Physical Activity Induced Alterations of Gut Microbiota in Humans: A Systematic Review

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Abstract

Background: Gut microbiota are considered to have a great impact on human health and disease. While it is widely recognized that the gut microbiota of healthy individuals differs from those with obesity, inflammatory bowel disease, metabolic syndrome, and other chronic diseases, the alterations of gut microbiota with mild and vigorous physical activity is not fully understood. Accordingly, we performed this systematic review to address the question regarding the effects of mild and intense exercise on the gut microbiota in humans.

Methods: The comparative analyses of gut microbiota were conducted following the PRISMA protocol to determine the differences in the active vs. nonactive individuals (phenotypes) (n=11), including the influence of physical activity intervention on the human gut microbiota (n=13); the differences in the gut microbiota of athletes vs. nonathletes (n=8); and the microbiota status at different stages of athletic performance or intervention (n=7). Literature searches were performed using four databases: PubMed, Web of Science, Scopus, and EBSCO, and 2090 articles were retrieved by using appropriate keywords.

Results: After excluding 2052 articles, we ultimately selected 38 articles that met the eligibility criteria for this review. The data analyses revealed that physical activity markedly influenced the microbiota ratio of *Firmicutes/Bacteroides*, and the relative abundance of short-chain fatty acid (SCFA) producers and other types of bacteria in the GI tract.

Conclusion: It is concluded that the level of physical activity modulates the gastrointestinal microbiota in humans. The vigorous exercise effect was most apparent among athletes compared to untrained individuals. The results showed that athletes harbor a more diverse type intestinal microflora than nonathletes, but with a relatively reduced abundance of SCFA- and lactic acid-producing bacteria, thereby suggesting an adverse effect of intense exercise on the population of gut microbiota.

Trial registration: Prospero CRD42021264064

Background

Human gut bacteria consist of mainly *Firmicutes* (60–80% of all gut bacteria), and *Bacteroidetes* (20–40%), as well as a small amount of *Proteobacteria* and *Actinobacteria*, but their relative abundance varies with anatomical location among individuals. While the composition of the gut microflora can change rapidly with antibiotic use, diet, and other environmental factors, the population remains relatively stable [1]. The physiological balance between the host and the gut microbiota has a major bearing on the host's health [1]. In fact, the host needs the gut microbiota to support various functions of the gut: nutrient metabolism, mutagen and carcinogen neutralization, development and function of the immune system, protection from pathogens, enterocyte and intestinal epithelium development, and short-chain fatty acid (SCFA) production. SCFAs initiate enterocyte proliferation and mucin secretion, which greatly impact on the tightness of the intestinal barrier. SCFAs are produced by bacteria from the genera *Clostridium*, *Eubacterium*, *Fusobacterium*, *Butyrivvibrio, Megasphera*, *Roseburia*, *Feacalibacterium*, and *Eubacterium* [2]. The composition of the microbiota, especially the presence of the above-mentioned bacteria, influences the permeability of the toxic metabolites from the gut barrier.

According to published studies, moderate exercise has a beneficial effect on intestinal permeability, absorption and assimilation of electrolytes and nutrients, and on the rate of excretion of toxic metabolic products [3]. By contrast, increasing the training load (i.e., extending the exercise time or increasing the intensity of physical exertion) may negatively affect the digestive system, and cause symptoms, such as abdominal pain, colic, flatulence, nausea, vomiting, or diarrhea. In this context, several normal physiological responses to exercise that disrupt and affect the integrity and function of the gastrointestinal tract are called "exercise-induced gastrointestinal syndrome" [4]. This syndrome is thought to affect 70% of athletes and occurs 1.5 to 3-times more often among qualified athletes than among amateurs [4]. It follows two distinct pathways: cardio–gastro-intestinal and neuroendocrine–gastro–intestinal signal pathways. The former causes redistribution of the blood flow to the working muscle and peripheral circulation, while the latter is associated with an increased sympathetic activation and the resulting decrease in the functional capacity of the gastrointestinal tract [4]. Camilleri [5] suggested that physical exercise may disturb the immune system of the digestive tract (i.e., damage the lumen of the digestive tract), which may result in an increased inflammatory response and gastrointestinal symptoms [5]. Further, Camilleri proposed that changes in the composition of the intestinal microbiota, characterized by an increase in its alpha diversity and the abundance of several dominant bacteria, such as *Bacteroides*, increase intestinal permeability [5]. Published literature shows the occurrence of acute and chronic diseases, not only of the digestive system, is associated with alterations in the composition of the intestinal microflora [6, 7]. "Dysbiosis" is the loss of commensal bacteria with possible beneficial metabolic activity and the overgrowth of opportunistic pathogens, as well as reduced biodiversity [6, 7].

