Training intensity-dependent increases in corticospinal but not intracortical excitability after acute strength training

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The purpose of this study was to determine whether the increases in corticospinal excitability (CSE) observed after one session of unilateral isometric strength training (ST) are related to changes in intracortical excitability measured by magnetic brain stimulation (TMS) in the trained and the contralateral untrained biceps brachii (BB) and whether such changes scale with training intensity. On three separate days, 15 healthy young men performed one ST session of 12 sets of eight isometric contractions of the right elbow flexors at 0% (control session), 25%, or 75% of the maximal voluntary contraction (MVC) in a random order. Before and after each session separated at least by 1 week, motor evoked potential (MEP) amplitude, short-interval intracortical inhibition (SICI), contralateral silent period (SP), and intracortical facilitation (ICF) generated by TMS were measured in the trained and the untrained BBs. Compared with baseline, MEPs recorded from the trained BB increased by ~47% after training at 75% of MVC ($P < .05$) but not after training at 0% (~4%) or 25% MVC (~5%, both $P > .05$). MEPs in the untrained BB and SICI, SP, and ICF in either BB did not change. Therefore, acute high-intensity but not low-intensity unilateral isometric ST increases CSE in the trained BB without modifications in intracortical inhibition or facilitation. Thus, increases in corticospinal neurons or α-α-motoneuron excitability could underlie the increases in CSE. Regardless of contraction intensity, acute isometric ST did not modify the excitability of the ipsilateral primary motor cortex measured by TMS.

KEYWORDS
cross-education, intracortical facilitation, ipsilateral M1, short-interval intracortical inhibition, silent period, strength training

1 | INTRODUCTION

Strength training (ST) is an effective means to increase maximal voluntary (MVC) force and muscle mass.1-3 The chronic increases in MVC force after ST are usually accompanied by neural adaptations at a supraspinal1,2 and spinal level.3 However, little is known about how fast such neural adaptations occur after beginning a ST program. Recent studies have shown that even just a single ST session can evoke spinal and cortical modulations4-6 as determined by electrical stimulation at the mastoid process and transcranial magnetic stimulation (TMS) over the contralateral primary motor cortex (cM1), respectively. Indeed, acute ST increased the synaptic efficacy of neural transmission in the corticospinal tract, α-motoneuron excitability, and/or cM1 excitability.5,6 Furthermore, there are indications for contraction intensity-dependent effects of ST on corticospinal excitability (CSE) measured by TMS because high vs low training
loads produced more pronounced and longer-lasting changes in neuronal excitability. However, changes in spinal excitability measured by cervicomedullary electrical stimulation did not produce such intensity-dependent effects. This suggests that cM1 is more sensitive to the intensity of muscle contraction used in acute ST compared with α-motoneurons, supporting the hypothesis that short-term neural adaptations to ST occur at the supraspinal level.

A dose-response relationship in the responses to corticospinal but not spinal stimulation following acute ST could reflect the involvement of cM1 circuits. Intracortical circuits can inhibit or facilitate the responses to TMS in cM1. Gamma aminobutyric acid (GABA) is the main inhibitory neurotransmitter in cM1, which acts mainly through interneurons with GABAa receptors, responsible for fast synaptic inhibition, and GABAb receptors, responsible for slower but longer-lasting inhibition. Both forms of inhibition can be measured with paired- and single-pulse TMS, respectively. Although both forms of inhibition are mediated by different populations of interneurons, these project to higher-threshold circuits that activate the corticospinal tract neurons, ultimately reducing cM1 excitability. Therefore, although there is still no evidence of a relationship between chronic changes in intracortical inhibition and the force of a muscle contraction, decreases in the efficacy of those inhibitory intracortical circuits can release cM1 from inhibition, increasing cM1 excitability, the efficacy of the motor command, and the drive to muscles to contract more forcefully. In fact, chronic ST tends to decrease short-interval intracortical inhibition (SICI) and silent period (SP) duration, suggesting that a release of intracortical inhibition could be one mechanism underlying the chronic increases in cM1 excitability and in the effectiveness of the motor command to increase MVC force. However, the time course of such adaptations is unclear because results from acute studies are inconsistent. In addition to reductions in SICI or SP, an increase in intracortical facilitation (ICF) could also contribute to the increase in CSE. ICF is thought to involve corticocortical pyramidal cells with glutamnergic synapses projecting to the cortical neurons that activate the corticospinal tract. However, little is known about changes in ICF after an acute session of ST, with two studies showing little or no changes.

