



1  
2  
3 **Abstract**  
4

5 During performance of a unimanual force generation task the primary motor cortices  
6 (M1s) experience clear functional changes. Here, we evaluated the way in which M1s  
7 interact during parametric increases in right wrist flexion force in healthy volunteers. We  
8 measured the amplitude and the slope of motor evoked potentials (MEP) recruitment  
9 curves to transcranial magnetic stimulation (TMS) in the left and right flexor carpi  
10 radialis (FCR) muscles at rest and during 10, 30 and 70% of maximal wrist flexion force.  
11 At rest, no differences were observed in the amplitude and slope of MEP recruitment  
12 curves in the left and right FCR muscles. With increasing right wrist flexion force, MEP  
13 amplitudes increased in both FCR muscles, with larger amplitudes in the right FCR. We  
14 found a significant correlation between the left and right MEP amplitudes across  
15 conditions. The slope of right and left FCR MEP recruitment curve was significantly  
16 steeper at 70% of force compared to rest and 10% of force. A significant correlation  
17 between the slope of left and right FCR MEP amplitudes was found at 70% of force only.  
18 Our results indicate a differential scaling of excitability in the corticospinal system  
19 controlling right and left FCR muscles at increasing levels of unimanual force generation.  
20 Specifically, these data highlights that at strong levels of unimanual force the increases in  
21 motor cortical excitability with increasing TMS stimulus intensities follow a similar  
22 pattern in both M1s, while at low levels of force they do not.  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

## Introduction

Previous studies demonstrated force-related changes in neural activation in the primary motor cortex (M1) contralateral to a moving arm. Electrophysiological studies in nonhuman primates have shown that the firing rate of pyramidal tract neurons in M1 contralateral is positively related to the magnitude of force (Evarts 1968; Hepp-Reymond et al., 1978). Functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies in humans have shown increased neural activation in M1 contralateral with increasing levels of force during isometric contractions (Dai et al., 2001; Dettmers et al., 1995).

Force-related changes have been reported in the M1 ipsilateral to a contracting arm as well. Neuroimaging (Dettmers et al., 1995; Thickbroom et al., 1998; Dai et al., 2001) and transcranial magnetic stimulation (TMS; Stedman et al., 1998; Muellbacher et al., 2000; Hortobagyi et al., 2003; Perez and Cohen 2008) studies in humans have reported an increased activity in M1 ipsilateral during high levels of force while performance of low levels of force has led to conflicting results in humans (Stedman et al., 1998; Liepert et al., 2001) and nonhuman primates (Donchin et al., 1998; Kazennikov et al., 1999). Although these studies described changes in neural activation in both M1s during unimanual force generation, the way in which motor cortical activity in the contralateral and ipsilateral M1 change relative to each other across force levels remains poorly understood.

Previous work showed increased inter-hemispheric coupling (Svoboda et al., 2002) and decreased interhemispheric inhibition (Perez and Cohen 2008) between M1s at increasing levels of unimanual force. Also, the contralateral M1 has a greater and

1  
2  
3 proportional level of BOLD percent signal change relative to the ipsilateral M1 at  
4  
5 increasing force (Dettmers et al., 1995; Spraker et al., 2007). Therefore, we hypothesized  
6  
7 that scaling of motor cortical excitability in both M1s could operate in a parallel way at  
8  
9 high levels of force. To address this question, we evaluated changes in motor cortical  
10  
11 excitability in both M1s associated with parametric increase in unimanual force  
12  
13 generation in healthy humans.  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

## Methods

### Subjects

Eight right-handed healthy volunteers (4 women, 4 male;  $24.2 \pm 6.9$ ) years participated in the study. All subjects gave their informed consent to the experimental procedure, which was approved by the NINDS ethics committee in accordance with the Declaration of Helsinki. All subjects participated in one session in which they performed 10, 30 and 70% of their maximal right wrist flexion force in a randomized order while the left arm was at rest.

### Motor task

Subjects were seated in an armchair with both arms flexed at the elbow by 90 degrees and the wrist in a neutral position. The right arm was attached to a custom 6-axis load cell (35-E15A; Woodland, CA, Fig. 1B). Custom software was written to acquire signals from the load cell and to display visual feedback equivalent to rest, 10, 30 and 70% of each subject's maximal right isometric wrist flexion force in real-time (Matlab R14SP3, Mathworks, Natick, MA; Figure 1A). Subjects were instructed to respond to the GO signal (target signal) presented on a computer monitor by moving a cursor to a target box. The maximal right wrist flexion force was measured three times at the beginning of each session and measurements were averaged. TMS measurements (see below) were taken at rest and during 10, 30 and 70% of force. Each TMS pulse was applied during the right FCR muscle burst in all force trials. The left arm was immobilized by a custom brace to ensure that the same testing position was maintained (for specific details see Perez and Cohen 2008). The left FCR electromyogram (EMG) was displayed as a

1  
2  
3 continuous line on an oscilloscope during right wrist force generation and visual feedback  
4  
5 was constantly provided to subjects and experimenters. As well, verbal feedback was  
6  
7 provided to the subjects to assure that the left FCR remained at rest at all times. Trials in  
8  
9 which left FCR activity was detected (more than 25  $\mu$ V; Muellbacher et al., 2000) were  
10  
11 excluded from further analysis.  
12  
13  
14  
15  
16

### 17 **Electromyographic recordings**

18  
19 Surface electrodes were positioned bilaterally on the skin overlying the flexor  
20  
21 carpi radialis (FCR) muscles in a bipolar montage (interelectrode distance, 2 cm). The  
22  
23 amplified EMG signals were filtered (band-pass, 25 Hz to 1 kHz), sampled at 2 kHz, and  
24  
25 stored on a PC for off-line analysis.  
26  
27  
28  
29  
30

