EFFECTS OF RESISTANCE TRAINING FREQUENCY ON MUSCLE STRENGTH, ACTIVITY AND MASS DURING A 24-WEEKS INTERVENTION IN THE ELDERLY

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Master's Thesis in Exercise Physiology

2014 – 2016

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ABSTRACT

Alonso Serrano, Javier. 2016. The effects of Resistance Training frequency on strength, power performance, muscle activity, hypertrophy and hormone concentration during a 24-weeks intervention in the. Department of Biology of Physical Activity, University of Jyväskylä. Master's Thesis in Exercise Physiology. 83 pp.

Elderly populations are increasingly affected by sarcopenia, dynapenia and osteoporosis. They all increase frailty and decrease quality of life and life-expectancy.

Resistance training (RT) has been reported extensively as a tool that can prevent, counter and in some cases reverse the course of the abovementioned diseases. Several studies covering RT adaptations in elderly populations have investigated periods between 6 up to 88 weeks with different frequencies, from 1 to 3 trainings / week and a wide range of intensities (30-85% or one repetition maximum) and different volumes.

The aim of this study was to investigate the effect of different training frequencies (one, two or three times / week) of periodized RT in older adults (60-75 years old) after a 36-week intervention period on strength adaptations and peak power, one repetition maximum dynamic leg press (1-RM) and explosive dynamic leg press with 50% of the 1-RM, muscle activity (measured by surface EMG, targeting vastus medialis and lateralis), lean mass (measured with Dual-energy X-ray absorptiometry) and basal serum hormones concentrations of testosterone (T), cortisol (COR), sex-hormone binding globulin (SHBG) and dehidroepiandrosterona (DHEA) .

In this study, RT intervention significantly increased 1-RM, especially towards the highest frequency intervention groups (3 times / week in both men and women). Without correlating with frequency, T and COR concentrations increased and on the other hand, a significant decrease in SHBG/COR ratio was observed in both men and women. Once and twice / week frequencies bring up similar strength outcomes. RT is an appropriate tool for increasing strength in both older men and women.

Keywords: resistance training, basal hormones, frequency, hypertrophy, muscle activity, elderly.

ACKNOWLEDGMENTS

This study was carried out through the Department of Biology of Physical Activity, at the University of Jyväskylä.

I would like to acknowledge the department and my supervisors, Simon Walker, Heikki Kyröläinen and Heikki Kainulainen for their continued support and assessment. Furthermore, I would like to thank the technical staff for their continuous cooperation and advice.

A special thanks to fellow students, Alistair Inglis and Elena Fernández Lezáun, for their contributions. I would also like to thank my family and friends for their endless support.

CONTENTS

1. INTRODUCTION

Increasing age is associated with declines in neuromuscular and cardiovascular systems along with drastic changes in body composition, resulting in an impaired capacity to perform daily activities. To counteract the biomechanical and physiological decline, regular resistance training seems to be one of the best strategies to improve together: muscle hypertrophy, power output, daily autonomy and other functional outcomes.

Nowadays the elder population faces disease associated with the increasing lack of regular muscular activity, such as sarcopenia (decrease of skeletal muscle mass) and dynapenia, a term proposed to describe the decrease in neuromuscular capacity of skeletal muscle (Manini & Clark, 2012).The decline in muscle strength and mass has been directly associated with aging, especially from the sixth decade onwards, for both men and women (Häkkinen et al. 1996, 1998) together the atrophy of muscle fibers, that has repeatedly been shown to be more pronounced in the type II fibers (e.g. Nilwik et al. 2013). Also, myofiber necrosis and myofiber type grouping have been reported (Lexell, 1995; Kent-Braun & Alexander, 2000).

Muscular strength is defined as the ability of a skeletal muscle or group of muscles to exert or generate force against a given load and power is the speed rate at which an individual can develop that strength. Resistance training (RT) refers to a specialized method of physical conditioning that involves the progressive use of a wide range of resistive loads, different movement velocities and a variety of training modalities including weight machines, free weights (barbells and dumbbells), elastic bands and others (Faigenbaum & Myer, 2010; Ratamess, 2009).

Many recommendations for exercise and physical activity are based on RT in the literature for the elderly (Cadore et al., 2008; Cadore et al., 2014; Garber et al., 2011). RT has been shown to be effective for improving muscle strength, power output, and muscle mass in healthy and frail elderly populations (Cadore et al., 2014; Cuoco et al., 2004; Fragala et al., 2014; Häkkinen et al., 2001; Izquierdo et al., 2001; Trappe et al., 2001). One Repetition Maximum (1-RM) is the maximum load that can be lifted in one contraction.. Training frequency is the number of workouts per period of time (usually a week). The recommended frequency for older adults is more than 2 days / week of

RT using major muscle groups during sessions, with an intensity between moderate and vigorous (ACSM, 2009).

The depolarization of the sarcolemma is one of the steps in the cascade that ultimately causes the muscle fiber to contract. The assessment of these action potentials forms the basis of electromyography (EMG). EMG is used for observing muscle activity of the target muscles as its amplitude at different force levels and its changes during the course of a submaximal contraction are dependent on the number of motor units active, their size, and firing rates (Suzuki et al., 2002).

Skeletal muscle responds to the secretion of hormones, such as Testosterone (T), Cortisol (COR) and Sex-Hormone Binding Globulin (SHBG) (Cadore et al., 2008; Crewther et al., 2011; Häkkinen, Pakarinen, et al., 2001; Kraemer et al., 1999; Kraemer et al., 1990; Smilios et al., 2007; Váczi et al., 2014; West, 2012). The decrease in T and SHBG concentrations and secretion with age has been studied in a cross-sectional fashion mostly (Gray et al., 1991a, 1991b; Kaiser et al., 1988). Additionally, other cross-sectional studies have demonstrated great differences between healthy young and healthy elderly individuals (Häkkinen et al., 2000; Izquierdo et al., 2001; Kraemer et al., 1999).

The purpose of the present study is to investigate the changes in strength (1-RM and power performance), muscle activity (EMG), lean mass (upper and lower limb), and basal hormonal levels (T, COR and SHBG) after a 6-month RT period with 3 different frequencies (one, twice and three times / week) in elderly untrained subjects for assessing the optimization of training frequency within this cohort, with the aim of furthering RT applications and recommendations.

2. LITERATURE REVIEW

2.1. Adaptations to strength training in untrained subjects

Untrained individuals respond favorably to a multitude of training stimuli. Adaptation capacity gets reduced along time with chronic exercise, therefore, scientific recommendations are needed to properly address program design in trained populations targeting strength and hypertrophy increases (Ratamess, 2009). Systematic RT in elderly untrained populations (both men and women) promotes positive (rather heterogeneous) changes in strength, muscle activity and hypertrophy (see table 2). Short bouts of RT improve protein synthesis and neuromuscular adaptations that are comparable to those of younger cohorts, despite a much lower pre-exercise rate (Newton et al., 2002). Therefore, disuse may be the underlying reason for skeletal muscle weakness and atrophy, rather than aging itself.

Motor nerves also demonstrate age-related changes where nerve fibers decrease in diameter (Mittal & Logmani, 1987) and nerve conduction slows (Arnold & Harriman, 1970). In addition, the neuromuscular junction (NMJ) where the motor neuron and the muscle fibers meet changes with aging where presynaptic nerve terminal branching and post-synaptic distribution of neurotransmitter receptor sites are increased and the NMJ has limited capacity to adapt (Deschenes et al., 2013). This may affect the ability of aged muscle cells to modulate calcium release with muscle contraction. Thus, age-related changes in neuromuscular activation appear to largely contribute to declines in both strength and power.

2.1.2. Maximal force production

Muscle strength is specific to the muscle group(s) and situation in which it is measured. Muscle strength can be measured isoinertially (lifting), isometrically or isokinetically (Enoka, 2002, 91). Strength loss during the aging process has been reported to be ranging from 1.5% to 5% loss / year after the 50 year old mark (Doherty, 2003; Frontera et al., 2000; Goodpaster et al., 2006; Marcell et al., 2014; Von Haehling et al. , 2010)(see table 1).

TABLE 1. Strength loss during the aging process. Adapted from (Keller & Engelhardt, 2013).

Study	**Strength loss**	**Comments**
Goodpaster et al., 2006	2,6-4,1%/year	Ethnic and sex specific differences
Frontera et al., 2000	1,7-2,5%/year	Longitudinal study over 12 years, starting age was in mean 65 life-years
von Haehling et al., 2010	1,5% between ages 50 and 60 and by 3% thereafter	-
Doherty, 2003	20-40% between 20th and 80th life year	-
Marcell et al., 2014	3.6-5%/year	Longitudinal study over approximately 5 years, starting age was 58.6±7,3 years

Maximal strength type training and hypertrophy type can improve force production, when total volume is equated, in both trained and untrained subjects, as it has been shown in studies like: Chestnut and Docherty (1999), that compared performance of 6 sets of 4RM with 3 sets of 10RM over the course of 10 weeks for upper body in untrained subjects, showing significant increases in hypertrophy and strength, but no significant differences between both groups; Campos et al. (2002), also in untrained individuals that, on the other hand, found greater lower-body strength improvements with low (3-5) vs. high (9-11) repetitions and additionally, Schoenfeld et al. (2014) with a similar setup but in trained subjects, equating volume and comparing maximal strength training with hypertrophic training, found coincident results, showing increased 1-RM in those that followed the maximal strength type protocol compared to the increases found in the hypertrophy type training group.

The RT volume is also associated with strength adaptations in older adults. Regarding the number of sets per exercise, some studies have investigated whether greater training volumes (i.e., 3 sets per exercise) result in greater magnitude of strength increases than lower volume (i.e., 1 set per exercise), (Cannon & Marino, 2010; Galvão & Taaffe, 2005). These studies reported that one and three sets per exercise induced similar strength gains after 10 weeks of strength training in elderly women and after 20 weeks in elderly men and women, respectively.

Regarding RT intensity in elderly, some studies have shown no differences in the strength enhancements among elderly when comparing moderate (50–65% of 1RM) to high (70–80%) intensities (Vincent and Braint, 2002; Brentano et al., 2008). Additionally, recent literature review and meta-analysis have shown that moderate to high training intensities (65–80% of 1RM) resulted in higher maximal strength (Hunter et al., 2004; Peterson et al., 2010; Steib et al., 2010; Borde et al., 2015).

Strength and muscle mass do not decrease concurrently, so strength may be a superior indicator of muscular dysfunction (Doherty, 2003), and longitudinal data suggests that muscle strength is a robust predictor of functional decline that may occur during aging (Pendergast, et al., 1993; Rantanen et al., 1999). The aging process is directly associated with a deficit in maximal voluntary muscle activation of the agonist and the antagonist muscle (Macalauso et al., 2002; Hortobágyi & Devita, 2006; Peterson & Martin, 2010; Billot, et al. 2014). In elderly populations, increases in force production are found predominantly in the literature after RT interventions between 6 and 88 weeks, and frequencies of 2-3 times / week, ranging from 13 to 41% increase of the 1-RM for lower or upper limb. Evidence shows that a dose-response relationship exists between the training intervention and the training induced strength gain (Liu & Latham, 2009), being the most popular statement among the literature, that 3 sets of 10 repetitions with an intensity of 70-80% of 1-RM, 2-3 times / week during a minimum of 8 weeks training is recommended for the elderly (Chodzko-Zajko et al., 2009; Garber et al., 2011).

A recent meta-analysis regarding RT dose-response relationship in elderly, reported that for enhancing both muscle strength and morphology, despite the large heterogeneity they found, a training period of 50–53 weeks, with a training frequency of three sessions per week, a training volume of two to three sets per exercise, seven to nine repetitions per set, a training intensity from 51 to 69 % of the 1RM, a total time under tension of 6.0 s, a rest of 120 s between sets, and a rest of 2.5 s between repetitions turned out to be most effective. (Borde et al., 2015). This data gets underpinned by what has been found previously in the literature (see Table 2). RT is considered to be a safe and effective method for increasing strength in older adults (Frontera et al. 1988; Fiatarone, et al., 1990; McCartney et al. 1996; Häkkinen, et al. 2000; Häkkinen et al. 2001; Hunter et al., 2004; Cannon et al., 2007; Correa et al., 2012; Radaelli et al., 2014; Walker et al. 2013; Walker et al. 2014a, 2014b; Unhjem et al. 2015).

2.1.3. Rapid force production and power

Power is defined as the amount of work / time unit or as the product of strength and speed, both influenced by the mechanical properties of the skeletal muscle (Moritani, 1993; Schmidtbleicher, 1992), and the relationship between length-tension and strength-speed, because the speed a muscle shortens depends on the load. Force production during a concentric contraction is inversely correlated with the speed of the contraction, so when the force production is lower, the faster the contraction is (Cormie et al., 2011; Haff et al., 1997; Haff et al, 2001; Kawamori & Haff, 2004) (See Figure 1 and Figure 2). A reduction of both slow-twitch (type I) and fast-twitch (type II) fibers, especially of type II is found in older adults (Macalauso & De Vito, 2004). The maximum velocity of shortening and power production are significantly higher in type II myofibers than in type I (Trappe et al., 2001). Power is lost at a faster rate than strength mostly due to the progressive type II muscle fiber impairment (Izquierdo et al., 1999). The reduced strength/power production is also related to the impaired excitation-contraction coupling and calcium release (Delbono et al., 1995). Older muscle fibers tend to be angulated in shape, reflecting the denervation of muscle fibers (Mosole et al., 2014).

