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IMPACTS OF PHYSICAL EXERCISE ON THE REGENERATION OF MUSCLE STEM CELLS

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Abstract: This review aimed to explore and analyze recent studies on the impacts of physical exercise on the regeneration of muscle stem cells and the effects on the health of these cells. For the research, different databases were used from 2015 to 2022, with the following indexing terms: "muscle cells", "stem cells", "physical exercises", "muscle regeneration" and "impact of exercises". Stem cells have a high capacity for regeneration and differentiate into specialized cells to promote cellular repair. Furthermore, the impacts of these cells on skeletal muscle tissue have received relevant attention in studies, being considered essential for the process, as they interact with several other regulatory pathways. Despite this, muscle regeneration also depends on a series of other interactions and mechanisms. When analyzing the relationship between muscle regeneration and exercise, physical activity can maintain muscle health and promote the proliferation of stem cells, as well as their rejuvenation, mainly in effect with resistance exercises, which promote the self-renewal of satellite cells. In conclusion, physical activity has a positive impact on the regeneration of muscle stem cells, however, strategies regarding exercise intensity and the mechanisms that specifically interfere with this process need to be better elucidated.
Keywords: exercise, stem cell, regeneration, muscle

INTRODUCTION

Physical exercise is recognized as an important tool for human health, and its practice is widely recommended as a drug-independent strategy for the treatment and/or prevention of various diseases [1]. Its impact on cellular health, particularly on muscle cells, has been increasingly studied, as regularly performed exercise is a stimulating factor that induces a series of adaptations and molecular modifications in skeletal muscle [2].

The mechanisms involved in cellular adaptations promote changes in the content of mRNA, proteins and enzyme activity, a fact that triggers the activation or repression of several signaling pathways, regulating the transcription and translation of proteins. Furthermore, the practice of physical activity leads to increased blood circulation, consequently providing more oxygen and nutrients to muscle cells [3]. Thus, physical activity activates regulatory molecules that coordinate skeletal muscle responses [4].

Studies have shown that physical exercise stimulates the rejuvenation and regeneration of skeletal and cardiac muscle stem cells [5,6]. Stem cells are undifferentiated cells with a high capacity for renewal and which have the ability to produce a specific, highly specialized cell type [7]. Researchers have reported that exercise can increase the number of skeletal muscle stem cells (MuSCs), improving their ability to differentiate and engage in regeneration processes. Furthermore, physical activity can also increase the number of muscle stem cells in the bloodstream and the production of growth factors, which promote muscle regeneration [5].

In this sense, it was found that performing physical exercises significantly increased the number of circulating stem cells and altered mitochondrial oxygen consumption, which was associated with better results in the resistance test [5]. Furthermore, practicing such activities significantly increases the number of muscle stem cells, which differentiate, increasing muscle strength [6].

Thus, knowing that physical exercise appears to have a positive effect on the health of muscle stem cells, as well as improving their quantity and capacity for regeneration, the objective of this work is to verify the mechanisms and processes through which physical exercise can influence the health of these cells.

METHODOLOGY

For the present review, a search was carried out in the PubMed, SciELO and Capes Periodicals databases between the years 2015 and 2022, in Portuguese and English. The following descriptors were used to search for articles, as well as the association of these terms and expressions: “muscle cells”, “stem cells”, “physical exercises”, “muscle regeneration” and “impact of exercises”. Furthermore, the Boolean operator AND was used as a search strategy between indexers. Additionally, other relevant works cited in the selected articles were consulted and referenced.

The titles and abstracts of all studies identified by the search on electronic platforms were selected according to the following inclusion criteria: studies of the impacts of physical exercise on animals and humans, evaluation of changes in muscle strength pattern after injury and analysis of regeneration of muscle stem cells. Furthermore, all articles with models that did not evaluate the effect of physical exercise on muscle cells and articles that did not analyze effects on stem cells were excluded, as well as articles without sufficient data and studies that did not consider the association of physical activity with endurance or muscular strength.

The articles that were related to the research object of the present work were read in full for evaluation according to the inclusion criteria, also excluding those that did not present a specific relationship with the topic covered in this study. Furthermore, other articles were included with the aim of contextualizing, enriching and justifying the topic covered.

RESULTS

In the search and selection process (Figure 1), 27 articles were obtained, which are analyzed in detail in Table 1, which presents a description of the selected articles according to: author, year of publication, type of study and results found.

