CORTICOSPINAL ADAPTATIONS TO STRENGTH TRAINING AND ITS ASSOCIATIONS TO RATE OF FORCE DEVELOPMENT

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ABSTRACT

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Introduction. Neuromuscular determinants underlying rate of force development during rapid muscle contractions may be more relevant compared to maximal strength in many athletic events characterized by power and speed, as well as in clinical relations with older adult and patient populations. Earlier studies have described various neuromuscular determinants associated with rapid muscle contractions, and while rate of force development is affected by both intrinsic neural and contractile properties the neural determinants seem to be particularly important at the onset and up to 75 milliseconds into rapid contractions. Variety of strength training modalities have been demonstrated to improve both the neural properties and rate of force development, and many associations between the two are evident. However, majority of strength training studies have addressed the associations considering the whole corticospinal tract but not in smaller segments. Therefore, the objective of this study was to investigate potential differences separately at cortical and spinal level.

Methods. Previously untrained (n=14, 28±5 years) participants completed a 7-week strength training intervention performed in conventional modality for whole body. The participants were measured for maximal voluntary contraction (MVC), and rate of force development (RFD) in three overlapping time frames (0–50, 0–75 and 0–100 ms) in isometric knee extension. Electrical stimulation of the peripheral femoral nerve was used for interpolated twitch technique (ITT) and maximal M-wave (M-max) of the rectus femoris (RF). Single-pulse electrical stimulation of the lumbar spine (LS) and transcranial magnetic stimulation (TMS) were used to measure changes in lumbar evoked potential (LEP) and motor evoked potential (MEP) peak-to-peak amplitude, as well as in spinal and corticospinal silent period (SP). All measures were taken over control period, at baseline prior to intervention, 3.5-weeks into the intervention and post to the intervention.

Results. No group level change in MVC or RFD in any time frame were observed following the strength training. Group level change in corticospinal and spinal excitability measured by MEP and LEP amplitudes remained unchanged across the intervention. Similarly, group level change in corticospinal and spinal inhibition measured by SP resulted in non-significant difference compared to baseline. Multiple regression analysis across all force and neurophysiological measures resulted in non-significant correlations.

Conclusions. No associations between rapid muscle contractions and corticospinal adaptations at either level could be demonstrated by the results of this study. Conventional whole body strength training may be suboptimal to improve rate of force development measured by unilateral isometric contractions. More importantly both corticospinal adaptations and early phase rate of force development present high intra- and inter-individual variation, thus various methodological considerations potentially compromising their assessment should be acknowledged.

Key words: strength training, rate of force development, transcranial magnetic stimulation, lumbar spine electrical stimulation, neurophysiology, exercise-induced neural plasticity

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Johdanto. Lihasten voimantuottonopeutta voidaan pitää merkityksellisempänä kuin lihasten maksimivoimantuottoa erityisesti nopeus- ja teholajeissa, sekä liikuntarajoitteisten ikäihmisten ja potilaiden kliinisessä kuntoutuksessa. Aiemmissa tutkimuksissa on kyetty osoittamaan useita erilaisia hermolihasjärjestelmätason muuttujia, joilla on vaikutus nopeisiin lihassupistuksiin. Nämä hermostolliset ominaisuudet vaikuttavat olevan tärkeitä erityisesti nopean lihassupistuksen alkuvaiheesta aina noin 75 millisekuntiin saakka, vaikkakin voimantuottonopeuteen vaikuttavat myös lihassolujen supistumisominaisuudet. Erilaisten voimaharjoittelumenetelmien on osoitettu parantavan sekä hermoston toimintaa että voimantuottonopeutta. Lisäksi näiden tekijöiden välisistä yhteyksistä on saatu tietoa. Suurin osa voimaharjoittelututkimuksista on kuitenkin tarkastellut yhteyksiä koko kortikospinaaliradan osalta, mutta ei erikseen kortikaali- tai spinaalitasolla. Näin ollen, tämän tutkimuksen tavoitteena on tutkia mahdollisia eroja kortikaali ja spinaali tasolla sekä niiden yhteyksiä voimantuottonopeuteen.

Menetelmät. Tutkimukseen osallistui aiemmin harjoittelemattomia aikuisia (n=14, 28±5 vuotta) ja he suorittivat seitsemän viikon voimaharjoittelujakson. Tutkittavilta mitattiin maksimaalista voimaa (MVC), sekä voimantuottonopeutta (RFD) kolmessa aikakehyksessä (0–50, 0–75 ja 0–100 ms) isometrisen polvenojennusliikkeen aikana. Perifeeristä reisihermon sähköistä stimulaatiota käytettiin tahdonalaisen lihasaktivaation (ITT) ja maksimaalisen M-aallon (M-max) tutkimiseksi suorasta reisilihaksesta (RF). Lannerangan sähköstimulaatiota (LS) ja transkraniaalista magneettista stimulaatiota (TMS) käytettiin mittaamaan muutoksia lihaksen herätepotentiaalissa (LEP ja MEP), sekä vasteen jälkeisessä ”hiljaisessa jaksossa” (SP). Kaikki mittaukset toteutettiin kontrollijakson aikana, ennen interventiota, 3,5 viikkoa intervention aloittamisen jälkeen ja sen päätyttyä.

Tulokset. Voimaharjoittelujakson seurauksena ei havaittu ryhmätason muutoksia MVC:ssä tai RFD:ssä. LEP- ja MEP-amplitudeilla mitatut herätepotentiaalit pysyivät ennallaan koko intervention ajan. Vastaavasti ryhmätason muutos SP:llä mitatussa ”hiljaisessa jaksossa” ei osoittanut tilastollisesti merkitsevää muutosta. Monimuuttuja-regressioanalyysi ei osoittanut korrelaatioita voima- ja hermostollisten muuttujien välillä.

Johtopäätöksiä. Tässä tutkimuksessa ei löydetty yhteyksiä nopeiden lihassupistusten ja kortikaali- tai spinaaliadaptaatioiden välillä. Perinteinen kokokehon voimaharjoittelu saattaa siis olla riittämätöntä nopeusvoimantuoton kehittämiseksi, ainakin jos sen tutkimiseksi käytetään yhden raajan isometristä voimamittausta. On tärkeää huomata, että kortikospinaaliset adaptaatiot ja nopeusvoimantuottokyky vaihtelevat suuresti yksilön sisällä sekä yksilöiden välillä. Näin ollen, luotettavan tiedon keräämiseksi on kyettävä kontrolloimaan useita metodologisia tekijöitä.

Avainsanat: voimaharjoittelu, voimantuottonopeus, transkraniaalinen magneettistimulaatio, lannerangan sähköstimulaatio, neurofysiologia, liikunnan aiheuttama hermoplastisuus

ABBREVIATIONS

RFD	rate of force development
MVC	maximal voluntary contraction
TMS	transcranial magnetic stimulation
LS	lumbar stimulation
MEP	motor evoked potential
LEP	lumbar evoked potential
M-max	maximal M-wave
aMT	active motor threshold

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1 INTRODUCTION

Explosive strength, also referred to as rapid muscle contractions in this work, describes the ability of an individual to increase force or torque as quickly as possible during a voluntary contraction. Explosive strength is suggested to be of more importance compared to maximal strength for many athletic, older adult and patient populations, since rapid muscle contractions share similarities with many sport-specific and functional daily activities (Tillin et al. 2013). Therefore, ability to interpret and understand the underlying mechanisms of rate of force development capacity of individuals is important not only for researchers exercise physiology, but also for clinical practitioners involved in physical training and rehabilitation.

Rapid muscle contractions are often measured as rate of force development (RFD) that is derived either from the force-time curves of maximal voluntary contraction (MVC) strength tests or more brief contractions released from a resting or low level of muscle activity (Aagaard et al. 2002). While maximal strength and explosive strength are strongly related, they may be governed by different neurophysiological mechanisms (Andersen & Aagaard 2006). The assessment of neuromuscular performance from rapid muscle contractions may be more sensitive to detect acute and chronic changes following strength training interventions. Moreover, the very early phase (<100 ms) rapid muscle contractions seem to be largely dependent on neural properties and less on the intrinsic properties of the skeletal muscle (Folland et al. 2014). The contribution from variety of neural modulators to rapid muscle contraction has been relatively widely studied in the past. Especially the integral effect of cortical neural drive, recruitment speed of motor neurons and the discharge rate of these motor neurons have been identified earlier (Del Vecchio et al. 2019, Dideriksen et al. 2019). Therefore, in depth identification of the critical neural characteristics underlying rapid muscle contractions will be helpful for designing strength training interventions again not only for athletes but for rehabilitation of patient populations as well as to sustain physical function and reduce injury risk of older adult populations.

The objective of this study is to characterize adaptations happening with rapid muscle contractions and corticospinal tract following strength training in previously untrained healthy

individuals. To achieve this measurement of rate of force development and stimulations of the nervous system was applied before, during and after a 7-week strength training intervention. Moreover, the novelty of the present study is to describe potential associations between rapid muscle contractions and neural adaptations separately at cortical and spinal level.

2 LITERATURE REVIEW

2.1 Neuromuscular determinants of rate of force development

2.1.1 Neural determinants

This literature review will provide an overview about the neurophysiological mechanisms underlying rapid muscle contractions that characterize physical performance features such as speed-strength, explosive strength and power. Different neural facilitatory and inhibitory mechanisms are involved in the regulation of human movement and affect rapid muscle contractions. According to current knowledge the prominent components affecting force production consist of the degree of motor unit recruitment, motor unit discharge rate and consequently the level of muscle activation. Therefore, also rapid muscle contractions are essentially an effect of the number of motor units activated (i.e. recruitment) and the rate at which action potentials are discharged (i.e. rate coding) by the motor neuron. In addition, association between muscle fibre conduction velocity and maximal rate of force development during the early phase (<50 ms) but not with later time points has been reported (Del Vecchio et al. 2018).

Maffiuletti et al. (2016) suggested that RFD is majorly determined by the capacity to direct neural drive to produce maximal voluntary activation over the first 50–75 ms (i.e. early phase) of rapid muscle contraction. Moreover, the capacity for high RFD during the early phase seems to be a result of increased motor unit discharge rate and the occurrence of double discharges (Duchateau & Baudry 2014; Kamen & Knight 2004; Patten et al. 2001; Sjøgaard et al. 2001). Similarly, Del Vecchio et al. (2019) also stated that the high initial discharge rate of the motor neurons seems to be determined by capacity of corticospinal input (i.e. neural drive). However, in the study significant correlation between maximal motor unit discharge rate, RFD and neural drive was found only during first 35 ms after the onset of the first detected action potential. Del Vecchio et al. (2019) suggested that the discharge rate at <35 ms into a volitional motor task represent changes specifically in cortical input since the very initial phase of contraction is only affected by efferent drive. Furthermore, the synaptic input received by motor neurons during

latter phase of rapid contraction may be affected by afferent feedback (e.g. muscle spindles or Golgi tendon organs) due to the electromechanical delay and nerve conduction times (Del Vecchio et al. 2019). Therefore, an estimate of the degree of corticospinal drive could be achieved by measuring the velocity of motor unit recruitment prior to afferent feedback.

Regardless of contraction velocity the motor unit recruitment always first follows a size principle of low threshold motor units being recruited before larger ones (Duchateau & Enoka 2011). However, there seems to be a contraction velocity dependent adjustment to the force level at which each motor unit is recruited. During slower contractions, motor unit recruitment increases progressively up to approximately 80–90% of the maximum force, which after the increase in force is a consequence of increased discharge rate. Whereas, during rapid contractions the same motor units seem to be activated at lower recruitment thresholds (Van Cutsem et al. 1997). In addition, Del Vecchio et al. (2019) evidenced that majority of motor units begin to discharge already before the onset of force production of rapid contractions. The maximal discharge rate of untrained subjects during sustained high-force isometric contraction can be two times slower (30–60 Hz) compared to discharge rate at the onset of rapid muscle contraction (60–120 Hz) (Duchateau & Enoka 2011). Kernell (2006) stated that discharge rate up to 100–200 Hz augmented the RFD of all motor units within the motor neuron pool, while further increases in discharge rate influenced only the faster motor units, thus indicating a speed-related difference in high- and low-threshold motor unit properties. Note, that trained individuals may reach discharge rates above 200 Hz. In addition, individuals have different proportions of slow and fast motor units with different intrinsic capacity to discharge. Therefore, the observed inter-individual differences in the motor neuron discharge rate may be determined by both the degree of corticospinal input and/or intrinsic characteristics of the neuron.

While maximal motor unit discharge rate is a substantial component of rapid force development at the onset of rapid voluntary contraction, it has been suggested that the synaptic input received by motor neurons even prior to onset of force would be the primary determinant of the rate of force development (Del Vecchio et al. 2019). Del Vecchio et al. (2019) reported that the maximal motor unit discharge rate occurs before the onset of force production. However, while rapid contractions are enhanced by a high initial discharge rate at the onset of muscle activation,

this rate coding pattern cannot be sustained for long, but plateau and decline progressively towards the maximum force level (Klass et al. 2008; Van Cutsem et al. 1998). In fact, discharge rates can be expected to decline already after the first action potentials (Miles et al. 2005). Unlike the discharge rate, Van Cutsem et al. (1998) stated that while also the major amount of motor units are recruited before the onset of force production in rapid contractions, the amount of recruited motor unit can be sustained far longer. The decline in discharge is greater in untrained than in trained individuals and further weakens with ageing suggesting that spinal inhibitory mechanisms and the intrinsic motor neuron properties modulate the descending command (Maffiuletti et al. 2016).

At the cortical level one of the underlying mechanisms for enhanced ability to produce rapid contractions may be faster recruitment of neurons within the cerebral cortex, since the activity of superior motor neurons determine the "all-or-none" response of inferior motor neurons (Del Vecchio et al. 2019). During maximal volitional drive a strong synaptic input is projected to the motor neuron pool, consequently determining both recruitment velocity and discharge rate. This transmission of cortical input by the motor neuron pool can be revealed by the association found between average discharges per motor unit per second and the recruitment velocity of motor neurons (Del Vecchio et al. 2019). However, the relative contribution of motor neuron recruitment velocity and discharge rate cannot be assorted as they both depend on the synaptic input projected to the motor neuron pool.

As discussed, as a consequence of motor unit recruitment and discharge rate the resultant level of muscle activity is one of the main factors of RFD (Maffiuletti et al. 2016). De Ruiter et al. (2004) studied the early phase of the torque and EMG time curves of the knee extensor muscles for possible deficiencies in RFD during voluntary contraction. The results revealed that the force attained at 40 ms into the rapid voluntary contraction was only 40% from the force of electrically induced tetanic contraction. Indicating that the ability to produce force rapidly is predominantly dependent on neural factors at the onset of muscle contraction rather than on muscular properties. Similarly, Andersen & Aagaard (2006) suggested that intrinsic muscular properties are not accounting for most of the variance of voluntary RFD after observing only moderate association (r=0.36) between voluntary RFD measured in the first 40 ms of a rapid knee extensor contraction and electrically evoked twitch contractile properties. In addition, by

examining the relative contribution of neural and contractile factors during voluntary and involuntary (supramaximal evoked twitch and octet) contractions Folland et al. (2014) made the notion that agonist EMG activity separated as a contributor to the variance in voluntary RFD particularly at 25–75 ms, whereas muscular properties were the primary determinant at 50–100 ms. Therefore, a conclusion can be made that neural factors emphasize foremost at the onset of rapid voluntary contraction (<75 ms) and is subsequently influenced by the contractile properties and MVC force at longer (>75 ms) durations (Maffiuletti et al. 2016).

There remains a large inter-individual variation in the intrinsic properties of the neuromuscular system and in the ability to produce force rapidly. It seems that neural factors contribute substantially to this variance, since the inter-individual variation is found to be most apparent in the early phase (40–50 ms) of voluntary contraction (Folland et al. 2014). Del Vecchio et al. (2019) suggested that the inter-individual variability in the ability to produce rapid muscle contractions seems to be determined by the level of neural activation preceding the force onset. Earlier, Duchateau & Enoka (2002) stated that numerous mechanisms at different levels of the corticospinal tract may interfere with the voluntary activation. An inability to generate sufficient volitional drive rapidly may be a part of the deficit in voluntary activation in general. However, the suboptimal output from the primary motor cortex may occur due to different causes in cortical centers involved in the initiation of a motor action. Nevertheless, Duchateau & Baudry (2014) stated that currently it is not possible to determine reasons for suboptimal volitional drive and insufficiency to maximally activate muscles during rapid movements.

