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Dietary influences on the gut-brain pathways: Mechanisms and therapeutic potential[★]

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ABSTRACT

There is emerging evidence that the gut-brain axis can be significantly influenced through a gut friendly diet. Indeed, nutritional neuroscience holds a significant role in managing the gut brain axis and mental health disorders as numerous pathways, chiefly, neurological, humoral and immune pathways are involved in the bidirectional communication of gut and brain. Moreover, these pathways are interlinked with the gut microbiota, performing a synergistic effect on gut-brain axis. Consequently, nutrients and gut metabolites have become crucial for managing the gut-brain communication and thereby handling various mental health disorders. Furthermore, the incorporation of dietary interventions through special diets can efficiently contribute to the maintenance of gut-brain health. Apart from this, advanced nutritional therapies, i.e., nutritional psychiatry, microbial biotherapies have been shown promising effects on altered gut brain signalling and health. Nonetheless, the role of nutritional diet in managing the gut brain axis is yet to be discussed in detail. Additionally, there is a growing need to investigate the impact of nutrients on healthy gut-brain communication within the field of nutritional psychiatry. On account of these gaps and findings, this review highlights the importance of diet and nutrition on a healthy gut-brain axis through the mechanism of action of different nutritional compounds, impact of special diets and novel nutritional and psychobiotic influenced strategies.

1. Introduction

The quote "Death lies in the bowel" by Hippocratis (Father of Medicine), stated in 400 BC signifies the importance of gut microbiota and gut health in regards with the overall wellbeing of the body [1]. Most of the nutrients and biomolecules are absorbed in the gut, thereby developing a cross communication with all the vital organs of the body. However, this interaction of the gut is more evident with the brain, through various pathways known as the gut-brain axis [2]. The pathways are influenced by various nutritional compounds and gut metabolites such as protein, fibre etc. [3]. Apart from this, gut microbiota exhibits a positive effect on brain health as well in managing mental health disorders such as anxiety, depression etc., through the stimulation of neurotransmitters [4]. Although the mechanism of gut brain axis is explored in previous studies, there are rare studies targeting interconnection of nutrition and diet in maintaining gut-brain communication and the therapeutic impact of food in gut-brain cross talk. Identifying this gap, this review explores the potential effect of diet and nutrition in the bidirectional communication of brain-gut-gut microbiota (BGM).

The gut-brain axis comprises a complex and interlinked network, connecting the gut and brain [1]. The major fundamental gut-brain communication pathways are composed of central, enteric, autonomic nervous system (ANS and ENS) and HPA axis [5]. Firstly, at neuro-autonomic level, direct action via autonomic nervous system (ANS) and vagus nerve, between brain and GI, and an indirect pathway that connects ANS and ENS. Secondly, the endocrine level, paraventricular (PVN) hypothalamic nucleus produce CRH and secretes

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adrenocorticotropic hormone (ACTH) through anterior pituitary stimulation, contributing to stress dependent HPA axis and finally, the immune pathway facilitated by cytokines and microbiota-immune interplay by gut-derived metabolites [6]. Additionally, gut microbiota, due to its characteristics, influences the role of diet on brain functioning by releasing, modulating the nutrients from the food via various bioactive molecules and metabolites [7]. However, the disruptions of a healthy microbiota collapses the gut-brain inter-communication contributes the pathogenesis of psychiatric disorders [8] as nutrient modified neurotrophic factors like brain-derived neurotrophic factor (BDNF) are necessary for the maintenance of synoptic plasticity [9]. Proper consumption of specific diets such as fibre rich and protein rich diets, prebiotics, fermented foods, traditional diets like Mediterranean diets exhibit a positive impact on gut-brain health [4,7]. Moreover, the altered gut-brain health can also be effectively managed through novel strategies and therapies including dietary interventions targeting psychobiotic strategy for modulating neurological diseases [10].

Despite the existing evidence on the role of nutrition in gut-brain axis, the importance of specific diet and nutrients on a healthy gut-brain crosstalk are yet to be explored in detail. There exists a lack of information regarding the interconnection of psychobiotics and gut friendly diet on gut-brain communication. Furthermore, the available studies have emphasised the role and mechanism of nutrients on gut-brain axis, but a comprehensive review on the importance of nutrients and gut friendly diet as well as an optimally managed psychobiotic concentration on a healthy gut-brain axis is lacking. Subsequently, nutritional interventions for altered gut-brain axis also need attention. Hence, in the light of the existing gap and above-mentioned potentials, this review focuses the significance of nutrition on gut-brain health along with an analysis of gut-brain-nutrition interconnection with mental health disorders. Additionally, on account of the profound impact of food, this review explores the novel insights of special diets and other intervention strategies for promoting an optimal gut-brain axis.

This review briefs an overview of the gut-brain axis, highlighting the major primary pathways, i.e., neural, humoral and immune pathways that regulates this intricate system. Besides, the mechanism of action of nutrients and gut metabolites on maintaining the gut-brain communication is highlighted. It reveals the interaction between gut microbiota, brain and nutrients. Additionally, this work underscores the significance of nutrition in managing mental health disorders and brain health. It explores the role of nutrients in optimum emotional and cognitive wellbeing. Also, this review provides insights about the importance of gut friendly diet in nutritional neuroscience. This covers key special diets that are effective in a healthy gut-brain communication. Moreover, this study contributes to a comprehensive understanding of novel

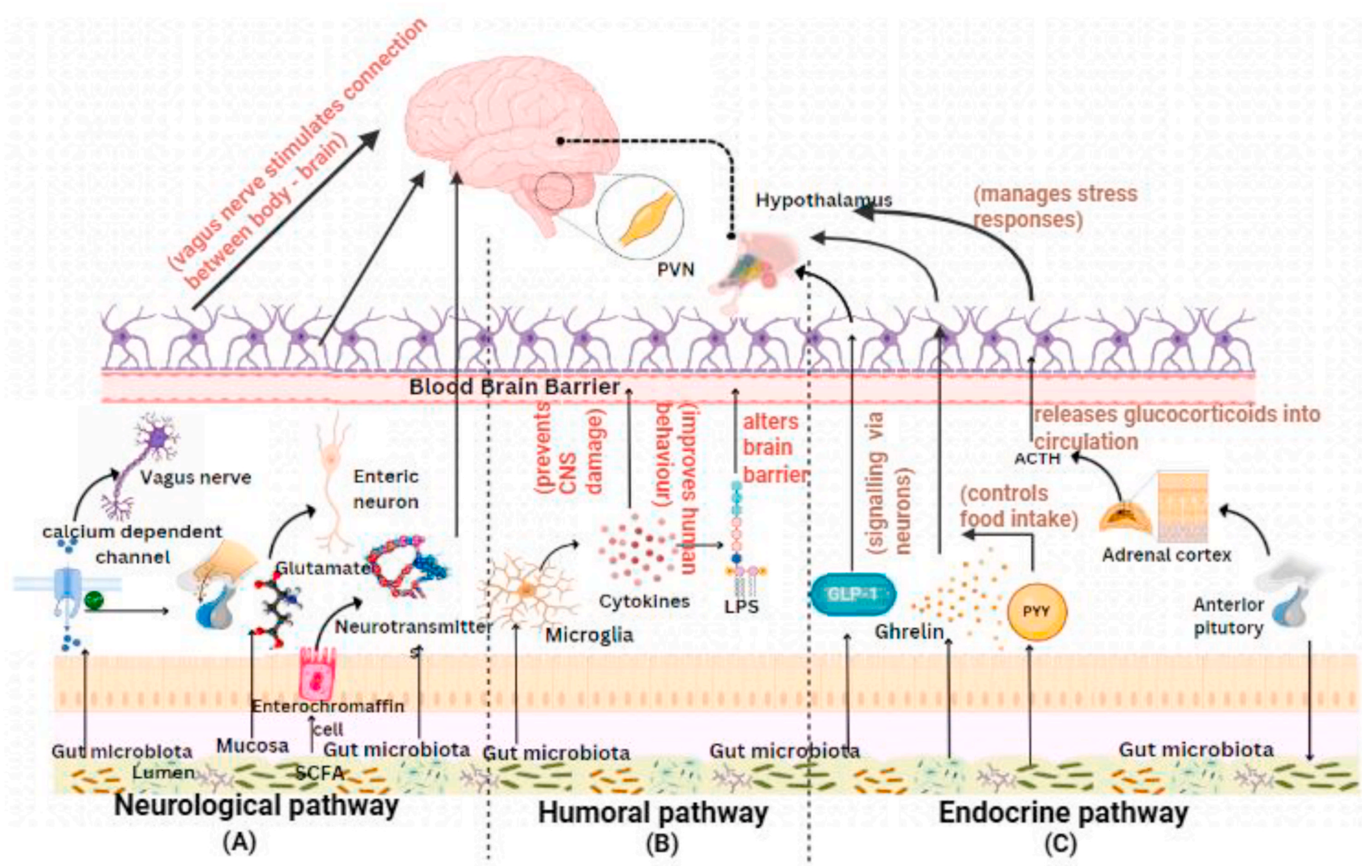

Fig. 1. Major signalling pathways of gut-brain axis including neurological, humoral and endocrine pathways.
(A) The neurological pathway involves the gut microbiome induced opening of calcium dependent channels for alteration of vagus nerves for the bilateral communication among brain, spinal code, enteric system and hypothalamus-pituitary-adrenal (HPA) system. Also, the gut mucosa transmits signals to glutamate- a neurotransmitter and sensory co transmitter for regulating visceral sensitivity in vagal pathway. Similarly, SCFA influences neurotransmitters from enterochromaffin cells to promote gut-brain connection.
(B) The humoral pathway includes the gut microbiota influenced modulation of microglia for cytokine production. These cytokines with LPS alter the brain barrier and function by changing the vascular permeability.
(C) The endocrine pathway includes, gut derived hormones ghrelin and PYY participates in the peripheral and central control of food intake in the gut-brain axis. The adrenal cortex releases glucocorticoids through the diffusion of adrenocorticotropic hormone (ACTH) from anterior pituitary into symmetric circulation. This leads to the management of gut brain axis, specifically in visceral sensations and behavioral stress response.

strategies for regulating altered gut-brain health. These outlined innovative methods encompasses nutritional and non-nutritional techniques to manage the disrupted gut-brain signalling.

2. Signalling pathways between gut and brain

The cross communication and signalling between brain and gut is mediated via functional lymphatic vasculature and blood brain barrier (BBB), through a physical and chemical connection that combines neurological, endocrine and immune pathways [11]. Specifically, the physiological and bidirectional communication between gut and brain is through cytokines, neurotransmitters and hormones [12]. This section highlights the major signalling pathways between gut and brain as illustrated in Fig. 1.

2.1. Neurological pathways

Neurotransmitters and neuroactive substances produced in the gut including γ-amino butyric acid (GABA), serotonin and short chain fatty acids (SCFA) can affect the brain functioning [13]. However, the signalling between gut-brain axis can be emphasised through the numerous neurological pathways. The alteration of afferent sensory nerves and saprophytic flora is essential for the activity of intrinsic sensory neurons by improving the gut motility using *Lactobacillus reuteri*, also resulting in the inhibition of calcium-dependent *potassium* channels opening [14,15]. This change in the gut motility initiates a bilateral communication among brain, spinal cord, enteric system and hypothalamus-pituitary-adrenal (HPA) system, as well as with the sympathetic and parasympathetic limbs that controls lumen driven afferent signals, thus getting channelled through enteric, vagal and spinal signals to the central nervous system [15]. Additionally, the microbiota send signals to the brain by activating afferent neurons of the vagus nerve via neuroendocrine and neuro-immune pathways [16]. Parallelly, researchers have proposed neurological relationship between both brain and GI tract. Particularly, 5-HT, a neurotransmitter exhibits a crucial role in managing the gut-brain communication [15]. Also microbial tryptophan induced release of 5-HT from enterochromaffin cells in the gut promotes gut-brain connection [17]. Additionally, the gut microbiota influence glutamatergic pathways through controlling L-tryptophan, that contributes to the synthesis of bioactive molecules, including 5-HT, kynurenine and indole derivatives through direct or indirect control of microbiota. Similarly, another neurotransmitter - glutamate (GLU) plays a major role in regulating visceral sensitivity by acting as a sensory co-transmitter in the primary afferent neuron, transmitting the information from mucosa to extrinsic primary afferent neuron and ENS [14]. In addition, gut microbiomes like *Ruminococcus gnavus* and *C. sporogenes* produces tryptamine in the brain that induces appetite and mood regulation [18].

