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Research Article

The effect of aerobic exercise on JAK/STAT signaling pathway

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Abstract

JAK/STAT is one of the key pathways in cell proliferation, growth, and differentiation. In most tissues, this path is known as the cause of inflammation and, in some cases, the induction and progression of diseases. In contrast, aerobic exercise regulates and modulates cell signaling by affecting signaling pathways and inflammatory and pro-inflammatory cytokines. In this article, we investigate the effect of aerobic exercise on the JAK/STAT signaling pathway.Classified articles were searched from reliable international and Iranian scientific databases. Articles were extracted from scientific databases such as Pubmed, Scopus, Science Direct, and Google Scholar. Also, articles were extracted from the scientific databases of Iran Magiran, SID, and Civilica. Out of 45 articles, 13 met this review article's criteria. Aerobic exercise affects the JAK/STAT signaling pathway in various tissues and organs. According to research results, aerobic exercise activates or inhibits this pathway differently depending on the tissue type. These effects of aerobic exercises were different in research tissues and models.Therefore, we emphasize the importance of further research on this signaling pathway and its response to exercise, especially aerobic exercise, to fully understand its effects and consequences. This research is necessary and significant in the field of exercise physiology and immunology.

Keywords:
aerobic exercise, JAK, STAT .

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1. Introduction

Aerobic exercise reduces oxidative stress, apoptosis, and inflammation. Aerobic activity can control, modulate, or inhibit these processes by activating and expressing various factors (1, 2). Among others, we can mention the increase in Nrf2 expression in aerobic exercise and the inhibition of the JAK2/STAT3 signaling pathway, ultimately leading to better cell function (3, 4). Regular aerobic exercise targets metabolic signaling pathways in cells, such as the liver and cardiorespiratory cells. Endurance exercise is a therapeutic strategy for many physiological functions in humans (5) and is currently considered as a preventive treatment for many common chronic conditions, including obesity, cancer, and diabetes (6, 7). Animal model studies showed significant suppression of mammary tumor growth in animals trained for endurance compared to sedentary mice (8, 9). Sports training, especially aerobic exercise, modulates cell growth, proliferation, and differentiation pathways. Various studies have shown that aerobic exercise, especially moderate-intensity, can reduce the JAK/STAT signaling pathway activity in various diseases. These include diabetes, cancer, and NAFLD. It can also moderate inflammation and cell proliferation (10, 11). In general, regular exercise reduces systemic cellular inflammation. This process can control or modulate systemic inflammation by affecting different signaling pathways (10, 12). The JAK2/STAT3 signaling pathway is involved in a wide range of cellular processes. The disruption of this pathway contributes to various diseases, including cancer. On the other hand, the JAK2/STAT3 signaling pathway is involved in muscle cell hypertrophy.

Some studies have shown that this pathway is activated by the cytokine IL-6. IL-6 and its related cytokines can activate the JAK/STAT signaling pathway in the myocardium and cause physiological hypertrophy of heart muscle (11, 13). White adipose tissue (WAT) produces inflammatory factors that activate the JAK2/STAT3 pathway and contribute to insulin resistance, impaired glucose metabolism, and increased risk of obesity-related complications (14, 15). JAK2/STAT3 pathways play a role in initiating and progressing inflammatory and immune responses in many pathological processes. It is known as a modulating pathway in various diseases (16, 17). Signal transducer and activator of transcription 3 (STAT3) belongs to the family of STATs, which is known as a transcription factor by binding to DNA in various pathological processes (10, 18). In addition to its multifaceted role in physiological processes, Janus kinase 2 (JAK2) plays critical roles in apoptosis, immune response, inflammation, and differentiation (13, 17, 19). Research observations show that aerobic exercise affects various cellular signaling pathways. One of these critical cellular pathways is JAK/STAT signaling, and studies showed that aerobic exercise affects this pathway. This review article was based on various studies to provide an update on the effects of aerobic exercise and activity on JAK2/STAT3 signaling pathways.

