International Journal of Sport Studies for Health

Journal Homepage

The Effect of Exercise Activity on Pannexin and NLRP3 in Neuromuscular Function with the Approach of The Role of New Peptides: A Narrative Review

Rasoul. Eslami[1*], Atefeh. Sadeghi[1]

[1] Department of Exercise Physiology, Faculty of Sports Science, Allameh Tabataba'i University, Tehran, Iran

*** Corresponding author email address**: eslami.rasul@gmail.com

A r t i c l e I n f o

Article type:
Review Article

How to cite this article:
Eslami, R., & Sadeghi, A. (2025). The Effect of Exercise Activity on Pannexin and NLRP3 in Neuromuscular Function with the Approach of The Role of New Peptides: A Narrative Review. *International Journal of Sport Studies for Health*, *8*(2), 85-95.
http://dx.doi.org/10.61838/kman.intjssh.8.2.10

A B S T R A C T

Objective: This study aims to investigate how exercise modulates pannexin channels, NLRP3 inflammasome activity, and exercise-induced peptides (irisin and interleukin-6), and their collective impact on neuro-muscular function.

Methods and Materials: This narrative review applied a systematic and comprehensive literature search strategy, targeting publications from 2013 to 2025. The databases used included PubMed, Web of Science, and Scopus. Keywords and MeSH terms such as “exercise,” “pannexin channels,” “NLRP3 inflammasome,” “irisin,” “interleukin-6,” and “neuro-muscular function” were employed. Articles were selected based on relevance to the interplay between exercise and molecular pathways affecting neuro-muscular performance. Both human and animal studies were considered, with emphasis on those presenting primary data, although relevant reviews were also included.

Findings: The review revealed that pannexin-1 channels play a vital role in ATP release during exercise, which supports muscle contraction, communication, and recovery. Exercise modulates pannexin-1 expression, potentially enhancing muscle strength and regeneration. NLRP3 inflammasome activation is influenced by exercise intensity and duration, with chronic training reducing its basal activation and inflammation, thereby promoting neuro-muscular adaptation. Novel peptides irisin and interleukin-6, secreted in response to exercise, were found to interact with pannexin-1 and NLRP3 pathways. Irisin enhances energy metabolism, insulin sensitivity, and muscle remodeling. IL-6 regulates inflammation and glucose metabolism and may exhibit dual roles depending on exercise context. Their interactions with pannexin-1 and NLRP3 are emerging areas of study with significant implications.

Conclusion: Exercise modulates critical molecular pathways including pannexin-1 channels, the NLRP3 inflammasome, and peptide mediators such as irisin and IL-6. These interactions collectively enhance neuro-muscular

Article history:
Received 22 January 2025
Revised 09 March 2025
Accepted 16 March 2025
Published online 01 Apil 2025

performance, suggesting therapeutic potential in disease prevention and functional improvement.

Keywords: *Exercise, Pannexin-1, NLRP3 Inflammasome, Neuro-Muscular Function, Irisin, Interleukin-6, Adaptation*

1. Introduction

Neuro-muscular function, the intricate interaction of the nervous system and skeletal muscle, is critical for the seamless execution of movement and physical activity as a whole. Exercise has been recognized for a long time as an immensely potent intervention to improve neuro-muscular function in a wide variety of populations (1, 2).

Molecular mechanisms by which exercise achieves these desirable effects await exploration, however. There is fresh evidence regarding the potential function of pannexin channels and NLRP3-inflammatory signaling in exercise adaptation, modulating their critical role in maintaining and enhancing neuro-muscular performance (3-5). Exercise has been found to strengthen muscles, increase nerve conduction velocity, and aid in improving motor coordination, all contributing to ultimate flawless neuro-muscular functioning (6). At the cellular level, exercise induces muscle hypertrophy and repair by a variety of mechanisms involving enhanced protein synthesis and satellite cell activation (6).

Exercise also has neuroprotective effects, inducing neurogenesis and improving cognitive function (7, 8). These intricate protective actions highlight the importance of elucidating the molecular mechanisms of exercise-induced adaptations. Pannexin channels, and pannexin-1 (Panx1) in particular, have been proposed as candidate key modulators of exercise-induced neuro-muscular performance. These hemichannels in gap junction serve a pathway by which small ions and molecules from the cytosol enter the extracellular space (9-11). Muscle tissue expresses very high levels of pannexin-1 and is sure to have an essential role to play as a component of excitation-contraction coupling activity involved in contraction of muscle (12, 13). Besides, it has been shown that pannexin-1 can potentially be implicated in the release of ATP that can cause muscle contraction and the modulation of inflammatory signals (9, 14), perhaps via high-intensity interval exercise (15). While there is evidence that exercise can modify pannexin-1 expression and function, the mechanism of this regulation is an area of active research (10). The NLRP3 inflammasome, a multi-protein complex that cleaves and activates caspase-1 and also generates pro-inflammatory cytokines such as interleukin-1 beta (IL-1β) and interleukin-18 (IL-18), has also been the focus of interest with respect to exercise-induced adaptations (16, 17). Acute exercise may result in an acute inflammatory response, but chronic inflammation may result in muscle pathology and dysfunction (18). Interestingly, exercise has a broad anti-inflammatory effect, perhaps by modulating the activity of NLRP3 inflammasome (17, 19). This two-way effect of exercise on inflammation highlights the complex interaction between physical exercise and cellular signaling pathways. To this complexity is added the effect of novel exercise-induced peptides, such as irisin and interleukin-6. Irisin, a recently discovered myokine secreted by skeletal muscle in an exercise-dependent fashion, elicits a cascade of beneficial effects including white adipose tissue browning, improved insulin sensitivity, and improved cognitive function (14, 20). Interleukin-6, another myokine, possesses pro-inflammatory and anti-inflammatory action based on context after exercise (21, 22).

