Effects of Muscle Action Type on Corticospinal Excitability and Triceps Surae Muscle-Tendon Mechanics.

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Running Head: Neuromechanical aspects of eccentric muscle action.

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Abstract

This study investigated if the specific motor control strategy reported for eccentric muscle actions is dependent on muscle mechanical behavior. Motor-evoked potentials , Hoffman reflex (H-reflex), fascicle length, pennation angle and fascicle velocity of soleus muscle were compared between isometric and two eccentric conditions. Ten volunteers performed maximal plantarflexion trials in isometric, slow eccentric (25º/s) and fast eccentric (100º/s) conditions, each on a different randomized testing session. H-reflex normalized by the preceding M-wave (H/M) was depressed in both eccentric conditions as compared to isometric ($P < 0.001$), while no differences in fascicle length and pennation angle were found among conditions. Furthermore, although the fast eccentric condition had greater fascicle velocity than slow eccentric ($P = 0.001$), there were no differences in H/M ratio. There were no differences in motor-evoked potentials size between conditions, and silent period was shorter for both eccentric conditions as compared to isometric ($P = 0.009$). Taken together, the present results corroborates with the hypothesis that the central nervous system has an unique activation strategy during eccentric muscle actions and suggests that sensory feedback does not play an important role in modulating these muscle actions.

Keywords

Motor evoked potentials, corticospinal excitability, muscle-tendon dynamics.

New & Noteworthy: The present study provided new insight into the motor control of eccentric muscles actions. It was demonstrated that task-dependent corticospinal excitability modulation does not seem to depend on sensory information processing. These findings support the hypothesis that the central nervous system has a unique activation strategy during eccentric muscle actions.

Introduction

According to the in vitro force-velocity relationship described for maximally activated muscle, peak forces generated during muscle lengthening have reached 150 –240% of maximum isometric force (Edman et al. 1978; Katz 1939;Linari et al. 2004). However, human in vivo studies yielded controversial results: some reported no differences between maximal eccentric and isometric moments (Chino et al. 2006; Duclay et al. 2011; Gruber et al. 2009), while some reported a greater eccentric moment or force (Finni et al. 2003; Hahn et al. 2012; Komi et al. 1973). Furthermore, twitch interpolation technique and electromyography (EMG) have often shown voluntary inability to fully activate the involved muscles, as demonstrated by a higher electrically evoked torque and lower EMG during maximal eccentric as compared with maximal isometric actions, respectively (Amiridis et al. 1996; Babault et al. 2001; Pinniger et al. 2000). Nevertheless, these results are also controversial since some studies have also shown no differences or even increased EMG during maximal eccentric compared to isometric actions (Hahn et al. 2010; Tilp et al. 2009).

The reduction of neural drive during maximal eccentric muscle actions may be due to spinal and/or supraspinal modulation. Several research groups have reported decreased Hoffman reflex (H-reflex; Duclay et al. 2005, 2011, 2014; Grosprêtre et al. 2014), and decreased motor evoked potentials (MEPs) using transcranial magnetic stimulation (TMS; Duclay et al. 2011, 2014). Additionally, a lower plateau and maximum slope in the input-output curve utilizing TMS during eccentric as compared with concentric muscle actions have also been reported, indicating different neural control strategies for these actions (Sekiguchi et al. 2001, 2003). Furthermore, Gruber et al. (2009) compared MEPs elicited in biceps brachii and brachioradialis by TMS and cervicomedullary motor-evoked potentials (CMEPs) obtained by electrical stimulation of the corticospinal tract. They found reduced MEPs and CMEPs in maximal eccentric compared with

isometric actions, however the decrease was greater for CMEP in both muscles, reflecting greater inhibition at spinal level. Furthermore, the MEP/CMEP ratio, which is an index of cortical excitability, was increased during eccentric actions (Gruber et al. 2009).

Unlike the direct comparison between MEP and CMEP, another approach that has been used to probe corticospinal excitability is to compare the H-reflex with MEP. H-reflex is a measure of efficacy of the synaptic transmission in the Ia reflex arc (Capaday 1997), and it is modulated not only by the excitability of spinal motoneurons (MN), but also by a variety of interneurons (Nielsen et al. 1999; Romanò and Schieppati 1987) and supraspinal centers (Heckman et al. 2008, 2009; Rudomin and Schimidt 1999). Furthermore, MEPs and H-reflexes of similar size do not necessarily reflect activation of the same population of motoneurons (Morita et al. 1999). Notwithstanding these limitations, Duclay et al. (2011) reported decreased MEPs and H-reflexes for soleus (SOL) muscle during maximal eccentric actions as compared with concentric and isometric actions, but no differences were found for medial gastrocnemius (MG). Duclay et al. (2011) reported a decreased silent period (SP) during the eccentric action for SOL suggesting decreased intracortical inhibition (Chen et al. 1999; Inghillerj et al. 1993; Roick et al. 1993). This finding corroborates with the increased cortical excitability proposed by Gruber et al. (2009).

