erably varies among groups classified by age at onset. This information may help prioritize specific SCA gene testing.

In conclusion, we provided detailed clinical and genetic characteristics of patients with 16q-SCA, which is not a rare AD-SCA subtype in the Japanese population. The range of the ages at onset of 16q-SCA patients is considerably broad, which might be explained by the presence of a modifying gene. Our finding of an exceptional patient who lacked the C-to-T substitution in the *puratrophin-1* gene emphasizes the importance of further genetic analysis of the candidate region of 16q-SCA.

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Disinhibition of the Premotor Cortex Contributes to a Maladaptive Change in the Affected Hand After Stroke

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Background and Purpose—The mechanism of reorganization after stroke remains uncertain. Several studies that have measured reaction time (RT) delay by transcranial magnetic stimulation (TMS) have revealed some substrates responsible for the reorganization of motor recovery. In this study, we evaluated the RT delay and inhibitory functions by examining the silent period (SP) in the primary motor cortex (M1) and premotor cortex (PMC) of the affected hemisphere. Using these data, we investigated whether a change in the inhibitory system might influence motor recovery.

Methods—This study was performed in 20 patients with chronic subcortical stroke. To evaluate the RT delay, TMS was applied to the affected hemisphere 100 ms after showing the cue that indicated paretic finger movement. The SP was induced by TMS over the affected hemisphere during voluntary contraction of the paretic hand.

Results—The RT delays of the PMC were more prominent in patients with greater disability. The ratio of SP duration to RT delay in the PMC decreased with the decline in motor function. Moreover, upper arm function was better than hand function in patients with a decreased SP in the PMC.

Conclusions—The inhibitory function of the PMC was disturbed in patients with poor motor function. Stroke patients with poor motor ability appeared to depend not only on the motor pathway from M1 but also on other parallel motor circuits to move the paretic side. However, this brain reorganization might result in the sacrifice of function of the affected hand. **(*Stroke*. 2007;38:1551-1556.)**

Key Words: disinhibition ■ stroke ■ transcranial magnetic stimulation

Functional imaging techniques have revealed a negative correlation between activation of secondary motor networks and motor function after stroke.[1,2] The role of the ipsilesional primary motor cortex (M1) is undoubtedly important for recovery of the affected hand[1,3]; however, it remains uncertain whether the activation of a motor-related area outside the ipsilesional M1 contributes to a maladaptive change or true recovery.[4–6]

In recent studies, reaction time (RT) delays induced by transcranial magnetic stimulation (TMS) have been considered for revealing the sites that contribute to motor recovery after stroke.[3,7,8] TMS temporarily delays but does not distort the execution of a motor command stored in strategically placed neurons within the neural substrate that is responsible for the motor response.[9] Therefore, a site where an RT delay was induced by TMS when a subject moved the paretic hand could be interpreted as the site contributing to motor recovery.

In this study, we investigated the correlation between RT delay and silent period (SP) duration in the M1 and premotor cortex (PMC) of the affected hemisphere. It has been reported that SP duration is considered to reflect an inhibitory function of cortical origin[10,11] and that RT delay is correlated with SP duration in healthy subjects.[10,12,13] However, we hypothesized that the SP duration in stroke patients might decrease compared with the RT delay at a site that contributed to the reorganization of the brain, particularly if this site was outside the M1. This hypothesis was formulated because several studies reported that a reduction in inhibitory function contributed to cortical plasticity.[4,14] In addition, we examined the correlation between the SP of the PMC and motor recovery to study whether a change in the inhibitory system of the PMC influences reorganization in the hand and upper arm regions of the cortex.

Subjects and Methods

The study population comprised 20 patients with a first-time ischemic subcortical stroke (Table 1). They were tested at a minimum of 6 months after stroke. Visual perceptions of all patients were within normal limits, and their Mini-Mental State Examination scores were normal. They had either mild or no spasticity (modified Ashworth scale).[15] Motor function was evaluated by the upper limb subset of the Fugl-Meyer scale (FMS).[16] The upper limb subset of the FMS (66 points) is divided into the upper arm subset (42 points) and the

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TABLE 1. Clinical Characteristics of Stroke Patients

