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Original Article

Pharmacological inhibition of PDE1 by vinpocetine attenuates 3-nitropropionic acid-induced behavioral and biochemical abnormalities in rats

Rahul Deshmukh*, P L Sharma

Neuropharmacology Division, I. S. F. College of Pharmacy, Moga-142001, Punjab, India.

Abstract

Enhancing cyclic nucleotide signaling by phosphodieterase inhibition (PDEs) has been reported to be beneficial in neurodegenerative disorders. The present study was designed to investigate the effect of vinpocetine (PDE1 inhibitor) in 3-nitropropionic acid (3-NP) induced experimental Huntington's disease. 3-nitropropionic acid was administered for 14 days (10 mg/kg i.p) in rats and these animals were treated with vehicle or different doses of vinpocetine (5, 10 and 20 mg/kg i.p). Changes in body weight, cognitive and motor behavior were assessed at different time points. Biochemically markers of oxidative stress, such as striatal glutathione and malondialdehyde levels were assessed terminally. Chronic administration of 3-NP produced significant decrease in body weight, showed marked abnormalities in cognitive and motor function and increased striatal oxidative stress. Vinpocetine dose dependently attenuated 3-NP induced behavioral and biochemical toxicity. Among the doses selected, vinpocetine at a dose of 10 mg/kg i.p was observed to be most effective in improving learning and memory in morris water maze and other motor functions such as grip strength, limb withdrawal and locomotor activity in rats. Further vinpocetine significantly attenuated oxidative stress in 3-NP treated rats. The above results suggesting that inhibition of PDE1 would be therapeutically beneficial in motor disorders including Huntington's disease.

Key words: Phosphodiesterase 1; Vinpocetine; Motor disorders; Huntington's disease; Oxidative stress

***Corresponding Author:** *Dr. Rahul Deshmukh, Associate Professor, Neuropharmacology Division ISF College of Pharmacy, Moga- 142001 Punjab, India. E-mail–login2rd@gmail.com