Title: Reduced contribution of the ipsilateral primary motor cortex to force modulation with short-term motor learning in humans: An NIRS study

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Abstract

How is muscle force modulated during hand exercise? Oxygenation in the contralateral primary motor cortex (M1) has been observed to vary considerably across trials of repetitive handgrip

exercise. No linear relationship was observed between the average value of oxygenation determined by a block design study and the force of the handgrip. We found reduced oxygenation in the ipsilateral M1 and unchanged oxygenation in the contralateral M1 during repetitive static handgrip exercises (40% and 60% maximal voluntary contraction; 10 s exercise/75 s rest; 5 sets), which might be due to short-term motor learning. These results support the hypothesis that the ipsilateral M1 might functionally compensate for the contralateral M1 in force modulation during unilateral exercises.

The main text

The brain-machine interface (BMI) enables support devices such as artificial hands to restore lost human capabilities. The development of these devices would be a breakthrough for neuroscientists in the field of movement control. Enabling individuals who have lost their hands to drink a cup of coffee through the use of an artificial hand would offer immense gratification to them. BMI technology can achieve this goal. However, if the artificial hand is unable to decipher the information transmitted by the brain for force modulation, it would breach or release the held object. Force modulation of an artificial hand by the brain is a key factor in the development of artificial hands through the application of BMI technology.

Studies to confirm the relationship between oxygenation in the contralateral primary motor cortex

(M1) and power output in humans have yielded contradictory results[1–3]. Recently, it was confirmed that the oxygenation in the ipsilateral M1 is considerably higher than that in the contralateral M1. This finding was attributed to precise force control during contractions[1]. Further, the function of the ipsilateral M1 complements or inhibits that of the contralateral M1[4–7]. In case of force modulation, the ipsilateral M1 may function complementarily to the contralateral M1.

Plasticity of the cerebral cortex often poses problems in studies on the oxygenation in the bilateral M1[8]. Some researchers have described the relationship between force modulation and the ipsilateral M1 oxygenation[1,8]. This relationship is not constant and is altered by the plasticity of the brain. The validation of M1 oxygenation measured at each trial especially fails to explain the force modulation. If the ipsilateral M1 modulates the muscle force in a complementary manner, the oxygenation in the ipsilateral M1 should decrease with the habituation of an exercise task. On the other hand, if the ipsilateral M1 does not control muscle force in a complementary manner or if the ipsilateral M1 modulates muscle force predominantly, then the oxygenation in the ipsilateral M1 should not decrease with the habituation of an exercise task.

Subsequently, we aimed to investigate the effect of motor learning on the contribution of the changes in the ipsilateral M1 to force modulation. We monitored the oxygenation in the bilateral M1 during a repetitive handgrip task using near-infrared spectroscopy (NIRS) (details in Supplementary Methods and Figure S1). Changes in bilateral M1 oxygenation were measured by NIRS during 5

repetitions of the handgrip task [exercise: 10 s, rest: 75 s; the tasks were performed at 40% and 60% of maximal voluntary contraction (MVC)]. Unlike functional magnetic resonance imaging (fMRI), NIRS can monitor the changes in oxygenation in the bilateral M1 at real time without the need for the superposition of the slices (details in Supplementary Methods).

The results of repeated two-way analysis of variance (ANOVA) for the peak changes in the oxygenation in the bilateral M1from resting values at 40% MVC (Experiment 1) and 60% MVC (Experiment 2) are shown in Table 1 and Table 2. The peak changes in the oxyhemoglobin (HbO_2) values in the contralateral M1 did not significantly differ across the MVC trials at both intensities (40% MVC: $F = 0.798$, $p = 0.5358$; 60% MVC: $F = 0.403$, $p = 0.8050$) (Figure 1 and 2). Correspondingly, the peak changes in deoxyhemoglobin (Hb) in the contralateral M1 did not differ significantly across the MVC trials at both intensities (40% MVC: $F = 3.154$, $p = 0.0281$; 60% MVC: $F = 2.929$, $p = 0.0371$) (Figure 1 and 2). The peak changes in HbO_2 in the ipsilateral M1 significantly differed across the MVC trials at both intensities (40% MVC: $F = 3.154$, $p = 0.0281$; 60% MVC: $F = 2.929$, $p = 0.0371$) (Figures 1 and 2). On the other hand, the peak changes in Hb in the contralateral M1 did not significantly differ across the trials, whereas those in the ipsilateral M1 significantly differed across the trials (40% MVC: $F = 6.711$, $p = 0.0005$; 60% MVC: $F = 3.057$, $p = .0317$) (Figures 1 and 2). A post-hoc test (paired t-test) revealed significant differences in the oxygenation (HbO_2 and Hb) changes in the ipsilateral M1 between the first and fifth trials (Tables 1

and 2).

