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Mini Review

Importance of Maintaining and Improving Immune Function by Physical Activity During the COVID-19 Pandemic

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Mini Review

In early December 2019, a novel coronavirus disease, designated as COVID-19, came into light in Wuhan, Hubei Province of China. With the first pneumonia cases of unknown origin being identified, it has become a pandemic worldwide. The World Health Organization (WHO) has declared it as a potential threat to the world population, and a public health emergency of international concern on January 30, 2020 [1]. Many countries and regions have advised people to reduce traveling and stay at home to avoid human-to-human transmission of the virus. As a result, most work, physical and recreational activities were suspended. However, staying at home can reduce the physical activity of the general population. Sedentary behaviors such as watching television and movies, browsing the Internet, using smartphones, and playing video games are associated with an increased risk of obesity [2-4], hypertension [5, 6], cardiovascular disease [4, 7], and type 2 diabetes mellitus [4, 7, 8]. Evidence showed that individuals with weak immunosuppression or immune defense mechanisms are more susceptible to severe disease [9-11]. However, there are several research suggested that physical activities such as moderate-intensity continuous training (MICT), resistance training (RT), and high-intensity interval training (HIIT) have a significant effect on modulating the immune system. Physical activity-induced immunoregulation has been recognized for more than 30 years, and there are about 5000 peer-reviewed original and review papers in the PubMed database [12].

Effects of MICT has been reported in many studies, i.e. MICT can improve cognitive function in patients with mild Alzheimer's disease [13], Parkinson's Disease [14], and schizophrenia [15], provide comparable reductions in resting blood pressure in adults with pre- to established hypertension [16], induce modest body composition improvements in overweight and obese individuals [17], and improve cardiorespiratory fitness in participants of cardiac rehabilitation [18]. MICT is also considered a preventive measure to bring down the further incidence of COVID-19 [19]. Evidence showed that even a slight increase in baseline maximal oxygen uptake (VO2max) may convert a significant proportion of high-risk patients to low-risk patients [20]. A randomized controlled trial assessed preventive effects of exercise on acute respiratory infection (ARI) illness, the results showed that 8 weeks of MICT contributed to the reduction in ARI illness, and the magnitude of observed benefit was similar to that from accepted medical interventions, such as influenza vaccination [21]. As shown in Table 1, a large number of randomized controlled trials have investigated the relationship between MICT and immune system function. Previous studies suggested that 12 weeks [22], 15 weeks [23, 24], or 12 months [25] of MICT had significant effects on the prevention of upper respiratory tract infections (URI), and the mechanisms were related to the improvement of vaccination responses, T-cell proliferative capacity, neutrophil phagocytic activity, NK cell cytotoxic activity, and leukocyte telomere lengths, and the depression of numbers of exhausted/senescent T cells, circulatory levels of inflammatory cytokines, and inflammatory response to bacterial challenge [26-31].

RT, a form of exercise that actively activates specific skeletal muscle groups against external resistance, has become a popular form of exercise and is recommended by the American Heart Association [32], the American College of Sports Medicine (ACSM) [32, 33], and the American Geriatrics Society [34]. RT has been proven to be an important strategy to improve muscle mass, muscle strength, and power output, as well as functional capacity [35]. And a growing number of studies strongly support the beneficial effects of RT on various aspects of cognitive performance, such as attention [36], memory [37], executive control [38], and mini-mental state examination (MMSE) score [39]. For example, Cassilhas et al. found that 24 weeks of moderate- and high-intensity RT had equally beneficial effects on cognitive functions in the elderly [40], and the mechanism was related to the increase of insulin-like growth factor-1 (IGF-1) [41]. In addition, RT has been shown to have significant effects on immune system function. Table 2 summarizes published evidence from randomized controlled trials on the relationship between RT and immune system function. Previous studies suggested that 10 weeks [42-44], 12 weeks [45], and 16 weeks [46] of RT had significant effects on improving the immunity of elderly people, and the mechanisms were related to the improvement of the resting natural killer cell activity [42], and monocyte and

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Table 1: *Research on the relationship between MICT and immune function.*

