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**Author(s):** Mason, Joel; Frazer, Ashlyn K.; Avela, Janne; Pearce, Alan J.; Howatson, Glyn; Kidgell, Dawson J.

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2 **Tracking the corticospinal responses to strength training**  
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6 Joel Mason<sup>1</sup>, Ashlyn K Frazer<sup>1</sup>, Janne Avela<sup>2</sup>, Alan J. Pearce<sup>3</sup>,  
7 Glyn Howatson<sup>4,5</sup>, and Dawson J Kidgell,<sup>1</sup>  
8  
9

10 <sup>1</sup>Department of Physiotherapy, School of Primary Health Care, Faculty of Medicine, Nursing and  
11 Health Sciences, Monash University, Melbourne, Australia.  
12

13  
14 <sup>2</sup>Faculty of Sport and Health Sciences, Neuromuscular Research Centre, University of Jyväskylä,  
15 Jyväskylä, Finland.

16 <sup>3</sup>College of Science, Health and Engineering, School of Allied Health, La Trobe University,  
17 Melbourne, Australia  
18

19  
20 <sup>4</sup>Faculty of Health and Life Sciences, Northumbria University, Newcastle-upon-Tyne, UK.  
21

22  
23 <sup>5</sup>Water Research Group, School of Environmental Sciences and Development, Northwest  
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34 **\*Corresponding author:**

35 Dr Dawson J Kidgell, PhD

36 Department of Physiotherapy, School of Primary and Allied Health Care, Faculty of Medicine,  
37 Nursing and Health Science, Monash University, PO Box 527 Frankston, Victoria, Australia, 3199.

38 Email: [dawson.kidgell@monash.edu](mailto:dawson.kidgell@monash.edu)  
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49 **Abstract**

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**Purpose:** The motor cortex (M1) appears to be a primary site of adaptation following both a single session, and repeated strength-training sessions across multiple weeks. Given that a single session of strength-training is sufficient to induce modification at the level of the M1 and corticospinal tract, this study sought to determine how these acute changes in M1 and corticospinal tract might accumulate across the course of a two-week heavy-load strength-training program.

**Methods:** Transcranial magnetic stimulation (TMS) was used to infer corticospinal excitability (CSE), intracortical facilitation (ICF), short and long-interval intracortical inhibition (SICI and LICI) and silent period duration prior to and following each training session during a two-week heavy-load strength-training period.

**Results:** Following two-weeks of strength-training, increases in strength (15.5%,  $P = 0.01$ ) were accompanied by an increase in CSE (44%,  $P = 0.006$ ) and reductions in both silent period duration (14%,  $P < 0.0001$ ) and SICI (35%,  $P = 0.0004$ ). Early training sessions acutely increased CSE and ICF, and acutely reduced silent period duration and SICI. However, later training sessions failed to modulate SICI and ICF, with substantial adaptations occurring offline between training sessions. No acute or retained changes in LICI were observed. Co-contraction of antagonists reduced by 36% following two-weeks of strength-training.

**Conclusions:** Collectively, these results indicate that corticospinal plasticity occurs within and between training sessions throughout a training period in distinct early and later stages that are modulated by separate mechanisms of plasticity. The development of strength is akin to the previously reported changes that occur following motor skill training.

**Keywords** Corticospinal excitability · Cortical plasticity · Intracortical facilitation · Short-interval cortical inhibition · Silent period · Strength training

94  
95 **ABBREVIATIONS**  
96  
97 **1-RM:** One-repetition maximum  
98 **AURC:** Area under the recruitment curve  
99 **AMT:** Active motor threshold  
100 **CSE:** Corticospinal excitability  
101 **CI:** Confidence interval  
102 **SD:** Standard deviation  
103 **ECR:** Extensor carpi radialis  
104 **EMG:** Electromyography  
105 **FCR:** Flexor carpi radialis  
106 **GABA:**  $\gamma$ -Aminobutyric acid  
107 **ICF:** Intracortical facilitation  
108 **LICI:** Long-interval cortical inhibition  
109 **MEP:** Motor-evoked potential  
110 **M<sub>MAX</sub>:** Maximal compound wave  
111 **MVIC:** Maximal voluntary isometric contraction  
112 **M1:** Primary motor cortex  
113 **rmsEMG:** Root-mean-square electromyography  
114 **RMT:** Resting motor threshold  
115 **sEMG:** Surface electromyography  
116 **SICI:** Short-interval cortical inhibition  
117 **SP:** Silent period  
118 **TMS:** Transcranial magnetic stimulation  
119 **rTMS:** Repetitive transcranial magnetic stimulation

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**Introduction**

Adaptations within the central nervous system (CNS) underlie training-induced improvements in motor performance. These adaptations commence as early as a single session of training and continue to change between training sessions, due to neural mechanisms associated with use-dependent cortical plasticity (Dayan and Cohen 2011). Use-dependent plasticity has been well studied in the context of skill acquisition (Mawase et al. 2017; Dayan and Cohen 2011), but is relatively lacking in the context of strength development. The process of acquiring a new motor skill has been linked to functional modifications in the intrinsic micro-circuitry of the primary motor cortex (M1), which include the expansion of motor representations (Monfils et al. 2005), the strengthening of existing (Riout-Pedotti et al. 1998; Riout-Pedotti et al. 2000) and the formation of new synapses (Kleim et al. 2004; Taube 2011). Importantly, early improvements in motor skill performance are rapid, and there are distinct mechanisms of cortical plasticity that are associated with the early and late stages of skill acquisition (Karni et al. 1998; Floyer-Lea and Matthews 2005; Dayan and Cohen 2011).

Although not as well examined as the motor learning literature, strength training can lead to rapid and substantial improvements in the ability to produce muscular force (Guizelini et al. 2018). Such increases in the force-generating capacity of the trained muscles are accompanied by changes in the excitability of the intrinsic micro-circuitry of the M1 due to use-dependant mechanisms (Kidgell et al. 2017). Although the rapid development of muscular strength is thought to occur as a result of changes in the CNS (Folland and Williams 2007; Duchateau and Enoka, 2002; Weier et al. 2012), the time-course, specific locus and mechanism of adaptation are poorly understood (Kidgell et al. 2017). Training-induced adaptations are reported to include reduced co-activation of antagonist muscles (Carolan and Cafarelli 1992), increased motoneurone excitability, revealed by increased H-reflexes and V-waves (Aagard et al. 2002) and alterations in motor unit behaviour (Kamen and Knight 2004; Del Vecchio et al. 2019). Many of these changes are reported to have a supraspinal influence that implicate the role of cortical plasticity in strength development (Kidgell et al. 2017).

Over last 30 years, transcranial magnetic stimulation (TMS) has been used as a technique to examine the acute and training-related effects of motor training on cortical plasticity. Single- and paired-pulse TMS can quantify cortical plasticity by inferring corticospinal excitability (CSE) through the measurement of the motor-evoked potential (MEP) and intracortical facilitation (ICF), as well as corticospinal inhibition (via the silent period duration) and intracortical inhibition (short and long-latency intracortical inhibition; SICI and LICI, respectively) (Di Lazzaro and Rothwell 2014). Changes in these TMS-evoked responses are regarded as indicators of cortical plasticity confined to the M1. Experimental evidence showed that strength training performed over three to four weeks either increased CSE (Griffin and Cafarelli 2007; Goodwill et al. 2012; Kidgell et al. 2010; Kidgell et

174 al. 2011; Weier et al. 2012; Pearce et al. 2013; Leung et al. 2015; Mason et al. 2017), decreased CSE  
175 (Carroll et al. 2002; Coombs et al. 2016; Jensen et al. 2005; Lee et al. 2009), and reduced the silent  
176 period duration (Kidgell and Pearce 2010; Coombs et al. 2016; Mason et al. 2017; Latella et al. 2012).  
177 Although these findings are mixed, a recent systematic review concluded that short-term strength  
178 training increases CSE, reduces the duration of the silent period and reduces SICI (Kidgell et al.  
179 2017). This suggest that use-dependent adaptations within the M1 support improvements in muscular  
180 strength. It is possible that the training-related responses following multiple weeks of strength training  
181 are simply the culmination of single training sessions. Hortobágyi et al. (2009) used TMS throughout  
182 a four-week strength training program to determine the effect of strength training on M1 plasticity. In  
183 this study, after every strength training session, real or sham repetitive transcranial magnetic  
184 stimulation (rTMS) was applied over the M1. Interestingly, when the M1 was disrupted via rTMS  
185 after each session, cumulative strength gains were diminished (Hortobágyi et al. 2009). Importantly,  
186 the diminished gain in strength was associated with reduced M1 plasticity. These data suggests that  
187 each individual strength training session plays a critical role in the process of acquiring strength, but  
188 also directly associates cortical plasticity with strength gains. Therefore, it is conceivable that a  
189 summation of the M1 responses could accrue from each session to the next; ultimately generating  
190 improvements in muscle strength. Therefore, the previously unexplored idea of tracking the cortical  
191 responses session by session might reveal a more detailed time-course of the neural adaptations to  
192 strength training.

