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Gut Microbiota, Dietary Metabolites, and Inflammation: Implications for Metabolic and Neurological Health

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ABSTRACT

The gastrointestinal tract contains a huge number of microorganisms, among which bacteria, viruses, fungi, and many others predominate. The influence of the gut microbiota on the digestion and absorption of nutrients, immunity, and the body's health in general, has been widely explored in recent years. The composition of microbiota is influenced by various factors, including food, environment, drug use, genetic predispositions. Human nutrition affects the composition and functional activity of the gut microbiota and contributes to the formation of metabolites. Microbes degrade various dietary components, including dietary fibers, resistant starch, polyphenols, protein, and fat. Short-chain fatty acids (SCFAs) are the most important metabolites produced by gut microbiota. SCFAs, such as acetate, propionate, and butyrate, are involved in the regulation of immunity and intestinal barrier function, as well as intermediary metabolism. The microbiota produces other bioactive metabolites, including bile acid derivatives, tryptophan metabolites, and trimethylamine-related compounds. This is a diverse group of compounds that are tightly linked to the gut-brain axis, have proinflammatory or anti-inflammatory effects, and are involved in the regulation of glucose and lipid homeostasis and the development of metabolic disease. Dysfunction of the gut microbiota can lead to a disruption of the intestinal barrier and a constant influx of bacterial products, resulting in low-grade systemic inflammation. In metabolic syndrome, the altered composition and function of microbiota are associated with adipose tissue dysfunction, disorders of glucose and lipid metabolism, and increased cardiovascular risk. The role of dysbiosis in the development of metabolic disease, particularly obesity, T2DM, and MASLD, is of great interest to researchers. The mechanisms connecting diet, microbiota, and inflammation are complex and multifaceted.

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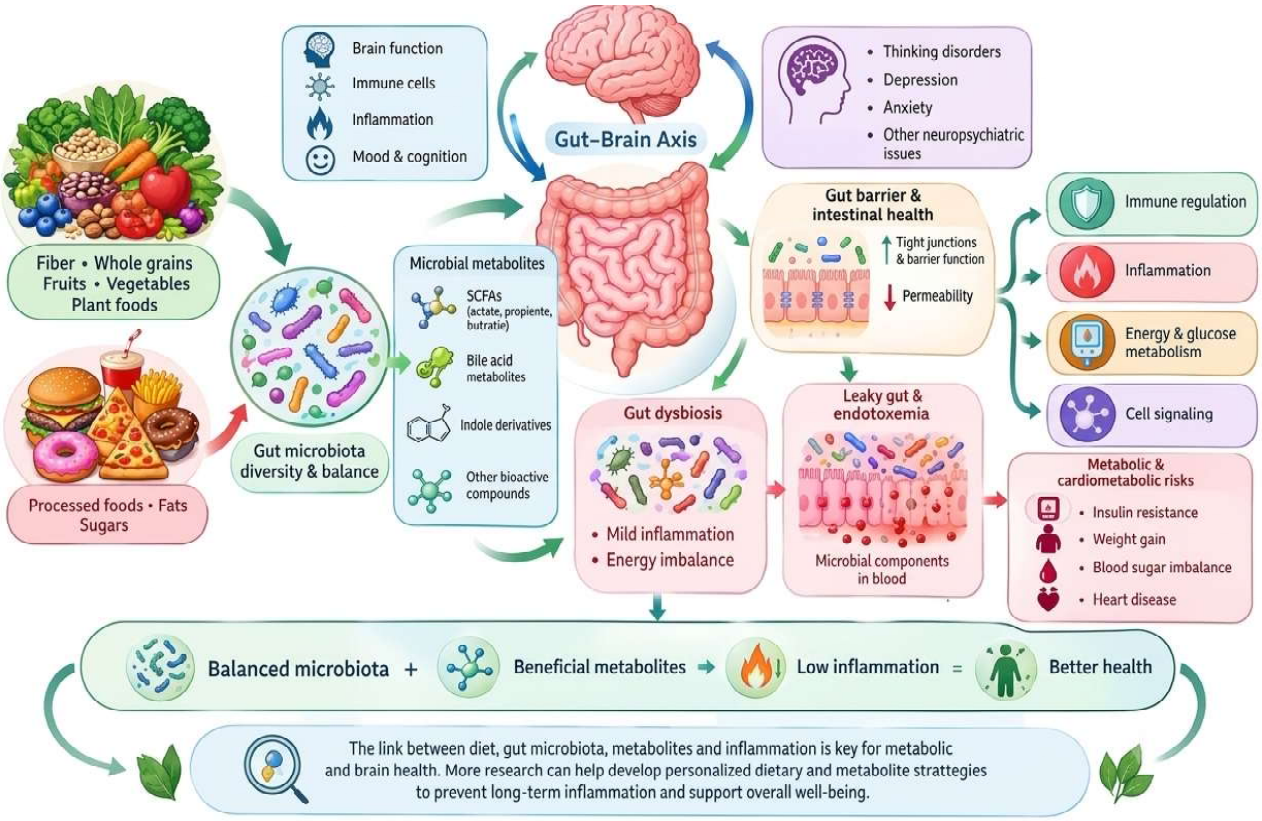
At the same time, there is growing evidence of the impact of the microbiota on the brain through the gut-brain axis, which involves a number of communication pathways. It follows from this that the gut microbiota and its metabolites are important players in the development and progression of neurological diseases. The connection between neurodegenerative diseases, such as Parkinson's and Alzheimer's, and the gut microbiome was also found. Furthermore, depression and cognitive function impairment were associated with changes in the microbiota and microbiota-derived metabolites. However, the contribution of dysbiosis to these diseases is controversial and requires further study. A balanced diet, rich in fiber, and biodiversity, as well as fermented foods, can improve gut health and increase the production of beneficial metabolites. Probiotics, prebiotics, and postbiotics are promising dietary supplements for restoring microbiota balance and improving health. Longitudinal and interventional studies are needed to identify causal relationships and biomarkers of disease. This will allow clinicians and medical researchers to develop and test individual treatments and conduct preventive therapies to achieve the best results. Thus, the study of the role of the microbiota in human health and methods to influence it will make it possible to find ways to reduce the burden of many metabolic and neurological diseases.