Therefore, explaining how these novel peptides act upon pannexin-1 and NLRP3 under exercise may provide valuable information about the control of neuro-muscular function. Therefore, here, we attempt to highlight the new functions for pannexin channels, NLRP3, and novel peptides such as irisin and interleukin-6 in the regulation of exercise-induced neuro-muscular function. We will present the existing knowledge on the mechanisms and their implications for future health and disease. Specifically, this review will include a critical discussion of pannexin-1 channels and their potential role in neuro-muscular activity, specifically the impact of exercise; a detailed analysis of NLRP3 and its impact on exercise-induced inflammation and how it may be modulated by exercise; and analysis of the emerging roles of irisin and interleukin-6 as exercise-secreted peptides and how they may have the potential to interact with pannexin-1 and NLRP3. Lastly, an in-depth appreciation of these molecular processes can translate into the design of targeted interventions to maximize exercise benefits and facilitate overall neuro-muscular wellness.

2. Methods and Materials

This review employed a systematic and comprehensive strategy to identify, evaluate, and synthesize relevant literature from 2013 to 2024 on the effect of exercise on pannexins, NLRP3 inflammasome, and novel peptides in

neuro-muscular performance. The research strategy was specifically designed to capture the most significant and up-to-date research in this rapidly developing area. PubMed, Web of Science, and Scopus were the primary scientific databases employed to carry out this review. These databases were chosen for their wide coverage of biomedical and life sciences literature. The search was conducted using a carefully written set of keywords and Medical Subject Headings (MeSH) terms to capture a comprehensive yet targeted retrieval of relevant articles. Key search terms included "exercise," "neuro-muscular function," "pannexin channels," "NLRP3 inflammasome," "irisin," and "interleukin-6," with appropriate synonyms and related ideas.

To ensure comprehensive coverage, reference lists of highlighted articles were meticulously searched for additional pertinent studies. Furthermore, review articles on related subjects present were read to obtain a general overview of the field and to identify potentially seminal studies that have helped shape our current understanding of the subject. Selection of articles to be included in this review had several criteria in ensuring quality and suitability of information. Primarily, studies were selected based on relevance to the intersection of exercise, pannexin channels, NLRP3 inflammasome, new peptides, and neuro-muscular functioning. Primary data articles containing original research work conducted on humans or animals were utilized to ensure inclusion of original information. However, noteworthy review articles and meta-analyses were also considered for their value in providing broader context and synthesizing existing knowledge. The search focus was primarily on studies published within the last decade. However, acknowledging the importance of foundational work, some earlier studies were included if they were deemed highly relevant to the topic. Due to resource limitations, this review primarily focused on studies published in the English language. The. scope of this review included a wide array of research that. ranged from molecular and cellular studies investigating. pannexin channels and NLRP3 inflammasome activation. mechanisms, to animal and human studies examining. the effects of various exercise modes on. these mechanisms. Focus was on investigations into the. function of novel peptides, including irisin and interleukin-6, during exercise-induced adaptations at the neuro-muscular. level.

3. Results

3.1 Exercise and Pannexin Channels

Pannexin channels, and particularly pannexin-1, are promising candidates in the complex interaction between exercise and neuromuscular performance. What follows reports the actual knowledge regarding pannexin channels, and in particular pannexin-1, and their hypothetical role in exercise adaptation. Pannexins are a family of transmembrane proteins forming large-pore channels in the cell membrane, differing from connexins to form gap junctions between cells. Of the three members of the pannexin family (pannexin-1, pannexin-2, and pannexin-3), pannexin-1 is the most widely expressed and found in almost all cell types (11). Pannexin-1 channels are permeable to a very broad range of molecules, including ions, ATP, and small metabolites, and play important roles in cellular signaling, inflammation, and potentially the excitation-contraction coupling in muscle (12, 23, 24). Exercise-evoked pannexin-1 channels are currently under investigation. Pannexin-1 channels have been suggested to contribute to physical activity-evoked release of ATP from muscle cells (9, 13). In turn, the released ATP can be a signaling molecule that is involved in muscle function and even influence various physiological responses to exercise (22). The functions of pannexin-1 in muscle contraction, fatigue, and recovery are under investigation now. It has been proposed in some studies that pannexin-1 is involved in calcium entry during muscle contraction and thus regulates muscle force production (12, 23). It has been demonstrated that pannexin-1 channels can associate with proteins involved in calcium signaling, but the exact mechanisms of such interaction remain to be elucidated (12). The role of pannexin-1 in muscle fatigue is unclear; however, opening of the pannexin-1 channel has been shown to play a significant role in muscle regeneration following injury or damage due to intense exercise. Satellite cells are myoblasts resident in the muscle and, when activated, begin to proliferate and migrate to the site of injury where they differentiate to create new muscle fibers. Pannexin-1 channels are involved in the control of these processes, myoblast fusion and migration, and extracellular matrix-myoblast interaction (12, 25). Furthermore, as a result of exercise lasting for extended periods, repeated pannexin-1 channel stimulation may lead to loss of ATP stores in muscle fibers and subsequent fatigue. However, activation of pannexin-1 channels is also a part of the recovery process after exercise. Released ATP can activate the activation of protein kinases such as

