Sustainable Microbiota Targeted Interventions in Psychiatric Disorders

Çağatay Han TÜRKSEVEN
Mersin University

To Cite This Chapter:
Turkseven, C. H. (2025). Sustainable microbiota targeted interventions in psychiatric disorders. In Ş. Demir, F. N. Takı, & Y. Uzun (Eds.), *Current studies for sustainable health* (pp. 1–22). ISRES Publishing.

Introduction

Major depressive disorder (MDD) and anxiety disorders represent two of the most widespread psychiatric conditions, contributing significantly to the global burden of disease. The World Health Organization (2023) ranks depression as the leading cause of disability worldwide, affecting an estimated 280 million people (World Health Organization, 2023). Anxiety disorders, similarly, impact over 300 million individuals globally (World Health Organization, 2025). These conditions often co-occur, share overlapping pathophysiological mechanisms, and carry significant personal, social, and economic costs. Standard first-line treatments for these disorders typically include pharmacological approaches such as selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs), as well as psychotherapeutic modalities like cognitive-behavioral therapy (CBT) (Cipriani et al., 2018). However, while these interventions can be effective, they are not without limitations. Approximately one-third of patients with MDD fail to respond adequately to initial antidepressant therapy, and relapse rates remain high even among responders (Rush et al., 2006). Moreover, adverse effects such as sexual dysfunction, gastrointestinal disturbances, sleep disruption, and weight changes are common with antidepressant use and significantly contribute to treatment discontinuation and decreased patient satisfaction (Campos et al., 2021). These limitations have catalyzed the search for novel, sustainable, and personalized therapeutic strategies. In this context, the gut microbiota has emerged as a compelling and rapidly expanding area of interest. The human gut harbors approximately 10^{13}-10^{14} microorganisms-primarily, bacteria-forming a complex, metabolically active ecosystem (Sender et al., 2016). These microbes influence host health through diverse mechanisms, including immune modulation, hormone secretion, neurotransmitter synthesis, and metabolic regulation. The bidirectional communication between the gastrointestinal system and the brain-referred to as the microbiota-gut-brain axis-involves multiple pathways: the vagus nerve, immune signaling, microbial metabolites, the enteric nervous system, and the hypothalamic-pituitary-adrenal (HPA) axis (Cryan et al., 2019). Disturbances in microbial composition (i.e., dysbiosis) have been linked to increased gut permeability, systemic inflammation,

altered neurotransmitter levels, and activation of neuroendocrine stress pathways-all of which are implicated in the etiology of mood disorders (Kelly et al., 2016; Foster et al., 2017). Recent clinical and preclinical evidence suggests that modulating the gut microbiome may offer a novel avenue for the prevention and treatment of depression and anxiety. Psychobiotics-live microorganisms that provide mental health benefits-alongside prebiotics and sustainable dietary interventions (such as the Mediterranean diet), represent promising adjuncts or alternatives to conventional therapies (Barber et al., 2023; Sarkar et al., 2016; Kazemi et al., 2019). These interventions may not only reduce symptom severity but also improve quality of life with fewer adverse effects, aligning with broader goals of sustainable healthcare.

This chapter explores the scientific basis and therapeutic potential of microbiota-targeted strategies in the management of depression and anxiety disorders. We begin by outlining the physiological mechanisms underpinning the gut–brain axis and its relevance to psychiatric illness. We then review current evidence on microbial dysbiosis in mental health, analyze the clinical utility of psychobiotics and dietary supplements, and assess the sustainability of microbiota-modulating dietary patterns. Finally, we discuss future directions in the field, including personalized microbiome-informed interventions and the integration of omics-based diagnostics.

The Gut–Brain Axis: Mechanistic Pathways and Clinical Relevance

The gut–brain axis (GBA) refers to the complex bidirectional communication system between the gastrointestinal (GI) tract and the central nervous system (CNS), involving neuronal, endocrine, immune, and metabolic signaling pathways. This cross-talk regulates not only gastrointestinal functions but also cognitive and emotional processes, making it central to understanding the pathophysiology of psychiatric disorders such as depression and anxiety (Carabotti et al., 2015)

Neural Communication via the Vagus Nerve and Enteric Nervous System

The vagus nerve plays a pivotal role in GBA communication. It provides an afferent conduit by which microbial metabolites and host immune signals influence brain activity, particularly in areas related to emotion and stress, such as the amygdala and prefrontal cortex (Bonaz et al., 2018). Experimental vagotomy in animal models abolishes the anxiolytic effects of certain probiotic strains, underscoring the vagus nerve's necessity in mediating psychobiotic efficacy (Bercik et al., 2011). The enteric nervous system (ENS), often termed the "second brain," comprises more than 100 million neurons and is capable of autonomous reflex activity. Gut microbes can influence ENS activity by producing neurotransmitters like γ-aminobutyric acid (GABA), serotonin (5-HT), and dopamine, which interact with local neurons and modulate gut motility, visceral sensitivity, and even mood (Strandwitz, 2018).

Neuroendocrine Pathways and the Hypothalamic-Pituitary-Adrenal (HPA) Axis

The HPA axis is a central stress response system that can be influenced by microbial signals. Under stress, corticotropin-releasing hormone (CRH) is secreted by the hypothalamus, triggering adrenocorticotropic hormone (ACTH) release from the pituitary gland and subsequent cortisol production from the adrenal cortex. Dysbiosis can lead to HPA axis hyperactivation, resulting in elevated cortisol levels, hippocampal atrophy, and impaired neurogenesis-all of which are implicated in depression (Mayer et al., 2014; O'Mahony et al., 2015). Interestingly, germ-free (GF) mice exhibit exaggerated HPA responses to mild stressors, a phenotype that is normalized by colonization with specific Bifidobacterium strains, further highlighting the microbiota's regulatory influence on neuroendocrine function (Sudo et al., 2004).

Immune System and Inflammation

The intestinal microbiota profoundly shapes both innate and adaptive immune responses. Commensal bacteria maintain mucosal homeostasis by promoting regulatory T cell (Treg) differentiation and modulating pro- and anti-inflammatory cytokine profiles (Arpaia et al., 2013). Disruption of this balance through dysbiosis enhances gut permeability-commonly referred to as "leaky gut" leading to the translocation of lipopolysaccharides (LPS) and other microbial components into systemic circulation (Fukui, 2016). These microbial signals activate peripheral immune cells, triggering the release of cytokines such as IL-6, TNF-α, and IL-1β, which cross the blood–brain barrier and promote microglial activation and neuroinflammation. This proinflammatory milieu is known to disrupt neurotransmitter metabolism and contribute to depressive and anxious symptomatology (Dantzer et al., 2008).

