Gait training with a wearable curara® robot for cerebellar ataxia: a single-arm study

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Research Article

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Abstract

Background: Ataxic gait is one of the most common and problematic symptoms in people with degenerative cerebellar ataxia. Intensive and well-coordinated inpatient rehabilitation has been shown to improve ataxic gait. In addition to therapist-assisted gait training, robot-assisted gait training has been introduced for several neurological disorders; however, only a small number of trials have been conducted for degenerative cerebellar ataxia. We aimed to validate the rehabilitation effect of a wearable "curara®" robot we developed in a single-arm study of people with degenerative cerebellar ataxia.

Methods: Twenty participants with spinocerebellar ataxia or multiple system atrophy with predominant cerebellar ataxia were enrolled. The clinical trial period was 15 days. We used a curara® type 4 wearable robot for gait training. We measured the following items on days 0, 7, and 14: Scale for the Assessment and Rating of Ataxia, 10-m walking time (10mWT), 6-min walking distance (6MWD), and timed up and go test. Gait parameters (i.e., stride duration and length, standard deviation of stride duration and length, cadence, ratio of the stance/swing phases, minimum/maximum knee joint angle, and minimum/maximum hip joint angle) were obtained using a RehaGait®. On the other days (days 1–6 and 8–13), the participants were instructed to conduct gait training for 30 ± 5 min with curara®. We calculated the improvement rate as the difference of values between days 14 and 0 divided by the value on day 0. Differences in the gait parameters were analyzed using a generalized linear mixed model with Bonferroni's correction.

Results: Eighteen participants were analyzed. The mean improvement rate of the 10mWT and 6MWD was 19.0% and 29.0%, respectively. All gait parameters, except the standard deviation of stride duration and length, improved on day 14.

Conclusions: The wearable curara® robot has the potential to facilitate gait training in people with degenerative cerebellar ataxia.

Trial registration: jRCT, jRCTs032180164. Registered 27 February 2019 - Retrospectively registered, https://jrct.niph.go.jp/en-latest-detail/jRCTs032180164

Introduction

Spinocerebellar ataxia (SCA) and multiple system atrophy with predominant cerebellar ataxia (MSA-C) are neurodegenerative diseases mainly affecting the cerebellum. There is no curative pharmacological therapy for SCA or MSA-C; however, some randomized case-control studies have shown that well-organized rehabilitation programs can improve ataxia temporarily [1–3]. As the gains by rehabilitation attenuate gradually after intervention, continuous, home-based rehabilitation is needed to maintain physical function [4, 5].

Robot-assisted gait training (RAGT) is one of the most popular applications in the field of robotics and rehabilitation [6–12]. RAGT has been applied to various diseases including stroke [8, 9, 11], Parkinson's

disease [10], spinal cord injury [7], and cerebral palsy [6], but only a few trials of RAGT for SCA or MSA-C have been conducted. We have developed a wearable “curara®” robot in order to help elderly or disabled people move. Furthermore, to apply this robot to people with stroke or cerebellar ataxia, we identified the assist conditions and evaluated its immediate effect on gait [13, 14]. We found that several gait parameters were improved temporarily in people with stroke or cerebellar ataxia while wearing curara® with certain assist conditions [13, 14]. The remaining issue to be resolved is whether curara® can improve gait through rehabilitation for a specified period. If so, this wearable robot could be introduced into home- and inpatient-based gait training in the future.

The present study was designed to validate the rehabilitation effect of curara® in people with degenerative cerebellar ataxia.

Methods

Participants and instrumentation

A total of 20 individuals (male: 8; female: 12) participated in this study. They fulfilled all of the inclusion criteria and did not fulfill any of the exclusion criteria. The inclusion criteria were: (1) definite diagnosis of SCA or possible or probable MSA-C by the second consensus criteria [15]; (2) aged 20 years or above; (3) able to walk 10 m or more independently with or without a walker and/or brace; and (4) Berg Balance Scale (BBS) score of 20 or above. The exclusion criteria were: (1) gait disturbance due to diseases other than SCA or MSA-C; (2) too thin or obese to fit into curara®; and (3) any other reasons that were considered to make the participants ineligible to participate in the clinical trial.