Initially, the search terms: "muscle stem cell regeneration", "impact of exercise in muscle", "stem cells regeneration muscle" and "physical exercise muscle impact" identified 28560 articles, 8448 articles in PubMed, 166 articles in Scielo and 19946 in Periódicos Capes. Repeated articles (57 articles) and studies that were not directly related to the topic (28352) were then excluded.

In this review, the research revealed 151 articles that were related to the object of study of this work, 5 in Scielo, 91 in Pubmed and 55 in Periódicos Capes. After reading the introduction and conclusion of the articles, only 37 articles met the pre-specified eligibility criteria, representing 10 from Pubmed, 1 from Scielo and 26 from Capes Periodicals. Finally, after reading the articles in full, 27 were selected for review.

DISCUSSION

STEM CELLS AND MUSCLE REGENERATION

It is known that there are numerous clinical applications for the use of stem cells in different medical specialties [8], considering that they are undifferentiated cells with a high capacity for renewal and that have the ability to produce a specific, highly specialized cell type [7]. Some research is already questioning whether the practice of physical activity has a certain relationship with the increase in the number of skeletal striated muscle stem cells. This fact would improve the ability to differentiate and engage in regeneration processes. [5].

Skeletal striated muscle regeneration is a highly coordinated process in which multiple factors and multiple cell types are activated to remove necrotic cellular debris and repair damaged myofibrils. Minor damage within the cell membrane of muscle fibers is reconstructed by the fusion of intracellular vesicles with the damaged sarcolemma. This muscle damage initiates a multi-step regeneration process in which satellite cells appear to play an essential role. The condition that initiates the cascade of reactions is the formation of inflammation at the site, resulting in the activation of MuSCs. The multiplicity of reactions and pathways that occur during this process means that many different substances are involved in it and not all mechanisms are well understood yet [6].

In the process described by Wosczyna [10] after skeletal muscle injury, MuSCs are activated and their rapid proliferation produces daughter cells that self-renew to maintain the MuSC pool or differentiate to become myoblasts for myofibril production and repair. Furthermore, complete regeneration of injured skeletal muscle depends on resident progenitor cells, infiltrating cells and the muscle extracellular matrix after injury [9].

According to Yamakawa [11], in adulthood, skeletal muscle maintains its function and size through regeneration and is formed by myofibrils, in which formation comes from the proliferation, differentiation and fusion of muscle progenitor cells during development and after injury; and such cells are derived from MuSCs. Furthermore, they show that these cells play a central role in the postnatal maintenance, growth, repair, and regeneration of skeletal muscle. In sedentary adult muscle, MuSCs are mitotically quiescent but are readily activated in response to muscle injury. At the individual cellular level, the nature of MuSCs differs in their self-renewal, proliferation, and myogenic differentiation potential. According to the authors, these