The maximal rate of rise in muscle force, or rate of force development (RFD) is a term derived from the force/torque-time curves recorded during explosive voluntary isometric contractions and has important functional consequences as it determines the force that can be generated in the early phase of muscle contraction, from 0 to 200 ms (Aagaard et al., 2002). Contractile RFD may be influenced by the level of neural activation, muscle size and fiber-type composition. Based on EMG recordings (see Figure 3), an enhanced neuromuscular drive has been demonstrated after heavy RT in elderly populations (see Table 2) and parallel behavior between EMG and RFD has previously been postulated to exist (Komi, 1986). Accordingly concurrent adaptations in efferent neural drive and contractile RFD may be expected in response to RT. Additionally, in the elderly, RFD significantly rises (≤40%) according to the literature in those RT protocols that ranged from 6-24 weeks and 2 times / week frequency (see Table 2).

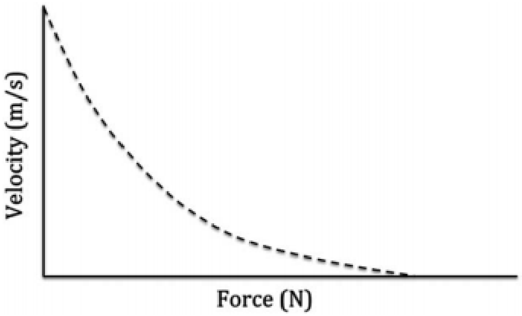

Figure 1. Inverse relationship between strength and speed variables towards muscle power. Source: Kawamori & Haff (2004).

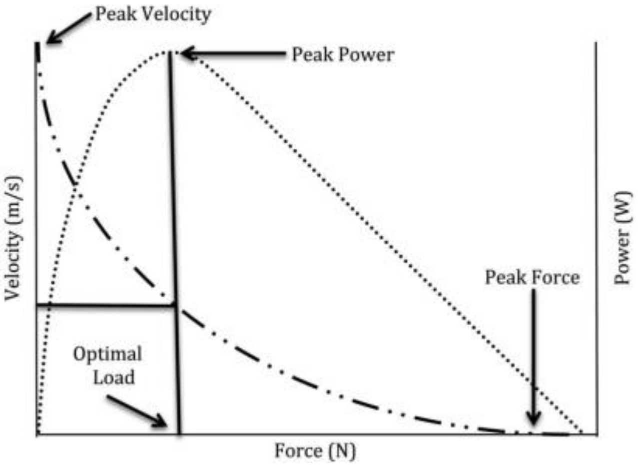

Figure 2. Maximum power expression and optimal relationship between strength and speed. Source: Haff & Nimphius (2012); adapted from Kawamori & Haff (2004).

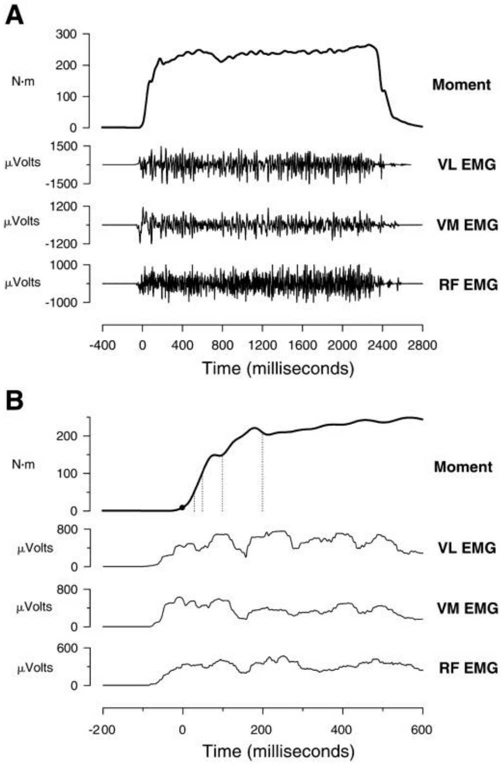

Figure 3. Rate of force development and simultaneous electromyography recordings. Source: (Aagaard et al., 2002).

A number of studies have demonstrated improvements in power production in older adults as a consequence of power-specific RT and this has also been seen at the single myofibrillar level. Power development is specific to the mode of training, indicating that a training program incorporating high-velocity contractions induces greater gains in the elderly (Earles et al., 2001).This is where power training in elderly populations gets a pivotal role, since the speed the repetitions are performed at, directly affects myofibrillar adaptations (i.e. intentionally faster concentric action will lead to more activity from type II fibers compared to slower ones).

2.1.4. Skeletal Muscle Mass

RT is considered to be a safe and effective method for increasing lean muscle tissues in older adults (Frontera et al. 1988; Fiatarone, et al., 1990; McCartney et al. 1996; Häkkinen, et al. 2000; Häkkinen,et al. 2001; Hunter et al., 2004; Cannon et al., 2007; Correa et al., 2012; Radaelli et al., 2014; Walker et al. 2013; Walker et al. 2014a, 2014b; Unhjem et al. 2015).

Muscle hypertrophy is virtually un-measureable during the initial stages of training, with the majority of strength gains resulting from neural adaptations. A study following 1,678 older adults aged between 70 and 79 years over 5 years, indicated that on average, older men lose approximately 1% of their thigh muscle area / year and older women lose 0.65% of their muscle thigh area / year (Delmonico et al., 2009). The rate of loss is not uniform across muscles. In an Magnetic Resonance of Imaging -based (MRI) study of 200 women and 268 men, the rate of loss of lower limb muscle was more than twice the rate of loss of upper limb muscle (Janssen et al., 2000), supporting previous evidence from computerized tomography (CT)- (Borkan et al., 1983) and Dual-Energy X-Ray Absorpiometry-based (DXA) (Gallagher et al., 2000) measurements. Results of a recent meta-analysis show that young subjects get greater increases in muscle mass compared with older subjects, although the data for both cohorts was rather variable and heterogeneous (Peterson et al., 2011).

During the hypertrophic phenomena, contractile elements enlarge and the extracellular matrix expands to support growth. Contractile hypertrophy can occur either adding sarcomeres in series or in parallel (Vierck et al., 2000), and fibers may increase in diameter, as is found in singly innervated muscles, to increase the number of myofibrils in parallel. These fiber diameter changes result in an increased muscle cross-sectional area (CSA) (Toigo & Boutellier, 2006). In skeletal muscle tissue, satellite cells (SCs) are pivotal for myofiber maintenance, repair and growth (Borneman et al. 1999; Roth et al. 2000; Verdijk et al. 2009; Verdijk et al. 2014; Vierck et al. 2000).

Training-induced hypertrophy in older men seems to take place in both fast and slow-twitch fibers. Verdijk et al. (2009) observed that, after a 3 month intervention RT protocol in untrained elderly men (aged 65-85 years), the skeletal muscle hypertrophy specifically increased for Type II fibers together with a specific increase in Type II muscle fiber SC content (see Figure 4).

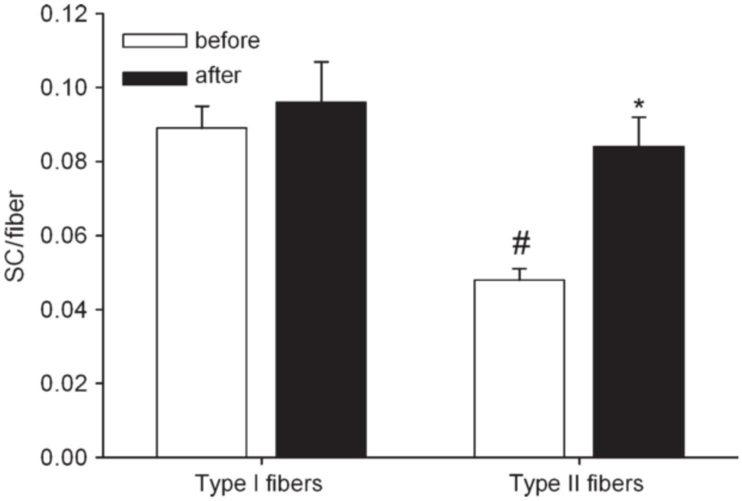

Figure 4. Mean number of SC in the Type I and Type II muscle fibers before and after the exercise intervention program. Source: (Verdijk et al., 2009).

A greater hypertrophic response to RT has been observed in the upper body muscles compared with lower extremity muscles in previously untrained individuals (Cureton et al. 1988; Welle et al. 1996). Several studies have shown that following RT protocols, CSA increases with protocols from 6 weeks until 88 (longest). Techniques like MRI, CT, and ultrasound can determine changes in CSA over relatively short training protocols (e.g. 8-12 weeks) (Mulligan et al., 1996). Hypertrophy becomes relevant for elderly populations, as low levels of muscle mass are strongly correlated with a loss of functional independence and mobility and an increased risk of disability and functional impairment (Janssen et al. 2002; Janssen et al. 2004; Delmonico et al. 2007).

Regarding SC, myofibers are permanently differentiated, multinucleated cells. In the multinucleated myofiber, the myonuclear domain is controlled, which theoretically maintains the genetic machinery for myofiber homeostasis (Barton et al., 1998; McCall et al. 1998). Myofiber growth or repair thus requires the addition of myonuclei. The SC that lie beneath the basal lamina of differentiated myofibers, are the primary source for the needed nuclei. Whether the SC pool declines in older muscles is as yet unclear (Bonavaud et al., 1997; Owino et al., 2001; Roth et al., 2000), although it is possible that a reduced capacity for SC activation appears with age (Bornemann et al., 1999). Type II muscle fiber SC content is strongly correlated with a greater increase in type II muscle fiber size in response to training. Correlation analysis has shown that type II muscle fiber size substantially declines as age increases. No such relationship has been found for the type I muscle fibers (Verdijk et al., 2014). In the young adult subjects, muscle fiber size seems to be greater in type II vs. type I muscle fibers. In contrast, in both the older and senescent subjects, muscle fiber size was significantly smaller in type II vs type I muscle fibers (see Figure 5).

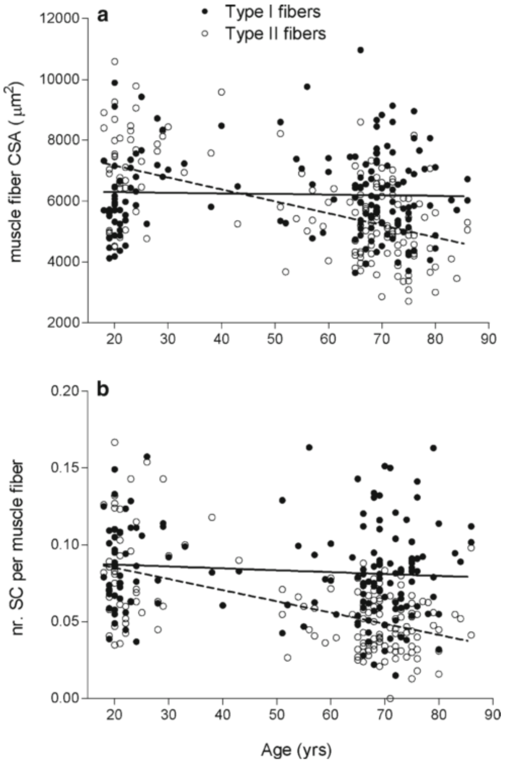

Figure 5. Scatter plots for adults aged 18-86 years (n=152), showing the correlation between age and (a) muscle fiber CSA and (b) the number of satellite cells (SC) per muscle fiber (Verdijk et al. 2014).

Genetic background, age, gender, and other factors have been shown to mediate hypertrophic responses to training protocols, affecting both the rate and the total amount of gains in lean muscle. Regarding regular RT, it becomes more and more difficult to increase lean mass, because it is directly proportional with the training experience (Alway et al. 1985; Kraemer et al. 1999). Further it becomes more and more important to design proper routines since muscle hypertrophy can be attained through a wide range of RT programs, the principle of specificity dictates that some routines will promote greater hypertrophy than others (Schoenfeld, 2013). It has to be pointed out that research has not been able yet to find the best approach for achieving this goal. There are several methods, normally varying in a wide range between higher intensities with large rests (i.e. powerlifting), focusing on mechanical tension and recruitment and low to moderate intensities with shorter rest intervals looking for metabolic stress and cell swelling (e.g. bodybuilding).

Greater mechanical stress associated with high-intensity resistance training may recruit more fast-twitch muscle fibers (due to their increased growth potential) and provide a greater stimulus for muscle hypertrophy than the metabolic stress associated with high-volume training (Clarkson et al. 1992; Ratamess et al. 2009, Mangine et al. 2015), but further research is needed examining the hypertrophic effects of protocols targeting mechanical and metabolic stress, or a combination of both.

Both approaches have been shown to promote hypertrophy, but the outcomes are different, especially considering the neuromuscular performance output, associated with the heavier protocols (Schoenfeld et al., 2014). In this study, when volume was equated, the hypertrophic outcome was relatively similar with different intensities and rest intervals, but the strength was greater in those subjects that performed higher intensities and the endurance together with time-under-tension tolerance were enhanced in those individuals that performed lower intensities and shorter rest intervals. A comparison between protocols with different intensities and equated volume in older populations has not been studied yet.

