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Possible contributions of ipsilateral pathways from the contralesional motor cortex to the voluntary contraction of the spastic elbow flexors in stroke survivors: a TMS study

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Abstract

Objective: The contribution of the contralesional motor cortex to the impaired limbs is still controversial. The purpose of this study was to investigate the role of descending projections from the contralesional hemisphere during voluntary elbow flexion on the paretic side.

Design: Eleven healthy and 10 stroke subjects performed unilateral isometric elbow flexion tasks at various submaximal levels. Transcranial magnetic stimulation (TMS) was delivered to the hot spot of biceps muscles ipsilateral to the target side (paretic side in stroke subjects or right side in controls) at rest and during elbow flexion tasks. Motor evoked potential (MEP) amplitudes of the contralateral resting biceps muscles, TMS-induced ipsilateral force increment, and reflex torque and weakness of spastic elbow flexors were quantified.

Results: The normalized MEP amplitude increased with force level in both healthy and stroke subjects. However, stroke subjects exhibited significantly higher force increment compared with healthy subjects only at low level of elbow flexion, but similar at moderate to high levels. The greater force increment significantly correlated with reflex torque of the spastic elbow flexors, but not weakness.

Conclusion: These results provide novel evidence that ipsilateral projections are not likely to contribute to strength, but are correlated to spasticity of spastic-paretic elbow flexors after stroke.

Keywords

Stroke; contralesional primary motor cortex; reticulospinal tract; spasticity

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Introduction

Weakness and spasticity (spastic paresis) are two common motor impairments after a stroke. Weakness is primarily caused by the stroke-related damage to the primary motor cortex (M1) and its descending corticospinal tract (CST). Integrity of the residual CST defines early and spontaneous recovery in the acute phase and predicts overall motor recovery[1]. Plastic reorganization occurs immediately after a stroke in both ipsilesional and contralesional cortices[2]. Ipsilesional reorganization facilitates and mediates recovery of voluntary movement on the paretic side [2]. For example, in a longitudinal function Magnetic resonance imaging (MRI) study, recovery of locomotor function in stroke patients is accompanied with a shift of activation from the contralesional primary sensorimotor cortex at the subacute stage to the ipsilesional side at the chronic stage [2]. The role of contralesional M1 reorganization to recovery depends on lesion location, size and motor impairment[3]. In case of severe motor impairment, activation of contralesional M1 provides additional neural resources to compensate for the severely damaged ipsilesional motor system, while such contralesional activation may interfere with motor performance in patients with only minor to moderate motor impairment.

Contributions of the contralesional activation are mediated by ipsilateral cortico-reticulo-spinal projections and uncrossed ipsilateral CST from contralesional M1, including premotor cortex[4]. Transcranial magnetic stimulation (TMS) to M1 primarily induces motor-evoked potentials (MEP), muscle contraction and force increment in the contralateral limb. Ipsilateral MEPs (iMEPs) are usually observed in healthy subjects when there is strong background activation of the target muscle and with high-intensity TMS[5]. iMEPs are easier to elicit in proximal impaired muscles in stroke patients, even at rest[6]. iMEP facilitation has been viewed to reflect a possible unmasking of cortico-reticulo-spinal pathways [6]. The finding that stroke patients who had no iMEPs in the acute phase developed iMEPs 6 months later supports the idea of unmasking [7]. Increased iMEPs following stroke may be indicative of an increased reliance on these unmasked pathways and these projections could contribute to abnormal inter-joint coupling during voluntary activation of impaired muscles [8–10]. In a recent study using high-resolution diffusion tensor imaging, Owen et al. [11] reported an increase in the size of contralesional reticulospinal tract and its correlation with increased synergy and impairment in chronic stroke. The findings further support plastic upregulation of the reticulospinal tract.

The contribution of reticulospinal upregulation and hyperexcitability to motor strength and recovery has been suggested by animal studies [12,13]. However, its role for post-stroke motor recovery in humans remains unclear [14,15]. On the other hand, reticulospinal hyperexcitability has been considered as the most plausible mechanism mediating post-stroke spasticity [16,17]. This pathophysiological mechanism of reticulospinal hyperexcitability is able to explain many clinical features associated with post-stroke spasticity. For example, the reticulospinal pathway plays an important role in maintaining normal anti-gravity posture. Reticulospinal hyperexcitability leads a shift in reference configuration and results in an abnormal resting joint angle. As such, objectively quantified by reflex torque in a laboratory setting, spasticity was found to be significantly correlated with the altered resting joint angle of the elbow joint

in chronic stroke, and clinical assessments as well (modified Ashworth scale, MAS, and Tardieu angle) [18,19].

