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RESEARCH ARTICLE

Short-interval intracortical inhibition of the biceps brachii in chronic-resistance versus non-resistance-trained individuals

Behzad Lahouti[1] · Evan J. Lockyer[2] · Shawn Wiseman[1] · Kevin E. Power[1,2] · Duane C. Button[1,2]

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Abstract

The purpose of this study was to investigate the effects of chronic resistance training on corticospinal excitability and short intracortical inhibition of the biceps brachii. Eight chronic resistance-trained (RT) and eight non-RT participants completed one experimental session including a total of 30 brief (7 s) elbow flexors isometric contractions at various force outputs [15, 25 and 40% of maximum voluntary contraction (MVC)]. Before the contractions, MVC, maximal compound muscle action potential (M_{max}) during 5% MVC and active motor threshold (AMT) at the three various force outputs were recorded. MVC force of the chronic-RT group was 24% higher than the non-RT group ($p \leq 0.001$; $\omega^2 = 0.72$). The chronic-RT group had lower AMTs at targeted forces of 15 and 25% MVC ($p = 0.022$ and $p = 0.012$, respectively) compared to the non-RT group. During 25 and 40% of MVC, the non-RT group exhibited decreased SICI in comparison to the chronic-RT group ($p = 0.008$; $\omega^2 = 0.35$ and $p = 0.03$; $\omega^2 = 0.21$, respectively). However, SICI did not differ between groups at 15% MVC ($p = 0.62$). In conclusion, chronic resistance training significantly reduces SICI. This suggests the presence of an adaptive process of inhibitory and facilitatory network activation, which may cancel out the SICI, allowing for increased corticomotor drive to the exercised muscle following a long period of resistance training.

Keywords Facilitation · Inhibition · Resistance training · Transcranial magnetic stimulation · Voluntary contraction

Introduction

Paired-pulse transcranial magnetic stimulation (TMS) protocols are useful methods for the non-invasive assessment of inhibitory and facilitatory circuits in the human motor cortex (Hallett 2000; Kobayashi and Pascual-Leone 2003). When pairing a subthreshold conditioning stimulus (CS) with a suprathreshold test stimulus (TS) at short interstimulus intervals (ISIs) of 1–5 ms, low-threshold intracortical inhibitory circuits are activated and the motor evoked potential (MEP) amplitude is reduced compared to that elicited by the suprathreshold TS alone (Kujirai et al. 1993). This phenomenon is called short-interval intracortical inhibition (SICI) and can be represented by the ratio of the conditioned MEP amplitude over the test MEP amplitude. There is ample evidence suggesting that SICI is mediated by inhibitory neural mechanisms located at the cortical level (Fuhr et al. 1991; Nakamura et al. 1997; Di Lazzaro et al. 1998; Chen 2000). Although multiple inhibitory mechanisms are involved in forming SICI, it has been shown that SICI reflects a balance between intracortical facilitation and inhibition (Ilic et al. 2002; Roshan et al. 2003).

Evidence from work using tonic contractions as a motor output indicates that a reduction in SICI is thought to be important for enhancing the excitability of corticospinal cells via reduced intracortical inhibitory input to the corticospinal pathway (Ridding et al. 1995; Chen et al. 1998). Additionally, it appears that the magnitude of SICI is highly task-dependent. For example, SICI is reduced during voluntary muscle contraction compared to rest (Fisher et al. 2002; Roshan et al. 2003; Zoghi et al. 2003). Furthermore, SICI reduction also occurs as force output increases in the first dorsal interosseous (FDI) (Ortu et al. 2008) and abductor pollicis brevis (APB) (Zoghi and Nordstrom 2007) muscles during submaximal contraction intensities. In addition to small hand muscles, Brownstein et al. (2018) reported the

✉ Duane C. Button
dbutton@mun.ca

[1] School of Human Kinetics and Recreation, Memorial University of Newfoundland, 230 Elizabeth Avenue, St. John's, NL A1C 5S7, Canada

[2] Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, Canada

same result from the rectus femoris muscle. However, none of the aforementioned studies have assessed SICI during various force outputs from the biceps brachii. Moreover, there have been very few studies illustrating the effect of resistance training on modulation of SICI.

Existing evidence from single-pulse TMS studies have reported inconsistent results regarding the central nervous system (CNS) adaptations to strength training. Carroll et al. (2002) reported a significant reduction in CNS excitability after short-term resistance training of FDI (Carroll et al. 2002), while others observed a significant increase in MEP size following short-term resistance training of tibialis anterior (Griffin and Cafarelli 2007) and the soleus (Beck et al. 2007) muscles. Indeed, the discrepancy in these results may be attributable to a number of factors, most notably the examined muscle group, the strength training protocols used, and/or the stimulation protocols employed (Carroll et al. 2011). In order to investigate potential mechanisms underlying changes in supraspinal excitability due to resistance training, Weier et al. (2012) applied paired-pulse TMS protocol to investigate SICI following a short-term resistance training protocol of the quadriceps femoris muscle. They observed that 4 weeks of heavy load squat strength training can lead to an increase in CNS excitability while significantly reducing SICI. In addition, acute motor skill training has also been shown to decrease SICI in tibialis anterior (Perez et al. 2004) and the FDI (Perez et al. 2007) muscles.

