

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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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 for 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) <sup>1,2</sup>. 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 <sup>3,4</sup>  
29 though it is believed that descending input is of greater importance in the control of human locomotor  
30 outputs <sup>5</sup>.

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 <sup>4,5</sup>. 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 <sup>6</sup>. 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 <sup>7</sup>. 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 humans<sup>8-14</sup>. 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 contraction<sup>15</sup>. 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 studies<sup>16</sup>. 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 cycling<sup>15</sup>.

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 groups<sup>17</sup>. This finding is supported by research that showed  
68 no reduction in lower extremity muscle activation at a SCCR during leg cycling<sup>18</sup>. 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<sup>8, 13-14</sup>. 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 FC arm cycling were different. It was hypothesized that corticospinal excitability as assessed via  
75 the amplitude of motor evoked potentials (MEPs) elicited via TMS of the motor cortex would not be  
76 different between a SSC and FC.

## 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;  $22 \pm 2.14$  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 arm<sup>19</sup>. Additionally, to screen for existing  
92 contraindications to physical activity each participant completed a Physical Activity Readiness

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

#### 95 *Experimental Set-up*

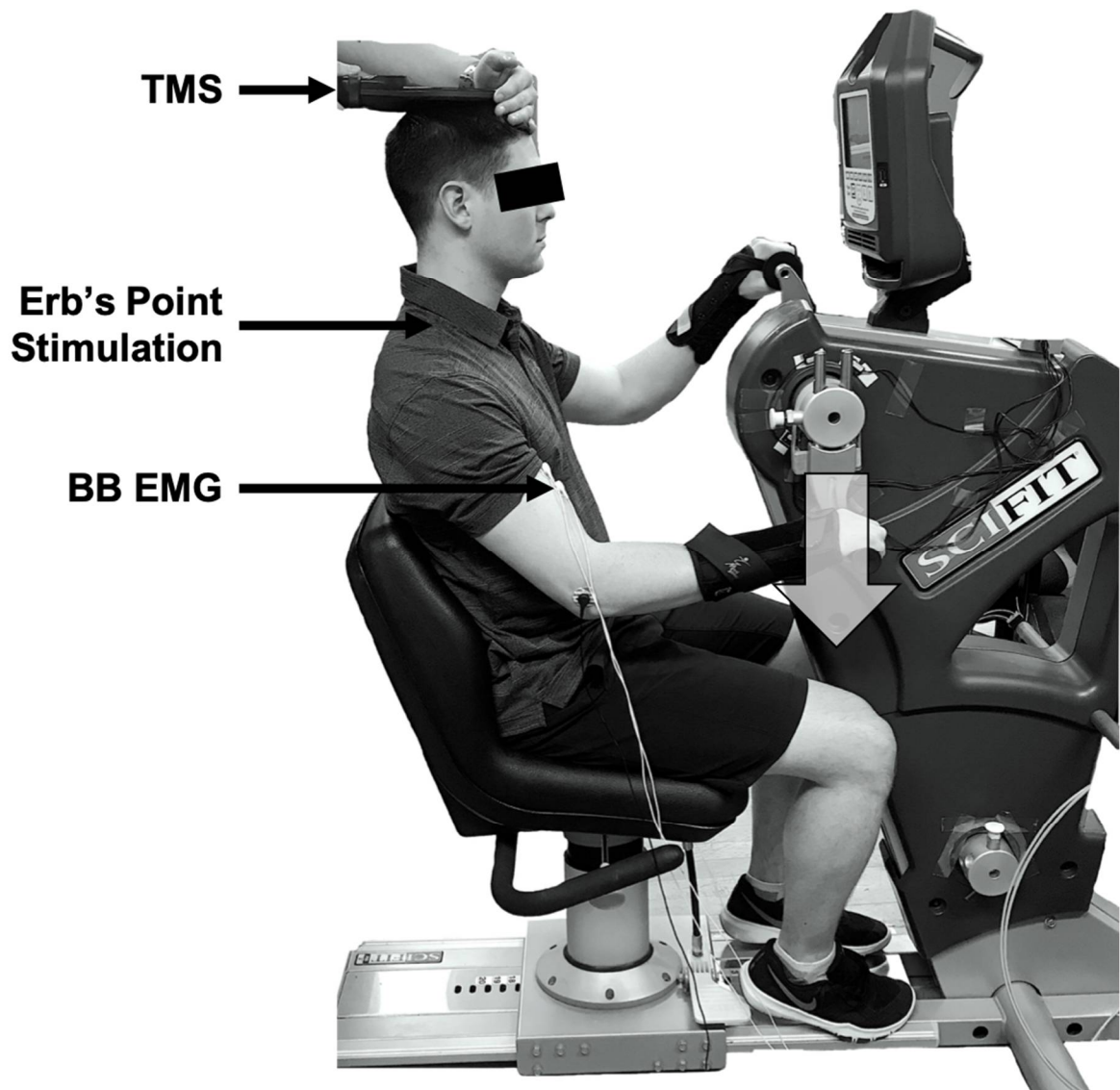
96 A one-group within-subjects design was used. Participants attended two lab sessions with at  
97 least 24 hours in between visits: the first visit was for a half-hour familiarization session and the  
98 second was the testing session, lasting approximately 1 hour. The experiment was completed on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

