# The Effect of Gut Brain Axis on Neurologic Diseases and Psychiatric Disorders

Huseyin Ugur Ozturk
California Institute of Behavioral Neurosciences and Psychology
Journal For International Medical Graduates

## Abstract

Neurologic and psychiatric diseases represent a huge health burden, as they impact many individuals worldwide irrespective of social class or age. Evidence suggests that these disorders represent approximately 12% of diseases globally. Human and animal models have been used to assess the impact of the gut-brain axis (GBA) communication pathways in the disorders' multi-causal perspective. Various mechanisms have been suggested; nevertheless, systematic reviews focusing on the latest developments in the area are minimal. This paper systematically reviews the influence of the gut-brain axis on psychiatric disorders and neurologic diseases. Using PRISMA 2020 Checklist, the findings reaffirm the microbiota-GBA bidirectional communication and its role in influencing various neuropsychiatric diseases. Understanding these mechanisms could be crucial in developing novel and targeted treatment approaches to treat these disorders for health practitioners. Besides, policymakers should come up with guidelines to regulate such interventions. However, the included evidence and the processes adopted were not without limitations; for this reason, future studies should address them.

**Keywords:** GBA, neurologic diseases, psychiatric disorders, microbiota, gastrointestinal microbiome, immune response.

## Introduction

For long it has been said "healthy body healthy mind". A lot of researches showed us healthy body leads to a healthy mind [1], Drossman. Even philosopher Jean-Jacques Rousseau describe this phenomenon as "Happiness: a good bank account, a good cook, and a good digestion."

On the contrary, intestinal permeability is increased by the gastrointestinal tract microorganism dysbiosis, enabling different inflammatory substances and metabolites to travel to the brain leading to a lack of social functioning and psychological symptoms. Similarly, [9] Appleton (2018), summarizes that the nerves, HPA axis, and autonomic nervous system in the gastrointestinal tract are connected to the brain and gut, enabling the brain to impact intestinal activities and the gut to influence mental health, cognition, and mood. Thus, a viable treatment method for BGA disorders is the therapeutic targeting of gut microbiota [10] O'Mahony et al. (2015).

Other studies have further investigated microbiota-GBA bidirectional communication. [11] Kumar et al. (2014), argue that more effectively understanding interactions between microbiota and GBA induces in-depth insights into the Parkinson's disease (PD) pathophysiology and allows timely diagnosis. Also, [12] Cryan et al. (2019), underscore the different communication routes of microbiota-GBA. The authors highlight that aging reduces microbial diversity, and stress may substantially affect the microbiota-GBA at each life stage. Using animal models to link neural processes' control and microglia microbiome activation, they add that the gut microbiota has been implicated in different disorders. Notably, human translational models are being undertaken. Recently, [13] Person and Keefer (2021), concluded by stressing that the brain-gut-microbiome axis (BGMA) represents a potential therapeutic target since employing postbiotics, probiotics, or prebiotics in mimicking gut microbial signals or modifying the gut microbiome may offer attractive therapies for resolving the debilitating conditions.

[14] Quigley (2017), found the real phenomenon as the microbiota-GBA in animal and translational models.

The human body contains trillions of microorganisms — outnumbering human cells by 10 to 1. Because of their small size, however, microorganisms make up only about 1 to 3 percent of the body's mass (in a 100 kg adult, that's 1 to 3 kg of bacteria), but play a vital role in human health.

Alterations in gastrointestinal (GI) function and GI symptoms have been reported to accompany an increasing number of central nervous system (CNS) disorders. [2-4]

Neurologic and psychiatric diseases represent a huge health burden, as they impact many individuals worldwide irrespective of social class or age. Indeed, evidence suggests that these disorders represent approximately 12% of diseases globally [5], Lami, Oliveira, de and Batista 2021 , et al. Research shows a bidirectional intestine-brain communication happens via the neural, endocrine, and immunological pathways ; thus, it has been hypothesized that this communication's imbalances might affect these diseases' development. Researchers have used human and animal models to assess the impact of the gut-brain axis (GBA) communication pathways in the disorders' multi-causal perspective. Accordingly, they have proposed various mechanisms; nevertheless, systematic reviews focusing on the latest developments in the area are minimal. This paper systematically reviews the influence of the gut-brain axis on psychiatric disorders and neurologic diseases.