It is generally assumed that when different muscle action types are tested in a specific joint angle, the muscle-tendon complex mechanical configuration (i.e. fascicle length and pennation angle) will be similar (Nordlund et al. 2002; Pinniger et al. 2001). Muscle-tendon mechanical configuration depends on the dynamics between the produced force and compliance of the series elastic component (SEC; Narici et al. 1996; Reeves and Narici 2003). SEC stiffness is dependent

on the applied force magnitude and velocity (Sugisaki et al. 2011; Theis et al. 2012, Tilp et al. 2012). Since the muscle's force production capability varies with velocity (Edman 1988; Hill 1938), and SEC behavior can also vary, the same joint angle may represent different mechanical configurations for different action types in different intensities and velocities. Furthermore, the angular velocity of limb movement differs from muscle velocity, as the movement velocity and the intensity of the muscle action will affect fascicle velocity (Chino et al. 2006; Finni et al. 2001; Narici 1996). Movement velocity during both passive joint movement and voluntary muscle actions have been reported to modulate H-reflex amplitude. Generally, higher velocity eccentric actions and passive muscle lengthening have lower H-reflexes than slower velocities for SOL, while diverging results have been shown for MG(Duclay et al. 2009; Grosprêtre et al. 2014; Nordlund et al. 2002; Romanò and Schieppati 1987). It remains unclear if the different velocities were capable of modifying muscle-tendon dynamics, and if the different afferent inputs would explain the larger inhibition at higher velocities. Although at higher velocities, increased Ia afferent discharge from muscle spindles is expected, increasing the excitability of the MN pool (Burke et al. 1978). Finally, changes in muscle architecture have been demonstrated to affect neural measurements utilizing EMG (Gerilovsky et al. 1989; Tucker et al. 2005).

The aim of the current study was to investigate if the specific motor control strategy reported for eccentric muscle actions is dependent of muscle mechanical behavior, and thus a reflection of differences in afferent information. We compared MEP and H-reflex modulation in SOL muscle between isometric and fast and slow eccentric conditions, while ultrasonography was utilized to access SOL and MG fascicle length (FL), pennation angle (PA) and fascicle velocity (FV). We hypothesized that all three conditions would have different fascicle velocities, although both

eccentric conditions would have equally lower corticospinal excitability compared to isometric. Furthermore, we also hypothesized that fascicle length and pennation angle would be similar among slow eccentric and isometric conditions, both having shorter FL and larger PA than fast eccentric. The first hypothesis was made under the assumption that there is a unique activation strategy for eccentric actions (Duchateau and Baudry 2014; Duchateau and Enoka 2008, 2016; Enoka 1996), while the second was based on an assumption of similar torque production among all conditions, but a higher joint passive resistance in the fast eccentric condition. While focusing on SOL muscle, we also report MG mechanical data because it is an important synergist muscle that has been shown to have a different control scheme from SOL (Duclay et al. 2009, 2011, 2014) and to have an influence on SOL mechanics (Bojsen-Moller et al. 2010; Finni et al. 2015). Neural measurements for MG were not performed as the number of maximal voluntary actions would have been too great for each testing session.

Methods

Subjects. Ten healthy male subjects (mean (SD) for age, height and weight were 23.8 yr (2.4), 1.81 m (0.05), 81.1 Kg (5), respectively) with no history of neurological injuries or diseases participated in the study. All subjects gave their written informed consent after explanation of the experiment and the risks involved. The procedures were approved by the local university ethics committee and performed according to the *Declaration of Helsinki*.

Study design. The study consisted of four testing sessions, all separated by 48 – 72 hours. The first session was a familiarization session, in which the subjects performed several trials of the different

maximal muscle action types (isometric, fast and slow eccentric), experiencing TMS, H-reflex, ultrasonography and EMG procedures. The subsequent three sessions were randomized and consisted of one isometric and two eccentric test conditions. At the beginning of each session a standard warm up, consisting of 10 muscle actions (matching the action type of the particular experimental condition) with progressively higher intensities (60-100% of maximal voluntary contraction; MVC) were performed. This procedure was important not only to prepare the subjects for the upcoming series of MVCs, but to take into account tendon conditioning with consecutive muscle actions, in an attempt to reduce tendon elongation variability in the initial MVC trials (Maganaris 2003). After warm up, subjects performed a series of MVCs matching the session muscle action type (isometric, slow or fast eccentric) in which evoked potentials, torque, ultrasound and EMG data were collected. Before every test session, subjects were asked to palpate their triceps surae muscle and perform a standing unilateral plantarflexion, tests were only carried out if subjects reported no muscle soreness.

Experimental setup. Subjects were seated with the knee joint fully extended, hip joint at 120° of extension and the ankle joint at an initial position of 90° (i.e. the sole of the foot at right angles to the tibial axis) in an ankle dynamometer (Neuromuscular Research Center, University of Jyväskylä, Finland). All measurements were performed on the right leg while the left leg rested quietly on a support. The right foot was firmly attached to a footplate mounted on the rotation platform so that the rotation axes of the ankle joint and the motor driven platform coincided. Subjects were securely stabilized by an assembly of straps that fastened both shoulders and connected to a waist belt. An additional strap with a foam support prevented the right knee joint from flexing. The torque around the rotational axis of the motor was measured by a piezoelectric

crystal transducer (Kistler Holding AG, Winterthur, Switzerland) and the ankle joint angle was monitored by a linear potentiometer. Furthermore, a small stiff metal wire attached to a spring system, located under the calcaneus, continuously monitored heel displacement from the footplate throughout the experiments. Torque, joint angle and heel displacement signals were sampled at 1 KHz utilizing a 16-bit AD converter (CED power 1401, Cambridge Electronics Design Limited, Cambridge, UK) and stored for later analysis.

