

PROTECTIVE EFFECT OF RESVERATROL ON 3NP INDUCED HUNTINGTON'S DISEASE RAT MODEL

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Introduction:

Huntington's disease (HD) is a neurodegenerative disorder caused by a mutation in the gene encoding Huntingtin. Mitochondrial defects have been suggested to play an important role in the mechanism of the pathogenesis of HD. The behavioural and anatomical similarities found between HD and models using the mitochondrial toxin 3-nitropropionic acid (3NP) in rats and primates support this hypothesis. Resveratrol has been shown to have a potent free radical scavenging activity in various in vitro and in vivo studies.

Methods:

The 3-NP was administered by osmotic mini pump. The pumps (Alzet; model 2ML4) were filled with 3-NP (Sigma-Aldrich) dissolved in saline to deliver 45 mg/kg/day to each rat. Resveratrol was prepared freshly by dissolving in 100% alcohol and injected intraperitoneally. Treatment of alcohol or resveratrol began from 3 days before surgery and continued for a total of 7 days. All 3NP treated animals and corresponding controls were evaluated for motor deficits. The striatum damage was evaluated by IHC, TUNNEL and Western blotting.

Results:

The IHC results show that 3NP could induce apoptosis and DNA oxidative damage. The tyrosine hydroxylase expression in striatum decreased after 3NP treatment. Rats treated with resveratrol have mild symptoms. Resveratrol administration reduced the cell damage and oxidative damage.

Conclusion:

From our study, we showed inhibition of mitochondrial complex II activity through neurotoxin 3-NP could lead to clinical symptoms of chorea in rats. Pathologically, striatal neuron apoptosis was revealed by positive TUNNEL staining, increased caspase-3 activity and morphological changes. The increased protein carbonyl level from striatum of the symptomatic animals suggested that oxidative stress might play an important role in the process of neuronal degeneration in PD. Resveratrol, a dietary polyphenol derived from plant sources may be a potential therapy in the future for the treatment of patients with HD.