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Biological Characteristics of Structural and Functional Remodelling in Skeletal Muscle: Effect of Exercise

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Abstract

For more than one and a half century, the effect of locomotory activity on skeletal muscle structure and function has been studied. It is clear that these changes depend on the mode of activity. Resistance and endurance exercise training differ in their intensity and duration as well as effects on metabolic pathways, structures of skeletal muscle, protein synthesis and degradation rate, neuromuscular junctions and muscle spindles. The purpose of this review was to compare differences and similarities in structural-functional rearrangements in skeletal muscle in endurance and resistance training and the effect of these changes on endurance and strength capacity. The main purpose of the study was to compare changes in mitochondrial and myofibrillar compartments and also changes in neuromuscular junctions in extra- and intrafusal muscle fibers. The comparison of morpho-functional changes in different skeletal muscle fiber types may help an

exercise biologist, sport physician, endurance and strength specialist to better understand the nature of specificity of different training modes on the functional capacity of an organism and build up exercise training strategies for both recreational and top athletes.

Keywords: muscle structure and function; adaptation to exercise training mode

Introduction

It is a well-known fact that a reciprocal relationship exists between structure and function in an organism. Structure creates function and function designs structure. The significance of this relationship increases in situations of increased functional demands such as exercise training. The effect of increased functional activity on morpho-functional changes has been successfully studied during the last one and a half century.

Endurance training (ET) influences the enzyme system of the Krebs cycle, electron transport chain, capillary supply, changes in key metabolic enzymes involved in fatty acid activation, and increased oxygen uptake in skeletal muscle [43,44,105]. ET does not result in hypertrophy of skeletal muscle fibers as the level of force production is relatively small compared to their maximal force generation [6]. Training in the aerobic zone of metabolism promotes a transition from type II to type I fibers in skeletal muscle, which occurs at the expense of type II fiber population [104]. The transition process is related to the myofibrillar apparatus as myosin is the regulator in the conversion of chemical energy into mechanical activity.

Protein synthesis is an energy consuming process that is related to the recovery period after exercise. A low cellular energy level induces activation of the 5'adenosine monophosphate-activated protein kinase (AMPK). AMPK reduces translational processes and a low energy status is associated with a high rate of protein turnover, which limits the increase of fiber size [110]. Lack of recovery also leads to changes in the skeletal muscle myofibrillar apparatus, particularly the destruction of contractile proteins and decreased exercise performance [83,84,91]. The decline in performance is largely related to skeletal muscle damage and a decrease in muscle oxidative capacity [42,91].

High volume ET disrupts body homeostasis and the body has to recover. Therefore, two responses must be paid attention to: the musculoskeletal system's response to an appropriate or inappropriate training load, and the effect this response or adaptation has on injury or the potential of injury. An inappropriate volume or intensity of exercise may cause a maladaptive cellular or tissue response due to an imbalance between load and recovery [27].

Resistance training (RT) improves muscle main function and mass as a result of an anabolic effect primarily in fast-twitch (FT) fibers [31]. Muscle hypertrophy is effectively achieved with loads exceeding 60% of maximal strength [60] as muscle protein synthesis rate increases due to a complex of translation of

mechanical signals [107]. At the same time, the downregulation of proteolytic genes has been shown [69]. RT expands the amount of the myofibrillar apparatus in order to enlarge fiber cross-sectional area [5] and a concomitant alteration in contractile protein phenotype and metabolic enzyme levels occurs in accordance with activity-induced changes in the muscle's fiber-type profile [75,89]. The repetition regime in the RT protocol plays an important role in the hypertrophy of muscle fibers. High numbers of repetitions in RT did not cause any significant hypertrophy of muscle fibers [15].

It is still not fully known how skeletal muscle responds to an increase in mechanical load. Compensatory hypertrophy is characterized by an increase in muscle mass, muscle protein content, and contractile force, and by a shift from the fast-to-slow myosin isoform type in FT muscles [75], but the exact mechanism of changed myosin isoforms during RT is poorly understood. In comparison with myosin heavy chain (MyHC) isoforms, much less is known about changes in myosin light chain (MyLC) isoforms during adaptation to RT.

The purpose of this review is to compare differences and similarities in structural and functional rearrangements in skeletal muscle in endurance and resistance exercise training. Attention has mainly been paid to the comparison of changes in the mitochondrial and myofibrillar compartments and also on the changes in neuromuscular junctions in extra- and intrafusal muscle fibers and the effect of these changes on endurance and strength capacity. A comparative study of morpho-functional changes during endurance and resistance training gives us better understanding about skeletal muscle adaptability to high volume and high intensity/power training and enables to create a basis for building up concurrent endurance and resistance exercise training strategy.

2. The effect of training volume and intensity on skeletal muscle fibers

Athletes' responses to exercise training are highly complex and individual [11,27]. The main problem is either finding the optimal training volume in case of endurance athletes [46], or the training intensity and power in case of speed and strength athletes [24,29]. Establishing the optimal training regimen is complicated as both the volume and intensity of the training and recovery period that are optimal for performance improvement in exercise training are also highly individual [7,64]. In athletes, the skeletal muscle response shows whether the training load is appropriate or inappropriate. An appropriate training regimen leads to performance improvement through a cascade of structural and functional changes (Fig. 1).

Adaptation of skeletal muscle to exercise depends on the training volume, intensity, frequency, and the half-life of the protein [18]. A unique ability to adapt and remodel during exercise training also includes changes in the transcription of a range of protective proteins [17].

