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Original Article

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Transcutaneous spinal stimulation combined with a long opponent-pronation orthosis (FAST-HAND) for upper extremity motor function in patients with chronic stroke: A randomized-controlled trial

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Abstract

Objectives: This study aims to assess the effect of functional assistive stimulation for the hand (FAST-HAND) in patients with chronic stroke.

Patients and methods: This single-blind, randomized-controlled study included 15 participants with a four-week follow-up between October 2021 and August 2024. All participants underwent task-oriented upper extremity (UE) rehabilitation twice weekly for four weeks. The FAST-HAND group received training with transcutaneous spinal stimulation and a long opponent-pronation orthosis, while the control group received rehabilitation without these devices. The Fugl-Meyer Assessment (FMA) upper extremity motor score (FMA-total), the modified Ashworth scale (MAS), the Motor Activity Log-14 amount of use (MAL-14 AOU), the Box and Block Test (BBT), the H-reflex, and reciprocal inhibition were assessed before, after, and four weeks after the intervention.

Results: Fifteen participants (13 males, 2 females; mean age: 53.0 ± 7.86 years; range, 38 to 67 years) were randomly allocated to the FAST-HAND (n=7) and control (n=8) groups. The mean FMA-total in the FAST-HAND group showed a significant change at post (42.6 ± 13.9) compared to baseline (39.0 ± 15.0) (p=0.025).

Conclusion: Our study results suggest that FAST-HAND can modestly improve UE motor function immediately after the intervention.

Keywords: Electric stimulation, rehabilitation, stroke, upper extremity.

Approximately 12.2 million new stroke cases were reported globally in 2019, alongside about 101 million individuals living with stroke worldwide.[1] Motor impairment of the upper extremity (UE) after stroke affects much patients with stroke, and recovery of function in the hemiparetic UE is

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noted in fewer than 15% of patients after stroke.[2] Many patients continue to face disabilities even after extensive rehabilitation therapy.[3]

The C7 spinal segment innervates the triceps brachii (triceps), which extends the elbow; the pronator teres (PT), which pronates the forearm; and the extensor digitorum communis (EDC), which extends the fingers.[4,5] These three muscles are key for inter-joint coordinate movements, making C7 an attractive target for neuromodulation to restore UE function. Many types of rehabilitation aim to improve UE function, although inter-joint coordinated distal and proximal movements are still challenging.[6] Restoring functional inter-joint coordinated movements with reaching, forearm pronation, and finger-flexion extension is critical to make their paretic UE useful in their activities of daily living (ADLs) for patients with moderate-to-severe hemiparesis.

Spinal cord stimulation was developed to enhance the activity of the spinal circuit.[7] Transcutaneous spinal stimulation stimulates the dorsal afferent root and evokes posterior root muscle reflexes.[8] Both epidural (invasive) and transcutaneous (non-invasive) spinal stimulation have been shown to improve UE function in patients with spinal cord injury.[9,10] Moreover, recent reports indicate that epidural spinal stimulation can produce significant motor recovery in chronic stroke patients.[11] Several studies have suggested that spinal cord stimulation may serve as an alternative strategy for enhancing motor recovery after stroke.[12] However, to the best of our knowledge, no clinical trials have evaluated the therapeutic effects of transcutaneous spinal stimulation on post-stroke UE impairment, yet.

Task-oriented training is crucial for patients with stroke,[13] particularly for the UE, where forearm pronation combined with elbow extension and finger pinching are critical for ADL. To address this, we developed a training protocol that uses transcutaneous spinal stimulation to C7 combined with a long opponent-pronation orthosis namely functional assistive stimulation for the hand (FAST-HAND). In the present study, we aimed to assess the effect of FAST-HAND in patients with chronic stroke.

PATIENTS AND METHODS

This single-center, single-blind, parallel-design, randomized-controlled study was conducted at Juntendo University Hospital, Department of Rehabilitation Medicine between October 2021 and August 2024. The study was carried out in accordance with the CONSORT 2010 guidelines (Supplementary Table 1).

Inclusion criteria were as follows: (1) patients with hemiparesis due to a first-onset stroke; (2) aged 20 to 80 years; (3) stroke onset longer than 60 days prior; (4) patients who could move their paretic fingers individually, but not smoothly or could not move their fingers individually (stroke impairment assessment set [SIAS] finger function test score ≤3);[14] (5) patients who could raise their paretic hand to the height of their nipple (SIAS knee mouth test score ≥2);[14] (6) patients who did not lose their light touch sensation in the affected UE (SIAS sensory score ≥1);[14] (7) muscle activities of the affected EDC could be detected by surface electromyography (EMG); (8) sufficient wrist range of motion (ROM) to wear an orthosis; and (9) modified Ashworth scale (MAS)[15] of the paretic finger score of 2 or less. Exclusion criteria were as follows: (1) severe cardiac disease; (2) uncontrolled hypertension; (3) acute illness or fever; (4) recent history of pulmonary embolism, acute cor pulmonale, or severe pulmonary hypertension; (5) severe liver or renal failure; (6) orthopedic complications preventing exercise; (7) severe cognitive impairment or mental illness; (8) other metabolic diseases that restrict rehabilitation; (9) less than two months since botulinum toxin treatment; (10) contraindications to electrical stimulation; and (11) use of a pacemaker. Finally, a total of 15 participants who met the inclusion criteria were recruited. The study flowchart is shown in Figure 1.