Microbial Metabolites and Neuroactive Compounds

Short-chain fatty acids (SCFAs)-primarily acetate, propionate, and butyrate-are metabolic byproducts of bacterial fermentation of dietary fibers. SCFAs exert broad neurobiological effects, including enhancing blood-brain barrier integrity, modulating gene expression via histone deacetylase (HDAC) inhibition, and promoting Treg activity (Dalile et al., 2019). Butyrate, a short-chain fatty acid produced by gut microbial fermentation of dietary fibers, has demonstrated antidepressant-like effects in preclinical studies. In particular, sodium butyrate has been shown to reverse stress-induced behavioral deficits and normalize molecular alterations in rodent models of depression, potentially through mechanisms involving histone deacetylase (HDAC) inhibition and neurotrophic factor modulation (Sun et al., 2018). Other microbial metabolites, such as tryptophan catabolites (e.g., kynurenine), influence serotonin synthesis and neuroplasticity. Dysbiosis can shift tryptophan metabolism toward the kynurenine pathway, decreasing serotonin availability and increasing neurotoxic quinolinic acid, both of which are linked to affective disorders (Agus et al., 2018).

Dysbiosis in Depression and Anxiety: From Clinical Profiles to Molecular Signatures

Dysbiosis refers to an imbalance in the composition, diversity, and function of the gut microbiota. It is characterized by reduced microbial richness, a loss of beneficial commensals, and an overrepresentation of potentially pathogenic species. Increasing evidence implicates dysbiosis as a key contributor to the pathogenesis of mood disorders, including major depressive disorder (MDD) and anxiety disorders (Jiang et al., 2015; Kelly et al., 2016). This section outlines both clinical and experimental findings regarding microbial alterations in these disorders and examines their immunological, neuroendocrine, and molecular consequences.

Clinical Microbiota Profiles in Mood Disorders

Recent metagenomic and 16S rRNA sequencing studies have identified reproducible alterations in the gut microbiota of individuals with depression and anxiety. In patients with MDD, studies consistently report a decreased abundance of short-chain fatty acid (SCFA) producing genera such as Faecalibacterium, Coprococcus, and Roseburia, which are important for maintaining intestinal barrier integrity and modulating inflammation (Valles-Colomer et al., 2019). In contrast, pro-inflammatory species from the Enterobacteriaceae family are often elevated, suggesting an immune-activating microbial profile. A well-cited study by Jiang et al. showed that patients with MDD had significantly lower levels of Firmicutes and increased Bacteroidetes, with a consequent shift in the Firmicutes/Bacteroidetes ratio (Jiang et al., 2015). Several studies have reported alterations in the gut microbiota of individuals with major depressive disorder. For instance, a systematic review found that members of the Lachnospiraceae family frequently differed between MDD patients and healthy controls, although the direction (increase vs. decrease) varied across studies. Moreover, genera such as Bacteroides and Alistipes were also observed to differ in abundance, but the findings were inconsistent across studies (Cheung et al., 2019). These alterations were associated with increased depressive symptom severity and may serve as potential biomarkers. In anxiety disorders, alterations in Lactobacillus and Bifidobacterium levels have been implicated. For example, a study involving patients with generalized anxiety disorder (GAD) demonstrated reduced Lactobacillus rhamnosus levels and disrupted microbial gene expression related to GABA metabolism-supporting the notion that the gut microbiota may influence neurotransmitter signaling relevant to anxiety (Bravo et al., 2018).

Molecular Signatures and Functional Pathways

Functional analyses of gut microbiota using metagenomic and metabolomic tools have revealed that dysbiosis in MDD is associated with altered expression of microbial genes involved in tryptophan metabolism, SCFA synthesis, and inflammatory cytokine regulation (Zheng et al., 2016). Specifically, dysbiosis is associated with an increased

flux of tryptophan along the kynurenine pathway rather than serotonin synthesis, leading to accumulation of neuroactive and potentially neurotoxic metabolites such as quinolinic acid (Agus et al., 2018). Gene expression studies also show increased microbial pathways associated with LPS biosynthesis and decreased genes for SCFA production in patients with depression (Valles-Colomer et al., 2019). These findings underscore how microbial function-beyond taxonomic composition-contributes to host inflammation and mood regulation. Furthermore, patients with mood disorders show altered intestinal gene expression. Biopsies from MDD patients reveal increased expression of Toll-like receptors (TLRs), pro-inflammatory cytokines, and tight junction protein deficits, indicating compromised mucosal immunity and barrier dysfunction (Kelly et al., 2017).

Causality and Bidirectionality

It is important to note that the relationship between gut microbiota and psychiatric illness is likely bidirectional. Chronic stress and depression can alter dietary intake, gastrointestinal motility, and immune function-factors that reciprocally influence microbial composition (Foster et al., 2017). Antidepressant medications, particularly SSRIs and TCAs, also exhibit antimicrobial effects that may shape the microbiota independently of disease mechanisms (Lukic et al., 2019). As such, future studies must carefully control for confounding factors, including diet, medication, and lifestyle variables. Nonetheless, evidence from fecal microbiota transplantation (FMT) studies strengthens the argument for causality. For example, one landmark study transferred microbiota from MDD patients into germ-free mice, resulting in the development of depression-like behaviors and altered neurotransmitter profiles (Kelly et al., 2016). These findings indicate that dysbiotic microbiota may contribute causally to the emergence of depressive phenotypes.

Psychobiotics and Nutritional Modulation of Mood: Evidence and Mechanisms

Psychobiotics are defined as live organisms-primarily bacteria-that, when ingested in adequate quantities, confer mental health benefits through interactions with the microbiota–gut–brain axis (Dinan et al., 2013). These benefits are mediated via mechanisms that include modulation of neurotransmitters, immunoregulation, and neuroendocrine signaling. Alongside psychobiotics, specific dietary components such as prebiotics, polyunsaturated fatty acids (PUFAs), vitamins, and polyphenols have also emerged as promising adjuncts or alternatives to conventional antidepressants and anxiolytics Mocking et al., 2016; Su et al., 2018).

Psychobiotics: Clinical Evidence and Mechanistic Insights

Most psychobiotics belong to the Lactobacillus and Bifidobacterium genera, which are common inhabitants of the human gut. Preclinical studies demonstrate that Lactobacillus rhamnosus can modulate GABAergic signaling and decrease anxiety-like behaviors

in a process found to be vagus nerve-dependent (Bravo et al., 2011). Similarly, Bifidobacterium longum 1714 has been shown to reduce cortisol levels and improve cognitive performance in human trials (Allen et al., 2016). A landmark double-blind, placebo-controlled trial using a combination of L. helveticus R0052 and B. longum R0175 found significant reductions in depression and anxiety scores among healthy volunteers (Messaoudi et al., 2011). Meta-analyses suggest modest but significant benefits of psychobiotic interventions for depression, although findings for anxiety remain more heterogeneous (Ng et al., 2018; Reis et al., 2018). The mechanisms of action include:

Neurotransmitter Modulation: Certain strains increase the production of GABA, serotonin, and dopamine, influencing mood and behavior.

Immune Regulation: Psychobiotics reduce systemic levels of pro-inflammatory cytokines (e.g., IL-6, TNF-α) and enhance anti-inflammatory mediators.

