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The Role of Gut Microbiota in the Pathogenesis and Treatment of Obesity: A Contemporary Review

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ABSTRACT

Background. Obesity is a chronic disease and a global health problem contributing to increased mortality. The gut microbiota supports energy homeostasis and modulates inflammation and appetite, and may influence obesity development.

Aim. To summarize evidence on the gut microbiota in obesity pathogenesis and microbiome-modulating treatments (diet, physical activity, pre-/pro-/synbiotics, postbiotics, selected pharmacotherapies).

Materials and methods. Major biomedical databases were searched for experimental and clinical studies on microbiota composition/function in obesity, dysbiosis-related mechanisms, and effects of interventions on microbiota and metabolic outcomes.

Results. Obesity is associated with heterogeneous but recurring alterations in microbial diversity, composition and function, including SCFA- and bile acid–related pathways and markers of impaired intestinal barrier function. Mediterranean/plant-based patterns, higher fiber intake and selected biotics most consistently improve these profiles; physical activity and some drugs show smaller, variable effects.

Conclusion. Dysbiosis may contribute to obesity via metabolic and inflammatory mechanisms, but findings are context-dependent, limiting the value of simple markers. Translation to practice requires standardized methods, robust biomarkers and personalized interventions integrated with sustained healthy diet and physical activity.

Keywords: obesity, gut microbiota, dysbiosis, diet, physical activity

1. Introduction

Obesity is a chronic metabolic disease that develops as a result of a prolonged positive energy balance, leading to excessive accumulation of adipose tissue in the body [1]. It is a major risk factor for other chronic diseases, such as hypertension, type 2 diabetes, cardiovascular diseases, colorectal cancer, and other malignancies[1]. It represents an increasing epidemiological

challenge worldwide, contributing to higher global morbidity and mortality. According to the WHO, in 2022 more than 1 billion people worldwide were living with obesity[2]. The etiology of obesity is complex and multifactorial, involving the interaction of biological, environmental, behavioral, and social factors[3]. Genetic factors account for as much as 40–70% of an individual's predisposition to obesity, influencing appetite regulation, metabolism, thermogenesis, and food preferences[4-6]. Both single-gene mutations (e.g., *MC4R*, leptin) and polygenic variants predisposing to excessive body weight are of importance[4-6]. Epigenetics also plays an important role, encompassing modifications of gene expression under the influence of environmental factors such as diets rich in simple sugars and saturated fats, chronic stress, and sleep disturbances[3]. Although obesity results primarily from a chronic energy surplus, the processes leading to this condition are far more complex than diet and physical activity alone[3].

In recent years, increasing importance has been attributed to the gut microbiota in the regulation of metabolic homeostasis[7-9]. The human gastrointestinal tract is inhabited by a complex community of microorganisms, comprising primarily bacteria but also archaea, viruses, and fungi. It is estimated that the gut microbiome contains trillions of cells[7]. Its composition is influenced by factors such as diet, lifestyle, environment, and medication use, and disturbances of the microbiota may affect energy metabolism, fat storage, inflammation, and appetite regulation[7-10]. Numerous studies have demonstrated that the composition and activity of the gut microbiota differ significantly between individuals with obesity and those with normal body weight, suggesting a role of dysbiosis in the initiation and maintenance of the disease state[7-10]. This has opened new therapeutic perspectives aimed at modulating the composition of the microbiome, such as dietary interventions, probiotics, prebiotics, and fecal microbiota transplantation, in the treatment of obesity and its accompanying metabolic disorders[11-13].

Based on a structured literature search and thematic analysis, we evaluated the current state of knowledge regarding the role of the gut microbiota in the pathogenesis of obesity, the key biological mechanisms linking dysbiosis with metabolic disturbances, and the effectiveness of interventions targeting the microbiome, such as probiotics, prebiotics, synbiotics, dietary modifications, and fecal microbiota transplantation[7-13].