Investigator	Study population	Research design	Key finding
Nieman et al. 1990[23]	36 mildly obese sedentary women (aged 34.4 ± 1.1 years)	Randomized to 15 weeks of moderate intensity walking program (45 min/day, 5 days/week; n = 18) or observational control (n = 18)	15 weeks of MICT was associated with elevated NK cell activity and reduced URI symptomatology
Nieman et al. 1993[22]	30 sedentary, healthy elderly women (aged 73.4 ± 1.2 years) and 12 highly conditioned elderly women (aged 72.5 ± 1.8 years)	Sedentary women randomized to 12 weeks of moderate intensity walking program (30-40min/day, 5 days/week; n = 14) or stretching control (45 min/day, 5 days/week; n = 16)	The incidence of URI was 8% in highly conditioned, 21% in MICT, and 50% in controls
Nieman et al. 1998[65]	91 obese women (aged 45.6 ± 1.1 years)	Randomized to 12 weeks of moderate intensity walking program (45 min/day, 5 days/week; n = 21), stretching control (45 min/day, 4 days/week; n = 22), diet or exercise and diet	The number of days with symptoms of URI was reduced in MICT group relative to subjects in the nonexercise groups
Chubak et al. 2006[25]	115 overweight and obese, sedentary, postmenopausal women (aged 61 ± 6.9 years)	Randomized to 12 months of MICT (45 min/day, 5 days/week; n = 53) or stretching control (45 min/day, 1 day/week; n = 62)	12 months of MICT reduced the incidence of colds among postmenopausal women
Barrett et al. and Rakel et al. 2012[66, 67]	149 elderly adults (27 men and 122 women; aged 59.3 ± 6.6 years)	Randomized to 8 weeks of MICT (n = 47), mindfulness meditation (n = 51), or observational control (n = 51)	Incidence, global severity, and duration of ARI illness were 29%, 31%, and 43% lower in the MICT group compared with controls
Sloan et al. 2012[24]	32 healthy postmenopausal women (aged 54.1 ± 5.3 years)	Randomized to 16 weeks of moderate intensity home-based walking program (30 min/day, 5 day/week; n = 16) or observational control (n = 16)	16 weeks of MICT increased the secretion of salivary immunoglobulin A, which constitutes the main specific immune defense mechanism in saliva
Barrett et al. 2018[21]	413 elderly adults (100 men and 313 women; aged 49.6 ± 11.6 years)	Randomized to 8 weeks of MICT (n = 137), mindfulness meditation (n = 138), or observational control (n = 138)	Proportional rate reductions of ARI incidence, global severity, and days-of-illness were 14%, 23%, and 31% for the MICT group compared with controls

T-cell-mediated immunity [45], and the reduction of the inflammatory reactivity and overall inflammatory milieu [43, 44], and C-reactive protein (CRP) levels [46].

HIIT can be described as "a short interval of vigorous activity interspersed with periods of low activity or rest", which can cause a strong acute physiological response [47]. A growing number of studies suggested that HIIT had effects on promoting cognitive function [48, 49], glucose and lipid metabolism in skeletal muscle [50], the expression of genes related to endogenous antioxidant enzyme activity and inflammation [51], the insulin sensitivity [52], the cardiopulmonary function [53], the aerobic capacity [54, 55], anaerobic capacity [56, 57], and the vascular endothelial function [58], and on reducing the oxidative stress level [59]. In addition, HIIT can provide comparable reductions in resting blood pressure in adults with pre- to established hypertension [16], induce modest body composition improvements in overweight and obese individuals [17], and improve cardiorespiratory fitness in participants of cardiac rehabilitation [18]. In addition to MICT and RT, HIIT has also been shown to have significant effects on immune system function. Table 3 summarizes published evidence from randomized or controlled trials on the relationship between HIIT and immune system function. Previous studies suggested that one single session [60, 61], 3 weeks [62], and 10 weeks [63, 64] of HIIT had significant effects on improving the immune function, and the mechanisms were related to the improvement of the potential anti-inflammatory benefits [60], the number of antimicrobial proteins in the saliva [62], and the innate immune functions [64], and the reduction of monocyte [63] and IFN-γ/IL-4 ratio [61].

In conclusion, different types of physical activity have significant effects on immune function, and maintaining physical activity levels during the current situation initiated by the COVID-19 pandemic will have significant physical health benefits.

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Conflict of interest

The authors declare no conflict of interest.

