Effects of periodic robot rehabilitation using the Hybrid Assistive Limb for a year on gait function in chronic stroke patients

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Abstract

Using a robot for gait training in stroke patients has attracted attention for the last several decades. Previous studies reported positive effects of robot rehabilitation on gait function in the short term. However, the long-term effects of robot rehabilitation for stroke patients are still unclear. The purpose of the present study was to investigate the long-term effects of periodic gait training using the Hybrid Assistive Limb (HAL) on gait function in chronic stroke patients. Seven chronic stroke patients performed 8 gait training sessions using the HAL 3 times every few months. The maximal 10-m walk test and the 2-minute walking distance (2MWD) were measured before the first intervention and after the first, second, and third interventions. Gait speed, stride length, and cadence were calculated from the 10-m walk test. Repeated one-way analysis of variance showed a significant main effect on evaluation time of gait speed ($F=7.69$, $p<0.01$), 2MWD ($F=7.52$, $p<0.01$), stride length ($F=5.24$, $p<0.01$), and cadence ($F=8.43$, $p<0.01$). The effect sizes after the first, second, and third interventions compared to pre-intervention in gait speed ($d=0.39$, 0.52, and 0.59) and 2MWD ($d=0.35$, 0.46, and 0.57) showed a gradual improvement of gait function at every intervention. The results of the present study showed that gait function of chronic stroke patients improved over a year with periodic gait training using the HAL every few months.

Keyword

Rehabilitation, Gait, Stroke, Robot, Hybrid Assistive Limb

1. Introduction

The motor function of stroke patients has been shown to recover rapidly by 3 months after onset[1], followed by an improvement trend to 6 months, and then a gradual decrease after reaching a plateau[2]. For this reason, there is no doubt that rehabilitation in the acute phase and subacute phase is important to accelerate recovery. On the other hand, about 30% of stroke survivors have some obstacles to walking even in the chronic phase[3]. Cessation of rehabilitation in the chronic phase of stroke is also associated with loss of functional ability because of the decline in daily activities due to the residual neurological deficits of the lower extremity. Therefore, continued rehabilitation for long-term after stroke is also important.

In recent years, gait training using robots for gait restriction after stroke has attracted attention[4]. The robot for gait training is considered a therapeutic device that can implement "intensive", "repetitive", and "task-specific" training, which are effective rehabilitation concepts for chronic stroke patients, in an accurate and reproducible manner. The wearable exoskeleton devices (Rewalk, Hybrid Assistive Limb; HAL, etc.) have been developed as a new type of robot[5, 6]. The HAL is a wearable robot for gait training that assists joint torque with the patients' electromyogram as a trigger. These features enable more task-specific gait training over-ground and to match the patients' intention to move their joint with the actual joint movements, rather than the robot providing a completely passive assist. Improved outcomes in learning motor control compared to other robots may be expected. Some previous studies indicated the possible superiority of gait training using the HAL compared to traditional rehabilitation [7, 8]. On the other hand, a recent study did not demonstrate the superiority of the HAL intervention in the improvement of gait ability compared to conventional physical therapy[9]. Therefore, there was a need for further study on the impact of the HAL on gait ability in stroke patients.

Gait rehabilitation for chronic stroke patients temporarily improves function, but that additional improvement is gradually lost after the intervention[10, 11]. With respect to this, we previously demonstrated in an observational study that the potentiation of the effects was maintained, with at least 3 months of improved gait function after the HAL intervention [12]. Therefore, periodic training programs using the HAL undertaken prior to functional decline may be effective for additional improvement and long-term maintenance of gait ability in chronic stroke patients. However, no clinical trials have evaluated the beneficial effects of the program including training, detraining, and retraining. The purpose of this study was to examine the effects of periodic training using the HAL for a year on gait ability in chronic stroke patients. We hypothesized that the periodic training program would result in stepwise improvements in gait ability for each gait training period, whereas the additional gait ability would be maintained during the detraining period.

2. Methods

2.1. Study design

A longitudinal, observational study with an intervention for a single group that adhered to the STROBE guidelines was performed. Patients who were receiving outpatient treatment in our hospital were told about the previous study[13] and this study from their doctor according to the inclusion and exclusion criteria. Patients who asked to participate in this study and could perform the interventions between December 2016 and July 2018 at Kyoto University Hospital were enrolled. They underwent the 3 interventions periods using the HAL with supervision by physical therapists. Each intervention period was conducted for 3 weeks during hospitalization, and patients were discharged from the hospital after each intervention period for several months (see the detraining periods in the Results section). Outcomes were measured before the first intervention and after each intervention (four times). Therefore, the total intervention period for each patient ranged from 9 months to a year (Fig. 1).

