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Research Article

Motor Improvement Induced by a Modified-Hybrid Assistive Neuromuscular Dynamic Stimulation (m-HANDS) Protocol of 3-hour EMG-controlled Neuromuscular Electrical Stimulation and Wrist Splint in Patients with Subacute Stroke: A Randomized Controlled Trial

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Keywords

- Stroke
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- Randomized controlled trial

Abstract

Background and objective: In the hybrid assistive neuromuscular dynamic stimulation (HANDS) protocol, patients use EMG-controlled neuromuscular electrical stimulation (NMES) with a wrist splint for 8 hours a day for three weeks. The HANDS protocol reportedly improves upper extremity motor function, but application of EMG-controlled NMES training for 8 hours might be difficult for many patients in many facilities.

Therefore, we developed an upper extremity training protocol using 3-hours of EMG-controlled NMES with a wrist splint, called the modified-HANDS protocol. This randomized controlled trial aimed to evaluate the efficacy of our modified HANDS protocol in subacute stroke patients.

Methods" The participants were 40 subacute hemiparetic patients in a rehabilitation hospital. Patients were randomly assigned to two groups. All patients in both groups received the same daily dose and duration of standard post-stroke multidisciplinary rehabilitation. Patients in the modified-HANDS group additionally used the the integrated volitional control electrical stimulator (IVES) combined with a wrist splint for 3 hours a day for 3 weeks. The primary outcome was the Fugl-Meyer Assessment upper extremity motor score (FMA) and the secondary outcome was the Motor Activity Log-14 amount of use score (MAL-14-AOU).

Results: All 20 patients in each group completed the interventions. Compared with the control group, the modified-HANDS group showed significantly greater gains in FMA ($P < .01$) and MAL-14-AOU ($P < .01$).

Conclusion: Our modified-HANDS protocol induced an improvement in upper limb motor function in subacute stroke patients. Further expansion of the use of the modified-HANDS protocol in rehabilitation hospitals would be beneficial.

INTRODUCTION

Stroke often causes motor paralysis, with upper extremity weakness being the most common impairment in stroke patients. Weakness of the upper extremity limits patient activity, restricts participation, and reduces independence in daily life [1]. However, recovery of impairment of the upper extremity is noted in fewer than 15% of patients after stroke [2].

The hybrid assistive neuromuscular dynamic stimulation (HANDS) protocol [3], which consists of a combination of closed-loop electromyography-controlled neuromuscular electrical stimulation (EMG-controlled NMES), named integrated volitional control electrical stimulator (IVES) [4], with a wrist-hand splint, reportedly helps improve motor function and facilitates the use of the paretic upper extremity in daily living in patients with moderate to severe hemiparesis [3].

The IVES is a portable surface EMG-controlled, single-channel NMES that continually changes its stimulus intensity in direct proportion to the amplitude of the voluntary EMG of the target muscles. In the HANDS protocol, patients wear a wrist–hand splint and carry a portable IVES with an arm belt for 8 hours during the daytime. Shindo et al., demonstrated the efficacy of the 8 hours HANDS protocol using the IVES and wrist splint in improving upper extremity motor function in patients with subacute stroke [5]. However, continuous use of IVES for 8 hours might sometimes be difficult due to management issues in some rehabilitation hospitals. The reason is that if the IVES is worn for 8 hours, the night shift staff would have to be on and off during the day, and wearing time overlaps with patient bathing time. Therefore, we devised a modified-HANDS protocol (m-HANDS), in which patients use IVES combined with a wrist splint for 3 hours a day.

In this study, we planned a randomized controlled trial to examine the effect of the 3-hour modified HANDS protocol in comparison with conventional rehabilitation in patients with subacute stroke who were admitted to a rehabilitation hospital. We examined the effects of a 3-hour daily m-HANDS protocol on upper extremity motor function and changes in use of the paralyzed hand.

MATERIAL AND METHODS

Participants

This single-blinded, randomized trial had a parallel design that conformed with CONSORT 2010 (Supplementary Table S1). Participants were recruited from among stroke inpatients at the Akabane Rehabilitation Hospital (240 beds, the average length of stay of the patients in this hospital is 78.3 days) from July 2020 to June 2022 using the following inclusion criteria: (*a*) time from stroke onset more than 30 days (*b*) age 20 to 90 years, (*c*) ability to raise the paretic hand to the height of the nipple (*d*) detectable surface EMG signals in the affected extensor digitorum communis (EDC) or extensor pollicis longus (EPL) muscles when the patient intends to extend their fingers, (*e*) passive extension range of motion (ROM) greater than 0 degrees in the affected wrist and −10 degrees in the metacarpophalangeal joints; (*f*) no pain in the paretic upper extremity; and (g) able to understand the study and provide consent even if there is aphasia. Cognitive function with a Mini-Mental State Examination (MMSE) score of 20 or higher.