It is proposed that ineffective synchronization of agonist, antagonist and synergist muscles involved in the task may be a part of the deficit in muscle activity (Duchateau & Enoka 2002). Maffiuletti et al. (2016) stated that the ineffective synchronization and/or coordination of voluntary activation may indicate both an inherent ability to focus efferent drive to the involved muscles as well as the training status of the individual. They theorized that the inter-individual differences during rapid actions are due to the rate of neural acquisition processes of new motor tasks, and that motor cortex is implicated in the motor learning. Especially, rapid improvement in high-speed actions seem to be result of short-term changes at the motor cortex (Maffiuletti et al. 2016). Lee et al. (2010) discovered this using transcranial magnetic stimulation (TMS) as increased corticospinal excitability accompanied the increase in index finger abduction

acceleration over short-term exercise. After 150 repetitions the peak abduction acceleration increased by 64% and the corticospinal excitability increased by 43%, respectively after 300 repetitions the increases were 93% and 63% from the base level. In addition, Muellbacher et al. (2001) found increased motor evoked potential (MEP) in TMS without change in MEP amplitude when the descending tract was stimulated at the cervicomedullary junction (i.e. cortical centers bypassed) indicating the involvement of the primary motor cortex in rapid motor learning.

Interestingly, Dideriksen et al. (2019) studied some of the neuromuscular determinants of rapid muscle contractions discussed in this chapter using a computational simulation model. The impact of three parameters: rate coding, recruitment, and contractile properties of a motor unit pool were analyzed in relation to maximal RFD during isometric contraction. Highest impact was found for the rate by which motor units were recruited, that is time interval between the first and last motor unit being recruited. Therefore, the computational simulations suggest that largest improvement in RFD should be achieved by reducing the motor unit recruitment interval (Dideriksen et al. 2019). However, the neurophysiological mechanisms are far more complex in vivo, thus the implemented simulation approach is insufficient to reliably designate the neuromuscular determinants related to rate of force development in natural settings.

2.1.2 Muscular determinants

As discussed earlier, the neural mechanisms are associated more with RFD at the onset of voluntary contraction and during the early phase (≤75 ms), whereas muscular properties such as muscle size (i.e. cross-sectional area) and architecture (e.g. fascicle length, pennation angle) may have more affect on late phase (≥75 ms) of the RFD (Andersen & Aagaard 2006). Therefore, the inter-individual variance in ability to produce force rapidly addressed so far requires further reasoning. As mentioned, individuals have different proportions of slow and fast motor neurons also meaning that the proportion of type I and type II muscle fibres differ accordingly, since the motor neuron always innervate fibres within the same type. Roughly 50% of the fibre type proportion is inheritable, while a high degree of adaptability for the fibres remain (Andersen & Aagaard 2000).

Fibre type composition is considered as fundamental factor influencing RFD based on the faster rate of tension development in type II than type I fibres. The faster rate of tension development is based on faster cross-bridge cycling rates resulted by greater total calcium (Ca^{2+}) release per action potential, faster time constants of Ca^{2+} currents, and fast myosin, troponin and tropomyosin isoforms of type II fibres (Bottinelli et al. 1996; Schiaffino & Reggiani 1996). In addition to large inter-individual variability there is also a distinct inter-muscular variation in fibre type composition. Luden et al. (2008) reported that knee extensor muscles vastus lateralis, vastus medialis and vastus intermedius contain approximately 50/50% of type I and type II fibres. However, Andersen (2001) reported type II fibres to vary between 25–80% in vastus lateralis muscle of young untrained men (n=21). Therefore, no universal fibre type composition average can be determined.

A moderate, albeit non-significant correlation (r=0.34) has been reported between the percentage of type II fibres in vastus lateralis and maximal voluntary knee extensor RFD (Taylor et al. 1997). However, a significant correlation (r=0.49) in young men has been reported between the area of type II fibres in vastus lateralis and knee extensor RFD measured to 50 ms (Hvid et al. 2010). This indicates that fibre type composition has a prominent role in the ability to produce force rapidly and likely accounts for some of the inter-individual and inter-muscular differences. Nevertheless, despite the importance of fibre type composition approximately 50–70% of the variance in voluntary RFD is expected to be caused by other reasons (Maffiuletti et al. 2016). Therefore, other factors in the muscle–tendon complex, such as the point of origin and insertion of muscles (i.e. lever arm), as well as the neural mechanism account for a considerable amount of the inter-individual variance and longitudinal adaptability.

As defined earlier, the faster rate of tension development of type II fibres is associated with differences in Ca^{2+} release mechanism resulting a greater Ca^{2+} release per action potential (Bottinelli et al. 1996; Schiaffino & Reggiani 1996). Therefore, at the neuromuscular junction and cellular level the desired adaptation with regards to gains in RFD involve increases in action potential stimulated Ca^{2+} release. Such adaptation may be achieved through increases in the total amount of sarcoplasmic reticulum, that consequently allows for a greater diffusion of excitatory potentials, greater total number of voltage-sensitive dihydropyridine and Ca^{2+} release from ryanodine receptors (Ørtenblad et al. 2000). In other words, the changes in these

mechanism result in greater rate and magnitude of Ca^{2+} release and thus likely increases RFD (Wahr & Rall 1997). Short-term effects of this occurrence have been demonstrated by the post-activation potentiation phenomenon where an increase in the sensitivity of the acto-myosin complex to Ca^{2+} influences RFD by allowing greater force production for a given Ca^{2+} release. Type II fibres have a lower sensitivity to Ca^{2+} compared to type I fibres, thus also making them more prone to stimuli focused on the sensitivity (Grange et al. 1993). However, training induced changes and fibre type dependent differences in Ca^{2+} sensitivity likely account for only small proportion of the inter-muscular and inter-individual variance in RFD (Hvid et al. 2011; Malisoux et al. 2006). In addition, it appears that influence of training on Ca^{2+} sensitivity in type II fibres is limited (Malisoux et al. 2006).

Furthermore, the influence of fibre type composition should be combined with neural drive components, as it seems that motor unit recruitment pattern and rate coding have a more relevant impact to rapid muscle contraction in muscles that contain greater proportion of type II fibres. Maffiuletti et al. (2016) explained that as a result of increased motor unit discharge rate and lower recruitment threshold may allow earlier utilization of high-threshold motor unit that contain type II fibres, thus influencing the RFD. Recruiting motor units that innervate type II fibres is beneficial due to their greater ryanodine receptor content (200%), higher number of junctional t-tubular segments and greater total sarcoplasmic reticulum development that account for the afore mentioned greater Ca^{2+} release per action potential (Ørtenblad et al. 2000). These differences in the intrinsic capacity of fibres can result in 3–8 times faster rate of cross-bridge formation (Metzger & Moss 1990). In addition, type II fibres have 200–300% greater sodium (Na^{+}) channel density making them more capable of conducting excitatory potentials at high rate (Schiaffino & Reggiani 2011). Therefore, the cumulative influence on Ca^{2+} release (i.e. rapid force output) is greater through the high discharge rate and recruitment of type II fibres.

Mirkov et al. (2004) reported that MVC is significantly correlated with voluntary RFD at least up to 100 ms, thus implying that the major factors such as neural drive and muscle cross-sectional area that influence MVC force also influence RFD. Andersen & Aagaard (2006) reported that MVC force explained the variance in voluntary RFD over the first 10 ms (18%), 50 ms (29%), 100 ms (57%) and 200 ms (78%) into a rapid voluntary contraction, thus the

relationship seems to present a sigmoidal increase with time from the contraction onset until force plateau.

Increases in muscle pennation angle allow for a greater muscle physiological cross-sectional area in relation to given muscle volume, further resulting as greater absolute rate of force rise, especially at late phase of the force rise. However, while both the muscle cross-sectional area and the ability to activate muscle at late phase (i.e. high force level) is expected to affect RFD, they may not be associated to rapid activation at force onset in equal proportion (de Ruiter et al. 2004). Moreover, with lower pennation angles the contractile force is transmitted to the corresponding tendon more directly (Maffiuletti et al. 2016). On the other hand, higher pennation angle increase the muscle gearing ratio (e.g. contraction velocity) through increased fibre rotation and origin-to-insertion shortening velocity during voluntary contraction (Maffiuletti et al. 2016; Azizi et al. 2008). The high gearing ratio may consequently increase the rate of force rise, especially in muscles that transfer force over long tendons. Nevertheless, further research is required to fully explore the pennation angle association on RFD (Maffiuletti et al. 2016).

Similarly, fascicle length growth, that is increase in the number of sarcomeres in series, is often suggested to contribute to higher shortening velocity and RFD (Stasinaki et al. 2019). However, Edman & Josephson (2007) discussed that the requirement to first remove the elastic compliance of the muscle fibres after contraction onset accounts for approximately 40% of the variance in the early force rise up to 50% of maximal force. Therefore, longer fascicle length could theoretically also result in slower force rise due to greater extent of elastic material in series, at very initial phase of contraction. Furthermore, the extension of actin–myosin filaments, titin protein and cross-bridges (i.e. fascicle material) may also require a longer internal aponeurosis (Maffiuletti et al. 2016). While muscle architecture likely affects RFD, further research is required to accurately determine the association of factors such as fascicle length on RFD.

Furthermore, the elastic compliance and stiffness of the entire muscle–tendon complex has also drawn research attention. Wiesinger et al. (2015) reported that training induced changes in

tendon stiffness are typically small (<50%) compared to normal inter-individual variability of approximately 500%. Comparably, Kubo et al. (2000) measured changes in vastus lateralis tendon stiffness (n=6) following a period of disuse and reported that the small reductions in tendon stiffness did not correlate with the RFD decline (r=0.19). Therefore, changes in tendon properties and RFD seem to be divergent, and similar affects may be seen both following training and detraining (Maffiuletti et al. 2016). The results indicate that considerably greater changes in tendon stiffness are required to cause significant impact on RFD, since the initial force transmission velocity of tendon material is already high (DeWall et al. 2014). Maffiuletti et al. (2016) discussed that similarly to tendon stiffness, it is proposed that changes in muscular stiffness should influence RFD, in case it is theoretically agreed that tissue stiffness affects force transmission rate. Moreover, taking into account the significant mass difference of muscle tissue and tendon tissue it could be expected that stiffness of the muscle affects RFD to higher degree compared to tendon. Currently no studies have evidently isolated the muscle stiffness effects on RFD, whereas the association of the muscle-tendon complex on late-phase RFD have been demonstrated (Hannah & Folland 2015). However, a notion was made that the association appeared to be dependent on maximum force, thus relative RFD had trivial association with the stiffness of the muscle-tendon complex. In theory, it seems that the variation in muscle-tendon complex stiffness may partly influence the inter-individual and inter-muscular RFD, although the current data remains lacking and inconsistent (Maffiuletti et al. 2016).

2.2 Neuromuscular adaptations to strength training

2.2.1 Adaptations in neural determinants

The training induced increases in strength and RFD appear to be caused by neural adaptations within the corticospinal tract. The adaptations along the descending pathways can occur at the cortical (e.g. corticospinal excitability and inhibition) and/or the spinal (e.g. spinal α-motor neurons and inhibitory-, excitatory interneurons) level (Kidgell et al. 2011). Essentially, all of the desired neural adaptations influencing RFD concern enhanced efferent drive focused to the trained musculature (figure 1). The diversity of potential effects in neural adaptations following strength training of different training modality, duration of the training intervention, type of

muscle contraction and of other acute training variables such as movement velocity and training load will be discussed ahead.

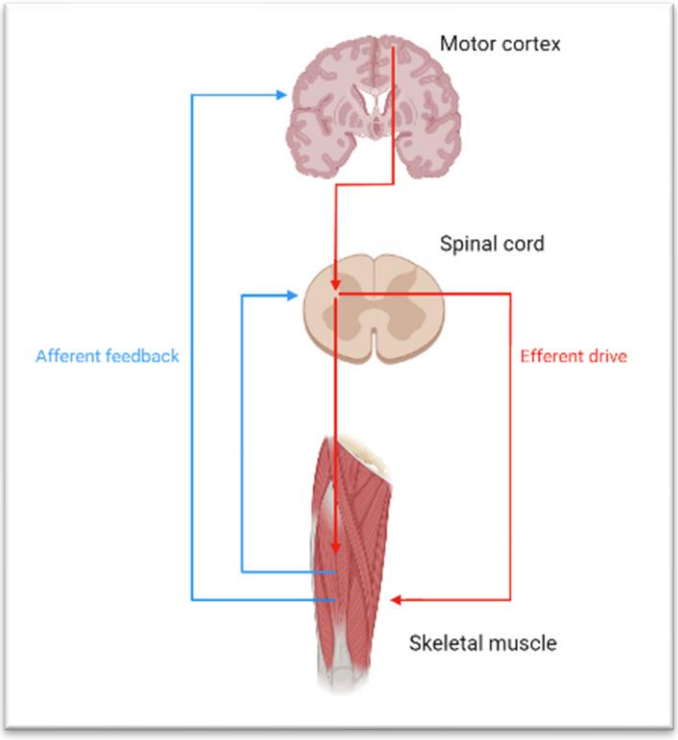

Figure 1. Schematic representation of neural segments within the corticospinal tract.

Various strength training modalities may induce variety of adaptations that improve the RFD as well as muscle activation. RFD related improvements in muscle activation may appear as increased H-reflex amplitude, EMG amplitude and rate of EMG rise over the initial >300 ms into a voluntary contraction (de Ruiter et al. 2012; Blazevich et al. 2008; Holtermann et al. 2007; Aagaard et al. (2002). The causative relationship between training induced adaptations in muscle activation and RFD can be indicated by the positive linear association found between integrated EMG and RFD (Klass et al. 2008; de Ruiter et al. 2007). Vila-Cha et al. (2010) recorded 33% improvement in knee extension RFD accompanied with 80–100% increase in EMG activity following 6 weeks of strength training. In addition, de Ruiter et al. (2012) and Blazevich et al. (2008) reported moderate to strong (r^2=0.46–0.81) positive association between RFD changes, EMG amplitude and rate of EMG rise for the quadriceps femoris, induced by 4

and 10 weeks of heavy strength training, respectively. These results indicate a strong contribution from training induced neural adaptations on RFD improvement.

Furthermore, Mason et al. (2020) reported that strength gains (15.5%) following only two weeks of strength training were accompanied by an increase in corticospinal excitability (44%) and reductions in silent period duration (14%) measured 72 hours after. In addition, the changes in corticospinal excitability and silent period duration were assessed pre and post to each training session, revealing that corticospinal input affected the force output also within training session and at early stages of training intervention. Similarly, Ruotsalainen et al. (2014) observed an initial increase in corticospinal excitability after the first set in an acute hypertrophic resistance exercise for elbow flexor muscles. However, this was followed by a gradual decline in corticospinal excitability and increased silent period measured immediately after each subsequent set. In addition, no change in M-max area was observed in peripheral nerve stimulation, thus suggesting that there was a supraspinal component for the central fatigue during the session (Ruotsalainen et al. 2014). Later, Latella et al. (2017) studied post training responses associated with heavy strength and hypertrophy training using transcranial magnetic stimulation. Corticospinal excitability and silent period were assessed at multiple time points up to 72 hours post training. The results revealed that corticospinal excitability was significantly increased only immediately post-training, but not at later time points for both heavy strength and hypertrophy training groups. In addition, silent period was significantly shorter immediately post-training and after 2 hours for both groups but remained shorter up to 24 hours after hypertrophic training only. Therefore, the results indicated that the acute neural adaptations are similar following heavy strength and hypertrophic training modalities (Latella et al. 2017).

As discussed, training induced adaptations can occur at different levels of the nervous system. First of all, cortical adaptations may account for changes in the neural plasticity during the early phase of new motor performances, such as strength training is for untrained individuals. In addition, early (≤4 weeks) changes may appear as more efficient agonist–synergist–antagonist coordination and enhanced force output, due to improved neural transmission facilitations and motor unit activation (Kidgell et al. 2011). Later (≥4 weeks) it is most likely that spinal circuitry modulation begins to contribute to improvements in RFD (Maffiuletti et al. 2016). Aagaard

(2003) suggested that improvement of spinal motor neuron excitability and/or Ia afferent synaptic transmission efficacy account for the modulation responsible of RFD gains, for one. This may be observed during maximal voluntary contraction as increases in H-reflex amplitude, that reflects the degree of pre-synaptic inhibition as one of the spinal-level modulators (Aagaard 2003). In addition, Van Cutsem et al. (1998) suggested that adaptive changes in spinal motor neuron discharge output such as very large increase of maximal motor unit discharge rate at the onset of voluntary contraction, and the ability to sustain high discharge rate over the first three interspike intervals influences RFD strongly.

In practice, both conventional strength training and explosive strength training have been found to elicit adaptations on neural circuits of both young and old individuals. Vila-Cha et al. (2010) trained subjects using dynamic lower extremity exercises at 60–85%/1RM loads and recorded 33% improvement in knee extension RFD and 80–100% increase in EMG activity after six weeks of training. Tillin & Folland (2014) divided subjects into maximal strength and explosive strength training groups and trained them using isometric knee extensor exercises for four weeks. Maximal force improvement and increase in EMG at maximal force level was greater following maximal strength training, while early phase force rise at 100 ms and increase in EMG during the first 50 ms was greater following explosive strength training. Earlier Tillin et al. (2012) trained recreationally active individuals for four weeks using only unilateral explosive isometric contractions 4 time 10 repetitions at >90%/MVC force on knee extensors. Following the brief intervention RFD for the first 50 ms after contraction onset improved by 54% and after 100 ms by 15%, while MVC force increased by 11%. Similarly, de Oliveira et al. (2013) trained recreationally active individuals for six weeks using maximal (>90%/MVC force) isometric knee extensions. Following the intervention, the very early phase (20 ms) RFD had improved by 22%, yet no improvement was apparent after RFD was normalized to MVC.