Keywords: *Gut Microbiota, Dietary Metabolites, and Inflammation: Implications for Metabolic and Neurological Health.*



Graphical Abstract

INTRODUCTION

Final version of our paper on interactions between gut microbiota, dietary metabolites and inflammation. The human gut microbiota is one of the most diverse and sophisticated ecological systems that involve a great variety of species of bacteria, viruses, and other microorganisms. It is also essential for the normal functioning of the human body and participating in the processes of digestion, regulating immunity, producing metabolites, and protecting from pathogens. Researchers have devoted significant attention to the interactions between the gut microbiota, its dietary metabolites, and inflammation, as well as the relationship between microbiota and the host's metabolic and neurological functions (Shen et al., 2021). The gut microbiota composition and diversity are usually changed under the influence of pro-inflammatory nutrition, environmental pollution, aging, and antibiotics application, while the balanced one ensures the appropriate digestion, immunity, and protection mechanisms. The major amount of plant dietary fiber, complex carbohydrates, proteins, and lipids are digested and broken down by the gut microbiota, leading to the formation of numerous metabolites. Short-chain fatty acids, secondary bile acids, indole derivatives, and other bacterial metabolites are considered to be important regulators of intestinal immunity, lipid and energy metabolism, intestinal barrier function, and glucose homeostasis. Moreover, the gut microbiota is involved and regulates the central nervous system and plays a significant role in neurodegenerative diseases. Dysfunctional microbiota leads to increased intestinal permeability and inappropriate immune response, resulting in chronic inflammation, which is a hallmark of cardiometabolic diseases. On the other hand, the inflammatory response is frequently the reason for obesity, metabolic syndrome, type 2 diabetes, cardiovascular diseases, and many other conditions. Meanwhile, it has been discovered that chronic pro-inflammatory responses are associated with particular immunoglobulin isotype patterns in individuals suffering from obesity and inflammatory bowel disease (Yang et al., 2021). Thus, intestinal permeability and inflammation appear to be a key mechanism by which dysregulated gut microbiota contributes to metabolic and immune dysfunction, while bacterial metabolites are capable of modulating the inflammatory response and the overall immune status. It is suggested that the gut-brain axis is one of the key mechanisms that connect the gut microbiota with other organs and systems, in particular the immune and endocrine systems. There is growing evidence that microbiota is functionally involved in the development and progression of neurological conditions such as Parkinson's disease and Alzheimer's disease, as well as depression and other mental disorders (Park et al., 2021). In this regard, understanding the nature of the interaction between the gut microbiota and the host will enable developing new therapies and preventative measures to treat and manage these conditions. Concludingly, the gut microbiota plays a critical role in human health and participates in various physiological functions, including digestion, immunity, neuroinflammation, cognition, and others. The modulation of the gut microbiota by a proper diet could be a far-reaching approach for managing and treating a wide range of diseases and physiological abnormalities, including obesity, diabetes, and cardiovascular diseases (Croci et al., 2021).