In this review, we will try to answer the question: how much physical effort is healthy for the human gut microbiota? We have scrutinized all published manuscripts on mild and vigorous physical activity on the population of microbiota, regardless of the size of participants. However, still a small amount of research has been done on the changes in microbiota in athletes. Especially, a small number of manuscripts were found about extreme physical effort and at various stages of training. There are some manuscripts about case studies because knowledge of extreme physical activity is still very low. We are cognizant of the fact that this is not the first review about the influence of physical activity on the population of microbiota, but our work supplements the knowledge from previous reviews on this topic [8–12], in particular extreme physical activity. The additional knowledge gained about this topic will also supplement current knowledge about the consequences of extreme physical exertion. In our analyses, we have examined the differences in the gut microbiota of active vs. nonactive individuals (phenotypes); the influence of physical activity intervention on the human gut microbiota; the differences in gut microbiota among athletes vs. nonathletes; and the microbiota status at different stages of athletic performance or intervention.

Methods

Literature search strategy

The current study is a systematic review of literature focusing on the effect of training load on the gut microbiota. The systematic review followed the PRISMA (Preferred reporting items for systematic reviews and meta-analyses) protocol and was registered in PROSPERO, the International Prospective Register of Systematic Reviews, under the registration number CRD42021264064. Four databases were searched: PubMed, Web of Science, Scopus, and EBSCO (Elton Bryson Stephens Company).

The literature search included original papers written in English and published before 17 June 2021. No year restriction was applied. The following index terms were used: “gut microbiota”, “composition”, “exercise”, and “physical activity”; all words were searched in all fields. Papers were browsed using only these key words to broaden the search.

Inclusion and exclusion criteria

After the database searches, the following inclusion criteria were applied: articles in the English language, studies involving males and/or females, adults, studies evaluating physical effort on composition of gut microbiota. The following exclusion criteria were adopted: underage subjects, subjects with disease (s), animal model studies, studies evaluating parameters other than physical effort or exercise, review papers, meta-analysis.

Data extraction and study design

Data were first evaluated by three investigators (H.D., A.K. and M.D.) and then checked independently by two other investigators (A.S.-S., and J.O.-K.). First, all articles retrieved using the keyword search were downloaded. Then, all replicates were removed, and article abstracts were analyzed using the eligibility criteria. Finally, whole text of articles that met the eligibility criteria (n = 38) was reviewed. Each publication selected for review was critically evaluated for inclusion in this review. If the full text of a publication was not publicly available, then its author was contacted for a pdf copy.

The articles selected for this review were divided into four groups for the following analyses (one article was used twice):

1. Differences in the microbiota of active and nonactive individuals (phenotypes) (n = 11);
2. Influence of physical activity intervention on the human gut microbiota (n = 13);
3. Differences in the gut microbiota of athletes and nonathletes (n = 8);
4. Microbiota status in athletes at different stages of preparation or intervention (n = 7).

The publications were grouped in this manner to facilitate data interpretation. Considering the study design, the article was included for analysis in four groups. Only data on the influence of physical exercise on gut microbiota were extracted for review.

Quality assessment

Following analysis described in subsection Methods the evidence level was assessed by three independent reviewers (H.D., A.K., and M.D.) using the 2011 method of the Oxford Centre for Evidence-Based Medicine (OCEBM), developed by an international group of investigators considering feedback from clinicians, patients, and researchers. The OCEBM method allows rapid identification of the likely best evidence encouraging clinicians, researchers, and patients to autonomously assess evidence [13] (Table 1).

Table 1
The 2011 Oxford Centre for Evidence-Based Medicine (OCEBM) levels of evidence [13].

Evidence level (treatment benefits).
Level 1: Systematic review of randomized trials or n-of-1 trials
Level 2: Randomized trial or observational study with dramatic effect
Level 3: Non-randomized controlled cohort/follow-up study
Level 4: Case-series, case control study, or historically controlled study
Level 5: Mechanism-based reasoning

Results

The literature search identified 2090 potential articles. After removal of 856 duplicates, and 460 records marked as ineligible by automation tools, 774 records underwent title and abstract screening. Full texts of 50 articles were evaluated, and 38 articles were included in the review (one came from citation). Results are summarized in four tables:

i. Table 2 shows differences in the microbiota of active and nonactive individuals.
ii. Table 3 shows differences in the gut microbiota of athletes and nonathletes.
iii. Table 4 depicts microbiota status among athletes at different stages of preparation or interventions.
iv. Table 5 shows the influence of physical activity intervention on the human gut microbiota.

We summarize articles this way to better understand the results of our review.

