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Review

Effects of high-/low-temperature and high-altitude hypoxic environments on gut microbiota of sports people: A retrospective analysis

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A R T I C L E I N F O

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A B S T R A C T

As an invisible "endocrine organ", gut microbiota is widely involved in the regulation of nervous system, endocrine system, circulatory system, and digestive system. It is also closely related to host health and the occurrence of many chronic diseases. Relevant literature shows that high temperature, low temperature, and high-altitude hypoxia may have negative effects on commensal microorganisms. The stimulation of exercise may aggravate this reaction, which is related to the occurrence of exercise-induced fever and gastrointestinal and respiratory diseases. The intervention of probiotics can alleviate the above problems to a certain extent. Therefore, this paper takes exercise in a special environment as the starting point, deeply analyses the intervention effect and potential mechanism of probiotics, and provides the theoretical basis and reference for follow-up research and application of probiotics in sports science.

Introduction

Trillions of microorganisms live in the human body, including the skin, oral cavity, nasal cavity, vagina, and intestinal tract. Amongst them, the intestinal tract has become the main place for microorganisms to inhabit due to its unique anatomical structure, forming a dense and diverse micro-ecosystem called the gut microbiota.[1] It has evolved with the host over a long time period to form a mutually beneficial and symbiotic stable system, and it has functions that the human body does not have.[2,3] As the largest and most complex micro-ecosystem in the human body, the composition and structure of gut microbiota have remarkable individual differences; gut microbiota is susceptible to high temperature, low temperature, high-altitude hypoxic and other external environments, as well as the host's own diet, exercise and age.[4] Present research on the gut microbiota of sports people carried out in sports medicine and other fields mainly focuses on the comparison between different sports events, exercise intensities, exercise levels (professional and amateur), exercise abilities (aerobic and anaerobic) and the impact of the correlation between gut microbiota and different tissue organs (e.g. intestinal tract, heart, lung and skeletal muscle). By contrast, research on the impact of the external environment of high temperature, low temperature and high-altitude hypoxia on the gut microbiota of exercise individuals is insufficient, and more studies are necessary from the perspective of disease prevention and treatment and nutritional supplements. The supplementation of probiotics can reduce the incidence and severity of sports-related diseases caused by sports personnel in a special environment from the perspective of improving the composition of gut microbiota and the integrity of the intestinal barrier structure, as well as improving the function of the body's immune system; probiotics even have the potential to alleviate sports fatigue and prolong the time of sports fatigue.[5–7] To date, probiotics, as a safe and convenient nutritional supplement, have been widely used in food, aquaculture, and other fields, as well as by scholars in sports medicine and other fields. This paper will search articles spanning nearly 10 years in the PubMed, Web of Science, EBSCO, and other databases for nearly 10 years with the keywords of 'exercise, gut microbiota, probiotics, high temperature, low temperature, and high-altitude hypoxia'. After the screening, only more than 20 relevant studies will be obtained and then summarise the relevant research on the impact of exercise on the gut microbiota under high temperature, low temperature, and high-altitude hypoxia in recent years. The intervention effect and possible mechanism of probiotics were reviewed (see Tables 1 and 2).

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Abbreviations

LPS	lipopolysaccharide
PPARs	peroxisome proliferator activated receptors
HACE	high altitude cerebral edema
HAPE	high altitude pulmonary edema
EHS	exercise-induced heat stress
URTI	upper respiratory tract infection
AMS	acute mountain sickness
TRP	tryptophan
IAld	indole-3-aldehyde
SCFA	short-chain fatty acid
IL-6	interleukin 6
TNF-α	tumor necrosis factor alpha
NF-κB	nuclear factor-κB
IgA	immunoglobulin A
IgM	immunoglobulin M
CRP	C-reactive protein
$\dot{V}O_{2max}$	maximal oxygen consumption
RH	relative humidity
CFU	colony forming units
CMV	cytomegalovirus
EBV	epstein Barr virus
FoxO1	forkhead box O1
TGF-β	transforming growth factor-beta
IL-22	interleukin-22

Table 1
Effects of exercise on gut microbiota in high-/low-temperature and high-altitude hypoxic environments.

