Advances in Research on the Anti-inflammatory Effects of Exercise in Ameliorating Neuroinflammation-Associated Depression

Authors: Zhang Zhixin, Guo Qi, Chen Xiaoyu, Chen Xiaoyu

Date: 2024-01-09T00:00:00+00:00

Abstract

Depression is a multifactorial affective disorder with an unclear pathogenesis. However, recent studies have revealed an association between neuroinflammation and depression, primarily manifested through the interplay between neuroinflammatory processes and the pathogenic mechanisms of depression, including abnormalities in cerebral monoamine neurotransmitters, hypothalamic-pituitary-adrenal (HPA) axis dysregulation, and dysfunctional neurogenesis. Currently, exercise as an antidepressant intervention has garnered widespread attention. Therefore, this review analyzes relevant literature to summarize how exercise alleviates neuroinflammation through its anti-inflammatory effects, thereby ameliorating depression via emotion-related pathways, and investigates the influence of different exercise prescriptions on the anti-inflammatory efficacy of exercise, aiming to provide novel scientific perspectives for the treatment of neuroinflammation-associated depression.

Full Text

Preamble

Research Progress on the Anti-inflammatory Effects of Exercise in Improving Neuroinflammation-Related Depression

Abstract: Depression is a multifactorial affective disorder with unclear pathogenesis. Recent studies have revealed an association between neuroinflammation and depression, primarily manifested in the interaction between neuroinflammatory processes and depression pathogenesis, including abnormalities in brain monoamine neurotransmitters, HPA axis dysfunction, and impaired neurogenesis. Currently, exercise has garnered widespread attention as an antidepressant intervention. This review analyzes relevant literature to summarize how exercise alleviates neuroinflammation through its anti-inflammatory effects, thereby

improving depression via emotion-related pathways, and explores how different exercise prescriptions influence these anti-inflammatory effects. The aim is to provide novel scientific insights for treating neuroinflammation-related depression.

Keywords: exercise, anti-inflammatory, neuroinflammation, depression, exercise prescription

Depression is one of the most common psychiatric disorders, characterized primarily by low mood, anhedonia, and social impairment. Globally, 14.3% of deaths—approximately 8 million annually—are attributable to mental disorders, with depression serving as a major cause of suicide and disability and contributing significantly to the global disease burden [1]. Pathological mechanisms associated with depression include abnormalities in brain monoamine neurotransmitters, HPA axis dysfunction, and impaired neurogenesis. Recent research has identified links between neuroinflammation and various neurological and psychiatric disorders, with notable connections to depression pathogenesis that warrant investigation.

Currently, pharmacotherapy remains the primary treatment for depression, yet long-term medication use causes significant side effects and imposes substantial economic burdens on patients. Appropriate physical activity helps delay brain aging and improve neurodegenerative diseases such as Alzheimer' s disease and multiple sclerosis. Most importantly, exercise has proven effective in treating depression, with studies demonstrating its anti-inflammatory properties. Therefore, this review examines the intervention effects of exercise in improving neuroinflammation-related depression through anti-inflammatory mechanisms and discusses how different exercise modalities, intensities, and frequencies influence these effects, providing scientific evidence for developing exercise prescriptions to alleviate depressive symptoms.

1. Depression Pathogenesis: Neuroinflammation

Depression is a multifactorial psychiatric disorder with unclear pathogenesis. However, recognized neurobiological alterations in depression primarily involve the monoamine neurotransmitter system, hypothalamic-pituitary-adrenal (HPA) axis, neurogenesis system, and neuroinflammation. Among these, neuroinflammation represents a critical factor that interacts with the other three neurobiological components of depression. Dysregulated neuroinflammation affects other neurobiological processes in depression, such as causing depletion of brain serotonin, HPA axis dysfunction, and impaired neurogenesis, thereby directly or indirectly influencing depression onset and progression [2], making it particularly noteworthy.

