Tailor-made Rehabilitation Approach Using Multiple Types of Hybrid Assistive Limb Robots for Acute Stroke Patients: A Pilot Study

Hiroyuki Fukuda, P.T.[1,2], Takashi Morishita, M.D., Ph.D.[1], Toshiyasu Ogata, M.D., Ph.D.[1, 3], Kazuya Saita, O.T.[1,2], Koichi Hyakutake, O.T.[1,2], Junko Watanabe, S.T.[1,2], Etsuji Shiota, M.D., Ph.D.[2], and Tooru Inoue, M.D., Ph.D.[1]

1. Department of Neurosurgery, Fukuoka University, Faculty of Medicine, Fukuoka, Japan
2. Department of Rehabilitation Medicine, Fukuoka University Hospital, Fukuoka, Japan
3. Department of Neurology, Fukuoka University, Faculty of Medicine, Fukuoka, Japan

Corresponding Author:
Takashi Morishita, M.D., Ph.D.
Department of Neurosurgery,
Fukuoka University Faculty of Medicine
Nanakuma 7-45-1, Jonan ward,
Fukuoka, Japan.
81-92-801-1011
81-92-865-9901 FAX
e-mail: tmorishita@fukuoka-u.ac.jp

Running Title: HAL-assisted rehabilitation for acute stroke

Keywords: Neurorehabilitation, physical impairment, stroke rehabilitation, robot, hybrid assistive limb

Title: Tailor-made Rehabilitation Approach Using Multiple Types of Hybrid Assistive Limb Robots for Acute Stroke Patients: A Pilot Study

Abstract

Objectives: To investigate the feasibility of a tailor-made neurorehabilitation approach using multiple types of hybrid assistive limb (HAL) robots for acute stroke patients.

Methods: We investigated the clinical outcomes of patients who underwent rehabilitation using the HAL robots. The Brunnstrom stage, Barthel index (BI), and functional independence measure (FIM) were evaluated at baseline and when patients were transferred to a rehabilitation facility. Scores were compared between the multiple-robot rehabilitation and single-robot rehabilitation groups.

Results: Nine hemiplegic acute stroke patients (five men and four women; mean age 59.4 ± 12.5 years; four hemorrhagic stroke and five ischemic stroke) underwent rehabilitation using multiple types of HAL robots for 19.4 ± 12.5 days, and 14 patients (six men and eight women; mean age 63.2 ± 13.9 years; nine hemorrhagic stroke and five ischemic stroke) underwent rehabilitation using a single type of HAL robot for 14.9 ± 8.9 days. The multiple-robot rehabilitation group showed significantly better outcomes in the Brunnstrom stage of the upper extremity, BI, and FIM scores.

Conclusions: To the best of our knowledge, this is the first pilot study demonstrating the feasibility of rehabilitation using multiple exoskeleton robots. The tailor-made rehabilitation approach may be useful for the treatment of acute stroke.

Introduction

Stroke is a debilitating disorder leading to disabilities such as hemiplegia, aphasia, and perceptual problems. Neurorehabilitation is an essential part of treatment for functional recovery from stroke, and studies have shown the efficacy of early rehabilitation intervention following stroke (Jauch et al., 2013; Morgenstern et al., 2010). In particular, recent studies have demonstrated the efficacy of robot-assisted rehabilitation (Basteris et al., 2014; Norouzi-Gheidari, Archambault, & Fung, 2012). Accordingly, hybrid assistive limbs (HALs; Cyberdyne Inc., Tsukuba, Japan) were invented to enhance neurorehabilitation (Kawamoto, Hayashi, Sakurai, Eguchi, & Sankai, 2009; Wall, Borg, & Palmcrantz, 2015). The HAL predicts the movement of the affected limb by detecting bioelectric signals from the muscles and assists the affected limb to achieve appropriate movement. Achievement of appropriate movement has been considered to provide sensory feedback and accelerate neuronal recovery (Watanabe, Tanaka, Inuta, Saitou, & Yanagi, 2014).

The first HAL robot was designed to provide bilateral leg support. As several studies have reported the usefulness of this robot-assisted rehabilitation (Cruciger, Tegenthoff, Schwenkreis, Schildhauer, & Aach, 2014; Kawamoto et al., 2010; Ueba et al., 2013), we have used this robot for gait and balance training after stroke. The single-leg version of HAL (HAL-SL) was invented to help patients become more independent than with HAL-BL at the advanced stage of gait training. Additionally, two types of single-joint HAL (HAL-SJ) for elbow and knee joints have been used to facilitate rehabilitation for more severe patients at the bedside, and these robots allow therapists to train both upper limbs and knees.