The disease subtypes of the participants were as follows: SCA type 2 (SCA2): 1 participant; SCA6: 4 participants; SCA31: 3 participants; SCA36: 1 participant; autosomal dominant cerebellar ataxia without genetic testing: 3 participants; idiopathic cerebellar ataxia: 3 participants; and MSA-C: 5 participants. The age at entry was 63.5 ± 10.5 years (mean ± standard deviation [SD]), range 45–84 years. The BBS and Scale for the Assessment and Rating of Ataxia (SARA) scores were 40.1 ± 7.1 and 11.3 ± 4.2 (mean ± SD), respectively.

We used a wearable “curara® type 4” robot in this study (Fig. 1). The curara® type 4 weighs approximately 5 kg (4 actuator units and the controller box) and has an exoskeletal structure that does not have a direct connection between the hip and knee joints. The basic mechanisms of curara® are characterized by a torque-sensing technique and synchronized-based control system. Detailed information regarding curara® is shown in our previous reports [13, 14]. Curara® is considered as a pseudo-passive device [12] that consists of a streamlined structural design of small actuators and a small rechargeable battery.

Measurements

The study period was 15 days in total. We evaluated the participants on days 0, 7, and 14. On these days, they were instructed to walk 10 m on a flat floor at a comfortable speed 9 times while wearing a RehaGait® (HASOMED, Magdeburg, Germany). We measured the 10-m walking time (10mWT) with a stopwatch. We collected the following gait parameters using RehaGait®: stride duration and length, standard deviation of stride duration and length, cadence, ratio of the stance/swing phases, minimum/maximum knee joint angle, and minimum/maximum hip joint angle. We also measured the 6-min walking distance (6MWD), SARA, and timed up and go (TUG) test on days 0, 7, and 14. The BBS was evaluated on days 0 and 14. We set the improvement rates of the 10mWT and 6MWD as the main outcome measures, which were calculated as the difference of values between days 14 and 0 divided by the value on day 0. All of the measurements shown above were taken without wearing curara®.

Rehabilitation Program

All of the participants were instructed to perform gait training with curara® for 30 ± 5 min per day through days 2–6 and days 8–13 (total, 12 days). One or two physical therapists accompanied each participant to operate curara® and to prevent falls (Fig. 1). The participants also received a combination of physical (except gait training), occupational, or speech therapy rehabilitation. The maximum rehabilitation time including gait training with curara® was 3 h per day.

We set the synchronization gain, gait cycle, and joint angles as the assist conditions of curara®. Among these, synchronization gain was fixed to 0.1 at the hip joint and 0.3 at the knee joint throughout the rehabilitation period in all participants. The gait cycle and joint angles varied from individual to individual, and they were set according to the gait parameters of the fastest gait performance on days 0 or 7. The amplitude of the joint angle was set at 140% at the hip joint and 110% at the knee joint. The conditions set on day 0 were effective for gait training on days 1–6, and those updated on day 7 were effective for days 8–13. These parameters meant that the amount of assistance from the robot was larger at the hip joint than at the knee joint, i.e., the device-in-charge robotic support was more influential at the hip joint than at the knee joint. With these assist conditions, curara® could support the participants to reproduce their best gait performance faithfully during gait training.

Statistical analysis

The differences of the SARA score, BBS score, and TUG test between days 0 and 14 were analyzed by a paired *t*-test. The differences of gait parameters obtained with RehaGait® were analyzed using a generalized linear mixed model with Bonferroni's correction. In the model, the day of measurement was set as the fixed effect, and subject factors and the number of measurements on the same day of measurement were set as random effects. All statistical analyses were performed using IBM SPSS Statistics 24 for Windows. The level of significance was set at $p < 0.05$ in all tests.

Results

Of the 20 participants, one (56-year-old male with SCA6, BBS score of 36, and SARA score of 17.5 at baseline) withdrew from the study on day 3 because he no longer wished to continue the trial. The other

19 participants completed the program without any harmful events. However, one participant (84-year-old female with SCA31, BBS score of 27, and SARA score of 17.5 at baseline) was excluded from the analysis due to extreme outliers in most of the measured items; therefore, the data from 18 participants (SCA: 13; MSA-C: 5) were analyzed. The detailed information on the participants and the results of the SARA, BBS, and TUG test are shown in Table 1. At baseline, the participants were aged 62.8 ± 9.8 years (mean ± SD) and the BBS and SARA scores were 41.0 ± 6.7 and 10.6 ± 3.9 (mean ± SD), respectively. There was no difference in the change of the SARA and BBS scores, but the TUG test improved on day 14 ($p = 0.002$).

