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Ability of electrical stimulation therapy to improve the effectiveness of robotic training for paretic upper limbs in patients with stroke

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ABSTRACT

We investigated whether untriggered neuromuscular electrical stimulation (NMES) can increase the effectiveness of shoulder and elbow robotic training in patients with hemiparesis. Thirty subacute stroke patients were randomly equally allocated to robot only (RO) and robot and electrical stimulation (RE) groups. During training, shoulder and elbow movements were trained by operating the robotic arm with the paretic arm, and the robotic device helped to move the arm. In the RE group, the anterior deltoid and triceps brachii muscles were electrically stimulated at sub-motor threshold intensity. Training was performed (approximately 1 h/day, 5 days/week for 2 weeks) in addition to regular rehabilitation. Active range of motion (ROM) values of shoulder flexion and abduction, and Fugl-Meyer assessment (FMA) scores were measured before and after training. Active shoulder ROM was significantly better after than before training in the RE group; however, no such improvement was noted in the RO group. FMA scores were significantly better in both groups, and there was no significant difference between the groups. Untriggered NMES might increase the effectiveness of shoulder and elbow robotic training in patients with hemiparesis. Additionally, NMES at a sub-motor threshold during robotic training might facilitate activation of paretic muscles, resulting in paralysis improvement.

1. Introduction

Robotic training has been reported to be an effective treatment for hemiparesis after stroke [1]. The InMotion ARM™ Robot (Interactive Motion Technologies, Inc., Cambridge, MA, USA) is a therapeutic robotic training tool for upper limb rehabilitation [2], and many studies have reported that robotic training improves paralysis in patients with stroke [3–5]. In robotic training using the InMotion ARM Robot, shoulder and elbow movements are trained by operating the robotic arm with the paretic arm during reaching tasks in a horizontal plane. During the reaching tasks, the robotic device helps to move the arm when the patient is unable to move the arm. Previous studies have applied the InMotion ARM Robot to hemiplegic patients with acute and subacute stroke and have shown improvements in the Fugl-Meyer assessment (FMA) scale, which indicates motor functional performance, and muscle strength of the hemiparetic upper limb [6,7]. Volpe et al. [4] and Finley et al. [8] have also reported that the robotic device improved the FMA score by 1–3 points in chronic stroke patients.

In recent years, it has been reported that further improvement in paralysis can be achieved in patients with stroke by combining electrical stimulation with upper limb rehabilitation programs, such as repetitive facilitative exercise [9], mirror therapy [10], and bilateral arm training [11]. Additionally, in stroke patients, a reduction in the synergy of shoulder abduction and elbow flexion has been reported with a combination of transcutaneous functional electrical stimulation to the triceps brachii muscle and shoulder movement training [12]. Although studies have reported on the effectiveness of electrical stimulation alone in patients with paralysis [13,14], electrical stimulation can be combined with robotic upper-limb training, as these approaches are compatible. Hu et al. reported that the improvement in upper-limb function with wrist movement training was greater when the combination of

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Table 1
Patient characteristics before training.

	RO group	RE group	*p*-value
Number of patients	15	15	
Age (years)	64.9 ± 9.4	56.9 ± 12.3	0.08
Sex (male/female)	12/3	9/6	0.22
Affected side (right/left)	5/10	6/9	0.70
Lesion type (hemorrhagic/ischemic)	9/6	7/8	0.46
Days after stroke onset	66.3 ± 11.2	65.7 ± 17.6	0.43

Data are presented as mean ± standard deviation or number.
RO, robot only; RE, robot and electrical stimulation.

electrical stimulation and robotic training was used than when only robotic training was used [15]. This previous study included patients with voluntary muscle contraction on the paretic side, and used triggered neuromuscular electrical stimulation (NMES). With triggered NMES, it is possible to contract muscles consistently with movement planning by the patient, and the improvement in paralysis is likely to be better with triggered NMES than with untriggered NMES that does not provide stimulation based on movement planning [16]. However, triggered NMES can be used only in patients with voluntary muscle contraction, while untriggered NMES can be used in patients without voluntary muscle contraction.

In the present study, we investigated whether untriggered NMES can increase the effectiveness of shoulder and elbow robotic training in patients with hemiparesis.

2. Materials and methods

The study enrolled 30 patients with stroke, who were hospitalized at Fujita Health University Nanakuri Sanatorium. The inclusion criteria were as follows: (1) first stroke in the cerebral hemisphere and (2) absence of sensory disorders (score of ≥ 2 for fine touch and joint position sense in the stroke impairment assessment set [SIAS] sensory evaluation) [17]. The exclusion criteria were as follows: (1) severe aphasia; (2) inability to maintain a sitting position; and (3) failure to provide consent.