Changes in CNS excitability following chronic resistance training (over a year) have also been examined (del Olmo et al. 2006; Pearcey et al. 2014; Philpott et al. 2015). Some authors have shown no correlation between increased muscle strength and changes in corticospinal excitability following chronic resistance training (del Olmo et al. 2006; Tallent et al. 2013) while others report significant CNS excitability modulation. For example, Pearcey, Power, and Button (2014) reported smaller MEP amplitudes from the biceps brachii muscle in a chronic resistance-trained (RT) group compared to a non-RT group during strong force outputs ($\geq 50\%$ MVC) (Pearcey et al. 2014). Also, Philpott et al. (2015) observed a significantly increased spinal excitability of the non-dominant biceps brachii during high force outputs (50 and 70% MVC) in chronic-RT group compared to non-RT group (Philpott et al. 2015). However, it remains unknown how SICI is altered in individuals who have been chronically resistance training. Several studies evaluated the long-term effects of motor training on intracortical excitability modulation in musicians who have undergone chronic training of their fingers. SICI and intracortical facilitation (ICF) were weaker in musicians than non-musicians (Nordstrom and Butler 2002). However, when SICI was evaluated across a range of CS intensities, it revealed that at higher intensities of CS, musicians have stronger SICI compared to non-musician participants (Rosenkranz et al. 2007). The differences in these results could be due to activation of other interneurons belonging to the ICF network. It has been shown that higher CS intensities may be able to activate these facilitatory interneurons (Ziemann et al. 1998). Thus, to avoid activation of the ICF network, a single subthreshold CS intensity, instead of applying a range of CS intensities, may better reflect overall changes in SICI.

To date, no study has investigated the effects of chronic resistance training on SICI. Since the SICI system influences corticospinal neurons by producing inhibitory postsynaptic potentials (IPSPs) (Ortu et al. 2008), it could change corticomotor drive to the exercised muscle and can be subjected to long-term neural adaptation. Therefore, the purpose of this study was to examine corticospinal excitability and SICI in chronically resistance-trained (chronic-RT) and non-resistance-trained (non-RT) individuals utilizing single-pulse and paired-pulse TMS protocols. There were two hypotheses for this study: (1) SICI of the biceps brachii will decrease as force output increases from weak to moderate elbow flexors contractions and (2) chronic-RT individuals will demonstrate reduced SICI compared to non-RT individuals.

Methods

Participants

Sixteen healthy, male individuals without a history of neurological disease volunteered for this study. The 16 participants were divided into two groups consisting of 8 chronic-RT (height 177.2 ± 10.5 cm, weight 84.6 ± 6.0 kg, age 27.5 ± 7.6 years, 1 left-hand dominant) and 8 non-RT (height 174.5 ± 6.1 cm, weight 77.3 ± 10.0 kg, age 29.1 ± 3.2 years, 2 left-hand dominant) individuals. For the chronic-RT group, participants were all non-competitive recreational athletes who were required to have had more than two continuous years of resistance training experience (at least three times per week) including a variety of multi-jointed weight training exercises. The participants in the non-RT group did not resistance train. Participants were verbally informed of the procedures being used for the experiment and signed a written consent form if they accepted. To detect any potential contraindications with magnetic stimulation procedures, all participants were asked to complete a magnetic stimulation safety checklist (Rossi et al. 2011) before participation. The University's Interdisciplinary Committee on Ethics in Human Research approved the study (#20190061-HK), which was in accordance with the Tri-Council guidelines in Canada with full disclosure of potential risks to participants.

Experimental set-up and recordings

Elbow flexor force

Participants were seated in a custom-built chair (Technical Services, Memorial University of Newfoundland, St. John's, NL, Canada) in an upright position, with the chest and head strapped in place to minimize movement, and the hips and knees flexed at 90°. The shoulder was placed at 0° and the elbow was flexed at 90°. At the 0° position, both arms were slightly abducted and rested on a padded support. The forearm was held horizontal, positioned midway between neutral and supinated positions, and placed in a custom-made orthosis that was connected to a load cell (Omegadyne Inc., Sunbury, OH, USA). The load cell detected force output, which was amplified 1000× (CED 1902, Cambridge Electronic Design Ltd., Cambridge, UK) and displayed on a computer screen. Data were sampled at 2000 Hz (Signal 4.0 software, Cambridge Electronic Design Ltd., Cambridge, UK). Participants were instructed to maintain an upright position with their head in a neutral position during contractions of the elbow flexors. Verbal encouragement and visual feedback were given to all participants during elbow flexor contractions (Fig. 1a).

Electromyography (EMG)

EMG activity of the biceps brachii muscle was recorded using 10-mm diameter MediTrace Pellet Ag/AgCl electrodes (disc shape, Graphic Controls Ltd., Buffalo, NY). The electrodes were placed 2 cm apart (center to center) over the mid-muscle belly of the participant's biceps brachii. A ground electrode was placed on the lateral epicondyle of the opposite upper limb. Before the electrode placement, skin was prepared for all electrodes including shaving hair off the desired area, using abrasive sand paper to remove dead epithelial cells from the desired area, followed by cleansing with an isopropyl alcohol swab. Before the recording, we obtained an inter-electrode impedance of < 5 kΩ to check the ratio of the signal-to-noise. EMG signals were amplified (1000×) (CED 1902) and filtered using a 3-pole Butterworth with cutoff frequencies of 10–1000 Hz. Analog-to-digital conversion of the signals was performed at a sample rate of 5 kHz using a CED 1401 interface and Signal 4 software (Cambridge Electronic Design Ltd., Cambridge, UK).