CaMKII, PKA, and PKC, which phosphorylate pannexin-1 channels and open them to release more ATP. This feedback maintains muscle contraction and supports the recovery process (13, 25). The potential role of pannexin-1 in muscle recovery following exercise is an area for future studies. The exercise regulation of pannexin-1 expression is another important feature of this field. There is not much evidence to indicate that exercise training can modulate the expression of pannexin-1 in skeletal muscle, but the findings are not entirely consistent (6). Nevertheless, chronic exercise activity can potentially bring about significant adaptations in the skeletal muscle system, including changes in muscle fiber type, enhanced muscle strength, and enhanced muscle endurance. These adaptations have the opening of pannexin-1 channels at their core. For example, muscle fibers' repeated electrical stimulation may lead to the phosphorylation of pannexin-1 channels and their opening with release of ATP. This may enhance muscle strength and endurance by increasing the force-generating ability of muscle fibers. Besides, pannexin-1 channel stimulation can influence gene expression involved in muscle growth and differentiation and lead to muscle hypertrophy and greater muscle mass (11, 25). Figure 1 demonstrates a summary of exercise effects on pannexin-1 channels. However, the potential differential effects of various types of exercise (e.g., endurance vs. resistance training) on pannexin-1 expression remain unclear and must be investigated. Understanding how various training protocols influence pannexin-1 concentrations may provide valuable information regarding the mechanisms of exercise-induced adaptations in muscle function.

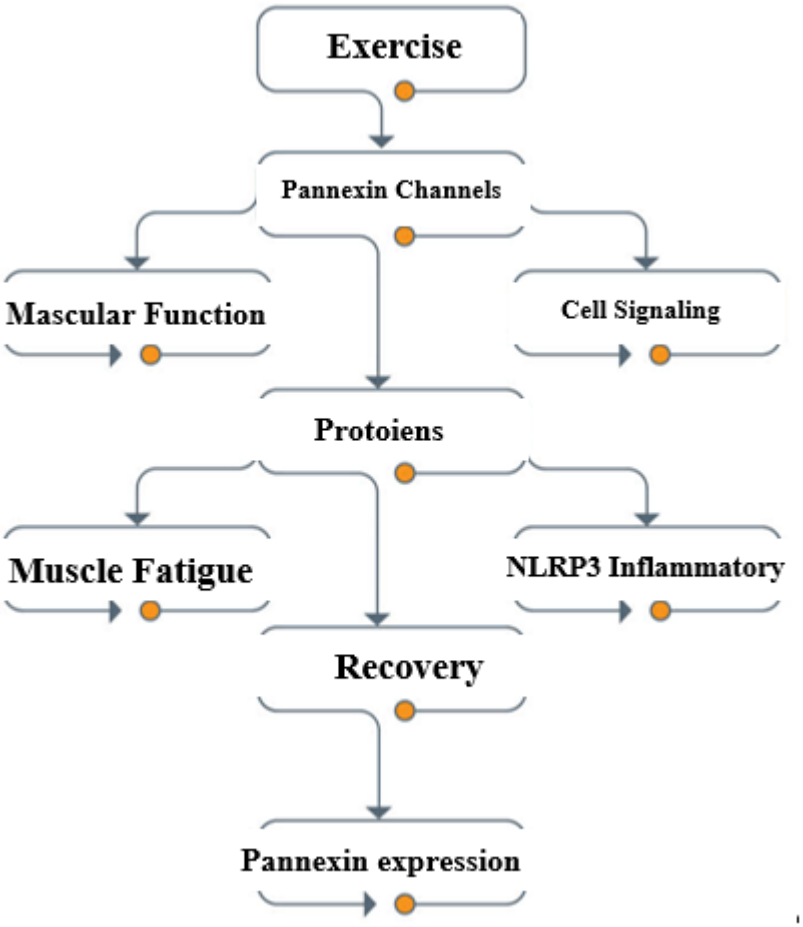

Figure 1. Overview of the effects of exercise on the pannexin-1 channel.

3.2 Exercise and NLRP3

NLRP3 is an intracellular multicomponent structure that is a key player in the immune response and now an undisputed key player in the area of exercise-induced adaptation. Activation of this complex triggers the discharge of pro-inflammatory cytokines interleukin-1 beta (IL-1β) and interleukin-18 through a process known as pyro ptosis (26, 27). Such inflammatory mediators, while necessary to fight infection, are involved in tissue damage in chronic inflammatory disorders (18, 19).

The relationship between exercise and NLRP3 activation is multifaceted and complex, with acute exercise exerting both activating (19) and inhibitory (17) effects depending on the intensity and duration of exercise. Acute exercise can activate NLRP3 in certain tissues, which can lead to acute muscle damage and inflammation (17, 28). This activation is attributed to mechanisms such as cellular stress and the generation of reactive oxygen species during high-intensity exercise (27, 29). Moderate exercise, on the other hand, may exert an anti-inflammatory effect by downregulating NLRP3 activation (19). This downregulation can be in the form of enhanced production of anti-inflammatory cytokines or inhibition of pro-inflammatory signaling cascades (21, 30). Chronic exercise training will increase long-term adaptations of the body that are able to modulate the activation of NLRP3 inflammasome. Chronic exercise will lower the basal level of activation of the NLRP3 inflammasome such that there is less chronic inflammation (16, 19). In line with this, exercise has also been reported to reduce NLRP3 activation and resultant inflammation in old individuals, pointing towards NLRP3-inflammatory response being key to exercise adaptation of neuro-muscular tissue (31). Exercise training may potentially induce muscle function and well-being via repression of NLRP3-pyroptosis, a form of programmed death of muscle cells (32). This action might be particularly critical to prevent sarcopenia, which is loss of muscle mass due to age. The association is further complicated by the presence of an interaction of pannexin channels with NLRP3 (32). During extended exercise activity of long duration, NLRP3-mediated inflammation has the ability to trigger extreme adaptations within the neuro-muscular system. For instance, IL-1β release can cause satellite cell proliferation and differentiation, the cells that play a role in muscle growth and regeneration. Also, inflammation augments remodelling of neuro-muscular tissues and plays a role in strength and endurance acquisition (33).

