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Title: Tracking the corticospinal responses to strength training

Year: 2020

Version: Accepted version (Final draft)

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Please cite the original version:

Mason, J., Frazer, A. K., Avela, J., Pearce, A. J., Howatson, G., & Kidgell, D. J. (2020). Tracking the corticospinal responses to strength training. *European Journal of Applied Physiology*, 120(6), 783-798. <https://doi.org/10.1007/s00421-020-04316-6>

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2 **Tracking the corticospinal responses to strength training**
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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:** γ -Aminobutyric acid
107 **ICF:** Intracortical facilitation
108 **LICI:** Long-interval cortical inhibition
109 **MEP:** Motor-evoked potential
110 **M_{MAX}:** 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 ± 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 ~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 200² 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 μ V
293 for RMT and greater than 200 μ 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 μ 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_{MAX} 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 2×7 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
404 analysis revealed by the end of the first week of strength-training, the strength-training group
405 increased their 1-RM strength of the wrist flexor by $6.3 \pm 4.5\%$ (CI -9.80 to -0.0995, $P = 0.04, d =$
406 1.24) compared to a $1.4 \pm 3.5\%$ increase in the control group (Table 1). Post hoc analysis also showed
407 after two-weeks of strength-training, the strength-training group increased their 1-RM strength by
408 $15.5 \pm 7.6\%$ (CI -18.5 to -8.76, $P < 0.001, d = 2.20$) compared to a $1.8 \pm 3.5\%$ increase in the control
409 group.
410

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

721 **Funding** This research did not receive any specific grant from funding agencies in the public,
722 commercial, or not-for-profit sectors.

723

724 **Compliance with ethical standards**

725

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

Accepted - uncorrected proof

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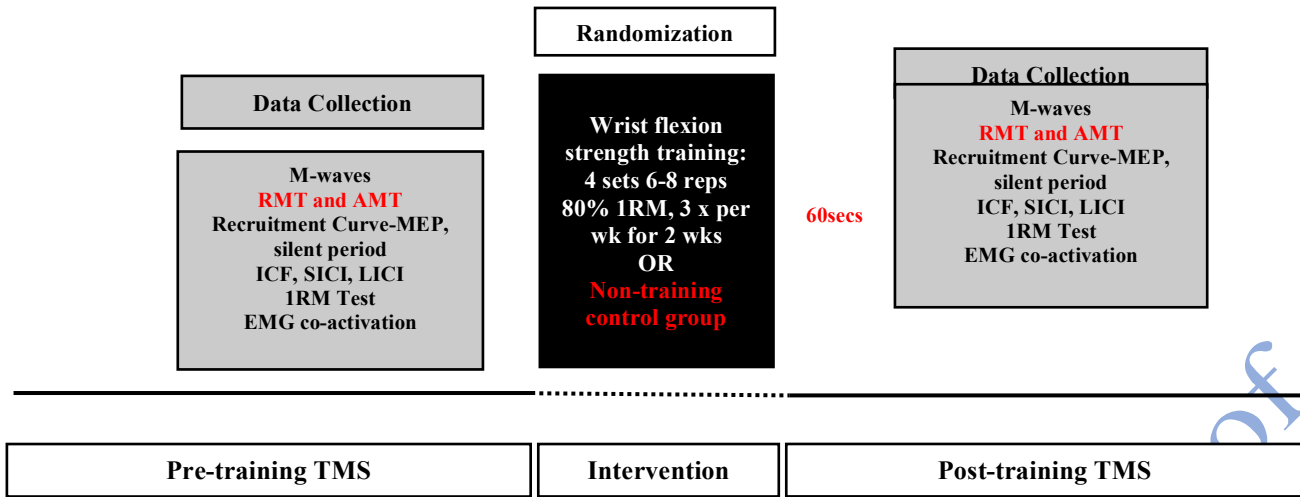


Figure 1: Schematic representation of the experimental design for the experimental group (heavy-load strength training of the wrist flexors) and the control group. Pre and post testing occurred prior to and following each strength-training session (repeated six times over two weeks, each separated by 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.

