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The Relationship Between Gut Microbes and Nutrient Absorption and Its Application Status

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Abstract: Gut microbiome research is one of the most groundbreaking directions in the life sciences of the 21st century, and its background involves the deep integration of medicine, microbiology, immunology and systems biology. Gut microbiome research has crossed the "correlation discovery" stage and is driving the underlying logic of treatment strategy through the integration of interdisciplinary technologies. In the next decade, microbiome medicine will form a "diagnosis-intervention-monitoring" closed loop, the core of which is dynamic precision medicine targeting the microbiome. The research of personalized nutrition and precision microbiome medicine needs to be further explored. This paper mainly analyzed the relationship between intestinal microbes and host nutrition metabolism, especially the effects of different nutrient intake on intestinal microbial composition, and how intestinal microbes affect host health through metabolic processes. It is clear how to use intestinal microbes to intervene in individual health and how to use different nutrient ratios to improve individual intestinal microbes. It provides a reference for future studies on the relationship between intestinal microbes and host nutrition metabolism and the relationship between intestinal microbial diversity and health. The study of the influence of different individual genotypes on intestinal microbiota and the detailed mechanism of the interaction between intestinal microbiota and host metabolic pathway have not been solved. Future research can focus on more human-based clinical research to apply AI to precision nutrition.

Keywords: Gut microbes, macronutrient metabolism, gut microbes metabolism.

1. Introduction

The gut microbes is a complex community of microorganisms inside the host intestinal tract. Gut microbes utilize undigested nutrients to synthesize beneficial compounds through intricate metabolic processes. Gut microbes change the body's absorption of nutrients, and different nutrients lead to different gut microbes compositions. The number of intestinal microbes is huge and the species are rich, and different microbes species have different metabolic mechanisms. Most of the gut microbes use dietary fiber and other nutrients, through a series of complex metabolism, for self-growth and have effects on the human body. However, under current dietary patterns, the intake of this group of substances beneficial to gut microbes is decreasing. The intake of fat, protein and refined carbohydrates is increasing. This has also led to an increasing incidence of intestinal diseases. Studies have shown that gut microbes ferment dietary fiber to produce some short-chain fatty acids (SCFAs) [1], which are used to meet microbial growth and development, maintain intestinal health and be utilized by the host. These SCFAs improve the intestinal environment and make some minerals better

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absorbed and utilized. At the same time, microbes produces some vitamins that are good for maintaining host health. Gut microbes facilitate the transformation of primary bile acids (BAs) into secondary bile acids, which possess a variety of functions and affect the absorption and digestion of lipids and glucose.

However, high fat intake leads to excessive bile acid production that disrupts the diversity of gut microbes, while contributing to obesity, type II diabetes and other symptoms. A decrease in beneficial bacteria and an increase in pro-inflammatory microbes work together on the immune system, causing some inflammation to occur. A decrease in secondary metabolites SCFAs of beneficial bacteria leads to leaky gut. Long-term high protein diet can lead to the decrease of Bacteroidetes [2]. Hydrogen sulfide, amines and other substances accumulate in large quantities, leading to cell poisoning and increasing the risk of inflammatory bowel cancer. Studies on the effects of different nutrient intake on gut microbes can promote the maintenance of a healthy gut, thereby enhancing individual nutrient absorption and immune function. Meanwhile, studies on the brain-gut axis also prove that gut microbes are related to host neurotransmitter secretion, and brain and gut can interact with each other to influence host mood. This paper will summarize the effects of intestinal microbes on the metabolism of macronutrients, the effects of different nutrient intake on intestinal microbes and how to promote the growth of beneficial bacteria to maintain body health. This review will summarize the role of the gut microbes and provide some suggestions on how to increase the diversity of the gut microbes to provide a healthier body for the host.

