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Microbial Champions: The Influence of Gut Microbiota on Athletic Performance via the Gut-Brain Axis

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Abstract: In recent years, exercise has shown a powerful ability to regulate the gut microbiota received with concern. For instance, compared with the sedentary group, high-level athletes showed a different gut microbiota composition and remarkable capability of physiological metabolism. In addition, different diet patterns (*eg*, high-fat diet, high carbohydrate diet *et.al*) have different effects on gut microbiota, which can also affect exercise performance. Furthermore, adaptations to exercise also might be influenced by the gut microbiota, due to its important role in the transformation and expenditure of energy obtained from the diet. Therefore, appropriate dietary supplementation is important during exercise. And exploring the mechanisms by which dietary supplements affect exercise performance by modulating gut microbiota is of considerable interest to athletes wishing to achieve health and athletic performance. In this narrative review, the relationship between gut microbiota, dietary supplements, training adaptations and performance is discussed as follows. (i) The effects of the three main nutritional supplements on gut microbiota and athlete fitness. (ii) Strategies for dietary supplements and how they exerted function through gut microbiota alteration based on the gut-brain axis. (iii) Why dietary supplement interventions on gut microbiota should be tailored to different types of exercise. Our work integrates these factors to elucidate how specific nutritional supplements can modulate gut microbiota composition and, consequently, influence training adaptations and performance outcomes, unlike previous literature that often focuses solely on the effects of exercise or diet independently. And provides a comprehensive framework for athletes seeking to optimize their health and performance through a microbiota-centric approach.

Keywords: gut microbiota, nutrition, exercise, gut-brain axis, metabolism, athlete performance

Introduction

The gut is a niche inhabited by the human microbiota, with the largest number of bacteria and the greatest number of species. Consistent with the function of the digestive system, the gut microbiota (GM) harbors an enormous metabolic capacity and helps to absorb and transform the nutrients. The GM alteration has a strong association with human health status, for example, colorectal cancer patients showed a lower diversity of GM.[1] Lots of factors could shape the GM, such as birth mode, antibiotic use, and nutrient intake. Besides, a great diversity of metabolic ways can affect the GM, which results in highly dynamic and individualized shapes of the gut ecosystem, such as absorption of short-chain fatty acids (SCFAs), vitamin synthesis, energy harvesting, inflammatory regulation, and host immune response.[2,3]

The nutrients are many and various, different nutrients that have a different effect on GM. For instance, researchers reported that rats fed a high-energy dense diet rapidly altered their GM with increases in *Firmicutes/Bacteroidetes* ratio and the abundance of pro-inflammatory *Proteobacteria* compared to those consuming a low-energy diet.[4] Moreover, poor nutrition and a sedentary lifestyle are linked to a high incidence of chronic metabolic diseases,[5] while exercise plays

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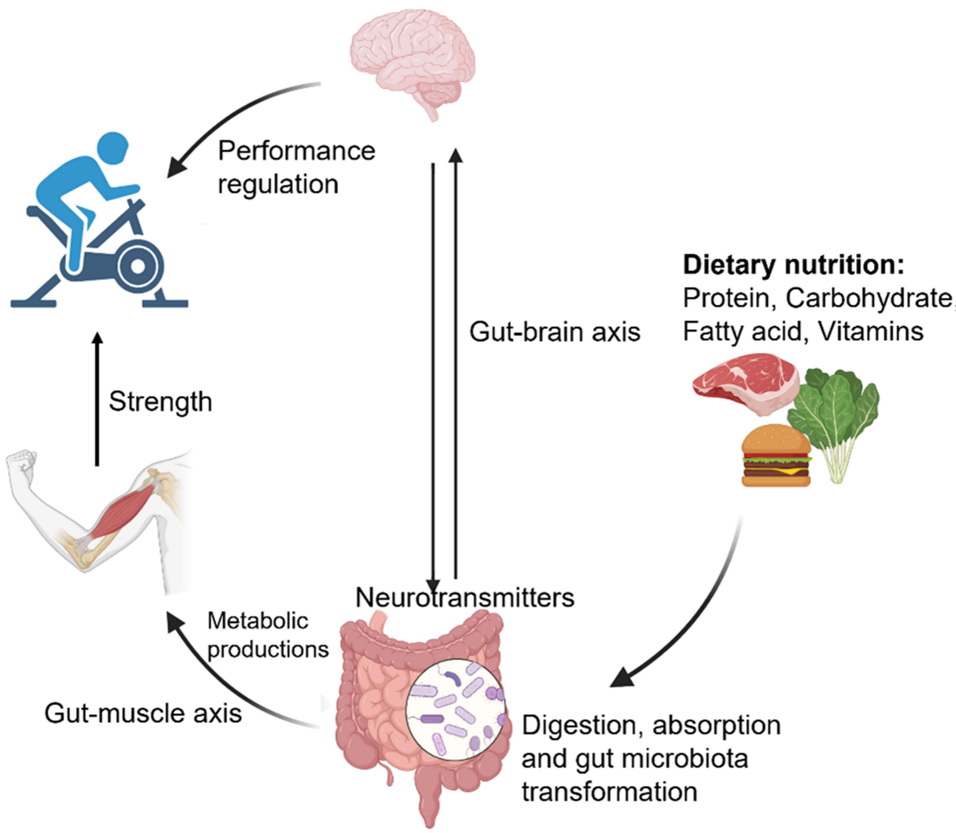
Graphical Abstract



a fundamental role in preventing and treating these pathologies.[6] Interestingly, studies also reported that the manipulation of GM and its by-products through exercise prescription might represent a promising novel approach in preventing and treating metabolic pathological conditions.[7,8] Nowadays, one conception is that the GM acts like an endocrine organ, sensitive to changes in homeostasis and physiology associated with training. Exercise alone also causes large-scale changes in GM, which then increases cognitive capacity and provides some relief from symptoms in some disease models.[9] In addition, a view that exercise promotes and helps maintain a healthy GM has gained momentum in recent years.[10] Furthermore, reports demonstrated regular exercise is associated with higher biodiversity and the beneficial function of GM, and the GM may thus represent a mediator of the exercise-induced health benefits.[11]

As a particular group, athletes significantly demand nutrition and exercise to pursue excellence. Hence, metabolic adaptations (including muscular strength and/or power, aerobic capacity, energy expenditure, and heat production) as well as the ability of the GM to absorb nutrients and regulate the immune system, are therefore particularly important at this juncture. In this process, GM exerted an important effect on athletic performance. For instance, researchers observed an increase in *Veillonella* relative abundance in marathon runners postmarathon, and the *Veillonella* methylmalonyl-CoA pathway is overrepresented. As a result, *Veillonella* species metabolize lactate into acetate and propionate via the methylmalonyl-CoA pathway, which acts to promote exercise performance.[12] Intriguingly, there is a high relevance between physical stress and changes in GM composition during exercise, specific microbiomes can correct various adverse events caused by strenuous exercise practice, which is associated with gastrointestinal discomfort, and training to exhaustion can also be associated with dysbiosis of the GM.[11,13,14] Besides, acting as the mediator in the gut-brain axis, GM plays a critical role in this bi-directional and integrated system (Figure 1). It can help to secret neurotransmitters and

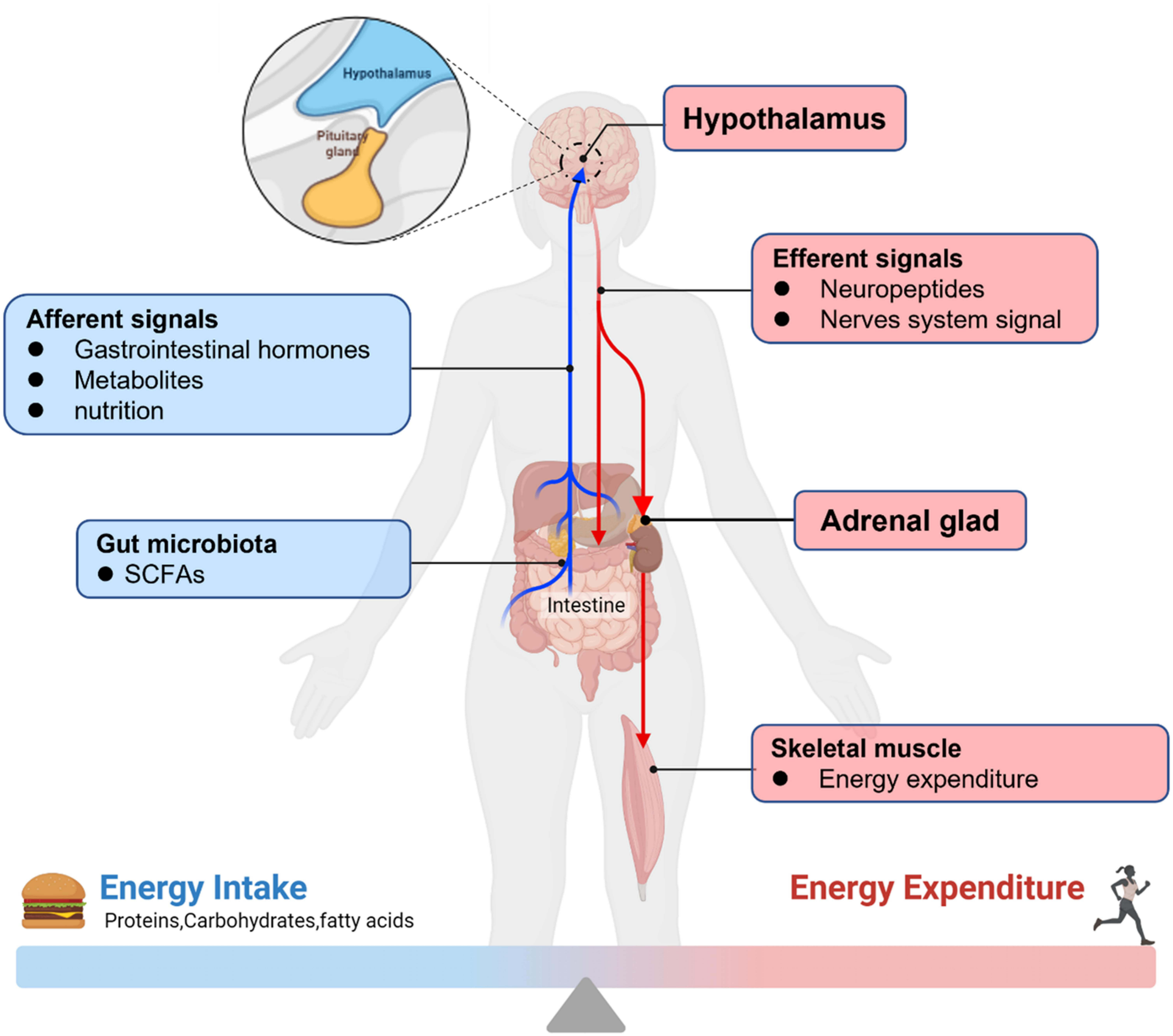


Figure 1 The mechanism of the gut-brain axis. Dietary nutrients are absorbed in the intestinal tract and interact with gut microbiota (GM) to synthesize neurotransmitters, which reach the central nervous system through the vagus afferent nerve. Neurons in the paraventricular nucleus of the hypothalamus secrete corticotropin-releasing hormone (CRH), which stimulates the anterior pituitary gland to release adrenocorticotropic hormone (ACTH). ACTH, in turn, prompts the adrenal cortex to synthesize glucocorticoids, which act on the skeletal muscle system via the vagus efferent nerve, participating in and enhancing the storage and utilization of skeletal muscle energy.

then through the hypothalamic-pituitary-adrenal (HPA) axis to maintain health and alleviate exercise depletion and oxidation.[15]

While moderate exercise generally benefits gut health, very intense or prolonged physical exertion can disrupt the delicate balance of the gut microbiota, potentially leading to dysbiosis[16]. This disruption may manifest as an increase in pro-inflammatory bacteria, a decrease in beneficial species, or both. For example, strenuous exercise has been linked to elevated levels of bacteria from the Enterobacteriaceae family, such as Escherichia coli and Salmonella. These bacteria are known to produce lipopolysaccharide, a potent endotoxin that can trigger systemic inflammation when it crosses a compromised gut barrier.[17] Additionally, intense exercise may increase the abundance of *Desulfovibrio* species, which produce hydrogen sulfide, another pro-inflammatory compound.[18] Several factors contribute to this phenomenon. During intense exercise, blood flow to the gut is reduced as it's redirected to working muscles. This can lead to intestinal hypoxia and increased intestinal permeability, potentially allowing harmful bacteria to cross the gut barrier and trigger inflammation.[19] And the physiological stress of intense exercise can alter gut motility and hormone production, further impacting microbial balance.[14] This exercise-induced gut dysbiosis has been linked to gastrointestinal symptoms often experienced by athletes, such as cramping, bloating, and diarrhea, and may even impair recovery and performance in the long run. Thus, optimizing gut health through diet, supplements, and appropriate training load is crucial for athletes and active individuals to maintain muscle function, minimize inflammation, and support efficient recovery.

