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Motor Improvement and Corticospinal Modulation Induced by Hybrid Assistive Neuromuscular Dynamic Stimulation (HANDS) Therapy in Patients With Chronic Stroke

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Background and objective. We devised a therapeutic approach to facilitate the use of the hemiparetic upper extremity (UE) in daily life by combining integrated volitional control electrical stimulation with a wrist splint, called hybrid assistive neuromuscular dynamic stimulation (HANDS). *Methods*. Twenty patients with chronic hemiparetic stroke (median 17.5 months) had moderate to severe UE weakness. Before and immediately after completing 3 weeks of training in 40-minute sessions, 5 days per week over 3 weeks and wearing the system for 8 hours each day, clinical measures of motor impairment, spasticity, and UE functional scores, as well as neurophysiological measures including electromyography activity, reciprocal inhibition, and intracortical inhibition were assessed. A follow-up clinical assessment was performed 3 months later. *Results*. UE motor function, spasticity, and functional scores improved after the intervention. Neurophysiologically, the intervention induced restoration of presynaptic and long loop inhibitory connections as well as disynaptic reciprocal inhibition. Paired pulse transcranial magnetic stimulation study indicated disinhibition of the short intracortical inhibition in the affected hemisphere. The follow-up assessment showed that improved UE functions were maintained at 3 months. *Conclusion*. The combination of hand splint and volitional and electrically induced muscle contraction can induce corticospinal plasticity and may offer a promising option for the management of the paretic UE in patients with stroke. A larger sample size with randomized controls is needed to demonstrate effectiveness.

Keywords: *Stroke; Hemiparesis; Upper extremity function; Transcranial magnetic stimulation; Intracortical inhibition; Reciprocal inhibition; Electrical stimulation*

Recovery of function in the hemiparetic upper limb is noted in fewer than 15% of patients after stroke.[1] Patients often compensate for their paretic upper limb by using their intact limb in the performance of everyday tasks.[2] It was supposed that strong reliance on compensatory overuse of the intact limb inhibited functional recovery of the impaired upper limb. Based on this hypothesis, forced-use therapy known as constraint induced movement therapy (CIMT) has been developed.[3] However, to participate in the CIMT, the candidates must be able to voluntarily extend their fingers and wrist at least 5 degrees, practice for 6 hours daily in a 2-week course, and spend waking hours with their nonparetic hand in a mitt.

To counter potential problems inherent in the intensive services needed for CIMT, we developed an alternative therapeutic approach to facilitate the use of the paretic upper extremity in daily living by combining assistive neuromuscular electrical stimulation with a wrist-hand splint for patients with moderate to severe hemiparesis. We call this hybrid assistive neuromuscular dynamic stimulation (HANDS). For assistive stimulation, we used integrated volitional control electrical stimulator (IVES),[4] which can automatically change its stimulation intensity in direct proportion to the changes in voluntary generated electromyography (EMG) amplitude recorded with surface electrodes placed on the target muscle. The stimulation was applied to the paretic finger extensors (extensor digitorum communis; EDC). The rationale for combining the stimulation system with a wrist-hand splint was derived from the work of Fujiwara et al,[5] who reported that a wrist-hand splint could reduce spasticity in finger, wrist, and elbow flexors, and facilitate finger extensor muscle activities. Therefore, the wrist-hand splint could make it

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Table 1
Clinical Details of Participants

					SIAS		MAS		
Patient	Diagnosis	Age	Paretic Side	TFO (Days)	Finger	Knee-Mouth	Elbow	Wrist	Finger
1	CI	53	Rt	180	4	4	2	1+	1+
2	CI	47	Rt	1095	1a	4	2	1+	2
3	CI	58	Lt	365	1b	3	3	2	3
4	CI	45	Lt	9750	1c	3	3	3	1
5	CH	28	Rt	630	1a	3	2	2	2
6	CI	58	Lt	1140	1c	3	2	2	1+
7	CI	75	Rt	330	1b	3	2	1+	1+
8	CI	64	Lt	160	1c	4	1	1+	1
9	CH	50	Rt	330	1b	3	1+	2	2
10	CH	73	Lt	3950	2	3	1	1	0
11	CI	27	Lt	3630	1a	4	2	2	2
12	CH	44	Lt	210	1b	3	1+	1+	2
13	CH	20	Lt	1050	1a	3	2	2	2
14	CI	61	Rt	600	1a	2	2	2	2
15	CH	43	Lt	200	1b	3	1+	1	1+
16	CI	58	Rt	450	1a	4	1+	1+	1+
17	CH	41	Lt	450	4	4	1	1	1
18	CI	30	Lt	165	1b	4	1	1	1+
19	CH	62	Rt	4320	1b	3	2	2	2
20	CI	58	Rt	900	1b	2	2	1+	1+

