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The Relationship Between Physical Activity Levels and Immune Function

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Abstract

The relevance of this study stems from the need to identify the relationship between the level of physical activity and the state of the immune system, including the incidence of infectious diseases and the rate of recovery. The study also examines myokines released in response to physical exercise that affect the immune system.

To assess the relationship between physical activity and immune system activity, a survey was conducted among 103 people. The results showed an ambiguous relationship between the level of physical activity and the rate of recovery; to clarify the results, a study with a larger sample size is required. Additionally, an analysis of empirical studies available in the PubMed database was conducted.

Keywords: Interleukins, Physical exercise, Immune system, Myokines.

Introduction

Throughout history, movement has been one of the most vital abilities for the survival of living organisms. Physical activity plays a crucial role in maintaining the normal functioning of the human body, ensuring the optimal course of physiological processes. In today's world of rapid technological, internet, and transportation infrastructure development, the need for physical labor has significantly decreased, leading to the spread of a sedentary lifestyle. Lack of physical activity is considered one of the major risk factors for the development of various diseases and functional disorders of the body [7]. Regular physical activity has a beneficial effect on various body systems. It has been proven that moderate physical activity increases the body's resistance to infectious diseases, including acute respiratory viral infections [3]. At the same time, it should be noted that physical activity must be appropriate to the body's functional capabilities.

During physical exercise, skeletal muscle functions as an immunoregulatory organ via myokines, influencing inflammation and leukocyte transport [9].

Myokines are biologically active substances produced by muscle fibers in response to stimulation, exerting autocrine, paracrine, or endocrine effects [9]. It has been established that myokines play a key role in regulating the immune system [9,5]. The main myokines affecting the immune system are:

1. Interleukin-6 (IL-6)

IL-6 was the first myokine identified and remains the most studied among them. Its synthesis is triggered by contracting myocytes in response to glycogen depletion, lactate accumulation, and increased calcium signaling [9].

Plasma IL-6 levels rise during exercise and peak upon its completion. During prolonged aerobic exercise (such as a marathon), IL-6 concentrations can increase 100-fold or more compared to baseline levels.

The functions of IL-6 as a myokine are diverse. In terms of metabolism, it stimulates glucose uptake by muscle cells via the GLUT4 transporter and activation of AMPK, and increases lipolysis and fatty acid oxidation. In the context of immune regulation, muscle-derived IL-6 induces the production of the anti-inflammatory cytokines IL-1ra and IL-10, suppresses TNF-α (tumor necrosis factor-alpha) production, activates NK cells, and stimulates T-helper differentiation [9]. In oncology, it promotes the mobilization of NK cells to the tumor via an IL-6-dependent mechanism [7]. IL-6 activates the STAT3 pathway, inducing the expression of M2 phenotype markers (CD206) and suppressing the activity of M1 macrophages [5]. IL-6 enhances T-cell motility through the translocation of STAT3 into the mitochondria and the maintenance of mitochondrial calcium homeostasis [5]. IL-6 promotes the differentiation of CD8+ T cells (which is critical for the clearance of intracellular pathogens, such as Brucella) and the maturation of dendritic cells, stimulating an antitumor T-cell response [5].

Interleukin-1 receptor antagonist (IL-1ra)

IL-1ra is an IL-1β receptor antagonist and one of the most important anti-inflammatory mediators. Its secretion is primarily driven by the stimulation of macrophages by muscle-derived IL-6, so its release follows an increase in IL-6 in the blood [9, 5].

Mechanism of action: IL-1ra blocks IL-1β signal transduction without activating any intracellular responses, i.e., it acts as a pure competitive antagonist [8]. This is important for protecting muscle tissue from hyperactivation of the inflammatory response during the recovery period following physical exercise.