The exclusion criteria were (1) history of major psychiatric or previous neurological disease, including seizures; (2) presence of a pacemaker or other implanted stimulator; and (3) patients with visuospatial neglect or apraxia.

The study was performed in accordance with the Declaration of Helsinki and was approved by the Akabane Rehabilitation Hospital Ethics Committee on June 12, 2020 (approval number: 2020C-001).

Intervention

The m-HANDS group received 3 weeks of m-HANDS, which consisted of the use of IVES and a wrist splint for 3 hours, in addition to standard rehabilitation. m-HANDS was provided via closed-loop, EMG-controlled NMES (MURO solutions, Pacific Supply Co., Osaka, Japan) combined with a wrist-hand splint (Wrist Support, Pacific Supply Co.). The stimulus intensity and duration were controlled by the EMG of the paretic EDC muscles [4]. This NMES continually changes its stimulus intensity in direct proportion to the amplitude of the voluntary EMG. The surface electrodes pick up EMG signals in the target muscle and simultaneously stimulate it in direct proportion to the detected EMG signal.

The rationale for combining the stimulation system with a wrist-hand splint was derived from the work of Fujiwara et al. [6], who reported that a wrist-hand splint could reduce spasticity in the finger, wrist and elbow flexors, and could facilitate finger extensor muscle activity. In our study, the HANDS system was active for 3 hours, and patients were instructed to use their paretic hand as much as possible while wearing it. Patients were also instructed to practice bimanual activities of daily living (ADLs).

The control group was asked to use their affected hand as much as possible in their ADLs, in addition to the standard rehabilitation program. All patients in both groups participated in the same standard rehabilitation program, consisting of 1 hour of physical therapy and 1 hour of occupational therapy daily. Speech therapy was applied if needed.

All exercises took place in the training rooms. Occupational therapy consisted of gentle stretching exercises of the paretic upper extremity and active muscle reeducation exercises manually performed by a therapist. Occupational therapists were directed toward patients' goals and focused on their particular impairments and disabilities; thus, the specific therapy that each patient received was individualized.

Outcome Measures

The primary outcome was the Fugl-Meyer Assessment upper

Supplementary Table S1

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	p1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	p2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	p4
	2b	Specific objectives or hypotheses	p4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	p5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	p5
	4b	Settings and locations where the data were collected	p5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	p5-6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	p6-7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	p5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	p5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	p7
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	p7
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	p7
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	p8 Figure 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	p8
Recruitment	14a	Dates defining the periods of recruitment and follow-up	p8
	14b	Why the trial ended or was stopped	p8
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	p8, Table1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	p8
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	p8 Table2
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	p8
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	p8
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	p8
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	p9-10
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	p9-10
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	p9-10
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	p12
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	p11-12

extremity motor score (FMA) [7]. In this score, the motor score of the upper extremity includes 33 items and possible scores range from 0 to 66. The FMA is a commonly used measure with excellent interrater reliability and construct validity [8].

The Motor Activity Log (MAL), which is a structured interview used to measure upper extremity disability in activities of daily living, was assessed as the secondary outcome. The MAL-14 includes 14 items that are scored on an 11-point amount of use (AOU) scale (range 0-5) to rate how much the arm is used [9]. The MAL is internally consistent and relatively stable in chronic stroke patients not undergoing an intervention [10], and high construct validity and reliability have been demonstrated in patients with chronic stroke [9,10].

All clinical measures were evaluated at hospitalization and pre- and post-treatment. The FMA and MAL-14-AOU were assessed by four occupational therapists not involved in the treatment of the participants.

Before the study, we trained the investigators in the use of the FMA and MAL-14-AOU, and confirmed good interrater reliability (intraclass correlation coefficients >.95) in 20 in-patients with stroke.

Statistical Analyses

The Mann–Whitney *U* test was used to compare non-parametric and parametric data between the two groups, and the $\chi 2$ test was used to compare nominal data. Repeated measures analysis of variance (ANOVA) was used in the analysis of pre- and post-treatment measurements in each group. Effects were considered significant if *P* was < .05. All statistical analyses were performed with SPSS version 28.

RESULTS

Of the 471 stroke patients admitted during the study period, 48 met the study criteria (Figure 1). In total, 40 of the 48 patients gave their informed consent for participation and were included in the trial. A computer-generated list randomly assigned the participants to either the m-HANDS group (n=20) or the control group (n=20).

All patients in each treatment group completed the study. The demographic data of the participants are shown in Table 1. There were no significant differences in any measurements between the m-HANDS group and the control group at baseline.