2. Gut Microbiota and Energy Homeostasis

2.1. Composition of the healthy human gut microbiota

The gut microbiota is a vast ecosystem located in the gastrointestinal tract, consisting of symbiotic and commensal microorganisms. Although there is substantial inter-individual

variability in the composition of the gut microbiome in healthy subjects, its basic structural principles remain relatively constant [14]. The majority of gut bacteria belong to five phyla: Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria and Verrucomicrobia [15], with Bacteroidetes and Firmicutes together accounting for more than 90% of the gut microbiota [14]. Gram-negative Bacteroidetes include species such as *Bacteroides*, *Prevotella*, *Parabacteroides* and *Alistipes*, whereas Gram-positive Firmicutes include important butyrate-producing species such as *Faecalibacterium prausnitzii*, *Eubacterium rectale* and *Eubacterium hallii* [16]. Revised quantitative estimates suggest that the total number of bacterial cells in the human body is of the same order of magnitude as the number of human cells (approximately 1:1), with most of these microorganisms located in the large intestine [17].

The abundance of bacteria is lowest in the proximal segments of the gastrointestinal tract: the stomach contains approximately 10^1 microbial cells per gram of content, and the number gradually increases along the small intestine to reach about 10^{12} microbial cells per gram of content in the colon [18]. Overall, more than 70% of all microorganisms in the human body reside in the large intestine [19].

Besides bacteria, the gut microbiome also comprises other microbial communities, including fungi (the mycobiome), viruses (particularly bacteriophages), Archaea and protozoa, which may play important roles in health and disease [20-22].

2.2. Functions of gut microbiota

The gut microbiota is a major contributor to human health, although its full functional repertoire is still not completely understood. Key functions of the gut microbiota include modulation of the immune response, in part through enhancement of epithelial barrier function and reduction of inflammation via the production of short-chain fatty acids (SCFAs) [23].

Another essential role is the ability to extract energy from otherwise indigestible dietary polysaccharides, thereby increasing the host's caloric yield from the diet [24,25]. The microbiota also protects against pathogenic microbes by competing for nutrients and attachment sites, producing antimicrobial compounds and shaping the mucosal immune system [26].

In addition, gut microbes influence appetite regulation, blood pressure control and glucose and lipid metabolism through the production of metabolites (such as SCFAs), modulation of enteroendocrine signalling and interaction with host metabolic pathways [27,28].

2.3. Differences in obesity

Numerous studies have indicated a correlation between gut microbiota composition and the development of obesity and related metabolic disorders [29,30]. Key differences observed in

individuals with obesity include reduced bacterial diversity and stability, as well as an increased proportion of Gram-negative bacteria [31].

Some studies suggest that non-bacterial components of the gut microbiome may also play an important role in obesity pathogenesis. In one study, an increased abundance of H_2-utilizing methanogenic Archaea was observed in obese patients compared with lean controls[32,33]. A possible explanation for this phenomenon has been proposed in animal models, in which methane-producing Archaea enhanced the capacity of polysaccharide-degrading bacteria to digest polyfructose-containing glycans, thereby increasing energy harvest and caloric intake [34].

Experimental research on mice has also suggested a link between increased viral DNA and RNA in the gut and obesity [35,36]. In a study conducted in obese children, a decreased abundance of *Saccharomyces* species compared with controls was reported, although the significance of this finding remains unclear [33]. Overall, the role of non-bacterial communities (virome, mycobiome, Archaea) in the development of obesity and other metabolic diseases remains a promising field for further investigation [33,35,36].

2.4. Current controversies in the Bacteroidetes–Firmicutes ratio

One of the earliest proposed markers distinguishing the gut microbiota of individuals with higher BMI from those with normal weight was the ratio between Bacteroidetes and Firmicutes. A higher Firmicutes-to-Bacteroidetes ratio (in contrast to the higher relative abundance of Bacteroidetes often reported in healthy, lean individuals) was suggested to characterize the microbiome of people with obesity in several studies [24,37-39].

However, other reports have found this association to be weak, non-significant or even inverted [40-43]. In a recent meta-analysis, the Bacteroidetes/Firmicutes ratio was considered a non-reproducible marker of obesity when evaluated in relation to BMI [44]. Another study suggested that this ratio might be more closely associated with measures of central adiposity, such as waist and body circumference, rather than BMI alone [45].

