



Letter to Editor

Could postbiotics improve mental health?

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The gut microbiota has emerged as a crucial component in the bidirectional communication between the gut and the brain, known as the gut-brain axis.¹⁻³ This complex network of interactions has been implicated in various mental disorders, including depression, anxiety, and schizophrenia. Recent literature suggests that an imbalance in gut microbiota, or dysbiosis, may contribute to the pathogenesis of these mental disorders by altering neurotransmitter levels, immune responses, and neuroinflammation.⁴

Mental disorders significantly impact individuals and society, leading to disability and reduced quality of life. While current treatments, including medications and psychotherapy, are effective for many, they may not be universally successful and can have undesirable side effects. This highlights the need for alternative approaches to prevent and treatment for mental disorders. Additionally, recent research indicates a direct link between gut health and mental health, with probiotics—live microorganisms known for their potential role in mental health—being less impactful than their metabolic by-products, termed postbiotics.⁵

Postbiotics, which include compounds like neurotransmitters, have shown promise in reducing inflammation and promoting intestinal health.⁶⁻⁸ Consuming probiotics through fermented foods or supplements and indirectly consuming postbiotics through probiotic-rich foods or fortified products may improve mental health outcomes. This letter focuses on the potential benefits of postbiotics in preventing and treating mental illnesses such as depression, anxiety,

bipolar and related disorders, and Psychotic disorders, aiming to explore new approaches for improving mental health.

Genetic variations and neurotransmitter imbalances contribute to depression and anxiety, which are prevalent mental health problems affecting millions globally.⁹ The World Health Organization reports that approximately 280 million people suffer from depression, with women being more likely to experience it than men.¹⁰ Various factors, including family history, stressful life events, and hormonal changes, contribute to the development of depression and anxiety. Conversely, the gut microbiota plays a significant role in the gut-brain axis, influencing stress responses and mental health.¹¹ Studies have also shown differences in the fecal microbiota of individuals with depression compared to healthy controls, suggesting a potential role for gut bacteria in modulating mental health.¹⁰

Moreover, psychotic disorders may be affected by gut microbiota. Probiotic supplementation may influence gut microbiota, reduce inflammation, and modulate immune responses, potentially benefiting patients with schizophrenia by increasing brain-derived neurotrophic factor levels and supporting cognitive function. Clinical trials have explored the effects of probiotics on cognitive impairment in schizophrenia, showing positive effects on symptom severity.^{12,13}

Furthermore, manic illnesses, characterized by elevated mood and energy, can lead to impulsive behavior. Studies suggest that diet and microbiota can influence manic-like behaviors. Probiotic strains have shown potential in reducing mania-like behaviors and improving mood



in animal models. Additionally, postbiotics have demonstrated benefits similar to probiotics, indicating their potential role in managing manic disorders.^{14,15}

The mechanisms by which probiotics and postbiotics influence mood are not yet fully understood. They may operate through the gut-brain axis, modulating gut microbiota composition and affecting neurotransmitter production. Probiotics can increase the production of GABA, a neurotransmitter with calming effects, and reduce markers of inflammation linked to mood disorders.^{16,17} Microbial metabolites, such as short-chain fatty acids (SCFAs), GABA, dopamine, serotonin, tryptophan, and oxytocin, play significant roles in mood regulation. SCFAs, produced during the fermentation of dietary fibers, can act as signaling molecules that influence mood-related pathways. GABA is crucial for decreasing neuronal excitability, while dopamine and serotonin are associated with feelings of pleasure and happiness. Tryptophan, an essential amino acid, is a precursor for serotonin synthesis and has been linked to mood regulation.¹⁸⁻²³

In conclusion, understanding the intricate relationship between gut microbiota and mental health status opens new avenues for therapeutic interventions targeting the gut-brain axis. Continued research into postbiotics and their effects on mood management and preventing and treatment of psychotic disorders could lead to novel approaches in psychiatry for treating individuals struggling with mental disorders, ultimately improving mental health outcomes and quality of life.