To compensate for athletes' increased energy consumption and maximize their adaptation to physical loads, they must adopt adequate dietary habits and nutritional supplements. Thus, we need to analyze the effects of mutual interactions between exercise, nutrient supplements, and GM on the overall general health and athletic performance to help them gain scientific guidance.

This narrative review offers new insights into the intricate interplay between gut microbiota, dietary supplementation, and athletic performance, emphasizing the role of the gut-brain axis. And moves beyond simply describing the impact of gut microbiota on muscle function. Instead, we delve into the crucial interplay between dietary supplements, training adaptations, and athletic performance, all mediated through the lens of the gut microbiome. By systematically exploring the impact of key dietary supplements on gut microbiota and outlining tailored strategies for their application based on exercise type, this review provides practical insights for athletes and practitioners seeking to optimize performance through targeted nutritional strategies.

The GM of Athlete Differs from Other Population

Since GM has a potential effect on performance-enhancing and in turn the exercise facilitates the GM alteration, in that way, the GM composition of athletes is certainly different from the other population (Table 1).

Several studies have explored differences in the composition of the GM between athletes and other populations (Table 1). A study of professional athletes from an international rugby union squad discovered that the athletes had lower inflammatory but improved plasma creatine kinase (an extreme exercise marker) and metabolic markers. Simultaneously, these professional athletes displayed a higher diversity of GM, which had a positive correlation with protein consumption and creatine kinase compared with control.[20]

Table 1 The Effect of Different Types of Exercise on Gut Microbiota

Type of Exercise	Country, Sex, Age, and BMI	Method of Gut Microbiota Analysis	Effects
Professional rugby athletes[20]	All subjects except one (Indian ethnicity) were of Irish ethnicity. Male (n=40); Mean age: 29 (±4) years old; Mean BMI: 29.1 (±2.9). Healthy controls: Male; Mean age: 29 (±6) years old; Two groups with group 1 (n=23) having a BMI≤25 and group 2 (n=23) having a BMI >28.	By 16S rRNA amplicon sequencing.	Athletes have a higher diversity of gut microbes, representing 22 different phyla. *Bacteroidetes* were significantly less abundant in the athletes. Notably, the proportion of *Akkermansiaceae* and *Akkermansia* in elite athletes was significantly higher than in the high BMI control group.
Professional rugby athletes[10]	Professional male athletes (n=40) Healthy controls (sedentary subjects) (n=46): Two groups with low BMI (n=22, BMI≤25.2) and high BMI (n=24, BMI≥26.5).	Further statistical and bioinformatic analysis of the metagenome based on 16S rRNA replicate sequencing.	Enhancement of microbial diversity in athletes compared with controls. Athletes had relative increases short-chain fatty acids (SCFAs) and excreted proportionately higher levels of the metabolite TMAO.
Professional and amateur level competitive cyclists[21]	All subjects were Americans. Professional group: Female (n=8); Male (n=14). Amateur group: Female (n=3); Male (n=8). Age: 19–49 (median age 33).	By metagenomic whole genome shotgun (mWGS) and metatranscriptomic (RNA-Seq) sequencing.	By mWGS sequencing, the 33 cyclists data of gut microbiomes split into three taxonomic clusters, marked by either high *Prevotella, Bacteroides* or a mix of many genera including *Bacteroides, Prevotella, Eubacterium, Ruminococcus, and Akkermansia*. Significant high abundance of the genus *Prevotella* (≥2.5%) was correlated with time reported exercising during an average week. Increased abundance of *Methanobrevibacter smithii* transcripts in a number of professional cyclists which comparison to amateur cyclists.

(*Continued*)

Table 1 (Continued).

Type of Exercise	Country, Sex, Age, and BMI	Method of Gut Microbiota Analysis	Effects
Bodybuilders[22]	All subjects were Korean and male. Bodybuilders (n = 15); Age: 25 (±3) years old; BMI=28.1 (±2.6). Elite distance runners (n = 15); Age: 20 (±1) years old; BMI=20.5 (±0.8). Healthy control (without exercise habits) (n = 15); Age: 26 (±2) years old; BMI=25.9 (±4.2)	The DNA of fecal samples was sequenced for the analysis of gut microbial diversity through bioinformatics cloud platform.	Highest level of *Faecalibacterium, Sutterella, Clostridium, Haemophilus*, and *Eisenbergiella* in bodybuilders, while Bifidobacterium and *Parasutterella* were the lowest. For species, intestinal beneficial bacteria widely used as probiotics (*Bifidobacterium adolescentis* group, *Bifidobacterium* longum group, *Lactobacillus sakei group*) and those producing short chain fatty acids (*Blautia wexlerae, Eubacterium hallii*) were the lowest in bodybuilders and the highest in controls.
Elite Race Walkers[23]	All subjects from Australia, Canada, Chile, Italy, Japan, Poland, South Africa, and Sweden. Male (n=30) Age: 20–35 years old	By 16S rRNA amplicon sequencing.	The microbiota profiles at the beginning could be separated into either a *Prevotella* or *Bacteroides* dominated enterotype. The Low Carbohydrate High-Fat diet resulted in a greater relative abundance of *Bacteroides* and *Dorea and* a reduction of *Faecalibacterium*.
Marathon runners[24]	Female and male (n=15); Sedentary controls (n=10)	By 16S rRNA amplicon sequencing.	After a marathon an increase in *Veillonella* and every gene in a major pathway metabolizing lactate to propionate is at the higher relative abundance in marathon runners.
Professional Wushu routine martial arts athletes[25]	All subjects were Chinese. Female (n=15), Male (n=16), Age: 20–24 years old. Two groups with 12 higher-level and 16 lower-level athletes	By 16S rRNA amplicon sequencing.	Higher-level athletes' gut microbial richness diversity was significantly higher than in the lower-level athletes. The genera *Parabacteroides, Phascolarctobacterium, Oscillibacter* and *Bilophila* were enriched in the higher-level athletes. The genus *Megasphaera*, on the other hand, is abundant in low-level athletes.
Strength athletes[26]	Polish, Male (n=16), Aged from 19 to 24 years or older.	High-throughput sequencing	*Alistipes communis* species showed an increase in abundance during the Wingate test (WT) specifically within the strength group, indicating a potential link to resistance training. *Dorea longicatena, Catenibacterium sp AM22 15*, and *Clostridium phoceensis* were identified as more abundant in strength athletes at various time points of analysis
Endurance athletes[26]	Polish, Male (n=15), Aged from 19 to 24 years or older.	High-throughput sequencing	*Blautia sp* AF19 10LB, which was found to be significantly more abundant in endurance athletes compared to both the strength and control groups at most time points. The presence of *Bacteroides faecis, Fusicatenibacter saccharivorans*, and *Ruminococcus sp* AF419 was also noted at different intervals, indicating their potential role in endurance performance

Another novel study showed a trend towards a decrease in GM diversity following a systematic reduction in training in swimmers, suggesting that GM is susceptible to change following changes in exercise levels.[27] In addition, *Coprococcus* and *Faecalibacterium* were also reduced during this process. *Faecalibacterium* was found to be enriched in athletes,[20] where it helped to reduce oxygen tension in the lumen and produce butyrate.[28] In previous reports, these microbiomes have been associated with increased physical activity and improved gut health through the fermentation of complex carbohydrates, which are also responsible for providing energy to the host.[29] In addition to the normal population, in a cross-sectional study of females, researchers observed the highest alpha diversity in athletes compared to anorexia nervosa patients, overweight, obese and normal weight controls, and the lowest diversity in anorexia nervosa patients,[30] possibly due to inadequate nutritional intake and physical activity.

Not only the GM of the athlete is different from the normal population but also there is a difference between the athletes. The professional athletes had distinct taxa composition characteristics and subsequently had functional metabolism features in the gut microbiota. Among professional martial arts athletes, a total of 10 different taxa of microorganisms were commonly found in high- and low-level athletes.[25] Typical examples in high-level athletes are *Parabacteroides* and *Phascolarctobacterium*, while the *Megasphaera* (belonging to family *Veillonellaceae*) has been most extensively studied in low-level athletes. Whereas *Parabacteroides* could bring advantages to exercise and cardiac function, furthermore, they were negatively associated with metabolic disorders.[31,32] However, *Megasphaera* has a relevance to nonalcoholic steatohepatitis and genital tract inflammation,[33] and also a potential to produce high levels of lipopolysaccharides.[34] That may suggest the elite athletes had more beneficial and abundant microbial taxa characteristics compared to low-level athletes, and these characteristics are associated with levels of physical activity to a certain extent.[35] In a survey of cyclists, the majority of cyclists (30 out of 33) had *Akkermansia*, and the relative abundance of *Prevotella* among them was high in cyclists who trained for more than 11 hours per week.[21] Among professional cyclists, *Methanobrevibacter smithii* had a higher probability of occurrence than at the amateur level. An important role of *M. smithii* is the fermentation of complex polysaccharides, through its utilization of hydrogen gas (H_2) and formate to reduce carbon dioxide (CO_2) to methane.[36,37] Once *M. smithii* disappeared, accumulated H_2 will inhibit bacterial NADH dehydrogenases and then decrease the production of ATP, SCFAs, and other important compounds.[36,37] Another stratification of athlete GM analysis showed that different levels of athletes have a different GM enterotype, in the aspects of taxonomical structure and functional composition, the majority of elite athletes assigned to a similar enterotype.[38] An enterotype-dependent GM is strongly associated with athlete performances. Further in-depth functional profiling revealed that elite athletes have an excellent in ATP metabolisms, multiple sugar transport systems and carbohydrate metabolisms depending on their enrichment microbial community.[38] Raised evidence revealed elite athletes are more tolerated various kinds of stress and overload,[39] the reason is elite athletes have a better GM community that can modulate excitatory and inhibitory neurotransmitters and neurotransmitters-like substances, especially in response to physical and emotional stress.[40,41]

GM Helps to Strength Skeletal Muscles to Enhance Exercise Performance

It is self-evident how important skeletal muscles are to exercise or athletes' performance. The requirement for skeletal muscle mass and function is widespread in all types of exercises/sports. Strength exercise depends on the explosive strength of the muscles and endurance exercise requires aerobic capacity and muscle metabolic ability to improve endurance. Dietary intake is undoubtedly the main factor influencing the deposition of muscle proteins. But recent research suggests a role for the GM in regulating skeletal muscle mass and function in mice. Furthermore, the gut microbiome may also influence muscle function through the regulation of the immune system and related gene expression.[42] Compared to pathogen-free mouse skeletal muscle, germ-free (GF) mouse skeletal muscle showed atrophy, decreased expression of insulin-like growth factor 1 (IGF-1), reduced transcription of genes associated with skeletal muscle growth and mitochondrial function, and reduced expression of genes encoding *Rapsyn* and *Lrp4*, which are important proteins for neuromuscular junction assembly and function.[42] Transplanting the GM from pathogen-free mice into GF mice could convert this situation.[42] One of the potential mechanisms is GM could modulate the muscle mass and function through the gut-muscle axis. For example, *Lactobacillus curvatus* CP2998 exerted a positive effect on muscles by suppressing glucocorticoid receptor activation and the improvement of glucose utilization.[43] In contrast, the evidence showed the gut microbiome may influence skeletal muscle via catabolic pathways. For instance, metabolites produced by the gut microbiota, such as trimethylamine N-oxide, have been linked to increased inflammation and oxidative stress, which can negatively impact muscle function and recovery.[19,44–46] Besides, a healthy GM (*eg, Propionibacteria* and *Lactobacillus reuteri*) can produce significant amounts of folate and vitamin B12, which may improve muscle anabolism and prevent hyperhomocysteinemia-induced oxidative stress and endothelial damage.[47] Another work focused on periodic diet strategies commonly used by athletes, which are, low-carbohydrate high-protein diet during physical training to improve fitness, and high-carbohydrate diets during competitions to improve athletic performance. The result showed GM stability was associated with greater athletic performance when highly trained individuals underwent dietary periodization.[48] These changes in the GM may also help to reduce inflammation and improve muscle function and recovery processes.