The specific aim of this experiment was to investigate the role of ipsilateral projections from the contralesional M1 to voluntary activation using TMS. As mentioned before, descending pathways from contralesional M1 include both ipsilateral CST and cortio-recticulospinal tracts. It is thus inferred that ipsilateral responses to TMS to the contralesional M1 during voluntary contraction of spastic-paretic elbow flexors could reflect its contributions to voluntary strength on the paretic side. Furthermore, there are evidence of reticulospinal hyperexcitability in stroke survivors with spasticity, and reticulospinal hyperexcitability is considered to mediate post-stroke spasticity. Therefore, the correlation between TMS-induced force increment from the spastic-paretic elbow flexors and reflex torque was also analyzed. It was hypothesized that ipsilateral force increment to TMS to the contralesional M1 would be greater in stroke subjects than in healthy controls, and the induced force increment would be correlated with elbow flexors spasticity, not weakness.

Methods

Participants

Eleven healthy adults (30.5 yrs ± 5.3 yrs; 2 women) and ten stroke patients (65.3 yrs ± 11.1 yrs; 4 women) participated in this study. All healthy subjects reported being healthy without any known neuromusculoskeletal impairments and were right-handed. Healthy subjects did not take any drugs that influence cortical excitability. Inclusion criteria for stroke subjects were: 1) hemiplegia secondary to an ischemic or hemorrhage stroke; 2) at least 6 months post-stroke; 3) right-handed with residual voluntary elbow flexion force (manual muscle testing (MMT) ≥ 3); 4) spastic hypertonia in upper limb of the impaired side, rated as Modified Ashworth Scale (MAS) less than 3; 5) able to understand and follow instructions related to the experiment; and 6) on stable anti-spasticity medications or no medications for anti-spasticity. Exclusion criteria for stroke subjects included: 1) a history of multiple strokes or bilateral involvement; 2) presence of contracture that would limit full elbow range of motion on the impaired side; and 3) visuolspatial neglect;Note that patients who received botulinum toxin injections to their spastic elbow flexors were recruited at least 4 months after last injections, if the above inclusion and exclusion criteria were met. Table 1 lists the detailed information of stroke patients. The Committee for the Protection of Human Subjects at the local institution approved the procedures of this study. All participants provided written informed consent prior to participating in this study.

Procedures

Subjects were seated a height adjustable chair comfortably in an upright position. Their test arm was secured against two adjustable metal plates with a padded strap approximately 2–4 inches proximal from the wrist in a custom device. The contralateral arm rested in a symmetrical position on a height adjustable table. The arrangement of the arms was as follows: the shoulder joint was positioned approximately in 30˚ of abduction and 45˚ of flexion, while the elbow was flexed to 90˚. The wrist and fingers were kept in the neutral position. Surface electromyography (EMG) electrodes were placed on the biceps muscles

bilaterally (a Bagnoli EMG system with 2.1 single differential configuration, Delsys Inc., Boston, MA, USA). The reference electrode was placed on the lateral epicondyle on the test side. The placement of surface electrodes followed the European Recommendations for Surface Electromyography [20].

A 20-inch computer monitor (Model: 2001FP, Dell Computer Corp., Texas, USA) was located 1 m away at the eye level in front of the subjects. The monitor was used to display the force produced by the subject (white line) and the target (redline) using a custom-written program in LabView® (National Instrument™ Inc., Texas, USA). All subjects affirmed that they could see the display clearly.

Each subject went through the following procedures within a single session: 1) locating hotspot; 2) maximal voluntary contraction (MVC) task; 3) TMS at rest; 4) TMS during 10%, 30%, and 60% of MVC isometric elbow flexion (contracting) tasks; 5) passive stretch. Sufficient rest breaks were given to the subjects to minimize any possible fatigue effect throughout the experiment.

Locating hotspot: To find the hotspot for resting biceps (left side for healthy subjects and non-impaired side of stroke patients), a single-pulse TMS stimulus (BiStim^2, Magstim Corp., UK) was set at an intensity of 75% of the maximum stimulator capacity (equal to 84.75% maximum stimulator output on Magstim 200^2, Magstim Corp., UK) while subjects were held their targeted forearm in about 90˚ of elbow flexion in the sagittal plane. TMS was delivered over the targeted primary motor cortex using a figure-of-8 shaped stimulation coil (a 35-mm mean diameter of each wing). The hotspot was determined when the largest increment in targeted elbow flexion was produced in 3 consecutive trials. We used a gel ink pen to mark the spot on the scalp and the hotspot was verified periodically throughout the experiments. The induced baseline MEPs were confirmed to vary within 10% to ensure consistency of hotspot localization and control of variability in responses.

TMS at rest: Followed by the MVC task, TMS was delivered to the hot spot for the resting biceps randomly between 7–11 seconds during a 12-second trial. Six trials were collected at rest.