Abbreviations: CI, cerebral infarction; CH, cerebral hemorrhage; Rt, right; Lt, left; TFO, time from onset of stroke; SIAS, Stroke Impairment Assessment Set; MAS, modified Ashworth scale.

easier to detect finger extensor activities with surface electrodes. It can also help reduce flexor muscles spasticity, which is likely to be induced by repetitive finger flexion-extension movement in daily life. Using this assistive stimulation combined with a splint, patients with moderate to severe hemiparesis, who cannot extend their paretic fingers voluntarily, could extend their fingers at their will, which could facilitate the use of their paretic hand in their daily activities.[6] To examine the effects of the HANDS system, we tested the changes in motor function and spasticity of the paretic upper extremity. Furthermore, we studied changes in selected markers of brain and spinal plasticity induced by the training program using EMG and transcranial magnetic stimulation (TMS).

Methods

Participants

The participants were 20 patients with hemiparetic stroke, who had met the following inclusion criteria: (1) the time from stroke onset longer than 150 days; (2) no cognitive deficits; (3) no pain in the paretic upper extremity; (4) passive extension range of motion (ROM) greater than 0 degrees of the affected wrist and −10 degrees of metacarpopharyngeal joints; (5) detectable surface electromyographic signals in the affected EDC when the patients intended to extend their fingers; (6) no severe proprioceptive deficit in the affected upper extremity; (7) the ability to walk without physical assistance in daily life (eg, including patients who could walk independently with a cane and/or an orthosis); and (8) no motor improvement in the last 1 month before starting the intervention was confirmed with physicians and patients' testimony. Study sample mean age was 49.7 years (SD 15.2) and the median time from stroke onset was 17.5 months (range, 5.3 to 32.5 months). Clinical details of the participants are shown in Table 1. The purpose and procedures of the study were explained to the participants and informed consent was obtained. The study was approved by the institutional ethics review board.

Intervention

The IVES is a portable noninvasive (surface) EMG controlled, single channel neuromuscular electrical stimulator developed by Muraoka.[4] The IVES continually changes its stimulation intensity in direct proportion to the amplitude of voluntary EMG and applies an electrical stimulation of subthreshold motor intensity (eg, no visible muscle contraction but tingling feeling) during no voluntary contraction. The surface electrodes pick up EMG signal at the target muscle and simultaneously stimulate it in direct proportion to the picked up EMG signal with the exception of the section of 25 milliseconds after delivering each stimulation pulses in which stimulation artifacts and M wave are observed. A pair of electrodes for EMG detection and stimulation (30×12 mm) placed 5 mm apart, and 1 electrode (30×30 mm) for reference and stimulation were placed on the affected EDC muscle. Three trains of biphasic square wave pulses with a duration of 300 μs (300 μs positive pulse, 300 μs off, 300 μs negative pulses, and 300 μs off were repeated 3 times) were

applied at 20 Hz. The stimulus intensity was continuously changed in proportion to the detected EMG amplitude of the target muscle. The maximum stimulus intensity was set at a level tolerable by the patients and at which extension of 4 fingers besides the thumb to 0 degrees was achieved during voluntary finger extension attempt.

The patients wore a wrist-hand splint (Wrist support PO, Sigmax, Japan) and carried a portable IVES in a waist-bag for 8 hours during the daytime (Figure 1). The system was active for 8 hours; patients were instructed to use their paretic hand as much as possible while wearing the HANDS system. Their nonparetic upper extremity was not restrained. The patients were also instructed to practice bi-manual activities in their daily lives.

