

A model of neuroinflammation and demyelination by intracerebroventricular injection of microbial neuraminidase

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Neuraminidase from *Clostridium perfringens*, which cleaves terminal sialic acid from carbohydrate chains, was injected in the lateral ventricle of rats. It diffused in the ipsilateral ventricle, the third ventricle, and also towards the periventricular brain parenchyma. Soon after, the complement system activated, and some ependymal cells detached and died. In the affected zones, there was an increased expression of GFAP in astrocytes, IBA1 in microglia, and ICAM1 in the endothelial cells of blood vessels. Cytokines, such as IL1 β secreted by activated macrophages and microglia, provoked the extravasation of leucocytes from about 4 h post-injection. The main sources of cells were large venules located in the choroid plexus, the meninges and the subependyma around the foramen interventricularis. Invading cells arrived orderly: first neutrophils, then macrophage-monocytes, and last lymphocytes (mainly CD8 α -positive T-lymphocytes). Leucocytes invaded the ventricle and the meninges, and also penetrated the brain parenchyma, sometimes passing through the ependyma and the glia limitans. As a result, some myelinated tracts suffered vacuolar degeneration, being the stria medullaris consistently affected. Oligodendrocytes in the damaged tracts were not affected. Vacuolated myelin recovered with time. Thus, the intracerebroventricular injection of neuraminidase may represent a novel reversible animal model to study experimental neuroinflammation and myelin vacuolization.

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