HPA Axis Attenuation: These strains blunt stress-induced HPA activation, normalizing cortisol output and restoring feedback sensitivity.

Despite encouraging data, challenges remain regarding strain specificity, dosage, delivery mode, and duration of intervention. Additionally, variability in individual microbiota composition may affect responsiveness to psychobiotic therapy (Westfall et al., 2017).

Prebiotics and Functional Dietary Components

Prebiotics are nondigestible dietary fibers-such as fructooligosaccharides (FOS) and galactooligosaccharides (GOS)-that selectively stimulate the growth and activity of beneficial gut bacteria. GOS supplementation has been shown to reduce cortisol awakening responses and improve emotional processing in healthy individuals, suggesting stress-buffering effects (Schmidt et al., 2015). Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), play crucial roles in synaptic plasticity, neuronal membrane fluidity, and inflammatory modulation. Deficiencies in omega-3 fatty acids have been associated with an increased risk of depression and cognitive decline (Mocking et al., 2016; Su et al., 2018). Meta-analyses indicate that omega-3 supplementation, especially formulations high in EPA, reduces depressive symptoms in both clinical and subclinical populations (Mocking et al., 2016). Vitamins and micronutrients such as vitamin D, folate, and vitamin B12 are also implicated in mood regulation. These nutrients affect homocysteine metabolism, methylation processes, and monoamine synthesis, all of which are relevant in depression pathophysiology (Young, 2007).

Polyphenols and Gut–Brain Interactions

Polyphenols are bioactive compounds found in fruits, vegetables, tea, and dark chocolate.

Although poorly absorbed in the small intestine, they undergo microbial fermentation in the colon, generating neuroactive and anti-inflammatory metabolites. These byproducts modulate gut microbial composition and SCFA production, thereby influencing brain function (Ammar et al., 2020). Resveratrol, quercetin, and epigallocatechin gallate (EGCG) have demonstrated antidepressant-like effects in preclinical studies, and some human trials suggest cognitive and mood benefits, though more rigorous studies are needed (Cione et al., 2019).

Dietary Synergy and Sustainability

A combined dietary strategy that includes psychobiotics, prebiotics, anti-inflammatory nutrients, and polyphenols may exert synergistic effects on the gut–brain axis. Such approaches are not only promising from a clinical perspective but also align with principles of sustainability by reducing dependence on long-term pharmacotherapy and enhancing self-managed mental health strategies. Emerging formulations, including synbiotics (combinations of probiotics and prebiotics), postbiotics (nonviable microbial byproducts), and fermented foods (e.g., kefir, kimchi, yogurt), offer accessible and culturally adaptable options for integrating microbiota-modulating strategies into everyday life (Dahiya et al., 2022; Agans et al., 2018).

Microbiota-Targeted Alternatives to Conventional Antidepressants

Conventional pharmacotherapy for mood disorders-especially selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs)-remains the mainstay of treatment. However, these agents are often limited by delayed onset of action, incomplete efficacy, and a high burden of side effects, including sexual dysfunction, weight gain, gastrointestinal distress, and cognitive blunting (Cipriani et al., 2018). Consequently, there is growing interest in microbiota-targeted interventions as complementary or alternative strategies that may exert therapeutic effects through different mechanisms with improved tolerability.

Limitations of Conventional Antidepressants

Antidepressants primarily target monoaminergic systems by modulating synaptic concentrations of serotonin, norepinephrine, and dopamine. While effective for many, response rates are modest, with only ~50% of patients achieving remission after first-line treatment (Rush et al., 2006). Furthermore, relapse rates are common, particularly in individuals with residual symptoms or poor adherence (Trivedi et al., 2006). Importantly, antidepressants may also affect the gut microbiota. Several studies indicate that SSRIs possess antimicrobial properties that can alter microbial composition in both beneficial and detrimental ways (Lukic et al., 2019; McGovern et al., 2019). For example, fluoxetine and sertraline reduce bacterial diversity in vitro and in vivo, potentially impacting mucosal immunity and inflammation (Lukic et al., 2019; McGovern et al., 2019).

Psychobiotics as Therapeutic Adjuncts or Replacements

Psychobiotics, including strains of Lactobacillus and Bifidobacterium, offer a promising microbiota-based intervention. These agents exert neuromodulatory effects via several pathways: regulating cytokine production, restoring tight junction proteins, modulating neurotransmitter availability, and balancing HPA axis output (Dinan et al., 2013; Sarkar et al., 2016).

A randomized controlled trial found that daily supplementation with L. helveticus R0052 and B. longum R0175 for 30 days led to significant improvements in depressive symptoms, sleep quality, and gastrointestinal comfort among participants with mild to moderate depression (Messaoudi et al., 2011). These findings suggest psychobiotics may not only alleviate core mood symptoms but also reduce somatic side effects frequently seen with antidepressants, such as gastrointestinal discomfort. In another study, administration of B. longum NCC3001 improved depression scores in patients with irritable bowel syndrome (IBS), further supporting the gut–brain axis as a viable therapeutic target in somatopsychic presentations (Pinto-Sanchez et al., 2017).

Dietary Interventions as Sustainable Strategies

Dietary interventions such as the Mediterranean diet have shown antidepressant effects, likely mediated via modulation of inflammation and microbiota composition (Sánchez-Villegas et al., 2009; Jacka et al., 2017). A landmark trial (the SMILES trial) demonstrated that adherence to a modified Mediterranean diet over 12 weeks significantly improved depressive symptoms, with remission rates nearly doubling compared to a control group receiving social support (Jacka et al., 2017). These diets are rich in fiber, omega-3 fatty acids, polyphenols, and vitamins-components that favorably influence gut microbiota diversity and SCFA production. Additionally, they are devoid of synthetic compounds, offer fewer side effects, and align with public health goals related to sustainable food systems and planetary health (Willett et al., 2019).

Combined Approaches and Clinical Integration

Microbiota-based interventions can be used in various clinical scenarios: As monotherapy in mild depressive or anxiety syndromes, especially in patients with treatment hesitancy or intolerance. As adjunct therapy to enhance the efficacy and tolerability of antidepressants. As maintenance therapy to prevent relapse by supporting immune, metabolic, and neuroendocrine resilience. However, standardization remains a challenge. Strain selection, dosing, delivery systems, and treatment duration vary across studies, making comparisons difficult. Moreover, individual variability in microbiota composition and host genetics may impact treatment outcomes. Personalized microbiota-informed interventions, guided by metagenomic or metabolomic profiling, hold potential for precision psychiatry but require further validation (Dinan & Cryan, 2017).

Sustainable Dietary Models and Microbiota–Mental Health Connections

Diet is a powerful modulator of gut microbiota composition and function, and in turn, of the gut–brain axis. Increasing evidence supports the role of specific dietary patterns not only in promoting general health but also in preventing and alleviating symptoms of mood disorders such as depression and anxiety. In this context, sustainable diets-those that are environmentally friendly, culturally appropriate, and health-promoting-offer a holistic approach to mental wellness that aligns individual well-being with planetary health goals (Willett et al., 2019).