Experimental Procedures. The ankle joint angle of observation in the isometric, slow eccentric and fast eccentric conditions was 80° (10° of dorsiflexion). Thus, nerve stimulation, TMS and ultrasound were always targeted and analyzed at this angle. In the isometric condition, the subject performed an isometric MVC lasting three seconds with the ankle joint at 80°. Stimulation timing for the isometric condition was 2 seconds after the initiation of the MVC, during a stable torque plateau. In the eccentric conditions the subjects were asked to perform a maximal isometric action lasting two seconds at 110° (20° of plantarflexion) ankle joint angle after which the foot plate moved to 75° at 25 °/s (slow eccentric) or 100 °/s (fast eccentric) while the subject maintained maximal effort throughout the movement. The stimulations were elicited 3.2 and 2.3 seconds after the initiation of the MVC for slow and fast eccentric actions, respectively. Maximal effort duration did not differ much between experimental conditions (3.00 s for isometric, 3.40 s for slow eccentric and 2.35 s for fast eccentric) minimizing variability in muscle-tendon mechanical behavior due to creep. Upon arrival at 75°, the subjects were instructed to relax and the footplate returned to the initial position at 20 °/s (Figure 1). Three maximal isometric, slow concentric (25°/s) and fast concentric (100°/s) dorsiflexions were performed at the end of the isometric, slow and fast eccentric conditions, respectively.

In each of the three experimental conditions the total number of trials varied from twenty to forty (mean = 32 trials). Ten trials were performed utilizing TMS, and a variable number of trials (never exceeding thirty) were used to gather H-reflex and maximal M-wave (Mmax) data. The order of TMS and nerve stimulation was randomized for every test session. Concomitantly, three trials were recorded utilizing ultrasound for each muscle (SOL and MG). All ultrasound images were immediately checked by one of the researchers, who was responsible for validating the trial (clear visualization of muscle fascicles, deep and superficial aponeurosis). Three minutes of rest were given between trials, and the test session had a mean duration of 130 minutes (range: 110-160). After a maximum of fifteen trials, the subject rested for 15 minutes to eliminate any possible fatiguing effects.

FIGURE 1– Representative recordings of EMG, joint angle, torque and evoked responses for isometric (left), slow eccentric (middle) and fast eccentric (right) conditions. From top to bottom: EMG activity for tibialis anterior and SOL muscles, joint angle displacement, torque during maximal plantarflexions, evoked responses for electrical stimulation and TMS.

Electromyography. EMG activity was recorded from SOL and tibialis anterior (TA) of the right leg using bipolar self-adhesive electrodes (Blue Sensor N, Ag/AgCl, 0.28 cm^2, Ambu, Ballerup, Denmark) and a ground electrode was placed on the head of the tibia. Additionally, a pseudomonopolar setting for SOL with a reference on the bony surface of tibia was employed. The pseudomonopolar electrode configuration was chosen to acquire SOL MEPs as it provides consistent waveforms, facilitating peak-to-peak and area analyses (Kumpulainen et al. 2012). Furthermore, although having the disadvantage of not having a common-mode rejection, the signal to noise ratio was still high, allowing easy MEP recognition and analysis.

Electrode placement and skin preparation were performed according to SENIAM (Hermens et al. 2000). Reference lines were drawn on the skin and a picture was taken to provide accurate replacement of the electrodes in the following sessions. The electrodes were adjusted on the muscle belly in accordance with the underlying fiber direction (interelectrode distance = 2 cm; interelectrode resistance < 2 kΩ). Alignment of the electrodes was checked according to the shape of the M-wave, which was ensured to be smooth during the maximal voluntary actions. EMG signals were amplified and high pass filtered (x1000, 10Hz) by a preamplifier (NL824, Digitimer Ltd., Hertfordshire, UK) then bandpass filtered (10 Hz to 1 KHz) by a differential amplifier (NL900D/NL820A Digitimer Ltd., Hertfordshire, UK). The signals were acquired on a personal computer at a rate of 5 KHz via a 16-bit AD converter (CED power 1401, Cambridge Electronics Design Limited, Cambridge, UK).

Transcranial magnetic stimulation. TMS was delivered using a single pulse, monophasic Magstim 200² stimulator with a 9-cm double batwing coil (Magstim, Whitland, UK), oriented to deliver posterior–anterior directed current to the motor cortex. The coil was optimally positioned to elicit at rest SOL MEPs with the greatest amplitudes while eliciting minimal TA MEPs (less than 50% of SOL MEP amplitude). A custom-made coil holder with a neck support and two elastic bands passing around the subject's chin were utilized to keep the coil's position constant. Additionally, marks were drawn on the subject's scalp to facilitate monitoring coil position throughout the testing session, and to enable accurate coil repositioning in the following sessions. Resting motor threshold (RMT) was defined as the lowest stimulus intensity to elicit a visible MEP with peak-to-peak amplitude of 70μV in three out of five consecutive trials (Opie and Semmler 2016). A

higher threshold than the standard bipolar practice (50µV; Rossini et al. 2015) was set because the pseudomonopolar electrode setup has a higher noise level (42.6 µV (SD 6.9). All experiments were performed with an intensity of 120% RMT (Temesi et al. 2014), corresponding to 67.1 % (SD 9.7) of maximal stimulator output.

