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Effects of Physiotherapy Interventions on the Function of the Locomotor System in Elder Age: View of Theory and Practice

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Abstract

The aim of this chapter is to give an overview about the aging processes in the neural and musculo-skeletal system at cellular and tissue level to highlight the demand for physiotherapy interventions. Searching the relevant literature published in the last decade, it was found that the loss of muscle mass (myofiber atrophy and decrease in the number of myofibers) is associated with decreased regeneration capacity of the skeletal muscle, deterioration of the neural control and bone remodeling as well as the impaired microcirculation leading to insufficient adaptation to the physical exercises. In the management of the aging-related deterioration of the skeletal muscle (sarcopenia), the first tool is the resistance training that improves the muscle mass and power as well as the functional outcomes regarding the mobility and physical performance. The endurance (aerobic) training improves the cardiovascular and respiratory status providing better blood supply to the skeletal muscle and exerts some effects directly to the skeletal muscle and bone (increases the mitochondrial functions, improves the bone remodeling). The combination of aerobic and resistance training seems to be more effective against the sarcopenia and osteopenia. The balance training gives additional benefits, so (together with increased muscle power and performance) improves the quality of life.

Keywords: skeletal muscle, skeleto-neuro-muscular system, aging, physiotherapy practice, physiotherapy and aging

1. Introduction

The homeostasis of the neuromuscular system requires preserved muscle structure and functionality with normal regeneration capacity as well as the intact motor control including peripheral innervation and upper control mechanisms. For the normal locomotion the healthy bone structure and function provide stable basis for muscle function and the proper blood supply is inevitable. All components may be influenced by aging and diseases to some extent causing dysfunction of motor activity.

The skeletal muscle fibers are multinucleated huge cells containing contractile proteins (actin and myosin) organized into sarcomeres. In the fetal life the

embryonal myoblasts fuse into long multinucleated structures. It is relevant to our topic that the skeletal muscle fibers are categorized basically into slow type (Type I) and fast type (Type II) twitch fibers based on the kinetics of contraction-relaxation cycle and metabolic properties. Recently, this simple model has become more complex and the diversity of muscle fibers has revealed [1].

The skeletal muscle fibers do not show spontaneous activity without innervation. The somatic motor nerves form neuromuscular junction (NMJ) with the endplate of the muscle fibers. The NMJ serves as the site of communication between the two structure. One motor neuron commonly innervates more than one muscle fibers constructing a motor unit in which the muscle fibers work together. The motor neurons and the muscle fibers influence the activity of each other, i.e. the motor neuron activates the myofibers, and the muscle fibers release cytokines that act on the motor neuron. The third component of the communication is the perisynaptic Schwann cell (PSC) population. The PSCs play stabilizer and trophic role in the NMJ. Recently, a new component, kranocyte has discovered that is a fibroblast-like cell covering the NMJ. The kranocytes may play role in the post-injury nerve regeneration [2].

The muscle stem cells (satellite cells) are responsible for the muscle repair after a cell damage caused by micro- or macro-traumatization. The satellite cells are located along the multinucleated muscle fibers between the muscle fiber and the basal lamina. On the adequate stimulation they can proliferate, fuse and form a new muscle fiber or – undergoing an asymmetric cell division – can regenerate the pool of the satellite cells [3]. Our knowledge about the factors regulating the normal function of the stem cells and the pathomechanism of impaired muscle repair in different conditions is ever-increasing and reported in many publications. Recently, Feige et al. [4] has reviewed the factors affecting the self-renewal capacity and repairing function of satellite cells in diseases and aging.

The healthy bone is a fundamental organ in the skeletomuscular system. There is an interesting concept to explore the crosstalk between the muscles and the bones. It means that the skeletal muscles and bones interact with each other and keep the homeostasis in normal stage [5]. The bone is a very dynamic structure with continuous bone resorption and counteracting bone formation. This process is called bone remodeling that plays important role in the bone homeostasis. The resident cells of the bone tissue are osteoblasts, osteocytes, osteoclasts and the bone lining cells originated from the mesenchymal stem cells located in the bone marrow. The osteoblasts are responsible for the bone formation characterized by intensive protein synthesis and release of proteins into the bone matrix. The osteocytes located in the lacunae surrounded with the mineralized bone matrix serve as mechanosensors coordinating the function of osteoblasts and osteoclasts. Osteoclasts are multinucleated cells with bone resorptive ability. Recently, information about their cytokine releasing activity and effects on other bone cells has emerged. Bone lining cells are quiescent osteoblasts covering the bone surfaces. Their role in the bone remodeling is poorly understood, but more and more data about their secretory activity and effects on the other bone cells has been published [6–8].