The advantage of having a variety of machines available is that therapists have the option of selecting the most appropriate treatment modality and tailoring the treatment plan for each patient at the different levels of stroke recovery. Although previous studies have reported the effects of a single type of HAL robot in rehabilitation, no studies have addressed tailoring treatments for individual patients using multiple types of HAL robots. We hypothesized that comprehensively treating the hemiplegic upper and lower limbs using multiple robots would be more effective than using only one robot. The aim of the present study was to investigate the feasibility of tailor-made rehabilitation for acute stroke patients with varying levels of motor weakness as a pilot study.

Methods

Participants

Acute stroke patients admitted to our hospital between September 2011 and September 2014 were recruited for this study following approval from our institutional review board to use HAL robots for rehabilitation in acute stroke cases. Patients with hemiparesis were included. HAL-assisted rehabilitation was performed with informed consent. To investigate the feasibility and usefulness of the multiple-robot approach, we classified patients treated with HAL-assisted rehabilitation into two groups: a multiple-robot rehabilitation (MR) group and a single-robot rehabilitation (SR) group. For the SR group, only HAL-BL was used for robot-assisted rehabilitation. Since the HAL-SL and the HAL-SJ became available in our hospital later than the introduction of the HAL-BL, the control data was collected from the early era of our robot-assisted rehabilitation program when the HAL-SL and the HAL-SJ were not available.

We excluded pediatric patients under 18 years old, those unable to follow instructions due to severe cognitive impairment, and those with severe body pain. Additionally, patients with complete paralysis in an upper or lower extremity were also excluded as the HAL robots require the bioelectrical signal from the muscles as a trigger for the assistive movements.

Rehabilitation protocol

In this study, we followed up with patients with motor weakness in both the lower and upper extremities treated with either multiple HAL robots or a single HAL robot. In addition to robot-assisted rehabilitation, all patients were treated with conventional rehabilitation therapy such as stretch and passive movements of the affected limbs. These conventional therapies were started at bedside prior to the use of robots.

In severe hemiplegic cases, we started the rehabilitation using HAL-SJ for either the upper or the lower extremity. As the HAL-SJ only supports single-joint movement, it was fully usable on the bed, even in the intensive care unit (Figure 1-A and B). With HAL-SJ, extension and flexion movements of the joint were repeated 100–150 times at each session.

Once sitting position was achieved, the HAL robot with bilateral leg support (HAL-BL) was introduced (Figure 1-C). We used the HAL-BL so that moving the intact lower limb joints helps the patient understand how the robot assists the affected limb. The patient repeated extension and flexion in the sitting position with the robot and practiced standing up from the sitting position. During these training sessions, the HAL monitor connected to the robot provided visual feedback to assist the patients in maintaining balance. Once the patient felt comfortable performing these tasks, treadmill training was initiated, and the HAL-SL was used for further gait training (Figure 1-D). Each session of HAL-assisted rehabilitation was performed for approximately 30 min. The timing of transition from HAL-BL to HAL-SL was determined by the degree of ataxia and balance problems.

Study Design

All sessions of robot-assisted rehabilitation were videotaped and evaluated by two therapists (H.F. and K.S.). We used Brunnstrom stages to evaluate motor function of the upper and lower extremities. We also evaluated activities of daily living (ADL) using the modified Rankin scale (mRS), Barthel index (BI), and functional independence measure (FIM) as the outcome measures prior to rehabilitation and at the time of transfer to a rehabilitation facility from our hospital.

Statistical Analysis

We performed a Wilcoxon signed-rank test to evaluate the changes in each parameter before and after rehabilitation in each group. Baseline scores and the change in clinical scores were also compared between the two groups. We used SPSS version 21.0 (IBM Corp., Armonk, NY, USA) for statistical analysis.

Results

Nine acute stroke patients (five men and four women; mean age 59.4 ± 12.5 years; four hemorrhagic stroke and five ischemic stroke) underwent rehabilitation using multiple types of HAL robots, and 14 patients (six men and eight women; mean age 63.2 ± 13.9 years; nine hemorrhagic stroke and five ischemic stroke) underwent rehabilitation using a single type of HAL robot (HAL-BL). Rehabilitation using robots was initiated on day 9.3 ± 6.8 and 9.4 ± 5.1 after onset of stroke in the MR and SR groups, respectively. Patient characteristics are summarized in Table 1.

