

RELATIONSHIP BETWEEN GUT-MICROBIOTA AND SPORT ACTIVITY

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^A Study Design; ^B Data Collection; ^D Manuscript Preparation

Abstract *Aim:* The purpose of this umbrella review is to bring together the most recent reviews concerning the relationship between gut-microbiota and sport activity.

Materials and Methods: A literature search was conducted through PubMed and focused on reviews and systematic reviews published between 2015 and June 2021 that dealt with the topic of microbiota and physical activity. Only articles written in English and published in peer-reviewed journals were considered. Key words related to the term microbiota alone or in conjunction with other terms such as “supplements”, “diet”, “probiotics”, “prebiotics”, “health”, “physical activity”, and “pathogens” were analyzed. The selection process was done first by analyzing the titles, then the abstracts, and finally the full text.

Results: After screening the title and abstract, 29 articles were excluded. Therefore, 20 studies were included in the present umbrella review. The figure shows the steps of the selection process (Figure 1). The specifications of the presented articles are listed in Table 2.

Conclusions: Exercise appears to be an environmental factor that can determine changes in the gut microbial composition with possible benefits for the host. Increased microbiota diversity improves metabolic profile and immunological responses and may provide a possible biomarker for health improvement. Exercise altered microbiota could be used to look for new approaches in the treatment of metabolic and inflammatory diseases.

Key words: endurance; exercise; immune response; microbiota; nutrition; probiotics

Introduction

Microorganisms

A wide variety of microorganisms, such as bacteria, archaea, viruses, and fungus, make up the human body. The microbiota is the aggregate name for these organisms, which are found within and on the body, including the lungs, oral mucosa, uterus, and skin. The gastrointestinal tract, particularly the large intestine, where it is estimated that there are up to 100 trillion microorganisms, is a crucial area for the microbiota. The human gastrointestinal system is home to 10^{13} – 10^{14} microorganisms, and its genome, known as the “microbiome,” has a gene repertoire that is 150 times larger than that of the human genome. This microbiome is predominantly composed of two bacterial phyla, Bacteroidetes and Firmicutes, and it originates from 1,000–1,150 bacterial species, the majority of which are anaerobes. Early childhood is when the microbiome develops. Upon delivery, the baby’s gut is exposed to a complex environment and the mother’s microorganisms, which start to colonize the Gastrointestinal tract (GIT) and develop a first microbiome with a maternal signature. The microbiome has an adult-like profile and a robust microbial population by the age of one (Monda et al., 2017; Conlon et al., 2015; Palmer et al., 2007; Tannock et al., 2007; Nicholson et al., 2012).

An individual’s core of resident microbiota, which is largely dominated by gram-positive Firmicutes and gram-negative Bacteroidetes phyla from birth to roughly three years of age, is assembled, and the resulting composition is as distinctive as a pair of fingerprints. The gut microbiota seems to have a substantial role in influencing the immune system and is necessary for digesting dietary components. It should come as no surprise that clinical researchers and the general public are becoming more interested in how the gut microbiota affects host health and the onset of illness. From metabolic illnesses to certain brain-related dysfunctions, altered gut microbiota composition and activity are connected to a rising range of ailments (Heintz-Buschart et al., 2018; Goodrich et al., 2014).

Those who are known to be ill may vary dramatically from healthy people in terms of the makeup of their gut flora. A common variety and composition of the genes in the gut, however, may be a more accurate indicator of physiological conditions, according to recent studies. Moreover, there are cases that support the opposite, as new research has linked greater gut bacteria diversity to a prolonged colonic transit time and systemic circulation of potentially hazardous protein breakdown products.

Low compositional diversity predicts worse health, but high compositional diversity does not necessarily imply better health. In order to evaluate the health of the microbiome, compositional diversity alone is inadequate. Functional variety, however, may be a crucial element in ensuring an ecosystem’s continued proper operation from an ecological standpoint. Measures of biological variety are often included in analyses that make sense of massive data sets produced by these high-throughput sequencing methods (Poretzky et al., 2014; Janda et al. 2007).

Several research in this study assessed alpha diversity, which is a measure of the variety of a sample. Several criteria that determine alpha diversity take into account the quantity of distinctive operational taxonomic units—referred to as “richness”—and their relative abundance—referred to as “evenness.” Beta-diversity, a measurement of how diverse communities are between samples, is also often utilized. When considering the phylogeny of the samples, beta-diversity measures are quantitative; however, when just assessing the presence or absence of samples, they are qualitative. Metabolomics is recommended as a supplement to sequencing-based methods since it provides information on the metabolic interactions between the host, nutrition, exercise, and the gut flora. While technology have enabled a fast expansion of gut microbiota research, the differences in microbial analyses

across studies might make it challenging to compare and contrast study results (Marcobal et al., 2013; Zierer et al., 2018). In addition to these considerations, it is worth exploring the potential impact of various factors, such as antioxidants, proteins, BCAA and glutamine, vitamin D, L-carnitine, caffeine, and carbohydrate-electrolyte.

Functions of the Intestinal Microbiome

Many crucial roles for the host's health are played by the gut microbiota. The gut microbiota is crucial for the gastrointestinal tract's motility, enabling peristalsis, and it plays a role in the barrier's fortification and the preservation of its homeostasis. The microbiota also performs protective roles by competing with pathogens for nutrients and receptors and by producing antimicrobial compounds to prevent pathogen colonization. The gut microbiota affects the growth and operation of the mucosal immune system via producing ligands. With the identification of certain molecules known as pathogen-associated molecular patterns, the innate immune system may also distinguish potentially harmful bacteria. As a result, there is an increase in cytokine production and T-cell activation, both of which are essential for proper immunological responses to infections. Moreover, the microbiota plays a crucial role in metabolic processes. In addition to creating short chain fatty acids (SCFAs), the gut microbiota also produces glycan, amino acids, and vitamins, contributing to the metabolism of the host (Samuel et al. 2008; Akira et al., 2003; Messina et al., 2014; Rakoff-Nahoum et al., 2004).

Microbiota and Diseases

In order to maintain homeostasis and typical gut physiology, the gut microbiota is crucial. Many disorders, including obesity, coronary heart disease, diabetes, and inflammatory bowel disease, have been linked to altered microbiome composition. The influence of the microbiota has been recognized as a significant environmental component in recent years. Genetically obese mice demonstrate a substantial decrease in Bacteroidetes and an increase in Firmicutes (Wen L et al., 2008; BSP, The Gut Microbiota and Lipid Metabolism, 2006; Bäckhed et al., 2005). In humans, the fecal microbiota of obese people is different from that of lean controls in that it contains less Bacteroides and more Firmicutes. Alterations in the microbiota's composition are also linked to inflammatory bowel disease, a digestive condition that includes both Crohn's and ulcerative colitis. Bacteroidetes and Firmicutes, as well as a rise in Proteobacteria (Rajilić-Stojanović et al., 2011; Quigley, 2009; Mawdsley et al., 2007). Exercise and food both favorably affect gut flora in different ways (Miranda-Comas et al., 2022). These changes are related to changes in transit time, bile acid composition, the synthesis of short-chain fatty acids (SCFAs), Toll-Like Receptors (TLRs), and the activation of B and T cells (Przewłócka et al., 2020). Also, in people who engage in regular physical activity, levels of heat shock proteins are decreased, maintaining the integrity of the intestinal barrier. Moreover, physical activity stimulates the synthesis of many hormones that might alter immune system function. Contrarily, high-intensity exercise increases intestinal permeability, which results in the translocation of microbial products, activation of TLRs, activation of the NF-κB pathway, generation of pro-inflammatory cytokines, and the initiation of an inflammatory response (Mohr et al., 2020). Moreover, in a vicious cycle, pro-inflammatory cytokines increase intestinal permeability (Fakharian et al., 2022). High-intensity exercise may also result in transient immunodepression, transient leukocytosis, leucopenia, reduced cellular immune activity, phagocytosis, and salivary immunoglobulin (Ig) A production. High-intensity exercise, on the other hand, boosts humoral immunity and natural killer (NK) cytotoxic activity, lowers the number of B lymphocytes in mesenteric lymph nodes, and boosts the production of interferon (IFN). Moreover, there is a decrease in the tight junction gene's expression. During a rigorous training

program, a greater level of T helper (Th)-2 (anti-inflammatory) cytokines causes a higher level of upper respiratory tract infections (Ruiz-Iglesias et al., 2023).

