Review Article

The Post-Exercise Window of Susceptibility to Infection: A Literature Review

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ABSTRACT

Objective

It is well-established that physical activity offers numerous health benefits; however, it should be performed with appropriate intensity and frequency. This literature review aims to explore the impact of irregular and intense exercise on immune function, with particular emphasis on the "post-exercise window of susceptibility" to infections.

Materials and Methods

Relevant articles were identified through a targeted search of the PubMed database, focusing on studies examining the effects of exercise on immune function. Selection was based on relevance to the topic and aimed to provide a broad overview of current perspectives.

Discussion

The current literature indicates that intense physical exertion is associated with exercise-induced muscle damage, inflammation, tissue hypoxia, and hormonal imbalances, all of which appear to contribute to a temporary suppression of immune function. This immune suppression is often manifested by an elevated incidence of upper respiratory tract infections. Furthermore, the literature highlights the protective role of regular, moderate physical activity in promoting long-term immune resilience and reducing the risk of infection. By comparing the short-term immune challenges induced by intense effort with the long-term benefits of consistent training, this review provides a balanced understanding of how exercise influences immune health.

Conclusion

Structured and sustainable physical activity practices are essential for optimizing immune function while avoiding the temporary immune suppression associated with irregular and excessive exercise.

Keywords

exercise; immunomodulation; inflammation; muscle tissue; cytokines

INTRODUCTION

Undoubtedly, physical activity is essential to the promotion of overall well-being. It is therefore fundamental for individuals to recognize its importance and integrate this understanding into their daily lives. In the Polish population exercise is relatively popular, however there is still a room for improvement. The 2021 report from the Polish Central Statistical Office revealed that 43.2% of urban residents engaged in physical activity, with 24.3% participating on a regular basis. Health-related motivations for engaging in sports were cited by 27.3% of Polish women and 21.9% of Polish men[1].

The effects of physical activity on health have been extensively investigated and continue to be a common focus of research. This is unsurprising, given that exercise is a regular

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part of life for a significant portion of the population, as previously mentioned. The literature encompasses a range of resources, including online and laboratory-based studies as well as systematic reviews and meta-analyses derived from these investigations[2,3].

Regular physical activity offers numerous health advantages, positively influencing various systems and functions of the body. It is essential in reducing the risk of obesity and attenuating metabolic complications associated with it, such as non-alcoholic fatty liver disease and type 2 diabetes. These profound metabolic effects are attributed not only to exercise-induced improvements in skeletal muscle metabolism but also to adaptive metabolic changes in multiple other tissues throughout the body[4].

Moreover, physical activity exerts a profoundly beneficial influence on mental health. Epidemiological studies show that low physical activity and prolonged sitting increase mental health risks, while higher activity reduces the likelihood of depression and anxiety[5].

Comprehensive research also highlights how significant is the impact of exercise on the immune system. Physical fitness and moderate-intensity exercise enhance immune responses to vaccinations, reduce chronic low-grade inflammation, and improve various immune biomarkers across various conditions, including cancer, HIV, cardiovascular disease, diabetes, cognitive impairment, and obesity[6].

Amid widespread recognition of physical activity's benefits, it is important to acknowledge that it can, at times, pose potential risks to health.

This study aimed to examine the phenomenon known as the window of susceptibility to infection following physical activity. The "open window" theory suggests that an acute session of endurance exercise may temporarily weaken the immune system, creating a brief period of heightened vulnerability, particularly to upper respiratory infections (URIs)[7].

It primarily occurs in individuals who do not engage in regular physical activity and undertake an intense workout. The mechanisms underlying its emergence primarily involve exercise-induced muscle damage, inflammation, hypoxia, and hormonal disturbances.

Exercise-induced muscle damage

Exercise-induced muscle damage (EIMD) is a condition described by prolonged impairment of muscle function, delayed-onset muscle soreness, stiffness, and swelling[8]. It is also associated with increased activities of intramuscular proteins in blood plasma, including creatine kinase, myoglobin, skeletal troponin I, and myosin heavy chains[9].

The predominant cause of EIMD is eccentric exercise, which involves exertion associated with the lengthening of the muscle, as the tissue works to decelerate or stop motion, rather than initiate it. This type of motion reduces the number of motor units recruited, consequently increasing the mechanical stress on the muscle. Moreover, metabolic stress can also contribute to EIMD, particularly in types of physical activity where eccentric contraction is less predominant[10].

