

1 Article

2 Corticospinal excitability to the biceps brachii is not 3 different when arm cycling at a self-selected or fixed 4 cadence

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10

11 **Abstract:** Background: The present study compared corticospinal excitability to the biceps brachii
12 muscle during arm cycling at a self-selected and a fixed cadence (SSC and FC, respectively). We
13 hypothesized that corticospinal excitability would not be different between the two conditions.
14 Methods: The SSC was initially performed and the cycling cadence was recorded every 5 seconds
15 for one minute. The average cadence of the SSC cycling trial was then used as a target or FC of
16 cycling that the participants were instructed to maintain. Motor evoked potentials (MEPs) elicited
17 via transcranial magnetic stimulation (TMS) of the motor cortex were recorded from the biceps
18 brachii during each trial of SSC and FC arm cycling. Results: Corticospinal excitability as assessed
19 via normalized MEP amplitudes (MEPs were made relative to a maximal compound muscle action
20 potential) were not different between groups. Conclusions: Focusing on maintaining a FC cadence
21 during arm cycling does not influence corticospinal excitability as assessed via TMS-evoked MEPs.

22 Keywords: motor evoked potential; MEP; arm cranking; pedaling; exercise

23

24 1. Introduction

25 It is well established that rhythmic locomotor outputs in non-human animals (e.g. cat, rat, dog)
26 are partially controlled by neural circuits located in the spinal cord, referred to as central pattern
27 generators (CPGs) ^{1,2}. Evidence, albeit indirect, has shown that the CPG also contributes to the
28 production of rhythmic motor outputs in humans by integrating descending and afferent input ^{3,4}
29 though it is believed that descending input is of greater importance in the control of human locomotor
30 outputs ⁵.

31 Arm cycling has been introduced as a model of locomotor output for examining changes in
32 neural excitability during rhythmic movement, with the vast majority of these studies using a set
33 cadence and power output for each participant ^{4,5}. While this may be necessary to maintain
34 experimental stringency, it is also acknowledged that: first, arm cycling may be regarded as a novel
35 task for some participants and second, that by setting the cadence at 60 rpm for example, participants
36 may not be cycling at a preferred cadence. Taken together, these two factors may act to alter
37 attentional demands, thus influencing measures of corticospinal excitability.

38 When humans engage in a novel motor task, they typically focus on how to perform said task,
39 placing them in what is known as the *cognitive stage* of motor learning according to the Fitts and
40 Posner model ⁶. This suggests that the level of cognitive effort, and thus, in all likelihood descending
41 input, would be greater during this stage of learning. This is supported by work examining the time
42 course of changes in corticospinal excitability when learning a novel motor task, albeit non-locomotor
43 ⁷. Holland et al. (2015) showed that the slope of the transcranial magnetic stimulation (TMS) evoked
44 input/output (I/O) curve decreased as learning progressed, with the majority of the change occurring

45 on the first of two training days. This suggests that as participants began the novel task, greater
46 cognitive effort was required thus enhancing corticospinal excitability, an effect that decreased as the
47 task lost its' novelty.

48 Arm cycling is a motor task that may be considered novel and a number of studies have been
49 published examining corticospinal excitability during cycling in humans⁸⁻¹⁴. Work from our lab has
50 shown that corticospinal excitability, assessed via TMS of the motor cortex projecting to the biceps
51 brachii, was shown to be higher during arm cycling in humans when the elbow was flexed (bottom
52 dead centre) compared to an intensity- and position-matched tonic contraction¹⁵. This effect was due
53 to enhanced supraspinal excitability as there were no differences in measures of spinal excitability.
54 In that study, participants were required to maintain a predetermined cadence (60 rpm) throughout
55 the trial by observing their cadence on the ergometer monitor and it was possible that this increased
56 the attentional demand of the task. Research has shown that directed visual attention can induce an
57 increase in neural activity in the fronto-parietal network as evidenced in functional brain imaging
58 studies¹⁶. It is thus possible that an increase in attention may increase corticospinal excitability during
59 arm cycling, though we hypothesized that the difference was task-dependent and not simply due to
60 increased attentional demands of arm cycling¹⁵.

