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THE MICROBIOTA–GUT–BRAIN AXIS: NEUROBIOLOGICAL MECHANISMS IN THE PATHOPHYSIOLOGY OF DEPRESSION

Milan Petković[1], Olivera Žikić[1,2]

[1]University Clinical Centre Niš, Center for mental health protection, Niš, Serbia

[2]University of Niš, Faculty of medicine, Department of Psychiatry with Medical Psychology, Niš, Serbia

Contact: Milan Petković

48 dr Zorana Djinjdića Blvd., 18000 Niš, Serbia

E-mail: milannpetkovic@gmail.com

Depression is one of the most common mental disorders and a leading cause of disability worldwide. Contemporary research indicates that, in addition to disturbances in monoaminergic neurotransmitter systems, neuroinflammation, dysfunction of the hypothalamic–pituitary–adrenal (HPA) axis, impaired neuroplasticity, metabolic alterations, and changes in the intestinal microbiota play a significant role in its pathophysiology. The microbiota–gut–brain axis represents a complex bidirectional communication system linking the gastrointestinal tract, intestinal microbiota, and the central nervous system through neural, immunological, endocrine, and metabolic mechanisms. A growing body of experimental and clinical evidence suggests that dysbiosis may contribute to the development of depression through increased intestinal permeability, translocation of bacterial components, activation of inflammatory processes and microglia, disruption of tryptophan metabolism and the kynurenine pathway, impairment of the blood–brain barrier, and reduced production of neuroprotective metabolites. The aim of this paper is to present current knowledge on the role of the microbiota–gut–brain axis and related

neurobiological mechanisms in the pathophysiology of depression, and to consider the potential clinical implications of these findings. Particular attention is given to psychobiotics, prebiotics, and nutritional interventions as potential novel personalized therapeutic approaches.

Keywords: depression; microbiota; gut–brain axis; neuroinflammation; hypothalamic–pituitary–adrenal axis

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MIKROBIOTA–CREVO–MOZAK OSA: NEUROBIOLOŠKI MEHANIZMI U PATOFIZIOLOGIJI DEPRESIJE

Milan Petković[1], Olivera Žikić[1,2]

[1]Univerzitetski klinički centar Niš, Centar za zaštitu mentalnog zdravlja, Niš, Srbija

[2]Univerzitet u Nišu, Medicinski fakultet, Katedra Psihijatrija sa medicinskom psihologijom, Niš, Srbija

Kontakt: Milan Petković

Bulevar dr Zorana Đinđića 48, 18000 Niš, Srbija

E-mail: milannpetkovic@gmail.com

Depresija predstavlja jedan od najčešćih mentalnih poremećaja i vodeći uzrok onesposobljenosti širom sveta. Savremena istraživanja ukazuju da, pored poremećaja monoaminskih neurotransmiterskih sistema, značajnu ulogu u njenoj patofiziologiji imaju neuroinflamacija, disfunkcija hipotalamo–hipofizno–adrenalne (HPA) ose, poremećaji neuroplastičnosti, metaboličke promene i promene intestinalne mikrobiote. Mikrobiota–crevo–mozak osa predstavlja složen dvosmerni komunikacioni sistem koji povezuje gastrointestinalni trakt, intestinalnu mikrobiotu i centralni nervni sistem putem neuralnih, imunoloških, endokrinih i metaboličkih mehanizama. Brojni eksperimentalni i klinički dokazi ukazuju da disbioza može doprineti razvoju depresije kroz povećanu intestinalnu permeabilnost, translokaciju bakterijskih komponenti, aktivaciju inflamatornih procesa i mikroglija, poremećaj metabolizma triptofana i kinureninskog puta, narušavanje krvno-moždane barijere i smanjenu produkciju neuroprotektivnih metabolita. Cilj ovog rada je da prikaže savremena saznanja o ulozi mikrobiota–crevo–mozak ose i neurobioloških mehanizama u patofiziologiji depresije i razmotri

potencijalne kliničke implikacije ovih saznanja. Posebnu pažnju privlače psihobiotici, prebiotici i nutritivne intervencije kao potencijalni novi personalizovani terapijski pristupi.

Ključne reči: depresija; mikrobiota; crevo–mozak osa; neuroinflamacija; HPA osa

INTRODUCTION

Depression represents one of the most significant public health challenges of modern society. It is associated with persistent psychological distress, impaired social and occupational functioning, increased somatic comorbidity and excess mortality. According to the World Health Organization, depressive disorders remain among the leading contributors to years lived with disability (1). Despite advances in psychotherapy and pharmacotherapy, a considerable proportion of patients experience only partial remission, recurrent episodes or treatment resistance. This clinical variability indicates that depression cannot be adequately explained by a single neurochemical disturbance.