Electrical stimulation. H-reflexes and M-waves were evoked in SOL by percutaneous electrical stimulation of the tibial nerve. A single rectangular pulse (1ms) was delivered from a constant current stimulator (DS7AH, Digitimer Ltd., Hertfordshire, UK). A circular cathode with a pickup area of 0.77 cm² (Unilect 4535M, Ag/AgCl, Unomedical Ltd., Redditch, UK) was placed over the tibial nerve on the popliteal fossa, and an oval shaped, 5.08 x 10.16 cm anode (V-trodes, Mettler Electronics corp., Anaheim, USA) was placed above the patella. The stimulation site providing the greatest amplitude of evoked responses in SOL while evoking minimal evoked responses in TA was first located by a hand-held cathode electrode which was later replaced by a self-adhesive electrode. Three to five trials utilizing supramaximal stimulation (1.5 times the maximum M-wave stimulus intensity) were performed and the mean value was considered Mmax for each experimental condition. Stimulation intensity was then decreased to elicit H-reflexes with a preceding M-wave of 20 ± 2% of Mmax, only values within this range were analyzed.

Ultrasound. A real-time ultrasound apparatus (SSD-α10, Aloka, Tokyo, Japan) was used to record continuously longitudinal images of SOL and MG during each test session. A B-mode linear array probe (scanning frequency = 7.5 MHz; field of view = 6 cm) was firmly fixed on the right leg using a foam pad and elastic tapes. The probe was coated with a water-soluble transmission gel and securely fixated to the dermal surface to ensure constant pressure. For SOL, the probe was

positioned at 50% of the distance between the popliteal crease and the lateral malleolus. Exceptionally, for one subject, the probe was positioned proximally at 30% of the same reference line, as only at this position the fascicle visualization was sufficiently clear for measurement. For MG, the probe was positioned proximally at 30% of the distance between the popliteal crease and the medial malleolus. Probe position was carefully selected so that the plane of the ultrasonogram was parallel to the muscle fascicles, avoiding fascicle length underestimation (Hodgson et al. 2006). The images were sampled at 100 Hz.

Data analysis

Digital data analysis was performed offline utilizing the Spike2 software (v4. CED, Cambridge, UK). The same software was programed to synchronize and control automatically the stimulation, dynamometer movement, ultrasound and EMG.

Torque, tendon force, heel displacement and EMG. For all experimental conditions, peak torque and mean heel displacement were calculated in a 50 ms window prior to stimulation (80°). Ten consecutive trials were selected pseudorandomly (i.e. chosen by chance using a standardized procedure) from which torque, heel displacement and EMG were averaged. SOL and TA EMG activity were quantified using root mean square (RMS) values of the EMG signal over a 50 ms window prior to the stimulation. SOL EMG was normalized by the Mmax measured in the same muscle action type. TA coactivation was normalized by TA RMS obtained in a 50 ms window during maximal dorsiflexion at the same ankle joint angle with the same velocity. Heel displacement was similar among the three experimental conditions, thus ankle rotation influenced

tissue displacement in a similar manner in all conditions. Additionally, torque and EMG were calculated in a 50 ms window before the onset of the eccentric movement (i.e. isometric pre-activation) for both eccentric conditions.

H-reflex. Peak-to-peak amplitudes for Mmax, M-wave and H-reflex were calculated between the initial deflection of the EMG from the baseline (i.e. response latency) to the second crossing of the horizontal axis (i.e. response duration). H-reflex amplitude values were normalized by the preceding M-wave of the same trial, and were expressed as H/M. Three trials were averaged.

MEP and SP. Peak-to-peak amplitudes and areas of MEPs were calculated between the initial deflection of the EMG from the baseline (i.e. MEP onset) to the second crossing of the horizontal axis (i.e. MEP offset). Peak-to-peak amplitude and area were normalized to the mean Mmax value measured in the same action type. Results for peak-to-peak amplitudes and areas were similar, and thus only peak-to-peak amplitudes are reported. The duration of the absolute silent period was assessed by visual inspection from the MEP offset to the return of EMG activity. Variables from ten TMS trials were averaged for each individual.

Fascicle Behavior. FL was defined as the distance between the insertions of the fascicle into the superficial and deep aponeurosis. PA was defined as the angle between the fascicle and deep aponeurosis. Measurement of PA was performed manually utilizing Image J (Bethesda, Maryland, USA). Moreover, FL and FV were tracked utilizing an automated fascicle tracking method based on the Lucas-Kanade optical flow algorithm with an affine optic flow extension (Cronin et al. 2011; Gillett et al. 2013) in a custom written Matlab graphical user interface (Matlab, The

MathWorks Inc. Massachusetts, USA). FV was obtained by differentiating the corresponding length change value with time (100 ms window). The mean of three measurements for each trial was utilized.