The Mediterranean Diet: A Paradigm of Anti-Inflammatory Nutrition

The Mediterranean diet (MD) is one of the most extensively studied dietary patterns in relation to both gut microbiota diversity and mental health. It emphasizes the consumption of olive oil, fruits, vegetables, legumes, nuts, whole grains, and fish, while limiting red and processed meats, refined sugars, and saturated fats.

This dietary pattern is rich in:

Polyphenols, which promote beneficial microbial species such as Faecalibacterium and Bifidobacterium (Singh et al., 2017),

Dietary fibers, which serve as prebiotics for SCFA-producing bacteria,

Omega-3 fatty acids, which exert anti-inflammatory effects and support neuronal membrane integrity (Su et al., 2018).

A randomized controlled trial (the SMILES trial) demonstrated that individuals with moderate to severe depression who adhered to a Mediterranean-style diet for 12 weeks experienced significantly greater reductions in depressive symptoms compared to a control group receiving social support, with remission rates of 32% versus 8% (Jacka et al., 2017). Moreover, adherence to the Mediterranean diet is associated with lower levels of CRP, IL-6, and TNF-α—key biomarkers of systemic inflammation implicated in depression pathophysiology (Estruch et al., 2018).

Traditional Dietary Models with Mental Health Benefits

Other regional and traditional diets also offer microbiota-supportive, anti-inflammatory properties: The Japanese Diet is rich in fermented foods such as miso and natto, seaweed, and fish, contributing to microbial diversity and neuroprotective compounds (Saji et al., 2021). The Scandinavian Diet includes whole grains like rye and barley, berries rich in anthocyanins, and fatty fish. It has been shown to reduce depression scores and improve cognitive function (Shakersain et al., 2018). The Brazilian Diet emphasizes fresh foods, legumes, and minimal ultra-processed items, showing protective effects against anxiety and depressive symptoms in adolescents (Mesas et al., 2019; Werneck et al., 2022).

These diets share a core of unprocessed or minimally processed whole foods, fiber-rich plant sources, and healthy fats, aligning with both gut microbiota health and sustainable food system goals.

Western Diet and Dysbiosis-Induced Neuroinflammation

Conversely, the Western diet-characterized by high intake of saturated fats, red meat, refined carbohydrates, and sugar, has been consistently associated with microbial dysbiosis, systemic inflammation, and increased risk of depression (Kanoski & Davidson, 2011). This diet depletes beneficial microbes such as Akkermansia muciniphila and Bifidobacteria, while promoting pathobionts like Proteobacteria. Studies in animal models show that high-fat, high-sugar diets reduce hippocampal brain-derived neurotrophic factor (BDNF) levels, impair neurogenesis, and induce behaviors akin to depression and anxiety (Kanoski & Davidson, 2011). Furthermore, these dietary patterns are environmentally unsustainable, contributing to greenhouse gas emissions, biodiversity loss, and chronic disease epidemics.

Sustainability as a Clinical and Ecological Imperative

Sustainable diets address the growing need to integrate personal health with ecological responsibility. According to the EAT-Lancet Commission, transitioning to a planetary health diet that balances nutrient adequacy, environmental preservation, and cultural relevance could prevent approximately 11 million premature deaths per year and mitigate climate change impacts (Willett et al., 2019). In mental health care, promoting sustainable dietary habits can reduce polypharmacy, improve treatment adherence, and empower individuals through lifestyle-based self-management. Integration of nutritional psychiatry into clinical settings-guided by dietitians, psychologists, and primary care providers-represents a multidisciplinary approach to addressing both mood disorders and global health challenges.

Future Perspectives: Personalized Microbiome-Based Therapies

As microbiome research advances, the prospect of personalized microbiota-targeted interventions is becoming increasingly viable. These approaches aim to tailor therapeutic strategies based on an individual's unique microbiome composition, metabolic activity, genetic predispositions, and symptom profile. Such precision-based interventions hold promise for improving the efficacy, safety, and sustainability of treatments for depression and anxiety.

The Rise of Multi-Omics in Mental Health

The integration of multi-omics technologies-including metagenomics, metabolomics, transcriptomics, and epigenomics-offers a powerful means to map host–microbe interactions in neuropsychiatric disorders (Mihailovich et al., 2024; Simpson et al.,

2022; Rosario et al., 2020). These tools can identify: Microbial signatures predictive of treatment response or resistance, Metabolite patterns associated with neurotransmitter production, Genetic and epigenetic markers linked to HPA axis sensitivity, inflammation, or neuroplasticity.

For example, metagenomic sequencing can identify deficiencies in SCFA-producing bacteria or the overrepresentation of pro-inflammatory species, while metabolomic profiling may reveal alterations in tryptophan–kynurenine metabolism, which has been linked to mood regulation and neurotoxicity (Agus et al., 2018; Zheng et al., 2016).

Stratification of Patient Subtypes

Future research should focus on identifying microbiome-based subtypes of depression and anxiety. These could include: Inflammatory subtype: elevated CRP, IL-6, dysbiosis, systemic endotoxemia. HPA axis–dysregulated subtype: altered cortisol rhythms, barrier dysfunction, vagus nerve hypoactivity. Neurotransmitter-deficient subtype: impaired microbial production of GABA or serotonin precursors. Such stratification may allow clinicians to select the most appropriate interventions-whether psychobiotics, prebiotics, synbiotics, or dietary regimens-based on specific biological profiles.

Emerging Interventions: Beyond Probiotics

Several next-generation interventions are under investigation: Postbiotics: non-viable microbial components or metabolites (e.g., SCFAs, polysaccharide A) that exert immunomodulatory or neuroactive effects without live organisms (Aggarwal et al., 2022).

Fecal Microbiota Transplantation (FMT): While still experimental in psychiatry, FMT has shown promise in small trials, including improved depressive symptoms in patients with IBS or autism spectrum disorder (Zhang et al., 2023).

Designer Probiotics: Genetically engineered strains that can produce targeted neurochemicals or modulate specific immune pathways.

While these innovations are promising, long-term safety, regulatory oversight, and ethical considerations must be addressed before widespread clinical adoption.

Challenges and Considerations

Key challenges in personalized microbiota-based psychiatry include: Individual variability: Microbiota composition is influenced by diet, geography, age, sex, medications, and genetics, complicating generalizations. Regulatory and standardization gaps: There is currently no consensus on optimal strains, doses, or treatment durations. Data interpretation: Integrating multi-omics data into actionable clinical insights requires

advanced bioinformatics and cross-disciplinary collaboration.

Nonetheless, computational modeling, machine learning, and AI-based decision tools are expected to facilitate patient-specific treatment plans, especially when coupled with longitudinal tracking of microbiome changes and symptom trajectories (Rea et al., 2019; Afroz et al., 2023; Cryan et al., 2019).

