STUDIES IN SPORT, PHYSICAL EDUCATION AND HEALTH
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Daniela Eklund

Different-day and Same-session Combined Strength and Endurance Training

Adaptations in Neuromuscular and Cardiorespiratory Performance, Body Composition, Metabolic Health and Wellbeing in Men and Women

JYVÄSKYLÄN YLIOPISTO

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"Maybe someday we will find,
that it wasn't really wasted time."

Eagles

ABSTRACT

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This thesis investigated 1) acute neuromuscular and hormonal responses to combined strength and endurance loadings with different orders and their long-term adaptations (women), 2) adaptations in neuromuscular, hormonal, cardiorespiratory and health variables following 24 weeks of volume-equated protocols of combined training (men and women). Subjects were assigned to one of three groups: strength and endurance training on different days (DD: men n=21, women n=18), training in the same-session with either endurance before strength (ES: men n=16, women n=15) or *vice versa* (SE: men n=18, women n=14). DD trained 4-6 d·wk^{-1} with strength and endurance on alternating days. ES and SE trained 2-3 d·wk^{-1} of [1E+1S] or [1S+1E] with strength and endurance in immediate succession. Training consisted of endurance cycling and hypertrophic and maximal strength training. Both ES and SE led to significant acute neuromuscular fatigue. Post-exercise growth hormone concentrations were significantly larger in SE than ES before and after the intervention. All three groups improvedd strength and endurance performance. The increase in maximal oxygen uptake was significantly larger in DD than in ES and SE in both genders. DD and SE increased voluntary muscle activation while ES did not. The individual changes in voluntary activation and maximal knee extension force were correlated in ES during weeks 13-24. Lean mass and vastus lateralis (VL) cross-sectional area increased similarly in all groups. Decreased fat mass was observed only following DD-training. Changes in blood lipids and abdominal fat were correlated in DD and the entire subject sample. Self-esteem and wellbeing improved and time-management behavior deteriorated in DD, but remained unchanged in the same-session groups. The results suggest that increased physical performance and muscle hypertrophy can be achieved with any of the training modes in previously untrained adults. Individuals adhering to ES training may be susceptible to neural interference, although it is unclear if strength development is affected. DD training simultaneously optimizes body composition and physical performance. DD-training does not result in a feeling of excessive general fatigue despite requiring more individual weekly training sessions than ES and SE.

Keywords: concurrent training, physical performance, neuromuscular adaptations, hormones, metabolic health, HRQoL

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This thesis has not only been read and evaluated by both of my supervisors but also by two experts in the field of exercise science. Prof. Gary Hunter and prof. Steven Fleck, thank you for accepting the invitation to review my work and thank you for the comments you provided to help me further improve my dissertation. I also want to thank prof. Dušan Hamar who agreed to be my opponent at the public defense of my dissertation. I am honoured to have been able to receive invaluable comments for my work from such distinguished researchers.

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Jyväskylä, May 2017
Daniela Eklund

LIST OF ORIGINAL PUBLICATIONS

The present thesis is based on the following original articles, which are referred to in the text by their roman numerals:

I Eklund, D., Schumann, M., Kraemer, W.J., Izquierdo, M., Taipale, R.S. & Häkkinen, K. (2016). Acute endocrine and force responses and long-term adaptations to same-session combined strength and endurance training in women. Journal of Strength and Conditioning Research 30(1):164-75.

II Eklund, D., Pulverenti, T., Bankers, S., Avela, J., Newton, RU., Schumann, M. & Häkkinen, K. (2015). Neuromuscular adaptations to different modes of combined strength and endurance training. International Journal of Sports Medicine 36(2):120-9.

III Eklund, D., Häkkinen, A., Laukkanen, J.A., Balandzic, M., Nyman, K. & Häkkinen, K. (2016). Fitness, body composition and blood lipids following three concurrent strength and endurance training modes. Applied Physiology, Nutrition, Metabolism 41(7): 767-74.

IV Eklund, D., Liukkonen, J., Vidal Diaz, F., Nyman, K. Häkkinen, K., Häkkinen, A. 2017. Wellbeing, self-esteem and time management following combined strength and endurance training. Submitted for publication.

Additionally, some previously unpublished results are included in this thesis.

CONTENTS

1 INTRODUCTION

In the early stages of human history, being able to lift heavy objects and travel long distances by foot were prerequisites for survival. While these capabilites were developed through necessity in everyday life, the modern human aims to achieve similar attributes of physical performance through pasttime activities e.g. by participating in guided exercise classes or by using modern equipment at gyms. While survival no longer depends on these traits, regular adherence to physical exercise is associated with better health and functional capacity (Farrell et al. 1998; Landi et al. 2014). Thus, exercise has become the remedy to the current sedentary lifestyle that is pestering the globe and negatively affecting its population.

The benefits and adaptations brought about by exercise are specific to the type of activity performed. While improvements in cardiorespiratory fitness and reduced premature mortality can be achieved through practicing endurance exercise (Murias, Kowalchuk & Paterson 2010; Farrell et al. 1998; Kodama et al. 2009), performing strength training results in increased muscle size and strength which subsequently sustains functional capacity throughout life (Häkkinen et al. 2001; Landi et al. 2014). Furthermore, regular adherence to exercise can improve self-esteem, perceived health-related quality of life and mood as well as alleviate depressive symptoms (Atlantis et al. 2004; White, Kendrick & Yardley 2009). Therefore, devoting time to a variety of exercise modes can be considered to be beneficial in most aspects of life.

However, simultaneously adhering to both strength and endurance exercise programs does not come without some concerns. As early research by Robert Hickson (1980) demonstrated, adverse effects on strength performance were quickly evident, if the overall volume and frequency of the training regimens were high. This interference in strength adaptations can be circumvented if adhering to more moderate amounts of exercise, which allows for simultaneous development of both muscle size and strength as well as aerobic capacity to similar extents as with single-mode strength or endurance training (Mikkola et al. 2012; Häkkinen et al. 2003).

Despite a large amount of research conducted on combined vs. single-mode training, knowledge on how different manners of combining strength and endurance training relate to each other is not as well established. Although combined training has been examined with strength and endurance performed on separate days (e.g. Dudley & Djamil 1985), on same days with >2h of recovery between modes (e.g. Hickson 1980), in the same session (e.g. Nelson et al. 1990), in the same session with different exercise orders (e.g. Collins & Snow 1993) in alternating shorter bouts integrated into the same session (Davis et al. 2008; Di Blasio et al. 2012) and with varying frequencies (Fisher et al. 2013) scarce documentation is available on how two or more of these modes, with equal training volumes, compare to each others in terms of measurable adaptations.

When similar volumes of training are maintained, training on different days requires a higher frequency of individual training occasions than if training would consistently be conducted as “double sessions”, with endurance and strength exercises performed consecutively in the same training session. These ways reveal distinctly different patterns of recovery: while training on different days allows for less recovery between the individual training sessions, same-session training never provides recovery before the exercise mode that is performed second in the training session, thus also raising concerns about the importance of the intra-session exercise order.

Therefore, the present dissertation aimed to investigate adaptations in neuromuscular and cardiorespiratory performance, elements of metabolic health as well as subjective perceptions of wellbeing following volume-equated different-day and and same-session combined strength and endurance training with different exercise orders in previously untrained, healthy men and women.

2 REVIEW OF THE LITERATURE

Regular adherence to physical activity provides a foundation for physical wellbeing and is a prerequisite for improving exercise performance and precursors of health. While strength (S) and endurance (E) training both provide beneficial adaptations specific to the training mode, adhering to both training modes concurrently is potentially more efficient than committing to only either one (Sillanpää et al. 2008). However, S and E result in distinctly different adaptations both in neuromuscular control (Vila-Chã et al. 2012), cardiorespiratory function (Bell et al. 2000) and muscle morphology (Farup et al. 2012), making simultaneous adherence to both modes susceptible to compromised adaptations (Hickson 1980).

Regardless of the specific exercise mode, all human locomotion relies on the function of the neuromuscular system. The commands mediated by the central nervous system (brain and spinal cord) are relayed to the peripheral nervous system, where the peripheral nerves transfer information to the muscles as well as to and from the central nervous system (McArdle, Katch & Katch 2001, p. 384). The smallest functioning unit of the neuromuscular system is the motor unit, which consists of an α-motoneuron and all the muscle fibers it innervates (Buchthal, Erminio & Rosenfalck 1959; Staudenmann et al. 2010). Muscle fibers connect to the motoneurons at the neuromuscular junction, where the terminal of the axon of the nerve cell reaches the fiber. An action potential traveling from the soma of the motoneuron and via the branches depolarizes the muscle membrane causing the motor unit to contract (Staudenmann et al. 2010), ultimately resulting in muscle contractions and human movement. The action potentials can be quantified as electromyogram recordings (EMG) and used to describe muscle activity (Folland & Williams 2007).

Myosin heavy-chain (MHC) content and metabolic properties of muscle tissue allow classification of muscles into type I (slow) and type II (fast) fiber types, with the MHC heavily influencing the contractile properties of the muscle (Pette & Staron 1997; Westerblad, Bruton & Katz 2010). While strength training has been shown to result in increased cross-sectional area of both type I and II muscle fibers (MacDougall et al. 1980), endurance training may leave the fiber size unchanged (Carter et al. 2001). Type I fibers typically produce less force and do not fatigue as fast as type II fibers. Correspondingly, Type II fibers consume energy (adenosine triphosphate, ATP) more rapidly than type I fibers. (Westerblad, Bruton & Katz 2010; Pette & Staron 1997).

Energy for muscle contractions is provided through different energy systems, depending on the type and duration of a given task. The pooled quantity of cell ATP and cell phosphocreatine (PCr) is utilized in maximal, short-duration (8-10 sec) activities, while prolonged work requires the aerobic system to oxidize ingested food into ATP. At light and moderate intensities, ATP can be generated through degradation of glycogen by the glycolytic system with the aid of oxygen (aerobic glycolysis). Vigorous exercise increases the energy needs beyond the supply of oxygen (anaerobic glycolysis) and results in the accumulation of lactate and hydrogen ions (Gastin 2001). While lactate can be used for energy turnover, the accumulation of hydrogen ions causes acidity and is one of the mechanisms that initiate the onset of fatigue (Gladden 2000; van Hall 2010).

Exercise-induced fatigue, defined as a reduced ability to exert or maintain muscle force or power is task-dependent and can occur due to both metabolic and neural causes (Booth & Thomason 1991; Bigland-Ritchie & Woods 1984). Fatigue is often described as being peripheral (occurring at or distal of the neuromuscular junction) or central (proximally to the neuromuscular junction) (Garner, Hicks & McComas 1989; Taylor & Gandevia 2008). Central fatigue is caused by a loss of motoneuronal output while peripheral fatigue is manifested e.g. as impairments in muscle contractility due to pH-lowering metabolic byproducts (Gandevia 2001).

The removal of metabolic byproducts is regulated by the interplay of the cardiovascular (the heart and blood vessels) and the ventilatory systems (the lungs and the respiratory tract). Together the systems are responsible for regulating the exchange of oxygen and carbon dioxide between an individual and the environment as well as providing the active muscle tissue with oxygen and nutrients (McArdle, Katch & Katch 2001, p. 253, 306). The highest rate of oxygen uptake and utilization during exercise is termed maximum oxygen uptake (VO_{2max}) and is considered to reflect the capacity of the cardiovascular system to deliver oxygen to the working muscles (Millet, Vleck & Bentley 2009; Hawkins et al. 2007; Bassett & Howley 2000). Long-term endurance training produces considerable increases in VO_{2max}, while little to no changes are typically observed after resistance training (Hickson 1980; Hurley et al. 1984).

The anabolic (building) and catabolic (breaking down) processes in the human body are regulated by the endocrine system, which consequently has a major role in the physiological responses and adaptations to exercise. The endocrine system aids the body in adapting to the changing conditions and disrupted homeostasis that is caused by stress (i.e. exercise), and is regulated through host organs (glands), chemical messengers (hormones) and targets or receptor organs (Kraemer & Ratamess 2005; Consitt, Copeland & Tremblay 2002; Guyton & Hall 2000, p. 836). Reactions are initiated through secretion of hormones into the bloodstream by host glands, after which they bind with specific target receptors (Guyton & Hall 2000, p. 836; McArdle, Katch & Katch 2001, p. 410). Hormonal release can occur either through a constitutive release (immediately upon synthetization) or regulated release (brief storage in the host gland) (Kelly 1985). After a hormone binds to a receptor, the receptor is temporarily unable to provide a binding site for any other chemical compound (Kraemer & Rogol 2005, p. 18). The immediate hormonal responses to exercise create the metabolic environment involved in e.g. tissue remodeling (Walker et al. 2015) and are affected by intensity, volume, duration, training status of the individual as well as the hormonal needs to maintain homeostasis (Viru 1992; Häkkinen & Pakarinen 1993; Viru et al. 1996).

2.1 Strength training: Acute responses and long-term adaptations in men and women

Muscle force is mainly determined by the number of active motor units, their firing rate, the size of the motor units and the muscle fibers (Milner-Brown & Stein 1975; Staudenmann et al. 2010; Folland & Williams 2007). Engaging in resistance training leads in the long term to several neurological and morphological changes, such as changes in fiber size and voluntary activation and ultimately increased muscle size and strength (Folland & Williams 2007), depending on the type of loading the muscle is exposed to (Campos et al. 2002). On the other hand, resistance training does not lead to major adaptations in the cardiovascular system (Fleck 1988).

The physiological demands of a strength loading can be shifted towards dominatingly metabolic or neural demands, depending on the acute strength loading variables: loadings of different types (Häkkinen, Kauhanen & Komi 1988; Campos et al. 2002), volumes (Häkkinen & Pakarinen 1993) as well as intensities and rest periods (McCaulley et al. 2009) result in different acute training responses as well as training outcomes (Table 1). The strength training intensities are commonly expressed as a percentage of the load an individual can successfully lift only once (one-repetition maximum, 1 RM).

TABLE 1 Loading intensities, quantity of repetitions and duration of inter-set rest define the primary demands and outcomes of a given strength loading. (Kraemer & Häkkinen 2002, p. 50-51; Kraemer & Ratamess 2004).

Training outcome	**Intensity (% of 1 RM)**	**Repetitions per set**	**Inter-set rest (s)**	
Power	30-60%	8-10	180	*Neural*
Maximal strength	80-100%	1-6	180	↓
Hypertrophy	70-80%	6-12	60-90	
Strength endurance	50-70%	15+	60	*Metabolic*

2.1.1 Neuromuscular fatigue and recovery following strength loadings

Strength loadings can cause drastic acute decreases in maximal force production and force-time characteristics of the working muscles (Häkkinen 1993). The magnitude of strength loading-induced fatigue is dependent on the acute programming variables both in terms of the magnitude as well as the underlying physiological mechanisms (Ahtiainen et al. 2004; Linnamo, Häkkinen & Komi 1998; McCaulley et al. 2009). While predominantly metabolic (hypertrophic) loadings result in greater impairments in maximal force production than neurally taxing (maximal) loadings, power loading protocols tend to be the least detrimental (Linnamo, Häkkinen & Komi 1998; McCaulley et al. 2009). Similarly, the highest blood lactate concentrations are typically noted immediately following a metabolically demanding loading, with submaximal and power loadings resulting in smaller post-exercise lactate concentrations (Linnamo et al. 2005; Häkkinen & Pakarinen 1993).

Any decrements seen in maximal force production following submaximal and power protocols typically recover within the first hours following cessation of exercise (McCaulley et al. 2009). However, 48-72 hours may be required for full recovery of maximal force following heavy hypertrophy and maximal type loadings (Häkkinen 1994; Ahtiainen et al. 2004; Linnamo, Häkkinen & Komi 1998).

When an individual regularly adheres to a training program, their ability to fatigue themselves increases at a given relative intensity, as does the capacity to accumulate a greater amount of metabolites before task-failure. However, despite that the magnitude of acute exercise-induced loss in maximal isometric force tends to be larger after prolonged training, the recovery of force may be more rapid (Izquierdo et al. 2009; Ahtiainen et al. 2004).

The initial phase of a rapid muscle contraction can be quantified as rate of force development (RFD) or a force produced within a certain time interval, e.g. 500 ms (McCaulley et al. 2009; Schumann et al. 2013). The highly metabolic, hypertrophic-type loadings tend to cause the biggest impairment in rapid force production variables. Maximal loadings are also potent in causing impairments, but power protocols likely affecting the rapid force production the least. (Linnamo, Häkkinen & Komi 1998; McCaulley et al. 2009). Despite metabolically strenuous strength exercise causing the largest decreases, recovery to pre-exercise values may be faster following a hypertrophy protocol than a maximal one. This could be due to maximal protocols having a larger disruptive effect on the neuromuscular system and causing central fatigue, while the origin of fatigue following a hypertrophic protocol is likely predominately peripheral. (McCaulley et al. 2009).

While the magnitude of fatigue in relation to the different types of strength loadings is similar in men and women, some evidence suggests that women are unable to fatigue themselves to the same relative extent as men. Consequently, women may also recover faster than men from a given strength loading (Linnamo, Häkkinen & Komi 1998; Häkkinen 1994). This difference is likely due to differences in peripheral rather than central mechanisms (Hunter et al. 2006) and has been attributed to men having a higher energy (Wüst et al. 2008).

2.1.2 Neuromuscular contributions to strength gains during strength training

The increase in maximal strength that is typically achieved with strength training is a result of both neural and morphological training-induced changes (Folland & Williams 2007). During the early stages of training the main contribution to increased muscle strength appears to come from neurological adaptations, with the morphological factors dominating later on (Moritani & deVries 1979). The neurological contributions to increased strength are likely a combination of increased descending neural drive and consequently increased motoneuron excitability (Vila-Chã et al. 2012), increased voluntary muscle activation (Knight & Kamen 2001) and increased agonist muscle activity (Häkkinen & Komi 1983). Changes in muscle morphology include increases in muscle cross-sectional area (Narici et al. 1996) and possibly changes in fiber subtype distribution (Carroll et al. 1998). When resistance training extends beyond 2-3 weeks and is performed in line with training prescriptions of 70-85% 1 RM loads and sets of 8-12 repetitions, muscle hypertrophy has been shown to occur in both men and women (Kraemer et al. 2004; Kraemer & Ratamess 2004, Kramer et al. 1997). A high amount of completed work (i.e. high volume) is considered to be preferential for maximizing gains in muscle size (Marx et al. 2001; Kramer et al. 1997).

The specific outcome of a strength training program both in terms of changes in muscle size and strength depends on the manipulation of the acute resistance training variables: number of repetitions and sets, intensity relative to 1 RM, and duration of inter-set rest (Kraemer & Ratamess 2004; Campos et al. 2002). As shown in FIGURE 1, an 8-week training program of low, intermediate or high repetitions resulted in adaptations specific to the given protocol. While the low repetition, high load protocol resulted in the largest gain in 1 RM, a high-repetition protocol was consequently the most efficient in improving the ability to perform as many repetitions as possible (Campos et al. 2002). Similar results displaying training specificity have been found in female populations (Kraemer et al. 2004). Furthermore, in order for an individual to increase muscular power or RFD in a given exercise, muscle actions during training need to be performed as rapidly as possible, so that consequently a given amount of work is performed in a shorter amount of time (Kraemer & Ratamess 2004).

It needs to be acknowledged that untrained individuals may initially experience gains in strength without any specific training program proving to be more advantageous than another (Juárez, González-Ravé & Navarro 2009). This rapid, initial improvement is thought to occur due to a "learning effect" in the nervous system consisting of increased intermuscular coordination, e.g. decreased antagonist and increased synergist activation as well as cross-education between limbs (Rutherford & Jones 1986; Folland & Williams 2007; Shima et al. 2002; Moritani & deVries 1979). In order to avoid stagnation of both the neural and morphological adaptations, progressively increasing loads need to be utilized in the training sessions. This way, the individual can further improve maximal muscle fiber recruitment hypertrophy and strength (Häkkinen, Alen & Komi 1985; Kraemer & Ratamess 2004).

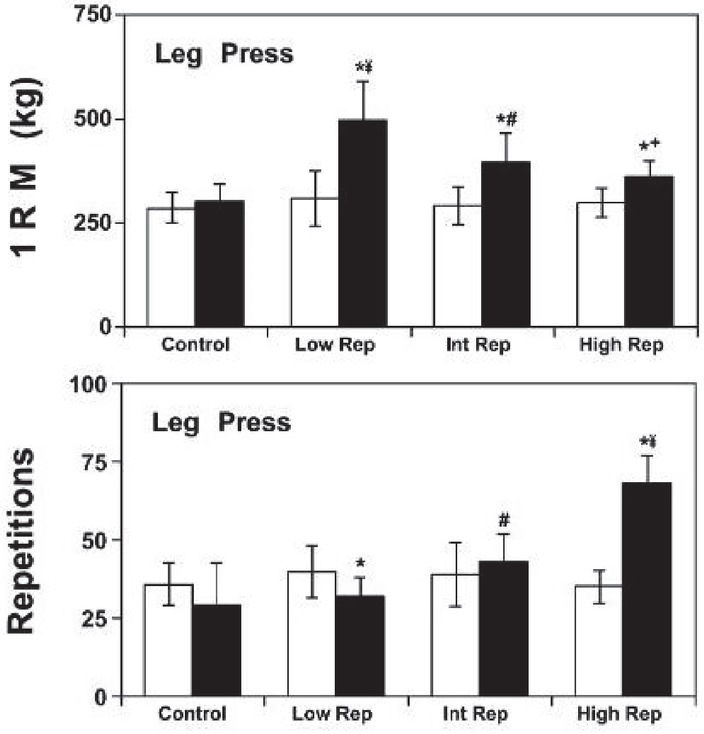

FIGURE 1 Performance in leg press 1 RM (above) and maximal repetitions (below) before (white bars) and after (black bars) 8 weeks of low, intermediate and high-repetition resistance training protocols. Modified from Campos et al. 2002.

2.1.3 Endocrine and metabolic responses and adaptations to strength loading and prolonged training

Both a single strength loading as well as prolonged strength training have the potential to influence the observed amounts of circulating hormones both in men and women (Consitt, Copeland & Tremblay 2002; Kraemer & Ratamess 2005). It is generally thought that the primary anabolic hormones testosterone (T) and growth hormone (GH) are involved in muscle tissue growth and remodeling while cortisol (C), a catabolic glucocorticoid, increases protein degradation (Kraemer 1988; Kraemer & Ratamess 2005). Significant acute elevations of these hormones are typically observed after metabolically demanding resistance exercise, with high-intensity (maximal and hypertrophic) exercise resulting in greater elevations than moderate-intensity (power and sub-maximal) protocols (Häkkinen & Pakarinen 1993; Kraemer et al. 1991; Raastad, Bjøro & Hallén 2000; Linnamo et al. 2005) (FIGURE 2). These exercise-induced elevations result from either reduced hepatic clearance (Cadoux-Hudson, Few & Imms 1985), receptor content regulation (Vingren et al. 2009), increased secretion or plasma volume reductions (Kraemer & Ratamess 2005). The magnitude of the responses are mostly dependent on the amount of activated muscle mass, and the number of sets and repetitions performed (Ahtiainen et al. 2004; Kraemer et al. 1999a; Linnamo et al. 2005; Vanhelder, Radomski & Goode 1984; Vanhelder et al. 1985) and less related to total volume (McCaulley et al. 2009).

The acute anabolic responses have in some studies with male populations been correlated to long-term physiological adaptations such as gains in muscle strength and hypertrophy (Hansen et al. 2001; McCall et al. 1999; Spiering et al. 2008; Walker et al. 2015), while other investigations have failed to distinguish this phenomenon (West et al. 2010). Reports regarding long-term adaptations in resting hormonal concentrations are inconsistent and mostly of insignificant magnitudes, but may be related to the training stimulus that the individual is exposed to (Kraemer & Ratamess 2005; Alen et al. 1988; Häkkinen, Pakarinen & Kallinen 1992).

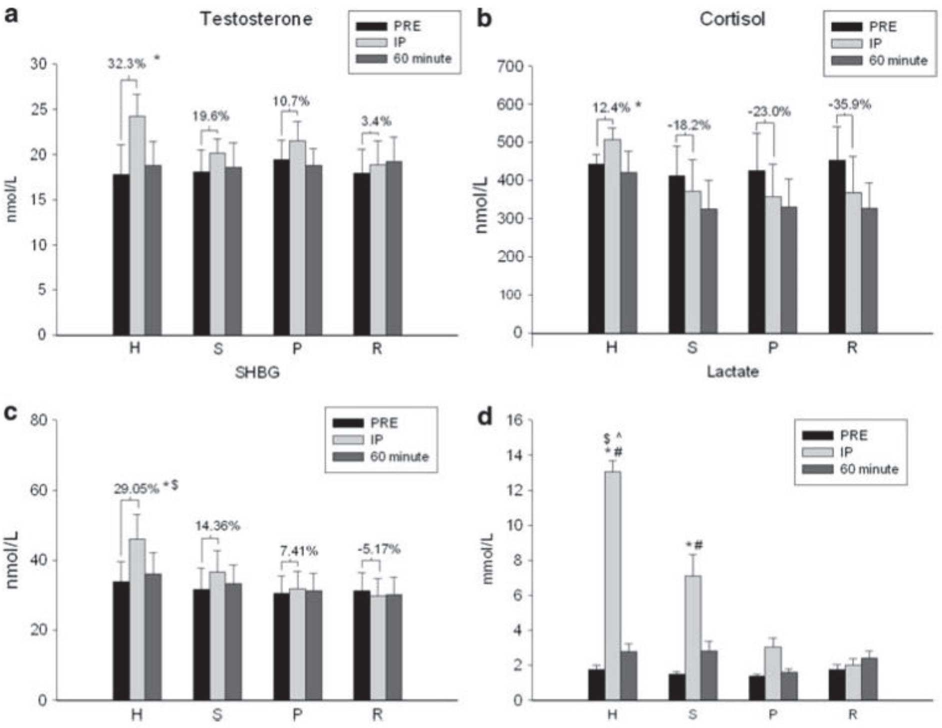

FIGURE 2 Changes in serum total testosterone (a), cortisol (b), steroid hormone binding globulin (SHBG) (c) and whole blood lactate (d) concentrations at rest (black bars), immediately post exercise (light grey bars), and at an 1 h following cessation of exercise (dark grey bars) for hypertrophy (H), strength (S), power (P) resistance exercise protocols as well as rest rest (R) in men. #Significant difference from pre value; *significant difference from R protocol; $signifcant difference from P protocol; ^significant ($p < 0.05$) difference from S protocol. Modified from McCaulley et al. 2009.

2.1.3.1 Acute hormone and lactate responses to strength loadings

Acute elevations of testosterone in response to metabolically demanding resistance exercise have commonly been observed in male populations (Linnamo et al. 2005; McCaulley et al. 2009) with trained individuals possibly displaying greater magnitudes than untrained counterparts (Tremblay, Copeland & Van Helder 2004). This phenomenon was well highlighted in a study by McCaulley et. al (2009) through comparing three volume-equated protocols of squat loadings: hypertrophy (4x10 repetitions at 75% 1RM), strength (11x3 repetitions at 90% 1RM) and power (8x6 repetitions of jump squats at 0% 1RM). Elevated testosterone concentrations were noted only after the hypertrophy protocol, which also elicited the greatest blood lactate response. Similarly, Häkkinen and Pakarinen (1993) reported elevated testosterone as well as significantly elevated lactate concentrations after 10x10 repetitions at 70%

1 RM in comparison to a 20x1RM protocol. This interaction between T and lactate could indicate that resistance-exercise induced elevations in circulating testosterone concentrations may be lactate-stimulated, possibly through mechanisms related to intracellular cyclic adenosine monophosphate (cAMP) (Lu et al. 1997).

In contrast to men, women demonstrate only minor, if any, elevations in T following heavy resistance training (FIGURE 3) (Copeland, Consitt & Tremblay 2002; Häkkinen & Pakarinen 1995; Linnamo et al. 2005). While some studies have reported acute elevations in young women (Nindl et al. 2001) the majority of studies describe a lack of change in T following resistance exercise (Häkkinen & Pakarinen 1995; Kraemer et al. 1991; Kraemer et al. 1993; Kraemer et al. 1998). As women lack testosterone-synthesizing Leydig cells and mainly rely on the peripheral conversion of androstenedione and dehydroepiandrosterone (DHEA) to T (Enea & Boisseau 2011; Consitt, Copeland & Tremblay 2002), it has been suggested that other endogenous anabolic hormone mechanisms may compensate for scarce T in order to meet the anabolic needs of resistance exercise sessions (Kraemer et al. 1991).

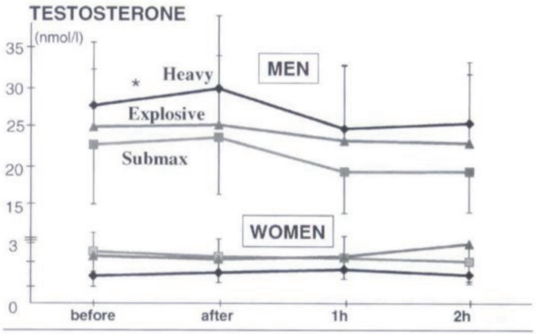

FIGURE 3 Serum testosterone concentrations before, immediately after as well as 1 and 2 hours after cessation of different strength loading protocols. Modified from Linnamo et al. 2005.

Despite gender-related differences in T responses, women display significant acute elevations in GH and C similarly to men in response to heavy strength exercise protocols (Consitt, Copeland & Tremblay 2002; Linnamo et al. 2005; Kraemer & Ratamess 2005; Kraemer et al. 1993; Smilios et al. 2003; Mulligan et al. 1996). High intensity protocols (Vanhelder, Radomski & Goode 1984; Kanaley et al. 1992) with short rest periods (Kraemer et al. 1991) and exercises involving large amounts of muscle mass (Hansen et al. 2001) seem to produce the highest responses. Furthermore, multiple- vs. single-set protocols appear to result in higher elevations of serum GH especially in women (Mulligan et al. 1996), and higher total volumes may also prompt greater magnitudes of acute GH concentrations (Smilios et al. 2003).

Similarly to T, correlations between serum GH and blood lactate concentrations in response to heavy resistance exercise protocols have been reported by several studies (Häkkinen & Pakarinen 1993). This has been proposed to be due to hydrogen ion accumulation influencing GH release either through affecting peripheral chemoreceptors or hypothalamic function, although the exact mechanism is unclear (Gordon et al. 1994; Sutton, Jones & Toews 1976). Strong correlations between C and lactate have also been frequently observed (Häkkinen & Pakarinen 1993; Kraemer et al. 1989).

2.1.3.2 Chronic changes in resting hormone levels

While the acute elevations of anabolic and catabolic hormones are involved in creating the environment for tissue remodeling, resting levels are considered to reflect the current state of the muscle and homeostasis or long-term training stress (Kraemer & Ratamess 2005). It has been suggested that untrained individuals may experience changes in resting-level hormone concentrations in the early phases of strength training, which possibly mediate e.g. nervous system adaptations in both men and women (Kraemer et al. 1998).

While resting levels of GH appear to remain unaffected in both men and women across several age ranges (Häkkinen et al. 2000; Kraemer et al. 1999b; Marx et al. 2001) and even in highly trained populations (Ahtiainen et al. 2003; Häkkinen et al. 1988), data regarding long-term changes in T and C is less conclusive. In men both decreases (Alen et al. 1988) and increases (Kraemer et al. 1999b) in T have been described as a result of training. In women, concentrations have been reported to remain unchanged (Häkkinen et al. 1990) or increased (Marx et al. 2001), but also to be of similar concentrations in athletic and untrained populations (Stoessel et al. 1991). Furthermore, basal levels of T have in women been suggested to correlate with strength-training induced gains in strength development and muscle CSA (Häkkinen, Pakarinen & Kallinen 1992; Häkkinen et al. 2000). It is possible that changes in training volume may shift basal concentrations of T down when training is intensive and close to overreaching, and subsequently up back to normal levels when high-volume training is reduced (Ahtiainen et al. 2003; Raastad et al. 2001). However, it needs to be kept in mind that seasonal variations could mask effects of long-term changes, as the annual testosterone cycle displays a zenith in October-November and a nadir in June (van Anders, Hampson & Watson 2006; Svartberg et al. 2003; Stanton, Mullette-Gillman & Huettel 2011).

Resting levels of cortisol have been considered to reflect general physiological stress with possible changes regulating tissue homeostasis and protein metabolism (Kraemer & Ratamess 2005). Much like with T, changes in C following training have been reported to be reduced in untrained men (Kraemer et al. 1998; Alen et al. 1988; Häkkinen et al. 1985) or unchanged (Ahtiainen et al. 2003; Häkkinen et al. 2000). Similarly, in women both unchanged (Häkkinen, Pakarinen & Kallinen 1992) and decreased (Kraemer et al. 1998) levels of C have been reported following strength training, with decreases possibly relating to larger training volumes (Marx et al. 2001). The T/C-ratio has been used as a simplified, indirect indication of an anabolic milieu (Fry & Kraemer 1997; Häkkinen 1989), but findings regarding its relation to performance are unclear (Alen et al. 1988; Ahtiainen et al. 2003; Häkkinen et al. 1985).

2.2 Endurance training: Acute responses and long-term adaptations in men and women

Endurance performance can be defined as the capacity to sustain a given velocity for a given time and can be quantified e.g. as a time trial and, in the case of cycling, peak power output (W_{max}) (Jones & Carter 2000; Bassett & Howley 2000). The changes in cardiorespiratory fitness are most often measured as changes in maximum oxygen uptake (VO_{2max}) (Bassett & Howley 2000), with an increased whole body VO_{2max} considered to be a result of endurance exercise-induced increased mitochondrial density and oxidative capacity of the trained muscles (Holloszy 1967). Thus, long-term endurance training has the potential to improve the metabolic profile of the specific muscle groups as well as facilitate O_2 transport and VO_{2max} (Millet, Vleck & Bentley 2009). The relationship between VO_2 and heart rate tends to be linear especially at low-to-moderate intensities (Lewis et al. 1983; McArdle, Katch & Katch 2001, p.242), making heart-rate-based training prescription a worthwhile practice in combination with the determination of aerobic and anaerobic thresholds (Bassett & Howley 2000; Hills, Byrne & Ramage 1998; Aunola & Rusko 1986).

The cardiorespiratory parameters as well as metabolic responses are influenced by the mode of endurance exercise, making both acute responses and long-term adaptations mode-specific (Millet & Lepers 2004). Cycling exercise consists mainly of concentric muscle work and does possibly not induce as much central fatigue or muscle damage as running (Millet & Lepers 2004; Lepers et al. 2002). It has consequently been suggested that acute exercise-induced loss of force of the knee extensor muscles may be of a greater magnitude following a set of sprints performed by cycling in comparison to running (Rampinini et al. 2016). As the endurance training in the present thesis consisted of lower body cycling exercise, it also remains the main focus of this section of the literature overview.

2.2.1 Cardiorespiratory responses and training adaptations to endurance exercise

Due to the duration of endurance exercise bouts, the energy is supplied by large through aerobic pathways, which is reflected as an increased oxygen uptake (VO_2) during exercise (Gastin 2001; Børsheim & Bahr 2003). During cycling, both ventilation and heart rate increase together with the VO_2 from the 10th minute of constant pace, moderate intensity cycling (Hagan, Weis & Raven 1992), and from the 5th minute of higher intensity cycling (Hagberg, Mullin & Nagle 1978). Following exercise, VO_2 does not return to baseline instantly, but may remain elevated for hours after cessation of exercise (Børsheim & Bahr 2003; Gaesser & Brooks 1984). This excess post-exercise oxygen consumption (EPOC) is dependent on both the exercise intensity and duration (Bahr et al. 1987; Bahr & Sejersted 1991; Bahr, Grønnerød & Sejersted 1992) and could also be larger in untrained individuals (Frey, Byrnes & Mazzeo 1993; Short & Sedlock 1997).

Previously untrained subjects can increase aerobic fitness with a training frequency of 2 d·wk^{-1}, but well-trained individuals may require a minimum of 3 d·wk^{-1} to experience further improvements (Wenger & Bell 1986). In addition to the training frequency, the long-term adaptations also depend on exercise intensity as well as the duration of the exercise bouts. (Wenger & Bell 1986; Jones & Carter 2000). Increases in VO_{2max} require that work is frequently completed at intensities close to VO_{2max}, while a frequency below 2 d·wk^{-1} at lower intensities than 40-50% of VO_{2max} for less than 10 min at a time may not be sufficient to elicit any long term adaptations in healthy adults (Wenger & Bell 1986; ACSM Position stand 1998). However, frequent, prolonged endurance training at low intensity could improve metabolic variables which are considered to be coronary heart disease (CHD) risk factors. This is suspected to occur through mechanisms which are unlikely to be associated to training-related changes in cardiorespiratory fitness. (Despres & Lamarche 1994). Typical increases in VO_{2max} following short term (3-8 weeks) endurance training programs remain around 10% (Murias, Kowalchuk & Paterson 2010; Hautala et al. 2003). Larger increases (30%) have also been observed after just 12 weeks of training, which may be related to larger amounts of high-intensity work (Murias, Kowalchuk & Paterson 2010).

2.2.2 Endurance cycling exercise-induced neuromuscular responses and adaptations

The fatigue induced by cycling endurance exercise is likely to be specific to the working muscles, with e.g. no effect noted on upper body performance despite fatigue-related acute decreases in lower body force (Elmer et al. 2013). The degree of fatigue is likely to be dependent on the workload (Theurel & Lepers 2008), with the magnitude of peripheral and central fatigue likely exacerbated with exercise intensity and duration, respectively (Thomas et al. 2016). On the contrary, pedaling cadence may not greatly influence the outcome as observed by Sarre et al. (2013) through comparing fixed vs freely chosen cadences (Sarre et al. 2003). Importantly, cycling performed at a constant workload (corresponding to ca 50% VO_{2max}) appears to result in less acute force loss and decrease in voluntary activation in comparison to cycling exercise performed at highly varying resistances (corresponding to 100-200% VO_{2max}) (Theurel & Lepers 2008) (FIGURE 4). Similarly, repeated maximal sprint efforts resulting in considerable voluntary activation deficits (Bentley et al. 1998). However, EMG recordings of the key muscles involved in cycling have been shown to not greatly differ between a freely chosen vs. a 20% faster cadence (Sarre et al. 2003). Nonetheless, sustained cycling of short to moderate duration could result in increased intracortical inhibition despite no concomitant increase in EMG (Sidhu et al. 2013). Fatigue-induced force loss following constant-load cycling of 30-60 min at 50-55% of peak power output has been found to range between 7 and 11 % (Theurel & Lepers 2008; Lepers et al. 2002) and between 9 and 17 % in higher intensity cycling bouts in endurance trained cyclists (Goodall et al. 2015; Goodall et al. 2012).

Alterations in the metabolic milieu of locomotor muscles may also in part mediate motor control. A reduced pH may affect the motor unit firing rate in an inhibitory manner, possibly as a regulatory response to mediate the level of peripheral locomotor muscle fatigue. (Amann 2011). Thus, afferent feedback following metabolically strenuous exercise may limit the further development of peripheral fatigue through inhibiting the central motor drive (Amann et al. 2009; Amann et al. 2013). In intermittent cycling exercise, peripheral fatigue develops early on, with central fatigue following later in the exercise protocol (Monks et al. 2016). When submaximal exercise is of long duration (>2 h), fatigue has been found to be of both central and peripheral origin in men but mostly central in women. This difference is probably more related to differences in metabolism rather than neural characteristics (Glace, Kremenic & McHugh 2013), or possibly a gender-related difference located within a given muscle. (Hunter et al. 2006). Furthermore, women may have a lower capacity for sustaining effort at near-maximal power output in comparison to men, but recovery patterns following intermittent exercise appear to be similar in both genders (Billaut, Giacomoni & Falgairette 2003). During extremely high intensity or all-out cycling exercise, men may be using greater anaerobic power reserves and thus produce higher peak lactate concentrations than women despite similar VO_2 utilization and heart rate values (Panissa et al. 2016). Women may also accumulate lactate at a slower rate than men during incremental cycling exercise to exhaustion (Sargent & Scroop 2007). Consequently, women may not fatigue to the same extent as men during this type of exercise (Murias, Kowalchuk & Paterson 2010).

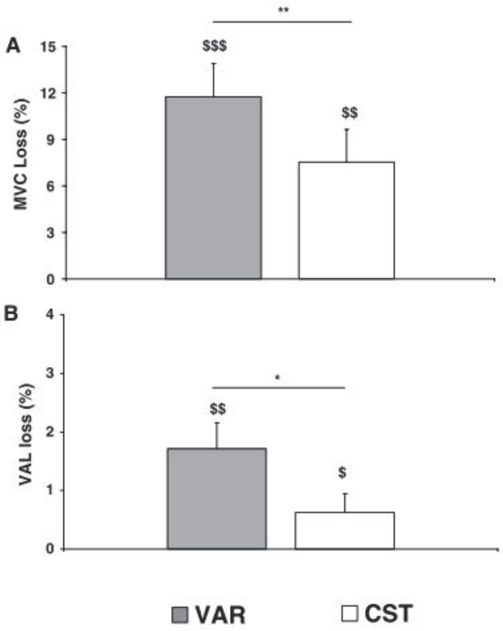

FIGURE 4 Reductions in maximal voluntary contraction (MVC) torque (A) and voluntary activation level (VAL) (B) immediately after constant power output condition (CST) versus variable power output condition (VAR) for each subject. Significant loss: $P < 0.05, $$P < 0.01, $$$P < 0.001; VAR > CST: *P < 0.05, **P <0.01 (Modified from Theurel & Leperes 2008).

In contrast to strength training, long term endurance training does not induce changes in voluntary activation percentage or EMG of the knee extensor muscles in sedentary or previously untrained subjects (Zghal et al. 2014; Knight & Kamen 2001). Furthermore, even though endurance training may increase motor unit conduction velocity, no changes are typically observed in discharge rate variability at maximal voluntary muscle effort after an endurance training intervention. On the contrary, the discharge rate at lower contraction levels may be reduced (Vila-Chã, Falla & Farina 2010; Vila-Chã & Falla 2016). Endurance training does also not appear to significantly affect muscle fiber size, area or type I/II distribution in either males or females, at least following running training interventions (Carter et al. 2001).

Peak power output (W_{max}) is commonly used as a measure of cycling performance in both untrained and athletic populations (Bentley et al. 1998; Hawley & Noakes 1992; Faria, Parker & Faria 2005; Mikkola et al. 2012; Bishop, Jenkins & Mackinnon 1998), and is commonly found to increase following cycling exercise training interventions. Murias et al. (2010) reported a 16% increase in W_{max} following 12 weeks while Mikkola et al. (2012) reported an 11% increase after 21 weeks of training in young, previously untrained men. Similarly, middle aged and elderly women displayed a 16% increase in W_{max} following 21 weeks of cycling endurance training (Sillanpää et al. 2010).

Inconsistencies in the magnitude of adaptations over various time periods could be attributed to the specifics of each training program, e.g. to differing amounts of high intensity training as well as programmed training progression.

2.2.3 Endocrine aspects of endurance exercise sessions and prolonged training

The magnitude of the acute hormonal responses to endurance exercise are reflections of exercise intensity, type (continuous vs. intermittent) and, to some extent, exercise duration (Kuoppasalmi et al. 1980; Gray, Telford & Weidemann 1993; Tremblay, Copeland & Van Helder 2005; Vuorimaa et al. 2008; Wilkerson, Horvath & Gutin 1980). Intense, intermittent anaerobic exercise typically results in greater acute T, C and GH responses in comparison to a low-intensity aerobic loading (VanBruggen et al. 2011; Kuoppasalmi et al. 1980; Gray, Telford & Weidemann 1993). Although intensity is considered a more important factor than duration in terms of influencing the magnitude of acute hormonal responses, it should be noted that at low exercise intensities T and C may require a more prolonged exercise session in order for significant elevations to occur (Tremblay, Copeland & Van Helder 2005). However, as T has been found to decline following ultra-duration endurance exercise despite increasing in response to shorter bouts, there may be a duration threshold after which the observed hormone concentrations start to decline (Guglielmini, Paolini & Conconi 1984; Tremblay, Copeland & Van Helder 2005). On the contrary, GH appears especially sensitive to exercise, as even short-duration sub-maximal loadings can elicit significant acute elevations from baseline (Bouassida et al. 2009).

The research on the effect of prolonged endurance training on resting hormone concentrations has to date not provided conclusive answers. It has been frequently demonstrated that endurance trained men display lower levels of basal testosterone than their untrained counterparts (Wheeler et al. 1984; Hackney 1989; Hackney, Fahrner & Gulledge 1998). Interestingly, previously untrained men have been reported to display a slight increase in T with 5 weeks of endurance training (Grandys et al. 2009), but a decrease when training is extended beyond 12 weeks (Bell et al. 2000). This could suggest that untrained individuals may experience an initial increase in T, followed by decreases when training is prolonged. In women, both reductions and no alterations of basal T have been observed (Keizer et al. 1987; Keizer et al. 1989). Keizer et al (1987) reported decreased basal T after an endurance training period, but only during the luteal phase of the menstrual cycle (Keizer et al. 1987). The menstrual cycle phase-specific fluctuations could be related to the training-induced changes in DHEA, DHEA-s and ACTH, which play a crucial role in T synthetization (Enea & Boisseau 2011; Keizer et al. 1987; Filaire & Lac 2000).

Even though an increased basal C level following high-intensity endurance training has been noted in a study by Kraemer et al. (1995), comparable concentrations have been reported in endurance trained and untrained men (Hackney, Sinning & Bruot 1988). In contrast, some studies with female populations report increased basal C and decreased basal T/C in elite athletes in comparison to non-athletic counterparts (Tegelman et al. 1990; Tsai et al. 1991), but in general there appears to be very little change on resting levels of C with endurance training in women (Keizer et al. 1989; Filaire, Duche & Lac 1998; Kiilavuori et al. 1999). As elevated basal C has been considered to be a reflection of an individual being in a state of overreaching or –training (Adlercreutz et al. 1986), fluctuations observed as a result of endurance training could be reflections of more intense training periods.

Previously untrained men and women may not experience any changes in resting GH levels when embarking on a low-to-moderate –intensity endurance training program (Bell et al. 2000). However, a prolonged period of endurance training may amplify the pulsatile GH release in women, when training includes exercising at or above the lactate threshold (Weltman et al. 1992). Consequently, the magnitude of an acute GH response to constant-load exercise may be reduced already after a short training period, if the intensity of the exercise is not of sufficient intensity (Weltman et al. 1997). While women may display greater absolute GH concentrations than men in response to endurance exercise, the incremental pattern of GH release is similar in both genders (Wideman et al. 1999).

2.3 Combined strength and endurance training

The association between consistent adherence to exercise for improved physical fitness and health has been established in various populations (Ghahramanloo, Midgley & Bentley 2009; Häkkinen et al. 2003; Sillanpää et al. 2009a) with strength and endurance training resulting in training-specific adaptations (Sillanpää et al. 2008). This paradigm of training specificity was established in the 1940's by Thomas DeLorme, who stated that each type of exercise would be incapable of producing results that were obtained by any other type of physical training (DeLorme 1945). Accordingly, endurance training has been shown to improve cardiorespiratory fitness (Murias, Kowalchuk & Paterson 2010) while strength training-induced adaptations include increased muscle size and strength (Häkkinen et al. 2001). As good cardiorespiratory fitness reduces premature all- cause and cardiovascular disease mortality (Farrell et al. 1998; Kodama et al. 2009) and improved or maintained muscle strength sustains functional capacity and reduces age-related loss of muscle mass (sarcopenia) (Landi et al. 2014), adhering to both exercise modes (combined training) can be considered to be of importance for all populations. However, incorporating both strength and endurance into the same training program could result in stagnation or even unfavorable adaptations if not planned correctly.