2.1. Effect of training volume

The most typical structural changes occurred in ET in type I and IIA muscle fibers (Fig. 2). The lesions in myosin and actin filaments, the distributed regularity of Z-disc in sarcomeres, the swelling and destruction of mitochondria, and the dilation of the terminal cristernae of the sarcoplasmic reticulum and T-system tubules are examples of these changes [68,87]. During ET, structural changes are considerably less evident in fibers, which have low oxidative capacity than in fibers with relatively high oxidative capacity (type I and IIA). ET also causes the most essential destruction in the myofibrillar apparatus of the nuclear-bag intrafusal muscle fibers in the region of type I fibers (Fig. 2). The increase in the number of satellite cells under the basal lamina of all muscle fibers studied in ET is a source of renewal of damaged structures [68,87].

2.2. Effect of training intensity

Typical destructive changes in fibers with low oxidative capacity have been registered in RT (Fig. 2). These changes include twisting of the myofibrils in a small area due to overtension in muscle fibers and loss of contact with the adjacent structures [87].

During RT, skeletal muscles show marked gains in strength in the group with less repetitions and a slower increase in power per training session [88]. This is due to both neuronal adaptations and an increase in the cross-sectional area (CSA) of muscle. There is consensus in literature that the gain in the CSA of muscle during RT is mainly due to an increase in myofibrillar proteins. The CSA of all fiber types has been shown to increase after RT with a tendency for larger increases in type II than in type I fibers [48]. Both slow-twitch (ST) and FT muscles hypertrophy in conditions when the power of exercise does not increase fast enough and the number of repetitions per training session is not high enough [88]. In the case of high repetitions and a rapid increase in training power, there is no hypertrophy of muscles or gain in strength. Testosterone concentration increases during RT, but the high level of corticosterone in the group with the rapid increase in training power and volume is responsible for the increased catabolism of muscle protein in this group [88]. If the power of RT is increased up to five percent per training session, there is less degradation of muscle protein. It means that in this case RT has an anticatabolic effect on skeletal muscle as the decrease of proteinase activity in muscle shows. A significant increase of FT fibers' CSA and the number of myonuclei without changes in the myonuclear domain size show the adaptation of skeletal muscle to RT [85]. The maintained myonuclear domain size tells us about the functional significance of myonuclear domain size in FT and ST muscle fibers during adaptation to RT.

3. Structural rearrangements in skeletal muscle fibers

3.1. Endurance training

In addition to the large mitochondria tightly packed with cristae in muscle fibers with higher oxidative capacity, small forms of mitochondria containing relatively few cristae also occur [87]. The intensive development of the mitochondrial apparatus in the post-training period vividly reflects the adaptive processes in ET, which is intended to supply the increased energy requirements of muscle cells with higher oxidative capacity [83]. In the peripheral sarcoplasm, both type I and type IIA muscle fibers contain short canals of the granular sarcoplasmic reticulum as well as polyribosomes and several Golgi complexes near the nucleus. The day following ET, significant destructive changes appeared in myofibrils in type I and type IIA muscle, including damage of myosin and actin filaments and the disturbance of the regularity of the Z-line in some sarcomeres [68]. The destruction of myofibrils is characteristic of both fiber types with relatively high oxidative potential, but it is still more typical of type I muscle fibers. In the A-disc, some myosin filaments in sarcomeres are absent and the destruction of these myofilaments may cover the whole sarcomere. During ET, actin filaments are less damaged than myosin filaments [87]. These structural changes are in accordance with biochemical ones, such as the increase in actin turnover rate after ET [68,85,86]. Relatively small structural rearrangements take place in type IIX/IIB muscle fibers during ET as these fibers are recruited less. A characteristic change in type IIX/IIB fibers is the focal destruction of myofibrils. The number of mitochondria in type IIX/IIB fibers did not increase significantly after ET. Mitochondria in type IIB fibers are located in small groups near nuclei and between myofibrils on the level of the Z-line but not in each sarcomere [87].

3.2. Resistance training

In type IIB muscle fibers, most structural changes are caused by speed and heavy RT [75,103]. Damaged myofibrils in a relatively small area, where myofibrils have twisted and lost the connection with the neighboring structures, are typical changes in type IIB fibers [87].

The morphological adaptations to RT involve an increase in the CSA of the whole muscle and individual muscle fibers, and an increase in myofibrillar size and number. The hypertrophy response is related to the activation of satellite cells in the early stages of training [26]. RT also causes other morphological adaptations, such as hyperplasia, changes in muscle fine architecture, myofilament density and the structure of connective tissue [26]. Changes induced by RT at the muscle-fiber level have been related to hypertrophy of different types of muscle fibers. RT causes an increase in the CSA of IIX and IIA fiber types, but in some human studies type IIX fibers have been shown to decrease [3].

Exercise-induced muscle damage often follows unaccustomed and sustained metabolically demanding activities [57]. The cellular damage in muscular tissue is caused by excessive strain in the contracting fiber, not the absolute force

developed in the fiber or the muscle [58]. The anatomic site of myofibrillar injury is the attachment of the myofibrils to the extrasarcolemic cytoskeleton [28]. Some degree of skeletal muscle adaptation occurs in response to each dose of exercise, whether normal or abnormal, and there can be various degrees of adaptation [58,68]. Well-trained athletes show increased neuromuscular excitability; reduced neuromuscular excitability shows an impaired signal transmission to target organs and is a parameter of peripheral fatigue [63,68].
Structural changes in skeletal muscle during exercise training with different duration and intensity are fiber specific (Fig. 2). FT fibers are more vulnerable to exercise damage than ST fibers [94]. The focal denervation of muscle fibers during exercise training was reversible and accompanied by the regeneration of new axonal terminals growing into pre-existing synaptic grooves [87]. Exercise training may cause complete and focal injuries of some muscle fibers as well as partial denervation of individual muscle fibers, which could be factors for the activation of satellite cells [68,89,108].

