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The gut–brain axis and mental health disorders: mechanisms, clinical evidence, and therapeutic implications

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ABSTRACT

The microbiota-gut-brain axis is a bidirectional communication network connecting gastrointestinal function with the central nervous system. We summarize the growing literature on the effect of altered gut microbiota composition and microbial metabolite production on the development and course of mental health disorders and neurodegenerative diseases in this review. The therapeutic potential of microbe-targeted treatments for mental health disorders will also be evaluated. This review used selected peer-reviewed articles, including prospective cohort studies, randomized controlled trials, mechanistic studies, and systematic reviews examining the relationship between gut microbiota and mental health disorders. The epidemiology literature provides strong evidence for a consistent association between gastrointestinal disorders and an increased risk of various psychiatric and cognitive conditions. Emerging interventional research suggests that interventions that modify gut microbiota (i.e., psychobiotics) can have positive effects on depressive symptoms, and on certain aspects of stress-related cognition and some cognitive functions. In contrast, the size of these effects appears generally moderate and specific to the strain used in each intervention. Therefore, the cumulative evidence provides a biologically plausible link between gut microbiota and mental health disorders; however, the diversity of study designs, types of microbial interventions, and studied populations underscores the need for further well-controlled clinical trials that include microbial characterization of the participants' microbiota, measurement of inflammatory biomarkers, and mechanistic outcomes to better define the therapeutic potential of interventions directed at modifying the microbiota.

Keywords: Brain–Gut Axis; Gastrointestinal Microbiome; Mental Disorders; Probiotics; Cognitive Dysfunction.

1. INTRODUCTION

Mental health disorders are a significant and increasing global health problem. There has been a greater than 50% increase in the occurrence of mood and anxiety

disorders since the last thirty years and this increase has contributed significantly to both disability and death globally. Roughly 3.8 – 10% of the world's population suffers from depression, whereas postpartum depression occurs in more than 10% of mothers and suicide is a cause of over 700,000 deaths per year (Verma et al., 2024). Mental illnesses such as schizophrenia also became more common between 1990 and 2019, with rates increasing by 65%, while around 1% of the population suffers from schizophrenia (Ju et al., 2023). All of these epidemiological patterns emphasize the need for improved understanding of biological systems that may be involved in susceptibility to mental illness, the course of the disease, and response to therapy. Recent studies suggest that the gut microbiota plays an important role in host physiology, extending its role beyond just gastrointestinal (GI) function and providing regulation of immune, metabolic, and neuroendocrine pathways. The human gastrointestinal tract houses between 10 and 100 trillion microorganisms. The GI tract contains around 150-400 different bacterial species (Verma et al., 2024).