The microcirculation comprises terminal arteriole, arteriovenous capillary, metarteriole, capillary bed and postcapillary venule. The microcirculation supplies the tissues with oxygen and nutrients, delivers carbon-dioxide and metabolic products and provides optimal milieu for cellular functions. Hendrickse and Degens reviewed the morphology and function of microvasculature including the role of these elements in the plasticity of skeletal muscle microcirculation. The adaptation of microcirculation to functional demand is an essential requirement for proper functioning of the muscle. The parallel change in the myofiber diameter and capillary density has been reported in many articles. The endothelial cells are

very important in vascular homeostasis and vascular adaptation. Nitric oxide (NO) promotes the release of the vascular endothelial growth factor (VEGF) that serves as the main angiogenetic molecule [9].

Another review article provides an overview on the systemic and local control of blood flow in the skeletal muscle microvasculature. The metabolic and endothelial regulations must be emphasized in relation to the topic of this chapter. The endothelium-derived relaxing (NO, endothelium-derived relaxing factor – EDRF, prostacyclin) or contracting (endothelin) substances play substantial role in the functional adaptation of microcirculation in normal and pathological states. Differences of microcirculation in oxidative and glycolytic muscles are also reviewed that worth to be considered in training protocols [10].

It is generally accepted that the physiotherapy (including various types of exercises) is a key factor in the management of sarcopenia. Basically, the physical exercises can be categorized into endurance (aerobic) and resistance type exercises. The endurance (aerobic) training works with large muscle groups, being sustained and rhythmic, e.g. swimming, burst walking, dancing, cycling, jogging, long distance running, etc. The most prominent functional outcome of this type of exercises is the improvement of the cardiorespiratory functions. The resistance training includes series of movements performed against static or dynamic resistances (e.g. weight, elastic band) that impacts also the major muscle groups and several joints. Usually it is repeated 2 or 3 times per week with increasing dosage. The primary aim of the resistance training is to improve the muscle power as functional outcome [11].

The aim of this chapter is to offer an overview about the aging processes in different elements of the locomotor system, to summarize the current results related to the physiotherapeutic interventions, and to give an insight into the undergoing processes influenced by exercises.

2. Aging-related alteration of the neural and musculo-skeletal system

In the past decade numerous evidences have been accumulated about the structural and functional changes during the aging process in muscle homeostasis including the loss of muscle mass and/or strength, the impaired repair mechanism and the disturbed adaptation of microvasculature to the metabolic demand. The loss of muscle mass and strength (sarcopenia) as well as the decrease in the bone mass (osteopenia, osteoporosis) together with the alteration of cardiovascular and respiratory system and disturbed metabolism cause the frailty syndrome [5, 12]. The regulation of muscle metabolism, its adaptation to nutrition and short-term or chronic physical exercise in young versus elder age have been overviewed in a recent review [13]. Further reviews also provide complex approach to aging process regarding the elements of muscle homeostasis (muscle fibers, motor unit, regenerative capacity, metabolic background) [14, 15].

To interpret the data, it is worth to distinguish the primary and secondary aging. The primary aging of skeleto-neuro-muscular system is manifested in a progressive deterioration in the structure and disturbed function. The secondary aging refers to the additional structural and functional changes caused by diseases and lifestyle factors. The aim of the therapeutic interventions can be to make slower the aging by limiting the secondary aging process [16].

2.1 Aging of skeletal muscle fibers and the whole motor units

Sarcopenia is the progressive loss of muscle mass and/or strength with consequent decline in functional outcome and activity of daily living (ADL) functions.