However, studies are ongoing as to how different types of exercise with different volumes and intensities influence NLRP3 activation and association with pannexin-1, and the precise mechanisms need to be researched. This is important as it has been shown that over-activation or chronic activation of NLRP3 may result in the development of neuro-muscular disease. For example, in intervertebral disc degeneration, NLRP3 activation through mechanical stress can lead to apoptosis, inflammation, and extracellular matrix degradation of disc tissue (34). Similarly, in type 2 diabetes and obesity, NLRP3 activation has been shown to play a role in the onset of insulin resistance and muscle atrophy (35). But other research has not found a direct correlation between pannexin-1 and exercise performance (36), and further research is needed to understand these complicated interactions. Figure 2 shows the effect of exercise on NLRP3.

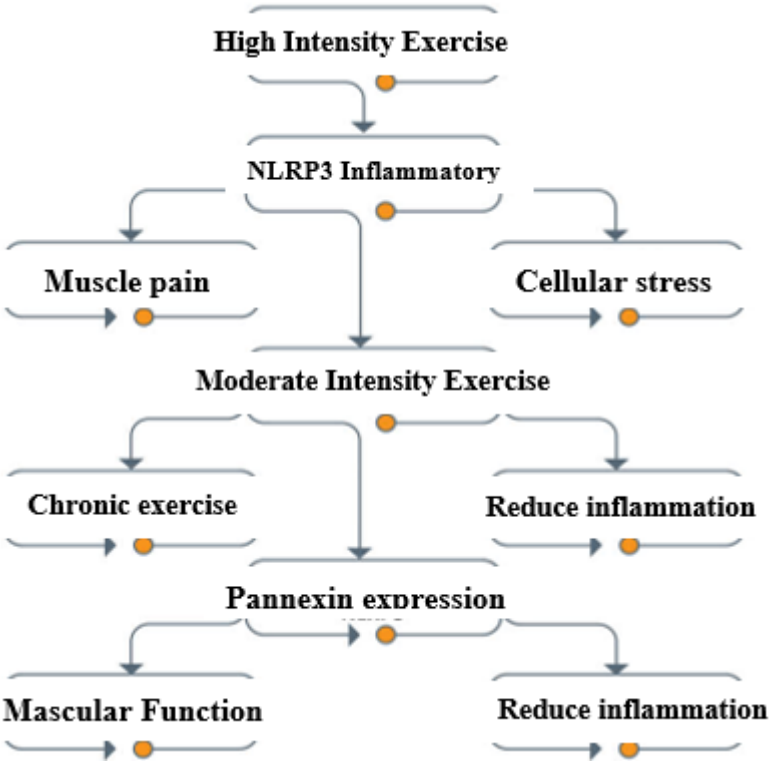

Figure 2. Overview of the effects of exercise on NLRP3

3.3 Exercise and Novel Peptides

3.3.1 Irisin

Irisin has been found in 2012 and has since become a major contributor in exercise physiology. This small peptide is a product of a large fibronectin type III domain-containing protein 5 (FNDC5), and it is released predominantly by muscle cells in a tightly controlled manner by exercise (21). The interaction between irisin and exercise intensity has been a topic of great interest in areas where it has been proposed to be a consequence of greater elevation in irisin than would be achieved through moderate-intensity exercise (17). Cumulative episodes of repeated exercise training would also cause a larger capacity for irisin production by the body and potentially to long-term changes in a direction towards good health with time (6). The exact mechanism through which exercise leads to irisin release remains obscure but is most likely through a process of PGC-1α upregulation, gene transcriptional coactivator of energy metabolism gene (37). Exercise-activated irisin release would be involved in muscle contraction and fatigue through influencing mitochondrial function, glucose uptake, and inflammation (38). Furthermore, long-term exercise training brings about strong neuro-muscular adaptations such as muscle type shifting to an adaptive type, muscle strength, and endurance. These are achieved through irisin release and opening of channels in pannexin-1 and affect gene expression, protein synthesis, and metabolism in muscle (11, 37). For example, exercise-activated irisin would lead to browning of white adipose tissue in contributing to generation of heat and metabolizing calories (20). Such a "browning effect" would lead to an elevation in energy exertion and would make irisin a therapeutically amenable target for health in metabolically. In addition to affecting muscle tissue, irisin is also found to regulate glucose uptake and metabolism in muscle tissue to induce increased insulin sensitivity (21, 30). Beyond affecting muscle tissue, irisin is also found to have effect on brain function and defense in some capacity with studies showing it may be beneficial to memory and anti-inflammation in the brain (8, 39). The potential interaction between irisin and pannexin-1 channels and NLRP3 is a new area of study with potential to shed more information about complex processes of exercise adaptation. Pannexin-1 channels responsible for ATP release have potential to indirectly affect irisin release through pathways of exercise signaling. The release of ATP through pannexin-1 is heightened with intense activity (9). NLRP3 is

a primary mediating factor of inflammation. Another layer of complexity is added to this process. While exercise has variable effects on NLRP3 activation with duration and severity of activity differing based on circumstances, long-term training in this activity may be a factor in contributing to reduced baseline inflammation (19). The potential anti-inflammatory effect of irisin is responsible for this regulation of inflammation with exercise activity and an interaction of irisin release and NLRP3 regulation of inflammation with routine physical activity is suggested (17). It is important to note, however, although this interaction between irisin, pannexin-1 channels, and NLRP3 is fascinating, this area of study is in its infancy. Exactly how these elements are involved with one another and how they work to have effect on exercise adaptations is yet to be discovered. Figure 3 is a summary of how exercise impacts irisin.