Early investigations of combined training programs utilized high overall training volumes and thus resulted in compromised strength gains but improved endurance performance ("the interference effect") (Hickson 1980). Thus, the emphasis was placed on the importance of utilizing moderate volume and frequency training programs to prevent adverse effects while still achieving significant increases in muscle strength and size as well as maximal aerobic capacity when adhering to a combined training protocol (Mikkola et al. 2012). However, while it is established that combined training protocols can yield similar benefits to standalone strength or endurance training both in terms of physical fitness and health (Dutheil et al. 2013; Ho et al. 2012; Lee et al. 2015; Sillanpää et al. 2008), comparisons between combined S and E training performed in the same training session or on different days (Sale et al. 1990) could elucidate the effects of both the acute and the chronic interference hypotheses (Leveritt et al. 1999). While the chronic hypothesis suggests that the muscle cannot adapt metabolically or morphologically to combined training because of the dissimilar adaptations that the two types of training induce, the acute hypothesis proposes that if the training modes are performed in immediate succession of each other, adaptations to the second mode may be compromised by residual fatigue from the preceding mode (Leveritt et al. 1999).

2.3.1 Interference in strength development related to combined training

The "interference effect" -concept was originally introduced by Robert Hickson in 1980 in order to describe the diminished strength gains when adhering to both strength and endurance training programs in parallel, in comparison to training for strength training only (Hickson 1980). With a training program consisting of both strength and endurance sessions at a frequency of 5-6 $d \cdot wk^{-1}$ (each), Hickson noted that gains in maximal strength stagnated after 4-6 weeks of training and thereafter started to decline towards the end of the 10-week training period. However, another group of similarly recreationally trained subjects that was adhering to the same strength training program and not participating in the additional endurance training sessions progressively increased maximal strength throughout the training period. Later research confirmed these findings, reporting either impaired maximal or explosive strength or muscle size following a wide range of training periods (6-24 weeks) of combined strength and endurance training in comparison to only strength training (Kraemer et al. 1995; Terzis et al. 2016; Hendrickson et al. 2010; Tsitkanou et al. 2016; Dudley & Djamil 1985; Dolezal & Potteiger 1998; Bell et al. 2000; Horne et al. 1997; Häkkinen et al. 2003; Mikkola et al. 2012). Furthermore, it has been noted that individuals with a higher level of aerobic fitness are not as susceptible to the interference effect as untrained individuals, thus underlining the importance of baseline training status when concurrently training for strength and endurance (Hunter, Demment & Miller 1987).

However, it was noted in both the research by Hickson as well as in other following investigations with various subject populations that the interference observed in strength adaptations did not extend to endurance performance variables (e.g. Bell et al. 2000, Häkkinen et al. 2003), but that strength training possibly even enhances endurance performance particularly in running (Millet et al. 2002; Mikkola et al. 2011). These findings consequently led to the suggestion that the interference effect is a manifestation of the muscle being unable to adapt to multiple divergent stimuli, ultimately resulting in compromised adaptations of some aspect of muscle strength or hypertrophy (Coffey & Hawley August 2016; Hawley 2009; Leveritt et al. 1999).

However, while some research has shown impaired maximal strength, reports from other studies have display increases comparable to strength-only training (ca 20% during 21 weeks, Häkkinen et al. 2003) but failing to see improvements in power variables or increases in force at certain velocities (e.g. Dudley & Djamil 1985, Häkkinen et al. 2003, Terzis et al. 2016). These inconsistencies in findings allude to the fact the interference effect is dependent on numerous variables relating to physiology and training programming, rather than simply being a result of concurrently adhering to both strength and endurance training programs (Docherty & Sporer 2000; Wilson et al. 2012).

2.3.1.1 Interference predicting model

Deriving from the acute and chronic interference hypotheses by Leveritt (1999), an interference-predicting model was developed by Docherty & Sporer (2000) (FIGURE 5). According to the model, interference in muscular adaptations would be the strongest if an individual would be concurrently adhering to metabolically strenuous high-intensity endurance training as well as hypertrophic strength training. In this situation, the muscle would be subjected to both hypoxia to increase capillarization as well as aiming to increase protein synthesis and consequently muscle size - two vastly different commands, which theoretically would result in impaired adaptations (Hawley 2009; Docherty & Sporer 2000). In a practical sense, it was proposed that continuous endurance exercise at lower intensities would be the least detrimental in terms of interference on strength development regardless of the utilized strength training protocol, but particularly minimal when the strength training would be mainly targeting neural adaptations (Docherty & Sporer 2000). In such a scenario, the processes responsible for increasing the oxidative capacity of the muscle and processes controlling the adaptations in the nervous system (e.g. increased firing rate) would be occurring at such different locations that interference would be unlikely to occur.

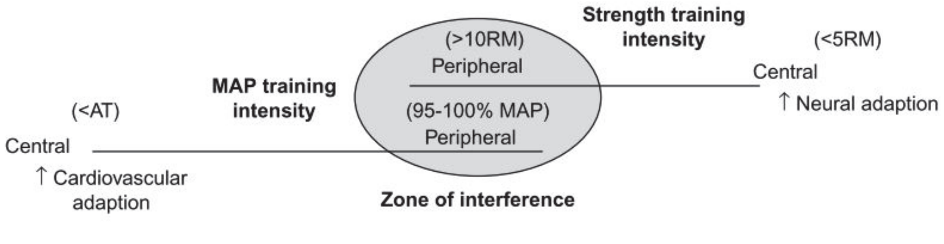

FIGURE 5 A model for predicting the occurrence of the interference effect, as proposed by Docherty & Sporer (2000). The model displays continuums and primary locations of adaptations for both maximal aerobic power (MAP) and strength training, and the possible overlap when both training modes are combined. AT = anaerobic threshold; RM = repetition maximum; ↑ = increased.

The model is partly supported by studies both in terms of avoiding the interference on maximal strength as well as being subjected to it (McCarthy et al. 1995; Häkkinen et al. 2003; Hickson 1980; Kraemer et al. 1995). Furthermore, studies investigating the effects of different endurance protocols on acute decreases in maximal strength have indeed noted that when both the strength and endurance protocols produce local peripheral fatigue, the acute impairment on maximal strength is the greatest (de Souza et al. 2007; Tan et al. 2014). However, acute studies without long-term changes in strength characteristics do not provide an answer regarding long-term adaptations. Additionally, the model is also opposed by the results of a number of studies (e.g. Dudley & Djamil 1985, Bell 2000). Consequently, it is likely that while models and acute studies could be used as guidelines to identify physiological factors influencing chronic interference, other aspects are also likely to play a role in its occurrence (Wilson et al. 2012).

2.3.1.2 Factors influencing the interference effect

Acute vs. chronic interference. It has been suggested that interference in neuromuscular performance is a manifestation of a long-term incompatibility of the muscle to adapt to different stimuli (Hawley 2009) or an individual being overtrained from large volumes of exercise (Kraemer et al. 1995; Hickson 1980). However, it is also possible that performing endurance and strength exercises in close proximity to each other leads to the second mode constantly being impaired by the preceding one and consequently suppresses the long-term adaptations (Cadore et al. 2012a). Fatigue from an endurance session can include reduced force output and rate of force development (Bentley et al. 2000; Lepers, Millet & Maffiuletti 2001) and a strength training bout can increase the oxygen costs of subsequent endurance exercise (Ratkevicius et al. 2006).

Training volume and frequency. The training intervention by Hickson (1980) (described in 2.3.1) can be considered to demonstrate the detrimental effects of long-term adherence to extremely high frequency and volume concurrent training. Despite the initial 4-6 weeks resulting in increased maximal strength, the strength performance significantly decreased during the latter half of the training period thus demonstrating a limited tolerance for high-volume combined training and a possible reason for the interference. Accordingly, interventions with more moderate training frequencies (S and E each 3 $d \cdot wk^{-1}$) have demonstrated that while no difference in maximal strength performance are observed after six weeks of either strength-only or combined training, a second six-week training period could still lead to compromises in some aspects of strength adaptations (Bell et al. 2000). Despite increases maximal dynamic bilateral leg press force, Bell et al. (2000) noted halted increases in unilateral isometric knee extension force, suggesting the susceptibility for interference of isometric muscle work to be higher than dynamic strength. In a similar manner, no interference was observed in maximal dynamic strength in a training program with an even lower frequency and volume (S and E each 2 d·wk^{-1}), while the development of explosive strength was halted (Häkkinen et al. 2003). Indeed, a meta-analysis by Wilson et al. (2012) revealed that total training volume does account for a small part of the interference effect, and that power and high-velocity variables are the most susceptible to suffer while maximal strength and muscle hypertrophy could remain unaffected (Wilson et al. 2012).

Endurance training mode. Even though moderate overall training volumes could preserve gains in muscular strength and size, the long-term training adaptations also have the potential to be influenced by the endurance training modality. When strength training is combined with a cycling endurance training program, these adaptations are less susceptible to be adversely affected than if strength training would be paired with running (Gergley 2009; Wilson et al. 2012). This could be due to the similarities in biomechanical patterns between cycling and multi-joint lower body strength exercises, which do not exist with running (Escamilla 2001; Gregor, Broker & Ryan 1991). Furthermore, contributions to exercise-induced fatigue could be different following cycling and running, which becomes relevant if strength and endurance training are performed in immediate succession (Leveritt et al. 1999; Millet, Vleck & Bentley 2009). Consequently, cycling exercise could be considered to augment maximal leg press strength development (Dudley & Djamil 1985; Gergley 2009; Häkkinen et al. 2003; Tsitkanou et al. 2016). Finally, running consists of repeated coupled concentric-eccentric actions and causes more muscle damage than cycling, which mainly relies on concentric muscle actions (Millet & Lepers 2004; Lepers et al. 2002; Koller et al. 1998). Thus, the choice of endurance training mode could also contribute to the interference in muscle strength and hypertrophy that has been observed in some (Hickson 1980; Hendrickson et al. 2010) but not all (Silva et al. 2012) studies.

2.3.2 Neuromuscular adaptations to combined training

While it has been proposed that combined training can provide all the benefits that S can alone, but to a lesser extent (Dolezal & Potteiger 1998), several studies have shown that performance can be improved as well as hypertrophy can be increased to the same and in some cases even a greater extent in comparison to adaptations following only either training mode (e.g. Mikkola et al. 2012). Even so, adaptations in rapid muscle actions and micro-level hypertrophy may differ from those of single-mode strength training, suggesting differing adaptations in the neuromuscular system (e.g. Häkkinen et al. 2003). As can be observed in TABLE 2A and TABLE 2B, most studies show some interference in rapid actions, while simultaneously allowing for increases of maximal strength. It can similarly be observed, that any possible interference tends to preserve adaptations hypertrophy and endurance performance, while the neuromuscular system seems to be the element more at risk to undergo unfavorable adaptations. This appears to hold true regardless of how the combined training regimens are structured.

TABLE 2 A Study designs of selected studies of combined strength and endurance training.

Study	Training details			
	Subjects	Training Description	Strength training	Endurance training
Same-session training				
Terzis et al. 2016	Young w	6 wks, S+E, 3d·wk^{-1}	Power-training	Running, 30 min, 60-70 % HR_{max}
Hendrickson et al. 2010	Active w	8 wks, S+E, 3d·wk^{-1}	3-12 reps, periodized	Running, 20-30 min, 70-85 % HR_{max}
Tsitkanou et al. 2016	Active m	8 wks, S+E, 2d·wk^{-1}	4 sets of 6 reps, 80-85% 1 RM	Interval cycling, 10 x 60s, 100% W_{max}
Dolezal & Potteiger 1998	Active m	10 wks S+E, 3d·wk^{-1}	4-15 reps, periodized	Running, 25-40 min, 65-85% HR_{max}
Nelson et al. 1990 Nelson et al. 1990 (11wks)	Active m	20 wks, S+E 4d·wk^{-1}	Isokinetic, 30.0 rad·s-1	Cycling, 30-60 min, 75-85% HR_{max}
Same-day training				
Hickson 1980	Active m + w	10 wks, S&E, 5-6 d·wk^{-1} each	3-5 sets of 5 reps, 80% 1 RM	Running 30-40min "as fast as possible"; Cycling 6 x 5 min close to VO_{2max}
Laird et al. 2016	Active w	11 weeks, S&E, 3d·wk^{-1} each	3-10 reps, periodized	Sprint running 8 x 20 s., 110-120%VO_{2max}
Different-day training				
Dudley & Djamil 1985	Young m + w	7 wks, DD, 3 d·wk-1 each	Isokinetic, 4.19 rad·s^{-1}	Interval cycling, 5 x 5 min, up to 180bpm
Bell et al. 2000 Bell et al. 2000 (6wk)	Active m + w	12 wks, DD, 3 d·wk^{-1} each	2-12 reps, periodized	Cycling 30-42 min at VT; 4-7 x 3 min at 90% VO_{2max}
Horne et al. 1997	Healthy m + w	12 wks, DD, 3 d·wk^{-1} each	Periodized	Running
Häkkinen et al. 2003	Healthy m	21 wks, DD, 2 d·wk^{-1} each	3-15 reps, periodized	Cycling, walking, 30 min >AT, 2-3 x 5-10 min AT > AnT and > AnT
Mikkola et al. 2012	Healthy m	21 weeks, DD, 2 d·wk^{-1} each	3-15 reps, periodized	Cycling, walking, 30 min >AT, 2-3 x 5-10 min AT > AnT and > AnT

m = men, w = women, reps = repetitions, S+E = Strength followed by endurance in the same session, S&E = Strength and endurance on same day, >2h between modes, DD = Strength and endurance on different days, W_{max} = peak watts during cycling, HR_{max} = Maximal heart rate, bpm = beats per minute, VT = Ventilatory threshold, AT = aerobic threshold, AnT = Anaerobic threshold, VO_{2max} = maximal oxygen uptake

TABLE 2 B Observed training adaptations and possible interference in comparison to single-mode strength or single mode endurance training.

A D A P T A T I O N S

Study	**Neuromuscular**			**Cardio-respiratory**		**Body composition**		**Interference in adaptations?**	
	Max S	**Explosive S**	**Neural**	**VO_{2max}**	**W_{max}**	**Hypertrophy**	**Body Fat**	**vs S-only**	**vs E-only**
Same-session training									
Terzis et al. 2016	↑	RFD↑, CMJ↔	FCV ↔	↑	-	Fiber hypertrophy ↔	-	Yes (CMJ)	-
Hendrickson et al. 2010	↑	LB ↔, UB ↑	-	↑	-	Lean mass ↔	↔	Yes (explosive LB)	No
Tsitkanou et al. 2016	↑	RFD 50ms ↓	-	-	↑	type I, IIa, IIx CSA ↑	-	Yes (explosive)	-
Dolezal & Potteiger 1998	↑	-	-	↔	-	↑	↓	Yes (UB strength)	Yes
Nelson et al. 1990	↑	-	-	↑	-	type I, IIa, IIb ↑,	-	No	Yes
Nelson et al. 1990 (11wk)	-	-	-	↑	-	type I, IIa, IIb ↔,	-	No	Yes
Same-day training									
Hickson 1980	↔	-	-	↑	-	Thigh circumference ↑	↓	Yes (max)	No
Laird et al. 2016	↑	↔	-	↑	-	↑	↔	No	-
Different-day training									
Dudley & Djamil 1985	↑ *)	-	-	↑	-	-	-	Yes (High angular velocity)	No
Bell et al. 2000	↑	-	-	↑	-	Type II CSA ↑	-	Yes (isom) / No (dyn)	No
Bell et al. 2000 (6 wks)	↑	-	-	↔	-	↔	-	No	No
Horne et al. 1997	↑	-	-	↑				Yes (unilateral 1RM)	No
Häkkinen et al. 2003	↑	↔	EMG ↑	↑	-	type I, IIa, IIb CSA ↑	-	Yes (explosive)	-
Mikkola et al. 2012	↑	↔	EMG ↑	↑	↑	↑	↓	Yes (explosive) / No (max)	No

↑ = increase, ↓ = decrease, ↔ = no change, - = data not available, ms = milliseconds, LB = Lower body, UB = Upper body, RFD = Rate of force development, CMJ = Counter-movement jump, CV = Conduction velocity, FCV = fiber conduction velocity, CSA = Cross-sectional area, VO_{2max} = maximal oxygen uptake, W_{max} = peak watts during cycling

Strength and power. The reduced gains in maximal strength that were originally associated with combined training (Hickson 1980) can most likely be avoided utilizing moderate to low training volumes and frequencies. This is demonstrated by numerous studies of various designs where maximal strength was found to increase to similar extents as with strength-only training (S and E performed in immediate succession, e.g. Nelson et al. 1990; S and E performed during the same day with ≥ 2h recovery between modalities, e.g. Robineau et al. 2014; S and E performed on different days, e.g. Häkkinen et al. 2003).

However, even though maximal strength has not been subjected to interference in a number of studies, adaptations in other neuromuscular variables have still been found to be impeded (FIGURE 6). Most commonly, velocity-related variables such as power (Hendrickson et al. 2010), rate of force development (RFD) (Häkkinen et al. 2003), counter-movement jump (CMJ) (Terzis et al. 2016) or isokinetic performance at high angular velocities (Dudley & Djamil 1985; Robineau et al. 2016) have been adversely affected or remained unchanged. In addition, unilateral (Horne et al. 1997) and isometric muscle actions (Bell et al. 2000) as well as fiber conduction velocity (Terzis et al. 2016) have also been reported to have been compromised with combined training.

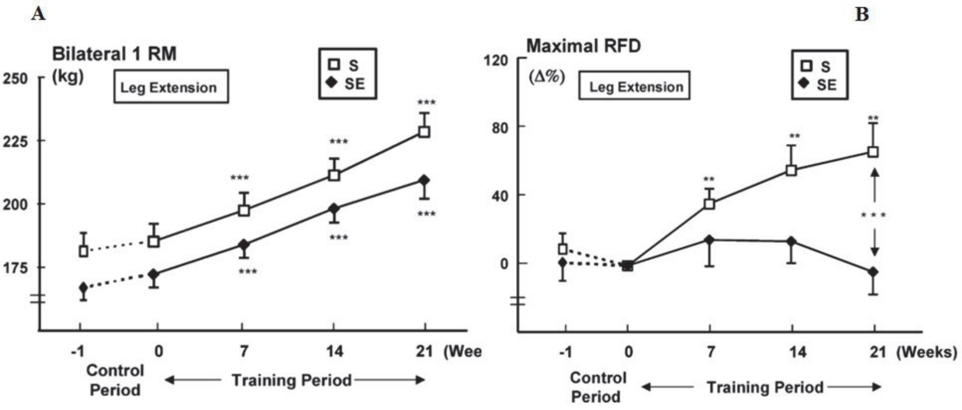

FIGURE 6 Changes in dynamic bilateral leg press 1 RM (A) and maximal RFD (B) over the course of 21 weeks in a strength training (S) and combined strength and endurance training group (SE). (Modified from Häkkinen et al. 2003).

Though it appears clear that some aspect of neuromuscular performance is compromised with combined training, the exact mechanism remains unclear. As cardiorespiratory variables mainly remain unaffected by the interference effect (e.g. Häkkinen et al. 2003), it appears lucrative to speculate that the site of interference is in the nervous system. This theory was questioned by McCarthy et al. (2002), who reported similar non-significant increases in surface EMG with both strength and combined training (McCarthy, Pozniak & Agre 2002), although it needs to be acknowledged that EMG alone as a representation of neural drive is a gross oversimplification (De Luca et al. 2006). Nevertheless, the discrepancies reported between adaptations in maximal strength vs. velocity-related variables could be due to neural rather than metabolic disturbances. It has been proposed that a neural, tension-limiting mechanism plays a major role in training-induced increases in muscle strength at slow contraction velocities with other neural factors being responsible for improvements in faster contractions (Caiozzo, Perrine & Edgerton 1981). In conjunction with the impaired velocity-related variables in numerous combined training studies, these results could suggest that combined training may not be able to alter the adaptability to the mechanisms improving fast contraction speeds, as opposed to strength-only training. Alternatively, differences in the time course of adaptations may explain these discrepancies. Initially, it may take longer for the individuals adhering to combined training to reach the adaptation level of a strength-only program (as observed in max strength) (Bell et al. 1991).

Muscle and fiber hypertrophy. There is theoretical support from molecular signaling models for blunted hypertrophy following combined strength and endurance training due to competing pathways (Fyfe, Bishop & Stepto 2014), and some studies have accordingly reported an absence of hypertrophy following combined training (Sillanpää et al. 2008). However, a practical examination of molecular signaling in humans revealed that despite differences in protein phosphorylation of selected pathways following combined training, hypertrophy of the trained muscles was observable (de Souza et al. 2013). In fact, several studies report increases in muscle cross-sectional area (CSA) following a variety of combined training protocols (Häkkinen et al. 2003; Tsitkanou et al. 2016; Bell et al. 2000; Mikkola et al. 2012; Lundberg et al. 2013; McCarthy, Pozniak & Agre 2002). However, even though macro-level hypertrophy (e.g. muscle CSA) may not be impaired per se, differences in fiber-type-specific hypertrophy may take place. McCarthy et al. (1995) reported similar increases in the S and combined training groups in quadriceps area as well in type II fiber area, but only S-training increased the area of type I fibers (McCarthy, Pozniak & Agre 2002). Similary, Bell et al. (2002) and Kraemer et al. (1995) reported unchanged type I area with combined strength and endurance training while strength-only training resulted in an additional increase in type I area. This attenuated hypertrophy of type I fibers has even been suggested to be one of the origins for the interference effect (Putman et al. 2004). However, some studies do report changes in all fiber types (Nelson et al. 1990; Häkkinen et al. 2003; McCarthy, Pozniak & Agre 2002), which could be attributed to differences in training duration, frequency, intensities or overall volumes, which ultimately affect muscular adaptations. It is also possible that short duration (6-11 weeks) training interventions may not be sufficient to induce hypertrophy (possibly due to an interfering stimuli), and instead more prolonged training is required for certain adaptations to take place (Nelson et al. 1990; Bell et al. 2000). Thus, an absence of either macro- or micro-level hypertrophy after a combined training intervention may be a difference in the time course of adaptations rather than a differential response to strength vs. combined training (Bell et al. 2000).

2.3.3 Adaptations in endurance performance following combined training

It is generally considered that a combined training program induces cardiorespiratory adaptations to a similar extent as an endurance-only training program with both running and cycling protocols yielding improvements in VO_{2max} (Dudley & Djamil 1985; Bell et al. 2000; Mikkola et al. 2012; Hendrickson et al. 2010). Furthermore, strength training may in fact aid endurance performance e.g. through enhancing exercise economy via neuromuscular mechanisms (Aagaard & Andersen 2010; Rønnestad & Mujika 2014). As endurance exercise mostly activates type I muscle fibers, performance may benefit from strength-training induced increases in type I strength as well as increased proportions of the oxidative, fatigue-resistant type IIa fibers (Kraemer et al. 1995; Rønnestad & Mujika 2014).

However, some investigations have reported diminished endurance adaptations following combined training when compared to the same endurance training program performed in isolation (Nelson et al. 1990; Dolezal & Potteiger 1998; Kraemer et al. 1995). In these studies it was proposed that muscle fiber hypertrophy induces decreases in capillary and mitochondrial densities as well as oxidative enzymes, which could be an underlying cause for attenuated VO_{2max} gains due to an increased diffusion distance (Rønnestad & Mujika 2014; Nelson et al. 1990). However, as both increases (e.g. Bell et al. 2000, Tsitkanou et al. 2016) and no changes (Vikmoen et al. 2016) have been reported following combined strength and endurance training interventions, it is likely that the adaptations are specific to the utilized endurance training.

The vast majority of studies of both short (6-11 weeks) and long (up to 24 weeks) duration do report increases in both VO_{2max} comparable to those of and endurance-only intervention in previously untrained subjects. Interventions of strength training paired with cycling have typically yielded increases of 6-11% (Dudley & Djamil 1985; Nelson et al. 1990) in shorter and 7-19% in longer interventions (Bell et al. 2000; Häkkinen et al. 2003; Mikkola et al. 2012). Similarly with running endurance training, increases in VO_{2max} have ranged between 6-20% (Terzis et al. 2016; Hendrickson et al. 2010; Hickson 1980; Laird et al. 2016; Horne et al. 1997) in 6-12 week interventions. Furthermore, in cycling studies W_{max} has been reported to increase ~16% in 8-21-week interventions (Tsitkanou et al. 2016; Mikkola et al. 2012). These magnitudes are by large comparable to those of single-mode training within similar time frames (eg. Häkkinen et al. 2003, Murias, Kowalchuk & Paterson 2010, Mikkola et al. 2012).

2.3.4 Endocrine considerations of combined training

While the changes in resting hormone concentrations have been well investigated following either strength- or endurance-only training, there is paucity in the knowledge regarding changes in hormone levels after long-term adherence to combined training in healthy adults. Based on the existing data it appears that resting levels of testosterone, cortisol and growth hormone remain unchanged, although slightly higher urinary cortisol concentrations has been observed in women after a 12-week training period (Bell et al. 2000; Kraemer et al. 1995; Horne et al. 1997). In contrast to these two 12-week interventions (Bell et al. 2000, Horne et al. 2007), a recent 24-week study reported increased basal cortisol and testosterone levels following the combined strength and endurance training intervention (Küüsmaa et al. 2016). Whether the discrepancies in these results are more related to the length of the training period or the specifics of the training programs cannot be fully established with the limited amount of existing data.

2.3.5 Health and motivation-related adaptations of combined training

Combined training has been found to have the potential of positively affecting body composition in healthy, non-obese individuals (e.g. Dolezal & Potteiger 1998, Sillanpää et al. 2009). Furthermore, it has been deemed beneficial for type 2 diabetics (Earnest et al. 2014), effective in improving risk factors of cardiovascular disease in older women (Lee et al. 2015), having positive effects on blood lipid profile (Mann, Beedie & Jimenez 2014) as well as subjective perception of physical capacity and quality of life (Tibana et al. 2014) in a variety of subject populations.

2.3.5.1 Changes in body composition following combined training

Lean mass. Despite possible differences in fiber-type hypertrophy following combined vs. strength-only training (as presented in chapter 2.3.2), changes in lean mass on a whole body-level and in muscle CSA have often been reported to be similar following both modes of training. Typical increases in lean mass at the whole body-level that have been observed with a variety of combined training modes range between 2 and 5% following 8-11 week interventions (Davitt et al. 2014; Dolezal & Potteiger 1998; Laird et al. 2016; Ghahramanloo, Midgley & Bentley 2009). At a macroscopic level, Hickson et al. (1980) noted a 5% increase in thigh girth after 10 weeks of combined training, and Häkkinen et al. (2003), Mikkola et al. (2012) and McCarthy, Pozniak & Agre (2002) reported 9, 11 and 14% increases, respectively, in the CSA of the quadriceps muscle group. In the studies that compared the combined training group to a strength training group, Mikkola et al. (2012) reported a larger CSA increase in the combined vs. the strength group, while the other studies reported comparable increases in lean mass (Dolezal & Potteiger 1998; Laird et al. 2016) and CSA (Häkkinen et al. 2003; McCarthy, Pozniak & Agre 2002) with the strength group. However, as Bell et al. (2000) reported no changes after 6 weeks of training similarly to Hendrickson et al. (2010) after 8 weeks, and with only minor (2%) changes noted after 8 weeks by Davitt et al. (2014), it could be that longer interventions are required for observable changes. Furthermore, running as the choice of endurance exercise (e.g. in Hendrickson et al. 2010) could interfere with gains in lean mass as opposed to cycling (e.g. in Davitt et al. 2014), which could even be considered to augment hypertrophy (Wilson et al. 2012; Mikkola et al. 2012)

Body fat. Significant decreases in fat mass has been observed after both combined training with both running and cycling protocols in younger and older adult males, comparable (Sillanpää et al. 2008; Hickson 1980) or more pronounced (Mikkola et al. 2012; Dolezal & Potteiger 1998) than after endurance-only training. Furthermore, in women a decreased body fat percentage but less pronounced than after endurance training has been reported in older adults (Sillanpää et al. 2009b) and obese adolescents (Damaso et al. 2014) after combined training. Some studies with women of normal weight have also reported unchanged body fat percentage or fat mass (Davitt et al. 2014; Hendrickson et al. 2010; Laird et al. 2016) after combined training. Differences between studies could be related to subject material or specifics of the training program variables or duration. According to a meta-analysis by Wilson et al. (2012), increased decrease of fat could be associated with a higher amount of high-intensity endurance exercise, possibly explaining differences in results between studies. Furthermore, there could be a biased dose-response relationship of exercise to fat loss in favor of males, as has previously been observed in overweight subjects following single-mode strength or endurance training; Fat loss with a given amount of exercise was found to be larger in men than in women (Donges & Duffield 2012).

2.3.5.2 The effects of combined training on blood lipids

Exercise has been shown to have beneficial effects on improving blood lipid profile, entailing reductions in total cholesterol, triglycerides, low-density lipoprotein (LDL) and increases in high-density lipoprotein (HDL) (Mann, Beedie & Jimenez 2014). Due to an abundance of evidence for endurance training being particularly effective (Tambalis et al. 2009; Mann, Beedie & Jimenez 2014), most studies investigating the consequences of combined training have only compared it to endurance training. However, with some studies having halved the endurance training for the combined training intervention in order to keep the exercise session duration the same between groups (Libardi et al. 2012), the comparison between different exercise modes and protocols is difficult. It does appear that a higher intensity of the endurance protocol affects the outcome, with faster and more pronounced improvements in body composition and lipid profiles with higher endurance training intensities (Dutheil et al. 2013; Schjerve et al. 2008). Because a dose-response relationship has been suggested to exist between training amount and improvement in blood lipid profile (Mann, Beedie & Jimenez 2014), the comparison of the effectiveness of CT to single-mode training is particularly challenging. There is also paucity in research on the effects of combined training in healthy adults, with most research focusing on either elderly (Sillanpää et al. 2009b; Lee et al. 2015; Rossi et al. 2016; Sillanpää et al. 2009a) or obese individuals (Bateman et al. 2011; Damaso et al. 2014) or type 2 diabetics

(Earnest et al. 2014; Sigal et al. 2007). Thus, the existing knowledge relies on the results from these specific subject populations.

Following short (8 weeks) and long (21 weeks) combined training interventions, lowered total cholesterol has been observed in elderly women (Lee et al. 2015; Sillanpää et al. 2009b) and in adult sedentary men (Ghahramanloo, Midgley & Bentley 2009). Furthermore, reductions in both low-density lipoprotein (LDL) and triglycerides and have been reported in both obese adults and adolescents as well as healthy adult men (Libardi et al. 2012; Bateman et al. 2011; Damaso et al. 2014; Ghahramanloo, Midgley & Bentley 2009). Conversely, some studies found no major changes in blood lipids in older men (Sillanpää et al. 2009a) or young women (LeMura et al. 2000), despite the endurance-only training groups in the respective studies experiencing some favorable adjustments to the blood lipid profile. Inconsistencies in the findings between different studies could be related to subject background and the underlying physiology or even baseline characteristics, as it has been suggested that subjects with dyslipidemia at baseline will experience more favorable adaptations in blood lipids with training (Laaksonen et al. 2000). It has also been proposed that a reduction in cholesterol occurs more frequently if loss of fat mass occurred simultaneously (Tran & Weltman 1985), or that there is a seasonal variation in cholesterol levels in both elderly and younger populations (Donahoo et al. 2000; Woodhouse, Khaw & Plummer 1993), both of which could further explain differences between studies. However, based on the existing knowledge, it is reasonable to assume that combined strength and endurance training could have a beneficial effect on blood lipid concentrations.

2.3.5.3 Self-perceived wellbeing and time management in relation to physical activity

Regular adherence to physical activity is associated with positive effects on health-related quality of life (HRQoL) (Bize, Johnson & Plotnikoff 2007) and self-esteem (White, Kendrick & Yardley 2009). The positive exercise-induced effects last only if physical activity is continuously practiced and made a permanent lifestyle choice (Brand et al. 2006). Positive effects on mood state and HRQoL have been noted after both long-term endurance (Annesi 2002) and strength training (Bampton, Johnson & Vallance 2015) interventions. Consequently, long-term adherence to concurrent strength and endurance training has been found to be effective in treating depressive symptoms, improving quality of life -related outcomes (Atlantis et al. 2004; Goldfield et al. 2016) and increase the perception of physical capacity (Tibana et al. 2014). In a recent study, combined training improved overall HRQoL more than endurance training in obese individuals, possibly relating to accompanying favorable changes in body composition (Goldfield et al. 2016).

However, individuals often mention lack of time as a reason for poor or no adherence to physical activity (Stutts 2002; Trost et al. 2002). Accordingly, deliberate planning plays a crucial role when implementing and maintaining healthy behavior (Schwarzer 2008) and may help in converting exercise into a long-term volitional lifestyle choice (Sniehotta, Scholz & Schwarzer 2005). Prescription of a higher frequency of training does not necessarily lower adherence (Perri et al. 2002) but could lead to a feeling of poorly managed time and, consequently, constitute as a source of stress similarly to a context of work overload at a workplace (Gillespie et al. 2010). Even though the positive effects of combined training on HRQoL-outcomes are recognized (Atlantis et al. 2004; Goldfield et al. 2016), documented effects of training programs with different training frequencies on time management perception and strategies is scarce.

2.3.6 Same-session and different-day combined strength and endurance training

The past decades of comparing combined strength and endurance training regimens to single-mode strength or endurance training has shown that physical performance can be improved to similar extents when adhering to both modes in parallel. However, despite an abundance of research conducted on combined vs. single-mode training, knowledge on how different modes of combined training compare to each other is unfortunately scarce. Even though combined training has been investigated with strength and endurance performed on separate days (e.g. Dudley & Djamil 1985), on same days with >2 h of recovery between modes (e.g. Hickson 1980), in the same session (e.g. Nelson et al. 1990), in the same session with different exercise orders (e.g. Collins & Snow 1993) and in alternating shorter bouts integrated into the same session (Davis et al. 2008; Di Blasio et al. 2012), very few studies have to date attempted to compare two or more of these modes in the same study.

Considering that the acute hypothesis by Leveritt et al. (1999) suggests that residual fatigue from one modality of training could affect the other, it could be postulated that either the intra-session exercise order (endurance before strength, E+S, or vice versa, S+E) or allowing for longer recovery between modes (i.e. assigning them to different days, DD) could affect training outcomes despite equal training volumes. Accordingly, early research has suggested that DD-training could be more effective in improving physical fitness (Sale et al. 1990). However, the tradeoff for achieving possible DD-related benefits could be considered the use of time: DD-training requires the individual to participate in more frequent (albeit shorter in duration) training sessions than someone adhering to same-session, so as to achieve the same volume of training.

2.3.6.1 Neuromuscular fatigue following same-session combined loading

When combining strength and endurance training into the same session, an individual is subjected to the so called acute interference (Leveritt et al. 1999; Leveritt & Abernethy 1999), stating that residual fatigue from one mode of exercise may affect the other, and possibly compromising long-term adaptations. While fatigue is almost certainly manifested following a combined loading in either the E+S or S+E order (Schumann et al. 2013) e.g. as decreased isometric force, the isolated effects of endurance exercise on strength performance and vice versa are dependent on several factors.

Acute physiological effects of endurance exercise on strength performance. Performing cycling endurance exercise tends to result in acutely impaired lower body strength, while upper body performance is likely to remain unchanged (Tan et al. 2014; Reed, Schilling & Murlasits 2013). However, there may be significant differences between endurance loading types and modes, as demonstrated by de Souza et al. (2007) who did not observe a reduction in lower body force immediately following a bout of continuous running, while intermittent running significantly affected leg strength immediately post-exercise (de Souza et al. 2007). However, only the maximal number of repetitions was negatively affected, while maximal strength remained unchanged. Conversely, when either heavy or submaximal strength training is performed, a subsequent endurance running session and its lactate responses appear to be unaffected (de Souza et al. 2011). This suggests that any hypothesized acute interference is perhaps not only due to residual peripheral fatigue, but may include a central component as well.

It should be noted that possible differences in acute responses regarding cycling vs running may lie in the biomechanical and physiological differences between the two modes, with differences in e.g. muscle recruitment patterns and time-under-tension explaining the slightly different outcomes (Millet, Vleck & Bentley 2009; Gergley 2009; Mikkola et al. 2012). Furthermore, the training status of the subjects as well as the volume and intensity of the exercise protocols are capable of producing slightly differing results (Cadore et al. 2012b; Goto et al. 2005; Schumann et al. 2013).

Acute physiological effects of strength exercise on endurance performance. The majority of studies investigating how a bout of strength exercise affects the underlying physiology of a subsequent endurance bout have been incorporated running protocols and by the least recreationally trained subjects (e.g. Palmer & Sleivert 2001). Based on these studies it has been concluded that resistance exercise affect endurance exercise economy (Palmer & Sleivert 2001; Taipale et al. 2015) or post-exercise oxygen needs (Drummond et al. 2005). The effects of strength exercise on cycling performance have been less studied, but any possible effects could be related to the type of strength exercise. While isokinetic strength exercise may not affect the oxygen demands of subsequent submaximal cycling, a plyometric session has the potential to affect oxygen costs of a following cycling bout (Ratkevicius et al. 2006; Crawford et al. 1991). These differences are most likely related to the differences in strength loading type, as plyometric exercise may cause muscle damage, while the damage following isokinetic may not be as significant (Alemany et al. 2014; Twist & Eston 2005).

2.3.6.2 Acute effects of same-session loading order on neuromuscular, cardiorespiratory, endocrine, and metabolic responses

Neuromuscular responses. Literature regarding acute neuromuscular responses to combined loadings with different orders and their adaptations to prolonged training in previously untrained subjects is extremely limited. In a study by Schumann et al. (2014) both E+S and S+E resulted in significant neuromuscular fatigue following the entire loading, both before and after a 24-week training intervention. When the strength protocol of mixed loading types was performed first, it resulted in larger decreases in force (MVC) in comparison to the opposite order. The S+E order also induced a larger degree of neuromuscular fatigue after the 24-week training intervention in comparison to the fatigue observed at baseline (Schumann et al. 2014). The recovery of force production was completed by 24 hours of recovery following both exercise order both before and after the training intervention.

Cardiorespiratory responses. Post-exercise oxygen kinetics after a combined loading could be affected more by the exercise order (Drummond et al. 2005) than the choice of specific endurance or strength exercise mode or oxygen consumption during the training session (Drummond et al. 2005; Vilacxa Alves et al. 2012). Even though Vilacxa Alves et al. (2012) and Di Blasio et al. (2012) found that the overall oxygen costs of a combined exercise session was not affected by the order, Drummond et al. (2005) concluded that oxygen consumption was greater 10 minutes post exercise when endurance exercise preceded the strength exercise. This was suggested to be because moderate aerobic exercise performed after strength exercise could possibly help in recovery, while conversely, strength exercise performed after endurance would disrupt the recovery process (Drummond et al. 2005). Whether this difference is enough to affect energy expenditure long-term is unclear.

Endocrine and metabolic responses. The present knowledge on hormonal responses to combined strength and endurance loadings mainly relies on findings from young, untrained male populations. Based on these investigations, a bout of endurance exercise may blunt the typical GH response to subsequent resistance exercise, thus resulting in lower post-exercise GH concentrations than if strength would be performed before endurance exercise (Goto et al. 2005; Schumann et al. 2013). The acute responses of testosterone and cortisol are less conclusive. While some studies have reported similar responses to both exercise orders (Schumann et al. 2013), others have found the first mode to always produce larger elevations in hormone concentrations, independent of the order (Cadore et al. 2012b). The specific characteristics are thus likely related to the intensity of both exercises modes. In terms of recovery, testosterone levels following the E+S order may initially show a delayed recovery to baseline in comparison with the opposite order as it was found to be depressed even 48 hours after cessation of exercise (Schumann et al. 2013).

This order-related difference has been found to disappear with prolonged training and to not contribute to long-term adaptations (Schumann et al. 2014). If more than 2 hours is allowed between the endurance and strength training modes, the recovery of endocrine variables to baseline appears to be the same following both modes (Johnston et al. 2017). This phenomenon highlights the possibility of different recovery needs for the training orders during the initial phases of training if strength and endurance are performed in immediate succession.

Both orders are likely to be similar in energy expenditure (Di Blasio et al. 2012) and also likely to produce similar post-exercise lactates (Schumann et al. 2014; Inoue et al. 2016). Lactate concentrations may remain slightly more elevated after the E+S loading after 10 minutes of passive recovery following cessation of exercise (Inoue et al. 2016), but are mainly similar between training orders both when subjects are untrained as well as accustomed to combined training (Schumann et al. 2014). The responses in creatine kinase (CK) may on the other hand be affected by the training status of the invidual. This indirect indicator of muscle damage was found by Schumann et al. (2014) to be diminished following a combined loading after a 24-week training intervention in individuals constantly adhering to the S+E training mode. The responses were also significantly smaller than following the E+S order. This could indicate an order-specific increased tolerance for combined strength and endurance loadings.

2.3.6.3 Effects of same-session training order on long-term neuromuscular and cardiorespiratory performance adaptations and body composition

The majority of research conducted on long-term adaptations to combined strength and endurance training with different exercise sequences as well as modest training frequency and volume show improvements for both orders in strength and endurance parameters after long-term training (e.g. Collins & Snow 1993, Davitt et al. 2014). This phenomenon has been found true both in development of upper and lower body strength, with circuit training protocols as well as with both cycling and running endurance exercise (Collins & Snow 1993; Davitt et al. 2014; Cadore et al. 2012a). However, some order-specific adaptations have been present in some studies, and are presented below.

Neuromuscular performance. Several studies employing a variety of populations have shown that the sequencing of strength and endurance training within a single training session does not affect the development of strength performance, but rather improves it to similar extents (Collins & Snow 1993; Gravelle & Blessing 2000; Chtara et al. 2008; Makhlouf et al. 2016; Küüsmaa et al. 2016). However, results from elderly populations suggest an order effect in favor of the S+E order for neuromuscular economy (Cadore et al. 2013; Cadore et al. 2012a). Furthermore, it appears that power and / or velocity related variables could be affected, as it has been reported that the S+E training order improved counter-movement jump performance, whereas E+S left it unchanged (Makhlouf et al. 2016).

Cardiorespiratory adaptations. Some studies have found the E+S order to results in impaired VO_{2max} (Gravelle & Blessing 2000) or improvements of slightly lesser extents in comparison to S+E (Cadore et al. 2012a; Chtara et al. 2005; Küüsmaa et al. 2016), but a finding of no order-related differences has also been reported (Collins & Snow 1993). Any possible impairment in endurance performance with the E+S order has been suggested to be related to disturbances in post-exercise oxygen kinetics interfering with recover (Drummond et al. 2005, Vilacxa Alves et al. 2012), which could be related to the specifics of the endurance training sessions.

Body composition and hypertrophy. It generally seems that both training orders behave similarly regardless of whether the main outcome has been increases in lean mass or muscle CSA (Davitt et al. 2014; Küüsmaa et al. 2016) or decreases (Sheikholeslami-Vatani et al. 2015) or unchanged body fat content (Davitt et al. 2014; Gravelle & Blessing 2000). Thus, it may be that the details of any given training program or subject material affect the outcome more than training order per se.

2.3.6.4 Same-session vs. different day training adaptations – review of existing literature

The limited data that exists on direct comparisons of same-session and different-day strength and endurance training does not allow for definite conclusions on how adaptations in performance and physiological variables differ between these training modalities. It could be argued that DD-training requires a higher frequency of training occasions in order to meet the volume of same-session training, which consequently allows for less recovery between the individual training sessions. Despite this, the different-day training mode allows for more recovery between the strength and endurance training modes, thus avoiding possible residual fatigue and the so called "acute interference" (Leveritt et al. 1999; Leveritt & Abernethy 1999). However, while it does appear that both methods are effective in increasing physical fitness and improving body composition, placing strength and endurance on separate days could provide an individual with some additional benefits, although this has not been consistent between studies (Sale et al. 1990; Robineau et al. 2016; Arazi et al. 2011; Makhlouf et al. 2016). Thus, it appears that more recovery between the training modes could be preferable.

Neuromuscular adaptations. The benefits of a longer recovery time between exercise modes was demonstrated by Robineau et al. (2014) when comparing same-session training with either 6 or 24 hours of recovery between training modes in rugby players. The 6-hour recovery resulted in larger gains in strength over 7 weeks than no recovery, but even larger gains were observed when allowing for a full 24 hours between modes (Robineau et al. 2014). Furthermore, an increase in the maximal voluntary activation level was the most likely to occur with a full day of recovery between strength and endurance exercise sessions. Similarly, Sale et al. (1990) reported that previously untrained subjects training on different days improved strength performance over 20 weeks more than those individuals who were training for both modes in the same session, even though both modes similarly improved both fast and slow twitch fiber area as well as muscle size. Conversely, two 12-week training interventions with physically fit subjects (Arazi et al. 2011) and soccer players (Makhlouf et al. 2016) reported no differences in strength performance between groups. However, Arazi et al. (2011) did not specify whether the same-session subjects consistently performed one mode before the other, while Sale et al. (1990) alternated between performing strength or endurance first and Robineau et al. (2014) reported that the training sessions were always initiated with strength exercise. Makhlouf et al. (2016) on the other hand compared DD-training to both same-session training orders, and found that the DD as well as the S+E -order both improved counter-movement jump performance while E+S did not. Thus, possible differences between same-session training orders and DD training are possible, but cannot be established based on the current data.

Cardiorespiratory adaptations. Conversely to strength performance, improvements in VO_{2max} were similar between same-session and different-day modes both in the studies by Sale et al. (1990) with untrained and Arazi et al. (2011) with trained subjects. However, Robineau et al. (2014) reported the largest increases in the different-day training group in rugby players. Also, even though Arazi et al (2011) reported no differences between the training groups, only the group training on different days showed a statistical difference to the non-exercising control group. It is possible that performing endurance training in an already fatigued state could have partly compromised the training adaptation (Ratkevicius et al. 2006), explaining the results of Robineau et al. (2014). As Sale et al. (1990) altered the same-session training order throughout the study, it is possible that enough endurance session were performed in a non-fatigued state so that group differences in cardiorespiratory adaptations did not emerge.

Body composition. Muscle size as measured by computer tomography (Sale et al. 1990) as well as lean body mass measured with bio impedance (Arazi et al. 2011) have been found to increase similarly after same-session and different day training. Arazi et al. (2011) also reported body fat percentage to decrease following both modes in normal weight, fit subjects, although different-day training appeared to decrease body fat to a larger extent than same-session training. It could be speculated, that performing more frequent, shorter sessions as opposed to fewer longer ones could affect energy expenditure, thus possibly explaining the results. This phenomenon has been demonstrated by splitting longer endurance sessions into shorter ones (Almuzaini et al. 1998), but has not been investigated in a combined training setting per se.

Based on existing data it appears plausible that DD-training could provide some advantages in selected measures of physical performance and body composition in comparison to same-session training. This can, however, not be stated with certainty, due to a small number of existing studies of varying durations. In order to establish more precise overview of the comparisons of same-session and different day training, further long-term training interventions are required.

3 PURPOSE OF THE STUDY

The purpose of the study was to examine adaptations to combined strength and endurance training performed on different days or with the same volume but performed in the same session with either strength preceding endurance or vice versa. More specifically, the aims of the study were:

1) To investigate acute endocrine and force responses and their long-term adaptations to same-session combined training with different intra-session exercise sequences in women.

2) To compare neuromuscular adaptations between same-session combined strength and endurance performed on different days or in the same session with different orders in men.

3) To investigate adaptations in strength and endurance performance, body composition, and blood lipid profile following combined strength and endurance performed on different days or in the same session with different orders in men and women.

4) To investigate long-term changes in subjectively perceived health-related quality of life, self-esteem and time management behavior in men and women following combined strength and endurance performed on different days or in the same session in men and women.

