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Article

The integrated relationship between type two muscle fibers and aging: An update study

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Abstract: Aging is an intriguing process that fascinates many researchers. This fascination is related to the impossibility of controlling time and its influence on human beings. Many theories have been studied to understand this complex process and the impact it has on the muscular system. The ability to control this influence and how to reduce the risk of falls, prevent illnesses, and improve the quality of life of the elderly has encouraged the development of many studies related to it. It is known that type two fibers undergo more denervation than type one fibers during aging, as well as the relationship between specific characteristics and their decline. However, some questions related to how this process actually happened and the ideal exercises that can enhance hypertrophy and the recruitment of type two fibers, although resistance training has been more accepted, are not clear and require further studies focused on this issue. Therefore, considering the importance of these type 2 muscle fibers in the aging process and how they impact the elderly, the objective of this study is to be pioneer in collecting recent and relevant information associated with this specific kind of fiber, show the current gaps on the subject and encourage new research to seek knowledge that improves science.

Keywords: aging; muscle system; type two fibers; denervation; exercises

1. Introduction

One of the big challenged in human life is understanding the impact of aging in the body. There are many issues associated with elderly people that can affect their quality of life [1], including the real importance of muscle fibers.

An important issue that is responsible for creating movement in the body and by applying force, causes movement in the body, is called muscle [2,3]. Muscle is the largest soft tissue in the body structure [4]. The work of skeletal muscles is one of the main functions of the skeletal and muscular system in the body [5,6]. Skeletal muscles play an essential role in movement, maintaining endurance, and performing various tasks to maintain body structure [7]. This important function is made possible by the interaction between muscles and bones [8,9].

In their study, Mita et al. [10] explained that muscle fiber is basically categorized into two types fibers: Slow-twitch fibers express myosin heavy chain (MyHC) I and are recognized by fatigue resistance and a high oxidative capacity. Fast-twitch fibres (also called type II fibers) express MyHC II and they have a high glycolytic property, power, and speed, but low endurance.

In addition, type 2 fibers can be divided into three different types: type IIa, type IIx/d, and type IIb [11]. Type IIa has many characteristics such as type 1: fatigue resistence, SDH (succinate dehydrogenase) activity, and Mitochondrial CK (miCK). However, from other viewpoints, type IIa has similar features to type IIx/d, and type IIb such as contractile speed [12].

Nowadays, it is known that this muscle mass is crucial to developing the elderly's functionality and performances including when they are associated with balance and confidence during activities [13].

These issues can impact how older people can improve their abilities against the risk of falls. Moreover, external and internal factors are situations that they need to deal with it all the time to avoid these risks. If it is easier, they will have more independence in a dairy routine; if it is not, they will have more probability of acquiring dangerous health issues.

Considering any matters that the body needs to deal with over time, such as heart failure, kidney, diabetes, sepsis, aging, hereditary muscle disorders, and denervation, it is necessary to preserve the balance between the degradation and biosynthesis of proteins related to muscle mass [12]. According to the type of fiber, distinguishing physiological character and metabolic activity, the muscle can show different physiological features for each specific situation.

Granic et al. [14] point out that due to the loss of innervation of large fast motor neurons in fast-twitch myofibers (type 2 fibers), reinnervation processes by collateral sprouting of slow motor neurons take place throughout life. It represents an adaptation and hemodynamic response to aging that impacts the quality of life of the elderly and what types of treatments they would need to seek to decrease the risk of falls and morbidities.

Considering all this information and the steady impact type 2 fiber preferentially undergoes a negative impact during the aging process [15], this paper is focused on reviewing notable and recent manuscripts related to type 2 fibers and the aging process to facilitate the search for data published in recent years related to the topic.

Moreover, approaches related to type 2 fibers are attached in various contexts as additional or secondary information, this study is the first to be conducted in the world that places this type of fiber as the center of the study. This is essential to give due importance to these muscle fibers that suffer mainly from aging and to encourage more studies to fill the gaps presented in the current literature.

2. Type two fibers

Fast-twitch motor units are further classified based on their fatigability as fast-twitch fatigue resistant (type FR), fast-twitch fatigue intermediate (type FInt), and fast-twitch fatigable (type FF) [16]. These motor units type comprises a specific fiber that expresses a single myosin heavy chain (MyHC) [17] isoform and these fibers are classified such as type IIa, IIx and IIb muscle fibers, sequentially.

It has been known that type 2 fibers are innervated by larger motor units. According to the size principle of motor unit recruitment [18] those will be recruited after smaller motor units that innervate type 1 fiber to control some signal related to fatigue, for example [19].