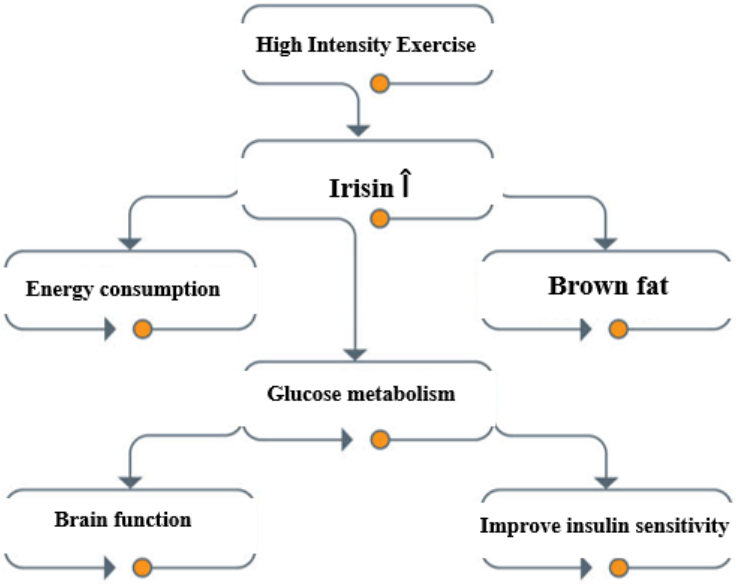

Figure 3. Overview of the effects of exercise on irisin

3.3.2 Interleukin-6

Interleukin-6 Interleukin-6 (IL-6), a major muscle-secreted myokine in exercise work, has emerged as an essential piece in clarifying multifaceted physiological responses to physical work. Muscle contraction is the major stimulus for IL-6 secretion by muscle fibers, and physical work intensity and duration are critical in regulating its expression (22). Intense physical work has been found to cause a tremendous surge in IL-6 production relative to moderate physical work (17). Moreover, long-duration training in exercise has been found to challenge the body to produce IL-6 to a larger magnitude, a long-term adaptive response to prolonged physical work (22). A number of potential pathways are likely to be responsible for coupling muscle contractions and IL-6 release including shifts in intracellular calcium balance, disruption in glucose supply, and production of reactive oxygen species (40). The purported function of IL-6 in exercise adaptation is complex and is the focus of active investigation. The most intriguing area of investigation is its influence on muscle metabolism. IL-6 plays a part in glucose metabolism and glucose uptake in skeletal muscle and possesses the potential to improve insulin sensitivity (21, 29, 30). The potential influence of metabolism would improve the body's ability to utilize glucose for fuel in response to exercise and result in improved endurance and performance. IL-6 is also involved in "browning" white fat to transform it into brown fat tissue more metabolically advanced in generating heat and consuming calories (19, 41). The browning effect would enhance burning calories and loss of adipose tissue and render IL-6 a viable therapeutic target in terms of metabolic health. Interestingly, whereas IL-6 is classically considered a pro-inflammatory cytokine, its production in response to exercise has a more complex function. Production of IL-6 in response to exercise might be anti-inflammatory in nature (42, 43) and possibly underlying the reported reduction in chronic, low-grade inflammation in response to regular

physical activity (19). Such an anti-inflammatory effect would be beneficial in repairing muscle and in recovery post-exercise and in eliciting the adaptive response leading to improved strength and endurance with duration. The interaction between IL-6, pannexin-1 channels, and NLRP3 is a new field of study with a potential to offer useful insight into the complex process of adaptations induced by exercise. Muscle pannexin-1 channels are responsible for ATP release to control IL-6 production (13). Exercise-induced IL-6 release has the potential to stimulate satellite cell proliferation and differentiation in muscle development and repair (11, 44). Pannexin-1 channel effects are also involved in gene profile and muscle synthesis of proteins in muscle to result in enhanced muscle endurance and muscle strength (11). How channels are involved in exercise-induced IL-6 release is unknown and merits in-depth studies (10). Exercise has variable effects on NLRP3 activation, where repeated training may result in decreased basal NLRP3 activity (19). The potential anti-inflammatory effect of IL-6 is potentially involved in this NLRP3 control of inflammation in response to regular physical activity (17), and it suggests a potential interaction between IL-6 production and NLRP3 inflammation control in response to regular physical activity. The inflammatory process has potential to positively or negatively influence neuro-muscular tissue. A moderate NLRP3 activation is involved in muscle remodeling and adaptability and has potential to cause development of neuro-muscular disease in case of long-term or excessive activation (11). The influence of exercise effect is represented in Figure 4. Overall, more studies are necessary to make definitive links between IL-6, pannexin-1 channels, and NLRP3, and to define specifically how physical exercise controls them. When progress in this area is made, new information about underlying molecular processes for positive impact of physical exercise on muscle metabolism, inflammation response, and overall health can be provided.

