SEVEN publicações acadêmicas

THE INFLUENCE OF THE MICROBIOTA–GUT–BRAIN AXIS ON MENTAL HEALTH AND INTESTINAL HEALTH

A INFLUÊNCIA DO EIXO MICROBIOTA–INTESTINO– CÉREBRO NA SAÚDE MENTAL E NA SAÚDE INTESTINAL

LA INFLUENCIA DEL EJE MICROBIOTA-INTESTINO-CEREBRO EN LA SALUD MENTAL Y LA SALUD INTESTINAL

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ABSTRACT

Background: The microbiota–gut–brain axis (MGBA) represents a complex communication network integrating neural, immune, endocrine, and metabolic systems, critically linking intestinal health to mental health. Scientific literature has consistently demonstrated that the gut microbiota plays a regulatory role in neurotransmitter synthesis, modulation of neuroinflammation, and significantly influences cognitive function and emotional state. Objective: This study aims to provide a comprehensive and critical review of the biological and dietary mechanisms that affect the functionality of the microbiota–gut–brain axis. Additionally, it seeks to explore the potential of dietary interventions as adjunct therapeutic tools in the management of neuropsychiatric disorders. Methods: A review of scientific evidence published between 2017 and 2024 was conducted. The databases consulted included PubMed, SciELO, and Scopus. Inclusion criteria encompassed articles in English and Portuguese addressing the relationship between gut microbiota, diet, and mental health, with a focus on systematic reviews, clinical trials, and experimental studies. Results: The literature review highlighted the significant impact of the Mediterranean diet and the regular intake of prebiotics and probiotics as promoters of mental health through positive modulation of the MGBA. In contrast, the deleterious effects of the Western diet—characterized by high intake of processed foods, saturated fats, and sugars— on mental health were noted,

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frequently associated with gut dysbiosis and increased neuroinflammation.Conclusions: Modulating the gut microbiota through dietary strategies emerges as a promising and relevant approach in the context of mental health. A deeper understanding of the mechanisms involved in the MGBA is essential for the development of personalized and effective nutritional interventions in the prevention and complementary treatment of neuropsychiatric disorders.

Keywords: Gut Microbiota. Mental Health. Microbiota–Gut–Brain Axis. Diet. Dysbiosis. Neuroinflammation.

RESUMO

Contexto: O eixo microbiota–intestino–cérebro (EMIC) representa uma complexa rede de comunicação que integra sistemas neurais, imunológicos, endócrinos e metabólicos, conectando de forma essencial a saúde intestinal à saúde mental. A literatura científica tem consistentemente evidenciado que a microbiota intestinal desempenha um papel regulador na síntese de neurotransmissores, na modulação da neuroinflamação e exerce influência significativa sobre a função cognitiva e o estado emocional. Objetivo: Este estudo tem como objetivo principal realizar uma revisão crítica e abrangente dos mecanismos biológicos e dietéticos que interferem na funcionalidade do eixo microbiota-intestino-cérebro. Adicionalmente, busca explorar o potencial de intervenções alimentares como ferramentas terapêuticas adjuvantes no manejo de transtornos neuropsiquiátricos. Métodos: Foi conduzida uma análise de evidências científicas publicadas no período compreendido entre 2017 e 2024. As bases de dados consultadas incluíram PubMed, SciELO e Scopus. Os critérios de inclusão contemplaram artigos em inglês e português que abordam a relação entre microbiota intestinal, dieta e saúde mental, priorizando revisões sistemáticas, ensaios clínicos e estudos experimentais. Resultados: A análise da literatura destacou o impacto significativo da dieta mediterrânea, do consumo regular de prebióticos e probióticos como fatores promotores da saúde mental através da modulação positiva do EMIC. Em contrapartida, foram observados os efeitos deletérios associados à dieta ocidental, caracterizada pelo alto consumo de alimentos processados, gorduras saturadas e açúcares, sobre a saúde mental, frequentemente correlacionados com disbiose intestinal e aumento da neuroinflamação. Conclusões: A modulação da microbiota intestinal por meio de estratégias dietéticas apresenta-se como uma abordagem promissora e relevante no contexto da saúde mental. A compreensão aprofundada dos mecanismos envolvidos no EMIC é fundamental para o desenvolvimento de intervenções nutricionais personalizadas e eficazes na prevenção e tratamento complementar de transtornos neuropsiquiátricos.

Palavras-chave: Microbiota Intestinal. Saúde Mental. Eixo Microbiota–Intestino–Cérebro. Dieta. Disbiose. Neuroinflamação.

RESUMEN

Contexto: El eje microbiota-intestino-cerebro (EMIC) representa una compleja red de comunicación que integra sistemas neurales, inmunológicos, endocrinos y metabólicos, conectando de manera esencial la salud intestinal con la salud mental. La literatura científica ha evidenciado consistentemente que la microbiota intestinal desempeña un papel regulador en la síntesis de neurotransmisores, en la modulación de la neuroinflamación y ejerce una influencia significativa sobre la función cognitiva y el estado emocional. Objetivo: Este estudio tiene como objetivo principal realizar una revisión crítica y exhaustiva de los mecanismos biológicos y dietéticos que interfieren en la funcionalidad del eje microbiota-intestino-cerebro. Adicionalmente, busca explorar el potencial de las intervenciones alimentarias como herramientas terapéuticas coadyuvantes en el manejo de trastornos neuropsiquiátricos. Métodos: Se condujo un análisis de evidencias científicas publicadas en el período comprendido entre 2017 y 2024. Las bases de datos consultadas incluyeron PubMed, SciELO y Scopus. Los criterios de inclusión contemplaron artículos en inglés y portugués que abordan la relación entre microbiota intestinal, dieta y salud mental, priorizando revisiones sistemáticas, ensayos clínicos y estudios experimentales. Resultados: El análisis de la literatura destacó el impacto significativo de la dieta mediterránea, del consumo regular de prebióticos y probióticos como factores promotores de la salud mental a través de la modulación positiva del EMIC. En contrapartida, se observaron los efectos deletéreos asociados a la dieta occidental, caracterizada por el alto consumo de alimentos procesados, grasas saturadas y azúcares, sobre la salud mental, frecuentemente correlacionados con disbiosis intestinal y aumento de la neuroinflamación. Conclusiones: La modulación de la microbiota intestinal mediante estrategias dietéticas se presenta como un abordaje prometedor y relevante en el contexto de la salud mental. La comprensión profunda de los mecanismos involucrados en el EMIC es fundamental para el desarrollo de intervenciones nutricionales personalizadas y eficaces en la prevención y tratamiento complementario de trastornos neuropsiquiátricos.