Considering the relationship between motor unit recruitment and resistance training, Morton et al. [18] assume that it is necessary to understand whether there is a basic threshold of external resistance to activate different types of fibers. Moreover, Grgic and Schoenfeld [20] point out that it is necessary to understand whether there is a basic threshold of external resistance to activate different types of fibers. On the other hand, there are other research that have been studying this interaction between muscle fibers and loads. Some authors mention that to active smaller motor unit (slow twitch) it is required to use a low load or repetition (30%1RM), while to stimulate the largest motor unit (fast twitch) it would be necessary to use a higher load or repetition (70%RM) [11,18,20,21].

In sequence, Paillard [22] believes that a high percentage of type 2 muscle fibers could be associated with the ability to react quickly in the case of external perturbations. It may enable a reduction in the risk of falls in elderly people.

In another study, Rowley et al. [23] analyzed that the total surface area of the presynaptic terminal is bigger at type IIx and IIb fibers than in type I and IIa fibers. Furthermore, the total number of active zones at presynaptic terminals is greater at type IIx and IIb fibers, and accordingly, the total number of synaptic vesicles released in response to a nerve action potential is greater in these types of fibers.

About the postsynaptic membrane at type IIx and IIb fibers, the total number of cholinergic receptors is greater in these fibers when compared to type I or IIA. Besides, the release of ACh and the density of voltage-gated Na^+ channels adjacent to the motor end-plate is higher than type I or type IIA fibers [24,25]. Hence, the membrane depolarization required to initiate a muscle fiber action potential is lower in type IIx and IIb fibers [26].

Recent studies [10,27] have shown that properties of muscle fiber are regulated by myokines in an auto/paracrine manner, such as muscle-derived brain derived neurotrophic factor (BDNF). It was reported as a regulator for type II fiber specification. For the authors, it is clear to speculate that there are distinct regulatory factors between the two types of fibers that could separate them.

2.1. Type two fibers and aging

The Neuromuscular Junction is an important structure that involves a motoneuron terminal and skeletal muscle fiber that includes three major components: the presynaptic terminal, the synaptic cleft, and the post-synaptic membrane [28].

During the aging process, there are many issues related to the neuromuscular junction. Electron Microscopy, morphology, physiology, and biochemical are some examples that can affect this connection between the neuro system and skeletal muscle system [28].

This multifactorial etiology involves changes in muscle metabolism, endocrine changes, nutritional factors, and mitochondrial-genetic factors [29]. This process is one of the big challenges faced by researchers because it is not clear to connect all this information in only one way of aging.

Granic et al. [14] mention nine known classic hallmarks of aging: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication. Besides, five new novel hallmarks have been analyzed: Inflammation, neural dysfunction, extracellular matrix dysfunction, reduced vascular perfusion, and ionic dyshomeostasis. All this effort to decipher the complex aging process has intrigued many researchers interested in this matter.

Because of that, authors have studied the loss of muscle mass with aging, which is largely associated with the progressive loss of motoneurons and the reduction in the number and size of muscle fibers [1].

In addition, approximately ten years before, Andersen [30] conducted a detailed study about muscle fiber adaptation in the elderly human muscle. He revealed that the most prominent phenotype in older people was fibers co-expressing Myosin Heavy Chain (MHC) I and MHC IIA.

They also explained that some old fibers switch fiber types along the length or there are some nuclear domains in which the MHC expression is different from the remaining part of the fiber.

Considering the fiber type, it is known that type 2 fibers decrease in number and lead to excitation-contraction uncoupling [15,28,31]. Tieland et al. [32] assume that these fast-twitch fibers are recruited later and this reduction affects muscle strength and may decline the ability to rise from a chair or to lift a heavy load.

A study carried out by Nilwik et al. [31] showed that quadríceps cross-sectional area (CSA) was smaller in older versus young men, as well as the type II muscle fiber size between these two groups (29%; $P < 0.001$). They could conclude that the impairment of muscle mass with aging is mainly attributed to smaller type II muscle fiber size and, as such, is unlikely accompanied by substantial muscle fiber loss.

Recently, Brown et al. [33] analyzed the diaphragm muscle (DIAm) in 24 month-older Ficher 344 rats proving that Type IIX-Type IIB is related to sarcopenia due to aging. The results showed that in this type of fiber, the mitochondrias were more fragmented and the Maximum velocity of Succinate Dehydrogenase Reaction (SDH max) per fiber volume decreased. This situation did not happen in type-IIA fiber.