DIET–MICROBIOTA INTERACTIONS AND METABOLIC TRANSFORMATION

Diet–microbiota interactions form a relationship where diet components shape the composition and function of the gut microbiota and the gut microbiota turns those diet components into metabolites that influence the body. The gut contains a microbial community that can break down carbohydrates, proteins, fats, polyphenols and other parts of diet that the body does not fully digest (Tanes et al., 2021). Diet fibre is especially important because gut microbes ferment carbohydrates into short chain fatty acids or SCFAs such as acetate, propionate and butyrate. These SCFAs help the body use energy keep the gut lining strong regulate the system and send signals to cells. Butyrate for instance supplies an energy source for colon cells in the gut and supports the gut lining while acetate and propionate can affect the body's overall metabolism. The gut microbiota also turns proteins from diet into substances such as branched chain fatty acids, indole derivatives, ammonia, phenols and other compounds (Socala et al., 2021). Some of these products help the body send signals but when diet pushes the gut microbiota to produce too much of potentially harmful substances it can lead to inflammation and problems with metabolism. Diet polyphenols found in fruits, vegetables, tea, cocoa and other plant foods are another group of foods that gut microbes can work on. Many polyphenols are not well absorbed in their form so gut microbes break them into smaller active pieces that can act as antioxidants fight inflammation and help metabolism. The gut microbiota also changes bile acids turning primary bile acids from diet into bile acids that can influence the body's metabolism by activating receptors like the farnesoid X receptor (FXR) and the Takeda G protein coupled receptor 5 (TGR5). In contrast a diet full of processed foods too much saturated fat and added sugar can alter the diversity and activity of gut microbiota creating a gut environment that promotes low grade inflammation (Yang et al., 2021). The shift in the gut microbiota can alter the intestinal permeability, the immune response signaling pathways and the production of microbial metabolites that enter the systemic circulation and, thus, disrupt the normal physiology of the host, for example, by affecting insulin sensitivity, lipid metabolism, adiposity or atherosclerosis. Importantly gut microbial metabolites can also talk to the brain through the gut–brain axis. SCFAs metabolites from tryptophan bile acid derivatives and other microbial products can interact with immune, endocrine, nervous and metabolic pathways that link the gut and the brain. Thus diet changes that affect gut metabolism can have consequences for both metabolic health and brain health. However these interactions differ from person to person. Depend on genetics, age, medications, lifestyle, disease and the existing gut microbiota. Understanding how diet changes gut metabolism gives a solid base, for creating nutrition plans that help keep metabolism balanced lower chronic inflammation and possibly support healthy brain function (Ma et al., 2022).

MAJOR DIETARY AND MICROBIAL METABOLITES

Dietary and bacterial metabolites regulate human health by controlling metabolic and immune processes and the communication between the gut and the brain. The former are formed as a result of the digestion and metabolism of food components, while the latter are created as products of microbial

transformation of dietary and endogenous compounds. The composition of the microbiota is influenced by many factors such as diet, age, genetic predispositions, lifestyle, and medications (Chakrabarti et al., 2022). Bacterial activity can create the short-chain fatty acids like acetate, propionate, and butyrate that are the most studied bacterial products. These molecules are formed as a result of the fermentation of dietary fibers and resistant starch carried out by commensal gut bacteria. For example, butyrate is an energy source for colonocytes, enhances the integrity of the gut barrier, and suppresses the inflammatory response. The other two SCFAs, acetate, and propionate, play a role in the regulation of energy homeostasis, lipid metabolism, and glucose utilization. Moreover, some SCFAs affect the activity of the hypothalamus and control appetite and body weight. The other class of bacterial metabolites is represented by bile acid metabolites formed by gut bacteria from primary bile acids that are synthesized in the liver (Ghasemian Sorboni et al., 2022). The secondary bile acids formed have an effect on the metabolism of lipids and glucose, immunity, and gut motility via particular receptors. One more class of bacterial metabolites is constituted by tryptophan derivatives. This essential amino acid, a part of which is transformed by intestinal bacteria into various metabolites, including indole, some of which (for example, indole derivatives) are involved in the regulation of the integrity of the intestinal barrier and immune response. In addition, deregulation tryptophan metabolism is often accompanied by inflammatory and neurodegenerative diseases. Trimethylamine is a bacterial metabolite involved in the pathophysiology of several diseases (O'riordan et al., 2022). Bacteria can indeed convert dietary nutrients such as choline or carnitine into trimethylamine, which can be oxidized in the liver to trimethylamine-N-oxide, which is associated with an increased risk of cardiovascular and metabolic diseases. The relationship between TMAO and these conditions, however, seems to be dependent on genetic background and environmental factors. Polyphenols represent micronutrients present in food, especially in tea, cocoa, fruits, vegetables, and wine, characterized by a wide range of biological activities, including antioxidant, anti-inflammatory, and vasoprotective effects (Marc et al., 2022). However, prior to their activation, polyphenols must be broken down in the gastrointestinal tract. Microbial transformation of proteins gives rise to the production of branched-chain fatty acids, ammonia, phenolic compounds, and hydrogen sulphide, amongst others. The impact of these metabolites on the body may depend on the dose, as well as individual characteristics of metabolism. Some microbial metabolites affect the gut-brain axis, thereby modulating intestinal immune responses, the hypothalamic-pituitary-adrenal axis, vagus nerve function, and the blood-brain barrier. This interaction leads to changes in neuroinflammation and thus to the functioning of the nervous system (Thomas et al., 2022).