193  
194 Theoretical frameworks for early and late phases of cortical plasticity have been established for the  
195 acquisition of motor skills (Dayan and Cohen 2011; Karni et al. 1998; Rosenkranz et al. 2007; Kleim  
196 et al. 2006; Floyer-Lea and Matthews 2005), which aid in the appropriate prescription and scheduling  
197 of skill-based training. However, no such frameworks are available for strength training. The  
198 establishment of similar frameworks identifying the cortical responses that shape the acquisition and  
199 consolidation of muscular strength would allow practitioners to prescribe training that directly and  
200 appropriately targets these underlying mechanisms in order to maintain and improve human health  
201 and performance. Therefore, the primary aim of this study was to track the progressive M1 responses  
202 prior to and following every strength-training session throughout a two-week strength-training period.  
203 It was hypothesised that as strength would increase throughout the training period, the acute  
204 excitatory and inhibitory responses (CSE, ICF, silent period, SICI and LICI) would accumulate within  
205 each session, leading to changes in M1 plasticity due mechanisms associated with use-dependent  
206 plasticity.

207

## 208 **Methods**

209

### 210 *Study Design and Participants*

211 Participants were randomly allocated to a control or experimental group that completed supervised  
212 heavy-load strength training of the wrist flexors, three times per week for two-weeks (Figure 1). All  
213 participants provided written informed consent prior to participation. Eighteen healthy individuals (8  
214 female, 10 male, aged  $23.45 \pm 4.2$ ) were selected on a voluntary basis and all experiments were  
215 conducted according to the standards established by the Declaration of Helsinki, and the project was  
216 approved by the Monash University Human Research Ethics Committee (MUHREC 11882). All  
217 participants were right handed according to the Edinburgh Handedness Inventory (Oldfield 1971) with  
218 a laterality quotient  $>85$ , were free from peripheral and neurological impairment, and had not  
219 participated in strength training for a period of twelve months prior to the commencement of the  
220 study. All participants were recruited from the University population and were required to complete  
221 an adult safety-screening questionnaire to determine their suitability for TMS (Keel et al. 2011).

222

### 223 *Experimental approach*

224 Participants attended a familiarisation session one-week prior to the commencement of baseline  
225 testing that involved one-repetition maximum strength testing (1-RM) of the wrist flexors, exposure  
226 to single-pulse and paired-pulse TMS, and peripheral nerve stimulation. Following randomisation,  
227 participants were allocated to either a strength-training group or a non-training control group. The  
228 experimental condition involved heavy-load isotonic strength-training of the right wrist flexors  
229 (dominant limb) six times over the course of two weeks, with at least 48 hours rest in between  
230 training sessions. Prior to and sixty seconds immediately after the cessation of each strength-training  
231 session, measures of motor cortical and corticospinal responses using TMS were obtained. A  
232 retention session including all assessments was completed  $\sim 72$  hours following the completion of the  
233 training intervention, and strength measurements were taken at baseline, following one week of  
234 training and following two weeks of training. The control group followed an identical protocol to the  
235 strength-training group, including frequency and volume of visits to the laboratory, pre- and post-  
236 session TMS testing, a retention session and strength testing. However, instead of heavy-load  
237 strength training, the control group sat quietly at rest for fifteen minutes.

238

### 239 *Voluntary strength testing*

240 Participants performed a standard unilateral one-repetition maximum (1-RM) strength test for the  
241 right wrist flexor at baseline, after three training sessions and following six training sessions and at  
242 retention (72 h following the sixth training session). Participants were seated in the isokinetic  
243 dynamometer, shoulders relaxed and elbow flexed at 90 degrees, with the forearm supinated and  
244 fastened firmly on the arm rest. The dynamometer attachment was removed and a weighted dumbbell  
245 was used to allow for a more sensitive and functional measure of dynamic strength. The wrist was  
246 positioned such that the styloid process sat just beyond the edge of the arm rest, and the relaxed hand

247 hung free in a supinated position. The researcher placed the dumbbell in each participant's hand and  
248 instructed them to grasp the dumbbell and completely flex the wrist, moving the hand upward. The  
249 exact same procedures were used for TMS positions, the strength training protocol, and for strength  
250 testing of the ECR, however, the forearm was pronated in the case of the latter. Following a warm-up,  
251 participants were asked what they considered their 1-RM to be, and this weight served as the starting  
252 point for 1-RM establishment. If the trial was successful, the weight of the dumbbell was increased  
253 accordingly (0.25-0.5 kg increments). This procedure continued until the subject could no longer  
254 complete one repetition, and their prior successful trial served as their 1-RM wrist flexor and extensor  
255 strength (Kidgell et al. 2011) and was subsequently used to calculate the intensity for subsequent  
256 training. Following each trial, subjects were given 3-mins recovery to minimise the development of  
257 muscular fatigue (Kidgell et al. 2011), and typically needed three to five trials to achieve their 1-RM  
258 strength.

259

### 260 ***Strength training protocol***

261 Participants performed supervised, loaded unilateral wrist flexion and extension through 20 degrees,  
262 with 0 degrees being the anatomical position, of the dominant arm monitored by a metronome (2 s  
263 concentric; 4 s eccentric; Kidgell et al. 2011) and electromagnetic goniometer (ADInstruments, Bella  
264 Vista, Australia). Participants completed four sets of 6-8 repetitions at 80% of their 1-RM, with 2.5  
265 min rest between sets. The principle of progressive overload was employed throughout the training  
266 period to maximise the training response. Specifically, when participants could complete four sets of  
267 eight repetitions, at the beginning of the next training session, the training weight (kg) was increased  
268 by 0.5kg. Control participants sat quietly at rest for 15 minutes, matching the time for strength-  
269 training completion in the intervention group.

270

### 271 ***Surface electromyography (sEMG)***

272 The area of electrode placement was shaven to remove fine hair, rubbed with an abrasive skin gel to  
273 remove dead skin, and then cleaned with 70% isopropyl alcohol. Surface electromyography (sEMG)  
274 was recorded from the right flexor carpi radialis (FCR) muscle using bipolar Ag-AgCl electrodes. As  
275 described by Selveanayagam et al. (2011) the electrodes for the FCR were positioned 9 cm from the  
276 medial epicondyle of the humerus with an inter-electrode distance (center to center) of 2 cm. As  
277 antagonist co-activation data was also collected, extensor carpi radialis (ECR) electrodes were  
278 positioned at 45% of the distance from the medial epicondyle of the humerus to the radial styloid  
279 process with an inter-electrode distance of 2 cm. A grounding strap was placed around the wrist as the  
280 common reference point for all electrodes. sEMG signals were amplified ( $\times 1,000$ ), band pass filtered  
281 (high pass at 13 Hz, low pass at 1,000 Hz), digitized online at 2 kHz, recorded (1 s), and analyzed  
282 using Power Lab 4/35 (ADInstruments, Bella Vista, Australia). The sEMG was used to record the test



283 and conditioned MEPs obtained during TMS prior to and following each training session throughout  
284 the two-week period and at retention 72 h following the intervention. sEMG was also used during the  
285 strength-training bout to provide an estimation of antagonist co-contraction.

286

### 287 *Transcranial magnetic stimulation*

288 During each testing session, TMS was delivered using two Magstim 200<sup>2</sup> stimulators (Magstim Co.,  
289 UK) to produce motor evoked potentials (MEPs) in the active FCR via a figure-8 coil. The motor  
290 hotspot for the FCR (with posterior-to-anterior-induced current flow in the cortex) was determined  
291 and resting motor threshold (RMT) and active motor threshold (AMT) were then established as the  
292 stimulus intensity at which at least five of ten stimuli produced MEP amplitudes of greater than 50  $\mu$ V  
293 for RMT and greater than 200  $\mu$ V for AMT (Rossini et al. 1999). Prior to and following each session  
294 throughout the strength-training intervention, RMT and AMT were retested and adjusted if required.  
295 To ensure that all stimuli were delivered to the optimal motor hotspots throughout testing, participants  
296 wore a tight-fitting cap marked with a latitude–longitude matrix, positioned with reference to the  
297 nasion–inion and interaural lines.

298 All single- and paired-pulse stimuli were delivered during a low-level isometric contraction of the  
299 right FCR. Participants were required to maintain a wrist joint angle of 20° wrist flexion in a position  
300 of supination. Joint angle was measured with an electromagnetic goniometer (ADInstruments, Bella  
301 Vista, Australia), with visual feedback provided on a screen visible to both the participant and the  
302 researcher (Hendy and Kidgell 2013). Holding the hand in this joint position equated to  $5 \pm 1\%$  of the  
303 maximal root-mean squared electromyography (rmsEMG). Because this position resulted in a low  
304 level of muscle activity, and to ensure that background muscle activity was consistent between TMS  
305 stimuli, rmsEMG was recorded 100 ms before the delivery of each TMS pulse. During the TMS trials,  
306 visual feedback was presented to the volunteer to display an upper limit of 5% rmsEMG; participants  
307 were instructed to maintain their muscle activation levels below this upper limit. The stimulus  
308 delivery software (LabChart 8 software, ADInstruments, Bella Vista, NSW, Australia) was set so that  
309 stimuli were not delivered if the rmsEMG value, 100 ms immediately prior to the stimulus, exceeded  
310  $5 \pm 1\%$  (Table 1).

311 Recruitment curves for the FCR were constructed to determine CSE (MEP amplitude) and silent  
312 period duration before and after each heavy-load strength-training bout. For a single stimulus-  
313 response curve, 10 stimuli were delivered at 130, 150 and 170% of AMT during a low-level isometric  
314 contraction of the FCR. Recruitment curves were also collected for the control group prior to and  
315 following 15 minutes of quiet sitting. This was repeated for each strength training session and at  
316 retention 72 h after the sixth training session.

