

MATRIX METALLOPROTEINASES AND THEIR RESPONSE TO NEURONAL STIMULATION

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The neurons of the adult brain are able to remodel their synaptic connections in response to various stimuli. Modifications of the peridendritic environment, including the extracellular matrix, are likely to play a role during synapse remodeling. Proteolytic disassembly of the extracellular matrix is a complex process utilizing the regulated actions of specific extracellular proteinases. One of best-characterized families of matrix modifying enzymes are matrix metalloproteinases (MMPs). We recently described changes in the expression and function of two well-known MMPs, MMP-9 and MMP-2, as well as their endogenous inhibitor, TIMP-1, in adult rat brain tissue before and after systemic administration of the glutamate receptor agonist kainate. Kainate application results in enhanced synaptic transmission and seizures followed by selective tissue remodeling, primarily in the hippocampal dentate gyrus. MMP-9, but not MMP-2, was highly expressed by neurons in the normal adult rat brain. MMP-9 protein was localized in neuronal cell bodies and dendrites. Kainate upregulated the level of MMP-9 mRNA and protein within hours of drug administration. This was followed several hours later by MMP-9 enzymatic activation. Within the hippocampus, MMP-9 mRNA and activity were increased selectively in the dentate gyrus, including its dendritic layer. Additionally, MMP-9 mRNA levels decreased in areas undergoing neuronal cell loss. This unique spatio-temporal pattern of MMP-9 expression suggests its involvement in activity-dependent remodeling of dendritic architecture with possible effects on synaptic physiology.