Among others, Wilkinson et al. [17] reviewed the characteristic changes in the skeletal muscle in elder age. It was revealed that the decline in the muscle mass derives from the muscle fiber atrophy and the decrease in the number of muscle fibers. The imbalance between the protein anabolism and catabolism was detected with conclusion that the protein turnover is mainly affected by the protein intake and the physical activity. The aged muscles seem to be resistant to the anabolic stimulation (e.g. insulin resistance) that causes loss of muscle proteins, i.e. atrophy. The sedentary lifestyle and the chronic, partial immobilization due to physical inactivity facilitate the loss of muscle mass [13, 17].

The impaired mitochondrial functions, mitochondrial dynamics and mitochondrial autophagy with consequent decrease in oxidative capacity of muscles are also associated with the aging-related sarcopenia, especially in the fast type myofibers [18].

A new approach is the investigation of the aging-related changes in the whole motor unit (motor neuron, NMJ and the innervated muscle fibers) together. We have found two review articles reported in the last decade that are closely related to our topic and give an excellent basis for interpretation of the effects of physical exercise on the neuromuscular functions [19, 20].

The loss of motor neurons, formation of very large motor units during reinnervation together with the decrease in the number and diameter of the muscle fibers (sarcopenia) impact negatively the mechanical performance and the fine motor control of the muscles. In the peripheral nervous system, the loss of motor neurons with high diameter is prominent, to large extent in the lumbar region. The effect of aging is muscle specific, i.e. the muscles in the lower limb are more affected than in the upper limb, the muscles being fast (type II) are more impaired than the muscles containing mainly slow fibers (type I). The upper motor control is also impaired by aging due to decreased excitability of corticospinal pathways [19].

The reorganization of the motor units, the decreased number of motor neurons and the increased number of myofibers innervated by an individual motor neuron seems to be the first step in the aging process. At cellular level, decrease in the rate of axoplasmic transport, the velocity of impulse propagation, and the speed of nerve regeneration were detected together with the fragmentation of the NMJ and impaired signal transduction [20].

The impaired neuromuscular function is manifested in the decreased maximum strength, power, and RFD (rate of force rise: DF/Dt) and in the attenuated functional capacity in daily living [19].

2.2 Aging-related decrease in the regeneration capacity of the skeletal muscle

It is widely accepted in the literature that the number of satellite cells with proliferative ability becomes progressively decreased in elder age resulting in the attenuated hypertrophy during exercise and the muscle regeneration after a muscle injury. The impaired self-renewal capacity has also been described in elder age leading to decreased number of satellite cells being in quiescence and become activated under stimulation. The imbalance between the symmetric and asymmetric cell division (resulting in proliferating cells and satellite cells returning to quiescent state) seems to be the key factor in the aging process of the muscle regeneration [3, 4].

The regeneration capacity can be influenced by the intrinsic and extrinsic factors determining the proliferation and differentiation of the satellite cells and the renewal of the quiescent satellite cell pool [21]. The extrinsic factors have been intensively studied [see ref. 4], but the intrinsic mechanisms occurring inside the muscle cells have been rather unknown. Blau et al. reviewed genetic experiments oriented to discover the intrinsic changes in satellite cells associated with aging [22].

In another review the aging-associated genetic changes are also reported. The stem cells become fragile with increasing chance of damage and death. The number of senescent cells (alive, metabolically active cells without cell division) increases that release pro-inflammatory cytokines with consequent inflammation. Replacing the lost myofibers, fibrosis and accumulation of adipose tissue is also characteristic in aging [23].

The first step in the muscle regeneration is the local inflammation when macrophages (M1 and M2) infiltrate the surroundings and eliminate the cell fragments. In elder age, the balance between the M1 and M2 macrophages is impaired leading to improper satellite cell activation. The extracellular matrix is also affected leading not proper milieu for satellite cells [24].

2.3 Aging and bone

The aging process of the bone is manifested in osteopenia and decreased mineralization of the bone (osteoporosis), in a disease with high prevalence and risk of pathologic fractures. The aging of bone (osteopenia) is frequently associated with sarcopenia therefore the physiotherapy interventions must be focused on treatment of sarcopenia and the osteoporosis parallel.