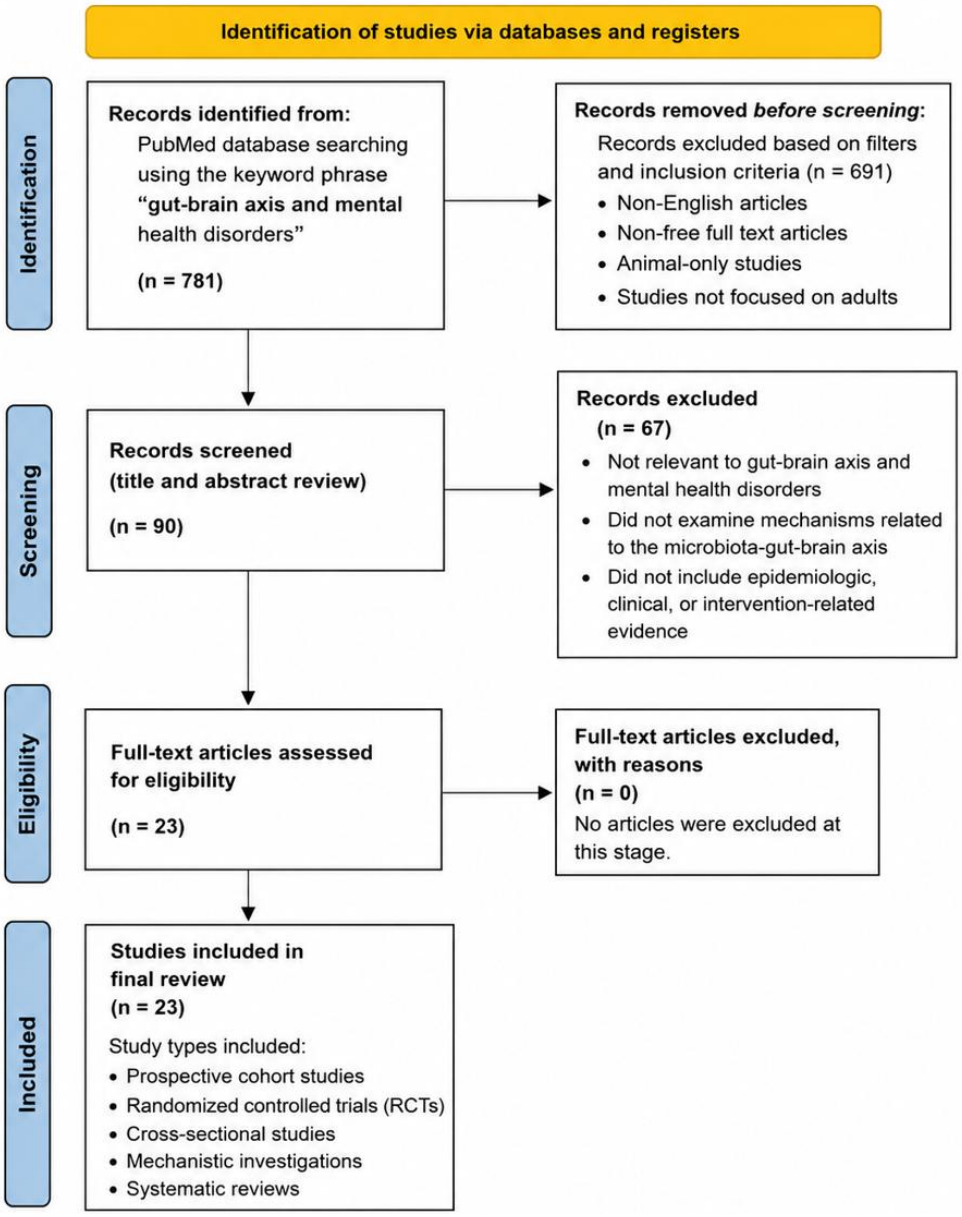

Figure 1. PRISMA 2020 flow diagram illustrating the identification, screening, eligibility assessment, and inclusion of studies related to the gut-brain axis and mental health disorders.

Dysbiosis involves reduced microbial diversity, caused by increased levels of pathogenic taxa. Lower expression of tight junction proteins, as well as systemic inflammation happen because of the dysbiosis. The MGBA represents a two-way communication network that links the GI tract and central nervous system (CNS) via neural, immune, endocrine, and metabolic pathways (Wadan et al., 2025).

Experimental studies are beginning to examine if microbiota-targeted treatments can be used as adjunctive therapy in the treatment of mental health disorders (Mosquera et al., 2024; van Nood et al., 2013); Clinical and epidemiological research support an association with mental health disorders and alterations in gut pathology (Yang et al., 2023; Feng et al., 2024). While most of these therapies have been tested in gastrointestinal diseases, they illustrate the possibility of using microbiome-based therapies for mental health disorders (Wadan et al., 2025).

Converging evidence from experimental, epidemiological, and intervention studies supports a clinically relevant relationship between the gut microbiota and mental health disorders. This review aims to examine current evidence linking the gut–brain axis to psychiatric and neurodegenerative conditions to clarify therapeutic implications, and identify future research priorities.

