MPP+-lesioned mice: an experimental model of motor, emotional, memory/learning and striatal neurochemical dysfunctions

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INTRODUCTION. The neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induces motor and nonmotor dysfunctions resembling Parkinson's disease (PD), however studies investigating the 1-methyl-4-phenylpyridinium (MPP+), an oxidative product of MPTP converted by monoamine oxidase B in astrocytes are scarce. **OBJECTIVE:** The present study investigated behavioral and neurochemical changes induced by intracerebroventricular (icv) administration of MPP+ in C57BL6 mice. **MATERIAL AND METHODS:** The male C57BL6 mice were treated with MPP+ (1.8-18 µg/mouse, icv) or vehicle. Twenty-four hours after the icv injection animals were tested in the open-field test (OFT) or rota-rod test or tail suspension test (TST) or forced swimming test (FST) or splash test (ST) or elevated plus maze (EPM) or step-down passive avoidance test. The striatum was dissected 2 hours after the behavioral test for immunoblotting or ELISA analysis. **DISCUSSION AND RESULTS**: MPP+ administration at dose of 18 µg/mouse reduced crossings and rearings responses in the OFT and rotarod time. MPP+ administration at dose of 1.8 µg/mouse produced a depressive-like effect in the FST and TST, loss of self-care in the ST, anxiogenic-like effect in the EPM and short-term memory deficit in the step-down inhibitory avoidance tasks. MPP+ increased tyrosine hydroxylase and α-synuclein and decreased the parkin immunocontent in striatum. The levels of the astrocytic protein S100B was decreased in striatum following MPP+ administration. MPP+ increased the Iba-1 immunocontent in striatum, suggesting microglia dyshomeostasis. MPP+ at dose of 18 µg/mouse increased TBARS and GSH levels and the gluthatione peroxidase and hemeoxygenase-1 immunocontent in striatum. MPP+ at high dose increased FGF-2 and BDNF levels in striatum. MPP+ decreased TrkB immunocontent in striatum. Finally, MPP+ increased serum corticosterone levels. **CONCLUSION:** These results indicate that MPP+ administration at low dose may be used as a model of emotional and memory/learning behaviour deficit in PD and that MPP+ administration at high dose could be useful for analysis of striatal dysfunctions associated with motor deficits in PD.

Palavra chave: MPP+; Parkinson's disease; Neurotrophic Factors, Glia, Oxidative stress.

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