4. Relationship between mitochondria and myofibrillar apparatus in muscle fibers

In the heart muscle, which has high oxidative capacity, intracellular phosphotransfer systems constitute a major mechanism linking the mitochondria and ATPases within specific structures – intracellular energetic units [82,93]. Mitochondria are precisely positioned between the myofilaments in muscle fibers with high or higher oxidative capacity [111]. The effectiveness of metabolic signaling strongly depends on structural-functional relationships of the interaction between mitochondria and sarcomeres [92]. Under conditions of hypoxia, the connections between mitochondria and sarcomeres are disturbed as sarcomeric components disintegrate the muscle cell structure and cause cell injury and death [92]. The activation of apoptosis may be partly responsible for the initiation of protein degradation and loss of muscle nuclei associated with local atrophy [23]. For example, the disruption of desmin impairs the linking of mitochondria to Z-disc and skeletal muscle exhibits impaired oxidative phosphorylation [81]. The 5'adenosine monophosphate-activated protein kinase (AMPK) becomes activated in skeletal muscle during acute bouts of exercise [4]. AMPK's main function is to monitor the energy status of muscle fibers and maintain muscle energy homeostasis [74].
Long-lasting endurance type exercise may lead to the depletion of the energy system, neuromuscular fatigue and muscle damage [1]. Children have less muscle mass than adults and generate lower absolute power during high-intensity exercise. Children's muscles were better equipped for oxidative than glycolytic pathways during exercise and had lower ability to activate their type II muscle fibers [77]. Skeletal muscle oxidative capacity increases with ET and an age-associated decline in oxidative capacity is related to the reduction in fitness [80].

Aerobic ET can positively influence structural changes to capillarity [37]. Type IIX/IIB muscles exhibit increased ADP concentrations in response to an increased workload, which conforms to the respiratory control theory in skeletal muscles [81].

5. Changes in neuromuscular apparatus

Exercise-caused synaptic remodeling is characterized by an impressive degree of specificity and sensitivity not only among different muscles but also among different fiber types within the same muscle [22]. Exercise training does not only result in the prevention of motor neuron loss or muscle fiber degeneration but supports a partial reversal of structural alterations that have already occurred [109]. Neuregulin has shown to support skeletal muscle adaptation to exercise training via metabolic regulation [33].

5.1. The effect of endurance training on neuromuscular junctions

The neuromuscular apparatus, which controls phasic motor impulses as well as neurotrophic influences, provides the plastic activity of the muscle tissue. Exercise training affects the structure of mammalian neuromuscular junctions with changes depending on age, type of muscle and character of exercise [87]. After one week of ET, a lot of neuromuscular terminals start branching [87]. ET causes the heterogeneity of the structures of the neuromuscular synapses, which is clearly expressed in type IIA muscle fibers (Fig. 3). The synapses of type IIA muscle fibers cover a large postsynaptic area as the well-developed synaptic apparatus provides intensive renewal of the structures of the muscle fiber [89].

The axon terminals of type I muscle fibers are relatively small, round or oval shaped and closely located. The surface of the neighboring neuromuscular contacts is smooth. The sarcoplasm near the terminals of the muscle fiber contains a great number of mitochondria, which contain a lot of cristae [87]. The axon terminals of type IIB fibers are elliptical and their synaptic vesicles are more generously provided with acetylcholine and other trophic factors. At the same time, the postsynaptic folds of the neighboring synapses have linked with each other. In comparison with type IIA muscle fibers, the postsynaptic folds of type IIB fibers are longer and more regular and they cover a much larger area of the sarcoplasm [87]. In type IIB fibers, the contact area is the largest between the ending and the surface of the muscle fiber.

In type IIB fibers, the postsynaptic folds extend near myofibrils and are separated from contractile structures by a thin sarcoplasmic layer. There is a large number of glycogen granules, few mitochondria and rarely any lysosomes in the terminals of neuromuscular synapses and in the postsynaptic area [87]. Coated vesicles appear in the sarcoplasm of the postsynaptic area of type IIA muscle fibers [87]. The occurrence of coated vesicles is not only related to the resynthesis of acetylcholine in nerve endings, but these vesicles also carry the proteins of choline receptors onto the postsynaptic membrane [87]. The connection with the

rough sarcoplasmic reticulum influences the regulation of muscle fiber protein metabolism [21]. If subsynaptic folds open into T-tubules, they participate in the formation of intermyofibril triads [19]. T-tubules in the sole plate form an extensive network, which together with the sarcoplasmic reticulum can form triads, the position of which makes them unusable for triggering muscle contraction [20].

6. Structural rearrangements in neuromuscular spindles

Muscle spindles monitoring muscle stretch are composed of nuclear bag1 (dynamic bag1), nuclear bag2 (static bag2), and chain fibers (static chain). During adaptation to increased motor activity, intrafusal muscle fibers show metabolic changes but do not cause hypertrophy [49]. Neuromuscular spindles are able to contract in the end regions and shorten simultaneously with muscle shortening during exercise. This allows the transmission of information about muscle length and the speed of contraction to higher centers of motor control at any time during exercise training. The motor zone of neuromuscular spindles is located near the poles, where the space under the capsules significantly diminishes. Each intrafusal fiber type has a distinct MyHC composition and a distribution of different MyHC isoforms along the whole length of intrafusal fibers [97]. Intrafusal fibers exhibit great variability in phenotypic expression. This variability is related to the plasticity of muscle precursor cells as muscle diversification apparently depends on heritable lineage derived properties interacting with environmental influences to give each muscle fiber its distinctive characteristics [95]. During muscle spindle regeneration, intrafusal satellite cells develop into extrafusal-like muscle fibers probably due to their motor innervation [96].