Neuroinflammation refers to the protective innate immune response in the central nervous system (CNS). However, persistent infection, psychological or physical stress-induced damage, or indirect peripheral stimulation can activate brain innate immune cells such as microglia, initiating inflammatory cascades that

release large quantities of inflammatory cytokines—including interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α)—which exert neurotoxic effects leading to depression [3]. Inflammatory cytokines released peripherally can signal to the brain through molecular, cellular, and neural pathways, thereby amplifying neuroinflammation [4]. Consequently, reducing peripheral inflammatory cytokine levels can also alleviate neuroinflammation.

Clinical data demonstrate that pro-inflammatory markers such as C-reactive protein (CRP), TNF-α, IL-1β, and IL-6 are significantly elevated in peripheral and central nervous systems of depressed patients compared to healthy individuals [5]. The causes of chronic low-grade inflammation observed in some depressed patients remain unclear. Current evidence suggests that infection, stress, autoimmune dysregulation, and unhealthy lifestyle factors (such as sedentary behavior, poor diet, and sleep disturbances) may trigger or enhance inflammatory responses [6]. Subsequent pro-inflammatory signals activate numerous downstream biological effects in neuroendocrine, monoaminergic, and oxidative stress systems [7], leading to "sickness behaviors"(such as low mood, fatigue, and appetite loss) that may progress to clinical depression. These depression-related sickness behaviors further reinforce unhealthy lifestyles, creating a vicious cycle that generates additional inflammatory responses and worsening depressive symptoms.

2. Biological Mechanisms of Exercise-Regulated Neuroinflammation in Improving Depression

Neuroinflammation can influence multiple emotion-related processes to induce depressive symptoms. First, inflammatory cytokines affect the production and metabolism of emotion-related neurotransmitters, representing one mechanism underlying neuroinflammation-related depression. For example, pro-inflammatory cytokines increase indoleamine-2,3-dioxygenase (IDO) activity, affecting tryptophan metabolism and resulting in reduced serotonin (5-HT) synthesis and increased kynurenine. Under neuroinflammatory influence, this leads to imbalanced kynurenine metabolism in microglia and astrocytes, increasing neurotoxic compounds (such as 3-hydroxykynurenine and quinolinic acid) that promote neuroinflammation-related depression [8]. Studies have found that exercise can suppress pro-inflammatory factor expression, reduce IDO enzyme activity, and thereby increase 5-HT concentration, exerting potential anti-inflammatory and antidepressant effects [9]. Additionally, exercise-induced peroxisome proliferator-activated receptor-γ coactivator 1α (PGC-1α) produced in skeletal muscle regulates peripheral kynurenine metabolism by shunting it toward kynurenic acid, which cannot cross the blood-brain barrier, thereby preventing kynurenine' s toxic central effects [10]. Furthermore, PGC-1α itself possesses anti-inflammatory properties [11].

Second, neuroinflammation affects neuronal growth and survival. Pro-inflammatory cytokines enhance oxidative stress, damaging glial cells in emotion-related brain regions such as the prefrontal cortex and amygdala

[12]. Additionally, cytokine-induced glutamate dysregulation causes excitotoxicity, reducing production of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) [13]. Preclinical studies have shown that neuroinflammation decreases BDNF in the prefrontal cortex and hippocampus, inducing depressive-like phenotypes in rodents [14]. Exercise can modulate neuroinflammation-related signaling pathways in microglia to promote neuronal repair; for instance, exercise activates the TLR4/miR-223/NLRP3 signaling pathway, exerting anti-inflammatory effects that alleviate neuroinflammation and promote repair of damaged hippocampal tissue [15]. Moreover, exercise not only inhibits pro-inflammatory factor release but also increases concentrations of antioxidants and anti-inflammatory factors, enhancing brain antioxidant capacity. Additionally, skeletal muscle PGC-1α induces FNDC5 cleavage to release irisin, which crosses the blood-brain barrier and induces BDNF upregulation in the hippocampus [16], improving synaptic plasticity and promoting neuroregeneration, ultimately alleviating depressive-like behaviors.

