LOCATION OF PRORENIN RECEPTORS IN PRIMATE SUBSTANTIA NIGRA. EFFECTS ON DOPAMINERGIC CELL DEATH

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Introduction: Local renin-angiotensin systems (RAS) play a major role in the development of several age related disorders, which are delayed but not totally abolished by blockage of angiotensin signalling. This may be explained by the discovery of a receptor (PRR) for renin and its precursor prorenin.

Aims: Location of PRR in monkey substantia nigra compacta (SNc) and determine its functional effects on dopaminergic cell death.

Methods: To determine the location of PRR we used double immunolabeling of monkey SNc and rat primary mesencephalic cultures. The functional effects of PRR was demonstrated with the administration of the PRR blocker HRP (handle region peptide), renin, and simultaneous blockage of angiotensin receptors in 6-OHDA-induced cell death in cultures.

Results: A large number of cells expressing PRRs were observed in the SNc and the ventral tegmental area (VTA) of Macaca fascicularis. In monkey SNc and rat primary mesencephalic cultures, double immunolabeling revealed colocalization of PRR labeling with neuronal (including dopaminergic) and microglial markers.

However, no significant co-localization of PRR was observed in astrocytes.

Administration of the HRP led to a significant decrease in 6-OHDA-induced dopaminergic cell death in cultures. Administration of renin with simultaneous blockage of angiotensin receptors led to an increase in 6-OHDA-induced cell death.

Conclusions: This suggests that All-independent PRR intracellular signaling also contributes to exacerbation of dopaminergic cell death, and that potential neuroprotective strategies should address both angiotensin and PRR signalling.