Effects of Dietary Supplementation on Gut Microbiota Profiles: Can They Affect Performance?

In light of this, we shall explain and examine the supplements that have reportedly had an impact on the makeup of the microbiota as well as the consequences of such interactions for the practice of physical activity and sports (Close et al., 2016)

Tab. 1. Supplements with impact on microbiota

Strong evidence	Moderate or emerging evidence	Lack of evidence
Antioxidants(<i>polyphenols</i>)	BCAA	Creatine
Probiotics	L-Glutamine	Taurine
Proteins	Sodium -bicarbonate	Beta- alanine
	Vitamin D	Beetroot juice
	Omga-3 PUFAs (Polyunsaturated fatty acids)	Collagen
	CHO- electrolytes sport drinks	Glucosamine
	L-carnitine	Vitamin C
	Caffeine	

Antioxidants

The frequency with which the aforementioned events occur in athletes nowadays reflects the popularity of sports nutrition supplements containing antioxidants. Polyphenols, a large class of naturally occurring chemicals originating from plants that are often included in dietary supplements meant for use by athletes and are also known to interact with microbiota, are a key category of antioxidants. Supplemental polyphenols and foods high in polyphenols have been shown to modulate gut microbiota, promoting the growth of beneficial bacteria like *Lactobacilli* and *Bifidobacteria*. These “prebiotic-like” effects of polyphenols have been observed using both in vitro studies with human gut microbiota and in vivo in pre-clinical and clinical trials. Polyphenols also encourage the establishment of other advantageous species, such as *Roseburia* spp., *Faecalibacterium prausnitzii*, and *Akkermansia* *Akkermansia* (Ismail et al., 2012; Espín et al., 2017).

Due to the favorable interactions between polyphenols and gut microbiota outlined above, Marchesi et al. noted that these polyphenols, which normally stay inactive in the diet, undergo biotransformation to become active molecules once the gut bacteria removes the sugar moiety. These metabolites show improved gastrointestinal absorption and bioavailability while retaining the antioxidant and pleiotropic activities of original substances. Hence, flavonoids may more readily enter the circulation and exhibit their physiologically significant effects at the systemic level thanks to the biotransformation carried out by bacteria (Liu et al., 2014; Etxeberria et al., 2015; Anê et al., 2015).

Regarding these outcomes, the conventional perspective of the health advantages associated to food and herbal supplement polyphenol fractions should be turned towards their absorbable gut microbiota metabolites. Therefore, it may be concluded that the mutually beneficial interactions between microbiota and polyphenols may work together to provide favorable circumstances that assist athletes in their practice of sports (Manach et al., 2005; González-Sarrias et al., 2017).

Proteins

As athletes may support and enhance performance and, indirectly, overall health, there has been growing interest in them in recent years. As was previously mentioned, immunological disturbances brought on by rigorous training and competition enhance vulnerability to URTI, have an effect on the GI, and thus have a big influence on performance. Depending on variables including the kind of sport, athletes' training level, and the sort and length of supplementation, probiotics significantly lower susceptibility to URTI and minimize its occurrence, duration, or severity. Investigated, in a randomized, double-blinded, placebo-controlled experiment, the effects of a multi-species probiotic supplementation on indicators of the intestinal barrier, oxidation, and inflammation, both at rest and after strenuous activity (Williams, 2010; Mishra et al., 2015).

After 14 weeks of treatment, they discovered that zonulin, a measure of increased gut permeability, fell to the normal range. TNF and exercise-induced protein oxidation were also favorably impacted. Therefore, following prolonged exercise, probiotic administration may influence intestinal barrier function, redox balance, and low-grade inflammation. The impact of a multistrain probiotic, prebiotic, and antioxidant intervention on endotoxin unit levels and GI permeability in recreational athletes was studied for 12 weeks prior to a long-distance triathlon. Six days after the race, the pre/probiotic treatment dramatically decreased endotoxin levels, but only LAB4ANTI was beneficial before the race (Lin et al., 1999; West et al., 2011; Gleeson et al., 2011).

In mice given *Plantarum* TWK10 supplements for six weeks while engaging in strenuous activity, it has been shown to provide greater muscular hypertrophy, performance, and fatigue resistance. The probiotics dramatically increased glucose content and endurance performance, indicating that TWK10 may aid in energy harvest. The effects of *Veillonella* on athletic performance may point to a potential use of these strains as a supplement to enhance performance (Kaushik et al., 2009; Soares et al., 2019).

Recent studies have shown that taking supplements of *Saccharomyces boulardii* has positive effects on the host metabolism. The effect of *Sb* supplementation on the oxygen consumption rate, mechanical efficiency, and aerobic performance of Wistar rats engaged in exhausting, incremental-speed exercise was assessed by the authors in this research. They discovered that supplementary *Sb* dramatically raises VO₂ max and aerobic performance but has little effect on resting aerobic metabolism. *KF* may change the makeup of the gut microbiota and reduce plasma levels of lactate, ammonia, and creatine kinase, enhancing exercise capacity and reducing physical exhaustion in mice. A probiotic-mediated increase in mood status may indirectly and favorably influence athletes' circumstances since probiotics are known to induce an improvement of mood state and disorders, according to the research (Huang et al., 2012; O'Brien et al., 2015).

Bravo et al. have provided a thorough analysis of the processes through which microbiota might affect mood and, more broadly, CNS. Based on the frequency of animal research, several writers claimed positive benefits of gut microbiota health on mood disorders that affect performance, like as anxiety and depression, despite the fact that there are relatively few studies specifically addressing this topic. Gruenwald et al. (2002) investigated the similar-

anxiolytic effects of supplementing with *Lactobacillus helveticus* and *Bifidobacterium longum* on healthy human volunteers. The effects of a six-month administration of a probiotic multivitamin preparation in adults experiencing stress or exhaustion were studied (O'Brien et al., 2015; Zeppa et al., 2020; Hsu et al., 2018; Benton et al., 2007).

According to the scientists, a 30-day supplementation program encouraged positive psychological reactions. The probiotic was eaten by research participants for four weeks, and even though none of them had been diagnosed with a mood problem, this greatly lowered their cognitive sensitivity to depressive states. Overall, the findings of the few human and animal research studies suggest that probiotics may improve mood, especially in those who have a history of mood disorders. Moreover, studies have shown a link between stress levels and physical activity, with physical exercise typically having positive impacts on mood and affective state (Gruenewald et al., 2002; Rao et al., 2009; Thomas et al., 2016).

Proteins should be ingested periodically throughout the day, before and after performances, to provide an adequate supply of necessary amino acids, especially as training and competitions are becoming longer and more intense. Protein amount, quality, processing history, and source must all be taken into account in order to understand how proteins affect the composition and functioning of the gut microbiota. Different protein sources' amino acid compositions may have varied effects on the gut flora. According to certain research, plant proteins are superior to animal proteins in terms of value to the host's metabolism and the microbiota (Desbonnet et al., 2008; Lyte et al., 2006; Mills et al., 2019).

The *Bacteroides* enterotype has been connected to a large intake of animal protein. Both high-protein groups showed a drop in fecal butyrate, which raises the possibility that a high-protein diet has a negative impact on colon health. Due to greater protein breakdown by the gut microbiota, the two high-protein diets also enhanced the quantity of bacterial metabolites generated from amino acids. They looked at how recreational endurance athletes' gut microbiome changed after receiving protein supplements for 10 weeks. The effects of long-term high-protein supplement usage on intestinal microbiota and amino acid fermentation in recreational athletes and protein supplement users have not been further studied. It has been shown that microbial diversity positively correlates with protein consumption and activity in top athletes. Therefore, exercise training is crucial for maintaining a balanced and healthy gut microbiota as well as for maintaining muscle growth and function. These findings suggest that an adequate consumption of protein should promote both intestinal health and athletic performance. While athletes have higher physiological needs for protein in their meals, high-protein diets may have negative effects on the gut flora and levels of protein fermentation. Although dietary guidelines for protein intake in this group are greater than for the general population, effects of protein supplementation on microbiota in athletes should be taken into mind (Moreno-Pérez et al., 2018).

BCAA and Glutamine

According to recent research, adding BCAAs to the diet helps piglets' immune systems and boosts intestinal growth, enterocyte proliferation, intestinal absorption of amino acids, and glucose. By reversing the effects of high-fat meals, increasing intestinal levels of endocannabinoids that regulate inflammation, improving the intestinal barrier, and promoting the intestinal peptide production, the *Akkermansia* genus has been shown to improve metabolic diseases and insulin resistance. To understand the effects of BCAA supplementation on gut microbiota in humans, however, specialized investigations are required since the aforementioned findings were acquired in

animals. In skeletal muscle, human blood, and the free amino acid pool, glutamine is the most prevalent amino acid (Ren et al., 2015; Zhou et al., 2018; Yang et al., 2016).