Stimulation conditions

Brachial plexus electrical stimulation (*Erb's point stimulation*) Stimulation of the brachial plexus was used to measure participants' maximal compound motor unit action potential

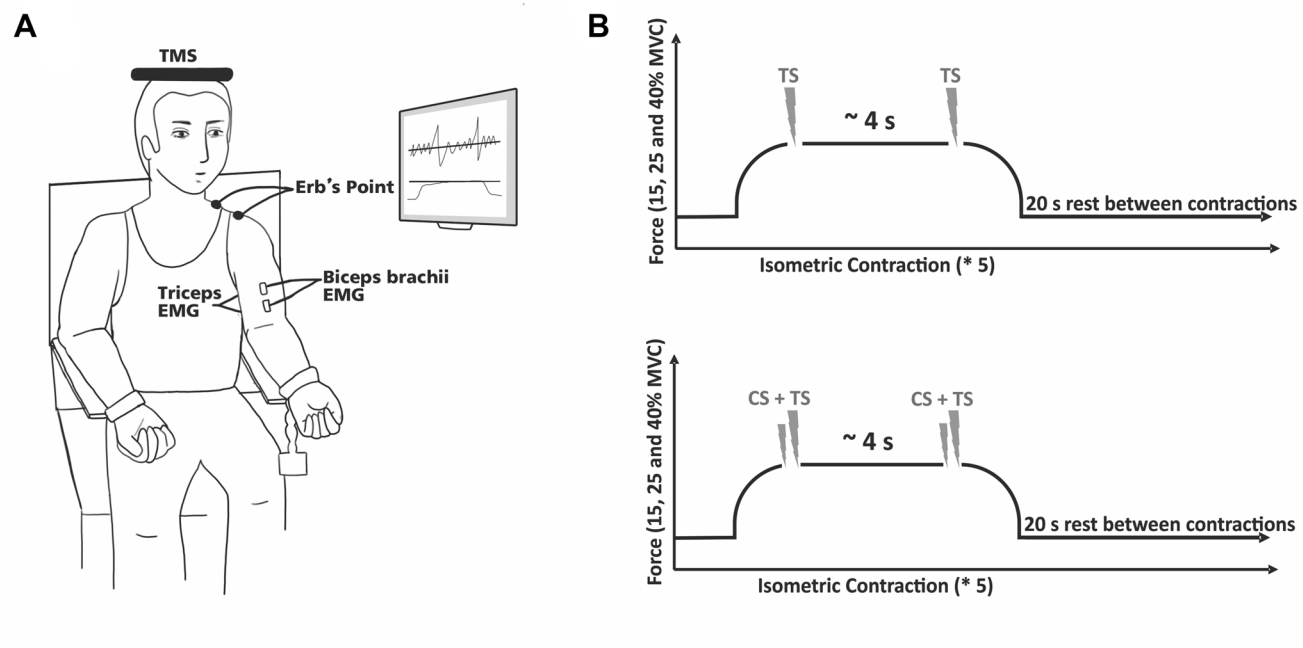

Fig. 1 Schematic diagram of the experimental set-up (**a**) and protocol (**b**). Participants were asked to complete 10, 7 s duration, elbow flexor contractions at 15, 25 and 40% MVC (total of 30 contractions, 10 at each %MVC). Participants received two (top panel **b**, a test stimulus to measure MEP) or four (bottom panel **b**, a condition and test stimulus to measure SICI) transcranial magnetic stimulations of the motor cortex during each contraction at 1.5 and 5.5 s. For each %MVC participants performed 5 contractions to measure MEP and 5 contractions to measure SICI

(M_{max}). Erb's point was electrically stimulated via a cathode and anode (Meditrace Ag–AgCl pellet electrode, disc-shaped 10 mm diameter, Graphic Controls Ltd., Buffalo, NY, USA) positioned on the skin overlying the supraclavicular fossa and over the acromion process, respectively. Current pulses were delivered as a singlet using a constant-current electrical stimulator (square wave pulse, 200 µs duration at 100–300 mA; model DS7AH, Digitimer Ltd, Welwyn Garden City, UK). The electrical current was gradually increased until M_{max} of the biceps brachii was reached during 5% MVC. M_{max} was measured during 15, 25 and 40% MVC using the stimulator intensity used to elicit M_{max} during 5% MVC.

Transcranial magnetic stimulation (*TMS*) TMS was delivered using a circular coil (13 cm outside diameter) attached to a BiStim module connected to two magnetic stimulators (Magstim 200, Dyfed, United Kingdom). The stimulating coil was positioned directly over the vertex of participants' head. The vertex was located by marking the measured halfway points between the nasion and inion and the tragus to tragus. The intersection of these two points was defined as the vertex and was clearly marked with a felt-tipped permanent marker. Electrical currents flowed in an anticlockwise direction through the circular coil. The coil was placed horizontally over the vertex so that the direction of the current flow in the coil preferentially activated the right or left primary motor cortex ("A" side up for right side, "B" side up for left side), for the elicitation of current in the dominant biceps brachii motor cortical representation. Two stimulation protocols were used during various force outputs of the biceps brachii: (1) a single-pulse TMS protocol (to elicit test MEP) and (2) a paired-pulse TMS protocol (to elicit conditioned MEP). For the paired-pulse protocol, a subthreshold stimulus (conditioned pulse) was delivered 2.5 ms prior to a suprathreshold stimulus (test pulse) to produce maximum SICI (Fisher et al. 2002). Also, the intensities of the conditioned and test pulse were set relative to the active motor threshold (AMT) of the MEP during each contraction intensity. AMT was defined as the lowest TMS intensity required to elicit a discernible MEP ($\geq$ 100 µV) in at least 50% of the trials (Rossini et al. 2015) for each contraction intensity. To find the intensity of the conditioned stimulus and the test stimulus, the mean stimulator output was decreased and increased, respectively, by 20% to determine each stimulation intensity for the remainder of the experiment (80% of each AMT for CS, and 120% of each AMT for TS) (Ortu et al. 2008; Hunter et al. 2016).

