, located in the surrounding gray matter, and showing IL-1ß and TNFα expression were the earliest glial cells producing cytokines, at 2-10 hours post-injection. Later on, cytokine positive glial cells were found inside the excitotoxically damaged area: reactive astrocytes expressed TNFα and IL-6 and microglia/macrophages mainly showed IL-1ß, but also TGF-ß. This maximal glial cytokine production paralleled the period of neuronal cell death, the peak of microglial reactivity and the onset of astroglial GFAP overexpression and hypertrophy. Finally, the expression of all cytokines analyzed was maintained in the glial scar until the last time examined. This specific pattern of cytokine production suggests an implication of these molecules in the evolution of excitotoxic neuronal cell death and the associated glial response during the inflammatory process.

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