317 To quantify short-interval intracortical inhibition (SICI), 10 single-pulse stimuli and 10 short-interval  
318 paired-pulse stimuli were delivered in a random order. The stimulator output intensity was set at  
319 120% AMT, which was determined during familiarization and adjusted if there was a change  
320 following each strength training session. The conditioning stimulus for paired-pulse stimulation was  
321 set at 80% AMT, the inter-stimulus interval was 3 ms, and subsequent posterior to anterior current  
322 flow was used. To quantify intracortical facilitation (ICF), 10 single-pulse stimuli and 10 paired-pulse  
323 stimuli were delivered in a random order. The stimulator output intensity was set at 120% AMT and  
324 the inter-stimulus interval was adjusted to 10 ms. Long-interval intracortical inhibition (LICI) was  
325 determined by a conditioning stimulus of 120% AMT followed by a test stimulus at 120% AMT with  
326 an inter-stimulus interval of 100 ms.

### 327 ***Maximal compound muscle action potential***

328 Direct muscle responses were obtained from the FCR muscle by supramaximal electrical stimulation  
329 (pulse width 200  $\mu$ s) of the Brachial plexus (Erbs point) during light background muscle activity  
330 (DS7A, Digitimer, UK). An increase in current strength was applied to Erbs point until there was no  
331 further increase observed in the amplitude of the EMG response ( $M_{MAX}$ ). To ensure maximal  
332 responses, the current was increased an additional 20% and the average  $M_{MAX}$  was obtained from five  
333 stimuli, with a period of 6-9 s separating each stimulus.  $M_{MAX}$  was recorded at baseline, prior to and  
334 following each training session and then at retention 72 h following the intervention to ensure that  
335 there were no changes in peripheral muscle excitability that could influence MEP amplitude.

### 337 ***Data analysis:***

338 Pre-stimulus rmsEMG activity was determined in the FCR muscle 100 ms before each TMS stimulus  
339 during pre- and post-testing. Trials were discarded when the pre-stimulus rmsEMG was greater than  
340  $5 \pm 1\%$  of maximal rmsEMG and then the trial was repeated. The peak-to-peak amplitude of MEPs  
341 was measured in the dominant right FCR muscle. MEPs were analyzed (LabChart 8 software; AD  
342 Instruments) after each stimulus and flagged automatically with a cursor, providing peak-to-peak  
343 values in mV, averaged and normalized to the  $M_{MAX}$ , and multiplied by 100. The total area under the  
344 recruitment curve (AURC) was calculated via the method of trapezoidal integration using the actual  
345 data collected during the construction of corticospinal excitability (MEP amplitude) and corticospinal  
346 inhibition (silent period duration) recruitment curves for the FCR before and after every strength-  
347 training session. The experimenter was blinded to each condition during all AURC analyses. Silent  
348 period durations were obtained from single-pulse stimuli delivered during the construction of the  
349 recruitment curve (130–170% AMT) and silent period durations were determined by examining the  
350 duration between the onset of the MEP and the resolution of background sEMG, which was visually  
351 inspected and manually cursored. The average from 10 stimuli was used to determine silent period  
352 durations. SICI and ICF were expressed as a percentage of the unconditioned single-pulse MEP

353 amplitude, while LICI was calculated and expressed as a percentage of the test to conditioning MEP  
354 amplitude for each individual paired stimuli. In regards to the changes in SICI, when the SICI  
355 percentage change increased following the strength-training sessions and the two-week intervention,  
356 this signified a decrease in cortical inhibition and when the SICI percentage change decreased  
357 following training this signified an increase in cortical inhibition. The same percentage changes also  
358 applied to LICI.

359

360 The extent of co-activation of antagonists was determined by calculating the percentage of the  
361 maximal ECR and FCR rmsEMG recorded during wrist flexion 1-RM strength testing, compared to  
362 the maximal ECR rmsEMG recording during wrist extension 1-RM testing.

$$363 \text{ Co-activation} = (\text{ECR}/\text{ECR}_{\text{MAX}})/(\text{ECR}/\text{FCR}) \times 100$$

364 Peak rmsEMG of the ECR was recorded during wrist extension 1-RM testing; the peak rmsEMG for  
365 the ECR was also recorded during wrist flexion 1-RM testing. In a similar manner, peak rmsEMG for  
366 the FCR was recorded during wrist flexion 1-RM testing; and during wrist extension testing. For all  
367 testing conditions, the rmsEMG max was obtained during the 1-RM tests and was calculated from a 1  
368 s segment that occurred during the peak of the surface EMG trace. The ECR/ECR<sub>MAX</sub> ratio,  
369 expressed as a percentage of total activation was then used to correctly interpret the extent of  
370 ECR/FCR ratio.

371

### 372 *Statistical analysis*

373

374 All data were screened with Shapiro–Wilk and Kolmogorov–Smirnov tests and were found to be  
375 normally distributed (all  $P > 0.05$ ). A  $2 \times 7$  repeated measures analysis of variance (ANOVA) with  
376 factors CONDITION (Control and Training) and TIME (Pre, post session 1, post session 2, post  
377 session 3, post session 4, post session 5, post session 6 and post session 7) were used to compare  
378 changes in pre-stimulus rmsEMG, M-waves, CSE, ICF, silent period, SICI and LICI between  
379 conditions and across time. In order to determine the effect of strength training on dynamic muscle  
380 strength and co-contraction indices, a separate two-way repeated measures ANOVA was used to  
381 compare group (trained vs. control) by week (week 1 vs. week 2) on the pooled changes in strength  
382 and the index of co-contraction. For all ANOVAs, if significant main effects were found, a Bonferroni  
383 post hoc test was used to analyze the percentage change comparing condition interaction (Control and  
384 Training) by time. For all comparisons, effect sizes (ES) of 0.2, 0.5, and 0.8 were established to  
385 indicate small, moderate, and large comparative effects (Cohen's  $d$ ), respectively. Prism 8 for  
386 Windows (GraphPad Software Inc, La Jolla, CA, USA) was used for all statistical analyses, with the  
387 level of significance set as  $P < 0.05$  for all testing. All data are presented as mean  $\pm$  95% CI in text,  
388 whilst mean  $\pm$  SD is presented in Tables and Figures.

389

## 390 **Results**

391

### 392 ***Pre-stimulus rmsEMG, maximal compound waves and motor thresholds***

393 Pooled weekly summary data for measures of electrophysiology is reported in Table 1. In summary,  
394 there were no significant differences between groups in M-waves, pre-stimulus rmsEMG, RMT or  
395 AMT at baseline and no main effects for TIME or TIME  $\times$  CONDITION interactions in any measure  
396 (All  $P > 0.05$ ; Table 1). Thus, in both the strength-training and control group, there were no changes  
397 in any of the aforementioned measures within any single session during the training program. Further,  
398 no changes were observed compared to baseline 72 h following the cessation of the training period in  
399 both the strength-training and control group (All  $P > 0.05$ ; Table 1).

400

### 401 ***Changes in Muscle Strength***

402 The percentage change in the dominant trained wrist flexor following strength-training or no training  
403 (control) is presented in Figure 2. Following strength training, there was a main effect for TIME [( $F_{2, 32} = 32.7, P < 0.0001$ )] and a GROUP  $\times$  TIME interaction [( $F_{2, 32} = 20.5, P < 0.0001$ )]. Post hoc  
405 analysis revealed by the end of the first week of strength-training, the strength-training group  
406 increased their 1-RM strength of the wrist flexor by  $6.3 \pm 4.5\%$  (CI -9.80 to -0.0995,  $P = 0.04, d =$   
407  $1.24$ ) compared to a  $1.4 \pm 3.5\%$  increase in the control group (Table 1). Post hoc analysis also showed  
408 after two-weeks of strength-training, the strength-training group increased their 1-RM strength by  
409  $15.5 \pm 7.6\%$  (CI -18.5 to -8.76,  $P < 0.001, d = 2.20$ ) compared to a  $1.8 \pm 3.5\%$  increase in the control  
410 group.

411

412 **— INSERT FIGURE 2**

413

### 414 ***TMS Measurements***

415 The primary aim of the TMS measurements were to investigate both the short-term and long-term  
416 adaptations to strength-training. Because none of the control group measurements showed any  
417 significant changes across testing sessions or training weeks (i.e., within group main effects, see Table  
418 2), the data presented in the short-term and long term responses to strength-training only include the  
419 main interaction effects between the strength-training and control groups.

420

421 ***Short-term MEP responses to strength training:*** Figure 3A illustrates the percentage change  
422 following each strength-training session across the two-week intervention for the strength-training  
423 group only. There was a significant main effect for increased CSE following the first session (CI -93.1  
424 to -22.9,  $P < 0.001, d = 1.82$ ), second session (CI -91.8 to -21.5,  $P > 0.001, d = 1.89$ ), third session  
425 (CI -77.3 to -7.11,  $P = 0.008, d = 1.17$ ), fourth session (CI -79.8 to -9.58,  $P = 0.004, d = 1.68$ ), fifth  
426 session (CI -81.9 to -11.7,  $P = 0.002, d = 1.42$ ), sixth session (CI -80.0 to -9.77,  $P = 0.004, d = 1.45$ )  
427 and 72 h after the last strength training session [session 7, retention] (CI -78.3 to -8.10,  $P = 0.006, d =$

428 2.12) compared to the control group. There were no differences in CSE between sessions for the  
429 strength-training group, thus the short-term effects of training seemed to be largest in response to the  
430 first training session and then sustained across subsequent training sessions (Figure 3A).