MVC task: After the hotspot was located, the subjects were asked to perform a maximum isometric elbow flexion and maintain the force for at least 3 seconds. For each side, MVC task was repeated 3 times and the highest force among 3 attempts was considered as the MVC force. The MVC forces of the target elbow flexors (right side for healthy subjects and impaired side for stroke patients) were used to predefine the target force.

TMS during isometric elbow flexion tasks: Subjects were asked to perform isometric elbow flexion tasks with the target biceps muscles at 10%, 30%, and 60% of their MVC. The order of the force levels was randomized for each subject. Real-time visual feedback was provided to the subjects. Briefly, a horizontal red line was presented on the computer screen, indicating the target level of force. A white line of real-time force signal run from left to right. The subjects were explicitly instructed to match the white line to the red line as closely as possible. To ensure the correct spot was stimulated, the hot spot was verified

intermittently throughout the experiment. Six trials were collected for each force level with TMS-induced responses. Subjects were instructed not to respond to the TMS stimuli, and to continue maintaining the force regardless of the TMS interruption.

Passive stretch: The resting elbow joint of stroke subjects was passively stretched, using a computerized stretching program[15,16]. In the aforementioned experimental configuration, the axis of rotation of the elbow joint was aligned with the axis of rotation of a servomotor (model: FHA-25C-50-US250, Harmonic Drive LLC, MA, USA). The initial position was selected at which the subject rested naturally, i.e., resting angle [18]. A total amount of 50° elbow extension was applied to the elbow joint at a constant speed (5°/s or 100°/s). When the elbow passively moved to the end position, it was remained at the end position for 2 seconds. The elbow joint moved back to the initial position at the same speed. Three trials were collected for each stretch speed. The order of speeds was randomized.

Both force and EMG signals were collected using an NI-DAQ card (Model: PCI-6229, National Instruments, TX, USA). Elbow flexion torque and resistance torque were measured with a torque sensor (Model: TRS-500, Transducer Techniques, CA, USA). The sensor was located in line with the center of the rotation of the active elbow joint. The force and EMG signals were sampled at 1000 Hz. All the collected data were stored on a personal computer.

Data Analysis

Force and EMG data were analyzed off-line with custom-written Matlab® programs (Math Works™ Inc., Natick, Massachusetts, USA). The raw force signal was low-pass filtered at 10Hz with a fourth-order, zero-lag Butterworth digital filter before further analysis. The following parameters were calculated the same as our recent analysis methods [21]:

For the impaired (target) side, we calculated the following parameters:

- *Background force.* Background force was calculated as the mean force over a 100-ms window prior to the TMS delivery during voluntary contraction tasks.
- *TMS-induced force increment.* During isometric elbow flexion tasks, TMS-induced force increment was quantified as the difference between the background force and the peak force after the TMS delivery. To be able to compare the force increment between subjects, the difference between the background force and the peak force after the TMS delivery was normalized to the background force.
- *Reflex torque:* as in our recent study[18], reflex torque was qualified as the difference between the peak resistance torque at 5°/s and the peak resistance torque at 100°/s.
- *Weakness:* For stroke subjects, weakness was quantified as the percent of the elbow flexion MVC on the impaired side with reference to the corresponding MVC force on the contralateral side.

For the resting contralateral side, we calculated the following parameters:

- *Motor evoked potential (MEP) latency.* MEP latency was quantified as the interval between the TMS delivery to the time when the EMG signal exceeded two standard deviations of the background EMG amplitude. It was averaged during the 100 ms window prior to the TMS delivery for each trial.
- *Normalized MEP amplitude.* To calculate the MEP amplitude, we quantified the peak-to-peak EMG amplitude of the resting biceps within the time window from the MEP onset to 50 ms after the TMS delivery. For each subject, the averaged MEP amplitudes during 10%, 30%, and 60% MVC tasks, respectively, were normalized by the averaged MEP amplitude at rest in order to make comparisons between subjects.

Statistical Analysis

The following dependent variables were calculated in this study: 1) MEP latency; 2) MEP amplitude; 3) TMS-induced force increment; 4) reflex torque; 5) weakness. Two-way mixed ANOVAs were used to compare TMS-induced force increment, MEP latency, and MEP amplitude, with a between-subject factor of GROUP (Healthy or Stroke) and a within-subject factor FORCE LEVEL (10%, 30%, and 60% of MVC). Paired t-tests were used to determine whether the MEP amplitude during each elbow flexion task was significantly higher than at rest. Pearson correlation was used to test whether TMS-induced force increment related to reflex torque and weakness, respectively for stroke subjects. The induced force increment at 10%MVC task was used for such correlation analysis. The alpha level for all statistical tests was 0.05. Data are reported as mean ± standard deviation (SD) within the text and as mean ± standard error mean (SEM) in the figures 2&3. Only the significant main effects are presented unless otherwise noted.