### 31 **TMS measurements**

32  
33 TMS was delivered to the optimal scalp position for activation of the FCR  
34  
35 muscles overlying left and right M1 (hot spot). Motor evoked potentials (MEPs) were  
36  
37 elicited by TMS stimuli delivered from a Magstim 200 stimulator (Magstim company,  
38  
39 Dyfed, UK) through a figure-of-eight coil (loop diameter, 8 cm; type no.: SP15560) with  
40  
41 a monophasic current waveform. The coil was held tangential to the scalp with the handle  
42  
43 pointing backwards and 45° away from the midline to activate the corticospinal system  
44  
45 preferentially trans-synaptically via horizontal cortico-cortical connections (Di Lazzaro  
46  
47 et al., 2004). Measures of motor cortical excitability included: resting motor threshold  
48  
49 (RMT) and MEPs recruitment curves amplitudes and slope.  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

### MEPs recruitment curves

Recruitment curves were measured in the left and right FCR while the right FCR was at rest and during 10, 30 and 70% of force. At rest, stimulus intensities started at 5% below the RMT, defined as the lowest TMS intensity required for eliciting MEPs of at least 50  $\mu$ V amplitudes in three of five consecutive trials. During right wrist force (10, 30 and 70%) stimulus intensities started at 5% below the intensity required to elicit a detectable MEP in three of five consecutive trials. Stimulus intensities were increased in 5% steps of maximal device output until the MEP amplitude did not further increase. Five MEPs were recorded at each stimulation intensity and each recruitment curve was repeated twice. TMS pulses were given every 10 sec. Several periods of rest were given to subjects in between trials to avoid muscle fatigue. MEP amplitudes were measured peak-to-peak, averaged off-line, and expressed as a percentage of the maximal motor response (M-max). To determine M-max, the median nerve was stimulated (1 ms rectangular pulse) with supra-maximal intensity using bipolar surface electrodes placed at the elbow. MEP recruitment curves were normalized to the individual RMT of each participant. Mean baseline activity for each recruitment curve was calculated, and values 1 SD above the baseline were included in a regression line. RMT values were determined by the intersection between the x intercept and the mean baseline using the following linear regression formula:  $y = a + bx$ . Then, measurements were binned at each stimulus intensity (range: 0.9–0.999). The same binning procedure was done at each stimulus intensity. All measurements were expressed as a percentage of the FDI M-max. Therefore, recruitment curves values are expressed relative to M-max responses and RMT for each

1  
2  
3 individual. Recruitment curves in the left FCR muscle used here as comparison to that of  
4  
5 the right FCR muscle, have been reported before (Perez and Cohen 2008).  
6  
7

## 8 9 **Data analysis**

10  
11 The slope of the MEP recruitment curves was calculated by using linear  
12  
13 regression analysis (see above MEPs recruitment curves). To ensure a proper fit of the  
14  
15 regression line all curves were visually inspected. Kolmogorov–Smirnov and Mauchly’s  
16  
17 tests were initially used to characterize the distribution and sphericity of data respectively.  
18  
19 Repeated measures ANOVA was used to determine the effect of TASK (rest, 10, 30 and  
20  
21 70%), SIDE (left and right) and stimulus INTENSITY (1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7,  
22  
23 1.8 and 1.9) on MEPs recruitment curves amplitudes. Multivariate analysis of variance  
24  
25 (MANOVA) was used to examine effect of TASK (rest, 10%, 30%, 70%), SIDE (left and  
26  
27 right) and their interaction (TASKxSIDE) on the slope of the MEP recruitment curves.  
28  
29 The covariance structure was assumed to be a compound symmetric structure. Bonferroni  
30  
31 post hoc test was used and corrected for multiple comparisons. Significance was set at  
32  
33  $p < 0.05$ . Variance is expressed as mean $\pm$ SD. Pearson correlation analysis was used to test  
34  
35 correlations as needed. Significance for correlation analysis was set at  $p = 0.01$ .  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

## 48 **Results**

### 49 50 51 **MEPs recruitment curve**

52  
53 Figure 2 illustrates right (A) and left (B) FCR MEPs recorded in a single subject  
54  
55 while the right FCR was at rest and during 10, 30 and 70% of force. Repeated-measures  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3 ANOVA showed effect of TASK on right FCR MEPs recruitment curves amplitudes  
4  
5 (F=1.7, p=0.02; Fig. 2C). *Post-hoc* testing showed a significant increase in MEP  
6  
7 amplitude at 70% (p≤0.001), 30% (p≤0.001) and 10% (p≤0.001) of force compared to  
8  
9 rest.

10  
11  
12 We also found a significant effect of TASK on left FCR MEPs recruitment curves  
13  
14 (F=1.7, p=0.02; Fig. 2D). *Post-hoc* testing showed a significant increase in recruitment  
15  
16 curves amplitude at 70% (p≤0.001) and 30% (p≤0.001) of force compared to rest. MEPs  
17  
18 were significantly larger at 70% compared to 30% (p≤0.001) and 10% (p≤0.001) of force.  
19  
20 No differences were observed between MEPs at rest and during 10% (p=0.3) of force.  
21  
22  
23  
24 EMG activity increased in the right FCR with increasing levels of force (F=6.0, p≤0.01),  
25  
26 while no changes were observed in left FCR EMG activity (F=0.3, p=0.72).