Therefore, because spinal mechanisms cannot fully account for the changes in CSE in relation to the ST intensity, changes in intracortical circuits could be the main mechanisms modulating CSE. Indeed, contrary to what happens with CSE, which increases with contraction intensity (up to a limit), SICI tends to decrease with the intensity of the voluntary drive. We could thus expect that high-intensity compared with low-intensity ST would have a greater potential to modify intracortical circuits, accounting for the greater responses to TMS after a single session of high- vs low-intensity ST.

A unilateral voluntary muscle contraction can also activate ipsilateral brain areas. Such cross-activation could be the source of adaptations in the untrained hemisphere, underlying increases in MVC force in the untrained homologous muscle when unilateral muscle contractions are repeated for a period of at least 3 weeks. However, it is unknown whether, akin to the trained side, neural modulations in the untrained hemisphere are already present after just one session of ST, or whether more training sessions are needed for neural changes to occur. Furthermore, because the excitability of the M1 ipsilateral to the contracting muscle (iM1) increases during discrete unimanual muscle contractions in an intensity-dependent manner, we hypothesize that acute ST would also induce intensity-dependent changes in iM1 excitability.

Therefore, the purpose of the present study was to determine whether the increase in CSE after one session of ST is related to changes in SICI, SP, and ICF and whether such changes would occur in an intensity-dependent manner in the trained and the untrained biceps brachii (BB). A detailed understanding of the time course of adaption to ST and its dependency on contraction intensity has important implications for patients with neuromuscular conditions and older adults who might be unable to participate in high-intensity ST protocols.

## 2 Material and Methods

### 2.1 Participants

Healthy, right-handed, and recreationally active men (2-3 hours per week of recreational sports activities or aerobic training, age, 23.93 ± 4.65 years, n = 15) with no reported contraindications to TMS and not currently taking any medications volunteered to participate in the study. One week before the start of the experiments, participants were familiarized with peripheral nerve stimulation, TMS, and MVC protocols. Participants were asked to refrain from consuming alcoholic or caffeinated beverages and from exercising for at least 24 hours before each experimental session. The Institutional Review Board of the Catholic University of Murcia approved the protocol. Written informed consent was obtained from all participants before the start of the study. The experiments were performed in accordance with the latest version of the declaration of Helsinki.

### 2.2 Experimental procedures

Each subject completed in a random order each of the three ST sessions at 0% (control [CON]), 25%, and 75% of MVC, one intensity per session, with each session separated by 1 week. The CON session consisted of 20 minutes of rest in
the posture used in training. ST sessions consisted of 12 sets of eight isometric right elbow flexor contractions ramped to 25% or 75% of MVC over 2 seconds. After reaching the target force, participants relaxed the elbow flexors and rested for 4 seconds. There was 1 minute of rest between sets.

Before (PRE) and after (POST) each intervention, one block of measurements with TMS (single- and paired-pulse) and brachial plexus stimulation was obtained from both arms during a low-level contraction of 5% of MVC. POST measurements started always in the left arm around 30 seconds after the last training set. Each block of measurement consisted of eight maximal compound muscle action potentials (M_max), 20 single-pulse motor evoked potentials (MEPs), and 40 paired-pulse stimulations (20 for SICI and 20 for ICF). All stimuli were separated by 5, and 30 seconds of rest was given after 15 pulses to avoid fatigue, so each block lasted for ~7 minutes. Additionally, five single-pulse MEPs at 120% of active motor threshold (MEP25%/M_max) and its respective SP were obtained in both BBs during 3-second-long contractions at 25% of MVC immediately before training or control period and at POST (approximately 10-15 minutes after training or control period ended; see Figure 1). Single-pulse stimulation during 25% vs 5% of MVC contractions allowed us to obtain clearer silent periods.

Before measurements, participants performed three MVCs with each arm separately. MVCs lasted for 3 seconds with 120 seconds of rest between trials. The posture during MVC tests and main measurements was identical. All trials were measured with two force transducers (NeuroLog System, Digitimer) firmly attached to the left or right wrist with a rigid strap. The highest MVC in each arm was used to determine the subsequent target force during measurements (5% and 25% of MVC) and training (25% or 75% of MVC).