Earlier Aagaard et al. (2002) has demonstrated that performing non-explosive training with ≥75%/1RM training loads can also be effective for evoking significant improvement in contractile RFD following longer training periods. The 14-week heavy strength training intervention induced significant (17–26%) increases in RFD measured for 50, 100 ms and longer durations. Improvements were also observed in EMG amplitude and rate of EMG rise over the respective times. However, in similar 14-week strength training intervention by

Andersen et al. (2010) no changes in early phase RFD were found, and even decrement was apparent after RFD was normalized to MVC. Therefore, the observed differences in adaptations may be explained by other training variables such as the movement velocity or periodization model. Although, Behm & Sale (1993) argued that improvements in early phase RFD should include exercises that are performed with maximal effort for acceleration regardless of the actual movement velocity. In the 16-week intervention subjects performed ballistic unilateral ankle dorsiflexions against isometric and isokinetic resistance using contralateral legs. Both legs demonstrated improvements (26%) in RFD despite high movement velocity was prevented in both exercise forms. It was suggested that the fundamental stimuli for improvement in RFD is the number of ballistic contractions and the degree of voluntary effort for acceleration, while contraction type (isometric or concentric) is of less importance (Behm & Sale 1993).

To compare different training modalities Peltonen et al. (2018a) divided subjects into hypertrophic strength and maximal-power strength training groups to compare whether the adaptations in RFD force differ following a long (20 week) training period. RFD was assessed every 3.5 weeks, and similar (44% versus 48%) increases were observed during the first 7-weeks. However, after 7-weeks RFD continued to increase only with the maximal-power strength group. Similarly, Balshaw et al. (2016) compared the effects of 12-week explosive and sustained-contraction training modalities to rate of force development. The explosive contractions were characterized by the intention to contract as fast as possible while sustained-contraction was performed by gradually increasing to 75%/MVC. Improvements in early phase (≤100 ms) rate of force development was only observed after explosive training (17–34%) and were associated with increased early-phase neural drive.

Moreover, Peltonen et al. (2018b) also studied the variety in inter-individual adaptations to training and RFD performance. The subjects of the afore mentioned maximal-power strength training group were retrospectively divided into groups according to whether the subject improved in RFD only following maximal strength training, only during the power training or did not improve. High inter-individual variability in adaptations was apparent as maximal strength responders (+100%), power straining responders (+ 53%) and non-responders (+ 3%) demonstrated distinctly different RFD improvements. Inter-individual adaptation patterns may help explain the contradictory of RFD adaptations observed in previous studies. The results of

the studies indicate that neuromuscular adaptations may be specific to the training stimulus and that maximal and explosive strength adaptations may be independent.

Collectively it seems that contractions performed with maximal voluntary RFD (i.e. explosive) is the most efficient training modality for maximal RFD improvement and muscle activation at the onset of muscle contraction, regardless of the training load. It may be that conventional strength training is less sufficient to induce such large improvements in motor unit discharge rate compared to explosive-type and ballistic training, considering that discharge rate may be even 2–3 lower during slow contraction format (Van Cutsem et al. 1998). Furthermore, Van Cutsem et al. (1998) demonstrated that prolonged (12 week) period of dynamic ballistic strength training began to engender increased incidence of double discharges in some motor units, denoting a transition towards extremely high (≥200 Hz) discharge rate at the onset of muscle contraction. Cheng et al. (2013) suggested that the underlying mechanism for this successive interspike interval of ≤5 ms (i.e. double discharge), that produces distinct increases in contractile force and RFD, is due to amplified magnitude of Ca^{2+} release from the sarcoplasmic reticulum to the cell cytosol that the arrival of double action potential at the motor end plate triggers. Nevertheless, both maximal strength training and explosive strength training seem to have strong influence on RFD over different phases. Along with neural adaptations additional contribution may occur from morphological adaptation such as increase in muscle cross-sectional area, proportion of type II muscle fibre and changes in tendon properties.

2.2.2 Adaptations in muscular determinants

Variance in RFD is not only limited to neural adaptations as improvements in RFD can occur independently from changes within the nervous system, denoting that also morphological adaptation account for training induced changes in performance (Maffiuletti et al. 2016). Expected muscular adaptations influencing RFD include growth in the anatomical muscle cross-sectional area and/or volume, since maximal contractile force and muscle size are significantly related (Andersen & Aagaard 2006). In addition, architectural changes such as the pennation angle alteration, fascicle length and muscle thickness growth may add to changes in RFD.

Muscle hypertrophy is a highly common finding following heavy strength training in all populations (Aagaard et al. 2001; Häkkinen et al. 1998). While type I fibre hypertrophy contributes to improvement of RFD via MVC development type II fibres have 10–50% higher specific force (Hvid et al. 2011). Furthermore, type II muscle fibre hypertrophy likely affects RFD to greater degree compared to equal proportional change in type I muscle fibres, due to the faster rate of tension development of type II fibres (Bottinelli et al. 1996; Schiaffino & Reggiani 1996). Similarly, Häkkinen et al. (1985) reported a positive relationship (r^2=0.30) with type II:I fibre area ratio and time to 30%/MVC following 24 weeks of explosive type strength training. Respectively, Andersen et al. (2010) reported a positive correlation (r^2=0.37) between decrease in the relative proportion of type IIx fibres and decrease in relative RFD at 0–50 ms into force onset following 14 weeks of non-explosive heavy strength training. Therefore, heavy strength training that target to stimulate type II fibre hypertrophy can be expected to cause greater relative change both in MVC and RFD, compared to less selective training modalities (Maffiuletti et al. 2016). Del Vecchio et al. (2018) suggested that also the adaptations of the muscle fibre contractile properties are likely induced by the neural stimulus, since a strong relationship between absolute explosive force and neural drive are frequently reported in recent studies.

According to Franchi et al. (2014) hypertrophy occurs with different morphological adaptations following concentric versus eccentric strength training, and argued that eccentric exercises may promote the addition of sarcomere in series, while concentric preferentially result in the addition of sarcomere in parallel. Therefore, eccentric contraction could induce increase in fascicle length with smaller changes in pennation angle, whereas concentric contraction could induce greater increase in pennation angle, with less change in fascicle length. Furthermore, Stasinaki et al. (2019) compared the effects of fast eccentric and slow eccentric training and reported that significant RFD improvement (10–19%) and increase (10.0±6.2%) in fascicle were only observed in the fast eccentric group. The results suggest that fast force production component in eccentric strength training may be more appropriate for increases in rapid contractions and may be partly due to increases in fascicle length. In addition, the regional morphological adaptations may differ as eccentric contraction is expected to cause greater muscle hypertrophy in the distal portion of the muscle, while concentric contraction should induce increases in the central portion of the muscle (Franchi et al. 2014). However, inter-muscle differences are

always apparent as for instance muscle vastus lateralis typically presents a more uniform architecture throughout its extent compared to vastus intermedius (Blazevich et al. 2006). The architectural differences may differ according to the contraction type as eccentric contraction induces greater myofibrillar disruption and degree of muscle damage compared to concentric contraction (Byrne et al. 2004).

Other morphological adaptations affecting RFD may include the reduction of type IIx myosin heavy chain isoforms in response to respective upregulation of type IIa myosin heavy chain isoform following prolonged heavy strength training (Ogasawara et al. 2013; Andersen et al. 2010; Andersen & Aagaard 2000; Kraemer et al. 1995). In addition, training induced changes in the muscle-tendon complex stiffness may influence RFD. Prolonged periods of strength training have been reported to increase patella and Achilles tendon stiffness by 15–25% together with positive relationship between tendon and aponeurosis stiffness and RFD (Waugh et al. 2014; Bojsen-Moller et al. 2005). Therefore, changes in muscular properties such as hypertrophy, pennation angle alteration, fascicle length and muscle thickness growth as well as changes in muscle-tendon complex stiffness can be expected to occur following strength training. However, their inter-relations and relative contribution to improvements in RFD have not been extensively studied.

3 RESEARCH QUESTIONS AND HYPOTHESES

The purpose of this study was to investigate neural adaptations within the corticospinal tract and potential improvement in early phase RFD in response to 7-weeks of conventional strength training. In addition, the objective was to compare the potential changes separately at cortical and spinal level. Moreover, any potential associations between adaptations at either level with early phase RFD was among the interests of this study.

First research question was whether 7-weeks of conventional strength training is sufficient to elicit improvements in early phase rate of force development? First hypothesis was that 7-weeks of conventional strength training will elicit improvements in early phase rate of force development, since earlier studies (e.g. Stasinaki et al. 2019; Tillin & Folland 2014; Vila-Cha et al. 2010) have demonstrated improvements in rate of force development following 4–6 weeks of strength training interventions.

Second research question was whether 7-weeks of conventional strength training is sufficient to elicit increment in corticospinal excitability? Second hypothesis was that 7-weeks of conventional strength training will elicit increment in corticospinal excitability, since earlier studies (e.g. Mason et al. 2020; Latella et al. 2017) have demonstrated significant increments in corticospinal excitability following only 2–3 weeks of strength training interventions, while there is some contradictory to how long the increments are sustained.

Third research question was whether 7-weeks of conventional strength training is sufficient to elicit decrement in silent period? Third hypothesis was that 7-weeks of conventional strength training will elicit decrement in silent period, since earlier studies (e.g. Mason et al. 2020; Latella et al. 2017) have demonstrated significant decrements in silent period following only 2–3 weeks of strength training interventions.

Fourth research question was whether the potential corticospinal adaptations and potential improvement in early phase rate of force development are associated? Fourth hypothesis was that corticospinal adaptations and improvement in early phase rate of force development are

associated, since earlier studies (de Ruiter et al. 2012; Blazevich et al. 2008) have demonstrated moderate to strong (r^2=0.46–0.81) positive association between RFD changes and the degree of muscle activation (EMG amplitude) following 4–10 weeks of strength training. In addition, this study will intend to evaluate differences in adaptations separately at cortical and spinal level, as well as their associations to rate of force development.

4 METHODOLOGY

4.1 Overview

The experiment was conducted in the laboratory of the University of Jyväskylä, Finland. The University Ethics Committee was informed about all presented experimental methods prior to the beginning of the study. All subjects participating in the experiment received a written and verbal description about the design, methods, and objectives of the experiment. All risks and benefits were explained to subjects and a written informed consent was obtained. All the subjects participated voluntarily, and they were allowed to withdraw from the experiment at will. The experiment began with familiarization, followed by a 2-week control period, and by a 7-week strength training intervention. Neural and strength measurements were performed prior to and after each separate phase of the experiment resulting in a total of five measuring points. More detailed description about the experimental design is presented in the following chapters.

4.2 Subjects

Screening resulted in seventeen selected subjects who were healthy young adults (28±5 years), both seven female (175±10 cm, 81±21 kg, 26±5%fat) and ten male (176±11 cm, 83±22 kg, 27±7%fat). By the end of the experiment three subjects had dropout from the experiment due to personal reasons. Therefore, data collected from (n=14) subjects were used for the final analysis. To be included in the final data analysis the subject may not miss more than one training session throughout the intervention.

Eligibility criteria. To be accepted the subject must not have any strength training experience in six months prior to the experiment. Further, the subjects were screened against concerns that could potentially compromise their health and safety to participate in strenuous training with existent risk of injury, while relatively low. Similarly, the eligibility criteria were designed for safe examination of the nervous system, and to avoid potential sources of error within the sensitive methods in use. Potential participants were excluded from the experiment in case they

had a pre-existing health condition such as epilepsy, seizures, depression, any implantable metal/electronic device (e.g. cochlear implants, cardiac pacemaker), any acute or chronic illness affecting the nervous system or musculoskeletal function, a prescription for medication affecting the nervous system, and/or any other condition that may compromise their ability to participate to training and testing. As secondary criterion the subjects were screened for amount of systematic endurance training during the preceding six months, and for the use of nutritional supplements that could potentially affect the exercise responses. Seven out of the 17 subject reported arbitrary/recreational endurance training of approximately 1–3 hours per week, and no subject reported use of additional nutritional supplements aside from those that are protein or carbohydrate based. The subjects were advised to retain their habitual level of daily physical activity but to retreat from other forms of exercise during the intervention to avoid possible cross effects. After eligibility was confirmed, the subject attended to a familiarization session during which all subjects were introduced to the neural measurement procedures, potential risk and discomfort and their rights.

4.3 Testing protocol

Each singular measurement session consisted parts for both neural and strength measurements. The subjects first visited the laboratory for a single familiarization session during which they were introduced to each separate stimulations and measurements. Later subjects underwent two separate measurement sessions during each measurement week. Total of 10 measurement sessions at 4 time points were performed starting with 1st control examination two weeks prior to intervention, 2nd examination at zero weeks prior to intervention, 3rd examination 3.5 weeks into training, and 4th examination post-training (table 1). The neural measurement included electrical stimulations of the peripheral femoral nerve, electrical stimulations of the lumbar spine, and transcranial magnetic stimulations of the motor cortex. The strength measurements included maximal voluntary contraction (MVC) force test and rate of force development (RFD) measurement in isometric knee extension. See chapter 4.5 for more detailed description of the methodology.

Table 1. Chronological order of the measurements.

Familiarization 1-week	**Control period 2-weeks**	**Intervention period 7-weeks**
Measurements performed once.	Measurements performed twice 2-weeks apart.	Measurements performed after 3.5-weeks and after 7-weeks.

Familiarization session. During the familiarization session the subjects were introduced to the neural measurements (i.e. peripheral nerve, lumbar, and transcranial magnetic stimulation) as well as to strength measurements (i.e. MVC and RFD). In the familiarization session optimal electrode locations were determined, and M-max, ITT, MEP, LEP and aMT stimulations were performed. In addition, the subject performed 2–3 MVCs, 3–4 RFDs and went through a randomized trial protocol where both lumbar and transcranial stimulations were triggered under relaxed and contracted conditions. The familiarization session was a brief version of the main neural measurements, since the aim was plainly to make the subject familiar and comfortable with the somatic sensation of the stimulations, and to perform the different maximal and submaximal effort contractions according to the experimental objectives.

Control period. Subjects underwent a control period during which each subject reported to the neural measurements at four separate occasions, twice two weeks prior to beginning of the intervention (control -2) and again twice on the initial week of the intervention (control 0) before the first strength training session. All sessions were divided into two separate sessions each lasting 90-minutes. The session one, consisted of MVC, RFD and lumbar stimulation assessment, whereas session two consisted of MVC, ITT and transcranial magnetic stimulation assessment. The two sessions were performed in 48-hour interval. The purpose of the paired control sessions was to function as baseline measurements, to detect the biologically normal inter-day variation, and to reveal potential variation caused by measurement errors.

Intervention period. Following the pre-intervention measurements, the subjects were randomly allocated into two intervention groups of equal size. While both of the training groups performed identically structured strength training program, the group division was arranged to ensure adequate supervision for each individual subject, to perform training safely and according to the designed loading paradigm. In addition, the group division was a precaution

for potential restrictions due to COVID-19. During the 7-weeks intervention training consisted of two strength training sessions per week, totaling of 13 strength training sessions by the end of the 7-week period. The strength training sessions were separated by 48 hours of recovery in between sessions. The training was performed at consistent time of day and week. The subjects were not allowed perform additional training during the intervention. After 3.5 and 7 weeks of training all subjects underwent strength and neural measurements for mid and post assessment of training responses (table 2)

Table 2. Contents of the first and second measurements session during each measurement week.

	Session 1	**Session 2**
1.	Pre - Maximal M-wave	Pre - Maximal M-wave (pre)
2.	Warm-up	Warm-up
3.	Pre - Maximal voluntary contraction (MVC)	Pre - Maximal voluntary contraction (MVC)
4.	Rate of force development (RFD)	Interpolated Twitch Technique (ITT)
5.	Randomized trial - lumbar stimulation (LS)	Randomized trial - transcranial magnetic stimulation (TMS)
6.	Post - Maximal M-wave	Post - Maximal M-wave
7.	Post - Maximal voluntary contraction (MVC)	Post - Maximal voluntary contraction (MVC)

The intervention measurements were identical to control measurement. The sessions were divided into two separate 60–90-minute sessions, separated by 48–72-hour inter-session interval and performed in a consistent time of day and week. The sessions were performed 72 hours after the cessation of last strength training session. The details of each part of the neural and strength measurements are discussed in chapter 4.5.