Palabras clave: Microbiota Intestinal. Salud Mental. Eje Microbiota-Intestino-Cerebro. Dieta. Disbiosis. Neuroinflamación.

1 INTRODUCTION

The intrinsic and dynamic connection between the gut and the brain, widely recognized in the scientific literature as the microbiota–gut–brain (EMIC) axis, has emerged as a research area of increasing relevance and impact in the health sciences. Recent and robust studies have consistently pointed out that the microbial community residing in the gut, the gut microbiota, not only plays crucial roles in digestive processes and in modulating the immune system, but also plays an essential and direct role in regulating behavior, cognitive functions, mood, and, consequently, overall mental health. This complex bidirectional communication is orchestrated through multiple interconnected pathways, which include direct neural pathways, such as afferent and efferent signaling through the vagus nerve, immune mechanisms involving cytokines and immune cells, hormonal pathways mediated by gut hormones and the hypothalamic-pituitary-adrenal (HPA) axis, and metabolic pathways, through the production of microbial metabolites such as short-chain fatty acids (SCFAs) and neurotransmitters (Berding et al., 2021).

In this multifaceted scenario, diet plays a central and decisive role, positioning itself as one of the main environmental factors capable of modulating the composition and functionality of the gut microbiota. Food choices can induce a state of microbial balance, known as eubiosis, characterized by a high diversity and predominance of beneficial species, or, conversely, promote an imbalance, called dysbiosis. Gut dysbiosis has been consistently associated with significant clinical repercussions, including increased intestinal permeability, chronic low-grade inflammation, and alterations in neuromodulator production, factors that are implicated in the development and exacerbation of a variety of neuropsychiatric disorders, such as major depression, anxiety disorders, schizophrenia, and autism spectrum disorders. The in-depth understanding of the influence of diet on EMIC therefore opens new perspectives for the development of nutrition-focused preventive and therapeutic strategies for the promotion of mental health (Gantenbein; Kanaka-Gantenbein, 2021).

2 OBJECTIVE

The main objective of the present study is to critically analyze the available scientific literature regarding the multifaceted mechanisms by which the gut microbiota influences mental health. The research will place particular emphasis on dietary modulation as a key factor in the interaction of the microbiota-gut-brain axis, the underlying pathophysiological factors involved in this complex communication, and nutritional strategies that demonstrate therapeutic potential in the management and prevention of neuropsychiatric disorders.

3 METHODS

This study is characterized as a systematic review of the scientific literature, conducted to analyze the interrelationship between gut microbiota, dietary patterns and mental health. Data collection was carried out through comprehensive searches in the PubMed, SciELO and Scopus databases, recognized for their scientific rigor and breadth of indexing. The search period included publications between 2017 and 2024, ensuring the inclusion of current and relevant scientific evidence on the topic investigated.

The search strategy resulted in the initial identification of 50 articles, of which 20 fully met the eligibility criteria and were included in the qualitative synthesis of this review. The inclusion criteria included: original and review publications in English and Portuguese; studies that directly addressed the relationship between gut microbiota, diet, and mental health; systematic reviews with or without meta-analysis; randomized controlled trials; and experimental studies (in vivo and in vitro) that investigated mechanisms of action in the areas of nutrition, psychiatry, microbiology and neurosciences.

The following were excluded from the analysis: opinion articles, editorials, letters to the editor, isolated case reports, studies with inadequately described methodology, and studies whose outcomes were not directly relevant to the scope of this review. The selection of studies was conducted independently by two reviewers, with divergences resolved by consensus, ensuring the methodological quality and reliability of the results presented.

4 RESULTS AND DISCUSSION

4.1 THE GUT MICROBIOTA: DEFINITION AND ESSENTIAL FUNCTIONS

The gut microbiota is made up of a vast and diverse community of trillions of microorganisms, which includes bacteria, archaea, fungi, viruses, and protozoa. These microorganisms coexist with the human host in a complex symbiotic relationship, predominantly colonizing the large intestine. This microbial community plays a fundamental and multifaceted role in the maintenance of human health, with a crucial role in the digestion of food components that are not digestible by the host, in the metabolism of nutrients and xenobiotics, in the maturation and modulation of the immune system and, in an increasingly evident way, in the regulation of central nervous system functions (Berding et al., 2021).

From the earliest moments of life, the composition of the gut microbiota is dynamically shaped by an intricate interaction of intrinsic to the host and extrinsic factors from the environment. These factors exert a profound and lasting influence on the immunological, metabolic and neurological development of the individual. Among the most impactful determinants of initial colonization is the type of delivery. Vaginal delivery facilitates the vertical transmission of microorganisms from the maternal vaginal and fecal microbiota, such as species of the genera Lactobacillus and Bifidobacterium, which are pioneers in the establishment of a healthy and resilient intestinal ecosystem. On the other hand, birth by cesarean section often results in an initial colonization dominated by microorganisms from the skin and the hospital environment, such as Staphylococcus and Corynebacterium, associated with lower microbial diversity in the early stages of life (Adak; Khan, 2019).

Feeding during the neonatal period represents another factor with a substantial impact. Exclusive breastfeeding is recognized for providing a rich variety of prebiotic substrates, notably human milk oligosaccharides (HMOs), which promote

growth of beneficial bacteria, with special emphasis on Bifidobacterium species. On the other hand, the use of infant formulas has been associated with a distinct intestinal colonization profile, sometimes with a greater abundance of potentially pathogenic microorganisms, such as certain species of Clostridium and Enterobacter (Järbrink-Sehgal; Andreasson, 2020).

Around three to five years of age, the gut microbiota tends to reach a state of greater stability, acquiring compositional and functional characteristics that resemble those observed in adult individuals. Among the microorganisms with widely recognized beneficial roles, the genera Lactobacillus and Bifidobacterium stand out, considered crucial for the maintenance of intestinal homeostasis. Species such as Lactobacillus acidophilus, L. casei, L. rhamnosus and L. plantarum actively contribute to strengthening the barrier function of the intestinal mucosa, participate in the regulation of the local and systemic immune system, and modulate the microbiota itself. These effects are mediated, in part, by the increased expression of intercellular occlusive junction proteins, such as occludin, and by the reduction of inflammatory processes through cytokine modulation, such as the increase in IL-10 and the decrease in IL-17. In addition, they demonstrate positive metabolic impacts, including improved insulin sensitivity and reduced circulating levels of bacterial lipopolysaccharides (LPS), a potent inflammatory inducer, especially evidenced in experimental models of high-fat diets. The species Bifidobacterium bifidum and B. longum, often prevalent in the intestines of infants, are notable for their ability to ferment complex dietary fibers, resulting in the production of short-chain fatty acids (SCFAs). These SCFAs exert anti-inflammatory and trophic effects on the intestinal mucosa, modulate dendritic cell activity, induce regulatory T cell differentiation (Treg), reduce the production of pro-inflammatory cytokines such as IL-6 and IL-1β, protect the integrity of the intestinal mucus layer, and positively influence the communication pathways of the gut-brain axis, with beneficial effects on behavior and cognitive function (Bremner et al., 2020).