Table 1
Characteristics of the participants and results of the SARA, BBS, and TUG test.

No.	Disease type	Age (years)/ Sex	SARA score		BBS score		TUG test (s)	
			day 0	day 14	day 0	day 14	day 0	day 14
1	SCA6	45/M	14.0	12.5	30	34	21.4	24.5
2	IDCA	77/M	9.5	7.5	44	53	18.6	11.0
3	MSA-C	65/F	5.0	3.5	51	53	12.6	10.2
4	IDCA	56/F	8.0	8.0	45	45	15.1	13.8
5	ADCA	57/F	7.5	7.0	49	51	6.8	8.3
6	SCA6	51/F	8.0	8.0	39	44	14.5	13.4
7	MSA-C	48/M	13.0	12.0	35	36	28.4	19.0
8	SCA6	61/F	13.5	12.0	35	40	25.1	22.7
9	MSA-C	72/F	13.5	11.5	33	39	26.5	20.6
10	SCA36	57/M	14.5	14.5	45	44	34.1	25.1
11	MSA-C	74/F	10.5	14.0	36	41	16.5	16.4
12	SCA31	72/M	19.5	21.0	34	19	43.1	32.4
13	SCA31	63/M	9.0	8.5	49	52	13.2	11.4
14	SCA2	50/F	11.0	11.0	37	40	14.1	12.3
15	IDCA	69/M	14.0	14.5	42	43	17.8	14.5
16	ADCA	69/F	2.0	2.0	53	54	10.2	8.9
17	ADCA	75/F	9.0	13.0	45	50	18.9	16.1
18	MSA-C	69/F	10.0	9.0	36	37	19.3	17.1
Mean ± SD			10.6 ± 4.0	10.5 ± 4.4	41.0 ± 6.9	43.1 ± 8.7	19.8 ± 8.9*	16.5 ± 6.5*

ADCA: autosomal dominant cerebellar ataxia without genetic testing; BBS: Berg Balance Scale; IDCA: idiopathic cerebellar ataxia; MSA-C: multiple system atrophy with predominant cerebellar ataxia; SARA: Scale for the Assessment and Rating of Ataxia; SCA: spinocerebellar ataxia; SD, standard deviation; TUG: timed up and go. *Statistically significant difference.

The results of the main outcome measures are shown in Fig. 2. The mean improvement rates of the 10mWT and 6MWD were 19.0% and 29.0%, respectively. Both rates showed considerable variability from individual to individual, and were not correlated with each other (correlation coefficient: 0.340, p = 0.168).

The improvement rate of the 6MWD, but not the 10mWT, correlated well with the SARA score (correlation coefficient: 0.626) and BBS score (correlation coefficient: -0.557) at baseline (Fig. 3).

The values of the gait parameters obtained by RehaGait® are shown in Fig. 4. All of the gait parameters, except for the standard deviation of stride length (Fig. 4b) and stride duration, were improved on day 14. When the values on days 0 and 14 were compared, the differences in stride length (Fig. 4a), cadence (Fig. 4c), ratio of the swing phase (Fig. 4d), and maximum flexion angles of the hip (Fig. 4e) and knee (Fig. 4f) joints were statistically significant.

Discussion

Ataxic gait is characterized by reduced walking speed and cadence, reduced stride length and swing phase, and increased variability of stride length and duration compared with the gait of healthy controls [16]. Thus, it is reasonable to use these gait parameters to evaluate the efficacy of RAGT for people with ataxia. In the present study, all of the gait parameters, except variability, improved during the 12-day rehabilitation program with curara® in people with cerebellar ataxia. The favorable change of each gait parameter was considered to account for the improvement in the 10mWT and 6MWD.