They were admitted for this therapy, and the length of the intervention was 21 days. They also received 40 minutes of occupational therapy per day, 5 days a week. Each session consisted of gentle stretching exercise of the paretic UE and active muscle reeducation exercise with the HANDS system by a therapist's manual contact. Occupational therapists were directed toward patients' goals and focused on their particular impairments and disabilities; thus, the specific therapy that each patient received varied.

Measurements

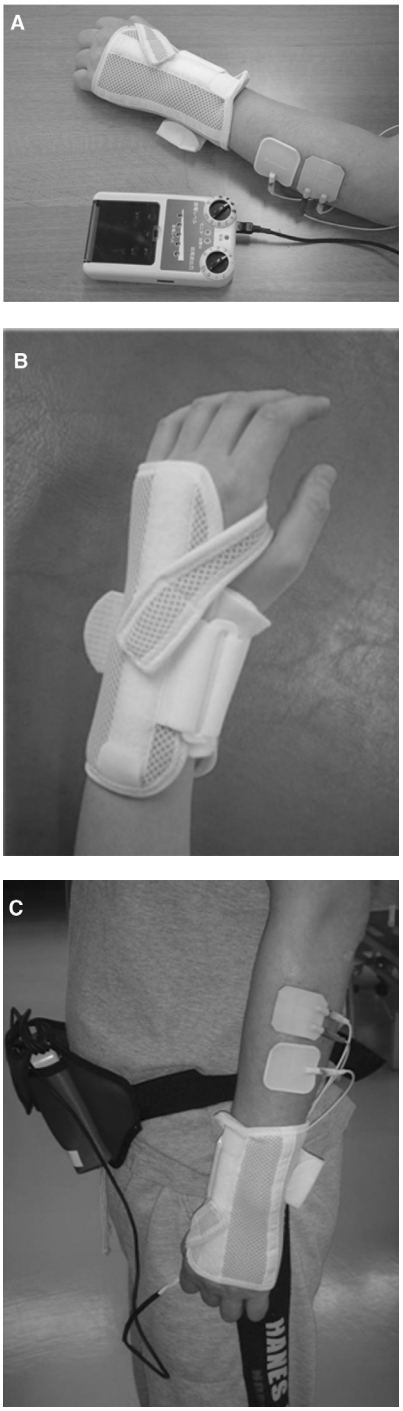
We used a pre–post test, cohort design for the following measurements. The pretests and posttests were performed 2 days before and 1 day after the intervention.

Clinical Evaluations

Practical utility of the paretic upper extremity was assessed using the utility score (UEUS).[7] UEUS consisted of 4 tasks performed with the paretic upper extremity: (1) pressing a sheet of paper on the desk, (2) hanging a bag, (3) drinking with a glass, and (4) turning over a page of a book. Each task was rated as 0, impossible; 1, partially possible; and 2, fully possible. The inter-rater reliability of the UEUS was satisfactory (weighted kappa 0.92 to 1.00). The Stroke Impairment Assessment Set (SIAS) motor test[8,9] and modified Ashworth scale (MAS)[10] were used as measures of motor function and spasticity in the affected upper extremity. The SIAS is a standardized measure of stroke impairment consisting of the 22 subcategories. The paretic side motor functions of the upper extremity are tested with the knee-mouth test and the finger test. They are rated from 0 to 5, for which 0 indicates complete paralysis and 5 no paresis. The score 1 for the finger test is divided into 3 subscales: 1a (mass flexion), 1b (mass extension), and 1c (minimal individual movement) (see Appendix).

All 3 outcome measures, that is UEUS, SIAS, and MAS, were scored by a masked examiner, who did not know which patients were recruited for this study to receive the HANDS therapy. This examiner assessed all the patients with stroke, who were admitted to our department during the study period, including patients not recruited for this study.