27  
28  
29 Repeated-measures ANOVA showed no differences on left and right FCR MEP  
30  
31 recruitment curves at rest (F=0.72, p=0.68; Fig. 3A). On the other hand, there was a  
32  
33 significant increase in recruitment curves amplitudes in the right compared to the left  
34  
35 FCR at 10% (F=7.9, p≤0.001; Fig. 3B), 30% (F=6.3, p≤0.001; Fig. 3C) and 70% (F=6.3,  
36  
37 p≤0.001; Fig. 3D) of force. We found a significant interaction between TASKxSIDE on  
38  
39 the slope of the MEP recruitment curves (MANOVA, F=31.2, p≤0.001). There are  
40  
41 significant differences across TASK on the right (F=7.8, p≤0.01) and left side (F=31.5,  
42  
43 p≤0.01). Post-hoc comparison revealed on both sides significant differences on the slope  
44  
45 of the MEP recruitment curve between rest and 70 % (left: F=73.4, p≤0.01, right: F=17.7,  
46  
47 p≤0.01) and 10 % vs. 70 % (left: F=46.7, p≤0.01, right: F=17.7, p≤0.01) but not between  
48  
49 30 % vs. 70 % (left: F=4.98, p=0.1, right: F=7.02, p=0.09).

### Correlation analysis

We found a significant correlation between left and right FCR MEP amplitudes across conditions (rest,  $r=0.73$ ,  $p\leq 0.001$ ; 10%,  $r=0.73$ ,  $p\leq 0.001$ ; 30%,  $r=0.73$ ,  $p\leq 0.001$ ; 70%,  $r=0.73$ ,  $p\leq 0.001$ ) indicating that subjects with larger MEP amplitudes in the right FCR were also the ones with larger MEP amplitudes in the left FCR. We also found a significant correlation between left and right FCR recruitment curve slopes across conditions ( $r=0.77$ ,  $p\leq 0.001$ ). The analysis of each separate condition revealed a significant correlation at 70% of force ( $r=0.83$ ,  $p\leq 0.01$ ; Fig. 4D) but not in the other conditions tested (rest,  $r=0.19$ ,  $p=0.6$ ; 10%,  $r=0.4$ ,  $p=0.28$ ; 30%,  $r=0.48$ ,  $p=0.22$ , Figs. 4A-C).

## Discussion

Here, we investigated changes in motor cortical excitability in both M1s during parametric increases in right wrist flexion force. We found that at increasing levels of right wrist force, there was a quantitatively different increase in MEP amplitudes in the right and left FCR muscles. Importantly, at strong levels of unimanual force generation, excitability changes with increasing TMS stimulus intensities follows a similar pattern in both M1s, a finding that was not present at weak levels of force.

Previous studies have demonstrated that during a unimanual force generation task motor cortical excitability, measured by the amplitude of MEPs evoked by TMS, increases in both the contralateral active M1 and the ipsilateral “resting” M1 (Stedman et al., 1998; Muellbacher et al., 2000; Hortobagyi et al., 2003). Therefore, since the shape of the input-output recruitment curve is influenced by changes in motor cortical cells and motoneuronal excitability (Devanne et al., 1997; Boroojerdi et al., 2001) their assessment can be used to characterize activity in corticospinal pathways from both M1s. In the present study we investigated the way in which motor cortical excitability measured by MEP recruitment curves in both M1s change in relation to each other during parametric increases in force generation.

We found a progressive increase in right FCR MEPs amplitudes at increasing levels of right wrist flexion force. This finding is in agreement with previous studies in other wrist muscles (Kirschka et al., 1993; Taylor et al., 1997). One important factor to consider in the increases in MEP amplitudes with increasing force levels is the

1  
2  
3 recruitment pattern of motor units (Palmer and Ashby 1992). In this regard, our results  
4  
5 confirm the findings of Kirschka et al. (1993) and Taylor et al. (1997) and show that the  
6  
7 size of MEP in the right FCR increases with the level of contraction at increasing  
8  
9 intensities of stimulation.  
10

11  
12 In the left resting FCR, we found a facilitation of MEPs at 30 and 70% of right  
13  
14 wrist force that was not present at rest and 10% of force. These findings are in agreement  
15  
16 with studies showing larger MEP in a resting arm during strong levels of force generation  
17  
18 by the opposite arm (Stedman et al., 1998; Muellbacher et al., 2000; Hortobagyi et al.,  
19  
20 2003). We observed no changes in left FCR MEP amplitudes at rest and 10% of force.  
21  
22 This result suggests that at low levels of force, the overall net interhemispheric balance  
23  
24 targeting M1 ipsilateral is more inhibitory and similar to rest, consistent with previous  
25  
26 reports (Liepert et al., 2001; Perez and Cohen 2008).  
27  
28  
29  
30