61 Several studies have examined the influence of cycling cadence on neuromuscular activation.
62 Marias et al., (2004) examined the effects of a spontaneous chosen crank rate (SCCR) and crank rates
63 20% higher and lower than the SCCR during arm cycling on integrated electromyography (iEMG)
64 levels in the biceps brachii muscles in humans. The researchers concluded that there were no
65 significant differences in iEMG between the crank rate conditions of the biceps brachii, suggesting
66 that the SCCR is not chosen to minimize the level of muscle activity and that the degree of muscle
67 activation was similar between the two groups¹⁷. This finding is supported by research that showed
68 no reduction in lower extremity muscle activation at a SCCR during leg cycling¹⁸. The iEMG assessed
69 in these studies is a measure of the electrical activity in the muscle representing the overall output of
70 the motoneurone pool and does not necessarily represent corticospinal excitability^{8, 13-14}. Therefore,
71 it is unknown how a SSC during arm cycling influences corticospinal excitability in comparison to a
72 FC.

73 The purpose of the current study was thus to determine if corticospinal excitability between SSC
74 and FSC arm cycling were different. It was hypothesized that corticospinal excitability as assessed
75 via the amplitude of motor evoked potentials (MEPs) elicited via TMS of the motor cortex would not
76 be different between a SSC and FSC.

77 **2. Materials and Methods**

78 *Ethical approval*

79 Prior to the experiment all participants were informed of the experimental protocol and written
80 informed consent was obtained. This study was in accordance with the Helsinki declaration and
81 experimental procedures were approved by the Interdisciplinary Committee on Ethics in Human
82 Research at Memorial University of Newfoundland (ICEHR #20171250). All experimental procedures
83 were in accordance with the Tri-Council guideline in Canada and potential risks of participation were
84 disclosed to all participants.

85 *Participants*

86 Eleven participants (7 male and 4 female; 22 ± 2.14 years of age) were recruited from the School
87 of Human Kinetics and Recreation (HKR) at Memorial University using a convenience sampling
88 technique. Prior to testing each participant completed a magnetic stimulation safety-checklist to
89 screen for existing contraindications to magnetic stimulation (Rossi et al, 2009). To determine hand
90 dominance participants completed an Edinburgh handedness inventory questionnaire to ensure that
91 all evoked responses were recorded from the dominant arm¹⁹. Additionally, to screen for existing
92 contraindications to physical activity each participant completed a Physical Activity Readiness

93 Questionnaire (PAR- Q+) ²⁰. Participants were excluded if they had any neurological deficits or
94 contraindications to magnetic stimulation and physical activity.

95 *Experimental Set-up*

96 A one-group within-subjects design was used. Participants attended two lab sessions with at
97 least 24 hours in between visits: the first visit was for a half-hour familiarization session and the
98 second was the testing session, lasting approximately 1 hour. The experiment was completed on an
99 arm cycle ergometer (SCIFIT ergometer, model PRO2 Total Body) with the arm cranks set at 180
100 degrees out of phase. Each participant was advised to sit upright at a comfortable position from the
101 arm cranks to ensure that they could maintain an upright posture throughout each cycling protocol.
102 The seat height was adjusted to ensure the participants shoulders were in line with the center of the
103 arm shaft. The participants were informed to lightly grip the handles with their forearms in
104 pronation. Each participant was required to wear wrist braces to limit wrist joint movement during
105 cycling to reduce the effects of the heteronymous reflex connections that exist between the wrist flexor
106 muscles and the biceps brachii muscle ²¹.

107 All measurements were taken at a single position; 6 o'clock relative to a clock face. This position
108 was relative to the participants dominant hand, such that TMS would be triggered when the right or
109 left hand was at the 6 o'clock position for a right or left-handed dominant individual, respectively.
110 We have examined this position previously ^{8-13, 15}, as it corresponds to a period of high bicep brachii
111 EMG activity during arm cycling since it occurs during mid-elbow flexion (i.e., movement from 3
112 o'clock to 9 o'clock)..

