ROLE OF MMP-9 IN STRIATAL BLOOD-BRAIN BARRIER DISRUPTION IN A 3-NITROPROPIONIC ACID MODEL OF HUNTINGTON'S DISEASE

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Introduction: 3-Nitropropionic acid (3-NPA) is a natural toxin that, when administered to experimental animals, reproduces the brain lesions observed in Huntington's disease, which mainly consist of selective neurodegeneration of the striatum. The lesions also include severe alterations to the blood brain barrier (BBB), which increase its permeability to several substances including blood components and exogenous fluorescent dyes, and the concomitant degradation of some of its constituents such as endothelial cells, tight junction proteins and the basement membrane.

Aims: To study the role of matrix metalloproteinases (MMPs) -2 and -9 in the degradation of the BBB in the striatal lesions induced by the systemic administration of 3-NPA to Sprague-Dawley rats.

Methods: 3-NPA was administered to rats for three days (20mg/kg/day) and after other three days, cerebral tissues were excised and cryostatic sections were obtained. Immunohistochemical and in situ zymography procedures were then applied and stainings were observed by fluorescence microscopy.

Results: In 3-NPA-treated rats, MMP-9 was present in most of the degraded blood vessels in the injured striatum, while it was absent in vessels from non-injured tissue. In the same animals, MMP-2 staining was barely detected close to degraded blood vessels. The combination of MMP-9 immunostaining, in situ zymography and inhibitory studies of MMP-9 confirmed that net gelatinolytic activity detected in the degraded striatal blood vessels could be attributed almost exclusively to the active form of MMP-9.

Conclusions: Our results highlight the prominent role of MMP-9 in BBB disruption in the striatal injured areas of this experimental model of Huntington's disease.