REVIEW ARTICLE

Mind Over Muffin: Probiotics as the Brain's Secret Weapon against Sugar Spikes

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Abstract

The gut-brain axis is an important regulator of metabolic homeostasis, modulating a variety of factors that contribute to glucose metabolism, food intake, inflammation, and neuroendocrine signaling. Recent developments in elucidating the role of probiotics in blood glucose control *via* the gut-brain axis are reviewed, with the analysis based on studies published in the past decade (2015-2025). Second, an analysis is conducted of both clinical and preclinical studies examining the effects of probiotic supplementation on glycemic responses and metabolic function. A randomized, double-blind, placebo-controlled study was conducted to examine the effects of a multistrain probiotic supplemented with *Lactobacilli* and *Bifidobacteria* in healthy individuals on glucose metabolism and gut-brain axis signaling. Clinical evidence suggests that probiotic supplementation may attenuate postprandial glucose excursions and improve glycemic regulation compared with placebo. These benefits are associated with favorable alterations in gut microbial composition, increased production of short-chain fatty acid-producing bacteria, enhanced insulin sensitivity, reduced systemic inflammation, and modulation of gut-derived neuroactive metabolites. Collectively, these findings support the potential role of probiotics in improving glucose homeostasis through gut-brain axis interactions, as well as in regulating appetite and supporting cognitive function. Preclinical and clinical studies have indicated that probiotics can modulate the gut-brain axis and improve glucose tolerance, metabolic stability, and other risk factors for metabolic disorders. Research suggests that alterations in the microbiota, inflammation, and neurotransmitter levels could also benefit cognition in a probiotic-dependent manner, but large clinical studies are necessary to confirm this.

Keywords: *Probiotics, gut-brain axis, glycemic control, neuroinflammation, psychobiotics.*

INTRODUCTION

Present-day eating habits, which contain high amounts of processed carbohydrates and sugar additives, prevent the body from maintaining stable blood sugar levels, resulting in repeated episodes of elevated blood sugar. These blood sugar fluctuations lead to both metabolic diseases, which include insulin resistance and type 2 diabetes, and to cognitive, mood, and brain function disturbances. Recent studies show that the gut microbiome, comprising multiple microorganisms in the digestive system, plays an important role in metabolic balance and brain health. Probiotics, defined as live microorganisms that confer health benefits to the host when administered in adequate amounts, have become popular gut-ecosystem-modulating agents because they can enhance blood sugar management and brain function by acting on the gut-brain axis [1]. Fig. (**1**) shows the intricate relationship among the digestive system, the body's metabolic systems, and the brain.

Probiotics should reduce postprandial glucose spikes by altering gut carbohydrate processing, enhancing insulin sensitivity, and modulating inflammatory pathways that affect both peripheral tissues and brain function. Current studies show that signals from the gut can control neural pathways that regulate energy levels, respond to stress, and process cognitive information. The relationship between probiotics and metabolic control serves as a metabolic secret weapon, helping protect and enhance brain function in areas with constant access to high-sugar foods, including muffins [2].

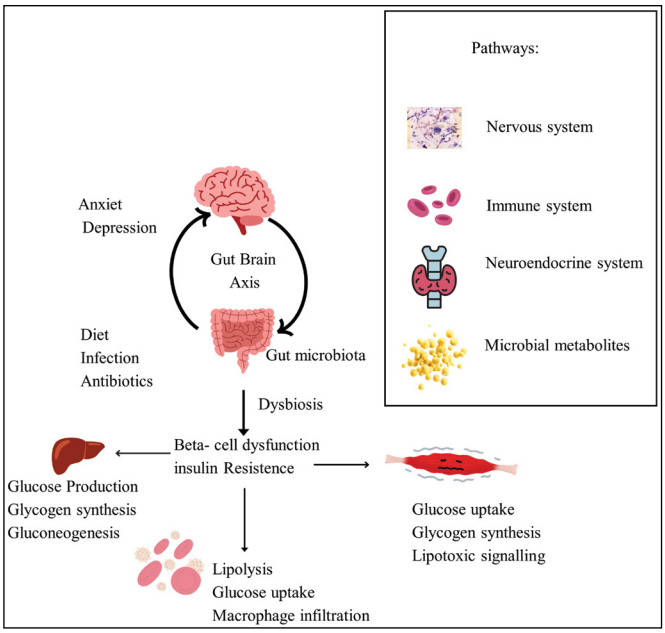


Fig. (1): Schematic representation of the gut-brain axis, which integrates neural, immune, neuroendocrine, and microbial metabolite signaling, whereby gut microbiota dysbiosis driven by diet, infection, antibiotics, and psychosocial stress induces pancreatic beta-cell dysfunction and systemic insulin impairment.

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Table 1: Comparative mechanisms and clinical effects of probiotics in modulating glycemic spikes and brain function *via* the gut-brain axis.

Probiotic Type	Mechanism of Action (Gut-Brain-Metabolic Axis)	Target Pathway	Glycemic Effects	Neurocognitive Effects	Clinical Significance	Reference
Multistrain probiotics	Modulation of gut microbiota composition; enhanced SCFA production	Gut microbiota-metabolic axis	Improved glycemic control; reduced fasting glucose	Indirect cognitive improvement *via* metabolic stabilization	Effective adjunct in T2DM management	[20], [21], [22]
Probiotic supplementation (general)	Increased insulin sensitivity; reduced systemic inflammation	Insulin signaling pathways	Reduced postprandial glucose spikes	Reduced neuroinflammation	Supports metabolic and brain health integration	[1], [24], [28]
Probiotics affecting β-cell function	Enhancement of pancreatic β-cell activity	Endocrine pancreas	Improved insulin secretion and glucose regulation	Indirect neural benefits *via* glucose stability	Potential therapeutic in glucose metabolism disorders	[2]
Psychobiotics	Modulation of neurotransmitters (serotonin, GABA); HPA axis regulation	CNS and stress-response pathways	Appetite regulation; improved glucose metabolism	Reduced stress, improved cognition and mood	Dual benefit in metabolic and mental health disorders	[32], [33]
Probiotics influencing gut hormones	Regulation of incretins (GLP-1, PYY)	Enteroendocrine system	Improved postprandial glycemic response	Appetite and satiety regulation	Useful in obesity and diabetes control	[27]
Probiotics with anti-inflammatory effects	Reduction of pro-inflammatory cytokines; immune modulation	Immune-metabolic interface	Reduced insulin resistance	Decreased neuroinflammation	Prevents progression of metabolic syndrome	[29], [30], [31]
Microbiota-targeted probiotic therapy	Restoration of microbial balance and diversity	Gut-brain axis	Stabilized glycemic variability	Improved brain signaling and metabolic regulation	Emerging therapeutic paradigm	[34], [35]
Synbiotic/probiotic interventions	Combined prebiotic-probiotic action enhancing microbial function	Integrated metabolic pathways	Improved glucose homeostasis	Indirect CNS benefits	Enhanced therapeutic efficacy over single interventions	[20]

Background on Sugar Metabolism, Glycemic Spikes

Sugar metabolism plays a fundamental role in a variety of physiological events, the most important of which is the regulation of blood glucose [1, 2]. Postprandial glycemic spikes are rapid increases in blood glucose after carbohydrate intake. They are modulated by various factors, including the type of carbohydrate consumed, insulin sensitivity, and the individual's metabolic response [3]. Since these spikes also cause oxidative stress, inflammation, and increased risk of chronic disease such as cardiovascular disease and type 2 diabetes, they are relevant not only in patients with diabetes but also to the general population [4, 5]. The deleterious effects of postprandial hyperglycemia highlight the need to develop novel dietary and lifestyle interventions to counteract blood glucose spikes [6, 10]. The key mechanisms underlying glycemic variability and its physiological consequences are summarized in Table **1**.

Rising Prevalence of Metabolic Disorders

Metabolic disorders, especially metabolic syndrome (MetS), are an important modern public health problem worldwide. MetS includes a cluster of central obesity, hypertension, dyslipidemia, and insulin resistance, with significantly increased chances for the development of cardiovascular diseases and type 2 diabetes mellitus (T2DM) [11]. The incidence of such symptoms has increased significantly in recent years; thus, there is an urgent need for effective prevention and management strategies [12].

However, the relevant data are not uniform across all regions and populations in terms of the prevalence of metabolic syndrome. In a comprehensive meta-analysis, the pooled global prevalence was reported as 32.4%, with higher prevalence in women (36.9%) than in men (26.7%) [11]. In America, data from the National Health and Nutrition Examination Survey (NHANES) revealed a rise in prevalence of MetS from 37.6% in 2011-12 to 41.8% in 2017-18 [13]. Likewise, a high-altitude study reported a pooled prevalence of MetS of 30.3%. The analysis demonstrated variability across altitude categories, with populations residing at higher altitudes generally exhibiting a lower prevalence (35.5%) than men (26.8%). The lower prevalence of MetS observed at higher altitudes has been attributed to physiological adaptations to chronic hypoxia, including improved insulin sensitivity, increased energy expenditure, and favorable effects on glucose metabolism. However, socioeconomic, dietary, and lifestyle factors may also contribute to these observations [14].

A population-based study in Chennai reported the prevalence of MetS in the general population as 25.8%; among people with T2DM, it was over 50% [15]. Simultaneously, the incidence of diabetes has increased worldwide. In 2022, more than 800 million individuals

Table 2: Comparative clinical and physiological outcomes of probiotic interventions on glycemic variability and brain-metabolic health.

Study Population	Probiotic Intervention Type	Study Design	Glycemic Outcomes	Metabolic Outcomes	Brain / Cognitive Outcomes	Key Conclusion	Reference
Adults with prediabetes and T2DM	Probiotic / synbiotic supplementation	Systematic review and dose-response meta-analysis of RCTs	Significant reduction in fasting glucose, HbA1c	Improved insulin sensitivity	Not directly assessed	Dose-dependent improvement in glycemic indices	[1]
Individuals with glucose metabolism disorders	Probiotic supplementation	Meta-analysis	Improved β-cell function	Enhanced insulin secretion	Indirect cognitive benefit *via* glucose regulation	Supports pancreatic function restoration	[2]
General population (variable metabolic responses)	Dietary carbohydrate exposure (baseline comparator)	Observational/ clinical studies	High inter-individual glycemic variability	Influenced by metabolic phenotype	Potential cognitive fluctuations	Highlights need for personalized interventions	[3]
Adults without diabetes	Low glycemic index diet (comparator)	Systematic review and meta-analysis	Reduced insulin resistance	Improved metabolic profile	Not assessed	Supports glycemic control strategies	[4]
T2DM patients	Multistrain probiotic supplementation	Randomized controlled trial	Improved fasting glucose and HbA1c	Reduced inflammation	Potential indirect CNS benefits	Effective adjunct therapy in diabetes	[27]
T2DM patients	Probiotic supplementation	Systematic review and meta-analysis	Improved glycemic control	Reduced lipid abnormalities	Not directly assessed	Beneficial short- and long-term metabolic effects	[21]
Individuals with metabolic disorders	Probiotic/ prebiotic/ synbiotic interventions	Meta-analysis of clinical trials	Improved glucose homeostasis	Reduced insulin resistance	Indirect brain benefits	Multi-target metabolic improvement	[20]
General population / metabolic syndrome	Probiotic supplementation	Systematic review	Stabilized blood glucose levels	Improved lipid and inflammatory markers	Not assessed	Supports prevention strategies	[22]
Patients with cognitive impairment	Probiotic therapy	Umbrella review of meta-analyses	Improved metabolic markers	Enhanced metabolic regulation	Improved cognition and mental performance	Links metabolic and cognitive improvements	[32]
Neurodegenerative / metabolic conditions	Microbiota-targeted probiotics	Review-based evidence	Modulation of glucose metabolism	Reduced systemic inflammation	Improved neurotransmission and brain signaling	Validates gut-brain-metabolic axis role	[25], [26]
Diabetes and metabolic disorders	Gut microbiota modulation (probiotics)	Expert forum / translational research	Reduced glycemic variability	Improved metabolic homeostasis	Potential CNS regulation	Emerging clinical application in diabetes care	[34]
General health population	Probiotic interventions	Comprehensive review	Improved glycemic stability	Enhanced immune-metabolic balance	Reduced neuroinflammation	Broad therapeutic potential	[35]

lived with diabetes, which was more than fourfold compared to the number of people with diabetes in 1990 [16]. More than 95% of cases of type 2 diabetes are associated with lifestyle factors and are preventable. Increased incidence of obesity, sedentary lifestyles, and unhealthy dietary patterns all play a significant role in the current epidemic [17].