ET does not change the myosin isoform profile in bag1 and bag2 fibers but does so in chain fibers [117]. At the intensity of 60–75% of VO_2max, a correlation was found between the recruitment of bag1 and extrafusal type I fibers, between bag2 and type IIA fibers and between nuclear chain and IIB fibers [118]. ET causes essential destruction in the myofibrillar apparatus of nuclear bag spindles (Fig. 2). Focal destruction of myofibrils occurs both in the extrafusal and intrafusal fibers [90]. Mainly peripheral myofibrils lyse [87]. There are sarcomeres in intrafusal fibers, where only single thick filaments are missing on the border of the H-zone. At the same time, there are sarcomeres where the majority of thick filaments in the A disc have completely lysed [87]. This gives an impression that actin filaments are more resistant to proteolytic enzymes also in intrafusal muscle fibers [90]. Muscle spindle sensitivity to RT was shown about three decades ago and as a result, the mechanical response of extrafusal muscle fibers or the respective motor units improved [35]. During brief intensive exercise, bag2 fibers play the most important role in the early phase of training [119]. Despite clearly expressed destructive processes in the fibers of spindles, the regeneration potential has been preserved therein. This is confirmed by a large number of polyribosomes, which

form numerous rosettes in the sarcoplasm between myofibrils and in the peripheral sarcoplasm [87].

7. Changes in nerve endings of neuromuscular spindles

The fibers of the neuromuscular spindle have separate motor neurons from extrafusal muscle fibers and the motor neurons controlling extrafusal muscle fibers are larger (alpha motor neurons), whereas the motor neurons that innervate the muscle spindles (gamma motor neurons) are smaller. The interaction of the alpha and gamma systems during muscle contraction in the training process is important because the central part of the intrafusal fibers must not become slack at any time [87].
There are two types of motor nerve endings of the intrafusal nuclear bag static muscle fiber. Those located near the centre of the spindle have postsynaptic membranes and they form postsynaptic folds around the gamma-axon terminal [87,90]. The synaptic cleft filled with the basal membrane is between pre- and postsynaptic membranes of synapses. The axon terminal contains a lot of round mitochondria, which are full of cristae. There are small vesicles containing acetylcholin located between mitochondria, and very few mitochondria in the postsynaptic area [90]. As intrafusal muscle fibers are destined to become slack when the extrafusal fibers shorten, unless they also shorten to the same degree due to the gamma motoneurons, these ultrastructural changes during ET and RT support the idea of an increase of alpha-gamma coactivation during regular exercise training [87]. Intrafusal muscle fibers located in the region of type I extrafusal muscle fibers adapt themselves to ET by using a response reaction very similar to that of extrafusal fibers. When comparing these structural rearrangements in the nerve-muscle synapses of the extra- and intrafusal muscle fibers, it is obvious that destructive changes occurring in the intrafusal fibers are considerably smaller than similar changes in the synapses of extrafusal fibers [87]. The reason for this is the effect of tension, which in case of ET in the synapses of intrafusal muscle fibers is much lower than in the synapses of extrafusal fibers [90]. The comparison of changes in the ultrastructure of different types of extrafusal and intrafusal muscle fibers, and their innervation and regeneration potential during ET and RT gives ground to conclude that all these links function in a mutual relationship depending on the character of exercise training (Fig. 2, 3).

8. Relationship between muscle fiber oxidative capactity and contractile apparatus

Skeletal muscle fibers with higher oxidative capacity are relatively small compared to fibers with low oxidative capacity pointing to an increase in relationships between fiber CSA and VO_2max [110]. It is significant that only

cardiocytes have high oxidative capacity among striated muscle cells, while skeletal muscle fibers have low (type IIB/X) and higher oxidative capacity (type I and IIA) [82,83,87,92].

VO_2max is proportional to succinate dehydrogenase (SDH) activity [8] or oxoglutarate dehydrogenase activity [9] and consequently to the number of mitochondria [47,78]. Muscle fibers with a relatively large CSA had low SDH activity and vice versa [56,79]. Fibers with higher oxidative capacity contain higher quantities of satellite cells, myonuclei, mitochondria, mRNA, and total ribosomal RNA content (i.e. components of the transcription machinery). Insulin-like growth factor 1 (IGF-1) expression, a stimulator of myofibrillar protein synthesis, is also higher in type I fibers [10,101]. Myostatin, the expression inhibitor of muscle hypertrophy, is higher in type II fibers [62,120]. At the same time, the components of the degradation machinery of muscle proteins, such as ubiquitin ligases MAFbx and MuRF, are about twofold higher in fibers with higher oxidative capacity [110]. The higher rate of protein degradation in muscle fibers with higher oxidative capacity is balanced by a high rate of synthesis. This may be an important factor limiting the size of these fibers [110]. As a result of that steady state, protein turnover rate is faster in muscle fibers with higher oxidative capacity. In these fibers, the half-life of mitochondrial proteins is the shortest although the turnover of cytochrome C is higher in the low oxidative fibers [41]. ET stimulates mitochondrial biogenesis and improves its functional parameters [45,66].