Figure 1
An Integrated Volitional Control Electrical Stimulator (IVES) Combined With a Wrist-Hand Splint



Note: (A) Electrical stimulation was applied to extensor digitorum communis (EDC) with the IVES. Electrodes were placed on the paretic EDC. (B) Wrist-hand splint. The splint, made of mesh materials, covered the area from approximately a quarter of the distal forearm to the MP joint. Two metal bars were attached both on the volar and palmer sides of the splint. To keep the thumb abducted, a Velcro strap was used passing through the thumb web from the palmer to the volar side of the splint. (C) The participants wear the wrist-hand splint and carry the IVES in the waist-bag for 8 hours (from 9 AM to 5 PM).

Computer-Aided Ratings

Handwriting was assessed using a system designed for measuring voluntary movements of the paretic upper extremities[11] (Human Technology Laboratory, Japan), which consisted of a pressure-sensitive digitizing tablet with a crystal display and a personal computer-based movement analysis software. First, a round target (1 cm in diameter) appeared on the crystal display and the patients were asked to track it with a stylus pen, with which they drew a circle 4 cm in diameter 3 times at a fixed speed (42º/s). The position data (x, y, coordinates) of the tip of the stylus pen on the digitizing tablet were stored on a personal computer at a sampling frequency of 40 Hz. The spatial resolution was 0.05 mm, and the distance (positioning lag component) between the target and the tip was calculated continuously. The axial pressure at the tip (pressure component) was also measured with 256 steps up to the maximum value of 204 N (2 kg). For each trial, 1028 points were subjected to off-line analysis. The participants were asked to avoid touching their elbows on the desk while they were being examined. The mean pen pressure and the mean distance from the target (tracking error) were calculated.

EMG Measurements

EMG activities were recorded with surface electrodes placed over the paretic EDC and flexor digitorum superficials (FDS) during the voluntary repetitive finger extension task. They were asked to extend their fingers as much and as fast as possible. The electrodes were applied with a center-to-center spacing of 20 mm, placed parallel to the muscle fibers, 1 electrode over and the other distal from the motor points of the EDC and FDS. Before attaching the electrodes, the skin areas were rubbed with alcohol, and the skin resistance was kept below 5 kΩ. An MEB-2000™ electromyography system (Nihon Kohden Co, Tokyo, Japan) was used to record and analyze the EMG data. The band pass filter was set at 30 Hz to 2 kHz. Co-contraction time ratio was calculated as the ratio between the time for FDS contraction and that for EDC contraction during finger extension. We also counted how many times the patients could repeat paretic side finger extension within 20 seconds.

H Reflex and Reciprocal Inhibition

With the patients seated and relaxed, H reflexes were elicited from the paretic flexor carpi radialis (FCR) muscle by submaximal electrical stimulation of the median nerve at the antecubital fossa with a 1-millisecond square-wave constant current. The reflex responses were measured as the peak-to-peak amplitude of the H reflex recorded by a bipolar disc electrode placed over the FCR muscle.[12]

Reciprocal inhibition was assessed using a FCR H reflex conditioning-test paradigm.[12] Ten conditioned and 10 test H reflexes were averaged at each time point. The test FCR H reflex amplitude was maintained at 15% to 20% of the maximal M wave amplitude (Mmax) for each block trial. Conditioning stimulation to the radial nerve was delivered at the spiral groove. Stimulus intensity of the conditioning stimulation was 1.0 motor threshold (MT). MT was defined as a 100 μV response of the extensor carpi radialis. The conditioning-test stimulus interval was set at 0, 20, and 100 milliseconds.

TMS Measurement

We assessed short intracortical inhibition (SICI) and intracortical facilitation (ICF) with paired magnetic stimulation methods.[13] Patients were seated in a reclining chair. Transcranial magnetic stimulation (TMS) was delivered with a Magstim 200 magnetic stimulator (The Magstim Company, Whitland, Dyfed, UK). Magnetic stimulation was applied over the motor cortex through a figure-of-eight coil having an external wing diameter of 9 cm and a peak magnetic field of 2.2 Tesla. The stimulating coil was placed over the optimal site for eliciting responses in the paretic/nonparetic EDC and oriented so that the current in the brain flowed in a posterior to anterior direction through this optimal stimulating site.