2.2. Humoral pathway

Immune cells like T and B lymphocytes play a critical role in modulating microbial challenges and regulating the GI-immune homeostasis [19]. The gut-brain axis is influenced by gut microbiota modulated immune cells including microglia and CNS mediated oligodendrocytes and astrocytes [11]. For instance, microglia are responsible for several immune activities including phagocytosis, immune activation and cytokine production [20]. In addition, studies have highlighted the influence of gut microbiota in the functioning of microglia as well as preventing CNS damage. Moreover, the gut microbiota influenced microglia positively affects human behaviours and can manage neurological disorder induced stress. Furthermore, the cytokines produced by microglia in the intestine passes through the bloodstream to the brain and affects the overall gut-brain axis [13,21]. These cytokines, along with LPS suppress microglial phagocytosis, alter the blood brain barrier and enhances neuronal apoptosis [22,23]. However, the gut microbiota also impacts the blood brain barrier (BBB) and its permeability, where BBB is known to prevent entry of infectious agents and immune cells [23,24]. Hence, the above immunological sensation in the blood barrier permeability demonstrates the connection between gut and brain through humoral pathway.

2.3. Endocrine pathway

Gut hormones including peptide YY (PYY), glucagon-like-peptide-1 (GLP-1) are are known for local efforts on gut motility [2]. Particularly, GLP-1 plays a key role in maintaining satiety, as its receptors are present in various tissues including gut, hypothalamus and activates these receptors in the vagal afferent pathway or ENS. Likewise, PYY participates in the peripheral and central control of food intake in the gut-brain axis. Similarly, ghrelin is another peripherally derived hormone in the gut that has a crucial role in expressing signals to the brain through vagal afferents in the nodose ganglion. In addition, reduction in the ghrelin levels leads to a decrease in the activity of the right dorsolateral prefrontal cortex, thus it can be attributed as a signalling molecule in modulating the gut-brain communication [25].

Similar signalling pathway between gut and brain is via the hypothalamic-pituitary-adrenal axis (HPA), where the paraventricular nucleus (PVN) releases corticotropin release factor (CRF). Moreover, CRF activates the HPA axis, whereas the adrenal cortex releases glucocorticoids through the diffusion of adrenocorticotropic hormone (ACTH) in symmetric circulation. This release of glucocorticoids leads feed back inhibition through transcriptional modulation in stress-responsive regions of brain. Additionally, this bidirectional communication between gut-brain and HPA axis is related with gut hormones, microbial metabolites, sensory and autonomic nervous system [26].

3. Impact of gut metabolites and nutrients on brain health: mechanisms of action

The diet-microbiome interactions are the key factors for the progression of microbiome-host communication, that ultimately affects brain health [7]. Hence, the mechanism of action of major nutrients and gut metabolites on brain health is discussed in this section as represented in Table 1.

3.1. Protein

Dietary protein is metabolised by the gut microbes to produce various neurotransmitters such as 5-HT, norepinephrine, GABA and dopamine [27]. Besides, studies have stated that gut microbiota induced the alteration of protein expression levels in multiple tissues of the gut–brain axis with depression-like phenotype [37]. However, the action of protein in the gut-brain axis is more prominent through the pathways linked with amino acids as mentioned below. Amino acids (AA) hold a major role in modulating the host's cognitive functions, either by acting as a neurotransmitter such as L-Glutamate (GLU) or by serving as a precursor for the synthesis of GABA, serotonin and dopamine [7]. For instance, GLU acts as a diet derived source of amino acid activates its receptors on either pelvic, splanchnic or vagal afferents takes part in conveying sensory inputs to parts of brain involved in gut-brain functions [14]. Similarly, glutamate is regulated by another AA derived compound N-acetylcysteine, an anti-inflammatory antioxidant that holds neuroprotective effects [4]. In addition, gut microbes such as *Bifidobacterium* and *Lactobacillus* is reported to produce GABA [38]. Besides, studies have highlighted the importance of different branched chain amino acids including phenylalanine and plasma tyrosine in the synthesis of norepinephrine [39]. Thus, due to its ability to metabolise AA and influence the neural transmissions, gut microbiota exhibits a crucial role in managing brain health, highlighting AA as a key component in microbiome-host interactions [7].

Table 1
Mechanism of nutrients on gut-brain health.

Nutrients	Mechanism on gut health	Mechanism on brain health	References
Protein	Protein is metabolised by the gut microbiome for the production of gut metabolites	Protein induces the release of various neurotransmitters like GABA, Dopamine etc.	[27]
Amino Acid	AA are involved in various processes for the production of end products that benefit intestinal barrier and gut microbiome.	AA can influence brain health through releasing and acting as neurotransmitters.	[7,28]
Fibre	Fibre nurtures the gut bacteria composition and diversity	Dietary fibre rich diet helps gut microbiota to produce neuromodulators such as g-aminobutyric acid (GABA)	[27]
SCFA	SCFA's reduce gut permeability, and regulates gut hormones like peptide YY (PYY) and glucagon-like peptide 1 (GLP-1).	SCFA's can modulate neurotransmitters and inhibits the release of histone deacetylases (HDAC).	[27,29]
Phenolic compounds	Phenolic compound decrease microbiota induced gut dysbiosis and metabolic syndrome.	Phenolic compounds can influence the production of neurotransmitters such as dopamine and boost microglial cell restoration	[30,31].
Vitamins			
Vitamin A	Vitamin A inverts the microbial impairments and disturbances in the gut.	Vitamin A reduces variations in hippocampal and prefrontal cortex BDNF concentration as well as reduces the symptoms of stress and anxiety.	[27].
B complex	B complex vitamins manage the gut permeability and reduce oxidative stress in the gut.	B complexes stimulate the release of various neurotransmitters	[32]
Gut metabolites			
Bile acids	Bile acids can influence the structure and function of gut microbiota.	BAs can influence regulation of BBB and gut permeability through tight junction disruptions, which in turn stimulates the fibroblast growth factor 15/19 (FGF-15/19) as well as GLP-1 production and activation of foresaid X receptors (FXR).	[33,34]
Tryptophan	Tryptophan metabolites like indole maintains the gut homeostasis by mucin production and inhibits gastrointestinal motility.	Tryptophan is a major factor in the gut microbiota regulated synthesis of kynurenine and serotonin as well as modulation of vascular endothelial growth factor B (VEGF-B) and growth factor-alpha (TGFα).	[35,36]

3.2. Fibre

Dietary compounds like fibre nurtures the development of gut microbiomes, that triggers the release of neurotransmitters, gut hormones and bioactive metabolites, thus influencing the brain through different signalling pathways [40,41]. SCFA- a metabolite of microbial fermented fibre present in the CNS can stimulate neurotransmitter synthesis and neurotrophic factors, thereby improving brain health through the regulation of neuron growth and differentiation [27]. Similarly, SCFA has a positive impact on brain health either through improving the gut microbiome levels or by regulating neurotransmitters [40]. In addition, studies have asserted that SCFA's transmit the electrical signals to regulate neurotransmitters in the brain through the stimulation of vagal afferents in the gastrointestinal tract [27]. Likewise, they exhibit the potential to decrease the symptoms of depression and psychosocial stress-induced intestinal permeability [42]. Subsequently, SCFA's contribute to the inhibition of histone deacetylases (HDAC), hence preventing anxiety related disorders [27]. Moreover, brain circuits are indirectly influenced by SCFA via the activation of G-protein-coupled receptor (GPCR) for secreting gut hormones like peptide YY (PYY) and glucagon-like peptide 1 (GLP-1) [29]. Furthermore, Ghrelin receptor - a major GPCR for food habits and mood are controlled by SCFA [43]. Thus, this mechanism represents the significance of SCFA and other microbiota metabolites through the modulation of GPCR in the gut-brain axis, thereby managing the functions of CNS [27].

3.3. Phenolic compounds

Phenolic metabolites can boost the production of neurotransmitters such as dopamine, that can deploy neurocognitive functions, thus improving the brain functions [44]. Studies highlighted the significance of phenolic compounds like Equol, a phytoestrogen that exhibits neuroprotective effect against β-amyloid plaque induced cytotoxicity [45]. Similarly, another phenolic compound as well as a gut microbiota induced substrate - proanthocyanidin, prevents oxidative stress induced neurodegenerative disorders by acting as a precursor of hippuric acid, DHPA (3-(3,4- dihydroxyphenyl)-propionic acid) and 3-hydroxyphenyl-acetic acid [46]. In addition, studies have highlighted the beneficial effect of phenolic compounds in the restoration process of microglial cells that are crucial in gut-brain communication [30].

3.4. Vitamins

Vitamins serve as a salient compound in CNS functioning as it is necessary for various neurological pathways due to its ability to cross the blood brain barrier [7]. Studies have emphasised the effect of vitamin A in stress and social anxieties. Moreover, vitamin A inverts the microbial impairments and disturbances along with variations in hippocampal and prefrontal cortex BDNF concentration [27]. Besides, B-complex vitamins contributes potential effects in alleviating symptoms of depression through various mechanisms including stimulating and modulating gut microbiome for the release of neurotransmitters like GABA, acetylcholine, dopamine and serotonin, decreasing inflammatory symptoms and oxidative stress, regulating epigenetics and managing gut permeability [32]. Significantly, vitamin B12 serves as a crucial component in regulating the muscle–gut–brain axis, which can be attributed to its ability to manage the functions at the intestinal, cerebral and muscular levels [47].

3.5. Gut metabolites

Gut metabolites like gut microbiota synthesized compounds such as bile acids (BA's) as well as metabolites produced from dietary amino acid like tryptophan by gut microbiota [48,49]. The two major gut metabolites that influence gut-brain axis including BA's and tryptophan are explained below.

3.5.1. Bile acids

Bile acids (BA) are generated by hepatic and bacterial enzymes to aid in digestion, regulation of inflammatory signalling, absorption and metabolism of lipids affects the microbiota interaction effect on brain function [48]. BAs can directly influence brain functioning via BBB regulation and gut permeability management, through tight junctions' disruptions, which in turn stimulates the fibroblast growth factor 15/19 (FGF-15/19) as well as GLP-1 production. This leads to the generation of signals in gut to the CNS through the activation of farnesoid X receptors (FXR) [34].

3.5.2. Tryptophan

Tryptophan is metabolised in the gut in different forms, although it is an essential amino acid from dietary protein [49]. It is a major factor in the gut microbiota regulated synthesis of kynurenine and serotonin that acts as messengers in the gut-brain cross talk [17]. Additionally, serotonin, metabolite of tryptophan leads to secretomotor reflex that stimulates the expression of 5-HT3 and 5HT-4 receptors in lamina propria via afferent nerve endings, ultimately contributes to the vasoactive intestinal peptide (VIP) and submucosal ganglionic neuronal activity [50]. Moreover, transformation of vascular endothelial growth factor B (VEGF-B) as well as growth factor-alpha (TGFα) are regulated by the microbial metabolites of tryptophan, thus modulating AhR induced transcription in astrocytes and neural disorders [51]. For instance, microglial regulation of astrocytes along with multiple sclerosis (MS) lesions formation in $CD14^{+}$ cells are performed by both TGFα and VEGF-B [52]. Apart from this, another tryptophan metabolite that can pass through the BBB - Kynurenine, holds significant influence on neural signalling through the direct transportation of neutral AA carriers that are transformed into QA and KA [50].

4. Role of Nutrition: brain health

Nutrition holds a significance on gut health, hence, indirectly influencing how gut microbiota can leverage brain health [53]. This section discusses the major role of nutrition on maintaining brain health via gut-brain axis as presented in Fig. 2.

4.1. Brain functioning

Specific diets and nutrition have a prominent role in managing cognitive and brain functioning [54]. Researchers have emphasised the importance of a diet rich in polyphenols for cognitive functions as they modulate cell and molecular processes involved in learning and memory, including neuronal signalling pathways involved in synaptic plasticity [55]. For instance, Mediterranean and other plant-based diets, rich in fibre and polyphenols are proven to improve cognitive function via gut-brain axis [56]. According to studies, diets rich in nuts and olive oil have exhibited a positive impact on the brain function of elderly population [57]. In addition, polyphenols like curcumin can positively influence brain health through memory boost and improved attention [58]. Moreover, studies have also emphasised the reversing effect of cognitive defects by consumption of polyphenolic compounds [59]. Furthermore, researches have reported an improved hippocampus functioning of the brain by supplementing fermented dairy products that increases the levels of beneficial gut microbes such as *Lactobacillus* [60].