In contrast, microorganisms such as those of the genera Staphylococcus and Corynebacterium, although common in the skin microbiota and considered commensal under normal conditions, may exhibit pathogenic behavior under certain circumstances, such as in cases of dysbacteriosis or impairment of the epithelial barrier, as observed in chronic wounds. Staphylococcus epidermidis, a usual healthy skin inhabitant, participates in local immune modulation and stimulates the production of antimicrobial peptides such as perforin-2, aiding in defense against pathogens such as S. aureus. However, Staphylococcus aureus, particularly certain strains, is strongly associated with chronic infections, such as diabetic foot ulcers. The genus Corynebacterium also includes species implicated in antimicrobial resistance processes and prolonged inflammation, such as C. striatum and C. jeikeium, which can modulate the immune response through the interleukin-23 (IL-23) pathway (Qiu et al., 2022).

In preterm infants, the gut microbiota exhibits particular characteristics. Studies show that, in the first weeks of life, there is a predominance of facultative aerobic and anaerobic microorganisms, such as Enterobacter and Clostridium. Clostridium colonization (particularly cluster I) demonstrated an increase from 16.1% in the first week to 41% in the fourth week in preterm newborns, a phenomenon more pronounced in babies born by cesarean section. This pattern may reflect the influence of the hospital environment, such as neonatal intensive care units (NICUs), and early exposure to antibiotic therapy, which can reduce bacterial diversity and favor the growth of opportunistic microorganisms. Enterobacter cloacae, in turn, was highly prevalent from the second week of life in preterm infants, reaching high mean counts (Góralczyk-Bińkowska; Szmajda-Krygier; Kozłowska, 2022).

The diversity and composition of the gut microbiota are dynamic and vary throughout the individual's life, being continuously modulated by a myriad of factors, including diet, the use of medications (especially antibiotics), the aging process, the presence of underlying diseases, levels of psychosocial stress, and environmental conditions. The predominant bacterial phyla in the healthy human gut include Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, Verrucomicrobia, and, to a lesser extent, Cyanobacteria. Of these, Firmicutes and Bacteroidetes generally represent the highest relative abundance in the microbiota of healthy individuals (Wang; Yang; Liu, 2023).

The phylum Firmicutes is largely represented by bacteria with strong fermentative capacity, such as the genera Lactobacillus, Clostridium (many commensal species) and Faecalibacterium. These microorganisms play an essential role in the fermentation of non-digestible complex carbohydrates and the subsequent production of SCFAs, such as butyrate, a metabolite crucial for the nutrition of colonocytes, the maintenance of intestinal mucosal integrity, and the modulation of the inflammatory response. An increase in the ratio of Firmicutes to Bacteroidetes has been associated, in some contexts, with greater efficiency in extracting energy from the diet, and is a finding frequently observed in individuals with obesity (Clemente-Suárez et al., 2023).

The phylum Bacteroidetes is also a predominant component of the human gut microbiota and plays relevant roles in the degradation of dietary fibers and complex polysaccharides. The balance between the populations of Firmicutes and Bacteroidetes is often considered an important marker of intestinal eubiosis. High-fiber diets tend to favor a higher proportion of Bacteroidetes, which generally correlates with a healthier metabolic profile (Marx et al., 2021).

Despite being less abundant compared to Firmicutes and Bacteroidetes, the phylum Actinobacteria plays a relevant role, especially during the first years of life. It is primarily represented by the genus Bifidobacterium, known for its ability to produce SCFAs, modulate the immune system, and protect against colonization by intestinal pathogens (Vahid et al., 2023).

The phylum Proteobacteria, although present in low proportions in healthy individuals, may have its abundance increased in situations of dysbiosis. An increase in the population of Proteobacteria is often considered indicative of microbial community instability and has been linked to inflammatory states and several pathological conditions, such as inflammatory bowel disease (ulcerative colitis), obesity, type 2 diabetes, and gastrointestinal cancer (Merlo; Bachtel; Sugden, 2024).

The bacteria of the phylum Fusobacteria are predominantly obligate anaerobic, typically found in low concentrations in the oral cavity and gastrointestinal tract. Under conditions of equilibrium, they participate in metabolic functions. However, the excessive proliferation of certain species of Fusobacteria, such as Fusobacterium nucleatum, has been associated with intestinal inflammatory disorders and the development and progression of colorectal neoplasms (Ljungberg; Bondza; Lethin, 2020).

The phylum Verrucomicrobia, although it represents a minority fraction of the microbiota, performs significant functions, and its main representative is the bacterium Akkermansia muciniphila. This species specializes in the degradation of mucin, the main component of the intestinal mucus layer, a process that promotes the renewal of the epithelial barrier and contributes to the control of inflammatory processes. The presence of A. muciniphila has been linked to improved insulin sensitivity, the maintenance of healthy body weight, and the reduction of chronic intestinal inflammations (Azad et al., 2018).

The phylum Cyanobacteria, on the other hand, is rarely detected in the human gut microbiota under normal conditions, and its presence is usually associated with environmental exposure or ingestion of contaminated water or food (Patel et al., 2022).

The gut microbiota can be classified into general profiles or enterotypes, based on the predominance of certain bacterial genera, such as Bacteroides (often associated with diets rich in animal proteins and fats), Prevotella (more related to the consumption of complex carbohydrates and vegetable fibers) and Ruminococcus (involved in the degradation of mucins and polysaccharides). It is important to note that these profiles are not fixed and may undergo modifications in response to changes in lifestyle, particularly in diet (Itani et al., 2017).

