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Traverse Galina[1], Horoshko Viktoriia[1],
Danylchenko Svitlana[2]

The Effect of Physical Activity on the Secretory Function of Muscles and Bone Tissue in Humans

[1]National University Yuri Kondratyuk Poltava Polytechnic
[2]Kherson State University, Kherson, Ukraine

The purpose of the study was to summarize new literature data on the effect of physical activity on the secretory function of skeletal muscles and their relationship with organs.

Materials and methods. Analytical methods were used in the study. The search for scientific information was carried out in databases of search systems.

Results. Muscles secrete proteins called myokines, which are involved in a variety of processes by interacting with tissues. Current research has shown that exercise, by stimulating the skeletal muscle system in vivo, leads to the release of myokines and causes several effects that explain the positive effect of exercise in the treatment of several diseases of the musculoskeletal system.

Skeletal muscles synthesize and secrete a wide range of myokines that contribute to various functions in organs, including the brain. Recent publications have focused much attention on one such myokine, the recently discovered protein irisin, which is secreted into the bloodstream from skeletal muscle during exercise from the membrane-bound precursor fibronectin type III. Irisin promotes metabolic processes such as glucose homeostasis and the darkening of white adipose tissue. Irisin also crosses the blood-brain barrier and initiates a neuroprotective genetic program in the hippocampus, which culminates in increased expression of brain-derived neurotrophic factors. Most studies report that irisin concentration is closely related to health status. For example, irisin levels are significantly lower in patients with obesity, osteoporosis/fracture, muscular atrophy, Alzheimer's disease, and cardiovascular disease.

Over the past decade, several myokines have been discovered, expanding our understanding of how muscles interact with other organs. In recent publications, a lot of attention is paid to the recently discovered protein irisin, which contributes to metabolic processes. A series of studies on irisin have provided new insights into the mechanisms of exercise to improve bone density, counteract cartilage degeneration, and maintain overall joint environmental homeostasis. These studies further contribute to the understanding of the role of exercise in the fight against osteoarthritis and may provide important assistance in advancing the prevention and treatment of this common disease.

Research on the exercise-induced muscle factor irisin will help to better understand and explain the beneficial effects of exercise on maintaining physical health, especially in the fight against aging and age-related degenerative changes.

Conclusion. Thus, exercise-induced stimulation of bioactive cytokines increases muscle anabolism, bone formation, mitochondrial biogenesis, glucose utilization, and fatty acid oxidation, and reduces chronic inflammation.

Keywords: skeletal muscles, myokines, protein irisin, bone density, environmental homeostasis, age-related degenerative changes.

Introduction. The skeletal muscle is the largest organ of the body. Skeletal muscles are primarily characterized by their mechanical activity required for posture, movement, and respiration, which depend on the contractions of the muscle fibers. However, skeletal muscle is not just a component of the musculoskeletal system. During the last decade, skeletal muscle has been identified as a secretory organ. Muscles have been shown to secrete proteins called myokines that are involved in a variety of processes by interacting with other tissues. Current research has shown that exercises can stimulate the skeletal muscle system in vivo, inducing the release of myokines, and generating new insights to explain the beneficial effects of exercise in the treatment of several musculoskeletal disorders.

Exercise is known to have a beneficial effect on improving metabolic disorders, and a combined therapeutic regimen of regular exercise and drug treatment is often recommended. The biology of exercise is complex and involves various metabolic and molecular changes that lead to changes in substrate utilization, enzyme activation, and conversely, improved physical performance. Over the past few decades, several myokines have been discovered, such as interleukin-6, irisin, myostatin, interleukin-15, brain-derived neurotrophic factor, β-aminoisobutyric acid, leukemia-inhibiting meteorin-like factor, and secreted protein. acidic and rich in cysteine, according to secretome analysis. The existence of myokines has

expanded the understanding of how muscles interact with other organs, such as bones and brain, adipose tissue, and the liver, to exert the beneficial effects of exercise at a whole-body level [1].