2. REVIEW METHODS

A literature search of the PubMed database was conducted to identify studies that examined the association between the gut-brain axis and mental health disorders. The literature search used the keyword phrase "gut-brain axis and mental health disorders". The initial literature search generated 781 publication results from the past fifteen years. Filters were then applied to identify studies that were free full-text articles written in English. In addition, the studies had to be conducted in human populations; studies focused solely on adults were also considered relevant for this review, whereas studies based solely on animal models were excluded. Once the inclusion criteria were applied to the literature search results, 90 articles remained to be evaluated to determine if they met the purpose of this review. The title and abstract of each study were reviewed to evaluate the relevance of the study to the objective of the review.

Studies that explored mechanisms related to the microbiota-gut-brain axis, epidemiologic associations between gastrointestinal and mental health disorders, and clinical or interventionist evidence relating to the gut-brain axis and mental health disorders were determined to be eligible. Based upon this evaluation, 23 studies were identified to be included in the final analysis of this review. The studies included in the final analysis consisted of prospective cohort studies, randomized controlled trials (RCTs), cross-sectional studies, mechanistic investigations, and systematic reviews examining the gut-brain axis and mental health disorders. The study selection process is presented in Figure 1.

3. RESULTS & DISCUSSION

Biological Foundations of the Gut–Brain Axis

The gut microbiota is a highly active ecosystem that has numerous systemic effects outside of the GI tract (Verma et al., 2024). These microorganisms can produce bioactive compounds including short-chain fatty acids (SCFAs), amino acid derivatives, lipids and neurotransmitter precursors that affect the host's immune regulation as well as neurobiological signaling (Verma et al., 2024; Wadan et al., 2025). An optimal balance of the gut microbiota is composed of beneficial bacteria such as Bifidobacterium and Lactobacillus that help to keep the intestinal epithelium intact and maintain a balance of the immune system. In contrast, when there is a loss of balance of the gut microbiota, referred to as dysbiosis, it results in low amounts of beneficial bacteria, high amounts of harmful bacteria, an inability of the intestine to properly close off the bloodstream, and the production of pro-inflammatory substances (Wadan et al., 2025).

Intestinal Barrier and Blood–Brain Barrier Integrity

One of the primary ways in which the gut microbiota influences the brain, specifically with respect to the development of neuropsychiatric disorders, is through the disruption of the endothelial barrier. The presence of a healthy number of beneficial bacteria in the gut will help promote the stability of tight junctions; however, stress and the imbalance of the gut microbiota will disrupt the expression of the tight junction proteins, claudin-1 and occludin, and increase the permeability of the intestinal lining (Verma et al., 2024). Once the intestinal lining becomes more permeable, bacteria and their metabolites such as lipopolysaccharide (LPS) pass into the bloodstream thus creating systemic inflammation (Wadan et al., 2025). In addition to its impact on the integrity of the epithelial barrier of the gut, the gut microbiota also plays a significant role in the integrity of the blood-brain barrier (BBB). Experimental evidence indicates that germ-free mice have decreased expression of the tight junction proteins, occludin and claudin-5, at the BBB, leading to increased permeability. However, once the germ-free mice were colonized with bacteria that produce SCFAs, the expression of the tight junction proteins and the integrity of the BBB returned to normal (Verma et al., 2024). Therefore, these studies demonstrate that the microbes directly regulate the tightness of the CNS barrier.

Immune and Inflammatory Signaling Pathways

The gut-brain axis operates by using immunological mechanisms. The studies demonstrate that there exists a connection between gut microbiota dysbioses and systemic inflammation. Dysbiosis of gut microbiota has been connected to elevated amounts of circulating inflammatory mediators as well as the inappropriate distribution of immune cells. (Wadan et al., 2025). A prospective cohort study indicated that inflammatory biomarkers (C-reactive protein (CRP), and neutrophil count) explained approximately 12.04% and 10.29% of the relationship between IBD and psychiatric conditions; thus indicating that the immune system participates in the creation of mental health problems (Feng et al., 2024). Studies investigating the molecular basis of neurodegenerative diseases also support the connection between the gut and the brain.