2. Materials and Methods

Searching for articles classified by key in this review study conducted from 2010 to 2024, articles in the medical databases Pubmed, Scopus, Science Direct, and Google Scholar and in the Iranian scientific databases Magiran, SID, and Civilica were analyzed. The collection of reviewed articles included 45 articles that included qualitative and quantitative research related to the last 14 years (from 2010 until now), of which 13 articles were eligible for this review article. Researches that had unclear sample size and method of implementation or were only conducted on unrelated factors were excluded from the study process. Also, articles without full text were excluded from the study. The keywords used in searching for article consists of: "Aerobic Training", "Aerobic Exercise", "Aerobic Activity", "JAK/STAT", "JAK2/STAT3", "JAK2" and STAT3. Criteria for selecting articles: Classified articles from 14 years ago to 2024 in this field. Articles whose full text is available. Articles that examined the relationship between aerobic exercise activity and the JAK/STAT or JAK2/STAT3 signaling pathway. Articles with unclear sample sizes referred to only one aspect of the methods used and lacked signaling pathways were excluded from the present study.

3. Results

The results of this review article show that aerobic exercise has had significant positive and negative effects on the JAK/STAT pathway in various studies. This pathway has various responses in cells of different tissues, and aerobic exercise has been able to modulate this signaling pathway (Table 1).

Binyu YAO et al. (2024) research on the subject. Endurance Training Inhibits the JAK2/STAT3 Pathway to Alleviate Sarcopenia, six-month-old SAMR1 male mice as the young group and one-month-old SAMP8 male mice were divided into two training groups (E group) and model group (control group – M). became an adaptive training protocol, which involved 10 minutes of training per day at a speed of 9 meters per minute for five days per week. The main training protocol was performed five days per week, one session per day, for eight weeks. Weeks 1-2 include running at a speed of 12 meters per minute for 30 minutes, week three running at a speed of 15 meters per minute for 30 minutes, week 4 15 meters per minute for 45 minutes, and weeks 5 to 8 15 meters per minute for 60 minutes and the inclination of the device was 0 degrees. Aging induced significant signs of sarcopenia in SAMP8 mice, and endurance training effectively improved muscle mass, muscle strength, and muscle function in SAMP8 mice. The expression of the JAK2/STAT3 pathway factor was decreased in group E compared to group M, and the expression of SOCS3, the STAT3 inhibitory gene, and NR1D1, as a factor associated with atrophy, increased significantly. Endurance training significantly improved sarcopenia-related phenotypes, and modulation of the JAK2/STAT3 pathway is a possible mechanism for ameliorating sarcopenia by endurance exercise, while NR1D1 may be its potential target.

Meng Li et al. (2024) conducted research on Treadmill training that improves neural function recovery in rats with spinal cord injury via JAK2/STAT3 signaling pathway and attenuates apoptosis. The statistical population was Sprague-Dawley rats, randomly divided into four groups: 1- Sham group. 2- SCI group; 3- SCI + treadmill exercise group (SCI/TT).

and 4- SCI/TT+AG490 group (a JAK2 inhibitor) (number = 12) were divided. Four days before spinal cord injury, all rats were monitored and trained to walk on a research treadmill daily. Treadmill training was started 24 hours after spinal cord injury (SCI) in SCI + TT group and SCI/TT+AG490 group and was performed twice a day for 15 minutes in running until the end of the experiment. After three days, the treadmill's speed reached 6 m/min. The results showed that treadmill training can improve the activation of the JAK2/STAT3 signal pathway and reduce apoptosis in the injured spinal cord, resulting in better functional recovery. These results emphasize the importance of synergistic treatment strategies for SCI.

Meiyan Sun et al. (2023) in the study Aerobic Exercise Ameliorates Liver Injury in Db/Db Mice by Attenuating Oxidative Stress, Apoptosis and Inflammation Through the Nrf2 and JAK2/STAT3 Signaling Pathways, which seven-week-old male mice with type 2 diabetes db/db and mice m/m of the same age were randomly divided into control group and experimental group (aerobic exercise). They received 12 weeks of aerobic exercise on a treadmill (10 m/min). Aerobic exercise was associated with reducing inflammation, oxidative stress, and apoptosis, which probably caused the increase in Nrf2 expression and inhibition of the JAK2/STAT3 cascade response. It reversed liver dysfunction in db/db mice with T2DM.

Yuan Shan et al. (2023) in their study that Exercise preconditioning attenuates cerebral ischemia-induced neuronal apoptosis, Th17/Treg imbalance, and inflammation in rats by inhibiting the JAK2/STAT3 pathway, 50 adult male Sprague-Dawley rats aged eight weeks and weight 250-280 grams, were divided into five groups of 10, including sham group, MCAO group, EP (Exercise Preconditioning) + sham group, EP + (Middle Cerebral Artery Occlusion) MCAO group and EP + MCAO + CA1 group according to a random table. Coumermycin A1 (CA1), a JAK2 agonist, activated the JAK2/STAT3 pathway. The EP protocol included three days of preparation and adaptation to the treadmill, performed at 15 to 20 m/min. The main training protocol was performed at a speed of 25 meters/minute, five days a week, each session lasting 30 minutes for four weeks. The results show that EP contributes to Th17/Treg imbalance, reduction of MCAO-induced neuronal apoptosis, and inflammation through inhibition of JAK2/STAT3 pathway, indicating its therapeutic potential in ischemic stroke.