2.1.5. Muscle activation

One of the variables responsible for the decline in strength among aging is the capacity of skeletal muscle to contract. Explaining the mechanism, a voluntary contraction needs the recruitment of motor neurons, and therefore, muscle fibers. Voluntary activation is commonly assessed using the interpolated twitch method (ITT) (Gandevia, 2001; Kent-Braun, 1997). The motor nerve to the muscle is electrically stimulated during a voluntary effort, termed Super-Imposed Twitch (SIT) (see Figure 6). During (usually an isometric) maximal voluntary contraction (MVC), SIT is applied at the level of the peripheral nerve, stimulating the motor axons of the contracting muscle. When the force output is increased by these SIT, the subject´s voluntary activation is considered to be sub-maximal (Shield and Zhou, 2004). Some motor units are not recruited or are not firing fast enough to produce maximal tension, which is termed neural deficit (Merton, 1954).

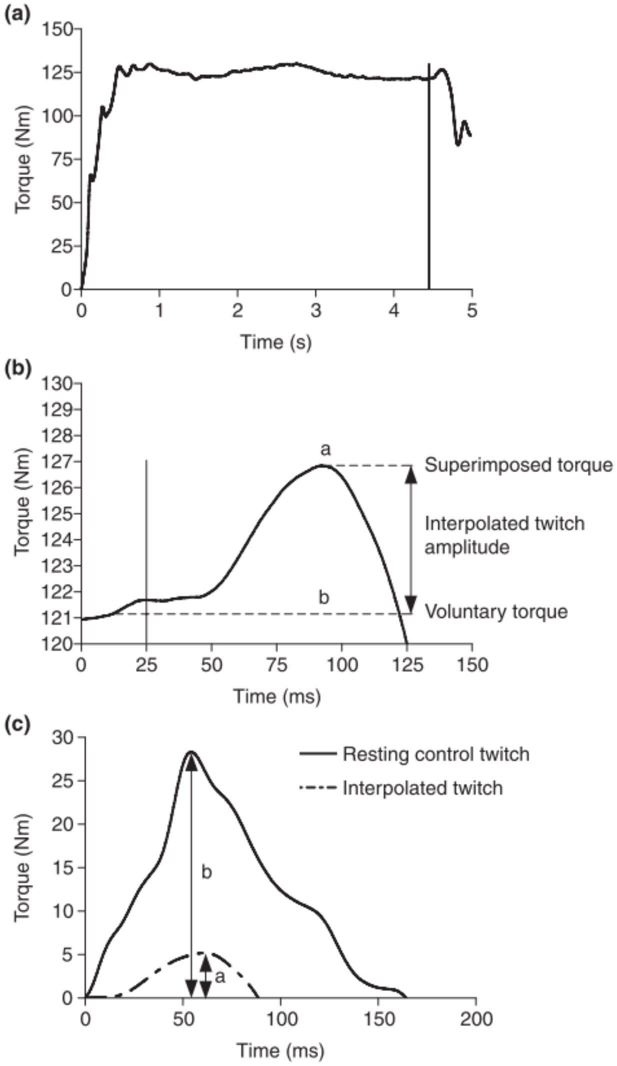

Figure 6. Method used to determine voluntary activation. a) Example of superimposed MVC contraction during the assessment of interpolated twitch amplitude. The vertical line intersecting the torque-time curve at approximately 4.4 s indicates the delivery of the electrical stimulus. b) Extracted superimposed twitch (SIT) from the same contraction as (a). The vertical line intersecting the torque-time curve at approximately 25 ms indicates the delivery of the electrical stimulus. c) Example of the method used to calculate voluntary activation from (a) and (b). Source: (Cannon et al., 2007).

Regarding the reliability of the MVC together with SIT, the variability in voluntary drive during a series of “maximal contractions” is reproducible within an individual from day-to-day, but the degree of variability in voluntary drive differs between subjects. Additionally, voluntary activation can be impaired by pain (Rutherford et al. 1986).

An increased force of contraction, results in increased activation of neurons in the primary motor cortex with increased firing of corticospinal neurons (Ashe, 1997). The rate at which the nerve impulse arrive is known as the motor unit firing rate and may vary from frequencies low enough to produce a series of single twitch contractions to frequencies high enough to produce a fused tetanic contraction. The increased strength presented after RT protocols in the elderly is mostly promoted after the first 6 weeks of training by an enhanced firing rate (Gabriel et al. 2006). There is an heterogeneous fiber type distribution pattern normally found in younger muscle, which is significantly altered in older muscles, and increased EMG amplitude can be found in the target muscles (vastus medialis, lateralis and biceps femoris) after protocols that last between 6 and 52 weeks (see table 2).

Training seems to decrease activation threshold of fast-twitch motor units and increase their initial firing rate during rapid contractions with 30-40% of the 1-RM (Van Cutsem et al. 1998). An increased rate of voluntary muscle activation was found in those subjects that had a lower level of voluntary activation capacity prior to the onset of training in the elderly who were investigated by Morse et al. (2004, 2005, 2007); this report was underpinned by Simoneau et al. (2006) and Scaglioni et al. (2002), who found that a lower baseline value of voluntary activation level was related with a greater gain in activation capacity after training and gain in MVC torque. Sensitivity of the ITT is subjected to a non-linear relationship between interpolated twitch amplitude (due to motor unit recruitment and/or firing frequency) and muscle force beyond 65% MVC, thus causing the inability of the interpolated twitch technique to detect the very small changes when above 65% MVC (Scaglioni et al., 2002).

Another mechanism contributing to the decrease in strength is an excessive co-activation of the antagonist muscle (Häkkinen et al. 1998; Macalauso, et al. 2002). Hortobágyi and Devita (2006), stated that the generation of high levels of voluntary force requires the co-activation of flexors and extensors to stabilize the joint and additionally, older individuals evidence exists for decreasing spinal reciprocal inhibition with age that might be responsible for the increased antagonist muscle activation. It has been also found, that before training, elderly women had significantly higher levels of co-activation than younger ones (Häkkinen et al., 1998, 2001).

Also a learning effect has been suggested as an explanation for the decrease in antagonist muscle co-activation after RT; this has been reported in young and older people (Häkkinen et al., 1998). The learning effect is assumed to occur the first 1-2 weeks of training, so the process in which the correct sequence of muscle contractions is laid down as a motor pattern in the central nervous system (Rutherford & Jones, 1986). However, Simoneau et al. (2007) attributed the fact that the initial significant increase of antagonist co-activation (during the first six months of training) decreased back to baseline levels after the second six months to a learning effect.

Arnold and Bautmans (2014) showed through meta-analysis that RT protocols increased muscle voluntary activation in the elderly (see Table 2), showing positive changes in EMG amplitude and RFD (Bottaro et al., 2007; Cadore et al., 2014; Cannon et al., 2007; Häkkinen et al., 1998; Izquierdo et al., 2001; Izquierdo et al., 1999; Kraemer et al., 1999; Walker et al., 2014a; Walker et al., 2013).

TABLE 2. Resistance training protocols in the elderly. Adapted from (Cadore et al., 2014)

Author	Period and weekly frequency	Training volume and intensity	Main results
Häkkinen & Häkkinen (1995)	12 wk; 2 times/wk	2-5 sets, 2-15 reps, 30-80% of 1RM. Slow and explosive muscle contractions	↑PT(20%) ;↑EMG VL; VM and RF(20%); ↑CSA QF (9%)
Häkkinen et al.(1996)	12 wk; 2 times/wk	2-6 sets, 8-15 reps (40-90% of 1RM) unilateral (UNI) and bilateral (BIL). Slow and explosive muscle contractions	↑ 1RM(13-19%); ↑EMG(9-19%); ↑CSA QF (11-14%)
Häkkinen et al.(1998)	24 wk; 2 times/wk	2-5 sets, 2-15 reps, 30-80% of 1RM. Slow and explosive muscle contractions	↑1RM(21%); ↑PT(36%); ↑RFD(40%); ↑SJ(24%); ↑EMG VL and VM
Kraemer et al.(1999)	10 wk; 3 times/wk	Undulating periodization: 2-5 sets of 3-5RM; 8-10 RM and 12-15RM.	↑1RM(10%); ↑CSA QF(6%)
Häkkinen et al.(1998)	24 wk; 2 times/wk	2-5 sets, 2-15 reps, 30-80% of 1RM. Slow and explosive muscle contractions	↑PT(16%); ↑EMG VL and VM; ↑CSA QF (8,5%) ↑CSA fiber type I and II
Häkkinen et al.(2000)	10 wk; 2 times/wk	3-6 sets of 6-15 reps(50-80% of 1RM). Slow and explosive contractions.	↑1RM(29%); ↑EMG VL and VM; ↑SJ(22%); ↑CSA QF(7%)
Häkkinen et al.(2001)	24 wk; 2 times/wk	3-5 sets, 6-15 reps, 30-80% of 1RM. Slow and explosive muscle contractions.	↑PT (36%); ↑EMG VL and VM; ↑RFD(40%); ↑1 RM (21%)
Häkkinen et al. (2001)	21 wk; 2 times/wk	3-5 sets, 8-20 reps	↓BFat(2%); ↑1RM LE(37%); ↑CSA QF(6-11%)
Izquierdo et al.(2003)	16 wk; 2 times/wk	2-5 sets, 3-15 reps, 50-80% of 1RM. Slow and explosive muscle contractions.	↑1RM(25-41%);↑PT(26%); ↑Power at 20-80% of 1 RM(15-60%); ↑CSA QF(11%)
Morse et al. (2005)	52 wk; 3 times/wk	2 sets,10-15 reps, 80%-100% RM	↑IPF (20%); ↑IPF(9,2%) = EMG DF
Morse et al. (2007)	52 wk; 3 times/wk	2 sets,10-15 reps, 80% -100% RM	↑1 RM IPF (23%); ↑EMG IPF (8%); ↑CSA(22%) = EMG DF
Izquierdo et al.(2007)	16 wk; 2 times/wk	3-4 sets, 10-15 reps, 50-80% of 1RM. Slow and explosive contractions.	↑CSA QF(11%); ↑maximal workload at cycle ergometer;↑load at 2 and 4mmol.L-1 at cycle ergometer
Bottaro et al. (2007)	10 wk; 2 times/wk	3 sets of 8-10 reps (40-60% of 1RM); Slow vs explosive contractions (EC)	↑1RM(25%) in both 2 groups ↑power at 60% of 1 RM, greater in EC(31 VS 8%)
Cannon et al. (2008)	10 wk; 2 times/wk	3 sets of 10 reps (50-75% OF 1 RM)	↑PT(18%); ↑EMG VL and VM(21%); ↑CSA QF (11%)
Slivka et al. (2009)	12 wk; 2 times/wk	3 sets of 10 reps (70% of 1 RM)	↑1RM (41%); ↑CSA QF (2%)
Nogueira et al. (2009)	10 wk; 2 times/wk	3 sets of 8-10 reps (40-60% of 1RM) Slow vs. explosive contractions (EC)	↑RF muscle thickness in EC (11%), ↑BB muscle thickness in both groups (7-14%)

Correa et al. (2013)	12 wk; 2 times/wk	First 6 weeks: 2 sets of 12-20 RM; Last 6 weeks: 3 sets of 8-12 RM; Threes ST groups: ST slow-speed (TG); High speed (PG); and plyometric training (RG).	↑1RM (20-22%) in the 3 groups;↑ QF MT (22%) in the 3 groups;↑EMG in the 3 groups; ↑RFD only in the RG group; ↑jump height (25%) only in the RG group
Pinto et al. (2013)	6 wk; 2 times/wk	2 sets. Intensity started at 20 RM, progressing to 10 RM.	↑1 RM (23%); ↑QF MT (8-18%); ↑QF MQ (15%)
Radaelli et al. (2014)	13 wk; 2 times/wk	1 (low-volumen group) or 3(high-volume group) sets / exercise; started at 20 RM, progressing to 10 RM.	↑1RM(23%); ↑EMG(22-28%); ↑MT (8-14%); ↑MQ (22-25%)
Walker et al. (2013)	20 wk; 2 times/wk	2-4 sets; 8-14 reps(60-80% of 1RM) – 2 groups, variable or constant load	↑LE and IKE variable 28±39%. ↑LE and IKE constant 33±54%; ↑ EMG; ↑CSA VL – variable 8±9% and constant 15±11%)
Walker et al. (2014)	20 wk; 2 times/wk	2-5 sets; 8-14 reps (60-80% RM)	↑ 10 RM load YM 35±11% and OM 27±15%. ↑LLM YM 4.9±2.7% and OM 3.1±2.9% (<1% some OM)

Wk: weeks; min, minutes; times/wk, number of training sessions / week; 1RM, 1 maximum repetition; PT, isometric peak torque; SJ, squat jump; CSA, cross-sectional area; QF, quadriceps femoris; MT: muscle thickness; VL, vastus lateralis; VM, vastus medialis; RF, rectus femoris; BB; biceps brachii; EMG, electromyographic signal; RFD, rate of force development; ECC, eccentric; EC, explosive contractions; YM, younger men; OM, older men; LE, leg extension; IKE, isometric knee extension.

