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RELATIONSHIP BETWEEN THE GUT MICROBIOTA COMPOSITION AND BODY MASS INDEX

The gut microbiome is a key topic for current research since it is known that intestinal microbiota has a great metabolic potential and contains not only thousands of taxa of various bacteria, but also microbes, viruses, archaea and, most importantly, more than three million genes, which makes it our “second genome”. A wide amount of research proves that the gut microbiome contributes to the health of the host. The function of the human intestinal microbiota involves the absorption of nutrients and the synthesis of vitamins, energy harvesting from the food, immune response and reduction of the inflammatory process. Human gut microbiome also takes part in lipid and glucose metabolism and production of short chain fatty acids that may act as energy substrates. It also takes part in neural and hormonal energy regulation of the body since hormone ghrelin, which is also known as the “hunger hormone” and acts as a stimulus for food intake, fat deposition, and growth hormone secretion, is positively correlated with the genera Bacteroides and Prevotella and negatively correlated with Lactobacillus, Bifidobacterium, Blautia coccoides, and Eubacterium rectale. The short-chain fatty acids stimulate the secretion of glucagon-like peptide-1 (GLP 1). GLP-1, in turn, stimulates the secretion of insulin and reduces appetite. It is also known that pre-, pro- and synbiotics as well as fecal transplantation from normal weight individuals to obese individuals may contribute to the obesity treatment. Still the precise mechanisms of gut microbiome regulation for further weight correction have not yet been established. The purpose of our study was to establish the relationship between the body mass index and the gut microbial composition in adults. Thus we conducted a literature search with inclusion criteria of studies on adults only, the mandatory presence of at least two groups - one with BMI < 25 (n>15), the other ≥ 25 (n>15).

Most results found no differences in alpha diversity between groups. It has been shown that obesity can affect beta diversity of microbes, as there are changes in bacterial taxa, as well as in the number of microorganisms. In individuals with excess body weight or obesity the Firmicutes/Bacteroidetes ratio is higher with more abundant Firmicutes, while Bacteroidetes are more abundant in normal weight individuals. Firmicutes are believed to be efficient in harvesting energy and absorbing nutrients, making food as accessible as possible and thus increasing the availability of calories consumed. People with a normal weight are characterized by bacteria Flavonifractor plautii, Faecalibacterium prausnitzii, Bacteroides faecichinchillae, Bacteroides thetaiotaomicron, Blautia wexlerae, Clostridium bolteae, Flavonifractor plauti, Lachnospiraceae that are naturally found in people with a healthy profile. The amount of Dorea, Blautia, Coprococcus, Subdoligranulum, Eubacterium ventriosum, Ruminococcus bromii, Ruminococcus obeum, Streptococcus, Dialister was higher in obese or overweight individuals. The difference in the microbial composition may be due to the gender. Further studies with a larger number of samples and observation of weight changes in dynamics, taking into account dietary interventions, are needed to understand the mechanism of the effect of bacteria on body mass index.

Key words. Gut microbiome and obesity, microbiota and weight, BMI and microbiome, microbiome in disease, microbiota in obesity

Analysis of recent research and publications. The human gut microbiota has a great metabolic potential and contains not only thousands of taxa of various bacteria, but also microbes, viruses, archaea and, most importantly, more than three million genes [1-3]. Thus, the number of

microbiota cells is approximately 10 times greater than the number of human cells, which makes the microbiome a "second genome" [4]. It is known that the microbial composition of a person is formed at an early age and varies greatly in quality and quantity, as it is influenced by many factors, such as the birth delivery method, diet, environment, antibiotics [5]. Normally, the components of gut microbiota coexist in symbiotic and antagonistic relationships, ensuring the protective functions of the host's organism. It was shown that the microbial composition of the large intestine can affect health [6]. Dietary interventions have a significant impact on the microbial composition, which can both strengthen the body's protective functions and weaken them [7]. The microbiota of the gastrointestinal tract contributes to the absorption of nutrients and the vitamins synthesis [8-10]. In addition, it is known about the correlation between the intestinal microbiota and the body's immune response, as well as the reduction of inflammatory processes [11-13].