4 METHODS

4.1 Subject material and experimental approach

4.1.1 Subject material

Healthy and recreationally physically active men (n=70) and women (n=70) in the age range 18-40 from the city of Jyväskylä, Finland volunteered to participate in the study. The recruitment was conducted through several public postings. The prospective subjects were required not to have participated in systematic strength or endurance training for a minimum of 1 year prior to the study. Subject candidates were required to be free of chronic illnesses and injuries, below a BMI of 30 $m^2 \cdot kg^{-1}$ and non-smokers. The use of medication that would contraindicate the performance of intensive physical training and hormonal function was prohibited. Female subjects were not pregnant or lactating. During the screening process, all subjects completed a health questionnaire and underwent a standardized resting electrocardiogram procedure, both of which were approved by a cardiologist.

Out of the 140 recruited and approved subjects, 15 men and 24 women were excluded from the analyses due to either a) failing to complete the intervention or b) due to a low training adherence. The demographics of the subjects included in the analysis are presented in TABLE 3**.** The study received ethical approval from the Ethics Committee of the University of Jyväskylä and was conducted in accordance with the Declaration of Helsinki. All participating subjects gave their written informed consent prior to the start of the study.

TABLE 3 Subject characteristics at Week 0.

	Women			Men		
	DD(n=18)	**ES**(n=17)	**SE** (n=15)	**DD** (n=21)	**ES** (n=17)	**SE** (n=18)
Age (y)	29.9±7.5	29.1±5.6	28.9±4.4	28.9±6.1	29.8±6.0	29.8±4.4
Height (cm)	168.0±5.0	168.0±7.0	164.0±5.0	180.0±0.07	178.0±6.0	179.0±5.0
Weight (kg)	66.5±8.2	66.7±10.1	62.4±8.0	80.5±11.1	80.3±12.0	75.2±8.5
BMI ($m^2 \cdot kg^{-1}$)	23.7±2.8	23.7±3.3	23.2±3.4	24.8±3.2	25.2±3.3	23.5±2.1

BMI = Body mass index; DD = Different-day combined strength and endurance training; ES = same-session combined training, endurance preceding strength; SE = same-session combined training, strength preceding endurance

4.1.2 Experimental approach

To examine the effects of combined strength and endurance training performed on different days (DD) or in the same session (with two different orders: ES and SE), each subject was assigned to one of three training groups for the entire duration of the 24-week training intervention. The measurement sessions took place before (Week 0), at the mid-phase (Week 12) and after (Week 24) the training intervention. The measured variables included maximal strength and endurance performance, neuromuscular function, hormonal concentrations, blood lipids and body composition. The subjects also filled in a food log as well as questionnaires regarding perceived health, self-esteem and time management aspects.

Additionally, the subjects in the ES and SE groups participated in an experimental loading session at both week 0 and 24 to assess acute responses to combined strength and endurance loading sessions with different orders. Due to the fact that this investigation was a part of a broader research project, only the female ES and SE data from the loadings are presented in this thesis. The corresponding male data has been previously reported and published elsewhere (Schumann et al. 2014). A schematic overview of the research design is presented in FIGURE 7.

4.2 Measurement procedures

4.2.1 Familiarization session

Prior to the start of the measurements, all subjects reported to the laboratory for a familiarization session during which all the equipment was adjusted and set up individually as well as allowing the subjects to be familiarized with all testing procedures, equipment and execution of the tested variables. To ensure repeatable electromyographic (EMG; article II) and ultrasound (US; articles I and II) measurements throughout the study, small marks were tattooed to the right limb to identify anatomical landmarks (Häkkinen & Komi 1983).

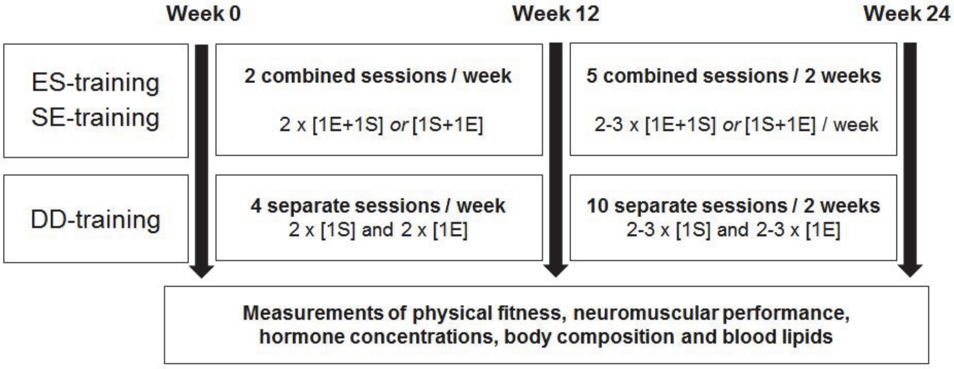

FIGURE 7 Overview of the study design.

All subjects were familiarized with the training and measurement protocols and equipment before the start of the study. All measurements sessions were separated from each other by a minimum of two days. For each subject, the measurements were conducted at the same time of day (±1 h). Abstinence from caffeine 12 h and alcohol 24 h prior to all measurements was required. The subjects arrived to the laboratory in a rested and hydrated state and at least two hours postprandial for the training sessions as well as the measurements of physical fitness. A minimum of two and a maximum of four days of rest took place between the last training session of each training period and the measurements.

4.2.2 Neuromuscular performance

4.2.2.1 Isometric strength measurements

Maximal bilateral isometric leg extension force (MVC) was determined both during acute (loading-induced changes: I) and chronic (long-term training adaptations: II, III) conditions on a leg press device (Department of Biology of Physical Activity, University of Jyväskylä, Jyväskylä, Finland) with a knee joint angle of 107^{o} (180^{o} representing full extension) (Häkkinen et al. 1998). The greater trochanter of the femur and lateral malleolus of the ankle of the right limb were used as anatomical reference points when determining joint angles. The subjects were instructed to perform an isometric bilateral leg press action as rapidly as possible, aiming to reach the maximum achievable force as early during the trial as possible and maintaining it for duration of approximately 3s.

In the chronic conditions (II, III), subjects were allowed a minimum of three trials separated by 1 min of rest. A fourth and fifth trial was allowed, if the difference from the third trial to the previous two exceeded 5%. In the acute (I) conditions, only two trials with minimal rest (10-15s) were allowed. The trial with the highest force value was selected for further analysis. Trials were analyzed for MVC as well as average force produced between 0 and 500 ms (MVC_{500}) (Häkkinen et al. 2003). Force signals were recorded with Signal 2.16 software (CED, Cambridge, UK), sampled at 2000 Hz and processed with a 20 Hz low-pass filter. Maximal unilateral isometric knee extension force along with electrical stimulation (see 4.2.2.4) was performed on a device designed and manufactured by the Department of Biology of Physical Activity (University of Jyväskylä, Jyväskylä, Finland). Subjects were seated in the device upright with a knee joint angle of the right limb at 107°. The left limb was lifted onto a chair and positioned parallel to the floor. A seatbelt at the hip and a pad strapped over the right knee secured the subjects to maintain the same position throughout the measurement. The right ankle was strapped to the device 2 cm above the right lateral malleolus with an adhesive fabric connecting to a strain gauge. Subjects were instructed to increase force gradually, reaching maximum voluntary knee extension force in approximately 3 s followed by maintenance of the reached force level for 3-4 s. Subjects performed three maximal isometric knee extension trials, of which the one with the highest voluntarily achieved force (prior to the electrical muscle stimulation) was accepted as the trial to be analyzed. Force signals were recorded and manually analyzed using the Signal software (version 4.04, Cambridge Electronic Design, Cambridge, UK), sampled at 2000 Hz and processed with a 20 Hz low-pass filter.

4.2.2.2 Dynamic strength measurements

Maximal bilateral concentric strength was assessed as one-repetition maximum (1 RM) using a David 210 weight stack horizontal leg press device (David Health Solutions Ltd., Helsinki, Finland). The subjects were seated in the device with a starting knee angle of 60° (58° ± 2°). In preparation for the 1 RM trials, the subjects performed 3 warm-up sets (5 × 70–75% estimated 1 RM, 3 × 80–85% estimated 1 RM, 2 × 90–95% estimated 1 RM) with 1 min rest between sets. When assessing 1 RM, a dynamic action to a full leg extension (knee angle 180°) was performed when verbally instructed. The load was increased following each successfully completed repetition. After a maximum of five maximal trials, the trial with the highest successfully completed load was accepted as the 1 RM.

4.2.2.3 Measurement of surface electromyography (EMG)

Electromyography of the Vastus Lateralis –muscle (VL) of the right limb was monitored during the isometric muscle actions in article I. Two adhesive electrodes (bipolar configuration Al / AgCl electrodes with an inter-electrode resistance < 5 kΩ, Blue Sensor N ECG Electrodes, Ambu A/S, Denmark) were placed in accordance with the SENIAM-guidelines (Hermens et al. 2000) on the distal third of the distance along the line between the anterior spina iliaca superior on the lateral side of the patella, on the muscle belly. This point was subcutaneously tattooed (Häkkinen & Komi 1983) onto the right limb during the familiarization session, and during the actual measurements the area over and around the tattoo was prepared for better signal conductivity using standard procedures of shaving, skin abrasion, and antiseptic rubbing alcohol. The electrodes were placed as close as possible to each side of the tattoo and aligned along the estimated pennation angle of the VL.

The raw EMG signal from the isometric leg press was amplified by 1000 and sampled at 3000 Hz. The signals were relayed from a portable transmitter to a receiver box (Telemyo 2400R, Noraxon, Scottsdale, AZ, USA) and further processed through an analog-to-digital converter (Micro 1401, Cambridge Electronic Design, Cambridge, UK). Customized, automated scripts for Signal 2.16 and 4.04 (Cambridge Electronic Design, Cambridge, UK) were used during the analysis of the isometric EMG and conversion into integrated EMG (iEMG, mV·s). Average maximum iEMG (mV·s) of the VL was determined during the 500-1500 ms time period after the onset of the contraction as a representation of the peak force phase.

The raw EMG signals from the unilateral isometric knee extension with super-imposed electrical twitch (see 4.2.2.4) were band-pass filtered (20–350 Hz) and manually converted to root mean square (rmsEMG, mV) during a 500 ms time frame of the peak force phase immediately preceding the super-imposed twitch (Signal 4.04 software, Cambridge Electronic Design, Cambridge, UK).

4.2.2.4 Measurement of voluntary activation of the knee extensors

Subjects performed three maximal unilateral isometric knee extension trials, of which the one with the highest voluntarily achieved force (prior to the electrical muscle stimulation) was selected for further analysis. Assessing the voluntary activation percentage (VA%) of the quadriceps femoris (QF) muscle group was conducted through delivering electrical stimuli during the maximal unilateral knee extension (described in 4.2.2.1) to the QF using the interpolated twitch technique (ITT).

Four galvanically paired self-adhesive electrodes (6.98 cm Vtrodes, Mettler Electronics Corp, USA) were placed on the proximal and intermediate regions of the quadriceps muscle belly of the right limb. Rectangular single pulses of 1 ms were delivered during rest, and increasing the stimulation intensity in 5 mA increments with a constant-current stimulator (400V, Model DS7AH, Digitimer, UK) until a plateau in the stimulation-induced force occurred. An additional 25 % intensity was added to the current which was observed to produce maximum twitch force during rest in order to ensure maximal effect during the knee extension. Supra-maximal single-pulse electrical stimuli were manually delivered to the muscle three separate times during each trial: 3 s before voluntary knee extension (at rest), during the plateau of maximal voluntarily exerted force (super-imposed twitch) during knee extension and 5 s after the end of the contraction (Merton 1954).

The voluntary activation percentage was calculated using the formula $VA\% = (1 - (P_{ts} / P_t)) \times 100$, in which P_{ts} represents the amplitude of twitch elicited by the electrical stimulation on top of the voluntary contraction and is divided by P_t, the control twitch delivered to the resting muscle 5 s after the maximal voluntary contraction (Bellemare & Bigland-Ritchie 1984). The same member of staff was always conducting the stimulation procedure.

4.2.3 Cardiorespiratory performance

Maximal oxygen uptake, maximal aerobic power and metabolic thresholds were determined for all subjects during a maximal endurance loading conducted on a cycle ergometer (Ergometrics 800, Ergoline, Bitz, Germany) utilizing a graded exercise protocol. The test was initiated for each subject at a load of 50 W, with 25 W increments applied every 2 min until volitional exhaustion. The subjects were asked to keep the pedaling frequency at 70 revolutions per minute (rpm) throughout the test, with the current rpm being visible throughout the test. When the participants failed to keep up the required rpm for longer than 15 s, the test was terminated. Verbal encouragement was provided throughout the test. The Borg Rating of Perceived Exertion (RPE)-scale was used at the end of each stage to monitor the subjective level of exhaustion. Heart rate was measured throughout the test (Polar S410, Polar Electro Oy, Kempele, Finland).

4.2.3.1 Maximal oxygen uptake and metabolic thresholds

Oxygen uptake was determined continuously, breath-by-breath, with a gas analyzer (Oxycon Pro, Jaeger, Hoechberg, Germany). Maximal oxygen consumption (VO2max) was averaged over each 60 s period during the test. The VO2-value from the last complete minute during the test was defined as VO2max. The aerobic and anaerobic thresholds were determined individually for each subject based on the deflection points in the curves of ventilation, oxygen consumption, production of carbon dioxide and blood lactate (Aunola & Rusko 1986).

4.2.3.2 Maximal power output

Maximal power output (Wmax) during the test (I, II) was calculated using the equation $W_{max} = W_{com}+(t/120)*25$, where W_{com} was defined as the load of the last completed stage and t the time of the last incomplete stage (Kuipers et al. 1985). Blood sampling

4.2.3.3 Serum hormone and creatine kinase concentrations

Venous blood samples were drawn to determine resting and acute concentrations of total testosterone (T), cortisol (C) growth hormone (GH, 22 kDa) and creatine kinase (CK) (I). In addition, concentrations of sex-hormone binding globulin (SHBG) and T/C and T/SHBG -ratios (I) were determined in a fasted state on the morning of the loading (I). Blood was drawn by a laboratory technician from the antecubital vein into a serum tube (Venosafe, Terum Medical Co, Leuven, Belgium). Samples were centrifuged for 10 min at 3500 rpm, after which serum was removed and frozen until analyzed. Hormones were analyzed with a chemical luminescence technique (Immulite 1000, Siemens, New York, USA) using hormone-specific immune-assay kits (Siemens, New York, USA). Creatine kinase (CK) was analyzed using chemical analysis (KoneLab 20 XTi, Thermo Fisher Scientific Oy, Vantaa, Finland). Sensitivities for T, C, GH, SHBG and CK were 0.5 $\text{nmol}\cdot\text{l}^{-1}$, 5.5 $\text{nmol}\cdot\text{l}^{-1}$, 0.03 $\text{mlU}\cdot\text{l}^{-1}$ and 0.02 $\text{nmol}\cdot\text{l}^{-1}$ and 0.7 mlU·l-1, respectively. Intra-assay coefficients of variation for T, C, GH and SHBG were 9.8 ± 3.9%, 7.1 ± 1.1%, 6.0 ± 0.5%, 3.1 ± 1.3%, and 1.5 ± 0.7%, respectively. Inter-assay coefficients of variation for T, C, GH, SHBG and CK were 12.0 ± 6.3%, 7.9 ± 1.2%, 5.8 ± 0.3%, 5.0 ± 1.0% and 3.6 ± 0.8%, respectively.

Serum hormone concentrations were not corrected for changes in plasma volume, but in order to monitor acute hemoconcentration (Dill & Costill 1974) in paper I, hemoglobin (HGB) and hematocrit (HCR) were analyzed with Sysmex KX 21 N (Sysmex America Inc., Mundelein, IL, USA) automated hematology analyser with a cyanide-free and cumulative pulse height detection method, respectively.

Due to recent reports having shown minimal influence of the menstrual cycle phase on anabolic hormone responses following strength (Timon et al. 2013) and endurance exercise (O'Leary et al. 2013), the loading sessions were conducted across several phases of the menstrual cycle. Seven subjects from the DD, four subjects from the ES and three subjects from the female SE groups reported oral contraceptive use and were excluded from the analyses of SHBG and T/SHBG-ratios.

4.2.3.4 Blood lactate concentration

To determine blood lactate (La) concentrations in article I, capillary blood samples were taken from the fingertip before, during and after the experimental loading into a reaction tube containing an anti-coagulant and hemolyzing agent. The samples were analyzed using a Biosen lactate analyzer (S-line Lab+ EKF, Magdeburg, Germany).

4.2.3.5 Blood lipids

Blood samples were drawn from the antecubital vein at 7:00-9:00 following a 12h overnight fast to obtain concentrations of total cholesterol (Chol_{tot}), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglycerides. Strenuous physical activity was not permitted during the 48 h preceding blood drawing. Blood samples were drawn by a laboratory technician from the antecubital vein into serum tubes (Venosafe, Terumo Medical Co., Leuven, Hanau, Belgium) adhering to standard laboratory procedures. Serum samples were stored for 10 min before being centrifuged at 3 500 rpm (Megafure 1.0 R, Heraeus, Germany) followed by immediate spectrophotometry analyzes

(Konelab 20XTi, Thermo Fisher Scientific, Vantaa, Finland). The Friedewald equation was used for estimating concentrations of LDL: LDL = total cholesterol - HDL-C - (triglycerides/2.2) (Friedewald, Levy & Fredrickson 1972).

4.2.4 Body composition

4.2.4.1 Lean and fat mass

Body composition was assessed by Dual-Energy X-ray Absorptiometry (DXA) (Lunar Prodigy Advance, GE Medical Systems, Madison, USA) (III). The DXA-scans were performed in the morning following a 12 h fast. Leg position was fixed throughout the scan with adhesive fabric around the knees and ankles. Arms were aligned along the trunk with the palms facing the thighs. Lean and fat mass were automatically analyzed (Encore-software, version 14.10.022). To analyze lower body fat (Fat_{lower}) and lean mass ($Lean_{lower}$), a region of interest (ROI) was created by separating the legs from the trunk by a horizontal line directly above the iliac crest. This adjustment was undertaken in order to include the gluteal area in the analysis. Total body and arm fat (Fat_{tot}, Fat_{arms}) and lean mass ($Lean_{tot}$, $Lean_{arms}$) as well as android fat mass (Fat_{andr}, centrally located fat mass) (Hind, Oldroyd & Truscott 2011) were obtained for each of the regions through the manufacturer's pre-defined ROI's.

4.2.4.2 Muscle cross-sectional area

Cross-sectional area (CSA) of the vastus lateralis muscle of the right limb was measured using a panoramic imaging technique with a B-mode axial-plane ultrasound device (SSD-a10, Aloka, Tokyo, Japan) (Ahtiainen et al. 2010). Images were taken at 50% and 70% of the femur length, i.e. the distance between the greater trochanter and the joint space on the lateral side of the knee. With the subject lying in a supine position, a 10 MHz linear-array probe was moved across the thigh in the medial-lateral direction. Leg position was fixed using a custom made support. Lines perpendicular to the measurement table were drawn across the thigh to ensure straight probe alignment and movement. Three images were taken at both 50% and 70% of the muscle length. Images were analyzed using ImageJ -software version 1.44 (National Institute of Health, USA) by manually outlining the muscles. The mean of the two closest values of 50% (as reported in paper II in men, with the same method applied to all groups in women) and the mean of the two closest values of 50% and 70%, respectively (as reported in paper I one from the ES and SE women, with the same method applied to DD women and all male groups), were averaged and used in the statistical analyses to assess total CSA.

4.2.5 Nutrition

Prior to the start of the study, all subjects received written and verbal nutritional recommendations according to the national guidelines. Subjects were asked to maintain a consistent dietary intake throughout the intervention. Nutritional intake was quantified as amount of energy consumed (MJ) and controlled through food diaries which were filled in by the participants for three consecutive days at weeks 0, 12 and 24. Energy intake was analyzed with a nutrient analysis software (Nutriflow, Flow-team Oy, Finland) based on the food diaries.

4.2.6 Questionnaires

Participants filled in all questionnaires both at baseline and after the 24-week training intervention. The questionnaires were filled in at the laboratory facilities following verbal instructions from a member of research staff. Men and women were pooled together group wise. The ES and SE subjects were combined to form one group (SS), due to the organizational nature of the training.

Self-esteem. The Rosenberg Self-esteem survey (Rosenberg et al. 1995) was used to assess self-esteem. The scale consists of ten statements related to general feelings about one's own self-image. Statements were responded to on a 1-4 scale: 1 - Strongly agree (3 points), 1 – Agree (2 points), 2 – Disagree (1 point), 3 - Strongly disagree (0 points). Negatively worded items (5 items) were reverse-scored. The sum of all items resulted in the self-esteem score, thus resulting in a 0-30 scale with a higher score representing better self-esteem. Scores between 15 and 25 are within normal range, while scores below 15 imply low self-esteem and above 25 high self-esteem.

Health-related Quality of Life. The Finnish version of a 36-item general health survey, RAND36 (Aalto, Aro & Teperi 1999) was used to assess the participants' health-related quality of life (HRQoL). The RAND36 is a well-validated questionnaire encompassing eight subscales (dimensions) of health: physical functioning, social functioning, role limitations because of physical functioning, role limitations because of emotional functioning, mental health, vitality, bodily pain, and general health perception. All scores within each dimension were converted to a scale of 0-100, with a higher score implying better health in the given dimension.

Time management behavior. Subjective time management behavior strategies (TMB) were assessed using selected items from a modified time management behavior questionnaire (Macan 1994), with 8 statements relating to time management and its link to exercise training. Statements were responded to on a 1-5 LIKERT scale (Likert 1932): 1 - Strongly disagree, 2 - Disagree, 3 - Neither agree nor disagree, 4 – Agree, 5 - Strongly agree. Statements were scored according to the scale. Negatively worded items (3 items) were reverse-scored. The mean of the scores of the individual questions resulted in the total TMB score. The total score as well as all questions were compared individually between groups. A higher score indicated a perception of better time management. The list of questionnaire items was as follows, with ^{o} indicating a reverse-scored item:

1. My training regimen leaves me sufficient time to rest.
2. My training regimen leaves me sufficient time for other leisure-time activities
3. My training regimen leaves me sufficient time for my family/friends.
4. I am having difficulties combining my training regimen with other aspects of my life. ^{o}
5. I am able to manage my time.
6. I have considered quitting my training regimen due to a lack of time. ^{o}
7. My training regimen makes me busy. ^{o}
8. I can usually focus well on my training regimen.

Fatigue and wellbeing. Subjectively perceived wellbeing and general fatigue were assessed on a 100-mm visual analog scale (VAS) (Dixon & Bird 1981) with a higher number representing a poorer subjective feeling.

4.3 Acute loading sessions

The experimental loading was intended to reflect the content of the 24-week training program, consisting of both endurance cycling and a dynamic leg press protocol. Loadings were conducted for each subject at the same time of day (±1h) at Week 0 and 24 and were performed in the same order as the training. Measurements of force and hormone responses during the loading were conducted before the initiation of the loading ("Pre"), after the first part ("Mid": E or S, respective to order) and after the complete loading ("Post") FIGURE 8. Recovery was monitored 24±1h and 48±1h after the cessation of the loading protocol ("24h" and "48h", respectively) (FIGURE 8). At Mid and Post subjects proceeded from the experimental exercise without any pause to perform an isometric leg press action to evaluate fatigue, after which blood was immediately sampled. Subjects were verbally encouraged throughout the loadings. Proper hydration on the day preceding the loading was encouraged. Consumption of 0.2 l of water was allowed between the two loading modes, after the "Mid" blood sample was taken.

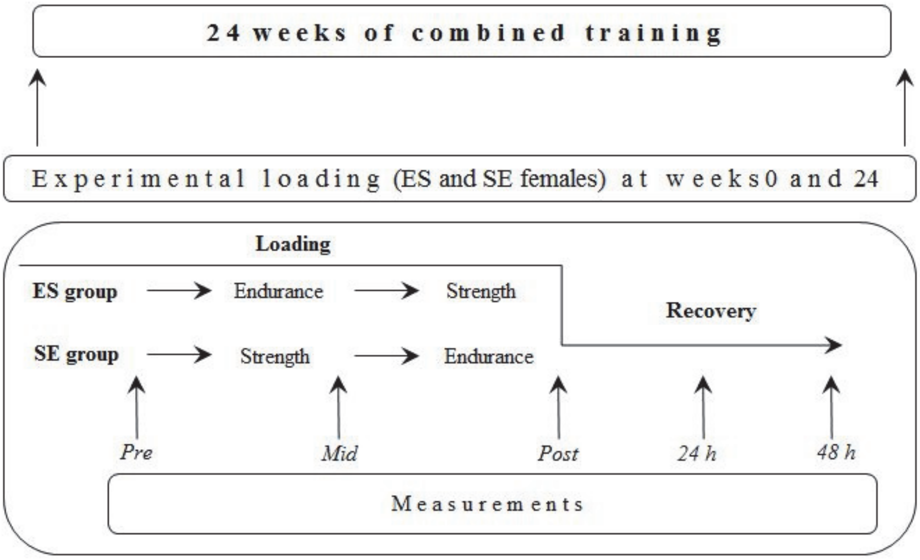

FIGURE 8 Overview of the experimental loading design to investigate acute responses of the ES (endurance preceding strength) and SE (strength preceding endurance) loadings in women. Pre = prior to starting the loading, Mid = between the exercise modes (after E or S for ES and SE, respectively), Post = immediately after the complete loading, 24h = after 24 hours of recovery, 48h = after 48h of recovery.

4.3.1 Strength loading

A David 210 weight-stack horizontal leg press (David Health Solutions Ltd., Helsinki, Finland) was used to conduct the strength loading. A detachable handle was available for assisting if necessary. The loading consisted of three protocols typically used in training for explosive strength (3x10 repetitions at 40% 1RM with 3 min rest between sets), maximal strength (4x3 repetitions at 75-90% 1RM with 3 min rest between sets) and muscle hypertrophy (4x10 repetitions at 75-80% 1RM with 2 min rest between sets). The loads were based on the 1 RM which was obtained during the basal measurements (see 4.2.2.2). In order to complete a true repetition maximum and standardize the loading conditions, additional resistance was added to at least one maximal and one hypertrophic set. In the explosive sets, subjects were instructed to perform the concentric phase as rapidly as possible and the eccentric phase in a controlled manner, without pausing between repetitions. For the hypertrophy and maximal sets, subjects were instructed to perform a full leg extension without locking knees. An even pace was kept throughout each of the repetitions in a set.

4.3.2 Endurance loading

The endurance loading consisted of 30 minutes of continuous cycling at an intensity of 65% W_{max} (Schumann et al. 2013) and was carried out on an electric resistance Monark cycling ergometer (Ergomedic 839E, Monark Exercise AB, Vansbro, Sweden). The intensity was based on W_{max} obtained during the basal measurements. Subjects were required to keep the pedaling pace at 70 revolutions per minute (rpm). The rpm was visible to the subjects throughout the loading and was additionally monitored by a member of staff. If the rpm dropped to 65 with the subject being unable to immediately increase it back to 70, the workload was lowered by 15W. If the subject was unable to keep up the pace for a full minute after the reduction, the intensity was further decreased by 15W. If necessary, the procedure was repeated until the subject could keep up the required pace and was able to complete the loading.

4.3.3 Measurements during the loading

4.3.3.1 Isometric force

Maximal isometric force production (MVC) of bilateral leg press was measured as described earlier (see 4.2.2.1). During the measurements at Pre, 24h and 48h subjects performed three trials with 1 min rest between. At Mid and Post subjects proceeded to the measurement and performed two trials with only ca 10s rest between for the purpose of recording exercise-induced fatigue. At all time points, the trial with the highest force was selected for analysis. Trials were analyzed for MVC and average force produced between 0 and 500 ms (MVC_{500}).

4.3.3.2 Blood lactate and serum hormones

To determine blood lactate concentrations, capillary blood samples were taken from the fingertip at Pre, Mid and Post as described earlier (see 4.2.3.4). In addition, venous blood samples were drawn at Pre, Mid, Post, 24h and 48h for determination of concentrations of T, C and GH. In addition, concentrations of the same hormones as well as sex-hormone binding globulin (SHBG) and T/C and T/SHBG –ratios at rest were determined on the morning of the loading (7:00-9:00 am) after a 12 h fast.

4.4 Training programs

The training program was designed to reflect recommendations for physically active individuals (Thompson et al. 2010). The 24-week training intervention was divided into two 12-week periods (Weeks 0-12 and Weeks 13-24). During weeks 0-12, all same-session combined subjects completed two weekly “double” sessions in their assigned order (i.e. either 2x[1E+1S] or 2x[1S+1E]).

During weeks 13-24 the training frequency was increased to five training sessions per two weeks (five sessions of [1E+1S] or [1S+1E], i.e. alternating weeks of 2 and 3 combined sessions). A break of 5-10 min was always allowed between the two training modes (S or E). The DD group adhered to the same training program, training S and E on alternating days. Thus, the DD-group completed four training sessions per week during weeks 0-12 (i.e. separate 2 S and 2 separate E sessions per week) and ten sessions per two weeks during weeks 13-24 (i.e. alternating weeks of [2S and 2E] and [3S and 3E].

All training sessions supervised by research staff to ensure completion and adherence to as well as proper execution of the training program. The subjects were encouraged to maintain normal daily activities but instructed to abstain from strenuous strength or endurance training in addition to that prescribed by the research.

4.4.1 Strength training

Strength training was performed for all major muscle groups focusing on knee extensors, hip extensor and knee flexors. The training program was initiated with circuit training (as general, preparatory training) and progressing through hypertrophy-inducing training towards maximal strength training (TABLE 4). The periodization for the extensors and flexors of the arms followed a similar pattern. In addition, exercises for the trunk were included in all strength sessions. The lower body exercises were performed with weight-stack devices while dumbbells and cable pulley machines were used for upper body exercises. Trunk exercises were performed both with machines as well as body weight. The periodization was repeated during weeks 13-24 with increased training intensity and volume. The duration of each strength session was 50-60 min.

4.4.2 Endurance training

The endurance training sessions were carried out on a magnetic resistance cycle ergometer. Training intensities were controlled by heart rate zones corresponding to the threshold values of the aerobic (AT) and anaerobic thresholds (AnT). During weeks 1-7 and 13-16 the training consisted of 30-45 min continuous cycling near the AT and progressed to interval training at and above AnT from weeks 8 and 17 onwards (TABLE 5). Thresholds were re-evaluated after week 12 and applied to the training during weeks 13-24. The duration of each endurance training session was 30-50 min.

TABLE 4 Strength training details for the lower extremities during the 24-week training intervention.

Weeks	**1-3**	**4-7**	**8-12**	**13-14**	**15-16**	**17-20**	**21-24**
Load	40-80%	70-85%	80-95%	40-60%	65-80%	80-85%	80-95%
Sets	2-3	2-3	3-5	3	2-3	2-4	2-5
Reps	10-20	10-15	3-10	12-20	10-12	8-10	3-10
Rest	None	1.5-2 min	1-3 min	None	1.5-2 min	1.5-2 min	2.5-3 min
				Exercises			
LP	Bilateral	Bilateral	Bilateral*	Bilateral	Bilateral	Bilateral	Bilateral*
KE	Bilateral	Bilateral	Unilateral	Bilateral	Bilateral	Bilateral	Unilateral
KF	Bilateral	Bilateral	Unilateral	Bilateral	Bilateral	Bilateral	Unilateral

*Explosive repetitions with a load of 40% in three training sessions (out of four) during weeks 11-12 and three sessions (out of five) during weeks 23-24, Load = % of estimated 1 RM, Reps = Repetitions per set, Rest = rest between sets and exercises, LP = leg press, KE = Knee extension, KF = Knee flexion.

TABLE 5 Endurance training details during the 24-week training intervention.

Weeks	**1-3**	**4-7**		**8-9**		**10-11**		**12**
Session	**I & II**	**I**	**II**	**I**	**II**	**I**	**II**	**I & II**
Intensity	<AT	<AT, >AT	<AT	<AT, ~AnT	<AT, >AT	>AT, >AnT	<AT, >AT >AnT	>AT>AnT
Mode	cont	cont	cont	int	cont	int	int	int
Duration	30	30	45	45	50	45	45-50	35-45

Weeks	**13-14**	**15-16**		**17-20**		**21-23**	**24**
	I & II	**I**	**II**	**I**	**II**	**I & II**	**I & II**
Intensity	<AT, >AT	~AT, <AnT	~AT	<AT, ~AnT	~AT, >AT	>AT >AnT	<AT, >AnT
Mode	cont	cont	cont	int	cont	int	int
Duration	40-45	30-35	30-45	25-45	30-50	35-50	25

I = First endurance session of the week, II = second endurance session of the week, Duration = session duration in minutes, AT= Aerobic threshold, AnT = Anaerobic threshold, < stands for 5-10 bpm below, > stands for 5-10 bpm above and ~ stands for at the threshold (±5 bpm), cont = continuous cycling, int = interval cycling

4.5 Statistical analysis

Data is presented as means ± standard deviations (SD) (I-III) and confidence intervals (CI 95%) (IV). All statistical analyses were carried out with IBM SPSS Statistics software (v. 20.-24, IBM Corporation, Armonk, New York, USA). Normality was checked using the Shapiro-Wilk test as well as through observing the Q-Q-plots.

In paper I, changes during the experimental loadings at Week 0 and 24 were analyzed with a five-level ANCOVA (i.e. Pre, Mid, Post, 24h and 48h) with absolute values for within-group changes and values relative to Pre for between-group differences. The Pre-values were used as covariates. In variables were a non-normal distribution persisted even after a log transformation, non-parametric statistics were used both for the within-group changes (Wilcoxon signed-rank test) and between-group comparisons (Mann-Whitney U-test). For the non-parametric tests a Bonferroni adjustment was applied by multiplying the pairwise p-values with the number of comparisons. Paired sampled t-tests were utilized for comparisons of experimental loading-induced within-group changes (i.e. Mid, Post, 24h and 48h) by comparing each loading time point with its corresponding value across 24 weeks.

Training-induced changes in basal hormones and basal measurements of 1 RM, W_{max} and CSA were analyzed with a two-way ANCOVA with baseline-values used as covariates, and between-group differences with an independent-samples t-test.

In papers II and III, normally distributed data was analyzed for within-group (time) changes with a repeated measures analysis of variance (ANOVA) using absolute values. Differences between the training modes (time×training) were analyzed using repeated measures ANCOVA with absolute values for main effects (II, III) and a One-Way ANOVA with absolute and relative changes for pairwise comparisons. Bonferroni post-hoc adjustments were used where appropriate. Non-normally distributed data was log-transformed to achieve normality and subsequently analyzed as described above.

All non-normally distributed data as well as all data in paper IV were analyzed as follows: within-group changes were analyzed using two-related samples Wilcoxon t-test and between-group differences with independent-samples Mann-Whitney U-test. The eight dimensions of RAND36 were analyzed separately. In RAND36, TMB and VAS a Bonferroni correction was applied for both within- and between-group comparisons by multiplying the pairwise p-values with the number of comparisons (i.e. the number of dimensions and questions, respectively).

The reported effect sizes are Cohen's d (difference of the means divided by the pooled SD), except for non-normally distributed data, where the effect size was defined as Z-score/$\sqrt{n}$. An effect size of ≥0.20 was considered small, ≥0.50 medium, and ≥0.80 large (I, II, III). The reported correlations are bivariate Pearson correlation coefficients (r) (I, II, III) and Spearman's rank correlation coefficients (r_s) for non-normally distributed data (I). The levels for significance were set at $p \leq 0.05$, $p \leq 0.01$ and $p \leq 0.001$ and a trend was accepted at $p \leq 0.06$.

5 RESULTS

5.1 Training adherence, nutritional intake and baseline performance

The training adherence in men was 99±2%, 99±2% and 100±1% in ES, SE and DD, respectively, and in women 98±4%, 99±2% and 99±2% in ES, SE and DD, respectively. Total self-reported energy intake (expressed in MJ) at week 0, 12 and 24 in men were as follows 9.3±1.8, 10.2±2.6 and 9.5±2.6 for ES; 9.4±2.0, 9.3±1.7 and 7.9±1.7 for SE; 8.4±2.3, 9.0±1.4 and 9.2±1.6 in DD, respectively. Total energy intake was in women 8±1.2, 7.8±1.8 and 8.2±2.1 for ES; 7.6±1.2, 7.7±1.6 and 7.1±2.1 for SE; 7.0±1.9, 6.9±1.6 and 7.0±1.8 for DD, respectively. The self-reported food energy intake did not significantly change in any of the groups over the intervention period. The baseline values of the strength and endurance performance variables as well as muscle cross-sectional area are presented in TABLE 6.

TABLE 6 Baseline performance and muscle cross-sectional area. 1 RM = maximal leg press strength, MVC = maximal bilateral isometric leg press force, VO_{2max}= maximal oxygen uptake, W_{max} = peak power output during maximal cycling, CSA50% = Vastus Lateralis cross-sectional area at 50% of femur length. DD = Different-day training, ES = Same-session training, endurance followed by strength, SE = Same-session training, strength followed by endurance

	WOMEN			MEN		
	DD (n=18)	**ES** (n=17)	**SE** (n=15)	**DD** (n=21)	**ES** (n=17)	**SE** (n=18)
1 RM (kg)	88±12	102±22 [*]	99±18	142±24	157±30	143±23
MVC (N)	1341±265	1610±302	1700±668	2332±590	2653±683	2338±540
VO_{2max} (ml/min/kg)	28±5	31 ± 4	34±5 *	36±7	42±7 *	43±7 *
W_{max} (W)	155±25	170±26	182±28 *	233±30	268±39 *	245±35
CSA50% (cm^2)	17±2	18±3	21±4 *	22±4	27±4 *	26±4

*indicates difference to same-gender DD.

5.2 Acute responses to combined loadings in women

5.2.1 Body weight, hemoglobin and hematocrit

No significant acute changes in body weight, HGB or HCR were observed during the loading at week 0 (body weight -0.3±0.3%, HGB +3.6±3.0%, HCR +2.6±2.9%) or week 24 (body weight -0.5±0.2%, HGB +4.2±3.8% or HCR +4.4±2.9%).

5.2.2 Isometric force and rapid force production

Week 0. MVC decreased significantly during the loading in both groups by Mid (ES -18±13% from 1740±235 N, P<0.01, effect size -1.305; SE -17±7% from 1810±633 N, P<0.01, effect size -0.515) and by Post (ES -20±11%, P<0.001, effect size 1.587; SE -18±5% P<0.001, effect size -0.532) (FIGURE 9). MVC$_{500}$ decreased significantly in ES by mid (-18±12%, p<0.01, effect size -1.24) and post (-20±14%, P<0.01, effect size -1.15) and for SE by post (-16±7%, P<0.05, effect size -0.611). No significant differences of MVC or MVC$_{500}$ to Pre were observed in either ES or SE at 24h or 48h.

Week 24. MVC decreased significantly for both groups by Mid (ES -16±9% from 1833±322 N, P<0.001, effect size -0.890; SE -21±8% from 1966±690 N, P<0.001, effect size -0.623) and by Post (ES -24±6%, P<0.001, effect size -1.66; SE -22±8%, P<0.01, effect size -0.731) (FIGURE 9). MVC$_{500}$ decreased significantly for both groups by Mid (ES -18±17% P<0.05, effect size -0.683 and SE -20±12%, P<0.05, effect size =-0.678) and post (ES -24±6%, P<0.001, effect size -1.43 and SE -25±23% P<0.05, effect size -0.637). Both groups recovered significantly (P<0.05-0.001) from Post to 24h and 48h. No between-group differences were observed during loading or recovery.

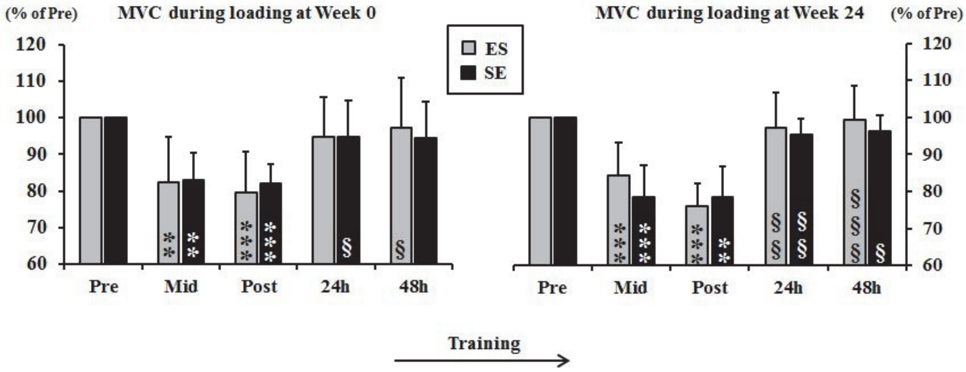

FIGURE 9 Acute mean (SD) changes (%) in maximal isometric force (MVC) for ES and SE during loading and recovery at weeks 0 and 24. Within-group differences: *significant from Pre, §significant from Post. **P< 0.01, ***P<0.001, §P<0.05, §§P<0.01, and §§§P<0.001. ES=same-session training endurance followed by strength, SE=same-session training, strength followed by endurance.

5.2.3 Serum hormone concentrations, lactate and creatine kinase

5.2.3.1 Serum hormone concentrations

Week 0. A significantly elevated T concentration was observed in ES at Mid (from 0.5±0.4 to 8.9±1.1 nmol·l^{-1}, $P<0.05$, effect size 0.513) (FIGURE 10). C concentrations remained statistically unaltered throughout the loading for both groups (TABLE 7). A trend ($P=0.051$, effect size 0.256) was observed in C for the ES group at Mid. C was significantly lowered from Pre for SE at 24h (-29±23%, $P<0.01$, effect size -1.53) and 48h (-29±14% $P<0.01$, effect size -1.70). GH was increased 5.6-fold at Mid in comparison to Pre for ES ($P<0.05$, effect size 0.888) and 5.2-fold at Post for SE ($P<0.05$, effect size 0.830) (FIGURE 11). A trend for significance was observed in SE between Mid and Post in GH ($P<0.06$, effect size 0.402). The Mid-Post change in GH was significantly different between groups ($P<0.001$) with a decrease in ES and trend for increase in SE.

Week 24. T concentrations were significantly elevated for ES at Mid (from 0.8±0.3 to 1.2±0.4 nmol·l^{-1}, $P<0.05$, effect size 1.247) and SE at Post (from 0.9±0.9 to 1.5±1.2 nmol·l^{-1}, $P<0.001$, effect size 0.536) (FIGURE 10). For SE, T significantly increased from Mid to Post ($P<0.01$, effect size 0.371). C concentration was decreased for SE from Pre at 48h (-28%, $P<0.001$, effect size -0.974) and near-significantly decreased at 24h (-26%, $P<0.06$, effect size -0.8254) in comparison to Pre (TABLE 7). A significant increase in GH was observed for both groups at Mid (ES 7.0-fold from, P<0.01, effect size 0.885 and SE 2.5-fold, P<0.05, effect size 0.790) and at Post for SE (3.6-fold, P<0.05, effect size 0.886) (FIGURE 11). GH decreased for ES between Mid and Post (from 68.3±31.7 to 14.7±11.3 mlU·l^{-1}, P<0.01, effect size -0.885). In GH, a between-group difference was observed at Mid (P<0.01), and the Mid-Post change was significantly different between groups (P<0.001). The GH response in ES was significantly different at Pre-Mid (P<0.01), Pre-Post and Mid-Post (P<0.05) in comparison to the corresponding changes at Week 0 (FIGURE 11).

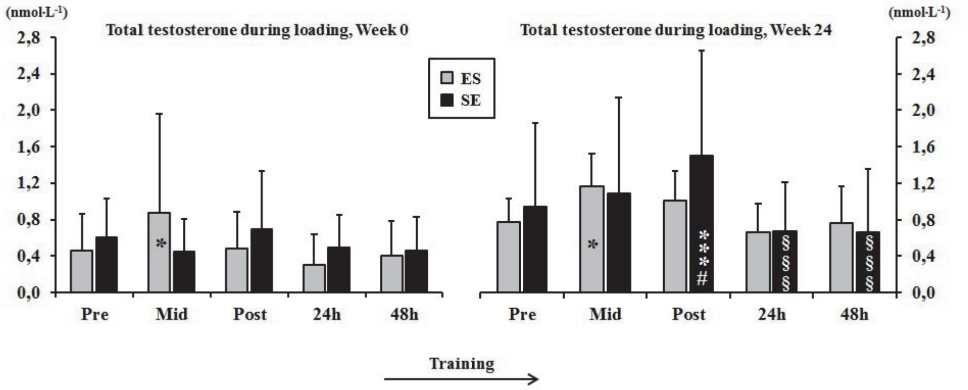

FIGURE 10 Acute mean (SD) responses in total testosterone for ES and SE during the loading and recovery at weeks 0 and 24. Within-group differences: * significant from Pre, # significant from Mid, § significant from Post. *P<0.05, ***P<0.001, #P<0.05, and §§§P<0.001. ES=same-session training endurance followed by strength, SE=same-session training, strength followed by endurance.

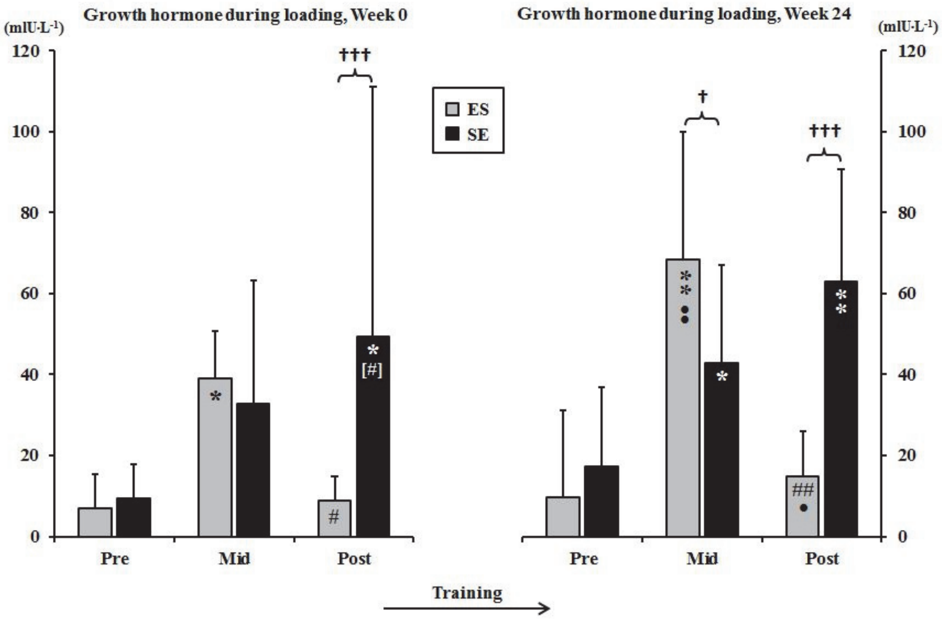

FIGURE 11 Acute mean (SD) responses in growth hormone responses for ES and SE during loading at weeks 0 and 24. Within-group differences: *significant from Pre, #significant from Mid, §significant from Post, ●significant from week 0; †between-group difference at given time point. *P<0.05, **P<0.01, #P<0.05, ## P<0.01, ●P<0.05, ●●P<0.01, †P<0.05, ††P<0.01, and †††P<0.001. ES=same-session training endurance followed by strength, SE=same-session training, strength followed by endurance.