2.2. Influence of serum hormone concentrations on training-induced adaptation

Hormonal environment is considered an important mediator for muscle growth, muscle quality and strength (Crewther, Keogh, Cronin & Cook, 2006; Kraemer & Ratamess, 2005). Changes in concentrations can be acute post-exercise (see table 3), changes in basal levels or in total concentrations after a larger training period (Deschenes & Kraemer, 2002).

In a study conducted by Nicklas et al. (1995), no alterations in resting concentrations of T were observed over 16 weeks of progressive training in men averaging 60 years of age, which was similar to the non-response in 70 year old men observed by Häkkinen and Pakarinen (1994) and the non-systematic changes found in middle-aged (40 years) and elderly men and women (70 years) after a RT intervention of 36 weeks (see figure 7) (Häkkinen et al. 2000). It had been previously stated that acute responses appeared to be more critical to tissue growth and remodeling than chronic changes in basal hormonal concentrations, as studies had not shown a significant change in basal levels of hormones during resistance training despite increases in muscle strength and hypertrophy (Kraemer & Ratamess 2005). However, in a recent study reviewing the hormonal responses after training, it was reported that post-RT elevations in anabolic hormones may not be necessary to acutely stimulate muscle protein synthesis or promote hypertrophy, meaning also that other non-hormonal mechanisms can dictate the hypertrophic response (Schroeder, et al. 2013). So it appears that basal hormone concentrations may reflect the current state of muscle tissue such that elevations or reductions may occur at various stages depending on substantial changes in the volume and intensity of training (Ahtiainen et al. 2003; Häkkinen et al. 1988; Kraemer & Ratamess 2005).

Some studies have demonstrated that increases in muscle hypertrophy can occur in the relative absence of post-RT hormonal increases (West et al., 2010; Wilkinson et al., 2006; West & Phillips, 2012). What remains equivocal is whether such hormonal elevations can potentiate the hypertrophic response, thereby maximizing muscle growth (Schoenfeld, 2013). On the other hand, exogenous administration of anabolic hormones (i.e., testosterone) has been shown to linearly increase lean tissue accruement (Bhasin et al. 2001), no studies have demonstrated a consistent relationship between elevations in the basal anabolic hormone response during resistance training interventions, using multiple joint structural exercises and increases in muscle mass in younger or elderly populations.

TABLE 3. Acute hormonal response to hypertrophic protocols. Adapted from: Crewther et al., 2006.

Study	**Subject (age)**	**Protocols:** **Exercise(s),sets x reps(load)**	**Testosterone** **(% or fold change)**	**Cortisol**	**Study**	**Subject (age)**	**Protocols:** **Exercise(s),sets x reps(load)**	**Testosterone(% or fold change)**	**Cortisol**
Häkkinen et al., 2000	10 Tra males	1 ex, 10 x 10 (10RM)	↑24 (↑22[b])	↑149	Gotshalk et al. 1997	8 Tra males	8 ex, 1 x 10 (10RM) 8 ex, 3 x 10 (10RM)	↑~14 ↑~32	↑~10 ↑~25
Kraemer et al., 1993	9 Tra females	8 ex, 3 x 10 (10 RM)	No change	↑~125	Volek et al. 1997	12 Tra males	1 ex, 5 x 10 (10RM)	↑7	No change
Mc Murray et al. 1995	8 Tra males	6 ex, 3 x 6-8(80% 1RM)	↑21	↑21	McCall et al., 1999	10 RTra males	8 ex, 3 x 10 (10RM)	No change	↑~27
Häkkinen and Pakarinen, 1995	8 UTra males 8 UTra females	1 ex, 5 x 10 (10RM) 1 ex, 5 x 10 (10RM)	↑9 No change	No change No change	Kraemer et al. 1998	8 UTra males	1 ex, 4 x 10 (10RM)	↑~38 ↑(40[b])	↑~78
Smilios et al. 2003	11 Tra males	4 ex, 2 x 10(75% 1RM)	No change	No change No change	Kraemer et al. 1999	8 UTra males	1 ex, 4 x 10 (10RM)	↑~37 ↑(29[b])	↑~80

[b]= Free testosterone ; ex= exercises; RM= repetition maximum; RecT=Recreationally Trained; Tra= trained; UTra=Untrained; ↑ indicates increase

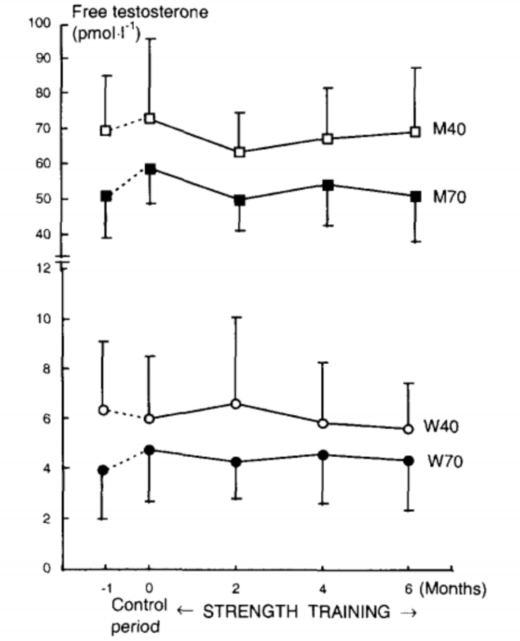

Figure 7.Serum free T concentration during a 1-month control period and a 6-month RT period in middle-aged and elderly men (M40, n=10; M70, n=11) and women (W40, N = 11; w70, n =10). M40= 40 year-old men; M70= 70 year-old men; W40= 40 year-old women; W=70 year-old women (Häkkinen et al. 2000).

Testosterone (T)

Testosterone is a steroid hormone from the androgen group and is found in humans and other vertebrates. In humans and other mammals, testosterone is secreted primarily by the testicles of males and, to a lesser extent, the ovaries of females. Small amounts are also secreted by the adrenal glands. It is the principal male sex hormone and an anabolic steroid. Anabolic effects include growth of muscle mass, increased bone density and strength. Additionally, T is also involved in energy expenditure and regulation of homeostasis and is pivotal for up-regulating muscle protein synthesis and decreasing protein degradation.

Testosterone interacts with an Androgen Receptor (AR), which is DNA-binding for attaching to cells and apply its characteristics. Approximately 1% to 3% of testosterone is free in the blood, and it is this free testosterone that is generally considered as biologically active. About 65 to 75% of the remainder of T is bound to sex-hormone binding globulin (SHBG), and 25 to 35% is bound to albumin. Recent evidence suggests that the amount of exercise time and the level of hormones, especially regarding the circadian rhythm, have some effects on physical and psychological performance (Ruige et al. 2011).

There are other variables that affect total testosterone and free testosterone values in humans: age, where pubertal and early adult stages show greater concentrations of T for both genders although it is 7-10 times greater in males (Taieb et al. 2003), gender, showing bigger concentrations in men but with a diurnal pattern similar to females (Dabbs & Mohammed, 1992). Circadian rhythms also affect testosterone concentration in healthy populations; it was reported by Miyatake et al. (1980) that testosterone levels increased regularly daily between 06:00 and 08:00 every morning even if there was sleep deprivation for all the subjects. So the time when testosterone is collected affects the measurement itself.

The normal T ranges are not completely standardized. Traditionally, normal was considered to be between 10.4 nmol/l and 34.7 nmol/L, but some commercial laboratories differ on this, considering ranges down to 4.2 nmol/L as normal for different populations and cases.

Some studies have observed a significant increase in basal testosterone levels and testosterone/SHBG (T/SHBG) ratio after RT period in athletes and previously untrained subjects (Häkkinen et al., 1998; Staron et al., 1994). Results of changes in basal testosterone concentrations during resistance training have been inconsistent or non-existent in men and women (Ahtiainen et al. 2003). Ahtiainen et al. (2003) reported significantly higher free and total testosterone concentrations after a 7-week high-volume training phase compared with pre-training values (see Figure 8).

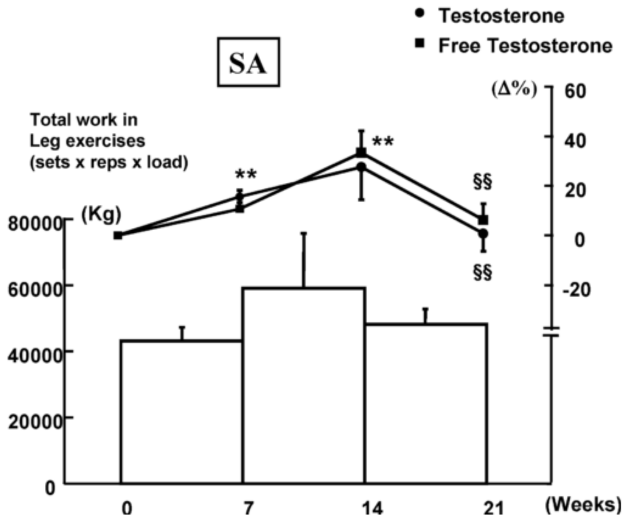

Figure 8. Relative changes in serum basal testosterone and free testosterone and total work during a 21 week RT period. Asterisks: significantly different (**P<0.01) from the pre-RT value (Ahtiainen et al., 2003).

On the other hand, when endogenous testosterone production is suppressed, lean mass increases are attenuated, storage of fat gets increased and muscle strength is abolished during RT in normal young men, thus being endogenous testosterone of paramount importance for the muscular adaptation to RT (Kvorning et al., 2006).

Sex-Hormone Binding Globulin (SHBG)

Sex-hormone Binding Globulin is a homodimeric plasma glycoprotein synthesized in the liver, that binds to both androgens and estrogens and is the major sex steroid carrier-protein in the bloodstream and functions also as a key regulator of steroid bioavailability within target tissues (Hammond, 2011). Evidence suggests that SHBG affects glycemic control, predicts metabolic syndrome in post-menopausal women, is affected by saturated fat intake, increasing it (Allen et al., 2002) and is low in obese and sedentary subjects (Weinberg et al., 2006). A change in SHBG concentrations may influence the binding capacity of T and free T available for diffusion across the cell membrane to interact with membrane-bound steroid receptors.

Production of SHBG depends on a multifactorial regulation with hormonal, nutritional, and metabolic factors influencing its levels (Toscano et al., 1992). One of the functions of SHBG is the control of metabolic clearing of steroids (Khan et al., 2002; Vermeulen & Ando, 1979), so the modification in SHBG concentrations may involve variations in the endogenous profile of urine steroids. Free androgen index (T/SHBG) is a good way to evaluate anabolic activity in sportsmen (Maynar et al., 2010).

Plasma concentrations of SHBG are affected by physical exercise (Cadore et al., 2008), and have a tendency to decrease with age (Gray et al., 1991). Differential responses have been observed during RT. Acute elevations have been reported (Rosner, 1991; Smilios et al., 2003), in some but not all studies (Izquierdo et al., 2007), whereas reductions (Hoogeven & Zonderland, 1996) and no changes in resting SHBG concentrations have been reported following 3-24 weeks of RT (Häkkinen et al., 1985,1990,1992,2000; McCall et al., 1999) following 1 week of intensive Olympic weightlifting (Häkkinen et al., 1988) and over a 2-year period in elite Olympic weightlifters (Häkkinen et al., 1988). Regarding SHBG in the elderly, after a 6-month RT intervention, no systematic changes were found in the basal concentrations of the hormone in men or women (Häkkinen et al., 2000).

Cortisol (COR)

Cortisol is considered the primary catabolic hormone, as it increases protein degradation and decreases protein synthesis (Crewther et al. 2006; Herbst & Bhasin, 2004; Viru & Viru, 2004). The general adaptation syndrome involves the adrenal cortex and COR response to exercise. It has been stated during last years of research that a decreased testosterone/cortisol ratio indicates a predominance of catabolism that is undesirable for adaptation and improvement of performance in athletes. COR exhibits a marked diurnal rhythm including a rapid increase in levels just before awakening. The levels peak around 30 minutes after awakening and decline during the day to reach their lowers levels in the evening during sleep. The level of blood COR is used for monitoring the stress response. However, the relationship among stress, well-being, and COR levels is very complex (Kudielka et al, 2009).

High-volume training programs have consistently elicited a greater COR response to training (Häkkinen & Pakarinen 1993; Crewther et al. 2008; Buresh et al. 2009; McCaulley et al. 2009; West et al. 2010). Although chronically high levels of COR are associated with decreases in lean muscle mass (Crowley & Matt 1996), the effects of transient elevations in COR are thought to mediate, in part, tissue remodeling but this remains poorly understood.

Chronic exposure to RT generally reduces or does not affect resting levels of COR (Staron et al. 1994; Ahtiainen et al., 2003; Kraemer & Ratamess 2005). Additionally, in a study conducted by Häkkinen et al. (2000), after 6 months of RT intervention in elderly subjects, no correlations or systematic change were found between the basal concentrations of COR and lean body mass or strength changes. Changes in resting cortisol may indicate the degree of long-term training stress imposed to the body (Kraemer & Ratamess, 2005). The literature shows that exercise-induced increase in the blood COR concentration is essential for the normal metabolic response to exercise and in the process of adaptation to repeated bouts of demanding exercise.

