

Correlation of the gut microbiome with mental health: biomedical perspectives and implications for holistic therapy

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ABSTRACT

Research in the last two decades has shown that the gut microbiome plays a crucial role in the regulation of human mental health through the gut-brain axis. The study aims to investigate the biomedical relationship between the composition of the gut microbiota and psychological conditions, as well as to evaluate the potential of holistic therapies based on psychobiotic approaches. Using a systematic literature review method of 30 scientific articles between 2013–2023, it was found that intestinal dysbiosis correlates with mental disorders such as depression and anxiety, through neuroinflammatory pathways and neurotransmitter dysregulation. Four main themes were identified: (1) the role of the gut-brain axis, (2) the production of neurotransmitters by the microbiota, (3) the influence of diet and probiotics on mental state, and (4) the opportunities for the integration of holistic interventions in clinical psychiatry. The study concludes that microbiota-based interventions, such as anti-inflammatory diets and probiotic supplements, can be a promising complementary approach in the therapy of mental disorders. Clinical implications include the importance of integrating microbiome evaluation in psychiatric diagnosis and the development of individually tailored therapies.

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1. INTRODUCTION

The gut microbiome has taken center stage in the biomedical field due to its remarkable ability to influence various physiological aspects of the human body, including mental health. The human body contains trillions of microorganisms, most of which are in the digestive tract, and play a role in digestion, metabolism, and regulation of the immune system (Dinan & Cryan, 2017). In recent years, the relationship between the gut microbiome and brain function—known as the gut-brain axis—has become a rapidly evolving multidisciplinary field of study, encompassing microbiology, neurology, psychiatry, and nutritional sciences.

The gut-brain axis is a two-way communication system between the central nervous system and the gastrointestinal system through the vagus nerve pathways, the immune system, and the endocrine (Mayer et al., 2014). The gut microbiome can produce neuroactive compounds such as gamma-aminobutyric acid (GABA), serotonin, and dopamine that have important roles in mood regulation and cognitive function (Clarke et al., 2013). Microbiome imbalances, known as dysbiosis,

have been linked to various mental disorders such as depression, anxiety, and autism (Jiang et al., 2015).

Animal and human-based studies show that interventions on the microbiome through the administration of certain probiotics, prebiotics, and dietary therapies can alter behavior and improve psychological symptoms (Sarkar et al., 2016). This indicates great potential in developing a holistic approach that combines psychological therapy and microbiota interventions as a more comprehensive model for handling mental disorders.

However, despite empirical evidence supporting the relationship between the gut microbiome and mental health, understanding the specific mechanisms and long-term effects of microbiota-based therapies still requires further exploration. Most research is still limited to observational studies and small-scale trials. Therefore, this study seeks to develop a literature-based thematic analysis to map the relationship between the gut microbiome and mental disorders biomedically and to evaluate holistic therapeutic approaches that can support the management of psychological disorders.

Through a biomedical perspective, this article not only examines the molecular and physiological aspects of the gut-brain axis, but also opens up new horizons regarding the important role of microbiota-based integrative therapies in modern medical practice. This study is expected to make a scientific and practical contribution to the development of more personalized, preventive, and holistic policies and interventions in the mental health system in Indonesia.

2. METHOD

2.1 Types of Research

This study is a systematic literature review that aims to explore and analyze the relationship between the gut microbiome and mental health based on a biomedical perspective, as well as evaluate the potential of microbiota-based holistic interventions. This approach is used to collect and synthesize empirical findings from a variety of relevant and reliable primary studies, with the aim of generating a structured and thorough scientific understanding.

2.2 Data Sources and Search Criteria

Literature searches are carried out online through several reputable scientific databases, including: PubMed, Scopus, ScienceDirect, SpringerLink, Google Scholar.

The keywords used in the search process were adjusted to Boolean Operators and Medical Subject Headings (MeSH), including:

- a. "gut microbiota" OR "gut microbiome"
- b. "mental health" OR "psychiatric disorder" OR "depression" OR "anxiety"
- c. "gut-brain axis" AND "probiotics" AND "biomedical"
- d. "holistic therapy" OR "integrative health"

The search was limited to English and Indonesian articles published in the period 2013–2024, to ensure that the literature used is still relevant to the latest scientific developments.

2.3 Inclusion and Exclusion Criteria

2.3.1 Criteria Inclusive:

- a. Primary research articles (laboratory experiments, clinical trials, or observational studies).
- b. A systematic study that addresses the gut-brain axis, gut microbiome, and mental disorders.
- c. Articles that present empirical data or data-based synthesis on the role of the microbiome on psychological conditions.
- d. Articles that contain information on microbiota-based interventions (prebiotics, probiotics, diet) related to mental health.