Participants were randomly allocated to two groups: the transcutaneous spinal stimulation combined with a long opponent-pronation orthosis (FAST-HAND) group and the control group. Randomization was performed via the permuted block method with a block size of 4. The intervention used in this study was performed according to a randomized list prepared by an individual not part of the study. A written informed consent was obtained from each

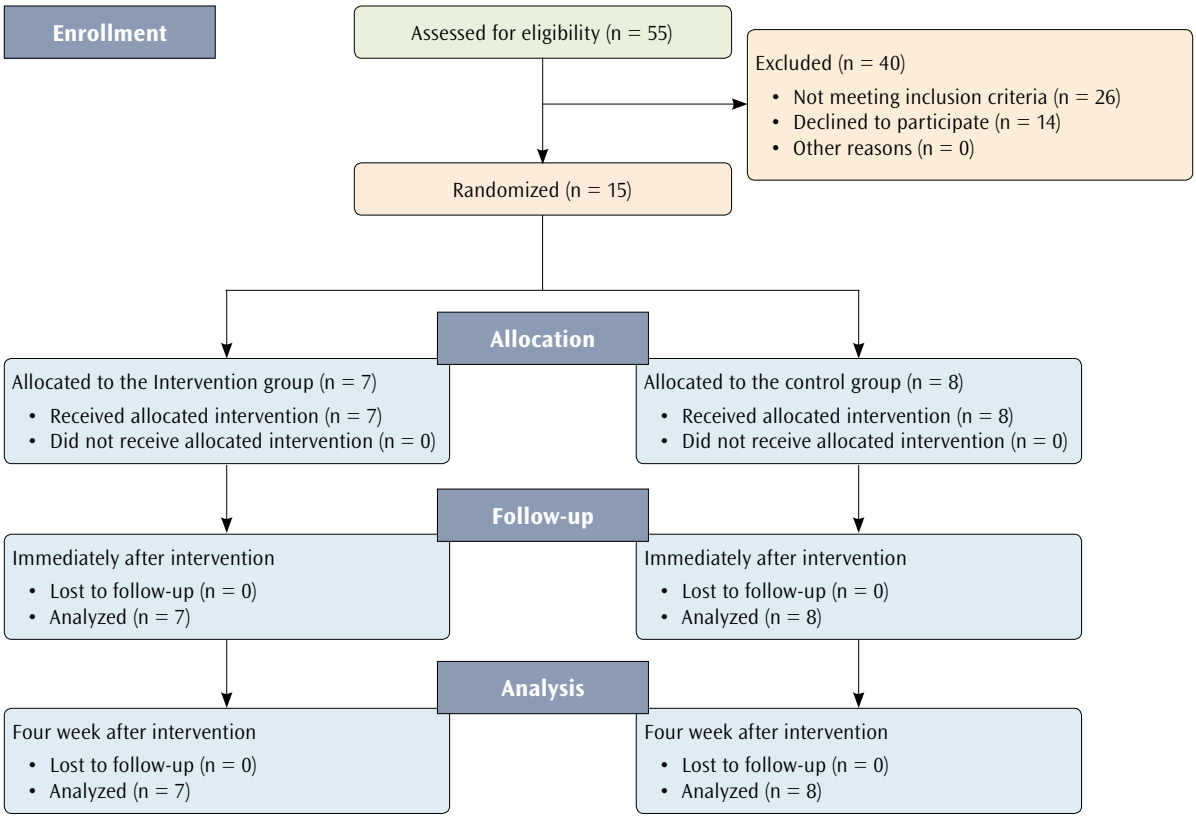

Figure 1. CONSORT flow diagram.

participant. The study protocol was approved by the Juntendo University Certified Review Board (Date: 13.09.2021, No: CRB3180012). The study was conducted in accordance with the principles of the Declaration of Helsinki. The study is registered at Japan Registry of Clinical Trials (jRCT) with the Registration No. jRCTs032210353 (https://jrct.niph.go.jp/).

Transcutaneous Spinal Stimulation

This transcutaneous spinal stimulation system was developed by our group. It was made by Pacific Supply Co. and is not commercially available. It was patented (Japan 6751881, USA 10,668,281, China ZL201680015103). We used the stimulation device system (model number: UE-16039-1C.2B.5A.6A, Pacific Supply Co., Ltd., Osaka, Japan), which delivered constant current stimulation (Figure 2a). We used two 7×5 cm self-adhesive ST-gel surface electrodes (Sekisui Kasei Co., Ltd., Tokyo, Japan) as stimulation electrodes. Stimulation electrodes were placed with the cathode positioned over the spinous process of the seventh cervical vertebra and the anode over the paretic Erb's point. It is easier for depolarization to occur beneath the cathodal electrode. In our previous study,[16] using the same device, we delivered transcutaneous spinal stimulation with an intensity set to twice the sensory threshold. This intensity was chosen to specifically recruit dorsal-root Ia afferent fibers. Thus, we applied this protocol to C7 stimulation to maintain methodological consistency. The sensory threshold was determined based on the participant's subjective perception. The stimulation frequency was set at 100 Hz, with a pulse width of 1 ms. The stimulation frequency was selected based on evidence that 100 Hz trains are sufficient to elicit tonic contractions of hand and arm muscles during intraspinal microsimulation.[17] To assess muscle activity, surface EMG electrodes were placed on the muscle belly of the paretic extensor EDC. The resulting muscle action potentials were wirelessly transmitted to the stimulation device

