Review Article

A narrative review of fatigue in exercise training: Relation between different organs

Zahra Hatami Nasab[1], Behzad Kia[2*]

Abstract

One of the harmful factors that affect athletic performance is exercise-induced fatigue, which results from excessive stress and leads to reduced physical and mental function. Physical fatigue resulting from physical activities, especially sports activities, affect the human immune system. Because the immune system responds to physiological and psychological stress, and like other physiological systems in our body, it causes temporary disorders in response to a session of exercise. The immune system is also affected by the intensity, duration, and type of exercise. As a result of exercise that leads to extreme fatigue, it also may affect immune function by causing stress responses, including inflammation, and cause immune system defects. Leukocyte blood flow and functional capacity may decrease over a long time with repeated strenuous exercise, possibly due to increased levels of stress hormones during exercise. Decreased blood glutamine levels have also been suggested as a possible cause of deficiency in one or more of the immune systems associated with strenuous exercise, although the evidence is less convincing. Also, during exercise, the production of reactive oxygen species increases and some functions of immune cells can be disrupted by excess free radicals. During exercise, exposure to airborne pathogens is higher due to the speed and depth of respiration. Therefore, the increased prevalence of infection in athletes is probably due to several factors: a variety of stressors (physical, psychological, or environmental, nutritional) can suppress immune function, and these effect, along with increased exposure to pathogens.

Key Words: **Exercise, Fatigue, Immune system**

1. Faculty of Physical Education and Sports Sciences University of Guilan, Rasht, Iran. 2. Assistant Professor, Department of Sport Physiology, Faculty of Sports Sciences, Islamic Azad University of Shoushtar, Shoushtar, Iran.

*Author for correspondence: kia_behzad@yahoo.com

Z H N: 0000-0002-1678-7181; B K: 0000-0003-1555-4551

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Introduction

Just as fatigue is a common and troubling complaint among people who engage in physical activity based on training or rehabilitation, the definition of sports fatigue can be defined as an interruption in muscle activity due to the depletion of substrate that provides energy for muscle contraction and accumulation of metabolites. In the body provides, be. Exercise can have both positive and negative effects on immune function and susceptibility to minor illnesses. The relationship between exercise and susceptibility to infection is modeled in a J-shaped curve. Also, many people believe that the more and more intense exercise they do, the more their body's resistance to disease increases, and they become healthier, which is due to the beneficial effects of exercise on some organs of the body, including the cardiovascular and respiratory systems. If the research shows the effects of repetition of intense and long-term exercise on the immune system, the prevalence of upper respiratory tract infection (URTI), and the destruction of immune factors. The relationship between physical exercise and fatigue has been considered by many researchers for more than a century and is very complex. Many research papers have been published on fatigue and its effect on physical and physiological performance. Fatigue that occurs during exercise seems to be a black box phenomenon that physiologists try to solve by creating physiological control models based on observations or various physical and physiological factors.

Fatigue

Fatigue is a common feature of many disorders in physiological processes, including physical, neurological, and mental disorders, and although fatigue is commonly recognized as a sign or symptom of illness or side effects of treatment, it is a mental experience. Fatigue is a term used to describe a decrease in physical performance associated with an increased perceived / actual difficulty of a task or exercise (Abd-Elfattah et al., 2015).

Exhaustion

In addition to fatigue, exhaustion is another psychological nature associated with physical exercise. Despite constant motor output during exercise, the "sense of effort" may gradually increase. Sometimes this sense of effort can be so intense that it affects a person's willpower to maintain motor output and forces the person to reduce or even stop their workload. This moment is defined as "exhaustion". When this amount of work or training is more than the physiological capacity of athletes, if the recovery period after training is not enough, it causes chronic fatigue and as a result, leads to illness or over activity syndrome and ultimately reduces the performance and ability of athletes. Feelings of tiredness and exhaustion are likely to be essential to maintaining our physical integrity. The phenomenon of fatigue and exhaustion during exercise is a field of interest in various scientific disciplines, especially physiology and psychology (Vygotsky, 2020).

Types of fatigue

Exercise-induced fatigue can be due to either peripheral (skeletal muscle) due to environmental pressures and disruption of body homeostasis, or central (CNS) due to stress and dysfunction. Central nervous system.