METABOLITE-MEDIATED IMMUNE AND INFLAMMATORY SIGNALING

Metabolite-mediated immune and inflammatory signalling is a way that what we eat and the gut microbes use it to affect the system and our overall health. Metabolites made by gut bacteria act as signals that help the gut microbiota talk to the gut walls immune cells and even organs away. Among these signals short-chain fatty acids (SCFAs) like acetate, propionate and butyrate are especially important. They come from bacteria fermenting

fibre and they can change how immune cells work how cytokines are made and how strong the gut barrier is. Butyrate for instance can help the gut lining stay healthy and control inflammation by blocking histone deacetylase and turning on G-protein-coupled receptors. When gut bacteria change tryptophan they make derivatives that can activate the aryl hydrocarbon receptor, which helps keep mucosal immunity balanced and the gut in harmony (Peterson et al., 2022). Bile acid metabolites also play a role in the regulation by activating receptors such as the farnesoid X receptor (FXR) and TGR5 associated with pro-inflammatory and metabolic pathways, respectively. Moreover, some bacterial metabolites may have pro-inflammatory effects if their concentrations are too high and / or the integrity of the intestinal barrier is compromised. For example when bacterial parts like move from the gut into the blood they can trigger innate immune pathways and add to chronic low grade inflammation. Metabolites coming from proteins, such, as phenolic compounds, indoles and other nitrogen rich products can act differently depending on how much there is, how they are built and the body environment (Meyers et al., 2022). Importantly metabolite-mediated signalling is not limited to the gut. Microbial metabolites can travel through the blood. Affect the liver, fat tissue, heart system and brain helping signal along the gut–immune and gut–brain axes. When these pathways get messed up they have been linked to metabolic problems and inflammatory diseases. What we eat strongly shapes this metabolic scene because fibre, polyphenols, proteins, fats and other food parts give the bacteria things to transform. Understanding metabolite-mediated signalling can explain how diet and gut microbes add to inflammation and can guide the creation of nutrition and microbiota focused plans to keep metabolic and brain health in check (Praveenraj et al., 2022).

MICROBIOTA-DERIVED METABOLITES IN METABOLIC DISORDERS

Microbiota-derived metabolites play a role in the relationship between the gut microbiome and metabolic health. The microorganisms living in the system change the food we eat and the substances made by the body into many active chemicals that can affect how the body uses sugar manages fats handles inflammation balances energy and responds to insulin. Short-chain fatty acids (SCFAs) acetate, propionate and butyrate are some of the most studied microbial metabolites (Castillo-alvarez et al., 2022). They are mainly made when the body breaks down fiber from food and can help keep the gut lining strong control the system affect how hungry we feel and change how the body deals with sugar and fats. Changes in how these fatty acidsre made or how they work have been linked to being overweight not responding properly to insulin and type 2 diabetes. Gut bacteria also change the food substance called tryptophan into chemicals made from indole. These can affect the system in the gut and the lining of the digestive tract through certain pathways like the aryl hydrocarbon receptor (Liu et al., 2023). Changes in these chemicals may lead to problems in the gut and more inflammation. Another important process of the gut microbiome is the transformation of bile acids by intestinal bacteria and their impact on the body. This biochemical process forms secondary bile acids that interact with nuclear receptors, such as FXR and TGR5, and modify glucose, lipid metabolism, and energy expenditure. The breakdown of choline, phosphatidylcholine, and carnitine, which can be found in food,

produces trimethylamine (Table 1). The liver oxidizes this substance to trimethylamine-N-oxide (TMAO). The role of this element in the development of cardiovascular and metabolic diseases has been confirmed by studies. The way the body breaks down proteins from microbes also makes chemicals like branched-chain fatty acids, phenols, ammonia and others that can affect how the body works (Nie et al., 2023). When the mix of microbes in the

Table 1: Gut microbiota- derived metabolites, dietary interactions, insulin resistance, metabolic dysfunction, and cardiovascular health: clinical relevance and therapeutic impications.