2.3 Setup

During testing, participants sat in a chair in front of a table with both shoulders flexed at 90° and the elbows flexed with forearms supinated and vertical (Figure 1). In this position, both forearms were fastened with a rigid strap to a force transducer (NL63-200 Kg; Digitimer) to measure voluntary force, which was displayed on a computer monitor in front of the participants.

Surface electromyography (EMG) was recorded from the right and left BB with Ag-AgCl surface electrodes in a belly-tendon montage (5-8 cm interelectrode distance). EMG was amplified (×200 or ×300 depending on the M_max amplitude), band-pass–filtered (10-1000 Hz), and sampled (2 kHz) with a Digitimer d440 isolated amplifier (Digitimer). Force recordings were band-pass–filtered (5-2500 Hz), amplified (×2500), and sampled at 2 kHz using a NeuroLog System (Digitimer). Both EMG and force recordings were simultaneously collected using an analog-digital board CED Micro1401-3 (Cambridge Electronic Design) for further analysis.

2.4 Brachial plexus stimulation

For recording the M_max in each BB, single-pulse stimulation (200 µs duration) was delivered to the brachial plexus with a DS7AH constant current electrical stimulator (Digitimer). The cathode (pre-gelled Ag-AgCl electrodes) was positioned in the supraclavicular fossa and the anode on the acromion. After defining the stimulation intensity needed to evoke the M_max in each BB, the intensity was set to 120% of this value for the measurements (range: 42-186 mA).

2.5 Transcranial magnetic stimulation

Single- and paired-pulse TMS was delivered to left (cM1) and right (iM1) motor cortices with a figure of eight coils (70 mm diameter) connected to two DuoMAG (Rogue Resolutions Ltd.) magnetic stimulators. The coil was oriented with the handle at ~45° posterolaterally to the midline, and the optimal stimulation location in each M1 was obtained by exploring the estimated center of the BB motor cortical representation. The point where stimulation produced the largest MEP in the contralateral BB was marked directly on the scalp with a permanent marker. Active motor threshold (AMT) was defined as the lowest stimulation intensity needed to obtain three out of five MEPs of a peak-to-peak amplitude >200 µV during a 5% MVC force, displayed as target on the monitor in front of the participant. To measure SICI and ICF, a paired-pulse protocol was used in which the conditioning pulse (CS) and the test pulse (TS) set at 80% and 120% of the AMT, respectively. The interstimulus interval was set to 3 ms (SICI) and 10 ms (ICF).

2.6 Data analysis

The peak-to-peak amplitudes of M_max and MEPs were measured. MEP amplitudes were normalized to M_max within each measurement block and averaged (MEP_5%/M_max and MEP_25%/M_max). Pre-stimulus rmsEMG activity was determined in a 150-ms window prior to each electrical or magnetic stimulus. Trials with rmsEMG larger or lower than the mean of each measurement block ±2 SDs were removed from the analysis. The SP duration was quantified as the time between the stimulus and the time at which the post-stimulus EMG returned to the 50% of the mean of the pre-stimulus (150-ms time window) background EMG activity.23
All data were first screened for normality using a Kolmogorov-Smirnov test. Intersession reliability of baseline \( M_{\text{max}} \), single-, and paired-pulse TMS responses across sessions was determined using intraclass correlation coefficients (ICC (2, 1) two-way mixed effect model) with 95% confidence intervals (95% CIs). The ICC was interpreted with values below 0.5 indicating low reliability, values between 0.5 and 0.75 indicating moderate reliability, values between 0.75 and 0.9 indicating good reliability, and values higher than 0.90 indicating excellent reliability. Then, a two-way repeated measures analysis of variance (RM-ANOVA) was performed with TIME (PRE and POST) and INTENSITY (CON, 25%, and 75%) as factors for pre-stimulus rmsEMG, \( M_{\text{max}} \), MEP\(_{5\%}/M_{\text{max}} \), MEP\(_{25\%}/M_{\text{max}} \), SP, SICI, and ICF. Limb was not included as a factor in the ANOVA because post-measurements in the trained and the untrained were not simultaneous (immediately after vs ~7 minutes after, respectively). If sphericity was violated (Mauchly’s test), degrees of freedom were corrected by Greenhouse-Geisser estimates of sphericity. When a nonsignificant main effect or interaction had a medium ES (\( \eta^2_p > 0.13 \)), paired comparisons and Cohen’s \( d \) effect sizes were also computed. Effect sizes are presented as partial eta-square values (\( \eta^2_p \); small: 0.02; medium: 0.13; large: 0.26). Unless indicated otherwise, data are reported as mean ± standard deviation. SPSS 20.0 software (SPSS) was used for statistical analysis. Statistical significance was set at \( P \leq .05 \).