2.2. Subjects

Eleven stroke patients with hemiplegia were enrolled in the previous study[13], which included one intervention period of gait training using the HAL (Cyberdyne Inc., Ibaraki, Japan) with the same protocol used in the present study, and seven of them agreed to participate in this study of periodic interventions. The remaining four did not opt for continued intervention for personal reasons. Their clinical characteristics are shown in Table 1. Walking ability was assessed by the Functional Ambulation Category (FAC; score range 0–5). Five patients used a T-cane to walk, and 2 patients used a quad-cane. All patients wore ankle-foot orthoses. All patients were fully informed of the procedures and purpose of the study, which conformed to the Declaration of Helsinki, and written, informed consent was obtained from all subjects. This study was approved by the ethics committee of Kyoto University Graduate School and the Faculty of Medicine (C0775). The clinical trial registration number of this study is UMIN000012764 R000014756.

2.3. Inclusion criteria and exclusion criteria

The inclusion criteria were: first-ever stroke and in the chronic phase (> 6 months from onset); the ability to understand an explanation of the study and to express consent or refusal; body size that can fit in the robotic suit HAL (height range, 145-180 cm; maximal body weight, 80 kg); and ability to walk at least 10 m. The exclusion criteria were: cognitive impairments that limit the ability to understand instructions; contracture restricting gait movements at any lower limb joint (hip, knee, or ankle); or cardiovascular or other somatic conditions incompatible with intensive gait training.

2.4. Gait training program

All patients performed the 3 intervention periods of at least 8 gait training sessions in each intervention period using the HAL. The training program and control mode of the HAL were in line with the previous study[13]. Some patients received several additional sessions due to their schedule of admission and discharge, but the outcomes were measured after the 8th session at each intervention period (see the number of intervention sessions in the Results section). Gait training was performed within 2-5 days/week for 3 weeks. They did not receive any other interventions for the lower extremity, such as conventional physical therapy, but some received occupational and/or speech therapy during the intervention period as needed and stretching therapy or exercise therapy of the lower extremity in the detraining period. One patient received Botulinum Toxin treatment for the lower limb in the detraining period. Each session lasted approximately 60 min, including a change of clothes, setup of the HAL, and gait training. The double-leg type HAL was used for gait training to control the motion of both lower limb, because many chronic stroke patients present with motor abnormalities on the non-paralysis side to compensate for the motion of their paralysis side. The gait training was performed on the ground or a treadmill with 3-4 physical therapists as needed for the operation of the HAL commands (1 therapist), supporting patients' stability (1-2 therapists), and handling a mobile suspension system (ALL-In-One Walking Trainer, Ropox A/S, Naestved, Denmark) (1 therapist) if needed. If the training session progressed and physical therapists' assistance of the support or handling the suspension was no longer needed, it was conducted with a physical therapist who operates the HAL commands. The physical therapists using the HAL had taken the learning program and had a license to use the HAL. Patients were encouraged to walk for as long as possible in time, such that distance and gait speed depended on the patients' tolerance. The settings of the HAL commands (magnitude and timing of assistance) were decided by the physical therapists based on their evaluation of patients' gait patterns and electromyography. The electromyographic signals from four muscles (rectus femoris, gluteus maximus, biceps femoris, and vastus lateralis) were detected and displayed on the mobile monitor of the HAL.

2.5. Outcomes

The outcome measures were measured before the first intervention and after the first, second, and third interventions (four times). The primary outcome measure was gait speed. Secondary outcome measures were stride length (m), cadence (step/min), and 2-minute walking distance (2MWD) (m). To calculate gait speed (m/s), stride length (m), and cadence (steps/min), walking time and number of steps were assessed on a maximum 10-m walk test (10MWT). The 10MWT was performed without the HAL. The faster time of two trials was selected for analysis. Patients were required to use the same device and/or orthosis during all measurements. A therapist supported the patients as necessary. The 2MWD was adopted as the measurement of walking capacity, which was recommended in the previous study[14]. The 2MWD was measured on the 30-m walking path in the rehabilitation room. Patients were told to walk as fast and as long as they could.