Topic	*Microbiota-Derived Metabolites*	*Major Function/ Effects*	*Clinical Relevance*	*Reference*
Short-chain fatty acids	Acetate, propionate, butyrate	Support gut-barrier integrity, regulate immune responses, appetite, glucose and lipid metabolism	Associated with obesity insulin resistance and type 2 diabetes	(Tiwari et al., 2023)
Dietary fibre fermentation	Mainly SCFAs	Gut bacteria ferment dietary fibre and produce beneficial metabolites	High-fibre diets may support metabolic health	(Liu et al., 2023)
Tryptophan metabolism	Indole and indole-derived compounds	Influences intestinal immunity and epithelial-barrier function through pathways such as aryl hydrocarbon receptor (AhR)	Alterations may contribute to intestinal inflammation and metabolic dysfunction	(Collins et al., 2023)
Bile acid metabolism	Secondary bile acid	Regulates glucose metabolism, lipid handling and energy expenditure through receptors such as FXR and TGR5	Changes are associated with obesity, diabetes and metabolic disorder	(Larabi et al., 2023)
Trimethylamine (TIMA) production	Trimethylamine	Produced by gut microbes from dietary choline, phosphatidylcholine and carnitine	Provides a pathway linking diet, gut microbiota and cardiovascular/ metabolic risk	(Shaw et al., 2023)
TMAO formation	Trimethylamine N-oxide (TMAO)	Formed mainly in the liver from TMA and involved in host metabolic processes	Elevated protein fermentation may contribute to an unfavourable metabolic environment	(Salminen et al., 2023)

Table (*Continued*)

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Topic	*Microbiota-Derived Metabolites*	*Major Function/ Effects*	*Clinical Relevance*	*Reference*
Protein fermentation	Branched-chain fatty acid, phenols, ammonia and other compounds	Microbial breakdown of proteins produces metabolites that can influence intestinal and systemic physiology	Excessive protein fermentation may contribute to an unfavourable metabolic environment	(Ullah et al., 2023)
Gut microbial dysbiosis	Reduced beneficial and/ or increased potentially harmful metabolites	Can impair gut-barrier function and promote inflammatory responses	Associated with obesity metabolic syndrome and type 2 diabetes	(Mann et al., 2024)
Inflammation and insulin function	SCFAs, bile-acid metabolites, indole compounds and others	Microbial metabolites can influence immune signalling and insulin sensitivity	Important in insulin resistance, fatty liver disease and metabolic syndrome	(Ross et al., 2024)
Diet-microbiota interaction	Multiple microbial metabolites	Fibre – rich, plant-based and diverse diets can modify microbial activity and metabolite production	Provides opportunities for dietary prevention and microbiota – based therapies	(Prasain et al., 2024)

gut or how they act becomes unbalanced there can be harmful chemicals and fewer helpful ones. This may disrupt intestinal barrier function, trigger an inflammatory response, lead to dysregulation of insulin signaling and alterations in lipid metabolism. Such pathophysiological mechanisms have been implicated in obesity, metabolic syndrome, type 2 diabetes, cardiovascular disease and non-alcoholic fatty liver disease associated with metabolic alterations. Eating fiber, plant-based foods and a wide range of foods can affect how the body makes these chemicals showing how important food is, in shaping the bodys chemical environment. Support future ways to use diet and microbes to prevent and manage health issues (Swer et al., 2023).

METABOLITES, GUT–BRAIN SIGNALING AND NEUROINFLAMMATION

Metabolites derived from the interaction of diet gut microbiota and host metabolism play an essential role in the function of the gut-brain axis. This bidirectional communication between the central nervous system and enteric nervous system involves neural, immune, endocrine, and metabolic pathways. In particular, the contribution of microbial metabolites derived from dietary fibers fermentation by gut bacteria was highlighted. Short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate are produced as fermentation by-products and modulate cellular signaling, maintain intestinal homeostasis, and regulate