431

432 **Longer-term MEP responses to strength training:** The longer-term adaptations to training are  
433 defined as the differences that occur when comparing the pre-training values obtained in the baseline  
434 test, the one-week test (session 3), the two-week test (session 6) and the retention test (session 7).  
435 These responses are illustrated in Figure 3B. For the strength-training group, AURC for CSE  
436 increased by  $53 \pm 43\%$  (CI 35.7 to 68.9,  $P < 0.0001$ ,  $d=1.67$ ) compared to the  $0.5 \pm 4.5\%$  increase in  
437 the control group at the end of training week 1, and by  $45 \pm 39\%$  (CI 30.4 to 60.5,  $P < 0.001$ ,  $d=1.60$ )  
438 compared to the  $0.2 \pm 2.6\%$  increase in the control group at the end of training week 2. The AURC  
439 for CSE was also increased from baseline 72 h following the strength-training intervention by  $44 \pm$   
440  $27\%$  (CI 23.6 to 62.8,  $P < 0.001$ ,  $d=2.13$ ) compared to the control group (Figure 3B).

441

442

#### INSERT FIGURE 3A-B

443

444 **Short-term corticospinal inhibitory responses to strength training:** Figure 4A illustrates the  
445 percentage change in silent period following each strength-training session across the two-week  
446 intervention for the strength-training group compared to the control group. In the strength-training  
447 group, there was a main effect for reduced silent period duration following the first session (CI 8.26 to  
448 20.3,  $P < 0.001$ ,  $d = 2.18$ ), second session (CI 7.74 to 19.8,  $P < 0.001$ ,  $d = 2.77$ ), third session (CI  
449 4.92 to 17.0,  $P < 0.001$ ,  $d = 1.73$ ), fourth session (CI 1.82 to 13.9,  $P = 0.002$ ,  $d = 1.72$ ), fifth session  
450 (CI - 2.59 to 14.7,  $P = 0.0004$ ,  $d = 2.46$ ), sixth session (CI 1.73 to 13.8,  $P = 0.002$ ,  $d = 2.35$ ) and 72 h  
451 after the last strength-training session (CI 8.25 to 20.3,  $P < 0.001$ ,  $d = 1.96$ ) compared to the control  
452 group. There was a significant difference in the duration of the silent period between session 1 and  
453 session 4 (CI -12.5 to -0.402,  $P = 0.025$ ,  $d = 0.92$ ) and session 1 and session 6 (CI -12.6 to -0.493,  $P =$   
454  $0.021$ ,  $d = 1.20$ ) for the strength-training group. Corticospinal inhibition appears to reduce rapidly  
455 following the first training session and then steadily return towards baseline across subsequent  
456 strength-training sessions (Figure 4A).

457

458 **Longer-term corticospinal inhibitory responses to strength training:** The longer-term adaptations to  
459 training are defined as the differences that occur when comparing the pre training values obtained in  
460 the baseline test, the one-week test, the two-week test and the retention test. These responses are  
461 illustrated in Figure 4B. For the strength-training group, AURC for silent period reduced by  $13 \pm$   
462  $6.3\%$  (CI 6.69 to 19.6,  $P < 0.001$ ,  $d = 2.56$ ) compared to the  $0.1 \pm 2.5\%$  increase in the control group  
463 at the end of training week 1 and reduced by  $8\% \pm 3.9\%$  (CI 2.77 to 15.6,  $P < 0.002$ ,  $d = 2.26$ )  
464 compared to the  $1.1 \pm 1.3\%$  increase in the control group at the end of training week 2. The AURC

465 for corticospinal inhibition also reduced 72 h following the strength-training intervention by  $14 \pm 10\%$   
466 (CI 9.33 to 22.2,  $P < 0.001$ ,  $d = 1.58$ , Figure 4B) compared to the control group.

467

468

#### INSERT FIGURE 4A-B

469

470 **Short-term SICI responses to strength training:** Figure 5A illustrates the percentage change in SICI  
471 following each strength-training session across the two-week intervention for the strength-training  
472 group. In the strength-training group, there was a main effect for a release in SICI following the first  
473 session (CI -56.3 to -10.9,  $P = 0.002$ ,  $d = 1.33$ ), second session (CI -60.0 to -14.6,  $P < 0.001$ ,  $d =$   
474 1.43), third session (CI -50.7 to -5.33,  $P < 0.003$ ,  $d = 1.55$ ), and 72 h after the last strength-training  
475 session (CI -58.3 to -13.0,  $P < 0.001$ ,  $d = 1.56$ ) compared to the control group. Interestingly, there  
476 were no differences in SICI release across strength-training sessions four, five and six for the  
477 strength-training group (all  $P > 0.05$ , Figure 5A).

478

479 **Longer-term SICI responses to strength training:** Again, the longer-term adaptations to training are  
480 defined as the differences that occur when comparing the pre-training values obtained in the baseline  
481 test, the one-week test, the two-week test and the retention test. These responses are illustrated in  
482 Figure 5B. For the strength-training group, SICI reduced by  $33 \pm 25\%$  (CI -52.6 to -12.5,  $P < 0.001$ ,  $d =$   
483 1.68) compared to the  $0.4 \pm 7.6\%$  increase in the control group at the end of training week 1. There  
484 were no differences in SICI release between the strength-training group and the control group at the  
485 end of week 2 (CI -35.8 to 4.29,  $P = 0.163$ ,  $d = 2.26$ ), despite a large effect. However, SICI was  
486 reduced for the strength-training group at 72 h following the strength-training intervention by  $35 \pm$   
487 25% (CI -54.7 to -14.6,  $P < 0.001$ ,  $d = 1.51$ ) compared to the control group.

488

489

#### INSERT FIGURE 5A-B

490

491 **Short-term and longer-term ICF responses to strength training:**

492 Figure 6A illustrates the percentage change in ICF following each strength-training session across the  
493 two-week intervention for the strength-training group. In the strength-training group, there was a  
494 main effect for increased ICF following the first session (CI -27.8 to -3.66,  $P = 0.001$ ,  $d = 1.48$ ) and  
495 second session (CI -25.2 to -0.231,  $P < 0.04$ ,  $d = 1.38$ ), compared to the control group. ICF also  
496 increased for the strength-training group following the fourth session (-24.5 to -0.396,  $P < 0.036$ ,  $d =$   
497 0.72), but the magnitude of this change was not different to the control group. There were no  
498 differences in ICF across strength-training sessions three, five and six (all  $P > 0.05$ , Figure 6A) and at  
499 retention for the strength-training group compared to the control group. For the strength-training  
500 group, ICF increased by  $13 \pm 10\%$  (CI -23.9 to -4.37,  $P = 0.002$ ,  $d = 1.86$ ) compared to the  $1.0 \pm 1.8\%$   
501 decrease in the control group at the end of training week 1 and increased by  $12 \pm 11\%$  (CI -21.4 to -

502 1.21,  $P = 0.023$ ,  $d = 1.57$ , Figure 6B) compared to the  $0.7 \pm 1.7\%$  decrease in the control group after  
503 the end of training week two. There were no differences in ICF between the strength-training and  
504 control groups at retention (CI -17.9 to 3.17,  $P = 0.245$ ).

#### 505 **INSERT FIGURE 6A-B**

506

#### 507 ***Short-term and long-term LICI responses to strength training:***

508 In the strength-training group, there were no main effects for a change in LICI from strength-training  
509 session 1 to strength-training session 6 ( $P = 0.463$ ) or following week 1 of training ( $P > 0.999$ ), week  
510 2 ( $P = 0.993$ ) or at retention ( $P = 0.99$ ) compared to the control group.

511

#### 512 ***Changes in Co-Activation of Antagonists:***

513 Figure 7 illustrates the antagonist co-activation index obtained during the weekly 1-RM strength  
514 testing following week 1 and week 2 for the strength-training and control group. There was a  
515 significant main effect for a reduction in antagonist co-activation from week 1 to week 2 for the  
516 strength training group compared to the control group (CI -3.08 to -2.30,  $P = 0.02$ ,  $d = 1.80$ ).

517

#### 518 **INSERT FIGURE 7**

519

## 520 **Discussion**

521

522 This study examined the time-course effects of strength-training on the formation of use-dependent  
523 cortical plasticity and how it contributed to improvements in muscular strength. The main findings are  
524 **1)** increases in strength were apparent after three sessions of strength-training, and further increases  
525 were observed following six sessions, **2)** following two-weeks of strength-training, CSE was  
526 increased with concurrent decreases in the duration of the silent period and SICI; however, **3)** the  
527 acute cortical responses to strength-training did not accumulate within each training session, rather **4)**  
528 the substantial and rapid responses to a single session of strength-training were either maintained  
529 (CSE), reduced (silent period) or abolished (ICF and SICI) during subsequent sessions, indicating that  
530 neural adaptations occurred between training sessions. Further, antagonist co-contraction during  
531 training was substantially reduced in week two compared to week one. These findings indicate that  
532 the MI undergoes substantial use-dependent plasticity from the first strength-training session onwards  
533 alongside reduced co-contraction of antagonists in order to drive improvements in muscular strength.  
534 These adaptations are rapid, and beyond the immediate cellular response to the initial strength-  
535 training session (such as increases in synaptic efficacy), occur primarily between strength-training  
536 sessions, and culminate in longer-term functional changes (i.e., neurogenesis).