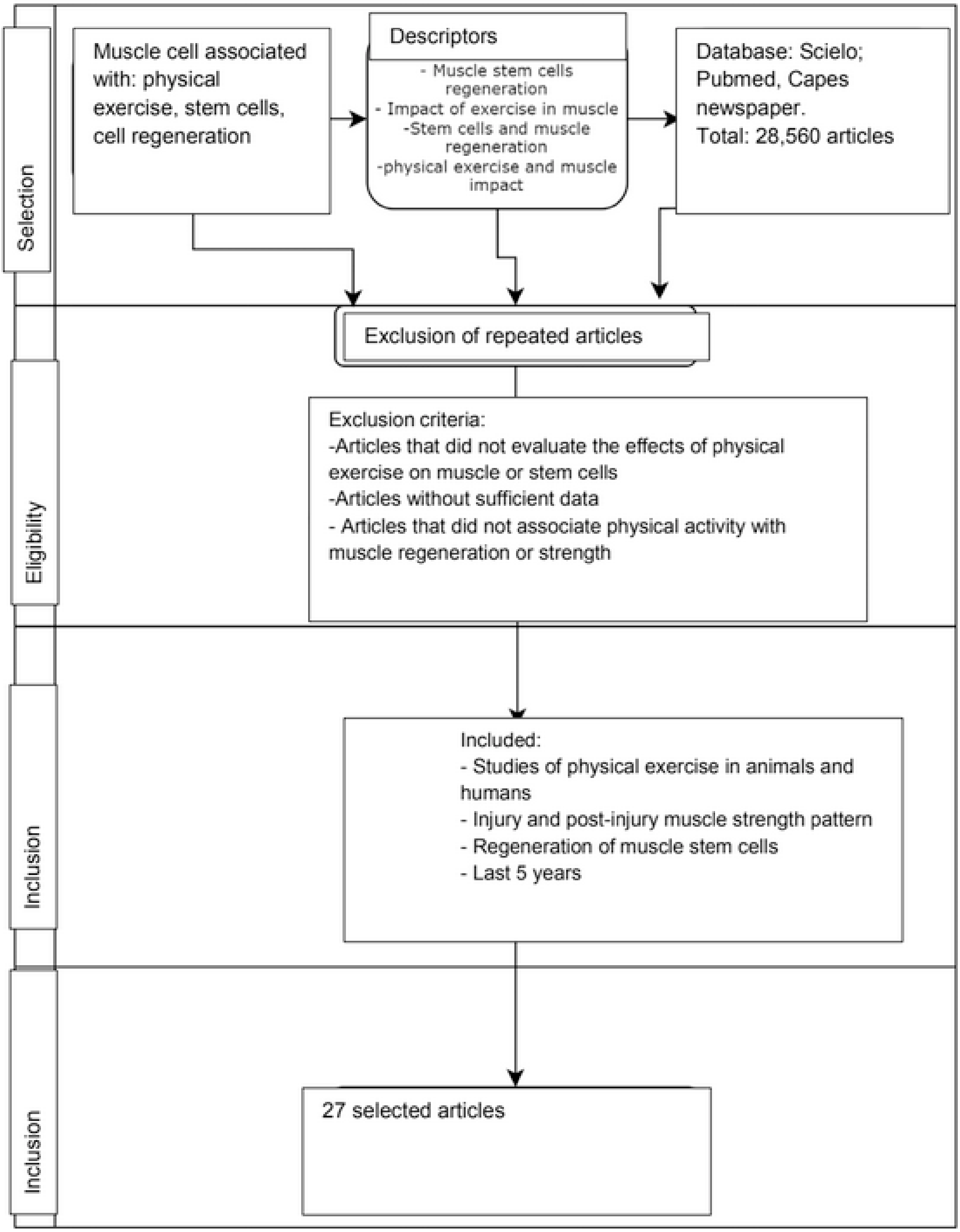

Figure 1. Flowchart of article search and selection. Source: Author

TITLE	AUTHOR/ YEAR OF PUBLICATION	METHOD	GOAL	RESULTS	CONCLUSION
Adult stem cells at work: regenerating skeletal muscle	Schmidt, et al. (2019)	Literature review	Discuss the properties of satellite cells, including heterogeneity in relation to gene expression	A highly orchestrated interaction between stem cell niche, satellite cell and other supporting cells is essential for proper skeletal muscle regeneration.	Satellite cells are the main drivers of skeletal muscle regeneration. Fine-tuned balance between states of quiescence, activation and differentiation is a prerequisite for proper regeneration.
Orienting Muscle Stem Cells for Regenaration in Homeostasis, Aging and Disease	Peter Feige, et al. (2018)	Literature review	Discuss the relationship between satellite cell heterogeneity and the establishment of polarity with asymmetric division.	Detailed characterization of long-term self-renewing satellite stem cells and the therapeutic outcome of the integration of multiple strategies to promote endogenous repair and regenerative potential of satellite cells were carried out.	The balance between symmetric and asymmetric satellite cell divisions significantly impacts regeneration efficiency by controlling the rate of generation of transient amplifying progenitors
Understanding muscle regenerative decline with aging: new approaches to bring back youthfulness to aged stem cells	Muñoz-Cánove, et al. (2019)	Artigo de revisão	Examine and discuss current understanding of satellite cell determinants of aging	The potential of stem cell interventions as rejuvenating strategies to prevent or delay age-related loss of muscle mass and strength.	The use of stem cells as a source of tissue repair and renewal introduces their potential as an inter-rejuvenator. In addition to contributing to the homeostatic maintenance of muscles, muscle fibers.
Exercise partially rejuvenates muscle stem cells	Larrick, et al. (2020)	Estudo de caso	Studying the effects of exercise on muscle stem cells in mice.	Preliminary work indicated that this voluntary running regimen did not alter the number of muscle stem cell pools in adult mice.	The extent and limits of the rejuvenating potential of physical exercise treatments for muscle stem cells were understood, and further studies were proposed to define them.
Stem Cell Aging in Skeletal Muscle Regeneration and Disease	Yamakawa, et al. (2020)	Literature review	Discuss the role of MuSCs in muscle regeneration and stem cell aging under physiological and pathological conditions	Age-related changes in skeletal muscle tissue and the host environment, such as increased prevalence of inflammation, affect MuSC function in response to injury.	The different characteristics of MuSCs contribute to the variety of physiological needs, such as (1) maintenance of a sustainable reservoir of MuSCs, (2) rapid production of a sufficient number of myogenic progenitor cells
Exercise/Resistance Training and Muscle Stem Cells	Fukada, et al. (2021)	Literature review	Elucidation of load-dependent mechanical changes in resident muscle cells, MuSCs,	Recent studies have demonstrated that myonuclear number reflects the size of myofibrils; therefore, it is crucial to know the properties of MuSCs and the mechanism of myonuclear accretion by MuSCs.	As the number of myonuclei directly influence the size of the myofiber, mediated by MuS, controlling these parameters can be an innovative therapeutic strategy.
Satellite cell self-renewal in endurance exercise is mediated by inhibition of mitochondrial oxygen consumption	Abreu, et al. (2020)	Estudo de caso	Investigate the effects of resistance training on skeletal muscle regeneration and satellite cell function.	Injured muscles from resistance-exercised mice exhibit enhanced regenerative capacity, higher densities of newly formed myofibers, as well as lower inflammation and reduced fibrosis.	Resistance exercise promotes self-renewal and inhibits differentiation into satellite cells, an effect promoted by metabolic reprogramming and respiratory inhibition.