Results

TMS was applied to the contralesional M1 during voluntary isometric elbow flexion on the impaired side or at rest. Such TMS application triggered an EMG response on the contralateral resting biceps muscle and induced force increment to the sustained isometric elbow flexion force on the ipsilateral (impaired) side. Figure 1 depicts a representative MEP response of the contralateral biceps muscle (A) and the TMS-induced force increment (B) from a stroke subject.

TMS effect on the MEPS of the contralateral resting biceps muscle

The MEP amplitude were all significantly higher during elbow flexion tasks than at rest for both healthy (10%: 130.5% ± 41.6%; 30%: 156.5% ± 57.7%; 60%: 257.8% ± 118.7%, all $p < 0.05$) and stroke subjects (10%: 177.6% ± 34.8%; 30%: 217.9% ± 42.0%; 60%: 267.9% ± 83.0%, all $p < 0.05$). Furthermore, there were significant FORCE LEVEL main effect ($F_{2,38} = 22.85$, $p < 0.01$) in Normalized MEP amplitude. Specifically, Normalized MEP amplitude was larger during 60% of MVC task compared with 10% ($p < 0.01$) and 30% ($p<0.01$) of MVC tasks (Figure 2). There were no significant main effects of GROUP nor FORCE LEVEL x GROUP interactions.

The MEP latency did not change regardless whether there was voluntary elbow flexion or at rest on the impaired side. There were no significant main effects of GROUP or FORCE LEVELS or their interactions for the MEP latency. The MEP latency was similar under all conditions for healthy (10%: 15.2ms ± 1.8ms; 30%: 15.1ms ± 1.6ms; 60%: 14.6ms ± 1.9ms) and stroke (10%: 14.2ms ± 1.3ms; 30%: 14.1ms ± 1.1ms; 60%: 14.1ms ± 1.6ms) subjects.

TMS effect on force increment in the ipsilateral side

TMS application altered isometric elbow flexion force on the ipsilateral side (Figure 3). There was significant main effects of GROUP ($F_{1, 19} = 5.86$, $p = 0.03$), FORCE LEVEL ($F_{2, 38} = 4.93$ $p = 0.01$) and FORCE LEVEL x GROUP interactions ($F_{2, 38} = 7.19$, $p < 0.01$) in TMS-induced force increment. Post-hoc analysis showed that stroke subjects exhibited significant higher TMS-induced force increment compared with healthy subjects during 10% MVC tasks (Stroke: 15.49% ± 17.70%; Healthy: 1.01% ± 0.46%, p = 0.01). The normalized and absolute values of TMS-induced force increment for each GROUP and FORCE LEVEL were listed in table 2.

Correlation between TMS-induced force increment and impairment severity (reflex torque and weakness)

One of the stroke subject was excluded in the correlation analysis because of inability to relax during the passive stretch tasks. There was a significant correlation between TMS-induced force increment and reflex torque in stroke subjects. Stroke subjects who had higher reflex torque exhibited higher TMS-induced force increment ($R^2 = 0.52$, $p = 0.03$; Figure 4). However, there was no significant correlation between TMS-induced force increment and weakness ($R^2 = 0.008$, $p = 0.82$).

Discussion

In this study, Single-pulse TMS was applied to the contralesional M1 in stroke subjects and healthy controls during voluntary elbow flexion on the impaired side in stroke subjects or on the right side in healthy subjects. We found that TMS-induced MEP amplitude on the contralateral resting biceps muscle was increased with the level of voluntary elbow flexion for both stroke and healthy subjects, i.e., force-dependent increase in the contralateral MEP. In contrast, the TMS-induced force increment on the ipsilateral side was not force-dependent, except that stroke subjects exhibited greater force increment during very light contraction (10% MVC tasks). Furthermore, there was a significant correlation between ipsilateral force increment and reflex torque, but not weakness of the paretic biceps muscle. These findings indicated that the contralesional hemisphere is not likely to significantly contribute to voluntary elbow flexion on the impaired side after stroke.

TMS effects on the ipsilateral and contralateral sides

The finding of force-dependent increase in the MEPs of the contralateral resting biceps muscle is suggestive of bilateral activation of M1 during unilateral elbow flexion of the impaired side in stroke subjects and in healthy controls. This is expected and consistent with the literature findings. It is well documented that, as compared to rest, there are decreased interhemispheric inhibition from activating M1 to the contralateral M1 and decreased short-

term intracortical inhibition in the resting (contralateral) M1, resulting in increased M1 excitability during unilateral activation in healthy subjects[22,23]. The interhemispheric M1 facilitation increases with level of activation of the target muscle [22], and is specific to the homologous muscle[23]. Recently, Cohen and colleagues reported similar changes in the resting (contralesional) M1 during unilateral activation of impaired muscles after stroke [24].