537

#### 538 ***The time-course of strength development***

539

540 The current study provides insight into the temporal scale of strength improvement, with significant  
541 increases in strength following just three strength-training sessions, and further increases following  
542 six strength-training sessions. The time-course of strength improvement supports the findings of  
543 Griffin and Cafarelli (2003) who observed strength increases following just two sessions of isometric  
544 strength training of the tibialis anterior, and further progressive increases throughout the rest of a four-  
545 week strength-training period. There are several lines of evidence suggesting that just one strength-  
546 training session can produce increases in strength upwards of 10% (Hood and Forward 1965; Christie  
547 and Kamen 2004; Nuzzo et al. 2019), and improvements in strength over a three-day strength-training  
548 period can be maintained three months following the cessation of training (Kroll 1963). The  
549 magnitude of strength gain following six sessions of training is comparatively large in reference to  
550 studies reporting improvements following longer strength-training periods (Ahtianen et al. 2003;  
551 Gomes et al. 2018; Serra et al. 2018). The difference is likely due to the subjects recruited in the  
552 current study being novices to any form of strength-training. Experimental evidence shows that  
553 inexperienced strength trainers obtain larger gains in strength across a multi-week training program  
554 when compared with subjects who are more experienced (Ahtianen et al. 2003). Further,  
555 discrepancies in the magnitude of strength improvements between studies might also be explained by  
556 the elements of the strength-training used in the current study, including heavy-load, dynamic  
557 contractions with external pacing (Leung et al. 2017; Kidgell et al. 2010; Mason et al. 2019). In  
558 summary, increases in strength begin very early after the onset of strength-training, and accumulate  
559 across training weeks, reinforcing the existing evidence that strength-training is an effective stimulus  
560 capable of producing rapid, lasting improvements in performance (Kidgell et al. 2017).

561

562 ***The training-related corticospinal and M1 responses are similar to the short-term acute responses.***

563

564 Seventy-two hours following the final session, substantial changes in M1 plasticity were observed  
565 when compared to baseline and to the control group, which is consistent with the literature (see  
566 Kidgell et al. 2017 for review). Similarly, the responses to the initial strength-training session were  
567 well-aligned with current evidence (see Mason et al. 2019 for review). With the exception of ICF, the  
568 corticospinal and M1 responses (or lack of, see LICI) to the initial strength-training session mirrored  
569 the responses measured at the retention period following the two-week strength-training period.  
570 However, from week one to week two, there appears to be no accumulation in the acute M1 and  
571 corticospinal responses to each individual strength training session as hypothesised. Rather, the M1  
572 and corticospinal responses are substantially and rapidly enhanced from the first strength-training  
573 session and are maintained (CSE), reduced (silent period) or eventually eliminated (SICI and ICF)  
574 following each individual training session across the course of the sixth strength-training session.  
575 Combined, these results indicate that substantial neural adaptations between strength-training sessions



576 could be influencing the corticospinal and M1 adaptations supporting the increase in strength  
577 throughout a training period.

578

579

### 580 *Identifying the neural mechanisms that accompany strength development*

581 Prior to discussing the mechanisms of cortical plasticity throughout the strength-training period, it  
582 may be useful to postulate what purpose cortical plasticity could serve. Alterations in corticospinal  
583 output during and following strength-training likely contributed to the development of strength  
584 through an influence on motor unit behaviour. The magnitude of muscle activation, and therefore the  
585 amount of force produced, is determined by the number of activated motor units (recruitment) and the  
586 rate at which the motoneurons are discharged (rate coding), with both being altered following  
587 strength-training (Farina et al. 2016). Recent evidence, using validated techniques previously  
588 unavailable (Farina et al 2016), indicates that strength gains following four-weeks of isometric  
589 strength-training are driven by decreased motor unit recruitment thresholds and increased discharge  
590 rates (Del Vecchio et al. 2019). This aligns with earlier evidence whereby increases in strength are  
591 due to adaptations in motor unit recruitment and rate coding following isometric strength-training  
592 (Duchateau et al. 2006; Van Cutsem et al.1998; Vila-Cha et al. 2010; Kamen and Knight 2004).  
593 Given that motor units are controlled by input to the motoneurone pool from the corticospinal tract,  
594 alterations in motor unit behaviour likely involve adaptive changes in the corticospinal tract from the  
595 M1 to the spinal motoneurone pool. Of these potential sites, adaptations at a supraspinal level are a  
596 primary candidate (Kidgell et al. 2017; Semmler and Enoka 2000; Schubert et al. 2008). Indeed, Del  
597 Vecchio and colleagues (2019) proposed that increased net excitatory synaptic input to the  
598 motoneurone pool was the likely mechanism driving motor unit adaptations as opposed to  
599 modification to the intrinsic motoneurone properties. This, paired with evidence that strength-training  
600 increases voluntary activation with no increase in cervicomedullary excitability (Nuzzo et al. 2017),  
601 suggests that modulation at the level of the M1 may be responsible for alterations in motor unit  
602 behaviour. Therefore, it is conceivable that in the current study, increases in CSE and decreases in  
603 inhibitory input to the motoneurone pool generated changes in motor unit recruitment and rate coding  
604 throughout the strength-training period, which ultimately underpinned the observed increases in  
605 strength. These corticospinal responses likely reflect an improved ability of the M1 to maximally  
606 recruit and discharge motor units, which is demonstrated by the increase in the input-output properties  
607 of the corticospinal tract following strength-training (i.e. change in AURC for CSE and silent period).  
608 However, a potential caveat to this line of inquiry is that there is evidence to suggest that the  
609 corticospinal tract is not the only descending motor pathway that provides synaptic input to the spinal  
610 motoneurone pool, which could alter motor unit behaviour (Riddle et al. 2009). For example,  
611 evidence shows that the reticulospinal tract is associated with force production (Baker and Perez  
612 2017), therefore, it could be the case that the reticulospinal tract was also modulated as a result of the

613 strength-training intervention. It is also likely that modulation in the reticulospinal tract also  
614 contributed to the increase in force, presumably through enhanced direct and indirect synaptic input to  
615 the spinal motoneurone pool. The time-course of these adaptations also supports this notion, as the  
616 increase in strength occurred rapidly and directly in line with the timeframes for alterations in motor  
617 unit behaviour (i.e. session by session, Christie and Kamen 2004). Further, reduced antagonist co-  
618 activation during the second week of strength-training is also consistent with existing evidence  
619 demonstrating rapid antagonist alterations following strength-training (Hight et al. 2017). Thus,  
620 changes in antagonist behaviour, alongside the agonist corticospinal responses, collectively contribute  
621 to increases in strength (Mason et al. 2019).

622  
623 The timing of cortical plasticity within this study warrants further discussion, as it provides insight  
624 into how the rapid cellular responses ultimately develop into longer-lasting functional changes  
625 following two-weeks of strength training. The presence of substantial adaptations between training  
626 sessions and the formation of cortical plasticity across the strength-training program add to the  
627 consistent comparisons between the development of strength and the acquisition of a motor skill  
628 (Leung et al. 2015; Leung et al. 2017; Jensen et al. 2005; Mason et al. 2019). In fact, it seems that  
629 strength-training induces neurogenesis that occurs between training sessions. Although there are no  
630 strength-training studies that have examined this notion alongside the time-dependent adaptations to  
631 strength-training, the use of skill acquisition frameworks may aid in the interpretation of the current  
632 result and the notion that strength-training induces neurogenesis.

633  
634 Diminishing responses to individual sessions and significant adaptations between strength-training  
635 sessions may be indicative of early and late phases of cortical plasticity supporting strength  
636 acquisition, resembling the distinct early and later phases of skill acquisition identified by imaging,  
637 behavioural and TMS studies (Karni et al. 1998; Rosenkranz et al. 2007; Kleim et al. 2006; Floyer-  
638 Lea and Matthews 2005). Early responses to skill training are commonly attributed to changes in  
639 existing synaptic strength, and later responses attributed to distinct functional processes such as  
640 synaptogenesis or neurogenesis (Rosenkranz et al. 2007; Kleim et al. 2006). Therefore, the early phase  
641 of strength development might also be characterised by changes in existing synaptic efficacy, which  
642 may occur both during training and at rest, whereas later changes may reflect structural changes that  
643 occur between training sessions. This idea is supported by the acute inhibitory responses to early  
644 training sessions, as a reduction in GABA-mediated inhibition is necessary for the early enhancement  
645 of synaptic efficacy (Hess et al. 1996; Hess and Donoghue 1994) and is associated with the  
646 acquisition of novel motor tasks (Stagg et al. 2011; Floyer-Lea et al. 2006; Butefisch et al., 2000;  
647 Kida et al. 2016; Mooney et al. 2019). Further, a lack of acute online inhibitory responses later in  
648 training is compatible with evidence that longer-term structural plasticity occurs between training  
649 sessions, not within training sessions (Mednick et al. 2011), and that synaptogenesis does not directly

650 contribute to initial acquisition, but occurs later in the learning process underpinning consolidation  
651 and retention of a skill (Kleim et al. 2004). However, the role of synaptogenesis and the functional  
652 reorganisation of M1 in strength development remains to be determined, despite evidence from  
653 animal models that unlike skill training, strength-training is incapable of inducing changes in motor  
654 map representations regardless of training stage (Remple et al. 2001). This is despite evidence of  
655 increased volume of excitable synapses onto motoneurons following strength-training (Adkins et al.  
656 2006).