In addition to taxonomic diversity, the variation in the anatomical distribution of the microbiota along the gastrointestinal tract stands out. The stomach, due to its acidic pH, has a low microbial density, with a prevalence of acidotolerant bacteria such as Lactobacillus, Streptococcus and, in some individuals, Helicobacter pylori. In the small intestine, microbial density gradually increases from the proximal to the distal portion, with a predominance of genera such as Lactobacillus and Enterococcus. The large intestine, in turn, is home to the highest density and diversity of microorganisms, with a predominantly anaerobic environment that favors the growth of bacteria such as Bacteroides, Clostridium, Faecalibacterium, and Ruminococcus (Canyelles et al., 2023).

Functionally, the gut microbiota plays a central role in the fermentation of dietary fibers and non-digestible carbohydrates, resulting in the production of SCFAs, mainly acetate, propionate, and butyrate. These metabolites are vital for the health of the host: butyrate is the main source of energy for colonocytes; Acetate and propionate are absorbed and used in other tissues. Collectively, SCFAs contribute to the reduction of inflammatory processes, modulate blood glucose and lipogenesis, and have been associated with reduced risk of developing colorectal cancer (QIU et al., 2022). The digestion of proteins by the microbiota also generates a variety of compounds, some bioactive such as polyamines and neurotransmitter precursors, and others potentially toxic in high concentrations, such as ammonia, phenols, and cresols (Olvera-Rosales et al., 2021).

The gut microbiota also plays a crucial role in lipid metabolism, including the transformation of primary bile acids into secondary ones, which act as signaling molecules. In addition, it participates in the conversion of various dietary compounds, such as polyphenols and choline. The metabolism of choline by the gut microbiota can result in the production of trimethylamine (TMA), which is subsequently converted in the liver to trimethylamine N-oxide (TMAO), a molecule that has been linked to increased cardiovascular risk in some studies. In addition, the microbiota is essential for maintaining the integrity of the intestinal epithelial barrier, stimulating the production of mucus and intercellular junction proteins (such as ZO-1, occludin, and claudiins), thus preventing increased intestinal permeability (a phenomenon known as "leaky gut"), which is implicated in the pathogenesis of several inflammatory, autoimmune, and metabolic diseases (Socała et al., 2021).

Trimethylamine N-oxide (TMAO) is a metabolite produced in the liver from trimethylamine (TMA), which is generated in the intestine by the action of microbial enzymes on dietary nutrients such as choline, L-carnitine, and betaine – compounds abundant in foods such as red meat, eggs, fish, and dairy products. The liver enzyme flavin monooxygenase 3 (FMO3) is responsible for the conversion of TMA to TMAO, which is subsequently excreted by the kidneys. Elevated levels of circulating TMAO have been consistently associated in epidemiological studies with an increased risk of atherosclerotic cardiovascular events. However, the direct causal relationship and precise mechanisms are still the subject of intense investigation, especially considering the role of renal function in regulating TMAO levels. Functionally, it is suggested that TMAO may favor atherosclerotic processes by promoting the formation of foamy cells in blood vessels, reducing reverse cholesterol transport, altering bile acid metabolism, and decreasing the bioavailability of endothelial nitric oxide. In addition, TMAO has been implicated in the stimulation of vascular inflammation, increased platelet reactivity and aggregation, and activation of the NLRP3 inflammasome, contributing to endothelial dysfunction and increased vascular permeability (Liu; Zhu; Yang, 2024).

The complex relationship between the gut microbiota and the nervous system is mediated by a diversity of interconnected mechanisms. These include the direct production of neurotransmitters by the microbiota (such as serotonin, GABA, dopamine, norepinephrine, and acetylcholine), the regulation of the hypothalamic-pituitary-adrenal (HPA) axis and, consequently, of the stress response, and the modulation of neuroinflammation. Significant changes in the composition and functionality of the gut microbial community (dysbiosis) have been consistently associated with a variety of neuropsychiatric conditions, including major depression, anxiety disorders, autism spectrum disorder, and neurodegenerative diseases such as Alzheimer's disease. Translational and clinical studies have shown, for example, that the administration of specific probiotic strains, such as Bifidobacterium longum, can exert anxiolytic and antidepressant effects, as observed in patients with irritable bowel syndrome (Gantenbein; Kanaka-Gantenbein, 2021).

The composition of the gut microbiota is also influenced by genetic factors of the host. Studies with monozygotic and dizygotic twins indicate that a portion of the variation in the microbiota can be inherited, with emphasis on the heritability of certain bacterial families, such as Christensenellaceae, which has been associated with the maintenance of a lean body mass index. Geographical, cultural, and lifestyle factors also exert a significant influence on microbial diversity and composition. Populations that maintain traditional lifestyles and high-fiber diets, such as some indigenous communities, often have greater microbial diversity compared to populations in urbanized and industrialized societies, who consume Westernized diets (Gantenbein; Kanaka-Gantenbein, 2021).

Disturbances in the composition and function of the gut microbiota – a state known as dysbiosis – are strongly implicated in the pathogenesis and progression of inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis. Under these conditions, a reduction in overall microbial diversity (alpha-diversity), an imbalance in the proportion of different bacterial phyla, and the predominance of species with pro-inflammatory or pathogenic potential, such as adherent-invasive strains of Escherichia coli (AIEC) and certain species of Ruminococcus gnavus, are often observed. Concomitantly, there is a decrease in the abundance of species considered beneficial and SCFA-producing, such as Faecalibacterium prausnitzii and Bifidobacterium longum (Berding et al., 2021).

Table 1

Bacterial species, predominant location and functions in the EMIC

Espécie/Gênero	Localização Predominante	Funções Principais
Lactobacillus acidophilus	Intestino delgado e grosso	Fortalecimento da barreira intestinal, regulação imune, produção de ácidos graxos de cadeia curta (SCFAs), modulação da microbiota
Lactobacillus casei	Intestino delgado e grosso	Regulação imunológica, melhora da integridade epitelial, efeito anti-inflamatório
Lactobacillus rhamnosus	Intestino delgado e grosso	Modulação da microbiota, aumento das proteínas de junção epitelial, efeitos metabólicos positivos
Lactobacillus plantarum	Intestino grosso	Redução de lipopolissacarídeos (LPS), aumento de IL-10 e IL-17, melhora da sensibilidade à insulina
Bifidobacterium bifidum	Intestino grosso (lactentes)	Produção de SCFAs, fermentação de fibras, modulação imune, proteção da mucosa intestinal
Bifidobacterium longum	Intestino grosso	Produção de SCFAs, indução de células T reguladoras (Tregs), efeito positivo no eixo intestino-cérebro
Faecalibacterium prausnitzii	Intestino grosso	Produção de butirato, efeito anti-inflamatório, manutenção da integridade epitelial