It has been reported recently that the dysfunction of osteogenic mesenchymal stem cells (MSCs) is the one sign of the aging process. The differentiation of MSCs is shifted towards adipogenesis instead of osteogenesis. The details of pathomechanism at cellular and molecular level has been reviewed by Infante and Rodríguez in 2018 [25].

The aging alters the number and function of osteoblasts (bone-forming cells) and causes impaired mineralization. In the background, the impaired organization of the cytoskeletal structure of the osteoblasts is supposed. The accumulation of the free oxygen radicals may be the reason of consequent series of altered processes [26].

In elder age, the adaptation of bone macro- and microstructure to the mechanical load is substantially impaired, mainly due to the inadequate control of osteoblasts and osteoclasts activity by the osteocytes as mechanosensors. Osteocytes are responsible for the balance between the activity of osteoblasts and osteoclasts (bone formation and bone resorption). In the elder age, the osteoclast activity exceeds the osteoblast activity mainly due to the impaired coordinator function of osteocytes. The current literature is heterogeneous related to the changes in the density and morphology of osteocytes, the shape of lacunae and canaliculi network. Differences may derive from species and sex differences as well as from different techniques used for measuring and analyzing the data. The type of bone (trabecular or compact) also may modify the changes and reactions of cellular elements [27].

2.4 Aging-related changes in the microcirculation

Evidences for the microcirculatory theory of aging has recently been reviewed. Decreased capillary density with reduced blood flow and insufficient tissue perfusion has been reported by several authors. Although, the experimental data are somehow conflicting according to the basal flow and post-exercise hyperemia in human leg; some evidences exist showing that the blood flow and reactivity of the vessels to exercise decline in elder age [9, 28]. It is suggested that the decrease in the capillary density precedes the sarcopenia [9]. Other data are not in agreement with this statement since neither capillarization nor arrangement of microvasculature seems to be affected by aging, but there are evidences for impaired endothelial functions including decreased NO and prostacyclin production and insufficient spread of vasodilation along the microvasculature [10].

It is widely accepted that the function of microvasculature is altered by aging itself and due to the accompanying diseases being frequently present in elder people. However, the possibility for *in vivo* investigation of microvasculature is limited by technical difficulties. A new promising tool is the contrast-enhanced ultrasound (CEUS) method that provides a relatively non-invasive imaging technique for clinical and research application [29]. By using this technique, impaired micro-vascular reaction to isometric exercise and attenuated, delayed post-exercise hyperemia were found in middle-aged subjects in comparison to young people without significant differences in vascular morphology and total leg perfusion [30].

Regarding the blood supply, the capillary: fiber (C:F) ratio is a determining parameter. The C:F ratio is lower in the patients with sarcopenia than in the patients at similar age without sarcopenia. The C:F ratio is mainly affected by aging in the skeletal muscle type II (fast) while is not changed in the muscles type I (slow). On the other hand, the increase in the fiber size (hypertrophy) is not associated to the increased capillarization [9].

It is also interesting that the capillary endothelium and the satellite cells act on each other, i.e. the vascular endothelium-derived growth factor (VEGF) stimulates the proliferation of the satellite cells and the angiogenesis is facilitated by the satellite cells. It is reported that the VEGF production is decreased in advanced age leading to loss of capillaries. Furthermore, the distance between the capillaries and satellite cells increases resulting in impaired regeneration of muscle fibers [9].

3. Physiotherapy on functional outcomes

It is widely accepted in the literature that the level of daily physical activity and the structured exercises contribute to the preservation of skeletal muscle structure and function and attenuates the aging-related decline acting directly on the neuromuscular or indirectly on the other system of organs, especially on the cardiorespiratory system [31].

The endurance (aerobic) exercises provide good basis for intervention against the decrease in muscle loss, while resistance exercises directly increase the muscle mass and performance. The combined training programs including resistance and aerobic exercises, completed with balance training provide the effective interventions in prevention of fall and improving the every-day functionality [9].