657  
658 It must be noted in contrast to the skill training literature (Kleim et al. 2006; Rosenkrantz et al. 2007),  
659 CSE remained substantially modulated by each strength-training session, despite all other indicators  
660 of cortical plasticity diminishing across the strength-training period. An increase in CSE immediately  
661 following a single session of strength-training appears to be an important factor for cortical plasticity  
662 underpinning strength development, as its abolishment via rTMS following strength-training reduces  
663 strength improvements considerably (Hortobágyi et al. 2009). Collectively, this suggested that CSE  
664 could contribute to both early cellular and later structural plasticity (i.e. neurogenesis) serving  
665 increases in strength, despite a lack of correlation between gains in strength and increased CSE  
666 following several weeks of strength-training (Jensen et al. 2005; Mason et al. 2017). The lack of  
667 correlation is likely due to other neural structures and systems being involved in strength  
668 development, especially the intrinsic spinal circuitry (Jensen et al. 2005). Thus, there is a need to  
669 examine multiple sites within the CNS in order to provide a greater understanding of which systems  
670 in the CNS are most related to changes in strength. However, CSE is not just an indicator of  
671 corticospinal plasticity, it is also thought to increase as a function of fatigue (Mason et al. 2019;  
672 Latella et al. 2017), representing a point of difference between strength-training and the typically low-  
673 fatiguing paradigms used in skill training. Whilst it is possible that repeated acute modulation of CSE  
674 through strength-training is sufficient to trigger mechanisms of structural plasticity (synaptogenesis)  
675 between strength-training sessions, conclusions regarding the functional consequences of increased  
676 CSE are preliminary in this context (Bestmann and Krakauer 2015).

677  
678 The current study has a number of limitations that must be considered when interpreting the findings.  
679 Firstly, a more precise temporal scale of strength improvements would have been generated through  
680 testing strength alongside every TMS testing day. However, this is logistically difficult, given the  
681 ability of even one maximum testing session to influence subsequent neuromuscular responses and  
682 performance (Nuzzo et al. 2019). Secondly, strength-training studies typically use more precise  
683 measurements of strength testing than 1-RM testing, such as maximal isometric voluntary  
684 contractions (MVIC) (Kidgell et al. 2017). However, previous strength-training studies have  
685 identified using different testing and training apparatus or techniques as a limitation. Indeed,  
686 adaptations are typically specific to the training involved (Brownstein et al. 2018), and are therefore

687 better assessed by identical protocols. Further, one plausible explanation as to why no changes in the  
688 LICI response were detected at any testing point is that LICI is highly dependent on factors such as  
689 contraction and stimulus intensities (McNeil et al. 2011). Therefore, the utilisation of other testing  
690 parameters may have been more appropriate in identifying potential changes. Additional limitations  
691 include a lack of a more comprehensive assessment protocol to assess spinal excitability, such as  
692 volitional waves and cervicomedullary evoked potentials. Future studies should also seek to track the  
693 responses to both skill and strength-training across an entire training period to discern differences.  
694 Importantly, beyond the assessment of peripheral excitability, the current study was unable to  
695 determine the contribution of fatigue to the single session responses. Therefore, similar upcoming  
696 studies should include techniques (such as cortical voluntary activation) to discern the role of both  
697 peripheral and central fatigue in mediating the acute and short-term responses to strength training, and  
698 how they relate to the process of acquiring muscular strength.

699  
700 In summary, this study provides new insight into how the rapid responses to a single bout of strength-  
701 training reflect the longer-term cortical responses that accompanies the increases in muscle strength  
702 following a two-week strength-training period. These results add to the notion that the repeated  
703 stimulus of strength-training is sufficient to induce long-lasting changes in muscle strength and  
704 cortical plasticity. Combined, the findings provide evidence for early and late phases of strength  
705 development, mediated by distinct cortical mechanisms similar to the frameworks observed for the  
706 development of motor skills. Importantly, the alterations in CSE and inhibition across the strength-  
707 training program occur acutely and between training sessions, conceivably to drive the changes in  
708 motor unit behaviour, which ultimately seem responsible, at least in part, for improvements in force  
709 production. Understanding the time-course and location of neural adaptation to heavy-load strength-  
710 training will allow practitioners to design more efficient training programs to develop and preserve  
711 skeletal muscle strength for maintenance of health and improve human performance. Finally, Kleim  
712 and Jones (2008) suggested that cortical plasticity underlying improvements in motor skill is perhaps  
713 best considered a process rather than a single measureable event, as it involves a cascade of events at  
714 the molecular, cellular and structural levels (Kandel 2001). The same must be considered for the  
715 adaptations underpinning improvements in strength. Thus, the relationship between corticospinal and  
716 M1 plasticity and strength development is an area ripe for further exploration.

717 **Author contributions** JM, AF, and DJK conceived and designed the study. JM, AF, GH and DJK  
718 conducted experiments, analyzed data, and drafted the first version of the manuscript. AJP, JA  
719 critically revised the manuscript. All authors read and approved the manuscript.

720

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723

724 **Compliance with ethical standards**

725

726 **Conflict of interest** None of the authors have potential conflicts of interest to be disclosed.

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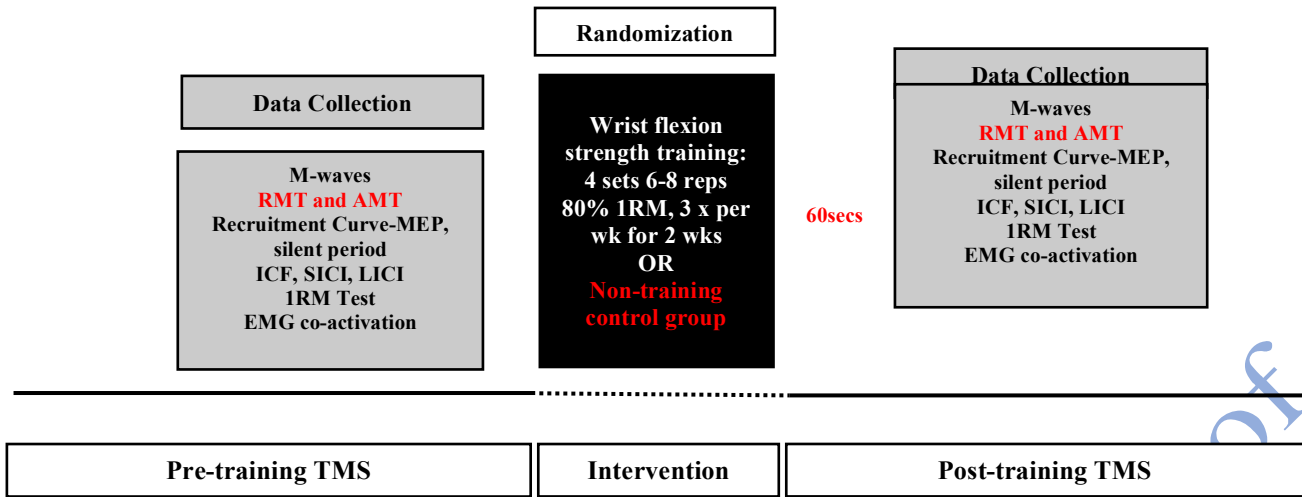
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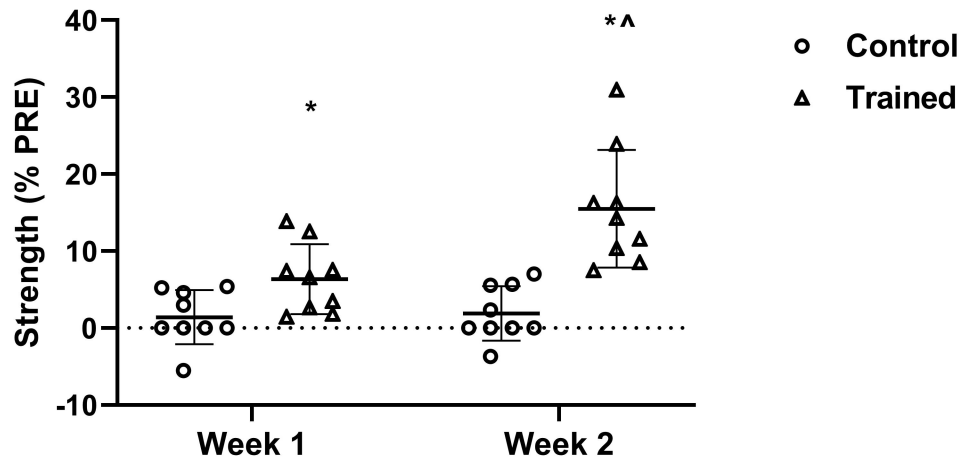
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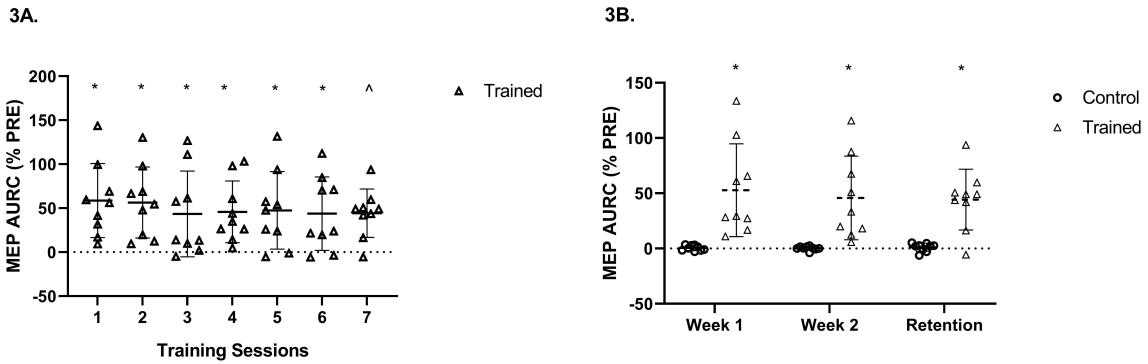