For the MR group, the mean number of total sessions of robot-assisted rehabilitation was 11.6 ± 3.9, including 6.3 ± 3.4 upper extremity sessions and 5.2 ± 1.6 lower extremity sessions during a period of 19.4 ± 10.3 days. Two of nine patients started with HAL-SJ for the lower extremity, and all patients reached a level where they used HAL-BL for gait training, although three patients were unable to undergo HAL-SL training due to a lack of muscle strength in the affected limb (cases 2 and 5) or balance disturbance (case 9). Rehabilitation details are summarized for the MR group in Table 2. On the other hand, the mean number of total sessions of robot-assisted rehabilitation was 4.9 ± 3.1 during a period of 14.9 ± 8.9 days for the SR group.

The MR group had lower baseline Brunnstrom stage of the lower extremity compared with the SR group (4.7 ± 1.1 vs 3.1 ± 3.6; $p = 0.037$). In the MR group, there were significant improvements in the Brunnstrom stage of the upper extremity ($p = 0.014$) and hand ($p = 0.046$) even though there was no significant improvement in the stage of the lower extremity ($p = 0.317$). On the other hand, no significant improvements were seen in the Brunnstrom stage of the upper extremity and hand in the SR group even though significant improvement was achieved in the stage of the lower extremity ($p = 0.014$).

Concerning the ADL scores, significant improvements in the mRS scores were seen in both the MR and SR groups ($p < 0.05$). The total BI improved from 34.4 ± 19.6 to 70.0 ± 20.9 ($p = 0.008$)

following multiple-robot rehabilitation, and the total FIM score improved from 57.8 ± 20.8 to 89.1 ± 22.8 ($p = 0.008$). In the SR group, the total BI and the total FIM scores changed from 31.1 ± 26.1 to 46.4 ± 27.4 ($p = 0.03$) and 56.2 ± 21.7 to 70.6 ± 28.3 ($p = 0.01$), respectively.

With regard to the degree of improvements in the outcome measures, the MR group showed statistically larger changes than the SR group in the Brunnstrom upper extremity stage, the total BI, and the total FIM scores. These clinical outcomes are summarized in Table 3. No adverse events associated with the robot rehabilitation were reported in our cohort.

Discussion

Since the first report of HAL for neurorehabilitation (Kawamoto et al., 2009), this new technology has been widely used for various disorders such as spinal cord injury, stroke, and orthopedic problems (Cruciger et al., 2014; Kawamoto et al., 2009; Kawamoto et al., 2010; Ueba et al., 2013; Wall et al. 2015). These studies have focused on the efficacy of robot-assisted rehabilitation using a single type of HAL robot in each study, but none of them reported how therapists may tailor the rehabilitation protocol using multiple HAL robots for each patient. As acute stroke has a varied etiology, the characteristics of the disease are heterogeneous and rehabilitation should be tailored.

There are several advantages of robot-assisted rehabilitation. Each robot is considered to provide a standardized rehabilitation protocol, and thus the robot could be a useful tool for research (Turner, Ramos-Murguialday, Birbaumer, Hoffmann, & Luft, 2013). Among the various types of rehabilitation robots, the HAL has advantages. It has a user-friendly system that does not require special training to use the robot. In addition, the HAL-SJ is small enough to enable therapists to introduce robot-assisted rehabilitation at the bedside setting in the stroke care unit, as was the case in our study. Moreover, HAL-BL and HAL-SL were available for patients at the advanced recovery stage after stroke or relatively mild paralysis, and the use of these types of robots helped prepare patients for transfer to a rehabilitation facility for more advanced rehabilitation programs.

As the HAL assists voluntary muscle movements, patients receive sensory feedback from the successful movements of the limbs, which motivates patients to move their limbs more eagerly. Taub, Uswatte, Mark, and Morris (2006) proposed the "learned nonuse" hypothesis as a mechanism of progression of paralysis after stroke, hypothesizing that unsuccessful movement of the affected limb due to stroke may result in reduced motivation to move the affected limb, thus complicating functional recovery. We believe that using HAL from the early stage of acute stroke would accelerate functional recovery by preventing "learned nonuse" and contribute to more favorable long-term clinical outcomes.

Although our study demonstrated favorable outcomes, there were important limitations. For instance, the sample size was small, and there was no control without robot therapy. It should be noted that the characteristics of MR and SR groups were not matched as they were enrolled from different study periods. Additionally, the number of rehabilitation sessions was not standardized in this study. Further studies with an increased number of cases and a control cohort will address these issues.