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 <sup>8-13, 15</sup>, 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

133 **Figure 1.** Experimental setup. Arm cycling was performed in the forward direction, with stimulations  
 134 occurring when the dominant arm passed the 6 o'clock position (i.e. bottom-dead centre) when the  
 135 biceps brachii is active. This position is denoted by the large grey downwards arrow.

### 136 **Simulation Conditions**

#### 137 *Brachial plexus stimulation*

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

#### 145 *Transcranial magnetic stimulation (TMS)*

146 Motor evoked potentials (MEPs) were measured during both cycling trials from the biceps  
 147 brachii and served as the dependent variable in the study. TMS (Magstim 200, Dyfed, UK) was used  
 148 to elicit MEPs in the biceps brachii by placing a circular coil (13.5 cm outside diameter) over the  
 149 vertex. TMS is a valid and reliable technique for eliciting MEPs, which are recorded from the muscle

150 as a measure of the excitability of the corticospinal tract (Rothwell et al., 1991). The vertex was located  
151 by measuring the mid-point between the nasion and theinion and between participants tragi and  
152 marks were placed for both measurements directly on the scalp. The intersection of the measurements  
153 was defined as the vertex<sup>13, 15, 23-24</sup>. The same researcher held the coil for each trial and was vigilant  
154 with ensuring the coil was held parallel to the floor and remained aligned with the vertex throughout  
155 each trial. The current preferentially activated the right or left motor cortex, depending on hand  
156 dominance. Stimulation intensity was set during cycling (60 rpm and 25W) with MEPs evoked when  
157 the dominant hand was at the 6 o'clock position. The stimulus intensity was measured as a percentage  
158 of the maximum stimulator output (MSO) and intensity was increased until the participants active  
159 motor threshold (AMT) was found. AMT was defined as the lowest stimulus intensity required to  
160 evoke 5 clearly discernable MEPs (~ 200  $\mu$ V) in 10 trials during cycling. Once AMT was found, MSO  
161 was increased by 10% to ensure clearly discernable MEPs were recorded and this stimulation  
162 intensity was then used for all trials.