The Role of Satellite Cells in Skeletal Muscle Regeneration—The Effect of Exercise and age	Kaczmarek, et al. (2021)	Literature review	The article presents the current state of knowledge on satellite cell-dependent skeletal muscle regeneration.	More severe muscle damage initiates a multi-step regeneration process in which satellite cells play an essential role.	The body's own satellite cell population is being rebuilt so that more fibers can be regenerated in the future.
Adaptation of skeletal muscle to physical exercise: molecular and energetic considerations	Abreu, et al. (2017)	Literature review	Summarize the main molecular responses suffered by skeletal muscle to physical exercise.	The constant practice of physical exercise generated a gradual and progressive change in protein content and enzyme activity, especially those involved in the production of ATP in cells.	Skeletal muscle undergoes molecular adaptations to physical exercise, which reflects an increase in the content of proteins involved in mitochondrial ATP synthesis, and efficient glucose transport/uptake.
Relationship between exercise volume and muscle protein synthesis in a rat model of resistance exercise	Ogasawara, et al. (2017)	Case study	Investigating the effects of relatively high-volume resistance exercise in Sprague-Dawley rats	Muscle protein synthesis reached a plateau after 3 or 5 sets of resistance exercise, and no increase was detected with additional sets.	The relationship between muscle protein synthesis and resistance exercise volume began to stabilize after approximately five sets of resistance exercise.
METTL3-Mediated m6A Metylation Regulates Muscle Stem Cells and Muscle Regeneration by Notch Signaling Pathway	Yu Lian, et al. (2021)	Research Article	Study the specific function of the METTL3 protein in regulating muscle stem cells and regeneration.	Knockout of METTL3 proteins culminates in a significant inhibition of muscle stem cell proliferation and blocks muscle regeneration after injury	METTL3 proteins, which can serve as a basis for the development of therapeutic strategies related to muscles, including injuries and dystrophies.
Role of damage and management in muscle hypertrophy: Different behaviors of muscle stem cells in regeneration and hypertrophy	Fukada, et al. (2019)	Literature review	Review the latest findings on the relationship between muscle satellite cells (MuSCs) and hyperpertrophy.	Degenerative myofiber damage is not required for MuSC activation/proliferation during hypertrophy. When considering MuSC-based therapy for atrophy it will be indispensable to elucidate MuSC behaviors in muscles with non-degenerative damage.	Overloaded muscle may require specific overload molecules and events. Degenerative damage to myofibrils is not necessary for both MuSC behavior and hypertrophy in overloaded muscle.
The Impact of Aerobic Exercise on the Muscle Stem Cell Response	Joanisse, et al. (2018)	Literature review	Advances regarding the influence of aerobic physical training on satellite cell function.	Increased satellite cell pool activation after aerobic training may make skeletal muscle repair effective	In addition to the role of satellite cells in mediating muscle growth, resistance exercise is capable of improving regeneration
Physical Exercise and Cardiac Repair: The Potential Role of Nitric Oxide in Boosting Stem Cell Regenerative Biology	Marino, et al. (2021)	Literature review	Present a new perspective on cardiac regeneration based on the relationship between physical exercise and nitric acid synthesis.	According to the article, studies have shown that physical exercise can have a beneficial effect on the regeneration of heart tissue after an injury and may be linked to the production of nitric oxide.	Studies on the relationship between physical exercise, nitric oxide production and cardiac regeneration are promising and may develop new therapies for heart disease.
Muscle Stem/ Progenitor Cells and Mesenchymal Stem Cells of Bone Marrow Origin for Skeletal Muscle Regeneration Muscular Dystrophies	Klimczak, et al. (2018)	Systematic literature review	Study of innovative therapies for skeletal muscle injuries and/or degeneration in dystrophic or traumatic patients.	Biological properties of BM-MSCs and the heterogeneous muscle stem cell population were found, based on hypothetical mechanisms that modulate muscle regeneration.	Stem cells are effective for muscle regeneration, dependent on time, dosage and signaling pathway, with potential for the treatment of diseases such as genetic and muscular dystrophies.