This rising prevalence of metabolic disorders calls for new and novel approaches that can both prevent and manage these conditions. Emerging evidence suggests that modulating the gut microbiota through probiotic administration is a promising approach to addressing some metabolic dysfunctions. Probiotics improve glucose metabolism, reduce inflammation, and enhance lipid profiles, which may serve as the brain's hidden defense mechanism against sugar spikes and metabolic disturbances [18-22]. Table **2** displays complete data on the clinical and physiological outcomes of different probiotic treatments.

The Emerging Link between the Gut Microbiota and Brain-Glycemic Control

Recent years have seen an increasing focus on the complex relationship that exists between the gut microbiota and the brain- the so-called microbiota-gut-brain axis [23]. This bidirectional means of communication plays an important role in homeostasis and has been implicated in multiple physiological mechanisms, including glycemic control [24]. Probiotics appear to offer new insight into the treatment of glycemic fluctuations by modulating the gut microbiota to influence brain function and/or metabolic pathways [25]. Probiotics have been reported to influence glucose metabolism through multiple mechanisms, including modulation of gut microbiota composition, enhancement of intestinal barrier integrity, regulation of inflammatory pathways, and production of bioactive metabolites that contribute to improved glycemic control [26]. Studies show that some probiotic strains may improve insulin sensitivity,

decrease inflammation, and affect the release of gut-derived hormones involved in glucose regulation [27]. For instance, a meta-analysis showed that probiotic treatment significantly improved glycemic control in people with T2DM [24, 28].

The gut microbiota may affect the CNS by producing neurotransmitters, modulating immunity, and altering hypothalamic-pituitary-adrenal axis activity [25, 29]. Changes in gut microbiota composition have been observed to affect neuro-inflammation and brain functional status, thereby influencing metabolism [30]. Probiotics could help restore balance in the gut microbiota, thereby potentially inhibiting neuroinflammation and aiding metabolic function [31].

Psychobiotics are probiotics that counteract the adverse effects of stress and confer mental health benefits, thereby demonstrating the potential of modulating the gut microbiota to affect brain function and behavior [32]. Thus, such treatments would facilitate cognitive functioning while also directly impacting appetite and glucose metabolism [33].

The recent association between the gut microbiota and brain glycemic control raises the prospect of probiotic therapy for managing glycemic variability [34]. By modifying gut microbial composition and functionality, probiotics represent a new paradigm in enhancing metabolic health and averting glycemic peaks [35].

MECHANISMS OF ACTION

A two-layered mechanism needs to be explored to understand how probiotics exert their health-promoting effects, including effects on glycemic regulation and brain function [36]. Probiotics act on host physiology through interconnected neural, metabolic, immune, and endocrine pathways; these pathways influence how our body responds to dietary sugars and how our brain processes glucose and metabolic signals [35]. That is the gut-brain axis, a bidirectional communication network that connects the gastrointestinal tract and the brain through neural pathways (like the vagus nerve), circulating metabolites, immune mediators, and hormonal signals [36, 37]. Modifications to this gut-brain axis arise from changes in gut microbiota composition, the production of bioactive metabolites such as short-chain fatty acids (SCFAs), and the modulation of gut hormone responses, all of which suppress postprandial hyperglycemic spikes while improving cognitive and metabolic resilience [37].

Metabolic effects of some probiotic strains can also be achieved by influencing carbohydrate digestion and absorption, for example, by inhibiting enzymes such as α-glucosidase, which breaks complex carbohydrates into glucose, thereby reducing the rate and amount of glucose entering the bloodstream [25]. Increases in insulin sensitivity and in the secretion of incretin-like glucagon-like peptide-1 (GLP-1) are additional mechanisms through which probiotics are believed to promote more effective glucose uptake by peripheral tissues [38].

Probiotics may exert beneficial effects by modulating immune and inflammatory pathways associated with low-grade chronic inflammation and metabolic endotoxemia, conditions that contribute to insulin resistance and impaired neuronal function. Short-chain fatty acids (SCFAs) and other gut microbiota-derived metabolites are involved in immune regulatory and scavenger functions. These bioactive compounds contribute to metabolic homeostasis by modulating adipose tissue function, reducing inflammatory responses, and influencing host energy metabolism [38-40].

Furthermore, in the central nervous system, probiotics modulate key signaling molecules and receptors involved in neuronal glucose transport and energy balance, as well as neurotrophic factors that influence synaptic plasticity, thereby affecting learning and memory. Probiotics similarly influence peripheral glucose homeostasis and may indirectly affect brain-related functions through mechanisms linked to metabolic stress, inflammation, and gut-brain axis signaling. These combined effects suggest a potential role for probiotics in regulating both glucose metabolism and cognitive health [25, 41].

Gut-Brain Axis

Probiotics are receiving considerable attention for their role in modulating the gut-brain axis, improving metabolic health, and reducing postprandial glucose spikes [42]. Several interconnected mechanisms have been proposed to explain how probiotics modulate gut-brain signaling and contribute to metabolic homeostasis [43]. Probiotics may influence the synthesis and regulation of important neurotransmitters, including serotonin, dopamine, and gamma-aminobutyric acid (GABA), which play essential roles in mood regulation, cognition, and behavior [44]. Specific probiotic strains can indirectly influence neurotransmitter biosynthesis by creating microbial metabolites such as SCFAs, modulating enteroendocrine cells, regulating the availability of precursors of neurotransmitters, and mediating signaling along the gut-brain axis. These may in part influence neurocognitive and metabolic outcomes [45].

The regulation of hormones by probiotic ingestion has also been observed. An increase in gut hormone secretion, such as GLP-1 (glucagon-like peptide-1) and PYY (peptide YY), has been demonstrated with probiotics, with implications for appetite and glucose homeostasis by influencing insulin secretion and sensitivity [46, 47]. Immune function can be modulated by altering the cytokine profile of the inflammatory response. Indeed, probiotics may decrease the expression of pro-inflammatory cytokines such as TNF-, IL-6, and IL-1, and increase the expression of anti-inflammatory cytokines such as IL-10, thereby preserving gut barrier function and reducing overall

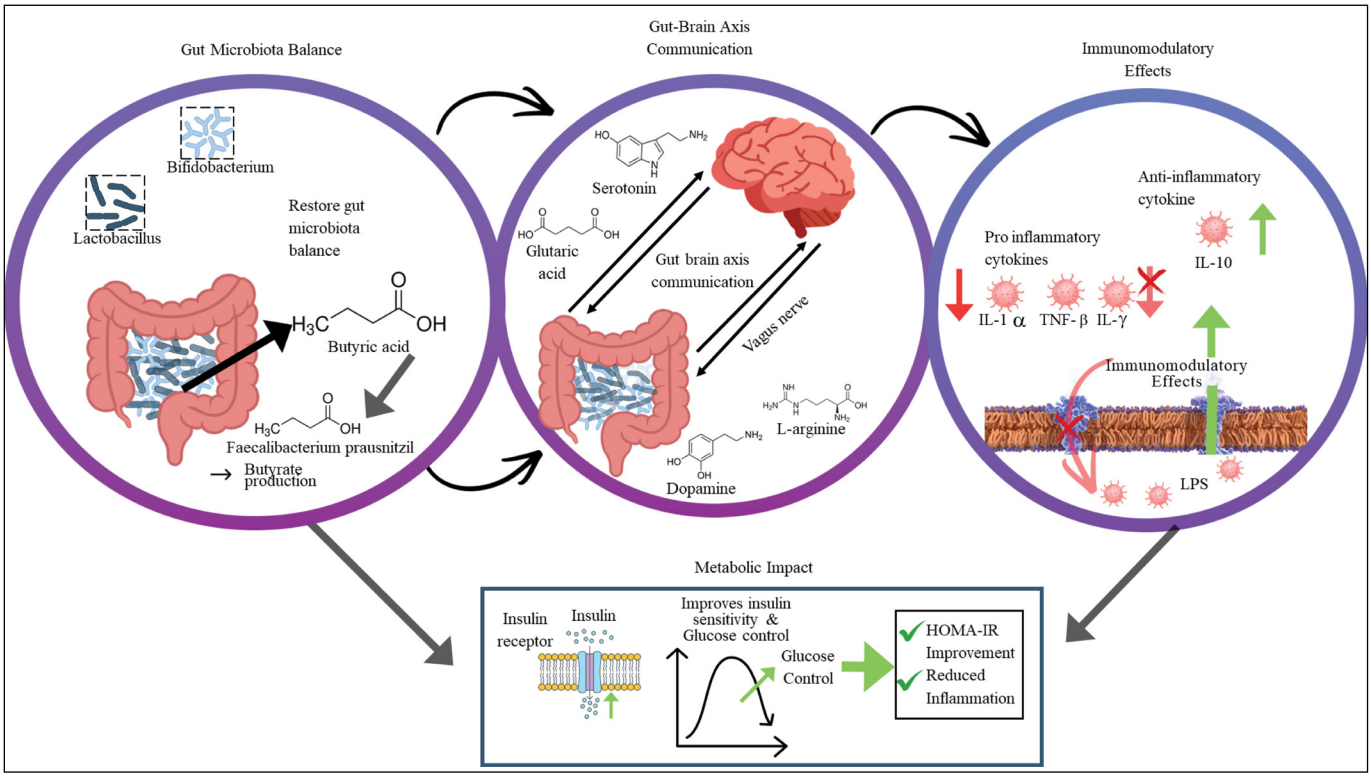


Fig. (2): Schematic representation of probiotic-driven restoration of gut microbiota (*e.g.*, *Lactobacillus*, *Bifidobacterium*, *Faecalibacterium prausnitzii*) leading to increased butyrate production, bidirectional gut-brain axis signaling (serotonin, glutamic acid, dopamine, L-arginine *via* the vagus nerve), immunomodulation (decreased pro-inflammatory cytokines, ↑IL-10) & consequent metabolic benefits including improved glucose control & reduced HOMA-IR.

inflammation. Inflammatory cytokines may, through the gut-brain axis, modulate hypothalamic activity and activate the hypothalamic-pituitary-adrenal (HPA) axis. Decreasing pro-inflammatory cytokine signals may allow the downregulation of HPA axis activity and cortisol release, thereby improving stress resistance [48].

Probiotics promote gut barrier function and inhibit the translocation of various endotoxins, including lipopolysaccharides (LPS), into the bloodstream. Endotoxins in the circulation trigger systemic inflammation, a risk factor for insulin resistance and metabolic diseases [49]. Thus, probiotics can modify metabolic pathways by altering the composition of the gut microbiota, thereby promoting lipid metabolism and energy homeostasis [50]. This would ultimately lead to better glycemic control and lower markers of insulin resistance [51]. These mechanisms are illustrated in Fig. (**2**).