This increased M1 excitability in the contralesional hemisphere during voluntary elbow flexion on the impaired side apparently did not contribute to force production of the impaired elbow flexors, however. In our study, the induced force increment did not increase with the level of force production in both healthy and stroke subjects (Fig 3). The ipsilateral responses to TMS are mediated by ipsilateral cortico-reticulo-spinal projections and uncrossed ipsilateral CST from the contralesional M1[4]. The finding of non-force dependent force increment demonstrated that these descending projections from the contralesional (or left) M1 did not contribute to voluntary elbow flexion in both healthy and stroke subjects. On the other hand, these results indicated that the enhanced excitability in the contralateral M1 is likely a result of overflow of M1 activation via interhemispheric facilitation during unilateral elbow flexion on the impaired side. Overall, our results are consistent with the literature that voluntary movement of paretic muscles is primarily mediated by the contralateral M1 activation in chronic stroke[2].

The role of ipsilateral descending projections from the contralesional hemisphere

In the context of no significant difference in force-dependent contralateral MEPs and non-force dependent ipsilateral force increment between healthy and stroke subjects, the result of greater force increment at 10% MVC tasks in stroke subjects is intriguing. Given the known reticulospinal hyperexcitability in chronic stroke with spasticity[25], and no contralelesional M1 hyperexcitability after stroke[26], the greater force increment at 10%MVC task is likely attributed to activation of cortico-reticulo-spinal pathways by TMS delivery and reticulospinal hyperexcitability.

This reticulospinal hyperexcitability-mediated force increment, however, is not likely to contribute to force production of spastic elbow flexors in this study. When the force increment is re-normalized by individual MVCs, i.e., the current values of force increment further divided by 10, 3.3, and 1.6 for 10%, 30% and 60% MVC tasks in Figure 3, force increment is equivalent to approximately 2%MVC across all levels in stroke subjects. The small induced force increment could not contribute significantly to the total force. This explains that there was no significant difference in percent change from the background force between stroke and healthy subjects, when the background level of force increased. This is also reflected by there is no significant correlation between force increment and weakness. Similar findings were reported in a recent study [15]. During sustained isometric elbow flexion by stroke subjects and healthy subjects, reticulospinal pathways were activated via startling acoustic stimuli. The induced force increment was in a small range of 1.5 to 4.5%MVC. There was no significant difference in force increment between healthy and stroke subjects, although stroke subjects had slightly greater increment with large variations. Our results are consistent with recent findings from other groups. Owen et al. reported that the size of reticulospinal tract on the paretic side was correlated with motor

impairment [11], this pathway was progressively recruited during expression of abnormal synergy [27]. For example, such expression of abnormal synergy may also account for the trunk muscle activation to compensate for functional limitations of the paretic arm [28,29]. In the course of motor recovery, this reticulospinal pathway was found to be related to motor mirroring or motor overflow, which subsides as voluntary movement recovers and progresses [30]. On the other hand, it was also found that there was a significant correlation between this greater force increment and reflex torque (i.e., severity of spasticity), but not weakness. These findings suggest that the TMS-induced greater ipsilateral force increment and spasticity could share a common pathophysiological process[31]

There were some limitations in this study. The age of healthy control group and stroke patient group was not matched. It is known that older adults show increased bilateral cortical activation during hand and finger tasks [32,33]. However, for proximal Biceps Brachii muscles, age-related muscle weakness is primarily attributed to motor-map reorganization and anterior shift of center of gravity[34], decreased intra-cortical inhibition[35], and decreased voluntary cortical activation[36]. Furthermore, the ipsilateral contribution to elbow flexion force was minimum, approximately 2%MVC for both healthy and stroke subjects at moderate to high levels. This finding argues against greater bilateral activation in older, stroke subjects during unilateral elbow flexion tasks on the paretic side. In this study, ipsilateral EMG responses to TMS were not analyzed. This is attributed to the fact that the TMS-induced force was small (on average only less than 2% of MVC), so that force related EMG burst could be captured only in some patients with large TMS-induced force (e.g. representative TMS-induced force and EMG burst showed in figure 1A). Another potential confounding factor is that we did not recruit stroke survivors with severe impairments and spasticity. Another limitation is lack of neuronavigational guidance for TMS. We took extra time to reassure localization of the hotspot throughout the experiments. The beneficial role of ipsilateral contributions from the contralesional M1 may be revealed in these stroke survivors[3,37]. However, stroke survivors were not be able to be positioned in the customized experimental apparatus due to spasticity and to perform voluntary elbow flexion due to paresis. Nevertheless, in this study with a relatively small sample size, the results were generally consistent with the literature. They provide evidence to advance our understanding the role of ipsilateral projections of the contralesional motor cortex, particularly its relation to post-stroke spasticity.