Studying the same issues related to it, Fogarty et al. [34] pointed out that in humans, the oxidative capacity of fast-type muscle is reduced with aging and suggested a reduction in mitochondrial oxidative capacity. It would be associated with DIAm and the sarcopenia process. According to them, the SDHmax activity of type I and type IIa fibers was significantly greater than type IIx and/or IIb. Furthermore, the reduction between rats with 6 m and 24 m were reduced by 36% SDHmax.

2.2. The decline

Since 1983, Lexell et al. [35] had been studying the effects of aging on the total number and size of fiber types in a skeletal muscular system. They analyzed that the size of the muscles of the older individuals was 18% smaller ($p < 0.01$) and the total number of fibers was 25% lower ($p < 0.01$) than young individuals. They observed a preferential reduction in type II fibers in the old group.

In addition, Sjöström et al. [36] carried out a study with the same muscle (vastus lateralis muscle) from childhood to old age. They explained that the proportion of type 2 (fast twitch) fibers on the border of fascicles is larger than the proportion internally, and during aging local and secondary factors commit the fiber type proportions.

After many years, this issue is a challenge among researchers. In 2012, Verdijk et al. [37] developed a study related to satellite cell numbers with spinal cord injury (SCI) and aging in humans. They compared skeletal muscle fiber characteristics between wheelchair-dependent young males with SCI, healthy elderly males, and young controls. In this study, satellite cells were substantially lower in the wheelchair-dependent SCI in both types I and II fiber. Furthermore, satellite cells were lower in the type II muscle fibers considering only elderly participants.

In sequence, other authors [38] realized that type II fibers were smaller in older adult men (4507 ± 268 vs. 6084 ± 497 μm, respectively, $P = 0.007$) when compared with the same kind of muscle: vastus lateralis of healthy young.

Considering the capillary contacts (CC) per muscle fiber, and the capillary-to-fiber perimeter exchange (CFPE), type I and type II muscle fiber CC and CFPE index were smaller in old compared with young muscle (CC type I: 3.8 ± 0.2 vs. 5.0 ± 0.3; CC type II: 3.2 ± 0.2 vs. 4.2 ± 0.2, respectively; both $P < 0.001$).

They also explained that the loss of muscle mass with aging is characterized by specific atrophy of the type II muscle fibers and a reduction in type II muscle fiber satellite cell (SC) content [39].

2.3. The denervation

According to Coletti et al. [11] type II fibers are preferentially sensitive to atrophy in aging and there are two additional phenomenon characteristics in this process: fiber type grouping and shifting. Grouping is when fibers (especially type I) have the presence of clusters of fibers of the same type, defined as a group of fibers with at least one enclosed fiber. Shifting is related to reinnervation when muscle fibers suffer genetic and enzymatic activities to influence the slow-twitch motor neuron act in a new NMJ. After this complex process, before being type II fiber, the new fiber will assume new features as it were type I fibers.

In 2023, Dowling et al. [40] carried out a review that confirmed fiber-type shifting in senescent animal models. When this issue was analyzed, the myosin heavy chains, myosin light chains, actins, troponins, and tropomyosins of fast versus slow isoforms of key contractile proteins. They suggested suitable bioanalytical tools of fiber-type transitions during aging.

Interested in understanding the effects of aging and denervation on the expression of uncoupling proteins in fast-twitch gastrocnemius muscles and slow-twitch soleus muscles of rats, Kontani et al. [41] realized that the sciatic nerve caused an increase in UCP3 (uncoupling proteins) mRNA levels in both muscles. However, the regulation of other genes contrasted between the two types of skeletal muscles. The reduction in the mitochondrial UCP3 and COX (cytochrome oxidase) proteins in type II fibers may have a negative effect on energy metabolism after the denervation of gastrocnemius muscles.

Another mechanism related to reinnervation is the regeneration of injured neurons or via collateral sprouting of neighboring uninjured afferents into the denervated territory [42]. In addition, Jablonka et al. [43] carried out a study that explained the role of sprouting of neighboring axon terminals when motoneuron disease and other neurodegenerative disorders appear. The importance of the axonal microtubule and actin cytoskeleton is crucial for the maintenance and plasticity of axonal branches and neuromuscular endplates.

In addition, other authors [1,44] support the idea that this denervation is associated with the decrease of protein synthesis in the neuronal cell body in that this alpha motoneuron would lose its functionality and be considered a sick structure. After that, the secondary consequence would promote axonal degeneration. The microtubules would suffer glycation of tubulin (nonenzymatic glycosylation) with a slowing of axoplasmic flow and the denervation would happen.