For example, studies examining postmortem brain tissue from patients who had Parkinson's disease and had comorbid depression found that the expression of certain microRNAs was significantly changed. More specifically, down-regulation of miR-199a-5p and miR-219a-5p, and up-regulation of miR-200a-3p resulted in increased expression of pro-inflammatory markers (TNF-α, IFN-γ, and NFκB1) and glial activation signals (Miquel-Rio et al., 2025). This finding suggests that the gut is able to send inflammatory signals to the brain through epigenetic and microRNA-mediated mechanisms.

Microbial Metabolite Modulation of Neurotransmitter Production

The microbial metabolites created by the gut microbiota serve as the primary functional interface between the gut microbiota and the CNS. SCFAs are produced through the fermentation of dietary fiber and have multiple physiological effects on the host (Wadan et al., 2025). SCFAs function as histone deacetylase inhibitors and signal through G-protein coupled receptors (such as GPR41 and GPR43) to modulate both inflammatory and neuroimmune responses (Verma et al., 2024). For example, the anxiety-susceptible mouse model showed increased levels of p-cresol in the prefrontal cortex compared to non-anxious control mice, and the administration of 4-ethyl phenyl sulfate caused anxiety-like behavior in the mice, suggesting that the gut microbiota produces metabolites that cause anxiety-like behavior (Verma et al., 2024).

Research has found a link between an elevated level of serum propionic acid in older adults and accelerated cognitive decline. This indicates the dysregulation of SCFAs is linked to the neurodegeneration process (Neuffer et al., 2022). The gut microbiota also produces Neurotransmitters. For example, certain bacterial genera such as Bifidobacterium and Lactobacillus have been shown to contribute to the production of GABA. In addition to GABA, there are various bacterial species that can affect the serotonin and dopamine pathways (Verma et al., 2024). The fact that microorganisms can produce neurotransmitters provides additional evidence that a shift in the microbial population can be related to both mood and cognition.

Neural Signaling and the Vagus Nerve

The vagus nerve communicates ascending signals from the GI tract to brain regions involved in cognition and emotion processing (Verma et al., 2024). A pilot clinical study examined the effectiveness of vagus nerve stimulation as an adjunctive therapy in the treatment of treatment resistant depression (TRD) and found that approximately 30-37 % of patients receiving vagus nerve stimulation showed clinically significant improvement; it also showed good tolerability and thus contributed to FDA approval of vagus nerve stimulation as a therapeutic option (Verma et al., 2024). Although this study did not specifically target the microbiome, these results support the physiological relevance of gut-brain neural pathways in modifying depressive symptoms.

The collective evidence provided here clearly illustrates that the gut-brain axis functions through tightly interconnected barrier, immune, metabolic, and neural systems. Each system can be affected by dysregulation of the others and dysregulation of any one of them may be associated with the pathogenesis of mental illness, and neurodegenerative diseases. Thus, this biological model serves as a foundation to understand epidemiologic associations and to evaluate therapeutic options that target the microbiota.

Epidemiological Evidence Linking Gut Disorders and Mental Health Outcomes

The majority of evidence relating to the mechanisms underlying GI pathology and its impact upon neuropsychiatric conditions is derived from population-based research designs. One of the largest prospective cohort analyses involved 491,131 participants from the UK Biobank. That analysis evaluated the association between inflammatory bowel disease (IBD) and incident psychiatric disorders over the follow-up period (Feng et al., 2024). After full multivariable adjustment, IBD was associated with an increased risk of all psychiatric disorders (HR 1.23, 95% CI 1.13-1.33), depression (HR 1.36, 95% CI 1.22-1.52), anxiety (HR 1.15, 95% CI 1.01-1.30), substance misuse (HR 1.23, 95% CI 1.09-1.38) and post-traumatic stress disorder (HR 1.87, 95% CI 1.00-3.51). People with Crohn’s disease or

ulcerative colitis developed psychiatric disorders more often than people without IBD (log-rank p<0.001). The mediation analysis also showed several possible ways in which IBD could increase the risk of psychiatric disorders. Specifically, it was determined that inflammatory and hematological biomarkers contributed to the association between IBD and psychiatric disorders. More specifically, neutrophil count mediated 12.04% of the association, CRP mediated 10.29%, systemic immune-inflammation index (SII) mediated 8.94%, red cell distribution width (RDW) mediated 16.51%, red blood cell count (RBC) mediated 9.76%, and albumin mediated 9.15% (Feng et al., 2024). These data supported the hypothesis that systemic inflammation and immune dysfunction are likely to represent mechanistic pathways connecting intestinal inflammation and psychiatric morbidity.