4.4 Training protocol

During the 7-week strength training intervention conventional strength training was performed two times a week, separated by 48 hours, and resulting in a total of 13 training sessions. All sessions were monitored by research staff to ensure safe training, sufficient technique and tempo on each exercise. The training sessions consisted of traditionally used single and multi-joint exercises such as leg press, knee-extension, bench press, bicep curl, and chest-supported seated row. In addition, low volume plyometric exercises were combined with the strength training. In the beginning of each training session a five-minute cycling with self-selected tempo and dynamic mobility exercises were performed for warm up purposes. The strength training paradigm included 3 sets with 8–10 repetitions for leg press, bench press, and chest-supported seated row, while knee-extension and bicep curl were performed with 5 sets of 8–10 repetitions. A two-minute inter-set interval was completed between each exercise. The selected exercises were performed in explosive fashion as the concentric phase was performed with effort for maximal velocity followed by two second eccentric phase, with no pause at change of movement direction. For each individual subject the loading was designed based on pre-intervention 1RM (knee-extension and biceps curl) or 3–5RM (leg press, bench press, and chest-supported seated row) strength tests. Furthermore, appropriate loading was redetermined on the latter session of each week using a failure set assessment. Based on the number of repetitions in “until failure” -set for each exercise the loading was adjusted accordingly for the consecutive week.

4.5 Measurements

During all measurements the subject sat on a rigid custom-built force chair (University of Jyväskylä, Finland) that restrained joint movement and disallowed possible compliance and distension to avoid uncontrolled changes in the joint angle that may affect the collected data. The distance of the back of the seat, and the height of the ankle strap (2.0 cm above the lateral malleoli) was adjusted via goniometer so that both the hip and knee ankle were fixed to 90° angle. The subjects were secured on the chair with a belt around the waist, seat belts around the

shoulders and a strap at mid-thigh (figure 2). All adjustable seating coordinates were documented on the first session and retained on the following sessions.

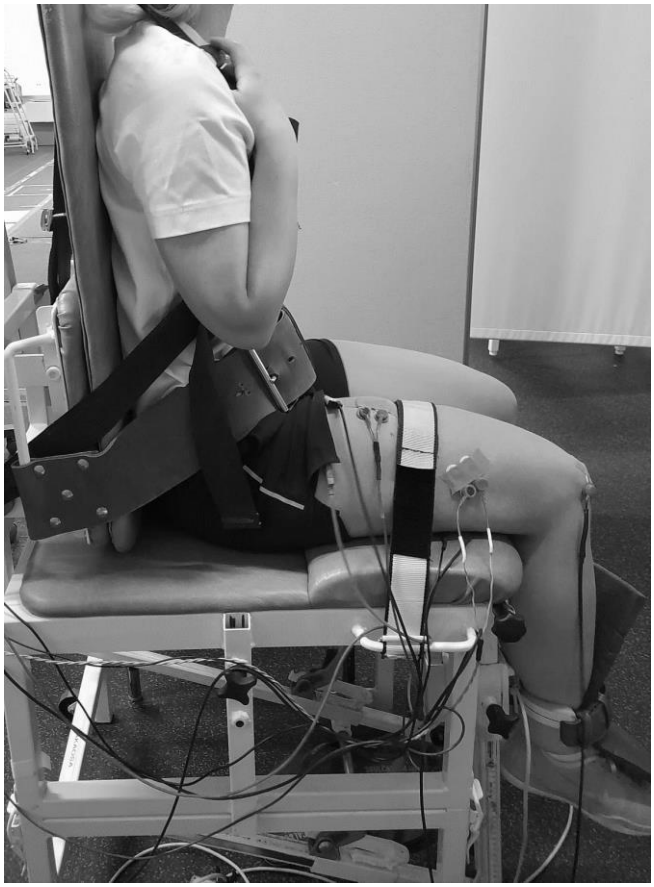

Figure 2. Positioning of the subject on custom-built force chair during all force and neural measurements.

4.5.1 Electromyography recordings

The main muscle of interest in this experiment was rectus femoris (RF) of the superficial knee extensors, while surface EMG (sEMG) recordings were also collected from vastus lateralis (VL) and bicep femoris (BF) muscles to receive signal information about optimal stimulation location and intensity during involuntary contractions, the level of coactivation, and general reference of agonist-antagonist muscle activity. All surface EMG recordings were performed using bipolar surface electrodes (Ambu® BlueSensor N 22x44 mm) with 10-mm pickup area,

20-mm interelectrode distance, and the EMG signal was interfaced with an analogue to digital converter (CED Power 1401-3, CED, Cambridge, UK). The recorded signal of each muscle was synchronized with the corresponding force signal using same analogue to digital converter and Signal 4.10 software (Cambridge Electronic Design Ltd., Milton, Cambridge, UK). All recording were performed with 3 kHz sample rate, x1000 gain, >120dB common-mode rejection ratio and 16–1000 Hz band pass filtering.

The electrode locations of the desired muscles were identified by palpating for muscle interfaces while performing isometric knee flexion and extension contractions, and by using anatomical landmarks according to SENIAM recommendations for sensor locations in hip or upper leg muscles. BF electrodes were placed to ½ distance on the line between the ischial tuberosity and the lateral epicondyle of the tibia. Similarly, RF electrodes were placed to ½ distance on the line from the anterior spina iliac superior to the superior edge of the patella, while VL electrodes were placed to ⅔ distance on the line from the trochanter major to the lateral side of the patella. Following a conventional preparation of the skin (e.g. shaving, abrading, and ethanol sterilization) an anode and cathode electrodes were placed at 20-mm inter-electrode distance over the muscle belly. The electrodes were placed parallel to the presumed orientation of the underlying fibres and the electrical conductance of the electrodes was verified to occur below 2 kΩ using a volt-ampere-ohmmeter. Finally, a single ground electrode was attached on the patella.

In the first session, after appropriate electrode location and signal was confirmed, markings were drawn around the electrodes using permanent pen, and the exact distances between the afore mentioned anatomical landmarks were documented to relocate identical electrode position in the later sessions. In addition, the subjects were given a permanent pen and advised to renew the drawings in case the color began to fade between measurements or training sessions, where the drawings were also remade each time.

4.5.2 Peripheral nerve stimulation

All collected sEMG recordings during the experimental paradigm were normalized to the maximal M-wave recorded in the beginning of each session. The maximal M-wave is a synchronous activation of muscle fibres caused by a supramaximal electrical stimulation to a peripheral nerve and is a commonly used reference value in a variety of neuromuscular research settings (e.g. Aagaard et al. 2002). Factors such as the electrode placement, preparation of the skin and thickness of the subcutaneous adipose tissue may influence the variance in sEMG amplitude, thus the normalization of voluntary sEMG amplitude to M-max improves intra- and inter-individual as well as intra- and inter-session data interpretation (Lanza et al. 2018). In this experiment the normalization was calculated in relation to M-max peak-to-peak amplitude as it is reported to be more reliable parameter than M-max area for removing the influence of electrode placement and to substantially reduce the influence of subcutaneous adiposity (Lanza et al. 2018). Similarly, at the end of the experimental paradigm the M-max threshold was redetermined, since the M-max amplitude is expected to decrease during the course of a prolonged experiment (Crone et al. 1999).

The M-max response was evoked via electrical stimulation of the peripheric femoral nerve of the right leg, while monitoring sEMG activity and torque. Appropriate electrode placement was assessed by palpating for pulse at the common femoral artery and placing the two circular surface electrodes (Polar Trode® 32mm diameter) on each side of the pulsating region in a similar direction with the inguinal ligament. This location was predicated on presumption that the femoral nerve is situated along the direction the common femoral artery. The subjects were also offered to place the electrodes independently according to instructions.

Single electrical stimuli of 1.0 ms were triggered from a computer and delivered via constant current stimulator (DS7AH, Digitimer Ltd, Welwyn Garden City, UK) under resting conditions and stationary limb position. The resting condition was controlled by supervising the EMG root mean square (EMG_{rms}) for potential preactivation over the preceding 100 ms prior to stimulus onset. The maximal M-wave was determined by gradually increasing the stimulus intensity until a plateau in the peak-to-peak amplitude of the M-wave of the rectus femoris muscle

occurred. The appropriate stimulus intensity was verified by evoking a stimulus of 150% of the alleged M-max intensity and if no further increase in the M-wave amplitude was caused the previous intensity was accepted. The applicable output stimulus intensity (mA) and M-max response (mV) was documented for the following LS and TMS experiments. See table 4 in chapter 4.5.6 for the stimulation intensities used during the experiment.

4.5.3 Rate of force development and maximal voluntary contraction

After the M-max determination the subjects performed a series of unilateral isometric knee extension contractions including warm-up, maximal voluntary contraction (MVC) and rapid contractions for rate of force development (RFD) assessment. Force signal was collected with 1 kHz sample rate and a rigid custom-built force chair (University of Jyväskylä, Finland) was used for the measurements. The force sensor that was integrated within the ankle strap was positioned perpendicular to tibial movement during the isometric knee extension. The strap around the ankle was made of nonelastic material to avoid excessive compliance. However, a 10 mm thick foam plastic pad was placed between the strap and the ankle for comfort. Therefore, in addition to the unavoidable compression of soft tissue minor compliance have occurred. Furthermore, to allow better assessment of the data the external lever arm was calculated on each subject, from the center of the force sensor to the lateral epicondyle of the femur, to convert force (N) to torque (N/m). Every subject performed the contractions using their right leg regardless of limb dominance. Only one subject reported left leg dominance.

Prior to force measurements a two-minute warm-up procedure was conducted, during which the subjects were allowed to practice contractions (e.g. no countermovement) on the force chair with immediate biofeedback provided. In addition, the subjects were advised to perform at least two contractions at subjectively estimated 50%/MVC and at 80%/MVC. The duration of the warm-up contractions was approximately 3–4 seconds and were separated by 10–20 seconds rest intervals. In addition to the practice during warm-up, prior to the first main measurement session each subject had undergone a supervised familiarization session where multiple acceptable contractions had been performed, thus increasing reliability of MVC and RFD measures already for the first pre-intervention session.

After the warm-up the subjects completed 3–4 MVC trials, separated by ≥60 s rest intervals, of the same isometric knee extension. In case the peak force of third MVC trial increased >5% from the preceding, a fourth attempt was performed. The subjects were instructed to perform the contraction "as hard as possible" without countermovement. The MVC contraction began in response to a vocal countdown "3–2–1–Push!" and continued for approximately 2–3 seconds. In addition to verbal encouragement visual biofeedback (e.g. marker of previous peak force) was provided during and between each trial. In addition, MVC was also completed at the end of each session to determine the degree of fatigue induced by the series of trials. The subjects were allowed only two trials to attain the pre-MVC value.

While MVC is relatively easy and valid method to evaluate neuromuscular capacity it has less temporal similarity than RFD with respect to many functional activities (Aagaard et al. 2002). Therefore, the main focus of this study was to examine rapid muscle activation using RFD because of the more positive correlation with many daily activities as well as sport-specific performance (Maffiuletti et al. 2010; Tillin et al. 2013a). Moreover, RFD is more sensitive than MVC to detect acute and chronic changes within the neuromuscular system (Penailillo et al. 2015; Jenkins et al. 2014; Angelozzi et al. 2012; Crameri et al. 2007).

As RFD measurements are sensitive to the given instruction the contractions used to measure RFD were separated from those used for MVC. Maffiuletti et al. (2016) suggested that the instruction should be specific to the objective of each contraction type to avoid suboptimal measures of the different parameters. Therefore, prior to each RFD trial the subjects were instructed to perform the contraction "as fast and as hard as possible" with an emphasis on the fast force production (i.e. maximal RFD). Similarly, to MVC the start of the contraction was imposed by vocal countdown "3–2–1–Push!", and visual biofeedback (e.g. force signal curve) was provided during and between each trial. This procedure was adopted for its common use, and since the current research provides no clear evidence about greater RFD values as result of self-selected start of the contraction.

During each session the subjects completed total of five rapid (i.e. RFD) contractions, separated by ≥60 s rest intervals. The RFD trials were kept short (~1 s) to avoid cumulative fatigue and

to enable performing all five contraction trials with the given rest intervals (Tillin et al. 2010; Van Cutsem et al. 1998). Criteria for acceptable trial consisted of no countermovement (monitored on a sensitive scale), and no change in EMG_{rms} activity or force baseline (>0.5 N) over preceding 100 milliseconds (Tillin et al. 2010; Blazevich et al. 2009; de Ruiter et al. 2004). Pre-tension (EMGrms) was monitored prior to the onset of contraction as they may alter the shape of the early phase force-time curve and peak RFD by influencing the initial torque-time integral (de Ruiter et al. 2006). In addition, as suggested by Folland et al. (2014) peak force of ≥80%/MVC had to be achieved on each contraction. That is due to the strong positive relationship between RFD and peak force of the same contraction (Folland et al. 2014; Van Cutsem et al. 1998). Any contraction insufficient to fulfill the criteria was rejected from the analysis. To ensure reliable and representative measures, the maximal RFD was determined by the average of two best efforts that met the criteria for acceptable trial.

4.5.4 Interpolated Twitch Technique

In the ITT assessment a paired electrical stimulus of 1.0 ms was delivered 10 ms apart to the peripheral femoral nerve of the right leg during a maximal voluntary contraction. During the measurement as the subject attained to reach maximal force output (100%/MVC) a paired electrical stimulus (i.e. interpolated twitch) was triggered at approximately 0.5–1.0 seconds into plateau at peak force to evoke a twitch like response and potentially an increment in force. In addition, another paired electrical stimulus (i.e. control twitch) was delivered 1–2 seconds after relaxation for comparison using the same stimulus intensity. Folland & Williams (2007) suggested that also recording the post-contraction control twitch seem to be more valid since the superimposed twitch at contraction are often potentiated. Therefore, later in the analysis the evoked twitch at relaxed condition is scaled in relation to interpolated twitch driven during the maximal contraction (formula 1).

To achieve reliable measures of voluntary activation and to minimize potential non-linear relationship between evoked and voluntary contraction the following points were considered during measurements (Shield & Zhou 2004; Button & Behm 2008). Similarly, to MVC and RFD tests the measurements were monitored with high resolution measurement of force and

sensitive EMG recordings to detect even small activation deficits. The investigator was provided with immediate feedback about the force signal to deliver the stimulus at appropriate timepoint, and only ±5% deviation from the previously recorded MVC value was allowed. In addition, the contraction onset was monitored for no change in EMGrms or baseline force for 100 ms prior to the contraction. The electrode positioning for ITT stimulation was the same as for all other electrical stimulations of the femoral nerve. The appropriate stimulus intensity was determined according to the intensity that generated highest torque value at relaxation collected during M-max stimulations. The stimulus was delivered with some subjective randomization, since Suter & Herzog (2001) suggested that some of the variability in ITT may be reduced with random time allocation. The ITT stimulations were performed total of four times, once during each of the respective measurement weeks as only single session seem not be adequate for a valid estimation of the degree of voluntary activation using the ITT (Button & Behm 2008). Paired stimulus was preferred over single-twitch as the variability in the ITT has been reported to decrease continuously with higher number of consecutive stimulations (Suter & Herzog 2001). The subjects were advised to try not to expect the irritating stimulation as the anticipation of the potential electrical stimulation may impair maximal performance (Button & Behm 2008; Folland & Williams 2007). Therefore, the validity of ITT results must be viewed with caution, since factors such as measurements resolution, ITT discomfort, anticipation of the stimulation may compromise the maximum force, especially among inexperienced subjects (Button & Behm 2008).

$$Voluntary\ activation = \left(\frac{1 - interpolated\ twitch\ (mV)}{control\ twitch\ (mV)}\right) \times 100$$

Formula 1. Bigland-Ritchie et al. (1983) calculation formula for the level of voluntary activation.

4.5.5 Electrical stimulation of the lumbar spine

The electrical stimulation of the lumbar spine (LS) was used to assess the corticospinal tract from the spinal level. The method allows examination of neural adaptations in isolation from

the cortical contributors, thus revealing potential segmental changes within the corticospinal tract (Škarabot et al. 2019). Therefore, when targeting the lower limb muscles LS is a useful method to examine the site of the adaptation, and to reduce the limitations associated with the use of transcranial magnetic stimulation alone.

During measurements the optimal electrode location was assessed by first palpating for the spinal process of the third lumbar vertebrae (L3), while the subject was standing. It was assumed that L3 is found at the horizontal line between the top of the right and left ilium bone, since the skin layers and subcutaneous adipose tissue around the pelvic bones elevate the palpated area to some extent. Once the spinal process of the lumbar vertebrae (L3) was identified at the supposed level the subject was asked to bend over for better palpation, and markings were drawn on skin once back at standing position. Finally, the subject was moved to a prone position, and a rectangular electrode (Polar Trode® 50x100 mm Rectangular) was placed on top the spinous process of L1. In addition, a circular electrode (Polar Trode® 32 mm diameter) was placed on top of the eighth thoracic vertebrae (T8). The inter-electrode space varied from 3.5 to 5.0 cm depending on the height of the subject (figure 3). This location was expected to produce the most sufficient (i.e. optimally concentrated, highest) electrical field around the area of T10–T12 spinal segments, that are associated with lower limb projections located inferiorly (Škarabot et al. 2019).