system using a dedicated wireless EMG system (model number: UE-16039-3A, Pacific Supply Co., Ltd., Osaka, Japan). These EMG and stimulation devices are controlled by an application called PSHS01-Measure Control Monitor (Pacific Supply Co., Ltd., Osaka, Japan). Electrical spinal stimulation was applied, when the amplitude of the EDC action potentials, as measured using surface electrodes, exceeded a predefined threshold. This threshold was set at a level that allowed detection during voluntary finger extension, but was not triggered by crosstalk during finger flexion.

Long opponent-pronation orthosis

Our newly developed long opponent-pronation orthosis helps patients maintain thumb opposition and forearm pronation. This orthosis has two components: the forearm component and the hand component. The forearm component was attached from the medial and lateral epicondyle to the distal end of the radius and ulna (Figure 2b). The forearm component was attached to the hand component with a metal bar (Figure 2c). The connection between the forearm

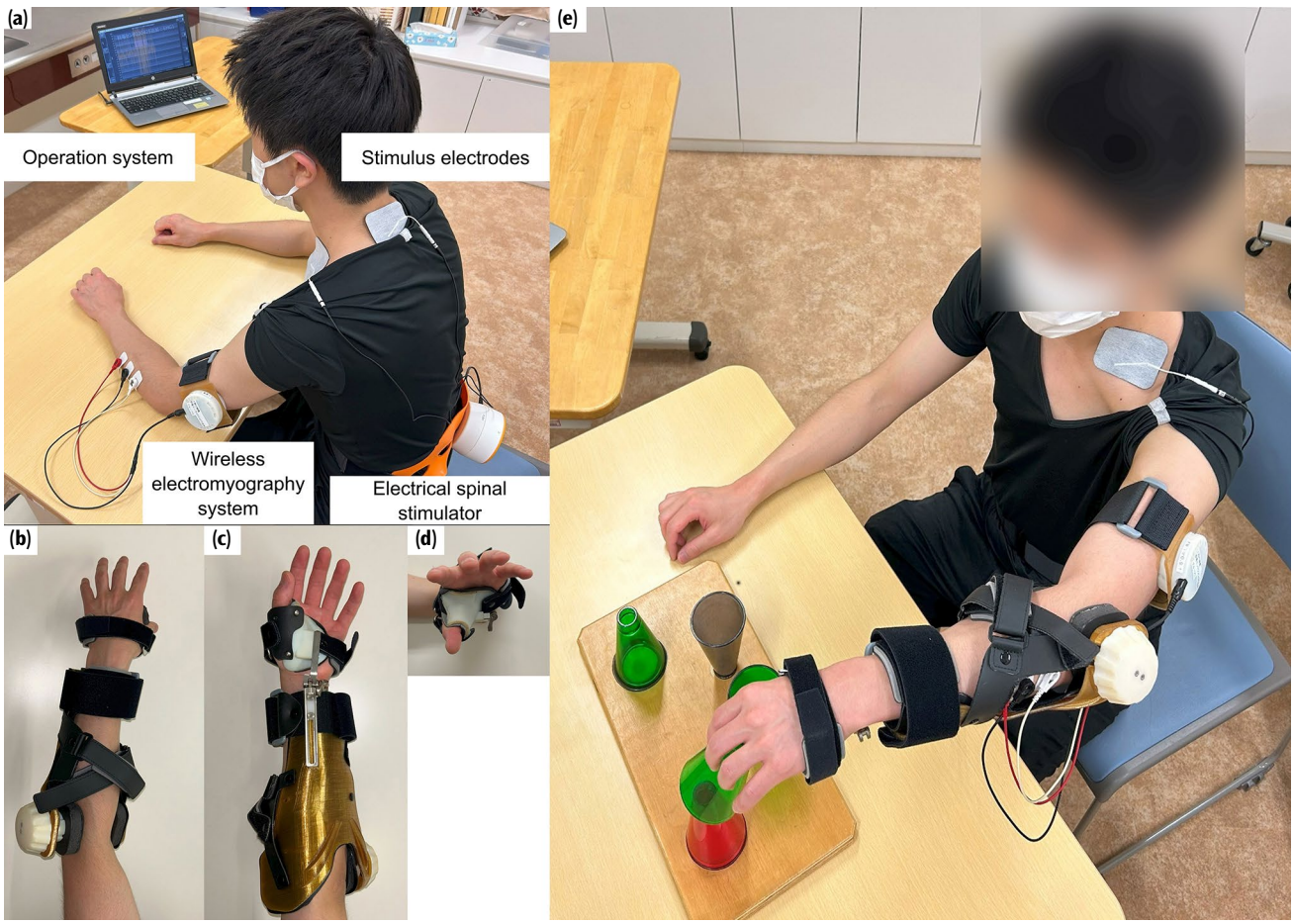

Figure 2. (a) This shows the overview of the transcutaneous spinal stimulation system. The wireless electromyography system obtains the muscle activity of the affected extensor digitorum communis from surface electrodes and sends it to the operation system. Stimulus electrodes are placed on the spinous process of the seventh cervical vertebra and at Erb's point. The operation system controls the electrical spinal stimulator. **(b)** This shows a top view of the newly developed long opponent-pronation orthosis. The proximal white valve is a screw-like system; rotating it can tighten it to secure it at the bilateral epicondyles. The distal part of the forearm compartment covers the distal parts of the radius and ulna and secures the forearm and the orthosis with bandages. **(c)** This shows the metal bar connecting the forearm compartment and the hand compartment. This bar restricts forearm supination and maintains the forearm in pronation. **(d)** This shows the hand component, which maintains thumb opposition. **(e)** This shows FAST-HAND, combined with transcutaneous spinal stimulation and long opponent-pronation orthosis.

FAST-HAND, functional assistive stimulation for the hand.

and the thumb in pronation by the orthosis restricts the forearm from being supinated and allows the forearm to remain in pronation. The hand component is a short opponent orthosis (Figure 2d).

Previous pronation orthoses, such as the Muenster and Sugar Tong orthoses, restrict elbow flexion and extension.[18] Our newly developed long opponent-pronation orthosis, however, allows elbow flexion and extension. Wearing this orthosis, participants can be more easily trained for reach and pinch-release.

FAST-HAND group