Repeatability and reliability of measurements. Since data were collected during 3 experimental sessions, it was important to verify repeatability for all variables. A pilot study (n = 4) consisting of 2 pairs of testing sessions with identical conditions for isometric and slow eccentric was performed. Intraclass correlation coefficient (ICC) was calculated using a 2-way fixed-effect model addressing random error (ICC 3.1, Weir 2005). Additionally, the coefficient of variation (CV) was calculated for each variable. CV and ICC are reported in table 1. These variables were not calculated for the automatic fascicle tracking method, as it has already been shown reliable and repeatable (Cronin et al. 2011; Gillett et al. 2013). Another important concern was to compare unfatigued maximal voluntary actions. Trials were only accepted when torque values were within a specific range from the mean of the first 6 trials. The acceptance range was determined utilizing 2 criteria simultaneously: (1) 2 standard deviations; (2) minimal difference (MI) constructed for a 99% confidence interval (CI).

MI 99% CI = standard error of the mean x 2.575 x $\sqrt{2}$,

The total number of trials for the 3 experimental conditions was 964, in which 42 (4.36%) were excluded due to low torque levels. A non-significant Pearson correlation coefficient between trial number and number of exclusions reflects their random distribution throughout the experiments and the fact that excluded trials were not associated with fatigue.

TABLE 1. Coefficient of variation (CV) for Isometric (Iso), slow eccentric (Slow Ecc) and fast eccentric (Fast Ecc) conditions and intraclass correlation coefficient (ICC) for Iso and Slow Ecc conditions (pilot study).

	CV (%)			ICC	
Variables	Iso	Slow Ecc	Fast Ecc	Iso	Slow Ecc
Torque	3.4	4.9	4.4	0.99	0.94
SOL EMG	13.6	12.5	15.1	0.89	0.85
TA EMG	12.4	13.9	13.5	0.91	0.92
HD	26.4	34.5	31.7	0.69	0.94
MEP	19.7	20.8	20.3	0.85	0.99
SP	6.9	11.2	10.9	0.95	0.99
Mmax	4.3	6.1	4.7	0.85	0.77
M-wave	8.1	6.9	6.4	0.82	0.69
H/M	9.3	23.2	25.4	0.77	0.82
PA	8.9	6.2	8.0	0.84	0.88

SOL and TA EMG = soleus and tibialis anterior electromyography; HD = heel displacement; MEP = motor evoked potential; SP = silent period; H/M = normalized H-reflex; PA = pennation angle.

Statistical analysis. All data are presented as mean (SD). Data normality was tested using the Shapiro-Wilks test. All variables except heel displacement and SOL EMG had a normal distribution. One-way repeated-measures ANOVA with a Holm-Sidak post hoc test was used to test differences between isometric, fast and slow eccentric conditions for all variables. The non-parametric analog Friedman repeated-measures ANOVA on Ranks test was used when appropriate. Two-way repeated-measures ANOVA with a Holm-Sidak post hoc was used to test differences between muscle action type and muscles for FL, FV and PA. Paired t-test was used to test differences in torque and EMG between the eccentric conditions in the pre-activation phase. Pearson correlation coefficient was calculated between neural (i.e. MEP, SP, H/M) and mechanical

(i.e. FL, FV) variables. All statistical analyses were performed using SigmaPlot v.10 (Systat Software Inc., San Jose, USA). Significance level was set at $P < 0.05$.

Results

Torque and EMG. Peak torque differed between experimental conditions ($F_{(2,10)} = 4.0$, $P = 0.037$). Post hoc tests identified that slow eccentric had higher torque than fast eccentric ($P = 0.015$). Regarding EMG, there were no differences in SOL activity ($P = 0.192$) or TA coactivation ($P = 0.160$) between experimental conditions. Table 2 presents torque, EMG and heel displacement measures for all experimental conditions. Pre-activation torque before the eccentric muscle actions was similar between fast and slow eccentric condition ($P = 0.487$). There were no differences in SOL EMG ($P = 0.934$) and TA EMG ($P = 0.846$) during the pre-activation phase.

TABLE 2. Effect of muscle action type on mechanical and neural variables.

Variables	Isometric	Slow Eccentric	Fast Eccentric
Torque (Nm)	224.4 (36.1)	228.9 (38.3)*	198.2 (34.7)
HD (mm)	4.4 (4.4)	3.1 (1.9)	3.6 (2.4)
SOL EMG (rms/Mmax)	0.029 (0.013)	0.023 (0.005)	0.024 (0.005)
TA (coactivation %)	10.3 (3.42)	11.9 (4.83)	14.1 (4.42)

Data are mean (SD). HD = heel displacement; SOL = soleus; TA = tibialis anterior; RMS = root mean square; Mmax = maximal M-wave. *Significant at $P < 0.05$: Slow Eccentric vs. Fast Eccentric.

Evoked potentials. Analysis of repeated measures for normalized MEP amplitude revealed no differences between experimental conditions ($P = 0.750$). Silent period was different among experimental conditions ($F_{(2, 9)} = 6.3$, $P = 0.009$); isometric had higher values than both eccentric conditions ($P < 0.01$; Figure 2a). Mmax ($P = 0.950$) and M-wave ($P = 0.981$) had similar amplitude values among the three experimental conditions. H/M was different among experimental

conditions ($F_{(2, 10)} = 12.6$, $P < 0.001$); isometric had higher values than both eccentric conditions ($P < 0.001$; Figure 2b).