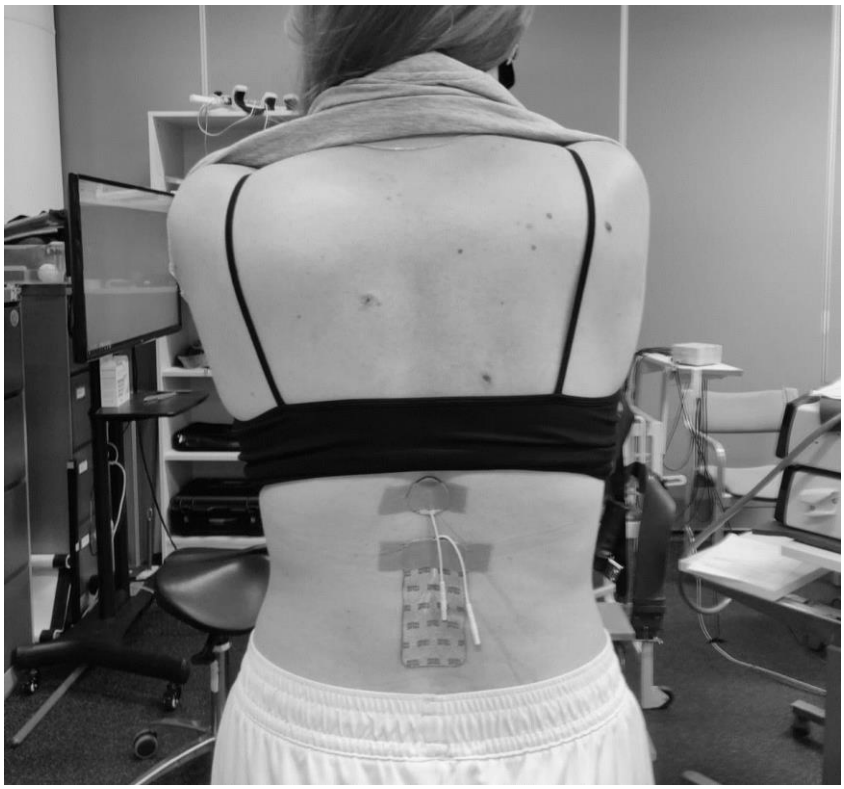

Figure 3. Electrode locations during the electrical stimulation of the lumbar spine.

Similarly, to the M-max determination a single electrical stimulus of 1.0 ms was triggered from a computer and delivered via constant current stimulator (DS7AH, Digitimer Ltd, Welwyn Garden City, UK) on the lumbar spine. First, two thresholds were set to 25 and 50% with respect to the M-max value attained at the peripheral nerve stimulation. The stimulatory intensities (mA) of 25%/M-max and 50%/M-max was later to be used in the randomized trial. The appropriate stimulatory intensities for the given thresholds were determined by gradually increasing the stimulus intensity until the desired level was attained. See table 4 in chapter 4.5.6 for the stimulation intensities used during the experiment. In relation to issues raised earlier (e.g. Hofstoetter et al. 2018; Škarabot et al. 2019; Petersen et al. 2002) a three-part validation protocol for electrode location was performed alongside the determination of appropriate stimulus intensities. The validation of the lumbar stimulation placement was confirmed at 2–3 separate occasions, both in the familiarization and the two control sessions prior to the intervention. The main concern with regards to inaccurate stimulation of the motor neuron pool was due to concurrent stimulation of the ventral and/or dorsal roots.

The three-part validation protocol began by confirming the normalization of the LEP. Meaning that the set stimulatory intensity for submaximal M-max levels must induce similar response consistently. First it was confirmed that no change in onset latency (i.e. from stimulus artifact until the start of the LEP) occurred with gradual increment in stimulation intensity. Decrease in onset latency of more than 1.0 ms in response to increase in stimulation intensity indicates targeting the ventral roots (Petersen et al. 2002). Later a given stimulation intensity had to produce 3/5 acceptable (±5%) responses at 25%/M-max. After gradual increment from 25 to 50%/M-max, again 3/5 acceptable responses had to be attained at 50%/M-max using a constant output intensity, respectively. Stimulations at both levels were given while the subject was at rest. The resting condition was controlled by monitoring the preceding 100 ms EMG_{rms} prior to stimulus onset for potential preactivation, throughout the validation protocol.

In the second part of the validation protocol a paired stimulation at 50 ms apart was applied using the stimulus intensity specified for 50%/M-max. The paired stimulation was given while the subject was at rest, and it was emphasized that the subject must not contract the muscles of the back while anticipating the stimulus. The peak-to-peak amplitude of both LEPs evoked by the stimulus were examined. It was determined that the latter M-wave must be of the same amplitude, or 10% lower at utmost. A reduction in M-wave amplitude of more than 10% indicates targeting the dorsal roots (Hofstoetter et al. 2018).

In the last part of the validation protocol motor neuron activation was examined under active conditions. A single stimulation was applied using the stimulus intensity specified for 25%/M-max under voluntary contractions of 10, 20, 50 and 60%/MVC, and once at rest. The conditions were performed in randomized order. It was expected that the output amplitude of the LEP should increase with respect to increase in the voluntary contraction intensity (Taylor et al. 2002). In case any responses demonstrated unexpected variance the electrodes were replaced slightly above the previous location.

After the same lumbar stimulation placement was validated at least in two separate occasions, the electrode locations were accepted to be used in the future sessions. Markings were drawn around the electrodes using a permanent pen, renewed each time the subject visited the

laboratory, and the subject were asked to renew the markings at home. In addition, pictures were documented, and the distance from the seventh cervical vertebrae (C7) to the superior edge of the higher circular electrode, and the inter-electrode distance was documented to reliably relocate the identical electrode position in all sessions.

In the randomized trial single electrical stimulus of 1.0 ms was delivered to the lumbar spine under total of six different conditions. The conditions were a combination of two different stimulus intensities (25 and 50%/M-max) and three different force levels (rest, 20% and 60%/MVC). During each setting the electrical stimulus was delivered 10 times resulting in a total of 60 stimulation by the end of the session (table 3). The inter-stimulus intervals for resting and 20%/MVC settings was 10 seconds, for higher force level (60%/MVC) 30 seconds, while the interval between different setting was 1 minute. The order in which the six different settings were performed was computer randomize at each session.

Table 3. Stimulus intensities, force level and number of stimulations performed during the randomized trial. Setting combination used in the present study appear bolded.

			Stimulus intensity (%/M-max)	**Force level (%/MVC)**	**Number of stimulations**
LS	**randomized order**	1.	25	0	x 10
		2.	25	20	x 10
		3.	**25**	**60**	**x 10**
		4.	50	0	x 10
		5.	50	20	x 10
		6.	**50**	**60**	**x 10**
					= 60 stimulations per session

4.5.6 Transcranial magnetic stimulation

Transcranial magnetic stimulation (TMS) allows a noninvasive measurement of potential changes occurring in the nervous system following strength training. In the technique a rapid high voltage magnetic stimulus is applied with an intention to activate axons of corticospinal neurons in the motor cortex to consequently evoke a muscle twitch (Kidgell et al. 2011). The passage of the generated electrical signal along the descending motor pathways can be recorded using sEMG electrodes in the muscle of interest. The measurable components over the passage are MEP latency, MEP amplitude, and duration of the post-MEP silent period (SP) when measured during voluntary activation of the muscle. Furthermore, these different components can provide information about occurrence of changes at cortical level (i.e. changes in corticospinal excitability and inhibition) and spinal level (i.e. changes in spinal motor neurons and inhibitory and excitatory interneurons) (Kidgell et al. 2011).

In this experiment TMS technique was performed to detect changes in total output of corticospinal tract (MEP), latency within the corticospinal tract and silent period duration. The stimulations were directed on the primary motor cortex, that is the region of cortex from which movements of skeletal muscles are regulated. Moreover, the area for the muscles of the lower extremity is typically present on the medial aspect of the hemisphere (Koeppen 2018). During measurements the optimal coil location (i.e. stimulation hotspot) was determined by first placing the large double cone coil over the primary motor cortex on the left hemisphere of the brain. After initial positioning of the coil on presupposed area the navigation for hotspot begun. All locations and respective size of motor evoked potential was quantified to determine the most optimal location for motor response of the rectus femoris muscle. Multiple TMS stimulations were delivered at various sites over the hemisphere until the largest MEP response was found (Rossini et al. 2015). After hotspot location was confirmed, markings were drawn around the coil using permanent pen, and the distances between potential landmarks were documented. The location of coil was kept consistent during the session and hotspot was redetermined in the beginning of each session.

Sufficient stimulus amplitude was determined by obtaining the motor threshold under voluntary activation (i.e. active motor threshold) of 10%/MVC using the relative frequency method. The search for active motor threshold (aMT) begun at subthreshold TMS intensity of 35% from maximal stimulator output. After initial stimulations the output intensity of the stimulation was gradually increase by 5% at a time until a positive MEP response (≥200μV peak-to-peak) was evoked. Furthermore, the stimulus intensity was shifted to 1% changes until less than 3 out of 5 acceptable (≥200μV) MEP responses appeared. The lowest intensity sufficient to produce ≥200μV peak-to-peak MEP amplitudes 3/5 trial was determined to be the active motor threshold. See table 4 for the stimulation intensities used during the experiment.

Table 4. Stimulation intensities in percent of maximal stimulator output for active motor threshold, and in milliamperes (mA) for peripheral nerve stimulation, lumbar stimulation.

	Pre	Mid	Post
Session 1 M-max (mA)	220±84	259±153	303±165
Session 2 M-max (mA)	184±84	170±114	236±153
LS 25%/M-max (mA)	253±93	227±62	255±93
LS 50%/M-max (mA)	325±104	343±110	340±94
aMT (%/max output)	35±6	34±6	32±5

In the randomized trial single magnetic stimulus of 1.0 ms was delivered (Magstim 2002 stimulator 9-cm, Magstim, Whitland, UK) to the motor cortex under total of nine different conditions. The conditions were a combination of three different stimulus intensities (120, 140 and 160%/aMT) and three different force levels (rest, 20% and 60%/MVC). During each setting the electrical stimulus was delivered 10 times resulting in a total of 90 stimulation by the end of the session. The inter-stimulus intervals for resting and 20%/MVC settings was 10 seconds, for higher force level (60%/MVC) 30 seconds, while the interval between different setting was 1 minute. The order in which the nine different settings were performed was computer randomize at each session (table 5).

Table 5. Stimulus intensities, force level and number of stimulations performed during the randomized trial. Setting combination used in the present study appear bolded.

			Stimulus intensity (%/aMT)	Force level (%/MVC)	Number of stimulations
TMS	**randomized order**	1.	120	0	x 10
		2.	120	20	x 10
		3.	**120**	**60**	**x 10**
		4.	140	0	x 10
		5.	140	20	x 10
		6.	**140**	**60**	**x 10**
		7.	160	0	x 10
		8.	160	20	x 10
		9.	**160**	**60**	**x 10**
					= 90 stimulations per session

4.6 Data analysis

4.6.1 Rate of force development and maximal voluntary contraction

MVC was determined during the measurements by choosing the best out of three attempts. In case the third attempt resulted in highest peak force a fourth attempt was given. Acceptable trial needed to meet two criteria; no countermovement prior to contraction and no change in EMG_{rms} activity or force baseline (>0.5 N) over the preceding 100 milliseconds. Highest peak force (Nm) from an acceptable trial was recorded as the MVC. For RFD, out of the various possible time frames a specific attention was set on the early phase. This was because the neural contributors were expected to be primary during the first 75 ms after the onset of a rapid voluntary contraction, while muscular properties and MVC force begin to influence increasingly from 75 ms onwards (Maffiuletti et al. 2016). However, during the early phase of

the RFD (e.g. 50 ms) the force may be only ~10% of MVC force. Therefore, variety of details in the recording apparatus and analysis were considered to ensure high quality signal, and reliable quantification of RFD for intra- and inter-individual comparison.

The RFD analysis was conducted automatically in Matlab R2021a (The MathWorks, Inc., US) using a custom-made script. The script algorithm detected the force onset at point where mean force of the following 9.0 ms was 5 N more compared to the mean force of the preceding 100 ms. After the automatic analysis each RFD contraction was manually reviewed by one of three members of the research staff. In case the automatic detection had made an apparent error the contraction onset was determined manually. The manual determination followed guidelines similar to what was proposed by Tillin et al. (2010) about systematic approach to manual determination of contraction onset. No countermovement, no change in EMG_{rms} activity or force baseline (>0.5 N) over preceding 100 milliseconds was allowed. For acceptable trials a horizontal cursor was placed along the force baseline, and the onset was robustly set following the definition of "the last trough before force deflects above the range of the baseline noise". The signals were viewed using a consistent scale of 500 ms versus 1 N. The data of the subjects (n=14) were divided for three investigators, thus recordings of one specimen were analyzed by the same investigator across all sessions. See formula 2 for the calculation of RFD value.

RFD was analyzed at three overlapping periods relative to contraction onset; 0–50 ms, 0–75 ms and 0–100 ms using average values of the two best efforts out of the five attempts. Folland et al. (2014) noted that the overlapping time frame method is unable to identify whether any transitions have occurred within the rising force–time curve, nor to isolate the potential physiological determinants responsible for possible divergences. Nevertheless, it provides a comprehensive profile of the rising force curve over the early phase of the contraction. The RFD (Nm/ms^{-1}) for each time frame was measured using the attained force value divided by the corresponding time. The peak force was quantified within three timepoints; 50 ms, 75 ms and 100 ms after the contraction onset.

$$RFD = \frac{Fpeak\ (Nm) - Fonset\ (Nm)}{t\ (ms)}$$

Formula 2. Calculation formula for the rate of force development.

The used dynamometer in the force measurements had low baseline noise amplitude, the signal was interfaced with an analogue to digital converter (CED Power 1401-3, CED, Cambridge, UK) and monitored from computer utilizing Signal 4.10 software (Cambridge Electronic Design Ltd., Milton, Cambridge, UK), thus providing enhanced signal accuracy a reliable determination of contraction onset (Tillin et al. 2013b; de Ruiter et al. 1999). After data collection the force signal was sampled at 1 kHz and EMG signal at 3 kHz, and analyzed using Spike 2 software (CED, Cambridge, UK). No smoothing or filtering of the signal was processed to maintain the baseline noise pattern and to prevent time shifts that allowed a reliable determination of the contraction onset as well as the comparison to the onset of muscle activity (Tillin et al. 2010; Konrad 2006). In addition, the low baseline provided a useful signal pattern for the manual review of the contraction onset determined by the automatic script.

4.6.2 Motor evoked potential and silent period

The motor evoked potentials (MEP) from both the transcranial magnetic stimulation of the motor cortex and electrical stimulation of the lumbar spine (LEP) were recorded and analyzed for muscle rectus femoris. The analysis was conducted automatically using a custom-made script in Matlab R2021a (The MathWorks, Inc., US). The size of single evoked potential amplitude was calculated from the difference between maximal positive and maximal negative peak value of each neural response (Groppa et al 2012). All recorded MEP and LEP responses were normalized to the determined M-max value and averaged across the 10 stimuli per each force level (0, 20 and 60%/MVC) and each stimulus intensity (25, 50%/M-Max and 120, 140, 160%/aMT). In the final analysis the MEP and LEP was expressed as peak-to-peak amplitude. The latency of the evoked potentials were manually calculated from the time of stimulation (i.e. trigger mark) to the start of the MEP or LEP response. The silent period was calculated from the time of stimulation (i.e. trigger mark) to the return of EMG activity back to baseline. All

recorded silent periods were averaged across the 10 stimuli per each force level (0, 20 and 60%/MVC) and each stimulus intensity (25, 50%/M-Max and 120, 140, 160%/aMT). However, for the resting force level (0%/MVC) the silent period was not always apparent.

4.6.3 Statistical analyses

After the automatic and potential manual analysis of the afore mentioned parameters, the results were averaged to a single value according to the subject, stimulation setting and session time point. Group level mean and standard deviation (SD) values were calculated for each respective parameter. In the statistical analysis the data was first tested for normality of distribution using the Kolmogorov-Smirnov and Shapiro-Wilk test. The repeated measures ANOVA was used to analyze the means of each parameter for significant ($p<0.05$) changes. The ANOVA compared the change in mean value across the pre-, mid-, and post-training repeated session. In case significant changes were observed the sessions were further analyzed using the Bonferroni post hoc test. Finally, the relationship within the changes in rate of force development and neural responses were analyzed using multiple regression analysis. All statistical analyses were conducted using IBM SPSS Statistics 26® (IBM Corporation, US) as well as Microsoft Excel 365® (Microsoft Corporation, US) software. Always the highest number of subjects with data from all measurement points were used for categorical analysis, thus a subject was not completely excluded from the study if data from singular parameter (e.g. 50%/M-max) was not present.