Conclusion

Taken together, the findings suggest that ipsilateral projections from the contralesional motor cortex are likely maladaptive. They are not likely to contribute to strength, but are correlated with spasticity of spastic-paretic elbow flexors after stroke with mild to moderate motor impairment.

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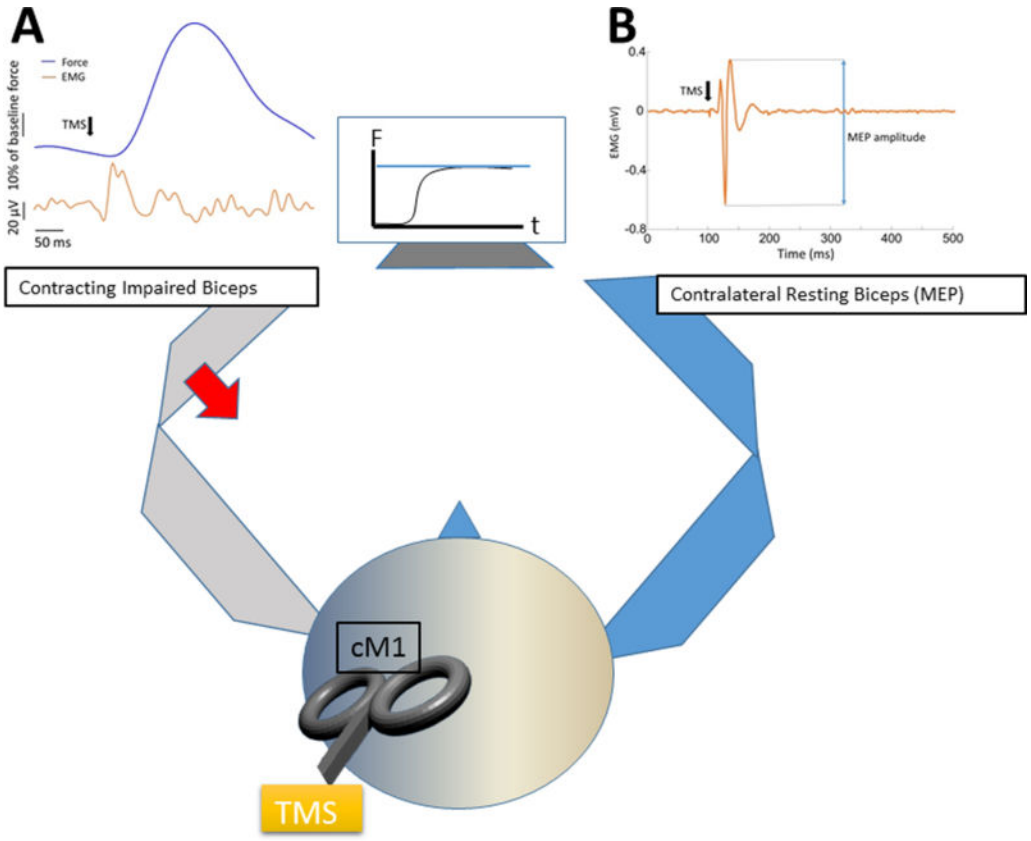

Figure 1.

A) A representative trial of MEP response during 10% of the MVC task from a stroke subject and B) Representative TMS-induced force increment from a stroke subjects during 10% of the MVC task. The blue trace was the force, and the orange trace was the EMG signals. The EMG signals were rectified and low pass-filtered at 50Hz in order to get smoothed EMG signals. Six trials of the raw force signals and modified EMG signals during 10% of the MVC task were averaged for the subject in order to represent the averaged results for the task. Note: the averaged force signals were normalized by the background force (mean force over a 100-ms window prior to the TMS delivery) in this figure.