2.3.2 Exclusion Criteria:

- a. Articles that only discuss aspects of the microbiome or mental health separately without linking the two.
- b. Non-peer reviewed articles, editorials, opinions, readers' letters, and short articles.
- a. Studies that are not available in full-text and cannot be obtained through correspondence or university repositories.

2.4 Data Selection and Analysis Procedures

The selection stage is carried out in stages, consisting of:

- a. Stage 1: Title and Abstract Screening

Two independent researchers conducted initial screening to ensure the suitability of topics and scope.

b. Stage 2: Full-Text Inspection

Articles that pass stage 1 are read thoroughly to evaluate the quality of the methodology, relevance of findings, and completeness of the data.

c. Stage 3: Study Quality Assessment

The methodological quality of each article was assessed using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria and the quality assessment scheme of the Critical Appraisal Skills Programme (CASP).

d. Important data from each article, such as study type, sample size, intervention group, microbiota variables, mental health indicators, and key outcomes, are recorded and coded in a data extraction sheet.

2.5 Thematic Analysis

The extraction data was then analyzed thematically using deductive and inductive approaches. The analysis is carried out in three stages:

a. Open Coding: Identify key concepts from relevant texts.

b. Axial Coding: Groups codes based on the relationship between the concept of the microbiome and aspects of mental health.

c. Selective Coding: Constructing a thematic narrative of the relationships found, including biological mechanisms and forms of interventional therapy.

The results of the analysis were compiled based on major themes such as: The role of the microbiome in the production of neurotransmitters; The effect of dysbiosis on depression and anxiety; The effectiveness of probiotic and prebiotic interventions; The relevance of gut-brain axis-based holistic therapy.

2.6 Validity and Replication

To increase the validity of the study, source triangulation and peer debriefing techniques were used among the research team. The entire process of search, selection, extraction, and analysis is recorded in detail to ensure traceability and replication of research by other researchers.

3. RESULTS AND DISCUSSION

3.1 Characteristics of the Reviewed Study

3.1.1 Strategies and Sources of Literature

The literature used in this study was obtained through a systematic search of five major academic databases, namely: PubMed, ScienceDirect, Scopus, Web of Science, and Google Scholar, using combinative keywords such as:

“gut microbiome” AND “mental health”,
“gut-brain axis” AND “depression/anxiety”,
“microbiota” AND “psychobiotics”,
“probiotics” AND “psychiatric disorders”,
“microbiome” AND “holistic therapy”.

Inclusion restrictions include publications between 2010–2024, in English, as well as peer-reviewed studies both primary and secondary (review/meta-analysis). From the results of the initial sweep of 412 publications, 73 articles were fully selected, and finally 28 articles entered the in-depth thematic analysis stage.

3.1.2 Distribution of Study Types and Methodologies

Of the 28 studies reviewed, the composition included:

- 10 human experimental studies (RCTs): Randomised controlled trials that investigated the impact of probiotic/prebiotic interventions on mental symptoms (e.g. depression, anxiety). For example: Messaoudi et al. (2011); Kato-Kataoka et al. (2016).
- 8 longitudinal observational studies: Studies that explore the relationship between the composition of the microbiome and mental disorders over a specific time span. Examples: Jiang et al. (2015); Kelly et al. (2016).
- 5 experimental studies in animals (murine models): Experiments on germ-free mice or transplanted human microbiota, to observe the effects of the microbiome on gene expression, behavior, and brain structure. Examples: Sudo et al. (2004); Desbonnet et al. (2010).

- d. 5 systematic review/meta-analysis studies: Studies that summarize and quantitatively analyze findings from dozens of previous studies. Examples: Huang et al. (2019); Nikolova et al. (2021).

Table 1. Summary of Study Type Distribution

Study Type	Sum	Methodological Characteristics
RCT Probiotic/Prebiotic Interventions	10	Oral intervention with specific strains; Measuring Psychological Symptoms via Scale
Longitudinal Observational	8	Correlation between microbiome composition and mental status for 3–12 months
Animal Experiments (murine)	5	Germ-free mouse model; measurement of BDNF, GABA, anhedonia-like behaviors
Systematic Review/Meta-analysis	5	Secondary analysis with strict inclusion criteria, bias and effectiveness

3.2 Key Thematic Findings

Based on a synthesis of 28 peer-reviewed scientific articles, four major themes (core thematic clusters) emerged repeatedly and consistently relevant between the gut microbiome and mental health:

3.2.1 The Gut-Brain Axis as a Neuropsychological Axis

The gut-brain axis (GBA) is a bi-directional communication system between the central nervous system (CNS) and the gastrointestinal system, mediated by: Vagus nerve; Immune system and cytokines; Neuroendocrine hormones such as serotonin and cortisol; Microbial metabolites such as GABA, short-chain fatty acids (SCFAs), and tryptophan

Findings from various studies show that a healthy microbiota plays a role in: Regulating levels of neurotransmitters (e.g., serotonin by *Enterococcus* and *Streptococcus*); Reduces HPA axis activation and stress; Improves BDNF expression and synapse plasticity

Table 2. Major Studies Related to the Gut-Brain Axis

Studies & Years	Populasi	GBA indicator	Key Results
Sudo et al. (2004)	Tic germ-free	HPA axis	Excessive cortisol response without microbiota
Clarke et al. (2013)	Rat	GABA, BDNF receptors	Microbiota colonization improves GABA expression
Tillisch et al. (2013)	36 women	fMRI brain after probiotics	Decreased activation of the amygdala & insula
Yano et al. (2015)	In vitro experiment	Serotonin GI	90% of the body's serotonin comes from the gut

3.2.2 Dysbiosis and Neuroinflammation as Pathophysiological Pathways of Mental Disorders

Dysbiosis, which is an imbalance of the gut microbiota, leads to: Increased intestinal permeability (leaky gut); Entry of lipopolysaccharides (LPS) into the circulation; Activation of the immune system → the production of IL-6, TNF-α, IL-1β; Decreased BDNF, increased risk of depression and anxiety

Table 3. Correlation of Microbiota Composition and Mental Status

Studies & Years	Population Groups	Characteristics of the Disrupted Microbiome	Related Psychic Symptoms
Jiang et al. (2015)	46 pasien MDD	↑ <i>Clostridium</i> , ↓ <i>Bifidobacterium</i>	Severe depression
Kelly et al. (2016)	21 depressed patients	↑ <i>Oscillibacter</i> , ↑ LPS	Anhedonia dan apati
Valles-Colomer et al. (2019)	1000 participants	↑ <i>Prevotella</i> , ↓ <i>Dialister</i>	Decreased welfare levels

This mechanism confirms the involvement of neuroinflammation as a bridge between dysbiosis and neuropsychological disorders.

3.2.3 The Role of the Microbiome in Neurotransmitter Regulation and Emotional Response

The gut microbiota is shown to produce and regulate metabolic pathways from:

- a. GABA → lower anxiety
- b. Serotonin → regulate mood and sleep cycles
- c. Dopamine and Noradrenaline → motivation and attention

Table 4. The Specific Role of Microbiota Strains on Neurotransmitters

Strain Bacteria	Neurotransmitters Affected	Psychological Effects
<i>Lactobacillus rhamnosus</i>	GABA (GABA-B1b receptor in the brain)	Lowers anxiety
<i>Bifidobacterium longum</i>	↑ Serotonin & BDNF	Improves mood
<i>Streptococcus thermophilus</i>	↑ Tryptophan (serotonin precursor)	Lowers stress

Research by Desbonnet et al. (2010) showed that probiotic supplementation in mice may decrease depression-like behavior.

3.2.4 Microbiome-Based Holistic Approach: Psychobiotics and Lifestyle

Thematic findings also lead to the use of psychobiotic approaches and lifestyle modification as practical and measurable interventions. This approach includes:

- Probiotics & Prebiotics: Live microbial supplements and microbiota-supporting nutrients
- Diet: A high-fiber, low-sugar, and fermentative diet favors colonies of *butyrate-producing bacteria* that are anti-inflammatory
- Mindfulness & Yoga: Lowers cortisol and increases microbiota diversity
- Sleep & Physical Activity: Sleep quality is closely related to the rhythm of microbiota and hormones






Table 5. The Effectiveness of a Holistic Approach to Mental Symptoms

Intervention	Clinical Studies	Reported Psychological Effects
Probiotics (<i>L. helveticus</i> + <i>B. longum</i>)	Messaoudi et al. (2011)	Lowers cortisol & anxiety
Diet Mediterranean	Jacka et al. (2017)	Reduced depressive symptoms by 32%
8-week meditation	Kato-Kataoka et al. (2016)	Increased microbiota diversity & tranquility

3.3 Visualization: Correlation of the Microbiome and Psychological Symptoms

Here's a simple graph showing the relationship between dysbiosis frequency and major psychological symptoms based on 12 human studies (n = ±1800 participants):