5 RESULTS

Group level average values in maximal voluntary contraction (MVC) and rate of force development (RFD) in response to 7-week strength training intervention are described in figures (4–5) below. Group level average in maximal voluntary contraction did not change significantly during the first 3.5-weeks of training nor after 7-weeks of training. Group level average in rate of force development did not change significantly in any time frame (0–50, 0–75, 0–100 ms) across the 7-week training intervention.

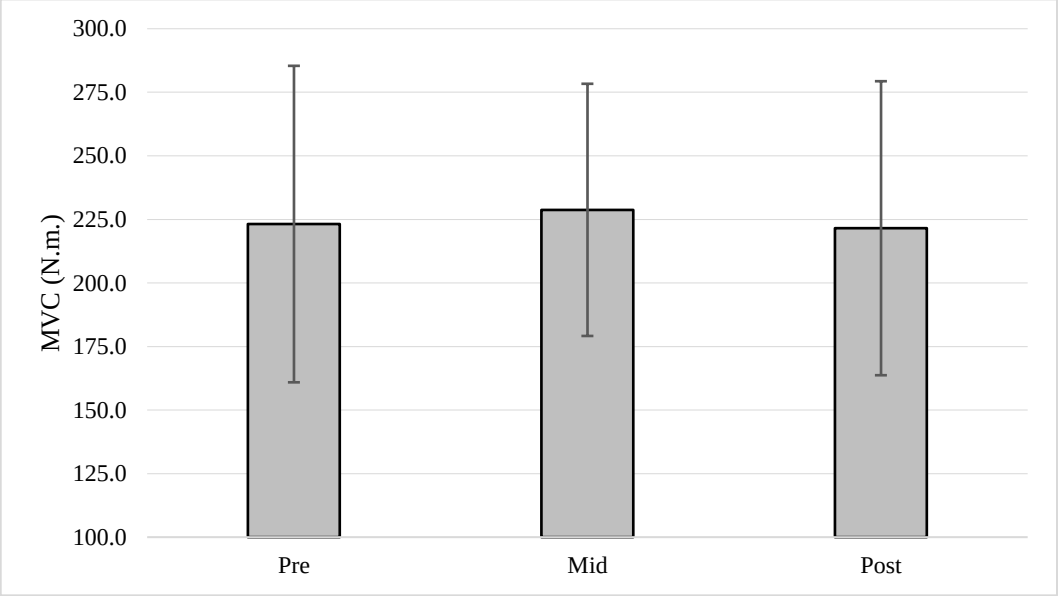

Figure 4. Maximal voluntary contraction prior to intervention (Pre), after 3.5 weeks (Mid), and after 7 weeks (Post).

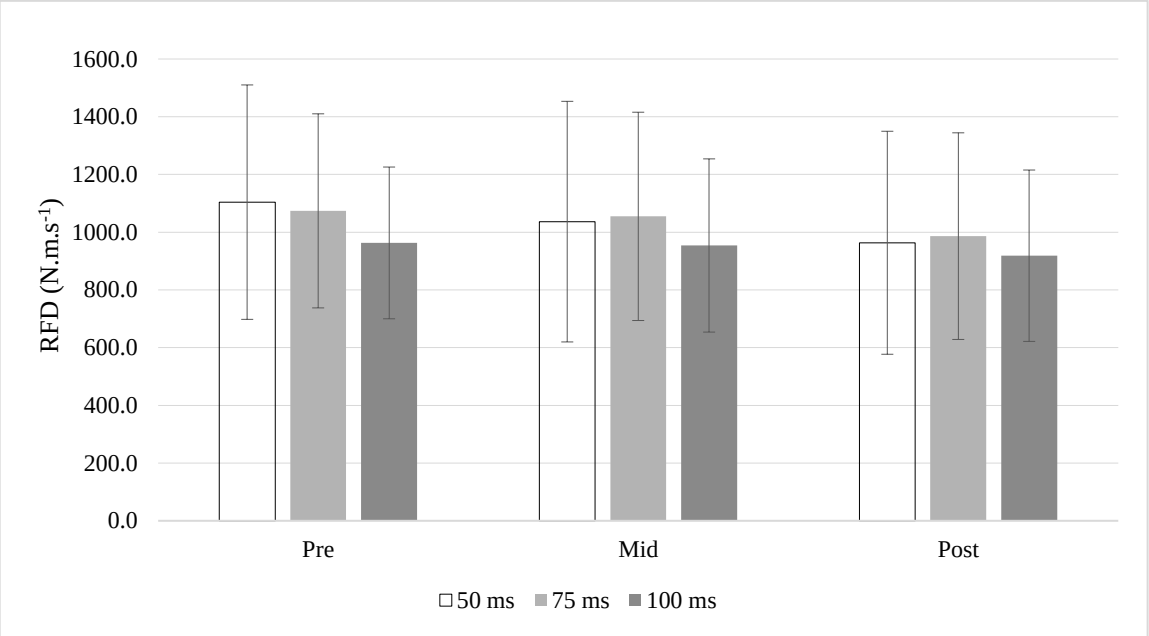

Figure 5. Rate of force development prior to intervention (Pre), after 3.5 weeks (Mid), and after 7 weeks (Post).

In addition, the measured voluntary activation during contractions at maximal force level varied between 91–100% and remained constant throughout the training intervention (97.4±2.4%) on group level. The group level percentual change and standard deviation for RFD and MVC measurements are presented in table 6.

Table 6. Group level mean and standard deviation percentual change in RFD and MVC across the 7-week training intervention.

	Δ% Pre-Mid	Δ% Pre-Post
RFD 0-50 ms	-5.3±21.0	-13.0±14.2
RFD 0-75 ms	-1.5±16.4	-8.7±14.0
RFD 0-100 ms	-1.3±14.7	-5.1±12.7
MVC	2.5±24.8	-0.7±27.0

All changes are non-significant ($p>0.05$).

Group level average values in lumbar evoked potential (LEP) and motor evoked potential (MEP) peak-to-peak amplitude in response to 7-week strength training intervention are described in figures (6–7) below. Across the 7-week intervention the group level average in lumbar evoked potential peak-to-peak amplitudes resulted in no significant changes for both stimulation intensities. The group level average maximal M-wave measured in millivolts and assessed prior to lumbar stimulations remained constant from 2.75±0.69 (Pre), to 2.35±0.87 (Mid) and 2.68±0.71 (Post).

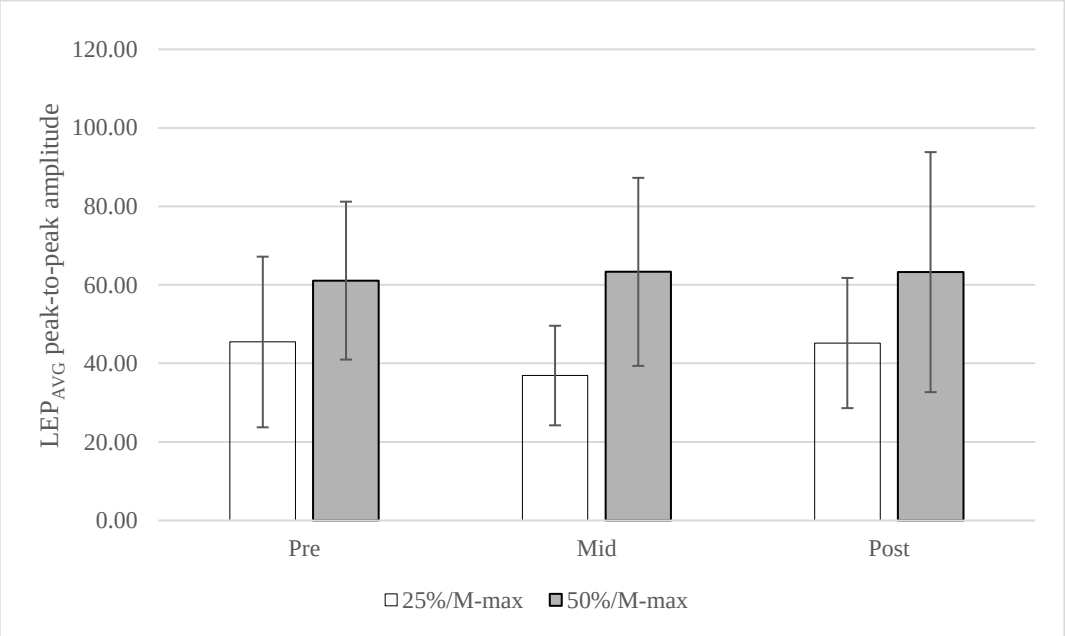

Figure 6. LEP peak-to-peak amplitude prior to intervention (Pre), after 3.5 weeks (Mid), and after 7 weeks (Post).

Similarly, across the 7-week intervention the group level average in motor evoked potential peak-to-peak amplitudes resulted in no significant changes for all stimulation intensities. The group level average maximal M-wave measured in millivolts and assessed prior to transcranial magnetic stimulations remained constant from 2.76±0.78 (Pre), to 2.54±0.74 (Mid) and 2.58±0.80 (Post).

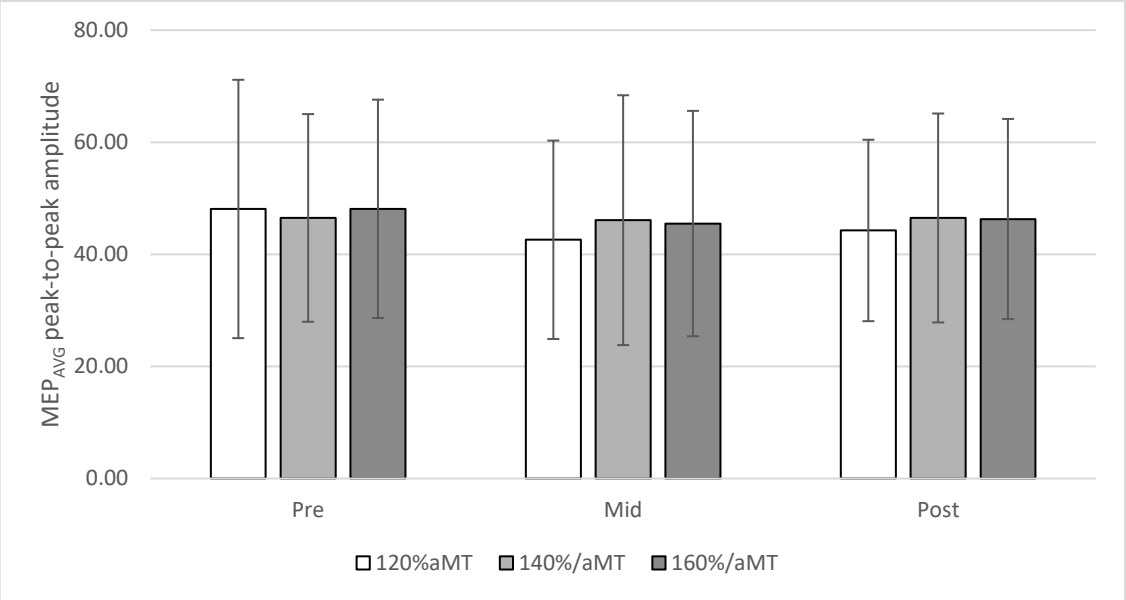

Figure 7. MEP peak-to-peak amplitude prior to intervention (Pre), after 3.5 weeks (Mid), and after 7 weeks (Post).

The group level percentual change and standard deviation for lumbar evoked potentials peak-to-peak amplitude with 25%/M-max and at 50%/M-max stimulation intensities and motor evoked potentials peak-to-peak amplitudes with 120%/aMT, 140%/aMT and 160%/aMT stimulation intensities at 60%/MVC contractions are presented in table 7.

Table 7. Mean percentual change in MEP and LEP peak-to-peak amplitude across the intervention evoked at different site and stimulus intensity.

	Δ% Pre-Mid	Δ% Pre-Post
LEP 25%/M-max	-18.8±41.1	-0.6±42.3
LEP 50%/M-max	3.7±35.4	3.5±40.6
MEP 120%/aMT	-11.4±44.8	-8.0±42.2
MEP 140%/aMT	-0.9±44.1	-0.01±40.0
MEP 160%/aMT	-5.5±42.4	-3.8±39.5

All changes are non-significant ($p>0.05$).

Group level average values in silent period (SP) duration following electrical stimulation of the lumbar spine and transcranial magnetic stimulation across the 7-week strength training intervention are described in figures (8–9) below. Across the 7-week intervention the group level average in silent period duration following lumbar stimulation resulted in no significant changes for both stimulation intensities.

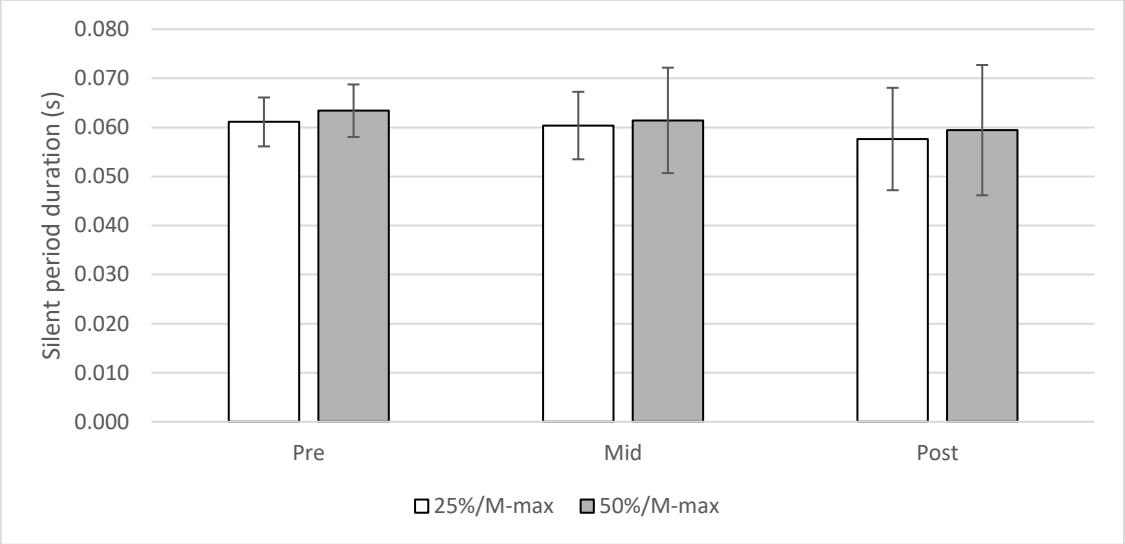

Figure 8. Silent period duration after lumbar stimulation prior to intervention (Pre), after 3.5 weeks (Mid), and after 7 weeks (Post).

Similarly, across the 7-week intervention the group level average in silent period duration following transcranial magnetic stimulation resulted in no significant changes for both stimulation intensities.

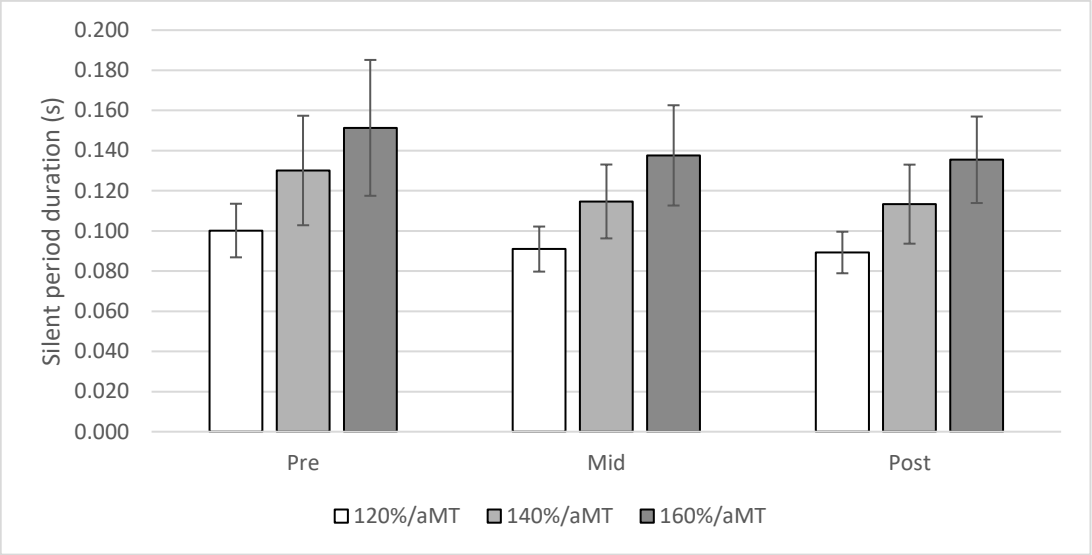

Figure 9. Silent period duration after transcranial magnetic stimulation prior to intervention (Pre), after 3.5 weeks (Mid), and after 7 weeks (Post).

The group level percentual change and standard deviation in silent period duration following electrical stimulation of the lumbar spine and transcranial magnetic stimulation are presented in table 8.