**Figure 1:** Schematic representation of the experimental design for the experimental group (heavy-load strength training of the wrist flexors) and the control group. Pre and post testing occurred prior to and following each strength-training session (repeated six times over two weeks, each separated by 48 h) and at retention, 72 h after the last training session for both the experimental and control groups. Pre- and post-measures for each strength-training session included assessment of peripheral muscle excitability (M-waves), resting- and active motor thresholds (RMT and AMT respectively), corticospinal excitability recruitment curves, corticospinal inhibition recruitment curves, short-interval intracortical inhibition (SICI), long-interval cortical inhibition (LICI) and intracortical facilitation (ICF) of the wrist flexors. **Not pictured:** 1-RM strength testing was conducted at baseline, following three sessions of strength training, following six sessions of training, and 72 hours after the sixth session together with antagonist co-activation assessment.



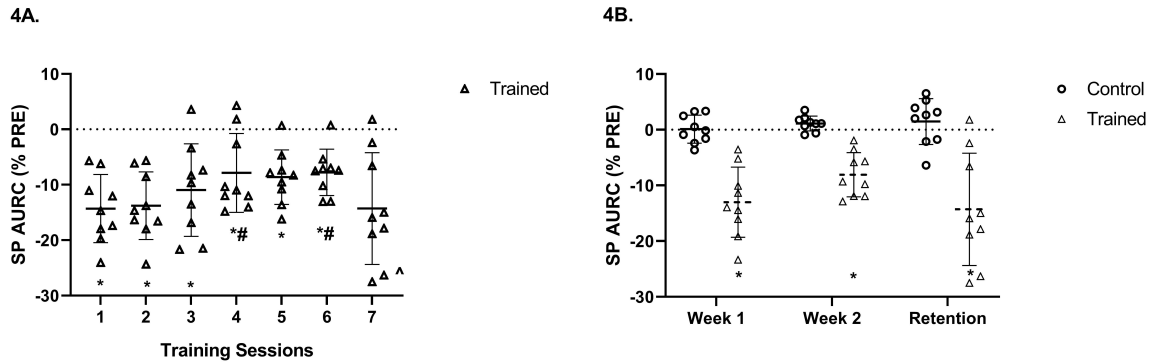
**Figure 2:** Change in 1-RM strength for the wrist flexor (mean  $\pm$  SD) following the strength-training condition at week 1 and week 2 compared to baseline strength and the control group. \*Denotes a significant increase in strength from baseline following heavy-load strength training compared to the control group, ^ denotes a significant increase in strength from week 1 following heavy-load strength training compared to the control group.

Accepted - uncorrected proof



**Figure 3A-B:** Changes in AURC for CSE of the trained wrist flexor (mean  $\pm$  SD) following heavy-load strength training across six training sessions and at the retention session (A). \*Denotes a significant increase in AURC for CSE from respective training sessions following training, ^denotes a significant increase in CSE 72 h following the cessation of the training period from original baseline data compared to the control group. Changes in AURC for CSE of the trained wrist flexor (mean  $\pm$  SD) at the one-week test, two-week test and retention test during and after two weeks of heavy-load strength training. \*Denotes a significant increase in AURC for CSE from baseline compared to the control group across the strength-training period.

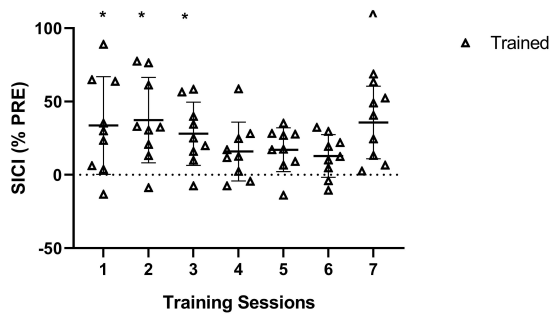
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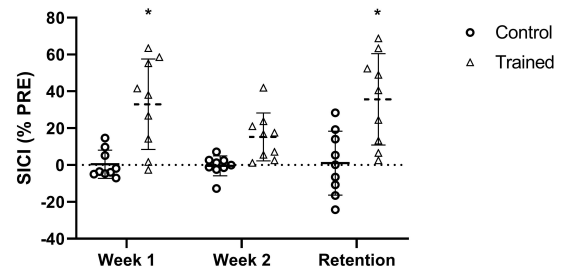
**Figure 4A-B:** Changes in AURC for silent period duration of the trained wrist flexor (mean  $\pm$  SD) following heavy-load strength training across six training sessions and at the retention session (A). \*Denotes a significant reduction in the AURC silent period duration from respective session baseline data following training, # denotes significant difference from session one, ^denotes a significant decrease in the AURC for silent period duration 72 h following the cessation of the training period from original baseline data compared to the control group. Changes in AURC for silent period duration of the trained wrist flexor (mean  $\pm$  SD) at the one-week test, two-week test and retention test during and after two weeks of heavy-load strength training (B). \*Denotes a significant decrease in the AURC for silent period duration from baseline compared to the control condition.

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5A.



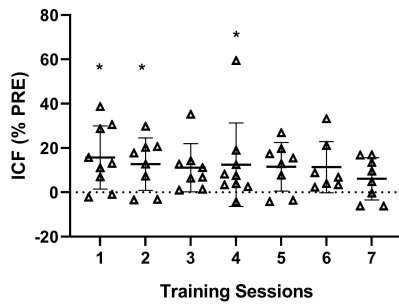
5B.



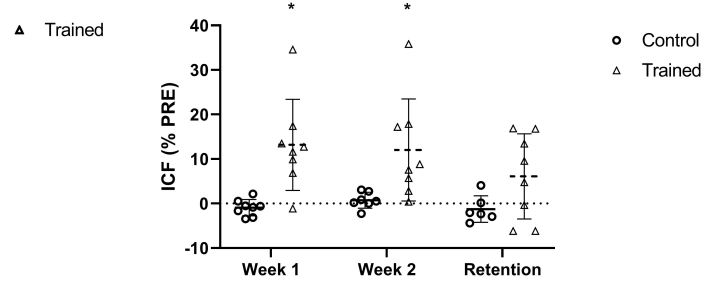
**Figure 5A-B:** Changes SICI of the trained wrist flexor (mean  $\pm$  SD) following heavy-load strength training across six training sessions and at the retention session (A). \*Denotes a significant release of SICI from baseline data following training, ^denotes a significant release in SICI 72 h following the cessation of the training period from original baseline data compared to the control condition. Changes in SICI of the trained wrist flexor (mean  $\pm$  SD) at the one-week test, two-week test and retention test during and after two-weeks of heavy-load strength training (B). \*Denotes a significant release in SICI from baseline compared to the control condition.

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6A.

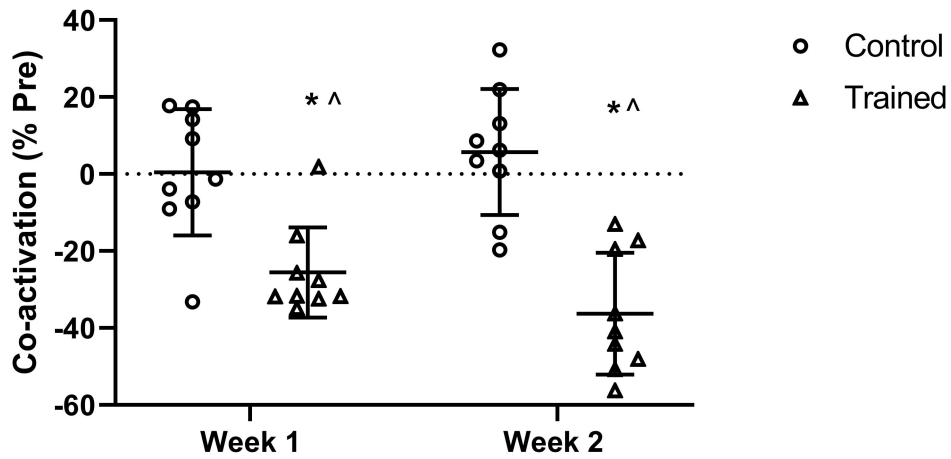


6B.