As an endocrine organ, skeletal muscle synthesizes and secretes a wide range of myokines that contribute to various functions in various organs, including the brain. Much attention has been paid in recent publications to myosin, the recently discovered protein irisin, which is secreted into the bloodstream from skeletal muscle during exercise from its membrane-bound precursor type III fibronectin [2]. Irisin promotes metabolic processes such as glucose homeostasis and white adipose tissue darkening. Irisin also crosses the blood-brain barrier and initiates a neuroprotective genetic program in the hippocampus, which culminates in increased expression of brain-derived neurotrophic factors. Most studies report that irisin concentration is closely related to health status. For example, irisin levels are significantly lower in patients with obesity, osteoporosis/fractures, muscle atrophy, Alzheimer's disease, and cardiovascular disease [3].

Many authors provide a significant role in the effect of irisin on bone metabolism, namely, the role of irisin in the regulation of bone mineral density, and bone metabolism, as well as its role in homeostasis and metabolism of chondrocytes is considered. A series of studies on irisin have provided new insights into the mechanisms of exercise to improve bone density, counteract cartilage degeneration, and maintain overall joint environmental homeostasis. These studies further contribute to understanding the role of exercise in the fight against osteoarthritis and may provide important assistance in advancing the prevention and treatment of such a common disease as osteoarthritis [4, 5].

The purpose of the study was to summarize new literature data on the effect of physical activity on the secretory function of skeletal muscles and their relationship with other organs.

Materials and methods. Analytical and bibliosemantic methods were used in the study. The search for scientific information was carried out in databases of electronic search systems.

Research results and discussion. It is known that skeletal muscles and bones are related anatomically and physiologically and play a crucial role in human locomotion and metabolism. Historically, the relationship between muscle and bone has been viewed in light of mechanotransduction, which dictates that mechanical forces applied to muscle are transferred to the skeleton to initiate bone formation. However, these organs also interact through an endocrine system driven by a family of cytokines, namely myokines (derived from myocytes) and osteokines (derived from bone cells). A third player in this biochemical crosstalk is adipose tissue and the secretion of adipokines (derived from adipocytes) [6].

Myokines, osteokines, and adipokines have local autocrine/paracrine effects, as well as through the endocrine system, regulating muscle, bone, and fat metabolism. Decreased physical activity and increased energy intake associated with aging lead to adipocyte hypertrophy and the involvement of immunological cells (macrophages). In turn, a decrease in physical activity releases pro-inflammatory adipokines, which cause chronic mild inflammation, a key link in the pathology of several diseases [7].

One of the chronic degenerative diseases of the musculoskeletal system is osteoarthritis (OA), which is characterized by pathological changes in articular structures, the frequency of this pathology increases with age. According to incomplete statistics, OA affects about 240 million people worldwide, which is about 3.8% of the total world population. The prevalence of OA is significantly higher among the elderly, and this prevalence among adults over 65 years of age is more than 1/3 of the general population [8, 9]. Its prevalence is expected to continue to rise significantly in the future, along with an aging population. OA has become a global public health problem.

Exercise is considered a key factor in the treatment of OA and is central to non-drug management. Physical activity is based on skeletal muscle activity, so exercise therapy may be effective in reducing pain associated with OA, improving physical function, and significantly reducing the risk of disability in OA. Remarkably, age does not seem to affect the benefits of exercise, and the improvement in joint function after exercise is similar in older and younger adults. In addition, exercise has been shown to delay skeletal sarcopenia and osteopenia and reduce the risk of diseases such as mechanical arthritis of the knee and hip that accompanies muscle loss [10]. Thus, exercise deserves further attention as a relatively safe treatment modality [11], but the mechanisms that modulate OA with exercise are still unclear.

Most studies have concluded that moderate-intensity resistance exercise significantly increases irisin levels [12]. However, different types of exercise showed very different effects on irisin induction. In a recent study, a resistance training experiment was designed for rats on a high-fat diet. After 12 weeks of training, in training rats, serum levels of total cholesterol and triglycerides decreased, and serum irisin concentrations increased. The authors suggested that the increased level of irisin in the blood serum of rats is associated with muscle contraction during exercise [13]. In a 2019 mouse experiment, exercise-induced irisin had an antioxidant stress effect and reduced smoking-induced emphysema [14].