Table 8. Mean percentual change and standard deviation in silent period duration across the intervention evoked at different site and stimulus intensity.

	Δ% Pre-Mid	Δ% Pre-Post
LEP SP 25%/M-max	-1.2±9.7	-5.7±13.1
LEP SP 50%/M-max	-3.1±13.0	-6.2±15.4
MEP SP 120%/aMT	-9.2±12.8	-10.9±12.5
MEP SP 140%/aMT	-11.9±18.5	-12.9±19.1
MEP SP 160%/aMT	-9.1±20.3	-10.5±19.2

All changes are non-significant ($p>0.05$).

The intraclass correlation (ICC) and coefficient of variance (CV) values during the two control period measurements prior to the 7-week strength training intervention are presented in table 9. During the control period none of the measured parameters changed significantly.

Table 9. Intraclass correlation and coefficient of variance values during the control period measurements.

	Intraclass correlation (ICC)	Coefficient of variance (CV%)
MVC	0.947	4.2
RFD 0–50 ms	0.867	15.0
RFD 0–75 ms	0.891	11.6
RFD 0–100 ms	0.897	9.7
LEP 25%/M-max	0.799	17.5
LEP 50%/M-max	0.698	15.7
MEP 120%/aMT	0.700	15.4
MEP 140%/aMT	0.793	10.9
MEP 160%/aMT	0.657	13.6
LEP SP 25%/M-max	0.290	4.5
LEP SP 50%/M-max	0.257	6.3
MEP SP 120%/aMT	0.403	9.6
MEP SP 140%/aMT	0.742	6.8
MEP SP 160%/aMT	0.297	14.4

The multiple regression analysis across all measurement points, all stimulation intensities, all RFD time frames and all neural parameters (i.e. peak-to-peak amplitude and silent period) resulted in non-significant correlations.

6 DISCUSSION

The purpose of this study was to investigate corticospinal adaptations and their associations to early phase RFD in response to 7-weeks of conventional strength training. Moreover, the objective was to compare the potential adaptations separately at cortical and spinal level. Therefore, transcranial magnetic stimulation and electrical stimulation of the lumbar spine were used to assess the corticospinal tract both from the level of the motor cortex and the lumbar spine. Across the training intervention RFD did not behave as was expected by the hypotheses. Similarly, corticospinal excitability did not improve, but predominantly remained constant across the intervention. In addition, potential associations between changes in early phase RFD and corticospinal adaptations were among the interest of this study, yet no statistically significant correlations were found.

The following four hypotheses were addressed by this study: (1) seven weeks of conventional strength training is sufficient to improve early phase rate of force development. However, the study resulted in no group level change in early phase rate of force development. (2) seven weeks of conventional strength training is sufficient to elicit increment in corticospinal excitability and (3) seven weeks of conventional strength training is sufficient to elicit decrement in silent period. However, no group level change in corticospinal or spinal excitability nor inhibition following the 7-week strength training intervention was detected. (4) changes in corticospinal adaptations and improvement in early phase rate of force development are associated. In addition, as a novel consideration, this study aspired to address any potential differences in adaptations at cortical and spinal level as well as their associations to rate of force development. However, no significant associations were found between early phase rate of force development and corticospinal adaptations.

6.1 Changes in rate of force development

The early phase rate of force development fluctuated across the strength training intervention but demonstrated no significant changes following 7-weeks of training. Therefore, the results of all RFD variables at different time points were opposite to expectations. It was initially

hypothesized that 7-weeks of conventional strength training would be sufficient to elicit improvements in early phase rate of force development, since earlier studies have demonstrated improvements in rate of force development following similar or shorter (4–6 week) strength training interventions. Tillin et al. (2012) found improved RFD for the initial 50 ms (54%) and 100 ms (15%). Similarly, Vila-Cha et al. (2010) found improvement for the initial 50 ms (33%), and Statinaki et al. (2019) recorded improvements (10–19%) across multiple time points varying between 0–250 ms.

However, the inter-individual differences in the ability to produce rapid muscle contractions have been reported to be high. Folland et al. (2014) discussed that the highest difference appears to be during the early phase of contraction and reported that the difference in RFD over first 50 ms into rapid contraction was 13-fold (CV=48%) among untrained individuals. In addition, many earlier studies have demonstrated associations between RFD improvements and increase in MVC force (e.g. Folland et al. 2014; Tillin et al. 2012; Andersen & Aagaard 2006; Mirkov et al. 2004). While the normalization of RFD to MVC was not performed in this study it may still be speculated whether the immutability and/or decrement of MVC observed across the intervention has affected the disimprovement of RFD. Folland et al. (2014) found 2.3-fold difference in isometric knee extension MVC of untrained individuals and 7.5-fold difference in RFD relative to MVC over first 50 ms. Andersen & Aagaard (2006) demonstrated a major effect of MVC on RFD as 18–57% of the variance in RFD was explained by MVC force over the first 100 ms into contraction. Similarly, Folland et al. (2014) reported that relative RFD represented variation for 50 ms (4–30%) and 150 ms (58–88%) even after RFD was normalized to subjects maximal voluntary contraction. Furthermore, after studying the effects of electrically stimulated octet force and EMG activity Folland et al. (2014) speculated that the inter-individual variability in RFD is mainly due to differences in ability to voluntarily activate agonist muscles and secondarily due to muscles intrinsic contractile properties.

Therefore, the twitch interpolation technique (ITT) was used during the experiment to assess participants ability to perform maximal muscle activation during MVC contractions. Previous studies have revealed that even healthy individuals may fail to activate number of skeletal muscles completely despite maximal effort (Shield & Zhou 2004). In this study the level of voluntary activation resulted to be 97.4±2.4%. However, deficits in voluntary activation

revealed by ITT may have varied across different muscles of the knee extensors (Shield & Zhou 2004). In addition, stimulation discomfort, choice of recorded muscle and measurements resolution may influence the assessment of maximal performance especially among inexperienced subjects (Button & Behm 2008; Folland & Williams 2007). Nevertheless, no change in ITT response was observed across the intervention, thus any impairment of voluntary activation has likely not affected the results.

6.1.1 Reliability and validity of force measurements

With respect to the reliability of RFD measurements and validity of signal analysis many methodological issues must be discussed. Buckthorpe et al. (2012) measured 13 males over three identical RFD sessions separated by 1-week and reported moderate-to-high reliability for RFD assessment in isometric knee extension using traditional test-retest correlation analysis. The RFD was measured in time windows of 0–50, 50–100, and 100–150 ms after the onset of force. The coefficient of variation (CV) of the initial 50 ms (16.6%) was distinctly higher compared to those at 50–100 ms (6.8%) and 100–150 ms (10.5%). In addition, Tillin et al. (2011) reported CV values of similar pattern with 2.8-fold difference between 50 ms and those at 100–150 ms. In this study the CV values were similar for 50 ms (15%), 75 ms (11%) and 100 ms (10%), respectively.

Intraclass correlation (ICC) values in earlier studies have been reported to be good and more consistent with the early and later phases of rapid contractions. Buckthorpe et al. (2012) reported ICC values for 50 ms (0.80), 50–100 ms (0.90) and 100–150 ms (0.62) across the three measurements. On a group level, the RFD assessment were stable across all time periods and consistent between sessions (Buckthorpe et al. 2012). Similarly, in this study the ICC values for 50 ms (0.867) was only slightly lower compared to 75ms (0.891) and 100ms (0.897). Buckthorpe et al. 2012 concluded that early phase RFD had high intra-individual variability but became consistent from 100 ms onwards (Buckthorpe et al. 2012). However, after multiple parameters (e.g. force, relative force, impulse) were considered the RFD within time period 50–100 ms became the most reliable, likely because peak RFD often occurs within this time period. It was also reported that rapid force production and early phase RFD remained highly variable

after comparing voluntary and involuntary evoked contractions, thus indicating an inherent variability in the neural drive. Therefore, if the intention was to examine intra-individual adaptations to longitudinal intervention within the initial 50 ms, the findings should be interpreted with caution due to the substantial variability.

Furthermore, the validity of early phase RFD assessment is affected by the force onset detection method in use. In this study an absolute threshold of 5 Nm was found most reliable and used for automatic detection of force onset. Maffiuletti et al. (2016) discussed that absolute thresholds may be unsuitable for comparisons of individuals and that relative thresholds should be preferred as they are based on a robust reference. Furthermore, it has been stated that commercially available dynamometers tend to have high inherent noise (~5 Nm) in comparison to custom-built dynamometers (<0.1 Nm), thus further compromising the use of high absolute onset thresholds (de Ruiter et al. 2007; Tillin et al. 2010). However, this study did use a custom-built force chair (University of Jyväskylä, Finland). Nevertheless, earlier studies using systematic manual onset detection have demonstrated that knee extensor torques of >5 Nm are not achieved until >25 ms after contraction onset even while using a low-noise dynamometer (Haider and Folland 2014; Hannah et al. 2012). Such degree of inaccuracy could invalidate RFD measurements during the early phase (50 ms) of contraction. This may explain part of the unexpected results of the present study, since onset detection threshold of 5 Nm was used in this study. Altogether, Maffiuletti et al. (2016) concluded that due to large intra-individual variability in rapid muscle activation capacity at the contraction onset, the reliability of RFD measures is consistently lower during the early phase of the contraction compared to the late phase. Furthermore, the accuracy and precision of the determination of contraction onset may be challenging, and potential imprecision of the onset time point will account for proportionally higher variance in early phase than those of longer time frame. Therefore, while particular care and time was focused on well controlled methodological protocols, to ensure the validity and reliability of the early phase RFD quantification, the results may have been affected by measurement imprecision.

In addition, the unexpected results may be partly due to the non-specific movement type selected for the RFD assessment, as strength training was performed in conventional concentric-eccentric fashion and the testing via isometric contraction. While different

contraction types (e.g. isometric, concentric, eccentric) share similar inherent neural mechanism, it must be acknowledged that there are differences in the characteristics of the resulting force. Tillin et al. (2012) reported that concentric contraction resulted in 60% greater RFD compared to eccentric and isometric conditions over multiple time points, even if appropriate normalization approaches were adopted to enable comparison. In addition, the force produced in seated unilateral isometric knee extension involves less contribution from synergistic and antagonist muscles compared to dynamic movements, which may partially impair force production. Similarly, Bogdanis et al. (2019) discussed that RFD measures have joint angle specific characteristics and that only unilateral training seems to result improvements in unilaterally tested RFD. However, while all contractions in the experiments were performed using the right leg, only one subject reported left leg dominance, thus at least leg dominance likely had no further effect to the results. Nevertheless, the unilateral isometric RFD measurement protocol was likely not optimal for revealing potential strength adaptations following dynamic training. It is left for speculation that to what degree is the observed variability and decrement in force measures a consequence of the detection method in use and/or non-specific movement type and/or the inherent variability in strength adaptations. Nevertheless, the force measurement results of this experiment denote that the first hypothesis of this study was negative.

6.2 Changes in neural determinants

The motor evoked potential induced by transcranial magnetic stimulation predominantly remained constant across the intervention while also demonstrating some, albeit non-significant decrements at mid (8.0%) and post training (11.4%) sessions using the 120%/aMT intensity. Similarly, lumber evoked potential demonstrated some non-significant fluctuation at mid-training session as LEP decreased at 25%/M-max (18.8%), but remained constant at 50%/M-max (3.7%) stimulus intensity. At post-training measurements the LEP was constant with pre-training values. The peak-to-peak amplitudes induced by both transcranial and lumbar stimulations did not change according to initial expectations. For the silent period an observable albeit non-significant group level average decrement from spinal level (5.7–6.2% or 3–4 ms) and cortical level (10.5–12.9% or 11–17 ms) resulted following the 7-week strength training intervention.

Previous studies have demonstrated contradicting findings in part of the corticospinal excitability. Latella et al. (2011) studied the effects of unilateral leg strength training on corticospinal responses on 18 previously untrained subjects. Following 8-weeks of training corticospinal excitability measured via TMS induced MEP did not change. However, corticospinal inhibition was significantly reduced as silent period decreased after 4-weeks (17.7 ms) and 8-weeks (17.3 ms). Similarly, Kidgell & Pearce (2012) studied the effects of 4-week strength training intervention on corticospinal responses yet found no significant differences in active motor threshold or MEP amplitude. However, a reduction in silent period duration of 16–25 ms was observed together with MVC force increase of 33.8%. Similarly, Mason et al. (2020) reported following only two weeks of training that strength gains (15.5%) were accompanied by an increase in corticospinal excitability (44%) and reductions in silent period (14%).

Furthermore, Carroll et al. (2002) found reduced MEP induced via TMS following 4-weeks of strength training for the index finger abductors. While Carroll et al. (2009) found no significant changes in MEP amplitude across muscles of the wrist following 4-weeks of strength training while isometric MVC increased (8.8–10.7%). Carroll et al. (2002) speculated that strength training seemed to induce such neural adaptations that corticospinal input of a given magnitude activated fewer motor neurons during muscle contraction following the training. The potential underlying mechanism proposed for this occurrence may involve changes in the efficacy of synapses between corticospinal tract and motor neurons, changes in inter-neuronal circuits on the descending neural drive or the excitability of the motor neurons, or even by alterations to the intrinsic properties of the motor neurons (Carroll et al. 2002). These results suggest that neural plasticity associated with increase in force may be mediated by variety of adaptations, and that all of them may not be revealed by a single parameter alone. Therefore, no change in MEP amplitude does not necessarily indicate a total immutability of the descending neural trajectories. Nevertheless, the neural measurement results of this experiment denote that the second and third hypothesis of this study were negative as the strength training intervention was not sufficient to elicit increment in corticospinal excitability nor decrement in silent period duration.

6.2.1 Reliability and validity of neural measurements

With respect to the reliability of the neural measurements and validity of signal analysis some methodological issues must be discussed. The essential aim of transcranial magnetic stimulation and electrical stimulation of the lumbar spine is to direct electrical current on the conductive neural tissues. In case a current of sufficient amplitude and duration is induced it will depolarize the interneuron axons that synapse with corticospinal neurons and lead to a motor response. Moreover, Kidgell et al. (2011) explained that the TMS stimuli will initially evoke a direct excitation of corticospinal motor neurons (D-wave) with a series of subsequent indirect activation (I-wave) via cortical interneurons. At the spinal level, the combination of these descending D and I-waves generate monosynaptic excitatory postsynaptic potentials that bring alpha motor neurons to their recruitment threshold, which will result in muscle twitch. However, Kobayashi & Pascual-Leone (2003) argued that TMS may be insufficient to accomplish the depolarization of all spinal motor neurons as MEP amplitudes via TMS are often observed to be substantially smaller than compound muscle potentials evoked by peripheral nerve stimulation. Therefore, in this experiment the motor evoked potentials were recorded under high voluntary contraction of 60%/MVC because the efficacy of the corticospinal tract seems to have activity dependent changes, and motor neuron excitability is altered during voluntary contractions as more alpha motor neurons are closer to their recruitment threshold (Taylor 2006). However, it is left for speculation whether there have been individuals for which the depolarization of spinal motor neurons by TMS and LS has been impaired. In such case the resulting MEP amplitude would be inaccurate.

Moreover, there are concerns in general practice with respect to the accuracy of the determined hotspot location and the stimulation intensity in use. According to Kidgell et al. (2011) the threshold to evoke an MEP is expected to be lower under the voluntary contraction of the target muscle due to increased excitability of both cortical and spinal level neurons. Therefore, in this experiment the sufficient current amplitude was determined by obtaining the active motor threshold using the relative frequency method. The search for active motor threshold begun at subthreshold TMS intensity of 35% from maximal stimulator output and was gradually increased first by 5% and 1% until most sufficient response was observed. Typically, somewhat higher TMS output intensities are required to evoke responses on the muscles of the lower

extremities compared to those for upper extremities (Rossini et al 2015). The method was used consistently throughout the experiment and there should be no concerns with the determination of the active motor threshold. However, while resulting MEP is affected by TMS stimulus intensity it also varies according to the intensity of the voluntary contraction (Rossini et al 2015; Groppa et al 2012). The size of the MEP may be larger, and the latency may be shorter under voluntary contraction due to larger number of neurons being near the recruitment threshold or because stimulation at relaxation reflects activation of low-threshold and more slow propagating pyramidal tract neurons (Rossini et al. 2015). As mentioned earlier, in this experiment the motor evoked potentials were recorded under 60%/MVC (±5% allowed), thus the variation in force level has likely had only minor influence on MEP amplitude. In addition, Bernardi et al. (1997) reported that the motor unit of agonist quadriceps muscles are recruited in a linear fashion up to this 60%/MVC during isometric knee extension. Therefore, no difference in MEP amplitude from 120%/aMT to 160%/aMT should be expected to occur if the maximal motor unit recruitment has been attained. However, single muscles may employ different motor unit recruitment strategies and all motor units may be recruited only at higher relative intensities, therefore, resulting in some variance in MEP amplitude. Nevertheless, multiple stimulus intensities (120, 140 and 160%/aMT) were applied in this experiment, since earlier Pellegrini et al. (2018) have reported that the reliability of TMS induced MEP increases with higher stimulation intensities at least in relation to the resting motor threshold. However, the stability of the coil location (i.e. hotspot area) is a common artifact in TMS measurements and may have affected the results of this experiment to some degree.