The FAST-HAND group received a task-oriented UE motor training program[13] with transcutaneous spinal stimulation and the long opponent-pronation orthosis (Figure 2e). The rehabilitation sessions were conducted for 40 min per session, twice a week, for a total of eight sessions. The patients were trained under the guidance of the physiatrist or the physical therapist. Using transcutaneous spinal stimulation with the orthosis, patients were asked to pick up and put down a peg, acrylic corn, and cue ball and move them to the designated location with reaching. These tasks involved movements such as reaching, grasping, and pinching. The difficulty of each task was adjusted according to the participant's condition by modifying factors such as object size, weight, range of motion, speed, and task complexity. By repeatedly performing these movements with the paretic UE, the training focused entirely on the recovery of the affected extremity.

Control group

The control group received the same rehabilitation program as the FAST-HAND group, excluding transcutaneous spinal stimulation and the use of the orthosis. The frequency and duration were matched to those of the FAST-HAND group (40 min per session, twice a week, for a total of eight sessions).

Assessments

All assessments were conducted by a masked examiner who was blinded to group allocation. Experienced physiatrists conducted these assessments. Evaluations were performed at three time points: before the intervention (pre), immediately after the intervention (post), and four weeks after the intervention (post-4w).

Clinical assessments

The primary outcome was assessed using the Fugl-Meyer Assessment (FMA) UE motor score.[19,20] The FMA ranges from 0 to 66 points (FMA-total). It includes 33 items and consists of four categories: (A) shoulder/elbow/forearm (FMA-A); (B) wrist (FMA-B); (C) hand (FMA-C); and (D) coordination/speed (FMA-D). Spasticity was assessed with the MAS of the elbow, wrist, and finger.[15] The amount of use scale of the Motor Activity Log-14 scale (MAL-14 AOU) was used to assess the amount of use of the paretic UE in ADL.[21] Paretic manual dexterity was assessed with the Box and Block Test (BBT).[22]

Electrophysiological assessments

The H-reflex and reciprocal inhibition (RI) were examined in the paretic forearm.[23] We used Nicolet EDX system (Natus Medical Inc., Middleton, WI, USA) to perform these examinations. With the patients seated and relaxed, H-reflexes were elicited from the paretic flexor carpi radialis (FCR) by submaximal electrical stimulation of the median nerve at the antecubital fossa with a 1-ms square-wave constant current. The recording window was 50 ms. The band pass filter was set at 3 Hz to 10 kHz. 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.

The RI was assessed using an FCR H-reflex conditioning-test paradigm. 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 M max for each block trial. Conditioning stimulation to the radial nerve was delivered at the spiral groove. The stimulus intensity of the conditioning stimulation was 1.0 motor threshold (MT). The MT was defined as a 100-μV peak-to-peak response of extensor carpi radialis. The conditioning-test stimulus interval was set at 0 (RI0ms) and 20 ms (RI20ms).

Statistical analysis

In a previous study of UE function in patients with chronic stroke,[24] the intervention group

showed a mean FMS change of 7.8 ± 5.1, and the usual rehabilitation group showed a mean change of 0.44. Based on a significance level of $\alpha = 0.05$ and a power of 80%, a sample size of 16 was calculated. Given that a similar or greater effect was anticipated in the intervention group of this study, the proposed target sample size was considered adequate.