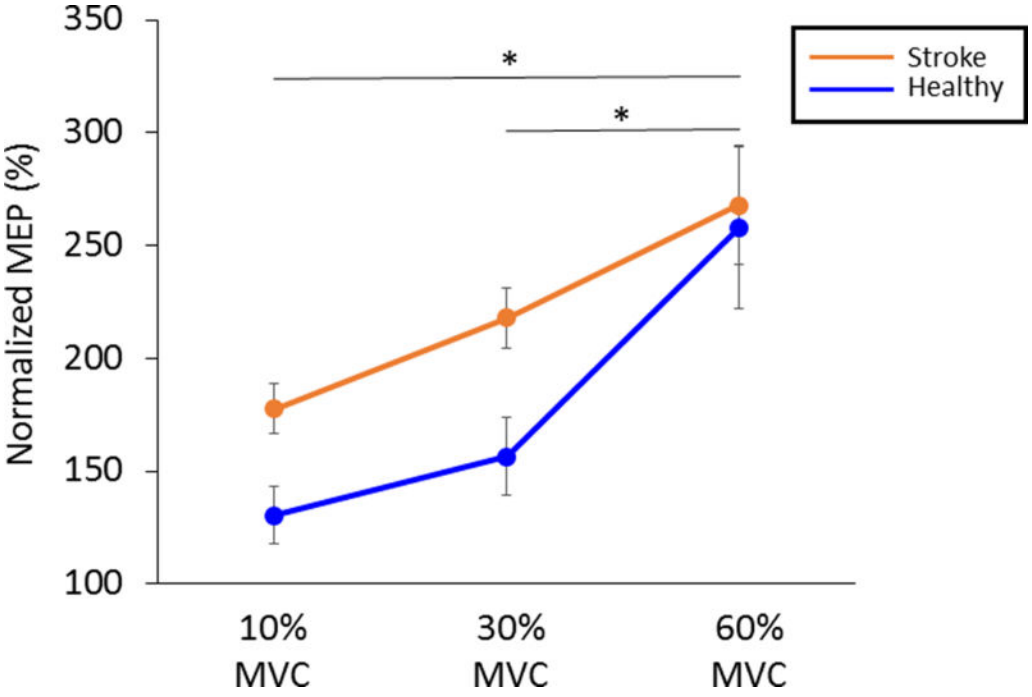

Figure 2.

Normalized MEP amplitude during 10%, 30%, and 60% of the MVC tasks for healthy and stroke subjects. The normalized MEP amplitude increased with increasing force for both healthy and stroke subjects. There were no significant differences between the two groups. * indicated significant difference between the two tasks within group ($p < 0.05$)

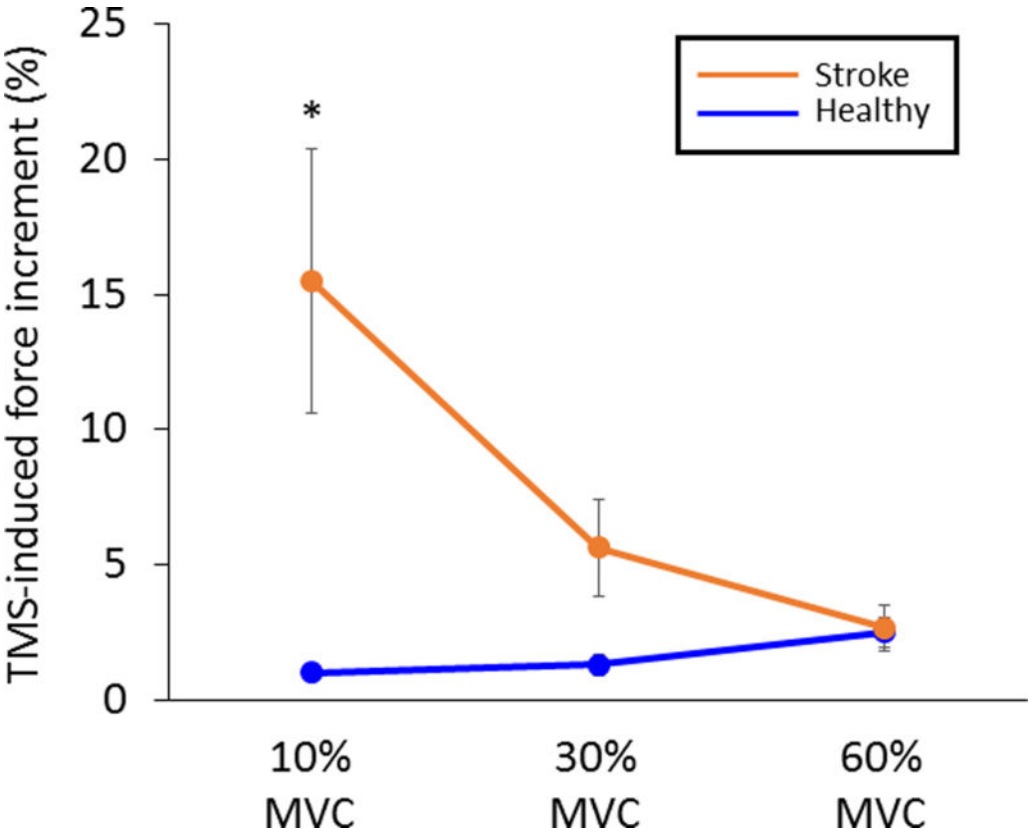

Figure 3.