### 163 *Experimental Protocol*

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

### 179 *Data Analysis*

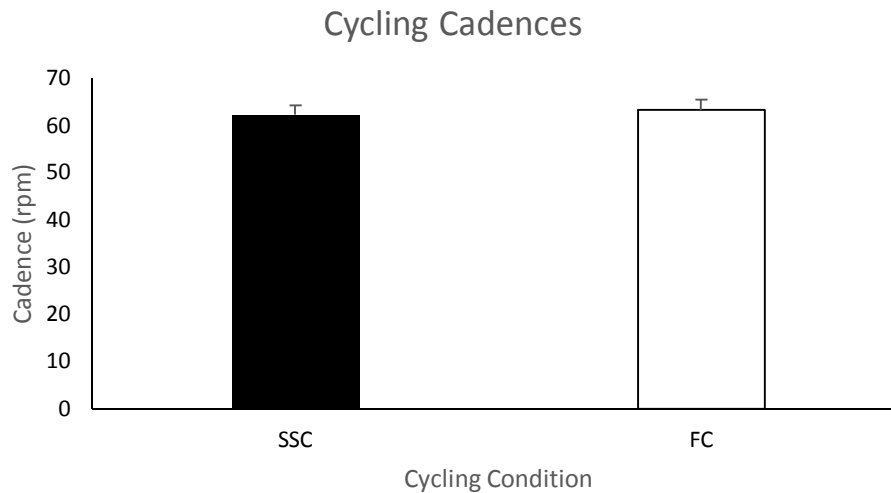
180 Data was analyzed off-line using Signal 5.11 software (Cambridge Electronic Design Ltd.,  
181 Cambridge, UK). To determine if central motor drive projecting to the biceps brachii was similar  
182 between the two arm cycling conditions the mean rectified EMG 50 ms prior to TMS stimulus artifact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

### 189 *Statistical analysis*

190 To compare pre-stimulus EMG between conditions (SSC and FC) paired- samples *t*- tests were  
191 utilized. Additionally, paired-samples *t*-tests were used to assess whether statistically significant  
192 differences in MEP amplitudes normalized to  $M_{max}$  occurred between the SSC and FC conditions. All  
193 statistics were completed on group data with a significance level of  $p < .05$ . All data is reported as  
194 mean  $\pm$  SE in Figures.

## 195 **3. Results**

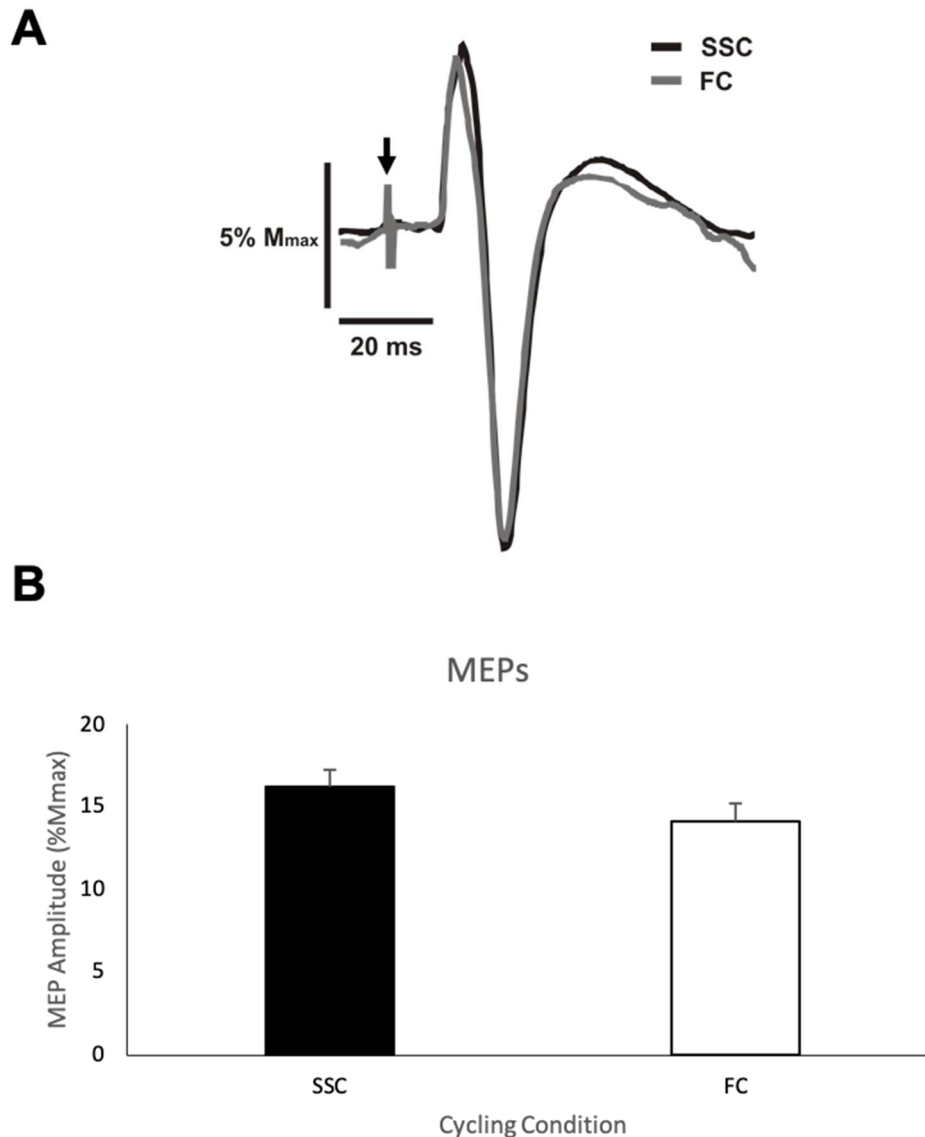
196 *Cycling cadence.* Figure 2 shows the group mean cycling cadence in revolutions per minute (rpm)  
197 during the SSC and FC arm cycling trials. The cycling cadences for each condition were not  
198 significantly different (mean cadence: SSC:  $62 \pm 6.4$  rpm and FC  $63 \pm 6.9$  rpm;  $p = .118$ ).