Exercise promotes satellite cell contribution to myofibers in a load-dependent manner	Masschelein, et al. (2020)	Case study	Evaluate the contribution of satellite cells to myonuclei mediated by increased load during physical training	First study to identify and evaluate the joint effect of satellite cells and myonuclear accretion in a physiological state of increased mechanical load via physical exercise.	Collectively, mechanical loading during exercise independently promotes the contribution of stem cells to myofibrils.
The role of satellite and other functional cell types in muscle repair and regeneration	Chen, et al. (2019)	Literature review	Study knowledge about satellite cells responsible for muscle regeneration, exercise and age	The multiplicity of reactions and pathways that occur during The regeneration process results in the participation and control of many factors that are activated and secreted during muscle fiber damage.	Some types of fibers are more prone to oxidative stress, which favors mitochondrial and respiratory damage. Furthermore, several signaling and control pathways are important for the regeneration process.
Use of cell therapy with stem cells in medical specialties in Brazil: Systematic Review	Barbosa, et al. (2018)	Literature review	Describe the clinical applications available in Brazil for the use of stem cells	Stem cell treatment is used definitively or as an adjuvant in therapies in medical areas, reducing the use of more aggressive therapies	The benefits of cellular therapies were identified, as well as their limitations, when compared to conventional therapies already used in various pathologies.
A Muscle Stem Cell Support Group: Coordinated Cellular Responses in Muscle Regeneration	Wosczyna, et al. (2018)	Literature review	Review of muscle regeneration studies.	The essential roles of cells such as macrophages and FAPs in the optimal performance of muscles during regeneration have been identified	He identified evidence of interference between many cells, signifying the importance of a cooperative cellular environment in muscle regeneration.
Effects of exercise on sciatic nerve regeneration in Wistar rats after axoniotmesis	Guerdert, et al. (2020)	Literature review	To study the effects of physical exercise (forced swimming) in rats undergoing axonotmesis.	They pointed out functional improvement, an increase in the production of neurotrophic factors (BDNF and NGF) and a decrease in the expression of the enzyme iNOS and the cytokine TNF–α in the exercised groups.	Physical exercise in the form in which it was used improved motor function and accelerated peripheral nerve regeneration.
Wnt Signaling in Skeletal Muscle Development and Regeneration	Girardi, et al. (2018)	Literature review	Provide a comprehensive view of the roles of Wnt signaling during muscle development	Discuss the crosstalk between the Wnt and TGFβ signaling pathways in skeletal muscle, verifying that these pathways are directly involved in skeletal muscle regeneration.	It was clarified that satellite cells need to receive cues from neighboring cells, such as macrophages or fibro-adipogenic progenitors to function correctly.
Single Stem Cell Imaging and Analysis Reveals Telomere Length Differences in Diseased Human and Mouse Skeletal Muscles	Tichy, et al. (2018)	Case study with mice	Methods to measure telomere length in skeletal muscle stem cells have not been demonstrated.	No differences were observed in telomere length between young and old MuSCs from uninjured wild-type mice but MuSCs isolated from young dystrophic mice exhibited significantly shortened telomeres.	Telomere wear is present in human dystrophics MuSCs, which highlights their importance in the regenerative failure of the disease