Patient No.	Age, y	Sex	Duration After Stroke, mo	Paretic Side	FMS for Upper Limb, %	FMS for Arm, %	FMS for Hand, %	Lesion Site
1	52	M	62	L	94	95	92	Thalamus
2	54	M	7	R	77	76	79	Internal capsule
3	59	M	54	R	82	83	79	Putamen and corona radiata
4	50	F	19	R	91	95	83	Basal ganglia, internal capsule
5	79	F	10	R	73	83	54	Basal ganglia, internal capsule
6	68	M	48	R	27	31	21	Putamen and corona radiata
7	76	F	24	L	89	95	79	Corona radiata
8	48	M	13	R	42	48	33	Corona radiata
9	45	M	60	R	32	33	29	Putamen and corona radiata
10	35	M	21	L	86	86	88	Thalamus
11	58	M	20	R	64	69	54	Thalamus
12	24	M	15	L	80	83	75	Corona radiata
13	57	F	6	R	30	33	25	Corona radiata
14	27	F	6	L	77	86	63	Putamen
15	59	M	39	L	26	26	25	Basal ganglia, internal capsule
16	64	F	28	R	77	86	63	Internal capsule
17	35	F	27	R	61	76	33	Basal ganglia, internal capsule
18	58	M	43	L	64	71	50	Internal capsule
19	52	M	10	L	82	83	79	Internal capsule
20	49	M	36	R	100	100	100	Putamen and corona radiata
Mean±SD	52.5±14.4		27.4±18.2		67.7±23.8	71.9±24.0	60.2±25.3	

hand subset (24 points). All subjects gave their written, informed consent, and the experimental protocol was approved by the local ethics committee of Hokkaido University Graduate School of Medicine.

Electromyographic (EMG) activity was recorded with Ag-AgCl electrodes positioned in a belly tendon montage on the skin overlying the first dorsal interosseous (FDI) muscle. The signal was amplified, filtered (50 to 2000 Hz), and digitized at a sampling rate of 5000 Hz for off-line analysis (Neuropack; Nihon Koden, Tokyo, Japan). A Magstim 200 stimulator (Magstim Co, Dyfed, UK) connected to a figure-of-8 magnetic coil was used for TMS. The coil was placed tangentially over the M1 at an optimal site for the FDI muscle. The optimal site was defined as the location where stimulation of a slightly suprathreshold intensity elicited the largest motor-evoked potentials in the FDI muscle. The resting motor threshold (rMT) was measured at the optimal site and was defined as the lowest stimulator output that could elicit motor-evoked potentials with peak-to-peak amplitudes >50 μV in at least half of 10 trials.

The RT experimental paradigm was displayed on a screen with the use of Labview (National Instruments, Austin, Tex). Each patient was comfortably seated in an armchair, 60 cm in front of a computer screen positioned at eye level. After a training session (3 blocks of 25 trials each), each participant was instructed to perform index-finger flexion movements as quickly as possible in response to a randomly (5- to 9-second) displayed "go" signal. TMS was delivered 100 ms after the "go" signal; its intensity was 80% of the maximum stimulator output. The order of stimulating the sites under examination (the M1, the PMC, and a sham stimulation) was randomized within and across subjects. We calculated 8% of the distance between the nasion and inion for each subject (typically, it was ≈2.8 cm) and defined the PMC area as the area corresponding to this distance anterior to the optimal site.[17,18] As a control for the specific effect of TMS, sham stimuli were applied with the Magstim coil perpendicular to the scalp at the vertex. Each block of stimuli consisted of 25 trials and was separated by 2-minute intervals to avoid fatigue. The RT was defined as the time interval between the "go" signal and the onset of the EMG burst (defined as the time when the EMG amplitude exceeded the mean value +3 SDs of the EMG amplitude in the 100 ms preceding the "go" signal). The RT at each site was determined for 25 averaged responses. In addition, the RT delay at each site was defined as the difference between the RT at each site and the RT in the case of sham stimulation.

We examined the SP duration of FDI muscle activity evoked by TMS at an intensity of 80% of the maximum stimulator output, during 20% of the maximal voluntary contraction of FDI muscle, and with visual feedback of muscle activity. Moreover, we used a stimulus at 130% of the rMT to exclude the possibility that a stimulus at a fixed level of stimulator output could not completely activate the inhibitory neurons in patients with a high rMT. The SP duration was measured in a single-trial EMG as the duration between TMS stimulus and the first recurrence of a sustained, voluntary EMG. The mean of 5 trials was used for further analysis. We excluded 6 patients who did not display the SP phenomenon from the SP study section, ie, an SP was not induced during tonic contraction, even with 100% stimulator output. For comparison of the SP duration relative to the RT delay at each site, the ratio of SP to RT was defined as SP duration/RT delay. Because RT delay was correlated with SP duration,[10,12,13] the disturbance of the inhibitory system increased with a decrease in the ratio of SP to RT. The RT delay induced by TMS was analyzed by repeated-measures ANOVA followed by a post hoc analysis with Scheffe's F test. Possible correlations among the various parameters were determined with Pearson's correlation coefficient test.

Results

The rMT of the patients with stroke was 65.1±4.3%. It tended to be higher in patients with poor recovery than in those with good motor performance. However, no significant correlation was observed between the rMT and FMS score ($r=-0.430$, $P=0.059$).