Environment	Literature source	Research object	Result	Conclusion
High temperature	Lundgren[20]	Healthy subjects (n = 12)	There is no significant difference in the diversity of dominant rectal flora before and after short-term heat exposure.	Short-term activities in a hot environment may have no effect on gut microbiota.
	Bennett et al.[21]	Athletes (n = 22)	The relative abundance of commensal flora is related to the integrity of gastrointestinal tract and the degree of gastrointestinal symptoms.	The relative abundance of commensal flora is related to the incidence of gastrointestinal diseases.
Low temperature	Meng et al.[28]	SD rats (n = 40)	Exercise in a continuous cold environment will change the structure of gut microbiota, promote browning of white fat and reduce the stimulation of cold exposure to the cardiovascular system.	Exercise in low-temperature environment can promote weight loss by improving the structure of gut microbiota.
	Sasaki et al.[29]	ICR mice	Cold living environment can inhibit the changes in caecal pH, short-chain fatty acid (SCFA) and microbiota induced by physical activity in mice.	The changes of gut microbiota caused by exercise can be suppressed by the decrease of environmental temperature.
High-altitude hypoxia	Li et al.[40]	SD rats (n = 120)	High-altitude training has obvious damage to the intestinal mucosal barrier, with relatively large bacterial growth, IL-6 and TNF-α, and NF-κB protein expression significantly increased.	High-altitude training may damage the small intestinal mucosal barrier, which allows the increase in IL-6, TNF-α and NF-κB levels to promote bacterial growth.
	Kleessen et al.[39]	Athletes (n = 7)	The structure of gut microbiota of the people who complete high-altitude mountaineering will change significantly. *Bifidobacteria* and strains belonging to *Atopobium, Coriobacterium,* and *Eggertella* will decrease, whilst the potential pathogenic bacteria will increase.	The changes in the composition of gut microbiota may be related to the immune level and may be an important factor leading to the increased health risk of mountaineers during mountaineering in high-altitude environments.

Abbreviations.
SCFA short-chain fatty acid.
IL-6 interleukin 6.
TNF-α tumor necrosis factor alpha.
NF-κB nuclear factor-κB.

Effects of exercise on gut microbiota in high and low temperatures and high-altitude hypoxic environments

High temperature

In general, the living environment above 35 °C and the working and sports environment above 32 °C are regarded as high-temperature environments, which can trigger the stress reaction in the body, affect the blood circulation system, inhibit the immune function, and cause irreversible damage to the nervous system. Exercise in heat can increase the heat production level of the body and deepen the degree of heat stress. In particular, blood redistribution during prolonged vigorous exercise can reduce intestinal blood flow by 80%.[8,9] The double stimulation of ischaemia and high temperature will aggravate the oxidative stress of the body and damage the intestinal epithelial cells and tight junction proteins that constitute the physical barrier of the intestinal mucosa, as well as the intestinal microbiota that constitutes the intestinal mucosal biological barrier and participates in the intestinal mucosal chemical barrier.[10] The destruction of the physical barrier increases the permeability of the intestinal mucosa, breaks the microecological balance in the healthy intestine, increases the abundance of harmful bacteria, and decreases the abundance of beneficial bacteria, further aggravating the damage of the intestinal barrier and causing bacterial translocation.[11–13] A large number of studies have proved that lipopolysaccharide (LPS), the cell wall component of Gram-negative bacteria, is related to the occurrence of spasm, heatstroke, heat stroke, heat sepsis and endotoxemia, which seriously threaten the physical and mental health and sports performance of sports personnel.[14–17] Costa et al.[18] found that the adverse effects of exercise on intestinal function under a high-temperature environment can be alleviated by improving intestinal permeability and bacterial translocation. Therefore, some scholars proposed that the gut microbiota, as a complex ecosystem, should be paid more attention in research on the aetiology and treatment of exertional heat illness.[19]

At present, studies on the influence of exercise on gut microbiota in a high-temperature environment are relatively few, and the results are not

Table 2
Effects of probiotics supplementation on sports population in high- and low-temperature environments.