neuroinflammatory processes. Among them, butyrate has a pronounced anti-inflammatory effect and protects the integrity of the blood–brain barrier (Deehan et al., 2024). Furthermore, gut microbiota produces proteinogenic amino acids and tryptophan metabolites from dietary proteins and amino acids. They also affect the gut–brain axis through their action on various receptors and the regulation of immune cell activity. In addition, bacteria perform transformation of primary bile acids into secondary ones by enzymatic activity. This transformation is connected with the regulation of metabolic and inflammatory processes via activation of nuclear hormone receptors, FXR, and TGR5 (He et al., 2024). Dysregulation of the gut–brain axis often leads to neuroinflammation, associated with the activation of microglial cells and the release of pro-inflammatory cytokines. Moreover, altered gut microbiota and increased gut permeability contribute to neuroinflammation by facilitating the translocation of bacterial endotoxins and pro-inflammatory mediators across the blood–brain barrier. Dysfunctional microbiota, altered by a high-calorie diet, can increase neuroinflammation, disrupt the integrity of the blood–brain barrier, and promote neurodegeneration. The composition and functionality of the gut microbiota, as well as its impact on the gut–brain axis, depend to a large extent on the diet. The interactions between diet and microbiota affect many downstream processes, from inflammatory responses to neuroendocrine regulation. The connection between the gut and the brain occurs through a variety of pathways, including the vagus nerve, endocrine routes, and direct humoral interactions. Thus, the gut–brain axis is a complex system in which signals from the gut can reach the central nervous system without involving neural connections (Loh et al. ,2024). At the same time, diet-induced disruptions of the gut microbiota and intestinal barrier function are often associated with deficits in the neuroendocrine-immune response. Overall, the gut–brain axis plays an important role in the regulation of physiological and pathological processes in the body. The ability of the microbiota to influence the brain and its functions is increasingly the subject of scientific research. This knowledge can be used to develop therapeutic and dietary strategies to regulate the gut–brain axis and maintain health (Aburto et al., 2024).

THERAPEUTIC POTENTIAL OF DIETARY METABOLITE MODULATION

Dietary metabolite modulation is an idea in food science that looks at how to change the way food parts make, change and work inside the body and how they talk to the bacteria in the gut. Because dietary metabolites can change inflammation, reactions, how the body handles sugar, how fats move, how the gut wall works and how the gut talks to the brain changing these ways can give us ways to stop or help long term sickness that involves metabolism and inflammation. Dietary fibre is an important target because when gut bacteria eat it they make short chain fatty acids (SCFAs) like acetate, propionate and butyrate (Arifuzzaman et al., 2024). Adding fibre foods such as whole grains, beans, vegetables, fruits and other plant foods can help good bacteria make food and help the body and gut stay healthy. Prebiotics and probiotics can also be used to change which bacteria are there and what foods they make. Their effects can be different for each person. Foods high in polyphenols give another way to try because gut bacteria turn dietary polyphenols into smaller useful foods that can