3 | RESULTS

3.1 | Reliability

Intersession reliability for \( M_{\text{max}} \), MEP\(_{5\%}/M_{\text{max}} \), SICI (%TS), ICF (%TS), SP, and MEP\(_{25\%}/M_{\text{max}} \) was good to excellent (ICC = 0.79-0.94, Table 1) in the trained and the untrained BB.

3.2 | Trained side

One subject was excluded from the statistical analysis only for the SICI variable because a consistent facilitation of more than 40% in both BBs. Pre-stimulus rmsEMG remained constant during all training sessions (See Table 2 in supporting information). MEP\(_{5\%}/M_{\text{max}} \) amplitudes increased by +46.7%
A single session of ST increases the responses to corticospinal tract stimulation at rest or during low-level isometric contractions suggesting increases in cortical or α-motoneuron excitability or an increased efficacy of the corticospinal-motoneuronal synapse. Our results are in line with previous studies by showing ~47% increase in CSE measured at 5% background MVC in the BB of the trained arm only after ST at 75% MVC. The present data confirm the previously described effect of intensity by showing a 75%—MVC intensity—threshold of acute ST to produce meaningful changes in CSE, suggesting that training intensity is a determinant of acute corticospinal plasticity in response to a bout of isometric ST.

Although the coil of TMS is placed over the cM1, the response to single-pulse TMS is not only affected by cortical neuron excitability. Single-pulse TMS reflects the excitability of corticospinal neurons and interneurons projecting onto these neurons in M1 as well as the excitability of α-motoneurons in the spinal cord, the neuromuscular junctions, and the muscle. Therefore, an increase in CSE measured by TMS could be due to changes at any or all of these structures. However, spinal mechanisms are unlikely to mediate the increases in CSE after acute ST. Previous studies showed that ST intensity affected CSE but not spinal excitability measured by cervicomedullary electrical stimulation. Furthermore, increases in corticospinal transmission and/or α-motoneuron excitability after acute ST are not always present. For that reason, mechanisms other than spinal changes were proposed to explain the increases in CSE after acute ST. Increases in corticospinal neuron excitability or reductions in the efficacy of the intracortical inhibitory circuits can both increase the efficacy of the excitatory input to α-motoneurones thereby increasing the response to TMS. However, we found no reductions in GABAa or GABAb receptor–mediated cortical inhibition.

Although two-way RM-ANOVA revealed a nonsignificant interaction between factors for SICI (Pre = .09, $\eta^2_p = 0.17$), paired comparisons showed a small increase in SICI (ie, reduced CS/TS ratio) after 75% of MVC ST session (from 76.8% to 69.1% of TS, Pre = .01, ES = −0.26, 95.0% CI = −0.41, −0.13). This small increase in SICI after high-intensity acute ST could be related to a methodological issue, that is, the test pulse MEP size. The amount of inhibition increases with increasing test pulse MEP size. Because we used PRE

### TABLE 1

<table>
<thead>
<tr>
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<th>Trained intersession ICC (95% CI)</th>
<th>Untrained intersession ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$M_{\text{max}}$</td>
<td>0.90 (0.77, 0.96)</td>
<td>0.83 (0.60, 0.94)</td>
</tr>
<tr>
<td>$\text{MEP}<em>{25}/M</em>{\text{max}}$</td>
<td>0.80 (0.52, 0.90)</td>
<td>0.82 (0.56, 0.93)</td>
</tr>
<tr>
<td>SICI (%)TS</td>
<td>0.82 (0.58, 0.93)</td>
<td>0.94 (0.85, 0.98)</td>
</tr>
<tr>
<td>ICF (%)TS</td>
<td>0.86 (0.66, 0.95)</td>
<td>0.85 (0.64, 0.94)</td>
</tr>
<tr>
<td>SP</td>
<td>0.79 (0.52, 0.92)</td>
<td>0.89 (0.73, 0.96)</td>
</tr>
<tr>
<td>$\text{MEP}<em>{25}/M</em>{\text{max}}$</td>
<td>0.91 (0.78, 0.97)</td>
<td>0.92 (0.82, 0.97)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confident interval; ICC, intraclass correlation coefficient; ICF, intracortical facilitation; MEP, motor evoked potential; $M_{\text{max}}$, maximal compound muscle action potential; SICI, short-interval intracortical inhibition; SP, silent period.