Experimental protocol

Participants completed a single experimental session (~ 1.5 h). The procedure involved performing isometric contractions of the dominant elbow flexors at different intensities of MVC. The participants first performed isometric contractions for 5 s at various low intensities to get accustomed to producing varying force outputs. Participants then completed two elbow flexors MVCs, which were required to have force measurements (N) within 5% of one another to ensure maximal force output; if not, a third MVC was performed. The MVCs were preceded by a 10-min rest period where the participants were prepped for EMG and stimulation conditions. Following 10 min of rest, the intensities for each stimulation type were set. M_{max} was recorded during 5% MVC by gradually increasing stimulus intensity until the M-wave of the biceps brachii reached a plateau. The stimulator intensity used to determine M_{max} at 5% MVC was used to evoke M_{max} for the remainder of the experiment. AMT was then determined at the three different force outputs (15, 25 and 40% MVC) of the dominant biceps brachii. After determining the stimulation intensities, the participants began the isometric contraction protocol. Three blocks of voluntary isometric contractions of the elbow flexors were performed at 3 different force outputs (15, 25 and 40% of MVC). Each block included ten contractions for 7 s duration. Participants were given 20-s rest between contractions and 5-min rest between contraction blocks. For each contraction, the target force for the participants was displayed on a computer screen. Participants were required to contract their elbow flexors and match the target force line and maintain it for 7 s. During each contraction, participants received 2 TMS pulses at two different time points (1.5 and 5.5 s) (Fig. 1b). The order of target forces and the type of TMS protocol were randomized. Following the isometric contraction protocol, participants performed three isometric contractions (one at each intensity) during which two M_{max} were recorded.

Data analysis and statistics

Average biceps brachii force during MVC performance was measured. Peak-to-peak amplitudes of test MEPs, conditioned MEPs and M-waves were recorded from the biceps brachii and then averaged for each target force. A total of 60 MEP responses were recorded (10 test and 10 conditioned MEPs at each of the three force outputs). Since the M_{max} amplitudes were not significantly different during different levels of force outputs, test MEPs peak-to-peak amplitudes were normalized to M_{max} (during 5% MVC) amplitude. To determine SICI, the mean amplitude of each conditioned MEP was measured and expressed as a percentage of the mean test MEP evoked by the suprathreshold pulse alone during the same contraction intensity. All data were analyzed off-line using Signal 4.0 software (CED, UK) and averages and ratios were calculated using Office Excel 2016 (Microsoft Corporation, Redmond, WA, USA).

Statistical analyses were completed using SPSS (SPSS 18.0 for Macintosh, IBM Corporation, Armonk,

New York, USA). Normality of the data was assessed using both Shapiro–Wilk and Kolmogorov–Smirnov tests and was found to be normally distributed. In the event of a violation of the assumption of sphericity, p values were adjusted using the Greenhouse–Geisser correction. First, a two-way ANOVA was applied to test the main effect of force output (15, 25 or 40% MVC) and training background (chronic-RT vs. non-RT) on each of the dependent variables (AMT, MEP size, AMT and SICI). Then, a series of between-group one-way ANOVAs were used to compare between-group differences during each target force separately. Data in text, table and figures are reported as means ± SD and significance was set at $p < 0.05$. To determine the effect size of dependent variables, ω^2 was calculated. This measurement is shown to be more appropriate for one- and two-way ANOVA. ω^2 values were set at small (0.01), moderate (0.06) or large (0.14). Pearson correlations were used to determine the relationship between AMT and SICI during the various force intensities.

Results

Elbow flexors force output

MVC force in the chronic-RT (471.5 ± 57.5 N; range 409–548 N) group was 57% higher than the non-RT group (298.6 ± 48.7 N; range 224–376 N) ($p \leq 0.001$; $\omega^2 = 0.72$).

Short-interval intracortical inhibition

Figure 2 shows the raw data of the test and conditioned MEP recorded from two participants, one non-RT (top row) and one chronic-RT (bottom row), during 15, 25 and 40% of MVC. Mean absolute values for SICI expressed as the ratio between the conditioned MEP over the test MEP are illustrated in Fig. 3a. During the 15% MVC condition, SICI was observed in all subjects, irrespective of resistance training background (range 41–100%, $p < 0.01$, $\omega^2 = 0.04$) with no difference between groups. However, the non-RT group exhibited higher SICI than the chronic-RT group at 25% (SICI 78 ± 13%, range 65–99%