5.2.3.2 Blood lactate and creatine kinase

Week 0. Blood lactate was significantly elevated from Pre in both groups at Mid (ES by 4.2-fold P<0.001, effect size 4.80; SE by 4.0-fold, P<0.001, effect size 2.8) and Post (ES by 5.0-fold P<0.001, effect size 2.84; SE by 4.0-fold, P<0.001, effect size 2.05) (TABLE 7). CK was significantly elevated from Pre in ES at Mid (13±9% from 93±21 mlU·l^{-1}, P<0.01, effect size 0.544), Post (16±9%, P<0.01, effect size 0.681) and 24h (57±32%, P<0.05, effect size 1.73) and for SE at Post (26±17% from 95±31 mlU·l^{-1}, p<0.01, effect size 0.679) but not at 24h (96±89%, effect size 1.29) (TABLE 7). A further increase in CK was observed in both groups between Post and 24h (ES P<0.05, effect size 1.337 and SE P<0.05, effect size 0.935). No between-group differences were observed during loading or recovery.

Week 24. Blood lactate was significantly elevated from Pre in both groups by Mid (ES 5-fold P<0.001, effect size 3.03; SE 6-fold for SE P<0.001, effect size 3.24) and Post (ES 5-fold P<0.001 effect size 4.81; SE 5.5-fold P<0.001, effect size 3.23) (TABLE 7). CK was significantly (P<0.05) elevated from Pre for SE at Mid (14±9%, from 108±72 mlU·l^{-1}, P<0.001, effect size 0.169) and Post (25±17%,

$P<0.01$, effect size 0.299), but not at 24h or 48h (TABLE 7). No between-group differences were observed during loading or recovery. The relative change in blood lactate was significantly larger after 24 weeks of training than the corresponding change at Week 0 for SE during Pre-Mid ($P<0.01$), Pre-Post ($P<0.05$) and Mid-Post ($P<0.05$) (TABLE 7).

TABLE 7 Acute mean (SD) changes in acute serum cortisol (C), creatine kinase (CK) and blood lactate (La) during loading and recovery for ES and SE at Week 0 and 24.

	WEEK 0		**WEEK 24**	
	ES	**SE**	**ES**	**SE**
C (nmol·l^{-1})	(n=10)	(n=10)	(n=8)	(n=10)
Pre	397±128	479±105	413±154	616±178
Mid	437±176	367±139	471±96	567±199
Post	426±207	435±211	423±108	778±252
24 h	312±111[*]	332±87**	284±134	459±200[*]§§
48 h	347±141	333±60**	322±116	445±170***§§§
CK (mIU·l^{-1})	(n=9)	(n=9)	(n=9)	(n=9)
Pre	93±21	95±31	103±44	109±72
Mid	103±19**	106±32	121±49	121±71 ***
Post	105±17**	118±35**+	123±55	131±75 **
24 h	143±36*	181±89§	145±80	148±81
48 h	128±38	132±55¤	141±116	123±70
La (mmol·l^{-1})	(n=12)	(n=11)	(n=12)	(n=11)
Pre	1.1±0.3	1.3±0.3	1.2±0.4	1.1±0.4
Mid	4.7±1.0***	5.0±1.9***	6.3±2.3 ***	6.8±2.4***••
Post	5.6±2.2***	5.2±2.3***	6.5±1.5 ***	6.0±2.1***•

Within-group differences: *=significant from Pre, +=significant from Mid, §=significant from Post, ¤ = significant from 24 h, •=significant from corresponding value at Week 0. *$P<0.05$. **$P<0.01$, ***$P<0.001$, +$P<0.05$, +$P<0.01$, •$P<0.05$, ••$P<0.01$, ¤ $P<0.05$, § $P<0.05$. §§ $P<0.01$, §§§ $P<0.001$. [*] within-group $P<0.06$ to Pre. ES=same-session training endurance followed by strength, SE=same-session training, strength followed by endurance.

5.2.4 Correlations

No significant correlations were observed between the acute changes in testosterone, cortisol or growth hormone and long-term 1RM, W_{max} or CSA development in either ES or SE. Changes in 1 RM or W_{max} or CSA were not correlated with basal levels of T, T/SHBG and T/C.

5.3 Training-induced neuromuscular adaptations

5.3.1 Maximal dynamic strength and isometric force

Dynamic strength. 1 RM significantly increased by week 12 in all groups in men (all $P<0.001$, effect sizes DD 0.620, ES 0.447, SE 0.772) and women (DD $P<0.001$, effect size 1.22; ES $P<0.05$, effect size 0.311; SE $P<0.01$, effect size 0.514) (FIGURE 12). By week 24 the increases were significant in all groups in men (effect sizes DD 0.738, ES 0.619, SE 1.07) and women (effect sizes DD 1.46, ES 0.578, SE 0.914). In women, the increase in 1 RM during weeks 0-12 was larger in DD than in ES ($P<0.01$) and near-significantly larger to SE ($P=0.058$). No significant time×group interactions were observed for any of the experimental groups during training. The changes during weeks 13-24 were significant both in men (effect sizes DD 0.139, ES 0.185, SE 0.293) and women (effect sizes DD 0.214, ES 0.260, SE 0.411).

Isometric bilateral leg extension force. Maximal isometric leg extension force (MVC) increased by week 12 in DD in women (15±9%, $P<0.001$) and all groups in men (DD 7±9%, $P<0.001$; ES 10±10%, $P<0.05$; SE 9±12%, $P<0.05$). The change in MVC was significant during weeks 0-24 in all groups (women: DD 21±13%, $P<0.001$; ES 22±18%, $P<0.001$; SE 12±13%, $P<0.05$; men: DD 11±12%, $P<0.001$; ES 9±13%, $P<0.05$; SE 13±18%, $P<0.05$). The change during weeks 13-24 was significant in DD in men (4±6%, $P<0.05$) and ES in women (13±12%, $P<0.01$). No between-group differences were observed during training.

Unilateral isometric knee extension force. Changes in isometric knee extension force (in men, paper II) between weeks 0–24 were not statistically significant in the DD and ES groups. The SE group increased knee extension force by 14% during 0–24 weeks (from 560±91 N, $P<0.01$, effect size 0.787). There were no significant between-group differences in changes for the experimental groups at any time point.

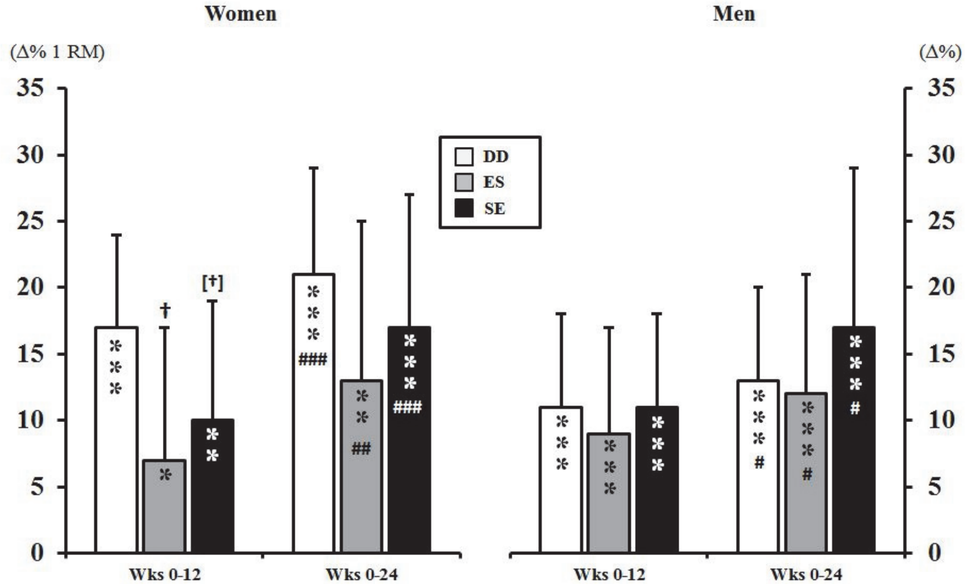

FIGURE 12 Mean (SD) changes (%) in 1RM in women (left) and men (right). *Significant within-group change, # significant within-group change weeks 13-24, † significant difference to same-sex DD. *P<0.05, **P<0.01, ***P<0.001, #P<0.05, ##P<0.01, ###P<0.001, †P<0.05, [†] P=0.058. 1RM, 1-repetition maximum; DD=different-day training, ES=same-session training endurance followed by strength, SE=same-session training, strength followed by endurance.

5.3.2 EMG and voluntary activation (male subjects)

The DD and ES groups increased average maximal VL iEMG during bilateral isometric leg press (at 500–1500 ms) during weeks 0–12 (DD by 26%, p<0.001, effect size 0.824; ES by 24% P<0.01, effect size 0.467). The DD and SE groups increased maximal VL iEMG significantly during weeks 0–24 (DD by 31%, P<0.001, effect size 0.376; SE by 42%, P<0.001, effect size 0.648). The change during 0–24 for ES was not significant. There were no significant between-group differences in changes for the experimental groups at any time point.

No significant change in maximal VL rmsEMG during maximal isometric knee extension was observed in the DD or ES groups at week 24 (FIGURE 13). The SE group experienced a significant (P<0.01, effect size 0.708) increase of 26% during weeks 0–24.

The DD and SE groups increased voluntary activation during weeks 0–12 and 0–24 (DD from 86.6±5.7 to 90.4±4.3%, P<0.01, effect size 0.829; SE from 86.9±8.8 to 91.2±6.9%, P<0.01, effect size 0.489) (FIGURE 13).

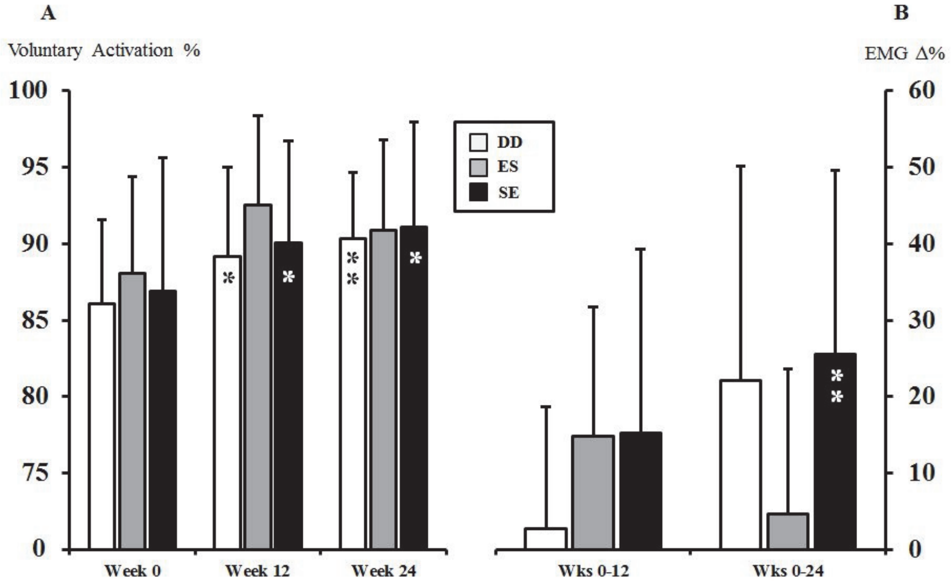

FIGURE 13 Mean (SD) voluntary activation percentage (A) and EMG (B) as measured during maximal knee extension. *=significant from pre. *P<0.05 and **P<0.01. DD=different-day training, ES=same-session training endurance followed by strength, SE=same-session training, strength followed by endurance.

In DD a significant correlation between the individual changes in voluntary activation percentage and changes in knee extension force was found during weeks 13-24 ($r=0.57$, $P<0.05$). A significant correlation was found for the ES group during weeks 0-12 ($r=0.70$, $P<0.01$), weeks 0–24 ($r=0.70$, $P<0.01$) and weeks 13–24 ($r=0.83$, $P<0.001$) (FIGURE 14). In the SE a significant ($r=0.50$, $P<0.05$) correlation between the two variables was observed during weeks 0-12.

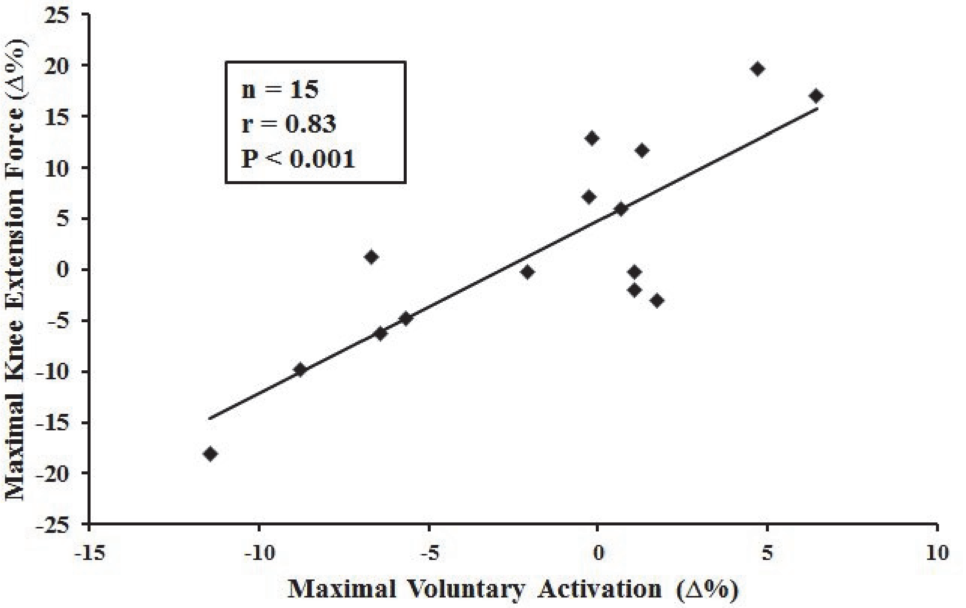

FIGURE 14 Correlation between the individual changes (%) in voluntary activation percentage and changes in knee extension force in the ES group during weeks 13-24.

5.4 Endurance performance and cardiorespiratory adaptations

5.4.1 Maximal power output during cycling

Increased maximal power output in the cycle ergometer test during weeks 0-12 was observed in all groups in men (DD by 14±10%, P<0.001, ES=1.11; ES by 8±9%, P<0.01, effect size; 0.499; SE by 9±7%, P<0.001, effect size 0.621) and in women in DD (16±15%, P<0.01 effect size 1.02) and ES (12±6%, P<0.01 effect size 0.740). The change in SE was not significant (effect size 0.40) All groups increased maximal power output during weeks 0–24 (effect sizes men: DD 1.56, ES 0.832, SE 1.07; women DD 1.20, ES 1.36, SE 1.05) (FIGURE 15A). The increases during weeks 13-24 were significant in all groups (men 5-6% P<0.009-0.001; women 5-9% P<0.05-0.004).

5.4.2 Maximal oxygen uptake (VO_{2max})

Increases in VO_{2max} during weeks 0-12 were significant in men in DD (12±9%, P<0.001, effect size 0.611) and SE (7±8%, P<0.01, effect size 0.388) as well as approaching significance in ES (7±8%, P<0.06, effect size 0.266). In women the increase during weeks 0-12 was significant in DD (16±10%, P<0.001, effect size

0.850) and ES (8±10%, $P<0.05$, effect size 0.348) but not in SE (7±9%, effect size 0.467). All groups increased VO_{2max} during weeks 0-24 (men: effect sizes DD 0.94, ES 0.38, SE 0.40; women effect sizes DD 1.23, ES 0.85, SE 0.67) (FIGURE 15B). The change during weeks 13-24 was significant in DD in men (6±7% $P<0.01$, effect size 0.352) and women DD (8±6%, $P<0.001$, effect size 0.470). There was a trend towards a between-group difference during weeks 0-12 in in men between DD and ES ($P<0.06$) and in women between DD and both same-session groups ($P<0.06$). The increase in VO_{2max} during weeks 0-24 was larger in the DD group in comparison to ES and SE both in men (both $P<0.01$) and women (both $P<0.01$).

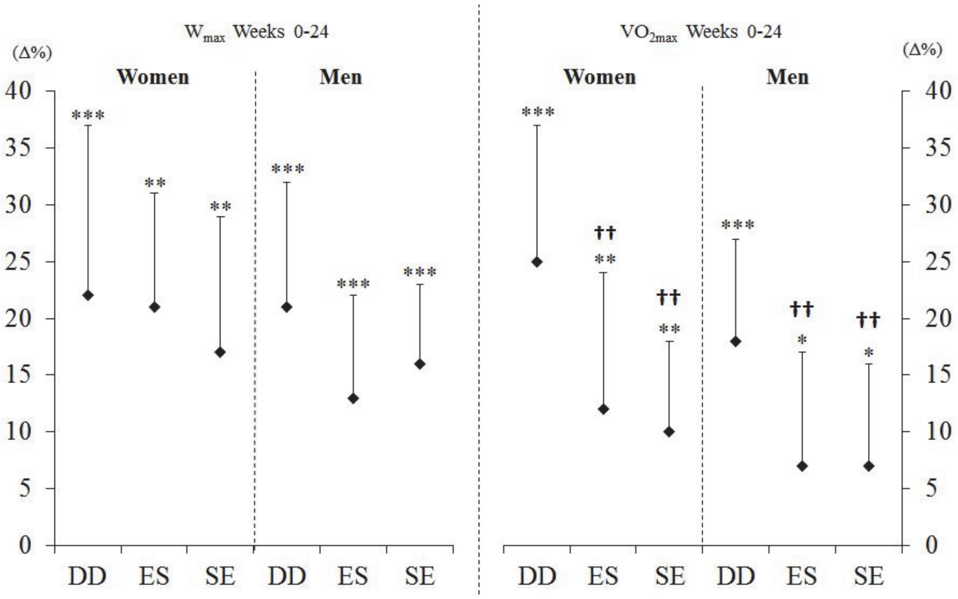

FIGURE 15 Mean (SD) changes (%) in W_{max} (A) and VO_{2max} (B) after training. * significant within-group change 0-24, †significant difference to same-sex DD. *$P<0.05$. **$P<0.01$, ***$P<0.001$, ††$P<0.01$. DD=Different-day training, ES=Same-session training, endurance followed by strength, SE=Same-session training, strength followed by endurance.

5.5 Body composition

5.5.1 Muscle cross-sectional area

Vastus lateralis CSA at 50% of femur length increased after training in all groups during weeks 0-12 in men (effect sizes DD 0.734, ES 0.319, SE 0.527) and in women in DD (effect size 0.913) but not in ES or SE (effect sizes 0.376 and 0.335, respectively) (FIGURE 16). The increase was significant during weeks 0-24 in all groups in men (effect sizes DD 0.928, ES 0.612, SE 0.896) and women (effect sizes DD 1.24, 0.818, SE 0.508). The increase during weeks 13-24 was significant in men in ES (5±6%, effect size 0.258) and SE (6±7%, effect size 0.407) but not in DD (3±9%, effect size 0.197). In women the increase during weeks 13-24 was significant in DD (4±4%, effect size 0.294) and ES (8±6%, effect size 0.497) but not in SE (3±5%, effect size 0.185). No significant between-group differences were observed during the training intervention in either gender.

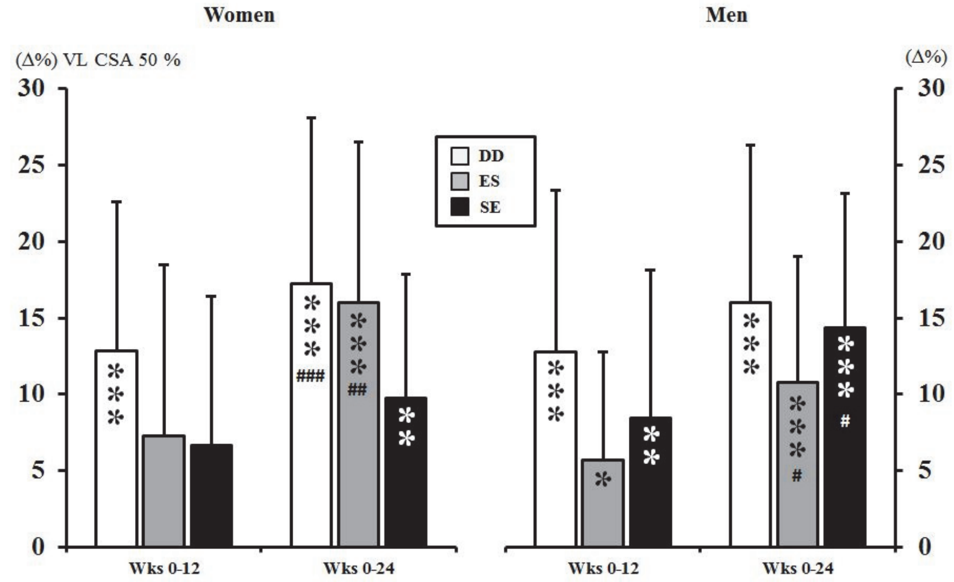

FIGURE 16 Training-induced mean (SD) changes (%) in Vastus Lateralis CSA. *, Significant within-group change during weeks 0–12; # significant within-group change during weeks 13–24. DD, different-day training; ES, same-session training, endurance followed by strength; SE, same-session training, strength followed by endurance.

Vastus lateralis CSA averaged of measurements taken at 50% and 70% of the femur length increased by week 12 in all groups in men (DD 9±5% from 23±3cm^2, P<0.001, effect size 0.737; ES 7±5% from 26±4cm^2, P<0.001, effect size 0.439; SE 8±8% from 25±3 cm^2, P<0.05, effect size 0.589) and in women in DD (11±9% from 15±2cm^2, P<0.001, effect size 0.920) and ES (8±6% from 17±2cm^2, P<0.01, effect size 0.725) but not in SE (6±10% from 19±3cm^2, effect size 0.384). The increases by week 24 were significant in all group in men (all P<0.001: DD 12±6%, effect size 0.952; ES 12±7%, effect size 0.784; SE 14±7%, effect size 1.04) and women (DD 14±10%, P<0.001, effect size 1.25; ES 15±10%, P<0.001, effect size 1.32; SE 10±8%, P<0.01, effect size 0.680). The increase during weeks 13-24 was significant in men in ES (4±5%, P<0.05, effect size 0.328) and SE (5±5%, P<0.05, effect size 0.405) but not in DD (2±6%, effect size 0.193). In women the increase during weeks 13-24 was significant in ES (6±4%, P<0.01, effect size 0.565) and SE (4±5%, P<0.05, effect size 0.305) but not in DD (3±5%, effect size 0.280). A significant difference at week 0 was observed between DD and ES in men and DD and SE in women. No significant between-group differences were observed during the training intervention in either men or women.

5.5.2 Whole body and regional lean mass

Training led to significantly increased total body lean mass in all three training groups in men (effect sizes DD 0.39, ES 0.32, SE 0.35) and women (effect sizes DD 0.55, ES 0.30, SE 0.38) (FIGURE 17). The regional changes in lean mass are presented in Table 3. The change in lower body lean mass was significant ($P<0.05$) in all groups except DD men. Trunk lean mass increased significantly in all groups ($P<0.05$) except in SE-women and ES-men. The change in lean mass of the arms was significant ($P<0.05$) in all groups except ES-women and SE-men. Time×group interactions were not observed in lean mass either in the separated regions or in the total body.

5.5.3 Whole body and regional fat mass

Fat mass decreased in all regions in the DD-groups. No significant changes in ES and SE were found during the training intervention (FIGURE 18 and TABLE 8). In women, significant time×group interactions were observed in Fat_{tot} ($P<0.05$), Fat_{lower} ($P<0.05$) and Fat_{andr} ($P<0.001$). The Fat_{tot} decrease in women was significantly greater in DD than in ES and SE during weeks 0-24 ($P<0.01$ and $P<0.05$, respectively; effect size DD 0.48, ES 0.03, SE 0.09) and weeks 13-24 ($P<0.05$; effect size DD 0.23, ES 0.01, SE 0.04). The decrease in fat_{lower} in DD women was significantly greater than in ES during weeks 13-24 ($P<0.05$; effect size DD 0.25, ES 0.03, SE 0.06) and approaching significance during weeks 0-24 ($P<0.06$; effect size DD 0.43, ES 0.07, SE 0.11). The magnitude of decrease in women in Fat_{andr} was greater in DD in comparison to ES and SE during weeks 0-12 ($P<0.001$ and $P<0.05$, respectively; effect size DD 0.34, ES 0.04, SE 0.07), weeks 0-24 ($P<0.001$ and $P<0.01$, respectively; effect size DD 0.51, ES 0.06, SE 0.06) and weeks 13-24 ($P<0.05$; effect size DD 0.17, ES 0.01, SE 0.0). In men, a significant time×group interaction was noted in Fat_{andr} ($P<0.05$) with the decreases in DD being of greater magnitudes than SE at weeks 0-12 ($P<0.05$; effect size DD 0.18, ES 0.13, SE 0.03), weeks 0-24 ($P<0.01$; effect size DD 0.45, ES 0.27, SE 0.03) and weeks 13-24 ($P<0.010$; effect size DD 0.27, ES 0.14, SE 0.06).

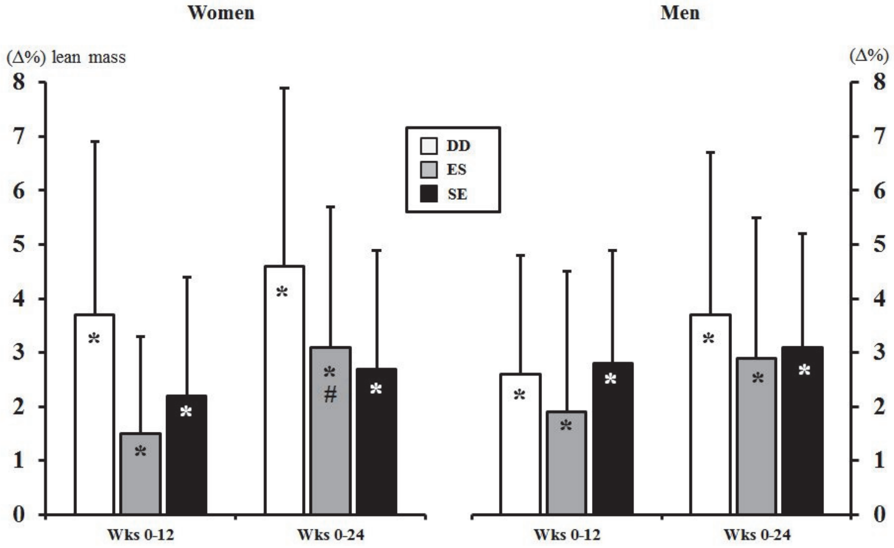

FIGURE 17 Training induced mean (SD) changes in total body lean mass. *, Significant within-group change during weeks 0–12; #, significant within-group change during weeks 13–24. DD, different-day training; ES, same-session training, endurance followed by strength; SE, same-session training, strength followed by endurance.

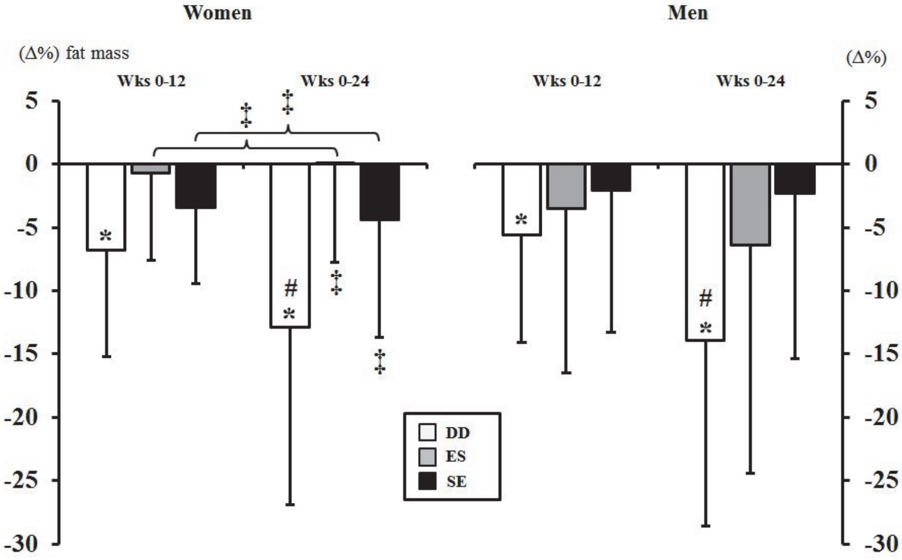

FIGURE 18 Training induced mean (SD) changes (%) in total body fat mass. *, Significant within-group change during weeks 0–12; #, significant within-group change during weeks 13–24; ‡, significant difference to same-session DD. DD, different-day training; ES, same-session training, endurance followed by strength; SE, same-session training, strength followed by endurance.

5.6 Blood lipids

Total cholesterol. Significant changes in total cholesterol were observed following training only in the male ES group (weeks 0-12 and 0-24, both $P<0.05$) (TABLE 9). The change in total cholesterol was significantly different from the same sex DD and SE (both $P<0.05$) groups at weeks 0-12.

HDL, LDL and triglycerides. HDL changed significantly only in DD women (weeks 0-12 and weeks 13-24, both $P<0.001$). Between-group interactions in HDL were observed in men between DD and SE (weeks 0-12 $P<0.01$ and weeks 13-24 $P<0.05$). Favorable changes in LDL were found in the male ES group (weeks 0-12 $P<0.05$) and triglycerides (weeks 13-24 $P<0.05$).

TABLE 8 Training induced mean (SD) changes (%) in body composition.

	Women			Men		
Weeks	**0-12**	**0-24**	**13-24**	**0-12**	**0-24**	**13-24**
Lean$_{\text{tot}}$						
DD	4±3***	5±3***	1±3	3±2***	4±3***	1±2
ES	1±2*[‡]	3±3***	2±2*	2±3*	3±3***	1±2
SE	2±2**	3±2***	1±3	3±2***	3±2***	0±2
Lean$_{\text{arms}}$						
DD	3±4*	3±4*	0±4	3±3***	5±4***	1±3
ES	2±4	2±4	0±5	1±3	3±4*	2±6
SE	3±4*	3±3**	0±4	2±3	3±4	1±4
Lean$_{\text{lower}}$						
DD	3±2 ***	4±2***	1±2	2±3*	2±4	0±2
ES	2±2[*]	3±3**	2±1**	2±3*	4±3***	1±2
SE	2±3*	3±2***	1±3	3±3***	4±3***	0±2
Lean$_{\text{trunk}}$						
DD	5±7	6±8*	1±7	3±3**	3±5	0±5
ES	1±4	4±6*	3±5	2±5	3±4*	1±4
SE	3±4[*]	3±6	0±6	4±4**	3±3*	-1±3
Fat$_{\text{tot}}$						
DD	-7±8*	-13±14**	-7±9*	-6±9**	-14±15***	-9±10***
ES	-1±7 [‡]	0±8‡‡	1±5‡	-3±13	-6±18	-3±11
SE	-3±6	-4±10‡‡	-1±7‡	-2±11	-2±13‡	0±11‡
Fat$_{\text{arms}}$						
DD	-5±9	-11±15*	-6±11	-3±9	-9±17*	-6±13
ES	-1±11	0±10	2±13	0±13	-5±15	-5±11
SE	1±9	-6±9	-6±10	1±12	-2±16	-2±15
Fat$_{\text{lower}}$						
DD	-5±8	-10±13*	-7±8*	-5±8*	-12±14**	-7±9**
ES	-1±7	-1±8[‡]	-1±4‡	-2±13	-5±16	-3±11
SE	-2±5	-4±9	-1±7	-3±11	-4±12	0±10
Fat$_{\text{android}}$						
DD	-11±10 **	-17±15**	-7±10*	-7±10*	-18±14***	-13±10***
ES	2±10 ***‡	3±8‡‡‡	2±8‡	-5±15	-9±21	-4±13
SE	-3±12 *‡	-4±15‡‡	-1±9‡	1±12‡	0±15‡‡	-1±12‡‡

*Significant within-group change. ‡ Significant difference to same-sex DD. *, **, *** p<0.05, <0.01 and <0.001, respectively. ‡, ‡‡, ‡‡‡ p<0.05, <0.01 and <0.001, respectively. [*] p<0.06 for within-group change, [‡] p<0.06 to same-session DD. DD, different-day training; ES = endurance followed by strength; SE = strength followed by endurance

TABLE 9 Blood lipid concentrations (mean±SD, absolute values of $mmol \cdot l^{-1}$).

	Women			Men		
	0	**12**	**24**	**0**	**12**	**24**
Chol$_{tot}$						
DD	4.8±0.7	5.1±0.8	4.7±0.8	4.6±0.8	4.7±0.8	4.6±0.9$^{\alpha}$
ES	4.9±0.9	5.1±1.0	4.9±1.0	4.8±0.9	4.4±0.7*‡#	4.5±0.8*
SE	4.6±0.7	4.7±0.8	4.7±0.9	4.6±0.8	4.6±0.8	4.6±0.6
HDL						
DD	1.9±0.3	2.1±0.3*	1.9±0.2$^{\alpha}$	1.4±0.3	1.5±0.4	1.4±0.3
ES	1.9±0.4	2.0±0.5	1.9±0.4	1.5±0.3	1.5±0.4	1.4±0.3
SE	1.9±0.4	1.9±0.5‡	2.0±0.4 §	1.4±0.3	1.3±0.3* ‡	1.4±0.3
LDL						
DD	2.4±0.6	2.5±0.7	2.3±0.8	2.6±0.9	2.7±0.8	2.5±0.8
ES	2.5±0.6	2.6±0.7	2.6±0.7	2.8±0.9	2.5±0.7*	2.7±0.8
SE	2.2±0.8	2.3±0.8	2.3±0.8	2.6±0.7	2.8±0.8	2.7±0.5
HDL/LDL						
DD	0.8±0.4	1.0±0.6	0.9±0.4	0.6±0.2	0.6±0.3	0.6±0.2
ES	0.8±0.3	0.9±0.4	0.7±0.3	0.6±0.3	0.6±0.2	0.6±0.3
SE	1.0±0.5	0.9±0.4	0.9±0.3	0.6±0.5	0.5±0.3	0.5±0.2
Triglycerides						
DD	1.2±0.5	1.1±0.5	1.1±0.6	1.4±0.8	1.3±0.5	1.2±0.7
ES	1.1±0.4	1.1±0.4	1.0±0.4	1.0±0.3	1.0±0.3	0.8±0.3$^{\alpha}$
SE	1.1±0.5	1.1±0.5	1.0±0.3	1.3±1.0	1.2±0.8	1.2±0.6

Chol$_{TOT}$: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; *significant within-group change from week 0, α significant within-group change from week 12. ‡ significant difference to same-gender DD at time point, # significant difference between same-gender ES and SE at time point. § significantly different from the other groups during weeks 12-24. DD=different-day training, ES=same-session training endurance followed by strength, SE=same-session training, strength followed by endurance.

Correlations with changes in body fat. The changes in Chol$_{TOT}$ and Fat$_{andr}$ had a low correlation during weeks 0-12 (r=0.280, P<0.01) and weeks 0-24 (r=0.283, P<0.01) among all participants. A moderate correlation between the two variables was observed in the DD-group including both sexes (weeks 0-12: r=0.601, P<0.001 and weeks 0-24: r=0.550, P<0.001).

5.7 Resting serum hormone concentrations

Resting serum concentrations are presented in TABLE 10. Testosterone increased by week 12 in all groups in men (DD P<0.01; ES P<0.05; SE P<0.05) but not in any group in women (Table 4). The change between weeks 0 and 24 was statistically significant in the ES and SE groups by week 24 in men (P<0.01 in both groups) and women (P<0.01 and P<0.05, respectively) but not in DD. The change from week 13 to 24 was significant in women in the ES (P<0.05) and SE (P<0.01) groups. A between-group difference was noted at week 24 between DD and the two same-session groups both in men (ES P<0.05; SE P<0.01) and women (ES and SE P<0.01). Changes in cortisol were noted in the SE group in men during weeks 13-24 and in women during weeks 0-24 (both P<0.05). The T/C-ratio increased in men during weeks 0-12 in SE (P<0.01) and a trend was noted in ES (P<0.06); during weeks 0-24 the increase was significant in ES (P<0.01) and SE (P<0.05). In women, the T/C-ratio increased significantly in ES (weeks 0-12 P<0.05, weeks 13-24 P<0.01). Between-group differences were noted in the change in T/C-ratio during weeks 0-12 between DD and SE (P<0.05) and during weeks 0-24 between DD and ES and DD and SE (both P<0.05).

TABLE 10 Resting hormone concentrations at weeks 0, 12 and 24 (mean±SD).

	Women			Men		
Weeks	**0**	**12**	**24**	**0**	**12**	**24**
T (nmol·L^{-1})						
DD	0.96±0.52	0.84±0.60	0.88±0.48	16.6.±5.7	21.9±10.2**	18.7±6-9
ES	0.63±0.31	0.73±0.43	1.07±0.32**#‡‡	13.5±3.2	16.1±4.9*	18.8±4.2**‡
SE	0.69±0.39	0.81±0.40	1.33±0.82*##‡‡	13.9±3.9	17.7±6.6*	19.5±4.4**‡‡
C (nmol·L^{-1})						
DD	547±212	569±202	560±191	504±150	481±119	494±124
ES	538±193	616±198	576±159	491±129	473±119	514±140
SE	542±176	539±234	660±134*	535±110	489±121	593±136 #
T/C × 10^3						
DD	2.3±1.6	1.7±1.4	2.0±1.3	33.6±8.4	47.9±25.5	39.6±17.0
ES	1.4±1.1	1.4±1.0	2.1±1.0*##‡	29.7±14.2	37.9±20.5[α]	38.8±12.2**
SE	1.4±1.0	1.7±0.9$‡	2.3±1.8‡	27.2±9.9	38.9±18.8**	34.1±9.9*

*significant within-group differences to week 0, #significant within-group differences to week 12, $ significantly different to same-gender DD during weeks 0-12, ‡significantly different to same-gender DD during weeks 0-24. *P<0.05, **P<0.01. #P<0.05, ##P<0.05. $ P<0.05. ‡ P<0.05, ‡‡ P<0.01 [α] within-group P<0.06 to week 0. DD=different-day training, ES=same-session training endurance followed by strength, SE=same-session training, strength followed by endurance.

5.8 Self-perceived health-related quality of life, wellbeing, time management and self-esteem

Health-related Quality of Life. There were no between-group differences in the changes of the RAND36 dimensions. Minor increases were observed in *Physical function*, *Vitality* and *General health* dimensions in the DD group and a minor decrease in *Social functioning* in the SS group during the intervention. However, the within-group changes in these dimensions were not significant after adjusting for multiple comparisons (TABLE 11).

General fatigue and wellbeing. There were no between-group differences in the changes of either general fatigue or wellbeing. General fatigue did not significantly change for either DD (23.9 ± 16.9 to 18.4 ± 15.3) or SS (22.2 ± 20.6 to 19.4 ± 18.4). General wellbeing score changed significantly for DD (19.5 ± 15.7 to 14.0 ± 12.2, $P<0.05$) but not for SS (16.2 ± 15.7 to 16.0 ± 15.9).

TABLE 11 Changes in self-esteem, time management behaviorand the dimensions of RAND36 health survey items following the 24-week training intervention.

	Pre		Change (95% CI)	
	DD	SS	DD	SS
Self-esteem	24.8 ± 4.3	25.9 ± 3.3	1.6±2.3 (0.87-2.3)*[‡]	0.4±1.9 (-0.8-1.0)
TMB	4.1±0.6	3.9±0.7	-0.2 (-0.3 - -0.08)*	-0.1 (-0.3 - -0.05)
RAND-36				
Physical function	97.0 ± 5.1	98.2 ± 3.7	1.8±4.7 (0.3 - 3.4)	0.8±3.1 (-0.08 - 1.7)
Role physical	92.8 ± 20.9	98.0 ± 11.0	0.7±22.1 (-6.6 - 7.9)	-2.5±15.2 (-6.7 - 1.8)
Role emotional	96.5 ± 10.4	96.1 ± 10.9	-7.0±25.9 (-15.5 - 1.5)	-2.0±16.9 (-6.7 - 2.8)
Vitality	69.1 ± 12.3	73.6 ± 11.3	4.4±12.0 (0.49 - 8.4)	-0.4±9.3 (-3.0 - 2.2)
Mental health	83.1 ± 10.1	84.3 ± 7.7	-0.9±6.4 (-3.0 - 1.2)	-0.8±6.0 (-2.5 - 0.9)
Social functioning	94.7 ± 10.3	98.3 ± 5.6	-3.6±12.6 (-7.8 - 0.5)	-3.9±12.4 (-7.4 - -0.4)
Bodily pain	87.7 ± 12.0	89.8 ± 14.1	1.3±11.1 (-2.3 - 5.0)	-2.0±13.0 (-5.7 - 1.6)
General health	78.4 ± 16.2	81.2 ± 12.2	5.7±13.2 (1.3 - 10.0)	4.0±10.5 (1.1 - 7.0)

* significant within-group change Pre-Post, [‡] $P<0.06$ between-groups Pre-Post, CI = confidence interval, TMB = Time management behavior questionnaire, DD = Different-day combined strength and endurance training SS = Same-session combined strength and endurance training (ES and SE)

Self-Esteem. A trend ($P<0.06$) for a difference in the change of the self-esteem score was observed. DD showed a significant ($P<0.001$) increase in the self-esteem score while the score for SS remained unchanged.

Time Management Behavior. There were no between-group differences in the change of the TMB total score or the individual questions. The DD group scored significantly lower at Post compared to Pre in questions 1 (“My training regimen leaves me sufficient time to rest.”, $P<0.05$), 2 (“My training regimen leaves me sufficient time for other leisure-time activities.”, $P<0.05$) and the reverse scale question 7 (“My training regimen makes me busy.”, $P<0.01$) as well as in the sum of all questions ($P<0.05$) (TABLE 11).

6 DISCUSSION

Performing strength and endurance training in parallel within the same training program is a practical solution to the exercise prescriptions that are suggested for general health and wellbeing of an individual (Thompson, Gordon & Pescatello 2010). While vast amounts of research during the past decades have focused on the existence and avoidance of "the interference effect" that affects strength gains during combined strength and endurance training, considerably fewer investigations have aimed to clarify the relationships between different manners of combining the two exercises modes.

The main objective of the present thesis was to evaluate the effects of different-day (DD) strength and endurance training and same-session combined strength and endurance training with different orders (endurance before strength, ES and vice versa, SE) on neuromuscular and cardiorespiratory performance, hypertrophy and body composition, blood lipid parameters, and subjective feeling of self-confidence and time management in healthy men and women. The thesis also investigated the acute neuromuscular and hormonal responses to the two same-session training modes with different orders in women.

The results of this study suggest that the gains in strength and endurance performance as well as muscle hypertrophy and lean mass can be achieved by previously untrained men and women with all of the present training programs. While the SE-loading order may result in slightly greater acute growth hormone responses in women, the adaptations in performance and muscle hypertrophy were similar between groups after long-term training. However, the results also indicated that performing ES-training for a prolonged period of time could put an individual at a disadvantage in terms of neuromuscular control, measured as maximal voluntary activation percentage, in comparison to the other two training modes. Furthermore, DD-training seemed to be the most effective in reducing both whole body and abdominal-region fat without resulting in an excessive feeling of general fatigue despite a higher frequency of individual training sessions. This study is the first long-term training intervention to compare these three training modes while monitoring a large variety of physiological and performance-related variables as well as taking into account subjective perceptions of health and wellbeing.

6.1 Acute responses to combined loadings with different orders in women

Acute decreases in force production. The results of the experimental loadings showed that the acute fatigue in terms of exercise-induced decreases in maximal and rapid isometric force were of similar magnitudes after both ES and SE conditions in women before and after the 24-week training period, which is similar to that observed earlier in men (Schumann et al. 2014).

In both loading conditions, the first part of the loading (E or S for ES or SE, respectively) produced the majority of the fatigue no further decreases inforce was accumulated during the second loading mode. Interestingly, an earlier investigation from our research group with male subjects performing the same loading showed that S performed after E resulted in a further decrease in force (Schumann et al. 2014). The additional fatigue produced by the S-loading could be attributed to the different types of loadings and the different muscle types they activate (Henneman, Somjen & Carpenter 1965), and is possibly undetectable in women due to the possible gender differences in fatigue accumulation (Häkkinen 1994; Linnamo, Häkkinen & Komi 1998). Fatigue in the quadriceps muscles may also be related to the fiber type distribution of an individual (Komi & Tesch 1979) and women tend to have a larger type I fiber ratio than men (Carter et al. 2001). Additionally, rather than a centrally mediated mechanism, the accumulation of metabolic byproducts could also be held liable for fatigue through disrupting muscle cross-bridge action (Westerblad, Bruton & Katz 2010). However, neither of our studies utilized methodologies to allow for a more invasive assessment to pinpoint the central and peripheral contributions to fatigue, thus not allowing for explanations of the different loading-induced fatigue between genders.

Neither maximal nor rapid force production was compromised from pre-loading values when tested at 24 hours post-exercise, which from the neuromuscular perspective implies that the subjects recovered from the loading within 24 hours after cessation of the combined loading. This implies that the overall strenuousness of the loading was likely diluted by the initial power sets, as full recovery from a heavy maximal or metabolic strength loading could take as long as 48-72 hours (Ahtiainen et al. 2004; Häkkinen 1994).

Acute hormonal responses.

No acutely elevated concentrations of testosterone (T) were observed in women in response to the full combined loading in either exercise order at week 0, when the subjects were unaccustomed to combined strength and endurance training. This outcome is in line with a previous investigation by our research group (Schumann et al. 2013) and was also expected due to the profile of the strength-part of the combined loading. The arrangement of explosive, maximal, and hypertrophic sets in the present strength loading were together likely not strenuous enough to elicit acute anabolic responses (Schumann et al. 2013), as large elevations in T would typically be expected in women after protocols with a large stress on the metabolic system (i.e. hypertrophic-type protocols) (Kraemer et al. 1993; Linnamo et al. 2005). However, this loading type was designed to mimic the content of the 24-week training program, and was thus likely to be well reflective of the training performed during the actual training intervention.

It is noteworthy that elevated concentrations of serum T were observed during the loading for ES at Mid-loading during weeks 0 and 24 and for SE at Post-loading during week 24. This may suggest the observed elevations to be primarily a result of the performed endurance exercise. This supports previous findings of endurance exercise inducing elevations in T in female populations (Enea et al. 2009; Keizer et al. 1987). Furthermore, the lack of significantly increased T at Post-loading for the SE group at week 0 is in line with earlier investigations in men (Cadore et al. 2012b; Rosa et al. 2014; Schumann et al. 2013), with unchanged concentrations of T after a combined loading in the SE order. However, the significant, acutely elevated concentration of serum T in SE at week 24 may be the result of training-induced increased sensitivity to adrenocorticotropic hormone (ACTH) (Loucks et al. 1989). ACTH stimulates the adrenal cortex and releases androgens as a by-product of C secretion (Johnson et al. 1997; Keizer et al. 1987), which together with the relatively higher rise in lactate after training could explain why acutely elevated T was observed during the loading in the SE group at Post at week 24, but not at week 0. However, as no such observation was made in the ES group, this mechanism remains speculative.

It needs to be acknowledged that we only measured total T during the loadings and did not detect any significant elevations in cortisol (C) during either order. Furthermore, the underlying causes of exercise-induced elevations in T in women are not fully elucidated, and not all plausible mechanisms were monitored in the present study. More accurate indications of T-kinetics could be obtained via monitoring the time course of androgen receptor regulation (Vingren et al. 2009) and reduced hepatic clearance as observed in men (Cadoux-Hudson, Few & Imms 1985). Hemoconcentration as a secondary cause for elevated T can likely be ruled out in the present study, as no changes were noted in hemoglobin or hematocrit during loading. Oral contraceptive use may be potent in affecting the secretion of T and the metabolites of dehydroepiandrosterone (Enea et al. 2009) and could thus affect the biosynthesis pathway of T during exercise. However, in the present study, a similar number of subjects in both groups reported oral contraceptive use and patterns of T response to endurance exercise was comparable in both orders.

