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Literature Review

The Link between Gut Microbiota and Athletic Performance

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Received: January 10, 2019; **Published:** March 26, 2019

Abstract

Around 20 years ago, gut bacteria was started to be studied in more depth. Along with the evolution of technology more knowledge was gathered and there was concluded that it offers many benefits to the human functions. However, it was discovered it can be altered by different factors like environment or diet. In case of athletes, gut microbiota can be also altered by exercise and vice versa. This change in human bacteria has a directly impact on host immunity which can trigger further other diseases or decrease performance. Starting from muscoskeletal problems to central fatigue, this chain reaction starting from the gut affects the athlete throughout the competitive season. Therefore, an increase in food products high in healthy microbiota could have a huge impact on sport performance. This mini-review summarises the current literature of the development and influence that gut microbiota has on athlete health and performance, highlighting the interactions that could lead to this.

Keywords: *Gut Microbiota; Athletic Performance*

Introduction

The human gut microbiota does not represent a new topic in research area, but is still not fully elucidated. Starting from 1680s, Anthonie Leewenhoek compared his oral and faecal microbiota with other samples from individuals that had different conditions, healthy or ill [1]. He observed thoughtful differences between the two conditions, but the study investigation was limited by the technology level. However, it is clear that the idea of gut microbiota investigation is as old as microbiology itself [1,2]. Each person contains around of 10 - 100 trillion symbiotic microbial cells, which are found primarily in the gut bacteria. The intestinal tract contains also viruses like archaea, fungi, protozoans, thus the microbial cells are altered by different conditions which sometimes reflect a positive or negative reaction to health [3-5]. These microbes take action in vitamin production, fibre digestion, immunity, consequently contributing significantly to health and disease [1,5-7].

There is a small amount of studies that looked at the impact of exercise on microbiomes [8-10]. One experiment that looked at elite rugby players showed evidence that athletes had greater microbiota diversity comparing to normal population [11]. This diversity of bacteria had been associated with an increase in protein intake and a higher creatine kinase level comparing to the control group [9]. Therefore, gut microbiota can depend on different nutritional factors and training level [8]. Athlete fatigue or mood instabilities during training and competitive environment or gastrointestinal distress are well known factors present in training or competition [12]. During intense effort, psychological and physical demands induce a stress response that activates sympathetic-adrenomedullary and hypothalamus pituitary adrenal (HPA) axes, which results further in a release of stress and catabolic hormones, inflammatory cytokines and microbial molecules [13]. This brain-gut axis of the bacteria is considered to be a key aspect which can influence host behaviour, intestinal barrier and immune functions [8].

The aim of this brief review is to critical analyse the current evidence of gut microbiota and to suggest the best way of recommendation to improve the athletic performance. Some researchers showed evidence that exercise can be an effective in decreasing levels of Turicibacter and increases Ruminococcus in the large intestine, that have key functions in removing the intestinal mucus and immunity [14]. Furthermore, microbiota diet have been promoted lately and represents an interesting area because it could modulate the gut microbiota composition [15]. Taking in consideration the variation of stress response periods in athletes, to plan a standard regime diet is difficult [16]. However, some researchers tried using probiotics and prebiotics and found that microbiota could act sometimes like an endocrine organ (e.g. secreting dopamine, neurotransmitters or serotonin), thus regulating the brain-gut axis in athletes [17]. The problem is that American Dietetic Association [18] or International Institute of Sport Nutrition [19] recommends high amount of carbohydrates (6 - 10 g/kg per day) intake to sustain muscle glucose and full fill muscle glycogen stores, high to moderate protein intake (1.2 - 1.7 g/kg per day) to assure the protein synthesis demands, low amount of fat intake (20 - 35% of the daily food) and low amount of fibre intake for an easy gastric emptying and to reduce the GI stress. Thus, inadequate intake of fibre can promote a reduction of microbiota diversity and function in GI [8].

Literature Review

Interest in gut microbiota have grown lately in athletic performance because it became linked with immune system, bone health and muscle mass [20-23]. Thus, through exercise normal homeostasis is altered from exercise stressors that trigger central fatigue and directly affect performance [12].