Characteristics of included studies:

Table 2
Changes in the gut microbiota (phenotypes) depending on the level of physical activity

OCEBM/Study design	Age (yrs.)	Study group	Method of fecal microbiota analysis	Diversity indexes, *F/B* ratio	Fecal results of group with high level of physical activity			
					Phylum/order	Family	Genus	Species
Level 2/Cross - sectional	18–40	Premenopausal women, N = 40	sequencing analysis 16S rRNA (V3, V4 region)	→Alpha diversity (Chao1, Shannon) ≠ Beta diversity (PCoA) →F/B	Phylum: no differences	*	↑*Bifidobacterium* ↑*Coprococcus* ↑*Paraprevotella* ↑ *Ruminococcaceae unclassified1* ↓*Odoribacter* ↓*Turicibacter* ↓*Ruminococcaceae unclassified2*	↑*Akker mucini* ↑*Faeca prautzi* ↑*Rosel homini*
Level 2/Cross - sectional	25.7 ± 2.2	Healthy adults (F, M), N = 37	sequencing analysis 16S rRNA	↑F/B	*	*	*	VO_{2max} 22% of individ bacteri
Level 2 /Cross - sectional	> 65	Older healthy adults (F, M), N = 207	sequencing analysis 16S rRNA (V3 region)	↑Alpha diversity (Observed Species) ↑Beta diversity (Bray–Curtis)	Order: ↑*Bifidobacteriales* ↑*Clostridiales*	*	*	*
Level 2 /Cross - sectional	18–35	Healthy adults (F, M), N = 39	sequencing analysis 16S rRNA (V3, V4 region)	↑Alpha diversity (Chao, Shannon, Simpson) ≠ Beta diversity (Bray–Curtis)	*	*	↑*Adlercreutzia* ↑*Coprococcus* ↑*Roseburia* ↑Unknown members of *Clostridiales*	*
Level 2/ Cross - sectional	69–76, 72 average	Seniors (M, F), senior orienteering athletes (n = 28), community-dwelling older adults (n = 70), N = 98	whole genome sequencing (WGS)	→Alpha diversity (Shannon) » Beta diversity (Jaccard, Unifrac)	*	*	*	↑*Feaca prausn* ↓*Bilop* unclass ↓*Paras excrem*
Level 2/ Cross - sectional	22.5 ± 2.9	Students, N = 140	sequencing analysis 16S rRNA	→Alpha diversity (Shannon) →F/B	*	*	↓*Dialister* ↓*Lachnobacterium* ↓*Megasphera* ↓*Paraprevotella*	*

OCEBM/Study design	Age (yrs.)	Study group	Method of fecal microbiota analysis	Diversity indexes, *F/B* ratio	Fecal results of group with high level of physical activity			
					Phylum/order	Family	Genus	Species
Level 2/ Cross - sectional	78–98, 84 average	Older healthy adults (M), N = 373	sequencing analysis 16S rRNA (V4 region)	→Alpha diversity (Shannon) » Beta diversity (Unifrac)	*	*	↑*Cetobacterium* ↓*Coprobacillus.* ↑*Feacalibacterium* ↑*Streptophyta* ↑*Clostriudium* ↑*Lachnospira* ↑*Prevotella* ↓*Aldercreutzia* ↓*Alistipes* ↓*Anaerotruncus* ↓*CC-1115* ↓*Clostridia SHA-98* ↓*Megasphera*	*
Level 2/ Cross - sectional	18 ± 0.6	Students (F, M), N = 373	sequencing analysis 16S rRNA (V4 region)	→Alpha diversity (Chao1, OTU) ≠Beta diversity (PCoA) →F/B	*	*	↑*Lachnospira* ↓*Enterobacteriales genus member*	*
Level 2/ Cross - sectional	23.1 ± 3.1	Students (F, M), N = 59	sequencing analysis 16S rRNA	*	Phyla: ↓*Firmicutes*	*	*	*
Level 2/ Cross - sectional	19–49	Premenopausal women, N = 71	sequencing analysis 16S rRNA	*	*	*	↑*Bacteroides* ↓*Enterobacteria*	↓*Eubac rectale* ↓*Clostr coccoi*
Level 2/ Cross - sectional	> 61	Older healthy adults, N = 897	sequencing analysis 16S rRNA	→Alpha diversity (Shannon)	*	↑*Bacteroidaceae* ↑*Campylobacteraceae* ↑*Clostridiaceae* ↑*Corynebacteriaceae* ↑*Fusobacteriaceae* ↑*Paraprevotellaceae* ↑*Peptostreptococcaceae* ↑*Turicibacteraceae* ↓Actinomycetaceae ↓Barnesiellaceae ↓Desulfovibrionaceae ↓Oxalobacteraceae ↓Pseudomonadaceae ↓S24-7		

Table 3
Changes in the gut microbiota depending on the level of physical activity in athletes.