As expected based on previous findings (Goto et al. 2005), the acute GH concentrations in the ES order both before and after training were significantly elevated after the endurance exercise bout, but were found to be reduced at Post-loading when also the strength-exercise has been performed. In contrast, the SE-loading order showed significantly elevated GH-concentrations throughout the combined loading. These differences in the kinetics of exercise-induced GH-responses were significantly different between groups both before and after training.

A possible mechanism for the dissimilar acute behavior of serum GH could originate in endurance-exercise induced lipolysis (Romijn et al. 1993). The release of free fatty acids (FFA) may affect anterior pituitary function (Casanueva et al. 1987), which could in turn suppress the release of GH. It is noteworthy that even though oral contraceptive ingestion could augment lipolysis during continuous cycling exercise (Casazza et al. 2004) such as that of the present loading protocol, the FFA content is likely to remain unaffected.

Similarly to the acute responses of T, the intensity of exercise is a major contributor to the magnitude of responses of GH in women (Linnamo et al. 2005; Weltman et al. 1992). In the case of GH, however, training needs to continuously be progressive in its intensity in order for GH to increase over baseline values, or else an exercise bout may not suffice to produce a significant GH response (Chang et al. 1986). The present study utilized exercise intensities that were kept relative to 1 RM and W_{max}, in order to match the training status of the subject at the moment of testing. Expectedly, this was reflected in the GH responses in both groups, as higher absolute concentrations at both Mid and Post in comparison with corresponding time points at week 0. Regardless of the fact that the magnitudes of the loading-induced changes in SE (Pre-Mid and Pre-Post) were not statistically larger than the corresponding magnitudes at week 0, the GH responses during loading at week 24 reached statistical significance. Thus, as the same relative exercise intensity was effective in acutely significantly elevating serum GH concentrations, this phenomenon serves as an indication of adaptation to training. Similar indications of training adaptations were found in the ES group, as the Pre-Mid and Pre-Post magnitudes were significantly greater during the loading at week 24 than at week 0.

Interestingly, despite the adaptations in GH release appearing to point towards the loadings still being strenuous at week 24, the examination of the behavior of CK may in fact suggest an improved tolerance of the experimental loading. Creatine kinase was slightly elevated both during loading and recovery in both groups at week 0 but during week 24 an increased concentration was only observed in SE during loading as well as being similar to resting levels during recovery. As CK can be considered to be an indirect indicator of muscle damage (Ebbeling & Clarkson 1989), the lack of its presence during recovery after training might suggest an increased tolerance for combined strength and endurance loadings. This finding of no significantly elevated concentrations CK after a prolonged training period is comparable to that observed in men with a similar loading (Schumann et al. 2014). Importantly, cycling as a choice of endurance training may in general not be as potent in inducing muscle damage as running, even following extremely prolonged exercise durations (Koller et al. 1998).

6.2 Training-induced adaptations in neuromuscular and cardiorespiratory performance

6.2.1 Maximal dynamic and isometric strength

The results of the present study showed that all three training modes in both genders were effective in increasing maximal dynamic leg press strength as well as maximal isometric leg press force with no statistical differences between groups after 24 weeks of training. However, after 12 weeks of training the gains in strength were larger in women in the DD-group in comparison to the ES-group. This difference in the time course of adaptations in favor of DD bears resemblance to the outcomes reported by Sale et al. (1990), whose results displayed a similar advantage for DD after 20 weeks in men. Hence, the researchers concluded that same- session combined training would be inferior to different day training in terms of gains in maximal dynamic strength, possibly due to the greater amount of recovery between the strength and endurance training modes (Sale et al. 1990). The effectiveness of a DD-training in comparison to same-session training was also recently reported in athletes following a 7-week training intervention. Rugby players adhering to DD-training were at an advantage in terms of strength gains compared to those who utilized immediate sequencing of the strength and endurance modes (Robineau et al. 2016).

Despite some emerging group differences in strength gains in the present study, which were most prominent in women between the DD- and ES-group at week 12, the strength gains were similar in all training groups after completion of the entire 24-week intervention. In order to clarify the greater increases in 1RM in the DD group in women at week 0 from the scope of the present study, the baseline difference in 1RM between the DD and ES groups also needs to be taken into account. The difference between DD and ES at baseline was approaching significance (p=0.06), putting the the DD-group at a slight disadvantage at the start of the study with a slightly lower baseline strength. However, this may have given an opportunity for more rapid and greater early strength gains (Cormie, McGuigan & Newton 2011). The possibility of this phenomenon is likely when also taking into account that the female DD-group did not statistically further increase 1 RM strength from week 12 to week 24.

The magnitude of 1RM gains in the present study can mostly be considered comparable to that of earlier studies of a similar duration and a similar design. Both the men and women in the same-session groups in the present study increased 1 RM by 12-17%, similar to the 13% reported by Sale et al. (1990) after 20 weeks. However, the men adhering to DD-training in the present study demonstrated smaller (13 %) gains in maximal dynamic leg press 1 RM strength in comparison to findings by both Sale et al. (1990) as well as Häkkinen et al. (2003) where strength increased 22-25% over 20-21 weeks. The earlier results are, however, similar to those observed in the DD women in the present study (21%). With the limited number of previous investigations utilizing a similar research design, the inconsistencies in the outcomes between the present study and the earlier ones is difficult to identify. Reasons for both the equality of the DD and same-sessions groups (as opposed to earlier studies) as well as slightly smaller strength gains in most groups than what has been reported earlier, could be linked to the details of the study design. Differences in the acute programming variables (e.g. training intensities), long-term periodization (e.g. progression schemes) as well as the varying subject populations with different training backgrounds may have affected the slightly inconsistent outcomes.

6.2.2 Electromyography and voluntary activation

Despite similar gains in strength in all training groups, the study revealed indications for differing adaptations of voluntary activation level and muscle EMG between the three combined strength and endurance training modalities during the 24-week training period. While the DD and SE –groups displayed a statistically significant increase in voluntary activation of the knee extensors, the same adaptation was not observed in the ES group. In addition to the unchanged voluntary activation percentage, a correlation was found in the same group between the individual changes in voluntary activation and maximal force development in isometric unilateral knee extension during the latter half of the training intervention.

The findings of the present study partly support those presented in earlier studies (Cadore et al. 2013; Cadore et al. 2012a). It was suggested by Cadore et al. (Cadore et al. 2013) that the ES sequence would in elderly subjects compromise neural adaptations, whereas no such compromise in adaptations was found in the SE order. These earlier findings also suggest the ES sequence to be unfavorable in terms of strength development in comparison to SE which was, however, not confirmed by the present study. Nevertheless, the present SE and DD groups demonstrated increased voluntary muscle activation during weeks 0–24 as typically seen with pure strength training (Knight & Kamen 2001; Reeves, Narici & Maganaris 2004), while the ES group showed no significant increases in the same variable. Furthermore, the significant interaction observed between individual changes in voluntary activation percentage and changes of knee-extension strength development during weeks 13–24 for the ES group demonstrated that individuals who experienced decreased voluntary activation percentage also reduced their strength gains in knee extension force.

Considering that the main difference between the training programming of the present three groups was the timing of the endurance modality in relation to the strength training, acute fatigue could be a contributing factor to the lack of increase in the ES group. While the DD group was consistently allowed a minimum of 24 h of recovery between the training modes and SE performed strength training in a recovered state, the ES group was the only one susceptible to performing their strength training in a fatigued state. Due to the fact that the quadriceps femoris muscle group contributes to continuous cycling with a significant percentage of its maximum activity even at relatively low workloads (Ericson et al. 1985) and the arising fatigue is manifested locally in the working muscles (Elmer et al. 2013), cycling exercise could be expected to compromise the quality of a following lower-body strength session. Prolonged cycling exercise may limit the force-generating capacity of the muscles via both central and peripheral mechanisms, consequently leading to a reduced capacity of the working muscles during subsequent activities (Amann 2011; Bentley et al. 1998).

Another plausible mechanism for residual fatigue from an endurance loading could be due to inhibitory feedback from type III and IV afferents due to a lowered pH or metabolite accumulation (Amann et al. 2013) or impairments in neuromuscular propagation (Duchateau & Hainaut 1985). Thus, strength-training induced adaptations could theoretically be at risk of being compromised, should strength training always be performed after fatiguing endurance training. In the present study, however, the ES group did improve both maximal dynamic and isometric strength despite the lack of increase in EMG activity and voluntary activation. Thus, it is worth noting that as increases in strength are not exclusively explained by neural adaptations but also rely on muscle hypertrophy (Häkkinen & Komi 1983; Moritani & deVries 1979; Narici et al. 1996). While the neural adaptations are initially responsible for strength gains, hypertrophy as a contributing factor typically follows later on in a training program (Häkkinen & Komi 1983; Moritani & deVries 1979; Narici et al. 1996). Thus, the significant gains in lower body muscle mass and Vastus Lateralis CSA during both training periods in the ES group (as discussed later in chapter 6.3) could partly explain the improvements in strength. In addition, cycling as the choice of endurance training mode is considered to possibly augment rather than hinder lower-body strength development to the same extent as e.g. running, due to biomechanical similarities with lower-body strength exercises (Gergley 2009; Mikkola et al. 2012). Thus, pertaining to the "interference effect" (which was not investigated in this study per se), it needs to be kept in mind that should the present study have utilized a running endurance protocol in place of cycling, the direction of the neuromuscular adaptations could have been different (see Wilson et al. 2012 for meta-analysis).

In summary, despite the ES order being the only group that is susceptible to having the quality of the strength loading compromised by the close proximity of endurance training, the present methodology does not allow to definitely conclude this to have occurred or where the compromised neural adaptations originate from. Whether fatigue-induced inhibitory neural responses from the endurance component alone can be considered to be responsible for unfavorable neural adaptations associated with the present ES training program, or whether the immediate addition of a strength-loading overloads the nervous system still requires further investigation.

6.2.3 Training- induced changes in peak power output and maximal oxygen uptake during maximal endurance cycling

Similarly to some of the strength variables, the peak power output during the maximal cycling test was significant in all groups in both genders when measured at week 24, which is similar to earlier findings with the SE and ES orders in men of different ages (Gergley 2009; Cadore et al. 2012a). However, some differences in the time course of adaptations emerged in women after the first half of the study. While the increases during weeks 0-12 were significant in DD and ES groups, the change in the SE group did not reach statistical significance. It is possible that adapting to the combination of a lower body strength and lower body endurance training took longer than 12 weeks to occur for the SE-order. As the performed strength exercise likely recruited most high-threshold motor-units (Henneman, Somjen & Carpenter 1965), the repeated push-pedal action during subsequent cycling may have become too demanding as both high- and low-threshold motor units are typically recruited (Vøllestad, Vaage & Hermansen 1984). Thus, in order to keep up the required pedaling frequency during the training sessions, lowering of the magnetic resistance on the endurance training equipment may have occurred. Ultimately, this could have initially led to an altered utilization of neuromuscular capacity during maximal cycling performance. Regrettably, the endurance training apparatus used in the present study was not equipped to monitor the exact resistance used. Thus, it is not possible to confirm the reason for initially differing adaptations in peak power output in women.

Interestingly, while the peak power output ultimately increased to similar extents in all groups, the gains in VO_{2max} differed between the DD and same-sessions groups both in men and women even after the full 24 weeks of training. The increases in DD were more than two-fold in comparison to both ES and SE in both genders, also resulting in significant between-group differences. This is in contrast to the results of Sale et al. (1990), who reported similar VO_{2max}-increases between different-day and same-session training after a similar time frame. On the other hand, findings by Robineau et al. (2016) mimic those of the present study, alluding to an advantage in cardiorespiratory performance in favor of DD-training. The difference to the study of Sale et al. (1990) could lie in the details of the strength training. As the present study included heavy or maximal strength training during the majority of the training sessions in opposed to the mostly submaximal loads in the study by Sale et al. (1990), our heavier strength training could have compromised oxygen utilization when performed in close proximity with endurance exercise. Drummond et al. (2005) have postulated that the creatine phosphate -depleting effect of endurance training (Dudley 1988; Tesch, Colliander & Kaiser 1986) could interfere with the metabolic processes of endurance exercise and its adaptations, if performed in close proximity. This could have resulted in a greater increase in VO_{2max} in the DD-group, which was consistent in both genders.

It is also possible that the slightly lower initial level of VO_{2max} in the DD-groups could have partly have contributed to the observed between-group differences, considering the possibility for a larger window of adaptation when starting a training program at a lower level of fitness. Despite this, the gains in DD were more than double to that of the ES and SE groups in both genders, suggesting the possibility that a DD-training mode may be more likely to positively affect VO_{2max}.

6.3 Body composition, serum hormones and metabolic and perceived health

6.3.1 Changes in muscle cross-sectional area and lean body mass

Due to different imaging methods of determining changes in size, comparing the magnitudes of change between different studies is cumbersome. However, in agreement with previously reported directions of change in muscle size over 20 weeks (Sale et al. 1990), the acquired increase of the Vastus lateralis CSA as well as whole body lean mass in the present study did not differ between the training groups in either gender after 24 weeks of training. However, in women no increases in ES and SE groups in the VL muscle was observed at week 12 when measuring at 50% of femur length. Interestingly, when averaging the measurements at 50% and 70% of femur length, the increase at week 12 reached statistical significance in ES but not in SE. Thus it seems that initially the ES mode provided a slight advantage in terms of muscle hypertrophy in comparison to SE.

While it has been suggested that endurance exercise performed immediately before strength exercise may interfere with the hypertrophic stimuli induced by the strength loading (Apro et al. 2015), it has recently also been suggested that it could augment hypertrophy in comparison to strength-only training (Lundberg et al. 2016) especially if incorporating high-intensity endurance exercise (Fyfe et al. 2016). This could provide explanations as to why the female ES group initially displayed some level of hypertrophy while the SE group did not. However, as this phenomenon was not observed in the male same-session groups and pinpointing the factual method was beyond the methodology of the present study, this hypothesis remains theoretical. Furthermore, the possibility of an uneven group distribution of potential non- or low-responders to exercise must also be considered (Ahtiainen et al. 2016; Walker et al. 2015).

The increases in muscle cross-sectional area and lean body mass were expected to occur due to the nature of the utilized strength training program. However, it has earlier been suggested that endurance training would blunt any hypertrophy that would be achieved with a concurrently performed strength training program (Fyfe, Bishop & Stepto 2014). Similarly to the "interference effect" relating to muscle strength, this hypothesis may apply to a greater extent when strength training is paired with running rather than cycling (see Wilson et al. 2012 for meta-analysis). Thus, running paired with strength training may not result in similar outcomes as the present study, where the cycling training could even have been considered to aid the hypertrophy (Mikkola et al. 2012).

6.3.2 Body fat and blood lipids

Despite similar changes in muscle CSA and whole body lean mass, body fat mass decreased only following DD training. These decreases were statistically significantly larger than those of the ES group in men, and significantly larger than both same-session modes in women, while the same-session training groups did not significantly differ from each other in either gender. Importantly, the same phenomenon was observed also in the abdominal region fat, as the accumulation of adipose tissue particularly in the abdominal cavity has been identified as a cardiovascular risk factor (Mottillo et al. 2010). Furthermore, abdominal fat may induce a pro-inflammatory environment associated with poor metabolic health e.g. through inducing metabolic syndrome (Ritchie & Connell 2007).

Our results support earlier findings stating that decreases in abdominal fat could be associated with a decrease in blood lipids (Dutheil et al. 2013). In the present study this was observed both in the total subject population as well as in the DD groups alone through correlations between the changes in total cholesterol and changes in abdominal fat. The present findings therefore indicate that DD training is may be an effective strategy in decreasing fat in the abdominal region and consequently contribute the improvement of both cardiovascular and metabolic health (Mottillo et al. 2010; Ritchie & Connell 2007). However, an inspection of the lipid fractions of the present study revealed decreased LDL cholesterol was observed in the ES group among men as well as a modest effect on HDL cholesterol following SE training in women, although not correlated to body composition. Thus, the effects of different combined strength and endurance training regimens on blood lipids is not fully elucidated solely based on the present study, although a strong indication was observed in terms of the DD contributing to an improved health profile.

Although the overall training volume was matched in all groups in the present study, a main difference in the training programming was that the DD group consistently performed the training sessions on alternating days while the same-session groups performed both modes in the same training sessions. It would thus seem lucrative to assume, that several shorter and more frequent exercise session would result in higher post-exercise oxygen consumption as has previously been demonstrated in endurance exercise (Almuzaini, Potteiger & Green 1998). Consequently, this possible difference could have accumulated over 24 weeks and resulted in larger overall energy expenditure, as has been observed to occur in older individuals after varying frequencies of combined strength and endurance training (Hunter et al. 2013). However, while the post-exercise energy demands have been investigated between ES and SE modes without any emerging differences (Di Blasio et al. 2012) or to a slight advantage for ES (Drummond et al. 2005), no study has attempted to compare these two modes to a combined training session performed in two parts on two consecutive days.

The slight differences in the baseline level of body fat also need to be considered when interpreting the results of the present study. Despite similar BMIs in both genders, both same-session groups were slightly leaner at the start of the study, which could partly contribute to the results. To attempt to overcome this, our statistical method was adjusted to take into account baseline differences in order to identify true adaptations. As the magnitude of change was more than 2-fold in the DD groups in comparison with the same-session groups and notably, without any change in fat mass in the same-session combined groups, it is possible that DD training is more potent in decreasing body fat mass in the present subject population. The effectiveness of the utilized training programs in overweight or obese individuals cannot be established based on the available results.

6.3.3 Acute and chronic hormonal adaptations

6.3.3.1 Acute exercise-induced hormones and associations to long-term adaptations in cross-sectional area (in women)

Despite that the GH responses showed distinctly different kinetics during the ES and SE exercise orders no between-group differences were observed in long-term training-induced increases in muscle CSA as well as no correlations to hypertrophy. Although an acute bout of exercise may stimulate variants of GH that are incapable of generating increases in biological activity, chronic resistance exercise may increase the circulating concentrations of other variants of biologically active GH (Kraemer et al. 2006). Thus, investigating baseline and acute concentrations of other GH splices than exclusively the present 22 kDa variant could provide further insight into possible associations with hypertrophy or lack thereof.

A similar lack of association was noted between acute responses of T and long-term performance adaptations. Although it has been proposed that tissue exposure to acute elevations in anabolic hormones would not be associated with hypertrophy or strength performance (West et al. 2010), such correlations have been reported after pure strength training in male subjects (Hansen et al. 2001; McCall et al. 1999) both with high-volume and high intensity strength training programs (Mangine et al. 2017). Furthermore, previously reported correlations of basal levels of T and T/SHBG ratios to strength development or CSA after strength training in women (Häkkinen, Pakarinen & Kallinen 1992; Hansen et al. 2001) were not found in the present study despite increased basal concentrations of T. Thus, it is possible that any linkages of resistance exercise–

induced anabolic responses and gains in strength and hypertrophy may be interfered when strength training is simultaneously accompanied by endurance training. This was previously demonstrated by our group in men in a different data set from the same subject population, where no association to performance was found between hormone concentrations (Schumann et al. 2014).

6.3.3.2 Adaptations in resting serum hormone concentrations in men and women

In the present study, increased basal concentrations of T were observed at week 12 in men both same-session groups as well as at week 24 in the same-session groups in both genders with a significant difference to same-gender DD. Similarly, no statistical changes were observed in the DD groups in the T/C-ratio, while it significant increases were observed in the same-session groups. Elevated basal concentrations of T following same-session combined training has previously been reported in male subjects after a 24-week training intervention similar to that of the present study (Küüsmaa et al. 2016), but comparisons to DD-training is lacking in presently available literature. It has previously been postulated that increases or decreases in resting concentrations of T following strength training may be due to substantial changes in training volume or intensity and may be transient in nature (for review, see Kraemer & Ratamess 2005). However, in the present study, the training volume was the same for all subjects, albeit differently allocated throughout the week. As the ES and SE groups performed a larger percentage of the weekly training volume per each individual training session, it may have provided a greater stimulus to the endocrine system which provoked an increased resting concentration of T.
Another possible mechanism for differences in basal concentrations could be related to the changes in fat mass that were observed following different-day training. It has previously been observed in post-menopausal women that exercise training results in decreased concentrations of T with the underlying mechanisms being related to changes in body composition (McTiernan et al. 2004). Due to the fact that adipose tissue is a source of androgens, reduced body fat could thus indirectly lead to reduced concentrations of T through changed aromatase activity and, consequently, reduced peripheral conversion of androgens to T (Enea & Boisseau 2011; Puche et al. 2002). However, whether this mechanism is fully applicable to the present subject population or not is debatable, and it remains hypothetical until further investigation.

6.3.4 Subjectively perceived wellbeing and time management

The present study assessed subjective perceptions of health-related quality of life, time management behavior (TMB), self-esteem, and perceptions of general fatigue and wellbeing. These measures were chosen due to the distinctly different organization of training in the different-day and same-session groups, which could potentially have led to different perceptions of time management and general wellbeing. Exercise in general is potent in improving health-related quality of life (HRQoL), self-esteem and treating depressive symptoms (Atlantis et al. 2004; White, Kendrick & Yardley 2009). In contrast, volitional excessive exercise may result in "exercise dependence", resulting in an obsessive attitude towards exercise which in turn may have negative psychological consequences (Hausenblas & Downs 2002).

In the context of the present study, it was hypothesized that the prescription of a higher exercise frequency could result in a feeling of stress or fatigue and poorly managed time due to the fact that exercise participation was a task assigned by the research staff that the participants were required to complete (Gillespie et al. 2010). In accordance with our hypothesis, the TMB-questionnaire revealed that the DD-subjects did indeed experience some degree of deterioration in time management behavior. More specifically, this manifested itself in questionnaire items dealing with a general feeling of "being busy", not having sufficient time for other leisure-time activities as well as not having ample time to rest.

The theory of planned behavior (TPB) (Ajzen 1991) states that in situations where the individual does not entirely control the behavior, the individual's behavior can most significantly be predicted by the individual's perceptions of his or her behavior. This in conjunction with the fact that lack of time is often cited as the main barrier for exercise (Dishman 1982; Dishman 1991) raises the question of the long-term sustainability of the DD training mode with up to 6 weekly exercise sessions. However, despite the worsened perception of time management behavior, the score on the visual–analog scale of perceived fatigue did not change during the study for DD. On the contrary, the wellbeing measured on the visual scale showed a slight improvement in the DD-group after 24 weeks of training. Similarly, self-esteem (Rosenberg et al. 1995) improved following DD-training with no change in the same-session groups. It needs to be noted, though, that already at the initiation of the study, the same-session groups scored over 25 points in the self-esteem questionnaire, placing those groups in the highest possible category of self-esteem, while the DD-group was initially bordering to the highest category (24.8). Thus a change in the same-session groups was not necessarily expected. Similarly for all groups in the questionnaire of HRQoL, scores were initially within expected values for healthy adults (Aalto, Aro & Teperi 1999). Thus, it is likely that a ceiling-effect limited the changes in these variables.

In general, it needs to be acknowledged that while certain personality traits have been associated with exercise adherence (Courneya & Hellsten 1998), the present study required participants to perform all their training sessions at the laboratory facilities, thus letting accountability possibly obscure the general courses of action that determine an individuals' participation success (Armitage & Conner 2008). Furthermore, as subjects were recruited through public postings, the sample may be biased towards subjects that were already motivated to participate, which may slightly limit the interpretation of the present results.

6.4 Methodological strengths and limitations

Long-term combined strength and endurance training interventions that focus on a variety of both acute exercise responses and long-term adaptations in both men and women are rare. The present study successfully evaluated three different volume-equated variants of combined training, bringing new and valuable information to the field of exercise science. However, some shortcomings in the methodology must be acknowledged.

First, as EMG as a representation of neural drive may be a gross oversimplification (De Luca et al. 2006; Folland & Williams 2007) the present study utilized voluntary activation measured with the interpolated twitch technique to further strengthen neuromuscular findings. However, both methods have some issues that need to be considered. In order to minimize possible inaccuracies in the EMG-recordings arising from technical, anatomical or physiological sites (De Luca et al. 2006), all procedures relating to the recording of EMG were carefully conducted by the same member of staff, and the EMG locations were permanently marked subcutaneously to ensure anatomical accuracy throughout the intervention. However, the EMG signal is also subject to fluctuations due to the amount of subcutaneous fat between the surface recording site and the active muscle, with a higher amount of fat resulting in a more deteriorated EMG-signal (De la Barrera & Milner 1994). With the present methodology we were, however, not able to isolate the exact volume of fat underneath the surface electrodes and are, therefore, not able to say, whether a change in subcutaneous fat over the VL muscle occurred and, whether or not, it affected the outcome of the EMG-signal. Regarding the ITT, percutaneous stimulation of the femoral nerve was found to be too challenging to perform in a repeatable manner. Thus, the present study used direct electronic muscle stimulation of the QF. Even though this method may be muscle and angle-specific and depend on the timing of the superimposed and resting twitches (Folland & Williams 2007), it has been suggested to be a valid alternative to nerve stimulation to assess voluntary activation level (Place et al. 2010). Furthermore, the results may depend on the timing of the superimposed and resting twitches (Folland & Williams 2007), which we to the best of our abilities counteracted by ensuring identical measurement settings throughout the study and always having the same member of the staff conducting the ITT-measurements. Nevertheless, the interpretation of our findings regarding neuromuscular adaptations needs to be done with caution, as it cannot be assessed to which degree the methodological issues may have been present.

Second, some concerns may also be present when interpreting the hormonal changes both in the male and female groups. The 24-week duration of the study inadvertently resulted in different seasons occurring with the first and last measurements of the study. Even though the present study showed changes in basal testosterone that are the opposite of what a typical seasonal shift would suggest (zenith around October and nadir in June), the seasonality could still have partly masked some otherwise pertinent changes (Svartberg et al. 2003; Stanton, Mullette-Gillman & Huettel 2011). Furthermore, due to organizational constraints it was regrettably not possible to control the phase of the menstrual cycle phase in the female participants. Due to ethical reasons it was also not possible to request the subjects to stop ingesting oral contraceptives. This may have affected the hormonal responses and adaptations (as previously discussed in 6.1 and 6.4, respectively).

Third, some further methodology that could have been used to confirm our findings regarding changes in body composition was unfortunately lacking. Measurements of post-exercise oxygen consumption as well as resting metabolic rate could have aided in explaining the reason as to why decreases in body fat were only observed in the DD-group.

Finally, some baseline differences were present in the final subject population. At the start of the study all groups were matched for baseline characteristics and performance, but due to some dropouts during the study the group-baselines were no longer similar at the end of the study. To counteract this, we used statistics that would take into account the effect of the baseline differences, but nonetheless, further studies with similar designs could help in confirming how the different training modes relate to each other.

However, the study also had several strengths in both its design as well as practical procedures. All measurements were conducted by well-trained staff and all procedures that required precision in measuring as well as analyzing was conducted by the same members of staff throughout the study. Furthermore, all training sessions were supervised and great care was taken in ensuring correct conduction and progression of the strength and endurance exercises.

The research setup with a large number of subjects (n=106) allowed for assessing both the effects of different intra-session exercise sequences as well as its comparison to the same volume of training performed with strength and endurance on separate days. The multitude of physiological variables explored over a 24-week training intervention in a large number of subjects can be considered to provide valid information for exercise prescription in individuals of similar anthropometric and physiological characteristics, which until now has not been investigated in such a comprehensive manner.

7 MAIN FINDINGS AND CONCLUSIONS

The purpose of the present thesis was 1) to investigate the acute neuromuscular and hormonal responses to combined strength and endurance loadings with different orders in women as well as and the adaptations to the acute responses over 24 weeks of combined strength and endurance training, 2) to investigate the adaptations in neuromuscular, hormonal, cardiorespiratory and health-related variables in men and women over 24 weeks of same-session combined training with different orders and different-day strength and endurance training with equated volumes. The results indicated that

1. Despite some order-related differences in the acute exercise-induced hormone kinetics of the same-session female groups, both training orders led to similar magnitudes of improved performance variables and increased whole body lean mass and muscle CSA.
2. All three training modes in both genders led to significant increases in strength and endurance performances as well as muscle size and lean body mass.
3. Decreased body fat mass was observed only in the DD-training groups.
4. Neuromuscular performance (quantified as EMG and voluntary activation percentage) in the ES group showed signs of being compromised and highly individual, while no compromises were observed in the DD and SE groups.
5. Increases in basal concentrations of testosterone were observed only in the same-session groups in both genders.
6. While the DD-group experienced some level of impaired time management, the general feeling of fatigue did not increase. Simultaneously, an increase in wellbeing was noted.

In summary, the present thesis demonstrates that the choice of a combined training mode may not be of great importance during the initial months of training if gains in strength and endurance performance or muscle hypertrophy are the main objective for previously untrained healthy adults. However, caution should be used in terms of neural interference if adhering to the ES training mode as it is unclear if compromised neural adaptations also could result in compromises in strength development. Furthermore, the DD training mode, although more time consuming, may be a more suitable option than same-session training if simultaneous optimization of body composition and cardiovascular health is desired.

YHTEENVETO (FINNISH SUMMARY)

Yhdistetty voima- ja kestävyysharjoittelu saman tai eri päivän aikana suoritettuna: Pitkäaikaisvaikutukset hermolihasjärjestelmään, sydän- ja verenkiertoelimistöön, kehon koostumukseen sekä metaboliseen terveyteen ja koettuun hyvinvointiin miehillä ja naisilla

Tämän väitöskirjan tarkoituksena oli tarkastella 1) kahden eri järjestyksin suoritetun yhdistetyn voima- ja kestävyyskuormituksen aikaansaamia vasteita veren hormonipitoisuuksissa sekä hermolihasjärjestelmän toiminnassa naisilla sekä näiden akuuttien vasteiden adaptaatioita 24 viikon yhdistettyyn voima- ja kestävyysharjoitteluun 2) 24 viikon voima- ja kestävyysharjoittelun aikaansaamia adaptaatioita hermolihasjärjestelmässä, sydän- ja verenkiertoelimistössä, suorituskyvyssä, hormonipitoisuuksissa sekä terveysmuuttujissa ja itse koetussa hyvinvoinnissa miehillä ja naisilla, kun voima- ja kestävyysharjoittelu toteutettiin joko eri päivinä (EP), tai samassa harjoituskerrassa eri järjestyksin (kestävyys ennen voimaa, KV, tai päinvastoin, VK).

Harjoittelu koostui kuntopyöräilystä sekä hypertrofisesta ja maksimivoimaharjoittelusta. EP-ryhmän koehenkilöt (miehet n=21, naiset n=18) harjoittelivat 4-6 päivänä viikossa, vuorotellen voimaharjoittelua ja kestävyysharjoittelua. KV-ryhmän (miehet n=16, naiset n=15) ja VK-ryhmän koehenkilöt (miehet n=18, naiset n=14) harjoittelivat 2-3 päivänä viikossa, mutta suorittivat aina voima- ja kestävyysharjoitukset peräkkäin siinä järjestyksessä, joka heille oli tutkimuksen alussa määrätty.

Tutkimuksen tulokset osoittivat kummankin harjoitusjärjestyksen johtavan akuuttiin hermolihasjärjestelmän väsymiseen. Akuutit hormonivasteet olivat samankaltaiset harjoitusjärjestysten välillä, mutta kuormituksen jälkeen kasvuhormonipitoisuudet olivat VK-ryhmällä suuremmat, kuin KV-ryhmällä niin ennen kuin jälkeen 24-viikon harjoittelujakson.

Kummatkin sukupuolet kaikissa kolmessa harjoitusryhmässä paransivat maksimivoimaa ja kestävyyssuorituskykyä, mutta EP-ryhmä paransi maksimaalista hapenottokykyä KV- ja VK- ryhmiä enemmän. Miehillä mitatun Vastus Lateralis-lihaksen (ulompi reisilihas, VL) maksimaalinen tahdonalainen aktivaatio parani EP- ja VK-ryhmillä, mutta ei KV-ryhmällä. Viikkojen 13-24 aikana havaittiin korrelaatio yksilöllisissä tahdonalaisen aktivaation ja polvenojennusvoiman muutosten välillä KV-ryhmässä.

Koko kehon rasvaton massa ja VL-lihaksen poikkipinta-ala suurenivat kaikilla ryhmillä. Merkittävää kehon rasvamassan vähenemistä havaittiin vain EP-ryhmässä. Keskivartalon rasvamassassan ja veren lipidien muutosten välillä havaittiin yhteys niin EP-ryhmässä kuin koko otoksessakin. Itsetunto sekä koettu hyvinvointi paranivat EP-ryhmällä ja pysyivät muuttumattomana saman harjoituskerran ryhmillä. Ajankäytön hallinta koettiin EP-ryhmässä hankalampana tutkimuksen jälkeen.

Tämän väitöskirjatutkimuksen tulokset osoittavat, että maksimivoimaa ja kestävyyssuorituskykyä voi parantaa samalla lihasmassaa kasvattaen kaikilla kolmella, käytetyllä harjoitusohjelmalla. KV-harjoittelun tuloksena saattaa kuitenkin ilmetä heikkenemistä lihaksen tahdonalaisessa aktivaatiossa, mutta tämän vaikutuksesta voiman kehitykseen ei ole varmuutta ilman pidempiaikaista harjoitteluseurantaa. Vaikka EP-harjoittelu koettiin ajankäytöllisesti haastavana, se ei vaikuttanut koettuun hyvinvointiin tai yleiseen jaksamiseen. Eri päivinä toteutettu harjoittelu vaikuttaisi olevan tehokkain keino suorituskyvyn ja kehonkoostumuksen ja metabolisen terveyden samanaikaiseen optimointiin.

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ORIGINAL PAPERS

I

ACUTE ENDOCRINE AND FORCE RESPONSES AND LONG-TERM ADAPTATIONS TO SAME-SESSION COMBINED STRENGTH AND ENDURANCE TRAINING IN WOMEN

by

D. Eklund, M. Schumann, W.J. Kraemer, M. Izquierdo, R.S. Taipale & K. Häkkinen.
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Title: Acute endocrine and force responses and long-term adaptations to same-session combined strength and endurance training in women

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Running head: Order effect in women: loading and training

Eklund, Daniela[1], Schumann, Moritz.[1], Kraemer, William J. [2], Izquierdo, Mikel. [3], Taipale, Ritva S[1], Häkkinen, Keijo[1]. 2014.

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ABSTRACT

This study examined acute hormone and force responses as well as strength and endurance performance and muscle hypertrophy before and after 24 weeks of same-session combined strength and endurance training in previously untrained women. Subjects were assigned one of two training orders: endurance preceding strength (E+S, n=15) or vice versa (S+E, n=14). Acute force and hormone responses to a combined loading (continuous cycling and a leg press protocol in the assigned order) were measured. Additionally, leg press one-repetition maximum (1RM), maximal workload during cycling (W_{max}) and muscle cross-sectional-area (CSA) were assessed. Loading-induced decreases in force were significant ($p<0.01$-0.001) before (E+S 20±11%, S+E 18±5%) and after (E+S 24±6%, S+E 22±8%) training. Recovery was completed within 24h in both groups. The acute growth hormone response was significantly ($p<0.001$) higher after S+E than E+S at both Week 0 and Week 24. Testosterone was significantly ($p<0.001$) elevated only after the S+E loading at Week 24, but was not significantly different from E+S. Both groups significantly ($p<0.001$) improved 1RM (E+S 13±12%, S+E 16±10%), W_{max} (E+S 21±10%, S+E 16±12%) and CSA (E+S 15±10%, S+E 11±8%). This study showed that the acute growth hormone response to combined endurance and strength loadings was significantly larger in S+E compared to E+S both before and after 24 weeks of same-session combined training. Strength and endurance performance and CSA increased to similar extents in both groups during 24 weeks despite differences in the kinetics of growth hormone. Previously untrained women can improve performance and increase muscle CSA utilizing either exercise order.

Keywords: concurrent training, testosterone, growth hormone, performance adaptations, order effect

INTRODUCTION

It has been well established in male populations, that metabolically demanding resistance exercise elicits large acute elevations of serum testosterone, growth hormone and cortisol (18, 25, 35). These acute anabolic responses in men have in some studies been linked to long-term physiological adaptations such as gains in muscle strength and hypertrophy (22, 31, 41), while in other studies this phenomenon has not been found (47). Even though the magnitude of exercise-induced elevations in hormonal concentrations may not be correlated to long-term adaptations per se, the hormonal responses are known to create the metabolic environment involved in tissue remodelling (e.g. 19, 45).

The hormonal responses to resistance exercise in women are similar to those of men, albeit smaller in magnitude. Typically, only minor or no acute elevations in testosterone concentrations are reported in women following strenuous resistance exercise protocols (e.g. (9, 19, 29). These limited magnitudes of testosterone responses are likely related to the intensity of exercise and amount of activated muscle mass (10, 26, 29, 32), but may possibly be counterbalanced by acute growth hormone release to meet the anabolic needs of resistance exercise sessions (25).

When combining strength (S) and endurance (E) into the same training session, the question arises regarding which exercise order (i.e. E+S or S+E) should be preferred. The acute effect of the exercise order on circulating hormones is of relevance considering the possible implications for long-term adaptations. As data from female populations is scarce, current knowledge of the hormonal responses to combined loadings relies mainly on findings from men. Based on earlier reports, a bout of endurance exercise seems to blunt the growth hormone response to subsequent resistance exercise, thus resulting in lower post-exercise concentrations than in the opposite order (16, 39). The findings regarding cortisol and testosterone (4, 37, 39) are less conclusive and may be related to the intensity or volume of the utilized exercise protocols or the training status of the subjects (4, 16, 39). Since most of these studies have incorporated a cross-sectional design, possible changes in the exercise-induced hormonal responses are not well understood. A previous study by our group noted that the S+E order could initially result in faster recovery of testosterone in men in comparison to the opposite order, possibly indicating different recovery needs (39). However, this difference was found to diminish with prolonged training, and did not influence the long-term strength gains. Furthermore, even though endurance exercise acutely impairs subsequent force production (12, 28) and has been suggested to attenuate strength development following prolonged E+S training (3), recent reports from both men and women show similar strength gains following long-term training (11, 14).

Despite a growing interest towards research regarding concurrent training in female populations (e.g. 11, 40), there is currently paucity in the knowledge regarding hormonal responses to combined exercise sessions in women. Although strength and endurance performance as well as lean mass are likely to increase to a similar extent following training in either order (11), the effects of prolonged training on exercise induced hormonal responses and the relevance for training adaptations has not been elucidated. Thus, the main purpose of the present study was to investigate the influence of the exercise order of combined strength and endurance loadings on acute hormone and force responses both before and after 24 weeks of combined training. A secondary purpose was to investigate whether the acute exercise-induced changes in hormone concentrations are associated with long-term training adaptations in strength and endurance performance or muscle cross-sectional area.

METHODS

Experimental approach to the problem

In order to examine the effect of prolonged training on acute exercise-induced force and hormone responses to combined E+S or S+E loadings and the chronic adaptations in strength and endurance performance and muscle cross-sectional area, a 24-week training intervention was conducted. As the focus of this study was to compare training-induced adaptations in acute loading responses, a cross-over design was not used and the subjects performed the experimental loading in their assigned loading order only. The acute loading responses and long-term adaptations in strength and endurance performance were determined before (Week 0) and after (Week 24) the intervention (Figure 1).

Subjects

Twenty-nine women participated in the present study. Recruitment was conducted by several public postings. Subjects were 1) recreationally physically active but without systematic strength or endurance training for at least 1 year prior to participation, 2) below a body mass index of 30 m^2/kg, 3) non-smokers 4) free from chronic illnesses and injuries and 5) not pregnant or lactating. A resting ECG screening was approved by a cardiologist. The subjects were informed about the study design, measurements and procedures. The subjects were matched by physical fitness at baseline into two training groups: endurance preceding strength (E+S, n=15, 29.1 ± 5.6 years, 168 ± 7 cm, 67 ± 10 kg and BMI 23.7 ± 3.3 kg/m^2) and strength preceding endurance (S+E, n=14, 28.9 ± 4.4 years, 164 ± 5 cm, 62.4 ± 8 kg and BMI 23.2 ± 3.4 kg/m^2). Due to organizational constraints, acute loading responses were assessed from 23 subjects (E+S n=12, S+E n=11), while changes in strength and endurance performance as well as muscle cross-sectional area were assessed for all subjects. The study received ethical approval from the Ethics Committee of the University of Jyväskylä, Finland, and was conducted in accordance with the Declaration of Helsinki. After written and verbal information about the study and its procedures had been provided, written informed consent was obtained from all subjects.

Procedures

Prior to the start of the measurements and training, subjects reported to the laboratory for a familiarization session during which the strength measurements were practiced and the equipment was adjusted to the specifics of the individual. Subjects wore the same shoes for all measurements and loading sessions. Blood sampling and all physical tests were conducted at the same time of day ± 1 h throughout the study. The measurements of maximal strength and endurance performance were separated from each other and the loading measurements by at least two days. The last training session of the 24-week training intervention was separated from the following basal measurements by 2-4 days of rest. Nutritional information according to the national guidelines was provided before the start of the study and the subjects were asked to keep their energy intake constant throughout the intervention. Ingestion of caffeine and alcohol was not allowed 12 h and 24 h (respectively) prior to the measurements and subjects were required to keep the nutritional intake prior to the measurements similar at Weeks 0 and 24.

As recent reports have shown minimal influence of the menstrual cycle phase on anabolic hormone responses to strength (43) and endurance exercise (33), the measurements were conducted across several phases of the menstrual cycle. Four subjects from the E+S and three subjects from the S+E groups reported oral contraceptive use.

*** Figure 1 near here ***

Basal measurements

Strength. Maximal bilateral dynamic leg press one-repetition maximum (1RM) was measured using a David 210 weight stack horizontal leg press device (David Health Solutions Ltd., Helsinki, Finland). Three warm-up sets (5 x 70-75%, 3 x 80-85% and 2 x 90-95% of estimated 1RM) with 1 min of rest between sets were performed before the 1 RM trials. Upon verbal instruction, subjects performed a full leg extension (knee angle 180°) from a starting knee angle of below 60º (58º±2º). After each successful completion the load was increased. Subjects were allowed a maximum of five trials. The trial with the highest completed load was accepted as the 1 RM.

Endurance. The maximal endurance test was conducted on a cycle ergometer (Ergometrics 800, Ergoline, Bitz, Germany) using a graded exercise protocol. The test was initiated at 50 watts (W) for all subjects with 25W increments applied every 2 min until volitional exhaustion. Maximal workload (W_{max}) was calculated as $W_{max} = W_{com} + (t/120)*25$ (39), where W_{com} represents the load of the last completed and t the time of the last incomplete stage. Aerobic and anaerobic thresholds were determined for each subject based on the points of deflection in the curves of ventilation, oxygen consumption, production of carbon dioxide and blood lactate (2).

Muscle cross-sectional area. Cross-sectional area (CSA) of the vastus lateralis muscle of the right limb was measured using a B-mode axial-plane ultrasound device (SSD-a10, Aloka, Tokyo, Japan) and a panoramic imaging technique (1). Images were taken at 50% and 70% of the femur length, i.e. the distance between the greater trochanter and the joint space on the lateral side of the knee. The 10 MHz linear-array probe was moved across the thigh from the medial to the lateral side with the subject lying in a supine position. Leg position was fixed using a Styrofoam support. Lines perpendicular to the measurement table were drawn across the thigh to ensure that the probe was moved in a straight line. Three images were taken at both 50% and 70% of the muscle length. Images were analyzed using ImageJ -software version 1.44 (National Institute of Health, USA) by manually marking the outlines of the muscles onto the image. The mean of the two closest values of 50% and 70%, respectively, were averaged and used in the statistical analyses to assess total CSA. The reproducibility of the measurement has been reported earlier by our research group (38).

Experimental loading protocol

The experimental loading was intended to reflect the content of the 24-week training program, which was designed to reflect the exercise recommendations for physically active individuals (42). The loading consisted of both endurance cycling and a leg press protocol. Loadings were conducted for each subject at the same time of day (±1h) at Week 0 and 24 and were performed in the order specific to the training. Measurements of force and hormone responses during the loading were conducted before the initiation of the loading ("Pre"), after the first part ("Mid": E or S, respective to order) and after the complete loading ("Post"). Recovery was monitored 24±1h and 48±1h after the cessation of exercise ("24h" and "48h", respectively).

Subjects were verbally encouraged throughout the loadings. Proper hydration on the day preceding the loading was encouraged. Consumption of 0.2 l of water was allowed between the two loading modes, after the "Mid" blood sample was taken.

Strength loading. A David 210 weight-stack horizontal leg press (David Health Solutions Ltd., Helsinki, Finland) was used to conduct the strength loading. A detachable handle was available for assisting if necessary. The loading consisted of three protocols typically used in training for explosive strength (3x10 repetitions at 40% 1RM with 3 min rest between sets), maximal strength (4x3 repetitions at 75-90% 1RM with 3 min rest between sets) and muscle hypertrophy (4x10 repetitions at 75-80% 1RM with 2 min rest between sets). Loads were calculated from the 1 RM obtained during the basal measurements. Additional resistance was added to at least one maximal and one hypertrophic set in order to complete a true repetition maximum and standardize the loading conditions. In the explosive sets, subjects were instructed to perform the concentric phase as fast as possible and the eccentric phase in a controlled manner, without pausing between repetitions. For the hypertrophy and maximal sets, subjects were instructed to fully extend their legs without locking their knees and to keep an even pace throughout the movement.

Endurance loading. The endurance loading consisted of 30 minutes of continuous cycling at an intensity of 65% W_{max} (39) on a Monark cycling ergometer (Ergomedic 839E, Monark Exercise AB, Vansbro, Sweden) equipped with electric resistance. The intensity was calculated based on W_{max} from the basal measurement. Subjects were instructed to keep the pedalling pace at 70 revolutions per minute (rpm). The rpm was visible to the subjects throughout the loading and was additionally monitored by a member of staff. In case of the rpm dropping below 65 with the subject unable to increase it, the workload was lowered by 15W. If the subject was unable to keep up the pace for a full minute after the reduction, the workload was further reduced by 15W. If necessary, the procedure was repeated until the subject was able to keep up the required pace and complete the loading.

Measurements during the experimental loading

Isometric force production. Maximal isometric force (MVC) was measured on a leg press device (Department of Biology of Physical Activity, University of Jyväskylä, Jyväskylä, Finland) with a knee joint angle of 107º (180º representing full extension) (20). The greater trochanter of the femur and lateral malleolus of the ankle of the right limb were used as anatomical reference points.

Subjects were instructed to perform an isometric bilateral leg press action as rapidly as possible with the aim of reaching the maximum force at the beginning of the trial and maintaining it for a duration of approximately 3s. At Pre, 24h and 48h subjects were allowed to perform three trials with 1 min rest between. At Mid and Post subjects immediately proceeded to the measurement and performed two trials with only 10s rest between for the purpose of recording exercise-induced fatigue. The trial with the highest force was selected for analysis. Force signals were recorded with Signal 2.16 software (CED, Cambridge, UK), sampled at 2000 Hz and processed with a low-pass filter of 20 Hz. Trials were analyzed for MVC and average force produced between 0 and 500 ms (MVC_{500}).