Table 2: *Research on the relationship between RT and immune function.*

Investigator	Study population	Research design	Key finding
McFarlin et al. 2005[42]	25 older, postmenopausal women (aged 72.1 ± 6.4 years)	Randomized to 10 weeks of RT (3 sets, 12 repetitions at 8RM, 3 days/week; n = 19) or observational control (n = 6)	10 weeks of RT improved the immunity of elderly women by increasing resting natural killer cell activity
Brooks et al. 2006[46]	62 Hispanic diabetic patients (40 men, 22 women; aged 66.0 ± 1.5 years)	Randomized to 16 weeks of RT (3 sets, 8 repetitions at 8RM, 3 days/week; n = 31) or observational control (n = 31)	16 weeks of RT reduced CRP levels in older diabetic patients
Phillips et al. 2010[43, 44]	35 healthy postmenopausal women (aged 72.1 ± 6.1 years)	Randomized to 10 weeks of RT (3 sets, 10 repetitions at 8RM, 2 days/week; n = 28) or observational control (n = 7)	10 weeks of RT reduced inflammatory reactivity and overall inflammatory milieu in elderly women
Shimizu et al. 2011[68]	24 healthy, sedentary, elderly adults (7 men, 17 women; aged 67.3 ± 0.9 years)	Randomized to 12 weeks of RT (3 sets, 10 repetitions, 2 days/week; n = 12) or observational control (n = 12)	12 weeks of RT upregulated monocyte and T-cell-mediated immunity in elderly people
Hagstrom et al. 2016[45]	39 breast cancer survivors (aged 51.9 ± 8.8 years)	Randomized to 16 weeks of RT (3 sets, 8-10 repetitions at 8RM, 2 days/week; n = 20) or observational control (n = 19)	16 weeks of RT was beneficial in improving the inflammatory profile in breast cancer survivors
Abd et al. 2018[69]	60 sedentary elderly adults (aged 66.2 ± 3.6 years)	Randomized to 6 months of RT (3 sets, 8-12 repetitions, 3 days/week; n = 30) or MICT (40 min/day, 3 days/week; n = 30)	Both RT and MICT reduced inflammation in elderly individuals

Table 3: *Research on the relationship between HIIT and immune function.*

Investigator	Study population	Research design	Key finding
Bartlett et al. 2017[63]	27 healthy, inactive adults (9 male and 18 female, aged 43 ± 11 years)	Randomized to 10 weeks of HIIT (18-25 min/day, 3 days/week, n = 14) or MICT (n = 13)	Expression of monocyte was reduced by training similarly in both HIIT group and MICT group
Durrer et al. 2017[60]	10 diabetic patients (aged 57.9 ± 5.4 years), 9 healthy adults (aged 55.8 ± 9.0 years)	Participated in an acute bout of HIIT (7 × 1 min at ~85% maximal aerobic power output, separated by 1 min of recovery) on a cycle ergometer	One session of HIIT had immunomodulatory effects and provided potential anti-inflammatory benefits to people with, and without, type 2 diabetes
Born et al. 2017[62]	28 recreational male runners (aged 25.0 ± 3.6 years)	Randomized to 3 weeks of HIIT (4 × 4 min of running at 90-95% of HR_{max} interspersed with 3 min of active recovery, n = 16) or long-slow distance training (LSD) (n = 12)	HIIT increased the number of antimicrobial proteins in the saliva as indicated by an elevated Immunoglobin-A secretion rate
de Souza et al. 2018[61]	10 sedentary obese men (aged 28.5 ± 2.7 years)	Performed three experimental sessions: HIIT (10 × 60 s at 90% of the HR_{max} alternated by 60 s of active recovery), MICT, and rest-control	A single HIIT session decreased IFN-γ/IL-4 ratio, indicating an anti-inflammatory response, without compromising the mucosal immune system
Bartlett et al. 2018[64]	12 physically inactive adults with rheumatoid arthritis (RA, aged 64 ± 7 years)	Participated in 10 weeks of high-intensity interval walking (10 × 60 s at 80-90% of $VO_{2reserve}$ separated by 50-60% of $VO_{2reserve}$, 30 min/day, 3 days/week)	10 weeks of HIIT in older adults with RA was associated with improved innate immune functions, indicative of reduced infection risk and inflammatory potential

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