Conclusions

We reported a pilot study presenting nine cases where stroke-related hemiparesis was treated with rehabilitation assisted by multiple HAL robots in comparison with 14 cases treated with a single robot to address the heterogeneous nature of stroke-related disability. This is the first study showing the feasibility of rehabilitation using multiple HAL robots for acute stroke patients.Selecting the appropriate treatment robot at each recovery stage of stroke to maximize the clinical benefits may be reasonable, and this new technology, HAL, has potential to improve stroke practice.

Acknowledgement

This study was partly supported by JSPS Grant-in-Aid for young scientists (B) 15K19984 and grant of the clinical research promotion foundation, Japan.

References

Basteris A, Nijenhuis SM, Stienen AH, Buurke JH, Prange GB, Amirabdollahian F. (2014). Training modalities in robot-mediated upper limb rehabilitation in stroke: a framework for classification based on a systematic review. *J Neuroeng Rehabil*, 11: 111.

Cruciger O, Tegenthoff M, Schwenkreis P, Schildhauer TA, Aach M. (2014). Locomotion training using voluntary driven exoskeleton (HAL) in acute incomplete SCI. *Neurology*, 83(5): 474.

Jauch EC, Saver JL, Adams HP, Jr., Bruno, A. Connors, J. J. Demaerschalk, B. M., ... Yonas, H. (2013). Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke,* 44(3): 870–947.

Kawamoto H, Hayashi T, Sakurai T, Eguchi K, Sankai Y. (2009). Development of single leg version of HAL for hemiplegia. *Conf Proc IEEE Eng Med Biol Soc*, 5038–5043.

Kawamoto H, Taal S, Niniss H, Hayashi T, Kamibayashi K, Eguchi K, & Sankai Y. (2010). Voluntary motion support control of Robot Suit HAL triggered by bioelectrical signal for hemiplegia. *Conf Proc IEEE Eng Med Biol Soc*, 2010: 462–466.

Morgenstern LB, Hemphill JC, 3rd, Anderson C, Becker, K. Broderick, J. P., Connolly, E. S., Jr., ... Tamargo, R. J. (2010). Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*, 41(9): 2108–2129.

Norouzi-Gheidari N, Archambault PS, Fung J. (2012). Effects of robot-assisted therapy on stroke rehabilitation in upper limbs: systematic review and meta-analysis of the literature. *J Rehabil Res Dev*, 49(4): 479–496.

Taub E, Uswatte G, Mark VW, Morris DM. (2006). The learned nonuse phenomenon: implications for rehabilitation. *Eura medicophys*, 42(3): 241–256.

Turner DL, Ramos-Murguialday A, Birbaumer N, Hoffmann U, Luft A. (2013). Neurophysiology of robot-mediated training and therapy: a perspective for future use in clinical populations. Front Neurol, November 13 [Epub ahead of print]

Ueba T, Hamada O, Ogata T, Inoue T, Shiota E, Sankai Y. (2013). Feasibility and safety of acute phase rehabilitation after stroke using the hybrid assistive limb robot suit. *Neurol Med*

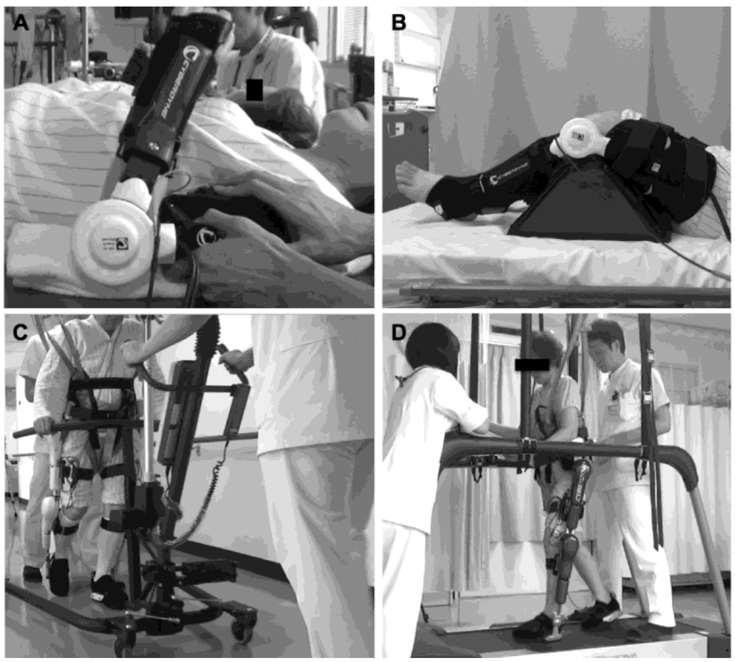
Chir (Tokyo), 53(5): 287–290.