It has recently been demonstrated that various types of exercise, including aerobic exercise, resistance and vibration exercise, and skeletal muscle electrical stimulation, increased irisin expression in the mouse myocardium. This resulted in the stimulation of mitochondrial phagocytosis, increased antioxidant function, and thus improved cardiac function with a more significant effect from resistance exercise. Resistance exercise plays an important role in increasing the serum concentration of irisin [15]. In addition, the study compared serum irisin levels at different stages of exercise in subjects with different levels of fitness in two different forms of exercise, cycling and sprinting, in detail. The researchers found that irisin expression was independent of the type of intense exercise and training status of the subjects, but that running caused a more sustained increase in irisin compared to cycling. The difference in the duration of irisin activation may be related to the higher rate of fat oxidation during running compared to cycling at the same relative intensity. A recent study reported that 35 minutes of high-intensity interval training during aerobic exercise induced a higher peak response to serum irisin in healthy adolescents compared to moderate, continuous-intensity exercise. High-intensity exercise induced a higher peak serum irisin response in healthy adolescents compared to moderate continuous exercise, while irisin induction was not evident with exercise in obese or overweight adolescents. Differences in the rate of fat oxidation provide a possible explanation for differences in irisin expression in different forms of exercise [16].

However, not all results of irisin modulation during exercise are consistent. Some studies have shown that chronic resistance training significantly reduced blood concentrations of irisin in a randomized controlled trial and that irisin also tended to decrease with endurance exercise. In the published literature, exercises that cause a decrease in serum irisin levels have included high-intensity circuit training, mixed physical training, intermittent sprint training, indoor aerobic training, and high-altitude mountaineering [17]. In addition, even in studies that report an increase in irisin levels after training, the timing of the increase in irisin levels is different. Additional research indicates that irisin activation occurs immediately after exercise. It has also been reported that the increase in irisin levels induced by short-term exercise in subcutaneous and visceral adipose tissue could persist for 1 week after exercise was stopped, and gradually returned to normal levels only 3 weeks after exercise was stopped.

Other authors have shown that cold environments can induce muscle tremors, which produce an irisin-raising effect similar to exercise. The study examined changes in serum irisin concentration after swimming in cold water. Interestingly, when cold was combined with exercise, winter swimmers unexpectedly experienced a significant decrease in serum levels of irisin [18], possibly due to different tissue sources and the metabolic environment of irisin. In addition, physical exercise does not always play a positive role in the metabolic processes of the body and may cause increased expression of some inflammatory factors. Excessive exercise has been shown to cause the activation of inflammatory factors [19].

However, despite some controversy, the positive role of irisin in the regulation of exercise-induced metabolism is generally recognized. Interesting data were presented by several authors on the relationship between irisin and aging. It has been shown that exercise-induced expression of irisin is associated with resistance to aging. A rat study compared the effects of age and exercise on irisin levels in rat heart, liver, and plasma samples. The results showed that aging reduces the level of irisin in the above tissues. Regular exercise increased irisin expression in all analyzed tissues compared to a sedentary lifestyle [19]. Recent studies have also shown that irisin is associated with improved neurocognitive function in the elderly and plays a key role in the stimulatory effects of exercise on learning and memory [20].

Thus, irisin has been proven to play a role in several diseases associated with aging. Aging can cause a decrease in the ability of articular cartilage cells to repair, destabilize the cartilage extracellular matrix, and stimulate its degradation. At the same time, irisin causes bone remodeling in the subchondral bone, causing changes in the mechanical stress of the joint, while stopping the progression of osteoarthritis.

Another study showed that irisin enhances the action of the antioxidant enzyme superoxide dismutase. Exogenous irisin suppresses the expression of apoptotic proteins in the postischemic myocardium and inhibits inflammation markers in it. Irisin also supported exercise-induced selective autophagy, and irisin expression correlated with the expression of markers of mitochondrial division and mitochondrial phagocytosis in myotubes [21]. Molecular experiments have shown that irisin also regulates telomerase activity by inhibiting phosphorylation and increasing telomerase activity in senescent hepatocytes, activating autophagy and improving mitochondrial function [22]. A similar association has been demonstrated in articular chondrocytes. In chondrocytes cultured in three dimensions in vitro, treatment with p-irisin significantly reduced phosphorylation levels while significantly reducing inflammatory markers by inhibiting chondrocyte catabolism via extracellular mechanisms [23]. Therefore, irisin promotes a protective effect on chondrocyte mitochondria, increasing chondrocyte

survival in an inflammatory environment and promoting anabolism.