Jiexiu Zhao et al. (2023) studied the effect of exercise combined with heat treatment to improve insulin resistance in diet-induced obese rats. For this purpose, 60 male Wistar rats were divided into two groups, a normal diet, and a high-fat diet, after 1 week of familiarization with the environment. After ten weeks of feeding, an oral glucose tolerance test (OGTT) was performed to determine whether the IR model of HFD group rats was successfully established. A total of 32 rats were randomly selected from successful IR modeling and divided into normal temperature + control (NC), normal temperature + exercise (NE), heat treatment + control (HC), and heat treatment + exercise (HE) groups. Became, with eight mice in each group fed a high-fat diet. Rats in NE and HE groups trained with incremental overload training on an animal treadmill for seven weeks. The first training session was 1 minute, and then each was increased by 2 minutesrats.

Training was done once a day for the first two weeks and then twice a day for weeks 3 to 7, 6 days a week. Rats of the NE group were trained in the animal room (temperature 23 ± 2 °C, relative humidity 50 ± 5%). Rats of the HE group were trained in a high-temperature environmental room (temperature 38 ± 2 °C, relative humidity 50 ± 5%). The results showed that aerobic exercise combined with heat treatment can effectively improve insulin resistance by regulating JAK2/STAT3 and HSF1/HSP27 pathways in the slow-twitch muscle of diet-fed obese rats. Importantly, aerobic exercise combined with heat treatment is more effective than exercise or heat treatment alone in improving insulin resistance in diet-fed rats. Moderate-to-low-intensity exercise that stimulates slow-twitch muscles, combined with heat treatment, is an effective strategy for treating insulin resistance.

Ziya Fallahmohammadi et al. (2023) investigated the Effect of Six Weeks of Treadmill Running on JAK1/STAT3 Pathway Gene Expression in the Basal Ganglia of Type-1 Diabetic Rats. 40 Wistar rats were divided into four groups of 10: healthy control group, exercise training control, diabetic control, and exercise training diabetes. Aerobic exercise protocol was performed for six weeks, five sessions per week, and with an intensity of 50-55% aerobic capacity. The mice were anesthetized 48 hours after the last training session, and the brain tissue was removed from the skull to separate the basal ganglia. The extracted tissue was measured using the qPCR method to measure gene expression. The results showed that the induction of diabetes did not change the JAK1/STAT3 pathway in basal ganglia. However, aerobic training decreased JAK/STAT signaling pathway gene expression in the basal ganglia compared to the diabetic group.

Yirou Lei et al. (2023) Sequential inspiratory muscle exercise-noninvasive positive pressure ventilation alleviates oxidative stress in COPD by mediating SOCS/JAK2/STAT3 pathway. For this purpose, 100 patients with COPD were randomly divided into respiratory muscle training (IMT), oxygen therapy (OT), non-invasive positive pressure ventilation (NIPPV), and IMT+NIPPV groups. The group did respiratory muscle training with the Power Breath device. Training intensity started at 40% of PImax for one week and increased by 10% after the first week to reach 80% of PImax. Training was done twice a day for 30 minutes. In the NIPPT + IMT group, patients received post-training IMT for 30 minutes per session, followed by NIPPV for 2 hours twice daily. The results showed that NIPPV, IMT, or sequential (NIPPV + IMT) significantly improved exercise endurance, quality of life, and dyspnea, reduced oxidative stress, promoted SOCS5 expression and inhibited JAK2/STAT3 pathway activation. COPD patients in the IMT+NIPPV group had better pulmonary function than the IMT and NIPPV groups.

Yi Chen et al. (2023) research An Acute Bout of Exercise Suppresses Appetite via Central Lactate Metabolism was conducted. 150 male C57BL/6J mice are eight weeks old and weigh 20-23 grams. After one week of environmental adaptation, 46 mice were divided into two groups with equal numbers (23): sedentary and training group. Another 76 mice were divided into four groups 19: saline inactivity group, lactate inactivity group, exercise training group + Examate, and exercise training group + normal saline. The exercise protocol was performed acutely with an intensity of 90% Vmax and was of HIIT type.