Role of SCFAs

There has been considerable scientific attention to the crosstalk among the gut microbiota, probiotics, and metabolic and nervous health. Most interestingly, probiotic-fermented, diet-derived fibers that produce SCFAs as active metabolites have been shown to affect glucose homeostasis and play a role in brain-level function through the gut-brain axis [52-54]. The potential of probiotics, *via* SCFA production, is considered in managing postprandial sugar spikes as well as their synergistic effect on cognitive performance.

Probiotics that produce SCFAs include *Lactobacillus*, *Bifidobacterium*, and *Ackermanns municipia*, which are bacteria that ferment indigestible carbohydrates and produce SCFAs (acetate, propionate, and butyrate)[40, 52, 53]. The SCFAs produced help regulate the host's metabolic well-being. The composition and concentration of these SCFAs depend heavily on the bacterial strains inhabiting the host intestine, the dietary fiber sources in the host's diet, and other related factors [55].

SCFAs modulate blood glucose balance *via* multiple biochemical pathways and signaling. Initially, they bind to G protein-coupled receptors (GPR41 and GPR43) in the intestines and pancreas, thereby controlling insulin secretion and increasing insulin sensitivity [40, 54, 55]. Propionate could, arguably, also act as a substrate for hepatic gluconeogenesis, thereby maintaining stable glucose levels during fasting [54, 56]. SCFAs have a range of beneficial metabolic actions, largely driven by butyrate. By modulating intestinal barrier function and pro-inflammatory cytokine production, butyrate attenuates systemic inflammation, thereby contributing to the development of insulin resistance and T2DM [53, 55]. Moreover, SCFAs have been reported to improve insulin sensitivity through effects on glucose and lipid metabolism and by increasing the release of gut hormones that regulate glucose homeostasis. Consequently, SCFAs might suppress postprandial

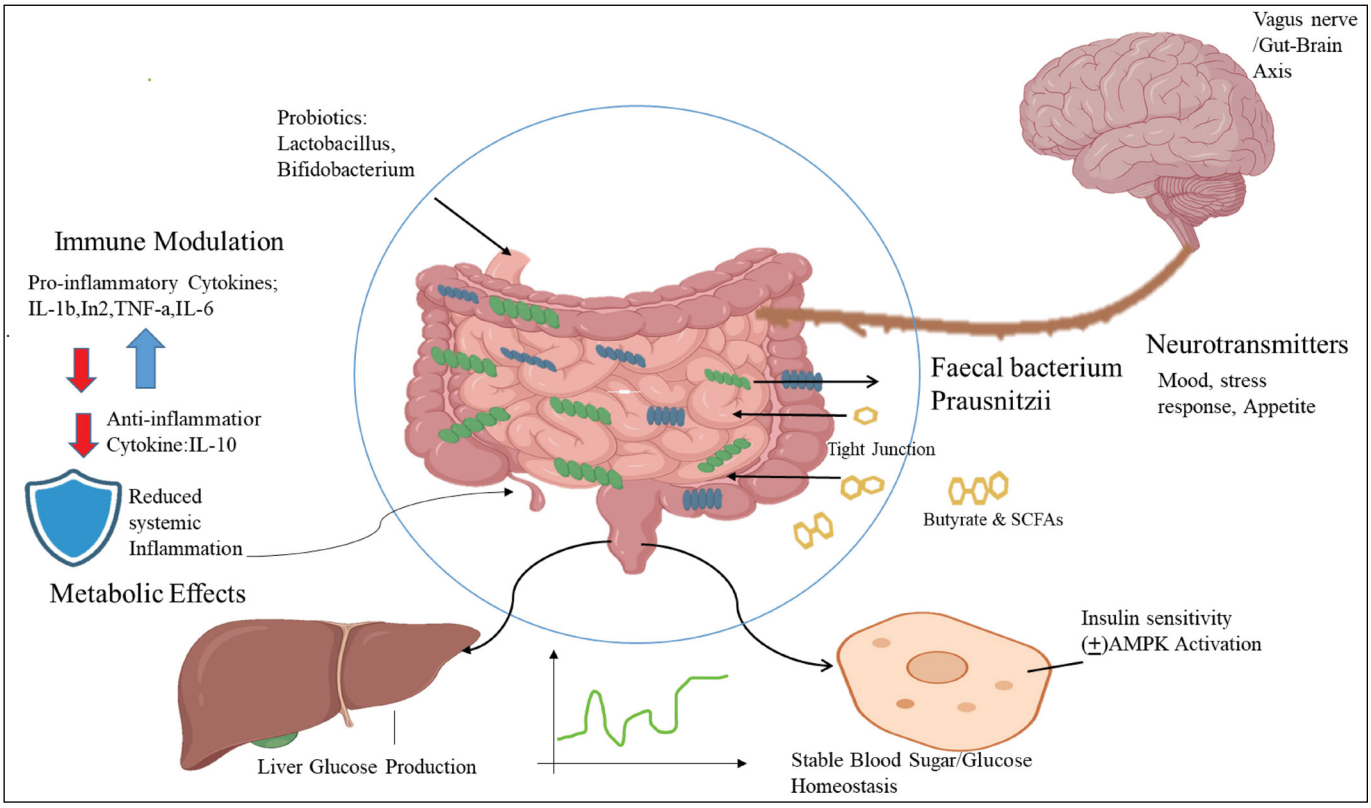


Fig. (3): Schematic representation of probiotic-driven gut microbiota restoration initiated by *Lactobacillus* and *Bifidobacterium* colonization and enrichment of butyrate-producing taxa (*e.g.*, *Faecalibacterium prausnitzii*), resulting in increased SCFA (butyrate) production, preservation of epithelial tight junctions, immune modulation (↓IL-1β, IL-2, TNF-α, IL-6; ↑IL-10) with reduced systemic inflammation, vagus nerve-mediated neurotransmitter signaling, enhanced AMPK-dependent insulin sensitivity and reduced hepatic glucose output, thereby promoting stable glucose homeostasis.

increases in plasma glucose and improve overall glycemic control, thereby diminishing many adverse effects of sustained hyperglycemia on metabolism.

Both butyrate and propionate can cross the blood-brain barrier and regulate the synthesis of neurotransmitters such as serotonin, dopamine, and GABA, which are involved in mood, cognition, and appetite regulation [54, 55]. Butyrate is known to upregulate BDNF expression and production. BDNF is a neurotrophin involved in neuronal survival, synaptic plasticity, learning, and memory, thereby enhancing cognitive abilities [57]. SCFAs, particularly butyrate, have been shown to strengthen the integrity of the blood-brain barrier and modulate microglial activity, the resident immune cells of the central nervous system. These effects may contribute to reduced neuroinflammation and improved communication along the gut-brain axis [50, 57].

One pathway by which SCFAs influence the brain is through vagus nerve signaling and appetite control. The vagus nerve is the main pathway between the gut and the brain. SCFAs also stimulate the release of gut hormones such as GLP-1 and PYY, which activate vagal afferents to signal satiety in the brain [40, 48, 49]. This may decrease appetite, slow gastric emptying, and reduce excessive sugar intake, thereby preventing spikes in blood glucose levels [40, 49].

Apart from metabolism, probiotic supplementation has been beneficial to memory, learning, and mood regulation, particularly among the aged and those with mild cognitive impairment (MCI). Studies using *Lactobacillus* rhamnosus and other strains have shown improved executive function, enhanced emotional well-being, and reduced neuroinflammation [55, 57]. These findings may result from increased production of SCFAs, with both gut-atmosphere effects and neuroprotective activities [40, 58]. Probiotics and SCFAs would serve as dual-functional health instruments in controlling sugars and improving brain function in combination with a high-fiber and probiotic-rich diet (including yogurt, kefir, kimchi, and fermented supplements), which may greatly contribute to controlling blood sugar levels to decrease the risk of developing T2DM and promote long-term clarity and cognitive endurance[46, 58]. These combined metabolic and neurocognitive effects are schematically represented in Fig. (**3**).

Inflammation Reduction

Probiotics may modulate inflammatory responses and contribute to blood glucose stabilization in pediatric populations through mechanisms involving the gut microbiota, immune regulation, and metabolic signaling pathways [59]. The probiotics mentioned above restore gut microbiota balance by helping essential bacteria to develop. Beneficial gut microorganisms include

Faecalibacterium prausnitzii, a major butyrate-producing bacterium that plays a critical role in maintaining intestinal homeostasis. Butyrate supports epithelial barrier integrity, regulates inflammatory pathways, and may influence metabolic and neurobiological processes through the gut-brain axis. The process of microbial modulation improves gut barrier integrity by promoting tight junction formation, reducing intestinal permeability, and preventing the entry of endotoxins, such as lipopolysaccharides, into the bloodstream [37]. Such enhancements in gut barrier function are essential for controlling systemic inflammatory events in metabolic disorders [60].

Probiotics also affect immune responses by downregulating pro-inflammatory cytokines, including interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6), and by upregulating anti-inflammatory cytokines, including interleukin-10 (IL-10) [36]. The modulation of these cytokines provides a balance to the immune response, thus decreasing any possible chronic inflammation that can interfere with insulin signaling and glucose metabolism [61].

Impact on Neurotransmitters, Insulin Sensitivity

Beyond their established effects on gut microbial composition, probiotics may influence metabolic health by modulating neurotransmitter signaling and insulin sensitivity [62]. Certain strains of *Lactobacillus* and *Bifidobacterium* can produce neuroactive compounds, including γ-aminobutyric acid (GABA) and serotonin precursors, which may affect appetite regulation, stress responses, and gut-brain communication through neural and immune-mediated pathways [62].

In addition, probiotic supplementation has been associated with improved insulin sensitivity, reflected by reductions in homeostatic model assessment of insulin resistance (HOMA-IR) and fasting insulin levels in individuals with metabolic disorders, including metabolic syndrome and polyendocrine metabolic ovarian syndrome. Collectively, these findings suggest that probiotics may contribute to metabolic homeostasis by influencing both neuroendocrine signaling and glucose regulation through the gut-brain-metabolism axis [63-66].

CURRENT EVIDENCE

Evidence from animal studies, clinical trials, and systematic reviews indicates that probiotics may improve glycemic regulation and influence brain function through interactions within the gut-brain axis. Despite considerable heterogeneity across studies and between probiotic types, findings indicate a modest positive impact of probiotics on glucose homeostasis through changes in gut microflora composition, improvements in the intestinal barrier, and reductions in peripheral inflammation. Probiotics can also act on the nervous system through microbial metabolites, immune mechanisms, and regulation of neurotransmitter levels, thereby reinforcing their potential as part of an integrative strategy to ameliorate diet-induced metabolic stress [59].

The findings of several randomized controlled trials (RCTs) and meta-analyses demonstrate that probiotic supplementation is associated with significant reductions in fasting blood glucose, fasting insulin, and insulin resistance in humans, suggesting that gut microbial modulation may improve glucose homeostasis and metabolic control [59, 67].

This clinical observation is further corroborated by animal studies showing that probiotics can normalize levels of brain glucose transporters, boost glucose metabolism, and control and reduce metabolic and pathologic symptoms related to neurodegenerative disorders. These findings illustrate the capacity of probiotics to alter brain glucose metabolism along with blood glucose control [43, 68].

Emerging results from human intervention studies show that probiotics can influence brain function, cognition, and emotional processing by altering the gut microbiome and facilitating communication between the gut and the brain [69]. Data are systematically presented in Table **3**.

The available evidence suggests a potential benefit of probiotics for glucose metabolism and brain function through modulation of the gut-brain axis, immune signaling, and metabolic pathways. Limitations in the evidence to date, including heterogeneous use of specific probiotic strains, dosages, treatment durations,

Table 3: Role of probiotics in modulating glycemic variability and brain function *via* the gut-brain axis.