PNS environmental fatigue

Physical activity due to metabolic events affects the balance of the internal environment. Metabolic origins currently include several systems that interact with each other to induce fatigue, all of which seek to maintain homeostasis. During exercise, metabolites and heat are produced that affect the stable state of the indoor environment. The greater the workload, the greater the effects of these variables on the indoor environment. Depending on the type of exercise, fatigue and tiredness may occur sooner or later. These feelings of exercise-related fatigue increase with the accumulation of metabolites. These feelings of exercise-related fatigue increase with the accumulation of metabolites. Occurs and are defined as changes in the internal environment and muscle fibers that predict the energy and impair muscle contraction (Cè et al., 2020; Vargas & Marino, 2014). Excessive exercise loads cause Increases the accumulation of blood lactate (OBLA) and changes in the internal environment (blood, extracellular fluid). Factors such as ammonia accumulation, heat accumulation, increased perspiration due to dehydration, lactate accumulation, buffering of hydrogen ions accumulated by bicarbonate, and increased release of carbon dioxide, which increases respiratory benefit, contribute to this type of fatigue (Vygotsky, 2020).

Other changes include

Accumulation of Pi (mineral phosphate), H+ and Mg+ ions in the sarcoplasm, reactive oxygen species ROS, the release of Ca^{+2} by calcium phosphate deposition, decrease in glycogen stores, decrease in conduction velocity of action potentials during sarcoma, increase in excretion of potassium + ions (K) of muscle fibers, and blockage of neuromuscular synaptic transmission.

Accumulation of Pi (mineral phosphate) in the sarcoplasm reduces the contractile force due to inhibition of the cross-bridge interaction. With Pi accumulation, Ca^{+2} release is inhibited by deposition of calcium phosphate in the sarcoplasmic reticulum duct and phosphorylation of Ca^{+2} release channels.

Decreased glycogen stores also lead to increased muscle fatigue, which in severe cases, along with low blood glucose levels and even short-term hypoglycemia, can severely impair CNS function. Glycogen depletion, lactate accumulation, pH reduction, and oxidative stress are considered to be the main factors promoting exercise-induced fatigue. One of the factors involved in muscle fatigue has been reported to be lactic acid accumulation, and it is possible that with increasing lactic acid accumulation, the degree of functional stability of individuals decreases, while the results of some other studies contradict this and state that lactate may If not a cause for fatigue, high lactic acid excretion is commonly used as an indicator of post-exercise fatigue (Ma & Suzuki, 2019; Siavash, 2010; Vygotsky, 2020).

Increased metabolic acidosis due to various pathways that cause a decrease in pH has also been suggested as a possible cause of muscle fatigue. Recently, the ATP hydrolysis reaction has been identified as the main source of acidification of the cellular environment, during which the formation of ADP, Pi and H + occurs during the decomposition of the ATP molecule (de Lima et al., 2018).

The increased flow of potassium ions (K+) from muscle fibers and increased potassium in the tubular duct t may lead to obstruction of the tubular action potential, resulting in less force due to weakened excitation-contraction coupling (Vygotsky, 2020).

The processes involved in transferring an axonal action potential to a sarcoplasmic action potential are called neuromuscular transmission. The decrease in conduction velocity of action potentials during sarcolemma is probably due to exercise-related biochemical changes in and around muscle fibers. The decrease in conduction velocity is reflected in the EMG (frequency content change) but has no definite immediate effect on the production of muscle force. In this type of fatigue, neuromuscular synaptic transmission may also be blocked; however, this factor seems to be of particular importance in myasthenia gravis. It is a type of muscle paralysis caused by immune activity against acetylcholine receptor proteins at the neuromuscular synapse. There is originally Ach or acetylcholine but no receptor, just like type 2 dia-

-betes This disease is specific to the end plates of the striated muscles that affect most women. Its maximum prevalence is in the third or fourth decade of life, but it can be seen at any stage of life, from childhood to old age, although older men and women are equally affected (Vygotsky, 2020)

Central fatigue

CNS function is complex and plays a vital role in maintaining a stable internal environment. The motor cortex of the brain is responsible for producing motor stimuli during exercise. We are aware of this motor stimulus, but we are not aware of the simultaneous motor control of the muscles that regulate our posture during exercise. In addition, the brain is the center of our cognition. Despite the complexity of all these tasks, our minds can focus on only one problem at a time; This is the goal of our consciousness. We have very limited awareness. We gradually become aware of the feeling of tiredness and tiredness during exercise. Physiologically, awareness of these emotions has a warning role (Vygotsky, 2020).