199

200 **Figure 2.** Mean cycling cadences for each group (SSC = black and FC = white). Data (n=11) is shown  
201 as mean  $\pm$  SE.

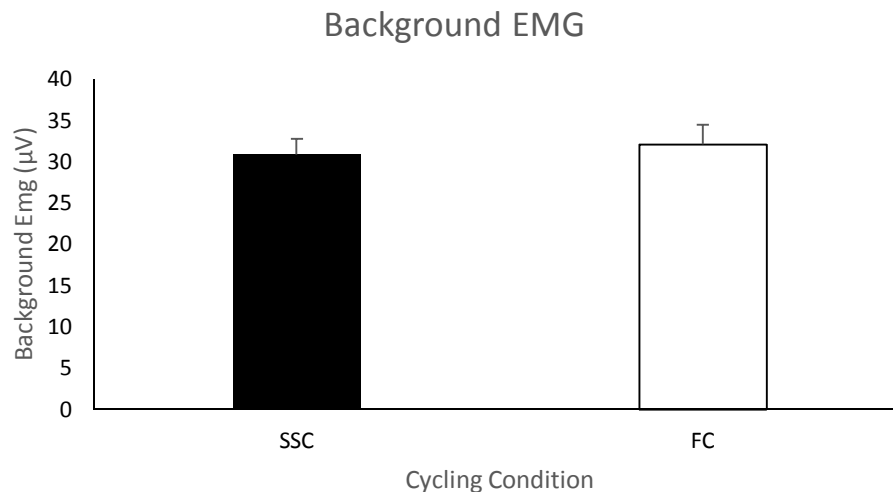
202 *MEP amplitude.* Figure 3A shows representative data for MEP amplitudes from one participant  
203 for both the SSC and FC cycling conditions. Figure 3B shows the group mean MEP amplitudes  
204 expressed as a percentage of  $M_{max}$  of the biceps brachii during the SSC and FC arm cycling trials. The  
205 average MEP amplitude (normalized/standardized to  $M_{max}$ ) when cycling at a SSC and FC was 16.2  
206 % ( $SD = 12.25$ ) and 14.1% ( $SD = 11.75$ ), respectively, with a mean difference of 2.1 %. This difference  
207 was not statistically significant ( $p = .146$ ).



208

209 **Figure 3.** (A) Representative MEP amplitudes from one participant for each cycling condition (SSC =  
 210 black and FC = grey). Downward arrow indicates location of stimulus artefacts that have been  
 211 adjusted in size for figure clarity. (B) Mean TMS evoked MEP amplitudes as a percentage of M<sub>max</sub>  
 212 for each group (SSC = black and FC = white). Data (n=11) is shown as mean ± SE.