Blood samples. To determine blood lactate concentrations, capillary blood samples were taken from the fingertip at Pre, Mid and Post into a reaction tube containing an anti-coagulant and hemolyzing agent. The samples were analyzed using a Biosen lactate analyzer (S-line Lab+ EKF, Magdeburg, Germany). In addition, venous blood samples were drawn at Pre, Mid, Post, 24h and 48h for determination of total testosterone (T), cortisol (C) and growth hormone (GH, 22 kDa) concentrations. Resting concentrations of the same hormones as well as sex-hormone binding globulin (SHBG) and T/C and T/SHBG -ratios were determined on the morning of the loading (7:00-9:00 am) in a fasted state. Samples were drawn by a laboratory technician from the antecubital vein into a serum tube (Venosafe, Terum Medical Co, Leuven, Belgium). Samples were centrifuged for 10 min at 3500 rpm, after which serum was removed and frozen until analysed. The hormones were analysed with a chemical luminescence technique (Immulite 1000, Siemens, New York, USA) using hormone-specific immune-assay kits (Siemens, New York, USA). Creatine kinase (CK) was analysed using chemical analysis (KoneLab 20 XTi, Thermo Fisher Scientific Oy, Vantaa, Finland). Sensitivities for T, C, GH, SHBG and CK were 0.5 nmol l^{-1}, 5.5 nmol l^{-1}, 0.03 mlU l^{-1} and 0.02 nmol l^{-1} and 0.7 mlU l^{-1}, respectively. Intra-assay coefficients of variation for T, C, GH and SHBG were 9.8 ± 3.9, 7.1 ± 1.1, 6.0 ± 0.5, 3.1 ± 1.3%, and 1.5 ± 0.7%, respectively. Inter-assay coefficients of variation for T, C, GH, SHBG and CK were 12.0 ± 6.3, 7.9 ± 1.2, 5.8 ± 0.3, 5.0 ± 1.0% and 3.6 ± 0.8%, respectively. Serum hormone concentrations were not corrected for changes in plasma volume. To monitor haemoconcentration (13), haemoglobin (HGB) and haematocrit (HCR) were analysed with Sysmex KX 21 N (Sysmex America Inc., Mundelein, IL, USA) automated haematology analyser with a cyanide-free and cumulative pulse height detection method, respectively.

Training

The training program has been described in detail previously (14). Briefly, the training was aimed to reflect recommendations for physically active individuals (e.g. 42) and was targeted at improving both maximal strength and endurance performance. During the first 12 weeks, the subjects completed two weekly sessions of [1E+1S] or [1S+1E] (respective to the assigned training order) and five sessions per two weeks (5x [1E+1S] or [1S+1E]) during weeks 13-24. Time between training modes was 5-10 min and recovery time between training sessions 48-72 h. Training sessions were supervised by research staff. Maintenance of normal daily activity was encouraged.

Strength training mainly targeted knee extensors and flexors as well as hip extensors. Exercises consisted of horizontal leg press, seated hamstring curls and seated knee extensions. The program was initiated with the exercises performed in a circuit (2-4 sets of 15-20 repetitions with up to 60% of 1RM) and continued through hypertrophy-inducing training (2-5 x 8-12 at 80-85% of 1RM, 1-2 min rest) towards maximal strength training (2-5 x 3-5 at 85-95% of 1RM, 3-4 min rest). A similar pattern of periodization was used for the upper body. Dumbbells and cable pulley machines were used for the upper body exercises and both machines and body weight for exercises of the trunk. The periodization was repeated during weeks 13-24 with increased training intensity and volume. The duration of each strength session was 50-60 min.

Endurance training sessions were performed on a cycle ergometer. Training intensities were controlled by heart rate zones corresponding to the threshold values of aerobic and anaerobic thresholds. Training consisted of 30-50 min continuous cycling near the AT (weeks 1-7 and 13-16), including interval training at and above the anaerobic threshold from weeks 8 and 17 onwards. The interval sessions were initiated and ended with 10-15 minute bouts below the aerobic threshold with 5-minute altering bouts on the anaerobic threshold and below the aerobic threshold in between.

Statistical analysis. Data are presented as means±SD. Statistical analysis for changes during the experimental loadings at Week 0 and 24 was performed using a five-level ANCOVA (i.e. Pre, Mid, Post, 24h and 48h) with absolute values for within-group changes and values relative to Pre for between-group differences, with Pre-values used as covariates. As GH during the experimental loading and basal SHBG were non-normally distributed even after a log transformation, non-parametric statistics were used both for the within-group changes (Wilcoxon signed-rank test) and between-group comparisons (Mann-Whitney U-test). For the non-parametric tests a Bonferroni adjustment was applied by multiplying the pairwise p-values with the number of comparisons. To compare the experimental loading-induced within-group changes (i.e. Mid, Post, 24h and 48h) across 24 weeks, paired-samples t-tests were applied for each measurement point.

Training induced changes in basal hormones and basal measurements of 1 RM, W_{max} and CSA were analyzed with a two-way ANCOVA with baseline-values used as covariates, and between-group differences with an independent-samples t-test. The individual ratios of changes in 1 RM and W_{max} were calculated as the percentage change in 1 RM divided by the percentage change in W_{max}.

Reported effect sizes (ES) are Cohen’s d except for non-normally distributed data, where ES was defined as Z-score/$\sqrt{n}$. Associations between the exercise-induced changes in serum hormone concentrations and training-induced adaptations were examined using bivariate Pearson correlation coefficient for normally and Spearman’s rank correlation coefficient for non-normally distributed data. A trend was accepted for p-values <0.06.

RESULTS

Training adherence was 99% in both E+S and S+E. All subjects completed at least 90% of the training sessions.

Acute loading responses at week 0

No significant changes in body weight (-0.3±0.3%), HGB (+3.6±3.0%) or HCR (+2.6±2.9%) were observed during the loading.

MVC decreased significantly during the loading in both groups by Mid (E+S -18±13% from 1740±235 N, *P*<0.01, ES=-1.305; S+E -17±7% from 1810±633 N, *P*<0.01, ES=-0.515) and by Post (E+S -20±11%, *P*<0.001, ES=-1.587; S+E -18±5% *P*<0.001, ES=-0.532) (Figure 2). MVC_{500} decreased significantly in E+S by mid (E+S -18±12%, *P*<0.01, ES=-1.24) and post (-20±14%, *P*<0.01, ES=-1.15) and for S+E by post (-16±7%, *P*<0.05, ES=-0.611). No significant differences of MVC or MVC_{500} to Pre were observed for either group at 24h or 48h.

*** Figure 2 near here ***

A significant increase in T was observed in E+S at Mid (from 0.5±0.4 to 8.9±1.1 $nmol \cdot l^{-1}$, *P*<0.05, ES=0.513) (Figure 3). C remained statistically unaltered throughout the loading for both groups (Table 1). A trend (*P*=0.051, ES=0.256) was observed in C for E+S at Mid. At 24h and 48h, C was significantly lowered from Pre for S+E (24h: -29±23%, *P*<0.01, ES=-1.53 and 48h: -29±14% *P*<0.01, ES=-1.70). A 5.6-fold increase from pre in GH was observed at Mid for E+S (*P*<0.05, ES=0.888) and a 5.2-fold increase at Post for S+E (*P*<0.05, ES=0.830) (Figure 4). A trend was found in S+E from Mid to Post (*P*=0.055, ES=0.402). The change from Mid to Post was significantly different between groups (*P*<0.001, ES=0.886).

Blood lactate increased significantly in both groups by Mid (E+S by 4.2-fold *P*<0.001, ES=4.80; S+E by 4.0-fold, *P*<0.001, ES=2.8) and Post (E+S by 5.0-fold *P*<0.001, ES=2.84; S+E by 4.0-fold, *P*<0.001, ES=2.05) (Table 1). CK was significantly elevated in comparison to Pre in E+S at Mid (13±9% from 93±21 $mlU \cdot l^{-1}$, *P*<0.01, ES=0.544), Post (16±9%, *P*<0.01, ES=0.681) and 24h (57±32%, *P*<0.05, ES=1.73) and for S+E at Post (26±17% from 95±31 $mlU \cdot l^{-1}$, *P*<0.01, ES=0.679) but not at 24h (96±89%, ES=1.29) (Table 1). CK further increased in both groups between Post and 24h (E+S *P*<0.05, ES=1.337 and S+E *P*<0.05, ES=0.935). No between-group differences were observed during loading or recovery.

*** Figure 3 and 4 near here ***

Acute loading responses at week 24

No significant changes in body weight (-0.5±0.2%), HGB (+4.2±3.8%) or HCR (+4.4±2.9%) were observed during the loading.

MVC decreased significantly for both groups by Mid (E+S -16±9% from 1833±322 N, $P<0.001$, ES=-0.890; S+E -21±8% from 1966±690 N, $P<0.001$, ES=-0.623) and by Post (E+S -24±6%, $P<0.001$, ES=-1.66; S+E -22±8%, $P<0.01$, ES=-0.731) (Figure 2). MVC_{500} decreased significantly for both groups by Mid (E+S -18±17% $P<0.05$, ES=-0.683 and S+E -20±12%, $P<0.05$, ES=-0.678) and post (E+S -24±6%, $P<0.001$, ES=-1.43 and S+E -25±23% $P<0.05$, ES=-0.637). Both groups recovered significantly ($P<0.05$-0.001) from Post to 24h and 48h. No between-group differences were observed during loading or recovery.

A significant increase in T was found in E+S at Mid (from 0.8±0.3 to 1.2±0.4 $nmol\cdot l^{-1}$, $P<0.05$, ES=1.247) and S+E at Post (from 0.9±0.9 to 1.5±1.2 $nmol\cdot l^{-1}$, $P<0.001$, ES=0.536) (Figure 3). For S+E, T significantly increased from Mid to Post ($P<0.01$, ES=0.371). C was decreased for S+E from Pre at 48h (-28%, $P<0.001$, ES=-0.974) and near-significantly decreased at 24h (-26%, $P=0.051$, ES=-0.8254) in comparison to Pre (Table 1). A significant increase in GH was noted for both groups at Mid (E+S 7.0-fold from, $P<0.01$, ES=0.885 and S+E 2.5-fold, $P<0.05$, ES=0.790) and at Post for S+E (3.6-fold, $P<0.05$, ES=0.886) (Figure 4). For E+S a decrease took place from Mid to Post (from 68.3±31.7 to 14.7±11.3 $mlU\cdot l^{-1}$, $P<0.01$, ES=-0.885). A between-group difference was observed at Mid ($P<0.01$), and the change from Mid to Post was significantly different between groups ($P<0.001$).

Blood lactate increased 5-fold for E+S by Mid ($P<0.001$, ES=3.03) and 6-fold for S+E ($P<0.001$, ES=3.24) (Table 1). Lactate at Post was increased 5-fold for E+S ($P<0.001$, ES=4.81) and 5.5-fold for S+E (*P*<0.001, ES=3.23) (Table 1). CK was significantly (*P*<0.05) elevated in comparison to Pre for S+E at Mid (14±9%, from 108±72 mlU·l^{-1}, *P*<0.001, ES=0.169) and Post (25±17%, *P*<0.01, ES=0.299), but not at 24h or 48h (Table 1). No between-group differences were observed during loading or recovery.

*** Table 1 near here ***

Differences in the acute loading responses before and after training

In E+S, the GH response was significantly different at Pre-Mid (*P*<0.01), Pre-Post and Mid-Post (*P*<0.05) in comparison to the corresponding changes at Week 0 (Figure 4). The relative change in blood lactate was significantly larger after 24 weeks of training than the corresponding change at Week 0 for S+E during Pre-Mid (*P*<0.01), Pre-Post (*P*<0.05) and Mid-Post (*P*<0.05) (Table 1).

Basal measurements

Both groups increased 1RM (E+S by 13±12% from 102±21 kg, *P*<0.001, ES=0.569 and S+E by 17±10% from 99±18 kg, *P*<0.001, ES=0.884) (Figure 5), W_{max} (E+S by 21±10% from 170±26 W, *P*<0.001, ES=1.36 and S+E by 16±12% from 182±27 W, *P*<0.001 ES=1.05) and CSA (E+S by 15±10% from 17±2cm^2, *P*<0.001, ES=1.32 and S+E by 11±8% from 19±3cm^2, *P*<0.001, ES=0.680). Basal hormone concentrations are presented in Table 2.

Correlations

No significant correlations were observed between the acute changes in testosterone, cortisol or growth hormone and long-term 1RM, W_{max} or CSA development in either E+S or S+E. Basal levels of T, T/SHBG and T/C were not correlated with changes in 1 RM or W_{max} or CSA.

*** Figure 5 and Table 2 near here ***

DISCUSSION

The main findings of the present study were that following the experimental loading at Week 0, significantly elevated serum GH was observed only in S+E, while serum T remained unchanged in both groups. At Week 24, both T and GH were significantly elevated in S+E but not in E+S at Post. The exercise order did not affect the magnitude of loading-induced fatigue measured as maximal voluntary isometric force and rapid force production either at Week 0 or 24. Additionally, muscle force production was recovered by 24 h following both exercise orders both at Week 0 and 24. The present 24-week combined strength and endurance training period resulted in significant increases in 1RM strength, W_{max} and muscle cross-sectional of similar magnitudes in both groups. These chronic adaptations were not associated with the acute exercise-induced changes of serum hormones in either order.

In accordance with our previous study with men performing the same experimental loading with the same relative intensity (39), we observed no acutely elevated concentrations of T in the present study at Post before the prolonged training period following either order. This outcome was expected, considering the combination of explosive, maximal and hypertrophic sets in the present strength loading. Thus, the protocol was likely not strenuous enough to elicit acute anabolic responses (39), as large elevations in T would be expected in women mainly following hypertrophic type protocols with a large stress on the metabolic system (26, 29). However, this design was purposefully chosen to reflect the content of the 24-week training program which was created based on common exercise recommendations (42).

Interestingly, as elevated concentrations of serum T were observed during loading for E+S at Mid (Week 0 and 24), and for S+E at Post (Week 24), our results suggest that the observed elevations may primarily have been a result of the present endurance exercise. Considering the likely absence of haemoconcentration in the present study, this supports previous findings of endurance exercise inducing elevations in T in female populations (15, 24). The lack of significantly increased T at Post for the S+E group at Week 0 is in line with earlier investigations in men (4, 37, 39), with unchanged concentrations of T following a combined loading in the S+E order. However, the significantly elevated concentration of serum T in S+E at Week 24 could be related to training-induced increased sensitivity to adrenocorticotropic hormone (30), which stimulates the adrenal cortex and releases androgens as a byproduct of cortisol secretion (23, 34). This together with the relatively higher rise in lactate after training could be related to why elevated T was observed in the S+E group at Post at Week 24, but not at Week 0. However, no such observation was made in the E+S group. Furthermore, as we only measured total testosterone and did also not detect any significant elevations in cortisol during the loadings in either order, this hypothesis remains speculative.

It also needs to be acknowledged that the underlying causes of exercise-induced elevations in T in women are not fully comprehended, and not all plausible mechanisms were monitored in the present study. Possible mechanisms include e.g. the time course of androgen receptor regulation (44) and reduced hepatic clearance as observed in men (5). Haemoconcentration as an indirect cause for elevated T can likely be ruled out in the present study due to unchanged hemoglobin and hematocrit during loading. It is also possible that oral contraceptive use affects the secretion of T as well as the metabolites of dehydroepiandrosterone (15) and, consequently, the biosynthesis pathway of T during exercise. However, in the present study, a similar number of subjects in both groups reported oral contraceptive use and, on a group level, the pattern of T response to endurance exercise was comparable in both orders.

Similarly to the exercise-related variables affecting the acute responses of T, the intensity of exercise is a major contributor to the magnitude of responses of GH in women (29, 46). As expected based on previous findings (16), the GH concentrations in the E+S order both before and after training were significantly elevated after endurance exercise but diminished following the strength loading. This pattern in the kinetics of exercise-induced growth hormone release was significantly different between groups both before and after training as S+E demonstrated elevated GH throughout the loading in contrast to E+S. These differing GH responses may have been caused by endurance exercise-induced lipolysis (36). The release of free fatty acids (FFA) is likely a major influence for suppressed GH release, possibly through affecting anterior pituitary function (6). It needs to be noted, that even though oral contraceptive use could amplify lipolysis during continuous cycling exercise, the FFA concentration is likely to remain unaffected (7).

Due to a critical relative threshold for GH secretion, the intensity of training would need to be continuously progressive in order for significant GH responses to occur within a loading session after prolonged training (8). In the present study, the loading was conducted with values relative to 1RM and W_{max} in order to keep the relative intensity the same at both weeks 0 and 24 and to be matched for the current training status and improved performance level of the subjects. This was reflected in the GH responses in both groups at Week 24 as higher absolute concentrations at both Mid and Post in comparison to corresponding time points at Week 0. In the S+E order, despite the fact that the magnitude of the loading-induced changes (Pre-Mid and Pre-Post) were not statistically larger than the corresponding magnitudes at Week 0, the GH responses during loading at Week 24 were statistically significant. This serves as an indication of adaptation to training, as the same relative exercise intensity was potent in significantly elevating serum GH concentrations. Similar indications for training adaptations were found in the E+S group, as the magnitudes of the Pre-Mid and Pre-Post changes were significantly larger at Week 24 than at Week 0. Interestingly, while the adaptations in GH release seem to indicate that the loadings were still strenuous at Week 24, changes in the behaviour of CK may suggests better tolerance of the experimental loading. CK was slightly elevated both during loading and recovery in both groups at Week 0, but during Week 24 only elevated in S+E during loading and similar to resting levels during recovery. As CK can be considered to be an indirect indicator of muscle damage, the lack of its presence during recovery after training may indicate an increased tolerance for combined strength and endurance loadings, similarly to what was recently observed in men (39).

Interestingly, although the GH responses clearly differed between the present exercise orders during loading, no between-group differences were observed in training-induced increases in muscle CSA. The implications of the present findings thus require further clarification e.g. through examining additional forms of GH than solely the present 22 kDa variant. While an acute bout of exercise may stimulate variants of GH that are incapable of generating increases in biological activity, chronic resistance exercise may increase the circulating concentrations of biologically active growth hormone (27). This may in part explain why the GH responses in the present study were not related to the changes in muscle cross-sectional area in either group and warrants further investigation of the mechanisms of several GH variants both during combined strength and endurance loadings as well as prolonged combined training.

In addition to a lack of a relationship between changes in muscle cross-sectional area and the magnitudes of acute GH release, we also observed no associations between acute responses of T and long-term performance adaptations. While it has been suggested that tissue exposure to acute elevations in anabolic hormones would not be associated with hypertrophy or strength performance (47), such correlations have been demonstrated in male populations following pure strength training (e.g. 22, 31). Furthermore, previously reported correlations of basal levels of T and T/SHBG-ratios and strength development and changes in CSA following strength training in women (e.g. 17, 21) were not found in present study despite significantly increased basal levels of T. Thus, it seems reasonable to suggest that the detection of possible linkages of resistance exercise-induced anabolic responses and gains in strength and hypertrophy may be interfered when strength training is simultaneously accompanied by endurance training both in men (39) and women. However, further studies with different training protocols are needed for more definite conclusions.

It is noteworthy that both exercise orders resulted in similar training-induced long-term gains in 1RM, thus challenging earlier suggestions of the order of S+E being superior to E+S in terms of adaptations in strength performance (3, 28). The experimental loading showed that the acute fatigue in terms of exercise-induced decreases in MVC and MVC_{500} were of similar magnitudes following both loading conditions both before and after training. Furthermore, as neither MVC nor MVC_{500} were no longer significantly depressed from Pre-loading values by 24h, the experimental loadings indicate that the recovery of maximal and rapid strength performance was completed within 24 hours of cessation of exercise. Consequently, it can be assumed that the recovery between individual training sessions was sufficient, as the sessions were consistently separated by at least 48-72h. Even though we only monitored recovery before and after 24 weeks of training, the loads utilized in the experimental loading were similar to those used during training. This may, in part, explain similar gains in 1RM in both groups.

However, it also needs to be noted that the findings regarding the effect of the mode of endurance exercise (i.e. running or cycling) on changes in strength performance are to date equivocal (40, 48). Thus, comparisons of the present training program, consisting of cycling endurance training, to other protocols should be done with caution. Interestingly, while no between-group differences were observed in long-term training-induced changes, the magnitude of gains in strength in relation to endurance performance was highly individual in both exercise orders (Figure 5). This warrants further investigation regarding the mechanisms of the underlying adaptations to same-session combined strength and endurance training in women.

To conclude, this study demonstrated that the acute hormone and force responses to a combined strength and endurance loading were by large similar between exercise orders in previously untrained women both before and after training, with the exception of differences in the kinetics of serum concentrations of GH during exercise. Furthermore, our results showed that strength and endurance performance as well as muscle cross-sectional area following 24 weeks of same-session combined strength and endurance training were similar in both exercise orders. Therefore, our data indicates that despite some differences in the acute anabolic responses to exercise, the present 24-week combined strength and endurance training program resulted in similar long-term performance and morphological adaptations in both groups.

PRACTICAL APPLICATIONS

As the present study did not show order-specific responses of recovery of force, the findings indicate that the exercise order does not seem to be of great importance for previously untrained women when combining strength and endurance into the same training session. Even though the growth hormone responses to exercise were significantly larger in S+E compared to E+S both before and after the training, this was not reflected in or associated with the long-term adaptations. Consequently, the gains in strength and endurance performance as well as muscle size were of similar magnitudes in the two training groups following 24 weeks of combined strength and endurance training. Thus, previously untrained women can achieve performance improvements and increases in muscle size by combining strength and endurance into the same training session with either exercise order, when sufficient recovery is allowed.

Captions and legends for figures

Figure 1. Overview of the experimental design. E+S = Endurance preceding strength, S+E = Strength preceding endurance.

Figure 2. MVC for E+S and S+E during loading and recovery at Week 0 and at Week 24. Within-group differences: *=Significant from Pre, §=Significant from Post. $^{**}P<0.01$, $^{***}P<0.001$, § $P<0.05$, §§ $P<0.01$ and §§§ $P<0.001$.

Figure 3. Responses in total testosterone for E+S and S+E during loading and recovery at Week 0 and at Week 24. Within-group differences: *=Significant from Pre, +=Significant from Mid, §=Significant from Post. $^{*}P<0.05$, $^{***}P<0.001$, $+P<0.05$ and §§§ $P<0.001$.

Figure 4. Growth hormone responses for E+S and S+E during loading at Week 0 and at Week 24. Within-group differences: *=Significant from Pre, +=Significant from Mid, §=Significant from Post, •=significant from Week 0. #=between-group difference at given time point. $^{*}P<0.05$. $^{**}P<0.01$, +P0.05, $+P<0.01$, •$P<0.05$, ••$P<0.01$, #$P<0.05$, ##$P<0.01$ and ###$P<0.001$.

Figure 5. Changes in 1RM (left), Maximal workload (middle) during the cycling endurance test and the individual ratios of the magnitude of gains in 1RM and workload (right). *=significant from Week 0. $^{***}P<0.001$.

Captions and legends for tables

Table 1. Exercise-induced changes in serum cortisol (C), creatine kinase (CK) and blood lactate (La) during loading and recovery for E+S and S+E at Week 0 and 24. Within-group differences: *=significant from Pre, +=significant from Mid, §=significant from Post, ¤ = significant from 24 h, •=significant from corresponding value at Week 0. *$P<0.05$. **$P<0.01$, ***$P<0.001$, +P0.05, +$P<0.01$, •$P<0.05$, ••$P<0.01$, ¤ $P=0.05$, § $P<0.05$. §§ $P<0.01$, §§§ $P<0.001$.

Table 2. Basal serum concentrations of total testosterone (T), cortisol (C), growth hormone (GH), sex-hormone binding globulin (SHBG), and ratios of testosterone and cortisol (T/C) and testosterone and sex-hormone binding globulin (T/SHBG) before and after the training intervention.

* within-group difference to Week 0; *$P<0.05$ and ***$P<0.001$

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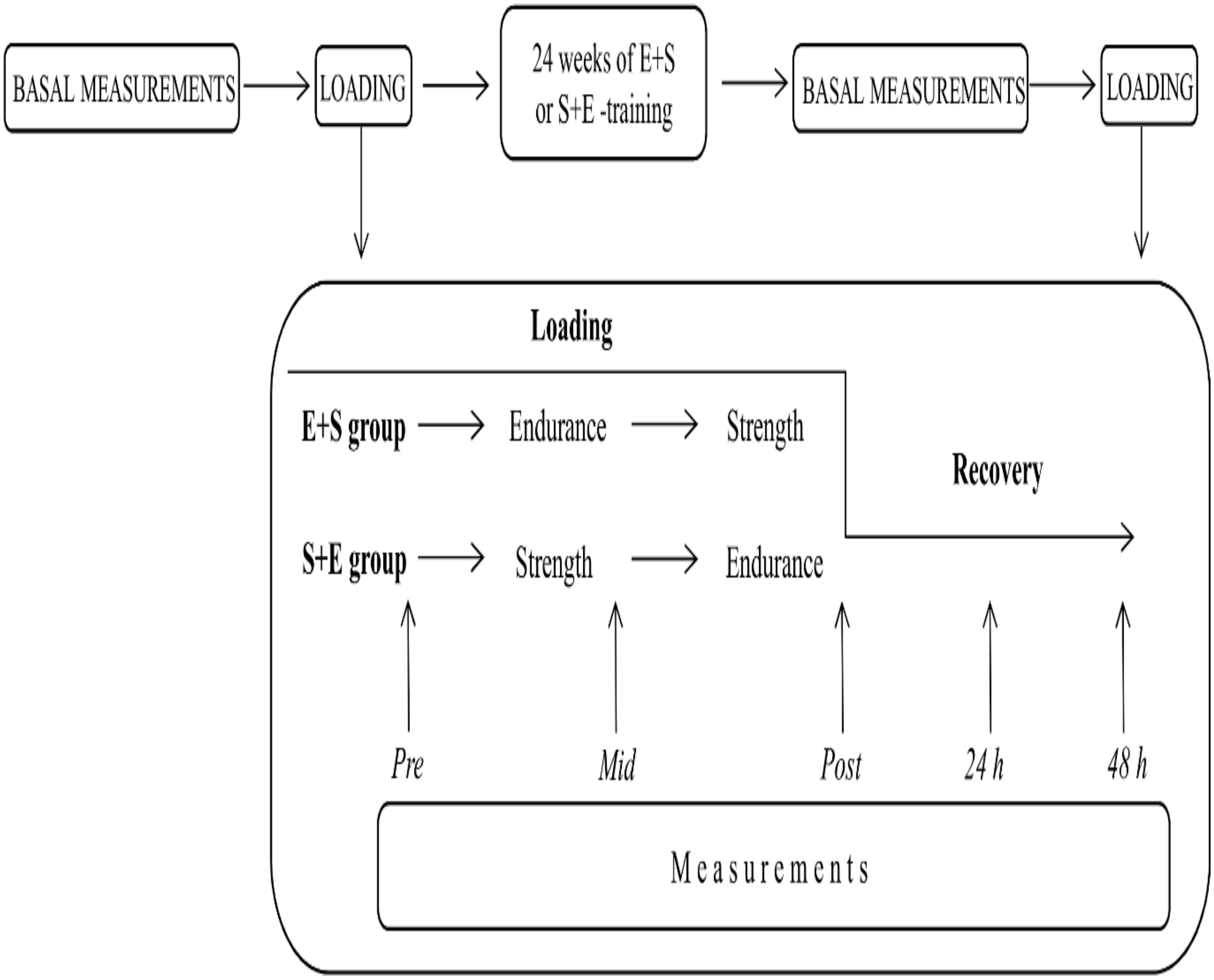
Table 1. Exercise-induced changes in serum cortisol (C), creatine kinase (CK) and blood lactate (La) during loading and recovery for E+S and S+E at Week 0 and 24. Within-group differences: *=significant from Pre, +=significant from Mid, §=significant from Post, ¤ = significant from 24 h, •=significant from corresponding value at Week 0. *$P<0.05$. **$P<0.01$, ***$P<0.001$, +*P*0.05, +$P<0.01$, •$P<0.05$, ••$P<0.01$, ¤ $P=0.05$, § $P<0.05$. §§ $P<0.01$, §§§ $P<0.001$.

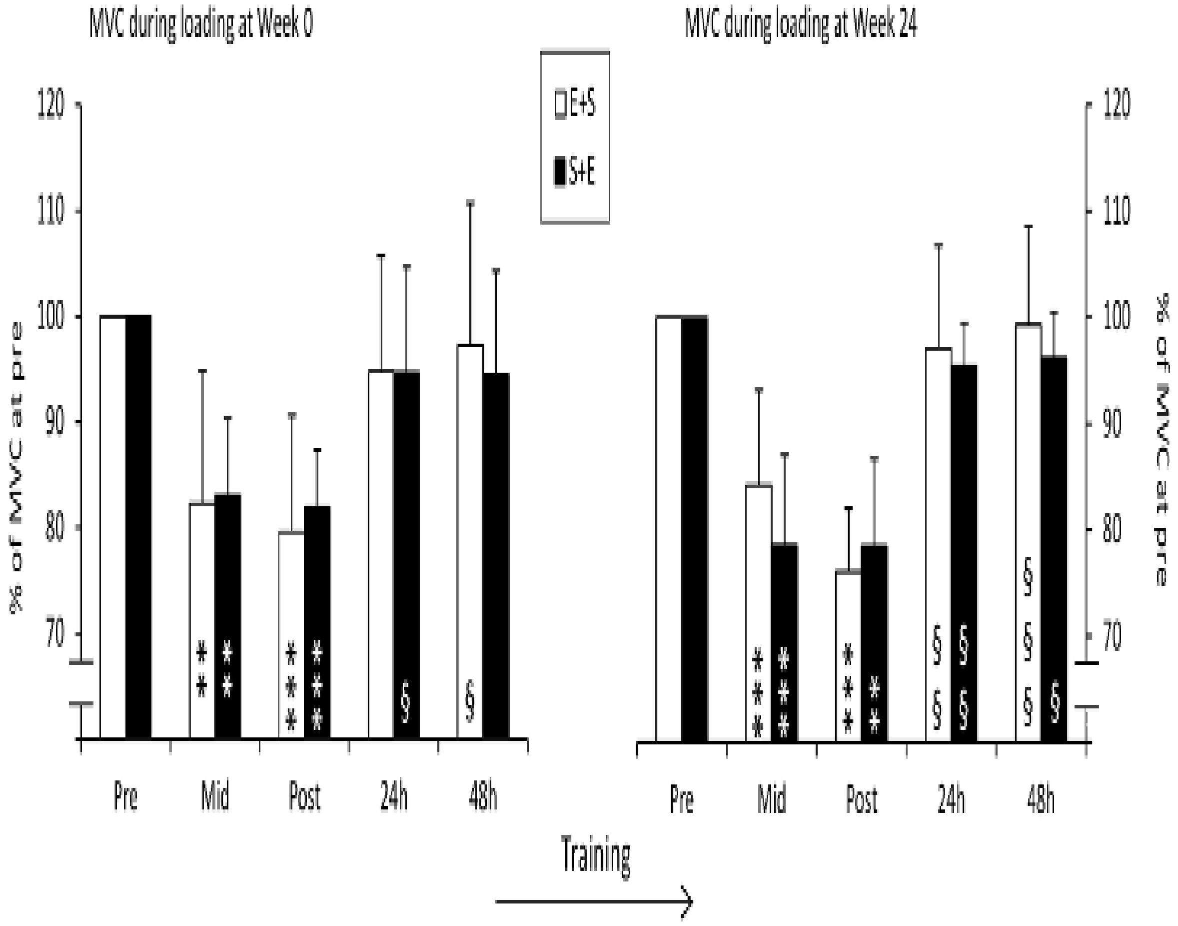
	WEEK 0		**WEEK 24**	
	E+S	**S+E**	**E+S**	**S+E**
C (nmol·l^{-1}*)*	*(n=10)*	*(n=10)*	*(n=8)*	*(n=10)*
Pre	397±128	479±105	413±154	616±178
Mid	437±176	367±139	471±96	567±199
Post	426±207	435±211	423±108	778±252
24 h	312±111 $^{[*]\ p=0.051}$	332±87 **	284±134	459±200 $^{[*]\ p=0.051}$§§
48 h	347±141	333±60 **	322±116	445±170*** §§§
CK (mlU·l^{-1}*)*	*(n=9)*	*(n=9)*	*(n=9)*	*(n=9)*
Pre	93±21	95±31	103±44	109±72
Mid	103±19 **	106±32	121±49	121±71 ***
Post	105±17 **	118±35 ** +	123±55	131±75 **
24 h	143±36 *	181±89 §	145±80	148±81
48 h	128±38	132±55 ¤	141±116	123±70
La (mmol·l^{-1}*)*	*(n=12)*	*(n=11)*	*(n=12)*	*(n=11)*
Pre	1.1±0.3	1.3±0.3	1.2±0.4	1.1±0.4
Mid	4.7±1.0 ***	5.0±1.9 ***	6.3±2.3 ***	6.8±2.4 *** ••
Post	5.6±2.2 ***	5.2±2.3 ***	6.5±1.5 ***	6.0±2.1 *** •

Table 2. Basal serum concentrations of total testosterone (T), cortisol (C), growth hormone (GH), sex-hormone binding globulin (SHBG), and ratios of testosterone and cortisol (T/C) and testosterone and sex-hormone binding globulin (T/SHBG) before and after the training intervention.

* within-group difference to Week 0; *$P<0.05$ and ***$P<0.001$

	WEEK 0		**WEEK 24**	
	E+S	S+E	E+S	S+E
T (nmol·l^{-1})	0.6±0.3	0.6±0.4	1.1±0.3 ***	1.3±0.9 ***
C (nmol·l^{-1})	546±186	564±185	614±225	673±136 *
GH (mlU·l^{-1})	7.9±12.1	11.0±10.0	6.1±11.1	14.0±20.6
SHBG (nmol·l^{-1})	52.3±17.5	65.3±42.0	68.6±12.7 *	81.6±43.4 *
T/C *10^3	1.4±1.1	1.3±1.0	1.9±1.1 *	2.1±1.8 *
T/SHBG *10^3	15.3±8.8	13.1±10.7	17.3±6.7	21.5±11.4


BASAL MEASUREMENTS
LOADING
24 weeks of E+S or S+E -training
BASAL MEASUREMENTS
LOADING
Loading
E+S group
Endurance
Strength
Recovery
S+E group
Strength
Endurance
Pre
Mid
Post
24 h
48 h
Measurements


MVC during loading at Week 0
MVC during loading at Week 24
□E+S
■S+E
% of MVC at pre
120
110
100
90
80
70
Pre
Mid
Post
24h
48h
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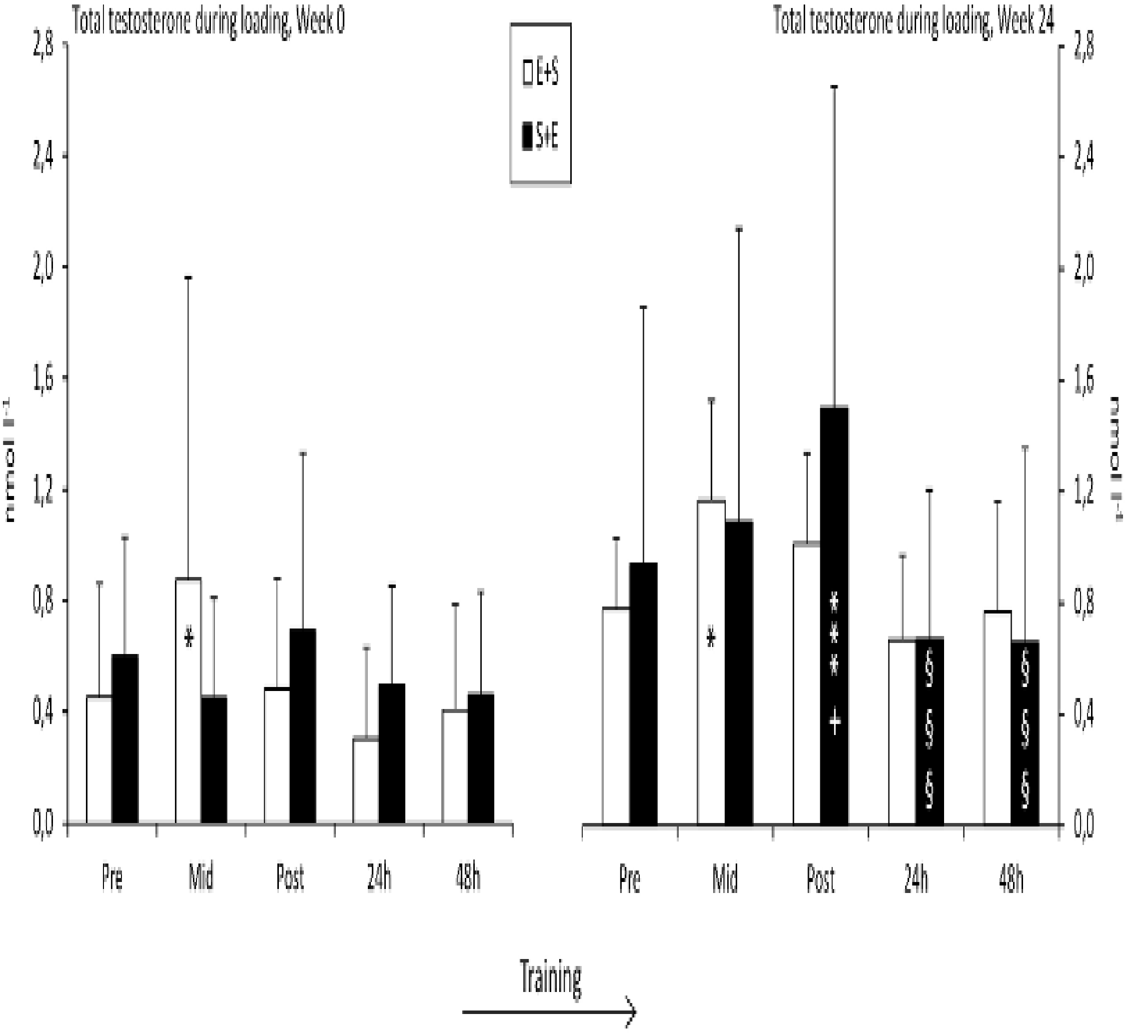
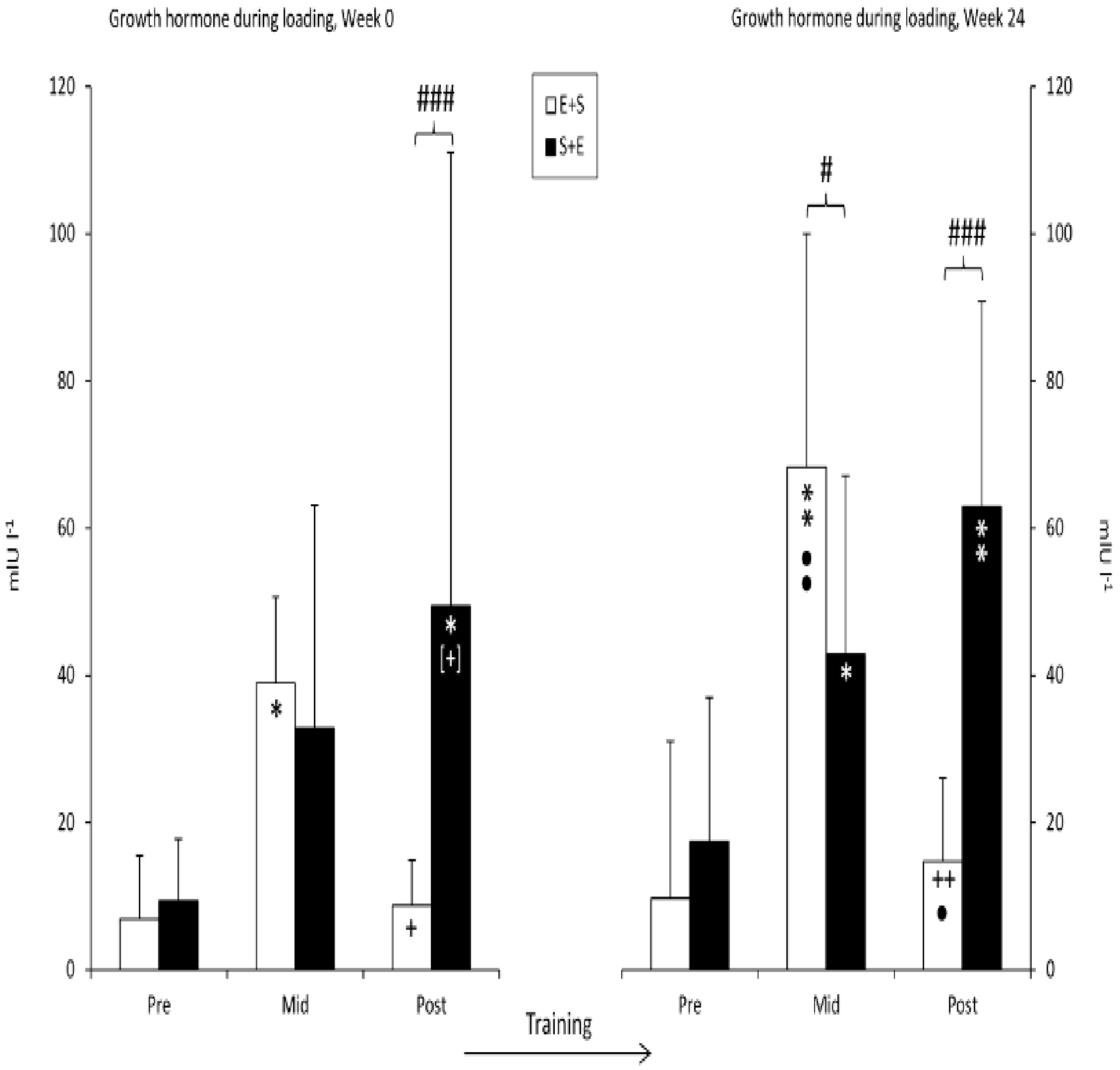
Training



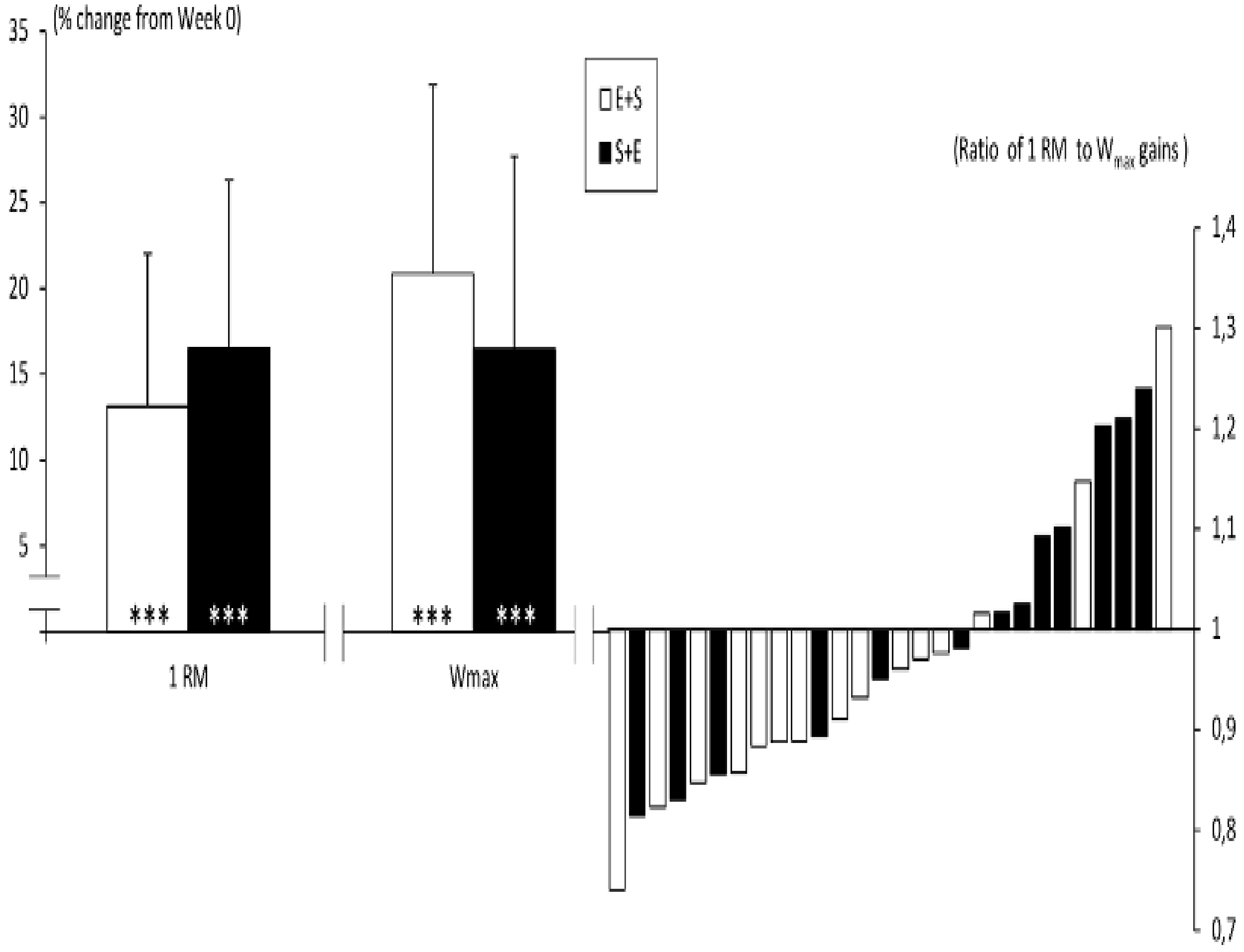
Total testosterone during loading, Week 0

Total testosterone during loading, Week 24



Growth hormone during loading, Week 0

Growth hormone during loading, Week 24


(% change from Week 0)
35
30
25
20
15
10
5
***
***
***
***
1 RM
Wmax
☐ E+S
■ S+E
(Ratio of 1 RM to W$_{max}$ gains)
1,4
1,3
1,2
1,1
1
0,9
0,8
0,7

II

NEUROMUSCULAR ADAPTATIONS TO DIFFERENT MODES OF COMBINED STRENGTH AND ENDURANCE TRAINING

by

D. Eklund, T. Pulverenti, S. Bankers, J. Avela, R.U. Newton, M. Schumann & K. Häkkinen. 2014.

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Title: Neuromuscular adaptations to different modes of combined strength and endurance training

ABSTRACT

The present study investigated neuromuscular adaptations between same-session combined strength and endurance training with two loading orders and different day combined training over 24 weeks. Fifty-six subjects were divided into different day (DD) combined strength and endurance training (4-6 $d \cdot wk^{-1}$) and same-session combined training: endurance preceding strength (E+S) or vice versa (S+E) (2-3 $d \cdot wk^{-1}$). Dynamic and isometric strength, EMG, voluntary activation, muscle cross-sectional area and endurance performance were measured. All groups increased dynamic one-repetition maximum ($p<0.001$; DD 13±7%, E+S 12±9% and S+E 17±12%) and isometric force ($p<0.05$-0.01), muscle cross-sectional area ($p<0.001$) and maximal power output during cycling ($p<0.001$). DD and S+E increased voluntary activation during training ($p<0.05$-0.01). In E+S no increase in voluntary activation was detected after 12 or 24 weeks. E+S also showed unchanged and S+E increased maximum EMG after 24 weeks during maximal isometric muscle actions. A high correlation ($p<0.001$, $r=0.83$) between the individual changes in voluntary activation and maximal knee extension force was found for E+S during weeks 13-24. Neural adaptations showed indications of being compromised and highly individual relating to changes in isometric strength when E+S-training was performed, but gains in one-repetition maximum, endurance performance and hypertrophy did not differ between the training modes.

Keywords: Concurrent training, order effect, voluntary activation

ABBREVIATIONS

CSA – Cross-sectional area
DD - different day strength and endurance training
EMG - Electromyography
E+S - Same-session combined strength and endurance training, endurance preceding strength
ITT - Interpolated twitch technique
QF - Quadriceps femoris
S+E - Same-session combined strength and endurance training, strength preceding endurance
VA - Voluntary activation
VL - Vastus lateralis

INTRODUCTION

Strength and endurance training are known to result in different neuromuscular adaptations. While strength training results in large gains in maximal strength and muscle hypertrophy [eg. 28], endurance training leads only to minor changes in strength performance but produces gains in endurance performance variables such as maximal oxygen consumption and maximal aerobic power output [22, 38, 49]. Previous research indicates that adaptations in strength, but not endurance, may be compromised when strength and endurance are trained for concurrently, in comparison to strength training alone [e.g. 24, 29]. This phenomenon has been observed with both different day [e.g. 6, 29] and same day combined strength and endurance training [e.g. 32]. The compromises in strength training adaptations with concurrent training in previously untrained subjects were originally annotated by Robert Hickson [24], when untrained subjects embarked on a training regimen with an overall remarkably high volume and frequency strength and endurance training. As a result of the strenuous training program, attenuations in strength gains were observed already after 5-6 weeks of combined training [24]. The same interference phenomenon has also been clearly observed in well-trained endurance athletes both in terms of maximal and explosive strength [43]. Conversely, when the total training volume of the concurrent training design is reduced both in a single session as well as over time, increases in maximal strength, maximal voluntary neural activation and muscle hypertrophy of the trained muscles have been found to be more likely to occur [29, 34, 45].

