Review Article

High-intensity exercise training and the immune system: A new role of lactate

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Abstract

High-intensity exercise training is one of the effective strategies to improve the performance of athletes to achieve excellent physical fitness. In the meantime, a look at the history of sports immunology reveals the idea of window theory, which has been of great concern. According to the history of exercise immunology, high-intensity exercise training can suppress the immune system leading to respiratory infections. It has recently been shown that high-intensity exercise training has no effect on suppressing the immune system. In this review, a new perspective on the immune system and high-intensity exercise training was presented to readers. Moreover, a new look at the history of high-intensity exercise training and the immune system and recent review studies was provided and some suggestions are offered.

Key Words: **High-intensity training, Immune system, Lactate, Metabolic stress, Training duration**

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Introduction

History of sport physiology has shown that exercise can be a major challenge for cellular homeostasis and causes extensive disorders in various tissues of the body (Hawley et al., 2014). However, the immune system constantly reacts to acute and chronic exercise (Improta et al., 2021; Kazemi et al., 2023). The immune system's response to exercise depends on exercise load and physiological stress (Souza et al., 2021). It has been shown that moderate-intensity exercise lasting less than 60 minutes can improve immune function (Moghadam, 2021). On the other hand, several reports have shown that high-intensity exercise can reduce the function of the immune system and increase the risk of infection by 3 to 72 hours (Gonçalves et al., 2020; Khammassi et al., 2020).

High-intensity exercise training with a short duration (2-4 minutes) is one of the most widely used exercise for fitness and health (Buchheit & laursen, 2013; Fasihiyan et al., 2022). But the point is to see whether strenuous exercise can be effective for the immune system. Numerous studies have shown that after high-intensity exercise, the immune system is temporarily suppressed (open window theory) (Ferreira et al., 2020; Kakanis et al., 2010). It has also recently been discovered that high-intensity exercise training can control inflammation in the body as an effective intervention (Khalafi & Symonds, 2020). Therefore, due to the hypothesis that high-intensity exercise can play a role in suppressing the immune system, some athletes refrain from doing this exercise. Nonetheless, it has recently been shown that high-intensity exercise training can improve the functioning of the immune system through various mechanisms. Thus, in this review study, we try to discuss the mechanisms of effective high-intensity exercise training on improving the immune system by reviewing new studies.

Lactate can have an anti-inflammatory effect on the immune system.

A hypothesis emerged between the 1980s and 1990s claiming

that acute high-intensity exercise training could suppress the immune system (Mackinnon, 1999; Walsh et al., 2011). These hypotheses show that long-term and acute high-intensity exercise training can increase the risk of infection, reduce IgA, and reduce the number of immune cells in the blood for a short time (Campbell et al., 2018). Summarizing these results led to the beginning of open window theory (Ahmadi Hekmatikar et al., 2019; Peake et al., 2017). It has been shown that during high-intensity exercise training, the pH level decreases and the production of lactate and hydrogen ions increases (Edge et al., 2006). Measuring blood lactate concentration provides information not only about changes in glycolysis (Medbo et al., 1993), but also provides information on metabolic changes. Also, it has been reported that peak blood lactate was observed in a 400 m run (Chen et al., 2022).

Looking at the history of exercise, it can be understood that there has been a lot of controversy for many years about the effectiveness of lactate during exercise. Lactate was discovered in 1780 and became known as a waste product in the body (Ferguson et al., 2018). But recent evidence suggests that lactate can play a very beneficial role in metabolic, physiological, and immunological processes (Certo et al., 2021). Lactate, the end product of the glycolysis cycle, has been shown to be produced and secreted by innate immune cells as inflammation increases (Palsson et al., 2013). Recent reports suggest that lactate production may suppress the immune system. This suppression of the immune system by lactate is called "immunoparalysis " (Hotchkiss et al., 2013). Studies have also shown that increasing lactate can reduce T cells and reduce the secretion of anti-inflammatory cytokines (Fischer et al., 2007). Therefore, to date, lactate plays a role in reducing and suppressing factor of the immune system.

New studies show that lactate can act like a double-edged sword. One study found that lactate could block IL-12 synthesis by dendritic cells (This could be in favor of producing interleukin-10) (Gottfried et al., 2006; Nasi & Rethi, 2007). In a study examining the effect of lactate on the immune system, it was reported that lactate is not only an excess but also can improve immune function and physiological health (Caslin et al., 2021). It has recently been shown that lactic acid can both suppress inflammatory macrophages and increase anti-inflammatory macrophages (Bohn et al., 2018; Zhang & Li, 2020). However, the exact mechanism of this process is not yet known, but recent data suggest that this polarization depends on the activation of hypoxia induction factors (HIFs) and inducible cyclic AMP early repressor (ICER) induction (Bohn et al., 2018; Zhang & Li, 2020).

HIFs can regulate both inflammatory genes and metabolic genes (Watts et al., 2019). One study found that immune cells can adapt to lactate, and that lactate can have strong anti-inflammatory effe-cts in the long run (Ratter et al., 2018). The point, however, is that lactate exerts its signaling effects depending on cellular conditions. For example, lactate in dendritic and macrophage cells can increase interleukin-10 (Manoharan et al., 2021). In conclusion, lactate can have both anti-inflammatory and inflammatory effects, depending on environmental conditions. However, its inflammatory effects are greater than its anti-inflammatory effects, and yet, it is not possible to say exactly which effect the lactic acid produced in high-intensity exercise training will have. However, what is clear is that if you do high-intensity exercise training for weeks and months in a row, your immune system will be strong.