FIGURE 2 – Effect of action type on evoked potentials. Figure 2a – Normalized MEP amplitude and silent period. MEP = motor evoked potential; SP = silent period. * Significant at $P < 0.01$: Isometric vs. Fast and Slow Eccentric. Figure 2b – Absolute M-wave and Mmax amplitude, and normalized H-reflex amplitude. # Significant at $P < 0.001$: Isometric vs. Fast and Slow Eccentric. Data presented as mean ± 95% CI.

Muscle fascicle behavior. There were no differences in SOL FL between conditions ($P = 0.722$), while MG FL differed ($F_{(2, 10)} = 4.4$, $P = 0.030$), being longer in fast eccentric as compared to isometric ($P = 0.01$). There was no significant interaction between conditions and muscles ($P = 0.426$). FV in SOL was different among the experimental conditions ($F_{(2, 10)} = 40.0$, $P < 0.001$); fast eccentric had higher values as compared with the other two conditions ($P < 0.001$). In MG, all experimental conditions had different FV values ($F_{(2, 10)} = 51.6$, $P < 0.001$); fast eccentric having the highest values and isometric the lowest ($P < 0.05$). There was an interaction between experimental conditions and muscles for FV ($F_{(2, 7)} = 6.1$, $P = 0.015$). FV values were similar in both muscles for the isometric condition, while MG had higher FV in both eccentric conditions as compared to SOL ($P < 0.05$). There were no differences in PA between the experimental conditions for SOL and MG ($P = 0.293$). In all conditions MG had smaller PA than SOL ($F_{(1, 9)} = 22.3$, $P < 0.001$). There was no interaction between condition and muscle ($P = 0.768$). Results for FL, FV and PA are presented in table 3. Figure 3 depicts FL behavior in a 900 ms window before stimulation for the three experimental conditions.

FIGURE 3 – Fascicle length values for SOL (left) and MG (right) acquired 900 ms before electrical or magnetic stimulation which occurred at time 0 s (arrow). Data points are presented as mean ± 95% CI of 100 ms window.

TABLE 3. Effect of action type on FL, FV and PA for SOL and MG, measured at 80° ankle joint angle.

	Isometric SOL/MG	Slow Eccentric SOL/MG	Fast Eccentric SOL/MG
FL (mm)	42 (8)/45 (8)*	43 (9)/52 (6)	44 (9)/54 (6)
FV (mm/s)	-0.1 (1)/0.1 (0.3)†	8.3 (3.1)/14.7 (4.9)†#	39(16)‡/56(17.1)†#
PA (°)	31.2 (5.3)/23.9 (6.9)#	32.0 (4.9)/24.4 (4.6)#	32.7 (4.2)/26.6 (6.2)#

Data are mean (SD). FL = fascicle length; FV = fascicle velocity; PA = pennation angle; SOL = soleus muscle; MG = medial gastrocnemius muscle. Negative values for FV = fascicle shortening. * Significant at $P < 0.05$: Isometric vs. Fast Eccentric. ‡ Significant at $P < 0.05$: Fast Eccentric vs. Isometric and Slow Eccentric. † Significant at $P < 0.05$: All conditions were statistically different. # Significant at $P < 0.05$: MG vs. SOL.

Correlations. FL had no significant correlation with H/M ($P > 0.6$), MEP ($P > 0.6$), and SP ($P > 0.416$) in all conditions . The only exception was a significant correlation between FL and SP for the isometric condition ($P = 0.045$, $r = 0.717$). Pooled data from all three experimental conditions yielded significant correlations between FV and H/M ($P = 0.004$, $r = -0.56$) and FV and SP ($P = 0.028$, $r = -0.43$). Changes in FL between isometric and both eccentric conditions (i.e. delta FL) were not correlated to changes in H/M between isometric and both eccentric conditions (i.e. delta H/M) ($P = 0.126$, $r = -0.43$; Figure 4).

FIGURE 4 – Correlation between changes in fascicle length and H/M. FL delta was computed as isometric FL – eccentric FL, positive values = muscle shorter in the eccentric condition. Delta H/M was computed as isometric H/M – eccentric H/M, positive values = lower H/M in the eccentric condition. Eccentric data from both slow and fast conditions were pooled together (2 data points for each subject, $n = 7$).

Discussion

The present study provided new data regarding the motor control of SOL eccentric muscle actions. We probed corticospinal excitability during maximal isometric and eccentric muscle actions while

monitoring muscle-tendon dynamics. The main finding was that SOL H/M was depressed during both fast and slow eccentric conditions as compared to isometric, while no differences in fascicle length and pennation angle were found among experimental conditions. Furthermore, although the fast eccentric condition had greater fascicle velocity than slow eccentric, there were no differences in H/M ratio. There were no differences in MEP size among experimental conditions, but SP was shorter for both slow and fast eccentric as compared to isometric condition. There was no significant correlation between the changes in FL and H/M between isometric and eccentric conditions.