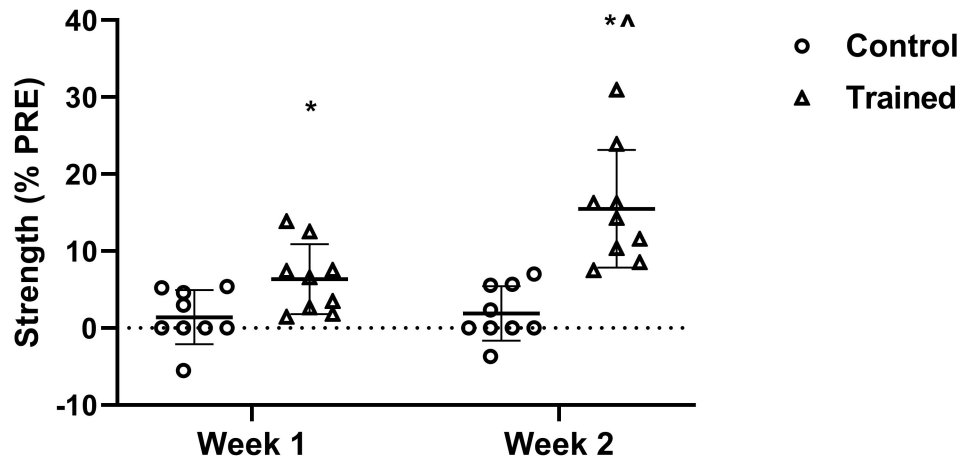


Figure 2: Change in 1-RM strength for the wrist flexor (mean \pm SD) following the strength-training condition at week 1 and week 2 compared to baseline strength and the control group. *Denotes a significant increase in strength from baseline following heavy-load strength training compared to the control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

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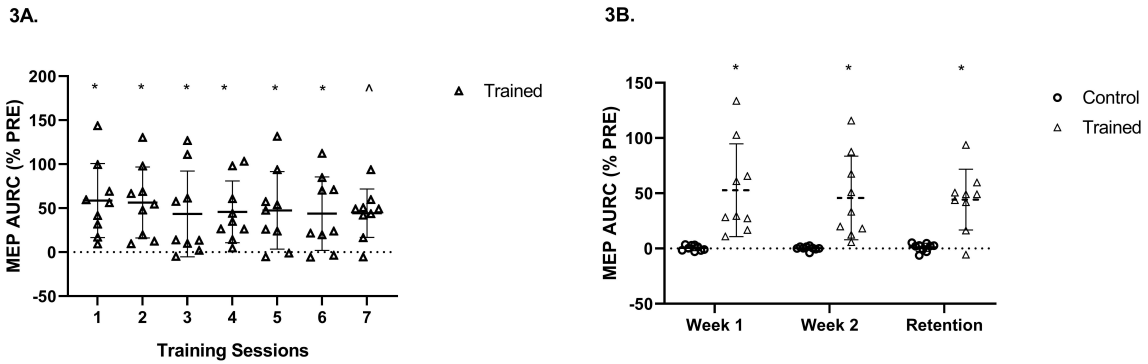


Figure 3A-B: Changes in AURC for CSE of the trained wrist flexor (mean \pm SD) following heavy-load strength training across six training sessions and at the retention session (A). *Denotes a significant increase in AURC for CSE from respective training sessions following training, ^denotes a significant 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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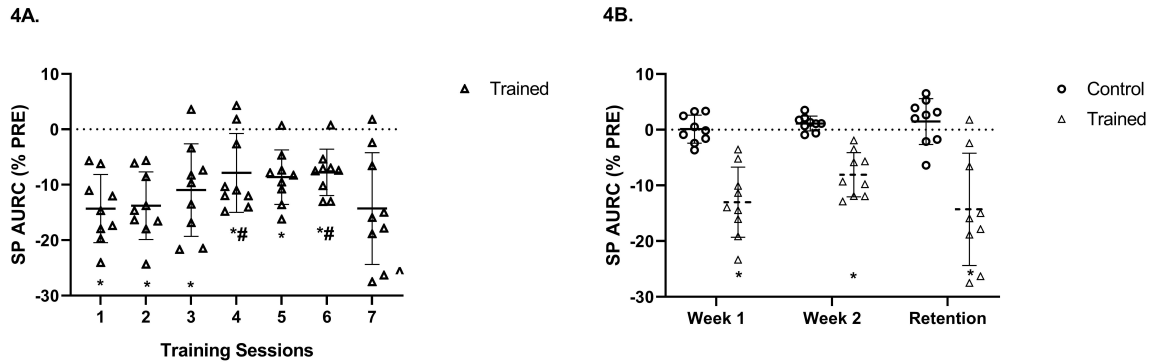
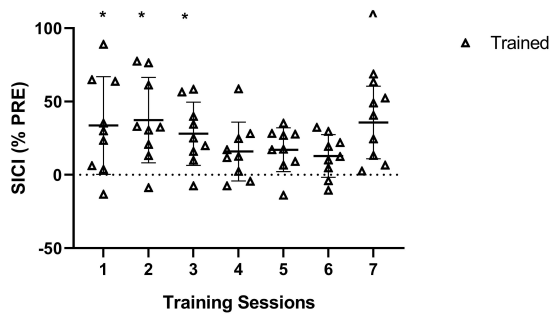


Figure 4A-B: Changes in AURC for silent period duration of the trained wrist flexor (mean \pm SD) following heavy-load strength training across six training sessions and at the retention session (A). *Denotes a significant reduction in the AURC silent period duration from respective session baseline 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.

