# The protective effect of voluntary exercise is mediated by the inhibition of NETosis and upregulation of Prdx6 in TNBS-induced rat colitis

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Inflammatory bowel diseases (IBD) are autoimmune disorders of the gastrointestinal tract. It is increasingly clear that voluntary exercise seems to be a non-pharmacological therapeutic option against this disease, but the exact mechanism behind the protection needs to be elucidated. This study was conducted to clarify the importance of NETosis, the process of the formation of neutrophil extracellular traps (NETs) and the antioxidant peroxiredoxin (Prdx) enzyme family in voluntary exercise-induced protection. Wistar-Hannover rats were randomly divided into 2 groups: sedentary and voluntary exercise (wheel running). After the 6-week training period, animals were challenged with 2,4,6-trinitrobenzene sulphonic acid (TNBS, 10 mg dissolved in 50% ethanol) as a model of colitis. Biochemical measurements were performed from the last 8 cm of the colon via Western immunoblotting and ELISA. Our results showed that voluntary exercise significantly decreased inflammation and ulceration of the colon in the TNBS-running group compared to TNBS-sedentary. In the case of the Prdx enzyme family, Prdx2 and Prdx4 isoforms were increased after TNBS treatment, but the impact of running was found to be significant only between the control groups. Voluntary exercise caused a significant increase in Prdx6 levels of the control and TNBS groups as well compared to sedentary. According to NETosis, we found that voluntary exercise significantly decreased the expression of citrullinated histone H3 (citH3), while myeloperoxidase (MPO) and protein arginine deiminase 4 (PAD4) were markedly decreased compared to the TNBS-sedentary group. Taken together, our results suggest that the protective effect of voluntary exercise seems to be mediated via the inhibition of NETosis and upregulation of the Prdx6 antioxidant.