Different Nutrients Intake Interacts with GM and Influence Exercise Performance

Both professional and amateur athletes take dietary supplements to help improve their performance. Athletes have always preferred different dietary patterns due to the different types of sports they play. According to a study of bodybuilders and distance runners, researchers found the bodybuilders prefer a high protein, high-fat and low carbohydrate/dietary fiber diet, while distance runners prefer a low carbohydrate and low dietary fiber diet.[22] *Faecalibacterium, Sutterella, Clostridium, Haemophilus*, and *Eisenbergiella* were found to be more abundant in bodybuilders, while abundance of *Bifidobacterium* and *Parasutterella* were less abundant. Meanwhile, some probiotics used as dietary supplements, such as *Bifidobacterium adolescentis, Bifidobacterium longum*, and *Lactobacillus sakei*, were at the lowest levels in bodybuilders.[22] This may be related to a dietary pattern of plentiful protein intake. Cross-sectional studies confirmed that only long-term diets were associated with enterotype clustering compared to short-term.[49] Based on the type of nutrients, further discussion will be categorized as follows (Figure 2) (Table 2).

Protein

When talking about athletes or sports, protein supplementation is always on our minds. Indeed, protein supplementation helps to increase muscle mass and strength gains during exercise.[61] However, malondialdehyde (MDA) levels are a marker of oxidative stress and are associated with excessive protein intake in resistance-trained athletes, with higher

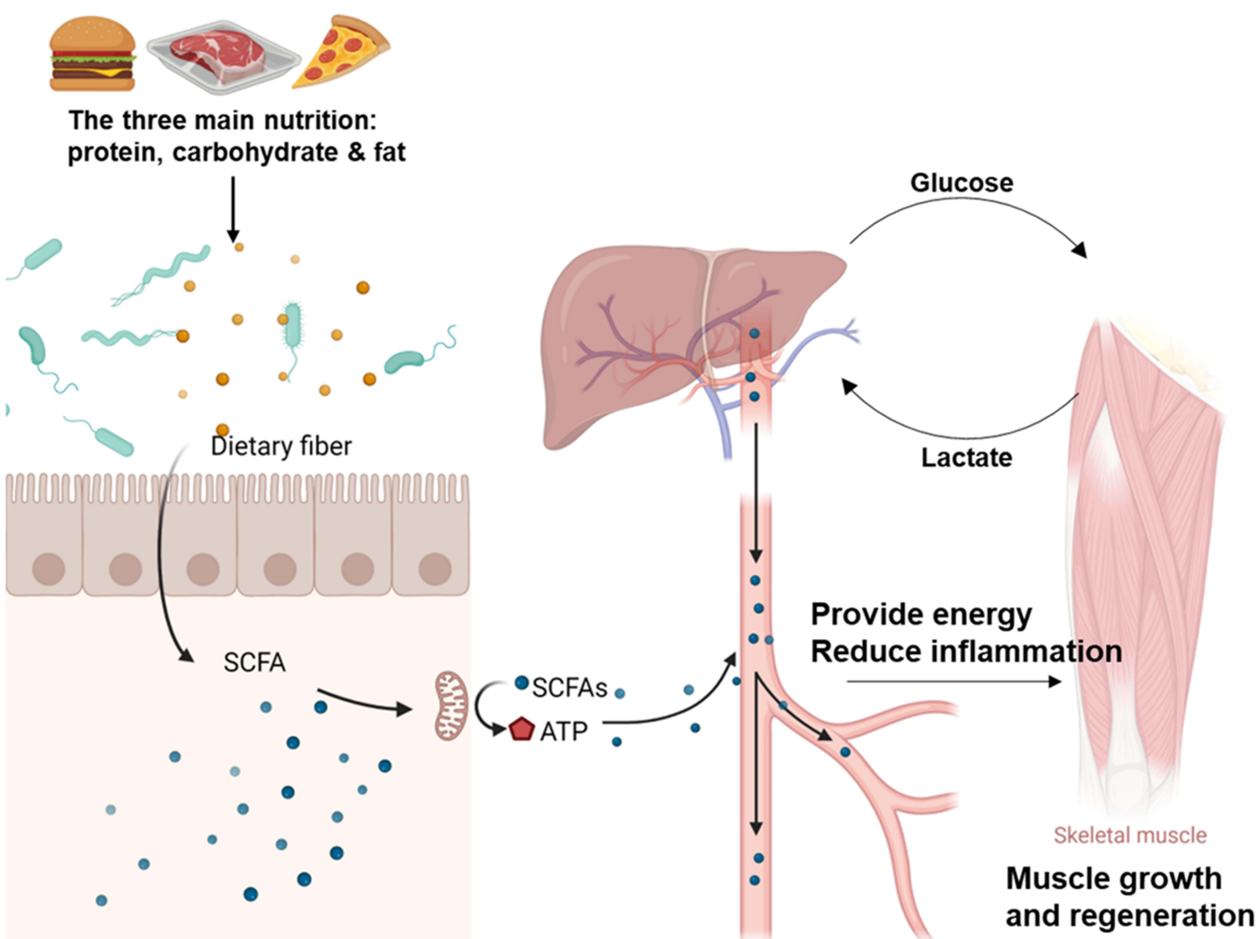


Figure 2 The three main nutrition effect on GM to provide the energy. The three main nutrition altered the gut microbiota (GM) composition to exert anti-inflammatory properties and provide the energy. Short Chain Fatty Acids (SCFAs) play an important role in glucose and lactate metabolism, it has been shown to increase the 5' adenosine monophosphate-activated protein kinase (AMPK) activity in liver and muscle tissue then triggers peroxisome proliferator-activated receptor (PPAR) gamma coactivator-1α expression, to control the transcriptional activity of several transcription factors and subsequently to regulate cholesterol, lipid, and glucose metabolism.

Table 2 The Effect of Different Nutrients and/or Diets on the Gut Microbiota

Nutrient and/ or Diet	Daily Intakes	Type of Gut Microbiota	Effects
Protein (g)	≥200 (Median 248)[20]	*Akkermansiaceae* and *Akkermansia* are predominant. *Prevotellaceae, Erysipelotrichaceae*, S24-7, *Succinivibrionaceae, Prevotella*, and *Succinivibrio* groups showed the biggest flux changes in relative abundance.	Exercise and protein intake drive gut microbiota diversity among athletes.
Carbohydrate (g/kg/d)	8.5[50]		A high-carbohydrate diet does not improve immune function or prevent a decrease in plasma glutamine concentrations following extensive training.[51,52] Simple and refined carbohydrates are not conducive to healthy gut microbiota composition or the production of beneficial SCFAs.[53]
Fat	20%-35% total energy[54] An athlete's fat consumption tends to be quite high (15–30% of dietary energy).[55] During prolonged exercise, endurance may benefit from a fat intake of 30–50% of dietary energy.[56]	High-fat and high-calorie diets increases intestinal permeability and plasma LPS along with a decrease in total bacterial density and an increase in the relative proportion of *Bacteroidales* and *Clostridiales* orders.[57]	Diets high in fat may also alter the gut microbiota unfavorably.
Polyunsaturated fat	Taking approximately 1–2 g of omega-3 polyunsaturated fatty acids daily, with eicosatetraenoic acid and docosahexaenoic acid proportions of 2:1, is optimal.[58]		During exercise, eicosanoids, cytokines, and ROS are decreased.
Fiber	Athletes trained in endurance consume less than 25 g a day.[59]	Microbiota diversity, SCFA production, and anti-pathogenic bacteria are reduced when fiber consumption is low.[56]	During the recovery period and training period, athletes should decrease the energy from processed foods high in added sugars, refined carbohydrates, and fat, since eating a high-fiber diet before intense training or competition could produce GI upset such as distension, gas, and bloating.[141]

levels of protein intake leading to lower malondialdehyde levels.[62] Some researchers believe that long-term protein supplementation may impair GM. Overfeeding protein caused butyrate concentrations to decrease in fecal samples, suggesting a possible negative effect of a high-protein intake on colon health.[63] Furthermore, the butyrate can significantly reduce the levels of MDA thus protecting the host from oxidative damage.[64] That may indicate overfeeding protein will reduce the butyrate concentration and result in a high-level MDA in our body.

Proteolysis produces α-amino acids, most α-amino acids are unable to synthesize by humans or synthesize at a rate far from the body's needs, which must be supplied by the extra food proteins. Among the α-amino acids, branched-chain amino acids and taurine are the most common functional sports drinks, which help athletes enhance the anabolic and adaptive effects of exercise on skeletal muscle and improve recovery ability.[65,66] However, it does not imply that the more taurine consumed, the more energy gained. In case of proteolytic metabolite production beyond the hosts' ability to assimilate, transform, or detoxify harmful metabolites, adverse effects on intestinal barrier function, inflammation, and colonic health will occur.[67] Evidence suggests that overfeeding of taurine has an association with colorectal cancer and is due to its ability to elevate taurocholic acid, deoxycholic acid, and hydrogen sulfide concentrations.[68]

GM also plays an important function in protein absorption and energy metabolism through the gut-muscle axis. For example, *Lactobacillus paracasei*, is a probiotic that can enhance the bioavailability of plant proteins by elevating essential amino acid concentrations.[69] Another probiotic, *Bacillus coagulans* (GBI-30,6086), shows anti-inflammatory properties and produces proteases to aid the absorption of amino acids by the host.[70] However, there are two different results in detecting the protein intake and alteration of GM in athletes. Clarke et al[20] draw a conclusion that overfeeding of protein supplementary enhanced the GM diversity, but Jang et al[22] demonstrated it decreased the GM diversity. However, this may be attributed to the different fiber intake between athletes, and the fibre intake exerts a great impact on GM too.

As mentioned above, protein intake is a necessary supplement for athletes, but overfeeding of protein may have the opposite effect. Appropriate supplementation of probiotics to enhance protein metabolism may be a safe and reliable solution to maximize protein utilization and enhance athletic performance.

Carbohydrate

As the main source of energy for long-distance running races, endogenous carbohydrates are stored in the liver and muscle, and glycogen requires catabolic reactions for proper energy production in the liver and muscle cells.[71,72] It has been recognized that the intake of a high carbohydrate (CHO) diet can improve endurance performance. Therefore, it is recommended that endurance athletes maximize CHO availability to enhance their performance during endurance sports competitions.[73] However, in the past several decades, the conception of the CHO has changed in the competition sports field. New guidelines in recent years have stated that a universal recommendation of absolute CHO intake is inappropriate.[74–76] The key points are threefold. Firstly, competitive exercise is highly variable, so CHO should be prescribed according to the expected fuel requirements of the exercise or sport. Secondly, high CHO intake is necessary and beneficial during high intensity or endurance exercise, but when exercise intensity becomes lower, consistent high CHO supplementation seems less important. Finally, how and when to supplement with CHO should consider the cyclical requirements of training and competition and be individualized.