There is little scientific knowledge about central fatigue. There is no doubt that CNS dysfunction can limit an athlete's athletic performance, but so far the exact mechanisms of CNS involvement in the development of fatigue, whether attributed to the CNS or the peripheral nerves, are not fully understood. It needs more research. Fatigue of the central nervous system during exercise greatly reduces the voluntary capacity of motor neurons, while peripheral fatigue is a loss of strength and power that manifests itself independently of nervous power. Davis and Fitz. 1998 Although mental factors can affect physical function, impaired neural conduction in active muscles is the most likely explanation for fatigue among most people during normal activities. It is also thought that the most likely explanation for fatigue associated with a bacterial or viral infection is a period of recovery or injury or surgery, a sign of acute fatigue, depression, discomfort from prolonged air travel, and central nervous system fatigue (Maughan, 2000).

Central fatigue included:

1. Conduction of action potentials may be blocked, leading to loss of muscle fiber activation.

2. The stimulation of motor neurons may be affected by reflexes from muscle afferents. Thus, the effects of central fatigue may be partially offset by mechanical receptor reflexes (types IA and II neurons from muscle spindles; type IB from Golgi tendon organs).

3. Stimulation of type III and IV nerves (chemical afferents and pain) slows the excitability of motor neurons and inhibits motor cortex output (brain).

4. The excitability of cells in the motor cortex of the brain may change throughout constant motor tasks, as shown by measurements using magnetic stimulation.

5. The synaptic effects of serotonergic neurons may increase, leading to increased feelings of tiredness and fatigue, which may result from increased entry of the serotonin precursor tryptophan into the brain. During prolonged exercise, such an increased influx of tryptophan may be due to a decrease in BCAA blood concentration. This hypothesis states that the duration of long-term activity increases with the recall of fatty acids and their levels in the blood, given that the carrier of these fatty acids in the blood is albumin and albumin also acts as a carrier of tryptophan, so the Binding of fatty acids to albumin increases the level of free tryptophan in the blood, which is an amino acid that can cross the blood-brain barrier and therefore after crossing the blood-brain barrier is converted to serotonin, which serotonin is one of The main theory of central fatigue is known (Abdollah, 2019; Vygotsky, 2020).

6. Release of exercise-induced cytokines. Interleukin 6 induces feelings of fatigue and interleukin 1 induces disease behavior in animals. In many diseases, the production of these cytokines increases (Shaun, 2015; Vygotsky, 2020).

Investigation of various physiological models and theories of fatigue:

From another point of view, concerning types of fatigue, there are also different theoretical and physiological models in relation to exercise-induced fatigue. We will explain some of them.

Cardiovascular model

The classical theory is also defined as the cardiovascular / anaerobic / sudden (severe) model of exercise physiology, stating that fatigue associated with high-intensity exercise due to skeletal muscle is "oxygen-free activation" that increases the muscle oxygen demand for exercise. It cannot be supplied by the heart. Thus, this insufficient oxygen supplies to exercise the muscles prevents the accumulation of increasing lactic acid accumulation, which Hill (1923) argues prevents skeletal muscle relaxation, which leads to skeletal muscle stiffness. However, it has been shown that it is the depletion of adenosine triphosphate (ATP) within skeletal muscle training that provides precision (Vygotsky, 2020).

Energy supply/discharge model

The cardiovascular/anaerobic model is later extended to another model called the energy supply/energy depletion model, which reduces fatigue during exercise by disrupting energy metabolic pathways to produce sufficient energy (ATP) to the muscles. Associates activation or reduction of endogenous substrates suc-

-h as as carbohydrates. This model demonstrates energy conservation through energy pathways (e.g., anaerobic system and aerobic system) and combines a strategy for the efficient use of metabolic energy resources available during exercise (Vygotsky, 2020).

Thermal regulation model

The thermoregulatory fatigue model suggests that fatigue occurs when the core temperature of the human body rises to a critical level of about 40 °C. This is because the central nervous system (CNS) is less able to maintain a constant neural stimulus at temperature. It has a critical temperature of 40 degrees Celsius. Under the prolonged exercise, the onset of hyperthermia (e.g., body temperature is too high, above normal) is associated with decreased cerebral circulation, which leads to a reduction in the supply of substrates or metabolic sources to or from the brain (Vygotsky, 2020).