Evidence also links altered gastrointestinal function to neurodegenerative risk. In a prospective cohort of 502,229 UK Biobank participants with a mean follow-up of 9.8 years, regular laxative use (defined as use on most days of the week during the prior four weeks at baseline) was associated with an increased risk of all-cause dementia (HR 1.51, 95% CI 1.30-1.75) and vascular dementia (HR 1.65, 95% CI 1.21-2.27), but not Alzheimer's disease (HR 1.05, 95% CI 0.79-1.40) (Yang et al., 2023). Risk increased with both higher laxative doses and the number of laxative types used (p-trend = 0.001 for all-cause dementia; p-trend = 0.04 for vascular dementia). Among users of a single laxative type, osmotic laxatives were linked to a higher risk of dementia (HR 1.64, 95% CI 1.20-2.24 for all-cause dementia; HR 1.97, 95% CI 1.04-3.75 for vascular dementia) (Yang et al., 2023).

Microbiome composition has also been examined in relation to neurodegenerative biomarkers. In a cohort of 170 participants from a memory clinic setting - including 33 individuals with Alzheimer's disease dementia, 21 with mild cognitive impairment, and 116 with subjective cognitive decline - machine learning models based on gut microbiota composition predicted amyloid positivity with an area under the curve (AUC) of 0.64 and phosphorylated tau positivity with an AUC of 0.63. Although the results were not very strong, SCFA-producing taxa were among the most important microbial features, suggesting possible biological relevance (Verhaar et al., 2022). Microbial metabolites were also linked to long-term cognitive changes. Older adults with higher serum propionic acid levels showed greater cognitive decline. This may suggest that altered SCFA metabolism may play a role in neurodegenerative processes (Neuffer et al., 2022). Even though the effects were moderate, the findings still showed a connection between gut-derived metabolites and cognitive decline over time. Functional gastrointestinal disorders were also linked with psychiatric symptoms.

In a study of 249 patients with fecal incontinence (mean age 63.4 ± 12.6 years; 93.6% female), the average number of additional disorders of gut–brain interaction (DGBI) was 2.2 (Li et al., 2024a). Therefore, these data provide additional evidence of the clinical overlap between gastrointestinal symptom burden and psychiatric distress in functional gut disorders. Similar associations have been reported in occupational and perinatal groups. In a cross-sectional study of 2,041 midwives, sleep quality (mean The Pittsburgh Sleep Quality Index (PSQI) 8.20 ± 3.64)) correlated with gut health scores (mean Gut Brain Health Questionnaire (GBHQ) 51.46 ± 10.85), with Pearson correlation coefficients ranging from r = 0.397 (PSQI-GBHQ) to r = 0.512 (PSQI-PHQ-9), all p < 0.01)) (Li et al., 2024b). After adjusting for multiple variables, a lower gut health score was associated with a higher risk of poor sleep (OR 1.042, 95% CI 1.03 - 1.054) (Li et al., 2024b).

During early pregnancy, a higher level of trait anxiety and depression has also been found to be associated with reduced alpha-diversity in the oral microbiome of a cohort of 224 pregnant women who were at a mean gestation of 17 ± 2 weeks (Alex et al., 2024). Although these studies were conducted in cross-section, they do provide some indication that microbiome and mental health are related even in physiologically vulnerable states. A second set of studies investigated whether the mental health effects of environmental exposures can be mediated through changes in the gut microbiome. A before/after study of 36 tunnel construction workers reported a significant decrease in their alpha diversity index values for the Shannon and Simpson indices, which measure diversity, after working on underground tunnels for approximately 21 days. More than half of the participants experienced at least one of the following symptoms of mental distress during their time underground: inattention, difficulty sleeping, loss of appetite, headaches, or irritable mood.