Dehydroepiandroesterone (DHEA)

The Dehydroepiandroesterone (DHEA) is an endogenous steroid hormone that serves as a precursor to the abovementioned sex steroid T. It is the most abundant circulating steroid hormone in humans, and is produced in the cortex of the adrenal glands which are located at the top of each kidney. DHEA is regulated by the Adrenocorticotropic hormone (ACTH). When DHEA is secreted into the blood stream, it gets carried bound to albumin. In its sulphated form

(DHEA-S), DHEA is the most abundant steroid hormone in the circulation. Concentrations of DHEA-S are between 250 to 500 times greater than the DHEA ones, for women and men respectively (Kroboth et al., 1999), and it has a similar variation pattern in concentration throughout the day to COR, so levels are highest in the morning, although DHEA-S levels are considered to not have a diurnal variation (Pruessner et al., 1997; Ahn et al., 2007; Heaney et al., 2012).

DHEA and DHEA-S positively modulate endothelial function, partly by stimulating the production of nitric oxide (NO) in the endothelial cells, which in turn have several beneficial effects on the cardiovascular system. Also, DHEA has been found to play a relevant role in the regeneration of tissues in the body (Theorell, 2009), so DHEA and DHEA-S levels could be used as biomarkers of regenerative and anabolic activity patterns.

The plasma levels of DHEA and DHEA-S decline approximately by 80% between the ages of 25 and 75. In a study conducted by Sato et al. (2016), after 12 weeks of RT, DHEA serum and muscle levels were restored to levels similar to young subjects. Also DHEA replacement has shown to significantly potentiate the effect of RT on muscle hypertrophy and strength in elderly women and men with a dose of 50mg/day (Villareal & Holloszy, 2006). According to Morales et al. (1998), a 100 mg/day DHEA therapy significantly increased the strength for their intervention group for the 8 men but not for the 10 women of the sample.

3. PURPOSE OF THIS STUDY AND HYPOTHESIS

In the literature, previous reviews have compared intervention and control RT programmes (Steib et al., 2010). Regading hypertrophy in younger populations, when comparing studies that investigated training muscle groups between 1 to 3 days per week on a volume-equated basis, the current body of evidence indicates that frequencies of two times / week promotes greater hypertrophic outcomes compared to one time (Schoenfeld, 2016). The dose of training that would be optimal for prescribing older populations remains unknown according to the latest meta-analysis made by Peterson, et al. (2010) and Arnold and Bautmans (2014). However, in a recent systematic review and meta-analysis of RT conducted by Borde et al. (2015), according to their data, a training period of 50-53 weeks, a training frequency of three sessions / week, a training volume of two to three sets per exercise, seven to nine repetitions per set, a training intensity from 51 to 69% of the 1-RM, a total time under tension of 6.0 seconds, a rest of 120 seconds between sets and 2.5 between repetitions, was the optimal dose considered among the literature reviewed.

Our primary hypothesis is that the subjects with the greatest frequency of training (3 times / wk) will present significantly more adaptations (strength, body composition, basal hormones) than those training once or twice a week.

The purpose of our study is to answer the questions regarding which relationship is there between RT and different workout frequencies and the changes in basal hormone concentrations, muscle activity, 1-RM and hypertrophy among the cohort after 24 weeks of periodized RT intervention. It is expected to see greater CSA and neuromuscular improvements (RFD and 1-RM) in the groups with higher frequency.

4. METHODS

4.1. Subjects

A letter was sent out in October 2014 to 2000 individuals between 65 and 75 years old in the Jyväskylä region. Information about the individuals was received from the central records bureau (Väestörekisterikeskus). After the 2000 letters were sent out, 450 registered for the study, 140 were invited to an information session and 115 signed informed consent forms and were medically screened. The medical examination was completed in January 2015; to participate in the study, individuals had to meet the following exclusion criteria: 1) Age: 65≥75; 2) Weekly physical activity: ≤3 hours of aerobic/endurance training; 3) Disabilities: None; 4) Smoking: None; 5) Obesity: Required <37 BMI; 6) Testosterone therapy: None in the last 10 years; 7) Reactions to exercise: None in the past 6 months. 8) Diabetes: No medicated.

After the selection criteria filter, 104 individuals were cleared to participate in the study. They were randomly divided into three training groups: once (n=26), twice (n=27) and three times / week (n=26) and a control group that performed no training during the intervention period (n=23). Ethical approval for the study was granted by the University Ethical Committee. The characteristics of the study sample, training groups and control group, can be seen in table 3.

TABLE 3. Anthropometric and sex characteristics of the training groups and control group.

Parameters	**Training group 1**	**Training group 2**	**Training group 3**	**Control Group**
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Age (yrs.)	69.8 (2.53)	68.85 (3.02)	69.38 (2.77)	69.3 (2.2)
Weight (kg)	76.5 (20.45)	79.99 (14.01)	80.28 (15.1)	75.1 (11.6)
Height (cm)	166.8 (8.82)	168.12 (7.37)	167.02 (9.58)	1.67 (0.08)
BMI	27.08 (3.2)	28.24 (4.31)	28.66 (4.01)	26.6 (2.5)
Sex	13 women 13 men	16 women 11 men	16 women 10 men	(12 women, 11 men)

Anthropometric data, including standing height (wall-mounted tape measure, accuracy 0.01 m) and weight (digital scale, accuracy 0.1 kg), were assessed pre-training. Body mass index was calculated using the formula:

$$\mathrm{BMI} = \frac{\mathrm{Weight\ (kg)}}{\mathrm{Height}^2\ \mathrm{(m)}}$$

4.2. Experimental design

4.2.1 Overall design

The experimental design of the study can been in Figure 9.

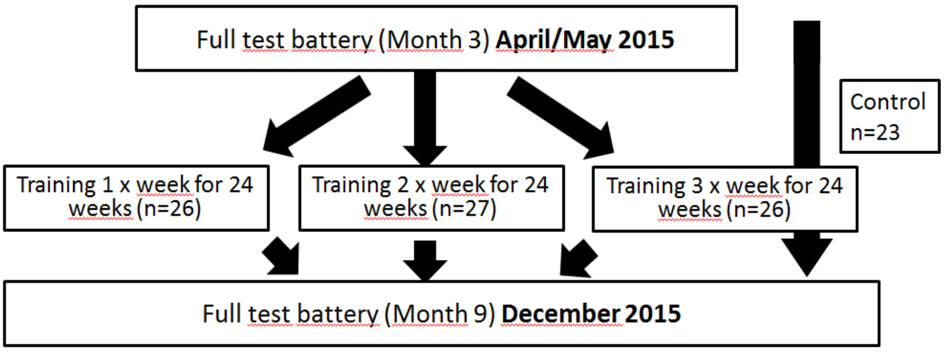

Figure 9. The overall experimental design of the study.

Baseline measurements were completed on all participating subjects. Following baseline measurements, subjects in the training group began the training protocol in March 2015, working out twice / week after the Month 0 testing session, while subjects in the control group maintained their normal daily activities. After the training group had completed 12 weeks of training, they were split into three groups: one session, two sessions and three sessions / week. Each time the measurements were conducted, the week before, a de-loading protocol was periodized, where both intensity and volume decreased for supercompensation. Training was then resumed for a further 24 weeks in the training group. The training protocol ended once the training group completed a total of 36 weeks of training. Post-training measurements were completed in December 2015. Both subjects in the training and control groups were instructed to maintain their normal daily physical activity and dietary habits external to the imposed testing and training of the study. Physical activity levels of the training and control group were tracked throughout the study period using diaries.

4.2.2 Training Protocol

The training protocol was conducted in the gym of the Liikunta building at University of Jyväskylä. Resistance training was performed in the gym using commercial resistance machines, cable and pulley systems and free weights (dumbbells and barbells). Training sessions were supervised, assuring that subjects were performing the session according to protocol, monitoring meanwhile their health and safety. Supervisors also controlled exercise technique and encouraged subjects to progressively overload and were assisted in case a repetition could reach failure. An information session was given, explaining the principles of RT together with the whole protocol. Subjects completed a short warm-up protocol previously, consisting of light aerobic exercises and some light stretching exercises. Sessions were designed to last approximately 1 hour. Subjects were asked to allow a 48-72 hours rest between training sessions.

The intervention period was divided into 9 mesocycles (1 mesocycle = 4 weeks) (see table 4). Written instructions were given before each protocol with the details of the protocol for each exercise. Supervisors were previously informed of the protocol for mesocycle, and were able to advise the subjects in the gym if any issues had to be countered. The details of the protocol for a given mesocycle included: the aim of the protocol, the exercises to complete, the number of repetitions and sets to complete, and the length of rest periods to observe. Subjects were to follow the protocol meticulously, and to record their training information (loads/resistances etc.) in personal training logs kept in a locked room at the gym. Training logs were constantly being monitored by supervisors, to ensure primarily that the subjects were progressing appropriately.

During each mesocycle, a pre-set range of repetitions (e.g. 10-12) was given to the subjects. Subjects were instructed to determine the load where concentric failure would occur during at least 1 set before they could complete all the reps in that range. Therefore, subjects were expected to be continually increasing their loads used during a mesocycle.

For the first 3 mesocycles (12 weeks), the training group (n=81) performed high-volume, full-body resistance training twice a week (2x) with limited rest between sets, focusing primarily on local muscular endurance for adapting the subjects for the next specific hypertrophy sessions.

The training protocol was then deferred for 1 week for measurements implicated in other studies. The measurements consisted of maximal bilateral isometric leg press, stimulation of the femoral nerve (Mmax), right leg unilateral isometric maximal knee extension (trials with and without super-imposed twitch), seated bilateral plantarflexion, bilateral 1-RM dynamic leg press and concentric power (using 50% of 1RM load) dynamic leg press. Following these measurements, training was resumed and for the subsequent 6 mesocycles, following a standard linearly periodized, full-body resistance training protocol, performed once, twice or 3 times / week. For these 6 mesocycles, subjects were instructed to perform 3 out of the 4 weeks at full intensity, and 1 week at reduced intensity (70% resistance). The 36 week training protocol can be seen below in Table 4.

TABLE 4 – Training protocol description.

Week	**Goal**	**Exercises**		**Sets x Repetitions**	**Rest period between sets**	**Special Instructions**
		Lower Body	**Up/ Body**			
1-4	Muscular endurance	-Leg press -Leg/knee extension -Leg/knee flexion -Sit-ups -Sitting calf raises	-Chest press -Latissimus pull-down -Triceps pulldown -Back extension -Shoulder press -Seated row -Biceps curls -Abdomen curls	2 x 16-20	1 min	N/A
5-8	Muscular endurance	-Leg press -Leg extensionperflexion -Sitting calf raises -Sit-ups	-Chest press -Triceps pulldown -Back extension -Shoulder press -Seated row -Biceps curls -Lat pull-down -Shoulder lateral raises -'Superman' body raises -Abdomen curls	2-3 x 14-16	See "Superset" protocol	"Superset" protocol: 2 exercises in succession (30s rest between), 2-4 mins rest after each superset
9-12	Muscular endurance	-Leg press -Leg extension/flexion -Sitting calf raises -Sit-ups	-Chest press -Triceps pulldown -Back extension -Shoulder press -Seated row -Biceps curls -Lat pull-down -Abdomen curls -Shoulder lateral raises	2-3 x 15	See "Superset" protocol	"Superset" protocol: 2 exercises in succession (no rest between), 1 min rest after each superset

			-‘Superman’ body raises			
13-16	Muscular hypertrophy	-Leg press -Leg extension/flexion -Sitting calf raises -Sit-ups	-Chest press -Triceps pulldown -Back extension -Shoulder press -Seated row -Biceps curls -Weighted trunk extension -Pectoralis fly -Lat pull-down -Abdomen curls -Shoulder lateral raises -‘Superman’ body raises	2-3 x 10-12	2 min	N/A
17-20	Strength, muscular hypertrophy	-Leg press -Leg extension/flexion -Lat pull-down -Sitting calf raises -Sit-ups	-Chest press -Triceps pulldown -Back extension -Shoulder press -Seated row -Biceps curls -Weighted trunk extension -Pectoralis fly -Abdomen curls -Shoulder lateral raises -‘Superman’ body raises	2-4 x 8-10	1-2 min	“Pyramid sets”: For 4 set exercises – 10 reps (set 1), 9 reps (set 2). 8 reps (set 3 and 4)
21-24	Maximum strength	-Leg press -Leg extension/flexion -Sitting calf raises -Sit-ups	-Chest press -Triceps pulldown -Back extension -Shoulder press -Seated row -Biceps curls -Weighted trunk extension	2-4 x 4-6	2-3 min	N/A

			-Pectoralis fly -Abdomen curls -Shoulder lateral raises -‘Superman’ body raises -Lat pull-down			
25-28	Muscular hypertrophy	-Leg press -Lunges -Leg flexion/extension -Straight leg calf -Squats leg extension -Deadlift	-Bench press -Single arm rowing -Shoulder raises -Abdomen exercises -Back exercises -Shoulder press -Assisted pull-ups -Pectoralis fly	3-4 x 8-12	1-2 min	Abdomen and back exercises (bw) performed in superset (no rest between sets)
29-32	Strength; emphasis on fatigue (high number of sets)	-Leg press -Leg extension/flexion -Sitting calf raises -Sit-ups abdomen curls (m), -Squats	-Chest press -Lat pull-down -Back extension -Shoulder press -Seated row -Shoulder press -‘Superman’ body raises	3-5 x 4-6	2-4 min	N/A
33-36	Power	-Leg press -Leg extension/flexion -Deadlift -Squat -Seated row -Standing calf raises	-Chest press -Assisted pull-ups -Abdomen curls -Shoulder press -Back extension	4-8 (at 30-50%; 60-80% (alternating) of maximum load from week 21-24 4	3 min	N/A

Daily physical activity was tracked during the study. The first 3 mesocycles using a high-volume protocol focusing on local muscular endurance were performed to prepare the subjects to adapt to RT and teach them how to perform the exercises with correct technique. Again, the aim was to acclimatize the subjects to RT and avoid using excessively high resistances. After the 3rd mesocycle, the protocol was changed to a more conventional linear periodized protocol to induce further gains in strength and muscle development.