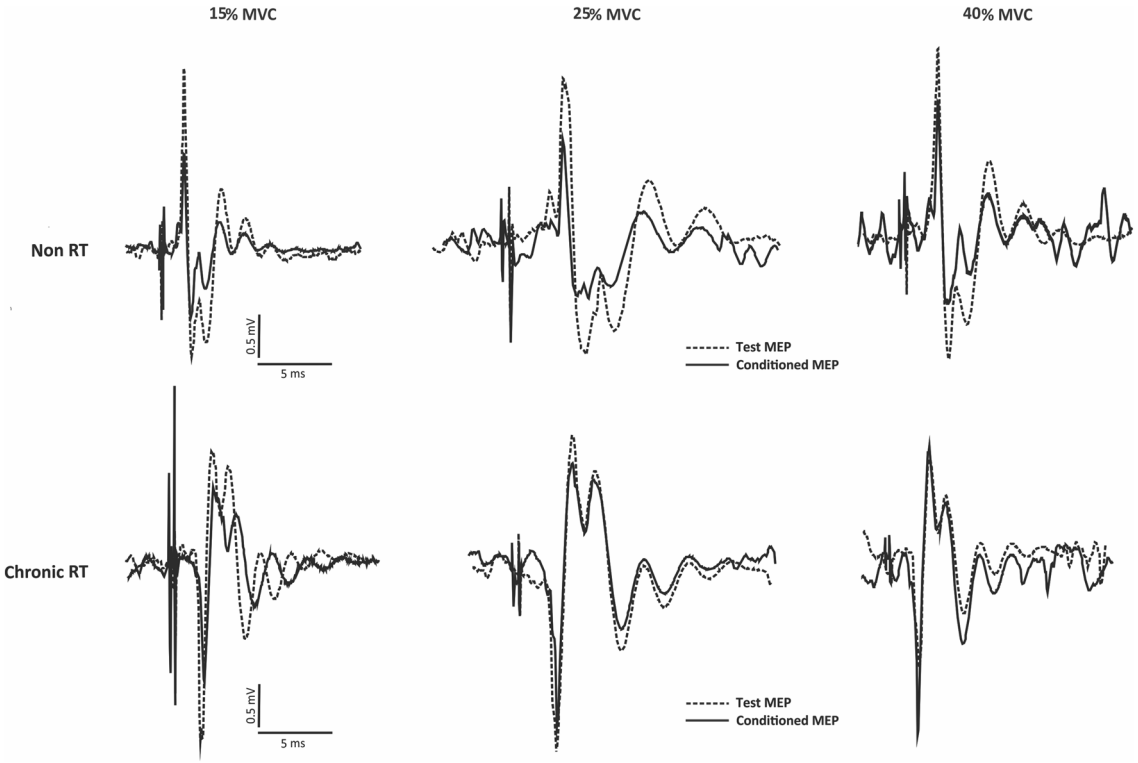

Fig. 2 Individual raw data from two participants. Corticospinal responses during 15, 25 and 40% MVC recorded from a non-RT (top) and chronic-RT (bottom) biceps brachii. MEPs recorded from the single-pulse stimulation protocol are shown with dash line and conditioned MEPs (recorded from paired-pulse protocol) are illustrated by the solid line. For the test pulse TMS protocol, stimulation intensity of 120% AMT was used. Conditioned stimulation intensity of 80% AMT was applied 2.5 ms prior to test stimulus to inhibit the test MEP during paired-pulse TMS protocol. Notice that SICI was not present in chronic-RT participants during stronger force outputs (25 and 40% MVC) while it was present at all force output levels in the non-RT participants

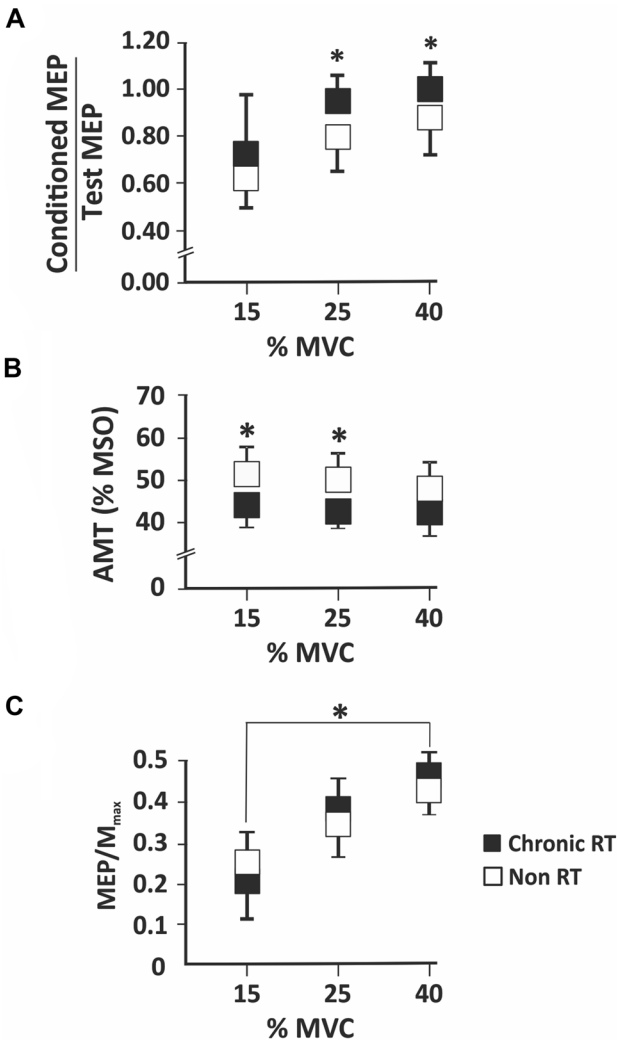

Fig. 3 The effect of chronic resistance training and contraction intensity on **a** SICI, **b** AMT and **c** MEP amplitude. **a** SICI was expressed as the ratio between conditioned MEPs and test MEPs. During 15% MVC both chronic-RT and non-RT groups exhibited SICI. However, during 25 and 40% MVC SICI was observed only in the non-RT participants. **b** The chronic RT had lower AMTs compared to the non-RT group (43 ± 1.8% vs. 50 ± 2.2%, 41 ± 1.3% vs. 49 ± 2.2%, 41 ± 1.9% vs. 47 ± 2.2%) at 15, 25 and 40% MVC, respectively. **c** Data is reported as normalized test MEP responses to M_{max}. As force increased, corticospinal excitability increased. MEP responses recorded during 15, 25, and 40 %MVC were all significantly different from one another. In all figures, data points represent means ± SD and asterisks represents statistical significance of $p < 0.001$, $p < 0.05$, $p < 0.05$ in **a**, **b** and **c**, respectively