The pathophysiology of EIMD is complex, and various mechanisms have been proposed to explain its causes. During eccentric exercise a forcible stretching of the myofibrils occurs parallel to their contraction. As some sarcomeres are more resistant to stretching than others, the more susceptible sarcomeres lose myofilament overlap. When the muscle contracts again, these overstretched sarcomeres may not reinterdigitate, resulting in sarcomere disruption. The accumulation of disrupted sarcomeres during repeated stretching damages sarcoplasmic reticulum, transverse tubules and the sarcolemma. This leads to increased membrane permeability and a rise in the sarcolemma Ca^{2+} levels[11].

Laterally, stretch-activated cation channels allow for influx of Na^{+} and Ca2+ into the sarcolemma, contributing to swelling and excessive Ca^{2+} levels[12]. The rise in Ca^{2+} concentration in the sarcolemma has a multitude of consequences.

Firstly, it results in increased passive muscle tension and a decrease in active tension[13]. Secondly, Ca^{2+} activates calpains and phospholipase A2. Calpains are cysteine proteases that cleave desmine, vimentine, and α-actinin located in the Z-disc regions, causing further damage to the sarcomeres. Phospholipase A2 exacerbates the damage to the cell membrane, allowing the efflux of intracellular molecules[14–16]. This manifests as a rise in the activity of muscle-specific proteins in blood plasma. Twenty-four hours after eccentric workout, there is an increase in circulating neutrophil counts[17]. The aforementioned structural and functional changes in EIMD lead to inflammation. It is possible that the efflux of muscle proteins cleaved by the calpains is the reason for leukocyte attraction. The first immune cells to invade damaged muscle are Ly6C+/F4/80- neutrophils.

They appear in the tissue as early as two hours post-injury, reaching the highest concentration between six and 24 hours. Phagocytic macrophages infiltrate second, followed by non-phagocytic macrophages.

The former appear around 24 hours and continue to rise until two days after muscle damage; after this period, their numbers decline rapidly. The latter peak around four days post-injury and remain in the tissues for over a week. Th1 cells produce interferon-γ and tumor necrosis factor-α, stimulating macrophages to differentiate into proinflammatory M1 CD68+ phenotype. M1 macrophages, along with neutrophils, generate reactive oxygen and nitrogen species, as well as myeloperoxidase, which further injure muscle tissue, but also help clear intracellular debris[18].

Inflammation

Physical activity serves as a stress factor and, immediately following exercise, can lead to inflammation[19].

Molecules, such as interleukin-6 (IL-6) and C-reactive protein are key mediators involved in the development and progression of inflammation during this process.

Il - 6

IL-6 is a pro-inflammatory cytokine produced by various cell types, including monocytes, macrophages, T and B cells, hepatocytes, endothelial cells, fibroblasts, keratinocytes, mesangial cells, adipocytes, tumor cells, and most importantly for this paper, by skeletal muscle cells[20].

IL-6 is secreted during exercise from muscle fibers, its release depends on exercise duration and intensity as well as glycogen exhaustion.

This interleukin facilitates communication between organs and muscles, contributing to homeostasis during physical activity. Studies have demonstrated that during prolonged endurance exercise, a noticeable increase in blood IL-6 levels of up to 100 times may occur[21,22].

The concentration of IL-6 may be higher in long-term resistance training compared to short-term resistance training[23]. During training, IL-6 levels increase non-linearly, with an exponential rise occurring immediately after exercise, the intensity of the training directly correlating with the level of IL-6.

Providing energy in the form of carbohydrates during exercise mitigates the rise in IL-6 levels by preventing the depletion of muscle glycogen stores[21]. In the inflammatory process, IL-6 stimulates the production of acute-phase proteins in the liver, including ferritin, CRP, and complement factors. It also activates the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased secretion of cortisol and catecholamines. Furthermore, IL-6 enhances the inflammatory response by inhibiting the regulatory function of T lymphocytes, promotes the differentiation of B and T lymphocytes, and directs neutrophils toward the site of damaged myocytes[24].

C-reactive protein

CRP is an acute-phase protein whose levels increase following strenuous physical activity. This elevation occurs because CRP production is provoked by IL-6[25]. Furthermore, research conducted by Stephen R. Hennigar et al. demonstrated that individuals engaging in physical activity while in an energy deficit exhibit slightly higher CRP levels compared to those in energy balance. Based on these findings, the researchers proposed a hypothesis suggesting a cooperative relationship between CRP levels and gluconeogenic processes[26].