To improve the performance of competitive sports, a new alternative view—a low-carbohydrate, high-fat (LCHF) diet has been come up to increase the fat utilization of muscle and the aerobic capacity of athletes. But that may impair performance in elite endurance athletes. A meta-analysis revealed a weak effect of ketogenic LCHF diet interventions through the index of maximum oxygen uptake (VO2max), rating of perceived exertion (RPE), time to exhaustion (TTE), maximal heart rate during exercise (HRmax), and rating of perceived exertion (RPE), but a significant effect on the respiratory exchange rate (RER).[77] Burke et al illustrated that the LCHF impairs performance in elite endurance athletes although a significant improvement in peak aerobic capacity.[78] Although a short-term adaptation to an LCHF diet in elite athletes increased exercise fat oxidation, it was not further enhanced with longer periods of exposure; nevertheless, the economy of exercise at intensities relevant to real-life endurance events is reduced by brief adaptation to a ketogenic LCHF when fat oxidation is maximized.[79] This suggests that the LCHF major increased the capacity for fat oxidation in the host physiology, it is not conducive to endurance exercise at sustained high intensity, where oxygen delivery to the muscles becomes limited.

For now, it's too early to say whether taking carbohydrates is beneficial or negates the performance of athletes. As the main resident of the gut, GM exerted a critical role in carbohydrate metabolism. Nida Murtaza et al divided elite race walkers into three groups: High Carbohydrate (HCHO), Periodised Carbohydrate (PCHO), and ketogenic Low Carbohydrate High Fat (LCHF) diet. After three weeks of intervention, LCHF decreased the abundance of *Faecalibacterium* and increased the relative abundance of *Bacteroides* and *Dorea* and showed significant negative correlations were observed between Bacteroides and fat oxidation.[23] While the production of *Faecalibacterium prausnitzii* includes a suite of metabolites and peptides with anti-inflammatory effects.[80]

Short-chain fatty acids (SCFAs) are the end product of fermentation of undigested carbohydrates and fiber from the diet by anaerobic gut microbiota. Significantly, SCFAs have gained sufficient attention in terms of GM alteration, health maintenance and athlete performance. There is growing evidence that SCFAs exert a variety of beneficial effects on energy metabolism, anti-tumor, anti-inflammatory, immune homeostasis and anti-pathogens in mammals.[81–84]

Athletes in the rankings, especially endurance athletes, rely on effective and efficient energy metabolism to enhance their performance. The report found that GF mice were significantly less capable of endurance exercise compared to mice with SCFAs-producing bacteria — *Bacteroides fragilis* in their colon.[85] This raises the hypothesis that the contribution of GM to aerobic activity may come from SCFAs. In animal experiments, hypoxia-induced remodeling of the intestinal microenvironment, which enhances SCFAs concentrations by increasing the abundance of related genera such as *Akkermansia* and *Bacteroidetes*.[86] The supplementation of acetate and butyrate significantly increased the biogenesis of muscle mitochondria. This may suggest that endurance capacity is enhanced by high concentrations of SCFAs in hypoxic conditions.[86] Another experiment also confirmed that multiple antibiotics treated in mice increased their exercise capability after continuous acetate infusion.[87] The depth analysis expounded that SCFAs may actively interfere with the mitochondrial biogenesis in the skeletal muscle. In addition, SCFAs have been shown to increase the adenosine 5'-monophosphate-activated protein kinase (AMPK) activity in liver and muscle tissue, which then triggers peroxisome proliferator-activated receptor gamma coactivator (PGC)-1α expression, and subsequently control the transcriptional activity of several transcription factors such as peroxisome proliferator-activated receptor (PPAR) α, PPARγ, PPARδ, liver X receptor (LXR), and farnesoid X receptor (FXR), which are all important in the regulation of cholesterol, lipid, and glucose metabolism.[82,88]

Fat

As we all know that both carbohydrates and fat are important substrates for oxidative phosphorylation and energy production in skeletal muscle. In exercise or competitive sport, lipid utilization is not the physical availability of fat to provide the energy but to bring the lipid to the site of oxidation in the muscles to furnish energy by the oxidative processes.[89] During the exercise, the main fuel substrates for athletes are triglycerides and adipose tissue.[90] Fat ingested from food is absorbed by intestinal mucosa under the action of bile acid lipase, and exogenous triglycerides are synthesized in intestinal mucosal epithelial cells. Triglycerides are stored in skeletal muscle cells as fat droplets. The content of triglyceride in skeletal muscle is affected by muscle fiber type, nutritional status, physical activity, and other factors. In addition, Intramuscular triglycerides are also thought to be an important source of substrate formation during prolonged endurance exercise in trained men. A study of trained men found that after prolonged endurance cycling, the intramuscular triglyceride content in the muscle was significantly reduced.[91]

In a study of high-fat diet and exercise training, untrained volunteers consumed a high-fat diet or high carbohydrate diet for 7 weeks and meanwhile with an aerobic endurance training program. The results indicated the activity of β-hydroxyacyl-coenzyme A dehydrogenase was increased by 25% which may suggest that diet can affect muscle enzymatic adaptation, presumably through an effect on the substrate flux and enhanced fatty acid (FA) metabolism, permitting enhanced FA oxidation.[92] But the intake of fat should also consider the type of fat, body composition, sport modality, training level, intestinal microenvironment, and so on. The amount and different types of fat are crucial for athletes' performance and the health of GM.[90,93]

For instance, the omega-3 fatty acid appears a potential function of influencing the metabolic response of muscle to nutrients and physiological functional response to exercise and post-exercise conditions, helping recovery and decreased injury/reduced risk of illness in athletes.[94] Further study also explored whether the omega-3 fatty acid influenced the GM. The GM occurred alteration after an omega-3 fatty acid supplement in humans. It decreased the abundance of *Faecalibacterium*, which have relevance to an increase in the Bacteroidetes and butyrate-producing bacteria.[95] This is consistent with the results we mentioned above that LCHF diet interventions altered the GM composition, both decreasing the *Faecalibacterium* and increasing the *Bacteroidetes*. In addition, the mountain of evidence illustrates that omega-3 has a positive action on the host, such as anti-inflammatory, helps to maintain the gut barrier, regulates the immune system, and interestingly, it could also increase the production of SCFAs.[96,97]

Vitamin

Most vitamins cannot be synthesized or not produced in sufficient quantities to satisfy the body's needs and must be obtained frequently from food, once the lack will cause vitamin deficiency disease and damage to human health (Figure 3). GM exerts a critical role in the process of vitamin synthesis. In athletes, vitamin deficiency causes long-term adverse cardiovascular effects, muscle damage, inducing high oxidative stress et al[98,99] Vitamins are a large family, and now we will discuss only a few representative ones.

For instance, vitamin D affects calcium and phosphate transport by muscles through cell membranes, phospholipid metabolism, and muscle cell proliferation and differentiation.[100] It is essential for skeletal calcium deposition and maintaining the balance of blood calcium. In the process of vitamin D synthesis, GM influences the vitamin D metabolism embodied in inhibiting fibroblast growth factor 23 and induced increased serum 25-hydroxyvitamin D, 24,25-dihydroxyvitamin D, and 1,25-dihydroxyvitamin D levels.[101]

In the vitamin B family, B2, B9 (Folate), and B12 are most strongly associated with exercise. B2 can improve redox reactions and energy production. Folate and B12 can prevent homocysteine-induced oxidative stress and endothelial damage.[102] The main strains of GM to help synthesize them include *Bacillus subtilis, Escherichia coli, Bifidobacteria* (main synthesis B2), *Bifidobacteria, Lactobacilli* (main synthesis folate), and *Propionibacteria, Lactobacillus reuteri* (main synthesis B12).[47]

The alterations in the oxidant/antioxidant balance are key factors in excessive reactive oxygen species (ROS) accumulation, and ROS accumulation can cause skeletal muscle injury.[103] Supplementing vitamins properly (eg, vitamin E) can interrupt lipid peroxidation reactions and remove free oxygen radicals, stabilizing cell membranes to alleviate muscle injury.[104] Studies in animals and humans show that GM can synthesize vitamin C and K and the B group vitamins.[105] Although it is not synthesized by GM, vitamin E has been demonstrated to alter the GM composition and protect the gut barrier integrity by inhibiting the loss of tight junction proteins.[106] Hence, further investigation is required for effective interventions targeting the GM composition and vitamin levels, to determine the mechanisms underlying vitamin regulation by the GM.

Summary

The four main nutrients do not play a single role in GM and exercise, and many athletes have their special eating habits. In terms of dietary choices, it is also impossible to achieve a single intake, for example, fat intake is usually accompanied

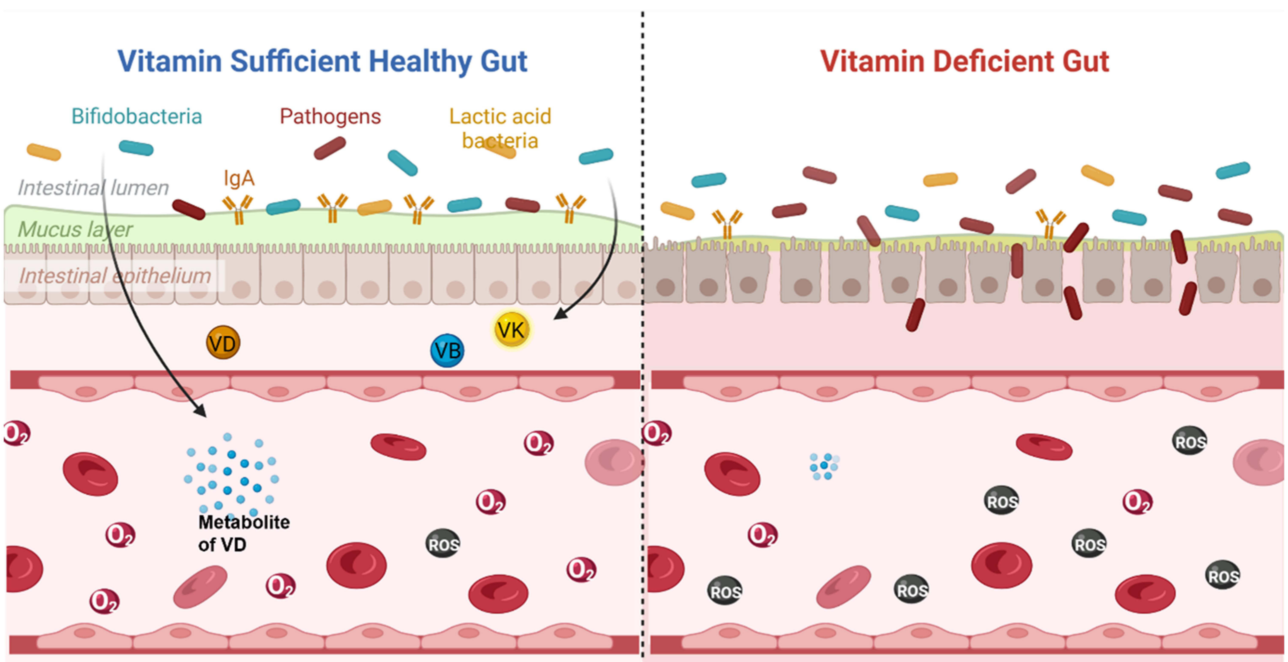


Figure 3 The effects of vitamin on athletes. The beneficial gut microbiota (GM) species can help to synthesize the vitamins to decrease the Reactive Oxygen Species (ROS) accumulation, interrupt lipid peroxidation reactions and remove free oxygen radicals, stabilizing cell membranes to alleviate the muscle injury.

by carbohydrate and ketogenic pattern. Athletes have a large requirement for energy intake, and different sports require different energy and nutrients, such as endurance sports and burst strength sports, they have a different diet pattern. This requires full consideration of athletes' physique and sports need in the process of nutrition intake and collocation. In such cases, it is important to fully consider the role of GM in digestion, absorption, metabolism, and athletes' performance.

