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Editorial

Fecal microbiota transplantation reverses obesity-induced neuropathic pain

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In the last years there have been several studies about the effects of fecal microbiota transplantation (FMT) on several diseases including major depression, schizophrenia, irritable bowel syndrome, Crohn's disease, and obesity.[1-4] Particularly, obesity is a clinical condition affecting millions of people around the world. This condition is a risk factor for several pathologies. Obesity can lead to prediabetes and insulin resistance, whereas that the latter condition may induce diabetic neuropathy before overt type 2 diabetes. There is evidence of pain in hands and feet of obese patients or prediabetic patients. Although chronic pain is one of the most common complications of obesity, treatment of neuropathic pain in these patients is not satisfactory. It has been shown that FMT and lipid metabolites reverse dysfunction of sensory nerves induced by a Western diet (high in lipids and sugar). Moreover, FMT in a diabetic obese patient reduced neuropathic pain in a case report. However, the role of FMT in obesity-associated neuropathic pain is currently unknown. The groups of Dr. Nigel A. Calcutt (University of California, San Diego) and Dr. Virginia Mansuy-Aubert (Loyola Universidad, Chicago) have studied this problem in a recent elegant study published in PNAS.[3] Researchers carried out FMT from lean to obese mice with insulin resistance. They found that FMT and a metabolite from bacteria found in feces of lean mice (butyrate) reduced neuropathic pain in obese mice. Obese mice treated with FMT had a major nerve density in the skin, which suggests that FMT is reversing sensory neuropathology induced by obesity. In addition, FMT reduced expression of genes that promote hyperexcitability in dorsal root ganglion neurons (DRG, pain receptors). In particular, FMT reduced expression lysine-specific methyltransferase 2A (KMT2A), ryanodine receptor 2 (RYR2), ABCA1, apolipoprotein E (ApoE) and PIEZO2 channels. FMT enhanced percentage of M2 macrophages (CD45+hiCD11B+CD206+) in DRG of obese mice. This implies that FMT induces a shift to the activation of macrophages with an anti-inflammatory profile. They found that FMT treatment increased 25 times expression of free fatty acid receptor 2 (FFAR2) in immune cells system. Furthermore, FMT treatment increased blood butyrate levels in obese patients. Tributirine, a butyrate donor, treatment diminished tactile allodynia in obese patients. Moreover, tributirine treatment in mice reduced activation of leucocytes (CD45) in DRG of obese mice. In vitro application of butyrate in neurons of DRG of mice enhanced expression of HDAC2 mRNA, which suggest that butyrate directly modulate HDAC2. Butyrate also modified TRPV1 channel activity. Interestingly, obese patients had lower levels of blood butyrate. Researchers suggest that FMT or butyrate could be helpful to treat early neuropathic pain in obese patients.

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