Espécie/Gênero	Localização Predominante	Funções Principais
Clostridium spp. (cluster I)	Intestino grosso (principalmente prematuros)	Produção de SCFAs, fermentação de carboidratos; em excesso, pode estar associado à disbiose
Ruminococcus spp.	Intestino grosso	Degradação de mucinas, produção de SCFAs, associado ao enterótipo *Ruminococcus*
Staphylococcus epidermidis	Pele (ocasionalmente intestino)	Modulação imune, proteção contra patógenos na pele
Staphylococcus aureus	Pele / intestino (em patologias)	Associado a infecções, inflamação, aumento de IL-23; presente especialmente em feridas crônicas
Corynebacterium spp.	Pele / intestino (prematuros ou disbiose)	Indução de inflamação prolongada, resistência antimicrobiana, modulação de IL-23
Enterobacter cloacae	Intestino de neonatos prematuros	Colonizador inicial, oportunista, frequente em unidades de terapia intensiva neonatal (UTIN)
Escherichia coli (AIEC)	Intestino grosso (disbiose, DII)	Espécie patogênica associada à Doença de Crohn, inflamação, comprometimento da barreira intestinal
Christensenellaceae (família)	Intestino grosso	Associada à magreza, influência genética na composição da microbiota
Prevotella spp.	Intestino grosso	Associada a dietas ricas em fibras, produção de SCFAs
Bacteroides spp.	Intestino grosso	Degradação de polissacarídeos; associado a dietas ricas em proteínas e gorduras
Akkermansia muciniphila	Intestino grosso (camada de muco)	Degradação de mucina, renovação epitelial, melhora da sensibilidade à insulina, efeito anti-inflamatório

Source: Prepared by the authors, 2025.

4.2 THE MICROBIOTA–GUT–BRAIN AXIS (EMIC): BIDIRECTIONAL COMMUNICATION PATHWAYS

The microbiota–gut–brain (EMIC) axis represents a fundamental two-way communication paradigm, which intricately interconnects the central nervous system (CNS), the enteric nervous system (ENS) – often referred to as the "second brain" – the gastrointestinal tract (GIT) and the vast community of microorganisms that reside within it, the gut microbiota. This complex signaling network is crucial for maintaining homeostasis It profoundly influences a myriad of processes, including digestive function, immune response, energy metabolism, and, increasingly recognized, behavior, mood, cognition and mental health (Adak; Khan, 2019).

Communication along the EMIC occurs through multiple parallel and interconnected pathways, which can be broadly categorized into:

Neural Pathways: The main neural pathway is the vagus nerve, which forms a direct link between the brain and the gut. Approximately 80-90% of vagus nerve fibers are afferent, transmitting sensory information from the intestinal lumen (including microbiota-derived signals such as metabolites and cellular components) to the CNS, specifically to the nucleus of the solitary tract in the brainstem. This information is subsequently processed in higher brain regions involved in regulating mood, stress, and behavior. The efferent pathways of the vagus, in turn, allow the CNS to modulate gastrointestinal motility, secretions, and local inflammatory response, indirectly influencing the environment and the composition of the microbiota (JÄRBRINK-SEHGAL; ANDREASSON, 2020).

Immune Pathways: The gut microbiota plays a coevolutionary role in the maturation and modulation of the host immune system. Microbial components, such as lipopolysaccharides (LPS) from gram-negative bacteria, peptidoglycans, and flagellin, are recognized by pattern recognition receptors (PRRs), such as toll-like receptors (TLRs), expressed on intestinal epithelial cells and immune cells residing in the lamina propria. This interaction triggers the production of pro-inflammatory (e.g., TNF-α, IL-1β, IL-6) or anti-inflammatory (e.g., IL-10) cytokines, which can have local effects in the gut or enter the systemic circulation and cross the blood-brain barrier (BBB), or signal through it, influencing neuroinflammation, glial function, and neurotransmission. Gut dysbiosis and increased gut permeability ("leaky gut") can lead to an increased translocation of microbial components and a state of chronic low-grade inflammation, implicated in the pathophysiology of depressive and anxiety disorders (Bremner et al., 2020).

Endocrine and Metabolic Pathways: the gut microbiota produces a wide range of metabolites from the fermentation of dietary components, mainly fiber. Short-chain fatty acids (SCFAs) – acetate, propionate and butyrate – are the most studied. Butyrate is the main source of energy for colonocytes and has potent anti-inflammatory effects, as well as strengthening the intestinal barrier. Acetate and propionate can cross BBB and influence brain function, including neuroinflammation and neuropeptides expression. SCFAs can also signal through G-protein-coupled receptors (GPCRs), such as GPR41, GPR43, and GPR109A, expressed in enteroendocrine cells, immune cells, and even the brain (Qiu et al., 2022).

Neurotransmitters and their Precursors: Gut bacteria are able to synthesize and/or modulate the availability of several neurotransmitters and their precursors, including serotonin (5-HT), gamma-aminobutyric acid (GABA), dopamine, norepinephrine, and acetylcholine. For example, approximately 90% of the body's serotonin is produced by enterochromaffin cells in the gut, and the microbiota can influence its synthesis and release. Tryptophan, an essential amino acid precursor of serotonin, is metabolized by the microbiota via the kynurenine pathway, whose metabolites (e.g., kynurenic acid, quinolinic acid) have neuromodulatory activity and have been implicated in psychiatric disorders (Góralczyk-Bińkowska; Szmajda-Krygier; Kozłowska, 2022).

Gut Hormones and Hypothalamic-Pituitary-Adrenal (HHA) Axis: The microbiota can influence the release of gut hormones (e.g., peptide YY, GLP-1) that signal to the brain, regulating appetite and metabolism. In addition, EMIC interacts with the HHA axis, the body's main stress response system. Studies in germ-free animals (without microbiota) demonstrate an exaggerated response to stress, which may be partially normalized by microbial colonization. Dysbiosis has been associated with dysregulation of the HPA axis, with changes in cortisol levels, a risk factor for depression and anxiety (Wang; Yang; Liu, 2023).

Intestinal Barrier and Blood-Brain Barrier: The integrity of the intestinal barrier is crucial to prevent the translocation of microorganisms and their products into the systemic circulation. The microbiota contributes to the maintenance of this barrier. Gut barrier dysfunction ("leaky gut") is associated with systemic inflammation and has been linked to blood-brain barrier (BBB) dysfunction, increasing the brain's vulnerability to inflammatory insults and toxins, which may contribute to the development of neuropsychiatric disorders (Clemente-Suárez et al., 2023).