Skeletal muscle and brain cross-talk in exercise-induced fatigue

In the human body, skeletal muscle is the most abundant organ and essential regulator of energy homeostasis. It is also responsible for generating strength and power, and in adaptations resulting from exercise is an important coordinator in other organs, including the liver, fat, or brain, and an essential coordinator of the body's total energy metabolism. It has recently been suggested in recent decades that skeletal muscle is a secretory organ and an endocrine tissue (Woodward et al., 2020).

In skeletal muscle, each motor neuron communicates with several muscle fibers. As a result, the musculoskeletal system consists of a central nervous system and motor units. Motor units and muscle fibers do not have the same physiological and biochemical properties. According to physiological studies, factors such as muscle contraction rate, maximum force, and fatigue resistance in motor units are completely different, so that type I fibers tend to resist fatigue and type II fast fibers are relatively fatigue. From a biochemical point of view. Also, the speed of cross-bridge cycle activity and ATPase activity of type 1 and 2 fibers are different. In addition, fatigue-resistant fibers have higher levels of activity of enzymes involved in oxidative metabolism than fatigue-sensitive fibers (Cè et al., 2020; de Lima et al., 2018; Vargas & Marino, 2014; Vygotsky, 2020).

Exercise quickly causes significant changes depending on factors such as intensity and duration. The energy produced during exercise will deplete the body of energy reserves, and the timing of the onset of fatigue depends on the type of exercise. Feeling tired is a gradual process and its physiological role protects the body against the destructive effects of exercise. And the ultimate effect is the feeling of fatigue, reduction or complete cessation of exercise.

And metabolic accumulation, related to muscle acidosis. But central fatigue is more related to central nervous system (CNS) events, which are associated with changes in neurotransmitters, changes in metabolic status, and high temperatures. CNS function is very complex. And plays a vital role in maintaining the stable state of the internal environment. Therefore, by increasing the workload and being affected by the internal environment of the body due to physiological stimuli such as exercise and environmental fatigue, it is conceivable that Directly by internal afferents and indirectly affect muscle function during exercise. Also physiologically due to the fact that motor stimuli are produced during exercise by the motor cortex of the brain.

Awareness of feeling tired has a warning role. This definition states that central fatigue reduces the activity of areas of the cerebral cortex that contribute to the use of skeletal muscle. In addition, changes that occur not only in the motor cortex but also in the supraspinal and spinal areas are important (Cè et al., 2020; de Lima et al., 2018; Pedersen, 2019; Pillon et al., 2013; Vargas & Marino, 2014; Vygotsky, 2020; Woodward et al., 2020).

The role of fatigue on athletes' performance

Every physical exercise is an energy-consuming activity that sooner or later depletes our body of energy reserves. Unlimited consumption of these reserves without replenishment will have detrimental effects on our physical health. Many diseases accelerate the depletion of energy reserves in the body. Thus, diseases enhance the effect of reduced energy storage associated with exercise. A detrimental factor that affects athletic performance is exercise-induced fatigue, which results from excessive stress and leads to decreased physical and mental function. Exercise fatigue can also act as a disruption in muscle activity due to the depletion of the substrate, which provides energy for muscle contraction, and the accumulation of metabolites in the body. According to the new records set in the World Championships, the motivation of athletes, especially professional level athletes, to increase the volume and intensity of their training is increasing day by day. As a result, fatigue caused by sports is one of the problems that athletes have always faced. Which the coaches are trying to postpone. Therefore, to improve athletic performance, it is necessary to examine how to delay the onset of exercise fatigue or reduce the development of fatigue during exercise, or how to effectively use the metabolic resources in the body to complete a physical activity without severe system defects. (Chuckravanen et al., 2019; Nourshahi, 2010; Salami. Fatemeh, 2000; Vygotsky, 2020).