2.6. Statistical analysis

Statistical analysis was conducted using SPSS (version 22.0, IBM Japan Inc., Tokyo, Japan). The normality of the data was evaluated using the Shapiro-Wilk test. Repeated measures one-way analysis of variance was used to analyze the effects on gait speed, stride length, cadence, and 2MWD. The effect size (Cohen's d) and 95% confidence interval (CI) of outcome changes in each intervention period compared to before the first intervention period were calculated using methods described previously[15, 16].

3. Results

The intervention compliance rate for the 7 subjects was 100%. Therefore, the statistical analysis included all patients' data. The median (quartile) of the total intervention period was 295 (266, 317) days. The number of intervention sessions was: 1^{st}, 9 (8, 10) sessions; 2^{nd}, 10 (9, 11) sessions; and 3^{rd}: 9 (8, 10) sessions. The detraining period between each intervention period was: 1^{st}-2^{nd} intervention period, 103 (83, 109) days; and 2^{nd}-3^{rd} intervention period, 145 (115, 187) days. All participants completed the entire protocol without any adverse events.

3.1. Gait function

The results for gait function are shown in Table 2, and individual changes of gait speed and the 2MWD are shown in Fig. 2. On repeated measures one-way analysis of variance, the gait speed showed a significant main effect ($F = 7.69$, $p < 0.01$). The effect size was gradually increased to $d = 0.39$, 0.52, and 0.59 after the first, second, and third intervention periods compared to pre-intervention period, respectively. Significant main effects were observed for both stride length ($F = 5.24$, $p < 0.01$) and cadence ($F = 8.43$, $p < 0.01$). Similarly, the 2MWD showed a significant main effect ($F = 7.52$, $p < 0.01$), and the effect size was increased gradually (pre-1^{st}: $d = 0.35$, pre-2^{nd}: $d = 0.46$, pre-3^{rd}: $d = 0.57$). The FAC did not change in any of the patients.

4. Discussion

This is the first report to indicate the long-term effects on gait function of repeated gait training interventions using the HAL. For healthy older adults, the previous study reported that the long-term training programs including training, detraining, and retraining periods contribute to the maintenance and/or improvement of physical functions for the long term[17]. Therefore, in the present study, whether gait ability can be improved by further gait training using the HAL several months after the first intervention and whether it can be improved over the long term by being repeated every few months in chronic stroke patients were investigated. It was found that gait speed and gait capacity were gradually increased by the 3 intervention periods with intervals of several months for approximately one year.

The results of the present study showed a near moderate effect size of improvement of gait speed (+ 0.14 m/s, d = 0.39) after the first intervention period. Perera et al.[18] showed the clinical meaningful change of gait speed to be 0.14 m/s, a substantial change in stroke patients. Therefore, the results of the present study showed that the gait training using the HAL induces a substantial effect in a single intervention period of the 8 sessions and additional effects in repeated intervention periods. The effect sizes of gait speed improvement in previous studies using the HAL for chronic stroke patients were reported as d = 0.16[19], d = 0.96[8], and d = 1.41[7], which were different from the effect size of gait speed improvement in the present study. Among these reports[7, 8, 19] and the present study, the subjects' characteristics or the intervention methods with the HAL were different. The degree of paralysis, injury site of the brain, or the setting of the assist parameter varied in each study. These differences in clinical settings might modify effect size, even though the same HAL robot was used in gait training. Other approaches to gait function in chronic stroke patients, including traditional gait practice[20], treadmill[21], split-belt walking[22], and circuit class therapy[23, 24], have been reported. However, all of the above approaches did not reach a moderate effect (0.14 m/s) defined by a previous study[18]. Furthermore, in the review of gait training using robots[4], it was reported that improvement of gait speed was 0.12 m/s for the end-effector type, 0.00 m/s for the exoskeleton type, and 0.12 m/s for the mobile device. Therefore, gait training using conventional robots was also regarded as not an efficient approach for gait speed in stroke patients. On the other hand, in some reports, the moderate effects on gait speed were exceeded by gait training using the HAL[7, 8], and one of them showed superiority to traditional rehabilitation[8]. Therefore, the HAL may offer a promising approach to gait dysfunction in stroke patients. It is needed further exploration from aspects of the context, dose, and timing in the training using the HAL.