vs. 97 ± 9%, range 88–116% of test pulse; $p = 0.008$; $\omega^2 = 0.35$, respectively) and 40% (SICI 86 ± 14%, range 65–101% vs. 102 ± 11%, range 93–116% of the test pulse; $p = 0.03$; $\omega^2 = 0.21$, respectively) of MVC.

Active motor threshold

For the TMS intensity required to elicit AMT, there was a main effect of resistance training background ($F_{1,42} = 17.657$; $p < 0.001$). However, there was no main effect of force output ($F_{1,42} = 0.819$; $p = 0.44$), or an interaction between force output and resistance training background ($F_{2,42} = 0.146$; $p = 0.86$). AMT for the chronic-RT group was 7% ($p = 0.022$, $\omega^2 = 0.26$), 6.5% ($p = 0.012$, $\omega^2 = 0.31$) and although not significantly, 7% ($p = 0.079$, $\omega^2 = 0.13$) lower than the non-RT group at 15 (chronic-RT range 39–51% MSO; non-RT range 44–65% MSO), 25 (chronic-RT range 37–48% MSO; non-RT range 41–62% MSO) and 40% (chronic-RT range 36–52% MSO; non-RT range 40–59% MSO), respectively of MVC (Fig. 3b).

Corticospinal excitability

Two-way ANOVA results showed that there was a main effect for force output ($F_{2,42} = 3.840$; $p = 0.02$), yet, no main effect for resistance training background ($F_{1,42} = 0.002$; $p = 0.96$) or an interaction between resistance training background and force output ($F_{1,42} = 0.030$; $p = 0.97$). Although MEP responses increased as a function of force output, there were no significant differences in MEP amplitudes between the chronic-RT and non-RT group at 15% (normalized MEP: 0.22 ± 0.28, range 0.09–0.33 vs. 0.24 ± 0.11, range 0.14–0.43; $p = 0.87$; $\omega^2 = 0.06$, respectively), 25% (normalized MEP: 0.37 ± 0.16, range 0.2–0.64 vs. 0.36 ± 0.22, range 0.2–0.9; $p = 0.94$; $\omega^2 = 0.06$, respectively) and 40% (normalized MEP: 0.45 ± 0.13, range 0.23–0.59 vs. 0.43 ± 0.28, range 0.23–1.07; $p = 0.86$; $\omega^2 = 0.06$, respectively) of MVC (Fig. 3c).

Compound muscle action potential

There was no significant difference in M_{max} amplitudes between the chronic-RT group (11.9 ± 6.53 mV, range 3.8–22.1 mV) and non-RT group (7.4 ± 2.49 mV, range 3.4–11.1 mV) during 5% MVC ($p = 0.09$, $\omega^2 = 0.12$). There were no significant differences in M_{max} amplitudes between the chronic-RT and non-RT group at 15% (9.8 ± 6.11 mV, range 2–20 mV vs. 6.7 ± 2.33 mV, range 3.3–11 mV; $p = 0.20$; $\omega^2 = 0.04$, respectively) 25% (10.4 ± 5.87 mV, range 2.7–19.6 mV vs. 7.1 ± 3.08 mV, range 2.9–11.7 mV; $p = 0.17$; $\omega^2 = 0.06$, respectively) and 40% (9.0 ± 5.06 mV, range 3.8–18.3 mV vs. 7.0 ± 3.12 mV, range 3.3–11.3 mV; $p = 0.19$; $\omega^2 = 0.04$, respectively) of MVC.

Correlation between SICI and AMT

Pearson correlations were performed to investigate the relationship between AMT and SICI during various force

outputs, regardless of resistance training background. During the 15% MVC condition, no correlation was observed between AMT and SICI ($r = -0.13$, $p = 0.63$). However, there was a strong linear relationship between these two variables during the 25% ($r = -0.57$, $p = 0.02$) and 40% ($r = -0.58$, $p = 0.02$) of MVC.

Discussion

This is the first study to directly examine the effects of chronic resistance training background on changes in SICI during various force outputs of the biceps brachii. The main findings of our study showed that regardless of resistance training background, SICI is reduced as force output increases. However, the magnitude of the reduction in SICI appears to be dependent on resistance training background. Specifically, during the more moderate strength force outputs (25 and 40% MVC), the amount of SICI in the chronic-RT group was significantly lower than the non-RT group. In fact, no SICI was even observed in the chronic-RT group during 40% MVC force. These findings suggest that neural adaptations in intracortical interactions may exist following chronic resistance training.