De Souza et al. (De-Souza et al. 2005). examined the impact of oral L-glutamine consumption of 30 g per day for a brief time on the makeup of the gut microbiota in overweight and obese people, showing substantial reductions in the waist circumference, circulating LPS levels, and insulin levels in overweight and obese participants (Everard et al., 2013; L'huillier et al., 2019; Swidsinski et al., 2005; Perna et al., 2019).

Vitamin D, L-carnitine and caffeine

The regulation of calcium and phosphorus homeostasis and the enhancement of endocrine effects on bones, intestines, parathyroid glands, and kidneys are all made possible by vitamin D's important contribution to skeletal mineralization. Moreover, there is mounting evidence that vitamin D controls a variety of other cellular processes, and its potential effects on skeletal strength and muscle mass are receiving a lot of attention. The biological impacts of vitamin D on the metabolism, development, and operation of muscle cells may take many distinct forms. High oral vitamin D consumption in the upper gastrointestinal tract decreased proteobacteria and increased bacteria, according to an investigation conducted on healthy volunteers (Veldurthy et al., 2016; Zeppa et al., 2019).

L-carnitine-containing supplements are popular and commonly used by athletes to improve physical performance due to their role in mitochondrial fatty-acid oxidation and their capacity to hasten recovery after exercise. Carnitine may be absorbed by both the small and large intestines. The quantity of gut microorganisms' present may influence how rapidly carnitine is absorbed by the large intestine. In reality, a variety of intestinal microorganisms may inhibit the absorption of carnitine. The metabolic carnitine pathways may also be impacted by insufficient dietary fiber consumption, which is linked to a higher risk of atherosclerosis and cardiovascular diseases. The capacity of the colonic microbiota to ferment fiber is maintained in part by carnitine. In reality, L-carnitine may undergo gut microbiota-dependent transformations that lead to metabolites that encourage thrombosis and atherosclerosis; the severity of this shift varies on the food pattern, i.e., omnivorous > vegan/vegetarian diets (Fielding et al., 2018; Ghonimy et al., 2018).

Caffeine usage is common among athletes because of its supposed advantages for performance. It is well known that caffeine competes with adenosine to offset its negative effects on neurotransmission, excitation, and pain perception in the CNS (Le et al., 2019). Although there is a lot of knowledge regarding the biological and pharmacological effects of caffeine, which is often supplemented by athletes, little is known about how caffeine affects the gut flora. There are several common and practical ways to take caffeine since it may be found in food, drinks, extracts, and coffee. The possible effects of caffeine usage on the makeup of the gut microbiota have not been the subject of much investigation. For instance, Jaquet et al. (Jaquet et al., 2009) found that drinking three cups of coffee led to a rise in the variety of the supposedly healthful Bifidobacteria strains. Nevertheless, as the authors themselves recognize, there were certain limitations to this experiment, such as the absence of a control group and a placebo. Janssens et al. recently found that taking Green Team (GT) supplements for 12 weeks (equivalent to a daily dosage of 0.27/0.45 g caffeine) had no appreciable effect on the makeup of the gut microbiota. The evaluated characteristics of fecal bacterial diversity and community structure did not change significantly between the treatment (green tea or placebo) and the period (baseline and week 12). They came to the conclusion that taking supplements of GT rich in catechin and caffeine had no long-term effects on the composition of the gut microbiota in healthy, normal-weight, and overweight individuals (Janssens et al., 2016).

Carbohydrate-Electrolyte Sport Drinks

Sports drinks containing carbs are much better for endurance than non-caloric control drinks. Usually, electrolytes are connected to carbs in numerous ways (liquid, gel, or solid). However, some authors claim that these supplements may make gastrointestinal discomfort worse depending on the intestinal absorption, formulation, and co-presence of certain components. There are no studies that emphasize changes in the abundance of the different bacterial strains of intestinal flora in response to the various formulations, thus further study is needed to understand how carbohydrate (CHO)-sports drinks interact with microbiota (Abboud et al., 2019).

The Relationships between Microbiota and Exercise

Regardless of nutrition, exercise has a distinctive impact on the microbiota. Exercise alters gut microbiota in a variety of ways, including gut transit duration, bile acid profile alteration, SCFA generation through AMPK activation, Toll-Like Receptor signaling pathway regulation, immunoglobulin A levels, number of B and CD4+ T cells, and eventually weight reduction. The alterations in various bacterial taxa were strongly linked with body mass index in research that examined active and sedentary women under 40 following exercise training. Lean people had larger concentrations of species with recognized anti-inflammatory effects and the capacity to create SCFAs, even though the participants' microbiota composition altered for a while after exercise (Stilling et al., 2015; Mailinget al., 2019; Luo et al., 2014; Frosali et al. 2015; Francaux et al., 2009; Hagio et al., 2010; Campbell et al., 2016).

It has been discovered that athlete microbiomes have unique microbial compositions that may be identified by their high concentrations of Veillonellaceae, Bacteroidetes, Prevotella, Methanobrevibacter, and Akkermansia. Prevotella and Methanobrevibacter smithii abundance levels were much greater in professional cyclists than in amateur riders, and they were connected with the frequency of training. It has been shown that Prevotella abundance predicts weight reduction in overweight persons who follow a diet high in fiber and whole grains for six weeks, indicating that enterotype should be taken into account in individualized dietary strategies to combat obesity. Humans produce more SCFAs after exercise, especially butyrate, a crucial indicator of gut health. In contrast to their sedentary counterparts, women who exercised three hours or more per week had higher relative abundances of butyrate-producing taxa, particularly certain species like Faecalibacterium prausnitzii, Roseburia hominis, and Akkermansia muciniphila, as well as the Coprococcus genus. Several species have been linked to benefits to health. A. muciniphila has been found in high concentrations in the microbiota of athletes, whereas low concentrations have been associated with metabolic abnormalities in inflammatory bowel disease patients. Prausnitzii is healthy and has a good influence on lipid metabolism and intestinal function (Machiels et al., 2014; Derrien et al., 2017; Clarke et al. 2014; Scheiman et al., 2019).

The Coprococcus species, which produces butyrate, was more prevalent in active women, which may have contributed to some of the positive health benefits of exercise. In another investigation, butyrate-producing taxa were found to rise exclusively in thin people who underwent a six-week controlled endurance exercise program. The obese ones did not. Additionally, Faecalibacterium species increased in lean adults while decreasing in obese individuals, while Bacteroides species showed the reverse pattern, supporting the effect of BMI. After adjusting for BMI, diet, and age, it is interesting to note that the abundance of butyrate-producing taxa was higher in those who had better levels of aerobic fitness. Long-distance running as a form of exercise resulted in a considerable rise in the Coriobacteraceae family. This aldosterone metabolite performs a variety of vital tasks, including cell signaling,

energy and fuel storage, and maintenance of membrane integrity. By sustaining glycemia throughout time, these byproducts of microbial fermentation may also be utilized as energy sources in the liver and muscle cells to enhance endurance performance. It is important to emphasize once again that the composition of the human gut microbiota is comparatively stable over time, resilient to perturbations, and reverting fully or partly to the prior composition following stimulus termination. The resistance to perturbations suggests that beneficial adjustments in diet and exercise habits intended to have long-term impacts on the microbiome to be successful (Braune et al., 2016; Van Hall, 2010; Trovato et al., 2016).

The Link between Diet, Physical Activity, and Microbiota

In order to preserve an athlete's ability to exercise, it is crucial for them to consume enough carbs, lipids, and proteins as well as to maintain a healthy gut microbiota. Carbohydrates and their storage as glycogen have a definite significance in appropriate muscular function during both aerobic and anaerobic exercise since they are the main indirect energy source for skeletal muscles. It has been shown that a person's capacity to store carbohydrates as glycogen affects mitochondrial biogenesis and function and functions as a particular regulator for the signaling pathway involved in training tolerance. By the control of carbohydrates, intestinal bacteria also contribute to the preservation of exercise ability. They encourage the fermentation of carbohydrates in the colon to create short-chain fatty acids from partially digested food (Elliott-Sale et al., 2018; Spriet, 2014; Philp et al., 2012).

