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Gut microbiota modulate distal symmetric polyneuropathy in people with diabetes

Aims: Peripheral neuropathy is a debilitating condition characterized by damage in the peripheral nervous system, and it is often associated with diabetes. Recent research has uncovered a significant and intricate connection between the composition of the gut microbiota and the development of diabetic sensorimotor polyneuropathy (DSPN). This article delves into a comprehensive study that explores the potential of fecal microbiota transplantation (FMT) to alleviate neuropathic symptoms in patients with DSPN.

***Methods*:** To lay the foundation, the study meticulously analyzed the gut microbiota composition in patients diagnosed with DSPN. This initial step aimed to discern any discernible patterns or imbalances in the gut microbiome associated with the condition. Researchers conducted a pivotal set of experiments by subjecting mice to FMT from DSPN patients with or without diabetes. In addition to the transplantation of microbiota from DSPN patients to mice, the research explored the effects of FMT from healthy donors to DSPN patients.

***Results*:** Notably, the transplantation of gut microbiota from DSPN patients into mice had profound effects compared to the transplantation of the microbiota from patients with normal glucose or diabetes. The outcomes provided crucial evidence of a causal link between gut microbiota and the worsening of peripheral neuropathy. This procedure also led to more severe gut-barrier dysfunction, higher antigen load, and systemic inflammation in the mice. Most significantly, the study revealed that FMT using microbiota from healthy donors played a pivotal role in significantly improving nerve function and alleviating neuropathic symptoms in DSPN patients. Additionally, the study revealed a significant improvement of gut barrier function and a reduction in systemic inflammation, characterized by lower levels of LBP, TNF-α, and IL-6 in DSPN patients after FMT.

***Conclusions*:** The research findings have profound implications, suggesting that FMT may hold great promise as a treatment for DSPN. Remarkably, the study indicates that the beneficial effects of FMT are not solely reliant on improvements in glycemic control or lifestyle modifications, as glucose and lipid metabolism remained similar between the FMT and placebo groups throughout the study. The study postulates that the improvement in DSPN may be attributed to the reduction of endotoxin production and an increase in butyrate-producing bacteria in the gut microbiome.

Comments. The study's sample size in the clinical trials was relatively small, indicating the need for larger cohort studies to validate and expand upon these preliminary findings. Furthermore, the study used only male db/db mice in the animal experiments, and future investigations should explore the potential influence of sex on the outcomes and using non genetic models since the leptin signaling may be involved in the outcomes. The molecular mechanisms underpinning the role of the gut microbiota in DSPN are not understood, necessitating further active research. Nevertheless, this study's innovative approach emphasizes the potential of FMT as a treatment option for DSPN, establishing a causal connection between the gut microbiome and peripheral nervous system disorders as it has been suggested by other groups in rodents these past years. The findings pave the way for more targeted and effective treatments for DSPN and suggest digging deeper into mechanisms in the future.

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Reference. Yang J, Yang X, Wu G, Huang F, Shi X, Wei W, Zhang Y, Zhang H, Cheng L, Yu L, Shang J, Lv Y, Wang X, Zhai R, Li P, Cui B, Fang Y, Deng X, Tang S, Wang L, Yuan Q, Zhao L, Zhang F, Zhang C, Yuan H. Gut microbiota modulate distal symmetric polyneuropathy in patients with diabetes. Cell Metab. 2023 Sep 5;35(9):1548-1562.e7. doi: 10.1016/j.cmet.2023.06.010. Epub 2023 Jul 13. PMID: 37451270.
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