## Materials & Methods

### Methods
The evidence for the current systematic review followed PRISMA (2020) guidelines. This encompassed a series of steps detailed below.

### Eligibility criteria
Studies included in this systematic had to meet certain eligibility criteria. They were articles published in English between 2012 and 2022, in indexed journals, and in reviews containing studies with animal or human models for psychiatric and neurologic diseases. The articles also needed to demonstrate how intestinal microbiota affects neuropsychiatric disorders.

These models have incriminated a disturbed gut microbiota in many CNS conditions, including Parkinson's disease; however, research involving human models is scanty due to significant logistical concerns. Overall, high-quality clinical trials are lacking despite the availability of theoretical microbiota-directed therapies for neurodegenerative conditions. In the study performed by [15] Chakrabarti et al. (2022), the researchers revealed that mechanisms and triggers that underlie the role of gut microbiota in the brain, or cognitive function should establish a standardized approach for human modeling studies, such as the necessity for further extensive samples analyses, strong guidance for given microbiota-GBA areas, and pertinent biomarkers' establishment.

### Results of syntheses

Most studies focused on microbiota-GBA bidirectional communication and its influence on neuropsychiatric diseases. They contend that new advanced in vivo and vitro studies and an emphasis on omics technologies alongside bioinformatics resources for efficient translation and pertinent target identification are the other urgent requirements. The primary strategy to build a validated evidence base is enhancing multi-disciplinary collaborations, knowledge sharing, and ongoing public-private funding. Such would be instrumental in enabling research on microbiota-GBA to get to the next phase to identify realistic opportunities in modulating the microbiota for improved brain health.

### Discussion

The general interpretation is that microbiota-GBA bidirectional communication and its role in influencing various neuropsychiatric diseases; Disruption of gastrointestinal system barrier and flora eventually leads to increased generation of pro-inflammatory cytokines which in turn leads to inflammation in all body including brain and especially blood vessels in the brain. This inflammation of blood vessels causes leakage and neuro-inflammation thus injury to neurons [16,17]. These injuries can turn up as psychiatric disorders or neurologic diseases. Inflammation in the brain also can lead up to microglia activation and amyloid plaque deposition. Also, not just microbial but communication with gut and brain importance can't be overlooked. Recently this communication, which is known as vagal nerve can be stimulated and used as treatment for resistant depression [18]. Likewise, how in the past, deficiency of vitamins and their outcomes were not known: in the near future microbiome and the deficiency of variety and needed flora for our will be an issue too.

### Information sources

The author searched the Cochrane library for the existing reviews. Others that were searched included PubMed, EMBASE, and SciELO. Following the final sample of review articles section, the author employed their reference lists as a source of secondary data.

### Search strategy

The investigator used a core strategy for the eventual bibliographic review. The strategy was adapted based on every database's structure. The strategy encompassed a combination of various search terms or descriptors, such as "gastrointestinal microbiome," "mental disorders," "nervous system conditions," "immune response," "neurosecretory systems," and "gastro," considering the databases' particularities. The search was deliberately kept wide to allow screening for eligibility of all studies on the subject.