9. Adaptability of different fiber types to endurance training

ET programs, in a variety of forms, improve the energetic potential of skeletal muscle and result in the effective functioning of the muscle contractile apparatus for longer periods of time [37,100,116]. High intensity interval training supplemented into the already high training volumes elicits improvements in skeletal muscle both during short-lasting intense and prolonged exercise performance [61]. It has been shown that low volume high intensity interval training maintains an athlete's endurance performance and muscle oxidative potential and increases intense exercise performance [50,51]. AMPK is activated in response to endurance training [114] and related to the metabolic adaptation of skeletal muscle. AMPK function includes induction of glucose transport, glycogen metabolism, fatty acid oxidation and transcriptional regulation of structural muscle genes [36]. The α1 isoform of AMPK has shown to be the regulator of skeletal muscle growth, while the α2 isoform regulates metabolic adaptation [70]. The peroxisome proliferator-activated receptor isoform δ (PPAR δ) is an important regulator of skeletal muscle endurance capacity as the Ppar δ gene increases skeletal muscle oxidative capacity by increasing type I fibers and by decreasing type II glycolytic fibers [67,113].

Aerobic exercise stimulates protein turnover by increasing muscle protein degradation and synthesis rate in the recovery phase after exercise [16]. Protein turnover is a rapid way for the redistribution of amino acids into new proteins as they are required because amino acids are derived from protein breakdown and incorporated into the newly synthesized protein. Protein turnover rate in skeletal muscle is relatively slow, particularly contractile proteins. The turnover rate of MyHC and MyLC isoforms provides a mechanism, by which the type and amount of protein can be changed in accordance with the needs of the contractile machinery during adaptation to ET [2,85]. Activity patterns of muscle fibers where MyHC I and IIa isoforms are dominant have relatively high oxidative capacity and are recruited during endurance exercise [86]. It has been shown that in rat FT *plantaris* (Pla) and extensor *digitorum longus* (EDL) muscles, the difference in oxidative capacity is about 10% [83]. Endurance exercise training increased the oxidative capacity in Pla muscle by 16% and in EDL muscle by 12% [83]. How much of gene expression of MyHC isoforms is due to genetic predisposition and how much to the specificity of training is unresolved [5]. Differences in MyHC isoforms' turnover rate between FT muscles show that the turnover rate is faster in muscles where oxidative capacity is higher [83]. Changes in MyHC isoforms' turnover rate in FT muscles during ET also characterize changes in the myofibrillar apparatus through protein metabolism. The latitude of changes in myosin isoforms' turnover rate also shows the significance of MyHC isoforms in the process of adaptation to ET (Fig. 3). Although the exact role of MyLC isoforms in FT muscles during ET is not fully known, changes in MyLC isoforms' relative content and their relation with the character of training show that they play an important role in the process of modulation of the contractile machinery during ET [2]. There is still no answer to the question whether other myofibrillar proteins can modulate the functional properties of myosin during ET and if it is dependent on the training volume. C-protein, which binds either myosin and actin or affects the mechanical properties of myosin cross-bridges by linking the S2 segment of myosin to the backbone of the thick filament [38], has shown to be very sensitive to high training volume [84]. C-protein together with MyHC isoforms plays the key role in changes of functional properties of the contractile machinery during an excessive increase in ET volume [84].

10. Adaptability of different fiber types to resistance training

Resistance exercise has become one of the fastest growing forms of physical activity for different purposes: improving athletic performance, enhancing general health and fitness, rehabilitation after surgery or an injury, or just for the pleasure of exercise [30]. The nervous system has shown to have an important role in athletes' training process leading to the peak in their maximal strength [34] and explosive exercise facilitates the neuromuscular system in this [65]. RT is a strong stimulus for growth of adult skeletal muscle due to muscle fiber hypertrophy [98]

and promoting signaling events arising from mechanical deformation of fibers, hormones and immuno/inflammatory responses [98]. Differences in resting and post-exercise concentrations of skeletal muscle testosterone and steroidogenic enzymes may be caused from species dependent reasons in muscle testosterone production, for example differences between humans and rats [112]. RT promotes protein synthesis due to increased transcription and translation [98]. RT enhances the synthesis rate of myofibrillar proteins but not that of sarcoplasmic proteins [73] and this is related to the mammalian target of rapamycin by activating proteins within the nitrogen-activated proteinkinase signaling [72]. A significant difference was observed between previously trained young and old participants in recovery from resistance training [71]. These results suggest a more rapid recovery in the young group. It seems that recovery from more damaging resistance exercise is slower as a result of age, whereas there are no age-related differences in recovery from less damaging metabolic fatigue [25]. Recovery from RT, during which the power of exercise increased less than 5% per session, caused hypertrophy of both FT and ST muscle fibers, an increase in the myonuclear number via fusion of satellite cells with damaged fibers or the formation of new muscle fibers as a result of myoblasts' fusion in order to maintain myonuclear domain size [88].

Contractile proteins turned over faster in type I and IIA fibers than in IIX/IIB fibers and the turnover rate of skeletal muscle proteins in skeletal muscle depends on the functional activity of the muscle [87]. RT increases of the turnover rate of skeletal muscle contractile proteins (Fig. 3). Adaptational changes first appeared in newly formed or regenerating fibers and these changes lead to the remodeling of the contractile apparatus and an increase in the strength generating capability of muscle. These changes are more visible in muscle fibers with higher oxidative capacity [88].

The recovery of skeletal muscle mechanical properties depends on the structural and metabolic peculiarities of the skeletal muscle and the character of RT [87]. For example, exhaustive RT results in a reduction in resting concentration of IGF-1 and an elevation in its binding protein 3 (IGF BP -3). This reaction may be seen as a compensatory reaction to accommodate the reduction in IGF-1 to preserve IGF availability [53].