The scores of outcome measures before and after the interventions are shown in Table 2.

In the FMA score, 2-factor [time (pretreatment, posttreatment), intervention (m-hands, control)] repeated measures ANOVA showed a significant interaction of time and intervention ($F(1,19) = 6.749$ $p=0.018$). The post hoc Bonferroni test showed a more significant difference between pre-FMA and post-FMA scores in the m-HANDS group ($P < .001$) than in the control group ($P = 0.002$). The mean gain in FMA was 8.6 points in the m-HANDS group (95% confidence interval: 5.051-12.149) and 3.8 points in the control group (95% confidence interval: 1.649-5.951), indicating a significant difference in gain in FMA between the two groups ($p<0.01$).

In the MAL-14-AOU score, 2-factor [time (pretreatment, posttreatment), intervention (m-hands, control)] repeated measures ANOVA showed a significant interaction of time and intervention ($F (1,19) = 7.871$ $p=0.011$). The post hoc Bonferroni test showed a more significant difference between pre- MAL-14-AOU and post- MAL-14-AOU scores in the m-HANDs group ($P < .001$) than the control group ($P = 0.036$). The mean gain of MAL-14-AOU was 0.87 points in the m-HANDS group (95% CI 0.498-1.244) and 0.28 points in the control group (95% confidence interval: 0.019-0.532), indicating a significant difference in gain in MAL-14-AOU between the two groups ($p<0.01$).

DISCUSSION

The m-HANDS protocol of 3 hours per day improved motor function and increased the amount of paretic hand use compared to conventional rehabilitation therapy alone. A previous study reported that electrical stimulation combined with voluntary contraction of the target muscle with closed-loop, EMG-triggered NMES induced downregulation of intracortical inhibitory interneurons, with subsequent facilitation of corticospinal activity in the intended movement [11]. The m-HANDS protocol provides day-to-day assistance whenever patients attempt to extend their paretic fingers.

The following are some of the reasons why the effect was observed even after wearing the device for 3 hours. The study participants were subacute stroke patients in a rehabilitation hospital with significant functional improvement, all of whom were receiving a sufficient amount of rehabilitation. In addition, hospital life also encouraged the use of the paretic hand.

We found that the m-HANDS protocol in addition to standard rehabilitation produced significantly larger improvements in FMA score compared with the control group in patients 4 weeks after stroke onset. Our findings support the effectiveness of the m-HANDS protocol, and the results were consistent with the findings of our previous study [3].

The effects of the m-HANDS protocol can be explained by the concept of the threshold of effective rehabilitation proposed by Han et al [12]. The concept states that if spontaneous arm usage is above a certain threshold, training can be stopped, as repeated spontaneous use provides a form of motor learning that further improves performance and spontaneous use. Below this threshold, training is in vain, and compensatory movements with the less affected hand are reinforced. In the m-HANDS protocol, participants were trained to use their paretic hand for 3 hours over 3 weeks using closed-loop EMG-controlled NMES and a hand splint. This amount of training might be above the threshold of effective rehabilitation.