OCEBM/ Study design	Age (yrs.)	Study group	Method of fecal microbiota analysis	Diversity indexes, *F/B* ratio	Fecal results of group with high level of physical activity			
					Phyla	Family	Genus	Sp
Level 2/Cross - sectional	12–26	Rowers (F): adult elite athletes, young elite athletes (n = 12), young nonelite athletes (n = 7), N = 19	sequencing analysis 16S rRNA (V3, V4 region)	↑Alpha diversity (Shannon, Simpson) » Beta diversity (Jaccard, Unifrac), ↑F/B	↑*Firmicutes*	*	↑*Clostridiales* unclassified ↑*Feacalibacterium* ↑*Lachnospiraceae* unclassified ↑*Ruminococcaceae* unclassified ↓*Prevotellla*	*
Level 2/Cross - sectional	19–28	Bodybuilders (n = 15), elite runners (n = 15), control group (n = 15) (M), N = 45	sequencing analysis 16S rRNA (V3, V4 region)	Diversity between groups: →Alpha diversity (Chao1) ≠ Beta diversity (PCoA)	*	*	↑*Clostridium* ↑*Eisenbergiella* ↑*Faecalibacterium* ↑*Haemophilus* ↑*Sutterella* ↓*Bifidobacterium* ↓*Parasutterella*	↓*E ac* ↓*E lo* ↓ *gr* ↓*E* ↓*E*
Level 2/Cross - sectional	20–24	Martial arts athletes (F, M), two competition levels (12 higher – level and 16 lower level athletes), N = 28	sequencing analysis 16S rRNA (V3, V4 region)	↑Alpha diversity (Shannon, Simpson)	*	↑*Porphyromonadaceae* ↓*Veillonellaceae*	↑*Bilophila* ↑*Oscillibacter* ↑*Parabacteroides* ↑*Phascolarctobacterium* ↓*Megasphaera*	*
Level 2/Observational study	34.4 ± 3.5	Marathon runners (F, M) (n = 14), cross-country skiers (F, M) (n = 11), sedentary controls (F, M) (n = 46), N = 71	sequencing analysis 16S rRNA	↑Alpha diversity (Shannon, Simpson, Chao1), ↑F/B	*	*	↑*Prevotella* Marathon runners only: Genus: ↑*Veilonella*	*
Level 2/Randomized control intervention trial	Elite athletes: 30.0 ± 9.9 Control group: 33.4 ± 7.9	Elite athletes (mainly cyclists and triathletes) (F, M) (n = 13), control group (F, M) (n = 11), N = 24	sequencing analysis 16S rRNA (V1, V2 regions)	→Alpha diversity (Inverse Shannon, Chao1) ≠Beta diversity (Bray–Curtis)	*	↑*Ruminococcaceae*	↑*Coprococcus* ↑*Parasutterella* ↓*Dialister* ↓*Odoribacter* ↓*Phascolarctobacterium*	*
Level 2/Cross - sectional	19–49	Cyclists training (for at least 2 years), N = 33	metagenomic whole genome shotgun sequencing (mWGS) and RNA sequencing (RNA-Seq)	*			↑*Prevotella*	↑*M sn*
Level 2/Cross - sectional	27 ± 5	Different sports classification groups (F, M) (n = 9 groups, 17 different disciplines); sports classification based on	sequencing analysis 16S rRNA	Moderate dynamic component that includes sports, such as fencing				↑*S* ↑*C* ↑*L ph* ↑*A ha*

OCEBM/ Study design	Age (yrs.)	Study group	Method of fecal microbiota analysis	Diversity indexes, *F/B* ratio	Fecal results of group with high level of physical activity			
					Phyla	Family	Genus	Sp
		peak static and dynamic components, N = 37		High dynamic and low static components, including sports, such as field hockey				↑*E ar* ↑*L ac* ↑*F in* ↑*F pr*
Level 2/Cross - sectional	29 ± 3	Rugby players (M) (n = 40), and two control groups: <25 BMI (n = 23), and > 25 BMI (n = 23), N = 86	sequencing analysis 16S rRNA (V4 region)	Rugby players in comparison with both control groups: ↑Alpha diversity (Shannon) »Beta diversity (Bray–Curtis)	↓*Bacteroidetes* ↑ *Firmicutes*	↑*Akkermansiaceae*, ↑*Ruminococcaceae*, ↑*Succinivibrionaceae*, ↑*Erysipelotrichaceae* ↑*Prevotellaceae* ↑*Succinivibrionaceae* ↓*Lactobacillaceae*,	↑*Succinivibrio* ↑*S24-7, RC9 gut group* ↑*Prevotella* ↑*Succinivibrio* ↑*S24-7* ↓*Bacteroides* ↓*Lactobacillus*	↑*A m*

Table 4
Microbiota status among athletes during sports preparation or interventions.