As a time-saving aspect rationalizes the idea of combining the two modes into the same training session, it raises the question of the possible differences between disparate intra-session exercise orders ("the order effect"). Considering that the first loading may result in residual fatigue compromising the second one, it can be thought to accumulatively suppress the favorable adaptations over a prolonged period of training [11, 44, 45]. Fatigue-induced acute adjustments in the nervous system following an endurance training session may include reduced force output of a particular muscle group and thus altered muscle recruitment [48], decreased rate of force development [8, 33] and reduced neural input to the muscle, ultimately resulting in decreased efficiency of the muscle contractile mechanisms [40]. Strength loading leads to acute decreases in neuromuscular performance [50] and, similarly, acute decreases in maximal force have also been noted following endurance exercise [46, 47].

Attention has previously been directed towards molecular adaptations as an explanation for possible difficulties in optimizing performance when training concurrently for strength and endurance [4, 15], whereas neural adaptations and differences between different modes of concurrent training have not been comprehensively investigated. Results from elderly populations point to an order effect in favor of strength preceding endurance with regard to training-induced neuromuscular adaptations [11, 12], although age-related declines in the same parameters [30] may complicate the interpretation. Furthermore, numerous different research designs make the comparison difficult, thus not elucidating how adaptations following different day and same-session combined strength and endurance protocols relate to each other. To the best of our knowledge, a long-term comparison of different day combined strength and endurance training and same-session combined training with different exercise orders has not been conducted. The purpose of this study was to examine possible differences or limitations in neuromuscular adaptations between same-session combined training with different loading orders and combined strength and endurance training performed on different days. Specifically, this object was achieved by monitoring adaptations in strength and force, voluntary activation, surface electromyography, muscle cross-sectional area and maximal power output during cycling over the course of a 24-week training intervention.

METHODS

SUBJECTS

Seventy healthy men aged 18-40 from the Jyväskylä, Finland region were recruited to participate in the study. Recruitment was conducted by several public announcements. Requirements for participation included the subjects to 1) be recreationally active (i.e. physically active but without systematic strength or endurance training for at least one year prior to the study), 2) have a body mass index of less than 30 kg/m^2, 3) not have been smoking for a minimum of one year prior to the start of the study, 4) be free from chronic illnesses and 5) have no injuries or ailments of the locomotor system. All subject candidates were interviewed in terms of general health and attended a health screening including resting ECG which was analyzed and approved by a cardiologist as a part of the pre-screening process. The selected subjects received detailed information about the study design, measurements and procedures and were required to give written informed consent prior to participation. The study received ethical approval from the ethics committee of the University of Jyväskylä and was conducted in accordance to the Declaration of Helsinki as well as the ethical standards of the International Journal of Sports Medicine [23].

Table 1 near here.

STUDY DESIGN

All subjects were initially familiarized with the training- and measurement protocols and equipment of the current study before proceeding to basal measurements of maximal strength, muscle cross-sectional area and endurance. The study spanned a 24-week period for the experimental groups and 12 weeks for the control period. The measurement protocols were repeated after the first twelve weeks as well as after the completion of the entire 24-week training period. The overview of the study design is presented in figure 1.

Figure 1 near here.

The strength and endurance measurements as well as measurement of muscle cross-sectional area were separated from each other by a minimum of 2 days. The measurements always took place at the same time of day (±1 h) to minimize circadian fluctuation. Subjects were instructed to abstain from caffeine 12 h and alcohol 24 h prior to the measurements as well as to consume a light snack 2 h before but allowing for at least 4 h between a main meal and the measurement session. The last session of both training periods was separated from the following measurements by a minimum of 2 and a maximum of 4 days.

After the basal measurements of ultrasound and strength and endurance performance, each subject was assigned into one of the three training groups for the entire duration of the study: different day strength and endurance training (DD), same-session combined strength and endurance training with strength preceding endurance (S+E) or endurance preceding strength (E+S). Assignment was done by pairwise matching physical characteristics. The control period lasted for 12 weeks and took place prior to the start of the study. During the control period a group of subjects (n=24) were asked to act as a control group. They were asked to refrain from strenuous physical strength and endurance activities, but were allowed to do light exercise and maintenance of daily activities. After the control period of three months, 21 subjects continued in the study to form the DD group. The entire 24-week program was completed by 56 subjects. Fourteen subjects did not finish the study due to minor injuries or medical issues, occupational changes or personal choices to drop out due to the demanding training program. Table 1 contains the data from subjects who completed the entire 24-week program.

FAMILIARIZATION SESSION

To minimize a possible learning effect to the tested variables, subjects participated in a familiarization session a few days prior to their first actual strength measurement. During the session, subjects were familiarized with the testing procedures, equipment and execution of the tested variables. For the isometric leg press and the isometric knee extension, knee angles of 107 º (180º representing full extension) were utilized [27]. A starting knee angle of below 60º (58º±2º) was utilized for the dynamic leg press. All knee angles were measured with a hand-held goniometer in the same measurement devices as the actual testing later took place. The greater trochanter of the femur and lateral malleolus of the ankle of the right limb were used as anatomical reference points. To ensure the device was set up in the same way throughout the study, the device settings were stored on both paper and in a computer file. To further reduce the sources of error, subjects were asked to wear the same shoes for all measurement sessions throughout the study. Small marks were tattooed to the right limb with a lancet and permanent ink to ensure repeatable electromyographic (EMG) measurements throughout the study [25].

NEUROMUSCULAR MEASUREMENTS

Dynamic strength. One-repetition maximum (1 RM) in bilateral leg press was measured using a David 210 weight stack horizontal leg press device (David Health Solutions Ltd., Helsinki, Finland). The subjects were seated with a starting knee angle below 60º (58º±2º). As a preparation for the 1 RM trials, subjects performed three warm-up sets (5 x 70-75% estimated 1 RM, 3 x 80-85% estimated 1 RM, 2 x 90-95% estimated 1 RM) with 1 min of rest between sets. When verbally instructed, subjects performed a dynamic action to a full leg extension (knee angle 180°). At successful completion, the load was increased. Subjects were allowed a minimum of three and a maximum of five maximal trials, after which the trial with the highest load was accepted as the 1 RM.

Maximal isometric bilateral leg press force. Maximal bilateral isometric leg press force was measured at a knee angle of 107º on a horizontal leg press device designed and manufactured by the Department of Biology of Physical Activity (University of Jyväskylä, Jyväskylä, Finland). When verbally instructed, subjects performed an isometric bilateral leg press action as rapidly as possible with the aim of reaching their maximum at the beginning of the trial and maintaining it for approximately 3 s. Subjects were allowed a minimum of three and a maximum of five maximal trials. A fourth and fifth trial was allowed, if the difference from the third trial to the previous two exceeded 5%. Force signals were passed in real-time to an analog to-digital converter (Micro 1401, Cambridge Electronic Design, Cambridge, UK) and transferred to a computer. Force signals were recorded with Signal 2.16 software (Cambridge Electronic Design, Cambridge, UK) and sampled at 2000 Hz and processed with a low-pass filter of 20 Hz. The trial with the highest exerted maximal force was used for further analysis. Trials were analyzed by a customized, automated script (Signal 2.16 software, Cambridge Electronic Design, Cambridge, UK).

Maximal unilateral isometric knee extension force and interpolated twitch technique. Maximal unilateral isometric knee extension force was recorded and electrical stimulation performed on a device designed and manufactured by the Department of Biology of Physical Activity (University of Jyväskylä, Jyväskylä, Finland). Subjects were seated upright with a knee joint angle of the right limb at 107°. The left limb was lifted onto a chair and positioned parallel to the floor. Subjects were secured to the knee extension device by a seatbelt at the hip and a pad strapped over the right knee. The ankle was strapped to the device 2 cm above the right lateral malleolus with a Velcro strap, which was connected to a strain gauge. Subjects were instructed to increase force gradually, reaching maximum voluntary force in approximately 3 s and maintaining the reached force level for a duration of approximately 4 s. Subjects performed three maximal isometric knee extension trials, of which the one with the highest voluntarily achieved force prior to the electrical muscle stimulation was accepted as the trial to be analyzed.

To assess voluntary activation (VA) of the quadriceps femoris (QF) muscle group, electrical muscle stimulation was delivered to the QF during the maximal unilateral knee extension using the interpolated twitch technique (ITT). Four galvanically paired self-adhesive electrodes (6.98 cm Vtrodes, Mettler Electronics Corp, USA) were placed on the proximal and intermediate regions of the quadriceps muscle belly of the right limb. Rectangular single pulses of 1 ms were delivered during rest, and increasing the stimulation intensity in 5mA increments with a constant-current stimulator (400V, Model DS7AH, Digitimer, UK) until a plateau in the stimulation-induced force was noted. To ensure maximal effect for the knee extension trials an additional 25 % of stimulation intensity was then added to the current which was observed to produce maximum twitch force during rest. The supra-maximal single-pulse electrical stimulation was delivered to the muscle at three separate times during each trial: 3 s before voluntary knee extension (at rest), during the plateau of maximal voluntarily exerted force (super-imposed twitch) during knee extension and 5 s after the end of the contraction [35]. The voluntary activation percentage was calculated as VA % = $(1 - (P_{ts} / P_t)) \times 100$ [7], ie. amplitude of twitch elicited by the electrical stimulation on top of the voluntary contraction (P_{ts}) divided by the following control twitch (P_t) delivered to the resting muscle 5 s after the maximal voluntary contraction. The stimulation procedure was always carried out by the same member of staff. Force signals were recorded with Signal 4.04 software (Cambridge Electronic Design, Cambridge, UK), sampled at 2000 Hz and processed with a low-pass filter of 20 Hz. Maximal force was manually analyzed on Signal version 4.04 (Cambridge Electronic Design, Cambridge, UK)

Electromyography (EMG). Muscle activity of the Vastus Lateralis (VL) muscle of the right leg was monitored through surface electromyography. Placement of two adhesive electrodes (bipolar configuration Al / AgCl electrodes with an inter-electrode resistance < 5 kΩ, Blue Sensor N ECG Electrodes, Ambu A/S, Denmark) was defined according to the SENIAM guidelines as two-thirds of the distance along the line between the anterior spina iliaca superior to the lateral side of the patella, on the muscle belly. This point was subcutaneously tattooed onto the right limb during the familiarization session, and during the actual measurements the area over and around the tattoo was prepared for better signal conduction by shaving, abrasion, and wiping with rubbing alcohol. The electrodes were placed as close as possible to each side of the tattoo, aligned with the estimated pennation angle of the VL. The activity of the VL muscle was recorded during the isometric muscle actions and electrical muscle stimulation.

The raw EMG signals from the maximal isometric bilateral leg press was amplified by a factor of 1000 and sampled at 3000 Hz. The signals were passed from a portable transmitter to a receiver box (Telemyo 2400R, Noraxon, Scottsdale, AZ, USA) from which the signal was passed on to a desktop computer via an analog-to-digital converter (Micro 1401, Cambridge Electronic Design, Cambridge, UK). Analysis of the isometric EMG and conversion into integrated EMG (iEMG, mV•s) was performed using a customized, automated script (Signal 2.16, Cambridge Electronic Design, Cambridge, UK). Average maximum iEMG (mV•s) of the VL was determined during the 500-1500ms time period after the onset of the contraction, representing the peak force phase for isometric bilateral leg press.

The raw EMG signals from the unilateral isometric knee extension with super-imposed electrical twitch were band-pass filtered (20–350 Hz) and manually converted to root mean square (rmsEMG, mV) during a 500 ms time frame of the peak force phase immediately preceding the super-imposed twitch using Signal 4.04 software (Cambridge Electronic Design, Cambridge, UK).

The neuromuscular measurements were performed in the following order: isometric force, electrical stimulation and dynamic strength.

CROSS-SECTIONAL AREA

Cross-sectional area (CSA) of the VL muscle was measured using a B-mode axial-plane ultrasound (SSD-a10, Aloka, Tokyo, Japan) by a panoramic imaging technique [1] where the 10 MHz linear-array probe was moved sagittally across the thigh, starting from the lateral side and moving over the thigh medially. Images were taken of the right limb at 50% of the femur length, defined as the midpoint between the greater trochanter and the joint space on the lateral side of the knee. The midpoint was measured with the subject lying on the left side while the anatomical landmarks were palpated, marked and the distance measured with a measuring tape. The midpoint was marked subcutaneously with ink to ensure that the measurement was conducted at the same point throughout the study. During the actual measurement, subjects were lying in a supine position with legs fixed with a Styrofoam knee support to prevent movement during the measurement. To ensure that the probe was moved in a straight line over the thigh, lines perpendicular to the measurement table were drawn across the thigh with a marker pen before every measurement session with the help of a specially crafted device. Three clear images from every measurement point were saved for analysis and the mean of the two values closest to each other were used as the final value in the statistical analyses. Images were analyzed with ImageJ -software (National Institute of Health, USA, version 1.44). The CSA was measured by manually marking the outlines of the muscles onto the image. The measurements were conducted by two members of staff trained for the task. The measurement for a given subject was always conducted and the images analyzed by the same person.

MAXIMAL POWER OUTPUT DURING CYCLING

A maximal endurance loading was conducted on a cycle ergometer (Ergometrics 800, Ergoline, Bitz, Germany) utilizing a graded exercise protocol. The initial load for each subject was 50W, with 25W increments applied every 2 min until volitional exhaustion. Maximal power output was calculated using the following equation: $W_{max} = W_{com} + (t/120)*25$, where W_{com} was defined as the load of the last completed stage and t the time of the last incomplete stage. The aerobic and anaerobic thresholds were determined individually for each subject by the points of deflection in the curves of ventilation, oxygen consumption, production of carbon dioxide and blood lactate [5].

At the end of each stage the Borg Rating of Perceived Exertion (RPE)-scale was used to monitor the subjective level of exhaustion. Heart rate was measured throughout the test (Polar S410, Polar Electro Oy, Kempele, Finland).

TRAINING

No supervised training was performed during the control period. However, light to moderate intensity physical activity 1-2 times per week for 30-60 min at a time was allowed. Additionally, maintenance of normal daily activities was encouraged. The 24-week training period was divided into two 12-week periods and was preceded by a preparatory phase with familiarization of the training procedures, equipment, loads and management of training programs and logs. During training period I, all same-session combined subjects completed two weekly “double” sessions of either [1E+1S] or [1S+1E], depending on which group they were assigned to. During training period II the training frequency was increased to five training sessions per 2 weeks (five sessions of [1E+1S] or [1S+1E]). A break of 5-10 min was allowed between the two training modes (S or E). The DD group adhered to the same training program, but trained S and E on alternating days, thus completing four training sessions per week during training period I and ten sessions per 2 weeks during training period II. All training sessions were under supervision of the project staff to ensure completion and adherence to the training program. In addition to the supervised training sessions the maintenance of normal daily activity was encouraged and the instructions for the subjects regarding additional physical activities were similar to those given for the control period.

Strength training was performed for all major muscle groups focusing on knee extensors, hip extensor and knee flexors. The training program was designed to be progressive and periodized, starting with circuit training and progressing through hypertrophy-inducing training towards maximal strength training (Table 2). The periodization for the exercises of the extensors and flexors of the arms followed a similar pattern. In addition, exercises for the trunk were included. All lower body exercises were performed with weight-stack devices, while some of the upper body exercises were performed with dumbbells.

Table 2 near here

All endurance training sessions were carried out indoors on a cycle ergometer equipped with a magnetic resistance. The training intensity was controlled by heart rate zones corresponding to the threshold values of aerobic (AT) and anaerobic thresholds (AnT), which were determined after the maximal cycle ergometer endurance test during the basal measurements. During weeks 1-7 and 13-16 the training consisted of 30-45 min continuous cycling near the AT and progressed to interval training at and above AnT from weeks 8 and 17 onwards (Table 3). The thresholds were recalculated from the endurance test performed after 12 weeks of training and applied during training period II.

Table 3 near here.

STATISTICAL ANALYSIS

Results are presented as means ± standard deviations. Data was analyzed with IBM SPSS Statistics v.20 software (IBM Corporation, Armonk, New York, USA). Repeated measures analysis of covariance (ANCOVA) with baseline values as covariates was used to assess training effects between groups. One-way ANOVA was used was used to assess differences in relative changes over time when time × group interactions were present. Within-group changes were analyzed with repeated measures ANOVA. Bonferroni post hoc procedures were applied when appropriate. The reported correlations are bivariate Pearson correlation coefficients (r). Significances were set at $^*p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$.

RESULTS

MAXIMAL STRENGTH

All groups significantly ($p<0.001$) increased bilateral concentric 1 RM during weeks 0-24 (DD by 13% from 142±23 kg ($p<0.001$, ES=0.775; E+S by 12% 159±30 kg, $p<0.001$, ES=0.631; S+E by 17% from 143±23 kg, $p<0.001$, ES=1.03) (Figure 2). A significant ($p<0.05$) difference was observed between DD and E+S at Pre, but no significant between-group differences were observed for any of the experimental groups after training. No significant change was observed 1 RM strength during the control period.

Figure 2 near here.

All groups increased maximal bilateral isometric leg press force during weeks 0-12 (DD by 7% from 2332±588N, $p<0.001$, ES=0.263; E+S by 11% from 2626±653N, $p<0.05$, ES=0.431; S+E by 9% from 2338±540N, $p<0.05$, ES=0.338) and during weeks 0-24 (DD by 11%, $p<0.001$, ES=0.413; ES by 12% $p<0.05$, ES=0.408; SE by 13%, $p<0.05$, ES=0.481). There were no significant between-group differences in changes for the experimental groups at any time point. No significant change was observed in leg press force during the control period.

Changes in isometric knee extension force between weeks 0-24 were not statistically significant for the DD and E+S groups (Figure 3). The S+E group increased knee extension force by 14% during 0-24 weeks (from 560±91N, $p<0.01$, ES=0.787). There were no significant between-group differences in changes for the experimental groups at any time point. No significant change was observed in knee extension force during the control period.

Figure 3 near here.

EMG AND VOLUNTARY ACTIVATION

The DD and E+S groups increased average maximal VL iEMG during bilateral isometric leg press (at 500-1500ms) during weeks 0-12 (DD by 26%, $p<0.001$, ES=0.824; E+S by 24% $p<0.01$, ES=0.467). The DD and S+E groups increased maximal VL iEMG significantly during weeks 0-24 (DD by 31%, $p<0.001$, ES=0.376; S+E by 42%, $p<0.001$, ES=0.648). The change during 0-24 for E+S was not significant. There were no significant between-group differences in changes for the experimental groups at any time point. No significant change was observed in average maximal VL iEMG during the control period.

No significant change in maximal VL rmsEMG was observed in the DD or E+S groups at week 24 (Figure 4). The S+E group experienced a significant ($p<0.01$, ES=0.708) increase of 26% during weeks 0-24. A significant ($p<0.05$) increase of 11% in maximal VL rmsEMG during unilateral isometric knee extension was observed during the control period.

Figure 4 near here.

The DD and S+E groups increased voluntary activation during weeks 0-12 and 0-24 (DD by 3.8% from 86.6±5.7 to 90.4±4.3, $p<0.01$, ES=0.829; S+E by 4.3% from 86.9±8.8 to 91.2±6.9, $p<0.01$, ES=0.489) (Figure 5). No significant change was observed in voluntary activation during the control period.

Figure 5 near here.

In the DD group a significant correlation between the individual changes in voluntary activation percentage and changes in knee extension force was found between weeks 13-24 ($r=0.57$, $p<0.05$). A significant correlation was found for the E+S group between weeks 0-12 ($r=0.70$, $p<0.01$), weeks 0-24 ($r=0.70$, $p<0.01$) as well as weeks 13-24 ($r=0.83$, $p<0.001$) (Figure 6). In the S+E group a significant ($r=0.50$, $p<0.05$) correlation between the two variables was observed between weeks 0-12.

Figure 6 near here.

CROSS-SECTIONAL AREA OF VL

All groups increased VL cross-sectional area during weeks 0-24 (DD by 16% from 22.3±3.7 cm^2, $p<0.001$, ES=0.928; E+S by 11% from 26.9±4.3 cm^2, $p<0.001$, ES=0.668; S+E by 14% from 26.2±4.0 cm^2, $p<0.001$, ES=0.884) (Figure 7). A significant ($p<0.05$) difference was observed between DD and E+S at Pre, but no significant between-group differences were observed for any of the experimental groups after training. A significant ($p<0.001$, ES=0.341) decrease in VL cross-sectional area was observed during the control period (-5% from 23.5±3.5 cm^2).

Figure 7 near here.

MAXIMAL POWER OUTPUT DURING CYCLING

All groups increased maximal power output during the cycle ergometer test during weeks 0-24 (DD by 21±11% from 233 W, $p<0.001$, ES=1.56; E+S by 13±8% from 266 W, $p<0.001$, ES=0.809; S+E by 16±7% from 245 W, $p<0.001$, ES=1.07). A significant ($p<0.05$) difference was observed between DD and E+S at Pre, but no significant between-group differences were observed for any of the experimental groups after training. No significant change in maximal power output was observed during the control period. RPE for the groups at the end of the last completed stage of the test were as follows: Ctrl Pre 19±1 and Post 18±1; Pre DD, E+S, S+E 18±1, 19±1, 19±1 and Post 18±1, 19±1 18±1. Maximal heart rate during the test was as follows: Ctrl Pre 196±7 and Post 195±8; Pre DD, E+S, S+E 195±8, 190±11, 193±8; and Post 193±8, 189±10 192±9.

Figure 8 near here.

DISCUSSION

The main finding of the present study was that gains in dynamic strength, hypertrophy and maximal power output during cycling were significant for all groups following the 24-week training intervention with no between-group differences. However, the study revealed indications for differing adaptations of voluntary activation level and muscle EMG between the combined strength and endurance training modalities during the 24-week training period. The statistically significant increase in voluntary activation percentage that was observed in the DD and S+E groups after 24 weeks of training was not present in the E+S group. Moreover, the individual changes in voluntary activation and maximal force development in isometric unilateral knee extension were correlated during the latter half of the training intervention for the E+S group.

The present findings in terms of training-induced gains in performance and muscle hypertrophy are by large in agreement with findings from previous studies. In agreement with previously reported changes in muscle thickness[9, 11], the relative gains in VL CSA did not differ between the present groups (increases of 16%, 11%, 14% for DD, E+S and S+E, respectively). The increases in maximal power output reported in the present study (21%, 13%, 16% for DD, E+S and S+E, respectively) are of similar magnitudes to what has been reported previously [11] for elderly subjects already after 12 weeks of either E+S or S+E training with a three-times-weekly regimen. In the corresponding time frame, the three groups in the present study performed one less endurance session weekly, improving maximal power output significantly (7-14%) and making further significant increases during weeks 13-24 with an increased training frequency. Similarly, the gains in maximal dynamic leg press did not differ statistically between the groups. The gains observed in 1 RM in the same-session combined groups (increases of 12% and 17%, for E+S and S+E, respectively) following 24 weeks of combined training can be considered comparable with earlier studies, albeit somewhat different in the time course of adaptations [13, 45]. With regards to different day strength and endurance training, the DD group demonstrated smaller (13%) gains in maximal dynamic leg press 1 RM in comparison to some earlier findings (22-25%) [29,45]. Sale [45] has suggested same-session combined training to be inferior to different day training in terms of gains in maximal dynamic strength, but this did not take place in the present study. The differences observed between results from earlier studies and the present study could be attributed to different training frequencies and volumes, acute variables of the training programs or even subject material.

Our findings with regards to the effects of same-session loading sequence on neural adaptations support in part speculations presented in earlier studies [9, 11]. Cadore et al. [9] suggested that the E+S sequence in elderly subjects would hinder neural adaptations of the strength training from occurring, whereas no such compromise in adaptations was found for S+E. These earlier findings also suggest the E+S sequence to be unfavorable in terms of strength development in comparison to S+E. In the present study we found no between-group differences in either strength gains or maximal power output. However, the present S+E group demonstrated increased VL EMG and force in isometric actions during weeks 0-24, whilst the E+S group showed no significant increases in the same variables during this time period. Furthermore, the highly significant correlation ($r=0.83$, $p<0.001$) observed between individual changes in voluntary activation percentage and changes of knee-extension strength development during weeks 13-24 for the E+S group demonstrated that individuals who experienced reduced strength gains also decreased their voluntary activation percentage. These findings suggest that potential inhibition or interference in the nervous system could occur in the E+S group in a further prolonged period of combined training. This type of inhibition could be due to increased firing and inhibitory feedback from type III and IV afferents [3] or impairment in neuromuscular propagation [17] following the endurance loading during training. Ultimately, this could affect the subsequent strength loading and, thus, strength-training induced adaptations. However, with the present methodology, we are unable to confirm these speculations.

It is worth noting that as increases in maximal force are not exclusively explained by neural adaptations but also rely on muscle hypertrophy [25, 37, 39], this could partly explain the improvements in strength for the E+S group despite the compromised adaptation in EMG activity and voluntary activation. The neural adaptations initially being responsible for improvements in force with hypertrophy following later [25, 37, 39] supports this assumption, as the E+S group experienced significant gains in VL CSA during both training periods. Furthermore, the stimuli for muscle hypertrophy that is produced by combined training has been suggested to override possible hypertrophy-blunting effects observed particularly after interval-type endurance training [15], which is reflected in the significant improvements of VL cross-sectional area for all groups in the present study. It is noteworthy, that even cycling alone has been found to induce a certain level of hypertrophy, as far as previously untrained subjects are concerned. The limited increase observed by Mikkola et al. [36] in the quadriceps femoris cross-sectional area was attributed to be the result of the repeated pedal push action, as the force produced was suggested to be high enough and the push-phase long enough for hypertrophy-inducing stimulus to occur. This could further clarify the increases in VL cross-sectional area despite the training program not being exclusively focused on hypertrophy.

Recent findings [10, 46] regarding the acute responses of combined strength and endurance loadings has brought forward concerns about the effects of possible residual fatigue that the first part of a combined strength and endurance loading may have on the subsequent part. Considering this, the obvious difference between the training programming of the present three groups was the timing of the endurance modality in relation to the strength exercises. The DD group had consistently a minimum of 24 hours of recovery between the training modes and S+E performed strength in a recovered state. Thus, E+S was the only group which continuously performed the strength exercises possibly in a fatigued state. Therefore, despite the fact that no acute variables were measured in the present study it is reasonable to discuss the possible role of the first part of the loading on the second one in order to find possible underlying mechanisms for the compromised neural adaptations. Possible residual fatigue from a cycling endurance loading could be expected to compromise the quality of a subsequent lower-body strength loading session, as it is known that the quadriceps femoris muscle group contributes to continuous cycling with a significant percentage of its maximum activity even at relatively low workloads [19]. Additionally, impairments in maximal voluntary neuromuscular function following fatiguing cycling appear to be specific to the working muscles [18] and prolonged cycling exercise appears to limit the force generating capacity to the muscles via both central and peripheral mechanisms, thus leading to a reduction in muscular capacity in the working muscles during subsequent activities [2, 18, 33]. Further clarification is needed as to whether fatigue induced neural responses from the endurance component alone through inhibitory mechanisms can be regarded responsible for disadvantageous neural adaptations following the present E+S training program, or whether the immediate addition of a strength loading is the factor overloading the nervous system. A recent study [46] investigating the order effect in an acute setting gives an indication for the latter, as in the E+S sequence both the first and second part of the loading significantly contributed to the total fatigue in terms of acute decreases in maximal isometric force and rapid force production. In the S+E condition, however, the measured variables were not further affected by the endurance loading, indicating that the strength loading was responsible for inducing most of the total fatigue when performed first. However, bearing in mind that all groups in the present study experienced gains in maximal power output during cycling, it appears that the possible strenuousness of strength loading does not prevent adaptations in endurance performance.

Despite the present differences in neural adaptations there were no significant differences in strength and hypertrophic adaptations between the groups. This, in turn, could partly be attributed to the periodized nature of the training program. The present strength training did not exclusively consist of high-load, neurally demanding strength training and did thus not provide a maximum stimulus to the nervous system [26]. Had this been the case, the unfavorable adaptations in muscle activity and voluntary activation may have appeared more pronounced as the strength training for the E+S group would continuously have been performed in an already fatigued state. However, as the voluntary activation percentage did significantly increase over 24 weeks for DD and S+E approximately to the same magnitude as would be seen after pure strength training [31, 42], the strength training protocol of the current study cannot be considered insufficient, but rather diluted by lighter, strength-endurance type training. This, on the other hand, supports previous suggestions of endurance training playing the inhibitory part in compromised strength performance related adaptations following combined training, via inhibiting the force-generating properties of the neuromuscular system [16, 24, 29]. Furthermore, cycling as the choice of endurance training modality may not hinder lower-body strength development to the same extent as e.g. running, due to similar biomechanical patterns as multi-joint lower-body strength exercises [21].

Methodological considerations and limitations. To investigate training-induced neural adaptations, the present study evaluated voluntary activation utilizing the ITT technique together with surface EMG. Increases or decreases in VA are not necessarily similarly reflected in the surface EMG-signal and thus, EMG as a representative of neural drive may be considered to be an oversimplification [14, 20]. In order to minimize possible additional inaccuracies in the EMG-recordings arising from technical, anatomical or physiological sites [14], all EMG-recording related procedures were carefully conducted and the EMG-locations were permanently marked subcutaneously. In the measurement setting of the present study, direct stimulation of the femoral nerve was found to be too challenging to perform to obtain highly repeatable results. Thus, we opted for direct electronic muscle stimulation of the QF, as this method has been suggested to be a valid alternative to nerve stimulation to assess activation level [41]. As the results of the ITT-measurements may be muscle and angle-specific and depend on the timing of the super-imposed and resting twitches [20], this was counteracted by identical measurement settings throughout the study and always having the same member of the staff performing the ITT-measurements. It should be noted, that in the present study both VA and EMG were found to follow the same direction of training-induced adaptations in the E+S group during the latter half of the 24-week training period when compromised adaptations were observed. Nevertheless, the interpretation of these findings needs to be done with caution with regard to neural adaptations, as both the EMG and ITT-procedures have their methodological limitations.

In conclusion, the choice of a combined training mode may not be of great importance in terms of gains in strength and endurance performance or muscle hypertrophy in previously untrained subjects. However, it could be speculated that either a longer training period than the present 24-week intervention or higher training volume and / or frequency might result in more severe neural interference or limitations in the E+S training mode. Whether this would also be reflected in compromises in strength development needs to be further investigated.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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CAPTIONS AND LEGENDS

FIGURES

Fig. 1 Overview of the study protocol. Different day training (DD, n=21) = Weeks 0-12: 2 d.wk-1 [1 strength, S] and 2 d.wk-1 [1 endurance, E], weeks 13-24: 2-3 d.wk-1 [1S] and 2-3 d.wk-1 [E]. Same session combined training = endurance before strength (E+S, n=17) and strength before endurance (S+E, n=18), weeks 0-12: 2 d.wk-1 [1E+1S] or [1S+1E], respectively; weeks 13-24: 2-3 d.wk-1 [1E+1S] or [1S+1E], respectively.

Fig. 2 Relative changes in maximal bilateral dynamic leg press 1RM for all experimental groups and during the control period. * = significant from pre; # = significant from mid. *** p<0.001 and # p<0.05. (DD, n=21; E+S, n=17; S+E, n=18; control period, n=24.)

Fig. 3 Relative changes in maximal unilateral isometric knee extension force for all experimental groups and during the control period. * = significant from pre. * p<0.05 ** p<0.01. (DD, n=21; E+S, n=15; S+E, n=18; control period, n=24.)

Fig. 4 Relative change in maximal VL rmsEMG during a 500ms epoch of maximal force phase during unilateral knee extension for all experimental groups and during the control period. * = significant from pre # = significant from mid. * p<0.05. (DD, n=16; E+S, n=14; S+E, n=15; control period, n=20.)

Fig. 5 Voluntary activation percentage for all experimental groups and during the control period. * = significant from pre.* p<0.05 and ** p<0.01. (DD, n=17; E+S, n=15; S+E, n=17; control period, n=21.)

Fig. 6 Correlation between the individual change in the voluntary activation percentage and the relative changes in maximal knee extension force in the E+S group during weeks 13-24.

Fig. 7 The relative change in VL cross-sectional area for all experimental groups and during the control period. * = significant from pre # = significant from mid.** p<0.01 *** p<0.001 and ## p<0.01. (DD, n=21; E+S, n=17; S+E, n=18; control period, n=24.)

Fig. 8 The relative change in maximal power output during cycling ergometer test for all experimental groups and during the control period. * = significant from pre # = significant from mid. ** p<0.01 *** p<0.001 ## p<0.01 and ### p<0.001. (DD, n=21; E+S, n=17; S+E, n=18; control period, n=24.)

TABLES

Table 1: Subject characteristics by group. DD = Different day training; E+S = same session training, endurance preceding strength; S+E = same session training, strength preceding endurance

Table 2: Strength training for the lower extremities during the 24-week training intervention. *Explosive repetitions with a load of 40% in three training sessions (out of four) during weeks 11-12 and three sessions (out of five) during weeks 23-24, Load = % of estimated 1 RM, Reps = Repetitions per set, Rest = rest between sets and exercises, LP = leg press, KE = Knee extension, KF = Knee flexion

Table 3: Endurance training (by cycling) during the 24-week training intervention. AT = Aerobic threshold, AnT = Anaerobic threshold, < = 5-10 bpm below, > = 5-10 bpm above, ~at the threshold (±5 bpm)

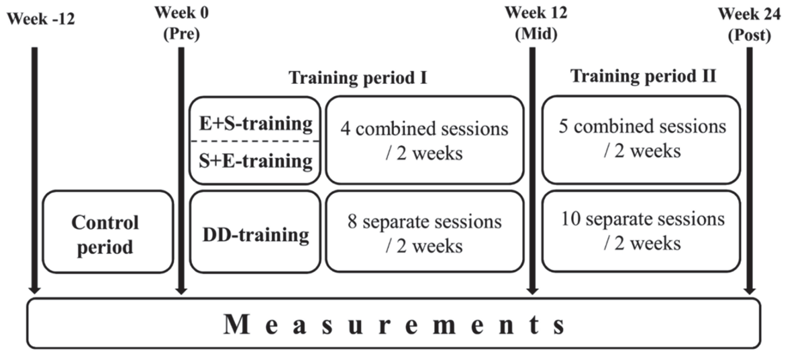


Figure 1

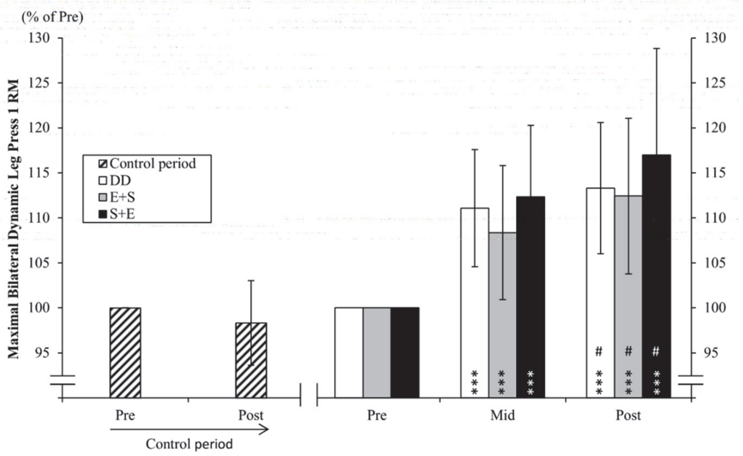


Figure 2

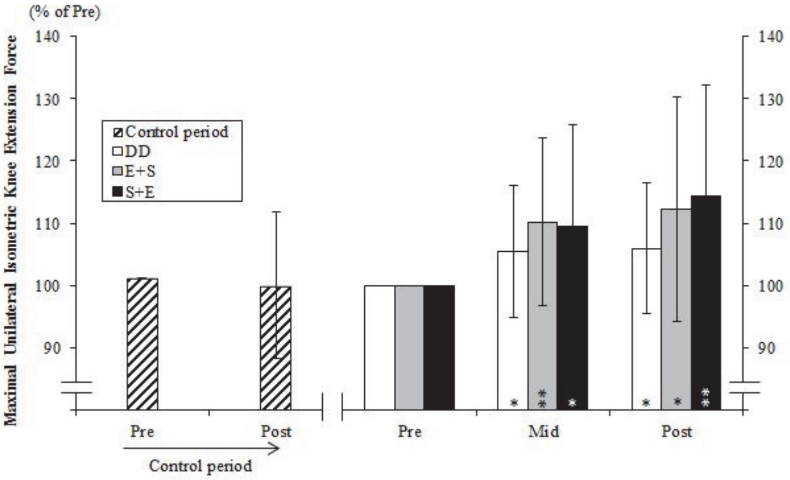


Figure 3

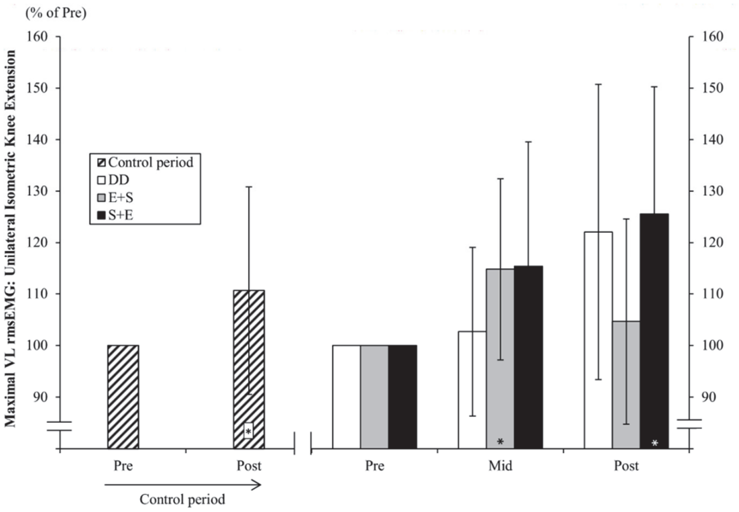


Figure 4

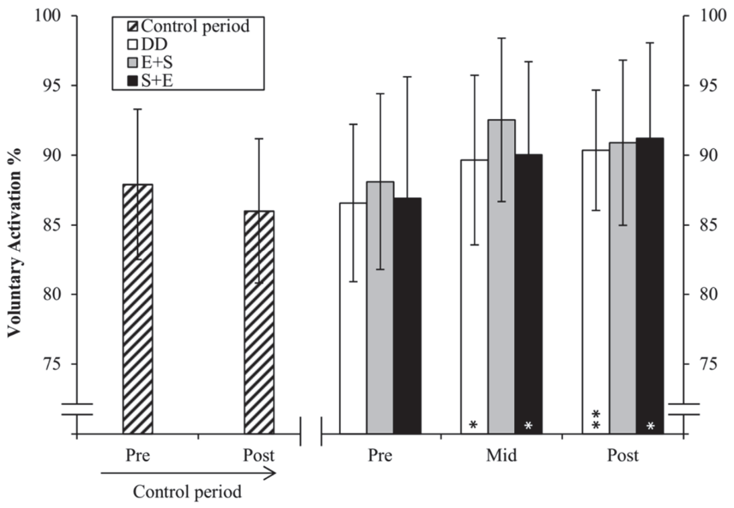
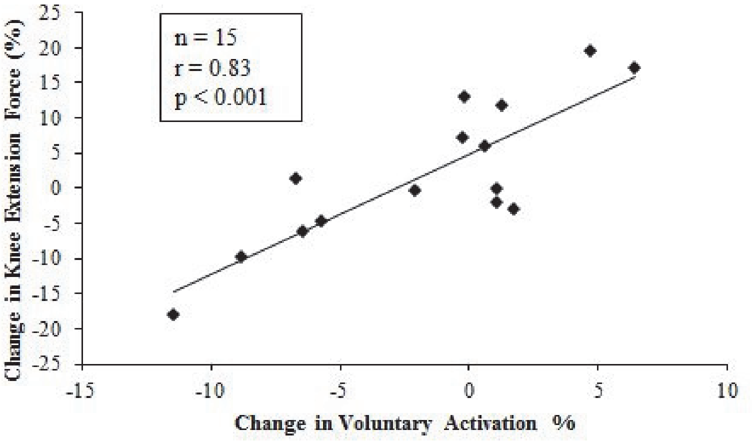


Figure 5



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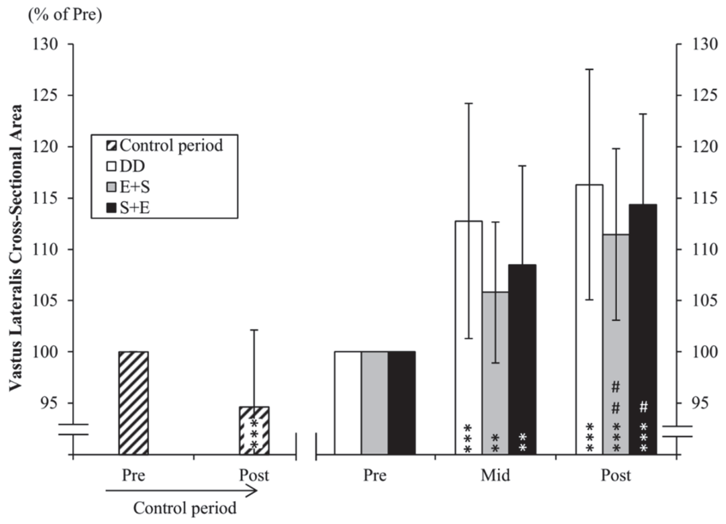

Figure 7

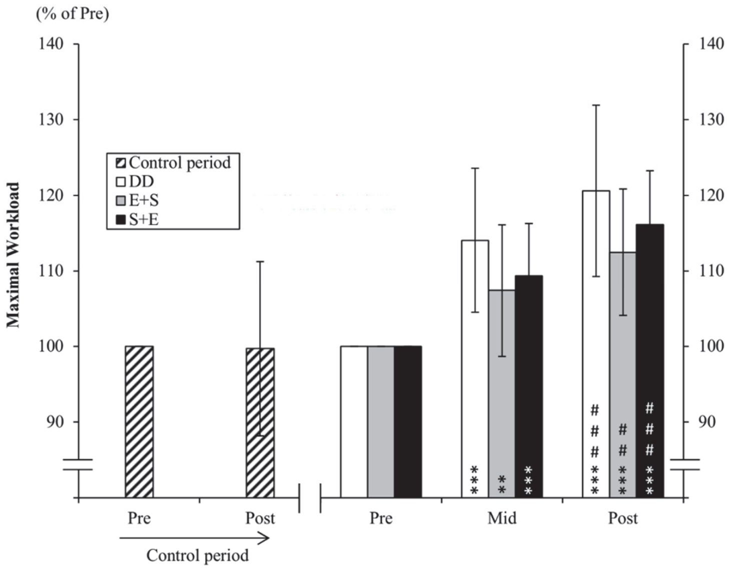

Figure 8

Table 1

Group	**n**	**Age (years)**	**Height (cm)**	**Weight (kg)**	**BMI (kg/m2)**
Control period	24	29.2 (±6.0)	180 (±6.0)	79.6 (±10.0)	24.5 (±2.9)
DD	21	29.2 (±6.0)	180 (±6.0)	80.5 (±11.1)	24.8 (±3.2)
E+S	17	29.4 (±6.1)	178 (±6.0)	79.7 (±11.9)	25.1 (±3.1)
S+E	18	29.8 (±4.4)	179 (±5.0)	75.2 (±8.5)	23.5 (±2.1)
total of training groups	56	29.4 (±5.8)	179 (±5.8)	78.8 (±10.4)	24.5 (±2.8)

Table 2

	Training period I			Training period II			
	Weeks 1-3	**Weeks 4-7**	**Weeks 8-12**	**Weeks 13-14**	**Weeks 15-16**	**Weeks 17-20**	**Weeks 21-24**
Load	40-80%	70-85%	80-95%	40-60%	65-80%	80-85%	80-95%
Sets	2-3	2-3	3-5	3	2-3	2-4	2-5
Reps	10-20	10-15	3-10	12-20	10-12	8-10	3-10
Rest	None (circuit)	1.5-2 min	1-3 min	None (circuit)	1.5-2 min	1.5-2 min	2.5-3 min
Exercises:							
LP	Bilateral	Bilateral	Bilateral*	Bilateral	Bilateral	Bilateral	Bilateral*
KE	Bilateral	Bilateral	Unilateral	Bilateral	Bilateral	Bilateral	Unilateral
KF	Bilateral	Bilateral	Unilateral	Bilateral	Bilateral	Bilateral	Unilateral

Table 3

Training period I

	Weeks 1-3	**Weeks 4-7**		**Weeks 8-9**		**Weeks 10-11**		**Week 12**
		Session I	**Session II**	**Session I**	**Session II**	**Session I**	**Session II**	
Intensity	< AT	<AT and >AT	< AT	<AT and ~AnT	<AT and >AT	>AT and >AnT	<AT, >AT and >AnT	>AT - >AnT
Mode	Continuous	Continuous	Continuous	Interval	Continuous	Interval	Interval	Interval
Duration	30 min	30 min	45 min	45 min	50 min	45 min	45-50 min	35-45 min

Training period II

	Weeks 13-14	**Weeks 15-16**		**Weeks 17-20**		**Weeks 21-23**	**Week 24**
		Session I	**Session II**	**Session I**	**Session II**		
Intensity	< AT and >AT	~AT, <AnT	~ AT	<AT and ~AnT	~AT and >AT	>AT - >AnT	<AT and >AnT
Mode	Continuous	Continuous	Continuous	Interval	Continuous	Interval	Interval
Duration	40-45 min	30-35 min	30-45 min	25-45 min	30-50 min	35-50 min	25 min

III

FITNESS, BODY COMPOSITION AND BLOOD LIPIDS FOLLOWING 3 CONCURRENT STRENGTH AND ENDURANCE TRAINING MODES

by

D. Eklund, A. Häkkinen, J.A. Laukkanen, M. Balandzic, K. Nyman & K. Häkkinen.
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Title: Fitness, body composition and blood lipids following three concurrent strength and endurance training modes

Running head: Health and combined training

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ABSTRACT

This study investigated changes in physical fitness, body composition and blood lipid profile following 24 weeks of three volume-equated concurrent strength (S) and endurance (E) training protocols. Physically active, healthy male and female participants (18-40 yrs) performed S and E sessions on different days (DD, men n=21, women n=18) or in the same session with E preceding S (ES, men n=16, women n=15) or vice versa (SE men n=18, women n=14). The training volume was matched in all groups. Maximal leg press strength (1RM) and endurance performance (VO_{2max} during cycling), body composition (DXA) and blood lipids were measured. 1RM and VO_{2max} increased in all groups in men (12-17% $p<0.001$ and 7-18% $p<0.05$-0.001, respectively) and women (13-21% $p<0.01$-0.001 and 10-25% $p<0.01$-0.001, respectively). VO_{2max} increased more in DD vs. ES and SE both in men (p=0.003-0.008) and women (p=0.008-0.009). Total body lean mass increased in all groups (3-5%, $p<0.01$-0.001). Only DD led to decreased total body fat (men -14±15% $p<0.001$, women -13±14% p=0.009) and abdominal-region fat (men -18±14% p=0.003, women -17±15% p=0.003). Changes in blood lipids were correlated with changes in abdominal-region fat in the entire group (r=0.283, p=0.005) and in DD (r=0.550 p=0.001). In conclusion, all modes resulted in increased physical fitness and lean mass, while only DD led to decreases in fat mass. Same-session SE and ES combined training is effective in improving physical fitness, while volume-equated, but more frequent DD-training may be more suitable for optimizing body composition and, possibly useful in early prevention of cardiovascular and metabolic diseases.