The Road Ahead: Interdisciplinary Integration

The future of sustainable, microbiota-focused psychiatry will rely on collaboration between: Psychiatrists and neuroscientists: to refine symptom-domain targeting and neurobiological mechanisms. Microbiologists and immunologists: to explore host-microbe immune crosstalk. Dietitians and public health professionals: to promote personalized yet scalable nutritional interventions. Bioinformaticians and data scientists: to analyze multi-omics data and develop predictive algorithms.

Ultimately, the integration of microbiota profiling into routine psychiatric care could represent a paradigm shift from symptom-based pharmacotherapy to systems-based precision medicine grounded in host–microbe interactions.

Conclusions

This chapter has synthesized the rapidly evolving body of evidence surrounding the microbiota–gut–brain axis and its relevance to the pathogenesis and treatment of major depressive disorder (MDD) and anxiety disorders. Accumulating clinical and preclinical findings demonstrate that disturbances in gut microbial composition-commonly referred to as dysbiosis-are associated with increased intestinal permeability, systemic inflammation, altered neurotransmitter metabolism, and stress axis dysregulation, all of which contribute to mood symptomatology.

We have shown that psychobiotics, prebiotics, and nutritional supplements (such as omega-3 fatty acids, B vitamins, and polyphenols) hold therapeutic promise by modulating microbial diversity, enhancing neuroactive compound production, and dampening inflammation. These microbiota-targeted strategies offer a sustainable and low-risk alternative or adjunct to conventional antidepressants, which often produce undesirable side effects and show limited efficacy in many patients.

In particular, adherence to anti-inflammatory dietary patterns-such as the Mediterranean diet-has been associated with reduced depressive and anxiety symptoms, improved cognitive function, and enriched microbial profiles. In contrast, Western dietary habits characterized by high sugar and saturated fat intake appear to exacerbate dysbiosis and neuroinflammation.

Looking forward, the application of multi-omics technologies-including metagenomics,

metabolomics, and transcriptomics-opens the door to precision microbiome-informed psychiatry. Stratifying patients into biologically relevant subtypes and tailoring interventions accordingly may dramatically improve treatment outcomes. Moreover, emerging tools such as designer probiotics, postbiotics, and computational modeling will likely play a central role in the next generation of mental health therapeutics.

From a public health perspective, microbiota-based interventions are particularly attractive because they are non-invasive, scalable, and ecologically sustainable. By reducing reliance on synthetic pharmacotherapy and supporting self-managed mental health, such strategies contribute to both individual and societal well-being.

This chapter contributes to the field of sustainable health sciences by bridging disciplines-psychiatry, microbiology, nutrition, immunology, and systems biology-to outline an integrative, evidence-based framework for mental health care. By placing microbiota-targeted strategies in the context of sustainability, we emphasize not only clinical innovation but also ecological responsibility, aligning therapeutic development with broader goals of planetary health.

The gut microbiome offers a new frontier in psychiatric research and clinical care. As scientific understanding deepens, microbiota-informed mental health strategies have the potential to shift paradigms from symptom suppression to system restoration; from generalized prescriptions to personalized care; and from treatment resistance to biological resilience.

References

Afroz, K., & Manchia, M. (2023). Gut microbiome and psychiatric disorders. BMC Psychiatry, 23. https://doi.org/10.1186/s12888-023-05003-4

Agans, R., Rigsbee, L., Kenche, H., Michail, S., Khamis, H. J., & Paliy, O. (2011). Distal gut microbiota of adolescent children is different from that of adults. FEMS microbiology ecology, 77(2), 404–412. https://doi.org/10.1111/j.1574-6941.2011.01120.x

Aggarwal, S., Sabharwal, V., Kaushik, P., Joshi, A., Aayushi, A., & Suri, M. (2022). Postbiotics: From emerging concept to application. , 6. https://doi.org/10.3389/fsufs.2022.887642

Agus, A., Planchais, J., & Sokol, H. (2018). Gut Microbiota Regulation of Tryptophan Metabolism in Health and Disease. Cell host & microbe, 23(6), 716–724. https://doi.org/10.1016/j.chom.2018.05.003

Allen, A. P., Hutch, W., Borre, Y. E., Kennedy, P. J., Temko, A., Boylan, G., Murphy, E., Cryan, J. F., Dinan, T. G., & Clarke, G. (2016). Bifidobacterium longum

1714 as a translational psychobiotic: modulation of stress, electrophysiology and neurocognition in healthy volunteers. Translational psychiatry, 6(11), e939. https://doi.org/10.1038/tp.2016.191

Ammar, A., Trabelsi, K., Boukhris, O., Bouaziz, B., Müller, P., M Glenn, J., Bott, N. T., Müller, N., Chtourou, H., Driss, T., & Hökelmann, A. (2020). Effects of Polyphenol-Rich Interventions on Cognition and Brain Health in Healthy Young and Middle-Aged Adults: Systematic Review and Meta-Analysis. Journal of Clinical Medicine, 9(5), 1598. https://doi.org/10.3390/jcm9051598

Arpaia, N., Campbell, C., Fan, X., Dikiy, S., van der Veeken, J., deRoos, P., Liu, H., Cross, J. R., Pfeffer, K., Coffer, P. J., & Rudensky, A. Y. (2013). Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. Nature, 504(7480), 451–455. https://doi.org/10.1038/nature12726

Barber, T. M., Kabisch, S., Pfeiffer, A. F. H., & Weickert, M. O. (2023). The Effects of the Mediterranean Diet on Health and Gut Microbiota. Nutrients, 15(9), 2150. https://doi.org/10.3390/nu15092150

Bercik, P., Park, A. J., Sinclair, D., Khoshdel, A., Lu, J., Huang, X., Deng, Y., Blennerhassett, P. A., Fahnestock, M., Moine, D., Berger, B., Huizinga, J. D., Kunze, W., McLean, P. G., Bergonzelli, G. E., Collins, S. M., & Verdu, E. F. (2011). The anxiolytic effect of Bifidobacterium longum NCC3001 involves vagal pathways for gut-brain communication. Neurogastroenterology and motility, 23(12), 1132–1139. https://doi.org/10.1111/j.1365-2982.2011.01796.x

Bravo, J. A., Forsythe, P., Chew, M. V., Escaravage, E., Savignac, H. M., Dinan, T. G., Bienenstock, J., & Cryan, J. F. (2011). Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. Proceedings of the National Academy of Sciences of the United States of America, 108(38), 16050–16055. https://doi.org/10.1073/pnas.1102999108

Bonaz, B., Bazin, T., & Pellissier, S. (2018). The Vagus Nerve at the Interface of the Microbiota-Gut-Brain Axis. Frontiers in neuroscience, 12, 49. https://doi.org/10.3389/fnins.2018.00049

Campos, A. I., Mulcahy, A., Thorp, J. G., Wray, N. R., Byrne, E. M., Lind, P. A., Medland, S. E., Martin, N. G., Hickie, I. B., & Rentería, M. E. (2021). Understanding genetic risk factors for common side effects of antidepressant medications. Communications medicine, 1, 45. https://doi.org/10.1038/s43856-021-00046-8

Carabotti, M., Scirocco, A., Maselli, M. A., & Severi, C. (2015). The gut-brain axis:

interactions between enteric microbiota, central and enteric nervous systems. Annals of gastroenterology, 28(2), 203–209.