(P = .04, ES = 0.43, 95% CI = 0.31, 0.58) only after ST at 75% MVC but not after ST at 25% MVC (+4.8%, $P = .44$, ES = 0.08, 95% CI = −0.18, 0.25) or CON (+4.4%, $P = .76$, ES = 0.04, 95% CI = −0.38, 0.36; Figure 2). Baseline (PRE) MEP5%/Mmax amplitudes were equal between sessions (CON vs 25% $P = .46$, CON vs 75% $P = .99$, 25% vs 75% $P = .19$); however, training at 75% of MVC produced higher post-training MEP5%/Mmax amplitudes than the CON session ($P = .04$, ES = 0.32, 95% CI = −0.01, 0.77) and revealed a trend toward significance compared with 25% session ($P = .06$, ES = 0.54, 95% CI = 0.29, 0.87).

A single session of ST at 0%, 25%, and 75% MVC did not affect MEP25%/Mmax, SP, ICF, and $M_{\text{max}}$ (Table 2 in supporting information). However, although RM-ANOVA did not show significant effects or interactions for SICI, there was a medium effect size for the Time*Session interaction ($P = .09$, $\eta^2_p = 0.17$) that revealed a small increase in SICI after the 75% of MVC ST session (from 76.8% to 69.1% of TS, $P = .01$, ES = −0.26, 95.0% CI = −0.41, −0.13).

### 3.3 Untrained side

Pre-stimulus rmsEMG remained constant during all training sessions (See Table 3 in supporting information). A single session of ST at 0%, 25%, or 75% MVC did not modify MEP5%/Mmax, MEP25%/Mmax, SP, SICI, ICF, and $M_{\text{max}}$ in the untrained BB (Table 3 in supporting information).

### 4 DISCUSSION

We determined the effects of acute unilateral isometric ST of the right elbow flexors at 0%, 25%, and 75% MVC on CSE, SICI, ICF, and SP in the trained and untrained arms. Only acute ST training at 75% MVC did increase CSE in the trained BB measured during a 5% background MVC. Contrary to the hypothesis, the increases in CSE were not accompanied by a decline in intracortical inhibition or an increase in intracortical facilitation. The effects of a single session of ST at 0%, 25%, and 75% MVC were limb-specific, as no changes occurred in any of the TMS measures obtained in iM1.

### 4.1 Trained side

A single session of ST increases the responses to corticospinal tract stimulation at rest or during low-level isometric contractions suggesting increases in cortical or α-motoneuron excitability or an increased efficacy of the corticospinal-motoneuronal synapse. Our results are in line with previous studies by showing ~47% increase in CSE measured at 5% background MVC in the BB of the trained arm only after ST at 75% MVC. The present data confirm the previously described effect of intensity by showing a 75%—MVC intensity—threshold of acute ST to produce meaningful changes in CSE, suggesting that training intensity is a determinant of acute corticospinal plasticity in response to a bout of isometric ST.