Environment	Literature source	Research object	Probiotics	Intervention time	Conclusion
High temperature	Shing et al.[5]	Athletes (n = 10)	*Lactobacillus*、 *Bifidobacterium*、 *Streptococcus strains*	4 weeks	Probiotics can prolong the running time of athletes from high temperature to exhaustion.
	Gill et al.[47]	Athletes (n = 8)	*Lactobacillus casei (L.casei)*	7 days	Supplementation of probiotics for 7 days before exercise-induced heat stress (EHS) did not provide more respiratory mucosal immune protection.
	Gill et al.[46]	Athletes (n = 8)	*Lactobacillus casei (L. casei)*	7 days	Short-term supplementation of large doses of probiotic beverages could not reduce endotoxemia caused by EHS.
Low temperature	Cox et al.[51]	Athletes (n = 20)	*Lactobacillus fermentum VRI-003*	4 weeks	Taking probiotics in advance by high-level long-distance runners can significantly reduce the days and severity of respiratory diseases.
	Marinkovic et al.[69]	Athletes (n = 50)	*Lactobacillus helveticus Lafti® L10*	14 weeks	Long-term supplementation of probiotics shortened the duration of upper respiratory tract infection (URTI) attacks during winter training of elite athletes.
	Strasser et al.[53]	Athletes (n = 33)	*Bifidobacterium bifidum W23*、 *Bifidobacterium lactis W51*、 *Enterococcus faecium W54*	12 weeks	Daily supplementation of probiotics can inhibit the decrease of tryptophan level caused by exercise and reduce the incidence of URTI, but it is not beneficial to exercise performance.
	Gleeson et al.[52]	Athletes (n = 58)	*Lactobacillus casei Shirota*	16 weeks	Regular intake of probiotics can effectively reduce the URTI incidence rate of athletes, which may be related to better maintenance of salivary IgA level during winter training and competition.
	Gleeson et al.[58]	Athletes (n = 243)	*Lactobacillus casei Shirota*	20 weeks	Regular intake of probiotics will not reduce the incidence of upper respiratory tract infection, but it can reduce the titre of antibodies such as cytomegalovirus in plasma and enhance the overall immune status.
	West et al.[7]	Athletes (n = 99)	*Lactobacillus fermentum* (PCC®)	11 weeks	*Lactobacillus fermentum* can be used as a beneficial nutritional adjuvant for healthy exercise men, but the impact on female URTI is uncertain and needs to be further solved.
	Kokubo et al.[63]	Athletes (n = 50)	*Lactococcus* lactis *JCM 5805*	13 days	It can reduce the incidence rate and severity of URTI and reduce the fatigue accumulation of athletes in continuous high-intensity sports, but it does not affect the index level of muscle injury and stress.

Abbreviations.
EHS exercise-induced heat stress.
URTI upper respiratory tract infection.
IgA immunoglobulin A.

uniform. For example, Lundgren et al. first explored the impact of moderate workload in heat on gut microbiota and found that the Shannon index and Simpson index of gut microbial diversity of subjects had not changed significantly; moreover, the abundance of *Lactobacillus* and *Enterobacteriaceae* had no significant difference, which may be due to the short stimulation time of 3 h.[20] However, some research results showed that the abundance and composition of the intestinal microbiota are related to the gastrointestinal symptoms caused by exercise heat stress. Although this correlation is not specific to a certain bacterium, the increase in the abundance of *Akkermansiaceae*, *Ruminococcaee*, *Tenericues*, *Verrucomicrobia,* and other bacteria is related to the increase in the level of intestinal epithelial injury markers. The presence or lack of symbiotic bacteria that produce short-chain fatty acids may be related to inflammation. Gastrointestinal symptoms are related to temperature regulation, suggesting that the abundance and composition of intestinal microbiota may be a potential indicator of gastrointestinal symptoms caused by intestinal epithelial injury, systemic inflammation, and labour heat stress.[21]