Nutrient delivery to the gut activates neuroendocrine mechanisms that control digestion and energy intake and utilization with the help of GM. GM can secrete vary such enzymes to help digestion and absorption and ferment fibers that cannot be absorbed by intestinal epithelial cells. These fibers ferment to produce SCFAs that are vital to the body, on the one hand, SCFAs are indispensable in maintaining colon health and act as an energy source for colonocytes. On the other hand, it is a neurotransmitter in gut-brain axis. In addition, GM also releases other mediators, including 5-hydroxytryptamine (5HT), glucagon-like peptide-1 (GLP-1), Peptide YY act on vagal afferent neurons regulating food intake and digestion.[107] A novel study reveals a new mechanism of GM that regulates digestion and absorption. They found that bacterial sensing via neuronal Nucleotide-binding oligomerization domain 2 (Nod-2) regulates appetite directly.[108] In other words, the bacteria in the gut can also manipulate people, making them crave what they want. To sum up, the GM has three main ways to influence the digestion: (i) To produce the enzymes to help digestion. (ii) To produce the neurotransmitters and regulate digestion through the gut-brain axis. (iii) Sensing of bacterial cell wall components by brain neurons directly to regulate the digestion. In short, GM may be more important in some ways than the brain in regulating and controlling appetite.

The Strategy of Diet Supplements

In the view of the above, it seems feasible to focus dietary supplementation on altering the gut microbiota. Numerous clinical and animal studies have shown that the GM displays endocrine organ functions, including the secretion of Serotonin (5-HT), dopamine, gamma-aminobutyric acid (GABA) and other neurotransmitters that control the HPA axis in athletes.[109] Alterations in the composition and function of the gut microbiota can therefore influence levels of these neurotransmitters, with potential implications for mood, cognition, and even muscle function. Several ways that the gut microbiome could influence neurotransmitter synthesis. One fascinating aspect is the direct production of neurotransmitters by certain gut bacteria. For example, specific strains within the Lactobacillus and Bifidobacterium genera have been shown to produce GABA.[110] Similarly, some strains of Escherichia coli, typically associated with the gut, can synthesize dopamine.[110] An indirect way the gut microbiome could alter neurotransmitter levels is through the production of precursor molecules, such as tryptophan, which is required for serotonin synthesis[111]. This bidirectional communication not only performs the neurotransmitter synthesis, but in return, the neurotransmitter can also modulate gut microbial composition through the autonomic nervous system and neuroendocrine regulation.[112] For instance, reduced serotonin levels, often associated with an imbalanced gut microbiota, have been linked to fatigue and impaired exercise performance.[113] GABA is also a key inhibitory neurotransmitter that can influence muscle tone and relaxation. For example, *Lactobacillus* and *Bifidobacterium* exhibit quite effective GABA production capacity.[114] 5-HT is a neurohormone that is regulated by physical exercise.[115] During intense exercise or competitive sports, high stress can affect GM composition through the release of neurotransmitters.[116] It is also a major regulator of intestinal secretion and motility and is a key neurotransmitter in the gut-brain axis.[117] The main strains that affect 5-HT synthesis are SCFAs, which are produced by bacteria belonging to Firmicutes and Bacteroidetes, the two most dominant phyla in human GM.[118] Many studies have shown that 5-HT plays a multifaceted role in gut homeostasis, including immunity, inflammation regulation, and wound healing, and that probiotics function through the HPA axis to maintain health and alleviate exercise depletion and oxidation.[15] Communication between the HPA and the gastrointestinal tract occurs through complex neuro-immune regulatory mechanisms. Neurotransmitters are received by the afferent vagus nerve and act on the hypothalamus and hippocampus regions of the brain, leading to the activation of the HPA.[119] While the hypothalamic paraventricular nucleus (PVN) has neurons with neuroendocrine functions, the PVN interconnects with the bed nucleus of the stria terminalis (BNST) to synthesize corticotropin-releasing hormone (CRH). CRH is then released into the hypothalamic portal circulation and is transported to the anterior pituitary, which stimulates the release of adrenocorticotropic hormone (ACTH) into the systemic circulation to regulate physical activity and participate in the control of stress responses.[120]

Although the role of GM in the control of exercise-induced stress adaptation remains to be explored, GF animal experiments may provide a new insight into the role of GM in regulating the development and function of the HPA axis in response to stress. Anxiety-like behavior and neuroendocrine responses to acute stress were enhanced in GF rats compared to specific pathogen-free (SPF) controls.[121] Hyperresponsiveness of the HPA axis was manifested by exaggerated release of corticosterone and ACTH induced by mild fasciculation stress, a process confirmed by enhanced expression of corticotropin-releasing factor in the hypothalamus and reduced expression of glucocorticoid receptor genes in the hippocampus.

The latest research provides new evidence that the hypothalamic neurons may directly sense the structural components of the GM to regulate feeding, nesting behavior and body temperature.[108] This study found out that the bacterial cell wall fragments derived from the intestinal microbiome can cross the intestinal barrier and enter the brain through blood circulation. Cell wall peptide acts on the pattern recognition receptor Nod2 (a pattern recognition receptor recognizing fragments of the bacterial cell wall termed muropeptides— develop alterations in food intake, nesting behavior, and body temperature control) in specific neurons in the hypothalamus, directly affecting the activity of these neurons.

In summary, through modulating vagus nerve afferent feedback, the GM can influence both brain and body function in this indirect way. And besides, it also has a direct way, which is a gut-brain communication mechanism to regulate the body's conditions. The GM is a critical modulator of muscle function, inflammation, and recovery processes through its production of bioactive metabolites, its impact on the immune system, and its bidirectional communication with the central nervous system via the gut-brain axis.

Probiotics

By definition, probiotics are living organisms that confer health benefits to their hosts by altering GM composition, improving gut barrier properties,[122] antioxidant status,[123] and attenuating the inflammatory response[124] following exhaustive exercise. For example, in cross-sectional studies in humans, the gold standard measure of cardiorespiratory fitness, peak oxygen uptake (VO_2peak), showed a correlation with GM diversity and butyrate concentration, and enhanced abundance of the butyrate-producing bacteria *Clostridiales, Roseburia, Lachnospiraceae*, and *Erysipelotrichaceae* may contribute to butyrate increase in the concentration of butyrate.[109] This suggests that butyrate and butyrate-producing bacteria play an important role in aerobic exercisers. A study isolated a strain of *Veillonella atypica* that increased post-marathon abundance from the marathon runner's stool samples and transplantation to mice. The results showed that *V. atypica* enhanced athletic performance by converting exercise-induced metabolism of lactate into propionate.[12] In another inoculation study, strains *B. longum subsp. longum* OLP-01 and *Ligilactobacillus salivarius subsp. salicinius* SA-03, isolated from a female Olympic medalist in weightlifting, significantly increased forelimb grip strength and endurance capacity in a swim-to-exhaustion test in mice.[125,126]

In endurance exercise review studies, the GM was shown to be key in controlling oxidative stress, and inflammatory responses as well as improving metabolism and energy expenditure during intense exercise.[116] In addition, GM-producing N-butyrate modulates neutrophil function and migration to inhibit inflammatory cytokine-induced expression of vascular cell adhesion molecule-1, therefore strengthening the intestinal epithelial barrier and exerting an anti-inflammatory effect.[127] A sustainable competitive sport, such as triathlon, always results in muscle damage, leading to exercise-related oxidative stress, which will lead to a decrease in skeletal function. The two main aspects to induce exercise-induced muscle damage are mechanical and inflammatory stress.[128] *Lactobacillus plantarum* PS128 supplementation may be a potential ergogenic probiotic on triathletes for possible physiological adaptation and health promotion by significantly improving the expression of pro-inflammation cytokines (TNF-α, IFN-γ, IL-6, and IL-8), anti- (IL-10) inflammation cytokines, kidney injury (TRX and C5a), and oxidative stress (MPO) markers induced by intense exercise.[129]

Prebiotic Like Effect Supplements

A prebiotic is an indigestible organic substance that can have beneficial effects on the host by selectively stimulating the growth or activity of one or a few species of bacteria in the colon, thereby enhancing host health. Including oligosaccharides, polysaccharides, extracts of natural plants (such as vegetables, herbs, wild plants, etc.), and so on. Nowadays, such saponin, polysaccharides, and other components extracted from herbal medicines have been proven to exert a prebiotic effect such as Lycium barbarum polysaccharide (LBP), ginseng saponin, jiaogulan saponin,[130–132] and so on.

Beyond exerted prebiotic effects, these organic substances also benefited exercise performance or exercise-related body conditions enhancement. In a recent study, *Platycodon grandiflorus* derived saponin enhances exercise function by ameliorating skeletal muscle protein synthesis and mitochondrial function. The potential mechanism is that saponin induced the expression of mitochondrial function proteins and increased the synthesis if skeletal muscle protein and muscle stem cell-related paired-box 7 and decreased the negative regulator myostatin, which indicates an enhancement of muscle regeneration.[133] Furthermore, *Platycodon grandiflorus* derived saponin attenuated the eccentric exercise-induced muscle damage through downregulating the muscle damage markers level including serum lactate dehydrogenase (LDH), creatinine kinase (CK) and C-related protein.[134] Ginseng is widely used and famous in the world, ginseng saponin also received the widely studied in the research laboratory. It is commonly suggested that it has the efficacy of improving performance on cognition and fatigue. Panax ginseng improved the speed of attention and some aspects of cognitive performance, although it lacks a further and clear mechanism of action and the paucity of sport-specific research.[135] But interestingly, the athletes ingested ginseng root extraction passed the urine test by the International Olympic Committee-approved laboratory, and there were no positive tests for any banned substances in any of the subjects.[136]

Polysaccharide is another common ingredient in herbal medicines. LBP exerted a health protection effect for thousands of years in China. A recent study found that LPB is an important participant in the anti-oxidative process. After exhaustive exercise, the mean endurance time of treadmill running to exhaustion of rats in LBP treated groups was significantly prolonged and decreased the anti-oxidative index compared with that in the normal control group.[137] The role of polysaccharide in scavenging Reactive Oxygen Species (ROS) is likely associated with hydrogen and hydroxyl of the polysaccharide chain.[138]

Taken together, these results provide a novel perspective on the biological function of homology of medicine and food against muscle damage and oxidation impairment. It is necessary to gain an insight into this project to help athletes make their body condition stronger and enhance performance. The schematic of probiotics that improves athletic performance through GM alteration is shown in Figure 4.

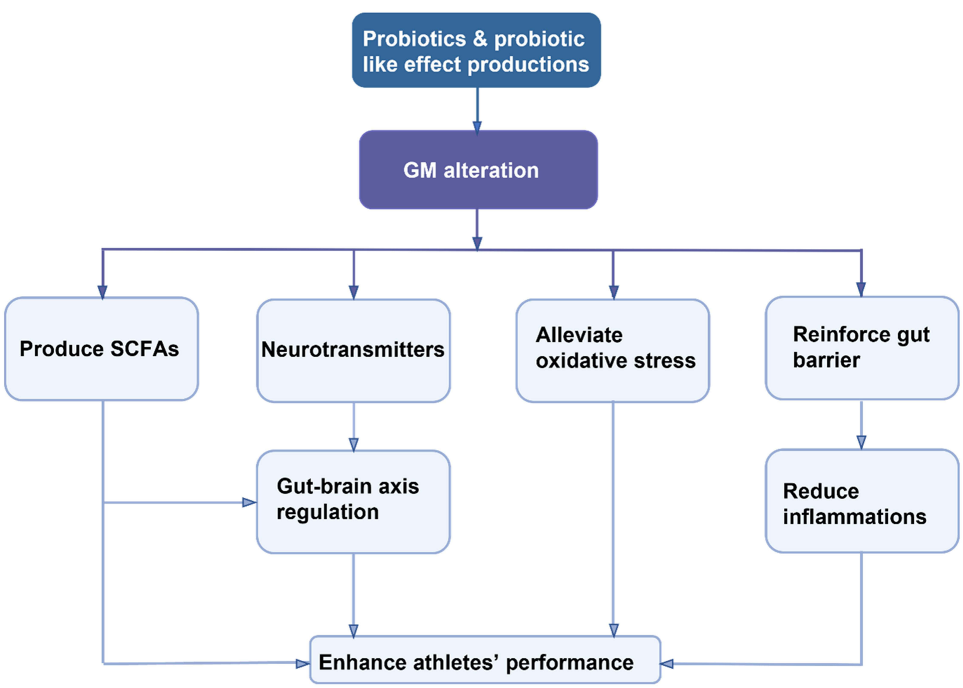


Figure 4 The schematic of how probiotics improves athletic performance through GM alteration.