The results of this study contradict the fact that the ipsilateral M1 partially contributes in force modulation. Muscle power output during exercise is fundamentally controlled by the contralateral M1. During the motor learning phase, the ipsilateral M1 may act in a complementary manner with regard to force modulation. In the present study, we used the handgrip ergometer (details in Supplementary Fig 1). The use of this instrument rather than a visual feedback system, as in previous studies[8,9], enabled easy evaluation of force modulation. In addition, the subjects practiced using the device over several days. Thus, the effects of motor learning on force modulation could be determined in relatively fewer repetitions of the exercise task. A previous study showed a decrease in ipsilateral M1 oxygenation during a sustained handgrip exercise performed at 30% MVC[9]. These results indicate that the contribution of the ipsilateral M1 to force modulation might be complementary to that of the contralateral M1. As shown by Newton et al.[10], the increased neural activation in the M1 of one hemisphere induces reduced neuronal activity in the M1 of the opposite hemisphere. Based on these results, oxygenation in the ipsilateral M1 should reduce neural activation in the contralateral M1.

However, NIRS cannot be used to determine the involvement of both hemispheres of the brain in force modulation because of technical drawbacks. The contribution of the ipsilateral and contralateral M1 to force modulation can be clearly studied using transcranial magnetic stimulation

(TMS). Thereafter, the uniformity of the contribution of the ipsilateral and contralateral M1 to force modulation remains unclear. The present results suggest collateral contribution of the ipsilateral M1 to force modulation, and that this contribution declines with motor learning. Further studies should focus on elucidating the contribution of the ipsilateral M1 to force modulation. This information will help achieve advances in BMI technology.

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AUTHOR CONTRIBUTIONS

This study was designed by all 3 authors. Data collection was performed by all 3 authors. K.S. was responsible for data analysis and writing the paper.

COMPETING INTERESTS STATEMENT

The authors declare competing financial interests.

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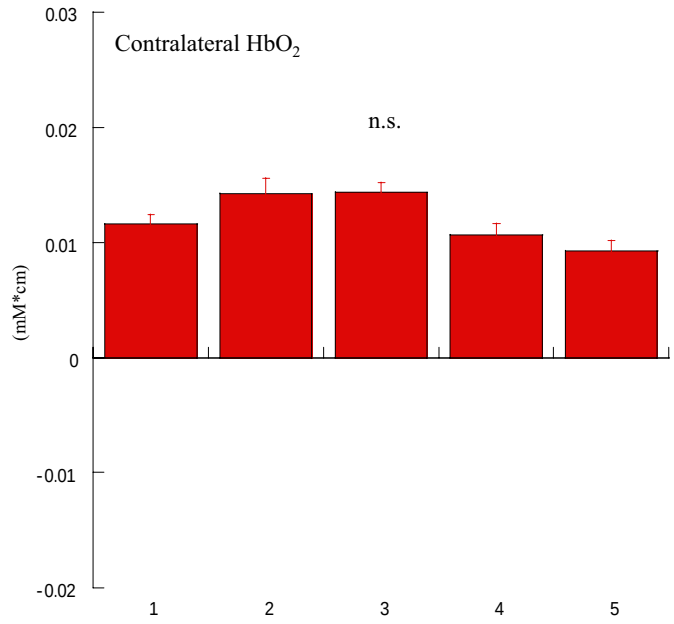
Figure legends

Figure 1. The peak value in oxygenation changes from resting levels at 40%MVC trials. The astarisks are shown the significant difference between the first trials. Upper panels represent the results of oxyhemoglobin (HbO_2) changes. Lower panels represent the results of deoxyhemoglobin

(Hb) changes. Right panels represent the results of contralateral primary motor cortex oxygenation changes, and left panels represent the results of ipsilateral primary motor cortex oxygenation changes. Asterisks show significant differences from the first trial ($p < 0.05$). Error bars indicate s.e.m.