4.2. Role in mood regulation

Nutrition has a major influence on mood regulation through the bidirectional communication of gut and brain [61]. According to studies, amino acids have a significant role in mood regulation, which can be attributed to its ability to synthesize the major neurotransmitters for mood regulation. These neurotransmitters include; GABA from glutamic acid, dopamine and norepinephrine from phenylalanine or tyrosine, serotonin from tryptophan [62]. Besides, bioactive compounds including vitamins, unsaturated fatty acids and polyphenols exhibit a defensive effect against mood related disorders [63]. In addition, regular consumption of probiotics along with certain bacterial strains are associated with improved mood regulation [64]. Moreover, studies have underlined that, supplementation of galactooligosaccharides (GOS) and fructooligosaccharides (FOS) - major prebiotic compounds have positive effects on mood related disturbances [53]. Apart from this, several bacterial strains such as *Bifidobacterium spp.* and *Lactobacillus spp.* are prominent in mood regulations as they are considered as psychobiotics [64].

4.3. Role in managing mental health disorders

Nutritional interventions have a significant impact on psychotherapeutic treatments that contribute to improved sleep quality and decreased symptom severities [4]. The involvement of gut-brain bidirectional communication is proven in managing psychiatric disorders [65]. Additionally, this sub-section elaborates regarding mental health disorders that can be managed with the help of gut microbiotas, as neurotransmitters, intestinal bacteria and nutrition are directly linked with each other.

4.3.1. Depression

Nutrition holds an important role in mental health as the pathogenesis of many mental disorders such as depression can be attributed to

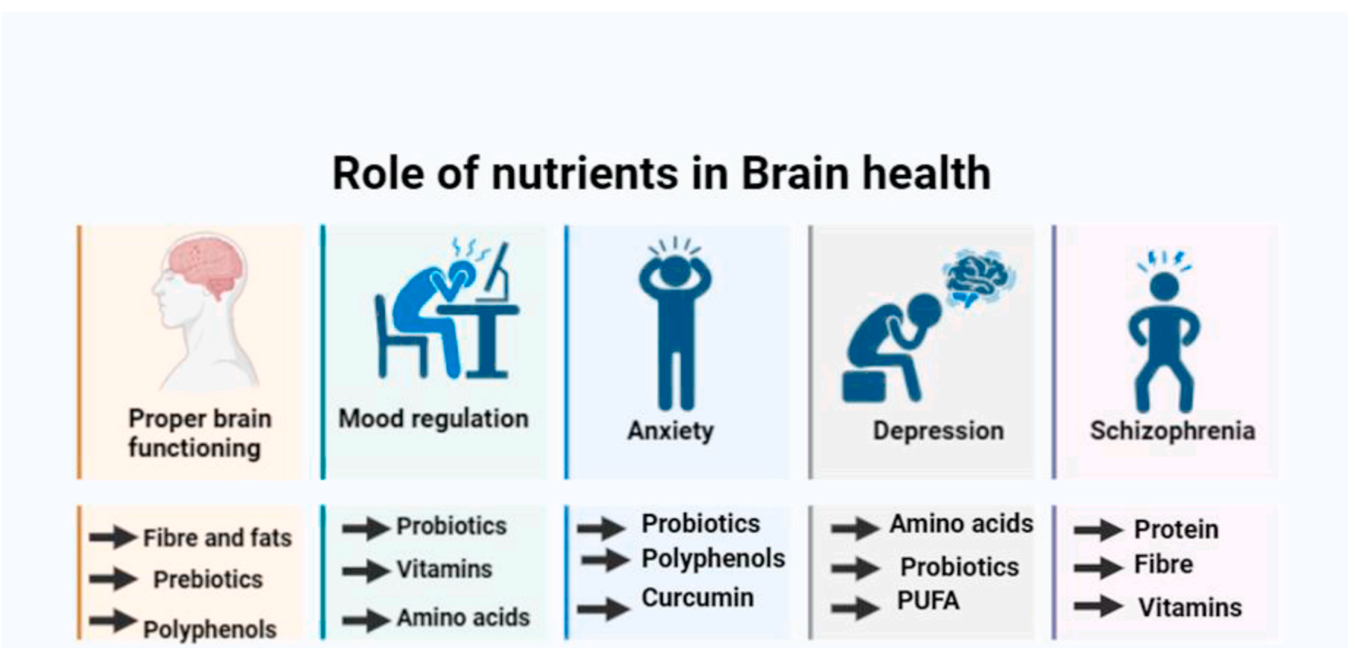

Fig. 2. Potential benefits of nutrients such as protein, Amino acids, fats, vitamins, probiotics and phenolic compounds on proper brain functioning, mood regulation, managing mental health disorders such as anxiety, depression and schizophrenia.

nutritional deficiencies [4]. Various nutrients are directly and indirectly associated with the management of depression [30]. Additionally, nutrients such as vitamin B3, B6, vitamin-C, inositol, folate and s-adenosyl-methionine that are present in gut friendly foods exhibit antidepressive effects [57]. Moreover, CNS has the highest concentration of polyunsaturated fatty acids (PUFA) including omega-3 and omega-6 fatty acids, that are known to reduce the complications of mental disorders like depression [66]. Evidence based studies suggests that nutrient rich diet with unprocessed foods will alleviate depressive symptoms. Hence, individualized dietary recommendations and prescriptions from dieticians by considering food intolerences, allergies, ethical and cultural preferences, socioeconomic status etc. [67]. Furthermore, in a randomized controlled trial, 152 aduts with depression were provided with Mediterranean diet for 3 months. The results showed that regular consumption of special diets such as mediterranean diet with fish oils has significantly decreased the symptoms of depression [68]. Besides, amino acid present in green tea - 'L-Theanine', exhibits protective effects against depressive symptoms [30]. Similarly, researches have highlighted the anti-depressive effect of stilbenoid resveratrol found in grapes, which can be attributed to its potential to hinder the reuptake of neurotransmitters such as serotonin and norepinephrine through gut brain axis [69]. According to studies, phenolic compounds also possess antidepressant effects through influencing the frontal cortex and hippocampal neurogenesis [30]. Besides, probiotics exerts a beneficial effect on managing depression by increasing BDNF and altering microbiota composition, via gut-brain axis [62]. Similar studies have also highlighted the positive effect of probiotic strains such as *Lactobacillus reuteri* NK33 and *bifidobacterium adolescentis* NK98 supplementation for depression [70]. Additionally, various systemic studies have also underscored the effect of probiotics as an antidepressant agent [71]. Likewise, regular consumption of fruits can influence gut microbiota due to the high concentration of fibre and phytonutrients in it, thus decreasing the risk of depression [64]. Hence, dieticians and clinical practitioners are trained to suggest appropriate therapeutic diets, dietary supplements and dietary counselling for ensuring lifestyle-based mental healthcare [67].

4.3.2. Anxiety

Nutrition has a significant role in managing behavioral disorders such as anxiety through the neuroendocrine system [72]. Studies have emphasised the positive effect of a ketogenic diet that limits high carbohydrates and high fat on anxiety related behaviours via altering the gut microbiota composition [4]. In addition, pro-inflammatory cytokines - IL-6 and IL-1β increase IDO expression in central and peripheral immune-competent cell types, whose activation degrades tryptophan, hence leading to anxiety symptoms [73]. Similarly, studies have highlighted that negative changes in intestinal bacteria composition due to nutritional deficiencies can cause anxiety related behavior [64]. Besides, the majority of mental disorders including anxiety are caused by elevated inflammatory markers and immunodeficiencies [74]. Such immunodeficiency and gut infection induced anxiety development can be managed with probiotics because generalized anxiety disorder has been noticed to be linked with altered gut microbiota composition which can be managed with probiotics [53]. For instance, fermented foods with probiotic strains are known for its inhibitory action against anxiety, as they exhibit direct association with immuno modulation and brain modulation [74]. In addition, an invivo study evaluated the effect of consuming a mix made of baru almond (*Dipteryx alata* Vog) and goat whey on aged mice models. The subjects were supplemented with the 2000 mg of baru + 2000 mg of goat whey/kg of body weight for 10 weeks and the results showed improved memory, decreased anxiety symptoms and reduction in pathogenic bacterial strains such as *Clostridia_UFC-014* [75]. Moreover, studies have emphasised the synergistic effect of curcumin on anxiety related behaviours induced by Dextran sulphate sodium salt (DSS), through altering the composition of gut microbiota [76].

4.3.3. Neurodevelopmental mental disorders (ASD and schizophrenia)

Various studies have stated the adverse impact of altered gut health in Autistic Spectrum Disorder (ASD) subjects, indicating the effect of gut microbiome with the pathophysiology of such disorders [57]. Researchers have reported that ASD patients exhibited a divergent abundance of gut microbiota composition that are composed of higher levels of harmful bacterias rather than the beneficial ones [77]. Moreover, a study conducted on ASD subjects concluded that diets with casein and gluten free products have a positive impact on reducing the symptoms of ASD as well as improved the non-verbal intellectual performance [78]. Similarly, another preclinical approach studied valproic acid induced ASD mice model to evaluate the effect of probiotic supplementation. The subjects were supplemented with fermented milk based on *Lactiplantibacillus plantarum* ST-III and the results showed improved autistic-like behaviors in male subjects through increasing the abundance of gut bacteria such as *Lachnospiracea* species [79]. Parallelly, schizophrenia is associated with poor nutritional intake, specifically during the symptomatic stage which can be linked with high intake of refined sugar and saturated fats [4]. Besides, studies have stated that glutamyle-thylamide, an amino acid present in green tea can be supplemented to patients suffering from schizophrenia [30]. Similarly, researchers have reported that schizophrenia patients exhibited enhancement in the communication between gut and CNS through incorporation of dietary fibre rich foods in daily diet [80].

5. Importance of gut friendly diet for brain health

Diet has a significant role on different gut microbial communities [81]. Gut friendly food has a major role in modulating the function and structure of the brain through gut-brain-microbiome (BGM) communication [57]. This section elaborates different diets for gut and brain health as represented in Fig. 3.

5.1. Protein rich food

Protein intake from food is known to improve episodic memory and working memory, particularly if the demands of tasks are very high [39]. Food groups like pulse that are rich in protein are closely linked with flourished microbiota composition and its metabolite synthesis [82]. For instance, studies revealed that regular consumption of chickpeas contributed to a significant increase in the levels of beneficial gut bacteria such as *Lactobacillus casei* and *Bifidobacterium* species whereas decreased the percentage of *Clostridium* cluster XI, I, II which are pathogenic in nature [27]. Moreover, due to its richness in essential nutrients, chickpeas are recognized as a functional food, particularly in the form of snacks, beverages, instant food products etc [83]. In addition, according to researchers, dietary pulse derived RS contribute to improvement in ageing associated neurocognitive functions [84]. Studies have highlighted that milk protein has a positive effect on CNS through influencing opioid receptors [85].