Fatigue, on the other hand, is defined as the inability of muscles to maintain the required level of strength during exercise. Likewise, it can be defined as an exercise that reduces a muscle's

ability to produce force. The term muscle fatigue is also used to indicate a transient decrease in muscle capacity for physical activity. In addition, in many sports (e.g., running and cycling), creating an effective rhythm organizes an athlete and maintains excellent physical function. Consequently, this rhythm affects musculoskeletal activity, mental control as well as psychological factors. These psychological factors can be self-motivation, level of consciousness, and mental accuracy, which are the product of several integrated factors such as physical fatigue or other unrelated sports stresses such as environmental conditions that are not in the athlete's personal control.

The athlete must be able to adapt to these unexpected environmental factors. Another aspect of coaching and external support/assistance for the athlete (in terms of nutrition, exercise technique, tactics, and training) is to have an aspiring competitor to succeed. Among all these, factors affecting athletic performance are a very important factor that cannot be ignored, and it is exercise-induced fatigue that reduces physical and mental function (Abd-Elfattah et al., 2015; Chuckravanen et al, 2019).

Fatigue and its effects on the immune system during exercise

Persistent fatigue from physical activity and frequent exercise can reduce performance, muscle pain, and mental and hormonal disorders that can last for weeks or months. Athletes usually intensify their training for a few days or weeks at certain stages of the season. This may lead to a state of over-maturity in which performance is temporarily reduced, but after a period of reduction with light training alone, leads to overcompensation and an increase in performance (Gleeson, 2007; Peake et al., 2017). Fatigue usually affects the components and functions of the immune system. That is, it seems that exercise that leads to severe fatigue may affect immune function by creating stress responses (Soraya, 2013). various studies have been shown that moderate-intensity exercise has a beneficial effect on the immune system (references). And reduces diseases, high-intensity exercise also suppresses the immune system and is considered as an increased risk factor for infection in athletes (Ebrahimi et al., 2016). Diseases or injuries (provide a verb for the sentence) when intense training occurs over a long period of time without sufficient balance between training and recovery, ie the body's ability to return to its original state between training and competition sessions is reduced (Peake et al., 2017; Shirvani et al., 2013).

Numerous studies in recent years have examined the effects of short periods of intense exercise on resting immune function and endocrine immune responses to endurance exercise. These studies show that several indicators, including leukocyte count and function, neutrophil and monocyte oxidative burst, CD4 / CD8 ratios, T lymphocyte, mitogen-stimulated lymphocyte proliferation , and antibody synthesis, and NK cell activity, increase exercise load in athletes. They are trained and sensitive. Even after relatively short periods (1-3 weeks) of intense exercise, a remarkable decrease in neutrophil function, lymphocyte proliferation, IgA, and circulating T cell counts has been observed. Thus, with chronic periods of very heavy training, several aspects of both innate and acquired immunity are impaired, but athletes are not clinically immunocompromised. In other words, exercise-induced immunosuppression does not put athletes at risk for serious illness, but it may be sufficient to increase the risk of common infections such as the flu. Also, during exercise, the production of reactive oxygen species increases and some functions of immune cells can be disrupted by excess free radicals. Therefore, the increased prevalence of infection in athletes is probably due to several factors such as psychological, environmental, and nutritional) can suppress immune function, and these effects, combined with increased exposure to pathogens, can make the athlete more susceptible to infection (Gleeson, 2007).

Open window

According to research, high-intensity sports activities during athletes' competitions cause changes and impairment of safety function. These changes lead to a period between 3 to 72 hours, which is called the open window. During the open window period, pathogens and pathogens can enter the host body and the risk of infection increases after exercise because, during exercise, exposure to pathogens is higher due to the speed and depth of respiration. Recent research has shown that athletes are more susceptible to certain diseases such as upper respiratory tract infections during strenuous training and sensitive competitions (Jafari et al., 2014; Shirvani et al., 2013). Athletes involved in intensive periods of endurance training are more prone to minor infections. For example, according to some studies, sore throats and flu-like symptoms are more common in athletes than in the general population, and when they have the disease, colds may last longer in athletes. Obviously, this is a concern for athletes, as it has generally been shown that even mild infections can lead to decreased athletic performance and ability to endure strenuous exercise (more severe viral infections may be associated with the development of persistent fatigue. There are very few studies that can show a direct link between any specific measure of exercise-induced impaired immune function and an increased prevalence of clinically confirmed infection (Gleeson, 2007).