4.2.3. Control group

The control group did not complete the training protocol. For the duration of the intervention, they were instructed to maintain their normal activities.

4.3. Data collection

All measurements were carried out in the Viveca building at the University of Jyväskylä. Prior to the beginning of the training protocol, baseline measurements (strength, body composition, lipid profile, hormonal baselines and inflammatory biomarkers) were made on the study sample. These same measurements were performed on the study sample following the 9 month training protocol. The complete details of all the measurements are described below.

4.3.1 Strength

Strength was assessed by a one repetition maximum (1-RM) test. A familiarization session for the 1-RM test was performed by all subjects prior to baseline measurements. Each subject completed a maximal dynamic horizontal 1-RM test in the seated position using a David 210 dynamometer (David Sports Ltd., Helsinki, Finland). 1-RM is the maximum load a subject can lift concentrically for one repetition. Leg extension in the subjects began at a knee angle of approximately 70° (mean = 68.4°, SD = 3.5). Subjects were instructed to hold the handles on the device tightly, and ensure that their buttocks and back remained in constant contact with the seat and backrest of the device throughout the test, and fully extend their legs (180°), without locking the knee joints. Verbal encouragement was given to all subjects. Prior to the start of the test, using the 1-RM value from the familiarization session, subjects executed a warm-up protocol of 6 reps at 50%, 4 reps at 70%, 2 reps at 90% and 1 rep at 95% of estimated 1-RM, with 1 minute rest between sets. Following the warm-up, the 1-RM test began with 1.5 minute rest between attempts. The aim was to complete the test within a maximum of 5 attempts. The greatest load that the subjects could fully lift was recorded as their 1-RM. Loads were increased or decreased in increments of 1.25, 2.5, 5 or 10 kg. Baseline, pre-training (Month 3) and post-training (Month 9) tests measurements were performed at the same time of day (±2 hour) and with similar ambient conditions.

The reliability of 1-RM leg press testing has been reported as high (Cuoco et al., 2004; Levinger et al., 2009), but there also are reported cases in the literature where some clinical systematic errors, although minimal, are found between 1-RM trials in the leg press (Phillips et al., 2004). In our case our ICC was 0.934 with a confidence interval of: 0.434 to 0.979.

Figure 10. Subject performing 1-RM in dynamic leg press

4.3.2. Peak Power

After the 1-RM test, 50% of the 1-RM load was calculated in order to perform a concentric power measurement in the same David 210 dynamometer (David Sports Ltd., Helsinki, Finland). The subjects were instructed to complete a single explosive repetition as fast as they could manage, in the concentric phase of the movement. According to Schroeder et al. (2007), power measurements in older men with leg press presents good reliability, since high correlation (r=0.96) has been found in between trials. In our study, the ICC for Peak Power was: 0.746 with a confidence interval of 0.643 to 0.822.

4.3.3. Electromyography

Surface electromyography (EMG) is commonly used to quantify the magnitude and timing of muscle activation during a given task. Ambu® Blue Sensors N bipolar Bipolar Ag/AgCl electrodes (5 mm diameter, 20 mm inter-electrode distance, common mode rejection ratio > 100 dB, input impedance > 100 MΩ, baseline noise < 1 μV rms) were positioned, following shaving and skin abrasion, for the assessment of the EMG. According to the SENIAM guidelines (Surface Electromyography for Non-Invasive Assessment of Muscles) (Hermens et al. 1999), tattoos were made for assuring that the electrodes were placed every measurement on the same spot for the targeted bellies of the muscles: Vastus medialis and Vastus Lateralis.

During the neuromuscular performance tests, surface electromyogram (EMG) was sampled at a frequency of 2000 Hz and amplified at a gain of 500 (sampling bandwidth 10–500 Hz). Raw signals were passed from a transportable pack to the receiving box (Telemyo 2400 R, Noraxon, Scottsdale, USA), were relayed to an AD converter (Micro1401, Cambridge Electronic Design, UK) and recorded by Signal 4.04 software (Cambridge Electronic Design, UK). After testing, EMG signals were band-pass filtered (20–350 Hz), and maximum integrated EMG was determined from 75° to 170° knee flexion (without locking the joing at maximum knee extension) angle during the dynamic concentric leg extension (sampled at 2000Hz) trials using customized scripts. Muscle activity was quantified as root mean square (RMS) amplitude for each of the muscles

4.3.3.1. EMG processing

In order to normalize the EMG signals analyzed, maximal M-waves were elicited by stimulating the femoral nerve using 1-ms square rectangular pulses, delivered by a constant-current stimulator (Model DS7AH, Digitimer Ltd, UK) and participant-specific current intensities (in between 100 to 1000μV). Supramaximal intensity for each participant was set at 1.25 times the intensity required to elicit the maximal M-wave. Maximum M-wave properties were analysed with Signal 4.02 software (Cambridge Electronic Design, UK) for peak-to-peak amplitude and peak-to-peak duration. The participants' individual EMG was normalized to highest amplitude value found in the M-wave stimulation.

4.3.4. Body Composition

Whole-body tissue composition was measured using DXA (Lunar Prodigy Advance, GE Medical Systems, Madison, United States). Measurements were performed in the morning after a 12 hour fast due to the fact that: body mass, lean mass and fat might present significant variations in mean values of trunk and legs, which seems to be moderate in men but more sensitive for women and also dependent in the meal size (Nana et al., 2012).

A technician instructed the subjects to remove any metal objects and take off excess clothing and gave further instructions. They were positioned so that their spine was aligned with the longitudinal line running down the middle of the bed. Their feet were secured with a footrest made out of Styrofoam and their arms were placed beside their body with palms facing in, with bean bags separating the hands from the thighs and upper arms from the torso. Subjects were to lie still throughout the duration of the scan; each scan took approximately 6 minutes. For the post-training measurements, the scan/image from baseline measurements was consulted to ensure that subjects were in the same position for both measurements.

Automatic analysis (Encore version 14.10.022) provided whole-body lean mass in grams (g), as defined in the user manual (lower boundary at pelvis cut; upper boundary above pelvis cut by 20% of the distance between pelvis and neck cuts; lateral boundaries are the arm cuts; Lunar User Manual, 2010).

Studies have consistently shown that DXA is a valid and reliable method of assessing body composition in subjects of all ages (Chen et al., 2007; Hart et al., 2015; Kaul et al., 2012; Nana et al., 2012).

4.3.5. Blood samples

Blood samples were drawn from the antecubital vein into serum tubes (hormones, lipids and glucose), [Vacuette®, Greiner Bio-One, Kremsmünster, Austria and EDTA-tube (BBC), K2E EDTA-Tube, Vacuette®, Greiner Bio-One, Kremsmünster, Austria, using needles, Vacuette®, Quickschield Complete PLUS, Greiner Bio-One, Kremsmünster, Austria and other standard laboratory procedures]. Whole blood was centrifuged at 3500 rpm (Megafuge 1.0 R, Heraeus, Hanau, Germany) for 10 minutes after which serum was removed and stored at -80°C until analysis (approximately 4 - 8 weeks).To examine the basal concentrations of serum hormones, blood samples were drawn from each subject after 12 hours of fasting and 8 hours of sleep in the mornings, two days before the strength testing took place (between 7:30 AM and 9:30 AM) during the whole training period.The analysis was conducted with IMMULITE 2000, solid-phase competitive chemiluminescent enzyme immunoassay, with one incubation cycle of 30 minutes. For COR and SHBG the amount of serum required was 10µl, while for T was 20µl. The analytical sensitivity for COR, T and SHBG was 5.5 nmol/L, 0.5 nmol/L and 0.02 nmol/L, respectively. The intra-assay variation was between 5.9-7.0% for COR, 9.2-10.9% for T and 6.0-7.2% for SHBG.

4.4. Statistical Analysis

Statistical analysis was completed using IBM SPSS Statistics Version 21 software (SPSS Inc., Chicago, IL, USA). Conventional statistical methods were used to determine mean and standard deviation (SD) values. The normality of the data was tested using Shapiro-Wilk ($n < 50$). Repeated measures ANOVA (4 group x 3 time x 2 sex) was used to identify main effects for all variables. Mauchly's sphericity test was performed, and where this assumption was violated, Greenhouse-Geisser adjustments were used. Within-group differences (pre-training (PRE) vs post-training (POST)) were analysed using a paired-samples t-test. Between-group absolute and percentage differences were assessed using one-way ANOVA (training groups versus control group). Pearson product-moment correlations were calculated between the percent change (Δ%), the absolute change (Δ) and baseline values (PRE) for each variables. The significance level for all tests was set $\alpha = 0.05$.

4.5. Reliability

The intra-class coefficient was calculated for assessing the reliability of the repeated measurements. The results can be seen in table 5.

TABLE 5. Intra-class coefficient (ICC) values for Testosterone (T), Cortisol (COR), Sex-hormone Binding Globulin (SHBG), Total Lean Mass (TLM), One Repetition Maximum (1RM), Peak power over 25ms (PPow) and Leg Lean Mass (LLM).

	1RM	Ppow	TLM	LLM	T	COR	SHBG
ICC	0.934	0.746	0.96	0.976	0.944	0.682	0.873
95% Confidence interval (Lower - Upper bound)	0,434-0,979	0,643-0,822	0,446-0,707	0,964-0,984	0,918-0,962	0,359-0,654	0,817-0,913

5. RESULTS

5.1. Strength

5.1.1. One Repetition Maximum

There was a significant main effect for time in men (F=9.2, $p<0.001$) and also for women (F=27.7, $p<0.001$) with a trend toward group x time (F=3.327, p=0.14). Post hoc tests did not reveal a significant main effect of time in 1-RM for the men that trained 2 times/week but the paired samples t-test with Bonferroni showed a significant difference (t(9)=4.8, p=0.001) from Pre-to-Mid measurements, and also for those who trained 3 times/week: (t(10)=4.1, p=0.002) from Pre-to-Post and (t(11)=6.2, $p<0.001$) from Pre-to Mid measurements. The women that trained 2 times/week increased their 1-RM significantly over time from Pre-to-Post measurements (t(14)=4.6, $p<0.001$), and the ones that trained 3 times/week also showed a significant effect of time in between the Pre-to-Mid measurements (t(15)=4.5, p=0.001) and the Pre-to-Post measurements (t(15)=0.001, $p<0.001$). The control group showed no changes in 1-RM. When comparing the change in the intervention groups with the control, it was found a significant difference between the 1-RM change in the men that trained 3 times / week and the control group from Pre-to-Post, showing and increase in 9.4%($p<0.001$) in 1-RM compared with the control group that decreased the 1-RM by 3%. Additionally in the women groups, after comparing the treatment groups with the control, they were found statistically significant differences between those women that trained twice / week from Pre-to-Post that increased 7% their 1-RM (p=0.14) and those who trained three times / week, increasing their 1-RM by 9% (p=0.001) compared with the decrease in 1-RM by 2% in the control group.

TABLE 6. 1-RM results (mean±standard deviation) for the training and control. Levels of significance within group: *=p≤0.05; **=p≤0.001 (Pre-to-Mid and Pre-to-Post).'~' symbol displayed for showing value close to significance (p=0.052).

Gender	Frequency (times / week)	1-RM (kg)			Δ%	
		PRE	MID	POST	Pre-Mid	Pre-Post
Men(n=11)	1	148±22	150±23	150±25		
Men(n=10)	2	160±20	166±21*	165±18~	3.6±2.3	3.4±4.3
Men(n=11)	3	151±31	160±31**	165±32**	8.12±5.25	9.4±5.7
Men(n=11)	0	141±16		137±19		
Women(n=13)	1	89±15	91±16	92±16		
Women(n=15)	2	105±20	108±19*	113±22**	3.4±5	7.7±6.3
Women(n=16)	3	103±17	111±20**	113±22**	8.12±5.25	9.55±7.76
Women(n=9)	0	97±20		95±20		

5.1.2. Peak power

No main effect of time or interactions were found within or between groups in the peak power analysis over 25 ms, during the dynamic leg press with 50% of the 1-RM load.

TABLE 7. Maximum leg press peak power (over 25 ms) using 50% of 1RM (mean±standard deviation).