5.2. Fibre rich food

A fibre-rich diet includes the combination of fruits and vegetables, whole grains, pulses that have a potential in overall gut health, thus contributing to improved brain functions like working memory and inhibitory control [27]. Studies have shown the increase in composition of beneficial microbiota including *Lactobacillus* and *Bifidobacterium*, simultaneously decreasing the levels of *Enterococcus* and *E. coli*, through regular consumption of fruits and vegetables [86]. In addition, studies have highlighted that a combination of fruits and vegetables contributes to recurrent consumption of fibre rich diets are cross linked with low risks of mental disorders and regulation of brain health [87]. Moreover, fibre rich foods promote, gastric acid release and increase gastric distension, contributing a trigger to the vagal nerves for a satiety signal to the brain [88]. Besides, regular consumption of fibre rich foods are

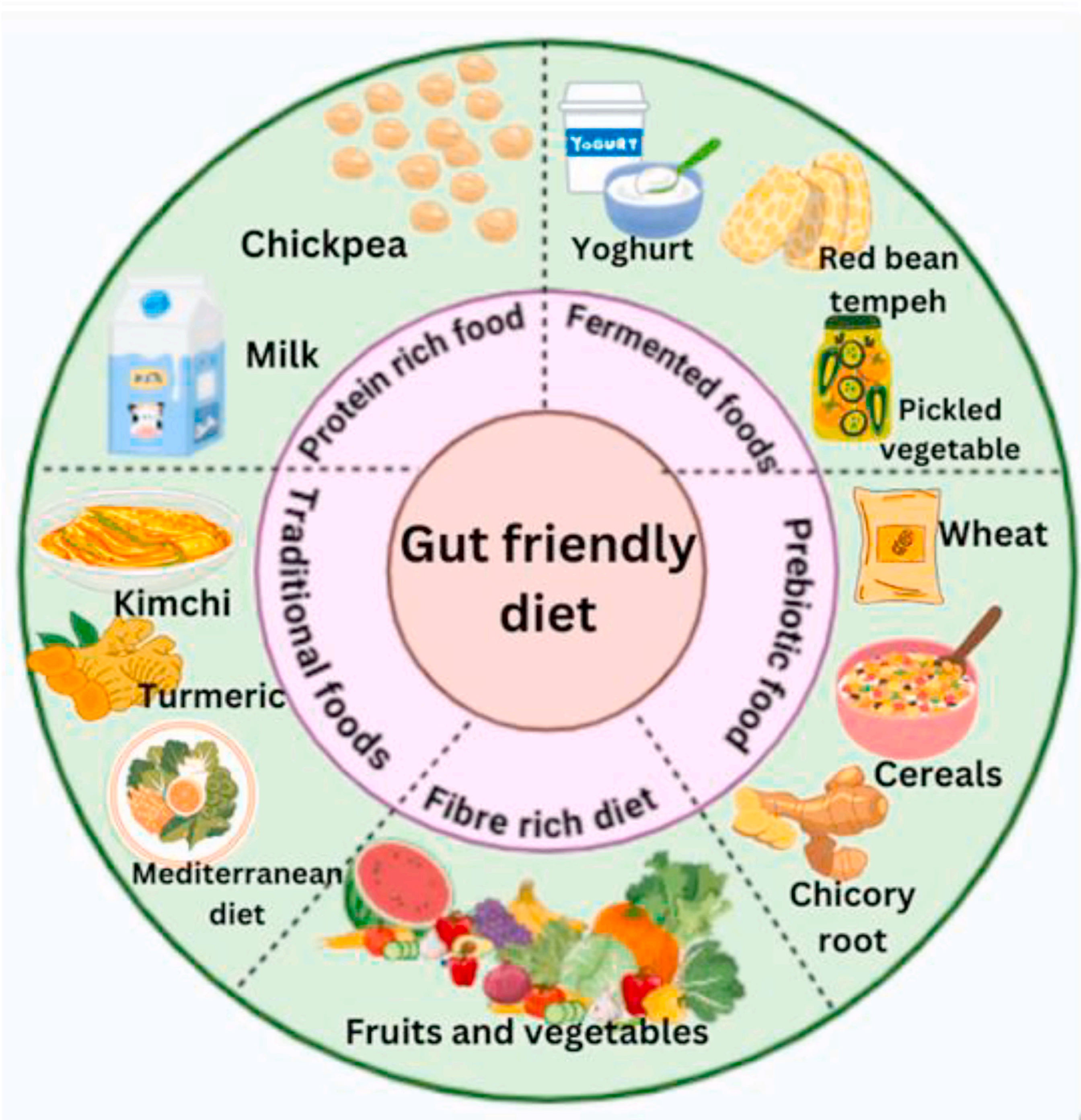

Fig. 3. Gut friendly diet including protein rich and fibre rich foods, fermented and prebiotic food products, traditional foods like Mediterranean diet, kimchi, turmeric has beneficial effects on brain health.

associated with mental well-being and decreased symptoms of depression [89]. Furthermore, foods rich in fibre also cause delayed gastric emptying, in correlation with cells for secretion of hormones like PYY, GLP-1, promotes satiety and decrease hunger [88].

5.3. Prebiotics

Prebiotics are food products that promote the growth of beneficial gut microbiomes as well as regulating immune cells hence contributing to a healthy brain [90]. Studies have stated that regular consumption of prebiotics may have positive effects of neurological disorders. Moreover, prebiotics are either consumed in the form of dietary supplements or as real foods such as cereals, wheat, chicory roots and onions. Furthermore, galactooligosaccharides and fructooligosaccharides are the two major prebiotics that are related to brain health [87]. For instance, a preclinical trial was performed on lipopolysaccharide (LPS)-induced CD1 adult mice models to analyse the effect of BGOS- a non-digestible galactooligosaccharide in anxiety. The subjects were fed with BGOS formulations for 3 weeks. Reduced cortical IL-1β levels were observed in BGOS fed mice, indicating formulation of prebiotic can regulate 5-HT2A (5-hydroxytryptamine 2A) and cortical IL-1b receptor expression. The study also highlights the significant role of prebiotics in managing neuropsychiatric disorders [91]. In addition, through the gut-brain axis, oligosaccharides in milk effectively flourishes the gut microbiome and manages stress induced during behavioral response [87]. Besides, prebiotic supplementation has been proved to modulate the sensory neurons of enteric nervous system (ENS) as well as improved growth of probiotic bacteria including *Lactobacillus* and *Bifidobacterium,* that plays a significant role on gut-brain axis [92].

5.4. Fermented food products

Fermented foods are foods and beverages developed through enzymatic conversions of major and minor food components with the help of microorganisms [93]. A diet rich in fermented food products is beneficial in maintaining brain health as it is considered as a source of good bacteria [94]. This can be attributed due to the presence of volatile compounds and alcoholic content in fermented foods, that influences the growth of gut microbiome [95]. Besides, fermentation of grains, lentils and vegetables are known to have a positive effect on the gut microbiota composition [94]. Additionally, non-dairy products like fermented grain products including sourdough bread have positive influence on insulin secretion and satiety, which can be attributed due to the acidic nature of fermented products [96]. Moreover, bioactive metabolites and probiotic factors are present in most of the fermented food products including sauerkraut, yoghurt and kefir [97]. Furthermore, these probiotic bacterias in fermented foods are well known for their ability to trigger the release of neurotransmitters like GABA [74]. Additionally, consumption of fermented foods with inulin-type fructans including cereals and chicory roots contributes to the growth of *Bifidobacterium Adolescentis and Faecalibacterium Prausnitzii*, that are beneficial gut microbiomes [94]. Besides, studies have highlighted the probiotic effect of milk kefir, a fermented product on dysregulation of glucocorticoid receptor expression in PVN that causes an alteration on the HPA axis [95]. Additionally, consumption of fermented foods such as red bean tempeh have shown to reduce anxiety levels in subjects with behavior disorders [98]. Similarly, studies have highlighted the restoration of beneficial gut bacteria and, through habitual consumption of a mixture of *Lactobacillus* sp. Obtained from fermented food products, namely fermented yoghurt, pickled Chinese cabbage and fermented milk product [99].

5.5. Traditional foods and herbs for gut-brain health

Traditional diets such as the Mediterranean diet, consisting of whole grains, pulses, fruits and vegetables, with limited red meat, sweets and refined products are prominent in brain health and reduced cognitive decline [30]. In addition, such diets could also influence the abundance of gut microbiota, thereby contributing to an antidepressant effect in the host [100]. Moreover, traditional chinese and korean fermented foods such as kimchi and kombucha have been known for its gut friendly effects and mood regulation [53]. Furthermore, turmeric (*Curcuma longa*), an Indian spice contributes to a positive effect on managing brain health and anxiety-like behaviours via gut brain axis, which can be attributed to the presence of curcumin in it [101]. Besides, a preclinical study evaluated the effect of 'Chaihu-Shugan-San'(CSS), a Chinese herbal mix is prominent for its potential to reverse stress induced by anxiety and depression. The study incorporated restraint stress (RS) induced depressive mice models with anxiety (male, 6 weeks old) were randomly categorized into 5 groups and were supplemented with the CSS water extract orally for 5 days. The results indicated potential decrease in RS-induced anxiety and depression in the subjects through suppressing NF-κB induced expression of BDNF [102].

6. Strategies for managing altered gut- brain signalling and mental health

The emerging strategies focusing on the gut microbiota comprises the incorporation of nutritional strategies and microbial bio therapies such as nutritional psychiatry, probiotic and paraprobiotic therapy and faecal microbiota transplantation (FMT) are discussed in this section. Table 2 represents different dietary interventions in mental health.

6.1. Nutritional strategies

The nutritional strategies for managing altered gut-brain health are explained below. 'Nutritional Psychiatry' is an emerging area of research that has great potential as an adjunctive tool for the prevention and treatment of diverse neuropsychiatric disorders [107]. This approach includes a combination of epidemiological and cross-sectional studies that are connected with brain health, mental disorders, diet and gut microbiome [57]. However, most of the psychiatric conditions are ameliorated with valuable nutritional approaches [107]. Furthermore, nutritional psychiatry fosters a diet that prevents metabolic endotoxemia, promotes brain health and structure [57]. Besides, it is based on the association between the consumption, bioavailability, metabolic function and body's exposure to particular nutrients with a wide range of psychiatric disorders, that are linked with regulation of synaptic plasticity and neuronal functions through direct and indirect pathways [108]. Supplementation of specific nutrients including B vitamins, Vitamin D, zinc, omega-3 fatty acids exhibit significant effects on managing gut-brain health [4]. Supplementation of microbiota-accessible carbohydrates (MAC) found in dietary fibre can contribute to improved cognitive impairments via the gut microbiota-brain axis induced by the consumption of an HF-FD [109]. In addition, supplementing such macro and micronutrients are emerging as a part of treatment for mental health disorders [4]. Similarly, individual supplementation of coca polyphenols, anthocyanin from blueberries, fiber (prebiotics) and blueberries either in dietary or extracted form can positively influenced mood, cognition and attenuated stress induced behavior [53]. In addition, studies states that following 'MIND diet', a combination of the DASH diet and Mediterranean diet can reduce the risk of neurodegenerative diseases like Alzheimer's disease, lower chances of age related cognitive decline [110]. However, due to inter-individual variation, the clinical response of different individuals with same conditions showed variability to different dietary interventions [111]. According to studies, integration of Mediterranean-based personliased dietery intervention reduced depressive symptoms in adults [112]. Studies are focusing on 'precision nutrition' under the field of nutritional psychiatry for designing tailored dietary and microbiome based interventions [111]. The hurdle in nutritional psychiatry is to have comprehensive and scientifically precise evidence-based studies to prove the contribution of nutrition in mental health. Current evidences suggests that in mental illnesses, poor nutrition is a modifiable risk factor that can be reduced with nutritional therapies [113]. For instance, studies have concluded that supplementation of vitamin D and Omega-3-fatty acids as an adjunctive strategy can modulate biological process in depression like inflammation, neurotransmitter activity and neuroplasticity [114]. Although, concerns exist in using dietary supplementation as a 'monotherapy' in severe mental health disorders like schizophrenia, bipolar disorder etc., instead it should be integrated with conventional care and if there are no contraindications to use as an adjunctive with the prescribed psychotropic drugs [113].

6.2. Microbial biotherapy

Microbial therapies are generally considered as a safe and effective strategy for treating dysbiosis that causes dysregulated immune responses [115]. The major microbial biotherapies such as probiotic and paraprobiotic therapy, faecal microbial transplantation (FMT) is elaborated below.

6.2.1. Probiotic and paraprobiotic therapy

The gut-brain axis has effect on regulating function of the brain and

Table 2
Dietary interventions in mental health.