113 The study required participants to cycle at two different cadences, both at a constant workload
114 of 25 W. The cadences (FC and SSC) served as the independent variable in the study. TMS and Erb's
115 point stimulation were delivered at the 6 o'clock position to elicit MEPs and M_{max} in the biceps brachii
116 muscle in each condition. MEP amplitude made relative to M_{max} and bEMG (see below), as a measure
117 of corticospinal excitability, served as the dependent variable. The SSC trial was completed first
118 followed by the FC trial and responses were triggered as the arm crank of the dominant arm passed
119 the 6 o'clock position.

120 *Electromyography (EMG) recordings*

121 EMG activity was recorded from the biceps brachii and lateral head of the triceps brachii of the
122 dominant arm using pairs of surface electrodes (Kendall™ 130 conductive adhesive electrodes,
123 Covidien IIC, Massachusetts, USA). EMG was recorded using a bi-polar configuration with an
124 interelectrode distance of 2 cm. Electrodes were placed in the middle of the muscle belly of the biceps
125 brachii. A ground electrode was placed over the lateral epicondyle on the dominant arm. Prior to
126 electrode placement the skin at the recording site was shaved to remove hair, abraded using an
127 abrasive pad to remove dead epithelial cells and cleaned with an isopropyl alcohol swab to reduce
128 impedance for EMG recordings. Signals were sampled online at 5 kHz using CED 1401 interface and
129 Signal 5.11 software (Cambridge Electronic Design (CED) Ltd., Cambridge, UK). EMG signals were
130 amplified (gain of 300) and filtered using a 3-pole Butterworth band-pass filter (10-1000 Hz) using a
131 CED 1902 amplifier.

132 **Simulation Conditions**

133 *Brachial plexus stimulation*

134 Electrical stimulation of the brachial plexus at Erb's point was used to measure M_{max} (maximal
135 M-wave) (DS7AH, Digitimer Ltd., Welwyn Garden City, Hertfordshire, UK). The anode was placed
136 on the acromion process and the cathode was placed over the skin in the supraclavicular fossa. A
137 pulse duration of 200 μ s was utilized and the stimulation intensity was gradually increased until the
138 M-wave amplitude of the biceps brachii reached a plateau, referred to as M_{max} . This stimulation
139 intensity was increased by 10% and used for the remainder of the experiment to ensure maximal M-
140 waves were elicited during each trial ²².

141 *Transcranial magnetic stimulation (TMS)*

142 Motor evoked potentials (MEPs) were measured during both cycling trials from the biceps
143 brachii and served as the dependent variable in the study. TMS (Magstim 200, Dyfed, UK) was used
144 to elicit MEPs in the biceps brachii by placing a circular coil (13.5 cm outside diameter) over the
145 vertex. TMS is a valid and reliable technique for eliciting MEPs, which are recorded from the muscle
146 as a measure of the excitability of the corticospinal tract (Rothwell et al., 1991). The vertex was located
147 by measuring the mid-point between the nasion and the inion and between participants tragi and
148 marks were placed for both measurements directly on the scalp. The intersection of the measurements
149 was defined as the vertex^{13, 15, 23-24}. The same researcher held the coil for each trial and was vigilant
150 with ensuring the coil was held parallel to the floor and remained aligned with the vertex throughout
151 each trial. The current preferentially activated the right or left motor cortex, depending on hand
152 dominance. Stimulation intensity was set during cycling (60 rpm and 25W) with MEPs evoked when
153 the dominant hand was at the 6 o'clock position. The stimulus intensity was measured as a percentage
154 of the maximum stimulator output (MSO) and intensity was increased until the participants active
155 motor threshold (AMT) was found. AMT was defined as the lowest stimulus intensity required to
156 evoke 5 clearly discernable MEPs (~ 200 μ V) in 10 trials during cycling. Once AMT was found, MSO
157 was increased by 10% to ensure clearly discernable MEPs were recorded and this stimulation
158 intensity was then used for all trials.