Taken together, current evidence indicates that the Bacteroidetes–Firmicutes ratio is an oversimplified and inconsistent marker of obesity-related dysbiosis, and that more refined taxonomic and functional indicators are needed to characterize obesity-associated alterations in the gut microbiota [44,45].

3. Mechanisms linking gut microbiota to obesity

Although the exact mechanisms by which the gut microbiota contribute to the development of obesity are still largely unknown, its dysbiosis has been proposed as one of the critical factors

of obesity pathogenesis. It has been suggested in numerous studies that the efficiency of digestible energy uptake is increased in obese patients mainly by promoting the synthesis of nutrient transporters and production of primary fermentation enzymes. [34,46] The increment in frequency of *Clostridium ramosum* (Fermicutes phylum) results in higher expression of Glut2 (a glucose transporter) and CD36 (a fatty acid translocase), therefore increasing the energy absorption and calorie intake. [46]

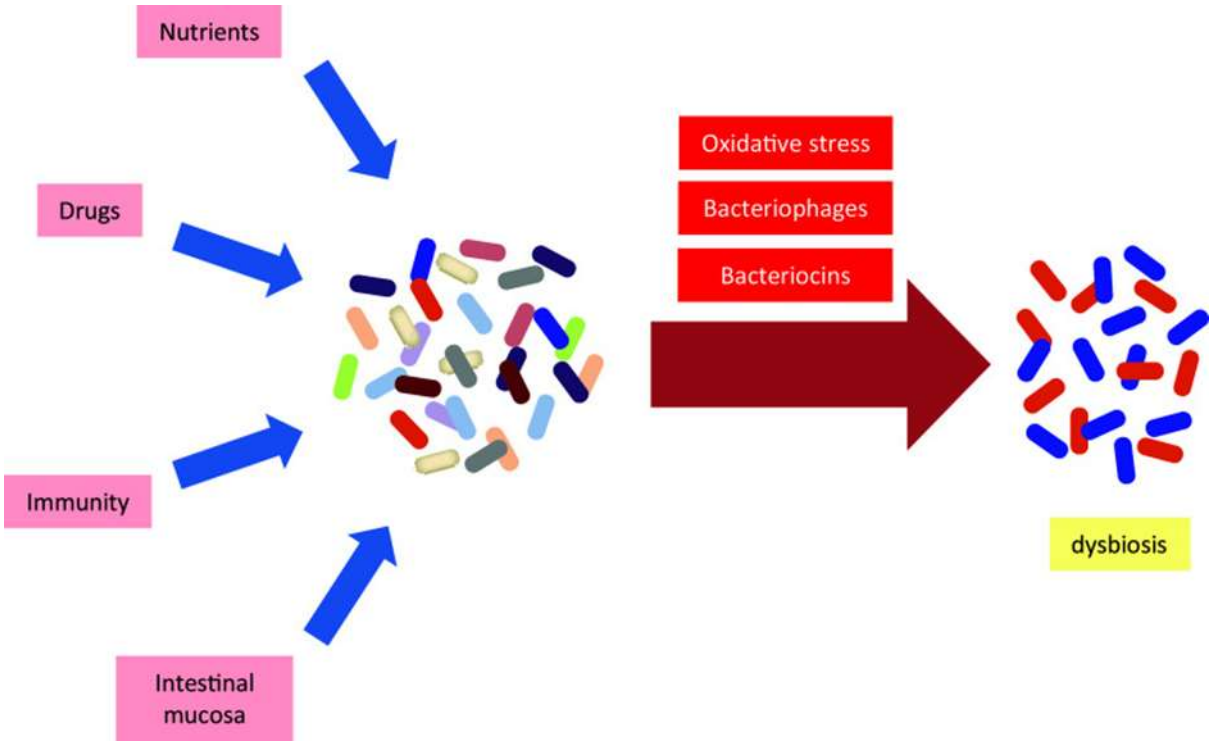
Apart from stimulating the energy uptake, the gut microbiota dysbiosis can also lead to decreased energy expenditure. In obese people, the abundance of *Bacteroides* and *Lactobacillus* is decreased, which results in reduction of bile acids. [47] Said reduction undermines energy usage via inhibition of TGR5/FXR-mediating signalling pathways in adipose tissue, which are activated by bile acid, therefore decreasing thermogenesis. [48-50]