The gut microbiome is involved in the process of lipid and glucose metabolism, and can also influence body weight by partially absorbing the amount of energy that an individual receives with food, so the microbial composition of the gut is exceptional for maintaining a healthy weight [14]. Moreover the gut microbial composition affects the athletic performance and endurance capabilities of athletes. Also the human gut microbiome is able to produce short-chain fatty acids, namely acetate, butyrate, propionate [15-17], which are known to be energy substrates necessary in endurance sports [18, 19].

What is more important, the results of numerous studies show that the use of pro-, pre- and synbiotics can have a positive effect on body weight loss, reducing such anthropometric indicators as body mass index, body weight and waist circumference [20-22]. In addition, the possibilities of fecal transplantation from individuals with a BMI within the normal range to obese individuals is being actively researched as a new method for treatment of obesity [23,24-26].

Despite the fact that the human gut microbiome is a key vector of modern research due to its connection with the body's protective functions, relatively few scientific works are devoted to the effect of the microbiome on the body mass index. Moreover, the precise mechanisms of gut microbiome regulation for further weight correction have not yet been established.

The purpose of our study is to establish the relationship between the body mass index and the gut microbial composition in adults.

Methods. The literature search was conducted using the keywords "gut microbiome", "intestinal microbiome", "gut microbiota and weight", "microbiota and obesity", "influence of the microbiome on body mass index" in the following databases: Medline (PubMed), Scopus (Elsevier), Google Scholar, Plos One. Data analysis was carried out in accordance with recommendations for conducting meta-analyses [27]. The criteria for inclusion in the analysis were studies on adults only, the mandatory presence of at least two groups - one with BMI < 25 (n>15), the other ≥ 25 (n>15). Thus, after excluding studies that do not meet the specified criteria, we selected 6 scientific works for analysis (Table 1).

Introduction. The human brain can influence energy balance through neural and hormonal signals through a special channel called "the gut-brain axis". Such signals mainly come from the gastrointestinal tract [28]. Moreover, the results of scientific works confirm that the gut microbial composition takes a direct part in such signals. The hormone ghrelin, which is also known as the "hunger hormone" and acts as a stimulus for food intake, fat deposition, and growth hormone secretion, is positively correlated with the genera *Bacteroides* and *Prevotella* and negatively correlated with *Lactobacillus*, *Bifidobacterium*, *Blautia coccoides*, and *Eubacterium rectale* [29,30]. The intestinal microbiota is also a producer of short-chain fatty acids, mainly acetate, butyrate and propionate, produced by the cells of the intestinal mucosa, which stimulate the secretion of glucagon-like peptide-1 (GLP 1). GLP-1, in turn, stimulates the secretion of insulin and reduces appetite. This process includes secondary bile acids, which are formed during the fermentation of bile acids by the microbiota and participate in the use of energy and the synthesis of GLP-1 [31-33].

Thus, we can state, and our statement has also been proved by the results of numerous researches, that the intestinal microbiota composition in individuals with a body mass index within the

normal range and people with excess weight or obesity differs both quantitatively and qualitatively [34]. The first such studies were conducted on mice, and it was shown that animals with normal weight had a greater microbiome diversity, with greater number of *Bacteroidetes* compared to *Firmicutes* [35].