Finally, neuroinflammation causes HPA axis feedback dysfunction. Large quantities of pro-inflammatory cytokines produced during neuroinflammation overactivate the HPA axis and disrupt glucocorticoid receptor function and expression, causing massive glucocorticoid release. High glucocorticoid concentrations elevate pro-inflammatory cytokines in depressed patients, triggering uncontrolled neuroinflammatory responses that further worsen depressive symptoms [17]. Exercise can improve hippocampal mitochondrial function and oxidative balance while reducing circulating glucocorticoid levels, restoring dysfunctional HPA axis feedback [18] and helping alleviate depressive symptoms.

In summary, the biological mechanisms through which exercise improves neuroinflammation-related depression can be explained by its anti-inflammatory effects.

3. Clinical Intervention Effects of Exercise on Depression and Neuroinflammation

Regular exercise provides numerous health benefits, including improved cardiovascular and respiratory function, reduced coronary risk factors, enhanced mood, and elevated cognitive performance. For patients with mild to moderate depression, exercise demonstrates efficacy comparable to classic antidepressant medications [19]. Although the biological mechanisms underlying exercise' s antidepressant effects remain unclear, studies indicate that exercise can regulate inflammatory factor levels in peripheral or central nervous systems to exert anti-inflammatory effects. For example, in a rat depression model induced by chronic unpredictable mild stress (CUMS), exercise alleviated depressive-like behaviors and downregulated CUMS-related peripheral and central inflammatory markers [20]. In a rat model of Alzheimer' s disease, exercise improved depressive-like behaviors, reduced brain TNF-α levels associated with depression, and increased IL-10 in the prefrontal cortex and BDNF in the hippocampus [21]. Importantly, changes in pro-inflammatory cytokine concentrations such as IL-6, IL-1β, and

TNF-α correlate with depressive symptom severity [22, 23]. While many studies demonstrate exercise' s anti-inflammatory effects, these can be influenced by factors including disease type and severity, exercise modality, intensity, and frequency. Therefore, we discuss how exercise form, intensity, and frequency affect intervention outcomes in neuroinflammation-related depression.

3.1.1. Aerobic Exercise

Aerobic exercise refers to activity powered primarily by aerobic metabolism, including running, brisk walking, cycling, and swimming. A meta-analysis identified aerobic exercise as the optimal intervention for improving depression, as it enhances cardiopulmonary function, promotes circulation, improves cognitive function, and reduces depression risk [24]. Studies show aerobic exercise significantly reduces TNF-α and IL-6 concentrations while increasing the anti-inflammatory factor IL-10 in sedentary elderly individuals [25]. In chronic hemodialysis patients, an 18-week cycling intervention improved depressive symptoms and significantly reduced IL-6 and IL-18 concentrations, with these changes correlating with symptom improvement [26]. Thus, long-term cycling exercise can ameliorate depressive symptoms in hemodialysis patients by modulating IL-6 and IL-18 levels. Similarly, a six-week aerobic exercise program in patients with mood disorders reduced TNF-α concentrations and alleviated depressive symptoms [27]. Nitric oxide (NO), a gaseous neurotransmitter, represents an important neuroinflammatory mediator whose synthesis increases due to inflammation-induced nitric oxide synthase (iNOS). High NO concentrations cause nucleic acid nitrosylation and neuronal damage. A study of depressed elderly patients over 50 found that 12 weeks of low-intensity aquatic exercise effectively reduced depression and anxiety by decreasing protein carbonylation-mediated oxidative stress and reducing NO concentrations [28].

Yoga, an ancient mind-body practice incorporating meditation and physical activity popular among women, has been identified through meta-analysis as an effective exercise modality for depression [29]. Research demonstrates yoga significantly reduces IL-6 concentrations and improves depression in patients with major depressive disorder [29], consistent with findings in rheumatoid arthritis patients with comorbid depression [30]. Additionally, a study comparing Tai Chi as an adjunctive treatment to medication alone found that adding Tai Chi produced greater improvements in cognitive function and depressive symptoms along with more significant reductions in the inflammatory marker CRP [31]. Tai Chi also reduces depression risk in elderly individuals by lowering IL-6 concentrations [32]. Furthermore, other aerobic activities including Qigong [33] and Pilates [34] have been shown to significantly reduce inflammatory factor levels and improve depressive symptoms.