The traditional monoamine hypothesis provided the dominant biological framework for understanding depression, and it was based on disturbances in serotonergic, noradrenergic, and dopaminergic neurotransmitter systems. However, contemporary research suggests that depression is a complex systemic disorder involving neuroinflammation, oxidative stress, impaired neuroplasticity, dysfunction of the hypothalamic–pituitary–adrenal (HPA) axis, and metabolic alterations (2,3). In this context, increasing attention has been directed toward the microbiota–gut–brain axis as a potential regulatory system involved in the development of psychiatric disorders.

The microbiota–gut–brain axis is a bidirectional communication network linking the gastrointestinal tract and the central nervous system. This concept has significantly transformed the traditional understanding of the relationship between the gut and the brain, highlighting the crucial role of the intestinal microbiota in the regulation of neuroendocrine, immune, and metabolic processes (4).

THE MICROBIOTA–GUT–BRAIN AXIS

The intestinal microbiota is a complex community of microorganisms that colonizes the human gastrointestinal tract. It is estimated that the human body contains approximately equal numbers of microbial and human cells, while the microbiome possesses a genetic repertoire that far exceeds that of the human genome (5).

The microbiota plays a crucial role in digestion, vitamin synthesis, bile acid metabolism, maturation of the immune system, and maintenance of intestinal barrier integrity (6). Under physiological conditions, a state of eubiosis is maintained, characterized by high microbial diversity and functional stability. In contrast, dysbiosis refers to qualitative and quantitative

alterations in the composition and function of the microbiota, which may result in a wide range of systemic consequences (7).

Gut-brain communication takes place through several partially overlapping pathways. Neural communication involves the enteric nervous system, vagus nerve, spinal afferents and autonomic nervous system. Endocrine communication involves the HPA axis and enteroendocrine signalling. Immune communication includes mucosal immune cells, cytokines, chemokines, lipopolysaccharide (LPS) and systemic low-grade inflammation. Metabolic communication is mediated by microbial products such as short-chain fatty acids (SCFAs), indole derivatives, secondary bile acids and metabolites related to tryptophan and neurotransmitter systems (3-5). These mechanisms continually interact, so that a change in barrier function, microbial metabolism or stress response may amplify downstream immune and central nervous system effects.

Table 1. Main signalling pathways of the microbiota-gut-brain axis

Pathway	Principal components	Potential relevance for depression
Neural	Enteric nervous system, vagus nerve, spinal afferents, autonomic nervous system	Interoception, stress regulation, visceral sensitivity, emotional processing
Endocrine	HPA axis, cortisol, CRH, ACTH, enteroendocrine hormones	Stress vulnerability, cortisol dysregulation, metabolic and immune effects
Immune	Gut-associated lymphoid tissue, cytokines, LPS, TLR4 signalling, microglia	Low-grade inflammation, neuroinflammation, altered neurotransmission and synaptic plasticity
Metabolic	SCFAs, indoles, bile acids, tryptophan metabolites, microbial enzymes	Barrier integrity, microglial homeostasis, epigenetic regulation, neuroplasticity
Barrier-related	Mucus layer, epithelial cells, tight junction proteins, blood-brain barrier	Translocation of microbial products, peripheral-to-central inflammatory signalling

NEUROBIOLOGICAL MECHANISMS

The neurobiological effects of the microbiota-gut-brain axis are mediated by several interdependent pathways. Neural signalling, stress-axis regulation, immune activation, barrier integrity, tryptophan metabolism, microbial metabolites and neuroplasticity are not competing explanations; rather, they represent different levels of the same biological system (4-8). This is particularly relevant in depression, where chronic stress, low-grade inflammation, metabolic disturbance, altered neurotransmission and impaired plasticity often coexist. Dysbiosis should therefore be considered a possible modifier of vulnerability, symptom expression and treatment response, not a universal primary cause of depression.

Neural Pathways

The enteric nervous system (ENS) is an intrinsic neural network of the gastrointestinal tract that regulates motility, secretion, mucosal blood flow and local reflexes with considerable autonomy (9). It communicates continuously with the central nervous system through autonomic pathways. The vagus nerve is the major route for rapid gut-to-brain signalling: most vagal fibres are afferent and transmit visceral information to the nucleus tractus solitarius, from where signals reach regions involved in interoception, affective regulation and stress responses, including the hypothalamus, amygdala and insula (2,5).