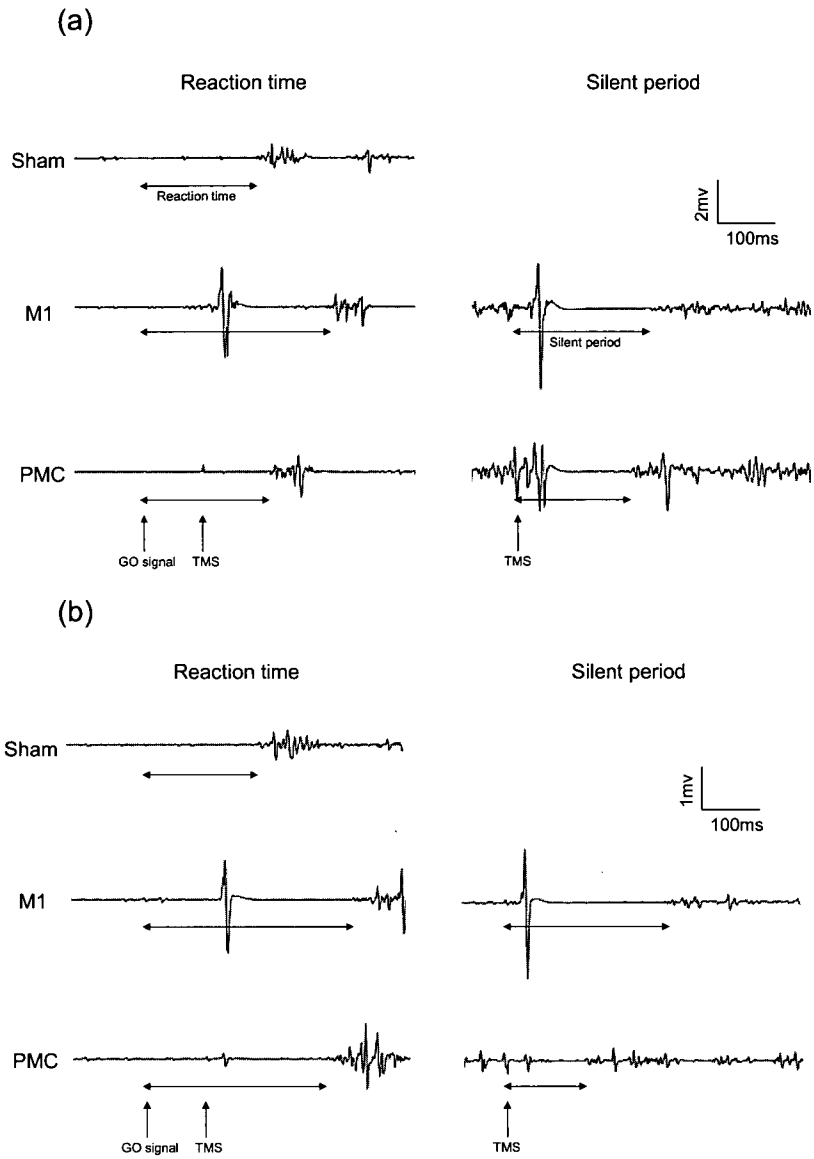

Figure 1. Examples of the raw data. a, A patient with good motor function and (b) a patient with poor motor function. TMS over the M1 induced an RT delay in individual patients with good and poor motor function. However, the RT delay of the PMC was more prominent in patients with poor motor function than in those with good motor function. Compared with the RT delay, the SP duration of the PMC was shorter in patients with poor motor function than in patients with good motor function.

Figure 1 shows the raw data for the RTs and SP durations in individual patients with good and poor motor function. Figure 2 shows the results of the RT delay that was induced after TMS over each site in the 20 patients. A repeated-measures ANOVA revealed a significant difference among RT delays at the stimulation sites [F (2, 38)=44.10, $P<0.001$]. Post hoc testing revealed that an increase in RT was apparent in the M1 and PMC when compared with the RT induced after sham stimulation (M1 $P<0.001$, PMC $P<0.001$). The RT delay was significantly associated with the SP in the M1 ($r=0.934$, $P<0.001$), but the RT delay was not significantly associated with the SP in the PMC ($r=0.272$, $P=0.347$).

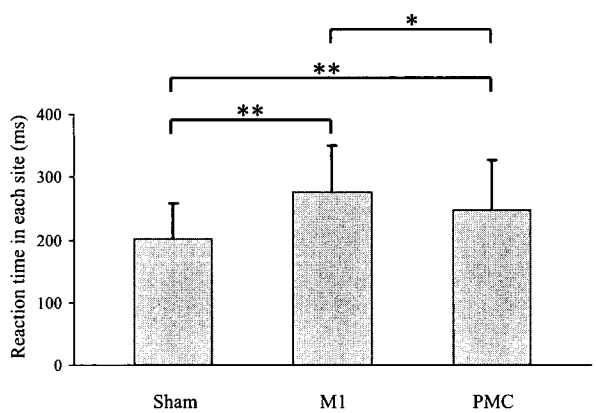

Figure 2. The RT change induced by TMS over each site. *$P<0.05$, **$P<0.01$. Error bar is the SD.