3.1 Effects of resistance training

The aging causes severe limitation in the every-day physical activity (walking, climbing stairs, rising from a chair etc.), predominantly in the lower extremities. To increase the physical performance, the improvement of the muscle power (the product of muscle force and contraction velocity) is the most important requirement. The widely used traditional resistance training (consisting heavy weights moved at a slow/moderate velocity) increases the power and functional performance but improves the contraction velocity to less extent than the power training (where the concentric movements are performed at high velocities). The power training with rating of perceived exertion is recommended to reach the best functional outcome [31].

The complex effects of strength (resistance) training has also been reviewed including improvement of muscle strength, reduction of sarcopenia and bone loss, as well as decrease in the risk of fall and injury by using different training parameters. Higher intensity of strength training results in more benefits even in old people. Significant improvement of functional and clinical outcomes was found also in patients suffering with different diseases [32]. The relationships between the

sarcopenia and physical activity were analyzed in a systematic review and meta-analysis where the resistance training was emphasized as a potent intervention against sarcopenia [33].

In a recent review, the controlled resistance training has been designated as the most powerful and fundamental tool for improvement of muscle strength, power and functional outcomes as gait speed, Timed Up and Go test (TUG), sit-to-stand test, Short Physical Performance Battery (SPPB) scores leading to a decrease in the risk of falls even in the frail persons [9].

Decline in the muscle power begins in the 4th–5th decades, so it is very important to start the progressive resistance training in middle age focusing on the muscles in lower extremity (gluteal muscles, quadriceps, and hamstrings) to prevent the further deterioration and progressive limitations in mobility. The leg press and knee extensor training resulted in similar improvement in the muscle power and functional outcomes. The exercise intensity seems not to be a significant moderator of the efficacy of resistance training improving the muscle force. It is suggested that the higher training intensity results in increase in the absolute force while the training at lower intensity increases the contraction velocity. The training volume (product of sets and repetition) has been in negative correlation with muscle power (the less volume resulted in higher power). The effect of variation in intensity and volume requires further meta-analysis [34].

Another systemic review and meta-analysis revealed that the most effective resistance training regarding the muscle strength was done with 2–3 session/week with 2–3 sets/exercise and 7–9 repetition at 70–79% of the 1RM for 50–53 weeks [35].

The multiple benefits of resistance training were reviewed including the facilitation of the physical functions and increasing the bone mineralization [36].

A follow-up study carried out in 6th and 18 months after a 12-week resistance training with 149 participants explored that the maintenance of benefits gained during a supervised resistance training was sustained only for a short period. 66% of participants self-reported doing the recommended level of physical activity (≥ 30 min/d) including walking, swimming, gymnastics and gardening, but only less than half of the participants continued the resistance exercises. The muscle strength of quadriceps decreased in comparison to the value at the end of the supervised training but remained higher than before the training program. In general, neither the leisure time physical activity nor the uncontrolled exercise training could completely prevent the decline in the muscle strength, only could limit the negative tendency. In contrast, the result of timed up and go test improved by exercise training was unchanged during the follow-up [37].

Recent review focused on the effect of physical activity in the prefrail or frail persons. Definition of frailty syndrome can be seen in a review article [12]. Although the intervention protocols were heterogenous, the most authors applied resistance training aiming to increase the muscle strength in frailty syndrome. It was generally reported that the physical activity reduced the frailty, improved the physical performance and caused a slight increase in the muscle strength [38].

Comparison of machine-based RT (M-SRT) on stable surface and RT on unstable surface (URT) either in machine-based (M-URT) or free-weight URT (F-URT) form resulted in similarly significant improvement in the muscle strength and power of lower extremities and balance in the groups of old participants (65 to 80 years). The lower extremity muscle strength was increased to highest extent in machine based URT, but the degree of muscle power improvement was independent on the form of exercises. The gait analysis revealed also important impact on parameters independently of the form of training. It has clinical relevance that the maximal training load of the squat-movement was significantly lower in F-URT in comparison to two other types of exercises [39].

3.2 Effects of endurance training

The numerous benefits of endurance (aerobic) training in old age are evidenced in several publications. Regarding the locomotor system, the increased aerobic capacity must be emphasized, but there are evidences for increased muscle strength on the effect of a long-term aerobic training [18].

The impact of endurance training on sarcopenia has been revealed less than of resistance training because the improvement of muscle mass and strength by resistance training is in the focus of investigators [13].