In the present study, patients performed 8 sessions in 3 weeks using the HAL. The other reports using the HAL involved 8 sessions[8] or 16 sessions[7, 19]. In the reports using other robots, the number of sessions was 20 [25, 26], 12 [27, 28], or 10 [29, 30]. Thus, there is high variability in the number of sessions in the reports, making it difficult to discuss whether the 8 sessions in the present study were appropriate. Although the number of gait training sessions in the present study was lower, and the expected total training amount was less than with other approaches using robots, the positive effect on gait ability in the present study would suggest that HAL rehabilitation has an advantage with respect to achieving high effects with even a small number of sessions.

The number of reports of the effects of the HAL is gradually increasing, with interventions occurring at various times after stroke onset. However, it is not clear when the intervention should be implemented from the acute to the chronic phase to achieve the highest final gait function. In individual reports of gait training using the HAL, it was reported that the gait ability improved in the acute phase[31, 32], the subacute phase[33-36], and the chronic phase[7, 8, 19]. It has also been reported that acute interventions were effective only in severe cases[37]. Moreover, the mid-term follow-up effect after gait training using the HAL was reported at the subacute[36] and chronic phases[12]. Therefore, it was desirable to investigate the long-term effect. The present study is the first to have examined the long-term gait function of stroke patients with periodic intervention. It was shown that gait function improved gradually with every intervention period, suggesting that continuing robot rehabilitation during the chronic phase of stroke has a positive effect on long-term gait function. The results of the present study provide a new concept for long-term rehabilitation strategies in stroke patients to be investigated further.

With respect to the limitations of the present study, first, the number of subjects was small, and there were large variations in age and degree of paralysis. To compensate for this weakness, the effect sizes and 95% CIs for all data compared were shown. Second, it is unclear whether function was maintained after the third intervention period. It might even be possible that additional intervention periods could lead to further improvements. In addition, the duration of the interval period between intervention periods varied by patients, and it is not clear whether the duration was appropriate. Future large-scale and long-term follow-up studies that use comparison groups including those receiving similar amounts of specialized physiotherapy designed to improve gait function are needed.

5. Conclusion

In the present study, gait training using the HAL, a wearable exoskeleton robot, was performed for the 3 intervention periods of the 8 sessions per intervention period in chronic stroke patients, and then the effect of periodic gait training on gait function was examined. It was found that both gait speed and gait capacity showed gradually increased effects with every intervention period, and gait function was improved continuously over approximately a year. The present study provides valuable information to be used in a larger, well-powered, controlled study.

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Table 1. Characteristics of the individual patients

Case	Sex	Age (y)	Height (cm)	Weight (kg)	Diag-nosis	Side of paresis	Period	BRS	FAC	FIM	Gait assistance aid	Gait orthosis
1	M	53	165.3	72.6	ICH	Left	52	II	3	70	Quad-cane	AFO
2	M	81	158.0	59.4	CI	Right	24	IV	4	121	Cane	AFO
3	M	71	166.0	66.0	CI	Left	72	V	4	121	Cane	AFO
4	F	60	156.8	59.5	ICH	Right	43	III	3	111	Quad-cane	AFO
5	M	21	170.2	51.5	ICH	Right	13	V	4	124	Cane	AFO
6	M	69	166.2	57.1	CI	Right	104	III	4	117	Cane	AFO
7	F	53	153.5	49.4	ICH	Right	53	III	4	118	Cane	AFO

M: Male, F: Female, CI: Cerebral infarction, ICH: Intracerebral hemorrhage

Period: Period from onset (months)

BRS: Brunnstrom recovery stage

FAC: Functional Ambulation Category (0–5 score range)