Probiotic/Strain	Primary Mechanism (Gut-Brain Axis)	Metabolic Effect (Glycemic Control)	Neurocognitive Effect	Key Biomarkers/ Pathways	Clinical Significance	Reference
General probiotics	Gut microbiota modulation	↓ Fasting glucose, ↓ insulin, ↓ insulin resistance	Indirect CNS modulation	Microbiota composition	Supports metabolic regulation strategies	[59], [67]
Multistrain probiotics	Gut-brain signaling	Improved glucose metabolism	Improved cognition and mood	Neurotransmitter signaling	Evidence for cognitive-metabolic link	[67]
SCFA-producing probiotics	SCFA-mediated signaling	Improved glucose homeostasis	Enhanced neuronal communication	SCFAs (butyrate, acetate)	Mechanistic link between gut and brain	[68]
Lactobacillus strains	Microbiome modulation	Improved metabolic profile	Improved cognitive outcomes	Microbiome diversity	Potential neuroprotective role	[69]
General probiotic therapy	Multi-pathway modulation	Variable glycemic improvements	Supports brain health	Inflammatory pathways	Requires further clinical validation	[70]

Probiotic/Strain	Primary Mechanism (Gut-Brain Axis)	Metabolic Effect (Glycemic Control)	Neurocognitive Effect	Key Biomarkers/ Pathways	Clinical Significance	Reference
Lactobacillus rhamnosus GG	Microbiota and amino acid metabolism modulation	↑ Insulin sensitivity, improved glucose metabolism	Reduced neuroinflammation	Amino acids, cytokines	Strong psychobiotic candidate	[38], [73]
L. rhamnosus	Cytokine modulation	Improved glucose metabolism	Reduced cognitive decline	IFN-γ/IL-10, TNF-α/ IL-10	Anti-inflammatory neuroprotection	[38], [74]
Bifidobacterium longum	SCFA production, gut barrier enhancement	Improved glycemic control	Enhanced cognitive function	SCFAs, gut barrier markers	Reduces inflammation and metabolic stress	[38], [71], [72]
B. longum BB68S	Gut-brain signaling	Not primary outcome	Improved cognitive performance	Neural signaling pathways	Cognitive enhancement in elderly	[38], [74]
Multi-strain (*L. rhamnosus* + *B. longum*)	Synergistic microbiota modulation	↓ HbA1c, ↓ postprandial glucose	Improved mood and cognition	Glycemic markers, SCFAs	Effective adjunct in T2DM and prediabetes	[38], [71], [72], [73]
Combined probiotics	Immune modulation	Improved metabolic balance	Reduced memory impairment	Immune pathways	Translational therapeutic potential	[38]
Probiotics (general use in elderly)	Gut microbiota-brain signaling	Improved metabolic stability	↑ Attention, memory, emotional well-being	Neurotransmitters, cytokines	Supports healthy cognitive aging	[73], [96]
Gut-brain axis-targeted probiotics	Neural network modulation	Indirect glycemic regulation	Improved brain network activity	Brain connectivity pathways	Basis for neuro-metabolic therapies	[75], [76], [77]
L. rhamnosus GG	Immune and microbiota modulation	Not primary outcome	Improved cognitive impairment	Inflammatory mediators	Disease-specific neuroprotection	[76]

study populations, and clinical outcomes, impede accurate comparisons among studies. Additionally, although generally considered safe, probiotics appear to be individual-specific in terms of efficacy. They may need to be used with caution in certain immunocompromised and/or critically ill patients. Probiotics, therefore, should be considered an adjunctive nutritional approach to support glucose management and cognitive function. Still, larger, high-quality randomized clinical trials should be conducted across various age groups and patient populations to determine specific probiotics, doses, treatment regimens, and long-term safety [63, 70].

Effects of Specific Probiotics Like *Lactobacillus* rhamnosus or *Bifidobacterium* longum

Previous studies have reported that probiotic strains, such as *Lactobacillus rhamnosus*, may exert beneficial metabolic and neurocognitive effects by modulating the gut-brain axis. These effects include improvement in glucose homeostasis, attenuation of postprandial glycemic excursions, and regulation of metabolic signaling pathways involved in insulin sensitivity. In addition, probiotic-mediated alterations in gut microbiota composition may influence short-chain fatty acid production and neurotransmitter signaling, thereby contributing to improved metabolic regulation and cognitive outcomes. Unlike rapidly digestible high-carbohydrate foods, these probiotic effects are associated with the stabilization rather than elevation of blood glucose levels [71]. Supplementation with *Lactobacillus rhamnosus* GG (LGG) in preclinical animal models, when compared with non-supplemented control groups, has been reported to improve insulin sensitivity and metabolic outcomes. These effects were associated with modulation of gut microbiota composition and alterations in amino acid metabolism. In addition, *Bifidobacterium* longum strains have demonstrated potential benefits for glycemic regulation in animal studies through increased production of SCFAs, enhanced intestinal barrier integrity, and subsequent reductions in systemic inflammatory responses, which collectively contribute to improved insulin signaling and metabolic homeostasis [38, 71, 72]. Furthermore, systematic reviews and randomized controlled trials show that multistrain probiotics containing *Lactobacillus rhamnosus* and *Bifidobacterium longum* are effective in lowering HbA1c levels and postprandial glucose peaks in people with prediabetes or type 2 diabetes [38, 71-73].

Emerging evidence from neurocognitive and gut-brain axis studies suggests that specific probiotic strains may exert beneficial effects on cognitive function, particularly in aging populations. According to a randomized, double-blind, placebo-controlled clinical trial involving healthy, older adults, *Bifidobacterium longum* BB68S supplementation (12 weeks, daily dose) resulted in objective cognitive gains compared to placebo. Cognitive measures assessed *using* validated neuropsychological tests, including the Mini-Mental State Examination (MMSE) and memory recall tests across various cognitive domains, showed a statistically significant increase in global cognitive scores in the intervention group compared to placebo. Supplementation with *Lactobacillus rhamnosus* in preclinical and clinical settings also appears to affect neuroinflammatory pathways; in animal and translational models, this probiotic was found to shift pro-inflammatory cytokine ratios, including IFN-/IL-10 and TNF-/IL-10, toward an anti-inflammatory state. This immunomodulatory effect directly affects neuroprotective mechanisms, as

decreased systemic inflammation is strongly correlated with preserved synaptic plasticity and resistance to cognitive decline. Although the magnitude of cognitive changes varies with the specific population and initial cognition, many studies found a slight yet significant augmentation in memory and executive function following supplementation. Together, these findings support the idea that probiotics can benefit cognition by modulating the gut-brain axis, reducing neuroinflammation, and regulating neurotransmitter function in vulnerable populations, including healthy older adults [38, 74].

A preclinical study and several clinical studies have shown that probiotic-specific effects exist and are associated with modulation of the gut-brain axis. In a preclinical colitis-associated cognitive deficit in mice, treatment with combined *L.rhamnosus* GG and B.longum (approximately 10^9-10^{10} CFU/day equivalent in experimental formulations) over the course of 3-4 weeks was correlated with both decreased neuroinflammation and ameliorated memory deficits, as shown by maze-based learning and behavioral cognition tests.

On the clinical side, an older population (mean age 60 years) showed cognitive and emotional improvements after receiving a multistrain probiotic containing *L. Rhamnosus* and *B. longum* daily for 12 weeks in a randomized controlled study. Cognitive performance was measured using standardized neuropsychological tests, including memory retrieval and attention performance tests, and validated mood questionnaires.

Neuroimaging studies using functional MRI (fMRI) to examine gut-brain axis connections have shown alterations in the activity of brain regions involved in emotional and cognitive processing in humans following probiotic consumption. These studies together confirm the hypotheses that *L. Rhamnosus* and *B. Longum* might exert neurocognitive and metabolic effects through anti-inflammatory action, restoration of the intestinal barrier, and neuromodulatory pathways, such as GABA or serotonin signaling. Hence, these probiotics could be used as adjuvant therapies for metabolic and neurocognitive diseases, including those characterized by poor glycemic control [75, 76]. The current literature is encouraging, but large-scale human trials are needed to determine the most effective probiotic strains, doses, and treatment durations for clinical use.

POTENTIAL USE OF PROBIOTICS IN MANAGING TYPE 2 DIABETES OR METABOLIC SYNDROME

Globally, populations are experiencing a surge in T2D and MetS, both characterized by insulin resistance, chronic inflammation, and altered glucose metabolism. In fact, the gut-brain axis appears to be an important probiotic target for improving glucose homeostasis and neuroendocrine signaling [77]. Clinical evidence from RCTs indicates that certain probiotic interventions can improve glycemic control and insulin sensitivity in T2DM and MetS. For instance, supplementation with *Lactobacillus rhamnosus* and *Bifidobacterium lactis* for 6 to 12 weeks resulted in reductions in fasting blood glucose and the homeostatic model assessment of insulin resistance (HOMA-IR).

A clinical study of patients with T2DM that used multistrain probiotics containing *Lactobacillus* and *Bifidobacterium* also observed a small yet significant decrease in HbA1c levels compared with placebo, along with favorable changes in inflammatory markers. Another RCT in patients with MetS who received a daily probiotic dose showed improvements in both insulin sensitivity and lipid parameters, indicating potential for strain-dependent improvements in metabolic measures.

While the effect sizes range with studies according to baseline metabolic state, the form of the probiotic, and the length of therapy, pooled data from randomized controlled trials have shown that probiotic administration appears to favorably influence glycemic measures including fasting glucose and insulin resistance indices, and although diverse outcomes have been seen with different trials, further studies with specific strains, dosages and longer periods of follow-up need to be carried out before recommending it clinically [78]. Neuroinflammation can be mitigated by probiotics, which suppress microglial activation and the release of pro-inflammatory cytokines, thereby improving brain function in metabolic diseases [79].

Probiotics have been a hot topic of research in recent years due to their role in regulating lipid metabolism and systemic inflammation, which are key factors in metabolic syndrome. Some meta-analyses and RCTs on the use of probiotics demonstrate an overall small but significant benefit in lipid parameters, with variable responses. In particular, improvements in plasma LDL-C were typically ~5-10%, depending on the probiotic strain, dosage, and treatment duration. Some trials also revealed slight improvements in total cholesterol and triglyceride levels, but these effects still vary across strains and appear heterogeneous [80]. By contrast, conventional statins reduce LDL-C by 30-50% or more, with increased potency at higher doses. Consequently, probiotics are unlikely to have LDL-C-lowering capabilities comparable to statins, but might provide a synergistic approach in patients with modest dyslipidemia or those unable to tolerate statins [81].

In addition to modulating lipid profiles, probiotics have anti-inflammatory properties, and clinical studies have shown reductions in circulating inflammatory biomarkers, including TNF and C-reactive protein, by about 10%- 25% in selected subjects. These effects are believed to be mediated by modulation of the gut microbiota, improved intestinal barrier integrity, and reduced endotoxemia, ultimately influencing systemic metabolic and inflammatory pathways.

