Neuroprotective effect of dimethyl fumarate in MPTP-mouse model of Parkinson's disease

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Oxidative stress is central in Parkinson's disease (PD) and nuclear transcription factor related to NF-E2 (Nrf-2) is involved in neuroprotection against PD. The aim of the present study was to investigate the neurotherapeutic action, Nrf-2 dependent, of DMF in a mouse model of PD. Mice received four injections of the dopaminergic neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Starting 24 h after the first administration of MPTP, animals were treated with DMF (10, 30 and 100 mg/kg, by oral gavage) daily for 7 days and, on the 8th day mice were subjected to behavioural test. DMF treatment significantly reduced neuronal degeneration of dopaminergic tract and behavioral impairments induced by MPTP administration. Moreover, treatment with DMF prevented dopamine depletion increasing tyrosine hydroxylase (TH) and dopamine transporter (DAT) and also reduced Î±-synuclein-positive neurons. Furthermore, DMF treatment up-regulated Nrf-2 pathway, increasing $NeuN^+$/$Nrf\text{-}2^+$cells in the striatum and inducing activation of manganese superoxide dismutase(Mn-SOD) and heme-oxygenase-1 (HO-1). Also, DMF reduced ciclo oxygenase 2 (COX-2), lowered nitrotyrosine (NT) and neuronal nitrite oxide synthase (nNOS) expression, restored nerve growth factor(NGF) levels and preserved by microtubule-associated protein 2 (MAP-2) alterations. These results support the thesis that DMF may constitute a promising therapeutic target for the treatment of PD.