ROLE OF NEURONAL PENTRA Xin 1 IN RODENT DA MODELS OF PARKINSON'S DISEASE

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Introduction: Neuronal pentraxin 1 (NP1), a member of the family long pentraxin family, is selectively expressed in the brain and is homologous to acute phase proteins of the immune system. Increased NP1 levels precede apoptosis in Alzheimer disease and fetal hypoxia models, suggesting that NP1 can act as a pro-apoptotic factor. NP1 is upregulated in the substantia nigra of sporadic Parkinsonian patients.

Aims: To investigate the role of NP1 in the 6-OHDA induced neurodegeneration we quantified expression levels of NP1, 2 and 6 hrs after neurotoxin administration into the substantia nigra and determined whether silencing of NP1 therein, influences neurotoxicity.

Methods: Rats were sacrificed 2 and 6 hrs after 6-OHDA injection, perfused with paraformaldehyde and brains processed for immunohistochemistry. Caspase 3 expression and the percentage of dopaminergic neurons expressing NP1 was assessed through a double immunolabeling with tyrosine hydroxylase (TH). Silencing lentiviral vectors were unilaterally injected in the substantia nigra 10 days before toxin infusion, controls rats received inactive vector. Amphetamine induced turning behavior was tested 2 weeks after 6-OHDA.

Results: Percentage of TH positive neurons expressing NP1 significantly increased after 6-OHDA. Silencing NP1 significantly increased lesion-evoked caspase activation and reduced the number of TH positive neurons in the substantia nigra. Lesion-induced rotational behavior was also enhanced.

Conclusions: These data suggest that lack of this protein might exacerbate 6-OHDA toxicity in the nigrostriatal pathway. On-going studies are examining the influence of NP1 deletion on MPTP-evoked toxicity and the role of NP1 in maintaining dopamine neuronal survival.