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Exercise as prescription for patients with various diseases.	Luan X, et al. (2019)	Literature review	The purpose of this article is to provide a summary of the latest exercise prescriptions for 26 different diseases, discussing the effects of exercise therapy on the prevention and rehabilitation of these diseases.	Identified the best exercise therapy program and its dosage based on evidence, experience and common sense. The review provided a scientific and methodological basis for choosing an exercise prescription based on the type of disease treated and the patient's health needs, which can assist in the prevention and treatment of diseases, thus promoting rehabilitation and improving quality of life. of patients.	Exercise therapy is safe and effective for improving physical performance and alleviating symptoms in various diseases. This study reviewed intervention methods for 26 common conditions, identifying recommended forms of exercise. Future research must focus on disease prevention through exercise and guide healthcare professionals in creating personalized prescriptions.
Exercise induces transient transcriptional activation of the PGC-1 alpha gene in human skeletal muscle.	Pilegaard H, et. Al. (2003)	Estudo de caso	Determine whether PGC-1a transcription is regulated by acute exercise and exercise training in human skeletal muscle. Furthermore, the study sought to investigate the role of PGC-1a in coordinating the activation of metabolic genes in response to exercise.	The results showed a significant increase in PGC-1a transcription and mRNA content after exercise, indicating its possible role in gene regulation in response to exercise.	The conclusion of the study was that exercise induces a significant transient increase in PGC-1a transcription and mRNA content in human skeletal muscle. This suggests that PGC-1a may play an important role in coordinating the activation of metabolic genes in response to exercise.
The "Omics" 'of Voluntary Exercise: Systems Approaches to a Complex Phenotype.	Kelly AS, et.al. (2015)	Literature review	To understand the underlying influences of variability in predisposition to exercise.	CC and DO mouse models are ideal for the simultaneous integration of many 'omics' approaches in a true systems context, moving from phenotype to genotype and understanding the space in between.	The use of 'next generation' mouse models offers a unique opportunity to explore the genetic and physiological complexity of exercise in a systems context, enabling the integration of multiple layers of 'omics' analysis.
Exercise and Steam Cells	Boppart MD, et.al. (2015)	Literature review	Review the response of adult stem cells to acute exercise and physical training, with special emphasis on hematopoietic stem cells, endothelial progenitor cells, and mesenchymal cells.	Exercise can influence adult stem cells, impacting feelings of tension, extracellular matrix, and inflammation. However, due to the early nature of stem cell biology, more research is needed to fully understand this relationship and its health benefits.	It highlights the importance of more research into the relationship between exercise and stem cells. Although there is evidence of exercise's influence on adult stem cells, the field of stem cell biology is still developing.
The therapeutic use of stem cells	Ferro C.A, et.al. (2019)	Literature review	The present study aimed to demonstrate the use of stem cells in diseases such as acute myocardial infarction, diabetes mellitus, liver cirrhosis, cerebellar ataxia and Parkinson's disease.	Stem cells have been shown to be capable of regenerating injured tissues and improving the functionality of affected organs. This suggests that stem cells have an important role in regenerative medicine, offering a promising treatment technology with a high rate of efficacy and a low risk of rejection.	The study concludes that the use of stem cells is effective in treating various pathologies, such as neurological, heart and liver diseases and diabetes.

Table 1. Description of selected articles according to: author, year of publication, type of study and results found. Source: Author.

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different characteristics of MuSCs contribute to the variety of physiological needs, such as maintenance of a sustainable reservoir, rapid production of a sufficient number of myogenic progenitor cells, and generation of functional cells.

Furthermore, the authors discuss physiological and chronological aging, which induce MuSC aging, leading to an impaired regenerative capacity. It is important to highlight that in pathological situations, repetitive muscle injury induces early impairment of MuSCs due to aging of stem cells and leads to early impairment of regeneration capacity [11].

Furthermore, it is noteworthy that the stimulus or damage to skeletal muscle resulting from physiological conditions (exercise, aging) or diseases (cachexia, sarcopenia, muscular dystrophies) trigger the regenerative process. In the regenerative process of skeletal muscle, different types of cells are involved, including stem cells in the muscle and cells involved in innate and adaptive immune responses, mainly those responsible for innate immunity, which allows adequate muscle regeneration [12]. The authors found, in a study with adult human muscle macrophages, that dysregulation in the cooperation between muscle progenitors and the cells responsible for adaptive and innate immune responses leads to impaired muscle regeneration and the deposition of non-functional adipose and fibrotic tissue, as occurs in muscular dystrophies.

According to Schmidt [13], skeletal muscle regeneration is a process involving the activation of several other cellular and molecular processes, whose satellite cells are indispensable, as their functioning is articulated by intrinsic signaling pathways, as well as by interactions with the cell niche. -stem. Thus, the authors discussed skeletal muscle regeneration, which is a process controlled by sequential expression of transcription factors on signaling pathways, cytoskeletal rearrangements and the contribution of non-satellite cells such as immune cells, fibro-adipogenic progenitors and interstitial cells. PW1-positive/Pax7-negative.