Intervention	Study population	Key findings	Reference
Ketogenic diet (metabolic therapy)	n = 23 with Bipolar disorder or schizophrenia	Participants showed 32 % reduction in psychiatric rating scale in schizophrenia and clinical global improvement in bipolar	[103]
Mediterranean diet	n = 72 with depression	The intervention for 12 weeks lead to reduced pressive symptoms in 36 % of participants. Also, the Beck Depression (BD) Inventory Scale score and Mediterranean Diet Adherence Score (MEDAS) was higher in MD group compared to control group.	[104]
Micronutrient supplementation	n = 33 (pregnant women) with antenatal depression	After 12 week micronutrient supplemnentation, the microbiome community structure increased hetrogenously. The higher abundance of Coprococcus, whose increased alpha diversity is related with anenatal depression scores.	[105]
Probiotics	n = 49 with major depressive disorder (MDD)	Multi strain probiotic supplementation for 8 weeks showed positive impact on gut microbiota concentration.This increase in beneficial strains like family Bacilleaceae are corelated with decreasing MDD symptoms.	[106]

behavior has been examined through preclinical trials [53]. Probiotics are live microorganisms that exerts potential health benefits to the host's health whereas, paraprobiotics are inactivated probiotic microbial cells or cell extracts for providing benefits when consumed in adequate amount [116]. Moreover, paraprobiotics include cell surface proteins, peptidoglycans, teichoic acid, polysaccharides from microbial cell walls etc. Indeed, probiotic and paraprobiotic therapies are prominent in the area of neuropsychiatry, through the modulation of gut microbiomes, thereby improving the gut-brain communication [117]. For instance, studies have reported that probiotics can influence the gut-brain axis through serotonin production in the gut [118]. Apart from this, oral gavage supplementation of paraprobiotic *Lactobacillus paracasei* PS23, inactivated at 100 °C has exhibited reduced symptoms related to anxiety and depression through hippocampal expression of BDNF [119]. Correspondingly, studies have also reported a decreased psychosocial discomfort, improved bowel movement and increased activity of parasympathetic nerves through the supplementation of beverage incorporating bacterial cells of *Lactobacillus gasseri* CP2305, a paraprobiotic pasteurised at 90 °C and freeze dried for inactivation [120]. Moreover, the gut microbiome composition can be a biomarker for psychiatric drug respondance and resistance, while the gut-brain axis holds a crucial role in the tolerability of such medications. Besides, the functioning network of insula- a region in brain that causes reduction of attention, stimulation of negative emotions and mood was reduced by the therapeutic supplementation of multi-strains of probiotics including *Bifidobacterium lactis, Streptococcus thermophilus, Lactobacillus lactis* and *Lactobacillus bulgaricus*. Apart from this, probiotic therapy also decreases emotional reactivity as well as reduction in cortisol response. Furthermore, studies have also reported a reduction in the inflammation and stress induced behavior in irritable bowel syndrome (IBS) which is interlinked with gut-brain axis dysbiosis, through supplementation of a probiotic strain - *Bifidobacterium infantis* [121]. In a randomized controlled trial proposed that there was significant reduction in depressive symptoms due to specific strains such as *Lactobacillus acidophilus, Lactobacillus paracssei, Bifidobacterium breve* etc. The study concluded that stain-specific probiotic approach can effectively reduce anxiety and depressive symptoms [118]. In addition, studies have showed improved symptoms in Generalized Anxiety Disorder (GAD) through sertraline with probiotic treatments as an adjuvant, rather than first line selective serotonin reuptake inhibitors (SSRI) alone [122]. Similarly, studies have been conducted to analyse the effect of probiotics as an adjunctive therapy to clinical medications on anxiety. The results indicated that there was reduced GAD symptoms with a synergistic approach combining 25 mg of sertraline (clinical drug) and probiotic capsules containing *Bifidobacterium bifidum, Bifidobacterium longom, Bifidobacterium lactis* and *Lactobacillus acidophilus* [117].

6.2.2. *Faecal microbial transplantation*

Faecal Microbial transplantation (FMT) is an emerging strategy for managing altered gut brain signalling, where a healthy donor donates their microbiota to the patient [123]. FMT has the ability to upgrade clinical symptoms and reassemble the gut ecosystem [113]. It is considered as an effective therapeutic treatment in recurrent *Clostridium difficile* infection (rCDI) [124]. After US Food and Drug Administration (FDA) approved FMT in 2013, the approach emerged as an effective treatment for microbiota dysfunction related disorders [124]. However, along with its therapeutic influence on gastrointestinal diseases, FMT also regulates gut-brain cross communication, thus boosting psychological and neurological health [125]. According to studies, the dynamic and personalized features of human microbiota has the ability to improve mental health. Based on the association between depression and gut microbiome, studies have incorporated FMT as an adjunct therapy with psychiatric treatment. The results showed improved depressive symptoms after 4–8 weeks of transplantation [126]. While FMT has shown therapeutic promises, it has several ethical and social regulatory concerns related to vulnerability of patient, informed consent, selection of appropriate donor and safety of the process. The donors should go through critical screening procedures and standard procedure is needed for avoiding the risk of disease transmission [127]. Also, the availability of self adminstratable (do-it-yourself) FMT kits in the market leads to hazardous risks and unfavorable results, as it should only be performed by certified healthcare professionals [128]. The privacy of the donor and patient is another ethical consideration of FMT, as studies have reported that individuals can be identified with distinct personal microbiome features overtime [127]. The method of administrating the bacteria is generally considered safe, even though it is associated with short term issues like bloating, constipation and diarrhoea [123]. However, the regulatory frameworks must ensure certain factors like carrier risks of pathogens during FMT, recipients immune status and the level of colonization antagonism of native microbiota towards the donor microbes [129]. These regulatory frameworks may vary across different countries, with some categorized FMT as a transplant while others as a drug, leading to an unharmonized safety standards at global level [128]. However, the US FDA approved fecal microbiota as a novel investigational drug and a biological product and the American Gastroenterology Association with National Institute of Health (NIH) has established an FMT National Registry for enrolling and tracking FMT patients over 10 years for follow up [128,130]. The emerging positive evidences and clinical acceptance categorizes FMT as an evolving field of microbiota-based therapeutics with diverse stakeholders including physicians, hospital administrators, patient advocacy groups, industries etc. [128]. Clinical trials of FMT on gut-brain related disorders are outlined as Table 3.

7. Conclusion and future directions

The bidirectional communication between gut and brain has a significant role in maintaining the overall functioning of the body. The gut microbiota regulates various neuronal functions through multiple pathways like immunal, hormonal and neurological pathways. Moreover, this gut-brain axis is closely associated with diet and nutrition through the regulation of beneficial gut microbiota. Furthermore,

Table 3
Clinical studies of Faecal Microbial Transplantation on gut and brain related disorders.

Clinical Diagnosis	FMT Method	Volume administered	Transplantation method	Outcome	Post FMT symptoms	References
Clostridiosis difficile infection (CDI)	Screening of donor and recipient, stool preparation	250 ml	Through colonoscopy followed by upper endoscopy.	98 percent of the subjects received effectiveness in a single trial with reduced CDI.	Diarrhoea/ constipation, bloating, abdominal pain.	[131]
Recurrent *Clostridiosis difficile* infection (rCDI)	Screening of donor and 16s rRNA gene amplicon sequencing for alfa diversity assessment	25 capsules per day for 3 days which contributes to a daily dosage of 10 gm in total.	Through oral cavity in the form of faecal microbiota capsules and FMT enema.	Successful transplantation with no recurrence of the disease, even after a span of 180 days.	No adverse events.	[132]
Depression	Screening of recipients (anthropometry and demography).	30 capsules per day with a dosage of 8.25 gm in total.	Through oral cavity in the form of frozen faecal microbiota capsules	Symptoms of depression reduced from severe to mild/ moderate level with increased abundance of gut microbiota.	No Serious Adverse events (SAE) reported.	[126]
Bipolar Disorder	Screening of recipient (multiple analysis of urine and stool), colonoscopy and panendoscopy.	250 mg per day	Through colonoscopy and enema	Improved symptoms of bipolar disorder including mood oscillations, anxiety etc.	Depressive and hypomanic period experienced	[133]

several nutrients and nutritional compounds such as protein, fibre, vitamins, bioactive compounds as well as its gut metabolites directly and indirectly influences gut brain axis. Apart from this, these nutrients through the alteration of gut microbiota as well as stimulation of neurotransmitters can significantly reduce the symptoms of neurological disorders like depression, mood and anxiety related behaviours. However, specific gut friendly diets including high fibre, high protein, prebiotics and traditionally followed food products are beneficial for maintaining brain health. In addition, recent techniques are getting prominent in the field of gut-brain health for the management of altered brain-gut-microbiota crosstalk that includes nutritional psychiatry, probiotic therapies, faecal microbial transplantation. While current findings depicts the effect of nutrition in managing mental health diseases, it can only be an adjunctive therapy along with psychotherapy. Looking ahead, future studies are required to analyse the proper mechanism of diet that influences gut-brain health The existing studies are limited in terms of variabilitiy in protocols, small sample size, insufficient data and lack of follow ups. Hence, further studies should focus on randomized control trials for evaluating microbiome based dietary strategies in mentally ill subjects. Moreover, longitudinal studies are required to examine the interplay between genetic factors, gender, age and lifestyle in terms of gut-brain axis. Furthermore, combined studies are required in the field of neuroscience and nutrition for exploring new pathways that connect nutrition with brain health as well as to foster diet related nutritional therapies in terms of mental health disorders. Additionally, personalized nutritional approaches based on microbiome profiling can improve the treatment outcomes and support the field of nutritional psychiatry.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Ethics approval consent

Not applicable.

Abbreviations

Availability of data and materials

No data set was generated for this article.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

AA	Amino Acid
ACTH	Adrenocorticotropic Hormone
AGRP/NPY	Agouti related peptide/Neuropeptide Y
ANS	Autonomous Nervous System
ARC	Arcuate Nucleus
ASD	Autism Spectrum Disorder
BA	Bile Acids
BBB	Blood Brain Barrier
BDNF	Brain-derived Neurotrophic factor
BGM	Brain-Gut-Microbiome
BGOS	Bifidobacterium Galactooligosaccharides
CCK	Cholecystokinin
CNS	Central Nervous System
CRF	Corticotropin Release Factor
CRH	Corticotropin Releasing Hormone
DHPA	(3-(3,4- dihydroxyphenyl)-propionic acid)
ENS	Enteral Nervous System
ERK 1/2	Extracellular Regulated Kinase 1/2
FG19	Fibroblast Growth Factor 19
FMT	Faecal Microbial Transplantation
FXR	Farnesoid X Receptors
GABA	γ- amino butyric acid
GLP-1	Glucagon like Peptide-1
GLU	L-Glutamate
GOS	Galactooligosaccharides
GPCR	G- Protein Coupled Receptors
HDAC	Histone Deacetylases
HPA	Hypothalamus-Pituitary-Adrenal
IBS	Irritable Bowel Syndrome
LPS	Lipopolysaccharides
MAC	Microbiota Accessible Carbohydrates
MS	Multiple Sclerosis
NF-κB	Nuclear Factor kappa B
PVN	Paraventricular Nucleus
PYY	Peptide YY
RA	Retinoic Acid
SCFA	Short Chain Fatty Acid
TGFα	Transforming Growth Factor- α
VEGF-B	Vascular Endothelial Growth Factor-B
VIP	Vasoactive Intestinal Peptide

References

[1] M. Bistoletti, A. Bosi, D. Banfi, C. Giaroni, A. Baj, The microbiota-gut-brain axis: focus on the fundamental communication pathways, PMBTS 176 (2020) 43–110, https://doi.org/10.1016/bs.pmbts.2020.08.012.

[2] H. Ahmed, Q. Leyrolle, V. Koistinen, O. Kärkkäinen, S. Layé, N. Delzenne, K. Hanhineva, Microbiota-derived metabolites as drivers of gut–brain communication, Gut Microbes 14 (1) (2022) 2102878, https://doi.org/10.1080/19490976.2022.2102878.

[3] N. Randeni, B. Xu, Critical review of the cross-links between dietary components, the gut microbiome, and depression, Int. J. Mol. Sci. 26 (2) (2025) 614.

[4] S. Mörkl, J. Wagner-Skacel, T. Lahousen, S. Lackner, S.J. Holasek, S.A. Bengesser, E. Reininghaus, The role of nutrition and the gut-brain axis in psychiatry: a review of the literature, Neuropsychobiology 79 (1) (2020) 80–88, https://doi.org/10.1159/000492834.

[5] A. Chakrabarti, L. Geurts, L. Hoyles, P. Iozzo, A.D. Kraneveld, G. La Fata, D. Vauzour, The microbiota–gut–brain axis: pathways to better brain health. Perspectives on what we know, what we need to investigate and how to put knowledge into practice, Cell. Mol. Life Sci. 79 (2022) 80, https://doi.org/10.1007/s00018-021-04060-w.

[6] A.P. Makris, M. Karianaki, K.L. Tsamis, S.A. Paschou, The role of the gut-brain axis in depression: endocrine, neural, and immune pathways, Hormones (Basel) 20 (1) (2021) 1–12, https://doi.org/10.1007/s42000-020-00236-4.