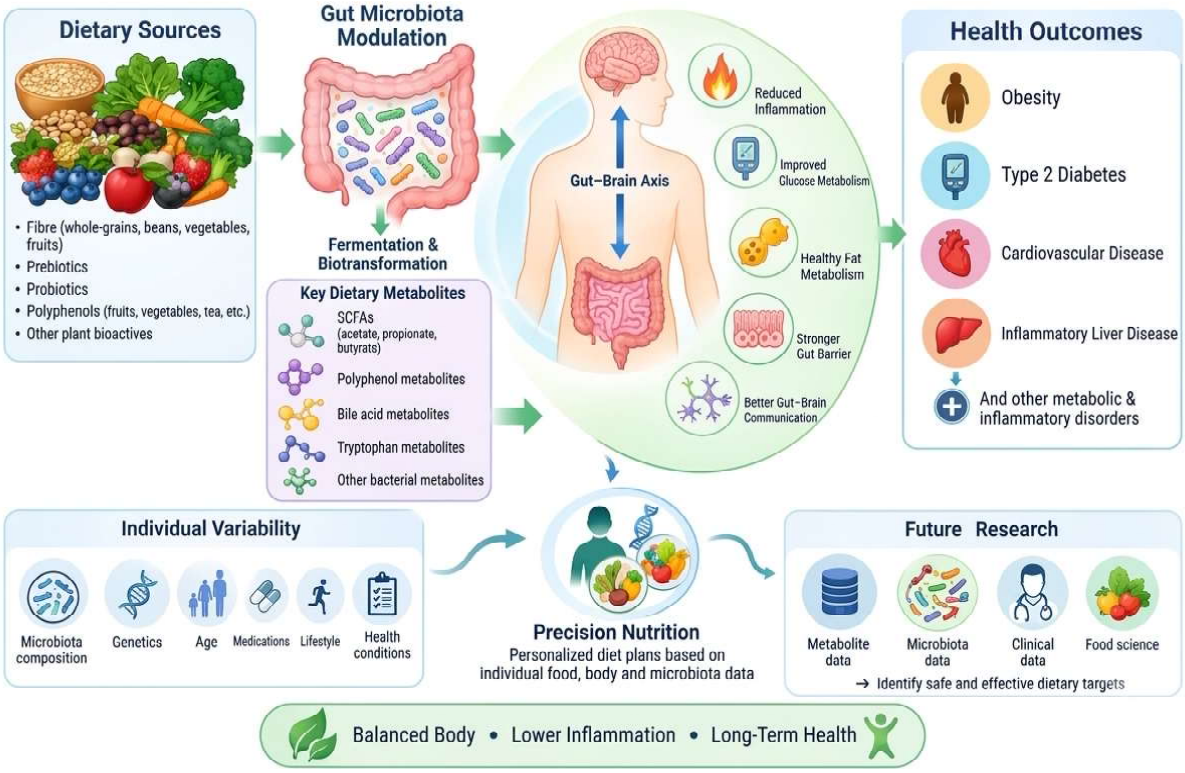

Fig 1. Dieatary modulation of gut microbiota and microbial metabolites influence gut-brain communication, inflammation, glucose and lipid metabolism, and disease risk, supporting precision nutrition strategies for long-term metabolic and neurogical health.

affect the body's defence and inflammation. Dietary change can also change how bile acids, tryptophan foods and other bacterial ways talk to the body (Fig. 1). These alterations may affect the utilization of sugars and fats in the body by modulating the receptors and signaling cascades involved in the regulation of homeostasis. The modulation of dietary metabolites has been considered for obesity-associated type 2 diabetes, cardiovascular and hepatic diseases that arise due to inflammation-associated disorders(Kim et al., 2024). Also bacterial foods can change the gut–brain link so dietary change could be a research area for brain health and thinking. The good effects of eating changes depend on each person's bacteria, genes, age, medicines, habits and health problems. So one diet plan may not give the metabolic results for everyone. Precision nutrition tries to use each person's food, body and bacteria data to make personal plans. Future studies that mix metabolite data, bacteria data, doctor data and food science may find which foods and ways can be safely targeted. Overall dietary metabolite modulation is a research field, for making food plans that keep the body balanced lower inflammation and keep people healthy for a long time (Hays et al., 2024).

CLINICAL EVIDENCE AND TRANSLATIONAL CHALLENGES

The increasing amount of clinical research has shown the gut microbiota's role in dietary

metabolites, inflammation, and the human metabolic and neurological functions. There are various metabolites which are produced by the microbiota, including short-chain fatty acids, bile acids, tryptophan metabolites, trimethylamine-N-oxide. These metabolites are found to be related to the improved understanding of inflammatory pathways, glucose and lipid metabolism, intestinal integrity, and the brain function. There is a documented association between decreased alpha diversity and obesity, type 2 diabetes, metabolic syndrome, and cardiovascular disease (He et al., 2024). There is also a link with various neurological diseases in the context of dysbiosis: Parkinson's, Alzheimer's dementia, depression, multiple sclerosis. Short-chain fatty acids (acetate, propionate, butyrate) modulate the immune system – for example, by maintaining the integrity of the intestinal barrier and reducing inflammation; tryptophan metabolites are involved in the communication between the gut and the brain. Trials assessing the role of probiotics, prebiotics, synbiotics, dietary interventions, and microbiota transplantation demonstrated inconsistent results; yet, they can be beneficial for certain individuals. The primary limitation to microbiota-based therapy is related to the fact that the same microbiome cannot be beneficial for all patients due to the significant interindividual variability of microbiota in health and disease (Lin et al., 2024). As a result, it is hard to determine what is a healthy microbiome, let alone find an applicable standard across the populations. Moreover, causality in microbiome-related associations has not been established. There is an urgent need for standardized, well-powered, and properly controlled studies that would evaluate the link between microbiome-related variables and clinical outcomes, as well as determine the optimal interventions and their mechanisms. It is also unclear whether they are merely indicators of disease or whether they directly undermine the functioning of other organs and systems. Multicenter randomized clinical trials are required to evaluate the role of microbiota and dietary interventions in health outcomes and establish the microbiome-based treatment's safety, effectiveness, and optimal duration and dosage. It is essential to design experiments that would utilize metabolomics and clinical genomics, along with dietary and microbiota information, to classify responders. Personalized diet recommendations and microbiota based treatment could enable people to optimize their benefits from dietary interventions (Trisal et al., 2025). However, there are several challenges to develop this kind of treatment at large scale. Thus, although there is an increasing amount of clinical evidence of the gut microbiome's role in dietary metabolites, inflammation, and the brain, more high-quality studies are needed to make microbiome-based diagnostics and treatment routinely available in the clinics (Nigam et al., 2024).