Additionally, a study by Bernat-Adell, María D., et al. investigated CRP levels in marathon runners and revealed a significant correlation between the duration of the run and CRP concentration. Their results indicated that longer runs were associated with higher CRP levels, with these elevated levels persisting for up to 48 hours post-exercise[27].

Hypothalamus-pituitary-adrenal circulation

During physical exercise, the body experiences stress due to increased energy requirements and disruptions in homeostasis, leading to the activation of the HPA axis. Intense exercise is known to elevate the secretion of stress-related hormones, including cortisol, adrenocorticotropic hormone (ACTH), and catecholamines[28].

Research has demonstrated that post-exercise cortisol levels in saliva and serum are significantly elevated[29]. However, individuals in good health who begin a workout routine may, over time develop a stronger immunity to the stimulating effect of the steroid. The release of cortisol correlates directly with the duration and frequency of exercise[30]. A minimal overlap exists between the cortisol increase induced by psychological stress and that caused by physical exertion. Cortisol

also contributes to the synthesis of catecholamines, which are simultaneously involved in the regulation of lymphocyte proliferation[31].

Catecholamines further influence the expression of intercellular adhesion molecule-1 (ICAM-1), assisting the release of lymphocytes from the vascular endothelium[24]. The number of leukocytes doubles or even triples within minutes of initiating exercise, and during prolonged physical activity, leukocyte levels can sustain an elevation of up to five times the baseline concentration[31].

Hypoxia and its immune effects

Hypoxia is a state of oxygen deficiency in the body's tissues that leads to a disruption of physiological processes in cells. It may arise from diverse etiologies and involve distinct mechanisms.

By comprehending the pathophysiology of a particular mechanism, we can perform differential diagnosis, which enables us to distinguish a number of causes i.e. hypoxemic hypoxia (the result of ineffective oxygenation of the blood due to disorders of perfusion, ventilation or diffusion), anemic hypoxia (deficiency or defect in the structure of hemoglobin), circulatory hypoxia (disorders of blood flow characteristic of cardiovascular disease, when the heart fails to provide necessary tissue perfusion), and histotoxic hypoxia (where there is a disruption of oxygen metabolism in cells, for example. due to cyanide poisoning)[32].

The intensity of oxygen deprivation varies from mild to severe. It occurs in acute forms lasting minutes-days, chronic forms that last days-years, and mixed acute and chronic forms [33]. The oxygen demand of cells varies from tissue to tissue. It depends on the functions performed, and the degree of activity, e.g., whether the body is in the exercise phase (in which case the oxygen demand of skeletal muscles increases) or at rest[34]. Ongoing pathological processes like inflammation and cancer that reduce available oxygen levels are also significant factors[35].

The boundary between the beneficial and harmful effects of physical exertion is individual and depends on many factors such as the current state of the immune system, ambient temperature, eating and sleeping habits, genetic predisposition and psychological influence[36]. Numerous studies confirm that intense exercise prompts systemic inflammation, resulting in increased synthesis and release of pro-inflammatory cytokines, while increased levels of anti-inflammatory cytokines are a secondary response[37]. A multitude of biochemical and molecular processes describe responses to hypoxia.

Hypoxia-induced factors (HIF), regulated by oxygen access, are responsible for homeostasis. They are mainly responsible for regulating the cell's adaptation to the prevailing conditions[38]. In the situation of acute hypoxia, HIFs are responsible for attempting to improve neutrophil survival and migration due to inhibition of apoptosis, increased chemotactic capacity and expression of neutrophil pro-inflammatory cytokines, e.g. IL-8, IL-4, TNF-alpha, vascular growth factor, which is a protective mechanism[39].

In the case of excessive exercise, the alpha/beta-adrenergic system, generates an immunosuppressive microenvironment of tissue scope by impeding the influx of effector immune cells (T cells and NK cells), releasing pro-inflammatory cytokines, blocking the activity and increasing the commitment of immunosuppressive cells, such as myeloid-derived suppressor cells (MDSCs), which condition T-cell anergy, block CD8+ T-cell activity, and increase programmed death-ligand 1 (PD-L1) expression. MDSCs are responsible for inhibiting Treg cell proliferation resulting in inhibition of T lymphocyte proliferation. Hypoxia also conditions the conversion of MDSCs to tumor-associated macrophages (TAM), related with the M2 immune evasive phenotype[40].