[7] G. Ezra-Nevo, S.F. Henriques, C. Ribeiro, The diet-microbiome tango: how nutrients lead the gut brain axis, Curr. Opin. Neurobiol. 62 (2020) 122–132, https://doi.org/10.1016/j.conb.2020.02.005.

[8] M. Dziedziak, A. Mytych, H.P. Szyller, M. Lasocka, G. Augustynowicz, J. Szydziak, T. Pytrus, Gut microbiota in psychiatric and neurological disorders: current insights and therapeutic implications, Biomedicines 13 (9) (2025) 2104.

[9] S.N. Hansen, D.H. Ipsen, A.M. Schou-Pedersen, J. Lykkesfeldt, P. Tveden-Nyborg, Long term westernized diet leads to region-specific changes in brain signaling mechanisms, Neurosci. Lett. 676 (2018) 85–91, https://doi.org/10.1016/j.neulet.2018.04.014.

[10] E. Sherwin, T.G. Dinan, J.F. Cryan, Recent developments in understanding the role of the gut microbiota in brain health and disease, Ann. N. Y. Acad. Sci. 1420 (1) (2018) 5–25, https://doi.org/10.1111/nyas.13416.

[11] E. Salvo-Romero, P. Stokes, M.G. Gareau, Microbiota-immune interactions: from gut to brain, LYMPHOSIGN J 7 (1) (2020) 1–23, https://doi.org/10.14785/lymphosign-2019-0018.

[12] J. Ojeda, A. Ávila, P.M. Vidal, Gut microbiota interaction with the central nervous system throughout life, J. Clin. Med. 10 (6) (2021) 1299, https://doi.org/10.3390/jcm10061299.

[13] M.G. Gwak, S.Y. Chang, Gut-brain connection: microbiome, gut barrier, and environmental sensors, Immune Netw 21 (3) (2021) 20, https://doi.org/10.4110/in.2021.21.e20.

[14] A. Baj, E. Moro, M. Bistoletti, V. Orlandi, F. Crema, C. Giaroni, Glutamatergic signaling along the microbiota-gut-brain axis, J. Mol. Sci. 20 (6) (2019) 1482, https://doi.org/10.3390/ijms20061482.

[15] B.M. Arneth, Gut–brain axis biochemical signalling from the gastrointestinal tract to the central nervous system: gut dysbiosis and altered brain function, Postgrad. Med. J. 94 (1114) (2018) 446–452, https://doi.org/10.1136/postgradmedj-2017-135424.

[16] K. Raj, N. Arora, A. Awasthi, M. Patel, A. Chaudhary, S. Singh, G.D. Gupta, Role of gut microbiota in neuroinflammation and neurological disorders, Frontiers in Clinical Drug Research-CNS and Neurological Disorders 12 (2024) 80–137, https://doi.org/10.2174/9789815179842124120l.

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

[18] M.K. Saraf, B.D. Piccolo, A.K. Bowlin, K.E. Mercer, T. LeRoith, S.V. Chintapalli, L. Yeruva, Formula diet driven microbiota shifts tryptophan metabolism from serotonin to tryptamine in neonatal porcine Colon, Microbiome 5 (1) (2017) 77.

[19] B.B. Yoo, S.K. Mazmanian, The enteric network: interactions between the immune and nervous systems of the gut, Immunity 46 (6) (2017) 910–926, https://doi.org/10.7907/1zv5-ve82.

[20] M. Prinz, D. Erny, N. Hagemeyer, Ontogeny and homeostasis of CNS myeloid cells, Nat. Immunol. 18 (2017) 385–392, https://doi.org/10.1038/ni.3703.

[21] R. Abdel-Haq, J.C. Schlachetzki, C.K. Glass, S.K. Mazmanian, Microbiome–microglia connections via the gut–brain axis, J. Exp. Med. 216 (1) (2019) 41–59, https://doi.org/10.1084/jem.20180794.

[22] R. Fu, Q. Shen, P. Xu, J.J. Luo, Y. Tang, Phagocytosis of microglia in the central nervous system diseases, Mol. Neurobiol. 49 (3) (2014) 1422–1434, https://doi.org/10.1007/s12035-013-8620-6.

[23] W. Tang, H. Zhu, Y. Feng, R. Guo, D. Wan, The impact of gut microbiota disorders on the blood–brain barrier, Infect. Drug Resist. (2020) 3351–3363.
[24] A. Alam, E.P. Thelin, T. Tajsic, D.Z. Khan, A. Khellaf, R. Patani, A. Helmy, Cellular infiltration in traumatic brain injury, J. Neuroinflammation 17 (1) (2020) 328.
[25] L.J. Sun, J.N. Li, Y.Z. Nie, Gut hormones in microbiota-gut-brain cross-talk, Chin. Med. J 133 (7) (2020) 826–833, https://doi.org/10.1097/CM9.0000000000000706.
[26] A. Farzi, E.E. Fröhlich, P. Holzer, Gut microbiota and the neuroendocrine system, Neurotherapeutics 15 (1) (2018) 5–22.
[27] K. Berding, K. Vlckova, W. Marx, H. Schellekens, C. Stanton, G. Clarke, J.F. Cryan, Diet and the microbiota–gut–brain axis: sowing the seeds of good mental health, Adv. Nutr. 12 (4) (2021) 1239–1285, https://doi.org/10.1093/advances/nmaa181.
[28] N. Ma, X. Ma, Dietary amino acids and the gut-microbiome-immune axis: physiological metabolism and therapeutic prospects, COMPR REV FOOD SCI F 18 (1) (2018) 221–242, https://doi.org/10.1111/1541-4337.12401.
[29] B. Dalile, L. Van Oudenhove, B. Vervliet, The role of short-chain fatty acids in microbiota–gut–brain communication, Nat. Rev. Gastroenterol. Hepatol. 16 (2019) 461–478, https://doi.org/10.1038/s41575-019-0157-3.
[30] B. Ekstrand, N. Scheers, M.K. Rasmussen, J.F. Young, A.B. Ross, R. Landberg, Brain foods-the role of diet in brain performance and health, Nutr. Rev. 79 (6) (2021) 693–708, https://doi.org/10.1093/nutrit/nuaa091.
[31] K. Kasprzak-Drozd, T. Oniszczuk, M. Stasiak, A. Oniszczuk, Beneficial effects of phenolic compounds on gut microbiota and metabolic syndrome, Int. J. Mol. Sci. 22 (7) (2021) 3715, https://doi.org/10.3390/ijms22073715.
[32] W. Śliwiński, O. Gawlik-Kotelnicka, Circulating B vitamins metabolites in depressive disorders-connections with the microbiota-gut-brain axis, Behav. Brain Res. (2024) 115145, https://doi.org/10.1016/j.bbr.2024.115145.
[33] S.L. Collins, J.G. Stine, J.E. Bisanz, et al., Bile acids and the gut microbiota: metabolic interactions and impacts on disease, Nat. Rev. Microbiol. 21 (2023) 236–247, https://doi.org/10.1038/s41579-022-00805-x.
[34] C. Xing, X. Huang, D. Wang, D. Yu, S. Hou, H. Cui, L. Song, Roles of bile acids signaling in neuromodulation under physiological and pathological conditions, Cell Biosci. 13 (1) (2023) 106.
[35] A. Agus, J. Planchais, H. Sokol, Gut microbiota regulation of tryptophan metabolism in health and disease, Cell Host Microbe 23 (6) (2018) 716–724, https://doi.org/10.1016/j.chom.2018.05.003.
[36] S. Taleb, Tryptophan dietary impacts gut barrier and metabolic diseases, Front. Immunol. 10 (2019) 2113, https://doi.org/10.3389/fimmu.2019.02113.
[37] Y. Liu, H. Wang, S. Gui, B. Zeng, J. Pu, P. Zheng, P. Xie, Proteomics analysis of the gut–brain axis in a gut microbiota-dysbiosis model of depression, Transl. Psychiatry 11(1) (202)568, https://doi.org/10.1038/s41398-021-01689-w.
[38] P. Strandwitz, Neurotransmitter modulation by the gut microbiota, Brain Res. 1693 (2018) 128–133, https://doi.org/10.1016/j.brainres.2018.03.015.
[39] A.K. Muth, S.Q. Park, The impact of dietary macronutrient intake on cognitive function and the brain, Clin. Nutr. 40 (6) (2021) 3999–4010, https://doi.org/10.1016/j.clnu.2021.04.043.
[40] H.M. Ng, C.L. Wall, S.B. Bayer, R.B. Gearry, N.C. Roy, The interconnection between dietary fibre, gut microbiome and psychological well-being, Proc. Nutr. Soc. (2025) 1–10.
[41] J. Kumar, K. Rani, C. Datt, Molecular link between dietary fibre, gut microbiota and health, Mol. Biol. Rep. 47 (8) (2020) 6229–6237.
[42] M. Van de Wouw, M. Boehme, J.M. Lyte, N. Wiley, C. Strain, O. O'Sullivan, J. F. Cryan, Short-chain fatty acids: microbial metabolites that alleviate stress-induced brain–gut axis alterations, J. Physiol. 596 (20) (2018) 4923–4944, https://doi.org/10.1113/JP276431.
[43] C. Torres-Fuentes, A.V. Golubeva, A.V. Zhdanov, S. Wallace, S. Arboleya, D. B. Papkovsky, H. Schellekens, Short-chain fatty acids and microbiota metabolites attenuate ghrelin receptor signalling, FASEB J. 33 (12) (2019) 13546–13559, https://doi.org/10.1096/fj.201901433.
[44] I. Domínguez-López, A. López-Yerena, A. Vallverdú-Queralt, M. Pallàs, R. M. Lamuela-Raventós, M. Pérez, From the gut to the brain: the long journey of phenolic compounds with neurocognitive effects, Nutr. Rev. (2024) 34, https://doi.org/10.1093/nutrit/nuae034.
[45] M.C. Tsai, S.H. Lin, K. Hidayah, C. Lin, Equol pretreatment protection of SH-SY5Y cells against Aβ (25–35)-induced cytotoxicity and cell-cycle reentry via sustaining estrogen receptor alpha expression, Nutrients 11 (10) (2019) 2356, https://doi.org/10.3390/nu11102356.
[46] I. Luzardo-Ocampo, M. Rebollo-Hernanz, Phenolic compounds and their impact on the gut-brain (2024), J. Funct.Foods 116 (2024) 106171, https://doi.org/10.1016/j.jff.2024.106171 axis.
[47] K.S. Batista, V.M. Cintra, P.A. Lucena, R. Manhães-de-Castro, A.E. Toscano, L. P. Costa, J.D.S. Aquino, The role of vitamin B12 in viral infections: a comprehensive review of its relationship with the muscle–gut–brain axis and implications for SARS-CoV-2 infection, Nutr. Rev. 80 (3) (2022) 561–578.
[48] P.K. Jena, L. Sheng, J. Di Lucente, L.W. Jin, I. Maezawa, Y.J.Y. Wan, Dysregulated bile acid synthesis and dysbiosis are implicated in Western diet–induced systemic inflammation, microglial activation, and reduced neuroplasticity, FASEB J. 32 (5) (2018) 2866, https://doi.org/10.1096/fj.201700984RR.
[49] X. Su, Y. Gao, R. Yang R, Gut microbiota-derived tryptophan metabolites maintain gut and systemic homeostasis, Cells 11 (15) (2022) 2296, https://doi.org/10.3390/cells11152296.
[50] W. Roth, K. Zadeh, R. Vekariya, Y. Ge, M. Mohamadzadeh, Tryptophan metabolism and gut-brain homeostasis, Int. J. Mol. Sci. 22 (6) (2021) 2973, https://doi.org/10.3390/ijms22062973.
[51] N. Ma, T. He, L.J. Johnston, X. Ma, Host–microbiome interactions: the aryl hydrocarbon receptor as a critical node in tryptophan metabolites to brain signaling, Gut Microbes 11 (5) (2020) 1203–1219.
[52] V. Rothhammer, D.M. Borucki, E.C. Tjon, M.C. Takenaka, C.C. Chao, A. Ardura-Fabregat, F.J. Quintana, Microglial control of astrocytes in response to microbial metabolites, Nature 557 (7707) (2018) 724–728, https://doi.org/10.1038/s41586-018-0119-x.
[53] T.L. Bear, J.E. Dalziel, J. Coad, N.C. Roy, C.A. Butts, P. K. Gopal, The role of the gut microbiota in dietary interventions for depression and anxiety. Adv. Nutr. 11 (4) (202) 890-907, https://doi.org/10.1093/advances/nmaa016.
[54] K. Moore, C.F. Hughes, M. Ward, L. Hoey, H. McNulty, Diet, nutrition and the ageing brain: current evidence and new directions, PNS 77 (2) (2018) 152–163, https://doi.org/10.1017/S0029665117004177.
[55] J. Bensalem, S. Dudonné, D. Gaudout, L. Servant, F. Calon, Y. Desjardins, V. Pallet, Polyphenol-rich extract from grape and blueberry attenuates cognitive decline and improves neuronal function in aged mice, J. Nutr. Sci. 7 (2018) e19, https://doi.org/10.1017/jns.2018.10.
[56] M.T. Melzer, L.M. Manosso, S.Y. Yau, J. Gil-Mohapel, P.S. Brocardo, In pursuit of healthy aging: effects of nutrition on brain function, Intermt. J. Sci. 22 (9) (2021) 5026, https://doi.org/10.3390/ijms22095026.
[57] J. Horn, D.E. Mayer, S. Chen, Role of diet and its effects on the gut microbiome in the pathophysiology of mental disorders, Transl. Psychiatry 12 (2022) 164, https://doi.org/10.1038/s41398-022-01922-0.
[58] G. Yang, W. Yang, F. Kiarasi, Polyphenol-based nutritional strategies combined with exercise for brain function and glioma control: focus on epigenetic modifications, cognitive function, learning and memory processes, Food Sci. Nutr. 13 (8) (2025) e70758.
[59] E. Schneider, K.J. O'Riordan, G. Clarke, J.F. Cryan, Feeding gut microbes to nourish the brain: unravelling the diet–microbiota–gut–brain axis, Nat. Metab. 6 (2024) 1454–1478. https://do8,i.org/10.1038/s42255-024-01108-6.
[60] C.N. Cannavale, A.R. Mysonhimer, M.A. Bailey, N.J. Cohen, H.D. Holscher, N. A. Khan, Consumption of a fermented dairy beverage improves hippocampal-dependent relational memory in a randomized, controlled cross-over trial, Nutr. Neurosci. 26 (3) (2023) 265–274, https://doi.org/10.1080/1028415X.2022.2046963.
[61] L.B. Martins, J.R. Braga Tibães, M. Sanches, F. Jacka, M. Berk, A.L. Teixeira, Nutrition-based interventions for mood disorders, Expert Rev. Neurother. 21 (3) (2021) 303–315, https://doi.org/10.1080/14737175.2021.1881482.
[62] M. Mueller, R. Ganesh, S. Bonnes, Gut health = mental health? The impact of diet and dietary supplements on mood disorders, Curr Nutr Rep 9 (2020) 361–368, https://doi.org/10.1007/s13668-020-00340-2.
[63] A. Arab, S. Mehrabani, S. Moradi, R. Amani, The association between diet and mood: a systematic review of current literature, Psychol. Res. 271 (2019) 428–437, https://doi.org/10.1016/j.psychres.2018.12.014.
[64] A.M. Taylor, S.V. Thompson, C.G. Edwards, S.M. Musaad, N.A. Khan, H. D. Holscher, Associations among diet, the gastrointestinal microbiota, and negative emotional states in adults, Nutr. Neurosci. 23 (12) (2020) 983–992, https://doi.org/10.1080/1028415X.2019.1582578.
[65] M. Van de Wouw, H. Schellekens, T.G. Dinan, J.F. Cryan, Microbiota-gut-brain axis: modulator of host metabolism and appetite, J. Nutr. 147 (5) (2017) 727–745, https://doi.org/10.3945/jn.116.240481.
[66] T. Larrieu, S. Layé, Food for mood: relevance of nutritional omega-3 fatty acids for depression and anxiety, Front. Physiol. 9 (2018) 1047, https://doi.org/10.3389/fphys.2018.01047.
[67] W. Marx, S.H. Manger, M. Blencowe, G. Murray, F.Y.Y. Ho, S. Lawn, A. O'Neil, Clinical guidelines for the use of lifestyle-based mental health care in major depressive disorder: World Federation of societies for biological psychiatry (WFSBP) and australasian society of lifestyle medicine (ASLM) taskforce, World J. Biol. Psychiatr. 24 (5) (2023) 333–386.
[68] N. Parletta, D. Zarnowiecki, J. Cho, A. Wilson, S. Bogomolova, A. Villani, K. O'Dea, A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: a randomised controlled trial (HELFIMED), Nutr. Neurosci. 22 (7) (2019) 474–487, https://doi.org/10.1080/1028415X.2017.1411320.
[69] S.M. Nabavi, M. Daglia, N. Braidy, S.F. Nabavi, Natural products, micronutrients, and nutraceuticals for the treatment of depression: a short review, Nutr. Neurosci. 20 (3) (2017) 180–194, https://doi.org/10.1080/1028415X.2015.1103461.
[70] Q. Huang, H. Liu, K. Suzuki, S. Ma, C. Liu, Linking what we eat to our mood: a review of diet, dietary antioxidants, and depression, Antioxidants 8 (9) (2019) 376, https://doi.org/10.3390/antiox8090376.
[71] I. Nadeem, M.Z. Rahman, Y. Ad-Dab'bagh, M. Akhtar, Effect of probiotic interventions on depressive symptoms, A narrative review evaluating systematic reviews PCN73 (4) (2019) 154–162, https://doi.org/10.1111/pcn.12804.
[72] P.M. Kris-Etherton, K.S. Petersen, J.R. Hibbeln, D. Hurley, V. Kolick, S. Peoples, G. Woodward-Lopez, Nutrition and behavioral health disorders: depression and anxiety, Nutr. Rev. 79 (3) (2021) 247–260, https://doi.org/10.1093/nutrit/nuaa025.
[73] L.A. Quagliato, A.E. Nardi, Cytokine alterations in panic disorder: a systematic review, J. Affect. Disord. 228 (2018) 91–96, https://doi.org/10.1016/j.jad.2017.11.094.
[74] H. Aslam, J. Green, F.N. Jacka, F. Collier, M. Berk, J. Pasco, S.L. Dawson, Fermented foods, the gut and mental health: a mechanistic overview with implications for depression and anxiety, Nutr. Neurosci. 23 (9) (2020) 659–671, https://doi.org/10.1080/1028415X.2018.1544332.
[75] R.D.C. de Araújo Bidô, D.E. Pereira, M. da Costa Alves, L.M.G. Dutra, A.C. dos Santos Costa, V.B. Viera, J.K.B. Soares, Mix of almond baru (Dipteryx alata Vog.)