Figure 2. The peak value in oxygenation changes from resting levels at 60%MVC trials. The astarisks are shown the significant difference between the first trials. Upper panels represent the results of oxyhemoglobin (HbO_2) changes. Lower panels represent the results of deoxyhemoglobin (Hb) changes. Right panels represent the results of contralateral primary motor cortex oxygenation changes, and left panels represent the results of ipsilateral primary motor cortex oxygenation changes. Asterisks show significant differences from the first trial ($p < 0.05$). Error bars indicate s.e.m.


Contralateral HbO_2
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0.02
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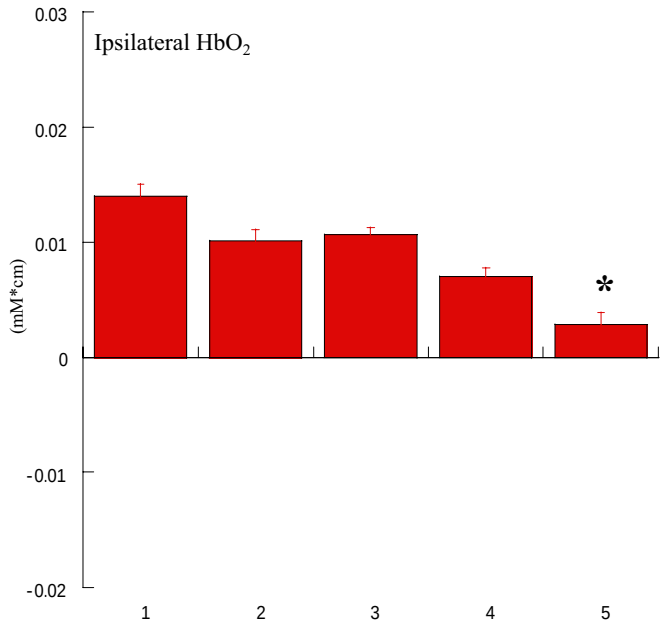
0
-0.01
-0.02
(mM*cm)
1
2
3
4
5


Ipsilateral HbO_2
*
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0.02
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(mM*cm)
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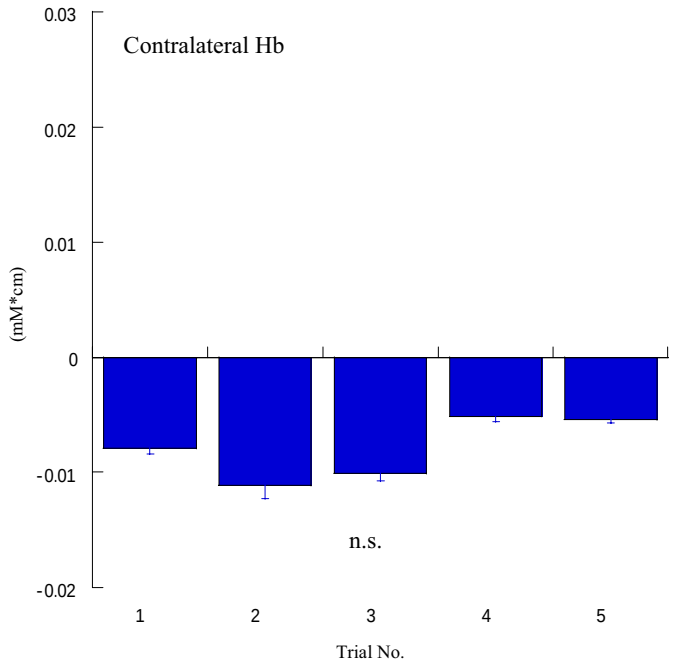
Contralateral Hb
n.s.
0.03
0.02
0.01
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-0.01
-0.02
(mM*cm)
1
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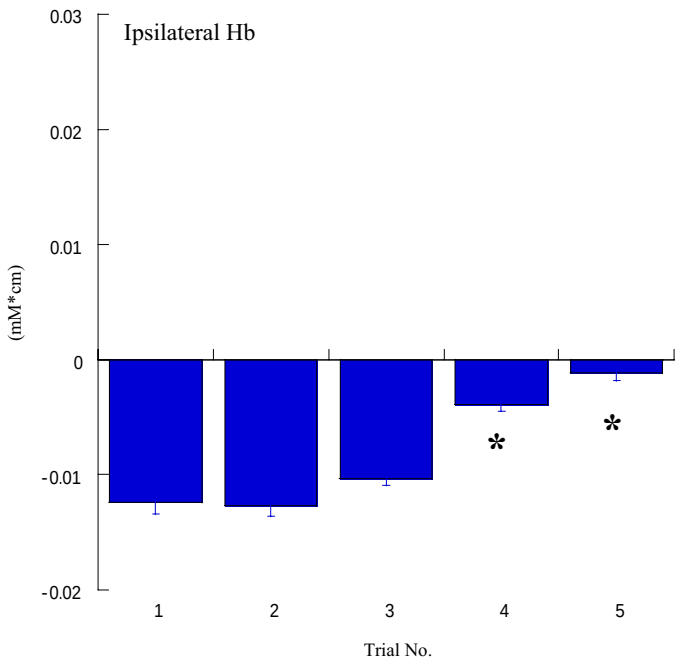
Trial No.