Authors' Contribution

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Competing Interests

The authors have no conflicts of interest to declare.

Ethical Approval

Not applicable.

References

1. Ansari F, Pourjafar H, Tabrizi A, Homayouni A. The effects of probiotics and prebiotics on mental disorders: a review on depression, anxiety, Alzheimer, and autism spectrum disorders. *Curr Pharm Biotechnol*. 2020;21(7):555-65. doi: [10.2174/1389201021666200107113812](https://doi.org/10.2174/1389201021666200107113812).
2. Forth E, Buehner B, Storer A, Sgarbossa C, Milev R, Chinna Meyyappan A. Systematic review of probiotics as an adjuvant treatment for psychiatric disorders. *Front Behav Neurosci*. 2023;17:1111349. doi: [10.3389/fnbeh.2023.1111349](https://doi.org/10.3389/fnbeh.2023.1111349).
3. Amirani E, Milajerdi A, Mirzaei H, Jamilian H, Mansournia MA, Hallajzadeh J, et al. The effects of probiotic supplementation on mental health, biomarkers of inflammation and oxidative stress in patients with psychiatric disorders: A systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med*. 2020;49:102361. doi: [10.1016/j.ctim.2020.102361](https://doi.org/10.1016/j.ctim.2020.102361).
4. Mhanna A, Martini N, Hmaydoosh G, Hamwi G, Jarjanazi M, Zaifah G, et al. The correlation between gut microbiota and both neurotransmitters and mental disorders: a narrative review. *Medicine (Baltimore)*. 2024;103(5):e37114. doi: [10.1097/md.00000000000037114](https://doi.org/10.1097/md.00000000000037114).
5. Johnson D, Thuraiarajasingam S, Letchumanan V, Chan KG, Lee LH. Exploring the role and potential of probiotics in the field of mental health: major depressive disorder. *Nutrients*. 2021;13(5):1728. doi: [10.3390/nu13051728](https://doi.org/10.3390/nu13051728).
6. Abbasi A, Aghebati-Maleki L, Homayouni-Rad A. The promising biological role of postbiotics derived from probiotic *Lactobacillus* species in reproductive health. *Crit Rev Food Sci Nutr*. 2022;62(32):8829-41. doi: [10.1080/10408398.2021.1935701](https://doi.org/10.1080/10408398.2021.1935701).
7. Ahmed H, Leyrolle Q, Koistinen V, Kärkkäinen O, Layé S, Delzenne N, et al. Microbiota-derived metabolites as drivers of gut-brain communication. *Gut Microbes*. 2022;14(1):2102878. doi: [10.1080/19490976.2022.2102878](https://doi.org/10.1080/19490976.2022.2102878).
8. Homayouni-Rad A, Abbasi A, Soleimani RA, Pouraga B. Could postbiotics substitute probiotics? *Curr Nutr Food Sci*. 2023;19(7):670-2. doi: [10.2174/1389201023666221004125745](https://doi.org/10.2174/1389201023666221004125745).
9. Cui L, Li S, Wang S, Wu X, Liu Y, Yu W, et al. Major depressive disorder: hypothesis, mechanism, prevention and treatment. *Signal Transduct Target Ther*. 2024;9(1):30. doi: [10.1038/s41392-024-01738-y](https://doi.org/10.1038/s41392-024-01738-y).
10. World Health Organization (WHO). Depressive Disorder (Depression). 2023. <https://www.who.int/news-room/fact-sheets/detail/depression>.
11. Clapp M, Aurora N, Herrera L, Bhatia M, Wilen E, Wakefield S. Gut microbiota's effect on mental health: the gut-brain axis. *Clin Pract*. 2017;7(4):987. doi: [10.4081/cp.2017.987](https://doi.org/10.4081/cp.2017.987).
12. Dickerson FB, Stallings C, Origoni A, Katsafanas E, Savage CL, Schweinfurth LA, et al. Effect of probiotic supplementation on schizophrenia symptoms and association with gastrointestinal functioning: a randomized, placebo-controlled trial. *Prim Care Companion CNS Disord*. 2014;16(1):26294. doi: [10.4088/PCC.13m01579](https://doi.org/10.4088/PCC.13m01579).
13. Ng QX, Soh AY, Venkatanarayanan N, Ho CY, Lim DY, Yeo WS. A systematic review of the effect of probiotic supplementation on schizophrenia symptoms. *Neuropsychobiology*. 2019;78(1):1-6. doi: [10.1159/000498862](https://doi.org/10.1159/000498862).
14. Pacchiarotti I, Anmella G, Colomer L, Vieta E. How to treat mania. *Acta Psychiatr Scand*. 2020;142(3):173-92. doi: [10.1111/acps.13209](https://doi.org/10.1111/acps.13209).
15. Swann AC, Moeller FG, Steinberg JL, Schneider L, Barratt ES, Dougherty DM. Manic symptoms and impulsivity during bipolar depressive episodes. *Bipolar Disord*. 2007;9(3):206-12. doi: [10.1111/j.1399-5618.2007.00357.x](https://doi.org/10.1111/j.1399-5618.2007.00357.x).
16. Liu X, Cao S, Zhang X. Modulation of gut microbiota-brain axis by probiotics, prebiotics, and diet. *J Agric Food Chem*. 2015;63(36):7885-95. doi: [10.1021/acs.jafc.5b02404](https://doi.org/10.1021/acs.jafc.5b02404).
17. Barrio C, Arias-Sánchez S, Martín-Monzón I. The gut microbiota-brain axis, psychobiotics and its influence on brain and behaviour: a systematic review. *Psychoneuroendocrinology*. 2022;137:105640. doi: [10.1016/j.psyneuen.2021.105640](https://doi.org/10.1016/j.psyneuen.2021.105640).
18. Moradi M, Kousheh SA, Almasi H, Alizadeh A, Guimarães JT, Yilmaz N, et al. Postbiotics produced by lactic acid bacteria: the next frontier in food safety. *Compr Rev Food Sci Food Saf*. 2020;19(6):3390-415. doi: [10.1111/1541-4337.12613](https://doi.org/10.1111/1541-4337.12613).
19. Abbasi A, Homayouni-Rad A, Ghasempour Z, Sabahi S, Samadi Kafil H, Hasannezhad P, et al. The biological activities of postbiotics in gastrointestinal disorders.

