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Sodium Butyrate Exacerbates Parkinson's Disease by Aggravating Neuroinflammation and Colonic Inflammation in MPTP-Induced Mice Model

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Abstract

The abnormal production of short chain fatty acid (SCFAs) caused by gut microbial dysbiosis plays an important role in the pathogenesis and progression of Parkinson's disease (PD). This study sought to evaluate how butyrate, one of SCFAs, affect the pathology in a subacute 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine hydrochloride (MPTP) treated mouse model of PD. Sodium butyrate (NaB; 165 mg/kg/day i.g., 7 days) was administrated from the day after the last MPTP injection. Interestingly, NaB significantly aggravated MPTP-induced motor dysfunction ($P < 0.01$), decreased dopamine ($P < 0.05$) and 5-HT ($P < 0.05$) levels, exacerbated declines of dopaminergic neurons (34%, $P < 0.05$) and downregulated expression of tyrosine hydroxylase (TH, 47%, $P < 0.05$), potentiated glia-mediated neuroinflammation by increasing the number of microglia (17%, $P < 0.05$) and activating astrocytes (28%, $P < 0.01$). In vitro study also confirmed that NaB could significantly exacerbate pro-inflammatory cytokines expression (IL-1β, 4.11-fold, $P < 0.01$; IL-18, 3.42-fold, $P < 0.01$ and iNOS, 2.52-fold, $P < 0.05$) and NO production (1.55-fold, $P < 0.001$) in LPS-stimulated BV2 cells. In addition, NaB upregulated the expression of pro-inflammatory cytokines (IL-6, 3.52-fold, $P < 0.05$; IL-18, 1.72-fold, $P < 0.001$) and NLRP3 (3.11-fold, $P < 0.001$) in the colon of PD mice. However, NaB had no effect on NFκB, MyD88 and TNF-α expression in PD mice. Our results indicate that NaB exacerbates MPTP-induced PD by aggravating neuroinflammation and colonic inflammation independently of the NFκB/MyD88/TNF-α signaling pathway.

Keywords: Colonic inflammation; MPTP; Neuroinflammation; Parkinson's disease (PD); Sodium butyrate.