In summary, aerobic exercise effectively modulates inflammatory factor levels and positively impacts depressive symptom improvement.

3.1.2. Resistance Exercise

Resistance exercise improves muscle strength, physical balance, and reduces fat accumulation, with muscle strength correlating inversely with depression risk. Studies demonstrate resistance exercise increases muscle strength and improves depressive symptoms in elderly individuals while reducing serum TNF-α and IL-6 concentrations [35]. A 24-week resistance training program in sedentary men significantly improved depressive mood and increased serum insulin-like growth factor 1 (IGF-1) levels [36]. IGF-1 is typically associated with neuroprotection in the central nervous system, but research also indicates anti-inflammatory effects in the brain, possibly by inhibiting astrocyte responses to inflammatory stimuli and modulating microglial phenotypes [37]. However, an eight-week moderate-intensity resistance exercise program in patients over 90 years old neither improved cognitive function nor reduced serum TNF-α concentrations [38], possibly due to advanced age and short intervention duration. When comparing resistance exercise to aerobic exercise, both modalities effectively improve depressive symptoms and reduce serum TNF-α in elderly individuals, though resistance exercise shows less significant reductions in serum CRP, IL-6, and IL-18 compared to aerobic exercise [39]. Conversely, a short-term 10-week study in sedentary individuals found resistance training reduced CRP levels by 32.8% versus only 16.1% with aerobic exercise [40]. Combining both modalities improves depressive symptoms and cognitive function in elderly patients with major depression while reducing IL-6 levels [41].

In summary, resistance exercise exerts anti-inflammatory effects and improves depressive symptoms, though limited research exists on its impact on inflammatory factor levels in depressed patients, necessitating further evidence. Therefore, combining resistance and aerobic exercise is recommended for patients.

Overall, aerobic exercise may represent a more effective training method for reducing inflammatory factor levels and improving depressive symptoms, while resistance exercise demonstrates promising anti-inflammatory and antidepressant effects in some studies, though conclusions remain controversial. Patients should select exercise modalities based on personal preferences. Importantly, exercise' s anti-inflammatory effects are influenced by factors including disease type and baseline inflammatory levels, requiring further research, particularly in depressed populations, to obtain more definitive conclusions.

3.2. Effects of Different Exercise Intensities on Depression and Inflammatory Marker Levels

Exercise intensity represents one factor influencing intervention efficacy. Whether different intensities produce distinct improvements in depressive symptoms remains unclear, with some studies indicating both moderate and high-intensity exercise effectively reduce depression severity in moderate depression, while very low-intensity exercise shows no effect [42]. Regarding inflammatory levels, a six-week comparison of high-intensity versus moderate-

intensity aerobic exercise found both improved depressive symptoms, but high-intensity exercise increased perceived stress and TNF-α and IL-6 concentrations compared to moderate-intensity exercise, which reduced TNF-α levels [43]. Thus, moderate-intensity exercise may represent the optimal intensity for depression improvement. Another similar study found no cytokine changes after low or moderate-intensity exercise [44], possibly due to different intensity classification standards—one using maximum power calculations, the other using the Borg 6-20 Rating of Perceived Exertion (RPE) scale. However, exercise intensity may not be a critical factor for exercise' s anti-inflammatory effects in depressed patients, as research indicates low, moderate, and high intensities all effectively reduce IL-6 concentrations and improve depressive symptoms without significant differences in IL-6 level changes between intensities [23]. Additionally, most studies show low-intensity aerobic exercise such as yoga and Ba Duan Jin also positively reduces inflammatory factor levels and alleviates depression, with greater patient acceptability compared to moderate or high-intensity exercise. In summary, while exercise exerts anti-inflammatory effects to alleviate depressive symptoms, the importance of exercise intensity remains unclear. Therefore, exercise intensity prescription should prioritize patients' functional capacity and cardiorespiratory fitness, incorporate personal interests, and most importantly, follow progressive overload principles to avoid injury.