At the same time, there were decreases in the abundance of several of the beneficial bacterial taxa, including Faecalibacterium and Roseburia (Lu et al., 2021), which are typically involved in the production of SCFAs. These different lines of evidence collectively demonstrate that there are strong associations between gastrointestinal pathology, alterations in the composition of the gut microbiome, inflammation, and mental health. The effect size is likely to differ based on the type of study design used. Still, the prospective cohort analyses provided temporal evidence for these associations, and the cross-sectional and biomarker-based analyses provided evidence for the mechanisms underlying these associations. Overall, the epidemiologic literature provides a rationale for testing microbiome-targeted treatments for psychiatric and neurodegenerative diseases.

Microbiota-Targeted Interventions: Current Evidence and Limitations

Psychobiotics are probiotics or prebiotics that modulate the gut-brain axis, conferring mental health benefits. Systematic reviews and meta-analytic evaluations of psychobiotic interventions have provided some evidence of their efficacy in reducing depressive symptoms. However, such reviews are often hampered by the diversity of psychobiotic strains used, as well as the variable dosages of those strains, differences in participant demographics, and differences in how the effectiveness of psychobiotics is measured (Mosquera et al., 2024; Casertano et al., 2024; Boehme et al., 2023; Kim et al., 2020; Reininghaus et al., 2020; van Nood et al., 2013; Wadan et al., 2025). Therefore, the variability of clinical responses to psychobiotic treatments likely reflects both interindividual differences in individual responses to psychobiotic treatments, as well as potential methodological limitations of prior research.

A recent systematic review including 51 RCTs comprising 3,353 participants evaluated the efficacy of psychobiotics for depressive symptoms across treatment durations ranging from 4 to 24 weeks (Mosquera et al., 2024). Approximately half of the subjects in this investigation received either a live or heat-killed active psychobiotic. Overall, the investigators found that the treatments resulted in a significant improvement in depressive symptoms. Still, they also noted that there was considerable variation in terms of both the strain of the psychobiotic used and the dosing regimen utilized by each investigator, along with other differences in population characteristics and outcomes measured by each investigator (Mosquera et al., 2024), which made it difficult to compare results among studies directly.

In addition to global benefits from psychobiotic-based treatments for individuals suffering from depressive disorders, a randomized, double-blinded, placebo-controlled cross-over trial demonstrated the strain-specific effects of GABA producing bacteria when administered to mildly stressed individuals (Casertano et al., 2024). Participants received Levilactobacillus brevis P30021 and Lactiplantibacillus plantarum P30025 for 12 weeks (n = 44 active arm; n = 43 placebo; mean age 29 ± 5.7 years; baseline DASS-42 score 18.7 ± 4.06). Responder analyses demonstrated increased abundance of probiotic genera in positive responders, including Lactiplantibacillus ($p = 0.009$) and L. brevis ($p = 0.004$). Clinical improvements may not directly reflect measurable changes in fecal neurotransmitter levels, as fecal neurotransmitter concentrations did not show a significant relationship with psychological test scores (Casertano et al., 2024).

Probiotics were also studied in older adults for their effects on cognitive function. A multicenter, randomized, double-anonymized, placebo-controlled trial involving 63 community-dwelling participants aged ≥65 years assessed supplementation with Bifidobacterium bifidum BGN4 and Bifidobacterium longum BORI for 12 weeks. Probiotic supplementation significantly improved mental flexibility test performance ($p < .05$) and stress scores ($p < .05$) compared with placebo, while also reducing inflammation-associated bacterial taxa ($p < .05$) (Kim et al., 2020). Together, these findings suggest that changes in the gut microbiome may affect cognitive and psychological function in older adults.

