Stress-induced immunosuppression and physical performance

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Abstract Sports training and competition are significant sources of stress. Elite athletes may be subject to specific exercise-related physical and mental stressors that promote the development of mood, anxiety disorders and depression. Psychological stress has been shown to adversely impact the function of the immune system and compromise host defenses against various infections. Inflammation may also play a role in neuropsychiatric diseases, including major depression. These associations between stress and inflammation are relevant. The current short review discusses psychological stress and the immune system in athletes, providing a comprehensive overview of the effect of the stress response on physical performance.

Keywords: immunosuppression, pro-inflammatory cytokines, depression, elite performance

Introduction

Psychological stress in humans causes physiological, immunological and behavioral alterations that can be maladaptive and negatively affect the quality of life1,2). The interaction between stress and the immune response has been studied using various experimental paradigms. It is well documented that exhausting physical activity and intense exercise training lead to inflammatory responses and immunosuppression, whereas regular physical exercise has a positive influence3). Furthermore, other factors associated with a high level of pressure to perform well, in addition to other stressors, contribute to the high prevalence of mental disorders among elite athletes, involving a physically debilitating condition that results in total compromise of their capacity to perform and compete4). Recent evidence indicates that inflammation and altered immune signaling significantly contribute to the etiology of many psychiatric symptoms and disorders5-7). Indeed, chronic psychological stress substantially enhances the pro-inflammatory profile8). These associations between stress and inflammation are relevant because immune activity potently regulates mood and behavior9). This article reviews psychological stress and the immune system in athletes, with a comprehensive overview of the stress response, and discusses the effect on physical performance.

Psychological stress and immune response

It is increasingly being recognized that social, psychological and physical stressors, such as anxiety, insecurity, social isolation or academic examinations, affect health1,2,10). Activation of the neuroendocrine and sympathetic systems stimulates physiological pathways linking stress and negative immune outcomes.

Psychological, emotional and physical stressors stimulate the autonomous nervous system, including efferent sympathetic and vagal pathways and the hypothalamic-pituitary-adrenal (HPA) axis, resulting in the release of pituitary and adrenal hormones11), with consequent immune alterations (Fig. 1). Various stressors may either increase or decrease the immune response, depending on kind and duration of stress12,13). Acute short-term low-intensity stressors or moderate stressors enhance the innate and adaptive immune system, which benefits the host14-16), while chronic stressors inhibit the immune function and increase susceptibility to infection, tumors, hypertension, heart attacks, stroke, autoimmunity and affective disorders17-22). Stress hormones, such as glucocorticoids and catecholamines, are known to regulate immune cell functions, particularly at the level of cytokine secretion23). Patients with major depression have been found to exhibit increased peripheral blood inflammatory cytokines, such as interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF)-α, which have been shown to access the brain and interact with virtually every pathophysiologic domain known to be involved in depression24-26). For example, normal volunteers challenged with lipopolysaccharide (LPS) exhibit acute increases in the symptoms of depression and anxiety27).
and the administration of typhoid vaccine to healthy individuals induces a depressed mood, fatigue, mental confusion and psychomotor slowing\(^{29}\). These findings suggest that the activation of the immune system can cause marked behavioral alterations, such as depression.

**Immune dysfunction and physical performance in athletes**

Regular moderate exercise reduces the risk of infection compared with a sedentary lifestyle; however, prolonged bouts of exercise and periods of intensified training are associated with an increased risk of infection against pathogenic agents\(^{3,30-32}\). Athletes with intensive training schedules or undergoing endurance competitions, such as marathons, experience chronic exposure to physical and/or psychological stress-induced hormones and cytokines. Hence, the accumulation of stress in elite athletes may lead to chronic immunosuppression and consequent increased susceptibility to opportunistic infections, resulting in the impairment of exercise performance\(^{30,32}\). It has been established that high-intensity exercise promotes a greater release of stress-associated hormones, such as catecholamines and cortisol, and modulates the immune system. Additionally, it is widely accepted that acute and chronic exercise alters the number and function of circulating immune cells\(^{3,31}\). Moreover, acute short-term exercise experienced at the time of immune activation may enhance innate and adaptive immune responses. In contrast, chronic or long-term exercise can suppress immunity by decreasing immune cell functions and/or increasing active immunosuppressive mechanisms (e.g. regulatory T cell pathways)\(^{33}\). Chronic or intensive training can also impair the balance of Th1/Th2 cytokines\(^{34}\), thereby modulating susceptibility to various immune-related disorders. Intensive exercise, excessive repetition of training and sports injuries stimulate local inflammation and generate a systemic inflammatory response, similar to that induced by infection\(^{35}\). Furthermore, higher serum levels of inflammatory cytokines, mainly IL-6 and TNF-\(\alpha\), have been observed after marathon races or long-distance cycling\(^{35,36}\). Although inflammation is a critical response to acute infection or injury, chronic or excessive inflammation may be detrimental to health. LPS, a potent stimulant
of cytokine release, and inflammatory cytokines signal the brain to produce changes in cognitive, behavioral and emotional functioning characteristic of sickness behavior\(^{1-7}\). Therefore, controlling immunological alterations is important during intensive training to avoid declines in exercise performance.

In addition to exercise-induced immune responses, other factors associated with a high level of pressure to perform well and other stressors, contribute to the immune suppression and high prevalence of mental disorders observed among elite athletes. The central nervous system, endocrine system and immune system are complex systems that interact with each other. Mental disorders and physiological maladaptations have been reported to be associated with a state of chronic low-grade inflammation and immunological dysfunction. This is a physically debilitating condition that results in total compromise of the capacity to perform and compete\(^6\). Therefore, considering the importance of knowledge regarding the relationship between exercise and the wide range of issues in the field of neuroimmune science involved in mental health, it is essential to avoid declines in physical performance in order to improve the success of athletes.

**Conclusion**

Elite athletes may be subject to specific exercise-related physical and mental stressors that favor the emergence of mood, anxiety disorders and depression. It should thus be emphasized that an athlete’s behavior and mental health may affect their performance. In conjunction with these considerations, athletes, coaches and medical support personnel should pay attention to the brain-to-immune and immune-to-brain communication that functions to regulate mental health and competitive performance.

**Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this article.

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