A link between the dysbiotic gut microbiota in obese people and increased production of short-chain fatty acids (SCFAs) has been reported in various studies. [51] Microbiota-derived SCFAs, mainly acetate, propionate and butyrate, are metabolites produced by gut microbiota by fermentation of undigested carbohydrates. [52-54] They play a vital role in the metabolism of lipids and carbohydrates, with butyrate and acetate being used as precursors for lipid synthesis and propionate working as a substrate for hepatic gluconeogenesis. [55,53] and are thought to maintain metabolic homeostasis in colonocytes through anti-inflammatory and anticarcinogenic effects. [56] Moreover, SCFAs might also activate the free fatty acid receptor 3 (FFAR3), therefore stimulating leptin expression in adipocytes. [57] Disturbances in leptin expression are frequent features in the pathogenesis of obesity. [58] It was also noted that SCFAs might indirectly induce insulin sensitivity by increasing systemic levels of gut-derived GLP-1 (glucagon-like peptide 1). [59] therefore stimulating the release of insulin from the pancreas, delaying gastric emptying and, by consequence, promoting satiety and weight loss. In a study on mice, SCFA were found to increase the expression of PPARs, an important mediator of adipogenesis. [60] Overall, the increased concentration of SCFAs in obese people seems to play an ambiguous role in the pathogenesis of obesity, and the exact pathomechanisms connecting obesity and increased production of these compounds need further investigation.

Another aspect possibly connecting gut microbiota dysbiosis and the development of obesity is the increased release of LPS. LPS is an endotoxin produced by Gram-negative bacteria, which were discovered to be more abundant in obese people. [61] LPS impairs the intestinal mucosal barrier and increases intestinal permeability, therefore resulting in the translocation of LPS from the intestine to systemic circulation. [62,63] In systemic circulation, LPS initiates an immune response in adipose tissue and liver, stimulating the secretion of proinflammatory cytokines and

chemokines. [64] Chronic low-grade systemic inflammation is regarded as one of the fundamental characteristics of obesity, affecting host metabolism and insulin resistance. [62,65] Taken together, gut microbiota alterations described in obese people contribute to the pathogenesis of obesity via a complex nexus of connections, with many mechanisms still unidentified, leaving a promising field for further research.

4.Dysbiosis



Dysbiosis is a term used to describe a disruption of the microbiota that alters its functional composition and metabolic activity. Such an imbalance may both promote the onset of metabolic diseases, such as obesity, and be further exacerbated by them, creating a bidirectional relationship. Such imbalance is an important factor in occurrence of many metabolic diseases, such as obesity, and prevent patients from getting better, or even make their condition more severe. [66]

By disrupting the intestinal barrier and gut-associated lymphoid tissues (GALT), bacterial components such as lipopolysaccharides (LPS) can more easily enter systemic circulation, activate inflammatory pathways, and induce insulin resistance.

Dysbiosis involving an increased growth of organism forms such as the Phylum Firmicutes (particularly the genus Clostridium), as well as the species such as Eubacterium rectale, Clostridium coccoides, Lactobacillus reuteri, Clostridium histolyticum, and Staphylococcus

aureus have been associated with obesity in some studies, whereas Akkermansia muciniphila is more often reported to be reduced in obesity and has been investigated for potential metabolic benefits [67,70,71].

High sugar and fats intake coexisting with low fiber content is characteristic for western type diet. It was shown repeatedly how significantly it influences the gut microbiom. [68] As demonstrated by [69], even a few days of such dietary intake may lead to microbiological and metabolic changes. According to [70,71] western diet is responsbile for decreased number of A. muciniphila. This bacterium affects the integrity of intestinal barrier, regulates glucose and LPS metabolism, and controls inflammation.

Moreover, Western Diet promotes the expansion of microorganism capable of mucin layer degradation, in consequence the susceptibility to translocation of bacterial PAMPs is increased[72]. A diet high in sugar and saturated fats favours the growth of Gram-negative bacteria and facilitates migration of LPS to the bloodstream. This phenomenon is known as the metabolic endotoxemia [62]. LPS activates TLR4 receptors further propagating inflammation and insulin resistance.