Moreover, a high fat diet may negatively impact the makeup of the gut microbiota, reducing the substrates available for the generation of SCFAs. Studies on animals have shown a rise in the number of bacteria that trigger the production of pro-inflammatory cytokines, raise plasma lipopolysaccharide levels, and boost NF- κ B expression, which is associated to activating pro-inflammatory genes. These bacteria may create sulfides, which weaken disulfide bonds in mucus and disassemble the goblet cell secreted MUC2 protein networks, which form gels. For maximum muscle response to training activities, which promotes hypertrophy and muscular strength, adequate protein intake is crucial. The number of protein-fermenting bacteria, such as *Clostridium*, *Desulfovibrio*, *Peptostreptococcus*, *Acidaminococcus*, *Veillonella*, *Propionibacterium*, *Bacillus*, *Bacteroides*, *Staphylococcus*, and other members of the Proteobacteria family, however, rises when protein consumption is high. Moreover, it has been linked to a decline in the population of bacteria that ferment carbohydrates, including *Bacteroides*, *Lactobacillus*, *Bifidobacterium*, *Prevotella*, *Ruminococcin*, *Roseburia*, and *Faecalibacterium*. The generation of byproducts including ammonia, biogenic amines, indole compounds, and phenols as a result of the fermentation of undigested protein residues in the colon poses a risk to the gut, metabolism, immune system, and neurological systems. These substances might enhance gastrointestinal symptoms, exacerbate the inflammatory response, and increase tissue permeability (den Hartigh, 2018; Shimizu et al., 2019; Gentile et al., 2018).

Increased carbohydrate intake, particularly non-digestible polysaccharides, which are the preferred substrate for gut bacteria, may counteract excessive protein consumption. High diversity and elevated levels of bacterial genes involved in protein and carbohydrate metabolism and SCFA synthesis have been linked to the microbiomes of different athletes. Also, studies on bikers revealed a correlation between exercise frequency and greater levels of microorganisms that metabolize carbohydrates. *Prevotella* Privately has also been shown to have a favorable impact on the metabolism of carbohydrates, lysine biosynthesis, alanine, aspartate, glutamate, and d-glutamine, as well as other amino acid metabolic pathways (den Hartigh, 2018; Barton Wet al., 2018; Mika et al., 2015; Chassardet

al., 2013; Churchward-Venne et al., 2012; Rinninella et al., 2019; Wu et al., 2011; Crawford et al., 2019; Burke et al., 2017).

More methane-producing bacteria from the *Methanobrevibacter smithii* family were found in high-performance athletes, and these bacteria were also linked to excessive energy generation and carbohydrate metabolism. Also, it seems that through controlling inflammation and influencing tryptophan metabolism, the ideal gut microbiota composition may benefit brain health and ward off sadness. As previously mentioned, excessive exercise may cause microecological imbalances by increasing intestinal barrier permeability, inducing intestinal ischemia, and elevating oxidative stress. As a result, inflammatory reactions are exacerbated, which increases catabolism and impairs muscular function.

The presence of more potentially hazardous bacteria, such as *Peptostreptococcus*, *Staphylococcus*, *Peptoniphilus*, *Acidaminococcus*, and *Fusobacterium*, as well as less anti-inflammatory species, such as *Bacteroides*, *Faecalibacterium*, *Collinsella*, and *Roseburia*, may also have negative consequences. They revealed an inverse correlation between lifestyle, skeletal muscle function, and gut microbiota composition. The production of ROS disrupts the components of muscle cell membranes, causing lipid and protein peroxidation and disrupting muscle function. As a result, oxidative stress is increased by both exercise overload and inactivity, as well as by immobility. (Churchward-Venne et al., 2012; Rinninella et al., 2019).

On the other hand, consistent exercise causes antioxidant enzymes to adapt, which raises the activity of catalase, glutathione peroxidase, and superoxide dismutase. Also, it lessens the harm done by free radicals and raises the antioxidant capacity and activity of the enzymes needed to repair ROS damage. They showed that individuals who engaged in leisure training had increased SOD and CAT activity as well as reduced ROS levels in their semen compared to sedentary participants or professional athletes. The decrease of oxidative stress may also be facilitated by the gut microbiota. They include the production of antioxidant enzymes, the reduction of inflammation brought on by the presence of pathogens or pro-inflammatory cytokines, and the control of metabolism through improved antioxidant absorption. According to certain research, SOD activity may be increased by bacteria such *Lactobacillus Plantarum*, *Lactobacillus gasseri*, *Lactobacillus fermentum*, *Lactococcus Lactis*, and *Streptococcus thermophilus*. Moreover, it has been shown that the *Lactobacillus*, *Lactococcus*, and *Bifidobacterium* genera increase intestine glutathione levels, which are essential for scavenging the hydroxyl radical. performed a study on athletes, demonstrating that the addition of the probiotic species *Lactobacillus rhamnosus* and *Lactobacillus paracasei* raised plasma antioxidant levels and reduced ROS production in response to high-intensity exercise (Martarelli et al., 2011; Spyropoulos et al., 2011; Qiao et al., 2013).

The precursor of metabolic syndromes: microbial dysbiosis and abnormal energy homeostasis

Obesity is caused by a persistent energy imbalance, genetic susceptibility, and inadequate physical exercise. Understanding the GIT microbiota has advanced significantly in recent years, pointing to its important intermediary function in energy balance. The gut microbiome's main jobs are to help the host by digesting food fibers and producing energy. Modifications in the GIT microbiota affect host metabolism and the effectiveness of digestion (Hassan et al., 2016; Grundlingh et al., 2011; Fothergill et al., 2016).

There is strong evidence to support the idea that sustained exercise improves energy balance and protects against a number of ORMDs. The mitochondrial biogenesis, muscle hypertrophy and angiogenesis, cardiovascular fitness, a more efficient energy supply chain, and activation of the HPA axis are the most important physiological

changes that happen in response to exercise. Energy balance is enhanced, and immune-inflammatory reactions are better controlled by the HPA axis. While they are not completely understood, the effects of exercise on GIT health have been a crucial area of focus in studies on cancer and metabolic diseases. Endurance exercise may alter GIT permeability, motility, immune-inflammatory and redox responses, as well as stool transit duration and consistency. These modifications in particular are somehow connected to the GIT microbiota. Also, it has been shown that specially created exercise therapy reduce GIT inflammatory illnesses by focusing on altering the metabolic profile and microbiome diversity. Several animal and human research have shown that physical activity has a favorable impact on the variety of the GIT microbiome. The microbial metabolic profile of the GIT and cardiorespiratory fitness have been linked by a number of writers to these variations in microbiome diversity. With less chemotaxis activity and improved microbial diversity, those with superior cardiorespiratory fitness also had lower levels of lipopolysaccharide production. The Clostridiales, Erysipelotrichaceae, Lachnospiraceae, and Roseburia families have a greater abundance of butyrate-producing bacteria, which may be the cause of the increase in microbial diversity and cardiorespiratory fitness in exercising patients. The most compelling evidence for the role of the microbiome in metabolic illnesses comes from research using gnotobiotic rats and probiotic/prebiotic treatment (Mika et al., 2015; Allen et al., 2018).

Gut permeability is related to these changes in the microbiota, metabolites, and inflammatory indicators under situations of physiological stress. Early-life exercise is more beneficial for improving the microbiota and creating stable lean body mass. Children with obesity often have a Firmicutes to Bacteroidetes ratio, which is known as an obesogenic characteristic and is characterized by microbiome enrichment with Firmicutes or depletion of Bacteroidetes. Moreover, an increase in bacteria that produce butyrate affects the metabolic pathways that cause fat formation and reduces obesity. Improvements in the production system for antioxidant enzymes, liver, muscle, and brown fat weight were all linked to an increase in exercise tolerance. Long-term exercise may enhance GIT microbial diversity, reducing the synthesis of the cytokines involved in tissue regeneration, even while the first reaction to severe exercise routines includes an increase in gut barrier permeability. Phylum of the Firmicutes supports a more favorable gut environment. Regular, moderate-intensity exercise enhances immune system performance and microbial diversity while lowering the risk of inflammatory illnesses (Evans et al., 2014; Welly et al. 2016; Petersen et al., 2017; Walsh et al., 2011).