Interleukin-10 (IL-10)

IL-10 is an anti-inflammatory cytokine produced primarily by monocytes and lymphocytes in response to physical exercise

IL-10 inhibits the synthesis of inflammatory mediators (TNF-α, IL-1α, IL-1β), suppresses the maturation of dendritic cells, and participates in the switching of B cells to IgA synthesis [5]. Additionally, IL-10 prevents the development of insulin resistance in muscle tissue [9]. IL-10, via the NF-κB pathway and STAT3, enhances M2 polarization and stimulates myoblast proliferation in damaged muscle [5]. IL-10 increases T-cell survival and enhances autoimmunity in the CNS by supporting CD4+ T-cells [5]. IL-10 is one of the main stimulators of B cells: it induces their proliferation, differentiation into plasma cells, antibody secretion, and immunoglobulin class switching—including stimulating IgA production in patients with IgA deficiency [5]. Thus, IL-10, released with a delay (30–60 min) following physical exercise, contributes to the long-term enhancement of the humoral immune response.

We also conducted a systematic review in accordance with the PRISMA guidelines [6]. Through April 2020, a search was conducted in seven databases (MEDLINE, Embase, Cochrane CENTRAL, Web of Science, CINAHL, PsycINFO, and SportDiscus) for randomized controlled trials and prospective observational studies that compared groups of adults with different levels of physical activity and reported on immune cell counts, antibody concentrations, the risk of clinically diagnosed infections, the risk of hospitalization, and mortality from infectious diseases [1].

The review found evidence of significant changes in certain immune markers as a result of regular physical activity. Physical activity, which lasted an average of 12 weeks and included aerobic (walking, running, cycling) or strength training, as well as a combination of both, was performed 3–5 times a week for an average of 30 minutes at moderate or high intensity. As a result, the concentration of CD4 T-helper cells and immunoglobulin IgA in saliva increased, while the concentration of neutrophils decreased [1].

In 1997, a survey was conducted involving 64,850 participants, of whom 26,124 had experienced at least one episode of infection or sepsis, and 4,708 died from infection or sepsis during the study period. In adjusted analyses, compared with less than one hour of physical activity per week, one hour of physical activity per week was associated with a lower risk of infection or sepsis, with a risk ratio (OR) of 0.93 (95% confidence interval (CI) 0.90–0.97), and a lower risk of death from infection or sepsis, OR 0.87 (95% CI 0.80–0.96). Further physical activity was associated with an even lower risk, and similar patterns were observed for walking. The risk of infection and death from infection or sepsis due to lack of physical activity was 2.6% and 4.5%, respectively [10].

Physical activity influences immune function [2] and cardiopulmonary health [4] and, thus, may reduce the risk of sepsis and death from it. Research findings have shown that physical activity can reduce the risk of sepsis and death from sepsis [11].

An analysis of randomized and prospective empirical studies across various populations demonstrates that the level of physical activity is closely linked to morbidity. Individuals with low levels of physical activity have a higher incidence of infectious and chronic diseases, whereas moderate physical activity is associated with a reduced risk of morbidity.

Methods

The objective of this study is to identify the relationship between the level of physical activity and immune system activity, specifically the rate of recovery and the incidence of infectious diseases.

The study included 103 participants, of whom 71 were women and 32 were men, with an average age ranging from 18 to 21 years. The primary method involved administering a questionnaire to all participants using the Global Physical Activity Questionnaire (GPAQ), supplemented with questions designed to assess immune status. Physical activity intensity was measured in MET-minutes per week (Metabolic Equivalent of Task). According to the WHO classification (IPAQ protocol), where:

Low activity: less than 600 MET-min/week – 16 people.

Moderate activity: 600–3000 MET-min/week – 59 people.

High activity: more than 3,000 MET-min/week – 28 people.

The frequency of infectious diseases was assessed using a 5-point ordinal scale (1 = "never," 5 = "very often"). Analysis by physical activity groups revealed the mean values shown in Table 1 and in the diagram in Figure 1.

MET Group	n	M (frequency)	SD
Low (<600 MET-min/week)	16	3.22	0.28
Moderate (600–3000)	59	2.64	0.24
High (>3000)	28	2.05	0.18

Table 1. Average incidence rates by physical activity groups.