OCEBM/ Study design	Age (yrs.)	Study group	Physical characteristics	Method of fecal microbiota analysis	Diversity indexes, *F/B* ratio	Results after the intervention		
						Phylum	Family	Genus
Level 2/Cross – sectional	20.7 ± 3.2	Competitive middle-distance runners F (n = 6) M (n = 8), N = 14	3 weeks of normal training 3 weeks of high-volume training 1-week taper	sequencing analysis 16S rRNA (V3, V4 region)	→ Alpha-diversity (Shannon Index, Chao1)		↓*Pasteurellaceae* Genus: ↓*Haemophilus*	
Level 4/Case study	32	World-class ultramarathon runner, N = 1	All stages of sports preparation	sequencing analysis 16S rRNA (V4 region)	↑Alpha diversity (Shannon) ↑F/B			↑*Haemophilus* ↑*Streptococcus* ↑*Veilonella* ↓*Alloprevotella* ↓*Subdolingranulum*
Level 2/Observational study	18–24	Swimmers (F, M), N = 13	Subjects recorded their total daily swimming yardage and the duration of daily practice	16S rRNA (V4 region)	Increase of training volume: ↑Alpha diversity (Shannon, Simpson) » Beta diversity (Bray–Curtis) ↑F/B		Increase of training volume: Family: ↑*Bacteroidaceae* ↑*Lachnospiraceae* ↑*Ruminococcaceae*	Decrease of training volume: Genus: ↓*Coprococcus* ↓*Faecalibacterium*
Level 4/Case study	26 ± 3	Rowers (M), N = 3	33 days, distance 5000 km	Shotgun sequencing	↑Alpha diversity (Shannon)			
Level 1, Randomized control trial	> 18	Soldiers (F, M), N = 73	4 days country-ski march, military training	sequencing analysis 16S rRNA (V3, V4 region)	↑Alpha diversity (Shannon) → Alpha-diversity (Chao1, OTU) ↑F/B			↑*Acidaminococcus* ↑*Fusobacterium* ↑*Peptoniphilus* ↑*Peptostreptococcus* ↑*Staphylococcus* ↓*Bacteroides* ↓*Collinsella* ↓*Faecalibacterium* ↓*Roseburia*

OCEBM/ Study design	Age (yrs.)	Study group	Physical characteristics	Method of fecal microbiota analysis	Diversity indexes, *F/B* ratio	Results after the intervention		
						Phylum	Family	Genus
Level 2/Single arm trial	18–50	Cross-country athletes (M), N = 40	Subjected to physical exertion until refusal, analysis before and after exertion	sequencing analysis 16S rRNA (V3, V4 region)	→Alpha diversity (Shannon, OTU) ≠Beta diversity (Bray–Curtis, Jaccard, Unifrac)			↑*Blautia* ↑*Rombutsia* ↑*Ruminococcocacea* USG-005 Species: ↑*Escherichia coli TOP48* ↓*Clostridium phoceensis* ↓*Ruminiclostridium* 9
Level 2/Observational study	23–54	Half-marathon runners (F, M)	Average period of training before the start time: 18 months; average time to finish: 115 minutes	sequencing analysis 16S rRNA (V3, V4 region)	After the run: →Alpha diversity ↑ OTUs	↑*Lentisphaerae* ↑*Acidobacteria*	↑*Coprococcus*_2 ↑*Collinsella* ↑*Mitsuokella* ↑*Pseudobutyrivibrio* ↑*Romboutsia*	

Symbols/Abbreviations used:

®, ≠ - unchanged

, » - increased

¯ - decreased

* - no data

F/B - Firmicutes/Bacteroidetes ratio

Alpha-diversity indexes: Chao1, Shannon, Simpson

Beta-diversity indexes: PCoA (Principal Coordinates Analysis), Bray–Curtis, Jaccard, Unifrac

Observed OTUs - Observed operational taxonomic unit

VO_2peak is the highest/maximum oxygen consumption achieved during a clinical/research graded exercise test

VO_2max is the maximal aerobic power defined as the maximum amount of oxygen that an individual can utilize during intense or maximal exercise

F - female; M - male

HR - heart rate; RM - repetition maximum; RTE - repetition time exercise

BMI - body mass index, RM - repetition maximum, RTE – resistant

Discussion

Diversity of the human gut microbiota

Diversity and richness are among the major parameters describing the human gut microbiota. Identification of dissimilarities in microbial diversity in different populations, for example, smokers vs. nonsmokers and ill vs. healthy, is a fundamental step of microbiome studies. For instance, reduced microbial diversity is associated with various host phenotypes, such as obesity, fatty liver disease, type II diabetes, inflammatory bowel disease, to name a few. Clinical interventions (e.g., antibiotic use) and environmental factors (e.g., diet, smoking, and physical activity) also affect the microbial diversity [56]. Accordingly, biodiversity (alpha diversity Shannon Index) parameters have been compared in athletic activity, and exercise studies. The microbial diversity was reported as unchanged regardless of the level of physical activity in five studies [15, 19, 20, 21, 25], while it was reportedly increased with increased physical activity in two studies [17, 18]. Although the diversity of gut microbiota of athletes was reported to be higher than that of nonathletes in four studies [26, 28, 29, 33]. In the current review, the diversity parameters did not respond to the stimulus of exercise in non-training individuals [44, 46, 47, 49, 50], but were affected by the