Table 2 shows correlations between motor function and the electrophysiologic data. The RT delay of the PMC was negatively correlated with the FMS score ($r=-0.787$, $P<0.001$; Figure 3a). However, the RT delay of the M1 was not correlated with the FMS score. The ratio of SP to RT in the M1 was not significantly associated with the FMS score. However, the ratio of SP to RT in the PMC was significantly associated with the FMS score (at fixed power, $r=0.563$, $P=0.036$, Figure 3b; at 130% rMT, $r=0.595$, $P=0.025$). This result indicated that compared with the RT delay, the SP of the PMC decreased with the decline in motor function. Moreover, the decreased ratio of SP to RT in the PMC was

TABLE 2. Correlations Between Motor Function and Electrophysiologic Data (Correlation Coefficients and *P* Values)

					SP/RT (M1)		SP/RT (PMd)	
	RT Delay (M1)	RT Delay (PMC)	SP (M1)	SP (PMC)	At Fixed Power	At 130% of rMT	At Fixed Power	At 130% of rMT
Upper limb subset of FMS	−0.137 (0.566)	−0.787 (0.000)†	−0.347 (0.224)	0.395 (0.162)	0.419 (0.136)	0.520 (0.057)	0.563 (0.036)*	0.595 (0.025)*
Ratio of upper arm subset to hand subset of FMS	−0.328 (0.158)	0.211 (0.371)	−0.069 (0.814)	−0.431 (0.123)	−0.436 (0.119)	−0.489 (0.076)	−0.704 (0.005)†	−0.689 (0.006)†

*$P<0.05$, †$P<0.01$.

correlated negatively with the ratio of the upper arm subset to the hand subset of the FMS (at fixed power, $r=-0.704$, $P=0.005$, Figure 3c; at 130% rMT, $r=-0.689$, $P=0.006$).

Discussion

The RT delays after TMS over the ipsilesional PMC were more prominent in patients with greater disability. In contrast, patients with good motor function demonstrated normal RT delay patterns of the paretic hand similar to those in healthy controls; RT delays induced by TMS were found in the contralateral M1 but not in the PMC.[13,19] These results indicated that the patients with good motor function had normal activation patterns during their hand movements because control from the PMC was either less important or suppressed. However, in patients with poor motor function, the motor control of the affected hand was dependent on the motor pathway from not only the M1 but also the PMC. This finding is consistent with that of a neuroimaging study that reported a negative correlation between motor function and multiple motor-related activations.[1,2] From another viewpoint, simple movements performed after stroke may require extensive motor cortical activity, similar to that associated with the more complex movements of "choice reaction time" of healthy controls. Other studies have noted that TMS over the contralateral PMC can induce RT delays during choice reactions of healthy controls.[19,20]

In healthy controls, a correlation between SP duration and RT delay has been noted.[10,13] This study also demonstrated a positive correlation between SP duration and RT delay of the affected M1 areas in stroke patients. However, in the PMC, SP duration was not correlated with RT delay, and we found that, compared with the RT delays, the SP durations of the PMC decreased with the decline in motor function. It has been postulated that the SP may reflect γ-aminobutyric acidergic inhibition of the cerebral cortex.[10,21] Several studies have reported that the loss of perilesional γ-aminobutyric acidergic inhibition contributes to the reorganization of the brain after stroke. This occurs by the unmasking of preexciting, functionally latent neural networks around the lesion and by an increased excitatory neurotransmitter release via removal of the inhibition of excitatory inputs.[4,14] The decreased SP duration in patients with poor motor function might reflect a disturbance in inhibitory function and the unmasking of latent excitatory connections in the PMC. Furthermore, this decreased SP duration of the PMC showed a negative correlation with relatively good function of the upper arm when compared with that of the hand. The projections from the PMC to the spinal cord are known to be less numerous and less excitatory than those from the M1.[22,23] Moreover, the projections from the PMC are more concerned with the control of muscle movements of the upper arm.[24,25] Regarding reorganization, it has been reported that hand and upper arm regions compete for areas within the cortex.[26] Considering these findings, the excitability that is unevenly distributed in the upper arm due to weak inhibitory function of the PMC might cause poor reorganization of the cortex that controls the hand. This hypothesis is consistent with the fact that the function of the upper arm was better than that of the hand in chronic stroke patients.[26,27]