Leukocyte count changes immediately after strenuous activity

Recent research also examines the effects of exercise on immune components to better understand the mechanisms by w-

-hich exercise affects immune resistance to infection (Shirvani et al., 2013). Exercise and immunosuppression are not clearly understood. Existing research shows a dual immune response to exercise. The reason for this can be the variety of sports activities in terms of intensity, duration and other physiological factors such as hormones as well as psychosocial factors (jafari et al., 2014).

Since the innate and acquired immune systems can be temporarily affected by a session of strenuous exercise (Jafari et al., 2014), this type of intense activity disrupts the body's homeostasis and causes a significant change and increase of 3 to 4 Equality in the number of leukocytes in the blood relative to resting conditions This increase is called leukocytosis and may persist for hours after exercise cessation. However, due to excessive and prolonged training pressure and its repetition, which leads to fatigue and overtraining, the number and functional capacity of leukocytes in the bloodstream are reduced. It seems that the amount of leukocytosis is directly related to the intensity and duration of the training and inversely to the amount of fitness.

An increase in the number of white blood cells during and immediately after exercise is often attributed to an increase in the number of neutrophils and, to a lesser extent, to lymphocytes. Neutrophils also make up 70% of white blood cells. An increase in the number of white blood cells during and after exercise is consistent with changes in the number of neutrophils. The number of neutrophils (and therefore the total number of leukocytes) often increases for a long time during the recovery period (up to 6 hours after cessation of exercise), especially if the training session is prolonged (2, 86 hours). This persistent "neutrophilia" is characterized by an increased presence of immature neutrophils, with less differentiation and precursor in the blood, which is likely in response to increased levels of soluble plasma agents, including

Glucocorticoids, growth hormone and cytokines such as IL 6 are produced. However, this neutrophilia after prolonged exercise is similar to what is seen during a bacterial infection. 24 hours of recovery is usually enough for the neutrophil count to return to normal. Delayed monocytosis is sometimes seen within 1 to 2 hours after prolonged exercise, but monocyte counts typically return to resting levels within 6 hours of cessation of exercise (Peake et al., 2017). Also, the results of Niemen et al.'s (1995) study of ten male endurance athletes showed that white blood cell counts increased by up to 250% in three hours of running on a treadmill, such as a marathon, and remained approximately three times the amount of rest. Six hours after exercise, this amount was 1.5 to 2 times the amount of rest (Jafari et al., 2014; Shirvani et al., 2013).

The results of this study also show that the number of neutrophils Increases significantly after 90 minutes of intense intermittent activity. Nehlsen et al. Suzuki et al. (1996) showed that in untrained men who exercised for seven consecutive days, each 1.5 hours a day, with an intensity of 70% VO2max, they cycled on a workhorse bike. Increases by 20% (Shirvani et al., 2013). In general, neutrophil concentrations increase during and after exercise and remain high for hours after exercise. The extent of these changes varies with the intensity and duration of exercise. The neutrophil count may have a two-step response as a small initial increase, then a decrease to about 30 to 60 minutes after exercise, followed by a further (double) increase in cell count in two to four hours after exercise. Be. This increase indicates the invocation of cells and possibly immature cells with less activity into the bloodstream (Shirvani et al., 2013).

Natural killer cell changes, T lymphocyte ratio of CD4 / 8 CD cells:

Intense training temporarily increases the number of circulating natural killer (NK) cells, but after training, the number of NK cells decreases to less than half normal for several hours. Normal amounts of rest usually return to normal within 24 hours (46 hours). NK cell cytolytic activity (per cell) decreases after exercise, and if the activity is both prolonged and intense, a decrease in NK cell count and cytolytic activity may begin during the training session. Exercise, number, and activity of activated killer cells are also lower than pre-exercise levels. Acute exercise has been shown to reduce the proliferative response of lymphocytes to mitogens and to reduce the expression of the primary activation marker (CD69) in response to mitogen stimulation. When physical activity is intense and prolonged (1.5 hours), the number of circulating lymphocytes may decrease below pre-activity levels for several hours after exercise, and the CD4 / CD ratio of T lymphocytes decreases (Gleeson, 2007).