To assess SICI and ICF, the conditioning stimulus and test stimulation were given using the same figure-of-eight coil connected to 2 magnetic stimulators. The conditioning stimulus was 80% of the active motor threshold. The test stimulus was set at 120% of the resting motor threshold or at a level capable of producing stable MEP of 0.2 to 1 mV. The participants received the test stimulus or conditioning test stimuli at interstimulus intervals (ISIs) of 2, 3, 10, and 15 milliseconds. SICI was calculated as the mean paired pulse amplitude at ISIs of 2 and 3 milliseconds as a percentage of the mean single-pulse amplitude. ICF was calculated in the same manner using ISIs of 10 and 15 milliseconds.

Follow-up

To assess long-term effects of the training protocol, clinical evaluations (the SIAS motor, MAS, and UEUS) and computer-aided ratings were assessed at 3 months after the end of the intervention.

Data Analysis

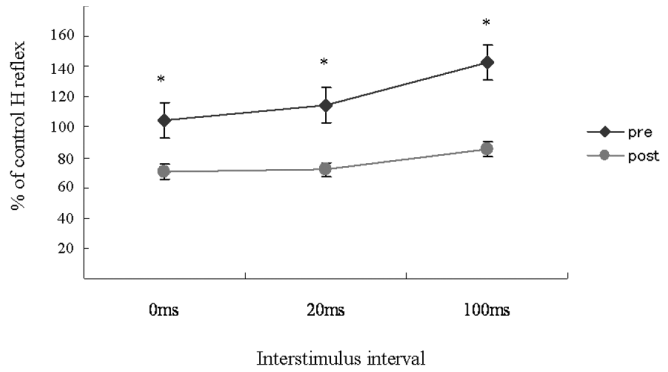
To calculate the mean value of the SIAS finger score, 1a, 1b, and 1c of SIAS finger score were transformed to 1, 2, 3, and 2, 3, 4, 5 of the SIAS finger score were transformed to 4, 5, 6 and 7. In the MAS score, score 1+ was transformed to 2, and score 2 and 3 were transformed to 3 and 4. The Wilcoxon signed rank test was used to compare nonparametric data as clinical evaluations, computer aided ratings and EMG parameters between pre treatment and posttreatment. Repeated measure analysis of variance (ANOVA) was used in the analysis of the reciprocal inhibition and paired pulse TMS studies. In the 3-month follow-up period, the main effect of time was examined with the Friedman test. The factors tested are explained in more detail in the Results section. The

Table 2
Summary of Scores of Clinical Evaluations, Computer-Aided Ratings, and EMG Measurements[a] (n = 20)

	Pretreatment	Posttreatment	*P* Value
UEUS			
Drinking with a glass	0.60 (0.75)	1.55 (0.68)	.001
Turn over a page	0.30 (0.57)	1.35 (0.74)	<.001
SIAS			
Finger	2.35 (1.49)	3.75 (1.11)	<.001
Knee-mouth	3.25 (0.63)	3.70 (0.57)	.02
MAS			
Elbow	2.50 (0.94)	1.10 (0.71)	<.001
Wrist	2.30 (0.86)	0.90 (0.78)	<.001
Finger	2.25 (0.96)	0.75 (0.63)	<.001
Grip strength	8.4 (5.17)	11.2 (4.46)	.015
Computer-aided ratings			
Pen pressure	53.1 (113.4)	106.8 (142.6)	.008
EMG measurements			
Co-contraction time ratio	0.84 (0.22)	0.45 (0.13)	.002
Repetitive extension	4.04 (1.90)	6.28 (2.14)	<.001

Abbreviations: EMG, electromyography; UEUS, upper extremity utility score; SIAS, Stroke Impairment Assessment Set; MAS, Modified Ashworth score.
[a]Values are mean value (SD). *P* value was calculated with Wilcoxon sign rank test.

Figure 2
Reciprocal Inhibition Before and After the Hybrid Assistive Neuromuscular Dynamic Stimulation (HANDS) Therapy



Note: The magnitude of the conditioned H reflex was expressed as a percentage of the control (unconditioned) H reflex at 3 (0, 20, 100 milliseconds) interstimulus intervals. Error bars indicate standard error. Asterisks indicate that the post hoc Bonferroni test showed a statistically significant difference between the pre- and post values at each interstimulus interval. The square symbol shows the pretreatment and the circle symbol shows the posttreatment mean percentage of control H reflex in each interstimulus interval.