The majority of published research examine exercise-induced microbiome alterations on a global scale, whereas just a small number identify particular taxonomic relationships between exercise and GIT microbiota. Yet, a few research on rodent activity have linked weight reduction to a rise in the Bacteroidetes /Firmicutes ratio. The Bacteroidetes /Firmicutes ratio is advantageous for metabolic health; however, conflicting evidence suggests that exercise-induced health advantages are associated with decreased Firmicutes populations and increased Firmicutes variety. The phylum Firmicutes members are particularly susceptible to alterations in the microbiome brought on by exercise. It is challenging to pinpoint certain bacterial genera that provide positive health effects or that cause systemic inflammation, however. The majority of the research we analyzed here found a correlation between changes in microbiome diversity and better health outcomes. Maybe the majority of these research reflect different taxonomic changes in the microbiome as a result of exercise, and they typically reveal more widespread alterations at the phylum level or in terms of alpha and beta diversity. To clarify host energy homeostasis in the manner and length of training that imprints good effects on the microbial population and its functional confinement, maybe further mechanistic research is needed. Future study on the effects of exercise on the microbiome should

aim to analyze immune-inflammatory pathways or neuroendocrine mediators in the gut and metabolic regions molecularly (Clarke et al. 2014; Matsumoto et al., 2008; Carbajo-Pescador et al., 2019).

The impact of exercise on microbiota diversity

Exercise-microbiota research are gaining popularity in the scientific community within a conceptual framework. The seminal study by Bäckhed et al., in which germ-free mice, as opposed to mice with gut microbiota, were protected against diet-induced obesity showing a persistently lean phenotype with increased levels of phosphorylated AMP-activated protein kinase in muscle and liver, was the study that first established the muscle-microbiota axis (Bäckhed, et al.(2005). A circulating lipoprotein lipase inhibitor that is generally inhibited in the gut epithelium by the microbiota, fasting-induced adipose factor, was not shown to protect GF mice against diet-induced obesity in the same research. The direct interaction of exercise therapies with intestinal microbiome and gut bacteria represented a further advancement. Mice colonized by several non-harmful bacteria had the highest potential for endurance, whereas GF mice performed worse during exercise than littermates with a single bacterial species. In that research, variations in the antioxidant system's activity were shown to have an impact on exercise performance. Exercise seems to be able to maintain the integrity and shape of the gut in obese mice even when they consume high fat diets, for example, by lowering inflammatory markers like cyclo-oxygenase 2 in both the proximal and distal gut. Exercise as the nexus between the immune system and the microbiota raises interesting concerns that might be tackled in exercise immunology. While this is happening, the breakdown of the epithelial barrier promotes the TLR-mediated detection of gut commensal bacteria. In this regard, a thorough examination of the dose-response relationship between levels of exercise and associated beneficial modifications in the microbial composition has not yet been undertaken. Aerobic and resistance exercise together may reduce pro-inflammatory cytokines and raise anti-inflammatory cytokines in T2D patients. Also, we have shown acceptable anti-inflammatory profiles in T1D patients who regularly engage in moderate aerobic activity (Samuel et al., 2008; Balducci et al., 2010; O'Sullivan et al., 2015; Hoffman-Goetz et al., 2008; Rodriguez-Miguel et al., 2014; Doyle et al., 2011; Hsu, et al., 2015).

Many animal models have shown that qualitative and quantitative changes in intestinal flora during exercise may affect immunity, the gut-brain axis, energy distribution, and nutrient absorption. The mice with one bacterium and the GF animals with the worst ones had the shortest times to weariness, whereas the whole microbiota group had the longest. Reduced amounts of SCFAs and other essential antioxidant enzymes for decreasing oxidative stress were seen in the absence of microbial colonization. As previously stated, SCFAs are one of the main byproducts of microbial fermentation. By influencing the immune system and lowering inflammation and oxidative stress, SCFAs help maintain intestinal energy homeostasis (Matsumoto et al., 2008; Cook et al., 2013).

Evans et al. found that voluntary wheel running reduced weight gain, changed the microbiota, and restored major-phylum levels in a model of high-fat diet-induced obesity. Voluntary wheel running prevented mice's gut microbial richness from changing after a two-day exposure to a polychlorinated biphenyl combination (Evans et al., 2014). A comprehensive microbial taxonomy was discovered via research into voluntary wheel- and forced treadmill exercise, perhaps linking it to gut immune cell homeostasis and microbiota-immune interactions (Choi et al., 2013; Queipo-Ortuño et al., 2013).

There is evidence that suggests exercise might help prevent the inflammatory insult that occurs in the stomach. The effects of high-intensity interval training on the microbiota of different gut segments in HFD fed mice were examined, and the results showed that exercise was unable to reverse the anxiety phenotypes dictated by

a high-fat diet. Segment-dependent modifications to the microbiota were made. In a model of human menopause, 11 weeks of voluntary wheel running that focused on low rather than high-aerobic capabilities changed the gut microbial populations in a distinct way. Age seems to affect how exercise affects gut microbiota. When exercise was started at a young age, it caused changes in the gut flora, which resulted in a leaner body mass compared to what exercise meant when it was done at an older age (Lin et al., 1999; Abboud et al., 2019; Stilling et al. 2015).

Many inflammatory disorders linked to insulin resistance, type 2 diabetes, and obesity have been linked to increased LPS translocation, which has been proposed as additional cause. LPS released from bacterial membranes may cause TLRs in the muscle to become active. TLR4 receptors caused persistent inflammation, obesity, insulin resistance, and muscular atrophy in LPS-injected rats. Despite receiving injections of LPS, voluntary wheel running increased insulin tolerance in mice fed the HFD (Frisard et al., 2010; Peppler et al. 2016).

The investigations of Hoffman-Goetz, in which exercise reduced TNF- and proinflammatory cytokine IL-17, discovered that intestinal immune response was positively controlled. In contrast, it raised the anti-inflammatory cytokine IL-10, catalase, and glutathione peroxidase. Balb/c mice with moderate activity had higher IgA levels in their duodenal lumen. Exercise may thus, to a certain degree, induce an ameliorated microbiota linked to variety, richness, and enhanced exercise performance. It is difficult to research the effects of exercise alone on the makeup and function of the human gut microbiota due to the dearth of sufficient numbers of well-planned and prospective controlled experiments. In fact, food interventions are a common part of research and are a significant confounding factor in changing the gut microbiota. Research on the microbiota involves a complex interaction that includes immunology and energy metabolism. Rugby players and low-BMI controls also showed higher proportions of *Akkermansia muciniphila*, which is indeed negatively correlated with BMI, obesity, and metabolic disorders, possibly because of improved gut barrier function. Furthermore, athletes' microbiota was more diverse than controls' in the Firmicutes phylum. Additionally, compared to controls, the top rugby players' microbial alterations were associated by stronger anti-inflammatory cytokines and lower inflammatory cytokines (Hoffman-Goetz et al., 2010; Hoffman-Goetz et al., 2009; Vilorio et al., 2011).

The effects of aerobic exercise and a low-carbohydrate diet on the microbiota of postmenopausal women and middle-aged pre-diabetic males with non-alcoholic fatty liver disease were studied for six months, and the results were followed up after six and twelve months. This strategy investigates the potential use of exercise-induced microbiome changes to prevent chronic illnesses. The body fat/muscle mass ratio of these women significantly correlated with a number of gut microbial populations. The researchers hypothesized that these results supported a program of exercise geared on ending sedentary habits while advantageously altering gut microbiome. 39 healthy individuals with various degrees of cardiorespiratory fitness were examined for fecal microbiota and fecal SCFAs after correcting BMI, diet, and age (Liu et al., 2014; Estaki et al., 2016; Bressa et al., 2017; Cerdáet al., 2016) confirmed the relationship between gut microbiota composition and cardiorespiratory fitness in 71 premenopausal women. Moreover, the gut microbial makeup of breast cancer survivors was significantly correlated with changes in cardiorespiratory fitness. The level of exercise intensity recommended in the different regimens is still up for debate. Yet, continuous vigorous exercise may change gut permeability, causing diarrhea, bacterial translocation into the bloodstream, gastrointestinal hemorrhage, and problems. Whereas moderate-intensity exercise lowers gut transit time (Yang et al., 2017; Paulsen et al., 2017).