Despite the use of a single session of ST, we observed a small increase in SICI after high-intensity acute ST. Although two-way RM-ANOVA revealed a nonsignificant interaction between factors for SICI ($P = .09$, $\eta^2_p = 0.17$), paired comparisons showed a small increase in SICI (ie, reduced CS/TS ratio) after 75% of MVC ST session (from 76.8% to 69.1% of TS, $P = .01$, ES = −0.26, 95.0% CI = −0.41, −0.13). This small increase in SICI after high-intensity acute ST could be related to a methodological issue, that is, the test pulse MEP size. The amount of inhibition increases with increasing test pulse MEP size. Because we used PRE
stimulation intensity during the POST measurements, the increase in the test pulse MEP size after high-intensity ST could have led to the slight, nonsignificant increase in SICI. Although this could be viewed as a limitation, the efficacy of SICI is related to the population of cortical circuits activated by the test pulse. The variable that determines which circuits are activated by TMS is the stimulation intensity and not changes in excitability. Therefore, reductions in stimulation intensity to adjust the test pulse size after a ST session could act as a confounding factor by affecting the cortical circuits activated the test stimulus and reducing the estimates of SICI because of a higher contribution of early indirect waves to the MEP, which are less affected by intracortical inhibition. Future studies should include both approaches (adjusted and not adjusted test pulse size) to further understand the effects of an acute ST session on SICI. Notwithstanding, the small increases in SICI in the present study partially agree with those in the acute ST characteristics such as intensity, level of peripheral fatigue, the type of contraction or the strategy of pacing the movement, or even the volume of exercise.

Therefore, combined results from the present and past studies suggest that spinal mechanisms or changes in intracortical circuits are not the main mechanisms underlying the acute increase in CSE after an acute bout of ST. Then, it is likely that the increases in the net excitatory output from cM1 to the muscle after an acute bout of ST are related to changes in the membrane excitability of the corticospinal neurons receiving input from the corticocortical neurons activated by the single-pulse TMS.

A methodological difference between the present and past studies is that we measured corticospinal changes at 5% or 25% background MVC and not at rest. Measuring responses to TMS during contraction represents more faithfully the adaptations that occur during training compared with the same measures obtained at rest. The increased MEP size after training during contraction could thus reflect plasticity associated with the task unlike the CSE measured at rest. Nevertheless, we found that a session of high-intensity but not low-intensity ST increased the CSE of the trained arm when measured during 5% of MVC contractions to a similar extent as when CSE was measured at rest in previous studies (+47% during contraction vs +76% at rest). The differences in the magnitude of change between both studies could be related to differences in the size of the baseline MEPs (7.05% of \( M_{\text{MAX}} \) vs. 4.57% of \( M_{\text{MAX}} \)). However, in both studies the absolute increase was similar (to a 10% vs to a 8% of \( M_{\text{MAX}} \)). This suggests that the increased responses to TMS after training have not become more facilitated by the muscle contraction compared with rest, suggesting that acute changes after ST occurred in the intrinsic properties of the cortical neurons that could be already measured at rest. Nevertheless, we did not find any increases in CSE when measured during 25% of MVC contractions. MEP size in BB tends to be progressively facilitated up to a 40%-50% of MVC. However, independent of contraction intensity, MEP size tends to peak at an amplitude around 60%-70% of \( M_{\text{MAX}} \). Therefore, a lack of change in MEPs during 25% of MVC after the high-intensity ST session could be related to the high baseline size of MEPs (~50%). The fact that baseline MEPs were already close to its maximum means that single-pulse TMS before training already recruited almost all of the excitable cortical neurons, limiting the scope for further increases. Also, because measurements were obtained during contractions, it is unknown whether spinal changes would have behaved in a similar manner as at rest.

Therefore, a direct comparison with previous studies is not possible and we cannot discard a concomitant increase in \( \alpha \)-motoneuron excitability contributing to the increase in CSE after high-intensity acute ST seen here. However, short-term ST periods have failed to produce adaptations at
the spinal level measured by cervicomedular electrical stimulation and H reflexes. This strengthens the support for the hypothesis that short-term increases in α-motoneuron discharge rate that lead to increases in MVC force are mediated by increases in the net excitatory input to the α-motoneuron pool from supraspinal centers.

Because we did not measure MVC force after ST, we cannot discard the possibility that fatigue has influenced our results. However, there is indirect evidence to suggest that fatigue was low or altogether absent. For example, we found no changes in the pre-stimulus rmsEMG, suggesting that any increase in neural drive was needed to maintain the force output as a consequence of reductions in muscle or α-motoneuron excitability. Also, in a previous study with an identical training, resting $M_{\text{max}}$-associated twitch forces did not decrease during the 30 minutes after the intervention, suggesting that there were no reductions in muscle contractile properties as a consequence of fatigue. Another factor that can potentially influence our results is central fatigue. The best indicator for the assessment of central fatigue is voluntary activation. Unfortunately, we did not measure voluntary activation in this study. However, as intracortical inhibition did not increase, we assume that central fatigue was low or altogether absent.
4.2 | Untrained side