3.3. Effects of Exercise Frequency and Duration on Depression and Inflammatory Marker Levels

Exercise frequency and duration constitute another factor influencing intervention efficacy. Research investigating exercise' s anti-inflammatory effects typically considers intervention duration, categorized as single-session (acute) exercise or repeated (chronic) exercise. Acute exercise acts as a stressor that triggers acute inflammatory responses, primarily due to IL-6 release during muscle contraction. However, this acute, transient IL-6 elevation induces increases in anti-inflammatory cytokines like IL-10 and inhibits pro-inflammatory TNF-α release, indirectly exerting anti-inflammatory effects. Studies show that patients with major depressive disorder do not experience exacerbated inflammation after a single acute exercise session [45]. Furthermore, research demonstrates that IL-6 reduction correlates with decreased depressive symptoms, and the number of exercise sessions completed during interventions shows significant correlation with IL-6 reduction [46]. Therefore, sustained exercise programs are recommended to better reduce pro-inflammatory status in depressed patients.

4. Summary and Outlook

Neuroinflammation represents a crucial pathogenic mechanism in depression that interacts with other depression-related pathological processes. Exercise serves as a therapeutic strategy for depression, either alone or as an adjunct to other treatments, exerting anti-inflammatory effects by modulating peripheral

or central inflammatory factor levels and signaling pathways to alleviate neuroinflammation and improve depressive symptoms. However, the influences of exercise modality, intensity, duration, and frequency on these anti-inflammatory effects require further investigation to develop optimal exercise prescriptions for neuroinflammation-related depression.

References

[1] Walker E R, McGee R E, Druss B G. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis[J]. JAMA Psychiatry, 2015,72(4):334-341.
[2] Troubat R, Barone P, Leman S, et al. Neuroinflammation and depression: A review[J]. Eur J Neurosci, 2021,53(1):151-171.
[3] Stein D J, Vasconcelos M F, Albrechet-Souza L, et al. Microglial Over-Activation by Social Defeat Stress Contributes to Anxiety- and Depressive-Like Behaviors[J]. Front Behav Neurosci, 2017,11:207.
[4] Beurel E, Toups M, Nemeroff C B. The Bidirectional Relationship of Depression and Inflammation: Double Trouble[J]. Neuron, 2020,107(2):234-256.
[5] Kohler C A, Freitas T H, Maes M, et al. Peripheral cytokine and chemokine alterations in depression: a meta-analysis of 82 studies[J]. Acta Psychiatr Scand, 2017,135(5):373-387.
[6] Kiecolt-Glaser J K, Derry H M, Fagundes C P. Inflammation: depression fans the flames and feasts on the heat[J]. Am J Psychiatry, 2015,172(11):1075-1091.
[7] Miller A H, Haroon E, Felger J C. Therapeutic Implications of Brain-Immune Interactions: Treatment in Translation[J]. Neuropsychopharmacology, 2017,42(1):334-359.
[8] Dantzer R, O' Connor J C, Lawson M A, et al. Inflammation-associated depression: from serotonin to kynurenine[J]. Psychoneuroendocrinology, 2011,36(3):426-436.
[9] 刘瑞莲, 屈红林. 有氧运动干预 CUMS 小鼠海马神经炎症及改善 NF- B、TNF-α/IDO/5-HT 信号通路的调控机制研究 [J]. 中国免疫学杂志, 2021,37(13):1563-1570.
[10] Agudelo L Z, Femenia T, Orhan F, et al. Skeletal muscle PGC-1alpha1 modulates kynurenine metabolism and mediates resilience to stress-induced depression[J]. Cell, 2014,159(1):33-45.
[11] Eisele P S, Furrer R, Beer M, et al. The PGC-1 coactivators promote an anti-inflammatory environment skeletal muscle vivo[J]. Biochem Biophys Res Commun, 2015,464(3):692-697.
[12] Leonard B, Maes M. Mechanistic explanations how cell-mediated immune activation, inflammation and oxidative and nitrosative stress pathways and their sequels and concomitants a role in the pathophysiology of unipolar depression[J]. Neurosci Biobehav Rev, 2012,36(2):764-785.
[13] Eyre H, Baune B T. Neuroplastic changes in depression: a role for the immune system[J]. Psychoneuroendocrinology, 2012,37(9):1397-1416.
[14] Zhang J C, Yao W, Hashimoto K. Brain-derived Neurotrophic Factor (BDNF)-TrkB Signaling in Inflammation-related Depression and Potential