The study had a modest sample size, which may limit how widely the findings apply of the findings. Probiotic therapy has also been studied as an adjunctive treatment for clinical depression. The PROVIT trial examined probiotic supplementation combined with vitamin B7 in patients with depressive disorders (Reininghaus et al., 2020). While the results of the study varied depending on the outcome measure used, the study provides support for the feasibility of using combinations of microbiota-targeted interventions and standard psychiatric treatment strategies. Such adjunctive approaches are consistent with the concept of microbiota modulation as a complementary, rather than replacement, treatment approach. Beyond a psychiatric indication, there is evidence that fecal microbiota transplantations (FMTs) provide the basis for large-scale microbiota manipulation. The use of donor feces in the treatment of recurrent Clostridium difficile infection demonstrated a complete resolution rate of 81%, when compared with a complete resolution rate of 31% for Vancomycin and 23% for Vancomycin combined with Bowel Lavage ($p < .001$) (van Nood et al., 2013). FMT is usually administered using 30-50 grams of donor stool. It can be delivered through colonoscopy, nasogastric tubes, or oral capsules (Wadan et al., 2025).

Restoring the microbiome may lead to meaningful clinical effects and probiotic dosing also differs depending on the condition being treated. In Clostridioides difficile infection (CDI), Saccharomyces boulardii is commonly given at 250-500 mg twice daily, while Lactobacillus and Bifidobacterium formulations are usually administered at 10-50 billion CFU/day (Wadan et al., 2025). Although several early findings were encouraging, the size of the effects in clinical psychiatric trials has been moderate at best, and there is considerable heterogeneity among studies. Most trials conducted so far have involved small sample sizes and short intervention periods ranging from 4 to 24 weeks. Different methods used to assess outcomes also make it difficult to clearly evaluate the effectiveness of microbiome-targeted interventions for psychiatric disorders (Mosquera et al., 2024). In addition, the use of cross-over trial designs and cohorts of healthy volunteers may not adequately reflect the psychiatric populations with whom such interventions will be used in the future (Casertano et al., 2024; Boehme et al., 2023).

Taken together, the current state of the evidence supporting interventional approaches targeting the microbiome suggests that these approaches do alter some psychological and cognitive end points associated with psychiatric disorders, especially those associated with depression, rumination, and perceived levels of stress, as well as specific aspects of executive function. However, the effects of these interventions appear to depend on the strains of microbes being administered, the population into which they are administered, and tend to be of relatively small magnitude. The findings also suggest that further research using well-designed and adequately powered randomized controlled trials with standardized microbial formulations and defined dosing protocols may provide more insight.

Future Directions and Clinical Implications

Future studies should also focus on combining microbial profiling with systemic biomarkers to help develop more individualized interventions. In the context of IBD, inflammatory markers such as neutrophil count and CRP partly explained the link between intestinal inflammation and psychiatric disorders. This suggests that inflammatory stratification may help identify individuals at higher risk (Feng et al., 2024). While the associations observed between gut microbiota composition and Alzheimer's disease biomarkers were modest, they were also replicable and thus, microbiome-informed risk modeling could potentially be used as a complementary approach to the traditional neurodegenerative markers for identifying patients at risk (Verhaar et al., 2022). Further studies looking at microbiota composition, inflammatory markers, and metabolomic features such as serum propionic acid, which has been associated with cognitive decline, could improve the accuracy of patient selection (Neuffer et al., 2022).

Large-scale microbial modulation is possible through high-response microbiota interventions. For example, FMT for recurrent CDI resulted in higher resolution rates than Vancomycin treatment (van Nood et al., 2013). Although this approach was used for a gastrointestinal condition, it suggests that restoring microbial diversity may lead to meaningful clinical effects under specific pathological conditions. However, it is unclear whether analogous large effect interventions can be achieved in psychiatric populations. Future research should focus on conducting longitudinal assessments that include integration of microbiome sequencing, inflammatory markers, tight junction integrity markers, and neuroimaging endpoints. Further research in humans is needed because many findings involving barriers and microRNAs were mainly based on germ-free models or postmortem analyses (Verma et al., 2024; Miquel-Rio et al., 2025).