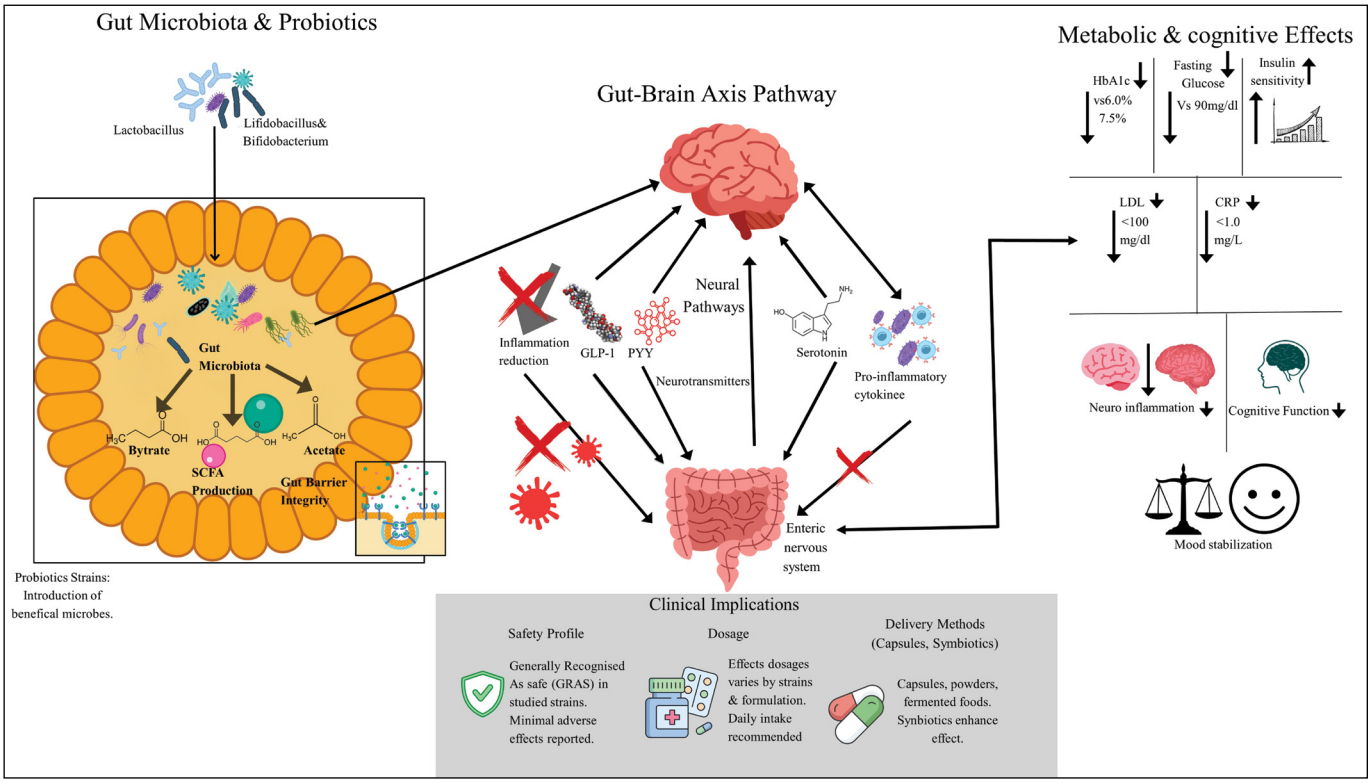


Fig. (4): The schematic diagram of probiotic-mediated alteration of gut microbiota and short-chain fatty acids production identifies the various gut-brain axis signaling pathways-neural, endocrine, and immune working together to diminish inflammation and, thereby, enhance metabolic regulation, neuroinflammation alleviation, and positive outcomes in cognition and mood.

Overall, while probiotics cannot replace first-line pharmacotherapy for dyslipidemia, emerging evidence supports their role as an adjunctive intervention in metabolic syndrome through modest lipid-lowering and anti-inflammatory effects [82].

Probiotics help restore gut barrier integrity, thereby curbing endotoxemia and reducing systemic inflammation associated with insulin resistance. The body regulates its blood sugar levels and eating patterns through hormonal control, and incretin hormone enhancement *via* GLP-1 and PYY improves this regulation. Probiotics work by modulating hypothalamic signaling systems, thereby helping maintain energy balance and reducing sugar cravings [83]. Previous studies assessing the effects of probiotics on incretin hormones are limited by variations in probiotic strains, dosages, and treatment durations, which limits the generalizability of the findings. In light of these limitations, we suggest designing and conducting large-scale, long-term clinical trials to arrive at a standardized probiotic therapy for T2D and MetS. Another possibility for intervention could be to capitalize on personalized probiotic treatment approaches tailored to each patient's unique microbiome profile to maximize therapeutic potential [69]. These integrated mechanisms and clinical outcomes are illustrated in Fig. (**4**).

SAFETY, DOSAGE, AND DELIVERY METHODS

Safety Profile: Probiotics are considered safe for healthy individuals and those with metabolic disorders [69, 84, 85]. GI discomfort is mostly mild and a common side effect. In immunocompromised patients or those with concomitant severe illness, probiotics should be administered with caution due to the extremely rare risk of bacteremia or fungemia. Regulatory bodies recommend strain-specific safety assessments; thus, the choice of probiotic strains should be strongly informed by well-documented safety profiles [86].

Dosage Considerations: Clinical trials assessing cognitive and metabolic effects typically use doses ranging from 10^8 to 10^11 colony-forming units (CFU) per day [83-85]. The dosage needs to be optimized for the strains used, indications, and population. To achieve the desired effect, the test strain needs to be taken daily for several weeks or months. A personalized approach based on a host's baseline microbiota and metabolic status may promote higher efficacy [85].

Delivery Methods: Probiotics can be administered as capsules, fermented foods, powders, or drinks. Encapsulation technologies can enhance their transit through the GI tract, improving clinical efficacy. Synbiotics (a combination of probiotics and prebiotics) might provide synergistic effects that promote colonization and metabolic activity [86]. For the system to be used safely, the user has to determine specific strains, doses, and delivery methods to achieve optimal efficacy. To date, the research needs large, randomized controlled trials to establish clinical standards. The overall clinical implications are also represented in Fig. (**5**).

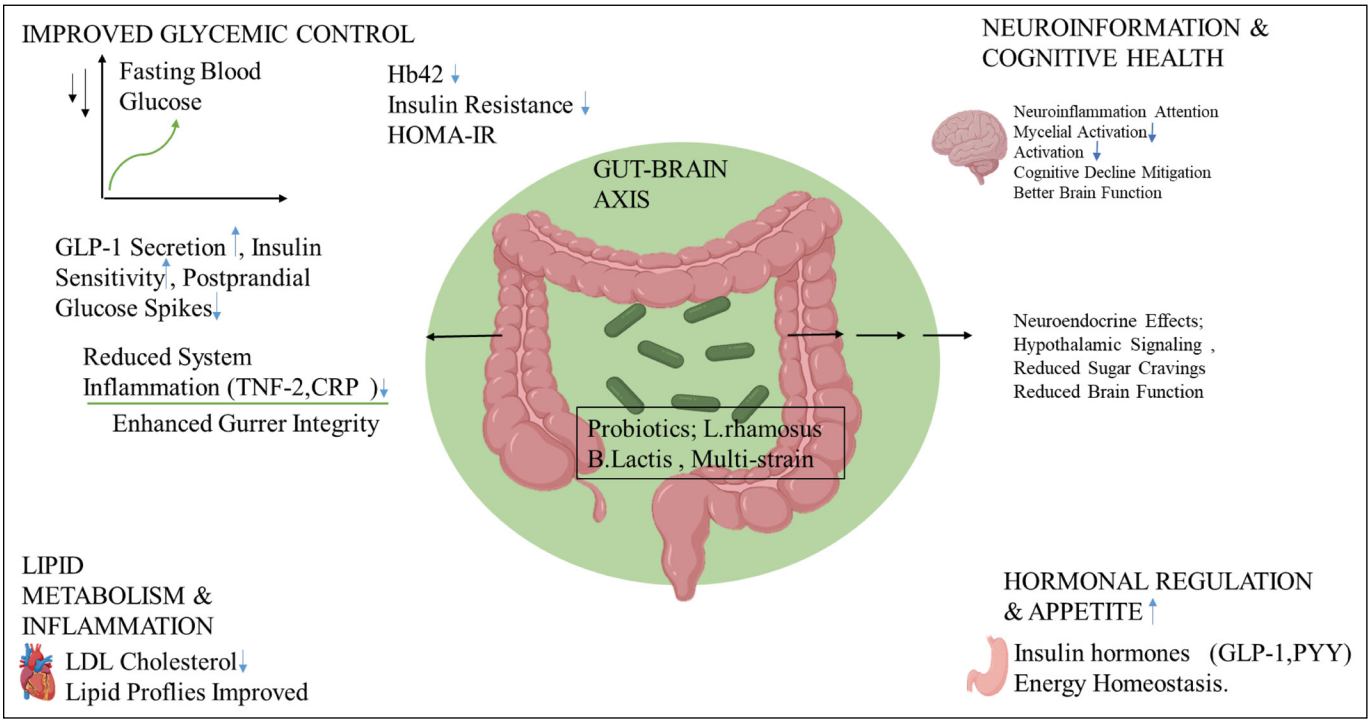


Fig. (5): Illustrated schematic diagram of probiotic-induced modulation of the gut-brain axis by improved glycemic control, increased insulin sensitivity, decreased systemic inflammation, improvement of lipid metabolism, regulation of appetite hormones, and attenuation of neuroinflammation, leading to metabolic homeostasis and improved cognition.

CHALLENGES & FUTURE PROSPECTS

In Mind Over Muffin: Probiotics as the Brain's Secret Weapon Against Sugar Spikes, we describe new evidence supporting the ability to manipulate the gut microbiome to influence metabolic control and communication within the gut-brain axis. This narrative review covers several areas currently being investigated regarding probiotic benefits. However, further well-designed preclinical and clinical studies are required to establish robust therapeutic guidelines and to translate these findings into evidence-based clinical applications. The different types of probiotic strains and formulations available create a major problem. Different probiotic strains produce distinct metabolic and neuroactive effects, which create two problems: first, they hinder researchers from drawing generalizable conclusions about probiotic use, and second, they prevent them from replicating results across various research projects [56].

The gut-brain metabolic axis is a complex system. People differ in their biological makeup, including their gut microbial composition, genetic makeup, dietary habits, stress response mechanisms, and daily activities. Probiotic effectiveness varies from person to person, making it challenging for scientists to identify a single effective probiotic. Most existing research studies require long-term clinical trials that use direct measurements of post-meal blood sugar increases, combined with cognitive and behavioral assessments, to achieve proper scientific validation [48].

Despite the limitations outlined, there is a bright future for this area of research. Advances in microbiome sequencing, combined with metabolomics and neuroimaging, will elucidate the biological pathways linking probiotic intervention to brain signaling and glucose metabolism. Tailored probiotics based on the individual microbiome profile, leading to personalized nutrition, will be key to effective treatment and greater uptake into medicine. Furthermore, the advent of new probiotic and synbiotic products, and the field of psychobiotics, offer considerable promise as these products target both the brain and the metabolic pathways that underpin sugar craving and disruption of glucose regulation [28].

The probiotic treatment could easily be part of an integrated system alongside digital health support, nutrition counseling, and behavioral therapies that guide an overall intervention to manage both sugar spikes and the cognitive aftermath of sugar restriction. The evolution from promoting metabolic health and supplements to evidence-based, brain-targeted therapy relies on research that integrates multiple disciplines to understand existing problems [43].

Individual Variability in Microbiome

The clinical effects of probiotics vary considerably among individuals due to the natural variability in gut microbiota and host genetic makeup [39, 68]. Individual differences among people pose obstacles for researchers seeking to develop standardized probiotic treatments and to study how probiotics protect against sugar-induced brain damage. The therapeutic benefits of personalized microbiome profiling and targeted probiotic formulations will reach their peak after scientific research solves the challenges of studying host-microbe

relationships [87]. This research uses advanced multi-omics techniques to analyze microbiome diversity and functionality, alongside clinical trials testing custom probiotic treatments tailored to each person's specific microbiota profile [88, 89]. Designing effective probiotic strategies that target brain health needs to overcome current challenges. Overcoming these challenges will create new opportunities to develop probiotic-based medical treatments to address brain health problems.