Hypoxia-induced adenosine has also been shown to cause heightened expression of immune checkpoints, including apoptosis, cytotoxic lymphocyte-associated protein-4, immunosuppressive cytokines (transforming growth factor-β) as well as regulatory T cells[41]. Hypoxic cells can evade the innate immune system due to the expression of molecules such as CD47 "don't eat me signal" as well as immune checkpoint inhibitor molecules PD-L1 and cytotoxic T-lymphocyte associated protein 4 (CTLA-4), which bind macrophages and effector T cells stopping their activity[42]. As a result of hypoxia, the mechanism of aerobic respiration takes over the process of glycolysis as the main source of the cell's energy resource. The product of anaerobic glycolysis is lactic acid, which evacuates to bloodstream and according to recent data, acts as a signaling molecule in escape from immune surveillance[43]. Lactates can also attenuate the degree cytotoxic activity of cytotoxic T (CTL) and NK cells[40].

Primary defence and upper respiratory tract infections

The "open window" theory suggests that after intense exercise, the immune system may temporarily weaken, which increases susceptibility to opportunity infections. Among trained athletes, URTIs are most frequently observed.

It is important to note that responses of the athletes immune system differ from the responses of the non-exercising individuals, making athletes more prone to infections.

The upper respiratory (UR) tract is continuously exposed to microorganisms from the external environment through respiration, therefore, it is essential to prevent the invasion of microorganisms and allergens[44,45]. By operating through two fundamental components, the immune system comprises innate and adaptive immunity.

Innate immunity provides both physical and chemical barriers against pathogens using germline-encoded molecular and cellular defense mechanisms, such as resident cells, blood components, antimicrobial peptides, proteins. In addition, it stimulates the activity of neutrophils, macrophages, mast cells, dendritic cells and NK cells. While innate immunity is the body's fastest defense mechanism, it is important to note that its responses are non-specific, which can sometimes render it insufficient. Concurrently, adaptive immunity consists of the coordinated action of B and T lymphocytes, antigen-presenting cells, antibodies and cytokines, including IFN-γ and TNF-α[35].

A fundamental component of the immune system closely linked to the occurrence of URTIs is the mucosal immune system. Interestingly, 70% of all lymphocytes in the body are found precisely in mucosal tissues. Its main role is to protect mucosal surfaces from invasion of microorganisms by employing in particular non-specific defense mechanisms, such as mucociliary transport and the secretion of bactericidal enzymes, to enhance its protective functions. The mucosal immune response is initiated at inductive sites, primarily located in the nasopharynx-associated lymphoid tissue (NALT) and gut-associated lymhpoid tissue (GALT), along with other, less well-defined lymphoid structures. These inductive sites are responsible for recognizing and processing antigens, while effector sites are involved in the production of secretory IgA.

The studies show that immunoglobulins A (IgA) play a crucial role in the mucosal immune system. Its primary function is to hamper the adherence of microorganisms to epithelial cells by nullifying and agglutinating them. Subsequently, microorganisms attached to secretory IgA (SIgA) are eliminated via mucociliary transport[45]. SIgA is a significant factor in the body's defense by facilitating immune exclusion at mucosal surfaces, intra-epithelial viral neutralization and immune elimination across mucosal barriers. Interestingly, studies have shown that athletes experience a temporary reduction in SIgA levels for up to 24 hours following intensive workout. This exercise-induced immunomodulation depends strongly on intensity, duration and frequency of the physical activity and can have diverse effects on the immune system. Therefore, it is essential to elucidate specific aspects of the particular exercise regimen, as one type of exertion can have detrimental influence on the immune system, while others can impact it in a disparate way[44].

Immunomodulatory effects of different workout intensities

As previously mentioned, the type, volume and intensity of a workout are critical factors in determining susceptibility to URTI. The researchers unanimously agreed that acute bouts of high-intensity or high-volume exercises can induce a temporary suppression of acquired immune functions, such as a reduction in immune cell counts[35]. Studies have shown that the correlation between exercise and the risk of developing URTI can be depicted by a J-shaped curve. This model suggests that the likelihood of experiencing URTI is average with low levels of exercise intensity and volume, below average with moderate levels, and significantly higher with acute or exhaustive exercise[46]. This correlation is also evident in the examples of endurance and resistance training. While endurance training primarily emphasizes volume, engaging large muscle groups in prolonged, moderate- to low-intensity activities, resistance exercise is typically characterized by higher intensity and shorter durations, aimed at improving muscle strength[47,48].