Among these processes, Liang [14] highlights the fundamental regulatory role of m6A modification mediated by the METTL3 protein in muscle stem cells and its influence on muscle regeneration. The post-transcriptional mechanisms underlying muscle stem cell fate and muscle regeneration have provided a molecular basis for the development of therapeutic strategies for muscle-related diseases, including injuries and dystrophies.

Furthermore, Girardi et al [15] identified that WNT proteins, a family of glycoproteins rich in cysteine, act as signals during muscle development. The signaling capacity of these compounds is strongly related to their ability to regulate the expression of Pax3, Pax7 proteins and MRFs genes, that is, Myogenic Regulatory Factors, thus contributing to the timing and maintenance of cellular regeneration and homeostasis muscle.

From the same point of view, Tichy et al [16] found that muscle stem cells contribute to muscle regeneration after injury and many muscle disorders, and repeated cycles of damage and repair lead to their dysfunction. Thus, telomere wear contributes to dysfunctional functions of these cells, observed through telomere length in mouse and human MuSCs. The researchers found that these cells from young dystrophic animals and humans exhibited significantly shortened telomeres, which highlights their importance in the regenerative failure of the disease. This has led to a better understanding of the molecular genetic events that, in relation to telomere dysfunction, can lead to the delineation of muscle regeneration limitations in etiological diseases in different MuSCs.

Furthermore, Feige [17] analyzed the impact of symmetric self-renewal and asymmetric division of stem cells on muscle regeneration and identified the effects of these processes on aging, disease and homeostasis. They found that asymmetric division affects the efficiency of regeneration in aging and disease. Symmetrical division promotes the expansion of satellite stem cells and maintains the homeostasis of the compartment. Furthermore, it has been shown that in aged muscle, the number of satellite cells becomes progressively reduced along with a loss of self-renewal and regenerative capacity. Therefore, this capacity of muscle requires a balance between self-renewal and myogenic commitment, with multiple lines of experimentation indicating that this balance is highly regulated.

Thus, stem cells have received greater attention in studies that investigate the cellular processes of skeletal muscle regeneration. However, the efficient ability to reconstruct this tissue also depends on additional cells and mechanisms in the environment. Therefore, understanding the complex interactions between muscle cell populations can help in the development of therapies that will help promote skeletal muscle regeneration in conditions where this process is necessary [18].

PHYSICAL ACTIVITY AND STEM CELLS

It is known that skeletal muscle has mononuclear stem cells, or muscle satellite cells (MuSCs), which are responsible for generating new muscle fibers. Myofibrils have plasticity, that is, they adjust their size in response to external stimuli, intrinsic factors or physical activity. Several studies indicate that resistance training and some types of drugs lead to an increase in muscle mass and function (i.e. hypertrophy). Regarding hypertrophy, studies indicate that proliferating MuSCs contribute to an increase in muscle size through fusion with the growing myofiber and the addition of new myonuclei [19]. As described by Damas [20], muscle "damage" represents physiological events, which disrupt the structure of the myofibril, decrease the stability of the sarcolemma and cause lethal damage to cells. Thus, there is evidence demonstrating the existence of ruptured myofibrils in resistance training, but evidence on degenerative damage of myofibrils in human muscle is still rare. Furthermore, MuSCs show different behaviors in regeneration and hypertrophy [21].

Authors Fukada [22] and Larricki, J. & Mendelsohn [23] discussed the impact of physical exercise on the rejuvenation and maintenance of muscle stem cells. They emphasize the aging of human beings as muscular changes that can harm their regeneration and metabolic function. Furthermore, the two articles highlight that physical exercise can have beneficial effects on muscle stem cells, including increasing the activity of the telomerase enzyme, reducing inflammation and increasing the production of growth factors. This emphasizes the importance of physical exercise for muscle health and to reduce the effects of aging on skeletal muscle.

Larricki, J. & Mendelsohn [23] focused on physical exercise in aged mice and found that resistance training exercise can partially reverse the aging of muscle stem cells through its action on telomeres. the importance of physical exercise to maintain muscle health, which can increase activity, resistance and proliferation of satellite cells, in addition to reducing the effects of aging on skeletal muscle, with a focus on muscle stem cells.