We observed that the SP duration of the PMC by stimulation at a fixed level of stimulator output was relatively decreased compared with the RT delay in patients with poor motor function. However, there is a possibility that fixed-power stimulation did not completely activate inhibitory neurons in patients with poor motor function after stroke. In these patients, the rMT was often high; therefore, to overcome this problem, we used 130% of the rMT as the stimulus while studying SP duration. The SP duration of the PMC by 130% of rMT stimulation, compared with the RT delays, decreased with the decline in motor function, as well as fixed-power stimulation. This result suggested that the decrease in SP duration of the PMC in these patients (poor motor function after stroke) was a peculiar epiphenomenon and did not occur due to insufficient stimulation power. The RT delay induced by fixed-power stimulation of the PMC was more prominent in patients with greater disability, who often had a high rMT. The power of the TMS had a positive correlation with RT delay.[10,13] It was considered that stimulation with 130% of the rMT might be more powerful and induce more prolonged RT delays in patients with poor motor function than those induced by fixed-power stimulation. Similarly, it was thought that the ratio of SP to RT in the PMC would have a more significant correlation with motor function, because the ratio of SP that was compared with the more prolonged RT delay after stimulation with 130% of the rMT might decrease more than fixed-power stimulation in patients with poor motor function. Because there was no possibility that an RT study with a stimulation of 130% of the rMT would have an outcome different from that obtained by the study with fixed-power stimulation, we did not conduct an RT study at 130% of the rMT.

Several studies have reported that the ipsilesional dorsal premotor cortex (PMd), particularly that in the PMC, plays an important role in motor recovery after stroke.[1,7] We did not stimulate the PMC by specifying the PMd in this study. Therefore, to enhance understanding of the role of the PMC

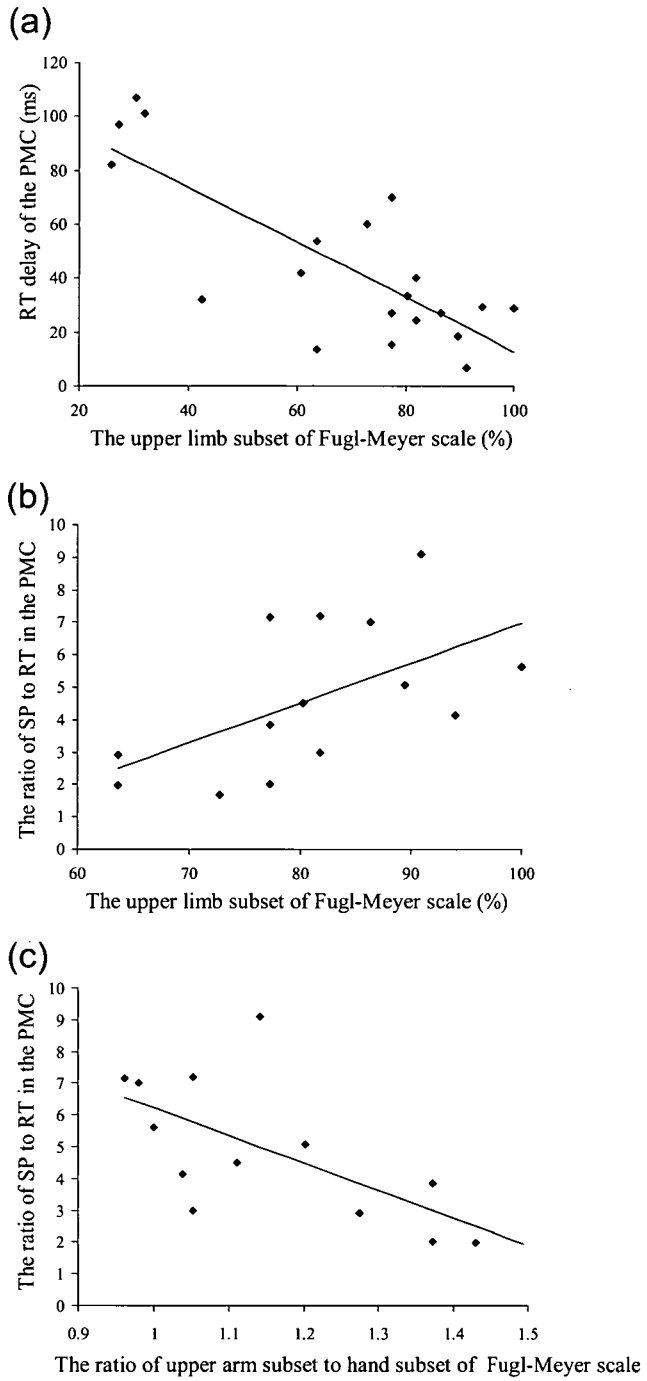

Figure 3. a, The RT delay of the PMC is negatively correlated with FMS score ($r=-0.787$, $P<0.001$). b, The ratio of SP to RT in the PMC had a significant correlation with the FMS score ($r=0.563$, $P=0.036$). (c) The ratio of SP to RT in the PMC had a negative correlation with the ratio of the upper arm subset to the hand subset of the FMS ($r=-0.704$, $P=0.005$).

in poststroke motor recovery, further studies are required to accurately stimulate the PMd by a stereotactic system integrated with magnetic resonance imaging data.