Regulatory Challenges

The major obstacle to the development of neuroprotection programs through probiotic use is regulatory challenges. The current situation lacks standardization because different strains, dosages, and formulations require standardization, creating variability in clinical outcomes and failing to establish a standard basis for regulatory classification. Further, health claims regarding brain function require substantial scientific backing-often with complex endpoints such as mood, memory, and attention, which are not easy to quantify or standardize in human trials [90]. Apart from that, key concerns would include the product's safety and quality control throughout its production, storage, and distribution, as safety legislation varies widely between countries. Meanwhile, the regulatory framework has become even more problematic, with probiotic medications typically regulated as dietary supplements by the FDA in the United States. At the same time, the European Food Safety Authority (EFSA) takes a tougher stance, imposing rigorous requirements and rejecting most health claims for lack of substantial evidence [91, 92].

Need for Large-Scale Clinical Trial

The therapeutic effects of probiotics on cognitive decline associated with sugar consumption need to be tested in large-scale randomized controlled trials with large participant groups. The study requires specific probiotic strains to be used at fixed doses while researchers conduct complete assessments of both cognitive function and metabolic health. The combination of metagenomics and metabolomics as multi-omic approaches provides a means to discover the biological pathways underlying personalized probiotic treatments. The assessment of the sustainability effects of probiotics requires long-term studies, as they must be evaluated alongside their ability to prevent chronic neurodegenerative disorders arising from metabolic disorders [70, 93, 94].

Probiotics might serve as an adjunctive treatment by reducing brain damage from sugar spikes through modulation of gut-brain communication. The scientific research process faces several major obstacles that prevent researchers from conducting large-scale experiments that need to assess treatment effectiveness and determine ideal product compositions and safety profiles. The expected benefits of these innovations will enhance both dietary treatments and medical therapies for cognitive health issues associated with metabolic disorders [95, 96].

Clinical Implications

Research on the gut-brain axis has changed our understanding of how dietary factors affect both metabolic systems and brain functions. The slogan "Mind Over Muffin: Probiotics as the Brain's Secret Weapon Against Sugar Spikes" reflects the clinical concept of the three scientific areas, nutrition, microbiota modulation, and neuroendocrine regulation, of glucose metabolism disorders that probiotics can affect. The sugar spikes that occur after meals create a pattern that overlaps with both metabolic disorders and the rising occurrence of cognitive development, mood disturbances, and insulin resistance, which progresses into cardiovascular and metabolic health dangers over time. The management of these spikes must encompass brain health issues, as they affect behavior that extends beyond glycemic control requirements [59].

Probiotics show potential as a non-invasive treatment option for dysglycemia and related neurological problems, as evidenced by their clinical applications. Certain probiotic strains can regulate glucose levels by modulating gut permeability, inflammatory signaling, short-chain fatty acid production, and enteroendocrine hormone release. These signals serve as a link between peripheral and central neural pathways that control appetite, stress responses, and reward processing, shaping sugar cravings and eating behavior patterns [59, 69].

The therapeutic application of probiotics in dietary and clinical treatments can reduce post-meal glucose spikes while safeguarding cognitive resilience and emotional control from excessive stress. The application of probiotics is potentially particularly helpful for people who suffer from prediabetes, metabolic syndrome, stress-related eating disorders, and certain neuropsychiatric disorders because their symptoms worsen with glycemic fluctuations. The establishment of these clinical foundations will guide the development of personalized nutrition approaches and microbiome-based treatments to enhance both metabolic and brain health [31].

CONCLUSION

Our research underscores the importance of integrating probiotics as a potential therapy in studies of metabolic health, which require researchers to examine the complex relationship between the gut microbiome and brain function rather than relying on traditional methods that measure calorie consumption and sugar levels. Growing evidence shows that probiotics can effectively lower post-meal blood glucose levels by acting on both peripheral metabolic systems and central nervous system functions that control appetite, stress responses, and reward-based eating patterns.

Probiotics have shown promise as an adjuvant therapy for blood glucose modulation and can benefit metabolic homeostasis by interacting with the gut-brain axis. Several probiotic strains can modulate glucose

regulation by balancing intestinal microflora, stimulating short-chain fatty acid production, promoting insulin sensitivity, and attenuating systemic inflammation.

Besides metabolic influences, the gut-brain axis is a mechanistic pathway through which probiotics can affect mood, stress, and behaviors by signaling neurotransmitters (such as serotonin and GABA). This suggests that probiotics may play a complementary role in metabolic and neurobehavioral states. Emerging preclinical and clinical research suggests benefits in dysregulated carbohydrate metabolism and sweet cravings. However, probiotics are probably best used as a complementary, not a therapeutic, treatment for metabolic disease at this time and need more robust, large-scale, randomized controlled studies to confirm strain specificity, dose, and long-term clinical effects. In conclusion, probiotic strategies appear to be a beneficial complementary approach for managing metabolic diseases, but further studies are necessary to define their potential therapeutic and clinical uses. Research in the area of probiotics has presented novel approaches to linking brain activity with metabolic regulation, in turn providing innovative means for personalized medication and disease prevention. As research further uncovers how probiotics act as effective agents in protecting brain metabolic health, they may become indispensable partners in its preservation.

Amplify the Central Theme: How the Probiotics Modify the Working of the Brain and Further Change the Metabolism Process of Sugar by Indirectly Affecting it

Intelligently organized almost imperceptibly between the gut and the brain, its all-natural neurobiological link establishes metabolic equilibrium with the help of probiotics. These useful microbes help modulate interactions between the gut and the central nervous system, which in turn regulate appetite, stress, and insulin sensitivity. Hence, by regulating neurotransmitter levels and decreasing inflammation, probiotics can help the brain metabolize sugars. This would help prevent unexpected spikes in blood sugar levels. Therefore, we see that the impact of probiotics extends beyond digestion; it also involves neurochemical pathways that modulate metabolic health. Hence, probiotic supplementation could be another promising approach for leveraging the brain's natural regulatory machinery to maintain blood sugar balance and improve overall cognitive and physical well-being.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Setayesh A, Karimi M, Karimi MA, Pirzad S, Heydari M, Asbaghi O, *et al.* Effects of probiotic and synbiotic supplementation on glycemic indices in adult individuals with prediabetes and type 2 diabetes mellitus: a grade-assessed systematic review and dose-response meta-analysis of RCTs. Probiotics Antimicrob Proteins 2026; 18(2): 3181-204.
DOI: https://doi.org/10.1007/s12602-025-10644-w
2. Xiang M, Sa X, Tuo Z, Bian J, Wang P, Zhang X. Effects of probiotic supplementation on islet β-cell function in subjects with glucose metabolism disorders: a meta-analysis. Front Nutr 2025; 12: 1668470.
DOI: https://doi.org/10.3389/fnut.2025.1668470
3. Wu Y, Ehlert B, Metwally AA, Perelman D, Park H, Brooks AW, *et al.* Individual variations in glycemic responses to carbohydrates and underlying metabolic physiology. Nat Med 2025; 31(7): 2232-43.
DOI: https://doi.org/10.1038/s41591-025-03719-2
4. Yu YT, Fu YH, Chen YH, Fang YW, Tsai MH. Effect of dietary glycemic index on insulin resistance in adults without diabetes mellitus: a systematic review and meta-analysis. Front Nutr 2025; 12: 1458353.
DOI: https://doi.org/10.3389/fnut.2025.1458353
5. Credali F, Venuti MT, Boffi D, Rossi P. Automatic computation of the glycemic index: data-driven analysis of the glucose standard. J Theor Biol 2026; 626: 112447.
6. Park W, Seo H, Kim J, Hong YM, Song H, Joo BJ, *et al.* In-depth correlation analysis between tear glucose and blood glucose using a wireless smart contact lens. Nat Commun 2024; 15(1): 2828.
DOI: https://doi.org/10.1038/s41467-024-47123-9
7. Han H, Kim Y, Gim M, Shin H, Jang H, Yoon WJ, *et al.* Effect of sugar-free jelly on glycemic metabolism and its potential health benefits in non-diabetic adults. Foods 2024; 13(6): 920.
DOI: https://doi.org/10.3390/foods13060920
8. Ayesh H, Suhail S, Ayesh S. Impact of allulose on blood glucose in type 2 diabetes: A meta-analysis of clinical trials. Metab Open 2024; 24: 100329.
DOI: https://doi.org/10.1016/j.metop.2024.100329
9. Kopec M, Beton-Mysur K, Surmacki J, Abramczyk H. Metabolism changes caused by glucose in normal and cancer human brain cell lines by Raman imaging and chemometric methods. Sci Rep 2024; 14(1): 16626.
DOI: https://doi.org/10.1038/s41598-024-67718-y
10. Wang D, Chen X, Lin J, Zhang T, Huang L, Leng D, *et al.* Maximal speed of glucose change significantly distinguishes prediabetes from diabetes. arXiv 2025; 2506.12567.
DOI: https://doi.org/10.48550/arXiv.2506.12567
11. Katagiri Y, Ozaku H, Kondo K. A method for evaluating the risks of glucose dysregulation in daily life by continuous measurement of glucose excursions under reduced glycemic load: a pilot study. Front Sens 2024; 5: 1382152.
DOI: https://doi.org/10.3389/fsens.2024.1382152
12. Dhatariya K, Umpierrez GE. Management of diabetes and hyperglycemia in hospitalized patients. In: Feingold KR, Adler RA, Ahmed SF, *et al.* Eds. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000.
13. Pigeot I, Ahrens W. Epidemiology of metabolic syndrome. Pflugers Arch 2025; 477(5): 669-80.
DOI: https://doi.org/10.1007/s00424-024-03051-7
14. Zila-Velasque JP, Grados-Espinoza P, Challapa-Mamani MR, Sánchez-Alcántara F, Cedillo-Balcázar J, Cs AD, *et al.* Prevalence

of metabolic syndrome and its components according to altitude levels: a systematic review and meta-analysis. Sci Rep 2024; 14(1): 27581.
DOI: https://doi.org/10.1038/s41598-024-77928-z

