Lactoferrin shows protective effects in a MPTP-induced mouse model of Parkinson's disease

J. Xie, J. Wang, H. Liu, H. Wu
Department of Physiology, Shandong Provincial Key Laboratory of Pathogenesis and Prevention of Neurological Disorders, Shandong Provincial Collaborative Innovation Center for Neurodegenerative Disorders and State Key Disciplines: Physiology, Qingdao University, China

Background: Lactoferrin (Lf), and the lactoferrin receptor (LfR), regulate cell membrane iron transport, are synthesized in the brain by activated microglia, and their expression is increased in dopaminergic neurons in Parkinson's disease (PD). We investigated the effects of iron-free Lf (apo-Lf) and iron-saturated Lf (holo-Lf) in a mouse model of PD and hypothesized that Lf protects against PD through altered iron metabolism. Methods: We examined the effect of daily intragastric doses of apo-Lf and holo-Lf for 7 days in an experimental 1-Methyl-4-phenyl-1,2,3,6-etrahydropyridine(MPTP)-induced mouse model of PD. Results: Apo-Lf and holo-Lf antagonized MPTP-induced symptoms including shortening pole climbing time, reducing weight loss, preventing tyrosine hydroxylase immunoreactive (TH-ir) neuron loss in the substantianigra (SN), and restoring dopamine in the striatum. Lf increased SOD1 and Bcl-2 expression, and decreased cleaved caspase-3 expression in the SN. Lf treatment down-regulated iron import protein divalent metal transporter (DMT1) and up-regulated iron export protein ferroportin1 (FPN1) normalizing MPTP-induced accumulation of nigral iron. Lf alleviated MPTP-induced increases in serum iron and ferritin, and decreased serum TIBC, spleen weight, and spleen iron content. Liver iron routine blood test remained unchanged. Conclusion: Apo-Lf and holo-Lf have a protective effect against MPTP-induced PD, with apo-Lf showing greater efficacy. Therefore, Lf is a new potential treatment for PD. More importantly, we put forward a hypothesis is that spleen weight loss and lower spleen iron levels might be the original source of iron overload in SN.