In conclusion, it appears that patients with poor motor function may use motor-related regions such as the PMC to move the paretic side. Disinhibition of the ipsilesional PMC might partly contribute to the reorganization of the brain in stroke patients with poor motor function. However, large-scale reorganization outside the ipsilesional M1 is a lengthy process that never results in complete recovery.

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Disclosures

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CASE REPORT

Repetitive Transcranial Magnetic Stimulation of the Unaffected Hemisphere in a Patient Who Was Forced to Use the Affected Hand

ABSTRACT

Takeuchi N, Toshima M, Chuma T, Matsuo Y, Ikoma K: Repetitive transcranial magnetic stimulation of the unaffected hemisphere in a patient who was forced to use the affected hand. Am J Phys Med Rehabil 2008;87:74–77.

We present a case report of a 56-yr-old chronic stroke patient with right hemiparesis who was treated with repetitive transcranial magnetic stimulation (rTMS) therapy. Before stroke, the patient had suffered an accident that led to paralysis and contracture of the left upper limb, and, subsequently, he was forced to use only his right upper limb for routine activities, despite right hemiparesis. We performed subthreshold rTMS (1 Hz, 25 mins) and sham stimulation of the contralesional primary motor cortex (M1) at different times. Immediately after rTMS, the patient was able to write characters with increased speed and accuracy, and this effect continued for more than 7 days; however, this was not the case after sham stimulation. Moreover, the writing practice after rTMS improved the patient's pinch force.

Key Words: Repetitive Transcranial Magnetic Stimulation, Rehabilitation, Constraint-Induced Movement Therapy, Stroke

Recent reports have demonstrated that repetitive transcranial magnetic stimulation (rTMS; 1 Hz) of the contralesional primary motor cortex (M1) improved the functioning of the affected hand in chronic stroke patients.[1–4] Inhibition of the excitability of the contralesional M1 by using 1-Hz rTMS results in a decrease in transcallosal inhibition from the contralesional to the ipsilesional M1 and an increase in the excitability of the ipsilesional M1; this ultimately leads to improved motor function in the affected hand.[1] It is expected that this method will be used as a new rehabilitation therapy for stroke patients; however, approaches to enhance and sustain the effects of rTMS are unclear.

We present a chronic stroke patient who was forced to use his affected hand for routine activities because of contracture of the unaffected hand. An improvement in the functioning of the affected hand was observed after the use of 1-Hz rTMS; this suggests that a combination of rTMS and motor training, such as forced limb use, can improve motor function in stroke patients. Therefore, we

studied whether rTMS therapy could improve the functional ability of this patient.

CASE REPORT

A 56-yr-old, right-handed male developed cortical cerebral hemorrhage (in the left precentral gyrus) 8 mos ago. He had suffered a fracture of the left forelimb and secondary infection of the left forelimb at 6 yrs of age, and subsequently he had been unable to move his left upper limb because of contracture of the wrist and elbow; however, he was able to move his left fingers. Therefore, he was forced to use his right upper limb despite the right hemiparesis caused by stroke. After physical and occupational therapy, he was able to walk and eat with a spoon, using his right hand. During testing of our protocol, his Fugl–Meyer score[5] was determined to be 60/66 (arm), 23/24 (hand), and 17/34 (leg). His modified Ashworth score[6] was 1/3 (arm), 1/3 (hand), and 1/3 (leg). The patient did not exhibit apraxia, aphasia, agnosia, or memory deficit. He provided written, informed consent, and the protocol for the use of rTMS was approved by the local ethical committee of the Hokkaido University Graduate School of Medicine.

A day before simulation, the patient familiarized himself with the task of writing and pinch force evaluation. Subsequently, the patient participated in two sessions that tested the influences of noninvasive cortical stimulation in the form of rTMS and sham stimulation. The rTMS session was conducted a week after the sham session to rule out the placebo effect of sham stimulation. The pinch force was measured before stimulation (pre) and after stimulation (post-1, immediately after stimulation; post-2, 30 mins after stimulation; and post-3, 7 days after stimulation). For more than 1 mo before the study, the patient practiced writing characters for more than 15 mins/day, because his chief complaint was related to the impairment of his writing ability. However, he was unable to write efficiently, and his ability of writing was stabilized. Therefore, in addition to the evaluation of the pinch force, we evaluated his writing performance, and we conducted further writing practices after rTMS. The patient practiced writing his address for 15 mins after the stimulation and for 15 mins/day until the post-3 session. We selected five Chinese characters (a part of his address) that he had frequently practiced writing before this study. The maximum pinch force of the affected hand was determined, using a pinch gauge (Pinch Meter SPR-641; Sakai Medical, Tokyo, Japan). To measure the pinch force, the subject was instructed to use only his thumb and index finger. In each session, 10 pinch force measurements were averaged.