Low temperature

Low temperature is the temperature that causes cold stress when the outside is lower than the comfort zone of the body. Acute and long-term cold exposure can harm the nervous, circulatory, and immune systems of the body, leading to hypertension, local frostbite, and life-threatening injury.[22] Moreover, exercise in a low-temperature environment will aggravate the heart load, increase the incidence rate and mortality of patients with cardiovascular diseases and reduce the body's exercise function and anti-fatigue ability, which is not conducive to the exercise abilities of athletes and competition performance.[22–24] Relevant studies have proven that low temperatures will change gut microbiota, which will promote the cold tolerance of the body. In other words, the gut microbiota may be the key factor to coordinate the energy homeostasis, metabolic heat production, and cold adaptation of the body.[25–27] Therefore, the effect of exercise on the gut microbiota under a low-temperature environment has attracted scholarly interest. Meng et al. took the lead in finding that the double stimulation of exercise under a low-temperature environment has more extensive changes in intestinal microbiota compared with simple cold exposure or exercise. Moreover, exercise even reverses intestinal microbiota in the cold exposure reaction. Changes in α-diversity and abundance of some bacteria (for example, *Proteobacteria* decreases when exposed to cold but increases when exercising in cold environments) occur, and the level of blood lipid markers related to the cardiovascular health of cold-exposed exercise individuals improves. This study showed that the health effects of exercise in cold environments may depend on changes in intestinal microbial populations and enhance interactions between some microbial species, thereby promoting the metabolism of the body.[28] In the process of studying the effect of exercise time on the microorganisms in the body, other scholars observed that, unlike the effect of simple exercise or low temperature on the composition of gut microbiota, exercise in a low-temperature environment will make the gut microbiota of mice close to that of ordinary mice in a normal environment. Thus, exercise can restore gut microbiota disorders caused by low temperatures.[29] Strenuous exercise will lead to an increase in core temperature and promote the secretion of exercise factors.[30–32] Recent studies have found that peroxisome proliferator-activated receptors (PPARs), an important exercise factor related to skeletal muscle metabolism and other functions, can realise the two-way regulation of PPAR expression and intestinal microbiota through the muscle gut axis.[33] In other words, exercise has a potential beneficial effect on regulating the gut microbiota disorder caused by low temperature, which may be related to regulating body temperature and releasing some myokines, but the specific mechanism remains unclear.

High-altitude hypoxic environments

The plateau environment is characterised by low pressure, hypoxia, thin air, cold, strong wind, long sunshine, and strong ultraviolet radiation.[34] Therefore, compared with high and low temperatures, the impact of a plateau hypoxic environment on the gut microbiota of the body is more complex.[35] At present, a large number of studies have proved that the gut microbiota disorder is easily affected by altitude, hypoxia, and other factors; it is related to the development of high-altitude diseases, such as high altitude reaction, high-altitude adaptation, high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE).[36–38] To date, there are few studies on the effect of exercise on the gut microbiota of the body under high-altitude or low-oxygen environments. Kleessen et al. tested the gut microbiota of people who completed high-altitude mountaineering, and they found that the composition of faecal flora not only showed a decrease in the abundance of beneficial bacteria and an increase in the abundance of conditionally pathogenic bacteria but also was accompanied by a decrease in serum IgM and/or IgA levels and a significant increase in the concentration of CRP, a systemic inflammatory index; hence, negative changes in the gut microbiota may be related to the decline in immune function.[39] Li and his colleagues used rats for high-altitude exercise training to simulate the human body's state of moderate-intensity exercise in a low-pressure and low-oxygen environment at high altitude; the research results showed that high-altitude training may promote the growth of bacteria and inflammatory cytokines (IL-6 and TNF-α) and damage the integrity of the intestinal mucosal barrier.[40] Machado et al. further demonstrated that exercise under hypoxic conditions can lead to a significant increase in plasma endotoxin concentration.[41] The above studies indicated that exercise may aggravate the destructive effect of high-altitude hypoxia on the composition of gut microbiota and intestinal mucosal barrier, leading to bacterial translocation and inflammatory reaction. However, some studies have shown that the negative changes in gut microbiota and the increase in intestinal permeability caused by hypoxia can be improved by exercise, and the crosstalk between host microorganisms and pro-inflammatory activities can also be effectively reduced.[42,43] Therefore, more studies may be needed to clarify the influence of exercise on gut microbiota under a high-altitude hypoxic environment. Altitude, ambient temperature, hypoxia duration, exercise degree and body health status may all be factors affecting the results. In short, personnel should not conduct sports activities in high-altitude areas before they adapt to the environment.