Both types of workout at high intensity can reduce immune function; however studies indicate that endurance exercise performed at moderate intensity and volume can actually enhance immunosurveillance and immunocompetence. This occurs due to the promotion of lymphocyte homeostasis and the enhancement of lymphocyte resistance to apoptosis.

As a result, it strengthens immune function and helps reduce chronic inflammation.

There are several reasons why acute exercise is associated with an increased risk of developing URTIs. Firstly, acute exercise interrupts a cell homeostasis by promoting immune system activation through the production of reactive oxygen species (ROS). The alpha/beta-adrenergic system also plays a crucial role, as it increases the levels of inflammatory cytokines and enhances the availability of immune cells, particularly natural killer cells and CD8+ T cells in peripheral tissues. Consequently, following acute exercise, lymphopenia is often observed, which is believed to be associated with redistribution of these immune cells. What is worth noting, the immune functions and the affected cell numbers usually recover to baseline within 24 hours of an exercise[35].

Additionally, it has been observed that acute exercise increases IgA levels only in trained subjects, particularly following particularly strenuous exercise, however, their baseline IgA levels are lower. Excessive exercise impairs immune function, thereby increasing the risk of infections. However, research indicates that regular moderate-intensity continuous training can enhance immune defense. This is attributed to the previously mentioned "J" curve. Studies demonstrate that moderate physical activity can be highly beneficial in reducing the risk of URTIs, but its benefits extend beyond that[44]. It is also well known that regular moderate exercise lowers the incidence of various cardiovascular diseases, including coronary heart disease, atherosclerosis and hypertension[49]. This improvement occurs because consistent exercise promotes mitochondrial integrity, reduces oxidative stress, and subsequently lowers inflammation, which in turn decreases the risk of developing inflammatory diseases[35].

Anti-inflammatory effects of exercise

As many studies throughout the years have shown that physical activity is beneficial for overall health it is not different when it comes to our immune system. Single bout of exercise when performed by a person who is not training on a regular basis results in a more pro-inflammatory reaction. It might also be strengthened by too intense exercise or insufficient resting time. However regular exercise with proper knowledge on regeneration period and training intensity is widely known to leave a positive mark.

Firstly, physical activity combined with diet enables us to reduce adipose tissue. The higher the body fat, the greater the risk of cardiovascular incidents, acquiring diabetes, and many other health issues. Adipocytes also produce multiple pro-inflammatory molecules, such as TNF-α, leptin, CCL2, CXC, RBP4, and IL-18. In addition, the tissue reduces the amount of anti-inflammatory cytokines. There is a direct correlation between the inhibition of adiponectin production and high amounts of fat in the body.

ICAM1 is a molecule involved in the infiltration of adipose tissue by T-cells and macrophages, which in turn causes inflammation. Its expression is known to be increased in the obese population. A group of patients who participated in six months of aerobic training showed a decrease in ICAM1 levels without changes in body weight. However, further studies on humans should be conducted[50].

Physical activity stimulates the sympathetic nervous system (SNS) and the HPA. The SNS causes the release of catecholamines, which inhibit the synthesis of pro-inflammatory cytokines dependent on lipopolysaccharides, such as IFNγ. The HPA axis, through ACTH, induces the increased production of cortisol, which is known to have anti-inflammatory effects.

As mentioned earlier, IL-6 is produced by contracting muscles during exercise. This is not the case with TNF-α or IL-1. Studies suggest[51] that IL-6 exhibits an anti-inflammatory effect by suppressing the pro-inflammatory synthesis of TNF-α and IL-1. IL-6 also induces the creation of IL-1ra, which is an IL-1 receptor antagonist, and IL-10[52]. Interleukin-10, also known as cytokine synthesis inhibitory factor (CSIF), is an anti-inflammatory molecule that inhibits the production of IFN-γ, IL-2, IL-3, IL-1α, and IL-1β. It also enhances B-cell proliferation and antibody synthesis. The cytokines mentioned above play a crucial role in activating the inflammatory response from granulocytes, monocytes, and NK cells[53].