Accepted - uncorrected proof

5A.



5B.

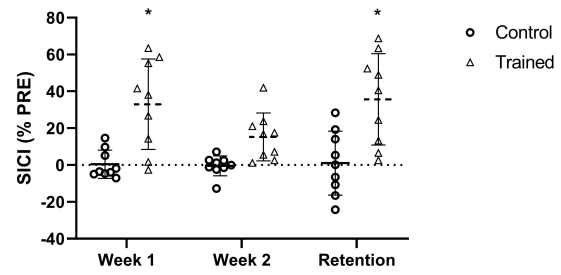
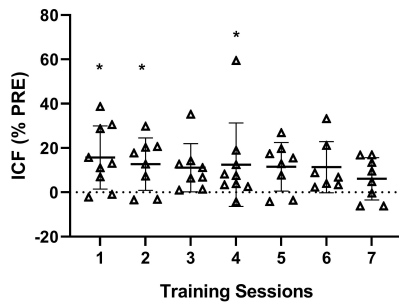


Figure 5A-B: Changes SICI of the trained wrist flexor (mean \pm SD) following heavy-load strength training across six training sessions and at the retention session (A). *Denotes a significant release of SICI from baseline data following training, ^denotes a significant release in SICI 72 h following 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.

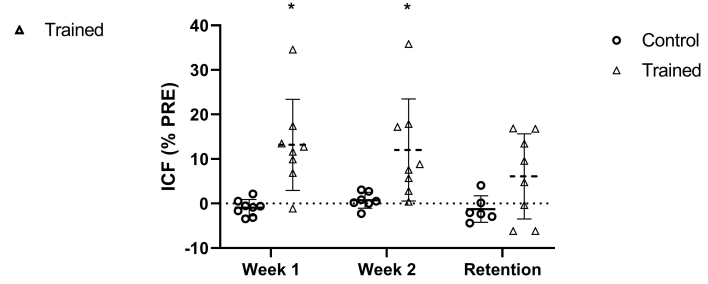


Figure 6A-B: Changes ICF of the trained wrist flexor (mean \pm SD) following heavy-load strength-training across six training sessions and at the retention session (A). *Denotes a significant increase of ICF from session baseline data following training. Changes in ICF of the trained wrist flexor (mean \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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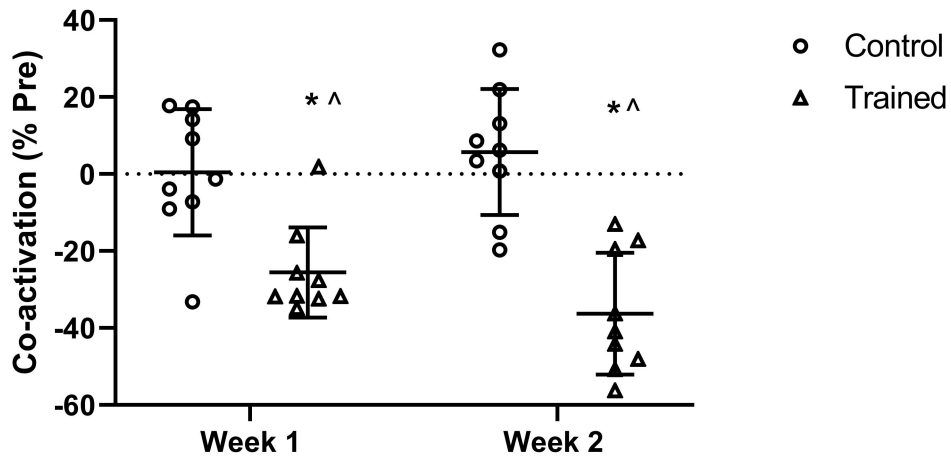


Figure 7: Changes in co-activation index following one week and two weeks of heavy-load strength training for the control and strength training groups. *denotes statistical significance from baseline, ^ denotes statistical significance from week 1 to week 2 compared to control ($P < 0.05$).

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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	9.33 \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.