- Crit Rev Food Sci Nutr. 2022;62(22):5983-6004. doi: [10.1080/10408398.2021.1895061](https://doi.org/10.1080/10408398.2021.1895061).
20. Thorakkattu P, Khanashyam AC, Shah K, Babu KS, Mundanat AS, Deliephan A, et al. Postbiotics: current trends in food and pharmaceutical industry. Foods. 2022;11(19):3094. doi: [10.3390/foods11193094](https://doi.org/10.3390/foods11193094).
21. Wu Y, Wang Y, Hu A, Shu X, Huang W, Liu J, et al. *Lactobacillus plantarum*-derived postbiotics prevent *Salmonella*-induced neurological dysfunctions by modulating gut-brain axis in mice. Front Nutr. 2022;9:946096. doi: [10.3389/fnut.2022.946096](https://doi.org/10.3389/fnut.2022.946096).
22. El Masry BH. Impact of Dietary *Lactobacillus plantarum* Postbiotics on Performance of Layer Hens under Heat Stress Conditions [dissertation]. Beirut, Lebanon: American University of Beirut; 2023.
23. Scheri GC, Fard SN, Schietroma I, Mastrangelo A, Pinacchio C, Giustini N, et al. Modulation of tryptophan/serotonin pathway by probiotic supplementation in human immunodeficiency virus-positive patients: preliminary results of a new study approach. Int J Tryptophan Res. 2017;10:1178646917710668. doi: [10.1177/1178646917710668](https://doi.org/10.1177/1178646917710668).