Effect of probiotics supplementation on sports population in high-/low-temperature and high-altitude hypoxic environments

Probiotics are living microorganisms that can produce beneficial effects on the host when administered in adequate amounts.[44] A large number of studies have proved that the use of probiotics can alleviate the fatigue of sports personnel and improve environmental stress such as high and low temperatures to a certain extent. However, there are few intervention studies on sports personnel in special environments. Therefore, to better understand the research status, the following is a summary of the effects of probiotics on sports people in high-temperature, low-temperature, and high-altitude hypoxia.

Effect of probiotic supplementation on sports population in a high-temperature environment

Exercise-induced heat stress (EHS) is a comprehensive response of the body to exercise in heat and humidity. Such exercise-related heat diseases have long troubled athletes. Therefore, scholars focus on how to effectively alleviate the discomfort of athletes, reduce the incidence rate of exercise-related heat diseases and inhibit the decline in exercise function.[44,45] Gill and his colleagues supplemented endurance athletes with a probiotic beverage containing *Lactobacillus casei* for 7 consecutive days and made them run for 2 h at 34 °C (60%$\dot{V}O_2max$ – maximal oxygen consumption and 32% RH- relative humidity). However, their research results showed that probiotics do not significantly improve endotoxemia and cytokinemia caused by EHS.[46] They also found that supplementation of probiotics before EHS cannot enhance the concentration of salivary antibacterial protein and does not play a significant role in improving respiratory mucosal immunity.[47] Some scholars speculated that the above negative results may be related to the intervention time, bacteria, and probiotic dose. Therefore, Shi et al. conducted a 4-week trial intervention by increasing the probiotic dose (containing 45 billion CFU *Lactobacillus*, *Bifidobacterium*, and *Streptococcus*) taken by athletes. The data showed that the supplementation of probiotics can effectively reduce the rising level of LPS caused by athletes' exercise at high temperatures and play a beneficial role in prolonging the time of exhaustive exercise.[5] Different from the ineffective intervention of short-term, single, and regular-dose probiotic research, long-term intake of high-dose compound probiotics can alleviate the adverse effects of exercise on the body to a certain extent. However, given the small number of studies, whether probiotic supplementation can significantly improve the discomfort related to exercise-induced fever needs further exploration. Notably, when choosing the type and dosage of probiotics, scholars should also fully consider factors such as the host's flora status (diversity) and the severity of exercise and/or heat stress experienced when supplementing probiotics, so as to better define the intervention role of probiotics in EHS.[44]

Effects of probiotic supplementation on sports population in a low-temperature environment

Long-term and high-intensity exercise can cause immunosuppression in athletes; exercises in cold weather can aggravate stress on the respiratory tract, gastrointestinal tract, and other organs, making the body highly susceptible to upper respiratory tract infections (URTIs), vomiting, diarrhoea and other diseases.[48,49] Amongst the athletes and staff who seek medical treatment during the Winter Olympics, the most common ones are patients with respiratory and gastrointestinal diseases.[50] Microorganisms are parasitic in the oral cavity, nasal cavity, intestinal tract, and other parts. They are closely related to the respiratory and digestive systems of the body, and they play an important role in the development of the mucosal immune system of the host. Therefore, many scholars have carried out intervention research on probiotics to explore their effects on the sports population in a low-temperature environment, especially the prevention and treatment of URTIs and other diseases. After applying probiotics to healthy athletes, Cox et al. found that probiotics can stimulate the immune system and improve interferon-γ levels. Probiotics can reduce the incidence rate and infection degree of respiratory tract infections of athletes during winter training.[51] Considering that the number of subjects in the aforementioned test was small, the intervention time was short and the results of some indicators were unclear, Gleeson and his colleagues expanded the subjects, recruited 84 athletes to carry out a 16-week probiotic intervention test, and proved that regular intake of probiotics can indeed reduce the incidence rate of URTI during winter training.[52] After the intervention with the unique *Lactococcus lactis* strain plasma, some scholars observed that the supplementation of probiotics can not only reduce the incidence rate and symptoms of URTI in athletes but also relieve the fatigue of athletes in continuous high-intensity sports.[6] In addition to a single strain, Strass et al. used compound probiotics to verify the athletes who completed the exhaustive aerobic exercise. The research results showed that supplementing compound probiotics during winter training can effectively reduce the incidence rate of URTI, inhibit the decrease of tryptophan level caused by exercise, and reduce the infection risk of athletes.[53]

Effects of probiotic supplementation on sports population in the plateau environment