It consisted of a 10-minute warm-up at 5 m/min, followed by ten high-intensity intervals of 4 min at 90% Vmax each session, followed by a 2-minute interval at 12 m/min. Acute exercise increased STAT3 and Jak2 phosphorylation in the hypothalamus, whereas central lactate inhibition significantly attenuated this effect. The expression of HIF-1α was increased after HIIT exercise, while it was decreased by central exam administration. Research data suggest that central lactate metabolism suppresses appetite and changes in exercise-induced neuropeptides, a mechanism likely through increased Jak2-STAT3 signaling.

Lili Lin et al. (2022) study Aerobic Exercise Improves Type 2 Diabetes Mellitus-Related Cognitive Impairment by Inhibiting JAK2/STAT3 and Enhancing AMPK/SIRT1 Pathways in Mice. The statistical population of diabetic mice aged eight weeks db/m and mice without leptin receptors (db/db) were divided into control and aerobic training groups. The training groups participated in treadmill acclimatization training for one week (5 m/min, 30 min/day), followed by 12 weeks (starting at 10 weeks) of moderate-intensity treadmill training (5 days/week at a speed of 8 meters per minute for 40 minutes in the first week - the second to the twelfth weeks at a speed of 8 meters per minute for 1 hour). Aerobic exercise improved cognitive impairment by activating the AMPK/SIRT1 signaling pathway and inhibiting the JAK2/STAT3 signaling pathway in type 2 diabetic rats. Long-term aerobic exercise improves cognitive impairment associated with type 2 diabetes by inhibiting JAK2/STAT3 and enhancing AMPK/SIRT1 pathways in mice.

Timothy S. Odermatt et al. (2020) Adipocyte-specific gp130 signaling mediates exercise-induced weight reduction International Journal of Obesity. Adipocyte-specific gp130 KO mice were purchased on a C57BL/6J background by crossing floxed gp130 mice with animals carrying Cre recombinase controlled by the Adipoq promoter (Adipoq).

Six-week-old male mice fed high-fat diet (HFD) ad libitum. were fed a 12-week HFD consisting of 59% of calories from fat and 15% of protein, followed by a 6-week, 5-day exercise protocol per week, which was increased by 1 cm/s every five days to reach a speed of 20 cm/s. Hypothalamic leptin and insulin signaling were increased in trained gp130F/F mice, but This was not the case in gp130Δadipo mice, which were shown to have increased protein levels of pSTAT3, pJAK2, and pAkt.

Almeida-Oliveira et al. (2019) Research Effects of aerobic exercise on molecular aspects of asthma: involvement of SOCS-JAK-STAT. For this purpose, 120 8-week-old C57Bl/6 mice weighing 20 grams were divided into four groups: control (Co), aerobic exercise (Ex), House Dust Mite (HDM), and HDM + Exercise (HDM + Ex). Aerobic training was performed in EX and HDM+EX groups five days a week; each training session was 60 minutes for four weeks and with moderate intensity. Aerobic exercise inhibited HDM-induced total cells such as lymphocytes, eosinophils, and neutrophils in the bronchoalveolar lavage and peribronchial space. Also, aerobic exercise reduced the levels of cytokines IL-5, IL-4, and IL-17 in Bronchoalveolar Lavage. Aerobic exercise decreased the expression of JAK2, STAT3, STAT6, and STAT5 by peribronchial leukocytes and airway epithelial cells. In general, aerobic exercise reduces the asthma phenotype involving SOCSJAK-STAT signaling.

Borjian Fard et al. (2019) Investigating the role of the JAK/STAT pathway in cardiac hypertrophy induced by the interval and continuous training in adult male rats. They paid; therefore, 16 Wistar rats were divided into two equal groups of 8 for aerobic exercise and control. The endurance training protocol was performed for eight weeks, five sessions per week

Warm-up 5-10 minutes with an intensity of 50-60% VO_{2max} - main exercise 50 minutes with an intensity of 65-70% VO_{2max}, final 5 minutes with an intensity of 50-60% VO_{2max}. The results showed that the heart muscle hypertrophy in the endurance training group was significantly higher than in the control group. However, the expression of JAK2, STAT3, CT1, and gp130 genes was not significantly different in the two groups.