When it comes to CRP, studies[54,55] have shown an increase in its levels near the end of and immediately after exercise. Others have discovered that it increases even one day after, but this might be due to the higher intensity of training. This marker has both pro- and anti-inflammatory features. Pue et al. concluded that it inhibits the production of pro-inflammatory molecules in macrophages[56]. On the other hand, regular exercise

reduces CRP levels[57].

There are two types of macrophages: M1, which promotes inflammation, and M2, which decreases inflammation and induces tissue regeneration. Their phenotypes can switch between each other. Studies have found that the development of M2 macrophages, as well as the phenotype switching from M1 to M2, is promoted by regular aerobic training. It also reduces macrophage infiltration into the tissue, as mentioned earlier[35,57].

TLRs are proteins that play a crucial role in the pro-inflammatory response to both exogenous and endogenous stimuli. Studies have discovered that patients who train regularly have decreased TLR4 expression on monocytes, which in turn reduces the inflammatory response. These monocytes divide into several types. One of them is CD14^low CD16^+ monocytes, which are characterized by two point five times higher TLR4 expression than other types. This makes them the most significant contributors to inflammation, despite comprising only 10% of the total monocyte population in the body. Regular exercise reduces the number of inflammatory monocytes, which may be due to increased cortisol levels in the plasma of CD14^low CD16^+ monocytes. Treg cells play a significant role in regulating immune system function and reducing inflammation. They release IL-10, which suppresses the development of other T-cells or NK cells. Studies have shown that regular high-intensity training increases the levels of Treg cells in circulating blood. As a result, they help reduce the inflammatory response in the body[50].

High-intensity exercise also increases B cell count in circulation, which promotes a more targeted response to pathogens rather than a non-specific inflammatory response.

CONCLUSIONS

The theory of open window susceptibility suggests that following intense exercise, there is a temporary period during which the immune system may become weakened. This transient state is characterized by alterations in immune cell counts and immunological responses, increasing vulnerability to infections, with URTI being the most commonly observed. Acute exercise disrupts cellular homeostasis, with the mucosal immune system playing a crucial role in this process. A key component of mucosal immunity is secretory SIgA, which facilitates immune exclusion at mucosal surfaces and immune elimination across mucosal barriers. Noticeably athletes experience a temporary reduction in SIgA levels for up to 24 hours following intensive physical activity, which may enhance pathogen invasion.

During physical exercise, the body experiences stress, leading to the activation of the HPA as a result, the levels of cortisol, ACTH, and catecholamines increase. This hormonal response, mediated via alpha/beta-adrenergic system, generates an immunosuppressive microenvironment within tissues. Such conditions promote lymphocyte proliferation, their release from the vascular endothelium, and elevated levels of pro-inflammatory cytokines and immune cells.

Hypoxia, as a part of physical exertion, contributes to alterations in cellular environments, thereby disrupting physiological processes. HIFs are responsible for neutrophil migration and the expression of neutrophil pro-inflammatory cytokines, including IL-8, IL-4, TNF-alpha, vascular endothelial growth factor. As a result of hypoxia, glycolysis becomes the primary energy source, producing lactic acid, which diminishes the cytotoxic activity of cytotoxic T lymphocytes and NK cells.

In addition to immunological adjustments, exercise-induced muscle damage, characterized by the accumulation of disrupted sarcomeres, further heightens susceptibility to infections. Sarcomere components become weakened, and calcium levels in the sarcolemma increase. Consequently, the levels of neutrophils, leukocytes, macrophages and pro-inflammatory cytokines increase. Among these, IL-6, originating from muscle fibers, plays a crucial role in the progression of inflammation. The intensity of the training directly correlates with the level of IL-6, stimulating the production of acute-phase proteins such as ferritin and CRP, while also inhibiting T lymphocytes and activating the HPA axis.

While strenuous physical activity may temporarily weaken the immune response and promote infections, the boundary between beneficial and detrimental effects of exercise is highly individual and influenced by various factors. However, acute exercise induces a temporary suppression of adaptive immune functions, the number of immune cells and mediators typically returns to baseline levels within 24 hours. The concept of the “open window” is particularly relevant for

individuals whose physical activity is not regular or sufficiently intense, as they may experience heightened susceptibility to infections during this period.

Despite the potential risks associated with intense exercise, the long-term benefits of regular physical activity for both mental and physical health far outweigh these temporary vulnerabilities. The open window of susceptibility is a transient state, and with consistent physical activity, the immune system adapts and strengthens over time.

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Conflict of interest statement

The authors declare no conflict of interest.

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