The patients were randomly allocated to a robot only (RO) group and a robot and electrical stimulation (RE) group, with 15 patients in each group (Table 1). In both groups, robotic training using the MIT-MANUS/InMotion2 system (Interactive Motion Technologies, Inc.) was performed (approximately 1 h/day, 5 days/week for 2 weeks) in addition to a regular rehabilitation program. During robotic training, patients repeated reaching movements in a horizontal plane at least 1000 times in approximately 1 h. In the RE group, NMES was delivered to the anterior deltoid and triceps muscles using the Trio300 system (Ito Co., Ltd., Tokyo, Japan) during robotic training. The parameters of NMES were a pulse width of 250 μs and a frequency of 20 Hz at sub-motor threshold intensity. NMES was continuously delivered during training.

We compared patient characteristics between the RO and RE groups, and used the Mann-Whitney *U* test for age and time since stroke and the χ^2 test for sex, side of stroke, and the hemorrhage/infarction ratio. Active range of motion (ROM) values of shoulder flexion and abduction, and FMA shoulder/elbow (FMA-SE) and FMA total (FMA-total) scores were measured before and after robotic training. The Wilcoxon signed-rank test was used to compare these parameters before and after training in each group, and the Mann-Whitney *U* test was used to compare the improvements in these parameters between the groups. All statistical analyses were performed using JMP® 9 software (SAS Institute Inc., Cary, NC, USA). A *p*-value < 0.05 was considered to indicate statistical significance.

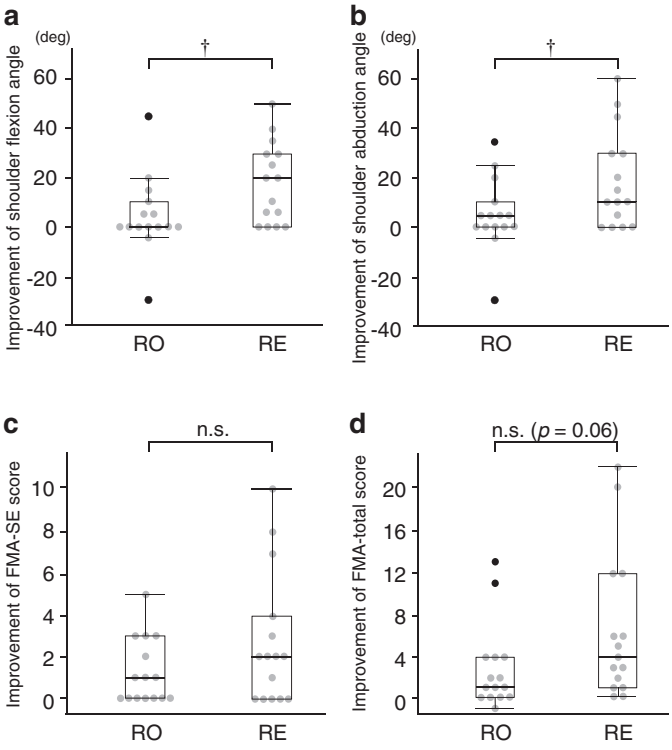

Fig. 1. Scatter plot (circle for each patient) and box-and-whisker plot (minimum, quartiles, and maximum) of the improvements in the robot and electrical stimulation (RE) group and the robot only (RO) group. The improvements in active range of motion values of shoulder flexion (A) and abduction (B) were significantly better in the RE group than in the RO group. There were no significant differences in the improvements in the FMA scores of the shoulder and elbow (C) and the FMA total score (D). $^{\dagger}p < 0.05$, n.s.: not significant; black circle: outliers over 1.5 × interquartile range.

3. Results

There were no significant differences in patient characteristics between the RO and RE groups prior to robotic training (Table 1). The clinical results before and after training are summarized in Table 2 and Fig. 1. Active shoulder ROM was significantly better after than before training in the RE group; however, no such improvement was noted in the RO group. Improvements in active ROM values of shoulder flexion and abduction were significantly higher in the RE group than in the RO group (20° and 10° vs. 0° and 5°, respectively). The FMA-SE and FMA-total scores were significantly better after than before training in both groups, and there were no significant differences between the groups, although the improvement in the FMA-total score tended to be greater in the RE group than in the RO group ($p = 0.06$).

4. Discussion

The combination of NMES and other therapeutic interventions, such as repetitive facilitative exercise and mirror therapy, has been reported to improve paralysis [9,10]. The present study showed that active ROM values of shoulder flexion and abduction were better with untriggered NMES combined with robotic training than with robotic training alone. Hsu et al. [13] reported better improvement in upper limb function with untriggered NMES (performed for a minimum of 10 h; 30 min/day, 5 days/week for 4 weeks) combined with a regular rehabilitation program than with a regular rehabilitation program alone. In the present study, robot training combined with continuously delivered untriggered NMES was performed for a total of 10 h over a period of 2 weeks, with improve-

Table 2
Clinical results.