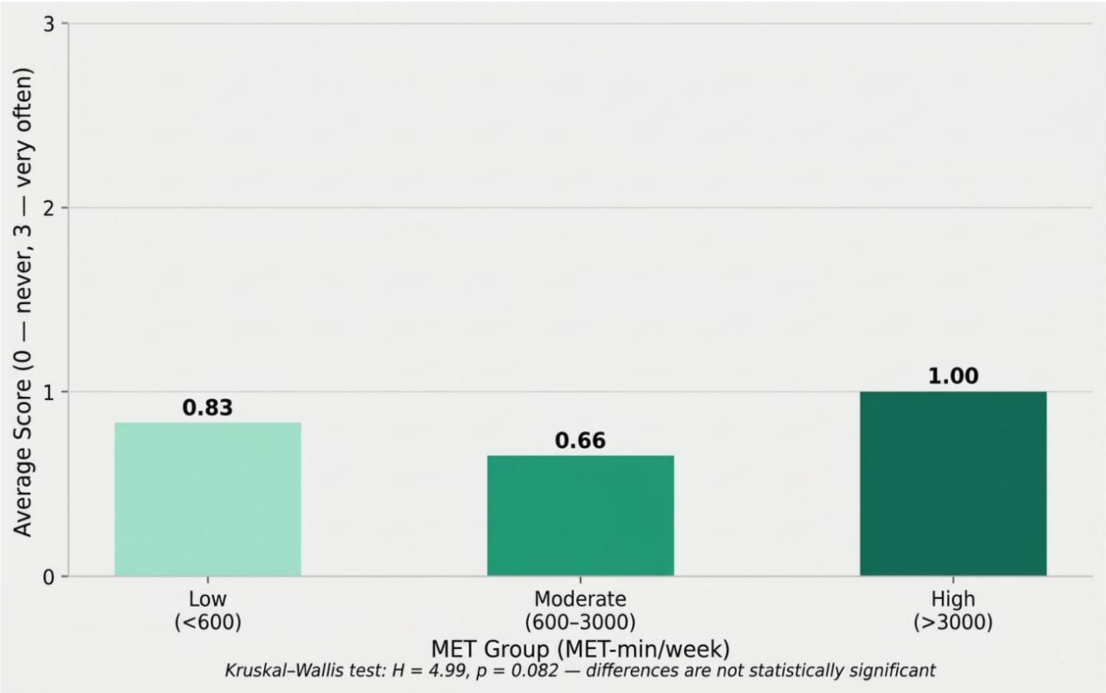

Figure 1. Mean incidence rates by physical activity groups (MET)

Where n is the number of people corresponding to one of the activity levels, M is the arithmetic mean, and SD is the standard deviation. Pearson's correlation analysis did not reveal a significant linear relationship between MET and disease incidence ($r = 0.168$, $p = 0.094$). Spearman's correlation coefficient confirmed the absence of a significant monotonic relationship ($r_s = 0.118$, $p = 0.241$).

Recovery speed was assessed on a scale from 1 to 6, where: 1 = very fast, 6 = very slow. Group indicators are presented in Table 2 and in Figure 2 as a bar chart.

MET group	n	M	SD	Median
Low (<600 MET-	16	4,500	1,295	5.0

min/week)				
Moderate (600–3,000)	59	4,211	1,359	5.0
High (>3,000)	28	3,704	1,589	3.0

Table 2. Recovery rate by physical activity group (1 = very fast, 6 = very slow).