### Selection process

Figure 1 shows the selection process of studies. The current study employed Endnote v. X7.8 in managing the references. It also followed the management and de-duplication techniques described by Peters (2017) and Bramer et al. (2016).
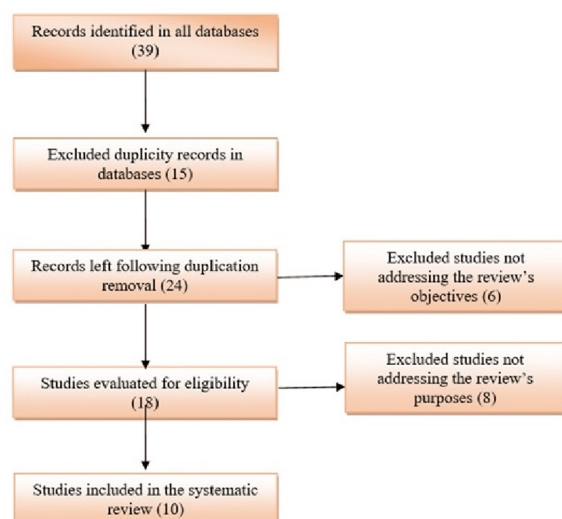


Figure 1: selection process of studies

On the other hand, this theory shows some promise for clinical field application such as Mediterranean diet which can be used as adjuvant treatment for depression by showing great promises [19] and not just by people who are suffering from any kind of psychiatric illness could benefit from it but also studies have shown adding free fatty acids to a patient's diet is beneficial for reduction of ADHD symptoms reduction and ketogenic diet reducing epileptic seizures [20].

The theory also explains by causing dysbiosis of gut microbiota antibiotics have psychiatric side effects [21]. Understanding these mechanisms could be crucial in developing novel and targeted treatment approaches to treat these disorders.

### Limitations

While these studies offer insightful evidence regarding how GBA affects neurologic diseases and psychiatric disorders, the evidence included was not without limitations. First, the articles were based on samples from developed countries and excluded the developing ones. Second, most papers may have reviewed data from the same samples. Thus, generalizability may have been a challenge. Notably, the review processes may have excluded certain aspects of PRISMA (2020) guidelines, as the evidence used was mostly reviews rather than random control trials.

### Conclusions

This systematic review has implications for practice, policy, and research. Regarding practice, the findings could inform novel therapeutic approaches for neuropsychiatric disorders owing to the overwhelming evidence that various studies have so far established. Conversely, regarding policy implications, it informs policy to enact policy guidance on how the proposed novel therapy administration. Finally, these findings show a scarcity of findings involving human models. Future should thus focus on high-quality clinical trials involving humans. Additionally, the studies could use a wide range of samples, including those from developing countries.

### References

1. Drossman DA. Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. Gastroenterology 2016.

### Data collection process

Data were extracted from records that met the criteria of the systematic review. This was done using a form with fields for population, study methodology, sample sizes, study duration, outcome measures, and results. Specifically, data regarding the precision and size of relationships established, adjustment effects, and result stratification by service type were obtained from the reviews. The pre-existing meta-analyses and articles' citation lists were searched to establish additional prospective studies.

### Quality assessment

The Crowe Critical Appraisal Tool (CCAT) was used to rate all the review papers. According to Austine (2019), CCAT is an appropriate tool for various methodological techniques, evaluating studies based on eight categories: preliminaries, introduction, sampling, design, data gathering, ethical considerations, results, and discussion. Every category is rated on a scale of 5, with all the categories having a total of 40 (transformed into %) after summation. Every study was assigned to 1 of the five categories in the current review based on the reviewers' average rating, where poorest quality (0-20%) and highest quality (81-100%) were coded 1 and 5, respectively. Inter-rater reliability was extremely good (k = 0.92, SE = 0.05).

## Results

### Study selection

From the 39 articles generated through descriptor combination, 15 and 6 were removed due to database duplication and unrelated to the review's objectives. From the full-text article assessed for eligibility, non-indexed articles published outside 2012 and 2012 never examined the connection between the gut-brain axis and neuropsychiatric disorders, and non-clinical trials with animal and human models were removed. Ultimately, ten reviews were used.