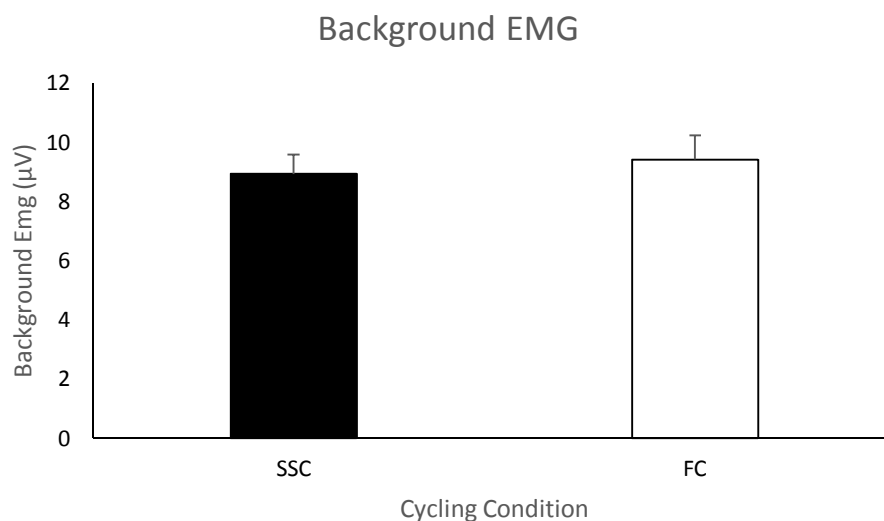
213 **Pre-stimulus EMG of the biceps brachii for MEPs.** The group mean (n = 11) pre-stimulus EMG  
 214 of the biceps brachii prior to the TMS stimulus artifact during SSC and FC arm cycling can be seen in  
 215 Figure 4. As a group, the mean pre-stimulus EMG for SSC and FC arm cycling trials was 30.2 ± 4.58  
 216 μV and 32.1 ± 5.82 μV, respectively. There was no significant difference between the values (p = .061).



217

218 **Figure 4.** Mean of the average rectified EMG amplitude for the biceps 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 *Pre-stimulus EMG of the triceps brachii for MEPs.* The group mean (n = 11) pre-stimulus EMG  
 221 of the triceps brachii prior to the TMS stimulus artifact during SSC and FC arm cycling can be seen  
 222 in Figure 5. As a group, the mean pre-stimulus EMG for SSC and FC arm cycling trials was  $8.9 \pm 2.12$   
 223  $\mu\text{V}$  and  $9.4 \pm 2.68 \mu\text{V}$ , respectively. There was no significant difference between the values ( $p = .58$ ).



224

225 **Figure 5.** Mean of the average rectified EMG amplitude for the triceps brachii prior to TMS-evoked  
 226 MEPs for each group (SSC = black and FC = white). Data (n=11) is shown as mean  $\pm$  SE.

#### 227 4. Discussion

228 This is the first study to compare corticospinal excitability projecting to the biceps brachii  
 229 between self-selected (SSC) and fixed cadence (FC) arm cycling. There were no significant differences  
 230 in corticospinal excitability as assessed via TMS-evoked MEP amplitudes recorded from the biceps  
 231 brachii between the two arm cycling conditions. Maintaining a predetermined cadence (FC) during  
 232 arm cycling does not increase corticospinal excitability when compared to cycling at a voluntarily  
 233 chosen cadence (SSC).