Furthermore, systematic evaluation of strain specificity must be conducted, since there appears to be a significant relationship between the type of probiotic bacteria and the effectiveness of the probiotic in terms of host context (Mosquera et al., 2024). Ultimately, the development of clinical application of psychobiotics will depend upon establishing harmonized trial designs, standardized microbial formulations, biomarker-stratified subpopulations, and mechanistically-integrated endpoints. Taken together, these findings may help determine whether microbial manipulation functions best as an adjunctive therapy, a prevention strategy, or a targeted intervention based on defined inflammatory or metabolic phenotypes. Table 1 shows the characteristics and main findings of selected studies included in the review.

Table 1. Study summary

Study	Study design	Population/sample size	Main findings
Feng et al., 2024	Prospective cohort study	491,131 UK Biobank participants	Inflammatory bowel disease (IBD) was associated with increased risk of psychiatric disorders, including depression, anxiety disorders, substance misuse, and post-traumatic stress disorder.
Yang et al., 2023	Prospective cohort study	502,229 UK Biobank participants	Regular laxative use was associated with increased risk of all-cause and vascular dementia during a mean follow-up of 9.8 years.
Mosquera et al., 2024	Systematic review of randomized controlled trials	3,353 participants across 51 RCTs	Psychobiotics demonstrated beneficial effects on depressive symptoms, although significant heterogeneity between studies was observed.
Casertano et al., 2024	Randomized, double-blind,	87 adults with mild-to-moderate stress	GABA-producing probiotic strains reduced cognitive reactivity to sad mood and

	placebo-controlled trial		overthinking but did not significantly affect overall perceived stress.
Boehme et al., 2023	Randomized, double-blind, placebo-controlled trial	45 healthy adults	Supplementation with *Bifidobacterium longum* NCC3001 significantly reduced perceived stress compared with placebo.
Kim et al., 2020	Multicenter randomized controlled trial	63 older adults	Probiotic supplementation improved cognitive flexibility and reduced stress-related measures in older individuals.
Verhaar et al., 2022	Observational cohort study	170 participants	Gut microbiota composition predicted amyloid and phosphorylated tau positivity with moderate discriminative ability.
Alex et al., 2024	Cross-sectional study	224 pregnant women	Altered oral microbiome alpha diversity was associated with higher anxiety and depressive symptoms.
Li et al., 2024	Cross-sectional study	2,041 midwives	Poor gut health was associated with impaired sleep quality and increased depressive symptoms.
Lu et al., 2021	Before-and-after observational study	Underground tunnel workers	Reduced gut microbiota alpha diversity and decreased SCFA-producing bacteria were observed after occupational underground exposure.

4. CONCLUSION

Current evidence indicates that the microbiota–gut–brain axis may play an important role in the development and progression of mental health disorders. Findings from experimental, epidemiological, and clinical studies suggest that changes in gut microbiota and microbial metabolite production can affect neuropsychiatric and cognitive function through interconnected immune, metabolic, and neural mechanisms. Nevertheless, differences in study design, probiotic strains, and treatment protocols make it difficult to draw firm conclusions regarding clinical effectiveness. Further large-scale and well-standardized studies are required to better determine the therapeutic value of microbiota-targeted interventions in mental health disorders.

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Authors' Contributions

Mateusz Szabat - contributed to the study conception and design, conducted the literature search and data analysis, wrote the manuscript, and approved the final version for publication.
Klaudia Samuła - conducted the literature search and data analysis.
Dominika Ruszel - conducted the literature search and data analysis.
Emilia Goc - conducted the literature search and data analysis.
Julia Rogała - conducted the literature search and data analysis.
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Martyna Sarzyńska - conducted the literature search and data analysis.
Sylwia Lepak - conducted the literature search and data analysis.
Zuzanna Irzyk - conducted the literature search and data analysis.

Informed consent

Not applicable.

Ethical approval

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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