Altitude training can improve the body's adaptation to the hypoxic environment by enhancing the functions of many systems such as respiration, cardiovascular system, and locomotor system. It has become a training method for many sports events, especially for middle- and long-distance endurance athletes to improve their sports ability.[54] The underlying mechanism has also been a concern amongst relevant scholars in sports medicine and other fields, and a large number of studies on the mechanism, methods, and nutrition intervention have been carried out. However, about half of the people who have entered plateau will have high-altitude gastrointestinal stress symptoms such as nausea and diarrhoea. With the increase in altitude, the incidence rate and severity of acute mountain sickness (AMS), HACE, and HAPE will also increase.[54,55] Therefore, how to quickly help sports personnel relieve discomfort and maintain good health is the key to assisting in the completion of scientific training. At present, people often use methods such as gradually increasing altitude; taking acetazolamide, dexamethasone, and other drugs; and dietary nutrition intervention to prevent and treat the high-altitude syndrome. However, as a result of certain side effects of drugs, time-consuming conventional methods, slow effects, and individual differences, no better solution exists at this stage.[56,57] Given that the high-altitude environment has an impact on the structure of gut microbiota, it is also related to the strength of the intestinal mucosal barrier and immune function.[57] Moreover, probiotic supplementation can improve the negative effects of exercise in a low-temperature environment by optimising the composition of the gut microbiota of the host, increasing the abundance of beneficial bacteria, and improving immune function.[7,52,58] Therefore, some scholars suggest that it may be applied to the sports population in the high-altitude environment to explore whether it also has special beneficial effects.[57] Ultimately, high altitude is accompanied with a low-temperature environment.

Possible mechanism of probiotic supplementation on an exercise population in high-/low-temperature and high-altitude hypoxic environments

At present, there is no clear statement on how probiotics can have beneficial effects on people who exercise under high and low temperatures and high-altitude hypoxia. Relevant scholars believe that such effects may be related to factors such as optimising the gut microbiota structure, improving intestinal integrity, and enhancing immune function of the body, which will be introduced separately below (Fig. 1).

Optimise the composition of intestinal microorganisms and increase the abundance of beneficial bacteria

Probiotic supplementation can affect the composition of the gut microbiota of athletes in a special environment. West and his colleagues studied the effects of probiotic supplementation on gastrointestinal and respiratory diseases of athletes during winter training; they found that the number of probiotic *Lactobacillus* in faecal flora of male and female athletes increased by 7.7 and 2.2 times, respectively.[7] Given that the abundance of *Lactobacillus* is inversely proportional to the inflammatory response, it also has the function of regulating immunity and changing lipid metabolism.[59] Supplementation of *Lactobacillus casei Shirota*, a beneficial bacterium related to *Lactobacillus*, has also been proven to be

