My First Medical Writing

SECTION EDITOR

Evguenia Alechine
ealechine@gmail.com

Editorial

Welcome to a new release of *My First Medical Writing*. In this edition, we bring you a contribution by Janaine Prata de Oliveira. As a former dentist with a PhD in Pharmacology, Janaine has worked throughout her scientific career on pain and inflammation research across Brazil, Belgium, and the USA. She is passionate about turning complex scientific and medical information into clear and relatable messages for a diverse audience, including children. Currently, she works as a post-doctoral researcher at St Louis University (USA) and as a freelance medical writer. You can find more information about her work at https://janawriteshealth.com. This article clearly shows her drive to communicate medicine and science-related topics to a broader audience. I hope you enjoy this read!

Evguenia

Gut feeling and chronic pain: Revisiting the microbiota connection

Janaine Prata de Oliveira
Freelance Medical Writer
St Louis, Missouri, USA
janaineprata@gmail.com

doi: 10.56012/bxad7017

Fibromyalgia, migraine, rheumatoid arthritis, irritable bowel disease (IBD), and neuropathic pain: Those conditions have one thing in common: chronic pain. Chronic pain is defined as pain that persists for three months or longer.[1] It affects nearly 20% of the global population and significantly impacts physical, emotional, and social well-being.[1,2]

Although chronic pain is a prevalent condition, treating it remains a challenge for patients and healthcare providers. Recent studies have shown a potential new player in this scenario: the gut microbiota.

The gut microbiota comprises thousands of microorganisms that perform essential functions beyond digestion. Emerging evidence highlights the role of the gut–brain axis in chronic pain, particularly through activation of immune cells and neuroinflammation. In this article, I explore how this interaction happens and how gut modulation might offer a potential strategy for chronic pain management. Let's dive into this microscopic world!

The gut microbiota: Beyond digestion

The gut microbiota is a microscopic world composed of over 1,000 microbial species and over 7,000 strains, primarily bacteria. In a balanced state (called homeostasis), the intestinal microbiota helps food digestion and immune regulation, as well as overall health.[3] On the other hand, when this balance is disrupted, the microbiome changes its composition, leading to dysbiosis. This condition can disturb the immune system and lead to chronic inflammation.[3-5]

In the past few years, the interaction between microbiota and the immune system has been investigated in many neurological and autoimmune conditions, such as Alzheimer's disease, multiple sclerosis, and chronic pain.[3] But how can small creatures make such an impact?

In the gut, microbial metabolism produces products such as lipopolysaccharides (LPS) and short-chain fatty acids (SCFAs). These microbial products can act as pro-inflammatory substances, activating immune cells that release cytokines and chemokines. Over time, this ongoing process exacerbates inflammation and can damage the intestinal barrier, a condition often referred to as "leaky gut". When the barrier is compromised, microbial products normally confined to the gut can cross into the bloodstream and reach distant organs, including the nervous system.[4-5]

Gut microbiota and chronic pain regulation

Gut microbes and their derivatives may contribute to peripheral sensitisation (pain) by directly activating specialised neurons in the peripheral nervous fibers (e.g., nerves in the skin, muscles, joints), called nociceptive neurons. Those gut microbes may also indirectly contribute to peripheral sensitisation by activating immune cells, and release of pro-inflammatory substances, such as IL-1β and TNF-β.[5,6]

> Importantly, recent clinical studies suggest that communication between the gut microbiota and microglia plays a key role in chronic pain development.

In the central mechanism, the gut microbiota interacts with the central nervous system, forming the gut-brain axis. Those microbial products (LPS and SCFAs) cross the blood-brain barrier that protects the brain from invaders. Then, they interact and activate the glial cells (microglia and astrocytes) and infiltrate immune cells. Those cells release additional inflammatory mediators and interact with neurons, causing neuroinflammation and exacerbating pain sensitisation.[5,7,8]

Importantly, recent clinical studies suggest that communication between the gut microbiota and microglia plays a key role in chronic pain development.[4,5,9-11] Therefore, restoration of gut microbiota homeostasis can reduce microglia activation, hence neuroinflammation and chronic pain. [4,5]