Effect of An Acute Exercise Session on Human Microbiota and Health

A single acute session of moderate-intensity exercise has several health benefits (70 percent VO₂max). Some of these beneficial benefits of moderate exercise on the host may be mediated by decreased intestinal permeability, which prevents pathogens from penetrating the intestinal barrier and consequently decreases systemic inflammation. In addition, a short session of moderate-intensity exercise has a variety of effects on the microbiota. The variety of functions may be used to gauge the effect on the microbiota. Although -diversity examines the distribution of different bacterial species across different samples, -diversity denotes the overall variety of samples. The gut microbiota's response to a half-marathon in novice runners revealed that twenty bacterial clades were more prevalent than seven species (Cook et al., 2013; Zhao et al., 2018). The top four genus-level biomarkers that changed after the race were *Pseudobutyrvibrio*, *Coprococcus*, *Collinsella*, and *Mitsuokella*, whereas *Bacteroides coprophilus* was the bacterial group that shrank the most. However, during this research, there were no food questionnaires or Bristol scores that would have shown gastrointestinal discomfort or a change in colon transit time. When omics approaches like shotgun metagenomics and metabolomics were used, minor changes in the make-up and functions of gut microbial genes were seen after increased physical activity (Cronin et al., 2018).

Exercise sessions with a high VO₂max (>70%) have a favorable effect on health. The evidence that is now available suggests that these sessions seem to have a greater effect than moderate exercise on the human body's homeostasis. After a brief time of activity, elite athletes have been shown to have considerable levels of inflammation (Castell et al., 1996), as seen by an increase in blood and urine inflammatory markers. Top rugby players, however, had a reduced inflammatory state as compared to controls [higher interleukin-10 (IL-10) and IL-8; lower IL-6, tumor necrosis factor-alpha (TNF-alpha), and IL-1] (Jeukendrup et al., 2000; Karl et al. 2017).

For endurance athletes in particular, digestive problems are a worry. Research conducted during a long-distance triathlon indicates that LPS does enter the circulation after ultra-endurance exercise. Thus, LPS may be to blame for these athletes' increased cytokine response, which led to gastrointestinal issues as well as muscular injuries. 68 percent of the participants had mild endotoxemia (between 5 and 15 pg/mL; endotoxemia is evident when LPS concentrations are >5.0 pg/mL) after this race. Immediately after the race, a 27-fold increase in IL-6 production was seen in parallel. Even though there was no statistically significant correlation between LPS and IL-6 concentrations, these results imply that increased intestinal permeability may occur simultaneously with an elevated cytokine response and may therefore contribute to an increased inflammatory response after exercise. Similar to this, intestinal permeability and inflammation increased in a military training environment under several stresses, regardless of the diet group. It's interesting to note that the relative abundance of actinobacteria before the training session, changes in blood IL-6 levels, and variations in stool cysteine concentrations may be responsible for 84 percent of the variability seen in the adjustments to intestinal permeability. The permeability of the small intestine was also increased by exertional heat stress. Nevertheless, in the glucose- or energy-matched whey protein hydrolysate groups, this increase was smaller than in the water-consuming control group. While these changes have a detrimental impact on the host's health, the benefits of such a high exercise load much exceed the temporary drawbacks (Karl et al., 2017; Keohane et al., 2019).

During a four-day cross-country ski trip in a high-stress military training environment, the microbiota of the subjects showed improved diversity and changes in the relative abundance of more than 50% of detected taxa. It's interesting to note that while other, less dominant species increased in population, the dominating *Bacteroides* shrank. Changes in microbial diversity, abundance, and metabolic capacity (assessed using 16S rDNA,

metagenomics, and meta proteomics, respectively) were also noted in a study focusing on four well-trained male athletes competing in a high-intensity, unsupported 33-day, 5,000-km transoceanic rowing race. Microbial diversity increased throughout the ultra-endurance event along with an increased abundance of butyrate-producing species as well as others associated with. Moreover, the microbial genes specifically involved in the synthesis of amino and fatty acids were overrepresented. It is noteworthy that many of these changes in the make-up and functioning of microbial communities persisted over the 3-month follow-up. Hence, microbial diversity increased even during periods of high activity (Keohane et al., 2019).

Acute exercise effects on the human gut microbiota

We examined the fecal metabolites and microbiota in 20 amateur runners before and after a half-marathon using metabolomics and 16S rRNA sequencing studies. Running a half-marathon increased the genus level abundance of Coprococcus and Ruminococcus bicirculans while lowering the abundance of Ezakiella, Romboutsia, and Actinobacillus. To find the gut bacteria linked to athletic performance and recovery states, Boston Marathon runners and a group of inactive controls were recruited. Surprisingly, following a half-marathon run, the pentose phosphate route, a metabolic mechanism similar to glycolysis that involves glucose oxidation, was the most enriched pathway. Up to one week before and one week after the marathon event, daily fecal samples were collected and submitted to 16S ribosomal DNA sequencing. The relative Abundance of the bacteria species Veillonella, which increased after the marathon, was the microbiological parameter that had undergone the most significant change between the pre- and post-exercise stages. Moreover, runners exhibited a greater incidence of Veillonella compared to non-runners. The methylmalonyl-CoA pathway is used by Veillonella species to transform lactate into SCFA acetate and propionate (Dhillon et al., 2019).

As post-exercise relative taxonomic abundances of Veillonella increased, the same outcomes were obtained. The post-exercise metagenomic samples within the group showed an overrepresentation of the Veillonella methylmalonyl-CoA pathway. Veillonella functionally modifies the metabolic repertoire of the gut microbiota. It indicates that after exercise, both the genus Veillonella and the metabolic pathway followed by Veillonella species for lactate metabolism are enriched. By providing a new method of processing lactate, Veillonella colonization in the gut may enhance the Cori cycle by turning systemic lactate into SCFAs that rejoin circulation. Veillonella atypica was found in a sample of one of the aforementioned marathon runners' feces, and it was given to mice to infect them. In a pre-clinical crossover study, mice given Veillonella injections demonstrated substantial reductions in inflammatory cytokines after exercise and an improvement of 13% in the time to exhaustion in running tests when compared to controls.

They also had higher conversion rates from lactate to the SCFA propionate. It was shown that systemic lactate may enter the lumen of these animals' guts and function as a substrate for microbial SCFA conversion. By metabolically converting exercise-induced lactate into propionate, atypically extended run times were achieved, demonstrating an enzymatic pathway that is naturally encoded by the microbiota and enhances athletic performance (Rycroft et al., 2000).

Probiotics as a Potential Ergogenic Aid to Enhance Physical Performance

Nutritional ergogenic aids are dietary supplements that people use to assist them exercise, increase their capacity for exercise, improve their training adaptations, and speed up their recovery after exercise. Safe, well-

researched ergogenic food supplements may help an athlete's competitiveness even if they just slightly increase performance. The most researched probiotics are from the genera *Lactobacillus* or *Bifidobacterium*, and probiotics are made up of many other bacterial species. Probiotic administration may prevent unfavorable physiological changes that may be brought on by vigorous exercise, according to animal studies that have examined associations between probiotics and physical performance and possible mechanisms behind these activities (Maughan et al., 2018; Ünsal et al., 2018; Lollo et al., 2012).

Probiotics may enhance gut barrier characteristics, the antioxidant status, and decrease the inflammatory response in animals after strenuous exercise, according to pre-clinical investigations. It is unknown how these protective benefits relate to outcomes of physical performance, however. Conclusions should be cautiously made since there are still relatively few clinical studies on the relationship between probiotics and physical performance, and each research typically only involves a limited number of individuals and makes use of various exercise regimes. Probiotics must be living organisms in order to meet the term (Martinen et al., 2020; Appukutty et al., 2015; Coffey V et al., 2017).

Probiotics as way to impact the gut microbiome

“A preparation of or a product containing live, specific microorganisms in adequate numbers, which alter the microbiota (through implantation or colonization) in a compartment of the host and hence have positive health advantages; on this host” is what is meant by “probiotics.” Probiotics have long been used to treat digestive issues brought on by taking antibiotics, traveling, or becoming ill. Up until recently, the only benefits associated with consuming probiotics were immunological regulation and a strengthening of the gut mucosal barrier. The mechanisms included physical adherence to the intestinal mucosa that may outcompete a pathogen or prevent its activation, changes to the composition of the bacteria in the gut, the microbiota's modification of dietary proteins, adjustments to the ability of bacteria to produce enzymes, and influence on the permeability of the gut mucosa (Schrezenmeir, 2018; Fooks et al., 2002). A change in cytokine production or interactions with immune intestinal cells, especially in the upper region of the gut, where probiotics may temporarily prevail, are further effects. For regulatory reasons, probiotics are limited to a small number of bacterial strains, often those belonging to the genera *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces* for yeasts, as contrast to the hundreds of commensal species that make up the human gut microbiome. During the longest periods of time, *Lactobacillus acidophilus* and *Lactobacillus casei* Shirota have been the most often utilized bacterial strains. The most common probiotics found in today's commercial supplements are *Bifidobacterium* spp. and *Lactobacillus* spp. As there is now widespread agreement that probiotics' therapeutic benefits are strain-dependent, probiotic properties should be characterized not only at the species level but also at the strain level (Rowland et al., 2010; Holzapfel et al., 1998).