TMS-induced force increment during 10%, 30%, and 60% of the MVC tasks for healthy and stroke subjects. The TMS-induced force increment was significantly higher in stroke subjects compared with healthy subjects during 10% of the MVC task. * indicated significant difference ($p < 0.05$)

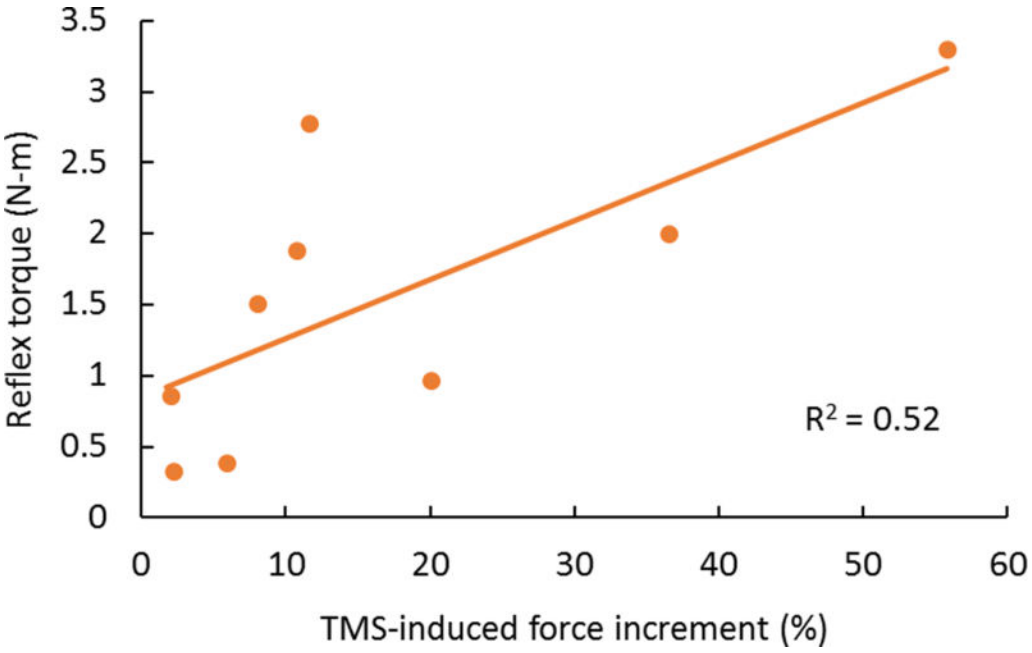

Figure 4.

Correlation between TMS-induced force increment and reflex torque. There was a significant correlation between TMS-induced force increment and reflex torque (R^2 = 0.52, p = 0.01). Stroke patients who have higher reflex torque also exhibited higher TMS-induced force increment during 10% of the MVC task.

Table 1.

Stroke patients list. Modified Ashworth Scale: MAS; Maximal voluntary contraction MVC; Middle cerebral artery: MCA; not available: NA; female:F; male: M; right: R; Left: L. Newton meter: Nm; Month: m.

Patient	Age	Gender	Paretic Side	Dominant Side	Elbow Flexor MAS	Wrist Flexor MAS	Finger Flexor MAS	Impaired biceps MVC (Nm)	Non-impaired biceps MVC (Nm)	Onset of Stroke (month)	Diagnosis	Location
Stroke_1	59	F	L	R	1	0	1	16.4	26.9	100	Hemorrhagic	Right MCA
Stroke_2	44	F	L	R	1	1	2	34.4	37	63	Ischemic	Right MCA
Stroke_3	70	M	R	R	1+	2	2	16.6	48.5	66	Ischemic	Left frontotemporal
Stroke_4	72	M	L	R	1+	2	3	6.24	23.85	64	Ischemic	Right MCA
Stroke_5	70	M	R	R	1	2	0	9.3	37.43	84	Ischemic	Left MCA (M1)
Stroke_6	63	F	L	R	1	1	2	7.4	30.1	171	Ischemic	Right MCA
Stroke_7	62	M	R	R	2	1	1	16	44.6	7	Ischemic	Left MCA
Stroke_8	72	M	R	R	1	0	0	26	39	82	Hemorrhagic	Left Frontoparietal
Stroke_9	56	M	L	R	1	0	1	10	29	27	Ischemic	Right MCA
Stroke_10	85	F	L	R	1	1+	1+	5	20	26	Hemorrhagic	NA

Table 2.

Normalized and absolute value of TMS-induced force increment. The values in the parentheses are standard deviation.

		10% MVC	30% MVC	60% MVC
Normalized force increment (%)	Healthy	1.01 (0.46)	1.30 (1.30)	2.51 (1.87)
	Stroke	15.49 (17.70)	5.65 (7.79)	2.67 (3.69)
Absolute force increment (N-m)	Healthy	0.85 (0.70)	0.98 (0.84)	1.61 (1.30)
	Stroke	1.78 (1.53)	2.18 (1.84)	2.46 (2.03)

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