31  
32 When we compared left and right FCR MEPs amplitudes, we observed larger  
33  
34 amplitudes at all levels of force in the right FCR muscle. This is in agreement with  
35  
36 previous results showing that at increasing force levels M1 contralateral shows a greater  
37  
38 level of BOLD percent signal change than M1 ipsilateral (Dettmers et al., 1995; Spraker  
39  
40 et al., 2007). As expected, we also found that the slope of MEP recruitment curves was  
41  
42 steeper in the right compared to the left FCR muscle. This is in agreement with a  
43  
44 previous study showing that ipsilateral M1 activation volumes across force (rate of  
45  
46 change of force) has a lower slope than that of the contralateral M1 (Spraker et al., 2007).  
47  
48 The slope, an input-output parameter in the MEP recruitment curve, most likely reflects  
49  
50 excitability properties of the population of corticospinal neurons contributing to the  
51  
52 MEPs and of those of the motorneuronal pool (Devanne et al., 1997; Boroojerdi et al.,  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3 2001). Therefore, at 70% of force, but not at other force levels, the greater slope and  
4  
5 MEP amplitudes found in both FCR muscles and their correlation, suggest that  
6  
7 excitability in both M1s is qualitatively scaled by force in a task-dependent manner,  
8  
9 quantitatively different. This is in agreement with studies suggesting that both M1s  
10  
11 operate in a similar manner at higher levels of force (Dai et al. 2001; Dettmers et al. 1995;  
12  
13 Svoboda et al. 2002). Because high firing rates during strong voluntary contractions  
14  
15 appear to limit the responsiveness of spinal motoneurons, similar limitations might be  
16  
17 expected in the response of cortical neurons. However, we found that the largest changes  
18  
19 in left resting MEPs amplitudes occurred at 70% of force at stimulus intensities when  
20  
21 right FCR MEPs were still increasing. Although it is unclear what portion of the cortical  
22  
23 neurons targeted by TMS are recruited or how fast these are firing during stronger efforts  
24  
25 (Evarts et al., 1983; Muir and Lemon 1983), our findings indicate that M1 ipsilateral best  
26  
27 follow the activation pattern of the M1 contralateral at strong force levels. Interestingly,  
28  
29 this did not happen at 10% of force, supporting previous results demonstrating that  
30  
31 interhemispheric coupling between motor cortices is not manifested under weak motor  
32  
33 effort but emerges under strong muscle contraction (Svoboda et al. 2002). Importantly, a  
34  
35 spinal contribution to changes in MEP size in the left resting arm has to be considered.  
36  
37 Meyer et al. (1995) reported the presence of the MEP facilitation in a resting arm during  
38  
39 a strong voluntary contraction of the contralateral arm in patients with callosal agenesis  
40  
41 suggesting that this effect might be partly mediated by subcortical structures. Further  
42  
43 studies in healthy volunteers have demonstrated that the size of cervicomedullary motor  
44  
45 evoked response (CMEPs) in the resting arm were unaffected by strong voluntary  
46  
47 contraction of the other arm (Hortobágyi et al., 2003) while the size of the FCR H-reflex  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3 is depressed (Hortobágyi et al., 2003) or unchanged (Delwaide et al. 1988) without  
4  
5 changes in the size of the M-wave (Muellbacher et al. 2000; Stinear et al. 2001).  
6  
7 Furthermore, the magnitude of reciprocal Ia inhibition between antagonistic arm  
8  
9 muscles is enhanced in a resting arm by strong contralateral voluntary contraction  
10  
11 (Delwaide et al., 1988). Thus, it is likely that the increase in size of the MEP involves  
12  
13 changes in excitability in the motor cortex but a spinal contribution can not be ruled out.  
14  
15 Another important issue to consider is that differences in the modulatory effect of force  
16  
17 on MEP size can be observed in left and right handed subjects. Indeed, previous evidence  
18  
19 has shown that the size of MEP facilitation in a resting arm is significantly different if the  
20  
21 task is performed with the dominant right hand rather than with the non-dominant left  
22  
23 hand (Stedman et al., 1998; Ziemann and Hallet 2001).  
24  
25  
26  
27  
28

29         The contralesional M1 in humans seems to play a significant role in the process of  
30  
31 recovery of motor function of the paretic hand after stroke (Murase et al., 2004; Lotze et  
32  
33 al., 2006). In healthy subjects, our results suggest that during weak unimanual  
34  
35 contractions, interactions between both M1s as measured by motor cortical excitability  
36  
37 changes are less similar, perhaps reflecting a higher influence of inhibitory interactions  
38  
39 (Murase et al., 2004), compared to a strong voluntary contraction. Consistent with this  
40  
41 postulation, changes in motor cortical excitability in M1 ipsilateral during a weak  
42  
43 unimanual voluntary contraction are in part inhibitory (Liepert et al., 2001). Therefore, it  
44  
45 is possible that in stroke patients parallel increases in excitability in M1s will better  
46  
47 manifest during strong voluntary contractions an issue for further investigation.  
48  
49  
50  
51

52         In summary, our results indicate a differential scaling of excitability in the  
53  
54 corticospinal systems controlling right and left FCR muscles at different levels of  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

unimanual force generation. We suggest that the ipsilateral M1 scales force in a similar pattern to that of the contralateral M1 at strong levels of unimanual force.

1  
2  
3 **References**  
4

5 Boroojerdi B, Battaglia F, Muellbacher W, Cohen LG. Mechanisms influencing stimulus-  
6 response properties of the human corticospinal system. *Clinical Neurophysiology*, 112:  
7 931-937, 2001.  
8

9  
10 Dai TH, Liu JZ, Sahgal V, Brown RW, Yue GH. Relationship between muscle output  
11 and functional MRI-measured brain activation. *Experimental Brain Research*, 140: 290-  
12 300, 2001.  
13

14 Dettmers C, Fink GR, Lemon RN, Stephan KM, Passingham RE, Silbersweig D, Holmes  
15 A, Ridding MC, Brooks DJ, Frackowiak RSJ. Relation between cerebral activity and  
16 force in motor areas of the human brain. *Journal of Neurophysiology*, 74: 802-815, 1995.  
17

18  
19 Delwaide PJ, Sabatino M, Pepin JL, La Grutta V. Reinforcement of reciprocal inhibition  
20 by contralateral movements in man. *Experimental Neurology*, 99: 10-16, 1988.  
21

22  
23 Devanne H, Lavoie BA, Capaday C. Input-output properties and gain changes in the  
24 human corticospinal pathway. *Experimental Brain Research*, 114: 329-338, 1997.  
25

26 Di Lazzaro V, Oliviero A, Pilato F, Saturno E, Dileone M, Mazzone P, Insola A, Tonali  
27 PA, Rothwell JC. The physiological basis of transcranial motor cortex stimulation in  
28 conscious humans. *Clinical Neurophysiology*, 115: 255-266, 2004.  
29

30  
31 Donchin O, Gribova A, Steinberg O, Bergman H, Vaadia E. Primary motor cortex is  
32 involved in bimanual coordination. *Nature*, 395: 274-278, 1998.  
33