Experimental studies have demonstrated that certain probiotic strains can influence animal behavior, while these effects are abolished following vagotomy, confirming the pivotal role of the vagus nerve in mediating communication between the gut microbiota and the brain (7). Translation to human depression, however, remains complex, because vagal signalling is strongly influenced by immune mediators, endocrine signals, enteroendocrine hormones and microbial metabolites.

The Hypothalamic–Pituitary–Adrenal (HPA) Axis

The hypothalamic–pituitary–adrenal (HPA) axis is the central neuroendocrine system involved in the physiological response to stress. Activation of the HPA axis results in increased cortisol secretion, which exerts numerous effects on the nervous, immune, and metabolic systems. Dysbiosis may contribute to HPA axis hyperactivity and the maintenance of a chronic stress response, a mechanism considered to play a key role in the pathophysiology of depression (10).

The microbiota appears to participate in the development and modulation of stress reactivity. Germ-free animals show exaggerated HPA-axis responses to stress, while early microbial colonization can partially normalize this phenotype (11). This suggests that microbiota may influence neuroendocrine programming during sensitive developmental periods. The relationship is bidirectional: chronic stress can alter gut motility, mucus secretion, permeability and microbial composition, while dysbiosis and immune activation may further increase stress vulnerability. Such a feed-forward loop is clinically relevant in patients whose depressive symptoms are accompanied by gastrointestinal complaints or inflammatory comorbidity.

Neuroinflammation

One of the most prominent contemporary models of depression is based on the concept of neuroinflammation. Increased intestinal permeability facilitates the translocation of bacterial components, particularly lipopolysaccharides (LPS), into the systemic circulation, thereby triggering inflammatory responses (11).

As a consequence, the production of pro-inflammatory cytokines, including interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), is increased. These mediators can influence central nervous system function and contribute to the development of depressive symptoms. Under persistent inflammatory stimulation, however, activated microglia may release cytokines, reactive oxygen species and excitotoxic mediators that disrupt neurotransmission, impair neurogenesis and reduce synaptic plasticity (12,13).

Meta-analyses have consistently shown significantly elevated levels of inflammatory markers in patients with depression compared with healthy individuals (14). This does not mean that all depression is inflammatory, but it supports the existence of biologically relevant subgroups in which gut-derived immune activation may be particularly important.

Table 2. Barrier dysfunction, dysbiosis and potential psychiatric implications

Parameter	Eubiosis / preserved barrier	Dysbiosis / increased permeability	Potential implication
Microbial ecology	High diversity; stable functional networks; adequate commensal activity	Reduced diversity; loss of protective microbial profiles; expansion of pathobionts	Shift from neuroprotective and anti-inflammatory metabolism toward pro-inflammatory signalling
Mucus layer	Compact mucus layer separating microbes from epithelium	Thinned or degraded mucus layer with closer microbe-epithelium contact	Facilitates epithelial stimulation and immune activation
Tight junctions	Adequate occludin, claudin and ZO-1 expression; regulated paracellular transport	Disrupted tight junction architecture; increased paracellular passage	Allows microbial products and antigens to enter systemic circulation
Immune response	Immune tolerance and balanced cytokine profile	TLR activation, increased IL-1 beta, IL-6 and TNF-alpha	Low-grade systemic inflammation and potential neuroinflammatory signalling
Blood-brain barrier	Preserved selectivity and protection of CNS parenchyma	Inflammation-related permeability changes	Increased access of peripheral inflammatory signals to the brain
CNS outcome	Microglial homeostasis, adaptive plasticity and mood regulation	Microglial activation, impaired neurogenesis and synaptic dysfunction	Biological substrate for affective, cognitive and somatic symptoms

Tryptophan, Serotonin, and the Kynurenine Pathway

Tryptophan metabolism is one of the most important biochemical intersections among microbiota, immunity and depression. Tryptophan is an essential amino acid and the primary precursor of serotonin. During inflammatory states, the enzyme indoleamine 2,3-dioxygenase (IDO) becomes activated, diverting tryptophan metabolism from serotonin synthesis toward the kynurenine pathway (14,15).

This shift results in reduced serotonin production and increased generation of potentially neurotoxic kynurenine metabolites, which may contribute to the development and progression of depression. Alterations in gut microbiota composition have been shown to significantly influence these metabolic processes (16). The microbiota influences this system by regulating tryptophan availability, shaping inflammatory tone and producing indole derivatives. The tryptophan-kynurenine pathway therefore provides a plausible mechanistic link between dysbiosis, inflammation, neurotransmission and depressive symptoms (14,30).