The growing understanding of these complex communication pathways has driven research on the therapeutic potential of modulating the gut microbiota, through probiotics, prebiotics, synbiotics, fecal microbiota transplantation (FMT), and dietary interventions, as a new frontier in the treatment and prevention of mental disorders. However, the research is still evolving, and more human studies are needed to fully elucidate the mechanisms and establish the clinical efficacy of these approaches.

Table 2

EMIC communication routes and their functions

Via de Comunicação	Função no EMIC
Neural (Nervo Vago)	Conecta intestino e cérebro; 80–90% das fibras são aferentes; regula humor, apetite e motilidade
Imunológica	Microbiota interage com TLRs → ativa citocinas (IL-6, IL-10, TNF-α); disbiose → neuroinflamação
Metabólica	Produção de AGCC → efeitos anti-inflamatórios, nutrição de colonócitos, influência na BHE
Neuroquímica	Microbiota sintetiza neurotransmissores (GABA, dopamina, serotonina); modulam comportamento e humor
Endócrina (Eixo HHA)	Influência no cortisol e resposta ao estresse; microbiota regula liberação de GLP-1, PYY
Barreiras Biológicas	Microbiota mantém integridade da barreira intestinal e BHE; disbiose → aumento da permeabilidade ("leaky gut")

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Barreiras Biológicas	Microbiota mantém integridade da barreira intestinal e BHE; disbiose → aumento da permeabilidade ("leaky gut")

Source: Prepared by the authors, 2025.

4.3 THE INFLUENCE OF DIET ON MICROBIOTA AND MENTAL HEALTH

Diet is recognized as one of the most potent and dynamic modulators of the composition and functionality of the gut microbiota. Daily food choices can induce significant changes in the gut microbial ecosystem over short periods, influencing the relative abundance of different bacterial taxa, the overall diversity of the microbiota, and its metabolic profile. These changes, in turn, have profound implications for host health, including mental health, through the communication mechanisms of the microbiota-gut-brain (EMIC) axis (M a r x e t a l. , 2 0 2 1) .

Dietary patterns rich in fiber, fruits, vegetables, and fermented foods, such as those characteristic of the Mediterranean diet, have been consistently associated with greater gut microbiota diversity and an increase in short-chain fatty acid (SCFA)-producing bacteria, such as Faecalibacterium prausnitzii and Bifidobacterium and Lactobacillus species. These SCFAs, particularly butyrate, not only nourish colonocytes and strengthen the intestinal barrier, but also have anti-inflammatory and neuromodulatory properties. Epidemiological and intervention studies have correlated adherence to the Mediterranean diet with lower risk of depression and better cognitive function (Vahid et al., 2023).

In contrast, the typical Western diet, characterized by high consumption of ultra-processed foods, saturated fats, refined sugars, and low fiber intake, has been linked to gut dysbiosis. This dietary pattern tends to reduce microbial diversity, promote the growth of potentially pro-inflammatory bacteria (e.g., some species of Enterobacteriaceae) and decrease the abundance of beneficial microorganisms. Dysbiosis induced by the Western diet can lead to increased intestinal permeability, low-grade systemic inflammation, and alterations in neurotransmitter production, all factors implicated in the pathogenesis of mood and anxiety disorders (Merlo; Bachtel; Sugden, 2024).

4.3.1 Specific dietary components also exert influence

Dietary Fibers: These are fermented by the microbiota in the colon, resulting in the production of SCFAs. Different types of fibers (soluble, insoluble, prebiotics such as inulin and fructooligosaccharides - FOS) can selectively modulate different bacterial groups. (Ljungberg; Bondza; Lethin, 2020).

Polyphenols: Compounds found in fruits, vegetables, teas, and cocoa, have antioxidant and anti-inflammatory properties. Many polyphenols are metabolized by the gut microbiota, generating bioactive metabolites that can influence EMIC (Azad et al., 2018).

Fats: The type and amount of fat in the diet can impact the microbiota. Diets high in saturated fats may promote dysbiosis and inflammation, while omega-3 fatty acids (found in fatty fish) have been linked to anti-inflammatory effects and may positively modulate microbiota and mental health (Patel et al., 2022).

4.3.2 Proteins: The amount and source of protein (animal vs. plant)

They can influence microbial metabolism, with protein fermentation resulting in products such as ammonia, phenols, and hydrogen sulfide, which in excess can be deleterious (Itani et al., 2017).

Probiotics: Live microorganisms that, when administered in adequate amounts, confer health benefits to the host. Certain strains of Lactobacillus and Bifidobacterium (psychobiotics) have shown potential in improving symptoms of anxiety, depression, and stress in preclinical studies and some clinical trials (Canyelles et al., 2023).

Prebiotics: Non-digestible substrates that selectively stimulate the growth and/or activity of beneficial bacteria in the colon. FOS, galactooligosaccharides (GOS), and inulin are examples. Studies suggest that prebiotics can modulate EMIC, reducing stress response and improving mood (Olvera-Rosales et al., 2021).

A detailed understanding of how different dietary components and patterns interact with the gut microbiota to influence mental health is critical for the development of personalized and effective nutritional strategies in the prevention and complementary treatment of neuropsychiatric disorders.

Table 3

Dietary components and their effects on EMIC

Componente Dietético	Efeito sobre o EMIC e Saúde Mental
Dieta Mediterrânea	↑ Diversidade microbiana, ↑ AGCC, ↓ inflamação, ↓ risco de depressão e ansiedade
Dieta Ocidental	↑ Disbiose, ↓ barreira intestinal, ↑ LPS, ↑ neuroinflamação
Fibras Prebióticas	Fermentadas por bactérias → produção de AGCC; fortalecem a barreira intestinal
Polifenóis	Antioxidantes e anti-inflamatórios; metabolizados pela microbiota → efeitos neuromoduladores
Gorduras	Saturadas → pró-inflamatórias; Ômega-3 → anti-inflamatórios e protetores neuronais
Proteínas	Excesso de proteína animal → compostos tóxicos; vegetais → melhor fermentação
Probióticos (psicobióticos)	*Lactobacillus*, *Bifidobacterium* → melhora de sintomas de ansiedade e depressão
Prebióticos	FOS, GOS, inulina → estimulam bactérias benéficas, reduzem resposta ao estresse

Source: Prepared by the authors, 2025.