Additionally, low fiber intake reduces accessible substrates for bacterial fermentation and lowers SCFA production [73], which plays an important role in the immune system regulation, epithelial integrity and appetite control. Western diet also increases pro-inflammatory bacterial growth, such as Bilophila wadsworthia. This leads to intestine inflammation, obesity and insulin resistance[74].

5. Modulating Gut Microbiota in the Treatment of Obesity

Obesity treatment leads to numerous changes in the gut microbiota. One of them is the introduction of a healthy diet - defined as understanding the role that different foods, essential nutrients, and other food components play in health and disease. [75] Researchers describe many dietary patterns that come closest to this definition.

One of them is the Mediterranean diet, rich in fruit and vegetables and olive oil, with moderate fish intake and minimal consumption of processed foods and red meat. [76] Due to its availability and health benefits, it is becoming increasingly popular. It has been shown that adherence to the Mediterranean diet is associated with a reduced incidence of cardiovascular disease, type 2 diabetes, and other metabolic disorders. [77] Human studies have reported an increased abundance of Bifidobacterium, along with higher levels of Prevotella, Bacteroides, and Enterococcus. [78] Other studies found that Faecalibacterium prausnitzii, Roseburia, and Lachnospiraceae were also more abundant [79], whereas Ruthenibacterium lactatiformans,

Flavonifractor plautii, Parabacteroides merdae, Ruminococcus torques, and Ruminococcus gnavus were less abundant. [79] An increase in Firmicutes and Lactobacillus was also noted. [78] Interestingly, changes in gut microbiome composition have also been observed after consumption of specific dietary components - for example, eating walnuts was associated with a higher relative abundance of Eubacterium eligens, Leuconostocaceae, Lachnospiraceae, and Roseburia. [80]

Another dietary pattern with beneficial effects is a vegetarian diet, which has been associated with reductions in metabolites linked to cardiovascular disease [81], including acylcarnitines and L-carnitine. [82] Changes in the gut microbiome - such as increased alpha diversity—have also been linked to vegetarian diets. [83] During such diets, increases in Eubacterium biforme, F. prausnitzii, and Eubacterium rectale have been observed [83], as well as an increase in Akkermansia. [82] Akkermansia has been shown to contribute to maintenance of epithelial energy balance and intestinal barrier integrity. [84]

In contrast, the Western diet increases the abundance of Bacteroides spp., Alistipes spp., and Bilophila spp., while reducing Lactobacillus spp., Roseburia spp., and E. rectale, which are described as beneficial to the host. [85] Scientists have identified dietary fat as a key driver of microbiome compositional changes, and these microbiota shifts have been linked to the development of obesity, diabetes, and localized inflammation in different tissues. [86] Foods typical of the Western diet promote the proliferation of potentially pathogenic bacteria while inhibiting beneficial taxa, disrupting microbiome balance and weakening intestinal barrier integrity. [86] Consequently, highly processed foods can alter the microbiota in ways that promote inflammatory diseases, including metabolic disorders, inflammatory bowel disease, and obesity. [87]

However, ketogenic diets (high fat, low carbohydrate), including very-low-calorie ketogenic diets (VLCKD), have been shown to contribute to weight loss and improvements in waist circumference and triglycerides; however, effects on LDL-cholesterol are variable, and in some individuals LDL-C may increase [88,89]. In one study, baseline microbiota showed higher Firmicutes abundance, followed by Bacteroidetes, Proteobacteria, and Actinobacteria; later, a reduced proportion of Firmicutes and Actinobacteria and an increased abundance of Bacteroidetes and Proteobacteria were observed. [88] Shifts in the Firmicutes/Bacteroidetes ratio are widely associated with obesity. Furthermore, VLCKD has been reported to significantly modulate the gut microbiota and may help restore homeostasis, suggesting a potential supportive role in treatment strategies for multiple diseases [88,89].