training load in highly trained athletes [35, 36, 37]. Therefore, the microbial diversity does not appear to be related to the physical exercise as per se, but to the appropriate “intervention”, i.e., the time or intensity of the physical effort. These conclusions are supported by studies in the rat model conducted by Allen et al. [55], who showed that forced vs. voluntary training differently impacts the gut microbiota composition. In addition, Grosicki et al. [35] analyzed changes in the intestinal microbiota at all stages of an athlete's preparation for an ultramarathon. They observed the highest alpha-diversity values during the training periods of the lowest intensity (the preparation period and post-start period), with the lowest values reported upon an increase of the physical effort load (the pre-start period) and immediately after the physical performance, i.e., the recovery period. Furthermore, Karl et al. [38] showed that greater microbiota alpha diversity is not always related to gut health but may be associated with the growth of potentially harmful bacteria. This is supported by an increased abundance of the potentially pathogenic genus *Veillonella* [56, 57, 58, 59] in the gut of marathon runners [29, 35, 42]. Although Sheiman et al. observed an increase in *Veillonella* relative abundance in marathon runners post-marathon and isolated a strain of *Veillonella atypica* from stool samples. Inoculation of this strain into mice significantly increased exhaustive treadmill run time probably because *Veillonella* utilizes lactate as their sole carbon source [60].

Changes in Firmicutes and Bacteroidetes abundance in the gut

Firmicutes and *Bacteroidetes* are the two most abundant phyla that inhabit the human gut. According to some reports, these bacteria account for up to 90% of the gut microbiota [2, 61]. The *Firmicutes* family contains several thousand species of highly diverse bacteria. *Bacteroidetes* are involved in food digestion, signal transmission, gut environment control, and inhibiting the growth of undesirable microorganisms in the gut [2]; however, their high abundance is associated with poor microbiota with low diversity [2]. Although, as mentioned earlier in section 4.1, high alpha diversity is not always associated with a healthy gut [38]. Only three studies reported increased *Bacteroidetes* abundance after exercise [47, 49, 52]. Further, an increase in the *Firmicutes/Bacteroidetes* ratio is reported in six studies [16, 26, 29, 35, 36, 38], mainly among athletes. In recently reported studies, the increased ratio is associated with obesity [62, 63]. However, the increased ratio in this particular group of microbiota can be explained by efficient energy extraction from food [64, 65], which is necessary for heavy physical exertion.

Changes in SCFA producer abundance in the gut

Bacteria from the *Clostridium* genus are major SCFA producers. They are also involved in the pro-inflammatory immune response [66]. An increase in the relative abundance of *Clostridium* genus upon physical activity was reported in two studies: one by Jang et al. [27], who compared the gut microbiota of body builders with that in a control group; and the other by Langsetmo et al. [21] in a large sample of elderly individuals. Two other studies reported a reduction in the relative abundance of *Clostridium genus* upon exercise intervention [47, 48]. Further, one study reported a decrease in *Clostridium difficile* abundance upon exercise [51]. This bacterium is a major source of infectious diarrhea associated with toxin production in the host’s gastrointestinal tract [67, 68], especially in the elderly [69, 70, 71] and obese individuals [72, 73]. These observations suggest that moderate exercise has a positive effect on the abundance of *Clostridium* bacteria.

Another SCFA-producing bacterium whose relative abundance is affected by exercise is the genus *Feacalibacterium* and its representative *Feacalibacterium prausnitzii*. An increase in the population of *Feacalibacterium prausnitzii* was noted in relatively active individuals [15]. Also, the population of genus *Feacalibacterium* was compared after a moderate exercise intervention [47], and in athletes versus non-training subjects [26, 27]. A decrease in its abundance was observed in professional athletes upon extreme physical exertion [36, 38]. Numerous authors have pointed out the anti-inflammatory effect of *Feacalibacterium prausnitzii* [74, 75], as well as of the entire *Feacalibacterium* genus [76], by associating the abundance of these bacteria with the alpha diversity of microbiota [77]. Overall, the appraisal of available data suggests a positive effect of moderate exercise compared with that of extreme exercise.

Another SFCA producer is the genus *Roseburia* [78, 79]. An increase in *Rosuburia* genus and its representative *Roseburia hominis* abundance was noted in various studies when comparing an individual’s normal physical activity and upon physical exercise [15, 18, 37, 41]. A decrease in its abundance was only observed upon extreme physical exertion [38], confirming the previous observations of a negative effect of extreme exertion on the gut microbiota. Further, the enhanced population in the family of *Lachnospiraceae* or genus *Lachnospira* confirms the positive impact of moderate-intensity exercise on the gut microbiota [21, 22, 26, 36, 41, 47].

Another important SCFA producer is the genus *Coprococcus* [80, 81]. It is associated with positive outcomes in the treatment of inflammatory bowel disease [82] and a reduced risk of *Campylobacter* infection [83]. A marked increase or abundance of *Coprococcus* genus was observed in comparative studies of active vs. inactive individuals [15, 30]. Furthermore, Hampton–Marcell et al. [38] reported a decrease in the relative *Coprococcus* abundance with a decreased physical exercise in swimmers during the starting season. Interestingly enough, the *Coprococcus_2* abundance tripled in runners after running a half-marathon [40], indicating that even extreme physical exertion can have a positive influence on the gut microbiota.