34  
35 Evarts EV. Relation of pyramidal tract activity to force exerted during voluntary  
36 movement. *Journal of Neurophysiology*, 31: 14-27, 1968.  
37

38  
39 Evarts EV, Fromm C, Kroller J, and Jennings VA. Motor cortex control of finely graded  
40 forces. *Journal of Neurophysiology*, 49: 1199-1215, 1983.  
41

42 Hepp-Reymond MC, Wyss UR, Anner R. Neuronal coding of static force in the primate  
43 motor cortex. *Journal of Physiology*, 74: 287-291, 1978.  
44

45 Hortobagyi T, Taylor JL, Petersen NT, Russell G, Gandevia SC. Changes in segmental  
46 and motor cortical output with contralateral muscle contractions and altered sensory  
47 inputs in humans. *Journal of Neurophysiology*, 90: 2451-2459, 2003.  
48

49  
50 Kazennikov O, Hyland B, Corboz M, Babalian A, Rouiller EM, and Wiesendanger M.  
51 Neural activity of supplementary and primary motor areas in monkeys and its relation to  
52 bimanual and unimanual movement sequences. *Neuroscience*, 89: 661-674, 1999.  
53

54  
55 Kischka U, Fajfr R, Fellenberg T, Hess CW. Facilitation of motor evoked potentials from  
56 magnetic brain stimulation in man: a comparative study of different target muscles.  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3 *Journal of Clinical Neurophysiology*, 10: 505-512, 1993.  
4

5 Liepert J, Dettmers C, Terborg C, Weiller C. Inhibition of ipsilateral motor cortex during  
6 phasic generation of low force. *Clinical Neurophysiology*, 112: 114-121, 2001.  
7

8 Lotze M, Markert J, Sauseng P et al. The role of multiple contralesional motor areas for  
9 complex hand movements after internal capsular lesion. *Journal of Neuroscience*, 26:  
10 6096-6102, 2006.  
11

12  
13 Meyer BU, Roricht S, Graf von Einsiedel H, Kruggel F, Weindl A. Inhibitory and  
14 excitatory interhemispheric transfers between motor cortical areas in normal humans and  
15 patients with abnormalities of the corpus callosum. *Brain*, 118: 429-440, 1995.  
16

17  
18 Muellbacher W, Facchini S, Boroojerdi B, Hallett M. Changes in motor cortex  
19 excitability during ipsilateral hand muscle activation in humans. *Clinical*  
20 *Neurophysiology*, 111:344-349, 2000.  
21

22  
23 Muir RB, Lemon RN. Corticospinal neurons with a special role in precision grip. *Brain*  
24 *Research*, 261: 312–316, 1983.  
25

26  
27 Murase N, Duque J, Mazzocchio R, Cohen LG. Influence of interhemispheric  
28 interactions on motor function in chronic stroke. *Annals of Neurology*, 55: 400-409, 2004.  
29

30 Palmer E, Ashby P. Corticospinal projections to upper limb motoneurons in humans.  
31 *Journal of Physiology*, 448: 397-412, 1992.  
32

33  
34 Perez MA, Cohen LG. Mechanisms underlying functional changes in the primary motor  
35 cortex cortex ipislateral to a moving hand. *Journal of Neuroscience*, 28: 5631-5640, 2008.  
36

37 Spraker MB, Yu H, Corcos DM, Vaillancourt DE. Role of individual basal ganglia nuclei  
38 in force amplitude generation. *Journal of Neurophysiology*, 98: 821-834, 2007.  
39

40  
41 Svoboda J, Sovka P, Stancák A. Intra- and inter-hemispheric coupling of  
42 electroencephalographic 8-13 Hz rhythm in humans and force of static finger extension.  
43 *Neuroscience Letters*, 334: 191-195, 2002.  
44

45 Stedman A, Davey NJ, Ellaway PH. Facilitation of human first dorsal interosseous  
46 muscle responses to transcranial magnetic stimulation during voluntary contraction of the  
47 contralateral homonymous muscle. *Muscle Nerve*, 21: 1033-1039, 1998.  
48

49  
50 Stinear CM, Walker KS, and Byblow WD. Symmetric facilitation between motor cortices  
51 during contraction of ipsilateral hand muscles. *Experimental Brain Research*, 139: 101–  
52 105, 2001.  
53

54  
55 Taylor JL, Allen GM, Butler JE, Gandevia SC. Effect of contraction strength on  
56 responses in biceps brachii and adductor pollicis to transcranial magnetic stimulation.  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

*Experimental Brain Research*, 117: 472-478, 1997.

Thickbroom GW, Phillips BA, Morris I, Byrnes ML, Mastaglia F. Isometric force-related activity in sensorimotor cortex measured with functional MRI. *Experimental Brain Research*, 121: 59-64, 1998.

Ziemann U, Hallett M. Hemispheric asymmetry of ipsilateral motor cortex activation during unimanual motor tasks: further evidence for motor dominance. *Clinical Neurophysiology*, 112: 107-113, 2001.