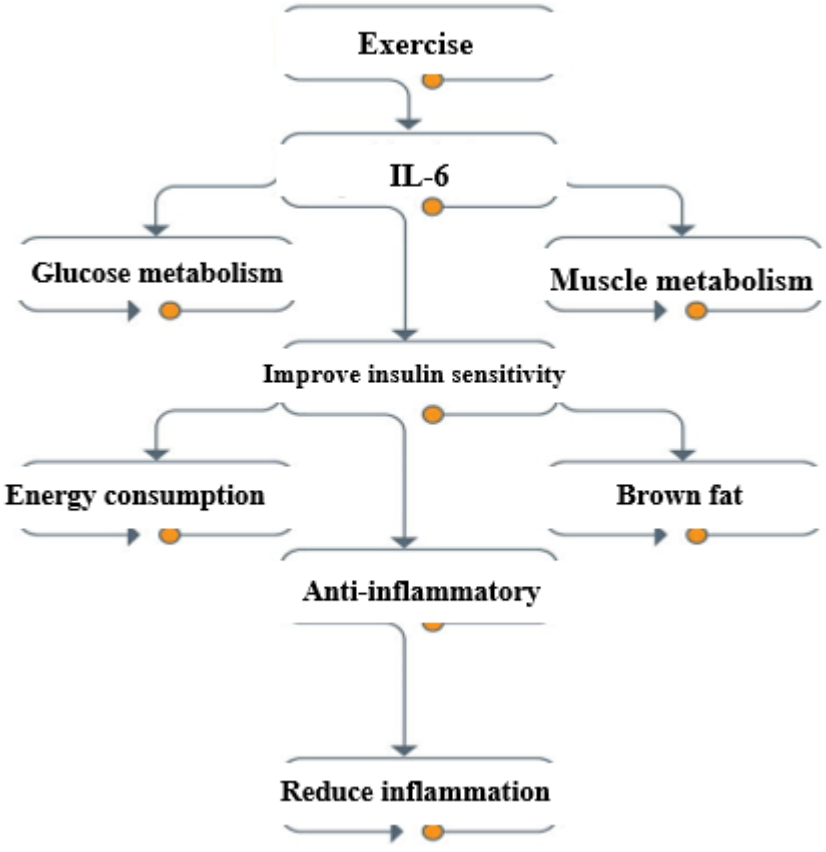

Figure 4. Overview of the effects of exercise on interleukin-6

4. Discussion and Conclusion

Exercise has deep influences on neuro-muscular performance by stimulating pannexin channels (specifically pannexin-1), the NLRP3 pathway, and novel exercise-derived peptides such as irisin and the myokine IL-6. Exercise-stimulated pannexin-1 activation and ATP release can influence muscle contraction, fatigue, and recovery. In addition, pannexin-1 expression could be controlled by exercis. Exercise, however, has a very deep influence on NLRP3 activation in neural and muscular tissues. The pathway also has a double role in exercise-induced inflammation and neuro-muscular adaptation. Additionally, novel exercise-induced peptides like irisin and interleukin-6 are able to act on pannexin channels and NLRP3 to influence the overall neuro-muscular exercise response.

Even with improved knowledge regarding the impact exercise has on the body at a molecular level, improvement is necessary. To gain the ability to tailor its benefits, further study in major pathways such as pannexin-1 (Panx1), NLRP3, and myokines such as interleukin-6 (IL-6) and irisin is essential. Scientists have to investigate if the blockade of Panx1 attenuates the release of IL-6 with exercise to ensure an immediate link. Furthermore, the function of NLRP3—a central inducer of inflammation—must be explored under different levels of exercise and over time to determine if chronic exercise suppresses its activity, possibly via the IL-6 pathway. Irisin, which induces the browning of calorie-storing white fat to energy-expending brown fat, must also be explored to determine the precise molecular mechanisms through which it functions in muscle and fat tissue. Interestingly, both genders will have to be involved in future research to consider the potential for variability and go beyond acute response to identify the chronic effect of prolonged exercise on these systems. By considering these factors, researchers can follow the complex interaction between Panx1, NLRP3, IL-6, and irisin, following the molecular chain reaction started by exercise. This further information can lead the way to personalized exercise routines founded on one's biology and potentially to new drugs that mimic the therapeutic effects of exercise in persons who cannot exercise. Unraveling these molecular relationships will ultimately enable us to maximize the disease-prevention, metabolic, and quality-of-life-promoting potential of exercise throughout life.

Authors' Contributions

All authors equally contributed to this study.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

Data are available for research purposes upon reasonable request to the corresponding author.

Acknowledgments

We would like to express our gratitude to all individuals helped us to do the project.

Declaration of Interest

The authors report no conflict of interest.

Funding

According to the authors, this article has no financial support.

Ethical Considerations

The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants.

References

1. Cicco TD, Pęziński M, Wójcicka O, Rottner K, Prószyński TJ. Cortactin Interacts With ADystrobrevin-1 and Regulates Neuromuscular Junction Morphology. 2023. [DOI]
2. Sanchís-Gomar F, López-López S, Romero-Morales C, Maffulli N, Lippi G, Pareja-Galeano H. Neuromuscular Electrical Stimulation: A New Therapeutic Option for Chronic Diseases Based on Contraction-Induced Myokine Secretion. Frontiers in Physiology. 2019;10. [PMID: 31849710] [PMCID: PMC6894042] [DOI]
3. Ge D, Lavidis NA. Climatic Modulation of Neurotransmitter Release in Amphibian Neuromuscular Junctions: Role of Dynorphin-A. Ajp Regulatory Integrative and Comparative Physiology. 2018;314(5):R716-R23. [PMID: 29341829] [DOI]
4. Ratliff WA, Saykally JN, Kane MJ, Citron BA. Neuromuscular Junction Morphology and Gene Dysregulation in the Wobbler Model of Spinal Neurodegeneration. Journal of Molecular Neuroscience. 2018;66(1):114-20. [PMID: 30105628] [PMCID: PMC6684170] [DOI]
5. Rebolledo DL, Aldunate R, Kohn R, Neira I, Minniti AN, Inestrosa NC. Copper Reduces A Oligomeric Species and Ameliorates Neuromuscular Synaptic Defects in a C. Elegans Model of Inclusion Body Myositis. Journal of Neuroscience. 2011;31(28):10149-58. [PMID: 21752991] [PMCID: PMC6623047] [DOI]