Microbiota-based therapies

Many chronic pain conditions present an imbalance in the gut microbiota, often marked by an increase of obligately or facultatively anaerobic and aerobic bacteria, such as *Clostridiaceae*, *Enterobacteriaceae*, and *Proteobacteria*.[4,5] At the same time, there is a reduction in the bacteria population that live in harmony with the body (also called commensal bacteria), disrupting the microbial ecosystem. In addition, pain may affect the microbiota profile across different types of painful conditions.[5,6] Thereby, some alternatives have been proposed to reestablish gut microbiota equilibrium.

Probiotics

Probiotics are active microorganisms that promote health benefits to the host, including immune modulation.[12] For instance, a study showed that probiotic supplementation of Lactobacilli, *Bifidobacterium,* and *Saccharomyces* for eight weeks reduced pain and improved sleep quality (i.e., getting uninterrupted and refreshing sleep), depression, and anxiety in patients with fibromyalgia.[13] Another study showed that supplementation of *Lactobacillus* for four weeks reduced pain in children with inflammatory bowel syndrome.[14] The positive effect of probiotic supplementation has also been confirmed in migraine after use of *Lactobacilli*, *Bifidobacteria,* and *Streptococcus* for ten weeks.[15]

Fecal microbiota transplantation

Fecal microbiota transplantation (FMT) transfers a small stool from a healthy donor into the gastrointestinal tract of a patient to modify intestinal flora and restore gut homeostasis.[16] In patients suffering from fibromyalgia, FMT reduced widespread pain, anxiety, and depression, and improved sleep quality after 3, 6, and 12 months after intervention.[17] FMT transplantation also reduced abdominal pain, discomfort, and severity in patients with inflammatory bowel syndrome after 12 weeks of the procedure; however, these effects were reduced over 1 year.[18]

Perspectives

The egg or the chicken? Which comes first, the neuroinflammation and chronic pain, or the dysbiosis? This is one of the questions that scientists are still uncovering. The relationship between gut microbiome and chronic pain is undeniable; however, we need to understand more about multiple microbiota profiles across different types of chronic pain and their clinical implications.

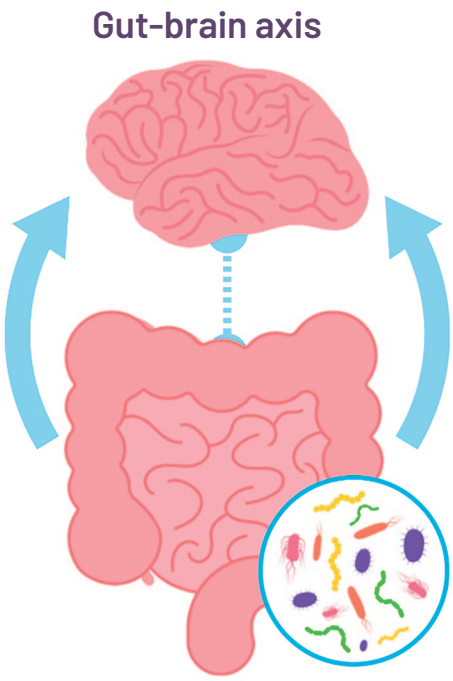
For now, a multidisciplinary approach remains essential. Additionally, patients should actively engage in their treatment plans to effectively manage chronic pain: following a balanced diet, practicing regular physical activity, working on mental health, and adhering to healthcare guidance. There is no simple solution. But the gut microbiota may offer new hope for chronic pain treatment.

Disclaimers

The opinions expressed in this article are the author's own and are not necessarily shared by their employers or EMWA.

Disclosures and conflicts of interest

The author declares no conflicts of interest.