After prolonged cessation of exercise (for example, 2 hours of cycling), the natural killer (NK) cells responsible for most exercise-induced lymphocytosis may be 40% less than baseline for 7 days after exercise. Exercise-induced lymphopenia shows the preferential movement of lymphocyte subtypes with strong effective functions (e.g., NK cells, T cells, and 8 CD cells outside the blood. Also, the rapid lymphopenia observed during the early stages of exercise recovery was initially of concern. Especially because early studies reported high levels of lymphocyte apoptosis (programmed cell death) after strenuous exercise; however, these findings have not been substantiated. It has been reported after exercise, even if the number of blood lymphocytes is up to 30-40% less than at rest. Lymphocytes and monocytes leave the blood in large numbers during the recovery period under the influence of glucocorticoids.

Long-term exercise may also reduce the migration and formation

of T cells, and the percentage of T cells that produce cytokines that are effective in responding to mitogen stimulation. Thus, the general trend during exercise recovery is that short-term results of moderate-intensity exercise have little (or may even) increase cellular immune function, while long-term outcomes appear (1). 5 hours) Heavy exercise reduces the normal function of all major immune cell types. These effects may predispose athletes to disease during recovery from competition or strenuous exercise (Peake et al., 2017).

Cross-talk of the musculoskeletal system and the immune system in exercise-induced fatigue:

For years, immunology has highlighted the inflammatory response, subsequent release of cytokines, and neural regulation during disease as important contributors to fatigue. Cytokines are a group of proteins that have paracrine/endocrine effects and their production is regulated by physiological stimuli such as exercise that play an important role in triggering inflammatory responses to inflammation and tissue damage (Vargas & Marino, 2014). In fact, Ofussen et al. Suggest an inflammatory response to link the environment to the brain through peripherally released cytokines and prostaglandins.

Recent studies have shown that the contraction of muscle myofibrils leads to the release of a type of cytokine called myokines, which in turn has many effects on other organs, including the brain. Skeletal muscle secretion in humans includes hundreds of myokines that are released in response to contractions and have a direct effect on the brain. The release of myokines and other mediators released during exercise speaks to the relationship between exercise and brain health and the existence of a muscle-brain endocrine ring, but it is unclear which environmental mechanisms elicit these positive effects of exercise.

Other effects of secreted myokines, hepatokines, and adipokines during exercise include their mediation on cognitive functional neurogenesis of appetite and metabolism, suggesting that they support the existence of a brain-muscle endocrine ring. As a result, exercise not only contributes to muscle growth and physical function but is essential for activating and increasing the number of neural connections (Agha Alinejad & Molanori Shamsi, 2010; Delezie & Handschin, 2018; Furrer et al., 2017; Pedersen, 2019; Pillon et al., 2013; Woodward et al., 2020; Yu et al., 2018).

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Immune glands such as bone marrow, liver cells, thymus and spleen are specific to the innate immune system. Answer: Mast cells and macrophages are activated when a foreign substance (eg, a virus) is detected in the body. For example, during the flu virus, the release of mast cells and macrophages causes the production of inflammatory cytokines such as interleukin-1. Tumor necrosis factor-alpha (TNF) and interleukin-6 increase to help systemic defense and prevent infection. It is thought that an increase in these cytokines is largely responsible for sending signals to the brain and producing all or some of the "disease behaviors "previously Research has also reported an increase in circulating serum cytokines IL6, IL1, TNF-α and TNF-β in some people with chronic fatigue syndrome. In addition, a relatively small increase in plasma IL6 levels has recently been shown to induce two anti-inflammatory cytokines, IL1 and IL10, along with CRP. During exercise, an increase in IL6 precedes an increase in these two cytokines, and it is argued that muscle-derived IL6 initiates this response. It is macrophages, and is considered one of the most important mediators of host defense against viral and bacterial infections. Resting level of inflammatory index TNF-α is associated with obesity and inactive lifestyle (Gleeson, 2007).

As with acute illness, fatigue from exercise is temporary, although it can be sustained in cases of overtraining. Exercise-hypothesis hypothesis - Cytokines show that continuous release of cytokines increases due to stress, limited recovery time, and sleep change (Vargas & Marino, 2014).