6. Bolotta A, Filardo G, Abruzzo PM, Astolfi A, De Sanctis P, Di Martino A, et al. Skeletal muscle gene expression in long-term endurance and resistance trained elderly. International Journal of Molecular Sciences. 2020;21(11):3988. [PMID: 32498275] [PMCID: PMC7312229] [DOI]
7. Gorgij E, Fanaei H, Yaghmaei P, Shahraki MR, Mirahmadi H. Maternal treadmill exercise ameliorates impairment of neurological outcome, caspase-1 and NLRP3 gene expression alteration in neonatal hypoxia-ischemia rats. Iranian Journal of Basic Medical Sciences. 2023;26(2):228.
8. Solimani Farsani M, Fathi M, Hemati Z, Gorgin Z. Investigating the Relationship between Neuromuscular Junction Preservation and Regeneration Factors and Hippocampal Inflammatory Factors under the Influence of Swimming Exercise in Alzheimer's Model Rats. Journal of Sabzevar University of Medical Sciences. 2024;31(2):248-34.
9. Cea LA, Riquelme MA, Vargas AA, Urrutia C, Sáez JC. Pannexin 1 channels in skeletal muscles. Frontiers in Physiology. 2014;5:139. [PMID: 24782784] [PMCID: PMC3990038] [DOI]
10. Wakefield B. Pannexin3 in exercise, obesity, and osteoarthritis: The University of Western Ontario (Canada); 2023.
11. Wakefield B, Penuela S. Potential implications of exercise training on pannexin expression and function. Journal of Vascular Research. 2023;60(2):114-24. [PMID: 36366809] [DOI]
12. Fernandez FJ. Role of pannexin in excitation-contraction coupling of skeletal muscle: Université de Lyon; 2021.
13. Riquelme MA, Cea LA, Vega JL, Boric MP, Monyer H, Bennett MV, et al. The ATP required for potentiation of skeletal muscle contraction is released via pannexin hemichannels. Neuropharmacology. 2013;75:594-603. [PMID: 23583931] [DOI]
14. de Resende e Silva DT, Bizuti MR, de Oliveira NR, Lima LZM, dos Santos Arraes VG, Zietz ACG, et al. Physical exercise as a modulator of the purinergic system in the control of sarcopenia in individuals with chronic kidney disease on hemodialysis. Purinergic Signalling. 2023:1-10. [PMID: 37368148] [PMCID: PMC11189381] [DOI]
15. Kazemi A, Eslami R, Karimghasemi L. The effect of high-intensity interval training on tumor necrosis factor-alpha levels in visceral and subcutaneous adipose tissue and insulin resistance in male rats. Sport Physiology. 2016;8(32):17-30.
16. Ding P, Song Y, Yang Y, Zeng C. NLRP3 inflammasome and pyroptosis in cardiovascular diseases and exercise intervention. Frontiers in Pharmacology. 2024;15:1368835. [PMID: 38681198] [PMCID: PMC11045953] [DOI]
17. Liu Z, Yang Y, Song L, Ruan X, He Y, Zou Y, et al. Aerobic exercise alleviates diabetic cardiomyopathy via attenuation of P2X4-mediated NLRP3 inflammasome activation and cardiomyocyte pyroptosis. [Add journal name]. 2024. [DOI]
18. Rayavarapu S, Coley W, Kinder TB, Nagaraju K. Idiopathic inflammatory myopathies: pathogenic mechanisms of muscle weakness. Skeletal Muscle. 2013;3:1-13. [PMID: 23758833] [PMCID: PMC3681571] [DOI]
19. de Paula Martins R, Lim CK, Ghisoni K, Staats A, Dallagnol K, Solano A, et al. Treating depression with exercise: The inflammasome inhibition perspective. Journal of Systems and Integrative Neuroscience. 2016;3(1):1-8. [DOI]
20. Zhang Y, Wang L, Kang H, Lin CY, Fan Y. Unlocking the therapeutic potential of irisin: Harnessing its function in degenerative disorders and tissue regeneration. International Journal of Molecular Sciences. 2023;24(7):6551. [PMID: 37047523] [PMCID: PMC10095399] [DOI]
21. Gomarasca M, Banfi G, Lombardi G. Myokines: The endocrine coupling of skeletal muscle and bone. Advances in Clinical Chemistry. 2020;94:155-218. [PMID: 31952571] [DOI]
22. Bustamante M, Fernández-Verdejo R, Jaimovich E, Buvinic S. Electrical stimulation induces IL-6 in skeletal muscle through extracellular ATP by activating Ca2+ signals and an IL-6 autocrine loop. American Journal of Physiology-Endocrinology and Metabolism. 2014;306(8):E869-E82. [PMID: 24518675] [PMCID: PMC3989743] [DOI]
23. Rami M, Fathi M, Rahmati M, Tabandeh MR. Effect of 6 weeks endurance exercise on hippocampal pannexin-1 and NLRP-1 protein levels in experimental diabetic male Wistar rats. Journal of Shahid Sadoughi University of Medical Sciences. 2020. [DOI]
24. Makarenkova HP, Shestopalov VI. The role of pannexin hemichannels in inflammation and regeneration. Frontiers in Physiology. 2014;5:63. [PMID: 24616702] [PMCID: PMC3933922] [DOI]
25. Luo Y, Zheng S, Xiao W, Zhang H, Li Y. Pannexins in the musculoskeletal system: new targets for development and disease progression. Bone Research. 2024;12(1):26. [PMID: 38705887] [PMCID: PMC11070431] [DOI]
26. Jorquera G, Russell J, Monsalves-Álvarez M, Cruz G, Valladares-Ide D, Basualto-Alarcón C, et al. NLRP3 inflammasome: potential role in obesity related low-grade inflammation and insulin resistance in skeletal muscle. International Journal of Molecular Sciences. 2021;22(6):3254. [PMID: 33806797] [PMCID: PMC8005007] [DOI]
27. Qiu Z, Lei S, Zhao B, Wu Y, Su W, Liu M, et al. NLRP3 inflammasome activation-mediated pyroptosis aggravates myocardial ischemia/reperfusion injury in diabetic rats. Oxidative Medicine and Cellular Longevity. 2017;2017(1):9743280. [PMID: 29062465] [PMCID: PMC5618779] [DOI]
28. Joukar S, Rajizadeh MA, Bejeshk MA, Alavi SS, Bagheri F, Rami M, et al. ATP releasing channels and the ameliorative effects of high intensity interval training on diabetic heart: a multifaceted analysis. Scientific Reports. 2024;14(1):7113. [PMID: 38532054] [PMCID: PMC10965991] [DOI]
29. Llanos P, Palomero J. Reactive Oxygen and Nitrogen Species (RONS) and Cytokines-Myokines Involved in Glucose Uptake and Insulin Resistance in Skeletal Muscle. Cells. 2022;11(24):4008. [PMID: 36552772] [PMCID: PMC9776436] [DOI]
30. Pillon NJ, Smith JA, Alm PS, Chibalin AV, Alhusen J, Arner E, et al. Distinctive exercise-induced inflammatory response and exerkine induction in skeletal muscle of people with type 2 diabetes. Science Advances. 2022;8(36):eabo3192. [PMID: 36070371] [PMCID: PMC9451165] [DOI]
31. Ding Y, Xu X. Effects of regular exercise on inflammasome activation-related inflammatory cytokine levels in older adults: A systematic review and meta-analysis. Journal of Sports Sciences. 2021;39(20):2338-52. [PMID: 34121608] [DOI]
32. Fu P, Gong L, Yang L, Tang S, Ma F. Weight bearing training alleviates muscle atrophy and pyroptosis of middle-aged rats. Frontiers in Endocrinology. 2023;14:1202686. [PMID: 37720530] [PMCID: PMC10499618] [DOI]
33. Higashikuni Y, Liu W, Numata G, Tanaka K, Fukuda D, Tanaka Y, et al. NLRP3 inflammasome activation through heart-brain interaction initiates cardiac inflammation and hypertrophy during pressure overload. Circulation. 2023;147(4):338-55. [PMID: 36440584] [DOI]
34. Chang HI, Chen CN, Huang KY. Mechanical stretch-induced NLRP3 inflammasome expression on human annulus fibrosus cells modulated by endoplasmic reticulum stress. International Journal of Molecular Sciences. 2022;23(14):7951. [PMID: 35887297] [PMCID: PMC9323355] [DOI]
35. Ramachandran R, Manan A, Kim J, Choi S. NLRP3 inflammasome: a key player in the pathogenesis of lifestyle disorders. Experimental & Molecular Medicine. 2024. [PMID: 38945951] [PMCID: PMC11297159] [DOI]