1  
2  
3 **Figure 1. Experimental set-up.**

4  
5 A, Diagram showing the visual display presented to all subjects during testing. The black  
6  
7 vertical line in the center shows the cursor that subjects was instructed to move by  
8  
9 performing right isometric wrist flexion force. The “GO” signal (dark gray box located to  
10  
11 the left of the cursor) was the target to where subjects had to move the cursor,  
12  
13 maintaining it in position for 3-5 seconds. B, Schematic of the experimental set-up.  
14  
15  
16  
17  
18

19 **Figure 2. Recruitment curves.**

20  
21 Average MEPs of a representative subject recorded from the right (A) and left (B) FCR  
22  
23 across conditions (rest, closed circles; 10, open circles; 30, closed triangles and 70%,  
24  
25 open triangles). In the graphs, the abscissa shows TMS stimulus intensity expressed  
26  
27 relative to the resting motor thresholds (RMT) and the ordinate shows MEP amplitudes  
28  
29 as a percentage of the FCR maximal motor response (M-max). Error bars indicate SEs;  
30  
31 \* $p < 0.05$ .  
32  
33  
34  
35  
36  
37

38 **Figure 3. Recruitment curve of left and right FCR.**

39  
40 **The same data is presented on Figure 2. Here, we illustrate left and right FCR**  
41  
42 **recruitment curves separately for each condition.** In all graphs the abscissa shows  
43  
44 TMS stimulus intensity expressed relative to the resting motor thresholds (RMT) and the  
45  
46 ordinate shows MEP amplitudes as a percentage of the FCR maximal motor response (M-  
47  
48 max) in the right (open circles) and left (closed circles) FCR muscles. Error bars indicate  
49  
50 SEs; \* $p < 0.05$ .  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3 **Figure 4. Correlations**  
4

5 In all graphs, the ordinate shows the magnitude of the slope of the MEP recruitment  
6  
7 curves in the right FCR, while the abscissa shows the magnitude of the slope of the MEP  
8  
9 recruitment curves in the left FCR. Note that at 70% of force the increase in the slope in  
10  
11 the right FCR is associated with an increase in the slope in the left FCR.  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

**Figure 1**  
[Click here to download high resolution image](#)

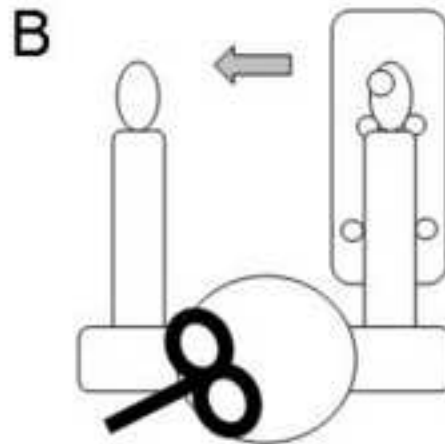
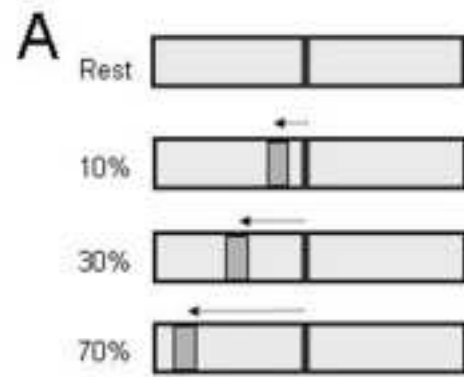


Figure 2  
[Click here to download high resolution image](#)