Conclusion

Growing evidence from animal and human studies indicates that gut microbiota composition plays a crucial role in host physiology and athletic performance. This influence is multifaceted, with key mechanisms including the production of performance-enhancing metabolites like short-chain fatty acids, modulation of the gut-brain axis impacting mood and motivation, and regulation of immune responses crucial for recovery. Dietary patterns and exercise types further shape the gut microbial community, highlighting the interconnectedness of these factors. While moderate, consistent exercise generally promotes GM diversity and health, intense or prolonged exertion can disrupt this balance, potentially leading to dysbiosis and inflammation. There is a delicate balance between the nutritional intake, GM and athletes, and GM is the undisputed center of the three. Manipulating GM may be an optimal and safe dietary supplement strategy to improve athletes' health, training response, adaptations, and performance. Exploring the relationship between nutritional intake, GM and athletes is a fascinating project. It is impossible to separate physical activity and dietary supplementation; none of them can be omitted. Understanding this intricate relationship between GM, diet, and exercise is paramount for developing tailored nutritional strategies for athletes. By analyzing individual GM profiles, we can personalize diet and training regimens to optimize athletic performance, enhance recovery, and potentially mitigate the negative impacts of intense training. This personalized approach holds immense promise for athletes of all levels, from supporting sub-elite athletes in reaching their full potential to assisting elite athletes in pushing their limits, all while considering the unique needs of individuals with specific medical conditions.

In this work, we 1) make a comprehensive overview of the multifaceted relationship between the gut microbiome, exercise, and athletic performance. 2) Emphasized the crucial role of the gut-brain axis in mediating the interplay between the gut microbiome and athletic performance. This bidirectional communication pathway is often overlooked in studies focusing solely on metabolic aspects. 3) Highlighted exercise intensity, which is an important consideration, as most research focuses on either moderate exercise or intense training, without directly comparing their impacts. 4) And our synthesis acknowledges both the beneficial effects of moderate exercise and the potential downsides of intense training on gut health. This balanced perspective is crucial for developing well-rounded recommendations for athletes.

By addressing these points, our work can make a valuable contribution to the field by providing a nuanced understanding of the gut microbiome's role in athletic performance and guiding future research towards personalized interventions for athletes.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Gao Z, Guo B, Gao R, Zhu Q, Wu W, Qin H. Probiotics modify human intestinal mucosa-associated microbiota in patients with colorectal cancer. *Mol Med Rep*. 2015;12(4):6119–6127. doi:10.3892/mmr.2015.4124
2. Hooper LV, Littman DR, Macpherson AJ Interactions between the microbiota and the immune system. *Science*. 2007;336(6086):1268–1273. doi:10.1126/science.1223490.Interactions

3. Postler TS, Ghosh S. Understanding the holobiont: how microbial metabolites affect human health and shape the immune system. *Cell Metab*. 2017;26(1):110–130. doi:10.1016/j.cmet.2017.05.008
4. Vaughn AC, Cooper EM, Dilorenzo PM, et al. Energy-dense diet triggers changes in gut microbiota, reorganization of gut-brain vagal communication and increases body fat accumulation. *Acta Neurobiol Exp*. 2017;77(1):18–30. doi:10.21307/ane-2017-033
5. Owen N, Sparling PB, Healy GN, Dunstan DW, Matthews CE. Sedentary behavior: emerging evidence for a new health risk. *Mayo Clin Proc*. 2010;85(12):1138–1141. doi:10.4065/mcp.2010.0444
6. Fiuza-Luces C, Garatachea N, Berger NA, Lucia A. Exercise is the real polypill. *Physiology*. 2013;28(5):330–358. doi:10.1152/physiol.00019.2013
7. Gonzalez-Freire M, de Cabo R, Studenski SA, Ferrucci L. The neuromuscular junction: aging at the crossroad between nerves and muscle. *Front Aging Neurosci*. 2014;6:1–11. doi:10.3389/fnagi.2014.00208
8. Silverman MN, Deuster PA. Biological mechanisms underlying the role of physical fitness in health and resilience. *Interface Focus*. 2014;4(5):20140040. doi:10.1098/rsfs.2014.0040
9. Kang SS, Jeraldo PR, Kurti A, et al. Diet and exercise orthogonally alter the gut microbiome and reveal independent associations with anxiety and cognition. *Mol Neurodegener*. 2014;9(1):1–12. doi:10.1186/1750-1326-9-36
10. Barton W, Penney NC, Cronin O, et al. The microbiome of professional athletes differs from that of more sedentary subjects in composition and particularly at the functional metabolic level. *Gut*. 2018;67(4):625–633. doi:10.1136/gutjnl-2016-313627
11. Ticinesi A, Lauretani F, Tana C, Nouvenne A, Ridolo E, Meschi T. Exercise and immune system as modulators of intestinal microbiome: implications for the gut-muscle axis hypothesis. *Exerc Immunol Rev*. 2019;25(96):84–95.
12. Scheiman J, Luber JM, Chavkin TA, et al. Meta-omics analysis of elite athletes identifies a performance-enhancing microbe that functions via lactate metabolism. *Nat Med*. 2019;25(7):1104–1109. doi:10.1038/s41591-019-0485-4
13. Chaves FM, Baptista IL, Simabuco FM, et al. High-intensity-exercise-induced intestinal damage is protected by fermented milk supplemented with whey protein, probiotic and pomegranate (Punica granatum L.). *Br J Nutr*. 2018;119(8):896–909. doi:10.1017/S0007114518000594
14. Clark A, Mach N. Exercise-induced stress behavior, gut-microbiota-brain axis and diet: a systematic review for athletes. *J Int Soc Sports Nutr*. 2016;13(1). doi:10.1186/s12970-016-0155-6
15. Huang W-C, Hsu Y-J, Huang H-CL C-C, Lee MC. Exercise training combined with bifidobacterium longum OLP-01 supplementation improves exercise physiological adaption and performance. *Nutrients*. 2020;13(1):1–16. doi:10.3390/nu13010001
16. Morishima S, Aoi W, Kawamura A. Intensive, prolonged exercise seemingly causes gut dysbiosis in female endurance runners. 2021. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8129978/. Accessed December 09, 2024.
17. Bhatia R, Sharma S, Bhadada SK, Bishnoi M, Kondepudi KK. Lactic acid bacterial supplementation ameliorated the lipopolysaccharide-induced gut inflammation and dysbiosis in mice. *Front Media*. 2022;13. doi:10.3389/fmicb.2022.930928
18. Larrosa BCMPJDP-SJFT-ARG-SM Gut microbiota modification: another piece in the puzzle of the benefits of physical exercise in health? 2016. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4757670/. Accessed December 09, 2024.
19. Zhang L, Wang Y, Sun Y, Zhang X. Intermittent fasting and physical exercise for preventing metabolic disorders through interaction with gut microbiota: a review. *Multidiscip Digit Publ Inst*. 2023;15(10):2277. doi:10.3390/nu15102277
20. Clarke SF, Murphy EF, O'Sullivan O, et al. Exercise and associated dietary extremes impact on gut microbial diversity. *Gut*. 2014;63(12):1913–1920. doi:10.1136/gutjnl-2013-306541
21. Petersen LM, Bautista EJ, Nguyen H, et al. Community characteristics of the gut microbiomes of competitive cyclists. *Microbiome*. 2017;5(1):1–13. doi:10.1186/s40168-017-0320-4
22. Jang LG, Choi G, Kim SW, Kim BY, Lee S, Park H. The combination of sport and sport-specific diet is associated with characteristics of gut microbiota: an observational study. *J Int Soc Sports Nutr*. 2019;16(1). doi:10.1186/s12970-019-0290-y
23. Murtaza N, Burke LM, Vlahovich N, et al. The effects of dietary pattern during intensified training on stool microbiota of elite race walkers. *Nutrients*. 2019;11(2):1–14. doi:10.3390/nu11020261
24. Girirajan S, Campbell C, Eichler E. Meta'omic analysis of elite athletes identifies a performance- enhancing microbe that functions via lactate metabolism. *Physiol Behav*. 2011;176(5):139–148. doi:10.1038/s41591-019-0485-4.Meta
25. Liang R, Zhang S, Peng X, et al. Characteristics of the gut microbiota in professional martial arts athletes: a comparison between different competition levels. *PLoS One*. 2019;14(12):1–13. doi:10.1371/journal.pone.0226240
26. Huminska-Lisowsk K, Zielinska K, Mieszkowski J, et al. Microbiome features associated with performance measures in athletic and nonathletic individuals: a case-control study. *PLoS One*. 2024;19(2):1–21. doi:10.1371/journal.pone.0297858
27. Hampton-Marcell JT, Eshoo TW, Cook MD, Gilbert JA, Horswill CA, Poretsky R. Comparative analysis of gut microbiota following changes in training volume among swimmers. *Int J Sports Med*. 2020;41(5):292–299. doi:10.1055/a-1079-5450
28. Campbell SC, Wisniewski PJ, Noji M, et al. The effect of diet and exercise on intestinal integrity and microbial diversity in mice. *PLoS One*. 2016;11(3):1–17. doi:10.1371/journal.pone.0150502
29. Ríos-Covián D, Ruas-Madiedo P, Margolles A, Gueimonde M, De Los Reyes-gavilán CG, Salazar N Intestinal short chain fatty acids and their link with diet and human health. *Front Microbiol*. 2016;7. doi:10.3389/fmicb.2016.00185
30. Mörkl S, Lackner S, Müller W, et al. Gut microbiota and body composition in anorexia nervosa inpatients in comparison to athletes, overweight, obese, and normal weight controls. *Int J Eat Disord*. 2017;50(12):1421–1431. doi:10.1002/eat.22801
31. Haro C, Montes-Borrego M, Rangel-Zúñiga OA, et al. Two healthy diets modulate gut microbial community improving insulin sensitivity in a human obese population. *J Clin Endocrinol Metab*. 2016;101(1):233–242. doi:10.1210/jc.2015-3351
32. Liu Z, Liu HY, Zhou H, et al. Moderate-intensity exercise affects gut microbiome composition and influences cardiac function in myocardial infarction mice. *Front Microbiol*. 2017;8:1–11. doi:10.3389/fmicb.2017.01687
33. Lennard K, Dabee S, Barnabas SL, et al. Microbial composition predicts genital tract inflammation and persistent bacterial vaginosis in South African adolescent females. *Infect Immun*. 2018;86(1):1–18. doi:10.1128/IAI.00410-17
34. He X, Ding L, Su W, et al. Distribution of Endotoxins in full scale pharmaceutical wastewater treatment plants and its relationship with microbial community structure. *Water Sci Technol*. 2018;77(10):2397–2406. doi:10.2166/wst.2018.162
35. Cronin O, Barton W, Skuse P, et al. A prospective metagenomic and metabolomic analysis of the impact of exercise and/or whey protein supplementation on the gut microbiome of sedentary adults. *mSystems*. 2018;3(3):1–17. doi:10.1128/msystems.00044-18