rTMS was performed using a 70-mm figure-eight coil and a Magstim Rapid stimulator (Magstim Company, Dyfed, UK). The coil was placed tangentially over the contralesional M1 at the optimal site for the first dorsal interosseous muscle. The optimal site was defined as the location where stimulation at a slightly suprathreshold intensity elicited the largest magnetically evoked potentials in the first dorsal interosseous. Electromyographic activity was recorded, using silver–silver chloride electrodes positioned in a belly tendon montage on the skin overlying the first dorsal interosseous, and the signal was amplified, filtered (50–2000 Hz), and digitized at a sampling rate of 5000 Hz for offline analysis (Neuropack, Nihon Koden, Tokyo, Japan). The resting motor threshold was defined as the lowest stimulator output that could induce magnetically evoked potentials with a peak-to-peak amplitude greater than 50 mV in at least half of the 10 trials. rTMS was applied for 25 mins at a frequency of 1 Hz and an intensity of 90% resting motor threshold. Sham stimulation was applied with the coil positioned perpendicular to the scalp of the contralesional M1 at the same frequency and intensity as real rTMS.

The pinch force was evaluated, using analysis of variance for repeated measures with time (pre, post-1, post-2, and post-3) and conditions (rTMS and sham). A post hoc analysis was performed, using the Bonferroni correction. The significance level was set at 0.05.

The patient did not exhibit any adverse side effects during the course of this study. After rTMS, he could write characters with increased speed and accuracy (Fig. 1). A repeated-measures analysis of variance demonstrated a significant interaction between the time and conditions ($P = 0.004$) and a significant effect of time ($P < 0.001$) on the pinch force. Post hoc tests revealed that the pinch force did not change immediately after rTMS (pre, 5.37 ± 0.27 kg; post-1, 5.51 ± 0.23 kg); however, it improved with subsequent writing practice (pre *vs.* post-2 [5.92 ± 0.21 kg], $p = 0.002$; pre *vs.* post-3 [5.90 ± 0.18 kg], $P = 0.003$). No significant change in the pinch force was observed during the sham session (pre, 5.38 ± 0.21 kg; post-1, 5.28 ± 0.27 kg; pre, 5.40 ± 0.28 kg; post-1, 5.37 ± 0.27 kg). The Fugl–Meyer and modified Ashworth scores of the patient did not change after rTMS.

DISCUSSION

This is the first report demonstrating the use of 1-Hz rTMS for improving the functioning of the affected hand of a chronic stroke patient who had suffered contracture in the unaffected hand.

Recent reports have demonstrated that the application of 1-Hz rTMS to the contralesional M1 improves the functioning of the affected hand in stroke patients.[1–4] In the present study, the improvement in the functioning of the affected hand

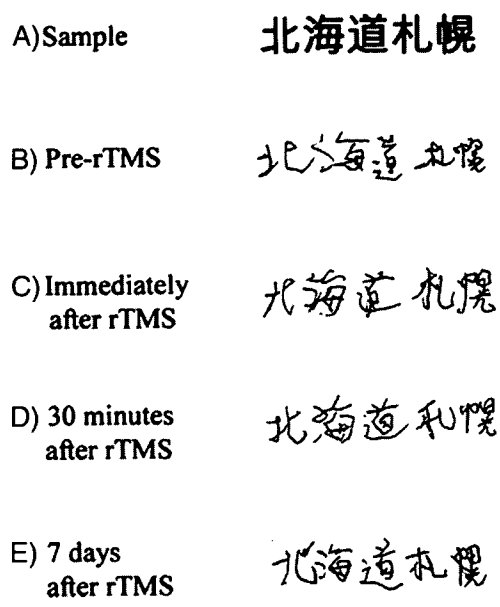

FIGURE 1 *The patient was able to write characters with increased speed and accuracy immediately after repetitive transcranial magnetic stimulation (rTMS). A, Sample: Five Chinese characters. B, Before rTMS: Total writing time was 39.1 secs. C, Immediately after rTMS (post-1): Total writing time was 34.1 secs. D, Thirty minutes after rTMS (post-2): Total writing time was 33.8 secs. E, Seven days after rTMS (post-3): Total writing time was 34.1 secs.*

after rTMS persisted for more than 7 days. However, it remains uncertain whether the effect of a single rTMS for stroke patients can be sustained[4] or not.[1] rTMS at 1 Hz can increase the excitability of the ipsilesional M1 by reducing transcallosal inhibition from the contralesional M1.[1,3] The increase in the excitability of the motor cortex was considered essential for motor learning.[7,8] Considering these findings, the increased excitability of the ipsilesional M1 after rTMS may contribute to reorganization of the ipsilesional M1 after motor learning. Therefore, interventions such as motor training after rTMS might be important for sustaining the effects of rTMS. In the present study, it is possible that motor function testing and writing practice after rTMS might have served as forms of motor training and helped to sustain the effects of rTMS.