36. Møller S, Hansen CC, Ehlers TS, Tamariz-Ellemann A, Tolborg SAR, Kurell ME, et al. Exercise training lowers arterial blood pressure independently of pannexin-1 in men with essential hypertension. Medicine & Science in Sports & Exercise. 2022;54(9):1417-27. [PMID: 35420578] [DOI]
37. Lin J, Liu X, Zhou Y, Zhu B, Wang Y, Cui W, et al. Molecular basis of irisin regulating the effects of exercise on insulin resistance. Applied Sciences. 2022;12(12):5837. [DOI]
38. Ning K, Wang Z, Zhang XA. Exercise-induced modulation of myokine irisin in bone and cartilage tissue-Positive effects on osteoarthritis: A narrative review. Frontiers in Aging Neuroscience. 2022;14:934406. [PMID: 36062149] [PMCID: PMC9439853] [DOI]
39. Karaji ZG, Fathi M, Mirnasori R, van der Zee E. Swimming exercise and clove oil can improve memory by molecular responses modification and reduce dark cells in rat model of Alzheimer's disease. Experimental Gerontology. 2023;177:112192. [PMID: 37119836] [DOI]
40. Fischer CP. Interleukin-6 in acute exercise and training: what is the biological relevance? 2002.
41. Kazemi A, Eslami R, Ghayed Ali M, Ghanbarzadeh M. Effects of 6 weeks of low volume high intensity interval training on serum levels of leptin, glucose, and body fat in young wrestlers. Scientific Journal of Kurdistan University of Medical Sciences. 2015;20(2):70-7.
42. Liu J, Jia S, Yang Y, Piao L, Wang Z, Jin Z, et al. Exercise induced meteorin-like protects chondrocytes against inflammation and pyroptosis in osteoarthritis by inhibiting PI3K/Akt/NF-κB and NLRP3/caspase-1/GSDMD signaling. Biomedicine & Pharmacotherapy. 2023;158:114118. [PMID: 36527845] [DOI]
43. Abbasi F, Pourjalali H, do Nascimento IBJ, Zargarzadeh N, Mousavi SM, Eslami R, et al. The effects of exercise training on inflammatory biomarkers in patients with breast cancer: A systematic review and meta-analysis. Cytokine. 2022;149:155712. [PMID: 34644675] [DOI]
44. de Sousa CAZ, Sierra APR, Martínez Galán BS, Maciel JFdS, Manoel R, Barbeiro HV, et al. Time course and role of exercise-induced cytokines in muscle damage and repair after a marathon race. Frontiers in Physiology. 2021;12:752144. [PMID: 34721075] [PMCID: PMC8554198] [DOI]