Conclusion. Exercise-induced stimulation of bioactive cytokines increases muscle anabolism, bone formation, mitochondrial biogenesis, glucose utilization, and fatty acid oxidation, and reduces chronic inflammation.

Perspectives of further research. Research on the exercise-induced muscle factor irisin will help to better understand and explain the beneficial effects of exercise on maintaining physical health, especially in the fight against aging and age-related degenerative changes.

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ВПЛИВ ФІЗИЧНОЇ АКТИВНОСТІ НА СЕКРЕТОРНУ ФУНКЦІЮ М'ЯЗІВ І КІСТКОВОЇ ТКАНИНИ ЛЮДИНИ

Траверсе Г. М., Горошко В. І., Данильченко С. І.

Резюме. *Метою* дослідження було узагальнення нових літературних даних про вплив фізичної активності на секреторну функцію скелетних м'язів та її зв'язок з іншими органами.

Матеріали і методи. У дослідженні використано аналітичний та бібліосемантичний методи. Пошук наукової інформації здійснювався в базах даних електронних пошукових систем.

Результати. Сучасні дослідження показують, що фізичні вправи стимулюють скелетну мускулатуру in vivo, що призводить до вивільнення міокінів та спричиняє низку ефектів, які пояснюють позитивні ефекти фізичних вправ у лікуванні багатьох захворювань опорно-рухового апарату. Скелетні м'язи синтезують і виділяють різні міокіни, які сприяють різним функціям органів, включаючи мозок. Іризин, який був синтезований порівняно нещодавно, виділяється зі скелетних м'язів під час фізичних вправ. Іризин сприяє таким метаболічним процесам, як гомеостаз глюкози і потемніння білої жирової тканини. Іризин також долає гематоенцефалічний бар'єр і ініціює програму нейропротекторного гена в гіпокампі. Це збільшує експресію нейротрофічного фактора мозку. Більшість досліджень показали, що рівень іризину тісно пов'язаний зі станом здоров'я. Останні публікації приділили багато уваги нещодавно відкритому білку іризину, який сприяє метаболічним процесам. Серія досліджень щодо іризину дозволила по-новому зрозуміти механізми впливу на покращення щільності кісткової тканини, протидії дегенерації хряща та підтримки загального екологічного гомеостазу суглобів. Ці дослідження можуть додатково сприяти розумінню ролі фізичних вправ у боротьбі з остеоартритом і надати важливу підтримку в просуванні профілактики та його лікування.

Висновок. Індукована фізичними вправами стимуляція біоактивних цитокінів збільшує анаболізм м'язів, формування кісток, мітохондріальний біогенез, утилізацію глюкози та окиснення жирних кислот, а також зменшує хронічне запалення. У перспективі розвитку дослідження іризину можуть краще пояснити сприятливий вплив фізичних вправ на підтримку фізичного здоров'я, особливо в боротьбі зі старінням і пов'язаними з віком дегенеративними змінами.

Ключові слова: скелетні м'язи, міокіни, іризин, щільність кісткової тканини, екологічний гомеостаз, вікові дегенеративні зміни.

ORCID and contributions:
Galina Traverse : 0000-0002-0905-7260 [E,F]
Viktoriia Horoshko : 0000-0002-5244-5648 [A,B,D,E,F]
Svitlana I. Danylchenko : 0000-0001-5312-0231 [D,F]

A – Work concept and design, B – Data collection and analysis,
C – Responsibility for statistical analysis, D – Writing the article,
E – Critical review, F – Final approval of the article

CORRESPONDING AUTHOR
Viktoriia Horoshko
National University Yuri Kondratyuk Poltava Polytechnic,
Department of physical therapy, occupational therapy
24, Pershotravneva Ave., Poltava 36011, Ukraine
phone: +380508009184, e-mail: talgardat@gmail.com

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