	RO group ($n=15$)			RE group ($n=15$)		
	Pre	Post	Gain	Pre	Post	Gain
Active ROM						
Shoulder flexion	75 (10–130)	85 (15–130)	0 (0–10)	85 (30–110)	120 (40–130)**	20 (0–30)†
Shoulder abduction	65 (40–100)	70 (45–120)	5 (0–10)	60 (40–100)	80 (50–130)**	10 (0–30)†
FMA shoulder/elbow	13 (6–21)	14 (7–22)**	1 (0–3)	12 (7–24)	18 (9–27)**	2 (0–4)
FMA total	14 (7–31)	16 (8–44)*	1 (0–4)	15 (10–41)	34 (13–45)**	4 (1–12)

Data are presented as median (lower and upper quartiles).
RO, robot only; RE, robot and electrical stimulation; ROM, range of motion; FMA, Fugl-Meyer assessment.
Gain indicates the extent of improvement (post minus pre training).
* Significant improvement after 2 weeks of training (**$p < 0.01$, *$p < 0.05$).
† Significant difference in improvement between the RO and RE groups ($p < 0.05$).

ment in paralysis, and this duration is similar to that in the previous study.

In our study, NMES was delivered at a sub-motor threshold. A review by de Kroon et al. reported that electromyography (EMG)-triggered NMES was more effective than untriggered NMES for improving paralysis [16]. Robotic training with triggered NMES is likely to be more effective than robotic training with untriggered NMES. However, our patients did not have sufficient voluntary muscle contraction for a detectable EMG level to evoke triggering in paretic muscles. Therefore, in this study, continuous sub-threshold electrical stimulation was delivered during training. Using untriggered NMES, Mang et al. stimulated the ulnar nerve [18] and Ridding and Uy stimulated its dominant muscles [19], and these electrical stimuli reportedly facilitated afferent inputs in the cerebral cortex, increasing the excitability of the corticospinal tract. Sawaki et al. [20] and McDonnell and Ridding [21] reported that the excitability of the motor cortex continued to increase after electrical stimulation, and somatosensory input from electrical stimulation could improve the effectiveness of training. Furthermore, it has been reported that the excitability of the motor cortex increased with a combination of electrical stimulation and voluntary movement [22,23]. Thus, it is possible that the excitability of the motor cortex is increased by untriggered NMES during robotic training, resulting in an improvement in paralysis.

Robotic training using the algorithm of InMotion2 assists in completion of the reaching movement when the patient cannot complete the movement independently. During repetition of the reaching movement (1000 times/day), NMES facilitated voluntary control of muscle, and patients had a high number of successful trials, leading to an increase in the effectiveness of training. Furthermore, NMES in peripheral nerves for more than 1 h has been reported to increase excitability of the motor cortex [24]. It is possible that paralysis improved because of an increase in the excitability of the motor cortex, as robotic training in our study required approximately 1 h for completing more than 1000 repetitions of the reaching movement.

FMA scores improved in both groups after robotic training, and there were no significant differences between the groups, although the improvement in the FMA-total score tended to be greater in the RE group than in the RO group ($p=0.06$). Keller et al. [12] explicitly applied untriggered transcutaneous functional electrical stimulation to the triceps brachii muscles of stroke patients with synergistic movement of the shoulder and elbow during shoulder abduction movement. The authors reported a co-contraction reduction with regard to the biceps brachii muscles and an increase in the activity of the triceps brachii muscles [12]. We believe that as the patients in our study could explicitly perform elbow movements because of electrical stimulation, consequent FMA score improvements were observed. In order to recommend the application of electrical stimulation with robot therapy, assessments of muscle activities are necessary. In addition, it is necessary to confirm the preserved effect of rehabilitation interventions through high-evidence level randomized controlled trials.

Because the patients in the present study were in the subacute phase (6–15 weeks) after stroke, the influences of spontaneous recovery could not be ignored. Hendricks et al. reported that spontaneous recovery contributes to motor function until 6 months after onset [25]. In order to exclude the possibility of natural recovery bias, we randomly divided the patients into two groups (RE and RO) and compared the groups. Although a statistically significant difference in age was not observed between the two groups, patients tended to be younger in the RE group than in the RO group. As the functional improvement in younger patients may be high in general, age-matched groups should be used in future studies.

In conclusion, untriggered NMES might increase the effectiveness of shoulder and elbow robotic training in patients with hemiparesis. Additionally, NMES at a sub-motor threshold during robotic training might facilitate activation of paretic muscles, resulting in paralysis improvement.

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Ethical approval

Patients provided consent prior to participation in the present study, and the study was approved by the ethics committee of Fujita Health University (HM15-132).

Conflict of interest

The authors of this article do not have any conflict of interest.

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