SICI as a function of contraction intensity

Irrespective of resistance training background, the amount of SICI observed in the present study was reduced as contraction strength increased from 15 to 40% MVC. Similar findings have been reported previously by several groups examining the modulation of SICI going from rest to weak muscle contractions (Ridding et al. 1995; Fisher et al. 2002; Zoghi and Nordstrom 2007) and over a range (10–50% MVC) of contraction intensities (Ortu et al. 2008) in hand musculature, as well as the rectus femoris muscle (Brownstein et al. 2018). In the latter two studies, SICI was completely abolished at moderate-to-strong contraction intensities (25–50% MVC) (Ortu et al. 2008; Brownstein et al. 2018). While the precise mechanisms underlying the reduction in SICI as muscle contraction strength increases is not fully understood, it has been proposed that it may be due to the concomitant activation of intracortical facilitatory networks, specifically short-interval intracortical facilitation (SICF), which ultimately results in little or no observable change in conditioned MEP size (Ridding et al. 1995; Ziemann et al. 1996; Zoghi and Nordstrom 2007; Ortu et al. 2008). Interestingly, in the current study however, unlike the complete abolishment observed in the above-mentioned studies, SICI was still measurable at 25% and 40% MVC in the non-RT group, but not in the chronic-RT group. We speculate that there may be several reasons for this discrepancy.

First, the lack of abolishment of SICI in the present study may be due to muscle-dependent SICI modulation. We examined SICI from the biceps brachii, whereas the majority of the aforementioned studies investigated the much smaller and more distal hand musculature (i.e., FDI and APB), which due to differences in motor control function, have different contributions from intracortical circuits than the biceps brachii (Abbruzzese et al. 1999). Secondly, for the paired-pulse TMS we used a CS intensity equal to 80% AMT at an ISI of 2.5 ms to produce the maximum SICI. However, in the previous studies, a wide range of CS intensities from 70 to 90% of AMT as well as various ISIs from 1 to 5 ms were utilized, potentially leading to a different quantification of SICI. For example, by applying a low CS intensity (70% of AMT), no inhibition was reported during weak contraction (20% MVC) of the FDI (Ortu et al. 2008).

SICI is reduced more in chronic-RT individuals as force output increases

The present results suggest that the magnitude of SICI reduction during various muscle contractions may also depend on resistance training background. Specifically, SICI was still measurable at 25% and 40% MVC for the non-RT group but was seemingly abolished in the chronic-RT group at 40% MVC. The mechanisms underlying the differences in SICI between groups are not known, however previous studies have shown that chronic resistance training can alter corticospinal excitability (Pearcey et al. 2014; Philpott et al. 2015). For example, using single-pulse TMS, Pearcey et al. (2014) evaluated changes in biceps brachii MEPs from the dominant arm of chronic-RT and non-RT participants over a range of force outputs from 10 to 100% MVC and found that MEP amplitudes increased progressively from weak to stronger elbow flexor contractions (up to 60% MVC) in both groups, however, at the highest contraction intensities (> 60% MVC), chronic-RT participants had lower MEP amplitudes than non-RT participants. The authors proposed that the discrepancy in MEPs at the high muscle contraction intensities between groups was likely mediated by enhanced spinal mechanisms underlying force output at the higher percentages of MVC (Pearcey et al. 2014). It was concluded that chronic resistance training may induce a potential neural adaptation at high contraction forces such that less descending input is required by the motor cortex to produce the appropriate force. However, the influence of inhibitory or facilitatory circuits on the development of MEP amplitudes in chronic-RT and non-RT individuals has not been compared until now.

Although not chronic resistance training, Latella et al. (2012) reported reduced corticospinal silent periods (indicating decreased inhibition) following 4–8 weeks of resistance training and suggested that the change in the corticospinal

silent period may have been due to increased intracortical inhibition (Latella et al. 2012). Additionally, Weier et al. (2012) and Goodwill et al. (2012), using similar paired-pulse TMS protocols, found that SICI was reduced following acute periods of either bilateral or unilateral strength training of the quadriceps. However, in these studies, SICI was only measured following acute resistance training and during a single force output (10% MVC), and thus may not be indicative of how SICI is modulated at various force outputs following training (Goodwill et al. 2012; Weier et al. 2012).

While both groups in the present study showed a reduction in SICI with increased force output from 15 to 40% MVC, SICI was observed in the chronic-RT group during elbow flexor force outputs equal to or stronger than 25% MVC but not at 40% MVC. Therefore, if SICI was the only mechanism responsible for MEP modulation, the same amount of intracortical inhibition should have been observed in both the chronic-RT and non-RT groups as they showed similar changes in MEP amplitudes from 15 to 40% MVC. The differences in SICI between groups are thus likely due to altered activation of a combination of intracortical inhibitory and facilitatory networks. We propose, though we cannot be certain, that with increasing contraction strength there is reduced intracortical inhibition that is accompanied by an increase in intracortical facilitation during moderate-to-strong muscle contractions as a way to produce higher force outputs without requiring greater descending input from the motor cortex. We suggest that this effect is larger for chronic-RT than non-RT individuals due to a reorganization of intracortical networks that may potentially represent a neural adaptation to long-term resistance training. Specifically, we postulate that at stronger contraction intensities, chronic resistance training may induce inhibition of the interneurons activating late I waves of the MEP response and activate facilitatory interneurons that produce early I waves at the same time, therefore resulting in an appeared abolishment of SICI (Zoghi et al. 2003; Ni and Chen 2008). Further work investigating both intracortical inhibitory and facilitatory networks in chronically resistance-trained individuals, however, is required before more conclusive statements can be made.