Statistical analysis was performed using the IBM SPSS for Windows version 29.0. software (IBM Corp., Armonk, NY, USA). To calculate the mean MAS score, a transformation was applied where a score of 1+ was adjusted to 2, and scores of 2 and 3 were modified to 3 and 4, respectively. The results were presented in mean ± standard deviation (SD). The primary goal of the statistical analysis was to evaluate the effectiveness of FAST-HAND in patients with chronic stroke. All analyses were conducted according to the intention-to-treat (ITT) principle. The paired t-test was used to compare parametric data, the Mann-Whitney U test was used to compare nonparametric between the two groups, and nominal data were compared using the chi-square (χ^2) test. The Shapiro-Wilk test was used to assess data normality. When normality was confirmed, a two-way repeated measures analysis of variance (ANOVA) with factors group (FAST-HAND and control) and time (before, post, and post-4w) was conducted to investigate whether FAST-HAND improve UE motor function (FMA, MAS, and BBT), daily activity (MAL-14 AOU), and electrophysiological outcomes (H/M ratio, RI0ms, and RI20ms). As post-hoc within-group comparisons, pairwise tests between time points were conducted using paired t-tests or Wilcoxon signed-rank tests, depending on data distribution. Bonferroni correction for multiple comparisons was applied. A p value of <0.05 was considered statistically significant with 95% confidence interval (CI).

RESULTS

The estimated sample size could not be fully enrolled, due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. A total of 15 participants (13 males, 2 females; mean age: 53.0 ± 7.86 years; range, 38 to 67 years) were enrolled and randomly allocated to the FAST-HAND group (n = 7) and the control group (n = 8). These 15 participants completed the four-week follow-up assessment. No adverse events related to the intervention were seen in both the FAST-HAND and control groups.

The baseline characteristics of the participants are shown in Table 1. The MAS of the fingers was higher in the FAST-HAND group than in the control group ($p = 0.03$), but the others showed no significant difference at baseline between the FAST-HAND group and the control group (Table 1).

The stimulation intensities for each participant in the FAST-HAND group are summarized in Supplementary Table 2. The threshold was confirmed prior to each intervention to ensure appropriate stimulation.

Table 2 shows the pre-, post-, and post-4w scores of the primary and secondary outcome measures in the FAST-HAND and control groups. The changes in the primary outcome measure, FMA-total, along with the mean ± SD for each group are shown in Figure 3 Two-way repeated measures ANOVA showed a significant main effect of time on FMA-total ($F(2,26) = 7.745$, $p = 0.002$, partial $\eta^2 = 0.373$), while the time × group interaction was not significant ($F(2.26) = 0.976$, $p = 0.390$, partial $\eta^2 = 0.070$). Post-hoc paired t-tests with Bonferroni correction in the FAST-HAND group showed a significant change in FMA-total (mean ± SD) from pre- (39.0 ± 15.0) to post-intervention (42.6 ± 13.9; 95% CI 1.24 to 5.62; $p = 0.014$, Cohen's d = 1.45). However, the change from pre- to post-4w after the intervention (43.6 ± 12.8) was not significant (95% CI 0.41 to 8.74; $p = 0.109$, Cohen's d = 1.02). In the control group, no significant changes were observed in FMA-total between pre- (44.0 ± 7.4) and post-intervention (49.4 ± 6.7) (95% CI 0.05 to 10.7; $p = 0.145$, Cohen's d = 0.84), or between pre- and post-4w after the intervention (47.1 ± 6.8; 95% CI –2.39 to 8.64; $p = 0.667$, Cohen's d = 0.47).

For the subgroup analysis, two-way repeated measured ANOVA revealed a significant main effect of time for both FMA-A and C (FMA-A: $F(1.54,20.0) = 4.438$, $p = 0.033$, partial $\eta^2 = 0.255$; FMA-C: $F(1.47,19.1) = 4.253$, $p = 0.040$, partial $\eta^2 = 0.246$), while the time × group interaction was not significant (FMA-A: $p = 0.663$; FMA-C:

Table 1. General characteristics of participants

	FAST-HAND group (n = 7)		Control group (n = 8)		
Variable	n	Mean±SD	n	Mean±SD	*p*
Age (year)		55.0 ± 6.7		51.25 ± 8.8	0.613
Sex					0.733
Male	6		7		
Female	1		1		
Body Mass Index (kg/m^2)		23.98 ± 2.45		25.46 ± 2.89	0.573
Stroke type					0.231
Ischemic	4		7		
Hemorrhage	3		1		
Hemiparetic side					0.378
Right	5		4		
Left	2		4		
Time from stroke (days)		1436 ± 1422		2255 ± 1606	0.445
FMA-total		39.00 ± 15.0		44.00 ± 7.4	0.463
A. Shoulder/elbow/forearm		21.57 ± 8.5		25.75 ± 4.4	0.232
B. Wrist		3.29 ± 4.2		3.63 ± 2.9	0.779
C. Hand		9.29 ± 3.6		10.00 ± 3.3	0.694
D. Coordination/speed		4.86 ± 0.7		4.63 ± 0.9	0.694
Modified Ashworth Scale					
Elbow		1.9 ± 0.7		1.8 ± 0.9	0.955
Wrist		1.3 ± 1.1		1.8 ± 0.7	0.397
Fingers		2.0 ± 0.6		1.1 ± 0.6	0.029
Motor Activity Log-14 amount of use average score		0.821 ± 0.75		0.460 ± 0.34	0.536
Box and Block Test		10.29 ± 17.4		8.12 ± 6.5	0.189
H/M ratio		0.63 ± 0.26		0.56 ± 0.39	0.534
Reciprocal Inhibition					
Interstimulus interval 0 ms		0.88 ± 0.28		0.89 ± 0.75	0.731
Interstimulus interval 20 ms		0.91 ± 0.28		0.77 ± 0.54	0.836