Askarabadi, S. H. et al. (2019) studied the effect of 6 weeks of aerobic training on peripheral neuropathic pain to inhibit the expression of the Notch-1 receptor and JAK/STAT signaling pathway in the posterior spinal cord of diabetic male rats. For this purpose, 40 8-week-old Wistar rats were divided into four groups 10: diabetic neuropathy control group, diabetic neuropathy + aerobic exercise group, healthy control group, and healthy control group + aerobic exercise. The protocol was performed in five sessions per week for six weeks. The speed and duration of the treadmill training is gradually increased from 10 meters per minute for 10 minutes in the first week, 10 meters per minute for 20 minutes in the second week, 14 to 15 meters per minute for 20 minutes in the third week, 14 to 15 meters per minute for 30 minutes in the fourth week, 17 to 18 meters per minute for 30 minutes in the fifth and sixth weeks. Aerobic exercise improves the pain caused by diabetic neuropathy by regulating and reducing the expression of Notch 1 proteins in the peripheral nerves of the spinal cord and reducing the number of inflammatory cytokines, which leads to the blocking of the JAK/STAT signaling pathway, followed by the reduction of STAT3 expression, which reduces pain sensation. It is practical and strengthens the therapeutic effect of aerobic exercises in diabetic neuropathy. Therefore, inhibiting the 1Notch receptor and the STAT/JAK signaling pathway without the use of drugs and prescribing regular aerobic exercises with mild to moderate intensity for diabetics can be a suitable method to control and treat the pain caused by it.

Table (1): Summary of results of aerobic exercise research and JAK/STAT signaling pathway

Researcher	Subjects	Aerobic Training Protocol	Results
Binyu YAO et al. 2024 (20)	Six-month-old male mice	Eight weeks, five sessions a week, running on the treadmill	↑muscle mass, muscle strength, and muscle function ↓JAK2/STAT3 expression
Meng Li et al. 2024(21)	Sprague-Dawley rats	Aerobic exercise of moderate intensity, twice a day for 15 minutes on the treadmill	↑ JAK2/STAT3 signaling pathway ↓ Apoptosis in the injured spinal cord
Meiyan Sun et al. 2023(3)	Seven-week-old male mice with type 2 diabetes	12 weeks of aerobic exercise on a treadmill (10 m/min).	↓ inflammatory, oxidative stress, apoptosis ↑ Nrf2 expression inhibits JAK2/STAT3
Yuan Shan et al. 2023 (22)	Adult Sprague-Dawley rats aged 8 weeks	Aerobic training 5 days a week for 30 minutes each session for 4 weeks	↓ Neuronal apoptosis and inflammation ↓ JAK2/STAT3 pathway
Ziya Fallahmohammadi et al. 2023 (23)	Wistar rats	Aerobic training for 6 weeks, 5 sessions per week	↑Aerobic exercise JAK/STAT signaling pathway gene expression in basal ganglia
Jiexiu Zhao et al. 2023 (24)	Wistar rats -	Aerobic training, 7 weeks, 6 days a week with moderate intensity	Regulation of JAK2/STAT3 and HSF1/HSP27 pathways in slow twitch muscle of obese rats
Yirou Lei et al. 2023 (25)	COPD patients	Respiratory muscle training group with Power breath device with an intensity of 40% to 80%	↑ Exercise endurance, quality of life ↓ oxidative stress ↑ SOCS5 expression Inhibition of the JAK2/STAT3 pathway
Yi Chen et al. 2023 (26)	Male C57BL/6J mice, at the age of 8 weeks	Acute HIIT training with an intensity of 90% Vmax	↑ Phosphorylation of STAT3 and Jak2 in the hypothalamus ↑ HIF-1α ↑Jak2-STAT3 -
Lili Lin et al. 2022 (27)	Diabetic mice at the age of 8 weeks	Aerobic training for twelve weeks, 5 days a week, at a speed of 8 m/min	↑ AMPK/SIRT1 Inhibition of JAK2/STAT3 signaling pathway -

Timothy S. Odermatt et al. 2020 (28)	C57BL/6J mice with adipocyte-specific gp130 KO	6 weeks of aerobic training, 5 days a week	↑ Hypothalamic leptin and insulin signaling In gp130Δadipo mice: ↑ pSTAT3, pJAK2 and pAkt protein levels
A R Almeida-Oliveira et al. 2019 (29)	8-week-old C57Bl/6 mice	4 weeks of aerobic training 5 days a week	↓ IL-5, IL-4 and IL-17 cytokine levels in Bronchoalveolar Lavage ↓ JAK2 STAT3, STAT6, and STAT5 expression in bronchial and airway epithelial cells
Borjian Fard et al. 2019 (11)	Wistar rat	8 weeks of endurance training, 5 sessions per week with an intensity of 50 to 70% VO2max	↑ Cardiac muscle hypertrophy in ↔Expression of JAK2, STAT3, CT1 and gp130 genes
Askarabadi, S. H., et al. 2019 (30)	8-week-old Wistar rat	6 weeks of aerobic training,5 sessions per week for	↓ Pain due to diabetic neuropathy ↓Notch 1 proteins in the peripheral nerves of the spinal cord Inhibition of the JAK/STAT pathway