Cheung, S. G., Goldenthal, A. R., Uhlemann, A. C., Mann, J. J., Miller, J. M., & Sublette, M. E. (2019). Systematic Review of Gut Microbiota and Major Depression. Frontiers in psychiatry, 10, 34. https://doi.org/10.3389/fpsyt.2019.00034

Cione, E., La Torre, C., Cannataro, R., Caroleo, M., Plastina, P., & Gallelli, L. (2019). Quercetin, Epigallocatechin Gallate, Curcumin, and Resveratrol: From Dietary Sources to Human MicroRNA Modulation. Molecules, 25. https://doi.org/10.3390/molecules25010063

Cipriani, A., Furukawa, T. A., Salanti, G., Chaimani, A., Atkinson, L. Z., Ogawa, Y., Leucht, S., Ruhe, H. G., Turner, E. H., Higgins, J. P. T., Egger, M., Takeshima, N., Hayasaka, Y., Imai, H., Shinohara, K., Tajika, A., Ioannidis, J. P. A., & Geddes, J. R. (2018). Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet (London, England), 391(10128), 1357–1366. https://doi.org/10.1016/S0140-6736(17)32802-7

Cryan, J. F., O'Riordan, K. J., Cowan, C. S. M., Sandhu, K. V., Bastiaanssen, T. F. S., Boehme, M., Codagnone, M. G., Cussotto, S., Fulling, C., Golubeva, A. V., Guzzetta, K. E., Jaggar, M., Long-Smith, C. M., Lyte, J. M., Martin, J. A., Molinero-Perez, A., Moloney, G., Morelli, E., Morillas, E., O'Connor, R., Cruz-Pereria, J.S., Peterson, V.L., Rea, K., Ritz, N.L., Sherwin, E., Spichak, S., Teichman, E.M., Wouw, M.V., Ventura-Silva, A.P., Wallace-Fitzsimons, S.E., Hyland, N., Clarke, G., Dinan, T. G. (2019). The Microbiota-Gut-Brain Axis. Physiological reviews, 99(4), 1877–2013. https://doi.org/10.1152/physrev.00018.2018

Dahiya, D., & Nigam, P. (2022). Probiotics, Prebiotics, Synbiotics, and Fermented Foods as Potential Biotics in Nutrition Improving Health via Microbiome-Gut-Brain Axis. Fermentation. https://doi.org/10.3390/fermentation8070303

Dalile, B., Van Oudenhove, L., Vervliet, B., & Verbeke, K. (2019). The role of short-chain fatty acids in microbiota-gut-brain communication. Nature reviews. Gastroenterology & hepatology, 16(8), 461–478. https://doi.org/10.1038/s41575-019-0157-3

Dantzer, R., O'Connor, J. C., Freund, G. G., Johnson, R. W., & Kelley, K. W. (2008). From inflammation to sickness and depression: when the immune system subjugates the brain. Nature reviews. Neuroscience, 9(1), 46–56. https://doi.org/10.1038/nrn2297

Dinan, T. G., Stanton, C., & Cryan, J. F. (2013). Psychobiotics: a novel class of psychotropic. Biological psychiatry, 74(10), 720–726. https://doi.org/10.1016/j.biopsych.2013.05.001

Dinan, T. G., & Cryan, J. F. (2017). The Microbiome-Gut-Brain Axis in Health and Disease. Gastroenterology clinics of North America, 46(1), 77–89. https://doi.org/10.1016/j.gtc.2016.09.007

Estruch, R., Ros, E., Salas-Salvadó, J., Covas, M. I., Corella, D., Arós, F., Gómez-Gracia, E., Ruiz-Gutiérrez, V., Fiol, M., Lapetra, J., Lamuela-Raventos, R. M., Serra-Majem, L., Pintó, X., Basora, J., Muñoz, M. A., Sorlí, J. V., Martínez, J. A., Fitó, M., Gea, A., Hernán, M. A., Martinez-Gonzalez, M. A., PREDIMED Study Investigators (2018). Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. The New England journal of medicine, 378(25), e34. https://doi.org/10.1056/NEJMoa1800389

Foster, J. A., Rinaman, L., & Cryan, J. F. (2017). Stress & the gut-brain axis: Regulation by the microbiome. Neurobiology of stress, 7, 124–136. https://doi.org/10.1016/j.ynstr.2017.03.001

Fukui H. (2016). Increased Intestinal Permeability and Decreased Barrier Function: Does It Really Influence the Risk of Inflammation?. Inflammatory intestinal diseases, 1(3), 135–145. https://doi.org/10.1159/000447252

Jacka, F. N., O'Neil, A., Opie, R., Itsiopoulos, C., Cotton, S., Mohebbi, M., Castle, D., Dash, S., Mihalopoulos, C., Chatterton, M. L., Brazionis, L., Dean, O. M., Hodge, A. M., & Berk, M. (2017). A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial). BMC medicine, 15(1), 23. https://doi.org/10.1186/s12916-017-0791-y

Jiang, H., Ling, Z., Zhang, Y., Mao, H., Ma, Z., Yin, Y., Wang, W., Tang, W., Tan, Z., Shi, J., Li, L., & Ruan, B. (2015). Altered fecal microbiota composition in patients with major depressive disorder. Brain, behavior, and immunity, 48, 186–194. https://doi.org/10.1016/j.bbi.2015.03.016

Kanoski, S. E., & Davidson, T. L. (2011). Western diet consumption and cognitive impairment: links to hippocampal dysfunction and obesity. Physiology & behavior, 103(1), 59–68. https://doi.org/10.1016/j.physbeh.2010.12.003

Kazemi, A., Noorbala, A. A., Azam, K., Eskandari, M. H., & Djafarian, K. (2019). Effect of probiotic and prebiotic vs placebo on psychological outcomes in patients with major depressive disorder: A randomized clinical trial. Clinical

nutrition (Edinburgh, Scotland), 38(2), 522–528. https://doi.org/10.1016/j.clnu.2018.04.010

Kelly, J. R., Borre, Y., O' Brien, C., Patterson, E., El Aidy, S., Deane, J., Kennedy, P. J., Beers, S., Scott, K., Moloney, G., Hoban, A. E., Scott, L., Fitzgerald, P., Ross, P., Stanton, C., Clarke, G., Cryan, J. F., & Dinan, T. G. (2016). Transferring the blues: Depression-associated gut microbiota induces neurobehavioural changes in the rat. Journal of psychiatric research, 82, 109–118. https://doi.org/10.1016/j.jpsychires.2016.07.019

Kelly, J. R., Minuto, C., Cryan, J. F., Clarke, G., & Dinan, T. G. (2017). Cross Talk: The Microbiota and Neurodevelopmental Disorders. Frontiers in neuroscience, 11, 490. https://doi.org/10.3389/fnins.2017.00490

