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Role of gut microbiota in obesity: A Comprehensive Review

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ABSTRACT

The gut microbiota, a complex community of microorganisms residing in the human gastrointestinal tract, plays a crucial role in various metabolic processes. Recent research has highlighted its significant influence on obesity, a growing public health concern globally. This review explores the relationship between gut microbiota and obesity risk, focusing on the mechanisms through which gut microorganisms influence energy balance, fat storage, and metabolic health. We also discuss potential therapeutic interventions targeting gut microbiota to prevent and treat obesity.

Keywords: Obesity, Gut microbiota, BMI

INTRODUCTION

Obesity is a multifactorial condition characterized by excessive fat accumulation, posing significant risks for numerous health conditions, including cardiovascular diseases, type 2 diabetes, and certain cancers (World Health Organization, 2020). Obesity is defined as abnormal or excessive fat accumulation (World Health Organization, WHO) and has been described as a 'global pandemic'(1),(2). Being overweight or obese are defined by measures of body mass index (BMI)(3). A BMI of obesity is over 30 kg/m^2 while a BMI of 25–29.9 kg/m^2 is defined as overweight(4). The standard for obesity and overweight are different in certain populations(5). For example, for Chinese people, the standard is different from that of WHO. According to the recommended criteria for Chinese people, the categories are defined as follows: underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–23.9 kg/m^2), overweight (BMI 24.0–27.9 kg/m^2), and obese (BMI ≥28 kg/m^2)(6). According to a WHO report published in 2021, more than 1 billion people were obese, including 650 million adults, 340 million adolescents and 39 million children based on data gathered in 2016. The global prevalence of being overweight or obese has increased by 27% in adulthood and 47% in childhood during 1980–2013(7). This number is still increasing, and the WHO estimates that it will increase by approximately 167 million people by 2025. Obesity is a risk factor for various diseases(8),(9), notably type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), cardiovascular disease (CVD) and some kinds of cancer(10). Obesity and related diseases impose a heavy burden on individuals, society, and on the economy, through greater public health costs, morbidity and mortality.

Obesity mainly develops as an imbalance between caloric intake and energy expenditure(11)When energy intake is more than needed, it will be stored as fat and glycogen in subcutaneous adipose tissue (SAT) and organs (12),(13). Adipose tissue (AT) consists of functionally distinct depots(14). White adipose tissue (WAT) is an active endocrine and a major and safe lipid storage organ, whereas brown adipose tissue (BAT) produces heat upon β-adrenergic stimulation or cold exposure, a process known as adaptive thermogenesis(15). In humans, WAT can be classified in two main depots: visceral WAT (VAT) and SAT, which have been widely studied for their association with the development of related diseases(16). BAT represents merely 1%–2% of fat, but it is vital in maintaining homeostasis and shows beneficial effects on blood glucose(17).

The gut microbiota, consisting of trillions of bacteria, viruses, fungi, and other microorganisms, has emerged as a crucial player in the development and management of obesity (18). This review aims to summarize current knowledge on the relationship between gut microbiota and obesity risk, examining both the underlying mechanisms and potential interventions.

1. THE ROLE OF GUT MICROBIOTA IN OBESITY

1.1. Energy Harvesting and Storage:

Gut microbiota influences the host's energy balance by enhancing the ability to harvest energy from the diet. Certain bacteria, such as Firmicutes, are more efficient at breaking down complex carbohydrates into short-chain fatty acids (SCFAs), which are absorbed and used for energy(18). Increased energy extraction from the diet can contribute to weight gain and obesity.

1.2. Metabolic Regulation:

The gut microbiota regulates various metabolic pathways through the production of metabolites like SCFAs, which have been shown to modulate appetite, insulin sensitivity, and fat storage(19). Butyrate, for instance, improves insulin sensitivity, while propionate reduces food intake by stimulating the release of satiety hormones (20).