The primary aim of the endurance (aerobic) training is the improvement of cardiovascular functions. Beside the impact on the cardiovascular health the aerobic physical activity influences the metabolism, increases the glucose tolerance, positively acts on body composition, and is an important factor in maintenance of the bone density [40].

3.3 Effects of combined training

There are a lot of publications regarding the effects of combined (multimodal) exercises on general fitness and especially the improvement of sarcopenia in old age. We summarize here the most relevant data gained from supervised, controlled exercise training programs consisting of aerobic (AT) and resistance training (RT) or RT and balance training. The functional outcomes are highlighted beside the feasibility and safety of the programs in old population without severe comorbidities.

Combined AT (2 times/week) and RT (2 times/week) were applied in a 6-week high-volume, moderate-intensity exercise program where the measurement of the functional outcomes (TUG test and the SPPB) was completed with the exploration of feasibility and safety of the training program for old untrained persons. The results showed unchanged TUG but significantly improved SPPB scores. The positive feedback about the subjective experiences during the follow-up in the semi-structured interviews and adherence to enter a longer program indicate that this exercise protocol is promising for the future and worth to consider these findings in planning the exercise interventions [40].

The functional outcomes (gained from the TUG test, the functional reach test, 30-second chair stand test and the 6-minute walk test) were analyzed comparing to the control on the effect of a 32-week aerobic training alone (3 times per week) or combined with resistance training (1 session of RT + 2 session of AT) in a randomized controlled trial carried out in a group of old (>65 ys) men ($n = 22$ in each group). It was found that the AT alone caused significant decrease in the time measured by TUG test and increase in the value of functional reach test and distance in the 6-minute walk test at the 24th weeks of the program and later. The combined training evoked greater improvement in parameters mentioned above with earlier manifestation (the walking distance became significantly higher as in the control group already at the 8th week). It was suggested by the authors that the improved functional outcomes might decrease the risk of fall [41].

The frequency (2 or 3 times per week) of combined (resistance and aerobic) training did not influence the functional outcomes in old men [42].

It was found in a randomized clinical trial (LIFE study) that the risk of fall in elder age cannot be attenuated by using resistance and balance training together with long-term structured physical activity (walking, strength and balance training) in the very old age (70–89 years) in sedentary people with functional limitations, but can reduce the rate of fall with consequent fracture and hospitalization, especially in men. The training program lasted for 24–42 months, partly in a supervised form (2 sessions/week with 63% attendance) and partly in the form of home-based activity (3–4 sessions/week) [43].

The effect of combined, high level balance and moderate intensity resistance training in long-term residential age care was also reported focused on the prevention of fall. Significant decrease in the rate of falls and increase in physical performance were found after a 25-week intervention period with progressive dosage followed by a maintenance program with low dosage up to 12 months [44].

4. Theoretical interpretation of practical experiences

It is interesting to see the theoretical findings regarding the effects of physical exercises on the structure and function at cellular and tissue level. These data may prove evidences for practical experiences and can help to design the training protocols.

4.1 Effect of physical exercise on the muscle itself and the whole motor unit

It is evidenced that the aerobic exercise improves the mitochondrial functions, the synthesis of insulin receptor and the myosin heavy chain protein even in the advanced age [13–15]. Impairment of the mitochondrial structure and function seems to be the consequence of decreased physical activity in older persons rather than the aging itself [14]. Not only the structured physical exercises, but the regular physical activity in the daily life promotes the mitochondrial protein synthesis [45].

It is generally accepted, that the resistance training increases the muscle mass and strength, although, some data show controversy results or the variability of the degree of improvement. The contractile properties of a single muscle fiber seem to be increased by both resistance and endurance training [14]. It is worth to mention that the skeletal muscle reacts to the resistance training in elder age less than younger age, due to the impaired protein synthesis [19].

The studies revealed differences in the remodeling of the muscle fibers on the effect of concentric (CON RET) vs. eccentric resistance training (ECC RET) at the 80% of one-repetition maximum for 4 weeks. Both type of training evoked hypertrophy and increased protein content of the muscles, while the CON RET increased the pennation angle and the ECC RET increased the myofiber length. It is suggested that the new sarcomeres are coupled in parallel to the old ones after a CON RET training but in series by using an ECC RET [46].