4.3.3 Biological mechanisms involving diet, stress, and mental health in the context of EMIC

Chronic stress is a well-established risk factor for the development of mental disorders such as depression and anxiety. The interaction between diet, stress, and the microbiota-gut-brain (EMIC) axis is complex and bidirectional, involving multiple biological mechanisms that may exacerbate or attenuate mental health outcomes (Socała et al., 2021).

Stress, both acute and chronic, can significantly alter the composition and function of the gut microbiota. Mechanisms include alteration of gastrointestinal motility, increased intestinal permeability, and modulation of mucus secretion and antimicrobial peptides, all influenced by activation of the HPA axis and the sympathetic nervous system. These alterations can lead to dysbiosis, characterized by a reduction in beneficial bacteria (e.g., Lactobacillus, Bifidobacterium) and an increase in potentially pathogenic or pro-inflammatory microorganisms. Stress-induced dysbiosis can, in turn, exacerbate the systemic inflammatory response and neuroinflammation, contributing to the symptomatology of mental disorders (Liu; Zhu; Yang, 2024).

Diet plays a crucial modulating role in this interaction. A diet rich in fiber, polyphenols, and omega-3 fatty acids can promote a more resilient and diverse microbiota, capable of mitigating some of the negative effects of stress on EMIC. For example, SCFAs produced from fiber fermentation have anti-inflammatory properties and may influence HPA axis regulation and neurotransmission. Polyphenols can reduce oxidative stress and inflammation. In contrast, a Western diet, high in saturated fats and sugars, may exacerbate stress-induced dysbiosis and increase vulnerability to mental disorders (Gantenbein; Kanaka-Gantenbein, 2021).

One of the central mechanisms is the modulation of intestinal permeability. Stress can compromise the integrity of intercellular junctions in the intestinal epithelium, leading to increased translocation of bacterial LPS into the circulation. LPS is a potent inducer of the inflammatory response, activating TLR4 receptors in immune cells and in the brain, which can trigger the production of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6). These cytokines can cross or signal through the BBB, promoting neuroinflammation, altering neurotransmitter metabolism (e.g., reducing serotonin availability by diverting tryptophan to the kynurenine pathway), and affecting neuronal plasticity. A diet that promotes gut barrier health (e.g., high in fiber, glutamine, zinc) can help counteract these effects (Bremner et al., 2020).

The tryptophan-kynurenine pathway is another point of convergence. Inflammation and stress activate the enzymes IDO (indolamine 2,3-dioxygenase) and TDO (tryptophan 2,3-dioxygenase), which divert tryptophan metabolism from serotonin synthesis to the production of kynurenine and its metabolites. Some of these metabolites, such as quinolinic acid, are neurotoxic and may contribute to the excitotoxicity and neuronal dysfunction seen in depressive disorders. The gut microbiota and dietary components can modulate the activity of these enzymes and the balance between the neuroprotective metabolites (e.g., kynurenic acid) and neurotoxic metabolites of this pathway (CANYELLES et al., 2023).

In addition, diet and microbiota influence the production of brain-derived neurotrophic factor (BDNF), a molecule crucial for neurogenesis, neuronal survival, and synaptic plasticity. Reduced levels of BDNF have been consistently associated with depression and the effects of chronic stress. Healthy diets and a balanced microbiota can promote adequate levels of BDNF, while inadequate diets and dysbiosis can reduce them (MARX, W. et al., 2021).

Finally, oxidative stress is an important component in the pathophysiology of mental disorders. Both psychological stress and a pro-inflammatory diet can increase the production of reactive oxygen species (ROS) and reduce antioxidant defenses. The gut microbiota can influence the redox state of the host, and a diet rich in antioxidants (vitamins C and E, selenium, polyphenols) can help mitigate oxidative damage in the brain (PATEL, B. K. et al., 2022).

Understanding these integrated biological mechanisms is essential for developing interventions that target EMIC, combining dietary and stress management strategies to promote mental health.

Table 4

Biological mechanisms integrating diet, stress, and mental health in the EMIC context

Mecanismo Biológico	Relação com Dieta, Estresse e Saúde Mental
Estresse e microbiota	Estresse crônico altera composição microbiana e ↑ permeabilidade intestinal
LPS e neuroinflamação	Aumento da translocação de LPS → ativa citocinas pró-inflamatórias (IL-6, TNF-α) → neuroinflamação
Via do triptofano-quinurenina	Inflamação desvia triptofano da serotonina → produção de neurotoxinas (ácido quinolínico)
BDNF	Estresse reduz BDNF; dieta equilibrada e microbiota saudável ↑ neuroplasticidade

Mecanismo Biológico	Relação com Dieta, Estresse e Saúde Mental
Estresse e microbiota	Estresse crônico altera composição microbiana e ↑ permeabilidade intestinal
LPS e neuroinflamação	Aumento da translocação de LPS → ativa citocinas pró-inflamatórias (IL-6, TNF-α) → neuroinflamação
Via do triptofano-quinurenina	Inflamação desvia triptofano da serotonina → produção de neurotoxinas (ácido quinolínico)
BDNF	Estresse reduz BDNF; dieta equilibrada e microbiota saudável ↑ neuroplasticidade

Source: Prepared by the authors, 2025.

4.4 DIETARY STRATEGY AND CLINICAL EVIDENCE OF EMIC MODULATION FOR MENTAL HEALTH

The growing understanding of the influence of diet and gut microbiota on mental health has driven the investigation of specific dietary strategies as therapeutic or preventive approaches for neuropsychiatric disorders. Several nutritional interventions have been explored, focusing on the modulation of the microbiota-gut-brain axis (EMIC) (SOCAŁA, K. et al., 2021).

Mediterranean Diet: As mentioned earlier, the Mediterranean diet is one of the most studied dietary patterns in relation to mental health. It is characterized by high consumption of fruits, vegetables, legumes, whole grains, nuts, seeds, extra virgin olive oil, and fish, with moderate consumption of dairy and poultry, and low consumption of red meat and processed foods. Randomized controlled trials, such as the SMILES study (JÄRBRINK-SEHGAL, E.; ANDREASSON, 2020), demonstrated that a dietary intervention based on the principles of the Mediterranean diet can lead to a significant improvement in depressive symptoms in adults with major depression. Proposed mechanisms include reducing inflammation, increasing SCFA production, improving microbiota diversity, and providing nutrients essential for brain function (e.g., omega-3 fatty acids, B vitamins, antioxidants) (Merlo; Bachtel; Sugden, 2024).