Ipsilateral Hb
*
*
0.03
0.02
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(mM*cm)
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Trial No.

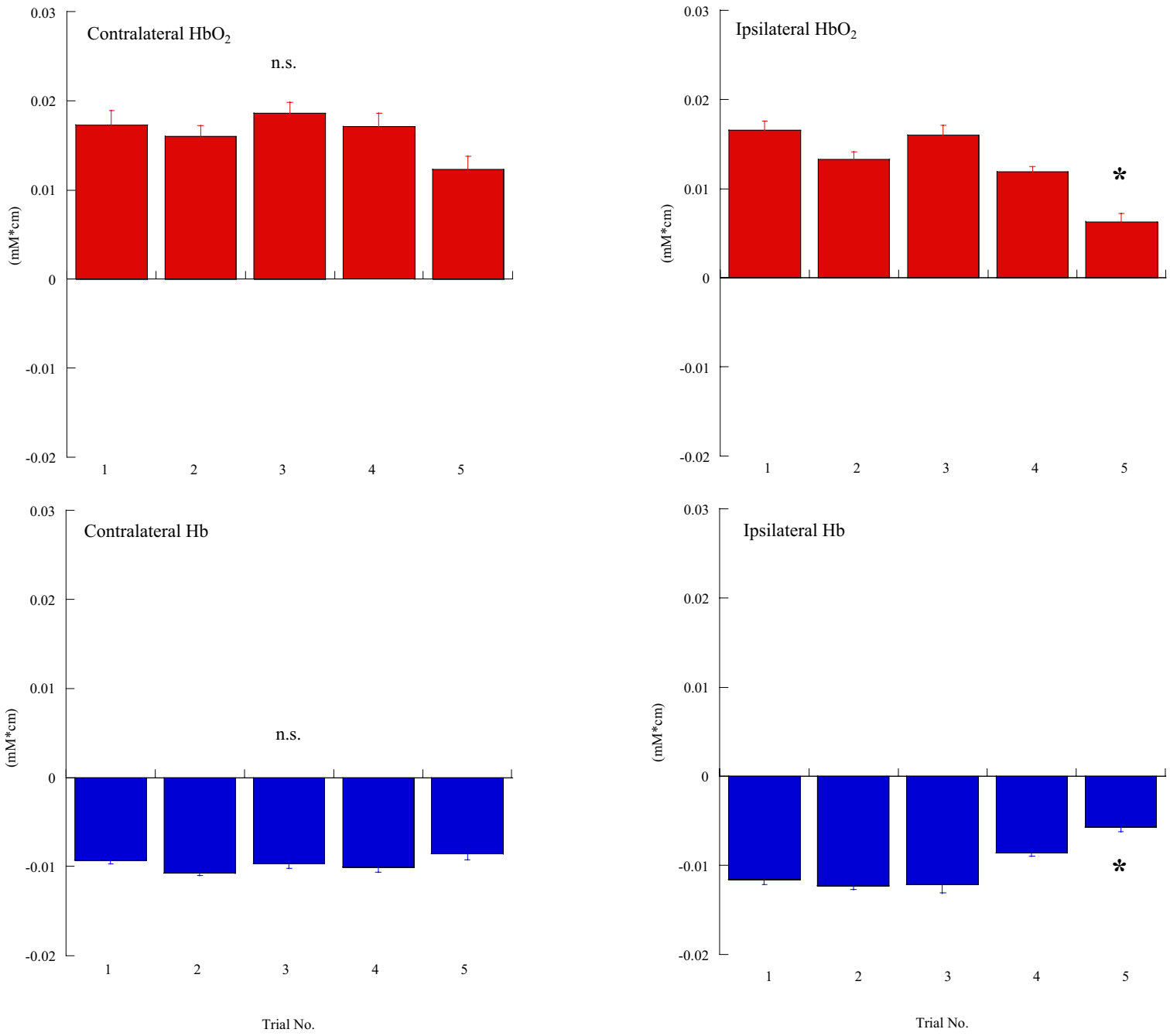
Contralateral HbO_2
n.s.
Ipsilateral HbO_2
*
Contralateral Hb
n.s.
Ipsilateral Hb
*
(mM*cm)
0.03
0.02
0.01
0
-0.01
-0.02
1
2
3
4
5
Trial No.