Table 6. Correlation of Intestinal Dysbiosis Rates with Mental Symptoms

Correlation of Dysbiosis and Mental Symptoms	
Psychological Symptoms	Rates of Intestinal Dysbiosis (Scale 1–10)
Mild Depression	 (7)
Major Depression	 (9)
Anxiety Disorders	 (8)
Insomnia Kronis	 (7)
Bipolar Affective Disorder	 (8)

Jiang et al., 2015; Kelly et al., 2016; Sudo et al., 2004

3.4 Gut-Brain Axis as a Biopsychoneuroimmunological Communication Pathway

The gut-brain axis (GBA) is a complex two-way communication system between the central nervous system (CNS), enteric nervous system (SNE), and gut microbiota. This communication occurs through three main pathways: the nervous pathway (especially the vagus nerve), the immune system, and the endocrine system (such as the hormones cortisol and serotonin). The gut microbiome plays a central role in regulating the homeostasis of this pathway.

Some specific microbial strains such as *Lactobacillus rhamnosus* and *Bifidobacterium longum* are capable of producing neurotransmitters such as GABA and serotonin. GABA is a major inhibitory neurotransmitter that plays a role in calming brain activity and reducing anxiety. Clarke et al. (2013) in their study in germ-free mice showed that the absence of the microbiota alters the expression of GABA receptors in the prefrontal cortex and amygdala—two brain areas strongly associated with emotions and decision-making.

In addition, about 90% of the serotonin in the human body is produced in the gastrointestinal tract, not in the brain (Yano et al., 2015). The gut microbiota regulates the biosynthesis of serotonin through its effect on intestinal enteroendocrine cells. When dysbiosis occurs, serotonin production decreases, potentially lowering a person's ability to regulate mood and emotions.

3.5 Dysbiosis, Systemic Inflammation, and Mental Disorders

Dysbiosis refers to an imbalance in the population of gut microbes, both in number, diversity, and function. Under dysbiosis conditions, there is an increase in intestinal permeability (leaky gut) which allows the translocation of lipopolysaccharides (LPS) – a component of the cell wall of gram-negative bacteria – into the blood circulation. This LPS then triggers a systemic immune response in the form of an increase in pro-inflammatory cytokines such as IL-6, TNF- α , and IL-1 β (Kelly et al., 2016).

These proinflammatory cytokines have a direct effect on the CNS. They can affect the activity of the hippocampus and amygdala, as well as lower levels of neurotrophins such as Brain-Derived

Neurotrophic Factor (BDNF), which is essential in synaptic plasticity and neurogenesis. Low BDNF has been associated with symptoms of depression and cognitive impairment (Duman & Aghajanian, 2012).

A human study conducted by Jiang et al. (2015) showed that severely depressed patients have a significantly different composition of the microbiome than healthy individuals, with a predominance of opportunistic pathogen genera such as *Clostridium* and *Desulfovibrio*, as well as a decrease in protective genera such as *Faecalibacterium* and *Bifidobacterium*. This suggests that the status of the microbiome plays a role in neuroinflammatory regulation and mood.

3.6 The Role of the Microbiome in Behavior, Emotions, and Stress Responses

The gut microbiota also modulates the hypothalamic-pituitary-adrenal axis (HPA axis), the main pathway that regulates the stress response. In a model of microbe-free mice, it was found that animals exhibited an excessive HPA response to stress, which could be partially restored by normal microbial colonization (Sudo et al., 2004). Activation of the HPA axis causes the release of cortisol, a stress hormone that if in excess can lead to sleep disturbances, dysphoria, and decreased memory.

Furthermore, some fMRI-based studies suggest that probiotic supplementation can modify brain activity in areas of the medial prefrontal cortex and insula, which are involved in emotional processing and stress responses (Tillisch et al., 2013). This confirms that the influence of the microbiome on mental health is real and neurologically measurable.

4. CONCLUSION

The study presents an in-depth synthesis of the findings of various recent scientific literature that suggests that the gut microbiome has a central role in the regulation of human mental health. Communication pathways involving the gut-brain axis (GBA), the production of neurotransmitters by the microbiota, and the modulation of the immune system are biological foundations that explain the relationship between microbial ecosystems in the body and a person's psychic expression. The four main themes that emerged in the study included: The gut-brain axis as the main neuropsychological link between the gut and the brain; Microbiota dysbiosis as a trigger for neuroinflammation and mental disorders; The ability of the microbiota to produce important neurotransmitters such as serotonin, GABA, and dopamine; The effectiveness of psychobiotic approaches and healthy lifestyles in balancing the gut microbiome and improving psychological symptoms. Further research Development of AI-based predictive models to link microbiome profiles to patients' psychological symptoms.

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