If dietary treatment fails to produce results, pharmacological treatment of obesity is introduced, which can also affect the gut microbiota. After a high-fat diet, the abundance of certain bacteria - such as Akkermansia, Bacteroides, Mucispirillum, Enterococcus, and Alistipes - has been reported to decrease significantly, while Faecalibaculum, Allobaculum, and Ileibacterium increased; intervention with tirzepatide facilitated restoration of gut microbiota homeostasis after a high-fat diet. [90] Correlation analyses showed that Akkermansia, Bacteroides, and Enterococcus negatively correlated with weight gain, blood glucose, and obesity-related indicators, whereas Ileibacterium and Allobaculum positively correlated with obesity-related characteristics. [90] Kato et al. described noradrenaline release into the intestinal lumen in vitro and activation of the sympathetic nervous system after acute GLP-1 receptor agonist administration, alongside a rapid increase in E. coli in vivo. [91] In the same line of evidence, liraglutide administration significantly reduced Bacteroidetes and tended to increase Actinobacteria, while Firmicutes and Proteobacteria remained unchanged; at the genus level, liraglutide significantly reduced Ruminococcus spp. and did not increase Akkermansia spp. [91] Despite the well-known efficacy of semaglutide in treating obesity, relatively little is known about its effects on the gut microbiome. [92] One human study reported significantly higher levels of the Lactobacillus genus and Lactobacillus gasseri after 8 weeks of treatment. [93] Orlistat reduced the relative abundance of Alistipes and Desulfovibrio in the fecal microbiome of high-fat-diet-fed mice. [94] However, other studies reported no significant changes in microbial diversity, dominant bacteria, enterotypes, or fecal short-chain fatty acids under the influence of orlistat. [95]

Given the key role of the brain–gut–microbiota axis in the etiopathogenesis of obesity, studies have evaluated obesity treatment strategies that directly target the gastrointestinal microbiota. Most commonly, microbiota composition has been modulated using prebiotics, probiotics, and postbiotics.

Prebiotics are indigestible food ingredients that selectively stimulate the growth or activity of one or a limited number of bacteria in the colon, benefiting the host and thereby improving health. [96] One example is inulin: it is not digested in the human small intestine, and nearly 90% reaches the colon where it is metabolized by bacteria. [97] Reported health benefits of inulin include reductions in blood lipogenesis and plasma triacylglycerol concentrations, reduced risk of gastrointestinal diseases, and increased calcium and iron absorption. [98] In studies involving obese children, inulin supplementation significantly promoted intestinal bacterial diversity and improved gut microbiome dysbiosis; these changes correlated with clinical and metabolic outcomes only in the inulin group, suggesting supplementation may be

a strategic approach to restore eubiosis and influence obesity in children. [99] Chitooligosaccharides can also modulate the gut microbiome by increasing Bacteroidetes, reducing Proteobacteria and Actinobacteria, and decreasing the Firmicutes/Bacteroidetes ratio. [100] Lactulose, in turn, resists hydrolysis by small-intestinal disaccharidases, reaches the colon intact, and is selectively metabolized by Bifidobacteria and Lactobacilli, producing lactic acid and/or carbon dioxide that acidify fecal biomass. [101]

Probiotics are live microorganisms that confer health benefits when consumed in adequate amounts; this definition was formalized by the World Health Organization in 2002. [102] "Next-generation probiotics" appear promising as preventive and therapeutic agents against obesity, including Akkermansia muciniphila, Faecalibacterium prausnitzii, Anaerobutyricum hallii, Bacteroides uniformis, Bacteroides coprocola, Parabacteroides distasonis, Parabacteroides goldsteinii, Hafnia alvei, Odoribacter laneus, and Christensenella minuta, which have shown encouraging results in preclinical models of obesity and obesity-related disorders. [103] Among these, Akkermansia muciniphila is one of the best studied and is often considered one of the most promising candidates. [104]

