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A gliotoxic factor and multiple sclerosis

Ménard A1, Amouri R, Dobránsky T, Charriaut-Marlangue C, Pierig R, Cifuentes-Diaz C, Ghandour S, Belliveau J, Gascan H, Hentati F, Lyon-Caen O, Perron H, Rieger F

Abstract

The pathogenesis of multiple sclerosis (MS) is unknown. Searching for possible toxic factors, it was found that 3-day exposure to heat-treated cerebrospinal fluid (CSF) from MS patients caused apoptotic death of astrocytes and oligodendrocytes, but not fibroblasts, myoblasts, Schwann cells, endothelial cells and neurons, in vitro. CSFs from other inflammatory or non-inflammatory neurological diseases showed no toxicity. Exposure of these glial cells to partially purified MS CSF produced DNA fragmentation, apoptotic bodies, chromatin condensation, cell shrinkage, and changes in the levels of known cytokines. A cytotoxic factor, called gliotoxin, was characterized chromatographically as a stable 17-kDa glycoprotein. Since this protein is highly cytotoxic for astrocytes and oligodendrocytes, it may represent an initial pathogenic factor, leading to the neuropathological features of MS, such as blood-brain barrier involvement and demyelination.

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