The effects of probiotics on gastrointestinal symptoms, inflammation, and oxidative stress have been studied in elite and competitive athletes. Men and females have differing impacts, and less study has been done on the latter group. The effects of probiotic supplementation on sports performance have not previously garnered considerable consideration. For instance, when tested on marathon runners, *Lactobacillus rhamnosus* strain ATCC 53103 had no effect on the frequency of GI symptom episodes, however the probiotic group's episodes were shorter overall. Professional cyclists who took the probiotic (*Lactobacillus fermentum* PCC) reported mild gastrointestinal symptoms more often and for longer on average (West et al., 2011).

Nevertheless, the severity of gastrointestinal illness considerably reduced as the mean training load increased in males. The burden of lower respiratory illness symptoms was significantly reduced in men but increased in women. In comparison to the control group, sprint athletes who consumed *Bifidobacterium bifidum* had significantly higher CD4 counts, IgA, IgM, lymphocyte, and monocyte percentages. Over a three-month period, *Lactobacillus helveticus* Lafti R L10 was supplemented with a population of top athletes (triathletes, bikers, and endurance athletes). The major markers of oxidative stress and antioxidant defense, such as malondialdehyde, advanced oxidation protein products, and superoxide dismutase, were lower in the probiotic group (Michalickova et al., 2018). The length of time that male runners could run before being worn out increased significantly when multi-strain probiotic supplementation was used. These probiotics included *Bifidobacterium lactis*, *Bifidobacterium breve*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus casei*, *Lactobacillus Plantarum*, *Lactobacillus fermentum*, and in addition, probiotic supplementation reduced intestinal permeability and mild to severe gastrointestinal discomfort (Pugh et al., 2019).

A 28-day probiotic supplementation period prior to a marathon race with *Lactobacillus acidophilus* (CUL60 and CUL21), *Bifidobacterium bifidum* (CUL20), and *Bifidobacterium animalis* subs p. *lactis* (CUL34) probiotics was linked to significantly lower incidence and severity of GI symptoms as well as a slight decrease in average speed in the probiotics group as compared to the control group. Nonetheless, there were no noticeably different completion times amongst the groups. Probiotic supplementation (*Streptococcus thermophilus* FP4 and *Bifidobacterium breve* BR03) was reported to likely improve isometric average peak torque production, attenuating performance declines and muscle tension in the days after a muscle-damaging exercise where subjects performed five sets of 10 maximal eccentric contractions (Jäger et al., 2016).

Similar studies have shown that *Bacillus coagulans* GBI-30 6086 significantly accelerated recovery 24 and 72 hours after exercise and decreased pain. Probiotic supplementation was linked to both performance maintenance and a small increase in creatine phosphokinase. Also, female college soccer and volleyball players' post-workout diet and intake of *Bacillus subtilis* during off-season training had no effect on their physical performance. The probiotic group, however, had much lower body fat percentages. These results show that probiotics may improve oxidative or inflammatory markers but have no discernible effect on performance. Recent research employing mice performance models and potential next generation probiotics, however, has shown encouraging results. The microbiomes of elite athletes who were exercising were where these probiotics were first found. Bacteria in the *Veillonella* genus break down lactic acid and produce propionate, which might increase endurance (Scheiman et al., 2019).

Prebiotics and Probiotics in exercise immunology

In terms of innate immune function, probiotics have been shown to enhance the phagocytic capacity of peripheral blood polymorphonuclear cells and monocytes as well as NK cells' cytotoxic activity. Acquired immunity also seems to have improved following probiotic supplementation, with significantly higher specific IgG, IgA, and IgM immunoglobulin levels. Local immunity is modified through enhanced intestinal barrier performance and enhanced local immune response. One of the important therapeutic implications of our in vitro studies is that specific probiotic strains reduce the prevalence of upper respiratory tract infections in both infants and adults (Haywood et al., 2014).

Despite the paucity of data on supplementation in athletes, it seems that this population might benefit from routine probiotic use. This is particularly intriguing since sustained, intense exertion may predispose athletes to

URTI. These beneficial effects occurred without any observable changes in the salivary levels of interleukin-4, -12, or IgA. The same sorts of effects, such as reduced respiratory illness, use of cold and flu drugs, and severity of gastrointestinal symptoms at higher training loads, were shown in male professional cyclists who took probiotics (Hughes et al., 2011).

It's intriguing that the researchers discovered a reduction in exercise-induced immunological disruptions, and it's possible that both pro- and anti-inflammatory cytokines were responsible for these outcomes. Two other trials on physically active persons and elite rugby union players found that probiotic supplementation had a beneficial effect on URTI incidence, but not severity or duration. Salivary IgA had positive outcomes in the experiment with persons who were physically active. In a different study, healthy volunteers going abroad had much less frequent and prolonged diarrhea when given 5.5 g/day of GOS supplementation. Lower levels of C-reactive protein have also been seen with FOS administration. More research should be done to see if these results are applicable to top athletes as preventative measures and rehabilitation tools (Cani et al., 2009; Tzounis et al., 2011).

Conclusion

The role of the gut microbiota in determining host health and disease development has been gaining clinical interest. Altered gut microbiota composition and function is linked to a growing number of conditions from metabolic disorders to some brain-related dysfunctions. The gut microbiota is also essential for processing dietary components and appears to have a significant role in shaping the immune system. The gut microbiota plays various vital functions in the host's health. Several diseases have been associated with altered microbiota composition. Metabolomics provides a 'functional' readout of the microbiome providing data on the metabolic interplay between the host, diet, exercise, and the gut microbiota. Gut microbiota is positively modified by physical exercise, independently of diet. Alterations in microbiota is also related to nutrient that has been consumed which can impact physical performance.