Wilcoxon signed rank test was used for post hoc analysis. Effects were considered significant if $P < .05$. All statistical analyses were performed with SPSS version 15.0J.

Results

Clinical Evaluations and Computer-Aided Ratings

The changes of UEUS, SIAS motor, muscle tone, grip strength, computer-aided ratings, and EMG parameters are shown in Table 2. The score of "drinking with a glass" and "turning over a page" of UEUS improved significantly ($P < .01$). Before the treatment, the mean score (SD) of "pressing sheet of paper" and "hanging bag" tasks of UEUS were 1.75 (0.55) and 1.90 (0.44). After the treatment, those mean scores were 1.9 (0.44) and 1.9 (0.44). The changes were not significant. The SIAS finger test improved significantly ($P < .001$) as well as the SIAS knee-mouth test ($P = .02$). The MAS scores of the paretic side at the elbow, wrist, and finger flexors were also reduced significantly ($P < .001$). But the improvement of motor function, as well as the other clinical improvements, was correlated neither with the time from onset nor with age.

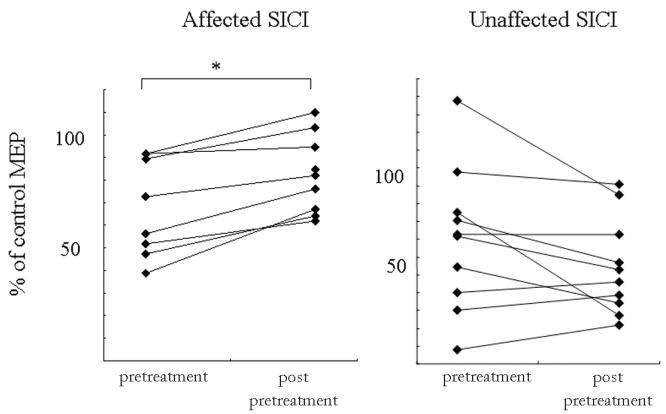
Computer-aided ratings showed that the pen pressure increased significantly ($P = .008$).

Electrical Physiological Outcomes: EMG, Reciprocal Inhibition, and TMS

EMG recordings showed that co-contraction of the antagonists (flexors) was reduced. The co-contraction time ratio was decreased ($P = .002$) (Table 2). In 19 patients, H reflex was evoked in their paretic FCR and changes of reciprocal inhibition were assessed as illustrated in Figure 2. The mean amplitude of test H reflex was 16.8% of M wave at pretreatment and 16.7% at posttreatment. A 2-factor [time (pretreatment, posttreatment), ISI (0, 20, 100 milliseconds)] repeated measure ANOVA revealed a significant main effect of time ($F(1,18) = 18.6$; $P < .001$). The post hoc Bonferroni test showed significant changes of reciprocal inhibition at all 3 interstimulus intervals after the intervention.

Using TMS, MEPs of the paretic EDC could be evoked in only 8 of 20 patients before the therapy, which increased to 9 patients after therapy. There was no significant change of active and resting motor thresholds in both the paretic and nonparetic sides after the therapy. The mean amplitude (mV) of the test MEP(SD) was 0.57(0.46) in nonparetic sides and 0.24(0.11) in paretic sides at pretreatment, and 0.46(0.35) in nonparetic and 0.22(0.09) in paretic sides at posttreatment. Three factors [time (pretreatment, posttreatment), side (nonparetic, paretic) and interstimulus intervals ISI (SICI; ICF)] repeated measure ANOVA showed significant effects of the ISI ($F(1,7) = 14.3$; $P = .007$). The effect of side was not significant ($F(1,7) = 5.33$; $P = .054$). Two-factor [time (pre, posttreatment), side (nonparetic, paretic)] repeated measure ANOVA for SICI showed a significant interaction of side and time ($F(1,7) = 18.7$; $P = .003$). The post hoc Bonferroni test showed a significant difference between the pre-SICI and post-SICI ($P = .005$) on the paretic side (Figure 3). Spearman's rank correlation test showed statistically significant correlation between the posttreatment SICI on the paretic side and

Figure 3
The Change of Short Intracortical Inhibition (SICI) Both in the Paretic and Nonparetic Hemispheres



Note: The asterisk indicates that the post hoc Bonferroni test showed a statistically significant difference. MEP, motor evoked potential.

posttreatment SIAS finger score (rs = 0.65; P = .03). There was no significant effect of side and time on ICF.