159 *Experimental Protocol*

160 After the stimulation intensities were set for TMS and Erb's point stimulation the cycling trials
161 were completed. The participant was first instructed to cycle forwards at a comfortable pace and the
162 monitor displaying the cycling cadence was moved out of the participants sight, such that the
163 participant was blinded to their cycling cadence. When the participant reached a steady cadence, as
164 observed by the researcher, the trial was started. Steady cadence was defined as a cadence that
165 fluctuated no more than ± 1 rpm over a 5 second period. While the participant was cycling the
166 researcher recorded the cadence every 5 seconds and calculated the average cadence over the
167 duration of the trial. After a 1- minute break the participant was instructed to cycle forward
168 maintaining a target cadence, as specified by the researcher, by observing their cadence on the
169 monitor. This target cadence (FC) was equal to the average of the cadence over the duration of the
170 SSC trial. During both trials the arm ergometer was set to a fixed power output of 25 W. While cycling
171 each participant received 12 MEPs and 2 M-waves per trial, which were delivered when the dominate
172 hand passed the 6 o'clock position. The order of the stimulations was randomized during the trial,
173 and the stimulations were evoked every 7-8 s. To prevent anticipation of the stimulation 2 frames
174 without stimulation were added. The total length of cycling was approximately 2 minutes per trial.

175 *Data Analysis*

176 Data was analyzed off-line using Signal 5.11 software (Cambridge Electronic Design Ltd.,
177 Cambridge, UK). To determine if central motor drive projecting to the biceps brachii was similar
178 between the two arm cycling conditions the mean rectified EMG 50 ms prior to TMS stimulus artifact
179 was measured (Forman et al., 2014). The peak-to-peak amplitude of all evoked responses (MEP and
180 M-wave) were measured from the initial deflection of the voltage trace from background EMG to the
181 return of the trace to the baseline level. MEP amplitudes can change as a result of changes to M_{max} ,
182 thus MEPs were normalized to M_{max} evoked during the same trial to account for potential changes in
183 peripheral excitability. All measurements were taken from the averaged files of all 12 MEPs and 2 M-
184 waves. All measurements were made from the dominant arm.

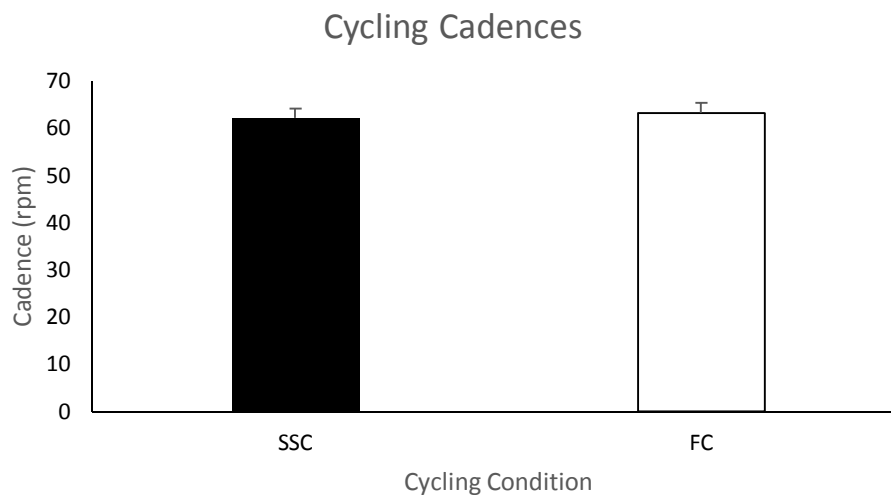
185 *Statistical analysis*

186 To compare pre-stimulus EMG between conditions (SSC and FC) paired- samples *t*- tests were
187 utilized. Additionally, paired-samples *t*-tests were used to assess whether statistically significant
188 differences in MEP amplitudes normalized to M_{max} occurred between the SSC and FC conditions. All

189 statistics were completed on group data with a significance level of $p < .05$. All data is reported as
190 mean \pm SE in Figures.