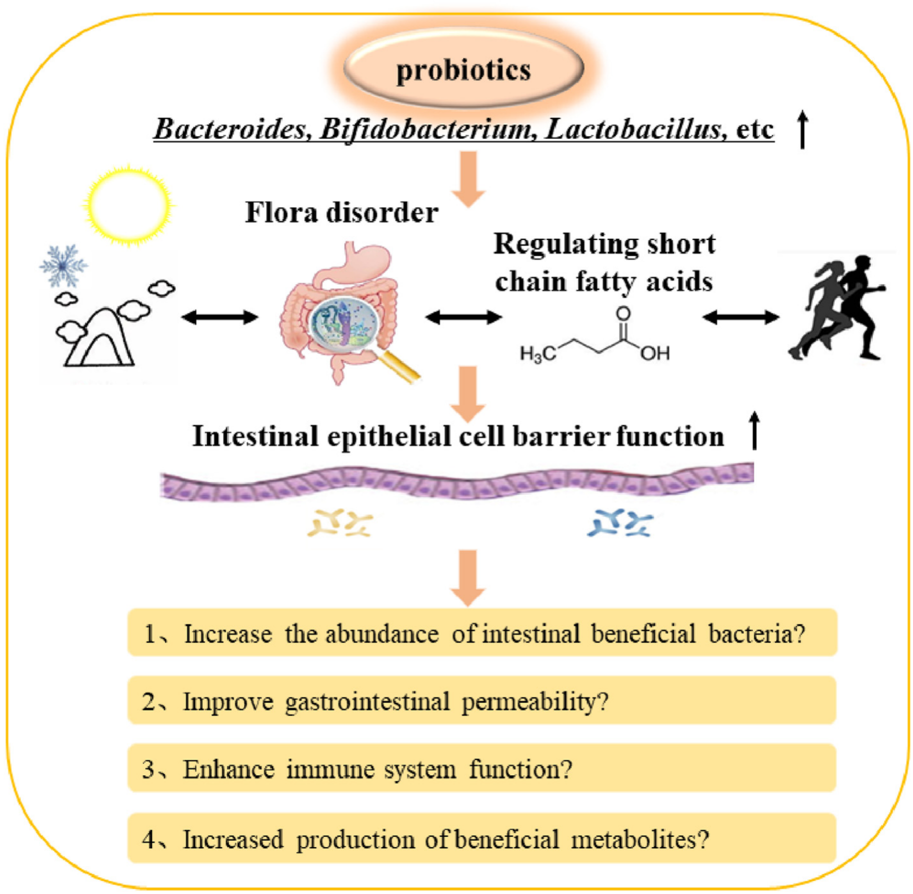

Fig. 1. Possible mechanism of probiotic supplementation on exercise population in high and low temperature and high-altitude hypoxia
The black upward single arrow represents the supplement of probiotics and enhancement of intestinal barrier function. The black double arrows indicate the interaction between the two factors.

effective in reducing the URTI incidence rate of athletes.[52] Therefore, the beneficial effects of probiotic supplements on sports people in special environments may be related to optimising the composition of gut microbiota and increasing the abundance of beneficial bacteria. Tryptophan (TRP), an essential amino acid of the human body, plays an important role in maintaining the health of the body. Some studies have found that the gut microbiota can regulate the host serotonin level by regulating TRP, and serotonin is related to fatigue in the body.[60] Therefore, the maintenance of the TRP content before and after exercise plays an important role in promoting the body to complete the exercise better. Relevant research results show that during winter training, the serum TRP concentration of athletes in the probiotic intervention group remains unchanged compared with the significant decrease in serum TRP concentration of athletes in the placebo group after exercise.[53] This difference may be due to the influence of probiotics on the composition of intestinal microorganisms, such as increasing the biosynthesis of TRP by specific bacteria.

Improve the gastrointestinal permeability

High temperature, low oxygen, exercise, and other factors can increase gastrointestinal permeability. The transmembrane entry of pathogens, endotoxins, and other substances into the blood will cause functional disorders of the intestinal barrier and trigger various inflammatory reactions, which are related to the occurrence and development of gastrointestinal diseases, endotoxemia and other diseases.[18,40,61] Shing et al. found that the supplementation of probiotics (*Lactobacillus*, *Bifidobacterium* and *Streptococcus* strains) for 4 weeks can prolong the exhausted exercise time of athletes in a high-temperature environment (35 °C and 40% humidity).[5] Although the study did not clarify the exact mechanism of improving exercise ability, it proved that probiotics can alleviate the rise of LPS levels after exercise, and improve gastrointestinal permeability.

Enhance immune system function

The double stimulation of a special environment and exercise may make the immune system of the body disordered.[58] Increasing studies showed that the occurrence of the disease is related to the decline in the immune function of the body. The gut microbiota participates in intestinal immunity through the common mucosal immune system, as well as in the regulation of the immune function of the whole body.[62] Many studies showed that long-term intake of probiotics has a good preventive effect on diseases related to immune system dysfunction. Gleeson et al. found that long-term intake of probiotics can significantly increase the saliva IgA content of athletes and effectively reduce the CMV and EBV antibody titre levels in plasma; moreover, they reported that long-term use of probiotics plays a role in enhancing the host immune system function.[52,58] Komano et al. observed that supplementation of *Lactococcus lactis* JCM 5805 can significantly reduce the incidence rate of URTIs and the days of feeling fatigued amongst athletes.[6] The animal experiments proved that this effect might be related to the enhanced expression of costimulatory factor CD8 by activated plasma cell-like dendritic cells, and probiotics can improve fatigue and reduce the risk of infection possibly due to the muscle degeneration gene FoxO1 and the fatigue regulatory cytokine TGF-β caused by inhibition.[63] Recent studies have also shown that probiotic supplementation can regulate the host immune system by regulating the gut microbiota-mediated TRP metabolism process. For example, probiotic *L. reuteri* can effectively promote the production of the TRP metabolite indole-3-aldehyde (IAld), activate T cells in the intestine, increase IL-22 levels, and protect the colon from inflammatory damage.[64]