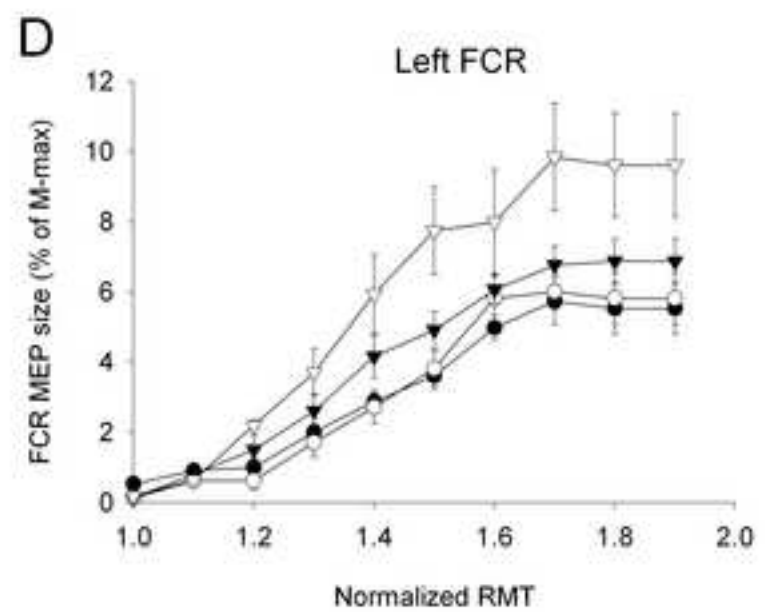
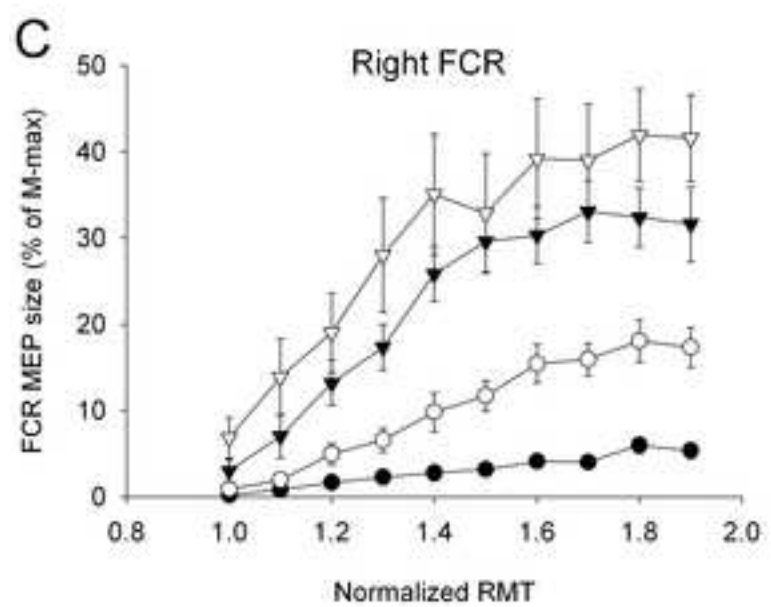
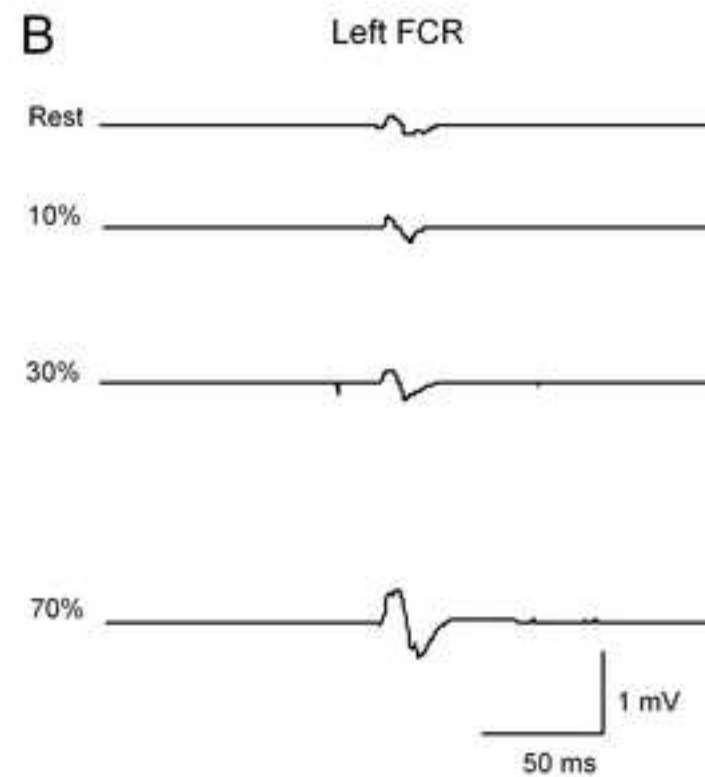
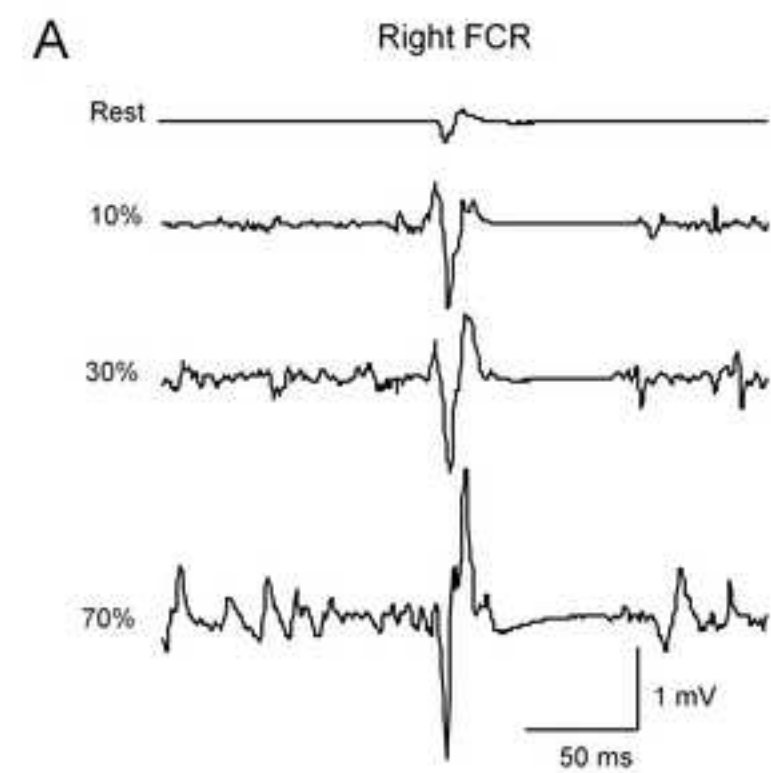


Figure 3  
[Click here to download high resolution image](#)