Central fatigue altering gut microbiota

Conform to the research review made by Purvis., *et al.*, approximately one to three thirds of athletes are under physiological and psychological stress, which were caused by the imbalance of high effort and recovery. Moreover, the stress level is considered greater in endurance athletes like swimmers, cyclists, triathlon athletes or long running marathons where the athlete trains around 4 - 6 hours per day during a macrocycle without a proper brake from the intense effort [13]. Therefore, in sport performance the focus is still on avoiding symptoms associated with the fatigue, declining performance [18].

In the GI tract can be found approximately 9 million genes and contains five phyla microbes that varies in approximately 160 species in large intestine [6]. Thus, the gut microbiota promotes food absorption, digestion and promotes energy to the human host. Besides that, it also provide folate, vitamin k2 and SCFAs [7]. Multiple functions are promoted by the intestinal microbiota, another example are the high glycemic index carbohydrates that are assimilated and burned for anaerobic energy production like acetate N-butyrate or propionate with gut bacteria help. Some evidence shows that microbiota it may also control the neurotransmitters which are in response to the physiological and psychological stress [24]. A lot of research have been made lately, on probiotics supplementation in athletes that looked at clinical outcomes and immune functions and linked them with fatigue [25-28]. For example, an initial study was made by Clancy., *et al.* (2016) supplemented healthy athletes with *L. acidophilus* at a dose of 2.0 x 10^{10} cells per day for four weeks. The results showed that fatigue athletes had lower T cells and were more predisposed to illness having decreased the immune functions. However, with probiotic therapy, immune homeostasis was less altered. This research was sustained by other results. A double blind cross over design supplemented 20 elite male runners with *L. fermnetum* over 4 months during winter and they looked at respiratory and gastrointestinal symptoms. The results showed that probiotics supplementation decreased the respiratory and GI illness symptoms. Measuring the faecal microbiota they discovered that following probiotics therapy the Lactobacillus bacteria increased 7.7 times in males. In females, the response to supplementation have been reduced to 2.2 times [29]. Thus, this paper suggest differences between sexes and environmental.

Many athletes suffer from training stress and if the proper time for recovery is not given they enter into a vicious cycle of exhaustion from training and competition, that results in fatigue and directly effects the performance [13]. There are a number of pathways that have been described along the years to lead to fatigue, insomnia or mood disturbances, but one of them is linked serotonin levels to microbiota [8,30]. During different fatigue stressors, serotonin neurotransmitters release is altered and have been associated with central fatigue leading to suboptimal performance [8]. Low levels of serotonin cause mood disturbance, deppresion also alters blood presure, gut transit and cardiac function [31]. Most of the body serotonin (95%) is produced in the enterochromaffin cells (EC) of the intestines, that

has imporant roles in driving and starting the sensory functions like gut pain awareness [32]. This connexion further stronger the idea of gut-brain bacteria imporantce. Moreover, the serotonin levels can be increased through gut microbiota synthesis during exercise [8]. Even thought, tryptophan hydroxylase (TPH) was believed to be the only gene encoding responsible serotonin synthesis, Wather., *et al.* (2003) discovered TPH1 and TPH2. Those tryptophan enzymes have been found in peripheral and pineal body, reflecting an adaptation of serotonin levels production by EC cells in brain and intestines [33].