11. Adaptability of hybrid fibers to exercise training

It is well known that physiological function of muscle fiber type is an outcome of MyHC isoform expressed within fiber. Some fibers, the so-called hybrid fibers, express a combination of two or more MyHC isoforms [13,99]. Laboratory animal experiments have shown that the relative proportions of hybrid fibers vary significantly from muscle to muscle [13]. In human skeletal muscle, hybrid fiber types represent a significant population of fibers, but the stability of this fiber phenotype is currently unclear. For example, electrical stimulation increases the proportion of hybrid fibers [76] and mechanical load and thyroid hormone

changes the proportion of hybrid fibers in skeletal muscle [14]. Running exercise decreases hybrid fibers in human skeletal muscle [59], whereas muscle hybrid fibers are relatively refractory to the effect of exercise in mice [32]. It is not clear yet what role hybrid fibers play in endurance and resistance training of athletes, particularly in changes of skeletal muscle oxidative capacity.

12. Concurrent endurance and strength training

It was shown about three decades ago that concurrent training for endurance and strength decreases the gain in muscle mass in comparison with training for strength alone [40]. This effect was explained by AMPK blocking the activation of the mammalian target of rapamycin complex-1 (TORC 1) by phosphorylating and activating the tuberous sclerosis complex-2 (TSC 2) [52]. This interference in skeletal muscle strength development was also explained by alterations in the protein synthesis induced by the high volume of endurance exercise or by frequent exercise training sessions [74] or related to the impairment of neural adaptations [12]. Based on recent studies, it seems that the effect of concurrent ET and RT on strength and endurance capacity depends on the trainability of athletes. Both, maximal and explosive strength training performed concurrently with ET have proved to be effective in improving strength, power and muscular activation in recreational endurance athletes [102]. Concurrent training improved performance in all occupational tasks and did not interfere with improvements in strength, power and endurance measures compared to ET or RT alone in recreational athletes [39].

Concurrent RT and ET in elderly men has shown that strength gain was similar to that observed with RT alone, although the volume of training was half of that in RT alone [115]. Using lower training volumes in concurrent training in older men [54] in comparison with ET and RT alone leads to similar strength enhancement with no presence of interference in this population [55]. It seems that the effect of concurrent ET and RT may be different in top athletes and recreational and elderly exercising subjects. The main complication in the current understanding about the concurrent training effect on skeletal muscle is that we do not know whether a muscle fiber is capable to undergo hypertrophy and maintain endurance capacity at the same time, and why it is different in top athletes and recreational athletes.

13. Conclusions

Athletes' responses to endurance and resistance training are individual. To find optimal training volume or intensity/power is complicated and the optimal recovery period for performance improvement is also individual. Only an appropriate training regimen leads to performance improvement through a

cascade of structural-functional changes. For both recreational and top athletes, the ratio between training load and recovery in endurance training has to support the development of the mitochondrial apparatus, which is able to supply the increased energy requirement of muscle fibers with higher oxidative capacity. Appropriate resistance training has to support an increase in the cross-sectional area of the whole muscle and individual fibers, an increase in myofibrillar size and number. The most remarkable structural changes in resistance training occur in fast-twitch muscle fibers as these fibers are more vulnerable to exercise damage than slow-twitch fibers. An inappropriate endurance and resistance training regimen leads to depletion of the muscle energy system, causes muscle damage and neuromuscular fatigue.

Skeletal muscle fibers with higher oxidative capacity are relatively small compared to fibers with low oxidative capacity. These fibers also have a faster protein turnover rate, higher 5'adenosine monophosphate-activated protein kinase activity, higher content of peroxisome proliferator-activated receptor isoforms δ, and faster skeletal muscle regeneration capacity. For designing and implementing training programs, it is suggested that coaches and athletes take into account physiological significance of structural-functional peculiarities of different muscle fibers, their specificity of adaptability to mode of exercise, and regeneration capacity.