Three-Month Follow-up

The clinical outcome measures and computer-aided ratings were assessed in 15 of the 20 patients 3 months after the end of the intervention. The Friedman test showed a significant effect of time in the drinking with a glass task and turning over a page task in the UEUS, the SIAS finger score, MAS (elbow, wrist, finger), pen pressure, and grip strength (Table 3). The post hoc Wilcoxon sign rank test showed that the pretreatment and 3-month follow-up values of drinking with a glass task score, turning over a page task score, the SIAS scores, and MAS scores were significantly different from the pretreatment values. When we compared the posttreatment values with those at the 3-month follow up, the post hoc Wilcoxon sign rank test showed significant difference in the drinking with a glass task and grip strength (Table 3).

Discussion

This study is the first to show that using a hybrid hand-wrist splint combined with closed loop EMG-controlled electrical stimulation training for 3 weeks resulted in both clinical improvement of the paretic upper extremity and corticospinal modulation in patients with chronic stroke. The improvement may be attributed to reduction of wrist and finger flexor spasticity as is evidenced by decreased co-contraction during the finger extension task. Partial restoration of reciprocal inhibition might explain this improvement. We assessed reciprocal inhibition with H reflex. The first phase of reciprocal inhibition (ISI 0 milliseconds) is considered to be mediated by disynaptic inhibitory pathways that were once thought to be analogous to the disynaptic Ia reciprocal inhibitory pathways.[12] The second phase of inhibition (ISI 20 milliseconds) is thought to be due to presynaptic inhibition of the terminals of Ia afferents responsible for the H reflex. The origin of the third phase (ISI 100 milliseconds) is less clear. It has been proposed that it is due to continued presynaptic inhibition and that the division between the second and the third phases is caused by superimposition of a short period of facilitation at around 50 milliseconds. An alternative hypothesis is that, because of its long latency, it may involve long loop inhibitory connections from radial nerve to brain stem (spino-bulbo-spinal connections) or even cerebral cortex (transcortical connections) and then back to the H reflex pathway in the spinal cord.[14] Like many other spinal pathways, it is hypothesized that reciprocal inhibition in the forearm is influenced by descending inputs from supraspinal centers that control the excitability of the systems at rest and during movement.[14] In the present study, not only the first phase but also the second and the third phases of reciprocal inhibition were modulated after the training. Therefore, it is hypothesized that supraspinal changes, as well as changes in the spinal reflex pathway, have been induced.

The change of intracortical circuitry in the motor cortex was assessed with paired pulse paradigm, and it was demonstrated that the paretic hemisphere short intracortical inhibition (SICI) was reduced after the intervention. Liepert et al[15] showed that disinhibition of SICI occurred as a compensatory mechanism in patients with early stroke. SICI has been, however, reported to be normalized in the chronic stage.[16] Our findings challenge such normalization as disinhibition of SICI occurred even in chronic stroke after the specific training protocol of our study. This disinhibition of intracortical interneurons is supposed to play an important role in motor learning, reorganization, and recovery after brain lesion.[17,18]

It was reported that repetitive electrical stimulation combined with voluntary drive of the target muscle increased corticospinal excitability more than repetitive electrical stimulation alone.[19] Cortico-cortical inhibition has been shown to be reduced during voluntary contraction, which was attributed to downregulation of intracortical inhibitory interneurons with subsequent facilitation of the activity of corticomotoneuronal cells involved in the intended movement.[20] Decreases in inhibition as well as increases in synaptic efficacy of neural circuits are some of the proposed mechanisms for rapid neuronal plasticity of sensorimotor areas during skill acquisition, learning, and memory.[21]