Torque and EMG. In a classical in situ experiment on cat SOL muscle the eccentric muscle force has been shown to be virtually independent of velocity above a certain initial velocity (Joyce et al. 1969). Also, previous human studies have reported triceps surae muscle maximal torques to be independent of eccentric velocity (Chino et al. 2006; Pinninger et al. 2000). Surprisingly, our study reports lower torque in fast compared to slow eccentric, which cannot be explained by pre-activation torque, TA coactivation and SOL EMG during or preceding (i.e. isometric pre-activation) the eccentric phases as these variables were similar in both conditions. By performing the pre-activation away from the force-length plateau (~83% of the maximal isometric torque at 80°), the time available to increase torque in the fast eccentric action was short (300 ms) compared to slow eccentric (1200 ms), possibly explaining the differences between conditions. It is important to ascertain that the subjects were able to perform maximal voluntary muscle actions in all three conditions, we propose that this was the case based on the following: 1) the familiarization session lasted 2 hours, and the subjects performed a mean of 15 MVCs for each condition; 2) the test-retest ICC for torque in the pilot measures was 0.94-0.99 (table 1); 3) during

each testing protocol, the subjects performed a mean of 36 MVCs, with stable torque values throughout, yielding very small CV (4.4%, Table 1). SOL EMG analysis had a low power (0.2) due to the large inter-subject variability (CV = 20 - 40%). Although not statistically different, SOL EMG during slow and fast eccentric conditions was 21 and 17% lower than isometric (ES = 0.61/0.51) respectively, suggesting neural inhibition and possibly explaining the lack of force potentiation during the eccentric conditions as compared to isometric. Force potentiation during eccentric actions has been reported in other studies (Grospretre et al. 2014; Hahn et al. 2012).

Corticospinal excitability and fascicle behavior. In the present study, both eccentric conditions had reduced H/M as compared with isometric, and although there was a tendency for lower values of H/M in fast eccentric (ES = 0, 43), it was not significantly different than slow eccentric. Reduced H-reflex during eccentric compared with isometric and concentric muscle actions have been consistently reported (Abbruzzese et al. 1994; Duclay et al. 2005, 2009, 2011; Grosprêtre et al. 2014; Romanò and Schieppati 1987). Duclay et al. (2009, 2011) reported the only exception for MG muscle, in which no differences in H-reflex were found between concentric, eccentric and isometric muscle actions. Regarding muscle action velocity, higher eccentric velocities (studied velocity range: 12°/s - 60°/s) have been reported to have lower H-reflex than slower velocities (Duclay et al. 2009; Romanò and Schieppati 1987).

The novel finding in this study is that SOL H/M was depressed during eccentric as compared with isometric muscle action, although muscle-tendon configuration (i.e. FL and PA) was the same. Additionally, the higher FV in fast eccentric condition which should have increased motoneuron excitability by increased Ia afferent discharge from muscle spindles did not occur, oppositely, fast

eccentric had a trend towards lower H/M. Although FV and H/M were significantly correlated (R^2 = 31%), the lack of significant correlation between the changes in FL and H/M (figure 4) suggests that afferent information coming from muscle spindles cannot be responsible for modulating the corticospinal excitability during eccentric muscle actions. Interestingly, the only participant engaged in regular track and field athletic training had a shorter FL at the test angle during the eccentric conditions (29,4% and 31,4% for slow and fast eccentric; Figure 4 upper-right corner), even though FV was positive indicating fiber lengthening in the last 100 milliseconds before the test angle. A high inter-subject variability in FL (CV = 19-21%) rendered the comparison between conditions a low power ($\beta = 0.05$); nevertheless, isometric FL was only 2.4% (ES = 0.11) and 4.8% (ES = 0.23) shorter than slow and fast eccentric conditions respectively. Thus, it seems reasonable to consider FL to be similar between experimental conditions. Furthermore, it is noteworthy that no differences in FV were found between slow eccentric and isometric protocols due to the large inter-subject variability ($\beta = 0.7$). Corroborating with Chino et al. (2006), our study showed that the effect of muscle action type and joint velocity on muscle fascicle dynamics was more pronounced in MG as compared to SOL, demonstrated by much greater differences in FL and FV. Duclay et al. (2011, 2014) reported no differences in MEP or H-reflex for MG during maximal eccentric muscle actions, contrasting with a consistent reduction of both parameters for SOL. Since the testing position in their study was the same as ours, it is plausible to suggest that the mechanical changes in MG did not affect corticospinal excitability, as afferent inputs were overwritten by centrally mediated inputs.

In the present study, no differences in SOL MEP size were found between isometric and eccentric muscle actions, corroborating with previous studies (Duclay et al. 2011; Hahn et al. 2012). Duclay et al. (2011), only found significant differences at the highest stimulation intensities, which

induced MEPs on or close to the plateau of the input-output curve. Direct comparisons between the effective stimulation intensity in these two experiments are not possible since different coil shapes were utilized (i.e. circular vs. batwing), generating different magnetic fields (Cohen et al. 1990). Lower MEPs during maximal and submaximal eccentric muscle actions have also often been reported for biceps brachii and brachioradialis (Abbruzzese et al. 1994; Gruber et al. 2009). Although obtaining the whole input-output curve for each muscle action type surely provides much more information about the task-dependent modulation of the corticospinal excitability (Devanne et al. 1997, Duclay et al. 2011; Sekiguchi et al. 2001, 2003, 2007), the number of trials in the current experiment would have been excessive, leading subjects into fatigue and affecting the results.