Gender	Frequency (times / week)	Peak Power at 25ms (W)		
		PRE	MID	POST
Men(n=11)	1	1571±419	1638±338	1722±438
Men(n=9)	2	1599±338	1773±383	1811±300
Men(n=10)	3	1836±823	1596±292	1740±366
Men(n=12)	0	1739±254		1635±226
Women(n=13)	1	712±157	769±202	789±239
Women(n=15)	2	931±198	936±207	1000±295
Women(n=17)	3	961±226	957±229	1052±326
Women(n=9)	0	846±228		832±235

5.3. Lean Mass

No significant main effect of time or interaction was found in between groups. No statistically significant differences were found between the changes in the intervention groups and the control groups for men and women. Pre and Post measurements presented in Table 8.

TABLE 8. Total Lean Mass changes over time, within groups (mean±standard deviation), among different training frequencies. Levels of significance within group: *=p≤0.05; **=p≤0.001.

Gender	**Frequency (times / week)**	**Total lean mass (kg)**	
		PRE	**POST**
Men(n=11)	1	54.5±8.5	54.2±8.6
Men(n=9)	2	55.8±5.6	55.5±6.01
Men(n=10)	3	53.58±6.7	53.8±7.1
Men(n=12)	0	51.76±4.81	51.63±4.9
Women(n=13)	1	35.58±2.82	35.18±3
Women(n=15)	2	37.94±4.51	37.96±4.62
Women(n=17)	3	38.99±3.5	38.82±4.3
Women(n=9)	0	37.48±8.6	37.39±8.9

TABLE 9. Legs' Lean Mass changes over time, within groups (mean+standard deviation) among different training frequencies. Levels of significance within group: *=p≤0.05; **=p≤0.001.

Gender	**Frequency (times / week)**	**Legs' lean mass (kg)**	
		PRE	**POST**
Men(n=11)	1	16.7±4.09	16.6±3.94
Men(n=9)	2	16.5±3.24	16.6±3.12
Men(n=10)	3	18.6±1.74	18.8±1.77
Men(n=12)	0	17.9±1.47	18.1±1.34
Women(n=13)	1	12.7±2.62	12.45±2.51
Women(n=15)	2	14.49±3.37	14.67±3.36
Women(n=17)	3	13.12±1.30	13.15±1.51
Women(n=9)	0	12.1±1.54	12.03±1.53

5.4. Serum hormone concentrations

Regarding the basal hormone levels, a main effect of time was found for T (F=21.5, p<0.001), but no significant interactions. Within groups, post hoc tests showed significant increases in T within groups for those men that trained once (t(10)=2, p=0.032), 3 times / week (t(11)=3, p=0.007), and also the control group (t(10)=3, p=0.010). Significant increases in T were observed in the women of all groups; increasing for all the intervention groups, once (t(11)=3.5, p=0.005), twice(t(11)=3.6, p=0.004), 3 times(t(11)=3.4, p=0.005) per week, and control (t(7)=3, p=0.015) (see table 10). Additionally when comparing the intervention groups with the control, no differences were found in between the changes in the treatment groups and the control group.

A significant main effect of time was found in COR (F=26, p<0.001) but no interaction. Post hoc tests showed that COR levels rose in all the intervention groups in men training once (t(10)=2.4, p=0.036), twice (t(8)=3.3, p=0.010), three times / week (t(11)=2.7, p=0.018) and control (t(10)=2.2, p=0.045), increasing proportionally with training frequency. In the women's case, those that trained 3 times / week (t(13)=2.8, p=0.013) and the control group (t(7)=3.9, p=0.005), showing this one the greatest increase (table 10). None of these comparisons between the changes in the intervention groups with the control was statistically significant.

Regarding T/COR ratio within groups, a main effect of time was found in men (F=5.681, p=0.022) and women (F=4.7, p=0.34) but not significant interactions (see table 11). Post hoc tests showed a significant decrease in those men that trained twice / week (t(10)=2.3, p=0.042). Regarding women groups T/COR ratio significantly increased in those ones that trained twice / week (t(14)=2.3, p=0.037) and the control group (t(7)=2.6, p=0.033).

The SHBG/COR ratio showed a significant main effect of time for men (F=15.4, p<0.001) and women (F=24.2, p<0.001) and no interactions (see table 11). Post hoc tests revealed a significant decrease within groups for the men that trained twice (t(11)=-3, p=0.007) and three times / week (t(11)=-3, p=0.007). Additionally a significant decrease was found for all the women´s groups, once (t(11)=-2.8, p=0.015), twice (t(13)=-2.7, p=0.018), three times (t(13)=-2.2, p=0.046) / week, decreasing proportionally with frequency, showing the greatest decrease in the control group (t(7)=2.3, p=0.050).

TABLE 10. Hormonal changes for Men and Women within groups (mean±standard deviation), among different training frequencies. Levels of significance within group: *=p≤0.05; **=p≤0.001. ’~’ symbol displayed for showing value close to significance (p=0.056)

Gender	Frequency (times / week)	Testosterone (nmol/l)		Δ%	SHBG(nmol/l)		Cortisol(nmol/l)		Δ%
		PRE	POST		PRE	POST	PRE	POST	
Men(n=11)	1	13.4±5.2	15.7±5.9*	24±29	46±15	45.6±15.6	371±105	438±78*	17±19
Men(n=9)	2	10.1±2.5	10.7±3.5	5±38	42.7±17	40.1±15.5	329±88	419±105*	29±28
Men(n=10)	3	10.5±2.6	13±3.1*	27±24	47.9±13.9	39±64	310±87	391±64*	37±48
Men(n=12)	0	14.9±4	18±5.6*	17±18	34.6±9.3	44.8±109	438±245	493±197*	24±10
Women (n=13)	1	0.2±0.2	0.5±0.4*	776±1590	55.5±22.6	45.5±24.5	339±73	367±147~	7±67
Women (n=15)	2	0.2±0.1	0.5±0.2**	396±657	56.8±16.8	55.5±14.7	315±95	395±114	22±18
Women (n=17)	3	0.4±0.3	0.8±0.5*	3331±11806	28.4±11.2	42.7±88.6	310±81	419±85*	48±60
Women (n=9)	0	0.3±0.2	0.7±0.4*	207±221	30.9±9.2	42.5±80	309±86	424±74*	45±41

TABLE 11. Testosterone/Cortisol ratio (T/COR) and Free Androgen Index (FAI). Levels of significance within group: *=p≤0.05; **=p≤0.001.

Gender	Frequency (times / week)	T/COR (nmol/l)		Δ%	FAI(nmol/l)		SHBG/COR(nmol/l)		Δ%
		PRE	POST		PRE	POST	PRE	POST	
Men(n=11)	1	0.038±0.019	0.036±0.013	-5±37.5	29.74±9.36	34.74±6.57	0.13±0.05	0.10±0.03	26±50
Men(n=9)	2	0.03±0.009	0.026±0.009*	-14±24	25.62±5.82	27.45±4.56	0.13±0.04	0.09±0.03*	-36±28
Men(n=10)	3	0.038±0.019	0.032±0.008	-17±81	22.87±5.98	28.29±5.44	0.17±0.08	0.12±0.04*	-44±62
Men(n=12)	0	0.036±0.02	0.036±0.017	0±16	29.37±10.45	30.70±8.71	0.17±0.1	0.13±0.04	26±85
Women(n=13)	1	0.0008±0.0006	0.0016±0.0011	66±58	0.718±0.497	1.3008±0.7880	0.17±0.04	0.13±0.05*	-26±27
Women(n=15)	2	0.0008±0.0005	0.0013±0.0006*	270±389	0.53±0.405	1.14±1.001	0.19±0.07	0.15±0.05*	-32±36
Women(n=17)	3	0.003±0.007	0.006±0.015	66±72%	0.79±0.49	1.49±1.06	0.19±0.1	0.12±0.03*	-47±70
Women(n=9)	0	0.001±0.0009	0.0017±0.0013*	116±176	0.372±0.2805	1.219±0.673	0.26±0.16	0.15±0.06*	-128±196

5.5. Muscle activity

Regarding muscle activity in absolute values, a significant main effect of time was found (F=6.2, p=0.017) in men's VM activity and also in men's VL activity (F=10.4, p =0.003). VM activity significantly increased for men that trained once / week (t(9)=2.5, p=0.030) from pre-to-post tests. VL activity significantly increased in men that trained 3 times / week (t(9)=2.4, p=0.038) from pre-to-post tests.

In the women's case, a significant main effect of time was found in VL (F=14.9, p<0.001) and VM activity (F=35.6, p<0.001). Within groups, post hoc tests showed significant increases in VM activity for those that trained once /week (t(8)=3.3, p=0.011), twice (t(13)=3, p=0.010) and three times / week (t(13)=5, p<0.001) from pre-to-post measurements. Additionally, there was a significant increase in VL activity from pre-to-post measurements in those women that trained twice / week (t(11)=3, p=0.012) and three times / week (t(13)=3.4, p=0.004). No significant interaction or significant change was found within or between the intervention groups and control. No significant changes were found either when the VL and VM activity data were normalized with the M-wave's data (see table 12, 13).

TABLE 12. Non-normalized muscle activity changes overtime, within groups (mean±standard deviation), among different training frequencies. Levels of significance within group: *=p≤0.05; **=p≤0.001. VL=vastus lateralis; VM=vastus medialis.

Gender	Frequency (times / week)	Vastus Lateralis EMG (mV)			Δ%	Vastus Medialis EMG(mV)			Δ%
		PRE	MID	POST	PRE-POST	PRE	MID	POST	PRE-POST
Men(n=11)	1	272±115	303±61	307±73	12±44	250±131	324±159	315±149*	23±12
Men(n=7)	2	232±84	217±87	274±121	16±36	207±85	226±90	247±102	17±18
Men(n=7)	3	190±97	209±119	226±128*	17±27	178±92	202±53	198±75	10±20
Men(n=9)	0	195±64		189±79	-3±20	205±73		209±85	2±15
Women(n=7)	1	77±41	77±27	80±39	3±5	95±64	115±91	113±78*	17±19
Women(n=12)	2	81±37	96±37	101±39*	21±5	77±42	111±53	99±49*	25±15
Women(n=14)	3	108±44	139±65	157±79*	36±57	103±30	115±40	150±49**	37±48
Women(n=8)	0	80±24		94±30	16±22	109±31		132±45	19±36

TABLE 13. Normalized muscle activity changes over time, within groups (mean±standard deviation), among different training frequencies. Levels of significance within group: *=p≤0.05; **=p≤0.001.

Gender	Frequency (times / week)	VASTUS LATERALIS EMG (µV)		VASTUS MEDIALIS EMG (µV)	
		PRE	POST	PRE	POST
Men(n=11)	1	0.11±0.12	0.08±0.08	0.05±0.03	0.07±0.09
Men(n=7)	2	0.06±0.03	0.11±0.10	0.04±0.02	0.04±0.02
Men(n=7)	3	0.08±0.05	0.07±0.03	0.11±0.15	0.04±0.02
Men(n=9)	0	0.04±0.02	0.06±0.05	0.05±0.03	0.06±0.06
Women(n=7)	1	0.05±0.018	0.04±0.027	0.04±0.024	0.04±0.027
Women(n=12)	2	0.04±0.027	0.06±0.031	0.04±0.033	0.04±0.024
Women(n=14)	3	0.05±0.033	0.06±0.061	0.07±0.038	0.06±0.04
Women(n=8)	0	0.04±0.02	0.05±0.02	0.04±0.03	0.07±0.07

5.6. Correlations

Bivariate correlation analysis was calculated for variables' percentage changes in between months 3 and 9. Regarding the trends found in both men and women intervention groups, the change in 1RM correlated positively with the change in PP (r=0.430**; p=0.004; n=42) for men and for women (r=0.456**; p=0.001; n=53). Additionally the change in T/COR correlated positively with the change in FAI in men (r=0.474*; p=0.001; n=43) and also in women (r=0.859**; p<0.001; n=44). Additionally, other correlations were found in the intervention groups, but not showing the same trend behaviour like abovementioned towards men and women (see Table 14).

Table 14. Correlations between the percentage change of the different variables. Levels of significance: *=p≤0.05; **=p≤0.001.