2. Relationship between gut microbes and macronutrient metabolism

2.1. Carbohydrate

The contribution of gut microbes in macronutrient absorption is to make the excess nutrients that the body cannot absorb and use for its own growth, and thus feed back to the host. Gut microbes mainly use nutrients that the body has not yet absorbed in the small intestine. The same is true for carbohydrates, the main source of carbon for gut microbes is complex polysaccharides that the body cannot absorb and use. Such molecules classified as soluble and insoluble based on their solubility. Soluble dietary fibers mainly include pectin, β-glucan, inulin and guar gum, etc. Insoluble dietary fibers mainly include cellulose, hemicellulose and lignin [3]. Complex polysaccharides have a wide variety of glucoside bonds, many of which the human body does not have the enzymes to hydrolyze, so the body cannot convert them into its own energy source. But some gut microbes produce enzymes that hydrolyze these glycoside bonds, so they can turn these macromolecules into nutrients for themselves. The diversity in glycosidic bonds among various types of dietary fibers allows different intestinal microorganisms to metabolize them accordingly. Analogous to how arabinoxylan is broken down into ethanol by Saccharomyces, and into acetate, propionate, and butyrate by Streptococcus and Bifidobacteria, β-glucan is metabolized into various SCFAs through the action of Saccharomyces, maitake, mushrooms, Lactobacilli, Enterococcus, and Bifidobacteria. Additionally, β-fructans are fermented into lactic acid and carbon dioxide by Kluyveromyces, marxianus, S. cerevisiae, and T. delbrueckii, while being converted into butyrate, a specific type of SCFA, by Bifidobacteria, Lactobacilli, Streptococcus, and Flavobacterium [4]. The breakdown of these dietary fibers results in the production of SCFAs, which are considered the most significant beneficial components among the metabolic products of gut microbiota. These SCFAs are typically thought to supply energy to colonic mucosal cells, support the integrity of the intestinal mucosal barrier, and offer therapeutic benefits for inflammatory bowel disease (IBD). Specifically, propionate has been shown to suppress cholesterol synthesis in the liver, whereas acetate and butyrate contribute to enhancing insulin sensitivity and regulating blood sugar levels. Additionally, butyrate plays a role in inducing apoptosis in cancer cells, thereby decreasing the risk of rectal cancer [5].

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The gut microbes-bile acid axis enables the expression of 7α-dehydroxylase via specific strains within the Firmicutes phylum, such as Clostridium scindens and Clostridium hylemonae. These strains transform primary bile acids (cholic acid [CA] and chenodeoxycholic acid [CDCA]) into secondary bile acids (deoxycholic acid [DCA] and lithocholic acid [LCA]). Notably, DCA acts as a strong agonist for the G protein-coupled bile acid receptor Gpbar1 (TGR5). This receptor stimulates the secretion of glucagon-like peptide-1 (GLP-1) by intestinal L cells, thereby enhancing insulin sensitivity and improving glucose metabolism through the TGR5-cAMP-PKA pathway.

2.2. Protein

Prior to entering the intestine, proteins are initially processed by host enzymes in the stomach and small intestine. In the stomach, pepsin catalyzes the breakdown of proteins into smaller polypeptide chains. These fragments subsequently move to the small intestine, where they are further hydrolyzed into amino acids and small peptides by enzymes like trypsin and chymotrypsin. This phase represents the primary location for protein digestion, during which most amino acids are absorbed into the bloodstream to fulfill the body's metabolic requirements.

Nevertheless, not all proteins are fully degraded and absorbed by host enzymes. Certain undigested protein remnants, such as specific anti-nutritional factors (e.g., plant protease inhibitors) or structurally intricate proteins (e.g., collagen), bypass digestion and reach the colon. Moreover, a diet high in protein may result in an overload of protein intake that exceeds the absorptive capacity of the small intestine, leading these excess proteins to enter the colon as substrates for intestinal microbes.

Various types of amino acids, including Branched chain amino acids (BCAAs), aromatic amino acids (AAA), sulfur-containing amino acids and others, can be metabolized by distinct microbial populations, producing a range of metabolites. BCAAs be broken down by microorganisms into (branched-chain fatty acids) BCFAs outward transport to induce insulin resistance. The primary bacteria involved in the metabolism of BCAAs are Clostridium and Bacteroides, with the main metabolic outcomes being BCFAs. These BCFAs serve as an energy source for colon cells; however, excessive levels of BCFAs have been linked to insulin resistance and obesity, potentially promoting fat accumulation through the activation of the mTORC1 signaling pathway [6].

For AAA (tryptophan, phenylalanine, and tyrosine), Lactobacillus and Bifidobacterium can transform tryptophan into indole derivatives. Indole compounds play a crucial role by activating the aryl hydrocarbon receptor (AhR), which enhances intestinal barrier integrity and exerts anti-inflammatory effects [7]. Simultaneously, the gut microbes has a close association with the in vivo kynurenine pathway involved in tryptophan metabolism. During this process, indoleamine 2,3-dioxygenase (IDO1) acts as a critical enzyme and plays an essential role. Moreover, inflammation triggered by the gut microbes might possibly influence the activity of IDO1 [8]. Phenylalanine and tyrosine, are primarily metabolized by Enterococcus and Escherichia coli. This metabolic process leads to the production of phenol, p-cresol, and 4-ethylphenol. At low concentrations, p-cresol has been shown to suppress the growth of harmful bacteria. Conversely, elevated levels of p-cresol may lead to damage in intestinal epithelial cells and enhance the risk of increased intestinal permeability.