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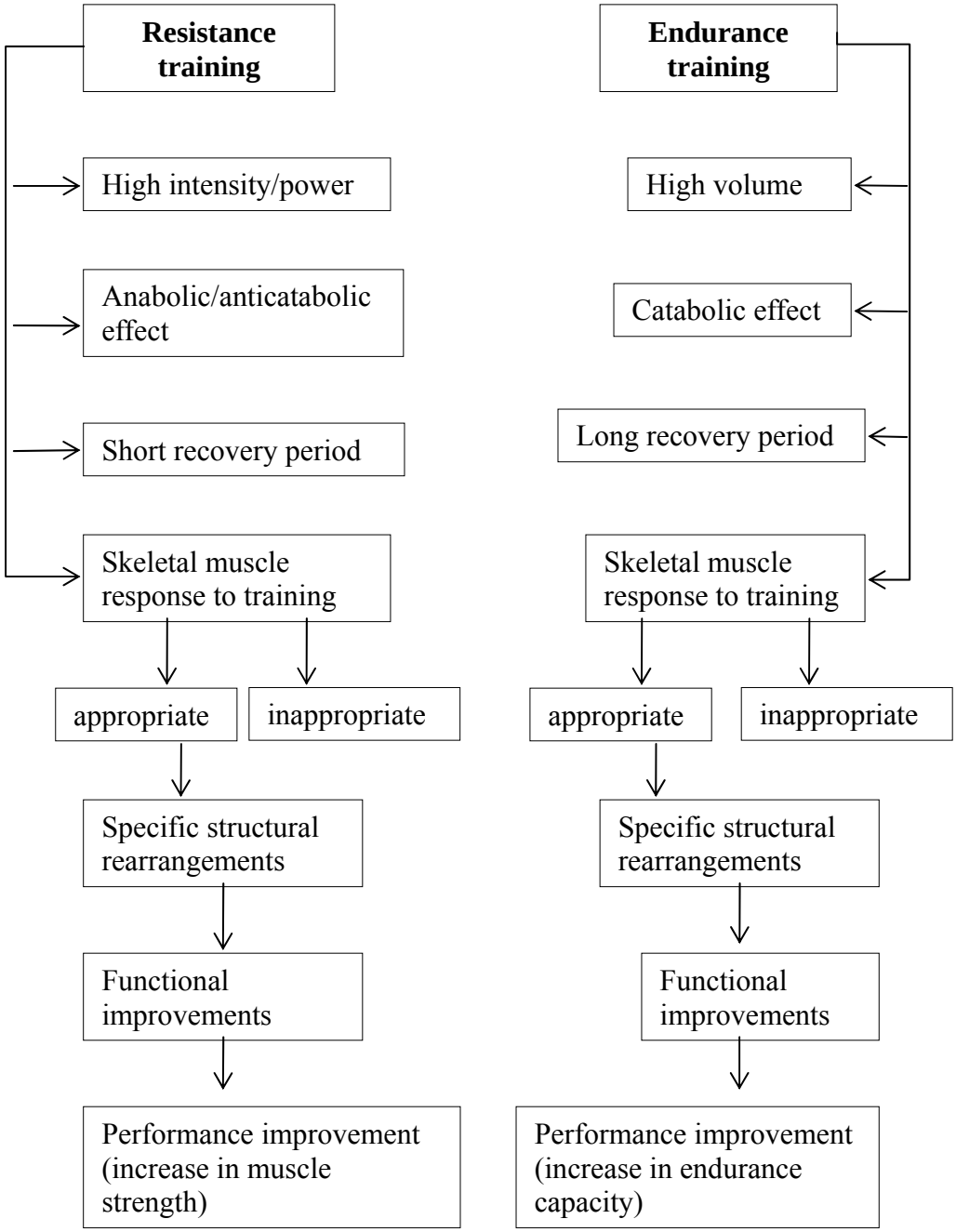
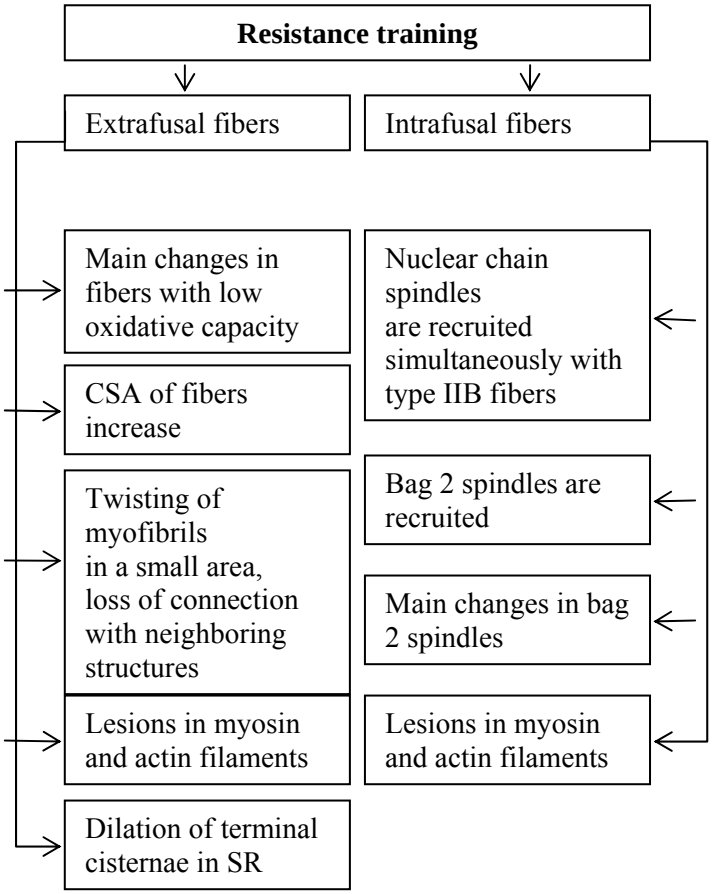


Figure 1.	Performance improvement through a cascade of strength and endurance training effects in skeletal muscle


Resistance training
Extrafusal fibers
Intrafusal fibers
Main changes in fibers with low oxidative capacity
CSA of fibers increase
Twisting of myofibrils in a small area, loss of connection with neighboring structures
Lesions in myosin and actin filaments
Dilation of terminal cisternae in SR
Nuclear chain spindles are recruited simultaneously with type IIB fibers
Bag 2 spindles are recruited
Main changes in bag 2 spindles
Lesions in myosin and actin filaments

