NEUROPROTECTIVE EFFECT OF LAMOTRIGINE AGAINST 3-NITROPROPIONIC ACID INDUCED HUNTINGTON'S LIKE SYMPTOMS: POSSIBLE GABA MECHANISM

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HD is a progressive neurodegenerative disorder that gradually reduces memory, cognitive skills and normal movements of affected individuals. Systemic administration of 3-NP induces selective striatal lesions in rodents and non-human primates. Therefore, the present study has been designed to elucidate the comparative mechanistic profile of, lamotrigine and its interactions with GABAergic modulators against 3-NP induced neurotoxicity. Systemic 3-NP (10 mg/kg) administration for 14 days significantly reduced body weight, locomotor activity, grip strength, oxidative defense (LPO, nitrite, SOD and catalase) and impaired mitochondrial complex enzyme-II activity in the striatum. 3-NP treatment also increased TNF-α level in the striatum. Lamotrigine (10, 20 and 40 mg/kg) treatment significantly restored behavioural, oxidative defense and mitochondrial complex enzyme activities and proinflammatory markers (TNF-α) as compared to 3-NP treated group. Systemic picrotoxin (1 mg/kg) pretreatment with sub effective dose of lamotrigine (20 mg/kg) significantly attenuated its protective effect. Further, muscimol (0.05 mg/kg) pretreatment with sub effective dose lamotrigine (20 mg/kg) significantly potentiated its protective effects which were significant as compared to their effect alone. The results of present study suggest that a GABAergic mechanism is involved in the protective effect of lamotrigine against 3-NP induced neurotoxicity.