Gender		Change in T	Change in SHBG	Change in COR	Change in TLM	Change in 1RM	Change in PPow	Change in FAI	Change in T/COR	Change in SHBG/COR	Change in VL	Change in VM	Change in LLM	Gender
Women (n=53)	**Change in T**		0.009	0.159	-0.014	0.038	-.0.072	**0.803****	**0.558****	0.058	0.239	0.84	-0.246	Men (n=43)
	Change in SHBG	-0.016		-0.020	-0.155	0.017	-.0.069	**-0.537****	0.010	**-0.459****	-0.137	-0.120	0.32	
	Change in COR	-0.158	0.253		0.193	0.173	-0.189	0.140	**-0.660****	**0.869****	-.117	-0.094	-0.194	
	Change in Lean Mass	-0.067	-0.173	-0.132		0.247	0.085	0.080	-0.136	0.272	**0.362***	**0.435***	0.297	
	Change in 1RM	-0.086	-0.049	-0.034	**0.430****		**0.430****	-0.012	-0.066	0.128	-0.049	0.141	**0.464****	
	Change in PPow	-0.056	0.093	**0.317***	0.188	**0.456****		-0.043	0.103	-0.083	-0.067	0.191	0.120	
	Change in FAI	**0.965****	-0.243	-0.072	-0.028	-0.092	-0.123		**0.474***	**0.328***	**0.342***	0.208	-0.263	
	Change in T/COR	**0.819****	-0.229	-0.172	-0.073	-0.072	-0.079	**0.859****		**-0.599****	0.275	0.150	0.013	
	Change in SHBG/COR	0.129	**-0.614****	**0.418****	-0.007	-0.051	0.095	-0.039	-0.127		-0.036	-0.004	-0.159	
	Change in VL	0.012	0.209	0.169	-0.062	0.179	0.165	-0.081	-0.179	0.031		**0.656****	-0.026	
	Change in VM	0.151	-0.036	-0.114	0.117	-0.101	0.067	-0.080	-0.003	-0.107	0.199		-0.123	
	Change in Legs Lean Mass	-0. 247	0.112	-0.062	**0.654****	0.248	0.055	-0.015	-0.171	-0.112	-0.026	0.243		
	Change in DHEA	**-0.341***	-0.070	0.043	-0.197	0.211	0.170	**-0.412***	**-0.391***	0.027	-0.192	-0.125	-0.245	

6. DISCUSSION

The main outcomes after the intervention were that the strength adaptations presented increases in 1-RM among 2 and 3 times / week frequencies, correlating positively with increasing training frequency. Regarding hormonal basal levels, significant changes were found in both men and women in T and COR, together with T/COR ratio and SHBG/COR but not a trend towards frequency was found. Muscle activity of the VL and VM showed significant increases but no relationship with different frequencies. On the other hand, TLM and LLM, together with muscle activity showed no significant changes in both genders.

The global population over the age of 65 is estimated to more than double between 2010 and 2050, growing from 40.2 million to 88.5 million (Vincent & Velkoff, 2010). Globally, the number of older persons is expected to more than double from 841 million people in 2013 to more than 2 billion in 2050. On average, people in longer-lived populations tend to spend more years living with disability than people in populations where the average lifespan is shorter. The average healthy life-expectancy is nowadays 62 years old and (World Population Aging, 2015). RT as an intervention has been used for improving muscle strength and morphology in old age although the dose-response relationship seems to be still inconsistent (Peterson et al., 2010). Due to the anticipated rise in the number of older adults in the next 40 years, RT has been being promoted as a countermeasure for enhancing quality of life and decreasing the health care costs by preventing muscle quality and strength natural declines with age.

6.1. Strength

Within groups, after 24 weeks of RT, 1-RM significantly increased in men among the frequencies: 2 and 3 times / week from pre-to-mid and mid-to-post measurements. Similar increases appeared in women in the frequencies: 2 and 3 times / week, also from pre-to-mid and pre-to-post measurements.

According to what has been observed in other studies with similar RT periodization, volumes and intensities, these increases remain modest compared with a 21% increase in 1-RM was found by Häkkinen et al. (2000, 2001) after 24 weeks of training; 37% increase after 21 weeks of RT by Häkkinen et al. (2001) and Walker et al. (2013, 2014), finding 28 % and 25 % increased 1-RM in the leg press. Also in longer interventions (52 weeks), it has been reported a significant increase >19% in Leg Press compared with the control group (Rhodes et al., 2000). These changes were reported in isometric bilateral leg press and knee extension devices which makes a big difference, since the difficulty is increased in the bilateral dynamic leg press.

Regarding intensity, based on the abovementioned studies, it has been suggested that moderate to high (65 – 80% of 1RM) training intensities induce greater strength gains. The same intensity range was used in this study supporting the increases in strength in the once /week, 2 times / week and 3 times / week intervention groups for both genders.

Regarding frequency, all intervention groups increased 1-RM but larger gains were observed with higher training frequency. This trend in elderly after RT interventions has also been reported after a meta-analysis by Borde et al. (2015), where they concluded that, in the elderly, a 3 times per week frequency seemed to be optimal for strength increase mainly and also hypertrophic adaptations. In another meta-analysis conducted by Silva et al. (2014) about RT in elderly, out of 21 studies, 17 of them chose a 3 / week intervention frequency and the strength of the subjects improved significantly in all of them. Farinatti et al. (2013) compared one vs. two vs. three strength training sessions per week in women over 60 years old. All three groups performed 1 set of 10RM in different exercises. These authors showed that the higher frequency (2 and 3 sessions) improved the strength and functional capacity in a greater extent than the lower frequency (1 session) of training with non-equated volume.

All these changes have to be considered within this intervention context, where the subjects performed a 3 months RT protocol with a twice / week training frequency before this data was analyzed. If the comparison had been made with the Month 0 baseline values, it is expected that more significant increases in 1-RM occurred after the intervention period. The rate of improvement has been reported in other studies to be greater in older untrained subjects with the onset of training as it can be seen for example in studies like the one conducted by McCartney et al. (1995) showing that 30 and 47% of the increase in 1-RM had occurred by 6 weeks and 12 weeks and almost half was evident by 12 weeks, finding a plateau afterwards but on the other hand other studies like Häkkinen et al. (1998) did not show a plateau in 1-RM increases in between an intervention period from 7 to 21 weeks.

In the present study, no significant differences were found between those groups that trained twice and three times / week, showing both similar increases in 1-RM. Statistically significant increased change in 1-RM in twice and three times / week when compared to once per week. According to the data, the total volume achieved by three sessions was not enough for furthering the strength adaptations in elderly compared to two but 2 and 3 times / week were enough for furthering the adaptations found in once / week by 9.5%.

6.2. Power

A non-statistically significant power increase pattern was found in all the intervention groups for men and women, 9±4% for those men that trained once per week, 12±12% for those who trained twice and 5±22% for the men that trained three times per week. Regarding the women, 10±40% increase for those which trained once, 7±40% increase training twice and 9±36% for those who trained three times per week. Additionally, the control groups both decreased the power in men by 6±11% and women showed a decrease of 1±3%.

These results contrast with other studies that found significant improvements in power production in older adults as a consequence of RT interventions by 21 ± 24% and 22 ± 28% in in 70 years-old men and women respectively after 24-weeks intervention (Häkkinen et al., 2001), 25 ± 16% power increase in leg press after 10 weeks intervention (3 times / week) in 57-65 year-old subjects (Newton et al., 2002); 22% power increase after a 12-week RT intervention focused in explosive movements in above-70 years old subjects with a 3 times / week frequency (Earles et al., 2001); additionally, after a 10-weeks intervention a significant increase in explosive contractions by 31±8% working with 60% of the 1-RM was found in another study conducted by Bottaro et al. (2007).

A dose-response relationship did not appear after the RT protocols, but all the intervention groups were found enhanced peak power, despite no differences between them. The periodization did not focus in power-oriented training until the last 4 weeks of the intervention period (33^{rd} to 36^{th} week in the full RT intervention period).

6.3. Muscle activity

Statistically significant increases in muscle activity for both VL and VM were found in some intervention groups for men and women. The men that trained 3 times / week showed an increased VL activity. Although the other groups didn't present significant changes in the VL activity, it increased progressively together with increasing frequency and a non-significant decrease appeared in the control group. The only frequency that showed significant increase in VL activity was the 3 times / week frequency. No statistically significant differences were found between men's groups. Similar pattern was found in women, increasing VL activity in parallel with frequency. Women that trained twice and three times per week showed a 21±5% and 36±57% increase respectively. Those who trained two and three times / week showed a significantly higher VL activity by 23 and 65%, respectively.

Regarding VM activity, no pattern towards frequency appeared in men's groups, since only those that trained once / week showed a significant increase of 23±12% but no significant changes were found in the other intervention groups or control. Furthermore, no statistically between-groups differences were found. When looking at women, the increasing muscle activity in parallel with increasing frequency appeared, in once, twice and three times / week, by 17±19, 25±15 and 37±48 respectively. Those who trained three times / week showed a significantly higher VL activity by 28% respectively when compared to once per week.

Different RT interventions have demonstrated significant increases in muscle activity in older adults: After 12 weeks, with a 2 times / week protocol, VL and VM activity increased by 20% (Häkkinen & Häkkinen, 1995), same duration and frequency showed a 9-19% increase in muscle activity (Häkkinen et al. 1996) and after a 24 weeks duration with same week frequency showed no significant increases in VL or VM (Häkkinen et al., 1998). Evidence reported by other studies contrasts with the muscle activity adaptations occurred in this study when looking at EMG normalized values. Regarding the absolute values, increases in muscle activity for both VL and VM show a similar trend in women than what has been reported in the literature.

6.4. Lean Mass

No significant changes were found in the intervention groups in TLM or LLM or in control. In studies with a similar setup (intervention duration, subjects' age, volume, intensity and training frequency), increases in LLM were found after 20 weeks intervention by 8±19% and 15±11% (Walker et al., 2013). Similar outcomes were found in studies conducted by Correa et al. (2013), reporting a 22% increase in quadriceps femoris after 12-week RT intervention, Pinto et al. (2013), finding a 8-18% increased quadriceps femoris mass after 6 weeks of RT and Radaelli et al. (2014), that reported a 8-14% increase in LLM of 8-14% after 13 weeks intervention. All these studies presented a frequency of 2 times / week.

It should be mentioned that increasing dietary protein favorably affects muscle and strength during RT periods (Bosse & Dixon, 2012). Age may reduce the acute anabolic response to protein intake with RT (Lockwood et al., 2008). Furthermore, the dose of ingested protein necessary to induce a maximal stimulation of muscle protein synthesis after resistance-type exercise appears to increase during conditions of energy deficit compared with conditions of energy balance (in short-term energy conditions) (Areta et al., 2014). Some studies in older adults when diet was intervened together with RT, showed no significant influence in hypertrophy or muscular strength (Campbell et al. 1994) after a 12-week progressive RT protocol and no significant change either in hypertrophy but a significant increase in knee extensor torque in a research conducted by Straight et al. (2012). One of the limitations of this study falls on the lack of control over dietary intake and life-style variables.

6.5. Basal hormones

Regarding hormonal basal levels, significant changes were found in both men and women in T and COR, together with T/COR ratio and SHBG/COR. It was not found a trend towards increasing training frequency and basal hormones besides the negative correlation between SHBG/COR ratio and increasing RT frequency in both men and women. Basal T concentrations have not shown systematic significant changes in older adults after a 6-month RT intervention (Häkkinen et al., 2000) or after a 12-week RT protocol (Craig et al., 2000). Suppression of T levels below 10% has been reported to attenuate the muscle mass increase after RT protocols (Kvorning et al., 2006).

There is not a single mechanism towards hypertrophic adaptations, and the ability to interact with the circulating levels of T suggests that the myocyte increase its sensitivity to the hormone by AR (Harridge, 2003). T has been reported to be affected by the disturbance of light-darkness exposure, ranging its influence between 5-48.6% in healthy men aged from 28-59 years (Cortés-Gallegos et al., 1998). In latitudes with less sun exposure, individuals receive less sun-radiation like the one in this study. Also, regarding energy intake, T basal concentrations significantly decrease in men that decrease the dietary fat content (Hämäläinen et al., 1984), especially of saturated fat (Lambert et al., 2004). In our study, subjects were exposed to less sun exposure than more southern latitudes compared to the average sun rate received in Finland, ranging from 5 (in December) in the last measurements to 19 hours (in July) (Finnish Meteorological Institute, 2016), during the first measurements of sun light. RT interventions have been reported to have no effect on SHBG levels (Häkkinen et al., 2002) and aerobic exercise appears to lower SHBG concentrations in postmenopausal women (Kim & Kim, 2012). The SHBG/COR ratio has not been recently used in any study for elderly populations. Tanskanen et al. (2011) reported SHBG increased after 12 weeks RT intervention and a decrease in COR and FAI. SHBG/COR ratio was higher after 4-7 weeks of training at the end of the basic training period in the military service, confirming their hypothesis that it would be useful for assessing if training is too strenuous. According to this hypothesis, the subjects in our study would have been able to handle a more strenuous intervention. Further insights into how basal hormonal concentrations affect strength and lean mass are needed to get a better understanding of the chronic endocrine responses to RT or if they don’t play a role at all.

7. CONCLUSIONS

This study provides evidence that shows RT as a consistent strategy for increasing strength and chronic hormonal responses in older untrained adults. In the literature, several studies set up RT interventions due to the increasing relevance of countering age-related diseases that directly affect longevity and life-quality as the population within this age-range keeps increasing year by year. RT protocols with 2 and 3 days / week are the most popular among the topic with a high variability of intervention durations, from 6 to 54 weeks.

In this study, the higher the frequency of training, the greater the increase in 1-RM was found in both men and women, finding statistical differences between once / week compared to twice and three times / week. Three times / week frequency showed no additional increase in 1-RM compared to two for both genders. Some chronic adaptations towards basal hormone concentrations were also found, with a significant increase pattern in T towards frequency and a constant decrease in the intervention groups for T/COR and SHBG/COR ratio appeared, Other variables, such as power, muscle activity, TLM and LLM, that in the literature show significant positive changes after different frequencies and intervention durations, have not been reported any relevant changes in this study.

From a dose-response perspective the results of this study suggest that for older populations, in order to increase strength, frequencies of one time / week are not enough for furthering improvements and seems like two and three times / week bring similar outcomes. Providing a sufficient duration of intervention and training frequency, RT is an appropriate tool for extending the years of independent living for both older men and women.

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