Electrical stimulation,[22] splint and combined use of electrical stimulation,[23,24] and splint alone[5] could reduce spasticity and improve motor function in the paretic upper extremity. The efficacy of EMG-triggered neuromuscular electrical stimulation has been likewise reported.[22,25] However, EMG-triggered neuromuscular electrical stimulators so far reported cannot control electrical stimulation in proportion to voluntary EMG, because it stops monitoring EMG after the stimulation. The IVES used in this study can control electrical stimulation

Table 3
Summary of 3-Month Follow-up Study[a] (n = 15)

	Pretreatment	Posttreatment	3-Month Follow-up	*P* Value
UEUS				
Drinking with a glass	0.60 (0.73)	1.50 (0.63)[b]	1.93 (0.25)[b,c]	<.001
Turn over a page	0.33 (0.61)	1.40 (0.7)[b]	1.33 (0.72)[b]	.001
SIAS				
Finger	2.60 (1.63)	3.86 (1.24)[b]	4.20 (1.26)[b]	<.001
Knee-mouth	3.33 (0.61)	3.73 (0.59)[b]	3.90 (0.25)[b]	.002
MAS				
Elbow	2.40 (1.05)	1.06 (0.79)[b]	0.66 (0.81)[b]	<.001
Wrist	2.13 (0.91)	0.86 (0.83)[b]	0.73 (0.79)[b]	<.001
Finger	2.06 (1.03)	0.73 (0.7)[b]	0.53 (0.83)[b]	<.001
Grip strength	8.2 (5.2)	11.7 (4.0)[b]	14.1 (5.0)[b,c]	.001
Computer-aided ratings				
Pen pressure	38.5 (81.0)	90.7 (114.9)[b]	80.1 (121.1)[b]	.001

Abbreviations: UEUS, upper extremity utility score; SIAS, Stroke Impairment Assessment Set; MAS, Modified Ashworth score.
[a]Values are mean value (SD). *P* value was calculated with Friedman test.
[b]Post hoc Wilcoxon signed-rank test showed significant difference from pretreatment ($P < .05$).
[c]Post hoc Wilcoxon signed-rank test showed significant difference between posttreatment and 3-month follow-up ($P < .05$)

continually in direct proportion to voluntary EMG. Patients can therefore use this stimulator at their will in daily life as long as 8 hours a day. It encourages the patients to use their paretic arm in their daily lives without the need to restrain the nonparetic upper extremity as is practiced in the CIMT.

During the use of the HANDS system, therapists do not have to spend long hours attending the patient as required during CIMT, making, we believe, the HANDS program more practical in daily clinical practice.

There are, however, several points to be considered in this study. The number of patients treated in this study was small. There was no age-matched control or sham treatment group.

The pilot data presented in this study provide the basis for designing and conducting a larger scale trial with more rigorous study design including masking and randomization to test the hypothesis that the HANDS training program is more effective and less labor intensive than CIMT or other strategies in the management of the chronically paretic upper extremity.

Appendix
Stroke Impairment Assessment Set (SIAS)

Motor Function (Upper Extremity)

1. Knee-mouth test: In the sitting position, the patient touches the contralateral knee with the affected hand and then lifts it to the mouth
   - 0 There is no contraction of biceps brachii
   - 1 Minimal voluntary movement is noted, but the patient cannot raise the hand to the level of nipple
   - 2 Synergic movement is noted in the shoulder and elbow joints, but the patient is not able to touch the mouth with the affected-side hand
   - 3 The patient carries out the task with severe or moderate clumsiness
   - 4 The patient carries out the task with mild clumsiness
   - 5 The patient carries out the task with as smoothly as on the unaffected side

2. Finger test: Individual finger movements are tested. The patient flexes each digit from thumb to little finger, in that order and then extends them from little finger to thumb
   - 0 No voluntary finger movement
   - 1a Minimal voluntary movement or mass flexion
   - 1b Mass extension
   - 1c Minimal individual movement
   - 2 Individual movement of each finger is possible, but flexion or extension is not complete
   - 3 Individual movement of each finger is possible with adequate flexion and extension of the digits; however, the patient carries out the task with severe or moderate clumsiness
   - 4 The patient carries out the task with mild clumsiness
   - 5 The patient carries out the task as smoothly as on the unaffected side

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