FAST-HAND, functional assistive stimulation for the hand; SD, standard deviation; FMA, Fugl-Meyer Assessment upper extremity motor score. The values are presented as the mean ± standard deviation. *P* values indicate the significance level of between-group differences with the Mann-Whitney U test or χ^2 tests.

p = 0.158). In the FAST-HAND group, post-hoc paired t-tests showed a significant change in FMA-A from pre- to post-intervention (p = 0.025, Cohen's d = 1.46), whereas the change from pre- to post-4 weeks after the intervention was not statistically significant (p = 0.167, Cohen's d = 0.89). In the control group, FMA-A showed no significant changes between pre- and post-intervention (p = 0.395, Cohen's d = 0.60), or between pre- and post-4 weeks after the intervention (p = 0.593, Cohen's d = 0.50). For FMA-C in the FAST-HAND group, no significant changes were observed between pre- and post-intervention (p = 0.309, Cohen's d = 0.73), or between pre- and post-4 weeks after the intervention (p = 0.334, Cohen's d = 0.71).

Among secondary outcomes, two-way repeated measures ANOVA showed a significant main effect of time for BBT (F(1.54,20.0) = 4.316, p = 0.036, partial η^2 = 0.249), while the time × group interaction was not significant (p = 0.669). Post-hoc paired t-tests showed no significant changes in either the FAST-HAND group or the control group between pre- and post-intervention, or between pre- and post-4w after the intervention (p > 0.05 for all time points). For the other secondary outcomes, MAL-AOU,[14] H/M ratio, RI0ms, and RI20ms, neither the main effect of time nor the group × time interaction reached statistical significance.

Due to non-normal distributions, MAS scores were analyzed using Wilcoxon signed-rank tests for within-group comparisons between pre- and post-intervention, and between pre- and post-4w intervention. No significant differences were found in either the intervention group or the control group for these comparisons (p > 0.05).

Table 2. The before, post, and post-4w scores of primary and secondary outcome measures

	FAST-HAND group					Control group				
				Mean difference (95% CI)					Mean difference (95% CI)	
	Before	Post	Post-4w	Post-before	Post-4w-before	Before	Post	Post-4w	Post-before	Post-4w-before
	Mean±SD	Mean±SD	Mean±SD			Mean±SD	Mean±SD	Mean±SD		
FMA-A	21.6 ± 8.5	23.0 ± 8.3*	23.6 ± 7.9	1.43 (0.53 to 2.33)	2.00 (-0.07 to 4.07)	25.8 ± 4.4	28.5 ± 3.9	28.1 ± 3.0	2.75 (–1.06 to 6.56)	2.38 (–1.57 to 6.32)
FMA-B	3.3 ± 4.2	4.1 ± 4.2	4.0 ± 4.3	0.86 (–0.27 to 1.98)	0.71 (–0.17 to 1.59)	3.6 ± 2.9	4.5 ± 3.0	3.9 ± 3.3	0.88 (–0.07 to 1.82)	0.25 (–0.72 to 1.22)
FMA-C	9.3 ± 3.5	10.4 ± 3.0	11.0 ± 2.3	1.14 (–0.31 to 2.60)	1.71 (–0.53 to 3.96)	10.0 ± 3.3	11.5 ± 1.8	10.3 ± 2.6	1.50 (–0.50 to 3.50)	0.25 (–1.22 to 1.72)
FMA-D	4.9 ± 0.7	4.9 ± 0.7	5.0 ± 0.6	0.00 (0.00 to 0.00)	0.14 (–0.21 to 0.49)	4.6 ± 0.9	4.9 ± 0.4	4.9 ± 0.4	0.25 (–0.49 to 0.99)	0.25 (–0.49 to 0.99)
MAS										
Elbow	1.9 ± 0.7	1.7 ± 1.3	1.7 ± 1.0	–0.14 (–0.98 to 0.69)	–0.14 (–0.78 to 0.50)	1.8 ± 0.9	1.5 ± 0.9	1.5 ± 0.5	–0.25 (–0.84 to 0.34)	–0.25 (–0.84 to 0.34)
Wrist	1.3 ± 1.1	1.1 ± 1.3	1.0 ± 1.0	–0.14 (–0.98 to 0.69)	–0.29 (–1.17 to 0.59)	1.8 ± 0.7	1.5 ± 0.8	1.3 ± 1.0	–0.25 (–0.99 to 0.49)	–0.50 (–1.27 to 0.27)
Fingers	2.0 ± 0.6	1.4 ± 0.8	1.6 ± 1.0	–0.57 (–1.07 to –0.08)	–0.43 (–1.16 to 0.30)	1.1 ± 0.6	1.1 ± 0.6	1.0 ± 0.8	0.00 (–0.45 to 0.45)	–0.13 (–0.66 to 0.41)
MAL-14 average score	0.82 ± 0.75	0.94 ± 0.98	1.05 ± 0.92	0.12 (–0.31 to 0.54)	0.23 (–0.08 to 0.53)	0.46 ± 0.34	0.56 ± 0.27	0.52 ± 0.28	0.07 (–0.14 to 0.33)	0.06 (–0.13 to 0.25)
BBT	10.3 ± 17.4	11.9 ± 19.8	12.2 ± 20.3	1.57 (–1.18 to 4.33)	1.93 (–1.46 to 5.32)	8.2 ± 6.5	11.1 ± 6.7	11.5 ± 6.6	2.88 (–1.82 to 7.57)	3.31 (0.57 to 6.06)
H/M ratio reciprocal inhibition	0.63 ± 0.26	0.54 ± 0.13	0.45 ± 0.11	–0.09 (–0.40 to 0.22)	–0.19 (–0.47 to 0.10)	0.56 ± 0.39	0.53 ± 0.22	0.53 ± 0.24	–0.03 (–0.48 to 0.43)	–0.03 (–0.51 to 0.50)
ISI 0 ms	0.88 ± 0.28	0.80 ± 0.22	0.87 ± 0.36	–0.08 (–0.53 to 0.38)	–0.01 (–0.48 to 0.47)	0.89 ± 0.75	0.90 ± 0.54	0.66 ± 0.27	0.01 (–0.64 to 0.65)	–0.23 (–1.01 to 0.55)
ISI 20 ms	0.91 ± 0.28	0.83 ± 0.22	0.93 ± 0.15	–0.08 (–0.32 to 0.16)	0.02 (–0.22 to 0.25)	0.77 ± 0.54	0.81 ± 0.25	0.90 ± 0.47	0.05 (–0.40 to 0.49)	0.13 (–0.63 to 0.89)