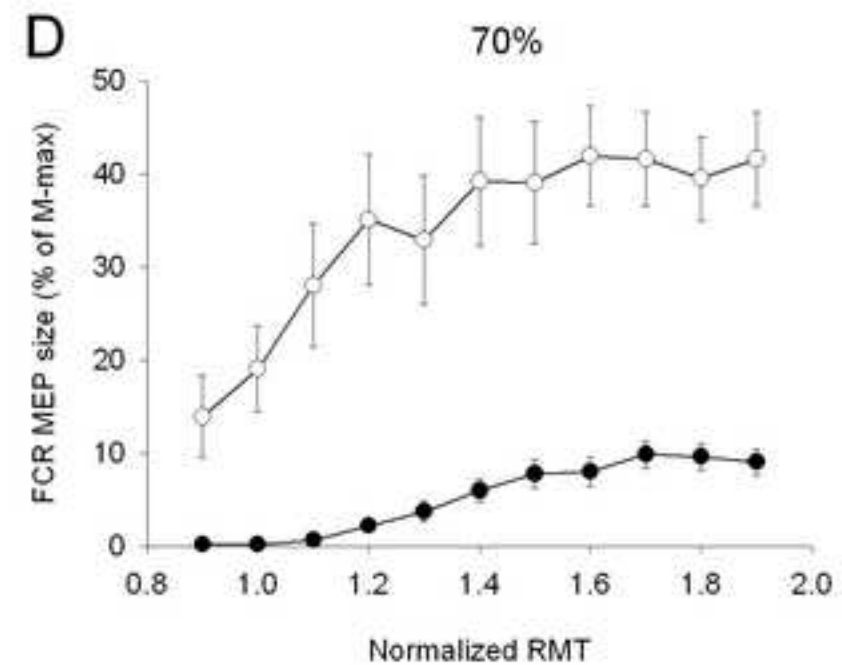
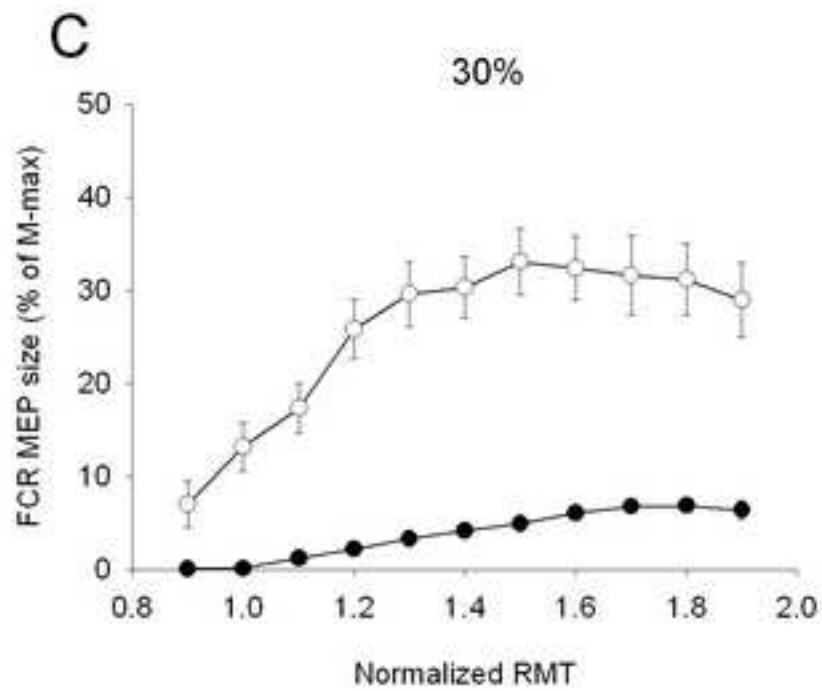
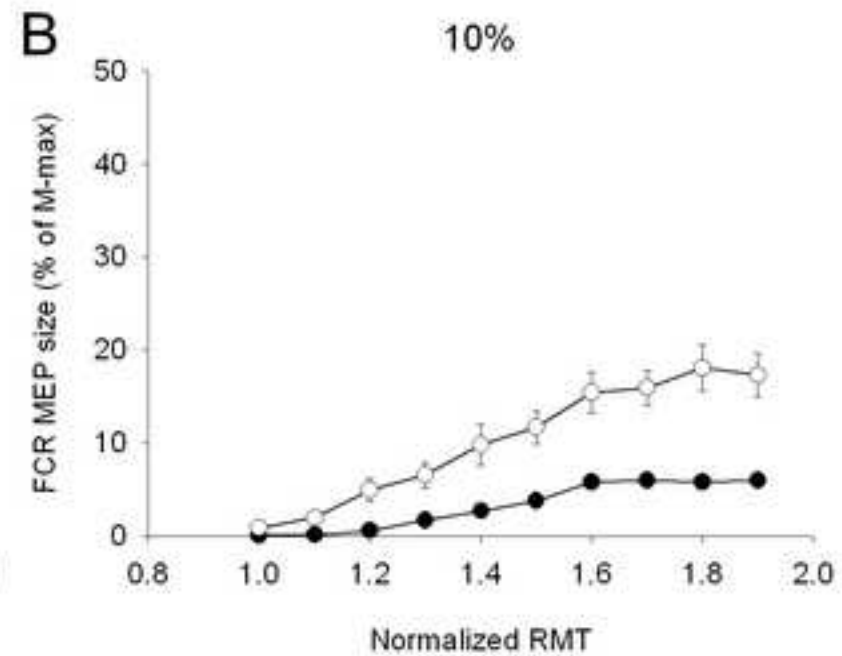
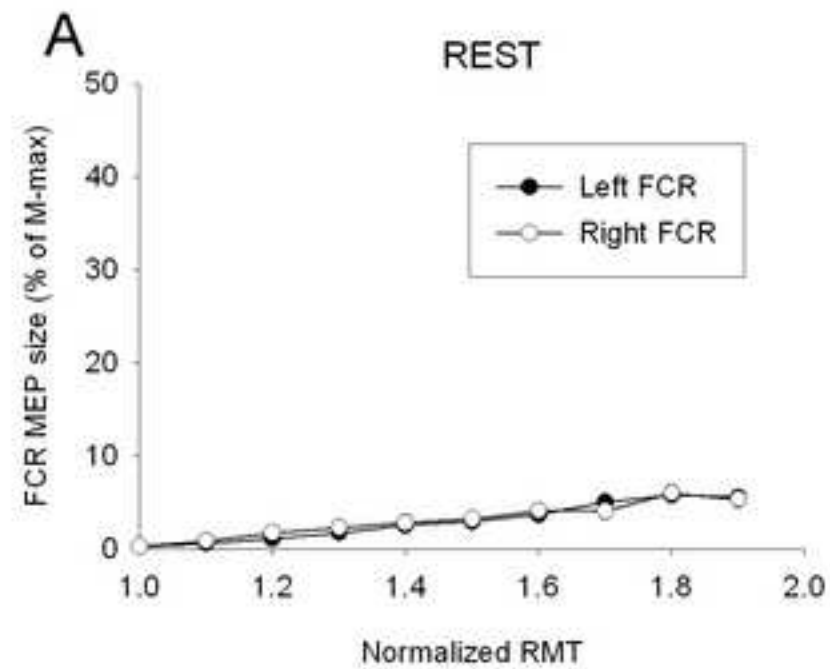


Figure 4  
[Click here to download high resolution image](#)