Our study has several limitations, one of which is the relatively

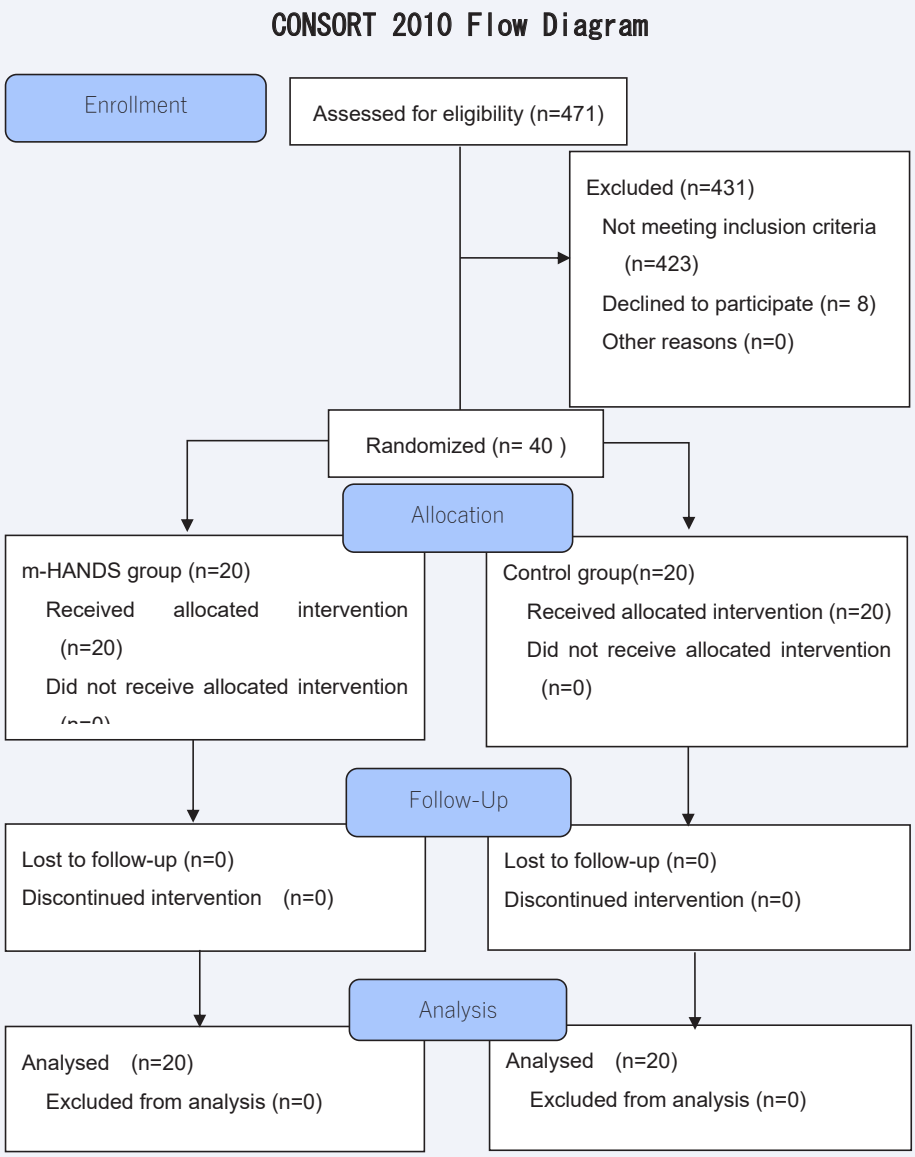

Figure 1 Flow diagram of the randomization procedure

Table 1: Patient Characteristics and Clinical Evaluations at Hospitalization

	m-HANDS Group (n=20)	Control Group (n=20)	P
Age,year	61.2±12.9 (43-85)	64.85 ±12.8 (42-80)	0.31
Gender	13males,7 females	11 males, 9 females	0.41
Type of Stroke	14 ischemic, 6 hemorrhagic	11 ischemic, 9 hemorrhagic	0.32
Time since stroke, day	75.7±40.7 (31-150)	60.5±28.0 (30-131)	0.27
Hemiparetic side	8 right, 12 left	12 right, 8 left	0.74
FMA	40.7±15.2 (6-59)	40.2±15.8 (4-66)	0.84
MAL-14-AOU	1.5±1.1 (0-3.7)	1.7±1.7 (0-4.8)	0.81

Values are given as mean ± standard deviation or median with range in parentheses.
P values indicate significance level of between-group differences with Mann–Whitney U test or $\chi 2$ tests
m-HANDS; modified-hybrid assistive neuromuscular dynamic stimulation
FMA; Fugl-Meyer Assessment
MAL; Motor Activity Log
AOU; amount of use scale of MAL

Table 2: The change of FMA, MAL-14-AOU

	m-HANDS Group (n=20)			Control Group (n=20)		
	Pre	Post	Gain	Pre	Post	Gain
FMA	40.7±15.2 (6-59)	49.3±13.9 (13-66)*	8.6**	40.2±15.8 (4-66)	44±15.8 (4-66)	3.8
MAL-14-AOU	1.5±1.1 (0-3.7)	2.41±1.33 (0.5-4.5)*	0.87**	1.7±1.7 (0-4.8)	1.98±1.71 (0-4.6)	0.27

Values are given as mean ± standard deviation with range in parentheses.
Comparision between pre- and posttreatment values in each group with Wilcoxon signed rank test: *($p < 0.001$)
Comparision between-group difference in gain with Mann-Whitney Utest: **($p < 0.01$)
m-HANDS;modified- hybrid assistive neuromuscular dynamic stimulation
FMA; Fugl-Meyer Assessment
MAL; Motor Activity Log
AOU; amount of use score

small sample size, which prevented us from examining the effect of differences in the severity of paresis using subgroup analysis.

In this study, we did not compare the difference in effectiveness between the traditional 8-hour HANDS protocols and 3-hour m-HANDS protocols. This could not be done at this time due to lack of hospital staffing, but will need to be compared in the future.

Another limitation is the lack of follow-up evaluation after the interventions; after finishing the 3 weeks of therapy reported here, patients in the control group also received the m-HANDS protocol. Since there is a possibility that the m-HANDS protocol simply sped up recovery, a follow-up survey is needed to confirm whether the effect is sustained.

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