Increased afferent feedback from the periphery also reduces SICI. Since increasing force output is accompanied by an increase in afferent feedback, SICI could be gradually reduced as force output increases as a secondary change to alterations in muscle afferent feedback. Ridding and Rothwell (1999) observed that a decrease in SICI during peripheral nerve stimulation and voluntary contraction, however, during motor imagery activity, where afferent feedback was absent, there were no changes in SICI (Ridding and Rothwell 1999). Increased neural activity generated by afferent feedback and voluntary command has been shown to be an important mechanism affecting intracortical inhibition during and following a repetitive task with hand muscles (Nordstrom and Butler 2002). Since chronic-RT individuals produce more force at a given percentage of MVC compared to non-RT individuals (Pearcey et al. 2014; Philpott et al. 2015), it is plausible that chronic-RT individuals have higher levels of afferent feedback, which subsequently reduce SICI. However, since we did not directly measure afferent feedback in the present study, we cannot be certain that this was the main mechanism modulating SICI.

Active motor threshold is reduced in chronic resistance-trained individuals

Another important finding of our study was that the chronic-RT group had lower AMT for MEPs of the biceps brachii during elbow flexor contractions at 15, 25 and 40% MVC than the non-RT group. However, to date, very little has been reported regarding the effects of resistance training on cortical motor threshold (CMT), including resting motor threshold (RMT) and AMT. According to the report of an International Federation of Clinical Neurophysiology, CMT including RMT and AMT is subject to intra-subject and inter-subject variations when repeatedly measured and consequently, it is of limited value to test corticospinal excitability (Groppa et al. 2012). However, the majority of neurophysiological studies report CMT and base stimulation intensities off variations of CMT. A given CMT (whether RMT or AMT) comprised a combination of mechanisms at the supraspinal and spinal levels as well as the peripheral nervous system (Di Lazzaro et al. 1998). Thus, the smaller AMT that was observed in the chronic-RT group in the current study, may be due to enhanced excitability (either by increased facilitation or decreased inhibition) anywhere along the descending corticospinal pathway. As discussed above, a reduction in intracortical inhibition observed in chronic-RT compared to non-RT individuals could be explained by a lower threshold for intracortical facilitatory circuit activation. Perhaps chronic resistance training affected the AMT in the same way; a reduced activation threshold for the interneurons responsible for facilitation of the MEP. A lower TMS intensity in the chronic-RT group may have been able to activate the intracortical facilitatory circuit and facilitate the corticospinal volley to evoke the MEP response, while in the non-RT group, a higher stimulation intensity was required to activate a similar proportion of cortical neurons to produce the target force.

We tested this hypothesis by investigating the correlation between AMT and SICI in all participants, independent of the resistance training background. The result showed a strong negative correlation between AMT and SICI during 25 and 40% MVC. Accordingly, the threshold for intracortical circuits activation could be correlated to the threshold needed to produce AMT. If this is the case, it is likely for

these two effects to be controlled by, at least in part, a common population of cortical neurons. Therefore, it is likely for the intracortical interactions to modulate AMT when the target muscle is performing a strong contraction. Potentially, with chronic resistance training, adaptative changes may occur in the intracortical network, allowing for a lower activation threshold of the intracortical facilitatory circuit.

Methodological considerations

In interpreting the aforementioned results, several methodological factors must be considered. First, although the sample size was similar to other studies investigating neurophysiological responses to resistance training (Latella et al. 2012; Weier et al. 2012; Pearcey et al. 2014; Philpott et al. 2015), a larger sample size would have provided better power for the study. Future studies should consider the variability in TMS-evoked MEPs and test more participants to ensure results are of the highest standard. Second, although most of the volunteers who participated had prior experience to the stimulation techniques and contraction intensity protocols, there were a few participants who were not completely familiar with all experimental protocols. While this could have potentially influenced the findings of this paper, we consider this to be a remote possibility given that there were individuals from both groups who were not completely familiarized, and the results were consistently different between groups. Lastly, we based our methods (i.e., stimulus intensities and ISIs) to elicit SICI from the biceps off previous papers who examined similar parameters. However, as eluded to by Goodall et al. (2018), as the field of neurophysiology continues to evolve, it is becoming more and more necessary to determine the appropriate methods to evoke SICI for each muscle, in order to optimize the true SICI response. Future work should attempt to characterize the SICI response to various contraction intensities using several CS/TS intensities and ISIs for each muscle examined.

Conclusion

In summary, regardless of resistance training background, SICI of the biceps brachii is reduced as elbow flexor force output is increased. However, chronically RT individuals show further reductions in SICI, with it being completely abolished by 40% MVC. This abolishment of SICI in the chronic-RT group may occur due to an adaptive neural process associated with training through which complex interactions between intracortical inhibitory and/or facilitatory circuits play a role. Furthermore, chronic-RT individuals also had reduced AMT at all contraction intensities compared to non-RT individuals. Reduced SICI and AMT of the biceps brachii during weak to moderate elbow flexor force outputs in chronic-RT individuals may, in part along with other mechanisms, underlie the greater absolute force production at these relative contraction intensities. We suggest that chronic resistance training leads to an adaptive neural process through the intracortical inhibitory and facilitatory circuits which can cancel out intracortical inhibition to some extent and maybe increase activation of the facilitatory circuits in the cortex during the generation of force. Future studies should determine the effect of chronic resistance training on SICF or ICF circuits.

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Compliance with ethical standards

Conflict of interest The authors declare they have no conflict of interest.

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