and goat whey modulated intestinal microbiota, improved memory and induced anxiolytic like behavior in aged rats, J. Psychiatr. Res. 164 (2023) 98–117, https://doi.org/10.1016/j.jpsychires.2023.05.046.
[76] F. Zhang, Y. Zhou, H. Chen, H. Jiang, F. Zhou, B. Lv, M. Xu, Curcumin alleviates DSS-Induced anxiety-like behaviors via the microbial-brain-gut axis, Oxid. Med. Cell. Longev. 2022 (1) (2022) 6244757, https://doi.org/10.1155/2022/6244757.
[77] R.G. Xiong, J. Li, J. Cheng, D.D. Zhou, S.X. Wu, S.Y. Huang, H.B. Li, The role of gut microbiota in anxiety, depression, and other mental disorders as well as the protective effects of dietary components, Nutrients 15 (14) (2023) 3258, https://doi.org/10.3390/nu15143258.
[78] J.B. Adams, T. Audhya, E. Geis, E. Gehn, V. Fimbres, E.L. Pollard, D.W. Quig, Comprehensive nutritional and dietary intervention for autism spectrum Disorder—A randomized, controlled 12-month trial, Nutrients 10 (3) (2018) 369, https://doi.org/10.3390/nu10030369.
[79] Y. Zhang, M. Guo, H. Zhang, Y. Wang, R. Li, Z. Liu, C. You, Lactiplantibacillus plantarum ST-III-fermented milk improves autistic-like behaviors in valproic acid-induced autism spectrum disorder mice by altering gut microbiota, Front. Nutr. 9 (2022) 1005308, https://doi.org/10.3389/fnut.2022.1005308.
[80] N. Munawar, A. Ahmad, M.A. Anwar, K. Muhammad, Modulation of gut microbial diversity through non-pharmaceutical approaches to treat schizophrenia, Int. J. Mol. Sci. 23 (5) (2022) 2625, https://doi.org/10.3390/ijms23052625.
[81] A. Tabrizi, L. Khalili, A. Homayouni-Rad, H. Pourjafar, P. Dehghan, F. Ansari, Prebiotics, as promising functional food to patients with psychological disorders: a review on mood disorders, sleep, and cognition, NeuroQuantology 17 (6) (2019) 1–9, https://doi.org/10.14704/nq.2019.17.06.2189.
[82] C.P.F. Marinangeli, S.V. Harding, M. Zafron, T.C. Rideout, A systematic review of the effect of dietary pulses on microbial populations inhabiting the human gut, Benef. Microbes 11 (5) (2020) 457–468, https://doi.org/10.3920/BM2020.0028.
[83] A. Ajay, S.S. Gaur, R. Shams, K.K. Dash, S.A. Mukarram, B. Kovács, Chickpeas and gut microbiome: functional food implications for health, Heliyon 10 (20) (2024) e39314, https://doi.org/10.1016/j.heliyon.2024.e39314.
[84] S. Kadyan, G. Park, N. Hochuli, K. Miller, B. Wang, R. Nagpal, Resistant starches from dietary pulses improve neurocognitive health via gut-microbiome-brain axis in aged mice, Front. Nutr. 11 (2024) 1322201, https://doi.org/10.3389/fnut.2024.1322201.
[85] S.R. Robinson, F.L. Greenway, R.C. Deth, F. Fayet-Moore, Effects of different cow-milk beta-caseins on the gut–brain axis: a narrative review of preclinical, animal, and human studies, Nutr. Rev. (2024), https://doi.org/10.1093/nutrit/nuae099 nuae099.
[86] J. Luo, X. Lin, M. Bordiga, C. Brennan, B. Xu, Manipulating effects of fruits and vegetables on gut Microbiota–A critical review, Int. J. Food Sci. Technol. 56 (5) (2021) 2055–2067, https://doi.org/10.1111/ijfs.14927.
[87] A. Tabrizi, L. Khalili, A. Homayouni-Rad, H. Pourjafar, P. Dehghan, F. Ansari, Prebiotics, as promising functional food to patients with psychological disorders: a review on mood disorders, sleep, and cognition, NeuroQuantology 17 (6) (2019) 1–9, https://doi.org/10.14704/nq.2019.17.06.2189.
[88] M. Akhlaghi, The role of dietary fibers in regulating appetite, an overview of mechanisms and weight consequences, Crit. Rev. Food Sci. Nutr. 64 (10) (2024) 3139–3150.
[89] O.G. Swann, M. Kilpatrick, M. Breslin, W.H. Oddy, Dietary fiber and its associations with depression and inflammation, Nutr. Rev. 78 (5) (2020) 394–411.
[90] M.K. Yadav, I. Kumari, B. Singh, K.K. Sharma, S.K. Tiwari, Probiotics, prebiotics and synbiotics: safe options for next-generation therapeutics, Appl. Microbiol. Biotechnol. 106 (2022) 505–521, https://doi.org/10.1007/s00253-021-11646-8.
[91] H.M. Savignac, Y. Couch, M. Stratford, D.M. Bannerman, G. Tzortzis, D. C. Anthony, P.W. Burnet, Prebiotic administration normalizes lipopolysaccharide (LPS)-Induced anxiety and cortical 5-HT2A receptor and IL1-β levels in Male mice, Brain Behav. Immun. 52 (2016) 120–131, https://doi.org/10.1016/j.bbi.2015.10.007.
[92] T. Cerdó, A. Ruíz, A. Suárez, C. Campoy, Probiotic, prebiotic, and brain development, Nutrients 9 (11) (2017) 1247, https://doi.org/10.3390/nu9111247.
[93] M. Casertano, V. Fogliano, D. Ercolini, Psychobiotics, gut microbiota and fermented foods can help preserving mental health, Food Res. Int. 152 (2022) 110892, https://doi.org/10.1016/j.foodres.2021.110892.
[94] D. Dahiya, P.S. Nigam, Probiotics, prebiotics, synbiotics, and fermented foods as potential biotics in nutrition improving health via microbiome-gut-brain axis, Fermentation 8 (7) (2022) 303, https://doi.org/10.3390/fermentation8070303.
[95] R. Balasubramanian, E. Schneider, E. Gunnigle, P.D. Cotter, J.F. Cryan, J. F, Fermented foods: harnessing their potential to modulate the microbiota-gut-brain axis for mental health, Neurosci. Biobehav. Rev. (2024) 105562, https://doi.org/10.1016/j.neubiorev.2024.105562.
[96] M.E. Rolim, M.I. Fortes, A. Von Frankenberg, C.K. Duarte, Consumption of sourdough bread and changes in the glycemic control and satiety: a systematic review, Crit. Rev. Food Sci. Nutr. 64 (3) (2024) 801–816.
[97] W. Marx, A. Scholey, J. Firth, N.M. D'Cunha, M. Lane, M. Hockey, F. Jacka, Prebiotics, probiotics, fermented foods and cognitive outcomes: a meta-analysis of randomized controlled trials, Neurosci. Biobehav. Rev. 118 (2020) 472–484, https://doi.org/10.1016/j.neubiorev.2020.07.036.
[98] Y.C. Chen, S.L. Hsieh, C.Y. Hu, Effects of red-bean tempeh with various strains of rhizopus on GABA content and cortisol level in zebrafish, Microorganisms 8 (9) (2020) 1330, https://doi.org/10.3390/microorganisms8091330.
[99] Y. Shi, X. Zhao, J. Zhao, H. Zhang, Q. Zhai, A. Narbad, W. Chen, A mixture of lactobacillus species isolated from traditional fermented foods promote recovery from antibiotic-induced intestinal disruption in mice, J. Appl. Microbiol. 124 (3) (2018) 842–854, https://doi.org/10.1111/jam.13687.
[100] T.G. DinaN, C. Stanton, C. Long-Smith, Feeding melancholic microbes: mynewgutrecommendations on diet and mood, Clin. Nutr. 38 (2019) 1995–2001, https://doi.org/10.1016/j.clnu.2018.11.010.
[101] R.G. Xiong, J. Li, J. Cheng, D.D. Zhou, S.X. Wu, S.Y. Huang, H.B. Li, The role of gut microbiota in anxiety, depression, and other mental disorders as well as the protective effects of dietary components, Nutrients 15 (14) (2023) 3258, https://doi.org/10.3390/nu15143258.
[102] S.K. Han, J.K. Kim, H.S. Park, Y.J. Shin, D.H. Kim, Chaihu-Shugan-San (Shihosogansan) alleviates restraint stress-generated anxiety and depression in mice by regulating NF-κB-mediated BDNF expression through the modulation of gut microbiota, Chin. Med. 16 (2021) 77, https://doi.org/10.1186/s13020-021-00492-5.
[103] S. Sethi, D. Wakeham, T. Ketter, F. Hooshmand, J. Bjornstad, B. Richards, L. Saslow, Ketogenic diet intervention on metabolic and psychiatric health in bipolar and schizophrenia: a pilot trial, Psychiatry Res. 335 (2024) 115866.
[104] J. Bayes, J. Schloss, D. Sibbritt, The effect of a mediterranean diet on the symptoms of depression in young males (the "AMMEND: a Mediterranean Diet in MEN with Depression" study): a randomized controlled trial, Am. J. Clin. Nutr. 116 (2) (2022) 572–580.
[105] A.J. Stevens, T.M. Heiwari, F.J. Rich, H.A. Bradley, T.L. Gur, J.D. Galley, J. J. Rucklidge, Randomised control trial indicates micronutrient supplementation May support a more robust maternal microbiome for women with antenatal depression during pregnancy, Clin. Nutr. 43 (11) (2024) 120–132.
[106] V.L. Nikolova, A.J. Cleare, A.H. Young, J.M. Stone, Exploring the mechanisms of action of probiotics in depression: results from a randomized controlled pilot trial, J. Affect. Disord. 376 (2025) 241–250.
[107] L.B. Martins, J.R. Braga Tibães, M. Sanches, F. Jacka, M. Berk, A.L. Teixeira, Nutrition-based interventions for mood disorders, Expert Rev. Neurother. 21 (3) (2021) 303–315, https://doi.org/10.1080/14737175.2021.1881482.
[108] R.A. Adan, E.M. van der Beek, J.K. Buitelaar, J.F. Cryan, J. Hebebrand, S. Higgs, S.L. Dickson, Nutritional psychiatry: towards improving mental health by what you eat, ECNP 29 (12) (2019) 1321–1332, https://doi.org/10.1016/j.euroneuro.2019.10.011.
[109] H. Shi, Q. Wang, M. Zheng, S. Hao, J.S. Lum, X. Chen, K. Zheng, Supplement of microbiota-accessible carbohydrates prevents neuroinflammation and cognitive decline by improving the gut microbiota-brain axis in diet-induced Obese mice, J. Neuroinflammation 17 (1) (2020) 77.
[110] M. Grajek, K. Krupa-Kotara, A. Białek-Dratwa, K. Sobczyk, M. Grot, O. Kowalski, W. Staśkiewicz, Nutrition and mental health: a review of current knowledge about the impact of diet on mental health, Front. Nutr. 9 (2022) 943998.
[111] A. Larroya, J. Pantoja, P. Codoñer-Franch, M.C. Cenit, Towards tailored gut microbiome-based and dietary interventions for promoting the development and maintenance of a healthy brain, Front. Pediatr. 9 (2021) 705859.
[112] F. Magzal, S. Turroni, M. Fabbrini, M. Barone, A. Vitman Schorr, A. Ofran, S. Tamir, A personalized diet intervention improves depression symptoms and changes microbiota and metabolite profiles among community-dwelling older adults, Front. Nutr. 10 (2023) 1234549.
[113] M.K. Mudd, C. Angelotta, Nutrition education in psychiatry residency programs: a call to action, J. Nutr. 154 (8) (2024) 2431–2436.
[114] M.L. Raza, S.T. Hassan, S. Jamil, W. Fatima, M. Fatima, Nutritional interventions in depression: the role of vitamin D and omega-3 fatty acids in neuropsychiatric health, Clin. Nutr. 45 (2025) 270–280.
[115] A. Oka, R.B. Sartor, Microbial-based and microbial-targeted therapies for inflammatory bowel diseases, Dig. Dis. Sci. 65 (2020) 757–788, https://doi.org/10.1007/s10620-020-06090-z.
[116] B. Yu, K.Y. Wang, N.R. Wang, L. Zhang, J.P. Zhang, Effect of probiotics and paraprobiotics on patients with sleep disorders and sub-healthy sleep conditions: a meta-analysis of randomized controlled trials, Front. Neurol. 15 (2024) 1477533, https://doi.org/10.3389/fneur.2024.1477533.
[117] S.B. Mudaliar, S.S. Poojary, A.S. Bharath Prasad, N. Mazumder, Probiotics and paraprobiotics: effects on microbiota-gut-brain axis and their consequent potential in neuropsychiatric therapy, Probiotics & Antimicro. Prot. 16 (2024) 1440–1464, https://doi.org/10.1007/s12602-024-10214-6.
[118] M. Rahmannia, M. Poudineh, R. Mirzaei, M.A. Aalipour, A.H. Shahidi Bonjar, M. Goudarzi, L.A. Sechi, Strain-specific effects of probiotics on depression and anxiety: a meta-analysis, Gut Pathog. 16 (1) (2024) 46.
[119] C.L. Wei, S. Wang, J.T. Yen, Y.F. Cheng, C.L. Liao, C.C. Hsu, C.Y.C. Tsai, Antidepressant-like activities of live and heat-killed Lactobacillus paracasei PS23 in chronic corticosterone-treated mice and possible mechanisms, Brain Res. 1711 (2019) 202–213, https://doi.org/10.1016/j.brainres.2019.01.025.
[120] K. Nishida, D. Sawada, Y. Kuwano, H. Tanaka, T. Sugawara, Y. Aoki, K. Rokutan, Daily administration of paraprobiotic Lactobacillus gasseri CP2305 ameliorates chronic stress-associated symptoms in Japanese medical students, J. Funct.Foods 36 (2017) 112–121, https://doi.org/10.1016/j.jff.2017.06.031.
[121] C.T. Peterson, Dysfunction of the microbiota-gut-brain axis in neurodegenerative disease: the promise of therapeutic modulation with prebiotics, medicinal herbs, probiotics, and synbiotics, JEBIM 25 (2020), https://doi.org/10.1177/2515690X20957225, 2515690X20957225.
[122] S. Eskandarzadeh, M. Effatpanah, K. Khosravi-Darani, R. Askari, A.F. Hosseini, M. Reisian, S. Jazayeri, Efficacy of a multispecies probiotic as adjunctive therapy in generalized anxiety disorder: a double blind, randomized, placebo-controlled trial, Nutr. Neurosci. 24 (2) (2021) 102–108.