Increase the production of beneficial metabolites

Relevant studies have proved that probiotics also play a role in preventing and treating a variety of diseases by increasing beneficial metabolites (e.g. short-chain fatty acids such as acetic acid and propionic acid) and participating in the regulation of energy metabolism, immune defence, antioxidant and other processes of the body. The research results of Okamoto et al. showed that the serum short-chain fatty acid level and exercise ability of mice treated with antibiotics decreases, but this phenomenon can be significantly improved by subcutaneous injection of acetic acid.[65] This experiment suggested that the short-chain fatty acids generated by gut microbiota can be one of the energy substrates to assist the host to complete the exercise. When probiotics *Lactobacillus acidophilus* NCFM and *Bifidobacterium lactis* Bi-07 were given to young rats for 28 consecutive days, the body increased the abundance of beneficial bacteria such as *Rothia*, *Bifidobacterium* and *Lactobacillus* and significantly increased the level of beneficial metabolites such as short-chain fatty acids. These changes promoted the maturation of the intestinal microbiome structure and function in weaned rats.[66] *Lactobacillus delbrueckii* subsp. *Bulgaricus* 2038 and *Streptococcus thermophilus* 1131 are also typical probiotics. Long-term intake of these probiotics can significantly increase the abundance of *Bacteroides* highly related to the production of butyrate and propionate.[67] However, the above studies were carried out in a normal environment, so whether probiotics also have beneficial effects through this mechanism for people exercising in a special environment has not been proved, and further research is warranted.

Conclusion and prospect

Gut microbiota is an important member to maintain the health of the body. High or low external temperature and hypoxia are factors that affect the composition of gut microbiota; cause damage to the intestinal mucosal barrier; and lead to a variety of gastrointestinal, respiratory, and other related diseases. Many studies have shown that probiotics have physiological activities such as regulating gut microbiota, anti-inflammation, and anti-oxidation. Probiotics have unique preventive and therapeutic effects on oral diseases, intestinal diseases, chronic metabolic diseases, and cancer, so they are becoming increasingly popular. However, for the sports population who is doubly stimulated by the external environment and sports, some unresolved problems limit the use of probiotics to some extent. Firstly, the effect of probiotic supplements has not been unified. It has obvious preventive and therapeutic effects on the incidence rate and severity of digestive and respiratory diseases of sports people in special environments, and it even has beneficial effects on alleviating fatigue of athletes during winter training and prolonging exercise time in the heat. However, endotoxemia and other symptoms caused by EHS have not been significantly improved, so the use of probiotic supplements is the focus of the research. Secondly, studies on the mechanism of probiotics can help explain the relationship between flora and human health and better serve human health. Although some scholars have proposed that the mechanism of probiotic supplement's impact on the exercise population under high-/low-temperature and high-altitude hypoxia may be related to increasing the abundance of probiotics, improving the permeability of intestinal barrier and enhancing immune function, research on the molecular mechanism is insufficient. In addition, circadian rhythm is essential to human physiological homeostasis and health. The oscillation of the host circadian rhythm affects the composition and function of intestinal microbiota; meanwhile, the normal operation of the host circadian rhythm depends on the diurnal changes in intestinal microbiota. The imbalance of intestinal micro-ecology or the disorder of the host circadian rhythm may lead to psychiatric disorders, whereas the intervention of plant polysaccharides may alleviate circadian rhythm disturbance and related psychiatric diseases.[68,70,71] Finally, to better meet the needs of sports personnel in special environments and provide them with more scientific and better use effects, the selection, collocation, and dosage of strains in probiotic preparations; the best way to eat; and other issues need to be explored by the majority of scientific research staff.

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All authors have read and agree with manuscript content. The manuscript has not been published and is not under consideration for publication elsewhere.

Authors' contributions

Each author contributed equally to the drafting of this manuscript.

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Conflict of interest

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