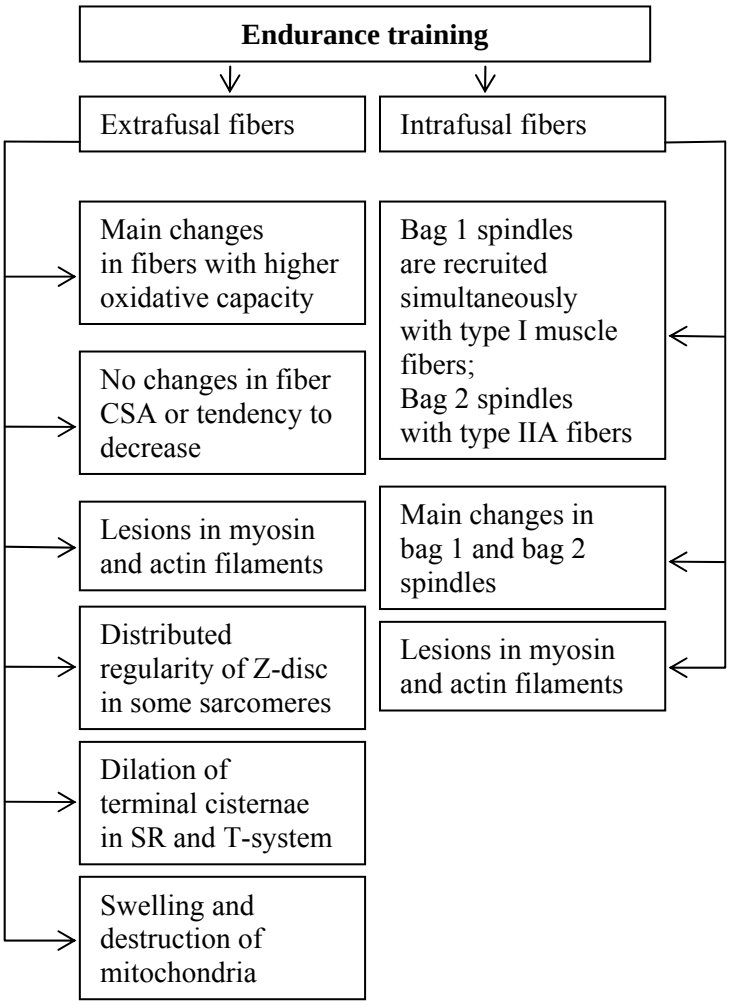


Figure 2.	Destruction in extrafusal and intrafusal muscle fibers during resistance and endurance training All these changes in skeletal muscle are specific and happen in a mutual relationship with training mode

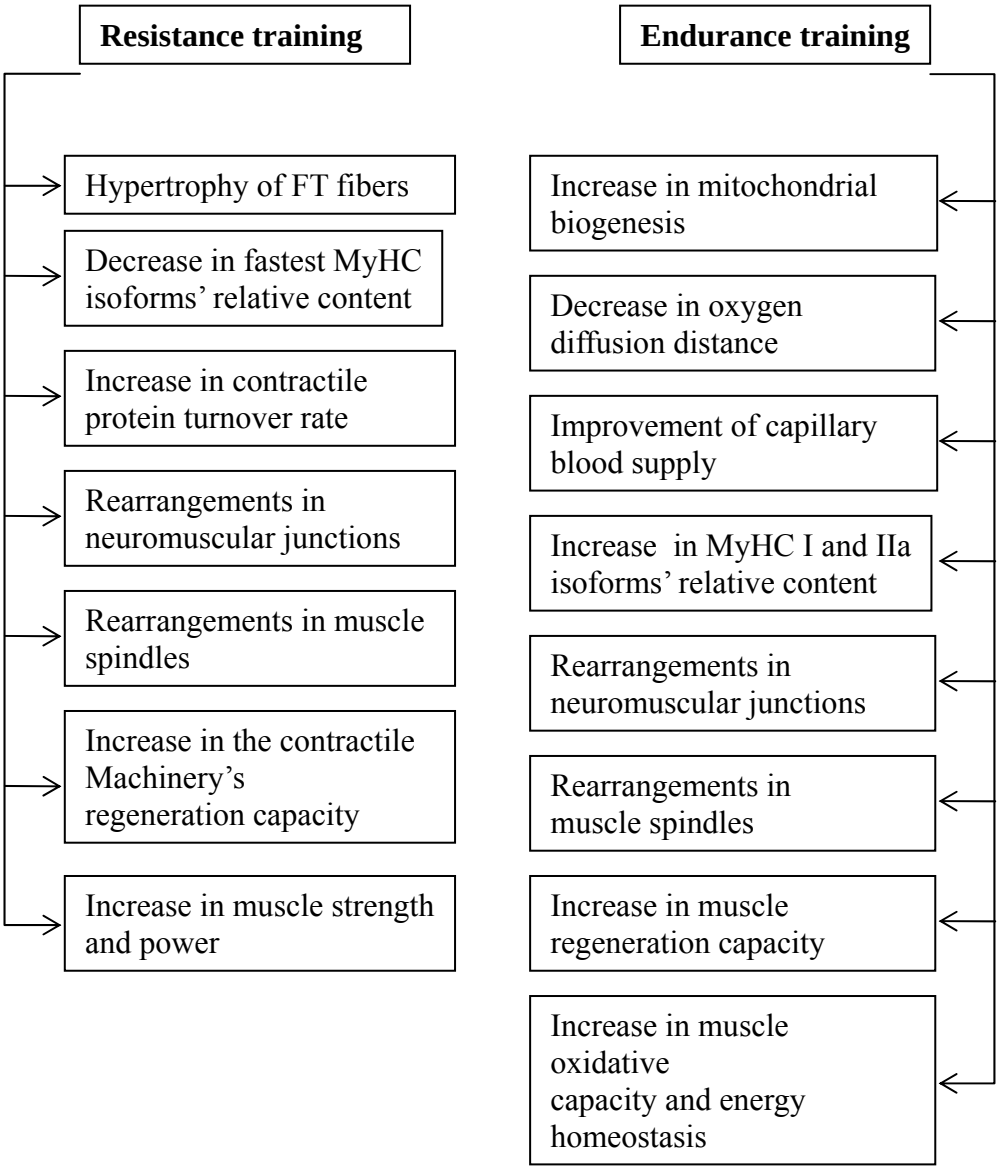


Figure 3.	Structural-functional rearrangements in skeletal muscle during resistance and endurance training

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