[123] X. Wang, D. Zhao, D. Bi, L. Li, H. Tian, F. Yin, H. Qin, Fecal microbiota transplantation: transitioning from chaos and controversial realm to scientific precision era, Sci. Bull. (2025), https://doi.org/10.1016/j.scib.2025.01.029.

[124] J.W. Wang, C.H. Kuo, F.C. Kuo, Y.K. Wang, W.H. Hsu, F.J. Yu, D.C. Wu, Fecal microbiota transplantation: review and update, J. Formos. Med. Assoc. 118 (2019) S23–S31, https://doi.org/10.1016/j.jfma.2018.08.011.

[125] K.E. Vendrik, R.E. Ooijevaar, P.R. De Jong, J.D. Laman, B.W. Van Oosten, J.J. Van Hilten, M.F. Contarino, Fecal microbiota transplantation in neurological disorders, FCIMB 10 (2020) 98, https://doi.org/10.3389/fcimb.2020.00098.

[126] J.P. Doll, J.F. Vázquez-Castellanos, A.C. Schaub, N. Schweinfurth, C. Kettelhack, E. Schneider, G. Yamanbaeva, L. Mählmann, S. Brand, C. Beglinger, S. Borgwardt, J. Raes, A. Schmidt, U.E. Lang, Fecal Microbiota transplantation (FMT) as an adjunctive therapy for depression—case report, Front. Psychiatr. 13 (2022) 815422, https://doi.org/10.3389/fpsyt.2022.815422.

[127] D. Thanush, H.C. Basavaraj, M.P. Gowrav, Current regulation and initial considerations for successful development and commercialization of microbiome therapies, Advanced Gut & Microbiome Research 2023 (1) (2023) 6657515.

[128] D.E. Hoffmann, G.H. Javitt, C.R. Kelly, J.J. Keller, S.M.D. Baunwall, C.L. Hvas, Fecal microbiota transplantation: a tale of two regulatory pathways, Gut Microbes 17 (1) (2025) 2493901.

[129] A.H.S. Wadan, M.K.A. El-Aziz, D.E.S. Ellakwa, The microbiota-gut-brain-axis theory: role of gut microbiota modulators (GMMs) in gastrointestinal, neurological, and mental health disorders, N. Schmied. Arch. Pharmacol. (2025) 1–30.

[130] E. Forth, B. Buehner, A. Storer, C. Sgarbossa, R. Milev, A. Chinna Meyyappan, Systematic review of probiotics as an adjuvant treatment for psychiatric disorders, Front. Behav. Neurosci. 17 (2023) 1111349.

[131] C.R. Kelly, E.F. Yen, A.M. Grinspan, S.A. Kahn, A. Atreja, J.D. Lewis, L. Laine, Fecal microbiota transplantation is highly effective in real-world practice: initial results from the FMT national registry, J. Gastroenterol. 160 (1) (2021) 183–192, https://doi.org/10.1053/j.gastro.2020.09.038.

[132] M. Chehri, A.H. Christensen, S.L. Halkjær, S. Günther, A.M. Petersen, M. Helms, Case series of successful treatment with fecal microbiota transplant (FMT) oral capsules mixed from multiple donors Even in patients previously treated with FMT enemas for recurrent Clostridium difficile infection, 0.00.0MEDICINE 97 (31) (2018) 11706, https://doi.org/10.1097/MD.0000000000011706.

[133] G. Parker, M.J. Spoelma, N. Rhodes, Faecal microbiota transplantation for bipolar disorder: a detailed case study, Bipolar Disord. 24 (5) (2022) 559, https://doi.org/10.1111/bdi.13187.