In agreement with these results, Pérez-López [24] evaluated the impact of physical exercise on the regeneration of muscle stem cells in healthy and elderly individuals. The study concluded that physical exercise can improve muscle regeneration, increasing the number of muscle stem cells and their activity. Furthermore, it demonstrated that the practice of physical activity can be particularly effective in muscle regeneration in older individuals.

However, despite studies that point to the benefit of physical activity on muscle stem cells, it is clear that further research is needed to understand the mechanisms that directly influence this regeneration process and what types and intensity of exercise are necessary to achieve this. get the most out of MuSCs.

PHYSICAL ACTIVITY AND RESISTANCE

According to Phablo [25], the practice of regular physical exercise generates numerous benefits for bodily health, in addition to also causing physiological adaptations that bring several improvements to the body. Thus, scientists observed that, when performing physical activity, skeletal muscle undergoes transformations in genes related to the regulation of myogenesis, carbohydrate metabolism, transport and oxidation of substrates and mitochondria metabolism. As a consequence, there is an increase in the content of proteins involved in mitochondrial ATP synthesis, an increase in proteins involved in the Krebs cycle, transport and oxidation of fatty acids, effective glycolytic metabolism, greater antioxidant capacity and efficient transport/uptake of glucose. Thus, it is clear the importance that physical exercise plays in skeletal muscles, especially in metabolic, energetic and molecular aspects.

Furthermore, according to Phablo [26] skeletal muscle stem cells are extremely important for the regeneration and maintenance of tissues over the years. In order to verify the function of these cells during resistance exercise, the researchers subjected mice to physical resistance training, aiming to study the function, differentiation and metabolic characteristics of satellite cells using in vivo and in vitro techniques. As a result, they discovered that the injured muscles of resistance-exercised mice had greater regenerative power, as there was an increase in the density of myofibers. Additionally, there was less inflammation and fibrosis. They then concluded that the resistance exercise promotes the self-renewal of satellite cells, through metabolic reprogramming and respiratory inhibition, generating a better muscular response to injuries. Therefore, it is a fact that physical exercise has a notable role in the renewal of muscle stem cells, as it promotes their proliferation through its practice.

From the same perspective, Ogasawara [27] demonstrated that resistance exercise (RE) is related, in some way, to the stimulation of the synthesis of general and muscle proteins. To do this, the researchers subjected some male Sprague-Dawley rats to several different series of resistance exercise, thus obtaining muscle samples every 6 hours after performing 1,3,5,10 or 20 series. As a result, they noticed that, after the sets, protein synthesis increased significantly, but reached a plateau after 3 or 5 sets. Furthermore, an increase in the phosphorylation of p70S6K at Thr389, a marker of mTORC1 (mammalian target of rapamycin complex 1) activity, was observed. However, the longer the resistance exercise series, the greater its action. As a result, they noticed that the relationship between p70S6K phosphorylation and ER resembled a straight line, but muscle protein synthesis stabilized after 5 sets. Finally, they concluded that physical activity is extremely important for increasing muscle activity in general, which provides numerous health benefits.

Therefore, it is clear that, although there are studies that relate the impact of physical activity on the regeneration of muscle stem cells, to date, there is no conclusive research on the mechanisms through which physical exercise influences the health of these cells. Furthermore, it is important to note that there are still some limitations in understanding this subject. Studies on how the type, intensity and duration of physical exercise affect muscle stem cell regeneration rates are being evaluated. Furthermore, the molecular mechanisms behind regeneration are being studied in order to better understand the interference of physical activity on muscle function.

In short, the results presented in research carried out in the literature allow us to conclude that physical exercise can have a positive effect on the regeneration of muscle stem cells. However, more studies are needed to better understand how such activities affect the regeneration of muscle tissues, how this influences injury recovery and improves muscle function.

CONCLUSION

Given the results discussed in this review, muscle stem cells play an important role in muscle regeneration and growth, however, the ability to efficiently remodel this tissue also depends on the interaction with other types of cells present in the skeletal muscle environment. In this sense, understanding better strategies and the effectiveness of this regeneration process depends not only on knowledge about stem cells, but also on the impact of the interaction of different cell types, pathways and mechanisms. In relation to physical exercise, especially strength training, the increase in muscle mass and improvement of its function stands out due to the increase in the proliferation and differentiation of muscle stem cells that cause hypertrophy of this tissue. Furthermore, exercise has a positive effect on the rejuvenation and maintenance of muscle stem cells, reducing the effects of muscle aging. Although there is evidence of these beneficial effects, there is still a lot of room for research, especially on the intercellular mechanisms involved and the best strategies applied to physical exercise to optimize the activity of muscle stem cells.

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