FAST-HAND, functional assistive stimulation for the hand; SD, standard deviation; CI: confidence interval; FMA, Fugl-Meyer Assessment upper extremity motor score; MAS, Modified Ashworth Scale; MAL-14, Motor Activity Log-14 Amount of Use; BBT, Box and Block Test; RI, reciprocal inhibition; ISI 0 ms, Interstimulus Interval 0 ms; ISI 20 ms, Interstimulus Interval 20 ms. Asterisks indicate significant differences between the baseline (before) and post or post-4w by a paired t-test (*$p < 0.05$).

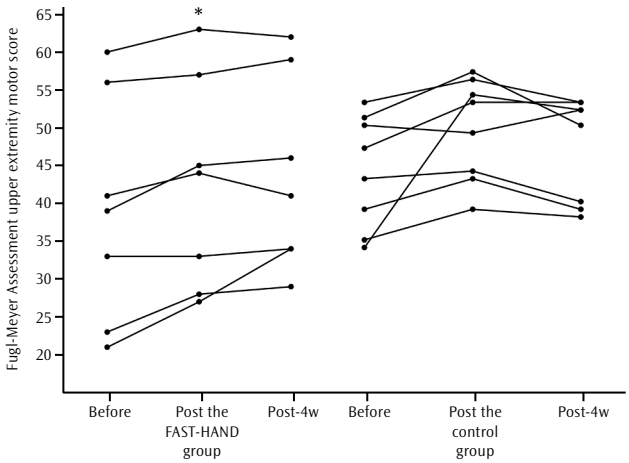

Figure 3. The change of the primary outcome measures for each group. Asterisks indicate significant differences between the baseline (before) and post or post-4w by a paired t-test.

* $p < 0.05$.

DISCUSSION

In the present study, we assessed the effect of FAST-HAND in patients with chronic stroke. To the best of our knowledge, this is the first randomized-controlled study to evaluate the effect of using transcutaneous spinal stimulation combined with a long opponent-pronation orthosis (FAST-HAND) for UE motor function in this patient population. Although our study was limited by a small sample size and did not demonstrate a significant time × group interaction, it showed a significant main effect of time. Post-hoc analyses suggested that the FAST-HAND improved in FMA-total and FMA-A.

Non-invasive spinal stimulation has been applied to patients with spinal cord injuries and cerebral palsy, and it demonstrated improvement in motor function.[10,25] Transcutaneous electrical spinal stimulation stimulates the posterior root afferent nerve, activates the motor neurons in the spinal cord, and boosts the excitability of spinal networks.[8,26] Among patients with stroke, functional inter-joint coordinated movements with reaching, forearm pronation, and finger-flexion extension are critical to use their paretic UE in ADL. The C7 spinal cord level innervates triceps, PT, and EDC. In the light of these data, it can be speculated that transcutaneous C7 spinal cord stimulation can activate motor neurons in the C7 spinal cord and help to activate triceps, PT, and EDC.