It is interesting, that not only the high-load but the low-load resistance exercise can stimulate the mitochondrial biogenesis and function besides the positive effects on the contractile machinery [47].

The electrical stimulation increases the size of the fast type muscle fibers parallel to the decrease in the diameter of the slow type myofibers, similarly to the resistance training in a 70y old population [48].

Although, the aging-related loss of motor neurons seems to be inevitable but physical exercise, especially the strength training can evoke adaptive changes in the motor units that compensate the decrease in the number of motor neurons. The reinnervation of deinnervated muscle fibers by the collateral axons can be promoted, but other data contradict to these findings [19].

Similar findings have recently been reported showing that the muscle cross-sectional area (CSA) in vastus lateralis has decreased by aging independently of different trainings. The number of motor units has been larger in young power training group compared to young controls but in elder age neither the power nor the endurance training have impacted this parameter. The size of motor units has increased by age without significant effect of power or endurance training. In conclusion, the benefit of regular training may be the improvement in motor unit remodeling [49].

The power training (concentric contractions at high velocity) evokes earlier activation and higher firing rate in the motor unit [31]. Overview of the spinal motor neuron plasticity, i.e. its adaptation to different exercises has recently been published. In human investigations, indirect approach has been used to get information about the motor neuron behavior analyzing the response of the motor unit by using surface or intramuscular electromyography. The heterogeneous training protocols make difficult to explore and interpret the association between the exercise features and the motor neuron response, so this field is open for further investigations [50].

4.2 Effect of physical exercise on the regeneration capacity of the skeletal muscles

Both the short- and long-term resistance training downregulate the M1 type and upregulate the M2 type macrophage expression. This shift facilitates the phagocytosis and satellite cell activation after an injury of muscle fibers improving the regeneration capacity of the skeletal muscle. The electric stimulation increases the number of Pax7 and neural cell adhesion molecule (NCAM) positive satellite cells (myogenic cells committed to differentiation) [48].

It is worth to consider that the mode of contraction used in a resistance training affects the muscle cell damage and regeneration at different way and to different extent. The eccentric muscle contractions (ECC) resulted in higher degree of damage than the concentric ones. The inflammatory cytokine concentration was increased due to the eccentric, but not the concentric exercises. The number of satellite cells increased in ECC group but remained unchanged after the concentric exercises [51]. The eccentric contractions stimulate the production of collagen type I, III and IV so restoring the extracellular matrix around the satellite cells. The fibrosis and adipogenesis seems to be attenuated [52].

It has been reported that the number of type I specific Pax7+ satellite cells has increased 96 h after resistance training alone or combined with endurance training but the number of type I specific MyoD+ (activated) cells have increased only after the resistance training. The number of type II specific satellite cells (Pax7+ and MyoD+) have not changed in any type of exercise in vastus lateralis of the middle-aged, overweight/obese, sedentary patients [53].

4.3 Effect of physical exercise on the bone

The loss of muscle mass and strength (sarcopenia) is frequently associated with the impaired structure (osteoporosis) and function of the bone (osteopenia).

Due to the technical difficulties in human (lack of non-invasive technique to measure the mechanical strain in the bone) there are no direct data about the effect of various types of physical exercises on bone cells. The indirect data derive from the measuring the markers for bone formation and bone resorption. The weight-bearing exercises (jumping, aerobics and running) and low impact exercises (as walking) are recommended in several authors and authorities for the prevention of bone loss. However, the effectiveness and feasibility of different trainings seems to be age dependent. In old age the concomitant diseases (joint and cardiovascular problems) make limitation in the choice of training type [54].

A recent publication has revealed a close correlation between the effect of a 3-month combined resistance and weight-bearing training on the bone remodeling and the muscle power in post-menopausal women. The number of circulating osteogenic cells has increased parallel to the bone-formation marker with significant correlation to the one-repetition maxim in the lower and upper extremities [55].

The osteoblast activity showed marked (but not significant) increase on the effect of a 10-week progressive aerobic training in women suffering from postmenopausal osteoporosis [56].