Gut microbiota alters athletes' health

Gut microbiota can affect health through many ways that could lead to immune and metabolic dysfunctions [34]. This process is doubled in many chronic diseases [14,20]. Because athletes are always, exposed to environmental conditions (e.g. cold air, chlorine) during exercise they often develops allergies [8]. These allergies increase the risk of respiratory tract infections affecting directly the athlete's bacteria [9]. The mucosal cover of the GI zone denotes the first barrier of protection against the entering pathogens and represents the key wall in the human immunity [14]. Studies made on animal and humans showed that microbiota is an important line between healthiness and illness, more specific the progression of mucosal wall increase the immunity resistance avoiding preventable inflammatory activity [35]. There was recognised by medical research that some illnesses like obesity, colitis or metabolic syndrome are influenced by genotype, age, and environmental issues (Binnendijk and Rijkers, 2013). Thus, suggesting this interface can likewise happen in the illness periods experienced by athletes [36]. This bacteria community is composed of genito-urinary tract, respiratory tract and mucosal lining of the gut. The gut being the largest compartment containing microbiomes (Brüls and Weissenbach, 2011). Therefore, theoretically any nutrient intake can have big influence on bacterial community, suggesting that daily dietary can represent a specific intervention around training or competition (Jumpertz., *et al.* 2011). Based on this relation researchers tried supplementation with more healthy bacteria (probiotic, prebiotic) looking at how this can influence more immune system in athletes [8-10]. Energy balance of an athlete during is the key in sport performance and besides the general nutrients (macronutrients and micronutrients), microbiota holds promises in sustaining the immune system by increasing the healthy days of an athlete. All is linked with the athletes' energy deficiency, following physiological and psychological stresses where the body is becoming sensible in the attempt of recovering [22]. Gut microbiota can become a useful tool in therapeutic interventions as reflects changes in hypothalamic - pituitary axis, where this hormonal axis reflects further an overtraining syndrome which can be linked with RED-S [26].

Besides respiratory and digestive illness symptoms, human microbiota also affects bone health [23]. The link starts with the relation of microbes with inflammatory responses like rheumatoid arthritis, spondyloarthropathies and gout. Bacterial DNA originated from gut and oral have been discovered in plasma serum and joint fluid proposing a contributor factor to degenerative musculoskeletal condition, osteoarthritis, rotator cuff tendon degeneration or tendinopathy [21]. Reducing the risk injuries by keeping the bone health at optimal level is essential. There is a chain reaction starting from the energy deficiency to immune system that is influencing hormonal regulation that further affects the bone mass and bone metabolism [8,26]. The bacterial metabolism has been impaired because of physiological and psychological stress reducing the cellular messengers to the bone.

Diet manipulation like increasing protein or change fibre intake modulates microbiome [8,36]. The effects can be seen if the diet is sustained a longer period, between 2 to 4 months [26]. The researchers found an additional method, to use pro- and prebiotics, an active bacterium that was found in food, essential for basic nutritional content [3]. Prebiotics are nutritional ingredient found in also in fruits and vegetables, which represents an option for those who are vegan, and is known to confer positive benefits to humans [6,37]. With supplementation, host microbiota is influenced, thus there can be increased the immune-inflammatory axes [3,38]. In mice experiments compared to controls, antibiotics have showed to increase bone mineral density by altering microbiome that affected bone resorbing osteoclasts. Therefore, bone improvement have been observed and linked with microbiome [21]. Another supplement that could affects the gut microbiota is the antibiotic [39], used really often by human population when combating diseases. For example, Panda., *et al.* 2007, examined the faecal microbiota in 21 patients after 7 days antibiotic treatment. They presented evidence of how antibiotic supplementation decreased the gut microbiota diversity by 25%, but in the same time the treatment increased the Bacteroidetes/Firmicutes ratio. Thus, antibiotic ingestion during illness provides space to grow for resistant strains to dominate the niche by reducing at first the number and diversity of gut bacteria [39]. These results suggest further that, supplementation with antibiotic can alters immune status in bone, affecting the bone mineralisation [23]. On the other hand, prebiotics have showed to increase bone mass, by influencing

the mineral bioavailability from the diet and increasing calcium absorption in both youths and adults. They used different prebiotics types like mixed short and long chain insulin variety frunctans, galacto-oligosaccharides have increased the total body mineral mass compared to the control group [40-42]. Also by analysing the faecal microbiota there was observed an increase in faecal bifidobacteria and calcium absorption [43].

Consequently there can be seen the connection between gut microbiota barrier - inflammation - bone health [8,21,26]. There are studies that demonstrated osteoarthritis is decreased when calcium was better absorbed by bone [21]. Evidence showed that cytokines and chemokines are produced in synovial fluid and mediates the inflammatory response. The synovial fluid and tissue have been discovered to contain bacterial DNA, strengthening the idea that during bone injuries these are present there but could be limited [44,45]. Therefore, supplementation could increase the microbiota level and reduce the non-inflammatory arthropathy [21]. Finally, a better absorption of calcium by human body will increase the cross-section area or will reduce the muscle wasting during an injury that keeps the athlete away from the physical activity for long periods [43,46].