In the present study, transcutaneous spinal stimulation was triggered with EMG activity of the paretic EDC. Synchronizing voluntary motor neuron activation with subthreshold spinal stimulation can strengthen the synaptic connections between the brain and spinal cord, according to the Hebbian rule.[27] Voluntary movement may effectively facilitate the spinal motor neuron and interneuron.[28-30] In these studies, the combination of voluntary movement and peripheral electrical stimulation demonstrated therapeutic effects. Similarly, in this study, the combination of spinal cord stimulation and voluntary movement may have produced comparable benefits. It is speculated that closed-loop control of spinal stimulation enhanced the therapeutic effect.[17]

Our newly developed long opponent-pronation orthosis helped the participants reach, grip, and release by maintaining thumb opposition and forearm pronation. Patients with moderate-to-severe hemiparesis often exhibit forearm supination and pronounced thumb adduction. These patients need assistance to reach or pinch-release during rehabilitation sessions or ADL. Previous pronation orthoses immobilized the upper arm18 and made such task-oriented training impossible. Wearing our long opponent-pronation orthosis, patients can increase the number of achievable task-oriented training during the 40-min sessions. A previous study has shown that stabilizing the paretic UE in a functional position enhances rehabilitation outcomes.[31] In our protocol, the orthosis provided mechanical support for forearm pronation and finger extension, while cervical transcutaneous stimulation augmented spinal excitability, together facilitating coordinated inter-joint movement practice. Therefore, transcutaneous spinal stimulation combined with a long opponent-pronation orthosis was presumed to have a therapeutic effect on UE function in patients with chronic stroke.

In the current study, both groups received task-oriented training. This training is reported to have effect for UE in patients with chronic stroke in the literature.[13] The control group exhibited

a numerically greater change of FMA-total between the pre- and post-intervention; however, this change was not statistically significant. In contrast, the intervention group showed a statistically significant improvement. One possible explanation for this is that the change observed in the control group exhibited greater variability, and when compared in terms of effect size, the FAST-HAND group demonstrated a larger effect, which may account for the observed difference.

Furthermore, the FAST-HAND improved inter-joint coordinated distal and proximal movements from the result of FMA-total change between pre- and post-intervention, but FMA-C was not significantly changed in our study. Some other studies have shown improvements in finger function.[32,33] These treatments focused specifically on finger function. In the present study, stimulation was centered on C7 and did not target the fingers specifically, which may explain the absence of significant changes.

Previous studies of moderate-to-severe hemiparesis in patients with chronic stroke included protocols such as 1-h sessions three times per week for 10 weeks.[34] Compared to these, FAST-HAND demonstrated comparable therapeutic effects with a shorter intervention schedule of 40-min sessions twice a week for four weeks, achieving outcomes similar to robotic rehabilitation treatment.[33] Outpatient rehabilitation for chronic stroke has some difficulties; for instance, limitations on medical resources lead to a mismatch between demand and supply in Japan[35] and worldwide.[36] The FAST-HAND is well-suited for outpatient rehabilitation, with limited time and resources. On the other hand, in the present study, no statistically significant change was observed in the FAST-HAND group at post-4 weeks after the intervention, which may have been influenced by the dosage of the intervention.

Since electrophysiological changes can also occur with task-oriented rehabilitation alone, we hypothesized that FAST-HAND would enhance these effects. However, in the present study, the interaction and the within-group comparisons in the post-hoc analysis were also not significant. Since these assessments were conducted at rest, they may not fully reflect the electrophysiological alterations during active movement. Notably, a previous study demonstrated that spinal RI of UE was modulated by motor imagery,[37] supporting the concept that spinal circuit plasticity can occur during movement planning even in the absence of overt contraction. Furthermore, studies of human gait have shown that spinal RI is modulated in a phase-dependent manner across the gaiting cycle,[38] suggesting that movement-related neural adaptations may be tightly linked to specific task phases. This discrepancy may explain why a significant improvement was observed in the FMA-total in FAST-HAND, while the electrophysiological measures did not exhibit statistically significant changes. It is also possible that increasing the intervention dose could lead to more pronounced and statistically significant changes.

Nonetheless, this study has several limitations. The first is the small sample size. Although impacted by the SARS-CoV-2 pandemic, the inability to reach the initially planned sample size may have affected the statistical power. This may have compromised the detection of a time × group interaction. Furthermore, the increased variability among cases may have amplified the influence of random fluctuations or individual differences. The second limitation is the absence of a three-group comparison among FAST-HAND, spinal stimulation alone, and orthosis alone. The third limitation is that the allocation of participants was not blinded. As the intervention requires a visibly apparent orthosis and perceptible spinal stimulation, it was not feasible to blind participants or therapists. To reduce assessment bias, all outcomes were assessed by evaluators blinded to group allocation. Future trials would incorporate a sham orthosis and sham stimulation protocol to achieve full double blinding. Moreover, larger multi-center, randomized-controlled studies with task-based electrophysiological measures are needed to confirm these findings and clarify the mechanisms underlying the observed functional gains.

In conclusion, the main effect of time was significant and the time × group interaction was not in the present study; however, a significant

improvement in the primary outcome measure was observed in the FAST-HAND group from pre- to post-intervention. These findings suggest that FAST-HAND can modestly improve UE motor function immediately after the intervention. Larger multi-center, randomized-controlled studies with double-blind designs, task-based electrophysiological assessments, and designs to separate the effects of stimulation and orthosis are warranted to confirm efficacy and clarify underlying mechanisms.

Declaration of Conflicting Interests

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Author Contributions

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Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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AI Disclosure

The authors declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the authors. The authors further confirm that AI tools were not used to generate, fabricate, or 'hallucinate' references, and that all references have been carefully verified for accuracy.

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