ACUTE VERSUS LONG-TERM EFFECTS OF 6-HYDROXYDOPAMINE ON OXIDATIVE STRESS AND NIGROSTRIATAL DEGENERATION IN PINK-1 KNOCK-DOWN MICE

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Introduction: PINK-1 mutations cause autosomal recessive early-onset Parkinson’s disease. PINK-1 is a protein with a mitochondrial signal sequence that confers protective effects to mitochondria. Deficiency of this protein may be correlated with an increased susceptibility to oxidative stress.

Aim: To study the acute and long-term effect of striatally administered 6-hydroxydopamine (6-OHDA) in PINK-1 knock-down (KD) mice.

Methods: In vivo salicylate trapping was applied to monitor the acute effects of 6-OHDA on ⋅OH formation in the striatum of PINK-1 KD and eGFP control mice. Salicylate perfused via the microdialysis probe reacts with ⋅OH and forms 2,3-dihydroxybenzoic acid (2,3-DHBA) which is measured by HPLC. The long-term effect was determined after striatal injection of 6-OHDA in separate groups. TH-immunostaining at the level of the striatum and substantia nigra (SN) 3 weeks after lesioning was performed and the size of the lesion was determined.

Results: Similar baseline levels of 2,3-DHBA were observed in eGFP and PINK-1 KD mice. In both groups, 6-OHDA perfusion caused a significant 2.5 fold increase in 2,3-DHBA concentration and returned to baseline after switching back to salicylate. The size of the lesion within the striatum and the SN was significantly higher in PINK-1 KD than in the eGFP mice.

Conclusion: Our data suggest that PINK-1 KD mice are not more susceptible to 6-OHDA induced acute oxidative stress than eGFP mice. However, the long-term effects of striatal 6-OHDA are more pronounced in PINK-1 KD mice, suggesting a higher susceptibility to oxidative stress long-term.