Postbiotics (also referred to as metabiotics) are defined as preparations of non-living microorganisms and/or their components that provide health benefits to the host. [105] Among microbial metabolites, short-chain fatty acids (SCFAs) appear to play a major role in reducing inflammation, strengthening intestinal barrier function, and modulating immune responses. In particular, butyrate has been linked to such properties, including increased energy expenditure and fat oxidation. [106] Moreover, mouse studies have highlighted that supplementation with 10-hydroxy-cis-12-octadecenoyl acid attenuated high-fat-diet-induced obesity without inducing arachidonic-acid-mediated adipose tissue inflammation, while improving metabolic status via free fatty acid receptors. [107]

6. Physical Activity, Sport Performance, and the Gut Microbiota

Physical activity is one of the factors determining the diversity and abundance of specific gut microbiota taxa, and its impact has in recent years become the subject of numerous studies in the context of obesity [108-112]. The results of many analyses indicate that regular physical exercise leads to beneficial changes in the microbiota, which may contribute to improved metabolic parameters and reduced inflammation [108-110]. The article by Hawley et al., providing a comprehensive review of current knowledge on the relationship between physical activity, gut microbiota and gastrointestinal health, showed that exercise increases both the alpha- and beta-diversity of the gut microbiota [108]. An increased prevalence of Succinivibrio,

Faecalibacterium prausnitzii, Roseburia hominis and Akkermansia muciniphila was also observed in athletes, as well as a lower abundance of the phylum Actinobacteria in physically active individuals [108]. Hawley et al. point out that the impact of physical activity depends on its type, intensity and duration. Moderate- and high-intensity training promotes the growth of beneficial microorganisms and increases the ability of the microbiota to ferment dietary fiber, whereas extreme competitive exercise may paradoxically transiently disrupt gut barrier function and increase the risk of dysbiosis, which is particularly relevant in endurance sports [108].

In the study by Allen et al., an increase in the abundance of short-chain fatty acid (SCFA)-producing taxa with anti-inflammatory properties and supporting gut barrier integrity was also found; however, this relationship was observed only in individuals with a normal BMI [109]. Ghaffar et al. conducted a meta-analysis on the effects of different types of physical activity (various sports disciplines) and their intensity on the gut microbiota, with particular emphasis on changes in taxonomic structure and the Bacillota/Bacteroidota ratio (formerly Firmicutes/Bacteroidetes, B/B ratio), sometimes used as a coarse indicator of microbiota shifts; however, its direction and clinical meaning are inconsistent across studies and it should not be treated as a standalone biomarker of dysbiosis or metabolic status. In approximately 80% of the included studies, they reported an increase in the Shannon index (alpha-diversity) in individuals engaging in high-intensity physical activity compared with those with lower intensity or less active lifestyles, indicating that more intensive and regular training promotes greater microbial diversity, regarded as a marker of a healthy and stable microbiota [110]. In about 50% of the studies, an increase in the B/B ratio was also observed in individuals who were more physically active or trained with higher intensity or greater workload (more hours per week), reflecting a change in microbiota structure [110].

In a 6-week study conducted by Hintikka et al. (2023) in 17 women with overweight who performed aerobic endurance training, no significant changes in body weight or body composition were observed, but clear alterations in the serum and fecal metabolome were noted (including increased concentrations of lysophosphatidylcholines in serum and glycerophosphocholine in feces), indicating enhanced lipid oxidation. At the same time, an increase in the abundance of the genus Akkermansia (particularly A. muciniphila) and its associated metabolic pathways was observed, suggesting that aerobic training alone, independent of weight loss, may beneficially modulate the gut microbiota and metabolic profile in individuals with excess body weight [111].

7. Integrative Approaches

An integrative approach to obesity is a more and more frequently discussed topic. Dietary habits, physical activity and the gut biome are put together as the interlinking factors. Microbiome diversity and an increased abundance of short-chain fatty acid (SCFA)–producing bacteria are associated with diets rich in fiber, polyphenols and unsaturated fats. This type of dietary habits supports glucose homeostasis and immune regulation [112].

Regular physical activity appears to further strengthen these effects, as it has been shown to enhance overall microbial richness and promote butyrate-producing taxa, including Faecalibacterium prausnitzii, a species linked to reduced systemic inflammation [113]. In this context, microbiome-targeted interventions such as probiotics, prebiotics, and synbiotics have gained attention for their potential to lower metabolic endotoxemia, improve intestinal barrier function, and positively influence host metabolic pathways [114]. Importantly, evidence suggests that combining lifestyle and microbiome-oriented strategies leads to more pronounced metabolic benefits than isolated interventions.