36. Nakamura N, Lin HC, McSweeney CS, MacKie RI, Rex Gaskins H. Mechanisms of microbial hydrogen disposal in the human colon and implications for health and disease. *Annu Rev Food Sci Technol*. 2010;1(1):363–395. doi:10.1146/annurev.food.102308.124101
37. Samuel BS, Hansen EE, Manchester JK, et al. Genomic and metabolic adaptations of methanobrevibacter smithii to the human gut. *Proc Natl Acad Sci U S A*. 2007;104(25):10643–10648. doi:10.1073/pnas.0704189104
38. Han M, Yang K, Yang P, et al. Stratification of athletes' gut microbiota: the multifaceted hubs associated with dietary factors, physical characteristics and performance. *Gut Microbes*. 2020;12(1):1–18. doi:10.1080/19490976.2020.1842991
39. Freitas CG, Aoki MS, Franciscon CA, Arruda AFS, Carling C, Moreira A. Psychophysiological responses to overloading and tapering phases in elite young soccer players. *Pediatr Exerc Sci*. 2014;26(2):195–202. doi:10.1123/pes.2013-0094
40. Clarke G, Stilling RM, Kennedy PJ, Stanton C, Cryan JF, Dinan TG. Minireview: gut microbiota: the neglected endocrine organ. *Mol Endocrinol*. 2014;28(8):1221–1238. doi:10.1210/me.2014-1108
41. Moloney RD, Desbonnet L, Clarke G, Dinan TG, Cryan JF. The microbiome: stress, health and disease. *Mamm Genome*. 2014;25(1–2):49–74. doi:10.1007/s00335-013-9488-5
42. Lahiri S, Kim H-J, García-Pérez I, et al. The gut microbiota influences skeletal muscle mass and function in mice. *Am Assoc Adv Sci*. 2019;11(502). doi:10.1126/scitranslmed.aan5662
43. Liu C, Cheung WH, Li J, et al. Understanding the gut microbiota and sarcopenia: a systematic review. *J Cachexia, Sarcopenia Muscle*. 2021;12(6):1393–1407. doi:10.1002/jcsm.12784
44. Costa AV. Exercise, nutrition and gut microbiota: possible links and consequences. *Int. J. Sports Exerc*. 2017;3(4):69.doi:10.23937/2469-5718/1510069
45. Solnick JV. Clinical significance of helicobacter species other than helicobacter pylori. *Clin Infect Dis*. 2003;36:349–354.
46. Nohesara S, Abdolmaleky HM, Zhou J, Thiagalingam S. Microbiota-induced epigenetic alterations in depressive disorders are targets for nutritional and probiotic therapies. *Multidiscip Digit Publ Inst*. 2023;14(12):2217. doi:10.3390/genes14122217
47. Ticinesi A, Lauretani F, Milani C, et al. Aging gut microbiota at the cross-road between nutrition, physical frailty, and sarcopenia: is there a gut–muscle axis? *Nutrients*. 2017;9(12):1–20. doi:10.3390/nu9121303
48. Furber MJW, Young GR, Holt GS, et al. Gut microbial stability is associated with greater endurance performance in athletes undertaking dietary periodization. *mSystems*. 2022;7(3). doi:10.1128/msystems.00129-22
49. Wu GD, Chen J, Hoffmann C, et al. Linking long-term dietary patterns with gut microbial enterotypes. *Science*. 2011;334:105–109. doi:10.1126/science.1208344
50. Achten J, Halson SL, Moseley L, Rayson MP, Casey A, Jeukendrup AE. Higher dietary carbohydrate content during intensified running training results in better maintenance of performance and mood state. *J Appl Physiol*. 2004;96(4):1331–1340. doi:10.1152/japplphysiol.00973.2003
51. Gleeson M. Dosing and efficacy of glutamine supplementation in human exercise and sport training. *J Nutr*. 2008;138(10):2045–2049. doi:10.1093/jn/138.10.2045s
52. Gleeson M, Bishop NC. Special feature for the Olympics: effects of exercise on the immune system: modification of immune responses to exercise by carbohydrate, glutamine and anti-oxidant supplements. *Immunol Cell Biol*. 2000;78(5):554–561. doi:10.1111/j.1440-1711.2000.t01-6-.x
53. De Filippo C, Cavalieri D, Di Paola M, et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. *Proc Natl Acad Sci U S A*. 2010;107(33):14691–14696. doi:10.1073/pnas.1005963107
54. American College of Sports Medicine and others. Nutrition and athletic performance: position statement. *Med Sci Sport Exercise*. 2009;32:709–731. doi:10.1249/MSS.0b013e318190eb86
55. Brown WMC, Davison GW, McClean CM, Murphy MH. A systematic review of the acute effects of exercise on immune and inflammatory indices in untrained adults. *Sport Med*. 2015;1(1):1–10. doi:10.1186/s40798-015-0032-x
56. Kočandrle R, Couprie DL. Generation. *SpringerBriefs Philos*. 2017;529(7585):73–85. doi:10.1007/978-3-319-49754-9_7
57. De La Serre CB, Ellis CL, Lee J, Hartman AL, Rutledge JC, Raybould HE. Propensity to high-fat diet-induced obesity in rats is associated with changes in the gut microbiota and gut inflammation. *Am J Physiol Gastrointest Liver Physiol*. 2010;299(2):440–448. doi:10.1152/ajpgi.00098.2010
58. Shei RJ, Lindley MR, Mickleborough TD. Omega-3 polyunsaturated fatty acids in the optimization of physical performance. *Mil Med*. 2014;179(11):144–156. doi:10.7205/MILMED-D-14-00160
59. Drenowatz C, Eisenmann JC, Carlson JJ, Pfeiffer KA, Pivarnik JM. Energy expenditure and dietary intake during high-volume and low-volume training periods among male endurance athletes. *Appl Physiol Nutr Metab*. 2012;37(2):199–205. doi:10.1139/H11-155
60. De Oliveira EP, Burini RC, Jeukendrup A. Gastrointestinal complaints during exercise: prevalence, etiology, and nutritional recommendations. *Sport Med*. 2014;44(SUPPL.1):79–85. doi:10.1007/s40279-014-0153-2
61. Cermak NM, Res PT, De Groot LCPGM, Saris WHM, Van Loon LJC. Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training: a meta-analysis. *Am J Clin Nutr*. 2012;96(6):1454–1464. doi:10.3945/ajcn.112.037556
62. Moreno-Pérez D, Bressa C, Bailén M, et al. Effect of a protein supplement on the gut microbiota of endurance athletes: a randomized, controlled, double-blind pilot study. *Nutrients*. 2018;10(3):1–16. doi:10.3390/nu10030337
63. Zeppa SD, Agostini D, Gervasi M, et al. Mutual interactions among exercise, sport supplements and microbiota. *Nutrients*. 2020;12(1). doi:10.3390/nu12010017
64. Liu J, Wang F, Luo H, et al. Protective effect of butyrate against ethanol-induced gastric ulcers in mice by promoting the anti-inflammatory, anti-oxidant and mucosal defense mechanisms. *Int Immunopharmacol*. 2016;30:179–187. doi:10.1016/j.intimp.2015.11.018
65. Caine JJ, Geracioti TD. Taurine, energy drinks, and neuroendocrine effects. *Cleve Clin J Med*. 2016;83(12):895–904. doi:10.3949/ccjm.83a.15050
66. Rahimi MH, Shab-Bidar S, Mollahosseini M, Djafarian K. Branched-chain amino acid supplementation and exercise-induced muscle damage in exercise recovery: a meta-analysis of randomized clinical trials. *Nutrition*. 2017;42:30–36. doi:10.1016/j.nut.2017.05.005
67. Oliphant K, Allen-Vercoe E. Macronutrient metabolism by the human gut microbiome: major fermentation by-products and their impact on host health. *Microbiome*. 2019;7(1):1–15. doi:10.1186/s40168-019-0704-8
68. Wolf PG, Gaskins HR, Ridlon JM, et al. Effects of taurocholic acid metabolism by gut bacteria: a controlled feeding trial in adult African American subjects at elevated risk for colorectal cancer. *Contemp Clin Trials Commun*. 2020;19:100611. doi:10.1016/j.conctc.2020.100611

69. Jäger R, Zaragoza J, Purpura M, et al. Probiotic administration increases amino acid absorption from plant protein: a placebo-controlled, randomized, double-blind, multicenter, crossover study. *Probiotics Antimicrob Proteins*. 2020;12(4):1330–1339. doi:10.1007/s12602-020-09656-5
70. Jäger R, Purpura M, Farmer S, Cash HA, Keller D. Probiotic Bacillus coagulans GBI-30, 6086 improves protein absorption and utilization. *Probiotics Antimicrob Proteins*. 2018;10(4):611–615. doi:10.1007/s12602-017-9354-y
71. Romijn JA, Coyle EF, Sidossis LS, et al. Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. *Am J Physiol*. 1993;265(3 28–3):380–391. doi:10.1152/ajpendo.1993.265.3.e380
72. Thomas DT, Erdman KA, Burke LM. Position of the academy of nutrition and dietetics, dietitians of Canada, and the American college of sports medicine: nutrition and athletic performance. *J Acad Nutr Diet*. 2016;116(3):501–528. doi:10.1016/j.jand.2015.12.006
73. Cermak NM, Van Loon LJC. The use of carbohydrates during exercise as an ergogenic aid. *Sport Med*. 2013;43(11):1139–1155. doi:10.1007/s40279-013-0079-0
74. Burke LM, Kiens B, Ivy JL. Carbohydrates and fat for training and recovery. *J Sports Sci*. 2004;22(1):15–30. doi:10.1080/0264041031000140527
75. Burke LM, Hawley JA, Wong SHS, Jeukendrup AE. Carbohydrates for training and competition. *J Sports Sci*. 2011;29(SUPPL. 1):S17–S27. doi:10.1080/02640414.2011.585473
76. Communications S. Nutrition and Athletic Performance. *Med Sci Sports Exerc*. 2016;48(3):543–568. doi:10.1249/MSS.0000000000000852
77. Cao J, Lei S, Wang X, Cheng S. The effect of a ketogenic low-carbohydrate, high-fat diet on aerobic capacity and exercise performance in endurance athletes: a systematic review and meta-analysis. *Nutrients*. 2021;13(8):2896. doi:10.3390/nu13082896
78. Burke LM, Ross ML, Garvican-Lewis LA, et al. Low carbohydrate, high fat diet impairs exercise economy and negates the performance benefit from intensified training in elite race walkers. *J Physiol*. 2017;595(9):2785–2807. doi:10.1113/JP273230
79. Burke LM, Whitfield J, Heikura IA, et al. Adaptation to a low carbohydrate high fat diet is rapid but impairs endurance exercise metabolism and performance despite enhanced glycogen availability. *J Physiol*. 2021;599(3):771–790. doi:10.1113/JP280221
80. Sokol H, Pigneur B, Watterlot L. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *PNAS*. 2008;105(43):16731–16736. doi:10.1002/path.1711620408
81. Tian Y, Xu Q, Sun L, Ye Y, Ji G. Short-chain fatty acids administration is protective in colitis-associated colorectal cancer development. *J Nutr Biochem*. 2018;57:103–109. doi:10.1016/j.jnutbio.2018.03.007
82. den Besten G, van Eunen K, Groen AK, Venema K, Reijngoud D-J, Bakker BM. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. *J Lipid Res*. 2013;54(9):2325–2340. doi:10.1194/jlr.R036012
83. Tang Y, Chen Y, Jiang H, Robbins GT, Nie D G-protein-coupled receptor for short-chain fatty acids suppresses colon cancer. *Int J Cancer G*. 2011;128:847–856. doi:10.1002/ijc.25638
84. LeBlanc JG, Chain F, Martín R, Bermúdez-Humarán LG, Courau S, Langella P. Beneficial effects on host energy metabolism of short-chain fatty acids and vitamins produced by commensal and probiotic bacteria. *Microb Cell Fact*. 2017;16(1):1–10. doi:10.1186/s12934-017-0691-z
85. Hsu YJ, Chiu CC, Li YP. Effect of intestinal microbiota on exercise performance in mice. *J Strength Cond Res*. 2015;29(2):552–558. doi:10.1519/JSC.0000000000000644
86. Huang L, Li T, Zhou M, et al. Hypoxia improves endurance performance by enhancing short chain fatty acids production via gut microbiota remodeling. *Front Microbiol*. 2022;12:1–13. doi:10.3389/fmicb.2021.820691
87. Okamoto T, Morino K, Ugi S, et al. Microbiome potentiates endurance exercise through intestinal acetate production. *Am J Physiol*. 2019;316(5):E956–E966. doi:10.1152/ajpendo.00510.2018
88. den Besten G, Lange K, Havinga R, et al. Gut-derived short-chain fatty acids are vividly assimilated into host carbohydrates and lipids. *Am J Physiol Gastrointest Liver Physiol*. 2013;305(12):900–910. doi:10.1152/ajpgi.00265.2013
89. Bjorntorp P. Importance of fat as a support nutrient for energy: metabolism of athletes. *J Sports Sci*. 1991;9:71–76. doi:10.1080/02640419108729867
90. Fritzen AM, Lundsgaard AM, Kiens B. Dietary fuels in athletic performance. *Annu Rev Nutr*. 2019;39:45–73. doi:10.1146/annurev-nutr-082018-124337
91. Van Loon LJC, Schrauwen-Hinderling VB, Koopman R, et al. Influence of prolonged endurance cycling and recovery diet on intramuscular triglyceride content in trained males. *Am J Physiol*. 2003;285(4 48–4):804–811. doi:10.1152/ajpendo.00112.2003
92. Helge JW, Kiens B. Muscle enzyme activity in humans: role of substrate availability and training. *Am J Physiol Regul Integr Comp Physiol*. 1997;272(5):41–45. doi:10.1152/ajpregu.1997.272.5.r1620
93. Shen W, Gaskins HR, McIntosh MK. Influence of dietary fat on intestinal microbes, inflammation, barrier function and metabolic outcomes. *J Nutr Biochem*. 2014;25(3):270–280. doi:10.1016/j.jnutbio.2013.09.009
94. Thielecke F, Blannin A. Omega-3 fatty acids for sport performance—are they equally beneficial for athletes and amateurs? A narrative review. *Nutrients*. 2020;12(12):1–28. doi:10.3390/nu12123712
95. Costantini L, Molinari R, Farinon B, Merendino N. Impact of omega-3 fatty acids on the gut microbiota. *Int J Mol Sci*. 2017;18(12):2645. doi:10.3390/ijms18122645
96. Li Q, Zhang Q, Wang M, Zhao S, Xu G, Li J. N-3 polyunsaturated fatty acids prevent disruption of epithelial barrier function induced by proinflammatory cytokines. *Mol Immunol*. 2008;45(5):1356–1365. doi:10.1016/j.molimm.2007.09.003
97. Watson H, Mitra S, Croden FC, et al. A randomised trial of the effect of omega-3 polyunsaturated fatty acid supplements on the human intestinal microbiota. *Gut*. 2018;67(11):1974–1983. doi:10.1136/gutjnl-2017-314968
98. Bhat M, Ismail A. Vitamin D treatment protects against and reverses oxidative stress induced muscle proteolysis. *J Steroid Biochem Mol Biol*. 2015;152:171–179. doi:10.1016/j.jsbmb.2015.05.012
99. Wang TJ. Vitamin D and cardiovascular disease. *Annu Rev Med*. 2016;67:261–272. doi:10.1146/annurev-med-051214-025146
100. Barker T, Henriksen VT, Martins TB, et al. Higher serum 25-hydroxyvitamin D concentrations associate with a faster recovery of skeletal muscle strength after muscular injury. *Nutrients*. 2013;5(4):1253–1275. doi:10.3390/nu5041253
101. Bora SA, Kennett MJ, Smith PB, Patterson AD, Cantorna MT. The gut microbiota regulates endocrine vitamin D metabolism through fibroblast growth factor 23. *Front Immunol*. 2018;9:1–11. doi:10.3389/fimmu.2018.00408