Since in the present study no differences were found in SOL MEP amplitude, which combined with stimulation intensity can modulate SP (Inghilleri et al. 1993; Säisänen et al. 2008), the decrease in SP during eccentric muscle actions suggests decreased cortical and/or spinal inhibition. The silent period has been used as an index of intracortical inhibition, as it is generally thought that it results from an early spinal inhibitory mechanism (< 50 ms) followed by later intracortical inhibition (Chen et al. 1999; Inghilleri et al. 1993; Roick et al. 1993). However, recent results have shown that the spinal inhibitory contribution can be much longer (i.e. up to 150 ms; Yacyshyn et al. 2016), casting doubt into the correct interpretation of SP data. Duclay et al. (2011) also found decreased SP during eccentric plantarflexion as compared to isometric, while other researches have shown evidence that supraspinal excitability seems to be higher during eccentric muscle actions (Fang et al. 2001, 2004; Gruber et al. 2009). Fang et al. (2001, 2004) reported greater movement-related cortical potential and a larger brain area involved during eccentric elbow flexion (maximal

and submaximal) as compared to concentric. The demonstrated differences suggest that the brain is more involved in the preparation, planning and execution of the movement and with the processing of sensory input during eccentric actions. Interestingly, in the present study eccentric velocity did not affect SP, suggesting that differences in afferent information (i.e. muscle spindle discharge) does not modulate these inhibitory mechanisms. Despite decreased cortical and/or spinal inhibition demonstrated by a shorter silent period in the present study and a higher MEP/CMEP ratio (i.e. higher cortical excitability demonstrated for elbow flexors; Grubber et al. 2009), the responsiveness of the SOL motoneuron pool is lower during eccentric muscle actions (i.e. lower H/M), indicating that changes in neural control during eccentric muscle actions possibly occurs both at spinal and cortical sites. However, contrary to the previously exposed results, Hahn et al. (2012) reported no differences in MEP and CMEP between isometric and eccentric muscle actions for SOL muscle, evidencing the need for further research in this area.

Proposed control mechanisms during eccentric muscle actions. Although it is currently not possible to pinpoint the exact neural pathways responsible for the eccentric motor control, several considerations are warranted: (1) Previous experiments have shown similar depression in muscle activation for submaximal and maximal eccentric muscle actions, suggesting that Ib afferents are not likely to contribute to the spinal inhibition observed (Abbruzzese et al. 1994; Duclay et al. 2014, Gruber et al. 2009; Sekiguchi et al. 2001); (2) since TA coactivation was similar among experimental conditions, reciprocal inhibition should not be responsible for the lower spinal excitability of SOL during the eccentric muscle actions; (3) recurrent inhibition mediated by Renshaw Cells can limit motor unit discharge rate (Windhorst 2007), and function as a variable gain regulator for motor output (Hultborn et al. 1979). Animal experiments have shown that

529 descending pathways can modulate recurrent inhibition (Baldissera et al. 1981), however indirect
530 recurrent inhibition assessment in humans has shown it to decrease as the contraction intensity
531 increased (Hultborn and Pierrot-Deseilligny 1979). Clearly, more information is needed in order
532 to ascertain if recurrent inhibition is a possible candidate for the modulation seen in our study; (4)
533 Presynaptic inhibition (PSI; Hultborn et al. 1987, Rudomin and Schmidt 1999) could reduce the
534 responsiveness of the motoneuron pool during eccentric muscle actions, by reducing the stretch
535 reflex gain (Bawa and Sinjær 1999; Nagazawa et al.1997, 1998). Grosprêtre et al. (2014)
536 conditioned the H-reflex with a subthreshold stimulation of the motor cortex and demonstrated
537 that descending pathways appear to control spinal inhibition during eccentric muscle actions. The
538 later study suggests that supraspinal modulation of PSI by primary afferent depolarization is a
539 possible candidate for lowering spinal excitability during eccentric muscle actions; (5) intracortical
540 inhibition (i.e. GABAergic inhibition) differences during eccentric and isometric muscle actions
541 have been recently shown by Opie and Semmler (2016). Utilizing a paired pulse TMS over M1,
542 they showed that short-interval intracortical inhibition was decreased whereas long-interval
543 intracortical inhibition was increased in eccentric muscle actions as compared to isometric.

544 ## Conclusion

545 The present study showed a decreased responsiveness of the SOL motoneuron pool to Ia excitatory
546 inputs (i.e reduced H/M) during eccentric muscle actions, while muscle mechanics (i.e. fascicle
547 length and pennation angle) remained the same as compared with isometric muscle action.
548 Although fascicle velocity was greater in the fast eccentric condition as compared with slow
549 eccentric, no differences in corticospinal excitability were found between conditions, suggesting
550 that Ia excitatory afferent input was not successful in increasing MN excitability. Additionally, the
551 decrease in SP during eccentric muscle actions, while MEP values remained similar among the

different test conditions, suggests increased supraspinal and/or spinal excitability, even though the responsiveness to Ia excitatory inputs was lower.

Taken together, the present results corroborate with the hypothesis that the central nervous system has an unique activation strategy during eccentric muscle actions (Duchateau and Enoka 2008, 2016; Duchateau and Baudry 2014; Enoka 1996). Furthermore, our results do not support the hypothesis that sensory information plays an important role in modulating spinal excitability during SOL eccentric muscle actions. A centrally mediated feedforward control scheme seems adequate to induce the observed excitability modulation, future studies are necessary to verify the exact mechanisms.

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