In addition, during prolonged submaximal exercise, blood glucose levels are strongly regulated by the release of IL-6 from glycogen breakdown in muscle, which in turn stimulates the release of hepatic glucose to maintain blood sugar. Robson-Ansley et al. Reported a 6-fold increase in plasma IL6 concentration after strenuous mountain biking training. Similarly, in overweight sedentary and sedentary indigenous populations, moderate to severe aerobic exercise (80% of maximal heart rate) has been shown to increase plasma IL6 by 2 and 5-fold, respectively. In addition, other studies report healthy and fit populations reporting a 5-fold and 9 to 10-fold increase in plasma IL6 during the 1-hour running cycle (Vargas & Marino, 2014).

Hormonal changes also occur in response to exercise, including increases in the plasma concentrations of several hormones, such as epinephrine (adrenaline), cortisol, growth hormone, and prolactin, which have immunomodulatory effects. Stress responses affect immune function, which is associated with a steady change and increase in stress hormones, especially cortisol and epinephrine. Muscle-derived interleukin-6 appears to be responsible, at least in part, for increasing cortisol secretion during long-term exercise, whereas other hormonal changes can

not be attributed to IL6. According to research findings, intense exercise increases the serum and salivary content of athletes, which in turn prolongs the amount of leukocytes in the bloodstream and reduces the effect of white blood cells and other immune cells, leading to a decrease. The body's defenses function against infections and viruses (Fathullah, 2003; Gleeson, 2007; jafari et al., 2014).

Immunoglobulin A:

Among other things, it can be stated that a decrease in salivary IgA concentration and the amount of secretion (the amount of IgA secreted in a fixed period) may make athletes prone to disease in the long run. Bacteria and viruses in the mucosa that can be destroyed by immune cells. However, short-term changes in salivary IgA concentration and secretion after repeated exercise vary. Saliva IgA concentration and secretion may decrease incrementally over longer periods. The repetitive exercise models used in many of the studies described above induce only acute fatigue. Accordingly, less exercise-induced changes in immune variables after repeated cessation of exercise may in fact indicate positive adaptation of the immune system, as opposed to reduced components and immune function that may lead to disease (Peake et al., 2017).

Prevention of fatigue and reduced immune function due to fatigue

Diet is one of the nutritional factors that play an important role in causing fatigue, which includes inadequate intake of complex carbohydrates, proteins, vitamins and minerals. The diet of professional athletes can also include the use of a range of medications, supplements and energy-boosters, and aspects of eating disorders, as well as eating habits in athletes, including low-carb diets, vegetarianism, or high-protein diets. Should be further investigated.

Impact of sleep and recovery

Sleep disorders can also reduce immunity, increase inflammation, and increase harmful health outcomes in the general population. Sleep disorders and circadian rhythm disturbances affect immunity through activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system and are associated with inflammation and lack of coordination of immune variables. Normal responses may increase the risk of infection, cardiovascular disease, and cancer in shift workers. Despite evidence that athletes experience poor sleep patterns compared to non-athletes, there is surprisingly little information in this area. However, the limited data available on how sleep disorders affect immune responses to exercise are inconsistent. Also, physical therapies used after exercise (eg, hydrotherapy and massage) may increase the athlete's sense of health and should be considered as adjunctive therapies to maintain safe health (Peake et al., 2017).

Conclusion

As mentioned, there are many factors that in frequent and high-intensity sports activities can play a role in the occurrence of fatigue and decreased functional quality of the immune system. The study of physiological changes during the process of muscle fatigue and central fatigue as well as the decline of immune system function indices in elite athletes and relatively active individuals indicates a large number of options as biomarkers of muscle fatigue and immune function. These changes are controlled to improve and relieve fatigue, prevent immunosuppression and infectious diseases in athletes. But in general, more accurate results regarding the prevention or delay of muscle fatigue as well as the dual response of the immune system to exercise in athletes of different disciplines still need more research. In general, the best solution for athletes in relieving fatigue and improving the immune system is to pay attention to the amount of sleep, intensity and duration of exercise, control of environmental factors and stress, accurate evaluation of diet including attention to adequate intake of carbohydrates, proteins, fats, fluids, Vitamins and antioxidants, etc., is a period of recovery and also attention to motivational and psychological factors in them.

What is already known on this subject?

One of the harmful factors that affect athletic performance is exercise-induced fatigue, which results from excessive stress and leads to reduced physical and mental function.

What this study adds?

The study of physiological changes during the process of muscle fatigue and central fatigue as well as the decline of immune system function indices in elite athletes and relatively active individuals indicates a large number of options as biomarkers of muscle fatigue and immune function.

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