4.4 Effect of physical exercise on the skeletal muscle microcirculation

In advanced age, the reactivity of microcirculation to various factors, especially the endothelium derived relaxing and contracting factors as well as the sympatholytic mechanisms during exercise are impaired. The vasodilation is reduced, and the vasoconstriction is higher than in younger people leading to lower blood flow and decreased tolerance to aerobic exercises [57].

According to the microcirculation theory of aging [28], the impairment of the microvasculature structure and reactivity in old age plays important role in deterioration of the neuromuscular homeostasis and can be an important target for physiotherapy interventions.

Endurance exercises stimulate the angiogenesis and oxidative metabolism in the muscle fibers, so it is recommended to precede the muscle mass increasing resistance exercises [9]. The better capillarization as a result of the long-term aerobic exercises or chronic electric stimulation usually precedes the increased activity of oxidative enzymes. Heavy resistance training does not stimulate the capillarization [10].

5. Recommendations to practitioners

The types of physical activity being feasible even in hospitalized and physically frail patient have been reviewed recently. Resistance exercises alone or in combination with other types of physical activity even done in bed at low to moderate intensity evoke positive changes in the physical performance. High speed, dynamic resistance exercise with concentric contractions are preferable in this situation. Resistance exercises performed by using elastic bands result in significant improvement in muscle power and functional outcome even in a short-term training program. Aerobic exercises with progressive duration (e.g. cycle-ergometer, treadmill or so simple exercises as steps-up, stationary cycling, walking) are strongly recommended [58].

The recently published position statement from the National Strength and Conditioning Association gives an excellent guideline for practitioners engaged in care of old people. Regarding the resistance training protocols directed to old people 2–3 sets of exercises acting on the large muscle groups and many joints with frequency of 2–3 sessions/week at 70–85% of 1RM and inclusion of power exercise with concentric movement at high velocity but moderate intensity (40–60% of 1RM) are recommended. There is a need to adapt the training program to neuromuscular disorders, limitation in movement, the comorbidities and frailty. The completion of resistance training with endurance and balance training is recommended to reach as benefits as possible [59].

The international practice guideline for sarcopenia elaborated by the participants in International Conference on Sarcopenia and Frailty Research strongly recommends the resistance training program for old persons based on evidences. It is noted that the individually tailored training program can be better than the group training but there is some cost limitation for this type of training program. The authors note that increase in physical activity in the leisure time is also advantageous [60].

The combination of aerobic and resistance training is also preferred by other authors to reach the possible maximal functional outcomes [5, 18, 53]. The best effects can be supposed if the aerobic training precedes the resistance training supporting the metabolic adaptation of neuromuscular system [9].

6. Conclusions

The main characteristics of the aging of skeleto-neuro-muscular system at cellular and tissue level is overviewed in a holistic approach with the aim of giving a theoretical basis for physiotherapeutic interventions. The muscle fiber atrophy and numeric decline in the muscle fibers are associated with the fundamental alteration of the motor neurons and NMJ accompanied by the remodeling of motor units. The regeneration capacity of the muscle fibers is attenuated due to the intrinsic aging of the satellite cells and the self-renewal ability of stem cell pool. The aging of neuromuscular system (sarcopenia) is frequently associated with the aging processes in the bone (osteopenia). The blood supply to the skeletal muscle is also affected by the aging of microvasculature leading to decreased vasodilation and increased vasoconstriction responses.

The implementation and functional outputs of resistance and endurance training is overview in the mirror of current literature. It is generally accepted that the resistance training is the most important interventions in the elder age with taking into consideration the aging-dependent limitations. Feasibility and safety relations are also cited. The endurance training alone improves the cardiovascular fitness with lower (but not zero) direct impact on muscle power and performance. The combined training (AT+RT) completed with the elements of balance training seems to be the more effective in old people. The data about the effects of the physical exercises at cellular and tissue level offer good background to interpretation of the practical experiences.

Based on the current literature, we recommend the combined exercise trading, fundamentally based on resistance training but completed with the endurance and balance training elements.

Conflict of interest

The authors declare no conflict of interest.

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