15. Liang X, Or B, Tsoi MF, Cheung CL, Cheung BM. Prevalence of metabolic syndrome in the United States National Health and Nutrition Examination Survey 2011-18. Postgrad Med J 2023; 99(1175): 985-92.
DOI: https://doi.org/10.1093/postmj/qgad008
16. Selvaraj P, Muthunarayanan L. Prevalence of Metabolic Syndrome and Associated Risk Factors among Men in a Rural Health Centre Area in Tamil Nadu. J Lifestyle Med 2019; 9(1): 44.
DOI: https://doi.org/10.15280/JLM.2019.9.1.44
17. Zhou B, Rayner AW, Gregg EW, Sheffer KE, Carrillo-Larco RM, Bennett JE, *et al.* Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants. Lancet 2024; 404(10467): 2077-93.
DOI: https://doi.org/10.1016/S0140-6736(24)02317-1
18. Noiman A, Fryar CD, Saif NT, Afful J. Prevalence of Overweight, Obesity, and Severe Obesity Among Children and Adolescents Ages 2-19 Years: United States, 1963-1965 Through August 2021-August 2023. In: NCHS Health E Stats [Internet]. Hyattsville (MD): National Center for Health Statistics (US); 2024 Sep. Health E-Stat 112.
19. Emmerich SD, Fryar CD, Stierman B, Ogden CL. Obesity and Severe Obesity Prevalence in Adults: United States, August 2021-August 2023. NCHS Data Brief 2021. Available from: https: // www.cdc.gov/nchs/products/index.htm
20. Paul P, Kaul R, Harfouche M, Arabi M, Al-Najjar Y, Sarkar A, *et al.* The effect of microbiome-modulating probiotics, prebiotics and synbiotics on glucose homeostasis in type 2 diabetes: A systematic review, meta-analysis, and meta-regression of clinical trials. Pharmacol Res 2022; 185: 106520.
DOI: https://doi.org/10.1016/j.phrs.2022.106520
21. Ayesha IE, Monson NR, Klair N, Patel U, Saxena A, Patel D, *et al.* Probiotics and their role in the management of type 2 diabetes mellitus (Short-term *versus* long-term effect): A systematic review and meta-analysis. Cureus 2023; 15(10): e46741.
DOI: https://doi.org/10.7759/cureus.46741
22. Wang Z, Li W, Lyu Z, Yang L, Wang S, Wang P, *et al.* Effects of probiotic/prebiotic/synbiotic supplementation on blood glucose profiles: a systematic review and meta-analysis of randomized controlled trials. Public Health 2022; 210: 149-59.
DOI: https://doi.org/10.1016/j.puhe.2022.06.012
23. Chandrasekaran P, Weiskirchen S, Weiskirchen R. Effects of probiotics on gut microbiota: an overview. Int J Mol Sci 2024; 25(11): 6022.
DOI: https://doi.org/10.3390/ijms25116022
24. Wang X, Chen L, Zhang C, Shi Q, Zhu L, Zhao S, *et al.* Effect of probiotics at different intervention time on glycemic control in patients with type 2 diabetes mellitus: a systematic review and meta-analysis. Front Endocrinol (Lausanne) 2024; 15: 1392306.
DOI: https://doi.org/10.3389/fendo.2024.1392306
25. Loh JS, Mak WQ, Tan LK, Ng CX, Chan HH, Yeow SH, *et al.* Microbiota-gut-brain axis and its therapeutic applications in neurodegenerative diseases. Signal Transduct Target Ther 2024; 9(1): 37.
DOI: https://doi.org/10.1038/s41392-024-01743-1
26. Abildinova GZ, Benberin VV, Vochshenkova TA, Afshar A, Mussin NM, Kaliyev AA, *et al.* The gut-brain-metabolic axis: exploring the role of microbiota in insulin resistance and cognitive function. Front Microbiol 2024; 15: 1463958.
DOI: https://doi.org/10.3389/fmicb.2024.1463958
27. Chaithanya V, Kumar J, Vajravelu Leela K, Ram M, Thulukanam J. Impact of multistrain probiotic supplementation on glycemic control in type 2 diabetes mellitus—randomized controlled trial. Life (Basel) 2024; 14(11): 1484.
DOI: https://doi.org/10.3390/life14111484
28. Oudat Q, Okour A. The role of probiotics in modulating gut microbiota and metabolic health for weight management: a mini review. Acta Microbiol Hell 2025; 70(1): 5.
DOI: https://doi.org/10.3390/amh70010005
29. Baroni I, Fabrizi D, Luciani M, Magon A, Conte G, De Angeli G, *et al.* Probiotics and synbiotics for glycemic control in diabetes: a systematic review and meta-analysis of randomized controlled trials. Clin Nutr. 2024 Apr 1; 43(4): 1041-61.
DOI: https://doi.org/10.1016/j.clnu.2024.03.006
30. Bock PM, Martins AF, Schaan BD. Understanding how pre-and probiotics affect the gut microbiome and metabolic health. Am J Physiol Endocrinol Metab 2024; 327(1): E89-102.
DOI: https://doi.org/10.1152/ajpendo.00054.2024
31. O'Riordan KJ, Moloney GM, Keane L, Clarke G, Cryan JF. The gut microbiota-immune-brain axis: Therapeutic implications. Cell Rep Med 2025; 6(3): 101982.
DOI: https://doi.org/10.1016/j.xcrm.2025.101982
32. Chen Y, Peng Y, Niu Q, Jiang Y, Ni H, Chen L, *et al.* The impact of probiotics therapy on cognitive and metabolic characteristics in patients with cognitive impairment: An umbrella review of meta-analysis of randomized controlled trials. Eur J Pharmacol 2025; 994: 177326.
DOI: https://doi.org/10.1016/j.ejphar.2025.177326
33. Pan I, Umapathy S. Probiotics: an emerging therapeutic approach towards gut-brain-axis oriented chronic health issues induced by microplastics: a comprehensive review. Heliyon 2024; 10(11): e32004.
DOI: https://doi.org/10.1016/j.heliyon.2024.e32004
34. Byndloss M, Devkota S, Duca F, Niess JH, Nieuwdorp M, Orho-Melander M, *et al.* The gut microbiota and diabetes: research, translation, and clinical applications—2023 Diabetes, Diabetes Care, and Diabetologia Expert Forum. Diabetes 2024; 73(9): 1391-410.
DOI: https://doi.org/10.2337/dbi24-0028
35. Sarita B, Samadhan D, Hassan MZ, Kovaleva EG. A comprehensive review of probiotics and human health-current prospective and applications. Front Microbiol 2025; 15: 1487641.
DOI: https://doi.org/10.3389/fmicb.2024.1487641
36. Latif A, Shehzad A, Niazi S, Zahid A, Ashraf W, Iqbal MW, *et al.* Probiotics: mechanism of action, health benefits and their application in food industries. Front Microbiol 2023; 14: 1216674.
DOI: https://doi.org/10.3389/fmicb.2023.1216674
37. Agustí A, García-Pardo MP, López-Almela I, Campillo I, Maes M, Romaní-Pérez M, *et al.* Interplay between the gut-brain axis, obesity and cognitive function. Front Neurosci 2018; 12: 329519.
DOI: https://doi.org/10.3389/fnins.2018.00155
38. Ķimse L, Reinis A, Miķelsone-Jansone L, Gintere S, Krūmiņa A. A narrative review of psychobiotics: probiotics that influence the gut-brain axis. Medicina (Kaunas) 2024; 60(4): 601.
DOI: https://doi.org/10.3390/medicina60040601
39. Liu Y, Tran DQ, Rhoads JM. tProbiotics in disease prevention and treatment. J Clin Pharmacol 2018; 58: S164-79.
DOI: https://doi.org/10.1002/jcph.1121
40. Chen K, Wang H, Yang X, Tang C, Hu G, Gao Z. Targeting gut microbiota as a therapeutic target in T2DM: A review of multi-target interactions of probiotics, prebiotics, postbiotics, and synbiotics with the intestinal barrier. Pharmacol Res 2024; 210: 107483.
DOI: https://doi.org/10.1016/j.phrs.2024.107483
41. Boyajian JL, Islam P, Abosalha A, Schaly S, Thareja R, Kassab A, *et al.* Probiotics, prebiotics, synbiotics and other microbiome-based innovative therapeutics to mitigate obesity and enhance longevity *via* the gut-brain axis. Microbiome Res Rep 2024; 3(3): 29.
DOI: https://doi.org/10.20517/mrr.2024.05
42. Petrut SM, Bragaru AM, Munteanu AE, Moldovan AD, Moldovan CA, Rusu E. Gut over mind: exploring the powerful gut-brain axis. Nutrients 2025; 17(5): 842.
DOI: https://doi.org/10.3390/nu17050842
43. Qin L, Fan B, Zhou Y, Zheng J, Diao R, Wang F, *et al.* Targeted gut microbiome therapy: applications and prospects of probiotics, fecal

microbiota transplantation and natural products in the management of type 2 diabetes. Pharmacol Res 2025; 213: 107625.
DOI: https://doi.org/10.1016/j.phrs.2025.107625

44. Kumar A, Sivamaruthi BS, Dey S, Kumar Y, Malviya R, Prajapati BG, *et al.* Probiotics as modulators of gut-brain axis for cognitive development. Front Pharmacol 2024; 15: 1348297.
DOI: https://doi.org/10.3389/fphar.2024.1348297

45. Nakhal MM, Yassin LK, Alyaqoubi R, Saeed S, Alderei A, Alhammadi A, *et al.* The microbiota-gut-brain axis and neurological disorders: A comprehensive review. Life (Basel) 2024; 14(10): 1234.
DOI: https://doi.org/10.3390/life14101234

46. Lu S, Zhao Q, Guan Y, Sun Z, Li W, Guo S, *et al.* The communication mechanism of the gut-brain axis and its effect on central nervous system diseases: a systematic review. Biomed Pharmacother 2024; 178: 117207.
DOI: https://doi.org/10.1016/j.biopha.2024.117207

47. Basnet J, Eissa MA, Yanes Cardozo LL, Romero DG, Rezq S. Impact of probiotics and prebiotics on gut microbiome and hormonal regulation. Gastrointest Disord 2024; 6(4): 801-15.
DOI: https://doi.org/10.3390/gidisord6040056

48. Liu Y, Wang J, Wu C. Modulation of gut microbiota and immune system by probiotics, prebiotics, and post-biotics. Front Nutr 2022; 8: 634897.
DOI: https://doi.org/10.3389/fnut.2021.634897

49. Zhang SM, Wu HC, Hung JH, Huang SL. Indole derivatives biosynthesis in *Bifidobacterium longum* subsp. *infantis* and the tryptophan substrate availability. Microb Biotechnol 2025; 18(6): e70167.
DOI: https://doi.org/10.1111/1751-7915.70167

50. Guo P, Wang W, Xiang Q, Pan C, Qiu Y, Li T, *et al.* Engineered probiotic ameliorates ulcerative colitis by restoring gut microbiota and redox homeostasis. Cell Host Microbe 2024; 32(9): 1502-18.
DOI: https://doi.org/10.1016/j.chom.2024.07.028

51. Schoeler M, Caesar R. Dietary lipids, gut microbiota and lipid metabolism. Rev Endocr Metab Disord 2019; 20(4): 461-72.
DOI: https://doi.org/10.1007/s11154-019-09512-0

52. Markowiak-Kopeć P, Śliżewska K. The effect of probiotics on the production of short-chain fatty acids by human intestinal microbiome. Nutrients 2020; 12(4): 1107.
DOI: https://doi.org/10.3390/nu12041107

53. Huang Y, Wang YF, Miao J, Zheng RF, Li JY. Short-chain fatty acids: important components of the gut-brain axis against AD. Biomed Pharmacother 2024; 175: 116601.
DOI: https://doi.org/10.1016/j.biopha.2024.116601

54. Li S, Liu Z, Zhang Q, Su D, Wang P, Li Y, *et al.* The antidiabetic potential of probiotics: a review. Nutrients 2024; 16(15): 2494.
DOI: https://doi.org/10.3390/nu16152494

55. Meher AK, Acharya B, Sahu PK. Probiotics: bridging the interplay of a healthy gut and psychoneurological well□being. Food Bioeng 2024; 3(1): 126-47.
DOI: https://doi.org/10.1002/fbe2.12081

56. Shen X, Ma C, Yang Y, Liu X, Wang B, Wang Y, *et al.* The role and mechanism of probiotics supplementation in blood glucose regulation: a review. Foods 2024; 13(17): 2719.
DOI: https://doi.org/10.3390/foods13172719

57. Xiao W, Su J, Gao X, Yang H, Weng R, Ni W, *et al.* The microbiota-gut-brain axis participates in chronic cerebral hypoperfusion by disrupting the metabolism of short-chain fatty acids. Microbiome 2022; 10(1): 62.
DOI: https://doi.org/10.1186/s40168-022-01255-6

58. Ding N, Hao X, Zhang Y, Zhang Y, Li Z. Benign regulation of short-chain fatty acids: the underlying mechanism of the beneficial effects of manual acupuncture on cognitive ability and the intestinal mucosal barrier in APP/PS1 mice. Front Neurosci 2025; 19: 1509581.
DOI: https://doi.org/10.3389/fnins.2025.1509581

59. Kim JH, Choi Y, Lee S, Oh MS. Probiotics as potential treatments for neurodegenerative diseases: a review of the evidence from *in vivo* to clinical trial. Biomol Ther (Seoul) 2024; 33(1): 54.
DOI: https://doi.org/10.4062/biomolther.2024.215