102. Kuo HK, Liao KC, Leveille SG, et al. Relationship of homocysteine levels to quadriceps strength, gait speed, and late-life disability in older adults. *J Gerontol - Ser a Biol Sci Med Sci*. 2007;62(4):434–439. doi:10.1093/gerona/62.4.434
103. Dzik KP, Kaczor JJ. Mechanisms of vitamin D on skeletal muscle function: oxidative stress, energy metabolism and anabolic state. *Eur J Appl Physiol*. 2019;119(4):825–839. doi:10.1007/s00421-019-04104-x
104. Ogan D, Pritchett K. Vitamin D and the athlete: risks, recommendations, and benefits. *Nutrients*. 2013;5(6):1856–1868. doi:10.3390/nu5061856
105. Steinert RE, Lee YK, Sybesma W. Vitamins for the gut microbiome. *Trends Mol Med*. 2020;26(2):137–140. doi:10.1016/j.molmed.2019.11.005
106. Liu KY, Nakatsu CH, Jones-Hall Y, Kozik A, Jiang Q. Vitamin E alpha- and gamma-tocopherol mitigate colitis, protect intestinal barrier function and modulate the gut microbiota in mice. *Free Radic Biol Med*. 2021;163:180–189. doi:10.1016/j.freeradbiomed.2020.12.017
107. Dockray GJ. Enteroendocrine cell signalling via the vagus nerve. *Curr Opin Pharmacol*. 2013;13(6):954–958. doi:10.1016/j.coph.2013.09.007
108. Gabanyi I, Lepousez G, Wheeler R, et al. Bacterial sensing via neuronal Nod2 regulates appetite and body temperature. *Science*. 2022;376 (6590). doi:10.1126/science.abj3986
109. Estaki M, Pither J, Baumeister P, et al. Cardiorespiratory fitness as a predictor of intestinal microbial diversity and distinct metagenomic functions. *Microbiome*. 2016;4:1–13. doi:10.1186/s40168-016-0189-7
110. Dicks LMT. Gut bacteria and neurotransmitters. *Microorganisms*. 2023;10:1838.
111. Hoffman JM, Margolis KG. Building community in the gut: a role for mucosal serotonin. *Nat Portf*. 2019;17(1):6–8. doi:10.1038/s41575-019-0227-6
112. Williams BB, Van Benschoten AH, Cimermančič P, et al. Discovery and characterization of gut microbiota decarboxylases that can produce the neurotransmitter tryptamine. *Cell Press*. 2014;16(4):495–503. doi:10.1016/j.chom.2014.09.001
113. Frankiensztajn LM, Elliott E, Koren O. The microbiota and the hypothalamus-pituitary-adrenocortical (HPA) axis, implications for anxiety and stress disorders. *Elsevier BV*. 2020;62:76–82. doi:10.1016/j.conb.2019.12.003
114. Barrett E, Ross RP, O'Toole PW, Fitzgerald GF, Stanton C. γ-aminobutyric acid production by culturable bacteria from the human intestine. *J Appl Microbiol*. 2012. doi:10.1111/j.1365-2672.2012.05344.x
115. D'Ascola A, Bruschetta G, Zanghì G, et al. Changes in plasma 5-HT levels and equine leukocyte SERT expression in response to treadmill exercise. *Res Vet Sci*. 2018;118:184–190. doi:10.1016/j.rvsc.2018.02.012
116. Mach N, Fuster-Botella D. Endurance exercise and gut microbiota: a review. *J Sport Heal Sci*. 2017;6(2):179–197. doi:10.1016/j.jshs.2016.05.001
117. O'Mahony SM, Clarke G, Borre YE, Dinan TG, Cryan JF. Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. *Behav Brain Res*. 2015;277:32–48. doi:10.1016/j.bbr.2014.07.027
118. Koopman N, Katsavelis D, Ten Hove AS, Brul S, de Jonge WJ, Seppen J. The multifaceted role of serotonin in intestinal homeostasis. *Int J Mol Sci*. 2021;22(17):1–23. doi:10.3390/ijms22179487
119. Hosoi T, Okuma Y, Matsuda T, Nomura Y. Novel pathway for LPS-induced afferent vagus nerve activation: possible role of nodose ganglion. *Auton Neurosci Basic Clin*. 2005;120(1–2):104–107. doi:10.1016/j.autneu.2004.11.012
120. Lin GG, Scott JG. Neural regulation of endocrine and autonomic stress responses. *Nat Rev Neurosci*. 2009;10(6):397–409. doi:10.1038/nrn2647.Neural
121. Crumeyrolle-Arias M, Jaglin M, Bruneau A, et al. Absence of the gut microbiota enhances anxiety-like behavior and neuroendocrine response to acute stress in rats. *Psychoneuroendocrinology*. 2014;42:207–217. doi:10.1016/j.psyneuen.2014.01.014
122. Ducray HAG, Globa L, Pustovyy O. Prevention of excessive exercise-induced adverse effects in rats with bacillus subtilis BSB3. *J Appl Microbiol*. 2020;128(4):1163–1178. doi:10.1111/jam.14544
123. Ünsal C, Ünsal H, Ekici M, et al. The effects of exhaustive swimming and probiotic administration in trained rats: oxidative balance of selected organs, colon morphology, and contractility. *Physiol Int*. 2018;105(4):347–357. doi:10.1556/2060.105.2018.4.25
124. Lollo PCB, Cruz AG, Morato PN, et al. Probiotic cheese attenuates exercise-induced immune suppression in Wistar rats. *J Dairy Sci*. 2012;95 (7):3549–3558. doi:10.3168/jds.2011-5124
125. Lee MC, Hsu YJ, Ho HH, et al. Lactobacillus salivarius subspecies salicinius sa-03 is a new probiotic capable of enhancing exercise performance and decreasing fatigue. *Microorganisms*. 2020;8(4):545. doi:10.3390/microorganisms8040545
126. Lee MC, Hsu YJ, Chuang HL, et al. In vivo ergogenic properties of the Bifidobacterium longum OLP-01 isolated from a weightlifting gold medalist. *Nutrients*. 2019;11(9):2003. doi:10.3390/nu11092003
127. Nicholson JK, Holmes E, Kinross J, et al. Host-gut microbiota metabolic interactions. *Science*. 2012;336(6086):1262–1267. doi:10.1126/science.1223813
128. Howatson G, Van Someren KA. The prevention and treatment of exercise-induced muscle damage. *Sport Med*. 2008;38(6):483–503. doi:10.2165/00007256-200838060-00004
129. Huang WC, Wei CC, Huang CC, Chen WL, Huang HY. The beneficial effects of Lactobacillus plantarum PS128 on high-intensity, exercise-induced oxidative stress, inflammation, and performance in triathletes. *Nutrients*. 2019;11(2):1–13. doi:10.3390/nu11020353
130. Xia W, Li X, Khan I, et al. Lycium berry polysaccharides strengthen gut microenvironment and modulate gut microbiota of the mice. *Evid Based Complement Altern Med*. 2020;2020. doi:10.1155/2020/8097021
131. Khan I, Huang G, Li X, et al. Mushroom polysaccharides and jiaogulan saponins exert cancer preventive effects by shaping the gut microbiota and microenvironment in Apc Min / + mice. *Pharmacol Res*. 2019;148:104448. doi:10.1016/j.phrs.2019.104448
132. Huang G, Khan I, Li X, et al. Ginsenosides Rb3 and Rd reduce polyps formation while reinstate the dysbiotic gut microbiota and the intestinal microenvironment in ApcMin/+mice. *Sci Rep*. 2017;7(1):1–14. doi:10.1038/s41598-017-12644-5
133. Kim YA, Jin SW, Oh SH, et al. Platycodon grandiflorum-derived saponin enhances exercise function, skeletal muscle protein synthesis, and mitochondrial function. *Food Chem Toxicol*. 2018;118:94–104. doi:10.1016/j.fct.2018.04.062
134. Kim YA, Oh SH, Lee GH, et al. Platycodon grandiflorum-derived saponin attenuates the eccentric exercise-induced muscle damage. *Food Chem Toxicol*. 2018;112:150–156. doi:10.1016/j.fct.2017.12.045
135. Baker LB, Nuccio RP, Jeukendrup AE. Acute effects of dietary constituents on motor skill and cognitive performance in athletes. *Nutr Rev*. 2014;72(12):790–802. doi:10.1111/nure.12157
136. Goel DP, Geiger JD, Shan JJ, Kriellaars D, Pierce GN. Doping-control urinalysis of a ginseng extract, Cold-FX (R), in athletes. *Int J Sport Nutr Exerc Metab*. 2004;1(69):5–24. doi:10.1123/ijsnem.14.4.473

137. Shan X, Zhou J, Ma T, Chai Q. Lycium barbarum polysaccharides reduce exercise-induced oxidative stress. *Int J Mol Sci*. 2011;12 (2):1081–1088. doi:10.3390/ijms12021081
138. Chi A, Tang L, Zhang J, Zhang K. Chemical composition of three polysaccharides from gynostemma pentaphyllum and their antioxidant activity in skeletal muscle of exercised mice. *Int J Sport Nutr Exerc Metab*. 2012;22(6):479–485. doi:10.1123/ijsnem.22.6.479