References

1. Treede RD, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain. 2019;160(1):19-27. doi:10.1097/j.pain.0000000000001384
2. Zimmer Z, Fraser K, Grol-Prokopczyk H, et al. A global study of pain prevalence across 52 countries: examining the role of country-level contextual factors. Pain. 2022;163(9):1740-50. doi:10.1097/j.pain.0000000000002557
3. Lloyd-Price J, Abu-Ali G, Huttenhower C. The healthy human microbiome. Genome Med. 2016;8(1). doi:10.1186/s13073-016-0307-y
4. Ustianowska K, Ustianowski Ł, Machaj F, et al. The role of the human microbiome in the pathogenesis of pain. Int J Mol Sci. 2022;23(21):13267. doi:10.1007/s12035-024-04663-x
5. Lou L, Zhou L, Wang Y. Gut microbiota: a modulator and therapeutic target for chronic pain. Mol Neurobiol. 2025 May;62(5):5875-90. doi:10.1007/s12035-024-04663-x.
6. Guo R, Chen LH, Xing C, et al. Pain regulation by gut microbiota: molecular mechanisms and therapeutic potential. Br J Anaesth. 2019;123(5):637-654. doi:10.1016/j.bja.2019.07.026
7. Ho T, Elma Ö, Kocanda L, et al. The brain-gut axis and chronic pain: mechanisms and therapeutic opportunities. Front Neurosci. 2025;19. doi:10.3389/fnins.2025.154599
8. Morreale C, Bresesti I, Bosi A, et al. Microbiota and pain: save your gut feeling. Cells. 2022 Mar;11(6):971. doi:10.3390/cells11060971
9. Boer CG, Radjabzadeh D, Medina-Gomez C, et al. Intestinal microbiome composition and its relation to joint pain and inflammation. Nat Commun. 2019;10(1):4881. doi:10.1038/s41467-019-12873-4
10. Kopchak OO, Hrytsenko OY, Pulyk OR. Peculiarities of the gut microbiota in patients with migraine comparing to healthy individuals. Wiad Lek. 2022;75(9 pt 2):2218-2221. doi:10.36740/WLek202209207
11. Chen J, Wang Q, Wang A, et al. Structural

Illustration: Janaine Prata de Oliveira

and functional characterization of the gut microbiota in elderly women with migraine. Front Cell Infect Microbiol. 2020;9:470. doi:10.3389/fcimb.2019.00470

12. Butel MJ. Probiotics, gut microbiota and health. Med Mal Infect. 2014;44(1):1-8. doi:10.1016/j.medmal.2013.10.002
13. Aslan ÇİN NN, Açik M, TertemİZ OF, et al. Effect of prebiotic and probiotic supplementation on reduced pain in patients with fibromyalgia syndrome: a double-blind, placebo-controlled randomized clinical trial. Psychol Health Med. 2024;29(3):528-541. doi:10.1080/13548506.2023.2216464
14. Weizman Z, Abu-Abed J, Binsztok M. Lactobacillus reuteri DSM 17938 for the management of functional abdominal pain in childhood: a randomized, double-blind, placebo-controlled trial. J Pediatr. 2016;174:160-64.e1. doi:10.1016/j.jpeds.2016.04.003
15. Martami F, Togha M, Seifishahpar M, et al. The effects of a multispecies probiotic supplement on inflammatory markers and episodic and chronic migraine characteristics: A randomized double-blind controlled trial. Cephalalgia. 2019;39(7):841-853. doi:10.1177/0333102418820102
16. Bowman KA, Broussard EK, Surawicz CM. Fecal microbiota transplantation: current clinical efficacy and future prospects. Clin Exp Gastroenterol. 2015;8:285-91. doi:10.2147/CEG.S61305
17. Fang H, Hou Q, Zhang W, et al. Fecal microbiota transplantation improves clinical symptoms of fibromyalgia: an open-label, randomized, nonplacebo-controlled study. J Pain. 2024;25(9):104535. doi: 10.1016/j.jpain.2024.104535
18. Holvoet T, Joossens M, Vázquez-Castellanos JF, et al. Fecal microbiota transplantation reduces symptoms in some patients with irritable bowel syndrome with predominant abdominal bloating: short- and long-term results from a placebo-controlled randomized trial. Gastroenterology. 2021;160(1):145-57.e8. doi:10.1053/j.gastro.2020.07.013.

Janaine Prata de Oliveira