Keywords: combined training; physical performance; health; resistance training; aerobic training; metabolic health

INTRODUCTION

The importance of consistent adherence to physical activity for improved physical fitness and health has been well established in various populations (Ghahramanloo et al. 2009, Häkkinen et al. 2003, Sillanpää et al. 2009). Regular physical exercise is associated with reduced levels of cardiovascular risk factors (Naghii et al. 2011), favorable changes in body composition (Ho et al. 2012, Sigal et al. 2007) as well as blood lipid profile (Tambalis et al. 2009). In terms of the choice of exercise type, endurance (E) and strength (S) training result in specific improvements in physical fitness as well as positive changes in health-related outcomes. While E-training has been shown to increase cardiorespiratory fitness (Murias et al. 2010) and consequently reducing premature all-cause and cardiovascular disease mortality (Farrell et al. 1998, Kodama et al. 2009), S-training leads to increased muscle size and strength (Häkkinen et al. 2001), thus sustaining functional capacity (Landi et al. 2014).

While it has been proposed that either E or S training alone can improve cardiovascular health and physical fitness (Spence et al. 2013), including both exercise modes into the same training regimen (combined training) may be even more effective than adhering to only either training mode alone (Sillanpää et al. 2008). Greater benefits in terms of cardiovascular health (Ghahramanloo et al. 2009, Ho et al. 2012, Sigal et al. 2007), reduced total body and abdominal fat as well as improvements in overall physical fitness profile have been observed with combined training in comparison to either S or E training alone in both obese (Ho et al. 2012, Dutheil et al. 2013) and elderly (Lee et al. 2014, Sillanpää et al. 2008) populations.

However, combined training regimens with an overall high volume and frequency can compromise strength gains especially in previously untrained individuals (Hickson 1980), emphasizing the importance of utilizing a moderate volume and frequency of training program to prevent adverse effects (Häkkinen et al. 2003). Moderate volume and frequency combined training seems to be effective in increasing muscle strength and size as well as maximal aerobic capacity in previously untrained adults, regardless of whether S and E are performed on different days (DD) or in the same training session with different orders (i.e. E immediately followed by S, ES, or vice versa, SE) (Eklund et al. 2015). However, data on health-related outcomes following these combined exercise training modes is still lacking.

Although a previous study by our group showed that 24 weeks of ES and SE-training produced similar adaptations in physical fitness and increases in lean mass in previously untrained men, no decreases in body fat mass were observed in either training group (Schumann et al. 2014). However, as split exercise sessions may result in increased post-exercise oxygen consumption in comparison to a long one (Almuzaini et al 1998) and could consequently contribute to increased overall energy expenditure, it is left unclear how splitting S and E onto different days affects body composition in the long term. As reductions in adipose tissue have been associated with an improved blood lipid profile (Dutheil et al. 2013), it is of interest to investigate the effects of different modes of volume-equated combined training programs on changes in body composition and blood lipid content.

The aim of the present study was to investigate possible differences in body fat and lean mass, blood lipid levels and physical fitness profile following 24 weeks of volume-equated different-day and same-session combined strength and endurance training in previously untrained healthy men and women. More specifically, this was achieved through comparing adaptations following strength and endurance training performed on different days (DD) or in the same session with two different orders (ES and SE). The present study expands on our previous work (Eklund et al. 2015, Eklund et al. 2016, Schumann et al. 2014) in order to provide a more comprehensive understanding of how adaptations to same-day combined strength and endurance training compares to strength and endurance training performed on separate days.

MATERIALS AND METHODS

Study design

Subjects. Following institutional ethical approval and in accordance with the Declaration of Helsinki, written informed consent was obtained from recreationally active male (n=70) and female (n=70) volunteers. The recruited subjects were required not to have participated in systematic strength or endurance training for at least 1 year prior to the study. All subjects were free from chronic illnesses and injuries, below a BMI of 30 $m^2 \cdot kg^{-1}$ and non-smokers. Female subjects were not pregnant or lactating. As a part of the pre-screening process, all subjects completed a health questionnaire and underwent a resting ECG, which were approved by a cardiologist. Out of the 140 recruited subjects, 15 men and 24 women did not complete the study or were not included in the analysis due to a training adherence below 90%. Subject demographics of the included subjects are presented in Table 1.

Experimental approach. To examine the effects of combined strength and endurance training performed on different days (DD) or in the same session (with two different orders: ES and SE) on physical fitness profile, body composition and blood lipids, the subjects were assigned to one of three training groups for the 24-week training intervention. The subjects were measured before (Week 0), at the mid-phase (Week 12) and after (Week 24) the training intervention. The measured variables included maximal strength and endurance performance, body composition and blood lipids as well as collection of food diaries.

All subjects were initially familiarized with the training and measurement protocols and equipment. The strength and endurance measurements as well as measurement of body composition and blood lipids were separated from each other by a minimum of 2 days. The measurements were conducted for each subject at the same time of day (±1h) to minimize circadian fluctuation. Subjects were instructed to abstain from caffeine 12 h and alcohol 24 h prior to all measurements. For training and measurements of physical fitness the subjects arrived to the laboratory in a rested and hydrated state and at least 2 h postprandial. The last session of both training periods was separated from the following measurements by a minimum of 2 and a maximum of 4 days.

After the basal measurements of body composition, blood lipids, maximal strength and endurance performance, each participant was randomly assigned to one of the three training modes for the entire 24-week duration of the study: 1) strength and endurance training performed on different days (DD, men n=21, women n=18), 2) strength and endurance performed in the same training session with endurance preceding strength (E+S, men n=16, women n=15) or 3) vice versa, i.e. strength and endurance performed in the same training session with strength preceding endurance (S+E, men n=18, women n=14).

Measurements of physical fitness

Maximal concentric strength. Bilateral leg press one-repetition maximum (1 RM) was measured using a David 210 weight stack horizontal leg press device (David Health Solutions Ltd., Helsinki, Finland). The participants were seated in the device with a starting knee angle of 60° (58° ± 2°). As a preparation for the 1 RM trials, participants performed 3 warm-up sets (5 × 70–75 % estimated 1 RM, 3 × 80–85 % estimated 1 RM, 2 × 90–95 % estimated 1 RM) with 1 min rest between sets. When verbally instructed, participants performed a dynamic action to a full leg extension (knee angle 180°). The load was increased upon a successful completion. After a maximum of 5 maximal trials, the trial with the highest successfully completed load was accepted as the 1 RM.

Isometric force. Maximal bilateral isometric leg press force (MVC) was measured at a knee angle of 107° (Häkkinen et al. 1998) on a horizontal leg press device designed and manufactured by the Department of Biology of Physical Activity (University of Jyväskylä,

Jyväskylä, Finland). Subjects were instructed to perform a bilateral leg press action to reach the maximum force as rapidly as possible and maintaining it for 2-3 s. A minimum of 3 and a maximum of 5 maximal trials were allowed. A fourth and fifth trial was allowed, if the difference from the third trial to the previous 2 exceeded 5 %. Force signals were recorded with Signal 2.16 software (Cambridge Electronic Design, Cambridge, UK) sampled at 2 000 Hz, processed with a low-pass filter (20 Hz) and analyzed using a customized, automated script (Signal 2.16 software, Cambridge Electronic Design, Cambridge, UK). The trial with the highest maximal force was used for further analysis.

Maximal oxygen uptake. A maximal endurance loading was conducted on a cycle ergometer (Ergometrics 800, Ergoline, Bitz, Germany) utilizing a graded exercise protocol. The initial load for each participant was 50 W, with 25 W increments applied every 2 min until volitional exhaustion. Participants were asked to keep the pedaling frequency at 70 revolutions per minute (rpm) throughout the test. The current rpm was visible for the participants throughout the test. When the participants failed to keep up the required rpm for longer than 15 s, the test was terminated. Oxygen uptake was determined continuously, breath-by-breath, with a gas analyzer (Oxycon Pro, Jaeger, Hoechberg, Germany). Maximal oxygen consumption (VO_{2max}) was averaged over each 60 s period during the test. The VO_2-value from the last complete minute during the test was defined as VO_{2max}.

Blood lipids. Blood samples were drawn from the antecubital vein at 7:00-9:00 following a 12h overnight fast to obtain concentrations of total cholesterol ($Chol_{tot}$), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglycerides. Participants were instructed to abstain from strenuous physical activity 48 before the blood samples were taken. Blood samples were drawn by a trained technician from the antecubital vein into serum tubes

(Venosafe, Terumo Medical Co., Leuven, Hanau, Belgium) adhering to standard laboratory procedures. Serum samples were stored for 10 min before being centrifuged at 3 500 rpm (Megafure 1.0 R, Heraeus, Germany) followed by immediate spectrophotometry analyzes (Konelab 20XTi, Thermo Fisher Scientific, Vantaa, Finland). The Friedewald equation (Friedewald et al. 1972) was used for estimating concentrations of LDL:

LDL = total cholesterol - HDL-C - (triglycerides/2.2)

Body composition. Body composition was assessed by Dual-Energy X-ray Absorptiometry (DXA) (Lunar Prodigy Advance, GE Medical Systems, Madison, USA). The DXA-scans were always performed in the morning with the participant in a fasted (12h) state. Leg position was fixed with Velcro-straps at the knees and ankles. Arms were aligned along the trunk with the palms facing the thighs. Automated soft tissue analyses were conducted for lean and fat mass (Encore-software, version 14.10.022). To analyze lower body fat ($\mathrm{Fat}_{\mathrm{lower}}$) and lean mass ($\mathrm{Lean}_{\mathrm{lower}}$), a region of interest (ROI) was created where the legs were separated from the trunk by a horizontal line directly above the iliac crest. Total body and arm fat ($\mathrm{Fat}_{\mathrm{tot}}$, $\mathrm{Fat}_{\mathrm{arms}}$) and lean mass ($\mathrm{Lean}_{\mathrm{tot}}$, $\mathrm{Lean}_{\mathrm{arms}}$) as well as android fat mass ($\mathrm{Fat}_{\mathrm{andr}}$, centrally located fat mass) (Hind et al. 2011) were obtained for each of the regions through the manufacturer's pre-defined ROI's.

Food diaries.

Nutritional intake was controlled through food diaries, which were filled in by the participants for three consecutive days at weeks 0, 12 and 24. Energy intake was analyzed based on the food diaries with a nutrient analysis software (Nutriflow, Flow-team Oy, Finland). The participants received written and verbal nutritional recommendations according to the national guidelines and were asked to maintain constant dietary intake throughout the intervention.

Training

The training program has been described in detail previously (Eklund et al. 2015). In short, the training was designed to reflect recommendations for physically active individuals as well as targeted at improving both maximal strength and endurance performance. During the initial 12 weeks, the same-session subjects completed two weekly sessions of [1E+1S] or [1S+1E] (respective to the assigned training order), and five sessions per two weeks (5x [1E+1S] or [1S+1E]) during weeks 13-24. The time between training modes was 5-10 min and recovery time between training sessions 48-72 h. The DD-group adhered to the same training program but performed S and E on alternating days, i.e. completing 4 weekly training sessions during the first 12 weeks and 10 sessions per two weeks during the latter 12 weeks. Training sessions were supervised by research staff.

Strength training mainly targeted the knee extensors and flexors as well as hip extensors, with the exercises consisting of horizontal leg press, seated hamstring curls and seated knee extensions. During the initial weeks, the exercises were performed in a circuit (2-4 sets of 15-20 repetitions with up to 60% of 1RM) and then continued through hypertrophy-inducing training (2-5 x 8-12 at 80-85% of 1RM, 1-2 min rest) towards maximal strength training (2-5 x 3-5 at 85-95% of 1RM, 3-4 min rest). A similar periodization scheme was used for the upper body. Dumbbells and cable pulley machines were used for upper body exercises, and both machines and body weight were utilized for exercises of the trunk. The periodization was repeated during weeks 13-24 with increased training intensity and volume. The duration of each strength session was 50-60 min.

Endurance training sessions were performed on a cycle ergometer. The training intensities were controlled through heart rate zones, which corresponded to the threshold values of aerobic and anaerobic thresholds. The training consisted of 30-50 min continuous cycling near the aerobic threshold (weeks 1-7 and 13-16), including interval training at and above the anaerobic threshold (weeks 8 and 17 onwards). The interval sessions were initiated and finished with 10-15 minute bouts below the aerobic threshold, with 5-minute altering bouts on the anaerobic threshold and below the aerobic threshold in between.

Statistical analysis. Data is presented as means ± standard deviations. All statistical analyses were carried out with IBM SPSS Statistics v.22 software (IBM Corporation, Armonk, New York, USA). Normality was checked using the Shapiro-Wilk test as well as through observing the Q-Q-plots. Normally distributed data was analyzed for within-group (time) changes with a repeated measures analysis of variance (ANOVA) using absolute values. Differences between the training modes (time×training) were analyzed using a repeated measures ANCOVA with absolute values for main effects and a One-Way ANOVA with absolute changes for pairwise comparisons. The covariates used were the baseline values for the variable in question. Bonferroni post-hoc adjustments were used where appropriate. Non-normally distributed data was log-transformed to achieve normality and thereafter analyzed as described above. The reported effect sizes are Cohen's *d* with an effect size of ≥ 0.20 being considered small, ≥ 0.50 medium, and ≥ 0.80 large. The reported correlations are bivariate Pearson correlation coefficients (r). The level for significance was $p \leq 0.05$. A trend was accepted at $p \leq 0.06$.

RESULTS

Training adherence

The training adherence in men was 99±2%, 99±2% and 100±1% in ES, SE and DD, respectively, and in women 98±4%, 99±2% and 99±2% in ES, SE and DD, respectively.

Measurement reproducibility

The measurement reproducibility was high (intra-class correlation 0.7-0.9) for all test measures, as has been reported earlier by our research group (Schumann et al. 2014).

Body composition

Lean mass. Total body lean mass increased significantly in all three training groups in both men (effect sizes DD 0.39, ES 0.32, SE 0.35) and women (effect sizes DD 0.55, ES 0.30, SE 0.38) (Figure 1). The regional changes in lean mass are presented in Table 2. The change in lower body lean mass was significant ($p<0.05$) in all groups except DD men. Trunk lean mass increased significantly in all groups ($p<0.05$) except in SE-women and ES-men. The change in lean mass of the arms was significant ($p<0.05$) in all groups except ES-women and SE-men. Time×group interactions were not observed in lean mass either in the separated regions or in the total body.

Fat mass. Fat mass decreased in all regions in the DD-groups, while significant changes in ES and SE were not found during the training intervention (Figure 2 and Table 2). In women, significant time×group interactions were observed in Fat_{tot} ($p=0.035$), Fat_{lower} ($p=0.048$) and Fat_{andr} ($p<0.001$). The decrease in Fat_{tot} in women was significantly greater in DD than in ES and SE during weeks 0-24 ($p=0.005$ and $p=0.028$, respectively; effect size DD 0.48, ES 0.03, SE 0.09) and weeks 13-24 ($p=0.016$ and $p=0.047$, respectively; effect size DD 0.23, ES 0.01, SE 0.04). In fat_{lower} the decrease in women in DD was significantly greater than in ES during weeks 13-24 (p=0.039; effect size DD 0.25, ES 0.03, SE 0.06) and approaching significance during weeks 0-24 (p=0.052; effect size DD 0.43, ES 0.07, SE 0.11). The magnitude of decrease in women in Fat_{andr} was greater in DD in comparison to ES and SE during weeks 0-12 (p=0.001 and p=0.028, respectively; effect size DD 0.34, ES 0.04, SE 0.07), weeks 0-24 (p<0.001 and p=0.002, respectively; effect size DD 0.51, ES 0.06, SE 0.06) and weeks 13-24 (p=0.012 and p=0.025, respectively; effect size DD 0.17, ES 0.01, SE 0.0). In men, a significant time×group interaction was noted in Fat_{andr} (p=0.038) with the decreases in DD being of greater magnitudes than SE at weeks 0-12 (p=0.038; effect size DD 0.18, ES 0.13, SE 0.03), weeks 0-24 (p=0.003; effect size DD 0.45, ES 0.27, SE 0.03) and weeks 13-24 (p=0.010; effect size DD 0.27, ES 0.14, SE 0.06).

Nutrition. Total energy intake (MJ) at week 0, 12 and 24 in men were as follows 9.3±1.8, 10.2±2.6 and 9.5±2.6 for ES; 9.4±2.0, 9.3±1.7 and 7.9±1.7 for SE; 8.4±2.3, 9.0±1.4 and 9.2±1.6 in DD, respectively. Total energy intake was in women 8±1.2, 7.8±1.8 and 8.2±2.1 for ES; 7.6±1.2, 7.7±1.6 and 7.1±2.1 for SE; 7.0±1.9, 6.9±1.6 and 7.0±1.8 for DD, respectively. The food energy intake did not significantly change in any of the groups.

Blood lipids. Total cholesterol changed significantly only in the male ES group (weeks 0-12 p=0.019 and 0-24 p=0.012) (Table 3). The change in total cholesterol was significantly different from the same sex DD (p=0.028) and SE (0.048) groups at weeks 0-12. $Chol_{HDL}$ changed significantly only in DD women (weeks 0-12 p=0.001 and weeks 13-24 p<0.001). Between-group interactions in $Chol_{HDL}$ were observed in men between DD and SE (weeks 0-12 p=0-005 and weeks 13-24 p=0.047). Favorable changes in $Chol_{LDL}$ were found in the male ES group (weeks 0-12 p=0.037) and triglycerides (weeks 13-24 p=0.017). The changes in $Chol_{TOT}$ and Fat_{andr} had a low correlation during weeks 0-12 (r=0.280, p=0.006) and weeks 0-24 (r=0.283, p=0.005) among all participants as well as a moderate correlation in the DD-group including both sexes (weeks 0-12 r=0.601 p<0.001 and weeks 0-24 r=0.550 p=0.001).

Strength and endurance performance. Changes in 1RM and VO_{2max} are presented in Figure 3 and have also partly been published elsewhere (Eklund et al. 2015, Eklund et al. 2016, Schumann et al. 2014, Schumann et al. 2015). 1 RM significantly increased in all groups in men (all groups $p<0.001$) and women (DD, SE $p<0.001$, ES $p=0.002$). In women, the increase in 1RM during weeks 0-12 was larger in DD than in ES ($p=0.013$). Maximal isometric leg extension force (MVC) increased in all groups by week 24 (Women: DD 21±13% from 1341±265 N $p<0.001$, ES 22±18% from 1610±302 N $p<0.001$, SE 12±13% from 1700±668 N $p=0.016$; Men DD 11±12% from 2332±590 N $p<0.001$, ES 9±13% from 2653±683 N $p=0.032$, SE 13±18% from 2338±540 N $p=0.024$). No significant time×group interactions were found in 1RM or MVC. Increases in VO_{2max} were significant in all groups (DD $p<0.001$, ES $p=0.037$, SE $p=0.013$) and women (DD $p<0.001$, ES $p=0.009$, SE $p=0.002$). The increase in VO_{2max} during weeks 0-24 was larger in the DD group than in ES or SE both in women ($p=0.009$ and $p=0.008$, respectively; effect size DD 1.23, ES 0.85, SE 0.67) and men ($p=0.003$ and $p=0.008$, respectively; effect size DD 0.94, ES 0.38, SE 0.40).

DISCUSSION

The main objective of the present study was to evaluate the effects of different-day (DD) strength and endurance training and same-session combined strength and endurance training with different orders (ES and SE) on body composition, blood lipid parameters and strength and endurance performance in healthy men and women. The primary finding of the study was that while all three training modes led to significant increases in lean body mass as well as strength and endurance performances, decreased body fat mass was observed only in the DD training groups. Only minor fluctuations in blood lipids were observed over the 24-week training intervention, but these changes were associated with the changes in fat mass.

Body composition and blood lipids

The increases in total body lean mass were similar following all three training modes in both sexes during the 24-week training period, despite the regional changes not reaching significance in all groups. These findings are in line with our earlier investigation (Eklund et al. 2015), in which similar increases in vastus lateralis cross-sectional area following different-day and same-session training with different orders in men were reported. While it has been suggested that endurance exercise performed immediately before strength exercise may interfere with the hypertrophic stimuli induced by the strength loading (Apro et al. 2015), the present intervention did result in considerable and statistically significant increases (3-4%) in lean mass measured by DXA in both same-session groups. However, as this investigation did not include a strength training-only group, it is not possible to conclude whether the gains in lean mass would have been larger without the coexistent endurance training. It also needs to be noted that cycling as the present choice of endurance exercise may aid rather than interfere with muscle growth, while running could have adverse effects on muscle hypertrophy (Wilson et al. 2012). Nonetheless, our results indicate that cycling endurance exercise performed in the immediate presence of strength training (either before or after) did not affect lean body mass differently than allowing for a full day of recovery through splitting strength and endurance training onto different days.

Interestingly, body fat mass was found to decrease only following the DD-training, even though changes in lean mass being similar in all groups and despite nutritional intake being maintained in each group. These decreases were significantly larger than those of the ES training in men, and significantly larger than both same-session modes in women. Similarly to what was observed in terms of lean mass, the same-session training groups did not significantly differ from each other in either sex in terms of decreases in body fat mass. This supports previous results in comparisons of prolonged ES or SE training in men (Schumann et al. 2014), where the training modes did neither result in significant fat loss, nor differed from each other.

Although the training volume was matched in all groups in the present study, the evident difference between the three groups was that the DD-group consistently performed the training sessions on different days while the same-session groups always performed both modes in the same training sessions. Even though the post-exercise energy consumption has not been investigated in a setting of combined training per se, split endurance sessions have been suggested to produce larger post-exercise energy costs than one long-duration session (Almuzaini et al. 1998), possibly contributing to a larger overall energy expenditure over time. As the DD-training could be considered to be a “split session” in comparison to same-session combined training, the assumption of a larger post-exercise energy consumption could be considered a feasible assumption to why the DD-training resulted in a larger degree of fat loss in comparison to combined session training. However, as post-exercise energy consumption was not measured in the present study, this hypothesis remains speculative until further investigation.

The excessive accumulation of adipose tissue especially in the abdominal area has been identified to be a cardiovascular risk factor (Mottillo et al. 2010) as well as to induce a pro-inflammatory environment associated with e.g. metabolic syndrome (Ritchie and Connell 2007). The present results are, therefore, of great importance from a public health perspective as a significant decrease in fat mass was prominently observed in the abdominal region in the DD-groups. Furthermore, these results support earlier findings that decreases in abdominal fat may be associated with decreased blood lipid concentrations (Dutheil et al. 2013), as observed in the present study both in the total subject population as well as in the DD-groups alone through correlations between the changes in total cholesterol and abdominal fat. Thus, the present findings suggest that DD-training could be an effective strategy for decreasing fat in the abdominal region (as represented by decreases in $\mathrm{Fat}_{\mathrm{andr}}$), and thus possibly contribute to improving both cardiovascular and metabolic health (Mottillo et al. 2010, Ritchie and Connell 2007). However, considering the lipid fractions, decreased LDL cholesterol was observed in the ES group among men as well as a modest effect on HDL cholesterol following SE training in women, without correlations to body composition. Therefore, the effects of different combined strength and endurance training regimens is important to investigate further in order to determine possible training protocol specific effects on lipid fractions.

When interpreting the results of the present study the slight differences in baseline level of body fat also needs to be taken into account. Despite the groups displaying similar BMI’s in both sexes, the ES and SE groups were slightly leaner at the start of the study. To overcome the difference in the baseline conditions, our statistical method was designed to take into account the baseline level in order to identify true adaptations. Thus, as the magnitude of change was more than two-fold in the DD-groups in comparison to the same-session groups and importantly, without any change in fat mass in the same-session combined groups, it is possible that DD-training is more potent in decreasing body fat mass. However, as comparisons between different-day and same-session training have mainly been conducted focusing on exercise performance rather than detailed comparisons of changes in body composition (Robineau et al. 2014, Sale et al. 1990), additional similar interventions are needed in order to gain a better perspective into the differences between these training modes following prolonged training periods.

Physical performance profile

All training modes resulted in significant gains in maximal concentric strength and isometric force of the lower extremities despite some initial differences in the time course of adaptations in women. Although DD-training in women resulted in improved isometric force as well as significantly larger gains in dynamic strength by week 12 in comparison to E+S and S+E, the adaptations after 24 weeks were similar in the three groups. While Sale et al. (Sale et al. 1990) reported larger strength gains following different-day than same-session training after 20 weeks in men, the results of the present study displayed a similar effect after 12 weeks in women. A recent investigation reported that following a 7-week training intervention in athletes a different-day S and E training mode appeared to be more beneficial for strength adaptations than immediate sequencing of S and E loadings (Robineau et al. 2014). However, with this limited number of studies examining differences between same- and different day S and E training, the inconsistencies in the outcomes between these studies is difficult to identify. The reasons could possibly be related to the specifics of the training programs (e.g. training frequency and/or intensities and training periodization scheme) as well as the subject populations. From the scope of the present study, the baseline difference in 1 RM between the DD and ES group may also explain the difference in the time course of adaptations. The DD-group starting at a slightly lower baseline level may have provided an opportunity for more rapid initial strength gains. Nonetheless, the present study showed similar long-term efficiency for improving maximal strength performance both in the same- and different-day training groups.

A difference to the findings from Sale et al. (Sale et al. 1990) was found in training-induced changes in VO_{2max}. In the present study the increase in VO_{2max} was significantly larger following DD-training than E+S or S+E -training in both men and women, while the earlier study reported no difference between groups. However, the results of the present study are in agreement with those of Robineau et al. (Robineau et al. 2014), who reported that different-day training appeared more likely to improve VO_{2max} than same-day training. In the present study, it may be likely that the lower initial level of VO_{2max} in the DD-groups partly contributed to this difference, considering the possibility for a larger window of adaptation when commencing training at a lower level of fitness. Despite this, the more than two-fold increases in VO_{2max} in the DD-group suggest that increases may be more likely to occur with the DD rather than ES or SE training, but further research is needed to establish the findings with its exact mechanisms.

CONCLUSIONS

In summary, the present study showed that all of the three modes of combined strength and endurance training were effective in increasing maximal strength and endurance performance as well as lean body mass in healthy individuals following 24 weeks of combined strength and endurance training. However, the increases in endurance performance were larger in magnitude when strength and endurance were performed on different days in comparison to that produced by same-session training. Furthermore, body fat mass was decreased only following combined strength and endurance training performed on different days. As the decreases in fat mass were associated with positive changes in blood lipids, combined strength and endurance training on different days may be an effective strategy for early prevention of cardiovascular and metabolic diseases. While the mechanism for this phenomenon was beyond the scope of the present study, separating strength and endurance training into more frequent sessions performed on different days seems to be a valid option for healthy adults who wish to simultaneously optimize body composition and improving physical fitness.

CONFLICT OF INTERESTS

The authors state that there is no conflict of interest.

ACKNOWLEDGEMENTS

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TABLES

Table 1. Subject characteristics at Week 0.

	Women			Men		
	DD (n=18)	**ES** (n=17)	**SE** (n=15)	**DD** (n=21)	**ES** (n=17)	**SE** (n=18)
Age (y)	29.9 ± 7.5	29.1 ± 5.6	28.9 ± 4.4	28.9 ± 6.1	29.8 ± 6.0	29.8 ± 4.4
Height (cm)	168.0 ± 5.0	168.0 ± 7.0	164.0 ± 5.0	180.0 ± 0.07	178.0 ± 6.0	179.0 ± 5.0
Weight (kg)	66.5 ± 8.2	66.7 ± 10.1	62.4 ± 8.0	80.5 ± 11.1	80.3 ± 12.0	75.2 ± 8.5
BMI ($m^2 \cdot kg^{-1}$)	23.7 ±2.8	23.7 ± 3.3	23.2 ± 3.4	24.8 ± 3.2	25.2 ± 3.3	23.5 ± 2.1
1 RM (kg)	88 ± 12	102 ± 22 *	99 ± 18	142 ± 24	157 ± 30	143 ± 23
VO_{2max} (ml/min/kg)	28 ± 5	31 ± 4	34 ± 5 *	36 ± 7	42 ± 7 *	43 ± 7 *
% BF	37.8 ± 5.0	34.8 ± 8.5	31.6 ± 7.2	26.5 ± 6.5	22.9 ± 8.2	20.6 ± 5.3 *

1 RM = maximal leg press strength, VO2max=maximal oxygen uptake, %BF = percentage of body fat

DD = Different-day training, ES = Same-session training, endurance followed by strength, SE = Same-session training, strength followed by endurance

* indicates difference to same-gender
DD

Table 2. Changes (%) in body composition

	Women						Men					
Weeks	**0-12**	**p**	**0-24**	**p**	**13-24**	**p**	**0-12**	**p**	**0-24**	**p**	**13-24**	**p**
Lean$_{tot}$												
DD	4±3*	0.001	5±3*	<0.001	1±3		3±2*	<0.001	4±3*	<0.001	1±2	
ES	1±2*$^{[\ddagger\ p=0.059]}$	0.024	3±3*	0.001	2±2*	0.011	2±3*	0.033	3±3*	0.001	1±2	
SE	2±2*	0.007	3±2*	0.001	1±3		3±2*	<0.001	3±2*	<0.001	0±2	
Lean$_{arms}$												
DD	3±4*	0.015	3±4*	0.040	0±4		3±3*	<0.001	5±4*	<0.001	1±3	
ES	2±4	0.133	2±4	0.297	0±5		1±3		3±4*	0.027	2±6	
SE	3±4*	0.035	3±3*	0.004	0±4		2±3		3±4		1±4	
Lean$_{lower}$												
DD	3±2*	<0.001	4±2*	<0.001	1±2		2±3*	0.049	2±4		0±2	
ES	2±2$^{[*]}$	0.056	3±3*	0.002	2±1*	0.002	2±3*	0.018	4±3*	0.001	1±2	
SE	2±3*	0.020	3±2*	<0.001	1±3		3±3*	<0.001	4±3*	<0.001	0±2	
Lean$_{trunk}$												
DD	5±7		6±8*	0.014	1±7		3±3*	0.005	3±5		0±5	
ES	1±4		4±6*	0.046	3±5		2±5		3±4*	0.041	1±4	
SE	3±4$^{[*]}$	0.053	3±6	0.338	0±6		4±4*	0.004	3±3*	0.015	-1±3	
Fat$_{tot}$												
DD	-7±8*	0.017	-13±14*	0.009	-7±9*	0.025	-6±9*	0.005	-14±15*	<0.001	-9±10*	0.001
ES	-1±7[‡]	0.059	0±8‡	0.005	1±5‡	0.016	-3±13		-6±18		-3±11	
SE	-3±6		-4±10‡	0.008	-1±7‡	0.047	-2±11		-2±13‡	0.043	0±11‡	0.036
Fat$_{arms}$												
DD	-5±9		-11±15*	0.020	-6±11		-3±9		-9±17*	0.026	-6±13	
ES	-1±11		0±10		2±13		0±13		-5±15		-5±11	
SE	1±9		-6±9		-6±10		1±12		-2±16		-2±15	
Fat$_{lower}$												
DD	-5±8		-10±13*	0.018	-7±8*	0.014	-5±8*	0.026	-12±14*	0.004	-7±9*	0.005
ES	-1±7		-1±8[‡]	0.052	-1±4‡	0.029	-2±13		-5±16		-3±11	
SE	-2±5		-4±9		-1±7		-3±11		-4±12		0±10	
Fat$_{android}$												
DD	-11±10*	0.003	-17±15*	0.003	-7±10*	0.030	-7±10*	0.027	-18±14*	<0.001	-13±10*	<0.001
ES	2±10‡	0.001	3±8‡	<0.001	2±8‡	0.012	-5±15		-9±21		-4±13	
SE	-3±12‡	0.028	-4±15‡	0.002	-1±9‡	0.025	1±12‡	0.038	0±15‡	0.003	-1±12‡	0.010

* significant within-group change, ‡ significant difference to same-gender DD (with p-value), # significant between ES and SE. DD = Different-day training, ES = Same-session training, endurance followed by strength, SE = Same-session training, strength followed by endurance

Table 3. Blood lipid concentrations (absolute values).

	Women			Men		
	0	**12**	**24**	**0**	**12**	**24**
Chol$_{tot}$						
DD	4.8±0.7	5.1±0.8	4.7±0.8	4.6±0.8	4.7±0.8	4.6±0.9$^{\alpha}$
ES	4.9±0.9	5.1±1.0	4.9±1.0	4.8±0.9	4.4±0.7*‡#	4.5±0.8*
SE	4.6±0.7	4.7±0.8	4.7±0.9	4.6±0.8	4.6±0.8	4.6±0.6
Chol$_{HDL}$						
DD	1.9±0.3	2.1±0.3*	1.9±0.2$^{\alpha}$	1.4±0.3	1.5±0.4	1.4±0.3
ES	1.9±0.4	2.0±0.5	1.9±0.4	1.5±0.3	1.5±0.4	1.4±0.3
SE	1.9±0.4	1.9±0.5‡	2.0±0.4 §	1.4±0.3	1.3±0.3* ‡	1.4±0.3
Chol$_{LDL}$						
DD	2.4±0.6	2.5±0.7	2.3±0.8	2.6±0.9	2.7±0.8	2.5±0.8
ES	2.5±0.6	2.6±0.7	2.6±0.7	2.8±0.9	2.5±0.7*	2.7±0.8
SE	2.2±0.8	2.3±0.8	2.3±0.8	2.6±0.7	2.8±0.8	2.7±0.5
HDL/LDL						
DD	0.8±0.4	1.0±0.6	0.9±0.4	0.6±0.2	0.6±0.3	0.6±0.2
ES	0.8±0.3	0.9±0.4	0.7±0.3	0.6±0.3	0.6±0.2	0.6±0.3
SE	1.0±0.5	0.9±0.4	0.9±0.3	0.6±0.5	0.5±0.3	0.5±0.2
Triglycerides						
DD	1.2±0.5	1.1±0.5	1.1±0.6	1.4±0.8	1.3±0.5	1.2±0.7
ES	1.1±0.4	1.1±0.4	1.0±0.4	1.0±0.3	1.0±0.3	0.8±0.3$^{\alpha}$
SE	1.1±0.5	1.1±0.5	1.0±0.3	1.3±1.0	1.2±0.8	1.2±0.6

* significant within-group change from week 0, $^{\alpha}$ significant within-group change from week 12

‡ significant difference to same-gender DD at time point, # significant difference between same-gender ES and

§ significantly different from the other groups 12-24

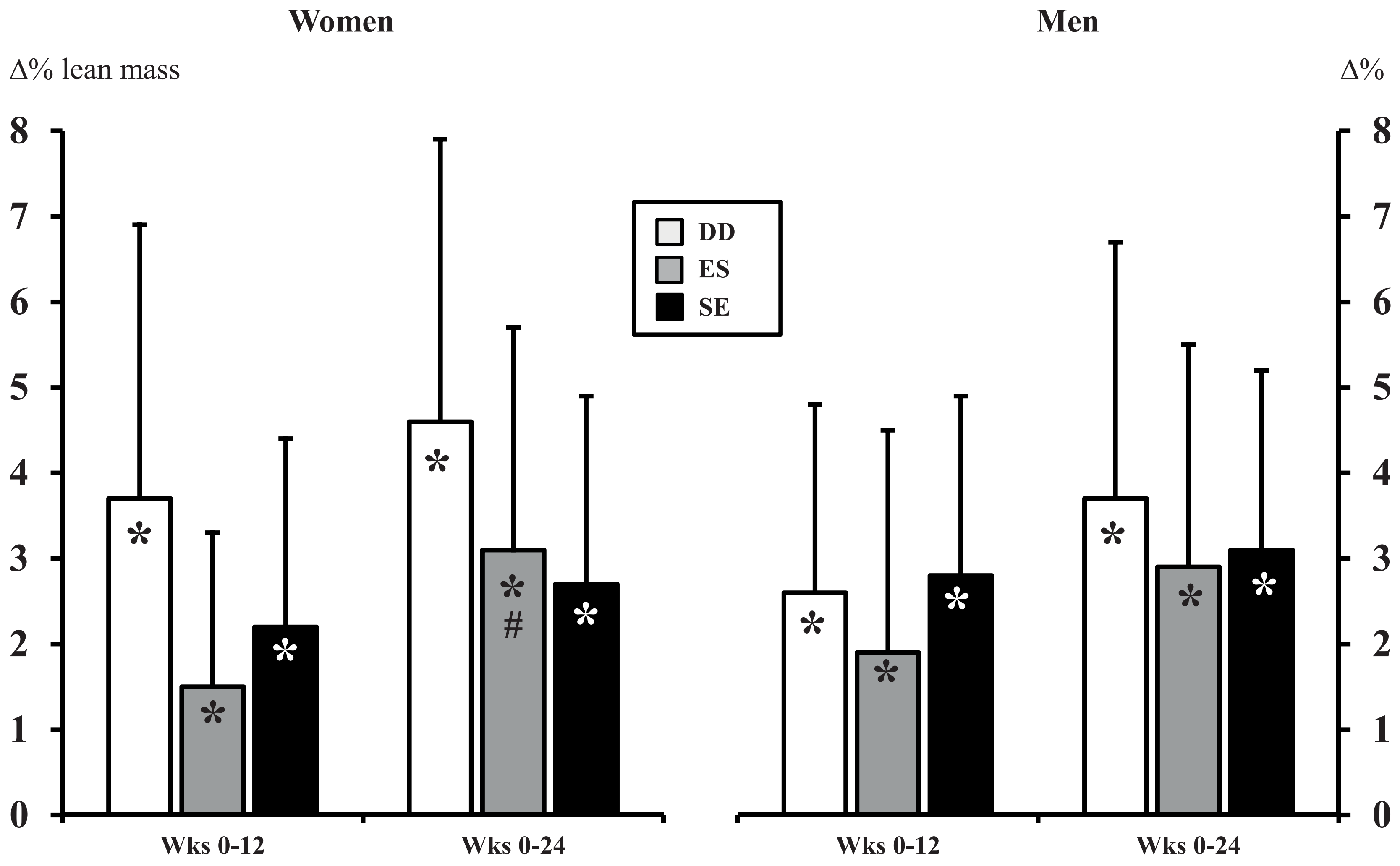
DD = Different-day training, ES = Same-session training, endurance followed by strength, SE = Same-session

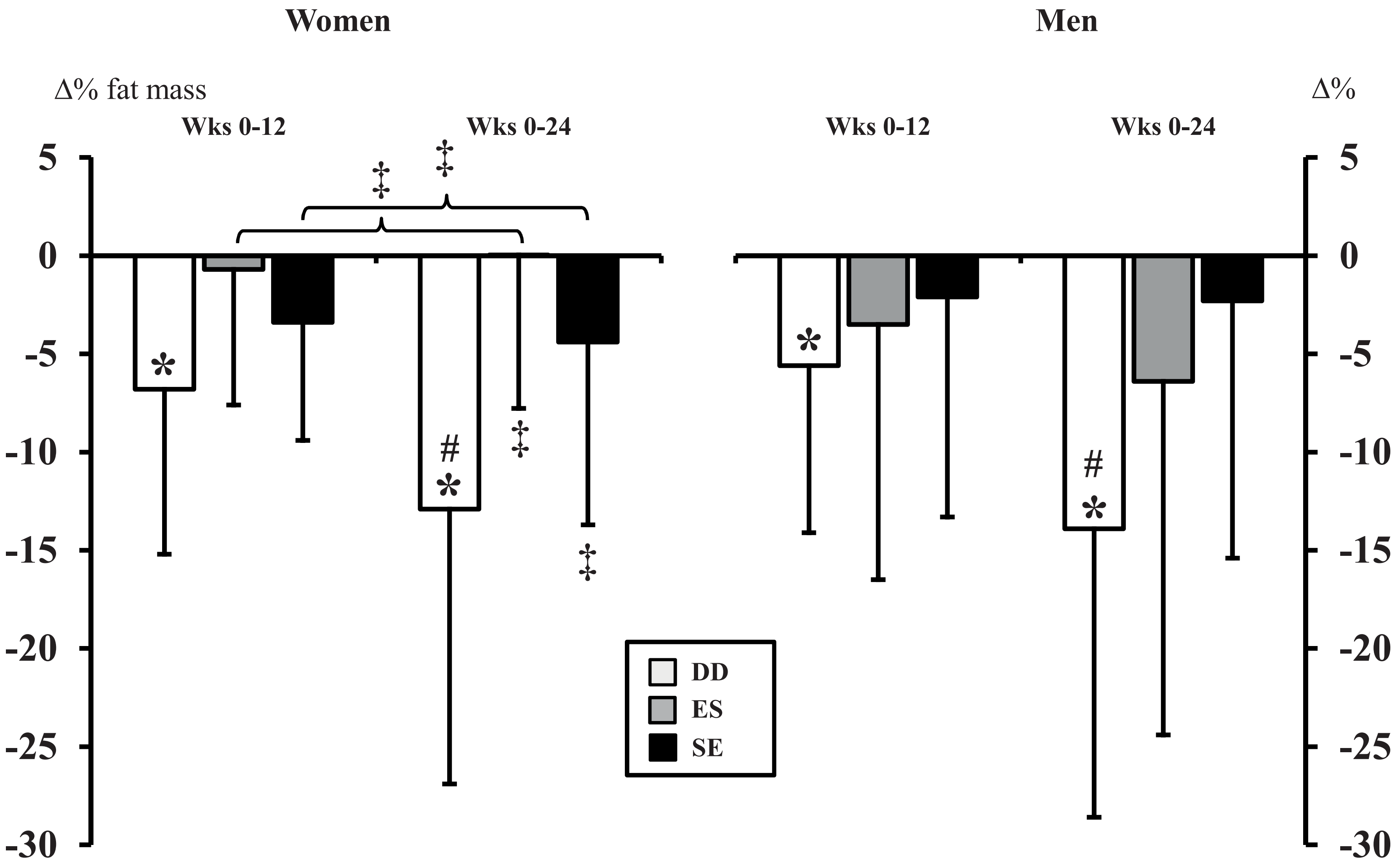
FIGURE CAPTIONS AND LEGENDS

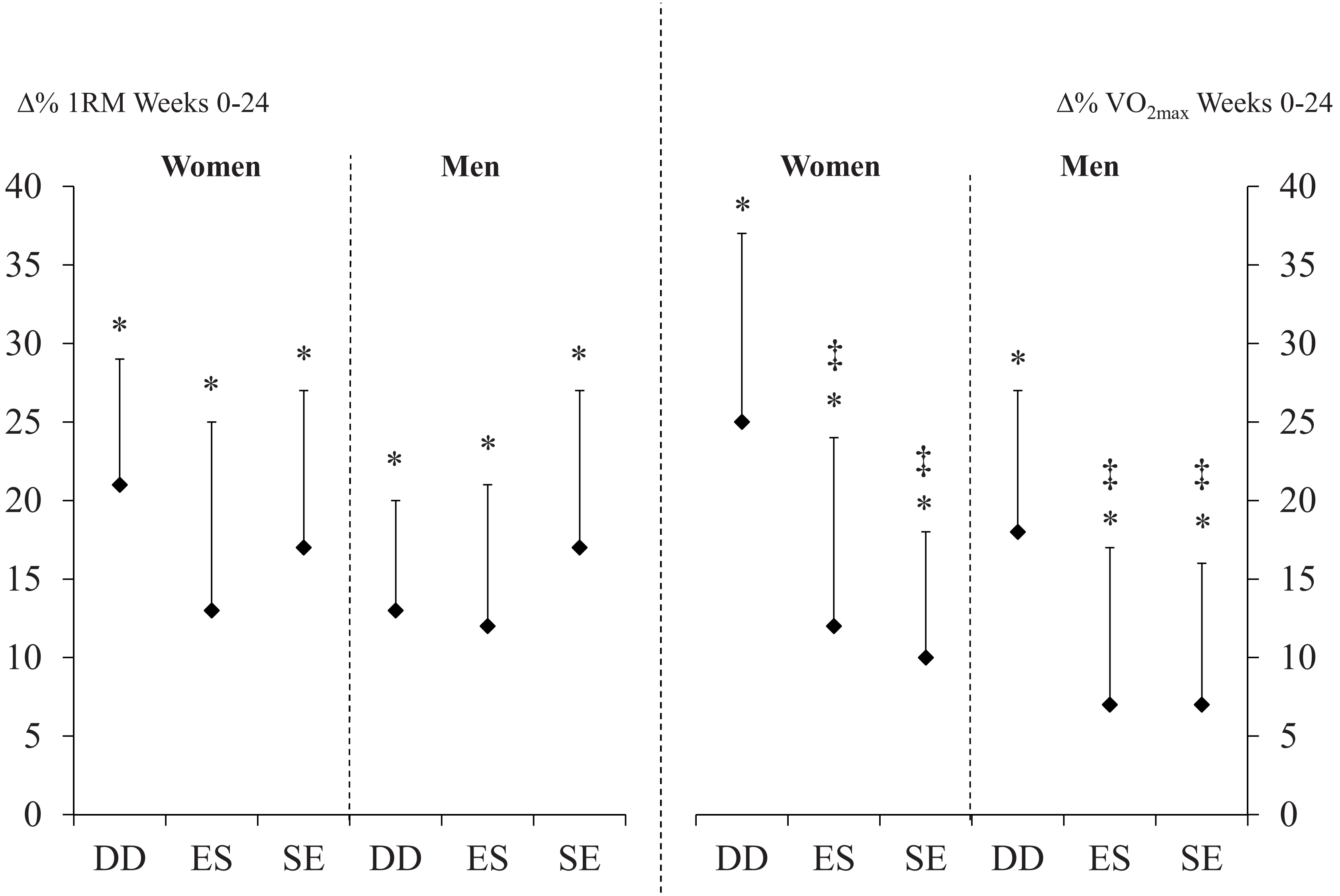
Figure 1. Mean (SD) changes in total body lean mass. * significant within-group change during weeks 0-12, # significant within group change during weeks 13-24. DD = Different-day training, ES = Same-session training, endurance followed by strength, SE = Same-session training, strength followed by endurance.

Figure 2. Mean (SD) changes in total body fat mass. * significant within-group change during weeks 0-12, # significant within group change during weeks 13-24, ‡ significant difference to same-session DD. DD = Different-day training, ES = Same-session training, endurance followed by strength, SE = Same-session training, strength followed by endurance.

Figure 3. Mean (SD) changes in 1 RM (left) and VO2max (right). * significant within-group change, ‡ significant difference to same-sex DD. DD = Different-day training, ES = Same-session training, endurance followed by strength, SE = Same-session training, strength followed by endurance


Women
Men
Δ% lean mass
Δ%
8
7
6
5
4
3
2
1
0
DD
ES
SE
*
#
Wks 0-12
Wks 0-24
Wks 0-12
Wks 0-24


Women
Men
Δ% fat mass
Δ%
Wks 0-12
Wks 0-24
Wks 0-12
Wks 0-24
5
0
-5
-10
-15
-20
-25
-30
*
#
‡
DD
ES
SE


Δ% 1RM Weeks 0-24
Δ% VO2max Weeks 0-24
Women
Men
Women
Men
40
35
30
25
20
15
10
5
0
DD
ES
SE
DD
ES
SE
DD
ES
SE
DD
ES
SE
*
‡

IV

SUBJECTIVE PERCEPTION OF WELL-BEING, SELF-ESTEEM AND TIME MANAGEMENT FOLLOWING 6 MONTHS OF COMBINED STRENGTH AND ENDURANCE TRAINING

by

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