Short-Chain Fatty Acids and Neuroplasticity

Short-chain fatty acids (SCFAs), particularly butyrate, are produced through the fermentation of dietary fiber by the intestinal microbiota. These metabolites exhibit anti-inflammatory and neuroprotective properties and play an important role in regulating the expression of genes involved in neuroplasticity (17).

Reduced butyrate production has been associated with increased inflammation, impaired blood–brain barrier function, and decreased expression of brain-derived neurotrophic factor (BDNF), all of which represent important mechanisms underlying the development of depressive symptoms (18).

Neurotransmitter-related signalling

Microbial effects on neurotransmission require precise interpretation. The microbiota does not simply supply the brain with neurotransmitters. Rather, it influences precursor availability, enteric neurotransmission, enteroendocrine activity, immune-metabolic signalling and vagal afferent activity. Most serotonin is produced in the gastrointestinal tract, but peripheral serotonin does not directly cross the blood-brain barrier in sufficient quantities to explain central mood effects. The more plausible mechanism is indirect: changes in tryptophan availability, intestinal

serotonin signalling, immune activation and vagal communication may modify central neurotransmitter systems (14,25,31).

Blood-brain barrier integrity

The blood-brain barrier (BBB) is a dynamic interface separating peripheral circulation from the central nervous system. Experimental studies indicate that gut microbiota can influence BBB permeability. Germ-free animals show increased BBB permeability and reduced expression of tight junction proteins, while microbial colonization or administration of SCFAs may improve barrier integrity (11).

This mechanism is clinically relevant because BBB dysfunction may increase the impact of peripheral inflammatory mediators on the brain. Within an integrative model of depression, dysbiosis may therefore act at two barrier levels: first by increasing intestinal permeability and systemic inflammatory exposure, and second by weakening the selectivity of the BBB. Direct human evidence is still limited, but the BBB provides an important mechanistic link between peripheral immune-metabolic disturbance and central neuroinflammatory change.

Neuroplasticity and BDNF

Depression is associated with impaired neuroplasticity, including altered synaptic function, reduced neurogenesis and changes in stress-sensitive brain regions. Brain-derived neurotrophic factor (BDNF) is a central mediator of neuronal survival, synaptic plasticity, long-term potentiation and adaptation to stress. Reduced BDNF signalling has been linked to depression and chronic stress, whereas successful antidepressant treatment may partly restore neuroplastic processes (12,23).

Microbiota may influence BDNF indirectly through several routes, including reduced neuroinflammation, modulation of HPA-axis activity, production of SCFAs, regulation of tryptophan metabolism and epigenetic effects on gene expression. In this framework, dysbiosis may not merely trigger acute inflammatory or neurotransmitter-related changes; it may also reduce the capacity of the brain to maintain adaptive plasticity over time. This perspective is relevant to mood symptoms, cognitive impairment, resilience and recovery.

Integrative network model

The mechanisms described above should be integrated into a dynamic network model. Dysbiosis may increase intestinal permeability, promote LPS translocation, activate cytokine

production, disturb HPA-axis regulation, redirect tryptophan metabolism, reduce SCFA availability, affect BBB integrity, activate microglia and weaken BDNF-dependent neuroplasticity. Conversely, eubiosis, intact barrier function and adequate production of protective metabolites may support immune tolerance, stress resilience and adaptive plasticity. This network model helps explain why depressive symptoms frequently coexist with gastrointestinal complaints, inflammatory comorbidities, metabolic abnormalities and heightened stress sensitivity.

THE GUT MICROBIOTA AND DEPRESSION

Over the past decade, many studies have reported differences in gut microbiota composition between individuals with major depressive disorder and healthy controls. Systematic reviews and meta-analyses suggest that depression is often associated with reduced microbial diversity and altered abundance of microbial profiles involved in SCFA production and immune regulation (17-21). Decreased abundance of Faecalibacterium, Roseburia and Coprococcus is among the more frequently reported findings, although the results vary considerably across studies.

This heterogeneity is expected. Microbiome composition is shaped by diet, geography, medication, antibiotic exposure, body mass index, sleep, physical activity, comorbid disease, sampling procedures and sequencing methodology. Depression itself can also change appetite, food choice, gastrointestinal motility, sleep pattern and medication exposure, all of which may secondarily alter the microbiota. For this reason, cross-sectional differences should be interpreted as associations rather than proof that dysbiosis is a primary cause of depression.