Therapeutic Targets[J]. Curr Neuropharmacol, 2016,14(7):721-731.
[15] 屈红林, 谢军, 陈嘉勤, 等. 有氧运动通过 TLR4/miR-223/NLRP3 信号通路轴介导 CUMS 抑郁小鼠海马炎症反应 [J]. 体育科学, 2019,39(02):39-50.
[16] Wrann C D, White J P, Salogiannnis J, et al. Exercise induces hippocampal BDNF through a PGC-1alpha/FNDC5 pathway[J]. Cell Metab, 2013,18(5):649-659.
[17] Rivest S. Interactions between the immune and neuroendocrine systems[J]. Prog Brain Res, 2010,181:43-53.
[18] Ignacio Z M, Da S R, Plissari M E, et al. Physical Exercise and Neuroinflammation in Major Depressive Disorder[J]. Mol Neurobiol, 2019,56(12):8323-8335.
[19] Hidalgo J L, Sotos J R. Effectiveness of Physical Exercise in Older Adults With Mild to Moderate Depression[J]. Ann Fam Med, 2021,19(4):302-309.
[20] Liu Y, Xu F, Liu S, et al. Significance of gastrointestinal tract in the therapeutic mechanisms of exercise in depression: Synchronism between brain and intestine through GBA[J]. Prog Neuropsychopharmacol Biol Psychiatry, 2020,103:109971.
[21] Naghibi S, Shariatzadeh J M, Barzegari A, et al. Treadmill exercise sex-dependently alters susceptibility to depression-like behaviour, cytokines and BDNF in the hippocampus and prefrontal cortex of with sporadic Alzheimer-like disease[J]. Physiol Behav, 2021,241:113595.
[22] Rethorst C D, Toups M S, Greer T L, et al. Pro-inflammatory cytokines as predictors of antidepressant effects of exercise in major depressive disorder[J]. Mol Psychiatry, 2013,18(10):1119-1124.
[23] Lavebratt C, Herring M P, Liu J J, et al. Interleukin-6 and depressive symptom severity in response to physical exercise[J]. Psychiatry Res, 2017,252:270-276.
[24] Morres I D, Hatzigeorgiadis A, Stathi A, et al. Aerobic exercise for adult patients with major depressive disorder in mental health services: A systematic review and meta-analysis[J]. Depress Anxiety, 2019,36(1):39-53.
[25] Abd E S, Al-Shreef F M, Al-Jiffri O H. Impact of aerobic exercise versus resisted exercise on endothelial activation markers and inflammatory cytokines among elderly[J]. Afr Health Sci, 2019,19(4):2874-2880.
[26] Zhao C, Ma H, Yang L, et al. Long-term bicycle riding ameliorates the depression of the patients undergoing hemodialysis by affecting the levels of interleukin-6 and interleukin-18[J]. Neuropsychiatr Dis Treat, 2017,13:91-100.
[27] Hartmann T E, Robertson C V, Miller T D, et al. Associations between exercise, inflammation and symptom severity in those with mental health disorders[J]. Cytokine, 2021,146:155648.
[28] Silva L, Tortelli L, Motta J, et al. Effects of aquatic exercise on mental health, functional autonomy and oxidative stress in depressed elderly individuals: A randomized clinical trial[J]. Clinics (Sao Paulo), 2019,74:e322.
[29] Nugent N R, Brick L, Armey M F, et al. Benefits of Yoga on IL-6: Findings from a Randomized Controlled Trial of Yoga for Depression[J]. Behav Med, 2021,47(1):21-30.
[30] Gautam S, Tolahunase M, Kumar U, et al. Impact of yoga based mind-body intervention on systemic inflammatory markers and co-morbid depression in