Table 1. The peak value in oxygenation changes from resting levels at 40%MVC trials. The astarisks are shown the significant difference between the first trials. Left panel represents the results of oxyhemoglobin (HbO_2) changes. Right panel represents the results of deoxyhemoglobin (Hb) changes.

HbO_2

Trial No.	Contralateral			Ipsilateral			
1	0.0116	±	0.0008	0.0140	±	0.0010	
2	0.0143	±	0.0013	0.0101	±	0.0010	
3	0.0144	±	0.0008	0.0107	±	0.0006	
4	0.0107	±	0.0010	0.0070	±	0.0008	
5	0.0093	±	0.0009	0.0029	±	0.0010	*
	F =0.798, p = 0.5358			F = 3.154, p = 0.0281			
				There was a significant difference between Trial 1 and 5: t = 3.017, p = 0.0235			

Hb

Trial No.	Contralateral			Ipsilateral			
1	-0.0079	±	0.0005	-0.0124	±	0.0010	
2	-0.0111	±	0.0012	-0.0127	±	0.0009	
3	-0.0101	±	0.0006	-0.0103	±	0.0006	
4	-0.0051	±	0.0005	-0.0039	±	0.0006	*
5	-0.0054	±	0.0003	-0.0011	±	0.0007	*
	F =2.215, p = 0.0911			F = 6.771, p = 0.0005			
				There were significant differences between Trial 1 and 4: t = 3.854, p = 0.0084; and between Trail 1 and 5: t = 6.429, p = 0.0007			

Table 2. The peak value in oxygenation changes from resting levels at 60%MVC trials. The astarisks are shown the significant difference between the first trials. Left panel represents the results of oxyhemoglibin (HbO_2) changes. Right panel represents the results of deoxyhemoglibin (Hb) changes.

HbO_2

Trial No.	Contralateral			Ipsilateral			
1	0.0173	±	0.0016	0.0166	±	0.0010	
2	0.0160	±	0.0012	0.0133	±	0.0008	
3	0.0186	±	0.0012	0.0160	±	0.0011	
4	0.0171	±	0.0015	0.0119	±	0.0006	
5	0.0123	±	0.0015	0.0063	±	0.0009	*
	F = 0.403, p = 0.8050			F = 2.929, p = 0.0371			
				There was a significant difference between Trial 1 and 5: t = 4.744, p = 0.0032			

Hb

Trial No.	Contralateral			Ipsilateral			
1	-0.0093	±	0.0004	-0.0116	±	0.0005	
2	-0.0107	±	0.0003	-0.0123	±	0.0004	
3	-0.0096	±	0.0006	-0.0121	±	0.0010	
4	-0.0101	±	0.0005	-0.0086	±	0.0004	
5	-0.0086	±	0.0006	-0.0057	±	0.0005	*
	F = 0.405, p = 0.8036			F = 3.057, p = 0.0317			
				There was a significant difference between Trial 1 and 5: t = 2.627, p = 0.0392			