PUBLIC HEALTH PERSPECTIVES AND FUTURE DIRECTIONS

The impact of the gut microbiota, its metabolites, and inflammation on the human body is a critical topic of public health importance. There is increasing evidence that dysbiosis driven by unhealthy dietary patterns, physical inactivity, antibiotic use, and other environmental insults may drive persistent low-grade inflammation that contributes to cardiometabolic dysfunction, obesity, and neurodegenerative diseases (Zhang et al., 2024). Consequently, the role of the gut microbiota in human health and disease emergence is gaining significant scientific attention and is

poised to become a critical component of public health. The public health community needs to invest in expanding and improving nutritional and microbiota health literacy to help populations make diet and lifestyle choices that support a healthy gut microbiota and prevent chronic disease. Emphasis should be placed on advocating for dietary fiber, whole grains, fruits, vegetables, legumes, and other nutrient-dense and microbiota-friendly foods while limiting ultra-processed foods, sugar, saturated fats, and unnecessary antibiotics. Educational programs related to nutrition and microbiota, targeted at children and adolescents, are of particular importance since they can help develop their decision-making and judgment abilities related to food choices (Mederle et al., 2024). The future of microbiome medicine will be dominated by the concept of personalized nutrition, which will take into account the unique characteristics of the microbiome-host ecosystem, including genetic and phenotypic traits. Innovative preclinical, translational, and clinical studies are needed to harness the power of metagenomics, metabolomics, artificial intelligence, and bioinformatics to decode the mechanisms by which specific bacteria and their metabolites contribute to the onset and progression of diseases. There is a need to develop microbiota-based pharmaceuticals and functional foods, including probiotics, prebiotics, synbiotics, postbiotics, and microbiota-derived metabolites, that have the potential to yield transformative therapeutic interventions. Such therapies need extensive, prolonged, and various clinical trials to provide credible evidence of their efficiency and safety before being approved for public usage. Moreover, the trials would need to include individuals of various socio-cultural and geographical origins and those with different dietary habits since there is a significant variation in the microbiome's structure and function from person to person (Dominguez-Lopez et al., 2025). Finally, future studies should focus on the gut-brain axis and the role of gut bacteria and metabolites in brain health, behavior, cognition, and affective and neurodegenerative disorders. Addressing the research agenda on the gut microbiota presents an unprecedented opportunity to re-engineer public health and transform patient care. By integrating nutritional, lifestyle, and clinical interventions, public health authorities and policymakers may reduce the global disease burden and improve human health (Ohara et al., 2025).

CONCLUSIONS

Gut microbiota, diet metabolites, and inflammation are deeply interconnected processes in the human body that tightly regulate various metabolic and neurobehavioral functions. The gut microbiome is an essential endocrine and immunological organ that produces numerous metabolites and molecules with regulatory effects, such as short-chain fatty acids, bile acid metabolites, and tryptophan derivatives, among others (Almahal et al., 2025). Dysbiosis, i.e., the imbalance of the gut microbiota, has been implicated in chronic low-grade inflammation, obesity, type 2 diabetes, cardiometabolic diseases, and neurological and psychiatric disorders. Despite the evidence of the beneficial role of the gut microbiota and its metabolites, there are still many questions to be answered. It is difficult to study the microbiome of the gut and to standardize prebiotic, synbiotic, and postbiotic treatments because of the complexity of the system and the number of variables such as nutrition, lifestyle, genetic predispositions, polypharmacy, age, environment, and others

(Srivastava et al., 2025). Therefore, there is a need for more intervention studies in humans that employ standardized measures of gut microbiota and diet (Diacova at el., 2025). Although the microbiota is highly individual and diverse, these studies are critical for establishing the causal relationships and implementing the personalized treatment in the future. A better understanding of the role of various microbiota-derived metabolites in the pathophysiology of different disorders will contribute to the development of novel therapeutic approaches and the improvement of current preventative and interventionist strategies (Tanes at el., 2025). To conclude, the gut microbiota is essential for humans; hence, it is critical to investigate its functions in detail through clinical, dietary, and microbiota studies conducted by interdisciplinary and multinational coalitions to ensure proper functionality for human metabolic and neurobehavioral health (Dalal at el., 2025).

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