60. Zhang D, Jian YP, Zhang YN, Li Y, Gu LT, Sun HH, *et al.* Short-chain fatty acids in diseases. Cell Commun Signal 2023; 21(1): 212.
DOI: https://doi.org/10.1186/s12964-023-01219-9

61. Ghorbani Z, Shoaibinobarian N, Noormohammadi M, Taylor K, Kazemi A, Bonyad A, *et al.* Reinforcing gut integrity: a systematic review and meta-analysis of clinical trials assessing probiotics, synbiotics, and prebiotics on intestinal permeability markers. Pharmacol Res 2025; 216: 107780.
DOI: https://doi.org/10.1016/j.phrs.2025.107780

62. Chen X, Yan L, Yang J, Xu C, Yang L. The impact of probiotics on oxidative stress and inflammatory markers in patients with diabetes: A meta-research of meta-analysis studies. Front Nutr 2025; 12: 1552358.
DOI: https://doi.org/10.3389/fnut.2025.1552358

63. Kearns R. Gut-brain axis and neuroinflammation: the role of gut permeability and the kynurenine pathway in neurological disorders. Cell Mol Neurobiol 2024; 44(1): 64.
DOI: https://doi.org/10.1007/s10571-024-01496-z

64. Jiang Y, Yang J, Wei M, Shou J, Shen S, Yu Z, *et al.* Probiotics alleviate painful diabetic neuropathy by modulating the microbiota-gut-nerve axis in rats. J Neuroinflammation 2025; 22(1): 30.
DOI: https://doi.org/10.1186/s12974-025-03352-3

65. Xiao B, Fu L, Yang Z, Yu G. Effect of probiotics on cognitive function and cardiovascular risk factors in mild cognitive impairment and Alzheimer's disease: an umbrella meta-analysis. J Health Popul Nutr 2025; 44(1): 109.
DOI: https://doi.org/10.1186/s41043-025-00816-3

66. Ruiz-Gonzalez C, Cardona D, Rueda-Ruzafa L, Rodriguez-Arrastia M, Ropero-Padilla C, Roman P. Cognitive and emotional effect of a multi-species probiotic containing *Lactobacillus rhamnosus* and *Bifidobacterium lactis* in healthy older adults: a double-blind randomized placebo-controlled crossover trial. Probiotics Antimicrob Proteins 2025; 17(5): 3525-37.

67. Eastwood J, van Hemert S, Stolaki M, Williams C, Walton G, Lamport D. Exploring the acute and chronic effects of a multistrain probiotic supplement on cognitive function and mood in healthy older adults: a randomized controlled trial. Am J Clin Nutr 2025; 121(6): 1268-80.
DOI: https://doi.org/10.1016/j.ajcnut.2025.04.002

68. Silva YP, Bernardi A, Frozza RL. The role of short-chain fatty acids from gut microbiota in gut-brain communication. Front Endocrinol (Lausanne) 2020; 11: 508738.
DOI: https://doi.org/10.3389/fendo.2020.00025

69. Quansah M, David MA, Martins R, El-Omar E, Aliberti SM, Capunzo M, *et al.* The beneficial effects of *Lactobacillus* strains on gut microbiome in Alzheimer's disease: a systematic review. Healthcare (Basel) 2025; 13(1): 74.
DOI: https://doi.org/10.3390/healthcare13010074

70. Lee SH, Ahmad SR, Lim YC, Zulkipli IN. The use of probiotic therapy in metabolic and neurological diseases. Front Nutr 2022; 9: 887019.
DOI: https://doi.org/10.3389/fnut.2022.887019

71. Crocetta A, Liloia D, Costa T, Duca S, Cauda F, Manuello J. From gut to brain: unveiling probiotic effects through a neuroimaging perspective—A systematic review of randomized controlled trials. Front Nutr 2024; 11: 1446854.
DOI: https://doi.org/10.3389/fnut.2024.1446854

72. Nemati M, Ebrahimi B, Montazeri-Najafabady N. Probiotics ameliorate endocrine disorders *via* modulating inflammatory pathways: a systematic review. Genes Nutr 2024; 19(1): 7.
DOI: https://doi.org/10.1186/s12263-024-00743-8

73. Gao T, Li R, Hu L, Hu Q, Wen H, Zhou R, *et al.* Probiotic *Lactobacillus rhamnosus* GG improves insulin sensitivity and offspring survival *via* modulation of gut microbiota and serum metabolite in a sow model. J Anim Sci Biotechnol 2024; 15(1): 89.
DOI: https://doi.org/10.1186/s40104-024-01046-z

74. Diotaiuti P, Misiti F, Marotta G, Falese L, Calabrò GE, Mancone S. The gut microbiome and its impact on mood and decision-making: a mechanistic and therapeutic review. Nutrients 2025; 17(21): 3350.
DOI: https://doi.org/10.3390/nu17213350

75. Park KJ, Gao Y. Gut-brain axis and neurodegeneration: mechanisms and therapeutic potentials. Front Neurosci 2024; 18: 1481390.
DOI: https://doi.org/10.3389/fnins.2024.1481390

76. Wang L, Zhao R, Li X, Shao P, Xie J, Su X, *et al. Lactobacillus rhamnosus* GG improves cognitive impairments in mice with sepsis. PeerJ 2024; 12: e17427.
DOI: https://doi.org/10.7717/PEERJ.17427

77. Peng X, Xian H, Ge N, Hou L, Tang T, Xie D, *et al.* Effect of probiotics on glycemic control and lipid profiles in patients with type 2 diabetes mellitus: a randomized, double blind, controlled trial. Front Endocrinol (Lausanne) 2024; 15: 1440286.
DOI: https://doi.org/10.3389/fendo.2024.1440286

78. Ma X, Shin YJ, Jang HM, Joo MK, Yoo JW, Kim DH. *Lactobacillus rhamnosus* and *Bifidobacterium longum* alleviate colitis and cognitive impairment in mice by regulating IFN-γ to IL-10 and TNF-α to IL-10 expression ratios. Sci Rep 2021; 11(1): 20659.
DOI: https://doi.org/10.1038/s41598-021-00096-x

79. Pan X, Guo A, Guan K, Chen C, Xu S, Tang Y, *et al. Lactobacillus rhamnosus* GG attenuates depression-like behaviour and cognitive deficits in chronic ethanol exposure mice by down-regulating systemic inflammatory factors. Addict Biol 2024; 29(11): e13445.
DOI: https://doi.org/10.1111/adb.13445

80. Cui Z, Wang S, Niu J, Ma J, Yang H. *Bifidobacterium* species serve as key gut microbiome regulators after intervention in gestational diabetes mellitus. BMC Microbiol 2024; 24(1): 520.
DOI: https://doi.org/10.1186/s12866-024-03680-z

81. Işık M, Köse F, Özbayer C, Budak Ö, Kaya RK, Erdoğan DG, *et al.* Promising antidepressant potential: the role of *Lactobacillus rhamnosus* GG in mental health and stress response. Probiotics Antimicrob Proteins 2025: 1-31.
DOI: https://doi.org/10.1007/s12602-025-10470-0

82. Kim WJ, Kil BJ, Lee C, Kim TY, Han G, Choi Y, *et al. B. longum* CKD1 enhances the efficacy of anti-diabetic medicines through upregulation of IL-22 response in type 2 diabetic mice. Gut Microbes 2024; 16(1): 2319889.
DOI: https://doi.org/10.1080/19490976.2024.2319889

83. Fekete M, Lehoczki A, Major D, Fazekas-Pongor V, Csípő T, Tarantini S, *et al.* Exploring the influence of gut-brain axis modulation on cognitive health: a comprehensive review of prebiotics, probiotics, and symbiotics. Nutrients 2024; 16(6): 789.
DOI: https://doi.org/10.3390/nu16060789

84. Bocchio F, Mancabelli L, Milani C, Lugli GA, Tarracchini C, Longhi G, *et al.* Compendium of *Bifidobacterium*-based probiotics: characteristics and therapeutic impact on human diseases. Microbiome Res Rep 2024; 4(1): 2.
DOI: https://doi.org/10.20517/mrr.2024.52

85. Kim CS, Cha J, Sim M, Jung S, Chun WY, Baik HW, *et al.* Probiotic supplementation improves cognitive function and mood with changes in gut microbiota in community-dwelling older adults: a randomized, double-blind, placebo-controlled, multicenter trial. J Gerontol A Biol Sci Med Sci 2021; 76(1): 32-40.
DOI: https://doi.org/10.1093/GERONA/GLAA090

86. Zhang C, Zhang Q, Zhang X, Du S, Zhang Y, Wang X, *et al.* Effects of synbiotics surpass probiotics alone in improving type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled trial. Clin Nutr 2025; 44: 248-58.
DOI: https://doi.org/10.1016/j.clnu.2024.11.042

87. Zmora N, Zilberman-Schapira G, Suez J, Mor U, Dori-Bachash M, Bashiardes S, *et al.* Personalized gut mucosal colonization resistance to empiric probiotics is associated with unique host and microbiome features. Cell 2018; 174(6): 1388-405.
DOI: https://doi.org/10.1016/j.cell.2018.08.041

88. Wang H, Lee IS, Braun C, Enck P. Effect of probiotics on central nervous system functions in animals and humans: a systematic review. J Neurogastroenterol Motil 2016; 22(4): 589.
DOI: https://doi.org/10.5056/jnm16018

89. Leeming ER, Johnson AJ, Spector TD, Le Roy CI. Effect of diet on the gut microbiota: rethinking intervention duration. Nutrients 2019; 11(12): 2862.
DOI: https://doi.org/10.3390/nu11122862

90. De Simone C. The unregulated probiotic market. Clin Gastroenterol Hepatol 2019; 17(5): 809-17.
DOI: https://doi.org/10.1016/j.cgh.2018.01.018

91. Li X, Zheng P, Cao W, Cao Y, She X, Yang H, *et al. Lactobacillus rhamnosus* GG ameliorates noise-induced cognitive deficits and systemic inflammation in rats by modulating the gut-brain axis. Front Cell Infect Microbiol 2023; 13: 1067367.
DOI: https://doi.org/10.3389/fcimb.2023.1067367

92. Smith RP, Easson C, Lyle SM, Kapoor R, Donnelly CP, Davidson EJ, *et al.* Gut microbiome diversity is associated with sleep physiology in humans. PloS One 2019; 14(10): e0222394.
DOI: https://doi.org/10.1371/journal.pone.0222394

93. Cryan JF, O'Riordan KJ, Cowan CS, Sandhu KV, Bastiaanssen TF, Boehme M, *et al.* The microbiota-gut-brain axis. Physiol Rev 2019; 99(4): 1877-2013.
DOI: https://doi.org/10.1152/PHYSREV.00018.2018

94. Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. BMJ 2018; 361: k2179.
DOI: https://doi.org/10.1136/bmj.k2179

95. Wang X, Zhang Y, Chang Y, Zhu Y, Xiang G, Chen K, *et al.* Alternating magnetic field-responsive engineered probiotics for anxiety therapy *via* gut-brain axis modulation. J Nanobiotechnol 2025; 23(1): 463.
DOI: https://doi.org/10.1186/s12951-025-03551-3

96. Martinez Guevara D, Vidal Cañas S, Palacios I, Gómez A, Estrada M, Gallego J, *et al.* Effectiveness of probiotics, prebiotics, and synbiotics in managing insulin resistance and hormonal imbalance in women with polycystic ovary syndrome (PCOS): a systematic review of randomized clinical trials. Nutrients 2024; 16(22): 3916.
DOI: https://doi.org/10.3390/nu16223916