191 3. Results

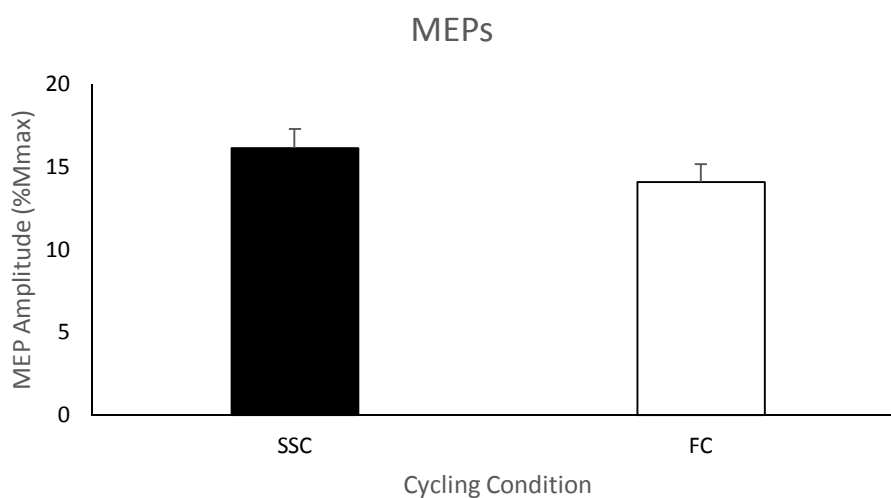
192 *Cycling cadence.* Figure 1 shows the group mean cycling cadence in revolutions per minute (rpm)
193 during the SSC and FC arm cycling trials. The cycling cadences for each condition were not
194 significantly different (mean cadence: SSC: 62 ± 6.4 rpm and FC 63 ± 6.9 rpm; $p = .118$).



195

196 **Figure 1.** Mean cycling cadences for each group (SSC = black and FC = white). Data (n=11) is shown
197 as mean \pm SE.

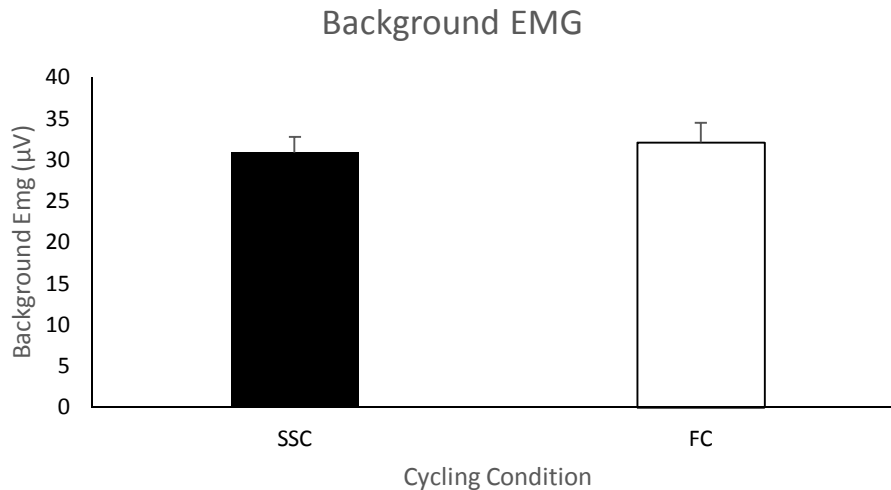
198 *MEP amplitude.* Figure 2 shows the group mean MEP amplitudes expressed as a percentage of
199 M_{max} of the biceps brachii during the SSC and FC arm cycling trials. The average MEP amplitude
200 (normalized/standardized to M_{max}) when cycling at a SSC and FC was 16.2 % ($SD = 12.25$) and 14.1%
201 ($SD = 11.75$), respectively, with a mean difference of 2.1 %. This difference was not statistically
202 significant ($p = .146$).



203

204 **Figure 2.** Mean TMS evoked MEP amplitudes as a percentage of M_{max} for each group (SSC = black
205 and FC = white). Data (n=11) is shown as mean \pm SE.