Wall A, Borg J, Palmcrantz S. (2015). Clinical application of the hybrid assistive limb (HAL) for gait training - a systematic review. Front Syst Neurochi, March 26 [Epub ahead of print]

Watanabe H, Tanaka N, Inuta T, Saitou H, Yanagi H. (2014). Locomotion improvement using a hybrid assistive limb in recovery phase stroke patients: a randomized controlled pilot study. *Arch Phys Med Rehabil*, Jul 7 [Epub ahead of print]

Figure Legends

Figure 1. Four types of hybrid assistive limb (HAL) robots. A. HAL-SJ (elbow joint), B. HAL-SJ (knee joint), C. The bilateral leg version of HAL (HAL-BL), D. The single leg version of HAL (HAL-SL)



	Multiple-robot group (N = 9)	**Single-robot group (N = 14)**
Age	59.4 ± 12.5	63.2 ± 13.9
Gender		
Male	5	6
Female	4	8
Onset to Start of Rehab (Days)	9.3 ± 6.8	9.4 ± 5.1
Rehab Periods (Days)	19.4 ± 10.3	14.9 ± 8.9
Type of Stroke		
Hemorrhagic	4	9
Ischemic	5	5
Number of HAL sessions		
HAL-BL	3.0±2.0	4.9 ± 3.1
HAL-SL	1.9±1.6	0
HAL-SJ (Knee)	0.3±0.7	0
HAL-SJ (Elbow)	6.3±3.4	0

Table 1. Demographic data of two groups. HAL = hybrid assistive limb; BL = bilateral leg version; SL = single leg version; SJ = single joint version

Table 2. Number of robot-assisted rehabilitation and the functional outcomes

	Upper Extremity	Lower Extremity					
	Number of HAL sessions	Number of HAL sessions				Total Number of all HAL Sessions	Rehabilitation periods (Days)
Case	**HAL-SJ (Elbow)**	**HAL-SJ (Knee)**	**HAL (Bilateral)**	**HAL (Unilateral)**	**Total**		
1	13	0	3	4	7	20	41
2	4	0	5	0	5	9	23
3	4	0	2	2	4	8	9
4	6	0	1	3	4	10	12
5	6	0	4	0	4	10	23
6	11	0	2	2	4	15	24
7	4	0	2	2	4	8	7
8	4	2	1	4	7	11	15
9	5	1	7	0	8	13	21
Mean±SD	6.3±3.4	0.3±0.7	3.0±2.0	1.9±1.6	5.2±1.6	11.6±3.9	19.4±10.3

	Multiple-robot group	**Single-robot group**	**P-value**
Br. Stage (U/E)			
Before	3.78 ± 1.71	3.43 ± 1.40	0.523
After	4.44 ± 1.33	3.64 ± 1.45	0.205
Δ Br. Stage (U/E)	0.67 ± 0.50	0.21 ± 0.70	0.025
Brunnstrom Stage (Hand)			
Before	3.78 ± 1.99	3.50 ± 1.87	0.518
After	4.22 ± 1.86	3.71 ± 1.90	0.311
Δ Br. Stage (Hand)	0.44 ± 0.53	0.21 ± 0.426	0.083
Brunnstrom Stage (L/E)			
Before	4.67 ± 1.12	3.14 ± 1.35	0.037
After	4.78 ± 1.09	3.57 ± 1.22	0.039
Δ Br. Stage (L/E)	0.11 ± 0.33	0.43 ± 0.51	0.014
mRS			
Before	4.00 ± 0.50	4.29 ± 0.83	0.408
After	3.33 ± 0.71	3.86 ± 0.86	0.084
Δ mRS	0.67 ± 0.50	0.43 ± 0.65	0.180
Total BI Score			
Before	34.4 ± 19.6	31.1 ± 26.1	0.137
After	70.0 ± 20.9	46.4 ± 27.4	0.018
Δ BI score	35.6 ± 17.6	15.3 ± 13.1	0.017
Total FIM Score			
Before	57.8 ± 20.8	56.2 ± 21.8	0.314
After	89.1 ± 22.8	70.6 ± 21.8	0.038
Δ FIM score	31.3 ± 11.0	14.4 ± 12.3	0.033

Table 3. Comparison in the clinical outcomes between two groups. Δ scores were calcuated as the difference between before and after robot-assisted rehabilitation. Wilcoxon signed-rank test was performed to compare two groups. The multiple-robot therapy group demonstrated significantly better outcomes in the Brunnstrom upper extremity stage, BI, and the FIM scores.