Changes in the lactic acid producer abundance in the gut

When discussing the role of gut microbiota, the lactic acid-producing bacteria from the genus *Bifidobacterium* and *Lactobacillus*, which are widely used in probiotics [2], must be mentioned. Their positive impact on human health is well documented [84]. When administered as probiotics, they reduce hypercholesterolemia [85], improve the parameters of diabetes mellitus [86], and regulate local and systemic immune responses [87, 88]. Further, their decreased population has been reported in individuals with severe depression [89]. In the context of the effects of exercise, an increase in their abundance was observed in one exercise intervention study [46], and in comparative studies done in athletes and non-athletes [32, 33]. By contrast, a reduction in their abundance is reported in highly trained athletes [42].

Other types of bacteria

Exercise affects the abundance of species from the gram-negative *Prevotella* genus. An increased abundance of *Prevotella* was noticed when comparing athletes to non-athletes [29, 33]. Moreover, the higher abundecne of *Prevotella* was seen during a 3300-Km row in rowers [37]. When accompanied by a high abundance of *Bacteroides* and *Akkermansia muciniphila*, this bacterium is a marker of good intestinal health [61]. However, that was not the case in the above

studies. When not accompanied by a higher abundance of *Bacteroides* and *Akkermansia muciniphila*, *Prevotella* are thought to support pro-inflammatory processes [90], opportunistic infections, and diseases related to intestinal dysbiosis, and are proposed to be a marker of intestinal dysbiosis [91]. These reported observations appear to confirm the negative impact of physical activity on the gut microbiota of qualified athletes.

The *Ruminaceae* family has been linked to a reduced intestinal permeability in 102 women [92]. An increase in its abundance upon physical exercise has been noted in numerous studies [15, 26, 30, 33, 36, 39], both when considering different phenotypes and athletes, which indicates the positive effect of physical activity on these bacteria. Two important geniuses belong to this family: *Ruminococcus*, proposed by Hills et al. as a marker of intestinal dysbiosis [61]. *Ruminoccocus* genus and its representative were decreased in intervention studies [46] and during sport preparation [34]. The second genus that belongs *to Ruminaceae* family is *Oscillospira*, which is closely related to human health [91] and lean individuals [93, 94]. The abundance of *Oscillospira* positively correlates with microbial diversity, high-density lipoproteins, and sleep-time duration, and is inversely correlated with blood pressure, fasting glucose levels, triglycerides, and uric acid [92]. In addition, *Oscillospira* abundance is reduced in Crohn's disease and fatty liver disease. From the literature reviewed for the current systematic review, an increase in *Oscillospira* abundance in intervention studies was only reported by Taniguchi et al. [51].

Another bacterium, proposed as a new probiotic [95], is *Akkermansia muciniphila*, the main representative of the *Verrucomicrobia* phylum. Zhai et al. consider it as a marker of a healthy gut [96], which is associated with lean people [77]. Although, its low abundance is observed in obese individuals and diabetics [97, 98]. That may be because the presence of *A. muciniphila* is associated with improved fat oxidation [99, 100, 101]. An increased relative *A. muciniphila* abundance was reported in relatively active people [15, 33] and after exercise intervention *Verrucomibrobia, Verrucomicrobiaceae, Akkermansia* respond [49], confirming the notion that moderate-intensity exercise positively affects gut health.

Exercise or physical activity may represent a strong modulator of gut microbiota composition. Moreover, the gut-muscle communication in human pathophysiology may be bidirectional, with gut microbiota representing a "cross-road" among environment, and skeletal muscle [101]. The well-known positive health effects of exercise may be mediated by its beneficial modifications to the gut microbiota. However, when there is an exercise overload, these possible beneficial effects are overweighed by increased intestinal permeability and oxidative stress, promoting inflammation and a catabolic state that negatively impacts the functionality of skeletal muscle [102].

The main limitation of the current systematic review is the limited number of studies reported on this research topic. The available literature on the effects of exercise on gut microbiota is rather scanty, and only a small number of participants were analyzed in the articles included in this review. This aspect is especially evident for data on high-performance athletes.

Conclusion

In light of the presented evidence, we conclude that the level of physical activity modulates the population of intestinal microbiota. That was apparent in athletes compared to untrained individuals. Athletes harbor a more diverse intestinal microflora than nonathletes, but with a relatively reduced abundance of SCFA- and lactic acid-producing bacteria, which may indicate an adverse effect of intense exercise on the gut microbiota.

Based on the reviewed studies, moderate-intensity exercise does not affect the diversity of the gut microbiota but impacts its composition, with an increased abundance of SCFA and lactic acid producers, also increasing the relative abundance of *Akkermansia muciniphila* and *Oscillospira*. These observations confirm the positive impact of moderate exercise on the diversity and function of the intestinal microbiota.