active Rheumatoid arthritis patients: A randomized controlled trial[J]. Restor Neurol Neurosci, 2019,37(1):41-59.
[31] Lavretsky H, Alstein L L, Olmstead R E, et al. Complementary use of tai chi chih augments escitalopram treatment of geriatric depression: a randomized controlled trial[J]. Am J Geriatr Psychiatry, 2011,19(10):839-850.
[32] Irwin M R, Olmstead R. Mitigating cellular inflammation in older adults: a randomized controlled trial of Tai Chi Chih[J]. Am J Geriatr Psychiatry, 2012,20(9):764-772.
[33] Cheung D, Chau P H, Yeung W F, et al. Assessing the effect of a mind-body exercise, qigong Baduanjin, on sleep disturbance among women experiencing intimate partner violence and possible mediating factors: randomized-controlled trial[J]. J Clin Sleep Med, 2021,17(5):993-1003.
[34] 陈金霞, 李元昊, 吴英清, 等. 普拉提锻炼对肥胖女大学生抑郁身体成分及血清炎症因子的影响 [J]. 中国学校卫生, 2020,41(05):783-786.
[35] de Castro D, Da C N D, Orsano V, et al. Effect of high-velocity and traditional resistance exercise on serum antioxidants and inflammation biomarkers in older women: A randomized crossover trial[J]. Exp Gerontol, 2020,139:111026.
[36] Cassilhas R C, Antunes H K, Tufik S, et al. Mood, anxiety, and serum IGF-1 in elderly men given 24 weeks of high resistance exercise[J]. Percept Mot Skills, 2010,110(1):265-276.
[37] Park S E, Dantzer R, Kelley K W, et al. Central administration of insulin-like growth factor-I decreases depressive-like behavior brain cytokine expression in mice[J]. Neuroinflammation, 2011,8:12.
[38] Ruiz J R, Gil-Bea F, Bustamante-Ara N, et al. Resistance training does not have an effect on cognition or related serum biomarkers in nonagenarians: a randomized controlled trial[J]. Int J Sports Med, 2015,36(1):54-60.
[39] Kohut M L, McCann D A, Russell D W, et al. Aerobic exercise, but not flexibility/resistance exercise, reduces serum IL-18, CRP, and IL-6 independent of beta-blockers, BMI, and psychosocial factors in older adults[J]. Brain Behav Immun, 2006,20(3):201-209.
[40] Donges C E, Duffield R, Drinkwater E J. Effects of resistance or aerobic exercise training on interleukin-6, C-reactive protein, and body composition[J]. Med Sci Sports Exerc, 2010,42(2):304-313.
[41] Nasstasia Y, Baker A L, Halpin S A, et al. Pilot Study of an Exercise Intervention for Depressive Symptoms and Associated Cognitive-Behavioral Factors in Young Adults With Major Depression[J]. J Nerv Ment Dis, 2017,205(8):647-655.
[42] Balchin R, Linde J, Blackhurst D, et al. Sweating away depression? The impact of intensive exercise on depression[J]. J Affect Disord, 2016,200:218-221.
[43] Paolucci E M, Loukov D, Bowdish D, et al. Exercise reduces depression and inflammation but intensity matters[J]. Biol Psychol, 2018,133:79-84.
[44] Perez M L, Raison C L, Coe C L, et al. Cytokine responses across submaximal exercise intensities in women with major depressive disorder[J]. Brain Behav Immun Health, 2020,2:100046.
[45] Boettger S, Muller H J, Oswald K, et al. Inflammatory changes upon a single maximal exercise test in depressed patients and healthy controls[J]. Prog

Neuropsychopharmacol Biol Psychiatry, 2010,34(3):475-478.
[46] Ventura J, McEwen S, Subotnik K L, et al. Changes in inflammation are related to depression and amount of aerobic exercise in first episode schizophrenia[J]. Early Interv Psychiatry, 2021,15(1):213-216.

Note: Figure translations are in progress. See original paper for figures.