Personalized medicine further builds on the recognition that gut microbiome composition varies between individual patients. The research on genetic and metabolic impact has enabled the identification of specific microbial patterns associated with obesity, impaired metabolic regulation, and heterogeneous dietary responses [115]. Researchers studied and proved that dietary recommendations tailored to an individual's microbiome profile may achieve superior glycemic control compared with conventional, population-based guidelines. Alongside microbial characteristics, host genetics and metabolic phenotypes increasingly inform individualized therapeutic decisions, including dietary planning and targeted probiotic supplementation [116]. As a result, personalized microbiome-based strategies are widely regarded as a promising direction for more effective obesity management.

Despite their potential, microbiome-targeted therapies face several limitations that currently restrict widespread clinical application. Differences in response to probiotics and dietary interventions remain a major challenge, as many commercially available products are not supported by solid clinical evidence [117]. Additional obstacles include the lack of standardized methodologies for microbiome analysis, difficulties in data interpretation, and the high cost of advanced sequencing techniques. Nevertheless, emerging approaches offer new perspectives. These include next-generation probiotics based on well-characterized strains such as Akkermansia muciniphila, which has shown favorable metabolic effects in early human trials [118]. Other innovative strategies, including engineered microbial consortia, personalized fecal microbiota transplantation (FMT), and postbiotic therapies targeting microbial metabolites such

as SCFAs or bile acid derivatives, are also under active investigation [119].

From a practical standpoint, maintaining microbiome health relies primarily on sustainable lifestyle modifications. Consistency in dietary patterns rich in whole plant foods, dietary fiber, and fermented products has been shown to consistently enhance microbial diversity and SCFA production [73]. Conversely, reducing the intake of ultra-processed foods, refined sugars, and saturated fats may help limit dysbiosis and metabolic endotoxemia. Regular, moderate physical activity further supports metabolic flexibility and gut microbiota. When used, probiotics and prebiotics should be selected based on scientific evidence, with strains from the genera Bifidobacterium and Lactobacillus currently supported by the strongest data in metabolic contexts [102]. Ultimately, long-term lifestyle consistency remains the base of maintaining a balanced gut microbiome.

8. Conclusions

The evidence reviewed in this paper shows that obesity can be associated with specific changes in the composition of the gut microbiota. Different dysbiotic patterns lead to functional changes such as increased energy harvest, decreased energy expenditure, altered SCFAs and bile acid concentration, as well as increased release of LPS leading to impaired intestinal barrier function and chronic low-grade inflammation. These mechanisms provide a possible link between the dysbiotic gut microbiota and metabolic adjustments resulting in obesity, providing a promising field for further research in order to expand the possibilities of obesity treatment.

On the other hand, many findings remain inconsistent between studies. Simple markers such as the Firmicutes/Bacteroidetes ratio have been proven non-reproducible. Additionally, the role of metabolites, including SCFAs and bile acids, is ambiguous and clearly based on context, depending on diet, host metabolism, tissue-specific signalling and other still unknown factors. The contribution of non-bacterial components of the gut microbiota to the metabolic dysregulation is apparent, yet data in humans is still limited and needs to be expanded.

The gut microbiota has been shown to be modifiable via lifestyle changes and therapeutic interventions. Introduction of dietary patterns rich in fiber and plant-based foods, regular physical activity, as well as selected pre-, pro- or postbiotics can result in increased diversity and more favorable functional profiles. On the other hand, Western-type diets and a sedentary lifestyle promote microbiotal dysbiosis. Findings presented in this paper could be translated into standardized clinical practice; however, the prominent limitations are interindividual variability, methodological differences and the predominance of animal and small human studies, therefore further research is essential.

In the future, researchers should focus on identifying reliable microbiological and metabolic markers, as well as interventions tailored to the patient. While the microbiota plays a crucial role, maintaining a healthy diet and regular physical activity is important to further improve the outcomes.

Disclosure

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