Probiotics (Psychobiotics): The term "psychobiotic" refers to probiotics that, when ingested in adequate amounts, confer mental health benefits. Specific strains of Lactobacillus (e.g., L. rhamnosus, L. helveticus, L. plantarum) and Bifidobacterium (e.g., B. longum, B. infantis, B. breve) have been investigated. Systematic reviews and meta-analyses suggest that probiotics may have a modest but significant effect on reducing depressive symptoms and anxiety, particularly in individuals with clinical symptoms (Liu; Zhu; Yang, 2024). Mechanisms may involve reducing inflammation, modulating the HPA axis, improving the integrity of the intestinal barrier, and producing neurotransmitters or their precursors. However, efficacy may be dependent on the strain, dose, duration of intervention, and characteristics of the individual. More research is needed to identify the most effective strains and populations that would benefit most (ADAK; KHAN, 2019).

Prebiotics: Prebiotics are non-digestible fibers that selectively promote the growth and/or activity of beneficial bacteria in the gut. Fructooligosaccharides (FOS), galactooligosaccharides (GOS), and inulin are common examples. Human studies have shown that supplementation with prebiotics can reduce the cortisol response in stressful situations and alter emotional processing, making individuals less attentive to negative stimuli (SOCAŁA, K. et al., 2021). These effects are probably mediated by the increase in Bifidobacterium and the production of SCFAs. Research on the direct impact of prebiotics on diagnosed disorders is still limited but promising (BREMNER et al., 2020).

Synbiotics: Combinations of probiotics and prebiotics. The rationale is that the prebiotic may increase the survival and activity of the probiotic in the gut. Some studies suggest additional benefits of synbiotics compared to probiotics or prebiotics alone, but evidence is still accumulating in the field of mental health (AZAD et al., 2018).

Omega-3 Fatty Acids: Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), found primarily in fatty fish, have anti-inflammatory properties and are important structural components of neuronal membranes. Meta-analyses of clinical trials suggest that omega-3 supplementation, particularly EPA-rich formulations, may be beneficial as an adjunctive treatment for depression (BREMNER et al., 2020). It is believed that omega-3s may influence mental health through modulation of inflammation, fluidity of cell membranes, neurotransmission, and possibly the composition of the gut microbiota (BREMNER et al., 2020).

Micronutrients: Deficiencies of certain vitamins (e.g., B vitamins, vitamin D) and minerals (e.g., magnesium, zinc, selenium) have been linked to an increased risk of depression and other mental disorders. These micronutrients play crucial roles as enzyme cofactors in neurotransmitter synthesis, antioxidant protection, and regulation of the inflammatory response. Correction of deficiencies through diet or supplementation may be important, although supplementation in individuals without deficiency has less consistent results (BREMNER, J. D. et al., 2020).

Avoiding Pro-Inflammatory Foods: Reducing the consumption of foods characteristic of the Western diet, such as those rich in refined sugars, trans fats, saturated fats, and food additives, is an important strategy. These foods can promote dysbiosis, chronic low-grade inflammation, and oxidative stress, all of which are implicated in the pathogenesis of mental disorders (PATEL, B. K. et al., 2022).

Table 5

Dietary strategies in the modulation of EMIC and their impacts on mental health

Estratégia Nutricional	Impacto no EMIC e Saúde Mental
Dieta Mediterrânea	Redução de sintomas depressivos (Estudo SMILES), ↑ diversidade da microbiota
Probióticos (Psicobióticos)	*L. rhamnosus, B. longum* → ↓ ansiedade, ↓ depressão, modulação do eixo HHA
Prebióticos	FOS, GOS, inulina → ↓ cortisol, ↑ Bifidobacterium, ↑ AGCC
Estratégia Nutricional	Impacto no EMIC e Saúde Mental
Simbióticos	Combinação de probióticos + prebióticos → efeitos sinérgicos na saúde mental
Ômega-3 (EPA, DHA)	Anti-inflamatórios, ↑ fluidez neuronal, modulação da microbiota intestinal
Micronutrientes	Vitaminas B, D, zinco, magnésio → cofatores na síntese de neurotransmissores
Redução de alimentos inflamatórios	↓ açúcar, gordura trans, processados → ↓ disbiose, ↓ inflamação, ↑ integridade intestinal

Source: Prepared by the authors, 2025.

5 CONCLUSION

The intricate relationship between gut health and mental health, mediated by the microbiota-gut-brain (EMIC) axis, represents a rapidly expanding field of research of considerable clinical relevance. The evidence accumulated over the past decade robustly demonstrates that the gut microbiota is not a mere commensal, but an active metabolic organ that plays crucial roles in modulating physiological processes ranging from digestion and immunity to the regulation of mood, cognition, and behavior.

The present systematic review of the literature, covering publications between 2017 and 2024, corroborates the premise that diet is one of the main modifiable factors capable of influencing the composition and functionality of the gut microbiota and, therefore, impacting mental health . Healthy dietary patterns, such as the Mediterranean diet, rich in fiber, polyphenols, and omega-3 fatty acids, are associated with a more diverse and resilient microbiota, reduced inflammation, and better mental health outcomes, including lower risk of depression and anxiety. By contrast, the Western diet, characterized by high consumption of processed foods, saturated fats, and sugars, is linked to gut dysbiosis, chronic low-grade inflammation, and increased vulnerability to neuropsychiatric disorders.

The mechanisms by which EMIC operates are multifaceted, involving neural (mainly the vagus nerve), immunological (cytokine modulation and neuroinflammation), endocrine (HPA axis regulation), and metabolic (SCFA production, neurotransmitter, and modulation of the tryptophan-kynurenine pathway) pathways. Chronic stress interacts in a complex way with diet and microbiota, and can exacerbate dysbiosis and inflammation, compromising mental health. Interventions aimed at restoring gut eubiosis and mitigating inflammation, such as the use of probiotics (psychobiotics), prebiotics, and the adoption of anti-inflammatory dietary patterns, demonstrate promising therapeutic potential.

However, despite significant advances, challenges remain. The heterogeneity of the studies, the complexity of individual interactions, and the need for large-scale, long-term randomized clinical trials are points that require attention. The identification of biomarkers that can predict individual response to dietary and microbiota-based interventions is a crucial area for the development of personalized approaches.

In summary, modulation of the gut microbiota through dietary strategies emerges as a promising and complementary frontier in the promotion of mental health and the management of neuropsychiatric disorders.

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