In addition, measurements of the MEP are always affected by many factors such as the intrinsic variability in the excitability of cortical and spinal motor neurons, environmental background noise, current direction, and state of arousal of the subject (Rossini et al 2015; Groppa et al 2012). In order to control the state of arousal, the subjects were instructed with an attention task (i.e. countdown from a hundred) during relaxations, while the muscle contraction served as an attention task during the active settings. Nevertheless, the mentioned factors will still result in some trial-to-trial variance in MEP amplitude that is unrelated to those induced by training. Similarly, there is inter-individual variability in MEP responses for similar stimulus intensities, yet evaluation of MEP is reliable after being controlled for type of motor action and torque (van Hedel et al. 2007). To further reduce possible artifacts for all TMS related measurements the

subjects were not allowed to consume caffeine containing beverages, did not perform training 12 and 48–72 hours prior to measurements, respectively. Furthermore, subjects were advised to sustain regular nutritional diet and sleep rhythms throughout the experiment, yet nutritional diaries were not employed. In addition, arousal was controlled by scheduling a consistent time of the day for the measurements, and the environmental background noise was reduced by isolated laboratory room.

While transcranial magnetic stimulation was moderately reliable (120%/aMT (ICC=0.700, CV%=15.4), 140%/aMT (ICC=0.793, CV%=10.9), 160%/aMT (ICC=0.657, CV%=13.6) to evoke excitatory responses in muscles through stimulation of corticospinal neurons it depends on the excitability of both cortical and spinal motor neurons, thus being insufficient to define changes in responsiveness at either level alone (Taylor 2006). Therefore, less commonly used method of lumbar spine electrical stimulation was applied in the present study to investigate the spinal excitability and alpha motor neurons innervating the muscle rectus femoris. The main issue of the method is the positioning of the stimulatory electrodes as on the spinal level both lumbar and sacral plexuses are associated with the major nerves that innervate the muscle fibres of the thigh (Glenesk & Lopez 2021). More specifically the femoral nerve that innervates the muscles of the anterior compartment (e.g. rectus femoris) of the thigh locates inferiorly to the lumbar plexus along the trajectory of the muscle psoas major, continues posteriorly to the inguinal ligament, and finally divides into anterior and posterior divisions (Swezey & Bordoni 2021). The anterior branch of the lumbar plexus is formed by the nerve roots of lumbar vertebrae L1–L4 as well as partly from the last thoracic vertebrae T12 (figure 10). In addition, the sacral plexus is receiving some branches from spinal nerves L4–L5, yet is predominantly formed by the sacral spinal nerves S1–S4 (Glenesk & Lopez 2021).

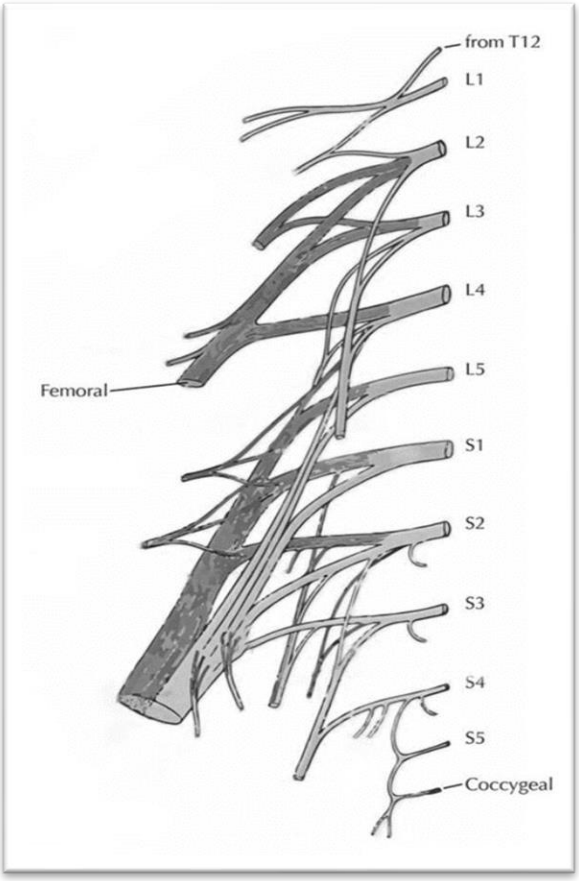

Figure 10. Schematic representation of the lumbar plexus and neural tract associations with the femoral nerve. Adapted from Gray's Anatomy illustrations.

Therefore, the electrical stimulation of the spinal cord was directed on the descending neural tracts just above L2–L4, that is the specific origin of the femoral nerve roots on lumbar plexus. In this experiment the electrodes were placed on the first lumbar vertebrae (L1) and the eight thoracic vertebrae (T8). This location was expected to produce the most sufficient electrical field around the area of T10–T12 spinal segments, that are associated with lower limb projections located inferiorly (Škarabot et al. 2019). Moreover, targeting of dorsal and ventral roots instead of the descending tracts superior to the motor neuron pool is a common issue in relation with the sensor locations. To account for this a three-part validation method was used in this experiment (described in section 4.5.5). Therefore, the sensor locations have been confirmed appropriately and the results should not have been affected by measurement errors. However, the sample size for stimulations at 50%/M-max was lower than for other stimulation

settings, since not all subjects could attain this level. This may have altered the average group level values and statistical power for the high intensity lumbar stimulations.

Finally, in relation to the reliability of silent period measurements, the duration is often measured from the onset of MEP to the return of voluntary EMG activity, however, in some cases it may be difficult to precisely define the end of the MEP (Kobayashi & Pascual-Leone 2003). Therefore, in contrast to Groppa et al. (2012) the silent period was not calculated from the onset of the MEP, but from the time of stimulation (i.e. trigger mark) to the return of EMG activity back to baseline. This was done to reduce the subjectivity of the manual analysis, since the data of the subjects (n=14) were divided for three different investigators. Furthermore, the detection of the return of EMG activity back to baseline remains more objective, since the deflection between the flat line signal during EMG activity suppression and return of EMG activity is rather clear cut. More importantly Orth & Rothwell (2004) reported that inter-hemispheric, inter-individual and inter-session variability affect to the duration of cortical silent period. The inter-individual differences and inter-session variability may be around 20–35%, while the inter-hemispheric variability is commonly of less significance. In addition, silent period duration is dependent on the TMS stimulus intensity and displays a gradual positive correlation in relation to increase in TMS stimuli intensity (Orth & Rothwell 2004). However, the SP duration is not influenced by the intensity of the voluntary muscle contraction in contrast to the motor evoked potential (Kimiskidis et al. 2005).

6.3 Associations between rate of force development and corticospinal adaptations

The results of this study were insufficient to reveal any associations between the rate of force development and adaptations either at cortical or spinal level. Relating to evidence established by earlier studies discussed in the previous chapters more apparent changes in RFD were initially expected to occur following the 7-week training intervention. Generally, as also discussed previously in the literature review, the time course of neural and muscular adaptations seems to follow a pattern where during the early phase (e.g. <8 weeks) strength training causes increases in RFD via increased motor unit discharge rates while no substantial muscle fibre hypertrophy or proportional fibre type transformation has yet occurred. Whereas prolonged

(e.g. >8 weeks) strength training seem to have lower influence to RFD, since that is when changes in motor unit discharge rate begin to decline and reduction in type IIx myosin heavy chain isoforms may begin to occur (Ogasawara et al. 2013; Andersen et al. 2010). Therefore, longer training intervention for the present study would likely not have benefited to reveal associations between rapid muscle contractions and corticospinal adaptations.

The studies discussed earlier (Mason et al 2020; Latella et al. 2011; Kidgell & Pearce 2012; Carroll et al. 2009; Carroll et al. 2002) have demonstrated that the adaptations in corticospinal inhibition via reduction in cortical silent period may in part account for increased force observed following strength training. While no improvements in RFD or MVC were observed in this study the potential mediators underlying adaptations in rapid muscle contraction should still be discussed. It seems more plausible that improvements in rate of force development following strength training, especially over short-term interventions, result from decreased neural inhibitory mechanisms, since reduced silent period duration is a more consistent finding compared to changes in motor evoked potentials. However, majority of the experiments have been conducted using sustained low to medium intensity contractions, therefore, it is not clear if improvements in rapid high intensity contractions are mediated by the same mechanisms. Del Vecchio et al. (2017) stated that the initial neural drive sent to the muscles, before any afferent feedback emerges, has the primary influence on the degree of early phase rate of force development. Therefore, indicating that the cortical inputs received by the motor neurons before force onset dictates the potential for rapid muscle contractions. Furthermore, it is likely that increased excitatory synaptic input to the motor neuron pool would bring about increased initial discharge rate and higher initial recruitment rate required for improving early phase rate of force development (Del Vecchio et al. 2017). Nevertheless, the reduction of inhibitory mechanism will allow more efficient neural drive to the motor neuron pool as less subsequent action potentials are suppressed. Consequently, there should also be higher potential for muscle activity at the neuromuscular junction and higher motor response if the innervated muscle fibres are able to receive such input. Therefore, an inverse correlation between the change silent period duration and sEMG amplitude as well as in rate of force development could be expected to occur following the strength training.

Furthermore, silent period duration typically varies between 50–300 milliseconds after TMS stimulation depending on the stimulus intensity (Kidgell et al. 2011). In this study the silent period durations varied between 90–150 ms following input delivered from the motor cortex and 58–63 ms delivered from spinal level. Certainly, silent period following TMS is of longer duration compared to LS as it is a combined consequence of both intracortical and spinal inhibition (Werhahn et al. 2007; Chen et al. 1999). The initial (50–60 ms) of silent period is often suggested to exist due to contribution from spinal inhibitory mechanisms involving changes in motor neuron excitability, afferent input, and recurrent inhibition (Fuhr et al. 1991). However, more recently Yacyshyn et al. (2016) suggested that the contribution from spinal inhibitory mechanisms to the silent period is considerably longer than reported previously and may last up to 150 ms, that was ~75% of the whole silent period duration. Furthermore, the spinal mechanisms are believed to include inhibition due to Renshaw cells, refractoriness of spinal neurons after excitation and postsynaptic inhibition due to activation of Ia inhibitory interneurons (Rossini et al. 2015; Groppa et al. 2012). Whereas the inhibition of later time frames (e.g. ≥150 ms) of the silent period has been suggested to reflect intracortical inhibition, potentially as consequence of γ-aminobutyric acid ($GABA_B$) mediated inhibitory mechanisms on motor cortex output (Ziemann 2004). Similarly, Kobayashi & Pascual-Leone (2003) stated that neuronal elements responsible for the silent period are most likely mediated by $GABA_B$ receptors. However, there are both short-lasting activity of GABAergic interneurons present at the spinal cord as well as long-lasting activity of cortical GABAergic neurons. Furthermore, it has been suggested that intracortical inhibition is likely present throughout the silent period (Škarabot et al. 2019). In addition, contribution from Ib inhibition via Golgi tendon organs and muscle spindles receptors are involved in the complex network of inhibitory signaling (Yacyshyn et al. 2016). Therefore, the relative contribution and durations resulting from cortical and spinal inhibition to silent period and the specific underlying mechanism are still a subject of debate (Škarabot et al. 2019).

Nevertheless, the group level fluctuations in silent period duration of the present study were statistically non-significant and it is left for speculation to what degree, if any, changes in inhibition have occurred in spinal or cortical level for individuals. Therefore, the inconclusive associations between the rate of force development and corticospinal adaptations denote that the fourth hypothesis of this study was negative as no correlations could be demonstrated.

6.4 Potential experimental limitations

In addition to the potential limitations of the non-optimal isometric force testing following dynamic training and the assessment protocol the nervous system, discussed above, there also potential limitations that concern the design of the intervention and the subject group. More optimal training protocol (e.g. lower body only, unilateral, isometric) could have been preferable as it can be speculated that the synaptic input resulting from the upper body strength exercises has not been sufficient reach the motor neuron pool associated with the lumbar plexus, thus decreasing the amount of stimulus directed for the specific neural projections of interest. In addition, the multiple high efforts required during the long lasting (60–90 min) measurements sessions may have caused acute fatiguing sensation at the end of the assessment of the corticospinal tract. Consequently, the accumulated neural fatigue could have induced changes spinal and cortical mechanism via afferent feedback, thus preventing the recruitment of high-threshold motor units and/or impair their discharge rate and resulting in reduced voluntary activation and strength. However, no decrement was observed in voluntary activation on group level average (97.4±2.4%), yet some individual did have impaired level of voluntary activation (91%) persistently.

Moreover, with potential suboptimal training protocol the variation within inter-individual adaptivity may have also affected the results. Earlier studies by Peltonen et al. (2018a; Peltonen et al. 2018b) have demonstrated that neuromuscular adaptations associated with maximal and explosive strength may be independent, specific to the training stimulus and have significant inter-individual variation. The results within the male (n=14) subjects revealed that high-responders improved RFD up to two-fold while some non-responders even demonstrated decrements in RFD (Peltonen et al. 2018a). This was apparent also within the data of this study as there were divergent adaptation profiles within the subject group. Furthermore, potential inter-individual differences in responsiveness between male and female subjects may complicate the group level changes even more. Latella et al. (2018) reported that between males (n=12) and females (n=10) the ratio of inhibition and excitability appeared to be similar following a single strength training session. However, males tended to have shorter silent period duration while females demonstrated increase in MEP amplitude, thus indicating that the acute mechanisms by which the net output of corticospinal excitability is modulated may be sex

specific (Latella et al. 2018). Nevertheless, potential between sex differences in neural adaptations over prolonged training interventions are unknown. More importantly, the definite inclusion criteria provided linearly distributed heterogeneity within the small subject group as there were initially seven females (175±10 cm, 81±21 kg, 26±5%fat) and ten males (176±11 cm, 83±22 kg, 27±7%fat) recruited with somewhat varying experience for strength training. Particularly for individuals with high body fat the thickness of the subcutaneous tissues may have complicated the conductance of the electrical stimulations and thus the neural assessments.

Nevertheless, the results of this experiment have most likely been compromised due to insufficient number of subjects. The initial objective was to acquire data from at least 15 subjects with even representation of both biological sexes, thus the 17 subjects were recruited to prepare for possible dropouts. While larger sample size would have provided higher statistical power, it was determined that a maximum of 15–20 subjects can be reliably examined within the intensive measurement periods, and safely processed through training in laboratory facilities under the local restrictions due to COVID-19. The number turned out to be insufficient to describe a profile for corticospinal adaptations induced by the intervention, or to reveal their associations to early phase rate of force development, both of which are characterized by high inter and intra-individual variability.

7 CONCLUSIONS

Four hypotheses were presented by this study: (1) seven weeks of conventional strength training is sufficient to improve early phase rate of force development. (2) seven weeks of conventional strength training is sufficient to elicit increment in corticospinal excitability. (3) seven weeks of conventional strength training is sufficient to elicit decrement in silent period. (4) changes in corticospinal adaptations and improvement in early phase rate of force development are associated. In addition, an effort was made to investigate any potential differences in adaptations at cortical and spinal level as well as their associations to early phase rate of force development. In contrast with the expectations the study resulted in no group level change in early phase rate of force development, no group level change in cortical or spinal excitability nor inhibition following the 7-week strength training intervention. Finally, the study resulted in inconclusive associations between changes in early phase rate of force development and corticospinal adaptations. Therefore, the present study failed to demonstrate any predominance of either spinal or cortical mediators to account for adaptations underlying improvement in rapid muscle contractions.

The results of this study may have been partially compromised by some methodological limitations discussed in the previous chapters. The main issues described included potential non-specificity of the strength training protocol and experimental assessment of force, high intra and inter-individual variability in neuromuscular performance, artifacts associated with analysis of early phase rate of force development, high sensitivity of the transcranial magnetic stimulation method, the uncertain reliability of the lumbar stimulation method, as well as low statistical power. Therefore, the methodological considerations are essential to provide more consistent evidence about neural adaptations and rapid muscle contractions in the future.

Despite no associations were found between changes in early phase rate of force development and corticospinal adaptations it should not be concluded that there are none. In contrary, even if predominant correlations were to be found between cortical or spinal adaptations with enhanced rapid muscle contractions it would not explain the causality. It is left for future experiments to determine whether there are divergent segmental adaptations within the

corticospinal tract. In addition, it should be addressed whether the adaptations differ according to training modality and if there is variation between individuals. Identifying these variants may be relevant to be identified in order to design optimal exercise for those with interests to enhance rapid neuromuscular performance. Therefore, future investigations should primarily address the topic using more homogenic groups and analogical experiments in relation to training interventions. Only later the interactions may be allocated according to different training modalities and individuals.

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