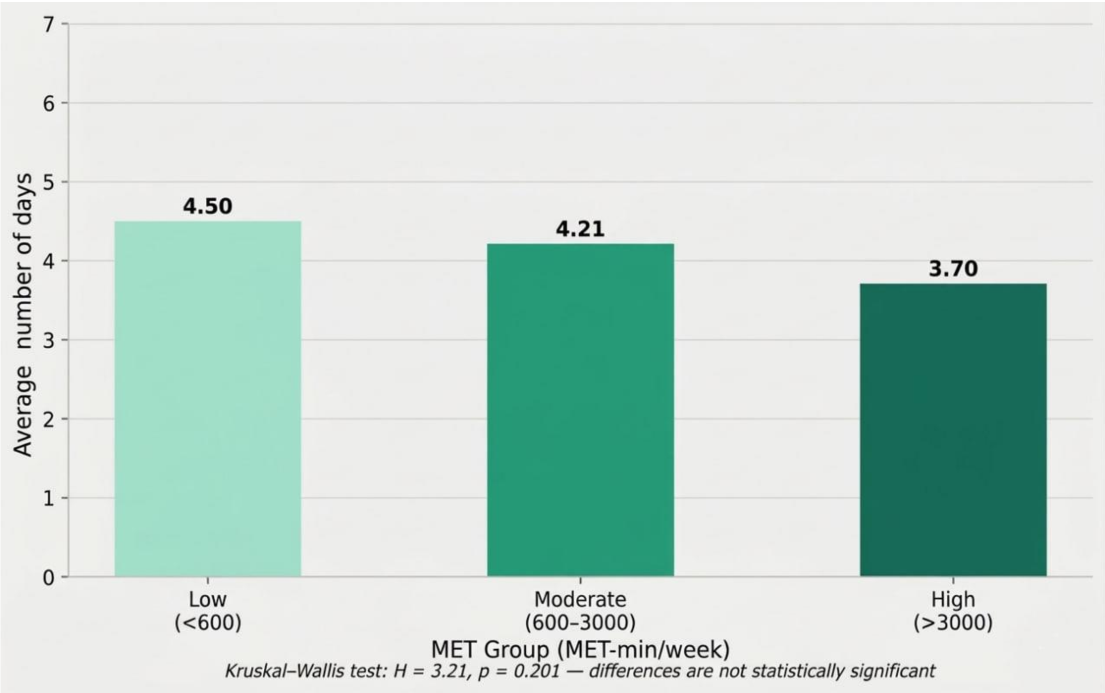

Figure 2. Average number of recovery days by physical activity group (MET)

Pearson's correlation revealed a negative but non-significant association ($r = -0.148$, $p = 0.138$). Spearman's correlation coefficient confirmed a similar result ($rs = -0.150$, $p = 0.132$). The negative sign of the coefficient indicates a trend: at higher MET levels, the median recovery duration is slightly shorter (3.0 days in the high-activity group versus 5.0 days in the low-activity group), suggesting a tendency toward faster recovery among physically active participants; however, this pattern is not statistically significant.

The relationship between the MET index and indicators of height, weight, and age is shown in Table 3.

Pearson's	Pearson's r	p	Spearman's rs	p	Significance
Growth	0.362	0.0002	0.317	0.001	***
Weight	0.301	0.002	0.226	0.023	**
Age	0.056	0.576	0.054	0.594	N/A

Table 3. Correlation between the MET index and anthropometric and age-related indicators.

(Note: ** $p < 0.01$; *** $p < 0.001$; n/s — not significant ($p > 0.05$). r — Pearson's correlation coefficient; rs — Spearman's rank correlation coefficient.)

Discussion

Numerous data obtained from a systematic review of various scientific articles indicate the beneficial effect of physical exercise on immune system activity due to the release of myokines such as IL-6, IL-10, and IL-1ra, which in turn contribute to the regulation of immune function. However, the data on recovery rates and incidence rates obtained from the analysis of survey results were statistically insignificant and require a larger sample size or the use of more objective methods of data collection than simple surveys.

Conclusions

In the questionnaire survey we conducted involving 103 participants, a statistically insignificant association was found between the level of physical activity and the rate of recovery from infectious diseases among the respondents. For a more accurate conclusion, it is advisable to increase the sample size and/or use more objective methods for collecting data on the immune system activity of each individual participant.

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