In stroke patients, constraint-induced movement therapy (CIMT) can enhance the functional recovery of the affected limb by enforcing its use.[9,10] The beneficial effects of this therapy are associated with an increase in the excitability of the affected motor cortex. The immobilization of the unaffected arm that induces a reduction in the excitability of the unaffected motor cortex is also considered important.[9] The application of 1-Hz rTMS to the contralesional M1 can induce downregulation of the contralesional M1[1] and upregulation of the ipsilesional M1.[3] Therefore, the mechanism of action of 1-Hz rTMS and CIMT may be related.[11] Considering that the conceptual basis for CIMT is that stroke patients must use only their affected hand for routine activities,[12] our patient underwent a type of CIMT because he was forced to use his affected hand, because of contracture of the unaffected hand. In our study, rTMS improved the motor function of the patient's affected hand, suggesting that rTMS therapy might enhance the effect of CIMT in stroke patients.

This study has some limitations that should be considered. First, the potential effect of rTMS-independent motor learning should be considered because of the crossover design of this study. However, the motor function of the affected hand was improved after rTMS and motor training, but not after sham stimulation and motor training. Moreover, it was considered that the motor function of the affected hand had reached a plateau because of the motor training before stimulation. Therefore, it was unlikely that motor training after sham stimulation had influenced the functional improvement of the affected hand after rTMS. Second, the patient might feel the difference between the active and sham stimulation. This sham stimulation produced no cortical stimulation, but it produced the auditory artifact as control stimulation.[13] We used a stimulation intensity of 90% resting motor threshold that did not induce contraction of the hand muscles. Moreover, the patient was naïve to rTMS and reported that he had received active treatment after sham stimulation. Therefore, it is unlikely that the difference between sham and rTMS influenced the results of this study. However, further investigation using a double-blind study with more subjects is required to evaluate the effects of rTMS.

Our results demonstrate that rTMS of the contralesional M1 can lead to improved motor function of the affected hand in chronic stroke patients with contracture of the unaffected hand. Further, the results of this study suggest that the combination of rTMS and CIMT might be useful in facilitating the recovery of stroke patients.

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BOOK REVIEW

EBM Guidelines für Allgemeinmedizin

Edited by Ikka Kunnamo, editor in chief, and editors Erwin Rebhandl, Susanne Rabady, Frank Mader. 1427 pages. Published 2006 by Verlagshaus der Ärzte, Wien, Austria. Printed in Slovenia. ISBN 3-901 488-27-8.

Like all other physicians, general practitioners have to cope with a rapidly growing amount of new medical knowledge. The textbook *Evidence Based Medicine for General Practice*, is the German translation of *Evidence Based Medicine Guidelines* [1] and is intended to support general practitioners in their clinical decisions, with the latest evidence available.

The book is organized into 48 chapters, thus reflecting both the WHO-ICD 10 classification and medical specialties. Each chapter is well structured and covers, in accordance with the ICD-10, the epidemiology and pathophysiology of respective human conditions and diseases. Therapeutic and management strategies are described profoundly and comprehensively, including prevention and rehabilitation procedures (although primarily as a therapeutic option or concept). A wealth of illustrations assists the user who may not be familiar with the physical appearance of a particular disease or condition. Using the GRADE Working Group recommendations,[2] the level of evidence is provided for both the treatment and for diagnostic tests, which makes this book unique.

The book shares an inherent weakness of textbooks: it does not provide cutting-edge knowledge, because it cannot take into account the most recent research. From a physical medicine and rehabilitation specialist's perspective, the book fails to provide general practitioners with the necessary information to optimally promote the functioning and health of their patients. Surprisingly enough, physical medicine is categorized as a subspecialty of orthopedics. The conceptual framework of preventive and rehabilitation medicine, as well as its salutogenetic approach to promote patients' functioning and health, remains undescribed. It is hard to comprehend why preventive and rehabilitative exercise and training, therapeutic interventions administered as physical medicine, and rehabilitation treatment modalities are summarized in a chapter entitled *Sports Medicine*.

In summary, this textbook, featuring the traditional medical perspective, can be recommended to both general practitioners and medical specialists seeking optimal diagnosis and treatment for their patients.

Rating: ****

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