FIM: Functional Independence Measure

AFO: Ankle-foot orthosis

Table 2. Changes in gait function

	Pre	1^{st}	2^{nd}	3^{rd}	F-Value	Effect size		
						Pre-1	Pre-2	Pre-3
Gait speed (m/s)	0.48 ± 0.28	0.62 ± 0.41	0.68 ± 0.45	0.70 ± 0.46	7.69**	0.39 (-0.66 - 1.45)	0.52 (-0.54 - 1.59)	0.59 (-0.48 - 1.66)
Stride length (m)	0.73 ± 0.35	0.81 ± 0.40	0.89 ± 0.40	0.86 ± 0.42	5.24**	0.23 (-0.82 - 1.28)	0.42 (-0.64 - 1.48)	0.33 (-0.72 - 1.39)
Cadence (step/min)	75.0 ± 24.1	84.4 ± 30.2	84.1 ± 30.0	92.0 ± 28.3	8.43**	0.34 (-0.71 - 1.40)	0.33 (-0.72 - 1.39)	0.64 (-0.43 - 1.72)
2MWD (m)	53.7 ± 31.6	67.3 ± 44.5	71.9 ± 45.7	76.6 ± 47.3	7.52**	0.35 (-0.71 - 1.41)	0.46 (-0.60 - 1.52)	0.57 (-0.50 - 1.64)

2MWD: 2-minute walking distance

Pre: Measurement before the first intervention

1^{st}, 2^{nd}, and 3^{rd}: Measurements after the first, second, and third interventions

**: $p < 0.01$

Fig. 1 Flowchart of this study

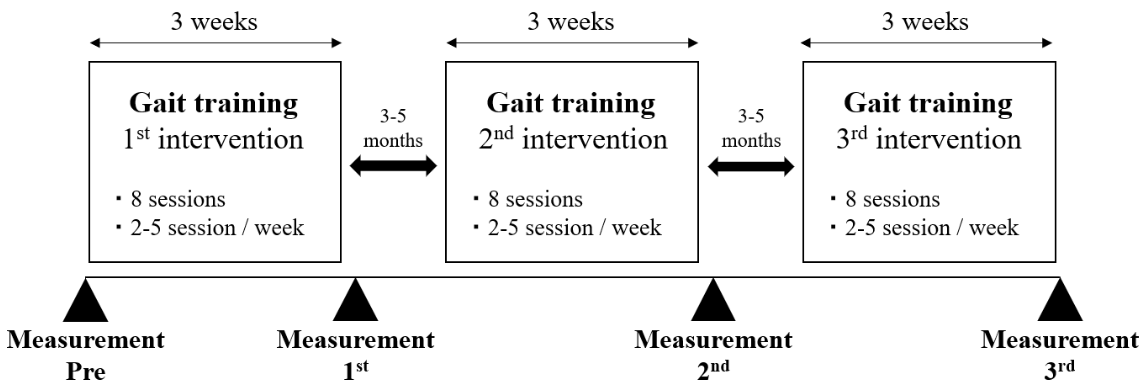
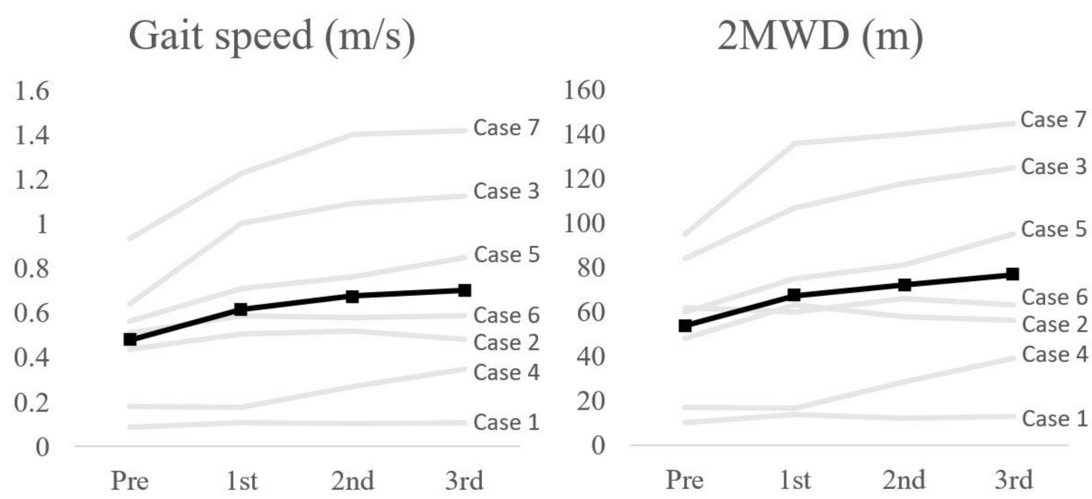


Fig. 2 Individual changes in gait function



2MWD: 2-minute walking distance

Black lines show mean values, and gray lines show individual change.