Sulfur-containing amino acids, such as methionine and cysteine, are metabolized by bacteria like Desulfovibrio and Clostridium, leading to the production of hydrogen sulfide (H_2S), mercaptans, and taurine. Elevated levels of H_2S can suppress cytochrome C oxidase activity, disrupt mitochondrial function, and trigger inflammation in the intestinal mucosa.

2.3. Fat

The interaction between gut microbes and bile acids represents a crucial area of research in the field of gut microbes studies. When Bacteroides becomes predominant in the gut microbes, the level of

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secondary bile acid DCA rises. DCA acts as a mild activator of the farnesoid X receptor (FXR), a nuclear receptor for bile acids that is abundantly expressed in both the liver and intestine. Upon activation, FXR promotes the expression of small heterodimer partner (SHP). As a transcriptional suppressor, SHP reduces the activity of sterol regulatory element-binding protein 1c (SREBP1c), which serves as a key regulator involved in the synthesis of fatty acids and triglycerides. Consequently, this pathway enables gut microbes to suppress lipid production.

Peroxisome Proliferator-Activated Receptor γ (PPARγ) belongs to the nuclear receptor superfamily and plays a key role in controlling adipogenesis, lipid accumulation, and insulin responsiveness. There is an established link between PPARγ and the gut microbes. For instance, butyric acid, which is generated through microbial metabolism in the gut, can serve as a ligand for PPARγ, thereby stimulating adipocyte differentiation and lipid storage. On the other hand, SCFAs enhance adiponectin expression via PPARγ, improving insulin sensitivity. Simultaneously, they suppress the expression of fatty acid synthase (FAS) in the liver. These two outcomes appear to be somewhat opposing in nature.

3. Effects of different nutrients on gut microbes

3.1. Carbohydrate

The effects of carbohydrates on gut microbes are complex and varied. It was mainly reflected in the two aspects that non-digestible carbohydrates (dietary fiber) increased intestinal microbes diversity and digestible carbohydrates decreased intestinal microbes diversity.

Dietary fiber as a prebiotic, it is fermented by bifidobacteria, prevotella, etc., which promotes the formation of SCFAs, maintains the acidic intestinal environment, and inhibits the proliferation of pathogens. Resistant starch (RS2) can enrich butyricogenic bacteria (such as Roseburia) and enhance intestinal barrier function. The study showed that after 4 weeks of RS2 intervention, firmicutes/Bacteroidetes ratio in prediabetic patients was optimized by 1.5 times ($p<0.05$), and insulin sensitivity was increased by 12% [9].

Refined sugars (such as sucrose and high fructose corn syrup) promote the proliferation of conditioned pathogens such as Proteobacteria and induce intestinal inflammation. Studies have shown that in healthy people, 2 weeks of eating a diet containing refined sugar (20% of total calories) resulted in a 40% reduction in the abundance of butyric-producing bacteria such as Faecalibacterium [10]. A high Glycemic Index (GI) carbohydrate diet significantly reduced the genetic diversity of the gut flora. Studies have shown that a long-term high GI diet (> 6 months) reduces gene expression in SCFA producing bacteria such as Roseburia by 25% [11].

3.2. Protein

Protein serves as a crucial nitrogen source for both humans and gut microorganisms, significantly influencing their development. A deficiency in protein consumption may result in energy shortages for certain gut microorganisms, triggering cell death and altering microbial diversity. Conversely, an overabundance of protein can also disturb the balance of gut microorganisms. In studies conducted on mice, when protein levels exceed 50%, there is a notable decrease in microbial diversity along with an increase in the presence of various colonic pathogenic bacteria [12].