Lukić, I., Getselter, D., Ziv, O., Oron, O., Reuveni, E., Koren, O., & Elliott, E. (2019). Antidepressants affect gut microbiota and Ruminococcus flavefaciens is able to abolish their effects on depressive-like behavior. Translational psychiatry, 9(1), 133. https://doi.org/10.1038/s41398-019-0466-x

Mayer, E. A., Knight, R., Mazmanian, S. K., Cryan, J. F., & Tillisch, K. (2014). Gut microbes and the brain: paradigm shift in neuroscience. The Journal of neuroscience : the official journal of the Society for Neuroscience, 34(46), 15490–15496. https://doi.org/10.1523/JNEUROSCI.3299-14.2014

McGovern, A. S., Hamlin, A. S., & Winter, G. (2019). A review of the antimicrobial side of antidepressants and its putative implications on the gut microbiome. The Australian and New Zealand journal of psychiatry, 53(12), 1151–1166. https://doi.org/10.1177/0004867419877954

Mesas, A., González, A., De Andrade, S., Martínez-Vizcaíno, V., López-Gil, J., & Jiménez-López, E. (2022). Increased Consumption of Ultra-Processed Food Is Associated with Poor Mental Health in a Nationally Representative Sample of Adolescent Students in Brazil. Nutrients, 14. https://doi.org/10.3390/nu14245207

Messaoudi, M., Lalonde, R., Violle, N., Javelot, H., Desor, D., Nejdi, A., Bisson, J. F., Rougeot, C., Pichelin, M., Cazaubiel, M., & Cazaubiel, J. M. (2011). Assessment of psychotropic-like properties of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in rats and human subjects. The British journal of nutrition, 105(5), 755–764. https://doi.org/10.1017/S0007114510004319

Mihailovich, M., Bajić, S., Dinić, M., Đokić, J., Živković, M., Radojević, D., & Golić, N. (2024). Cutting-Edge iPSC-Based Approaches in Studying Host—Microbe

Interactions in Neuropsychiatric Disorders. International Journal of Molecular Sciences, 25. https://doi.org/10.3390/ijms251810156.

Mocking, R. J., Harmsen, I., Assies, J., Koeter, M. W., Ruhé, H. G., & Schene, A. H. (2016). Meta-analysis and meta-regression of omega-3 polyunsaturated fatty acid supplementation for major depressive disorder. Translational psychiatry, 6(3), e756. https://doi.org/10.1038/tp.2016.29

Molendijk, M., Molero, P., Ortuño Sánchez-Pedreño, F., Van der Does, W., & Angel Martínez-González, M. (2018). Diet quality and depression risk: A systematic review and dose-response meta-analysis of prospective studies. Journal of affective disorders, 226, 346–354. https://doi.org/10.1016/j.jad.2017.09.022

Ng, Q. X., Peters, C., Ho, C. Y. X., Lim, D. Y., & Yeo, W. S. (2018). A meta-analysis of the use of probiotics to alleviate depressive symptoms. Journal of affective disorders, 228, 13–19. https://doi.org/10.1016/j.jad.2017.11.063

O'Mahony, S. M., Clarke, G., Borre, Y. E., Dinan, T. G., & Cryan, J. F. (2015). Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. Behavioural brain research, 277, 32–48. https://doi.org/10.1016/j.bbr.2014.07.027

Pinto-Sanchez, M. I., Hall, G. B., Ghajar, K., Nardelli, A., Bolino, C., Lau, J. T., Martin, F. P., Cominetti, O., Welsh, C., Rieder, A., Traynor, J., Gregory, C., De Palma, G., Pigrau, M., Ford, A. C., Macri, J., Berger, B., Bergonzelli, G., Surette, M. G., Collins, S. M., … Bercik, P. (2017). Probiotic Bifidobacterium longum NCC3001 Reduces Depression Scores and Alters Brain Activity: A Pilot Study in Patients With Irritable Bowel Syndrome. Gastroenterology, 153(2), 448–459.e8. https://doi.org/10.1053/j.gastro.2017.05.003

Rea, K., Dinan, T., & Cryan, J. (2019). Gut Microbiota: A Perspective for Psychiatrists. Neuropsychobiology, 79, 50 - 62. https://doi.org/10.1159/000504495

Reis, D. J., Ilardi, S. S., & Punt, S. E. W. (2018). The anxiolytic effect of probiotics: A systematic review and meta-analysis of the clinical and preclinical literature. PloS one, 13(6), e0199041. https://doi.org/10.1371/journal.pone.0199041

Rosario, D., Borén, J., Uhlén, M., Proctor, G., Aarsland, D., Mardinoğlu, A., & Shoaie, S. (2020). Systems Biology Approaches to Understand the Host–Microbiome Interactions in Neurodegenerative Diseases. Frontiers in Neuroscience, 14. https://doi.org/10.3389/fnins.2020.00716

Rush, A. J., Trivedi, M. H., Wisniewski, S. R., Nierenberg, A. A., Stewart, J. W., Warden, D., Niederehe, G., Thase, M. E., Lavori, P. W., Lebowitz, B. D., McGrath, P. J.,

Rosenbaum, J. F., Sackeim, H. A., Kupfer, D. J., Luther, J., & Fava, M. (2006). Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. The American journal of psychiatry, 163(11), 1905–1917. https://doi.org/10.1176/ajp.2006.163.11.1905

Saji, N., Tsuduki, T., Murotani, K., Hisada, T., Sugimoto, T., Kimura, A., Niida, S., Toba, K., & Sakurai, T. (2021). Relationship between the Japanese-style diet, gut microbiota, and dementia: A cross-sectional study.. Nutrition, 94, 111524 . https://doi.org/10.21203/RS.3.RS-255821/V1

Sánchez-Villegas, A., Delgado-Rodríguez, M., Alonso, A., Schlatter, J., Lahortiga, F., Serra Majem, L., & Martínez-González, M. A. (2009). Association of the Mediterranean dietary pattern with the incidence of depression: the Seguimiento Universidad de Navarra/University of Navarra follow-up (SUN) cohort. Archives of general psychiatry, 66(10), 1090–1098. https://doi.org/10.1001/archgenpsychiatry.2009.129

Sarkar, A., Lehto, S. M., Harty, S., Dinan, T. G., Cryan, J. F., & Burnet, P. W. J. (2016). Psychobiotics and the Manipulation of Bacteria-Gut-Brain Signals. Trends in neurosciences, 39(11), 763–781. https://doi.org/10.1016/j.tins.2016.09.002

Schmidt, K., Cowen, P. J., Harmer, C. J., Tzortzis, G., Errington, S., & Burnet, P. W. (2015). Prebiotic intake reduces the waking cortisol response and alters emotional bias in healthy volunteers. Psychopharmacology, 232(10), 1793–1801. https://doi.org/10.1007/s00213-014-3810-0