Intestinal microbiota and the link to BMI. Companys et al. in their study compared obese/overweight people to those with a normal BMI. It was found that the ratio of *Firmicutes* to *Bacteroidetes* was higher in the first group. *Firmicutes* are believed to be efficient in harvesting energy and absorbing nutrients, making food as available as possible and thus increasing the availability of calories consumed. It was also shown that the first group had a greater diversity of the microbiome, while the second was characterized by a greater abundance (ie, a greater number of bacteria). In the first group, bacteria that are producers of short-chain fatty acids, namely *Faecalibacterium prausnitzii*, *Lachnospiraceae*, especially *Roseburia* and *Lachnospira*, which are significantly more prevalent in people with normal body weight, were less represented. Interestingly, bacteria which belong to the phylum *Firmicutes* in overweight and obese individuals were mainly substituted by others also belonging to *Firmicutes*, namely *Dorea*, *Blautia*, *Coprococcus*, *Subdoligranulum*, *Collinsella aerofaciens* and *Bifidobacterium*, which are producers of propionate and acetate, also prevailed in the first group. Acetate, in turn, stimulates the synthesis of fatty acids [34]. In a study of a Japanese population, Kasai et al. concluded that the gut microbial composition has a correlation with both obesity and normal body weight. In this study, patterns of positive correlation with various bacteria were revealed. In the group of obese individuals, *Blautia hydrogenotrophica*, *Coprococcus catus*, *Eubacterium ventriosum*, *Ruminococcus bromii*, *Ruminococcus obeum* prevailed, while the gut microbiome of normal weight individuals was characterized by *Bacteroides faecichinchillae*, *Bacteroides thetaiotaomicron*, *Blautia wexlerae*, *Clostridium bolteae*, *Flavonifractor plautii*. Obese individuals showed a greater diversity of microbial composition, a higher ratio of *Firmicutes/Bacteroides*, but less *Bacteroides*, which was also confirmed by other researches [36].

Gallè et al. have found that the genus *Streptococcus*, as well as *Dialister* and *Dorea*, prevailed in obese individuals. Interestingly, *Dialister* and *Dorea* are also more abundant in individuals with a low activity level. No difference was found in the biodiversity and *Firmicutes/Bacteroides* ratio, but this finding is probably due to the the result of a small sample [37].

Borgo et al., have observed that obesity and excess body weight may be predicted by the presence of certain bacterial taxa. There are special bacteria markers, especially those producing short-chain fatty acids (i.e., butyrate, propionate etc), the presence of which can be considered as an indicator of reduced risks of inflammation. The authors declared *Flavonifractor plautii* and *Faecalibacterium prausnitzii* to be such indicators, which according to the results of the study significantly prevailed in people with normal body weight and are less represented in overweight or obese people [38].

Assmann et al., in a recent study also found no differences in the alpha-diversity of the gut microbiome between a group of normal weight individuals and another group with overweight or obese participants. Interestingly, the differences in beta-diversity were found. These results confirm the possible influence of obesity on changes in taxa and in the number of bacteria [39].

Hato et al. conducted research and investigated the relationship between the gut microbiome, body mass index and gender. The authors found no differences in alpha diversity between men and women which correlates with previous research. However, when dividing the participants into three groups according to body mass index (13 men and 13 women with BMI < 30; 13 men and 10 women with BMI ≥ 30 - ≤ 33; and 13 men and 13 women with BMI > 33) it was shown that men in the second group had a higher ratio of *Firmicutes/Bacteroidetes*, but in the third group this ratio was lower in men than in women. Interestingly, the level of *Bacteroidetes* remained stable in women with higher body mass index, while in men this level decreased with increasing BMI. Also, in the first group, *Bifidobacterium adolescentis*, *Oxalobacter formigenes*, *Eubacterium bifforme* prevailed in men of the first group, while the level of these bacteria was lower in women. No such differences were found in the second and third groups [40].

Table 1.