Animal studies provide stronger support for a functional role of microbiota in depressive-like phenotypes. Germ-free animals show changes in stress responsivity, behaviour and neurochemical systems, while FMT from depressed donors to microbiota-depleted or germ-free animals can induce behavioural and physiological changes resembling depressive-like states (5,21). These findings support biological plausibility and demonstrate that microbial communities can transfer aspects of disease-related phenotypes under experimental conditions.

Nevertheless, animal models cannot fully reproduce human depression, which is shaped by cognition, subjective experience, developmental history and social context. Translational findings therefore support the microbiota as a contributor to depressive pathophysiology rather than as a universal cause. The most defensible interpretation is that microbiota-related

mechanisms may be particularly relevant in specific biological subtypes or vulnerability states, especially when depression is accompanied by inflammation, metabolic disturbance or gastrointestinal symptoms.

The relationship between depression and the gut microbiota is bidirectional. Dysbiosis, increased permeability and immune activation may contribute to depressive symptoms, while depression-related behavioural and physiological changes may further disturb the intestinal ecosystem. Reduced physical activity, poor sleep, altered diet, alcohol use, stress-related motility changes and psychotropic medication may all affect microbial composition and function. This bidirectional view is clinically important because many patients with depression present with fatigue, appetite change, abdominal discomfort, irritable bowel symptoms and metabolic comorbidity.

A growing area of research concerns interactions between antidepressant medication and the microbiota. Antidepressants may alter microbial composition or function, while baseline microbial profiles may influence treatment response. Some reports suggest that selective serotonin reuptake inhibitors may have direct or indirect antimicrobial effects and may also influence peripheral serotonergic signalling, gut motility and vagal communication (21,31). These data are not yet sufficient to guide routine antidepressant selection, but they are relevant for future biomarker development and precision psychiatry.

THERAPEUTIC IMPLICATIONS

Understanding the microbiota-gut-brain axis has opened new therapeutic possibilities for depression. These approaches should not be viewed as replacements for established psychiatric treatment. At present, they are best conceptualized as potential adjunctive strategies aimed at immune, metabolic, barrier-related and stress-regulatory pathways that are not directly targeted by conventional antidepressants. Because the microbiota is responsive to diet, medication, stress, sleep, physical activity and environmental exposures, it represents a modifiable therapeutic target. Clinical translation, however, requires careful evaluation of efficacy, strain specificity, dose, treatment duration, safety and patient selection.

Psychobiotics

Psychobiotics are a class of probiotics that exert beneficial effects on mental health through their influence on the microbiota–gut–brain axis (34). The most extensively studied

strains belong to the genera Lactobacillus and Bifidobacterium. Proposed mechanisms include modulation of inflammatory signalling, improvement of barrier function, regulation of HPA-axis activity, changes in tryptophan metabolism, increased SCFA production and effects on vagal signalling.

Clinical studies have demonstrated that certain psychobiotic formulations may reduce symptoms of depression and anxiety, most likely through the modulation of inflammatory pathways, regulation of the hypothalamic–pituitary–adrenal (HPA) axis, and effects on neurotransmitter systems (23,24). These strategies are biologically plausible, but stronger clinical trials are needed before they can be recommended as standard treatment for major depressive disorder.

Diet and Nutritional Interventions

Diet is one of the most important factors influencing the composition and function of the gut microbiota. Diets rich in dietary fibre, polyphenols, legumes, fruit, vegetables, whole grains, nuts, fermented foods and unsaturated fats are associated with greater microbial diversity and increased SCFA production. The Mediterranean diet has been associated with greater microbial diversity, increased production of short-chain fatty acids, and reduced systemic inflammation (26, 28).

In contrast, a Western-style diet, characterized by high consumption of processed foods, saturated fats, and refined sugars, has been linked to a higher prevalence of dysbiosis and inflammatory alterations. Growing evidence suggests that nutritional interventions may contribute to the improvement of depressive symptoms in selected patient populations (24,25).

The SMILES trial provided important clinical evidence that structured dietary improvement can reduce depressive symptoms in adults with major depression (39). This does not prove that the benefit was mediated exclusively through microbiota-related pathways, but it supports the relevance of nutritional psychiatry. Lifestyle factors such as physical activity, sleep regularity and stress reduction may also influence the microbiota-gut-brain axis and should be considered within an integrated clinical approach.