The central nervous system adapts quickly to motor practice in the trained and the untrained muscle. Therefore, several studies have examined whether the acute changes occurring after a single session of unilateral ST in the trained hemisphere would also occur in ipsilateral, untrained brain structures. Notwithstanding, results from those studies are contradictory, with one study showing increases in CSE and reductions in SICI after a session of dynamic ST, whereas another study reported no effects of an acute unilateral isometric ST session on CSE, SICI, ICF, and IHI of the untrained hemisphere. Our results agree with these latter data, showing no effects of a single session of isometric unilateral ST of the elbow flexors on TMS outcomes in iM1. Furthermore, despite cross-sectional studies demonstrating that iM1 excitability increases and intracortical inhibition decreases more during high- compared with low-intensity contractions, our results revealed no intensity effects on the responses to TMS in iM1 after a single session of unilateral isometric ST.

Discrepancies between the effects of a session of unilateral ST on iM1 could be related to the type of contractions used during training. Eccentric compared with concentric contractions activate iM1 more strongly. This higher cross-activation is probably a consequence of the greater neural resources needed for programming and planning eccentric compared with static or concentric contractions, or related to inhibitory and facilitatory influences from the dorsal premotor and posterior parietal cortices in the cM1 and iM1. Another important aspect with regard to cross-activation is the intensity of a contraction. It is known that contractions need to be at moderate-high intensity to result in cross-activation of the ipsilateral hemisphere. The slowly ramped isometric contractions used in the current study result in relatively short periods of contractions at moderate-high intensity (>50% MVC). These short periods at moderate-high intensity might in turn have resulted in limited cross-activation during the contractions, reducing the scope for modulation of the corticospinal tract projecting to the untrained BB. Therefore, the absence of changes in iM1 after a unilateral isometric ST session could be related to an insufficient level of cross-activation during progressive isometric contractions, compared with unilateral dynamic ST mixing high-intensity eccentric and concentric contractions.

Therefore, although iM1 adaptations occur after chronic periods of ST, even with isometric contractions, the time course of those adaptations is longer than a single session, even if the intensity of ST is high. Indeed, previous studies showed that interlimb transfer of voluntary force and correlated increases in iM1 excitability to occur might require at least 10 sessions or 500 isometric contractions. Therefore, it is not possible to infer the long-term effectiveness of different ST configurations (ie, intensity and volume) based on the effects of just one session of ST. Consequently, longitudinal studies will be needed to determine the effectiveness of different ST configurations on iM1 plasticity. Furthermore, acute and chronic changes may occur in other ipsilateral structures that single-coil TMS cannot probe that are also bilaterally activated during unilateral contractions, such as supplementary motor area, sensory regions, prefrontal, premotor, cingulate, and parietal cortices, or cerebellum.

5 | CONCLUSIONS

High- but not low-intensity isometric ST of the elbow flexors increased CSE in the BB when measured at a background MVC of 5%. However, such increases were not accompanied by decreases in intracortical inhibition or increases in intracortical facilitation. These results suggest that increases in corticospinal neurons or α-motoneuron excitability are the main mechanisms underlying the increases in CSE. In contrast, no effects on CSE and intracortical circuitry occurred in the untrained hemisphere, suggesting that more than one session of unilateral isometric ST is needed to evoke adaptations in the untrained corticospinal tract independent of training intensity.

6 | PERSPECTIVES

Peripheral and neural adaptations to ST have different time courses. Adaptations in the central nervous system usually precede changes in the muscle and tend to underlie most of the early gains in MVC force. Therefore, it is important for coaches training healthy individuals and also patients with neuromuscular conditions or older adults, to know how modifications in training variables, such as training intensity, could affect early adaptations to ST. We show that training intensity is a key determinant of the acute increases in cortical or α-motoneuron excitability occurring in the early stages of training, which could explain the better effectiveness of chronic high-intensity ST in producing MVC force increases. However, just one session of unilateral isometric ST does not lead to acute changes in the iM1.

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CONFLICT OF INTEREST

None of the authors declare conflict of interest.

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REFERENCES


**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

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