**Figure 6A-B:** Changes ICF of the trained wrist flexor (mean  $\pm$  SD) following heavy-load strength-training across six training sessions and at the retention session (A). \*Denotes a significant increase of ICF from session baseline data following training. Changes in ICF of the trained wrist flexor (mean  $\pm$  SD) at the one-week test, two-week test and retention test during and after two weeks of heavy-load strength training (B). \*Denotes a significant increase in ICF from baseline compared to the control group.

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**Figure 7:** Changes in co-activation index following one week and two weeks of heavy-load strength training for the control and strength training groups. \*denotes statistical significance from baseline, ^ denotes statistical significance from week 1 to week 2 compared to control ( $P < 0.05$ ).

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**Table 2:** Mean ( $\pm$  SD) for MEPs, silent period duration, ICF, SICI and LICI prior to and following each training session throughout a two-week training program. \*Denotes a significant increase within the individual training session ( $P < 0.05$ ), † denotes a significant difference from baseline and control group 72 h following completion of the training period.

		MEP amplitude (AURC)		Silent period duration (AURC)		ICF		SICI		LICI	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Session 1	Control	926.11 $\pm$ 291.73	933 $\pm$ 307.60	5.78 $\pm$ .75	5.82 $\pm$ .82	116.33 $\pm$ 13.53	113.79 $\pm$ 10.95	23.81 $\pm$ 12.15	22.83 $\pm$ 10.69	46.03 $\pm$ 12.97	47.47 $\pm$ 13.05
	Training	945.09 $\pm$ 321.12	1433.89* $\pm$ 409.06	5.72 $\pm$ .47	4.89* $\pm$ .41	113.91 $\pm$ 9.90	131.80* $\pm$ 20.16	24.73 $\pm$ 9.43	32.41* $\pm$ 13.24	47.01 $\pm$ 13.76	49.29 $\pm$ 11.63
Session 2	Control	936.98 $\pm$ 265.81	932.52 $\pm$ 253.75	5.66 $\pm$ .74	5.63 $\pm$ .70	117.83 $\pm$ 13.75	115.13 $\pm$ 11.32	23.28 $\pm$ 11.75	23.92 $\pm$ 11.68	54.72 $\pm$ 20.95	51.77 $\pm$ 15.24
	Training	930.85 $\pm$ 286.45	1401.16* $\pm$ 391.46	5.63 $\pm$ .50	4.84* $\pm$ .37	118.05 $\pm$ 10.56	132.86* $\pm$ 17.66	25.24 $\pm$ 8.58	33.76* $\pm$ 10.85	43.40 $\pm$ 10.39	45.18 $\pm$ 9.76
Session 3	Control	912.63 $\pm$ 261.49	922.48 $\pm$ 260.80	5.72 $\pm$ .71	5.71 $\pm$ .68	115.08 $\pm$ 11.84	116.01 $\pm$ 10.93	24.48 $\pm$ 9.28	23.66 $\pm$ 8.11	53.64 $\pm$ 18.48	55.39 $\pm$ 21.54
	Training	1031.27 $\pm$ 318.00	1413.77* $\pm$ 468.58	5.42 $\pm$ .32	4.82* $\pm$ .51	118.46 $\pm$ 10.55	131.33 $\pm$ 15.44	26.98 $\pm$ 9.07	33.47* $\pm$ 9.23	51.50 $\pm$ 18.64	54.80 $\pm$ 17.28
Session 4	Control	920.61 $\pm$ 280.50	932.91 $\pm$ 301.91	5.87 $\pm$ .66	5.99 $\pm$ .62	120.76 $\pm$ 11.77	122.46 $\pm$ 15.78	25.26 $\pm$ 10.72	25.64 $\pm$ 10.73	43.93 $\pm$ 12.28	45.40 $\pm$ 11.85
	Training	1206.39 $\pm$ 252.04	1716.88* $\pm$ 406.72	5.12 $\pm$ .32	4.72* $\pm$ .45	116.67 $\pm$ 11.13	130.04* $\pm$ 16.96	30.87 $\pm$ 11.09	35.44 $\pm$ 12.56	51.34 $\pm$ 17.44	52.14 $\pm$ 14.57
Session 5	Control	937.59 $\pm$ 301.23	939.93 $\pm$ 291.20	5.65 $\pm$ .60	5.71 $\pm$ .63	117.12 $\pm$ 10.68	118.64 $\pm$ 11.50	24.33 $\pm$ 9.22	23.76 $\pm$ 9.46	48.39 $\pm$ 11.01	48.77 $\pm$ 8.83
	Training	1161.02 $\pm$ 285.29	1632.79* $\pm$ 377.65	5.11 $\pm$ .36	4.68* $\pm$ .53	121.84 $\pm$ 15.45	135.41 $\pm$ 18.97	31.78 $\pm$ 10.41	36.90 $\pm$ 11.02	48.54 $\pm$ 15.75	51.49 $\pm$ 16.29
Session 6	Control	930.00 $\pm$ 281.07	920.17 $\pm$ 281.07	5.79 $\pm$ .67	5.80 $\pm$ .69	118.95 $\pm$ 11.50	118.66 $\pm$ 11.05	22.94 $\pm$ 10.77	22.58 $\pm$ 10.17	46.81 $\pm$ 11.03	47.21 $\pm$ 10.71
	Training	1241.72 $\pm$ 311.10	1710* $\pm$ 447.61	5.02 $\pm$ .33	4.63* $\pm$ .41	21.83 $\pm$ 12.04	135.16 $\pm$ 14.27	33.28 $\pm$ 8.94	37.35 $\pm$ 9.88	50.75 $\pm$ 13.83	51.78 $\pm$ 11.79
Retention	Control	936.29 $\pm$ 303.08		5.86 $\pm$ .78		117.17 $\pm$ 11.47		22.82 $\pm$ 9.80		47.08 $\pm$ 9.43	
	Training	1306.11* $\pm$ 314.50		4.88 $\pm$ .50		120.66 $\pm$ 13.25		32.61 $\pm$ 10.95		48.82 $\pm$ 12.52	

MEPs: Motor-evoked potentials. AURC: Area under the recruitment curve. ICF: intracortical facilitation. SICI: Short-interval cortical inhibition. LICI: Long-interval cortical inhibition.

**Table 1:** Mean ( $\pm$  SD) for resting motor threshold stimulus intensity, active motor threshold stimulus intensity,  $M_{MAX}$  and single and paired pulse pre-stimulus rmsEMG prior to and following each session across a two week training period.

		RMT SI %			AMT SI (%)			$M_{MAX}$ (mV)			SP rmsEMG			PP rmsEMG		
		Pre	Post	P-value	Pre	Post	P-value	Pre	Post	P-value	Pre	Post	P-value	Pre	Post	P-value
Baseline	Control	48.15 $\pm$ 2.14			39.49 $\pm$ 2.86			2.43 $\pm$ .77			2.14 $\pm$ .61			2.45 $\pm$ .48		
	Training	46.84 $\pm$ 1.96			37.99 $\pm$ 2.61			2.54 $\pm$ .43			2.71 $\pm$ .48			2.61 $\pm$ .64		
Pooled Week 1	Control	49.13 $\pm$ 2.44	48.14 $\pm$ 2.13	.66	39.10 $\pm$ 2.45	40.17 $\pm$ 3.01	.89	2.59 $\pm$ .50	2.49 $\pm$ .43	.99	2.34 $\pm$ .53	2.41 $\pm$ .39	.63	3.19 $\pm$ .47	3.02 $\pm$ .40	.49
	Training	47.45 $\pm$ 1.99	47.86 $\pm$ 2.31	.97	36.47 $\pm$ 2.43	35.98 $\pm$ 2.34	.36	2.61 $\pm$ .55	2.53 $\pm$ 1.34	.92	2.55 $\pm$ .31	2.61 $\pm$ .81	.71	3.01 $\pm$ .67	2.75 $\pm$ .64	.67
Pooled Week 2	Control	47.47 $\pm$ 1.60	47.97 $\pm$ 1.86	>.99	39.59 $\pm$ 2.13	39.03 $\pm$ 1.88	.98	2.48 $\pm$ .71	2.62 $\pm$ .60	.73	2.97 $\pm$ .29	3.01 $\pm$ .47	>.99	2.78 $\pm$ .88	2.20 $\pm$ .69	.18
	Training	46.80 $\pm$ 2.01	47.01 $\pm$ 2.00	.86	36.78 $\pm$ 1.87	35.99 $\pm$ 2.31	.41	2.70 $\pm$ .81	2.42 $\pm$ .79	.57	2.45 $\pm$ .39	2.73 $\pm$ .66	.83	2.94 $\pm$ .73	2.62 $\pm$ .74	.41
Retention	Control	48.01 $\pm$ 2.39		.93	38.75 $\pm$ 1.99		.33	2.61 $\pm$ .69		.39	2.48 $\pm$ .46		.24	2.20 $\pm$ .61		.58
	Training	46.47 $\pm$ 2.24		.77	37.03 $\pm$ 2.58		.91	2.81 $\pm$ .47		.36	2.49 $\pm$ .52		.44	2.56 $\pm$ .43		.94

RMT SI: resting motor threshold stimulus intensity. AMT SI: active motor threshold stimulus intensity. Single (SP) and paired-pulse (PP) rmsEMG was pooled across stimulus intensities.