In recent years, there has been growing appreciation for plant-based proteins. Unlike animal-derived proteins, plant-based alternatives tend to be more favorably viewed by individuals because of their environmental benefits and positive impacts on gut microbiota. Studies indicate that excessive consumption of red meat and processed meat products significantly raises the likelihood of developing colon cancer. Conversely, adhering to a balanced and regulated dietary regimen can help decrease the risk of colon cancer [13]. Plant-based food proteins typically lead to a greater amount of

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nitrogen reaching the large intestine. Unlike animal-derived proteins, these compounds contribute differently to the regulation of gut microbes and the production of gut microbial metabolites (GMMs) [14]. Proteins sourced from animals, including casein and whey, are inclined to enhance the growth of proteolytic Bacteroides species, leading to an increase in potentially detrimental metabolites, such as trimethylamine N-oxide. This is linked to an elevated risk of cardiovascular diseases. On the other hand, proteins derived from plants, such as those from legumes, stimulate glycolytic fermentation processes. This encourages the expansion of advantageous bacteria, including Bifidobacterium and Lactobacillus, and results in the production of beneficial SCFAs like butyrate.

3.3. Fat

Fat is the one thing that people often avoid in today's society. As one of the three major macronutrients of the human body, the intake of fat is necessary. But high fat intake is a risk factor for obesity, insulin resistance, and non-alcoholic fatty liver disease (NAFLD). The harm is not limited to the human body; a high-fat diet can also reduce the diversity of gut microbes. In the above discussion on the role of gut microbes on fat intake, the primary bile acid-secondary bile acid pathway is an important part of fat digestion. About 95% of bile acids are reabsorbed in the ileum via apical sodium-dependent bile acid transporters (ASBTs) and returned to the liver via the portal vein for recycling, with the remaining 5% excreted in the stool. On the other hand, high fat intake can cause a large amount of secondary bile acids to accumulate in the gut, reducing the abundance of intestinal flora. At the same time, a large amount of bile acid accumulation is also the cause of intestinal leakage. Studies have shown that DCA can destroy intestinal epithelial tight junction proteins (such as Occludin) by activating the NLRP3 inflamome, thereby increasing intestinal permeability [15].

4. Applications

4.1. Probiotics, prebiotics and biostime

Prebiotics and probiotics are an important branch when it comes to the use of gut microbes in actual therapy. The targeted therapy of probiotics and probiotics is a hot topic in this field. In the past, antibiotics were usually used as the first choice to treat infectious diseases. They were lethal, but they often destroyed the diversity of intestinal flora, causing diarrhea, inflammation and other symptoms. At present, there are still some challenges in the application of probiotics, prebiotics and Biostime, which will produce specific differences due to different individual genes. Omics technology is a new challenge for the application of probiotics, prebiotics and Biostime to develop personalized nutrition programs and provide precise nutrition supplements to the human body. Omics technology mainly includes three aspects, namely genomics, proteomics and metabolomics.

4.2. Disease control and management

Probiotics plays a therapeutic role in many diseases. For non-alcoholic fatty liver disease (NAFLD), related studies showed that Lactobacillus + Bifidobacterium + Streptococcus combination effectively reduces liver enzymes (AST, ALT, GGT) [16]. At the same time, probiotics has been used in type 2 diabetes (T2DM), studies showed that probiotics have shown potential positive effects in T2DM management, particularly in improving blood glucose control and lipid parameters [17]. Intestinal microbes also play a certain role in mental diseases. With more and more in-depth studies on the brain-gut axis, people have gradually found that intestinal microbes have an impact on the secretion of many nerve signals such as 5-hydroxytryptamine (5-HT) and gamma-aminobutyric acid (GABA), and the use of intestinal microbes can have a certain positive effect on mental diseases.

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5. Conclusion

This paper explores the relationship between gut microbiota and host nutrient metabolism, focusing on the effects of different nutrient intake on gut microbiota composition and how gut microbiota affect host health through metabolic processes. This paper provides an important theoretical basis for understanding the role of gut microbiota in human health, and provides a possible way to improve gut health and prevent diseases through diet adjustment and microbial intervention. There are different treatment plans for different people to adjust their physical fitness. In most conditions, increasing the intake of dietary fiber in daily life can greatly promote the diversity of intestinal flora. Pay attention to personal diet adjustment and rationalize the intake ratio of protein, fat and carbohydrate. However, at present, many studies on gut microbes are based on animal experiments, and there are still some limitations in their real application to human beings. In addition, when considering the application of probiotics and Biostime in the treatment of related diseases, it is necessary to take into account the differences caused by different host genotypes. This kind of data is huge, and the trend of applying AI to personalized nutrition programs has become inevitable, and the research on personalized nutrition will be more in-depth in the future. It is hoped that subsequent precision microbiome medicine will enable individualized mental illness management.

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