Dietary recommendations

Under stress factors, nutritional combat is one way of maintaining the haemostatic balanced [8,13,18]. Gut microbiota have been showed to be altered by nutrient availability (carbohydrates, protein, fat, fiber) that are known to contribute to energy systems [18], but also by antibiotic, prebiotic or probiotic supplementation [8]. Thus, different methods of practical actions can be taken. In table 1 below are presented the ways of altering the diet for an increase in gut microbiota.

Nutrient	Dose	Effect
Carbohydrates	7 - 12 g/kg/day (endurance athletes)	High doses of CHO ad libitum during intense training reducing fatigue and improving performance and mood.
Protein	1.2 - 1.6 g/kg/day (elite athletes)	Inadequate protein intake decrease T cells functions affecting immunity, consequently increasing the infection incidents.
Fat	15 - 30% of the diet/day	Fat diets with good amount of omega 3 and omega 6, has shown to reduce the intestinal inflammation, bacterial translocation and gastro intestinal stress. However, a high fat diet may reduce the total gut microbiota.
Fiber	38 g/day man 25 g/day women	Low fibre diet is associated with lower level of gut microbiota, antipathogenic bacteria, thus there will be an increase in gut inflammation and less sympathetic nervous system stimulation. However, high fibre diet may cause gastrointestinal stress.
Probiotics	Highly variable depending on the strain, microbial composition and metagenome. Because of gut microbiota diversity in humans, there was not established a standard dose.	Supplementing the diet with fermented food can stimulate the expansion of microorganism like Bifidobacteria and Lactobacillus that have beneficial metabolic functions. E.g. improving SCFA, results in an increasing immune and barrier functions.

Table 1: *Presented different diets alternation for improving gut microbiota based on literature [8,18,19,26].*

Based on literature review, and taking in consideration the athletes daily needs for maintaining the haemostasis level proper avoiding central fatigue a high carbohydrate diet in which is inserted some fermented food like once daily (fekir, Greek yoghurt or milk) can be suggested [16]. Carbohydrates are known to be a key nutrient in athletic performance because intake of it fuel the muscle glycogen and maintain or restore the liver glycogen, improving time to exhaustion and performance [19]. Thus, during intense effort avoid an increase in stress hormones levels like cortisol, and decrease the immunosuppression [13]. However, a diet high in carbs does not promote immune functions [8]. Consequently, inserting a Greek yoghurt in the diet can increase the gut microbiota further affecting positively the immune functions and digestibility of the athlete [8,16]. Based on the gut-brain relation increasing gut microbiota a chain reaction could be triggered affecting microbiota from synovial fluid promoting bone and tendon health [21] or increasing TPH adaptation for serotonin

production that decrease mood disturbances, depressions and changes in blood pressure [30]. Therefore combining probiotics with a high carbohydrate diet could increase the healthy days of an athlete, further indirectly increasing performance [8,16,19,47].

Conclusion

Gut microbiota represents an interesting topic in sport performance where further research needs to be made [8,11,26]. Currently research data presented evidence of how this can be altered by athletes stressors like fatigue, mood, anxiety, that can further alternate different hormonal factors affecting haemostasis [16]. Different methods have been used to increase or to recover gut microbiota diversity after physiological and psychological stressor, like antibiotics [39], pre and probiotics [28], an increase in the fibre or protein intake [26], or altering carbohydrates and protein intake depending on the goal [19]. However, there is still not established a dose, or a diet that could be used by medical clinics or sport performance institutions for different aims [10,28].

Nevertheless, research area became more aware of the bacteria importance in the human immunology development, and habits from different cultures started to be analysed as environment or birth method, proved to be critical [48,49]. Regarding athletes, training camps at different altitudes and zones for developing gut microbiota represents an interesting research area for future [50-55]. In consequence, increasing the healthy days of an athlete has a long-term positive affects enhancing performance [8,16,28].

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