## Risk of bias in studies

### Results of individual studies

[6] Carabotti et al. (2015), revealed that microbiota-GBA linkages emanate from the interaction of dysbiosis and functional gastrointestinal and central nervous system (CNS) diseases. For instance, irritable bowel syndrome exemplifies these complex association disruptions.

2. Bove C, Travagli RA. Neurophysiology of the brain stem in Parkinson's disease. J Neurophysiol 2019;121:1856–1864. [PubMed: 30917059]

3. Brain-gut-microbiota axis in Parkinson's disease Agata Mulak, Bruno Bonaz DOI: 10.3748/wjg.v21.i37.10609

4. Fung TC, Olson CA, Hsiao EY. Interactions between the micro-biota, immune and nervous systems in health and disease. Nat Neurosci. 2017;20:145–55.

5. Lami, K. F., Oliveira, V. F. de and Batista, K. Z. S. (2021: Gut-brain axis and immunoneuroendocrine modulation in neurological and psychiatric disorders: A systematic review,. Research, Society and Development, 10(4), p. e28110414185. 10.33448/rsd-v10i4.14185

6. Carabotti, M.: The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems,. Annals of gastroenterology. 28:203-209.

7. Rutsch, A., Kantsjö, J. B. and Ronchi, F. (2020: The gut-brain axis: How Microbiota and host inflammasome influence brain physiology and pathology,. Frontiers in immunology, 11, p. 604179. 10.3389/fimmu.2020.604179

8. Jang, S.-H.: The brain-gut-microbiome axis in psychiatry,. International Journal of Molecular Sciences. 21:19. 10.3390/ijms21197122

9. Appleton, J. (2018: "The gut-brain axis: Influence of Microbiota on mood and mental health," Integrative medicine (Encinitas, Calif.). 17:28-32.

10. O'Mahony, S. M.: tryptophan metabolism and the brain-gut-microbiome axis,". Behavioural Brain Research, 277, pp. 32-48. 10.1016/j.bbr.2014.07.027

11. Thakur, Dr. Ajit & Shakya, Anshul & Husain, Gulam & Emerald, Mila & Kumar, Vikas. (2014). Gut-microbiota and mental health: Current and future perspectives. Journal of Pharmacology and Clinical Toxicology. 2. 1-15.

12. Cryan, J: F. et al. 2019, 99:1877-2013. 10.1152/physrev.00018.2018

13. Person, H., and Keefer, L. (2021: Psychological comorbidity in gastrointestinal diseases: Update on the brain-gut-microbiome axis,. Progress in neuro-psychopharmacology. 107:110209. 10.1016/j.pnpbp.2020.110209

16. Dinan TG, Cryan JF. Gut instincts: microbiota as a key regulator of brain development, ageing and neurodegeneration. J Physiol. 2017;595:489–503

17. Pistollato F, Sumalla Cano S, Elio I, Masias Vergara M, Giampieri F, Battino M. Role of gut microbiota and nutrients in amyloid formation and pathogenesis of Alzheimer disease. Nutr Rev. 2016;74:624–34

18. Carreno FR, Frazer A. Vagal Nerve Stimulation for Treatment-Resistant Depression. Neurotherapeutics. 2017 Jul;14(3):716-727. doi: 10.1007/s13311-017-0537-8. PMID: 28585221; PMCID: PMC5509631.

19. Dinan TG, Stanton C, Long-Smith C, et al. Feeding melancholic microbes: MyNewGut recommendations on diet and mood. Clin Nutr 2019;38:1995–2001. [PubMed: 30497694]

20. Adan RAH, van der Beek EM, Buitelaar JK, et al. Nutritional psychiatry: Towards improving mental health by what you eat. Eur Neuropsychopharmacol 2019;29:1321–1332. [PubMed: 31735529]

21. Antibiotics: neuropsychiatric effects and psychotropic interactions H Sternbach 1, R State PMID: 9427014 DOI: 10.3109/10673229709000304