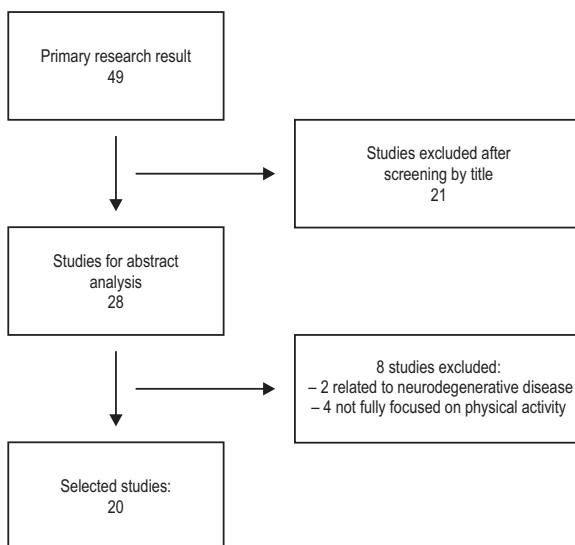


Fig. 1. Selection criteria for the analyzed papers

Table 2. Characteristics of included studies

Titles	Author	Years	Finding(s)
Crosstalk between gut	Luiz Fernando Freire Royes	2020	Exercise promotes microbial diversity and the preservation of an intact mucin layer and intestinal barrier in a healthy gut-brain axis. Contrarily, intestinal permeability, a rise in LPS, and the generation of cytokines are brought on by gut dysbiosis brought on by a hyperresponsive HPA axis during demanding (stressful) exercise.
Endurance exercise and gut microbiota: A review	Núria Mach a,b, *, Dolors Fuster-Botella	2016	The present research provides a comprehensive review of the gut microbiota's possible importance in controlling oxidative stress and inflammatory reactions, boosting metabolism, and increasing energy expenditure during severe exercise.
Review Article Exercise Modifies the Gut Microbiota with Positive Health Effects	Vincenzo Monda, Ines Villano, Antonietta Messina, Anna Valenzano, Teresa Esposito, Fiorenzo Moscatelli, Andrea Viggiano, Giuseppe Cibelli, Sergio Chieffi, Marcelino Monda, and Giovanni Messina	2017	Exercise may be used as a remedy to preserve the microflora's balance or to correct his future dysbiosis, resulting in an improvement in the patient's health. To completely comprehend the processes governing the changes in the microbiota's composition and capabilities brought on by exercise, further research is required.
Upper Respiratory Symptoms, Gut Health and Mucosal Immunity in Athletes	Candice Colbey • Amanda J. Cox • David B. Pyne• Ping Zhang • Allan W. Cripps • Nicholas P. West	2018	The respiratory system's equilibrium is significantly influenced by the oral microbiota (URS). According to authors, a greater knowledge of this link will result in improved diet and training methods to enhance gut and immune function and lessen the effects of URS on athletes.
Exploring the relationship between gut microbiota and exercise: short-chain fatty acids and their role in metabolism	Ryan A Carey, Doreen Montag	2021	SCFA have been found, and they may have a physiological role in how well you exercise.
the microbiota: an exercise immunology perspective	stéphane Bermon, Bernardo Petriz, alma Kajėnienė, Jonato Prestes, lindy castell, Octavio I. Franco	2015	Exercise may likely have a good impact on the gut microbiota, which is closely linked to the immune system.
Exercise and immune system as modulators of intestinal microbiome: implications for the gut-muscle axis hypothesis	Andrea Ticinesi, Fulvio Lauretani, Claudio Tana, Antonio Nouvenne, Erminia Ridolo, Tiziana Meschi	2019	The balance that comes from the relationship between the intestinal microbiota and immunology may have a substantial influence on the functioning of the gut-muscle axis and the health of the muscles.
Exercise influence on the microbiome–gut–brain axis	Alyssa Dalton, Christine Mermier & Micah Zuhl	2019	It has been shown that exercise increases the stomach and brain's synthesis of probiotics. <i>Firmicutes</i> and Actinobacteria, which include the genera <i>Lactobacillus</i> and <i>Bifidobacterium</i> , are the two primary phyla that have been identified as responding to exercise.
Interplay Between Exercise and Gut Microbiome in the Context of Human Health and Performance	Matthieu Clauss, Philippe Gérard1, Alexis Mosca and Marion Leclerc	2021	In endurance sports, the length and intensity of the activity have an impact on the microbiota. Reductions in inflammation and gastrointestinal symptoms may result from changes in the variety and composition of the gut microbiota.
Effect of Probiotics Supplementations on Health Status of Athletes	Bhagavathi Sundaram Sivamaruthi , Periyannaina Kesika and Chaiyavat Chaiyasut	2019	Athletes are advised to use probiotic supplements to maintain or enhance their health state and combat disease. Several strains or mixtures show protective effect against GI and URTI symptoms. The positive impact of uncommon probiotic strains in the context of sports has to be further investigated.

Titles	Author	Years	Finding(s)
Mutual Interactions among Exercise, Sport Supplements and Microbiota	Sabrina Donati Zeppa, Deborah Agostini , Marco Gervasi , Giosuè Annibalini , Stefano Amatori , Fabio Ferrini, Davide Sisti, Giovanni Piccoli, Elena Barbieri , Piero Sestili and Vilberto Stocchi	2019	Exercise type, timing, and intensity may all affect the gut microbiota's makeup. The metabolism and distribution of nutrients, hormones, and vitamins necessary to support exercise are regulated by the gut bacteria. By creating useful metabolites like the antioxidant bioactive compounds, some gut bacterial species might benefit athletes.
Gut-Muscle Axis Exists and May Affect Skeletal Muscle Adaptation to Training	Katarzyna Przewłócka , Marcin Folwarski , Karolina Kaźmierczak-Siedlecka , Karolina Skonieczna-Zydecka and Jan Jacek Kaczor	2020	Dysbiosis may impair physiological adaptability, increase the production of inflammatory markers and ROS, as well as the destruction of free radical macromolecules, all of which contribute to the atrophy of skeletal muscle. The key mechanism(s) through which the microbiota effect training adaptation are thought to be the modulation of the immune response, oxidative stress, metabolic processes, and nutrients bioavailability.
Gut Microbiota, Probiotics and Physical Performance in Athletes and Physically Active Individuals	Maija Marttinen , Reeta Ala-Jaakkola, Arja Laitila and Markus J. Lehtinen	2020	Probiotic-rich diets may increase the frequency of successful races and healthy training days while also reducing physiological reactions during recuperation periods after exercise. Probiotics may also help athletes perform better by facilitating training adaptations and increasing post-exercise mood and mental responses.
The athletic gut microbiota	Alex E. Mohr1, Ralf Jäger , Katie C. Carpenter , Chad M. Kerksick , Martin Purpura , Jeremy R. Townsend , Nicholas P. West , Katherine Black , Michael Gleeson , David B. Pyne , Shawn D. Wells, Shawn M. Arent, Richard B. Kreider, Bill I. Campbell, Laurent Bannock, Jonathan Scheiman, Craig J. Wissent, Marco Pane, Douglas S. Kalman, Jamie N. Pugh, Carmen P. Ortega-Santos1 , Jessica A. ter Haar, Paul J. Arciero and Jose Antonio	2020	Exercise, accompanying nutritional parameters, and body composition promote a more "health-associated" gut microbiota. Yet, in sedentary individuals, exercise seems to have a favorable impact on the composition and metabolic capacity of the human gut microbiota.
Exercise has the guts: How physical activity may positively modulate gut microbiota in chronic and immune-based diseases	Roberto Codellaa, Livio Luzi , Ileana Terruzzi	2017	Indicators of the gut's health, such as taxonomic richness and diversity, are connected with cardiorespiratory fitness. Physical exercise has the potential to boost gut microbial diversity via a number of mechanisms, including the promotion of an anti-inflammatory state.
Protein Supplements and Their Relationship with Nutrition, Microbiota Composition and Health: Is More Protein Always Better for Sportspeople?	Anna Kárlund 1, Carlos Gómez-Gallego 1 , Anu M. Turpeinen , Outi-Maaria Palo-oja , Hani El-Nezami and Marjukka Kolehmainen	2019	The information is fairly ambiguous and inconsistent when it comes to the function of dietary protein and supplements in the nutrition of sedentary and recreational athletes. Compared to a low-protein diet, high-protein meals cause more protein-derived substances to pass through the large intestine. The colon is where most bacterial amino acid metabolism occurs, which has an impact on the host's metabolism and overall system.
Aging, Gut Microbiota and Metabolic Diseases: Management through Physical Exercise and Nutritional Interventions	María Juárez-Fernández , David Porras , María Victoria García-Mediavilla , Sara Román-Sagüillo , Javier González-Gallego , Esther Nistal and Sonia Sánchez-Campos	2020	A variety of physiological and pathological processes involve the gut microbiome. Its potential as a therapeutic target stem from its function in obesity and other metabolic illnesses. Strategies to alter gut microbiota in the elderly may have a dual goal of reshaping the microbial communities linked to aging and combating intestinal dysbiosis brought on by metabolic disorders.

Titles	Author	Years	Finding(s)
Impact of Physical Exercise on Gut Microbiome, Inflammation, and the Pathobiology of Metabolic Disorders	Muhammad U. Sohail ¹ , Hadi M. Yassine, Aaqib Sohail, and Asmaa A. Al Thani	2019	The findings discussed here offer a chance to investigate fresh methods for preventing metabolic diseases in extremely lethargic individuals who are unable to exercise voluntarily to manage their weight. They also offer a plausible microbiome basis for exercise-induced prevention of metabolic diseases. Although while the bulk of the beneficial health impacts are unrelated to interactions between the microbiome and the host, there is evidence to indicate that some of the benefits may be mediated by variations in gut bacteria brought on by exercise.
Physical exercise, gut, gut microbiota, and atherosclerotic cardiovascular diseases	Jingyuan Chen, Yuan Guo, Yajun Gui and Danyan Xu	2018	SCFA butyrate may be one of the mechanisms by which physical activity promotes health because it has the ability to inhibit histone deacetylases and as a result affects gene regulation, immune modulation, intestinal barrier regulation, oxidative stress reduction, diarrhea control, visceral sensitivity, and intestinal motility modulation.
Role of exercise in preventing and restoring gut dysbiosis in patients with inflammatory bowel diseases: A review	Tilemachos Koutouras, Anastassios Philippou, George Kolios, Michael Koutsilieris, Maria Gazouli	2021	The results of this analysis suggest that studying the effects of exercise on the microbiome in IBD represents a viable area of study. The question of whether the microbiota participates actively or passively in the systemic changes brought on by exercise has to be clarified.

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