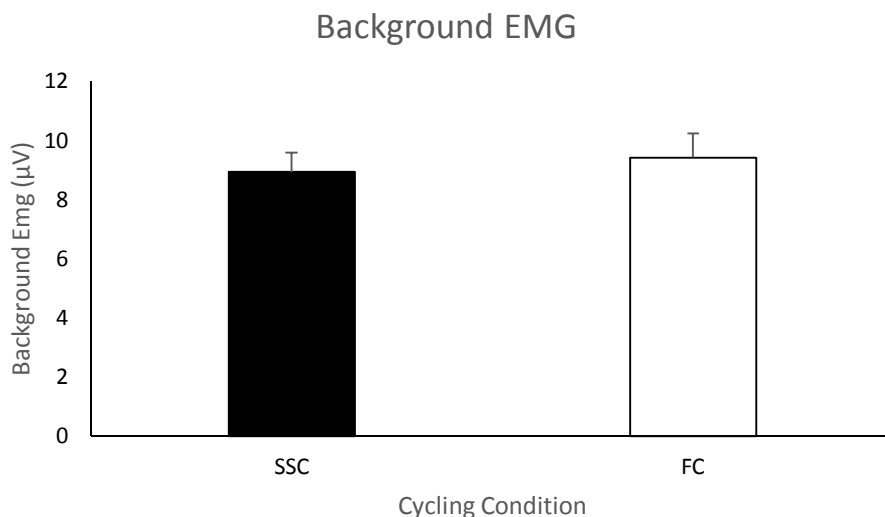
206 **Pre-stimulus EMG of the biceps brachii for MEPs.** The group mean ($n = 11$) pre-stimulus EMG
 207 of the biceps brachii prior to the TMS stimulus artifact during SSC and FC arm cycling can be seen in
 208 Figure 3. As a group, the mean pre-stimulus EMG for SSC and FC arm cycling trials was 30.2 ± 4.58
 209 μV and $32.1 \pm 5.82 \mu\text{V}$, respectively. There was no significant difference between the values ($p = .061$).



210

211 **Figure 3.** Mean of the average rectified EMG amplitude for the biceps brachii prior to TMS-evoked
 212 MEPs for each group (SSC = black and FC = white). Data ($n=11$) is shown as mean \pm SE.

213 **Pre-stimulus EMG of the triceps brachii for MEPs.** The group mean ($n = 11$) pre-stimulus EMG
 214 of the triceps brachii prior to the TMS stimulus artifact during SSC and FC arm cycling can be seen
 215 in Figure 4. As a group, the mean pre-stimulus EMG for SSC and FC arm cycling trials was 8.9 ± 2.12
 216 μV and $9.4 \pm 2.68 \mu\text{V}$, respectively. There was no significant difference between the values ($p = .58$).



217

218 **Figure 4.** Mean of the average rectified EMG amplitude for the triceps brachii prior to TMS-evoked
 219 MEPs for each group (SSC = black and FC = white). Data ($n=11$) is shown as mean \pm SE.

220 4. Discussion

221 This is the first study to compare corticospinal excitability projecting to the biceps brachii
 222 between self-selected (SSC) and fixed cadence (FC) arm cycling. There were no significant differences
 223 in corticospinal excitability as assessed via TMS-evoked MEP amplitudes recorded from the biceps
 224 brachii between the two arm cycling conditions. Maintaining a predetermined cadence (FC) during

225 arm cycling does not increase corticospinal excitability when compared to cycling at a voluntarily
226 chosen cadence (SSC).

227 A prior concern in studies from our lab and also the work of others was that the attentional
228 demands of maintaining a set cadence could inadvertently alter (likely increase) measures of
229 corticospinal excitability. The current finding that corticospinal excitability is not different between
230 SSC and FC arm cycling lends support to our previous finding that corticospinal excitability is task-
231 dependent and is higher during arm cycling than an intensity- and position- matched tonic
232 contraction¹⁵. In that study the participants were required to maintain a pre-determined cadence (60
233 rpm) while arm cycling rather than a voluntarily chosen cadence (Forman et al., 2014). Thus, it was
234 unknown if the increase in supraspinal excitability projecting the biceps brachii at the 6 o'clock
235 position was due to the arm cycling task or if it resulted from a greater attentional demand to
236 maintain the set cadence. The results from the current study indicate that focusing on maintaining a
237 fixed cadence does not increase the overall excitability of the corticospinal tract compared to arm
238 cycling at a SSC. Thus, the increase in corticospinal excitability during arm cycling that we reported
239 was likely task-dependent and not attributable to the fact that the participants had to focus on
240 maintaining a cadence of 60 rpm¹⁵. This is indirectly supported by prior work assessing EMG of both
241 arm and leg muscles during either arm¹⁷ or leg¹⁸ cycling, respectively. In the aforementioned studies,
242 there was no influence of SSC or FC on EMG amplitudes, though there were no measures of
243 corticospinal excitability.