1.3. Inflammation and Immune Response:

Obesity is often associated with chronic low-grade inflammation People who are overweight or obese has been linked with a low-grade, chronic inflammatory state, which is associated with increased infiltration into AT from the circulation by macrophages of the M1 or 'classically activated' phenotype(21). These macrophages can be recruited to AT where they secrete inflammatory cytokines (TNF-α, IL-6, IL-8, etc.)(22). Pro-inflammatory cytokines (e.g. IL6) can influence adipocyte function, lipid metabolism, homeostasis, blood pressure and insulin sensitivity and thus play a major role in the development of diabetes, atherosclerosis and cardiovascular diseases(23). However, IL6 can also be anti-inflammatory, regenerative and homeostatic by controlling acute-phase response and modulating glucose and liver metabolism (24),(24). Dysbiosis, an imbalance in gut microbiota composition, can disrupt the intestinal barrier, allowing bacterial endotoxins to enter the bloodstream and trigger inflammatory responses(25). This inflammation can exacerbate insulin resistance and fat accumulation.

1.4. Gut-Brain Axis:

The gut microbiota communicates with the brain via the gut-brain axis, influencing behavior and appetite. Neuroactive compounds produced by gut bacteria, such as neurotransmitters and SCFAs, can affect mood, stress response, and eating behaviors (26).

2. FACTORS INFLUENCING GUT MICROBIOTA AND OBESITY

2.1. Diet:

Diet is a primary modulator of gut microbiota composition. High-fat and high-sugar diets promote the growth of Firmicutes over Bacteroidetes, a ratio associated with obesity(27). Conversely, diets rich in fiber enhance the growth of beneficial bacteria that produce SCFAs.

2.2. Antibiotics:

Antibiotic use can disrupt gut microbiota, leading to dysbiosis. Early-life exposure to antibiotics has been linked to increased obesity risk later in life(28). This highlights the importance of judicious antibiotic use to maintain gut microbiota balance.

2.3. Genetics:

Host genetics also play a role in shaping gut microbiota. Twin studies have shown that genetics can influence the abundance of specific bacterial taxa, which in turn affect obesity risk (Goodrich et al., 2014).

2.4. Lifestyle:

Factors such as stress, sleep, and physical activity influence gut microbiota composition. Chronic stress and sleep deprivation can disrupt gut microbiota and promote weight gain, while regular physical activity is associated with a more diverse and healthy microbiota (29).

3. THERAPEUTIC INTERVENTIONS TARGETING GUT MICROBIOTA

3.1. Probiotics and Prebiotics:

Probiotics, beneficial live bacteria, and prebiotics, non-digestible fibers that promote the growth of beneficial bacteria, have shown promise in modulating gut microbiota and improving metabolic health. Specific strains of probiotics, such as Lactobacillus and Bifidobacterium, have been associated with reduced body weight and fat mass(30).

3.2. Dietary Interventions:

Dietary modifications, including increased fiber intake and reduced consumption of processed foods, can positively influence gut microbiota. The Mediterranean diet, rich in fruits, vegetables, whole grains, and healthy fats, has been shown to enhance gut microbiota diversity and reduce obesity risk (31).

3.3. Fecal Microbiota Transplantation (FMT):

FMT involves transferring fecal matter from a healthy donor to a recipient to restore gut microbiota balance. Clinical trials have demonstrated that FMT can improve insulin sensitivity and reduce body weight in obese individuals (32).

3.4. Pharmacological Approaches:

Emerging therapies targeting gut microbiota, such as microbial metabolites and bacterial-derived peptides, are being explored for their potential to treat obesity. These interventions aim to modulate gut microbiota composition and function to achieve metabolic benefits (33).

CONCLUSION

The gut microbiota plays a crucial role in the development and management of obesity through its effects on energy harvesting, metabolic regulation, inflammation, and the gut-brain axis. Understanding the complex interactions between gut microbiota and host metabolism opens new avenues for preventing and treating obesity. Future research should focus on personalized interventions that consider individual microbiota profiles and lifestyle factors to optimize obesity management strategies.

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