Fecal Microbiota Transplantation

Fecal microbiota transplantation (FMT) represents one of the most recent therapeutic strategies aimed at restoring microbial homeostasis and correcting dysbiosis. Although the results of experimental studies appear promising, current evidence remains insufficient to support the

routine clinical use of FMT in the treatment of depression. Further well-designed randomized controlled trials are required to establish its efficacy, safety, and long-term clinical benefits.

Table 3. Potential microbiota-targeted interventions in depression

Intervention	Proposed mechanisms	Current clinical status
Psychobiotics	Immune modulation, HPA-axis regulation, vagal signalling, tryptophan metabolism, SCFA production	Promising but strain-specific; mainly adjunctive and investigational
Prebiotics / synbiotics	Stimulation of beneficial microbial activity and SCFA-producing microbial profiles	Biologically plausible; evidence still heterogeneous
Postbiotics	Direct effects of microbial metabolites or inactivated microbial products	Emerging field; limited psychiatric trials
Mediterranean-style diet	Higher fibre and polyphenol intake, greater microbial diversity, reduced inflammation	Best supported lifestyle approach; should be integrated with standard care
FMT	Direct ecosystem-level microbiota replacement	Experimental in psychiatry; not recommended for routine treatment of depression
Medication-microbiota profiling	Prediction or monitoring of antidepressant response	Translational potential; not yet clinically established

LIMITATIONS OF CURRENT EVIDENCE AND FUTURE RESEARCH DIRECTIONS

Despite rapid progress, several limitations constrain interpretation of the microbiota-depression literature. First, many human studies are cross-sectional and cannot establish temporal or causal relationships. Second, microbiome findings are sensitive to sampling procedures, sequencing platforms, bioinformatic pipelines and statistical approaches. Third, depression is clinically heterogeneous, and microbiota alterations may differ across inflammatory, melancholic, atypical, anxious and treatment-resistant subtypes. Fourth, confounders such as diet, medication, body mass index, smoking, alcohol use, physical activity, sleep and comorbid disease are difficult to control completely.

A further challenge is the distinction between taxonomic and functional findings. Two individuals may have different microbial profiles but similar metabolic functions, or apparently similar microbial profiles with different functional output. Future studies should therefore combine metagenomics, metabolomics, immune profiling, neuroendocrine markers, neuroimaging and detailed clinical phenotyping. Longitudinal designs are particularly important for determining whether dysbiosis precedes depressive episodes, follows depressive behaviour, reflects treatment exposure or changes during recovery.

Future research should focus on the identification of specific microbiota-based biomarkers of depression, the development of personalized therapeutic strategies, and the application of advanced metagenomic and metabolomic technologies. Particular importance should be given to large-scale, multicenter longitudinal studies that would enable a more precise understanding of the causal relationships between dysbiosis and depression. Such investigations may provide valuable insights into the underlying biological mechanisms of the disorder and facilitate the development of novel diagnostic and therapeutic approaches targeting the microbiota–gut–brain axis. Microbiota-targeted interventions are unlikely to be equally effective for all patients. The strongest candidates may be patients with gastrointestinal symptoms, elevated inflammatory markers, metabolic syndrome, poor diet quality, recent antibiotic exposure or partial response to standard treatment. In this context, the microbiota-gut-brain axis is most useful not as a universal explanation of depression, but as one component of personalized and mechanism-based psychiatry.

CONCLUSION

The microbiota–gut–brain axis represents a complex regulatory network that links the gastrointestinal tract, intestinal microbiota and the central nervous system through neural, immune, endocrine, metabolic, and barrier-related mechanism. Available evidence suggests that alterations in the intestinal microbiota may contribute to the development of depression through mechanisms involving intestinal barrier dysfunction, neuroinflammation, hypothalamic–pituitary–adrenal (HPA) axis dysregulation, altered tryptophan-kynurenine metabolism, and decreased neuroplasticity.

Microbiota alterations should not be interpreted as a universal or independent cause of depression. Nevertheless, the microbiota-gut-brain axis provides a coherent biological framework for integrating somatic, immune, metabolic and affective dimensions of depressive disorders. Microbiota-targeted strategies, including psychobiotics, prebiotics, synbiotics, dietary interventions and, in selected research settings, FMT, may become useful adjunctive approaches. Although further research is required to achieve a more comprehensive understanding of these mechanisms, modulation of the gut microbiota represents one of the most promising strategies for the development of novel diagnostic and therapeutic approaches in contemporary psychiatry.

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APPENDIX