Link between intestinal microbiota and body mass index

	Authors, year of publication	Participants	Results	Source
1	Companys et al., 2021	First group of individuals with BMI* ≥ 25 i ≤ 35 (n=96). Second group with BMI < 25 (n=32)	The first group had a higher ratio of <i>Firmicutes/Bacteroidetes</i> , and also contained <i>Dorea</i> , <i>Blautia</i> , <i>Coprococcus</i> , <i>Subdoligranulum</i> . Second group had a higher number of <i>Faecalibacterium prausnitzii</i> , <i>Lachnospiraceae</i> , especially <i>Roseburia</i> i <i>Lachnospira</i> .	34
2	Kasai et.al, 2015	First group of individuals with BMI < 20 (n=23). Second group with BMI ≥ 25 (n=23)	Second group had a greater diversity of bacteria, a higher ratio of <i>Firmicutes/Bacteroidetes</i> and less presented <i>Bacteroidetes</i> , <i>Blautia hydrogenotrophica</i> , <i>Coprococcus catus</i> , <i>Eubacterium ventriosum</i> , <i>Ruminococcus bromii</i> , <i>Ruminococcus obeum</i> were present. The first group was dominated by <i>Bacteroides faecichillae</i> , <i>Bacteroides thetaiotaomicron</i> , <i>Blautia wexlerae</i> , <i>Clostridium bolteae</i> , <i>Flavonifractor plauti</i> .	36
3	Gallè et al., 2020	Students (n=140), the first group with BMI < 25 (n=113), second group with BMI ≥ 25 (n=27)	The genus <i>Streptococcus</i> , as well as <i>Dialister</i> and <i>Dorea</i> , predominated in obese individuals. No difference was found in biodiversity.	37
4	Borgo et al., 2018	First group of individuals with BMI < 25 (n=20). Second group with BMI ≥ 30 (n=20)	<i>Flavonifractor plautii</i> and <i>Faecalibacterium prausnitzii</i> were more abundant in the first group and less represented in the second group.	38
5	Assmann et al., 2020	First group of individuals with BMI ≥ 30 - ≤ 40 ; (n=78). Second group with BMI ≤ 25 (n=25)	No differences were found in alpha-diversity, but distinct features were found in beta-diversity due to the effect of obesity on changes in taxa and bacterial abundance	39
6	Haro et al., 2016	75 individuals divided into 3 groups according to the BMI: 13 men and 13 women with BMI < 30 ; 13 men and 10 women with BMI ≥ 30 - ≤ 33 ; and 13 men and 13 women with BMI > 33	Men in the second group had a higher ratio of <i>Firmicutes/Bacteroidetes</i> , but in the third group this ratio was lower in men than in women. The level of <i>Bacteroidetes</i> remained unchanged in women with increasing BMI, while in men this level decreased with increasing BMI. In the first group, <i>Bifidobacterium adolescentis</i> , <i>Oxalobacter formigenes</i> , and <i>Eubacterium bifforme</i> prevailed in men of the first group, while the level of these bacteria was lower in women. No such differences were found in the second and third groups.	40

*BMI - body mass index calculated by the formula::

$$\text{BMI} = \text{body mass (kg)/height (m)}^2$$

Conclusions. To the best of our knowledge, the gut microbial composition may have positive correlation with the body mass index. Even though most scientific works have not found differences in alpha diversity, it has been shown that obesity can affect beta diversity of microbes, as there are changes in bacterial taxa, as well as in the number of microorganisms. In addition, in people with excess body weight or obesity, the ratio of *Firmicutes* to *Bacteroidetes* is higher and *Firmicutes* predominate, while *Bacteroidetes* are considered to be the characteristic feature of the gut microbial composition of people with a normal weight. The increased number of *Firmicutes* in overweight and obese individuals is quite logical since *Firmicutes* are believed to be efficient in harvesting energy and absorbing nutrients, making food as accessible as possible and thus increasing the availability of calories consumed. People with a normal weight are characterized by bacteria that are naturally found in people with a healthy profile, namely *Flavonifractor plautii*, *Faecalibacterium prausnitzii*, *Bacteroides faecichinchillae*, *Bacteroides thetaiotaomicron*, *Blautia wexlerae*, *Clostridium bolteae*, *Flavonifractor plauti*, *Lachnospiraceae*. *Dorea*, *Blautia*, *Coprococcus*, *Subdoligranulum*, *Eubacterium ventriosum*, *Ruminococcus bromii*, *Ruminococcus obeum*, *Streptococcus*, *Dialister* predominate in obese or overweight individuals. It was also found that the difference in the microbial composition may be due to the gender of the individuals. Further studies with a larger number of samples and observation of weight changes in dynamics, taking into account dietary interventions, are needed to understand the mechanism of the effect of bacteria on body mass index.

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