Sender, R., Fuchs, S., & Milo, R. (2016). Revised Estimates for the Number of Human and Bacteria Cells in the Body. PLoS biology, 14(8), e1002533. https://doi.org/10.1371/journal.pbio.1002533

Shakersain, B., Rizzuto, D., Larsson, S. C., Faxén-Irving, G., Fratiglioni, L., & Xu, W. L. (2018). The Nordic Prudent Diet Reduces Risk of Cognitive Decline in the Swedish Older Adults: A Population-Based Cohort Study. Nutrients, 10(2), 229. https://doi.org/10.3390/nu10020229

Simpson, J., & Redinbo, M. (2022). Multi-omic analysis of host-microbial interactions central to the gut-brain axis.. Molecular omics. https://doi.org/10.1039/d2mo00205a

Singh, R. K., Chang, H. W., Yan, D., Lee, K. M., Ucmak, D., Wong, K., Abrouk, M., Farahnik, B., Nakamura, M., Zhu, T. H., Bhutani, T., & Liao, W. (2017). Influence of diet on the gut microbiome and implications for human health. Journal of translational medicine, 15(1), 73. https://doi.org/10.1186/s12967-017-1175-y

Strandwitz P. (2018). Neurotransmitter modulation by the gut microbiota. Brain research, 1693(Pt B), 128–133. https://doi.org/10.1016/j.brainres.2018.03.015

Su, K. P., Tseng, P. T., Lin, P. Y., Okubo, R., Chen, T. Y., Chen, Y. W., & Matsuoka, Y. J. (2018). Association of Use of Omega-3 Polyunsaturated Fatty Acids With Changes in Severity of Anxiety Symptoms: A Systematic Review and Meta-analysis. JAMA network open, 1(5), e182327. https://doi.org/10.1001/jamanetworkopen.2018.2327

Sudo, N., Chida, Y., Aiba, Y., Sonoda, J., Oyama, N., Yu, X. N., Kubo, C., & Koga, Y. (2004). Postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response in mice. The Journal of physiology, 558(Pt 1), 263–275. https://doi.org/10.1113/jphysiol.2004.063388

Sun, J., Wang, F., Hu, X., Yang, C., Xu, H., Yao, Y., & Liu, J. (2018). Clostridium butyricum Attenuates Chronic Unpredictable Mild Stress-Induced Depressive-Like Behavior in Mice via the Gut-Brain Axis. Journal of agricultural and food chemistry, 66(31), 8415–8421. https://doi.org/10.1021/acs.jafc.8b02462

Trivedi, M. H., Rush, A. J., Wisniewski, S. R., Nierenberg, A. A., Warden, D., Ritz, L., Norquist, G., Howland, R. H., Lebowitz, B., McGrath, P. J., Shores-Wilson, K., Biggs, M. M., Balasubramani, G. K., Fava, M., & STAR*D Study Team (2006). Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. The American journal of psychiatry, 163(1), 28–40. https://doi.org/10.1176/appi.ajp.163.1.28

Valles-Colomer, M., Falony, G., Darzi, Y., Tigchelaar, E. F., Wang, J., Tito, R. Y., Schiweck, C., Kurilshikov, A., Joossens, M., Wijmenga, C., Claes, S., Van Oudenhove, L., Zhernakova, A., Vieira-Silva, S., & Raes, J. (2019). The neuroactive potential of the human gut microbiota in quality of life and depression. Nature microbiology, 4(4), 623–632. https://doi.org/10.1038/s41564-018-0337-x

Werneck, A., Vancampfort, D., Oyeyemi, A., Stubbs, B., & Silva, D. (2020). Joint association of ultra-processed food and sedentary behavior with anxiety-induced sleep disturbance among Brazilian adolescents.. Journal of affective disorders, 266, 135-142 . https://doi.org/10.1016/j.jad.2020.01.104

Westfall, S., Lomis, N., Kahouli, I., Dia, S. Y., Singh, S. P., & Prakash, S. (2017). Microbiome, probiotics and neurodegenerative diseases: deciphering the gut brain axis. Cellular and molecular life sciences : CMLS, 74(20), 3769–3787. https://doi.org/10.1007/s00018-017-2550-9

Willett, W., Rockström, J., Loken, B., Springmann, M., Lang, T., Vermeulen, S., Garnett,

T., Tilman, D., DeClerck, F., Wood, A., Jonell, M., Clark, M., Gordon, L. J., Fanzo, J., Hawkes, C., Zurayk, R., Rivera, J. A., De Vries, W., Majele Sibanda, L., Afshin, A., Chaudhary, A., Herrero, M., Agustina, R., Branca, F., Lartey, A., Fan, S., Crona, B., Fox, E., Bignet, V., Troell, M., Lindahl, T., Singh, S., Cornell, S.E., Reddy, K.S., Narain, S., Nishtar, S., Murray, C. J. L. (2019). Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. Lancet (London, England), 393(10170), 447–492. https://doi.org/10.1016/S0140-6736(18)31788-4

World Health Organization. (2023). Depressive disorder (depression). Retrieved from https://www.knowledge-action-portal.com/en/content/depressive-disorder-depression?utm_source

World Health Organization. (2025). Anxiety disorders. Retrieved from https://www.who.int/news-room/fact-sheets/detail/anxiety-disorders?utm_source

Young S. N. (2007). Folate and depression--a neglected problem. Journal of psychiatry & neuroscience: JPN, 32(2), 80–82.

Zhang, J., Zhu, G., Wan, L., Liang, Y., Liu, X., Yan, H., Zhang, B., & Yang, G. (2023). Effect of fecal microbiota transplantation in children with autism spectrum disorder: A systematic review. Frontiers in Psychiatry, 14. https://doi.org/10.3389/fpsyt.2023.1123658

Zheng, P., Zeng, B., Zhou, C., Liu, M., Fang, Z., Xu, X., Zeng, L., Chen, J., Fan, S., Du, X., Zhang, X., Yang, D., Yang, Y., Meng, H., Li, W., Melgiri, N. D., Licinio, J., Wei, H., & Xie, P. (2016). Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism. Molecular psychiatry, 21(6), 786–796. https://doi.org/10.1038/mp.2016.44

About The Author

Dr. Çağatay Han TÜRKSEVEN is an Assistant Professor in the Department of Biophysics at the Faculty of Medicine, Mersin University. He completed his PhD in the same department, where he conducted research focusing on Alzheimer's disease, neurodegenerative mechanisms, neuroplasticity, hemodynamic parameters, electrophysiology, and cellular toxicity. He has contributed as a researcher to numerous national and international scientific projects and has authored several book chapters in the fields of biophysics and neuroscience. Recognized for his interdisciplinary scientific approach, Dr. Türkseven's work bridges basic science and clinical applications-extending from the molecular foundations of neurodegenerative diseases to bioelectrical processes, experimental animal models, and clinical research design.

Email: turkseven@mersin.edu.tr; cagatayhanturkseven1923@gmail.com

ORCID: 0000-0002-0584-0661

Similarity Index

The similarity index obtained from the plagiarism software for this book chapter is 6%.