4. Discussion

The JAK/STAT signaling pathway shows up-regulation in many diseases, especially chronic diseases, such as obesity, type 2 diabetes, and cancer. However, in some tissues, this enhanced regulation improves the condition of that tissue. In the studies of sports training, it increases the expression of JAK2/STAT3 in muscle cells. Therefore, this inflammatory reaction causes muscle cell growth and development and increases muscle tissue capacity.

The JAK2/STAT3 signaling pathway also plays a role in osteoarthritis. Inflammatory and pro-inflammatory cytokines such as IL-1β activate this signaling pathway and increase inflammation in osteoarthritis patients. Aerobic exercise has been studied as a modulator of the JAK/STAT pathway, especially in the JAK2/STAT3 pathway (17). Most research shows that aerobic exercise controls this process by increasing the expression of factors inhibiting the JAK/STAT signaling pathway.

The research by Lili Lin et al. 2022 researched aerobic exercise done on diabetic mice. The results showed that aerobic exercise activated the AMPK/SIRT1 pathway, and the JAK2/STAT3 signaling pathway inhibited this process, and diabetic mice improved cognitive disorders (26). On the other hand, Meiyan Sun et al. 2023 showed that aerobic exercise increased Nrf2 expression, followed by inhibition of the JAK2/STAT3 cascade response. This reversed liver dysfunction in db/db mice with type 2 diabetes (3). Research results from Askarabadi, S. H., et al. (2019) 6 weeks of moderate-intensity aerobic exercise in diabetic neuropathy in rats showed a decrease in the expression of Notch1 proteins in the peripheral nerves of the spinal cord, accompanied by a reduction in the number of inflammatory cytokines that lead to the blocking of the JAK/STAT signaling pathway and was followed by a decrease in STAT3 expression (29).

Aerobic exercise for 4 weeks reduced inflammatory factors, inflammatory cytokines, JAK2/STAT3 pathway, and STAT5 and STAT6 gene expression in peribronchial, bronchial, and airway epithelial cells in rats exposed to House Dust Mite, and inflammation in these lung tissues. Were controlled (28). In some studies, aerobic exercises have an increasing effect on the expression of the JAK/STAT signaling pathway. This improves the disease or target tissue condition. Borjian Fard et al. (2019) showed that aerobic training causes hypertrophy of rats' heart muscle, but this hypertrophy does not increase in the JAK2/STAT3 signaling pathway (11). Yi Chen et al. (2023) research in C57BL/6J mice showed that a session of HIIT training increased the expression of JAK2 and STAT3 in the hypothalamus of mice and suppressed appetite in them (25). In another study, aerobic exercise increased the expression of the JAK2/STAT3 signaling pathway. This can improve the reduction of apoptosis in the injured spinal cord. This can lead to better functional improvement in rats with spinal cord complications (21).

conclusion

From the research results, it can be said that the JAK/STAT signaling pathway is selective. This is in the sense that it has different functions in various tissues. As a result of its increase, chronic diseases develop as a result of inflammation. Aerobic exercises modulated the expression of this pathway in different conditions and tissues. This review article shows that research should be done on the effect of aerobic exercise on this critical cellular signaling pathway. This is so that the behavior of aerobic exercise on this pathway under different conditions and tissues is better understood.

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Compliance with ethical standards

Conflict of interest None declared.

Ethical approval the research was conducted with regard to the ethical principles.

Informed consent Informed consent was obtained from all participants.

Author contributions

AH.SF: This author helped extract and analyze data, interpret results, update reference lists, perform software analysis, and create a summary of findings tables.

MA. A: This author helped write the report, arbitrating potentially eligible studies, extracting and analyzing data, and interpreting results. He contributed to data extraction and provided feedback on the report.

F. RR: This author helped in searching and screening potentially eligible studies

M.P: This author helped in searching and screening potentially eligible studies

H.MH: This author helped in searching and screening potentially eligible studies

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