As a consequence, according to Larsson et al. [1] muscle function progressively declines because motoneuron loss is not adequately compensated by reinnervation of muscle fibers by the remaining motoneurons.

After the denervation and the attempts to solve the aging issues, the atrophy can be installed. This situation can be involved with other factors, such as a reduced regenerative capacity, organelle dysfunction (including lysosomes and mitochondria), changes in sarcomeres and endoplasmic reticulum, ultimately leading to defects in calcium handling [11]. This process can influence lifestyle, biological, and psychosocial issues on elderly skeletal muscle performance [32].

In short, it is clear that although many studies have focused on this issue for a long time, it remains unclear whether sarcopenia is initiated and driven primarily by changes in nerves, myofibres, or both [14].

2.4. Exercises related to the performance of type two fibers

Considering the strong relationship that exists between aging and the muscle system, much research has focused on issues related to type 2 fibers. It is clear the necessity to study type 2 fast fibers since they preferentially undergo denervation and reinnervation by slow-twitch motor neurons is a good reason to be understood.

According to Coletti et al. [11] physical activity is the key to enhancing muscle function in older sarcopenic adults, preferentially resistance training. It includes dynamic movements related to concentric and eccentric contractions during the exercises. Furthermore, the relevance of recruitment with motor units and the activation of specific types of fibers are relevant in this type of training.

For resistance training to induce a physiological response that will improve muscle mass and strength, a training load of greater than 70% of the one-repetition max (1-RM) is needed. Furthermore, another study [21] supports the idea that the initial load, in the elderly participant, should be 40% RM with gradual evolution until the final load is estimated at 80% RM.

Freire and Seixas [13] applied this muscle strengthening protocol to two groups of elderly people (84.6 ± 8.4 years). While in the control group participants underwent only muscle strengthening, in the interventionist group they trained the same protocol associated with sensorimotor exercises. They realized that after the interventions, significant differences between the groups were observed only in the dominant quadriceps muscle strength.

Furthermore, when evaluating intragroup differences, it was possible to note that improvements in the strength of all muscle groups evaluated were analyzed. However, considering that both groups improved in muscular strength, a new variable reflecting differences in muscular strength (final assessment—initial assessment) was verified for both groups, and no significant differences were found in improvements in muscular strength between them.

Recent findings demonstrate that endurance exercise induces the appearance of hybrid fiber alterations in seniors consistent with what was previously observed [45].

In this study, they analyzed the role of exercise-based interventions to spare muscle wasting and pinpointed the peculiar role of denervation-reinervation processes.

Morton et al. [18] pointed out that although performing resistance exercises with heavier loads is often proposed to be necessary for the recruitment of larger motor units and activation of type 2 fibers, they support the idea, that type 1 and type 2 fibers glycogen depletion was determined by nether load nor repetition during resistance exercise performed to task failure. They believe that muscle fiber activation is supported by reductions in peak torque and anabolic protein signaling.

On the other hand, Grgic and Schoenfeld [20] state that there is still a need for long-term studies that answer this question: if the training with blood flow restriction performed with low loads (30%1RM) produces type 1 fiber hypertrophy or not [46].

In other words, it is necessary to understand whether there is a basic threshold of external resistance to activate different types of fibers. In short, more studies should be developed on this interaction between resistance training and fiber type.

Considering the entire complex system that involves aging and sarcopenia, other types of exercises have currently been analyzed, such as aerobic exercises, balance training, and flexibility training.

Recent authors, such as Coletti et al. [11] argue that a combination of these exercises can be efficient for elderly people due to their variety. It allows the exerciser to periodize the training program with more motivation and encouragement.

3. Conclusion

Issues related to the effect of time on the human body have generated many doubts over the years. Although much research seeks information related to the impact of aging on the muscular system, little is known about the preference of the process to primarily affect type 2 muscle fibers. Type 2 muscle fibers preferentially suffer a decline, denervation, loss of number and size, reinnervation by regeneration of injured neurons, or collateral sprouting of neighboring uninjured afferents in the denervated territory.

However, it is not clear what happens for all these mechanisms to initially occur with type 2 fibers, as well as what is the best exercise for this damaging mechanism to be alleviated or prevented in these types of fibers.

Although evidence shows that elderly people suffer from decreased muscle functionality, more studies related to fast-twitch fibers need to be carried out. It is based on these questions that more specific interventions can be developed so that the elderly can achieve quality and prosperity in their lives.

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Conflict of interest: The author declares no conflict of interest.

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