High-intensity exercise, anti-inflammatory effect

It is found that salivary immunoglobin-A (sIgA) levels increased as a result of nine sessions of high-intensity exercise training (Born et al., 2018). The latter assumption, however, presumes that the mucosal immune system needs to be stressed in some way to adapt and improve its capacity to neutralize and defend viral pathogens in a similar way as muscles becomes stronger when exposed to regular training stress and adequate overload (Basuini et al., 2022). High-intensity exercise training seems to be replacing moderate-intensity exercise for inflammatory responses. In this regard, researchers in their study discussed the effect of endurance training and high-intensity exercise training on inflammatory responses (Farhani et al., 2022). The studies found that people who use HIIT exercises achieve health benefits in a shorter time and have faster and more adapted inflammatory responses than people who do endurance exercises (Kaspar et al., 2016; Khoramipour et al., 2020). However, it cannot be said with certainty that high-intensity exercise training can be effective in reducing inflammation because its exact mechanism remains unclear. However, according to the existing studies, it can be understood that high-intensity exercise training in the long run and chronically can change the orthography of immune cells (Liu et al., 2017).

Nevertheless, emerging evidence suggests that high-intensity training can induce a more advanced anti-inflammatory response which is favored in the prevention and treatment of diseases associated with chronic inflammation such as cardiovascular disease (Handzlik et al., 2013). According to this hypothesis, it can be stated that elite athletes who train have better metabolic health (Laine et al., 2016). This means that both the innate and adaptive immune systems have both improved themselves with high-intensity exercise over the long term. The key player in the immune system is the white blood cells, which can travel throughout the body through the blood vessels. The immune system is divided into two categories (the innate immune system and the adaptive immune system) (Agha-Alinejad et al., 2022;

-pond to initial infection and disease and does not retain the memory of previous responses. The innate immune system has several components. These components include skin, cellular processes such as phagocytosis and humoral components such as soluble proteins (Pérez, 2016). If pathogens persist in the body, the adaptive immune system is recruited. Therefore, the adaptive immune system can exert a longer immunity in the body (Simpson et al., 2020). However, the concern is that high-intensity exercise in beginners, regardless of intensity and duration, can increase the risk of upper respiratory infections (Dhabhar, 2014).

Conclusion

In this review study, we examined a new look at the effects of lactate on immunological changes. The present review study showed that lactate produced by high-intensity exercise training can act both as an immunosuppressant and as an anti-inflammatory agent. Looking at the history, it can be seen that lactate has been mentioned as an unnecessary factor for many years. Recent studies, however, have shown that lactate can act like a double-edged sword. Meanwhile, high-intensity exercise training has recently gained a lot of fans among athletes. These exercises improve metabolic health in a short period of time.

Throughout different decades of life, researchers have reported the importance of the immune system in the health of the body to people around the world. In this regard, training can establish a very good relationship with the immune system as a friend. Thus, the significant breakthroughs in this field were properly compiled in the so-called Exercise Immunology (Terra et al., 2012). But the point is to probe if strenuous exercise can be effective for the immune system. Moderate intensity training (40%-69% VO2max, 30 to 60 minutes, 3-5 days/wk) to relatively intense volumes (70 to 85% VO2max, 30 to 45 minutes, 2-3 days/wk) are directly associated with a lower upper respiratory tract infection (URTI) incidence (Nieman et al. 2019; Sellami et al., 2018). Moreover, recent studies have shown that exercise can increase the level of exercise-induced extracellular vesicles as a promising therapeutic approach (Alehossein et al., 2023).

It is still true that high-intensity exercise training can play a role in suppressing the immune system, but why? The present study showed that in people who have not exercised, high-intensity exercise training, regardless of the duration and intensity of exercise, increases the lactate and this increase in lactate suppresses the immune system. Recent studies, however, have shown that adherence to these exercises can improve immune function. However, we cannot claim that high-intensity exercise training is harmful for the immune system. In addition, this adaptation that occurs in high-intensity exercise training can increase the level of lactate threshold and compatibility between the immune system and lactate, and therefore it can be stated that lactate at this level can have anti-inflammatory effects.

What is already known on this subject?

Previous studies have shown that exercise can be effective in improving the immune system but inspecting the types of exercise effects on the immune system is still unclear. Moreover, a few studies have reported that lactate can play a very important role in immune response after training. Due to the amount of metabolic stress in different types of exercises, the secretion of lactate is very different and for this reason, investigating the high-intensity interval training effects on the immune system could be useful.

What this study adds?

In this review study, we explored the new role of lactate in high-intensity exercise training and its relationship to the immune system. However, we still cannot say with certainty that increasing lactate due to high-intensity exercise training can be beneficial or harmful to improve the functioning of the immune system. Therefore, it is suggested that in future research, researchers study the effect of high-intensity exercise training on lactate levels at different times on the immune system by focusing on lactate and the immune system.

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Table 1. Recommended high-intensity exercise training protocol for anti-inflammatory effect

Level	intensity	Duration	Recovery time	Number of sessions per week	Type of exercise
Beginner	It is better to start with moderate intensity training (40 to 65% Vo2max) *	30-40 min	24 h	3-5 sessions per week	Treadmill running, cycling, ball games
trained	65-85 % Vo2max	2-4 min	24-72 h	3 sessions per week	Running on a treadmill, cycling or speeding
Elite athletes	85-100 % Vo2max	30s-2min	24-72 h	3 sessions per week	Running on a treadmill, cycling or speeding

* In beginners, high-intensity exercise suppresses the immune system. Starting a moderate exercise can turn a beginner into a trained person.

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