244 *Attentional Focus and Corticospinal Excitability*

245 Prior work has shown that visual attention modulates corticospinal excitability and directing
246 visual attention towards specific features of an observed action facilitates corticospinal excitability
247 more than passive observation²⁵⁻²⁶. Attention can be directed to highly salient stimuli based on their
248 physical properties (i.e. brightness, colour, speed) or towards stimuli that is important for one's
249 current task²⁷. In this study during the FC condition participants were instructed to focus on the
250 monitor that displayed the cadence they were cycling at and were instructed to maintain a set cadence
251 and speed up or slow down based on the observed cadence. In contrast, during the SSC condition
252 participants were not able to see the monitor and were not instructed to focus on any particular object
253 in the external environment. Although participants were instructed to focus on the cadence on the
254 monitor throughout the FC trial, corticospinal excitability projecting to the biceps brachii was not
255 increased when compared to the SSC trial. A possible explanation for the lack of increase in
256 corticospinal excitability during the FC trial is that it is unknown if the participant maintained their
257 focus on the cadence displayed on the monitor throughout the entire trial as eye tracking devices
258 were not used. Also, much of the literature regarding increases in corticospinal excitability with
259 focused attention has been on the observation of human movement and the activity in the putative
260 mirror neuron system. Notably, corticospinal excitability is facilitated during action observation and
261 more so during goal-directed actions (i.e. grasping an object) when attention is directed to task-
262 relevant features of the observed action²⁸. In this study, the participants were not observing an action
263 but were rather observing numbers on a monitor that were relevant to their behavioural goal
264 (maintaining a set cadence). Thus, the theory that corticospinal excitability is facilitated during action
265 observation due to the increased activity in the mirror neuron system may not apply in the present
266 study.

267 *Methodological Considerations*

268 Additional factors should be considered when interpreting the present results. This study
269 assessed MEP amplitudes and therefore conclusions can only be made regarding the overall
270 excitability of the corticospinal tract. In future research assessing spinal excitability, with TMES for
271 example, to the target muscle to determine if changes in corticospinal excitability are occurring at the
272 spinal and/or supraspinal level may be of interest²⁹. For instance, it is possible that supraspinal
273 excitability increased during the FC trial and the increase was masked by a reduction in spinal
274 excitability, resulting in no change in the overall excitability of the corticospinal tract. In order to

275 decipher between supraspinal and spinal excitability both TMES and TMS need to be utilized. The
276 reason we chose the 6 o'clock position, however, was because in our prior work we have shown that
277 corticospinal excitability is higher during arm cycling than a tonic contraction at that position while
278 spinal excitability is not. Thus, it is unlikely that spinal excitability was different in the present study.
279 Additionally, some participants in this study had previous experience with arm cycling and therefore
280 may have required less attentional focus to execute the task. However, we purposely included a
281 familiarization session for all participants to minimize this threat to internal validity by allowing
282 participants to practice arm cycling.

283 5. Conclusions

284 The novel finding in this study is that corticospinal excitability, as assessed by changes in MEP
285 amplitude, projecting to the biceps brachii is not different between SSC and FC arm cycling. We can
286 indirectly (because attention was not directly measured) conclude that corticospinal excitability
287 during arm cycling is independent of attentional demands as corticospinal excitability is not different
288 when focusing attention on maintaining a set cadence compared to cycling at a voluntarily chosen
289 cadence.

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294 All authors have approved the submitted version of this manuscript.

295 **CONFLICTS OF INTEREST:** The authors declare no conflict of interest.

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