234 A prior concern in studies from our lab and also the work of others was that the attentional  
 235 demands of maintaining a set cadence could inadvertently alter (likely increase) measures of



236 corticospinal excitability. The current finding that corticospinal excitability is not different between  
237 SSC and FC arm cycling lends support to our previous finding that corticospinal excitability is task-  
238 dependent and is higher during arm cycling than an intensity- and position- matched tonic  
239 contraction<sup>15</sup>. In that study the participants were required to maintain a pre-determined cadence (60  
240 rpm) while arm cycling rather than a voluntarily chosen cadence (Forman et al., 2014). Thus, it was  
241 unknown if the increase in supraspinal excitability projecting the biceps brachii at the 6 o'clock  
242 position was due to the arm cycling task or if it resulted from a greater attentional demand to  
243 maintain the set cadence. The results from the current study indicate that focusing on maintaining a  
244 fixed cadence does not increase the overall excitability of the corticospinal tract compared to arm  
245 cycling at a SSC. Thus, the increase in corticospinal excitability during arm cycling that we reported  
246 was likely task-dependent and not attributable to the fact that the participants had to focus on  
247 maintaining a cadence of 60 rpm<sup>15</sup>. This is indirectly supported by prior work assessing EMG of both  
248 arm and leg muscles during either arm<sup>17</sup> or leg<sup>18</sup> cycling, respectively. In the aforementioned studies,  
249 there was no influence of SSC or FC on EMG amplitudes, though there were no measures of  
250 corticospinal excitability.

#### 251 *Attentional Focus and Corticospinal Excitability*

252 Prior work has shown that visual attention modulates corticospinal excitability and directing  
253 visual attention towards specific features of an observed action facilitates corticospinal excitability  
254 more than passive observation<sup>25-26</sup>. Attention can be directed to highly salient stimuli based on their  
255 physical properties (i.e. brightness, colour, speed) or towards stimuli that is important for one's  
256 current task<sup>27</sup>. In this study during the FC condition participants were instructed to focus on the  
257 monitor that displayed the cadence they were cycling at and were instructed to maintain a set cadence  
258 and speed up or slow down based on the observed cadence. In contrast, during the SSC condition  
259 participants were not able to see the monitor and were not instructed to focus on any particular object  
260 in the external environment. Although participants were instructed to focus on the cadence on the  
261 monitor throughout the FC trial, corticospinal excitability projecting to the biceps brachii was not  
262 increased when compared to the SSC trial. A possible explanation for the lack of increase in  
263 corticospinal excitability during the FC trial is that it is unknown if the participant maintained their  
264 focus on the cadence displayed on the monitor throughout the entire trial as eye tracking devices  
265 were not used. Also, much of the literature regarding increases in corticospinal excitability with  
266 focused attention has been on the observation of human movement and the activity in the putative  
267 mirror neuron system. Notably, corticospinal excitability is facilitated during action observation and  
268 more so during goal-directed actions (i.e. grasping an object) when attention is directed to task-  
269 relevant features of the observed action<sup>28</sup>. In this study, the participants were not observing an action  
270 but were rather observing numbers on a monitor that were relevant to their behavioural goal  
271 (maintaining a set cadence). Thus, the theory that corticospinal excitability is facilitated during action  
272 observation due to the increased activity in the mirror neuron system may not apply in the present  
273 study.

#### 274 *Methodological Considerations*

275 Additional factors should be considered when interpreting the present results. This study  
276 assessed MEP amplitudes and therefore conclusions can only be made regarding the overall  
277 excitability of the corticospinal tract. In future research assessing spinal excitability, with TMES for  
278 example, to the target muscle to determine if changes in corticospinal excitability are occurring at the  
279 spinal and/or supraspinal level may be of interest<sup>29</sup>. For instance, it is possible that supraspinal  
280 excitability increased during the FC trial and the increase was masked by a reduction in spinal  
281 excitability, resulting in no change in the overall excitability of the corticospinal tract. In order to  
282 decipher between supraspinal and spinal excitability both TMES and TMS need to be utilized. The  
283 reason we chose the 6 o'clock position, however, was because in our prior work we have shown that  
284 corticospinal excitability is higher during arm cycling than a tonic contraction at that position while  
285 spinal excitability is not. Thus, it is unlikely that spinal excitability was different in the present study.

286 Additionally, some participants in this study had previous experience with arm cycling and therefore  
287 may have required less attentional focus to execute the task. However, we purposely included a  
288 familiarization session for all participants to minimize this threat to internal validity by allowing  
289 participants to practice arm cycling.

## 290 5. Conclusions

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

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

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