Furthermore, the reviewed studies confirm the notion that intense physical activity may be detrimental to the intestinal microbiota. The exercise-induced gastrointestinal syndrome may be responsible for changes observed in the gut microbiota of athletes, and the effect of exercise on the gut microbiota appears to be much stronger than anticipated. On the other hand, moderate physical activity enhances the biodiversity and function of the microbiota. Nonetheless, this issue requires further research.

In the case of physical activity understood as an environmental issue affecting the intestinal microbiota, future research should focus on the impact of various types of activities, especially in the context of training load, intensity, or frequency of exercise. Such knowledge will allow us to design an effective intervention (diet supplementation or diet strategy) to keep the gut microbiota in large biodiversity and richness, especially under unfavorable gut conditions associated with intense or vigorous exercise.

List Of Abbreviations

SCFA: short-chain fatty acid

EBSCO: - Elton Bryson Stephens Company

PRISMA: - Preferred reporting items for systematic reviews and meta-analyses

OCEBM: - Oxford Centre for Evidence-Based Medicine

F/B: - Firmicutes/Bacteroidetes ratio

Observed OTUs: - Observed operational taxonomic unit

F: female,

M: male,

HR: heart rate,

RM: repetition maximum,

RTE: repetition time exercise,

BMI: body mass index,

RM: repetition maximum,

RTE: resistant training,

VO_2max: maximal oxygen consumption,

PCoA: Principal Coordinates Analysis.

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Table 5

Table 5 is available in the Supplementary Files section.

Figures

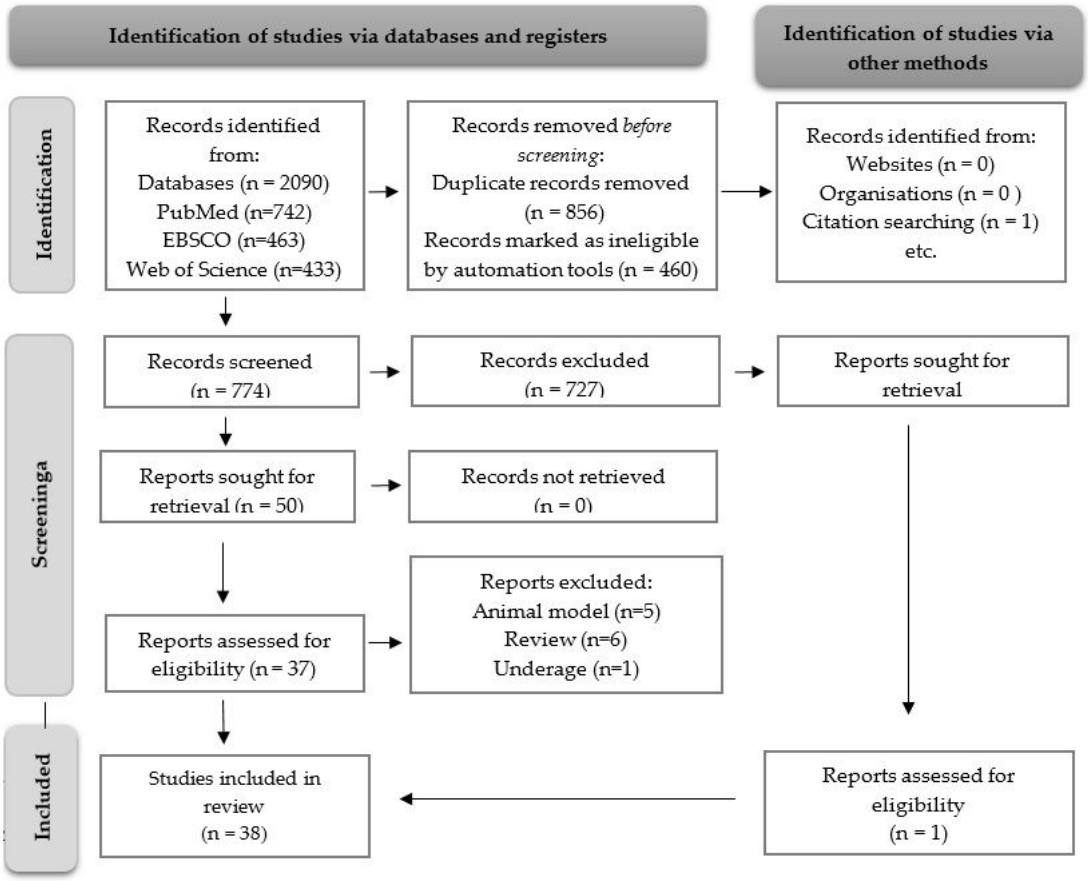

Figure 1

Profile of data extraction (the figure was made by the statement of PRISMA protocol [14])

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table5.docx
- PRISMA2020checklist.docx