Moreover, the improvements of the 10mWT and cadence observed in this study were comparable with those reported previously (19.0 ± 2.8% vs. 19.6 ± 4.1% and 9.2 ± 2.3 vs. 4.7 ± 1.6, mean ± standard error, respectively) in a multidisciplinary, intensive, inpatient rehabilitation program of 28 days for Japanese people with cerebellar ataxia [5]. The distribution of the SARA score and disease duration of the participants in the present study were also comparable with those of this previous study at baseline (10.6 ± 0.9 vs. 12.2 ± 0.7 and 9.2 ± 1.4 years vs. 9.3 ± 1.3 years, mean ± standard error, respectively) [5]. As for gait function, it is likely that the 12-day RAGT with curara® had an equivalent effect to the 28-day intensive, therapist-assisted gait training, although the former study by Miyai et al. focused not only on ataxic gait but also on broad ataxic symptoms [5].

We set the improvement rates of the 10mWT and 6MWD as the main outcome measures, but these parameters did not parallel each other. The improvement rate of the 6MWD, but not of the 10mWT, correlated well with the SARA and BBS scores at baseline. Simply speaking, this means that more severe cerebellar ataxia at baseline might predict a better outcome in the 6MWD by RAGT with curara®. In other words, this may indicate a ceiling effect for the improvement in the 6MWD. The main reason for this is that we used the rate, but not the actual measurement value, to determine efficacy. Conversely, it is apparent that people with severe cerebellar ataxia cannot tolerate RAGT with curara®. According to our preliminary screening, we set a BBS score of 20 or above as one of the inclusion criteria, but we need to clarify further the severity of ataxia that is the best fit for RAGT with curara®.

The methods and optimal timing of therapist-assisted gait training have yet to be standardized for degenerative cerebellar ataxia. Further, the mechanism underlying the temporary restoration of ataxic symptoms by intensive rehabilitation is not understood fully. As RAGT with curara® did not change the standard deviation of stride length and duration, it is unlikely that curara® improved cerebellar ataxia

directly during the clinical trial period. At present, we have not assessed the neuromodulative effects of curara®; however, it may enable people with ataxia to perform gait training for a longer period of time by reducing gait-associated burden on the body. We think that repetitive, well-programmed RAGT can be a valid option for gait training for people with cerebellar ataxia.

Study limitations

The major limitation of this study was that it was a single-arm study of 20 participants. Therefore, we do not know to what extent curara® contributed to the effect observed in this study. We did not use a non-weight-bearing device on gait training with curara®, so we only enrolled participants who had the ability to walk for 30 min while burdened with curara®. It is reasonable to assume that 30-min walking under such a condition might itself be important for the favorable results. Further, we did not examine how long the effect lasts after RAGT with curara®. To address these issues, we are now planning a randomized case-control study for people with cerebellar ataxia.

Conclusions

RAGT with curara® is potentially useful for people with cerebellar ataxia. We believe that long-term, home-based RAGT with curara® may help people with ataxia to maintain an ambulatory status.

Abbreviations

6MWD: 6-min walking distance; 10mWT: 10-m walking time; BBS: Berg Balance Scale; MSA-C: multiple system atrophy with predominant cerebellar ataxia; RAGT: robot-assisted gait training; SARA: Scale for the Assessment and Rating of Ataxia; SCA: spinocerebellar ataxia; TUG: timed up and go

Declarations

Funding:

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Availability of data and materials:

Anonymized data during this study will be provided upon request made to the corresponding author.

Author contributions:

AM, MH and KY conceived the study. AM, YM, NM, MT, MH and KY contributed to study design. NM, MT and MH developed a wearable “curara® robot”. YM maintained “curara® during the clinical trials. AM, YM and KY contributed to data collection. AM performed statistical analysis. AK, YM and KY interpreted data.

AK and KY drafted the manuscript. AM, YM, NM, MT, MH and KY revised and approved the final manuscript.

Competing interests:

Dr. Matsushima, Mr. Maruyama and Mr. Tetsuya have no competing interests.

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Consent for publication:

Not applicable.

Ethics approvals and consent to participate:

Study procedures were approved by the Ethics Committee of Shinshu University School of Medicine (No. 3999), and registered in Japan Registry of Clinical Trials (No. 032180164: https://jrct.niph.go.jp/en-latest-detail/jRCTs032180164) on Feb. 27, 2019. All the participants were provided with all necessary information about the study, and gave us written informed consent before the clinical trials. All aspects of the study confirmed to the principles described in the Declaration of Helsinki.

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Figures

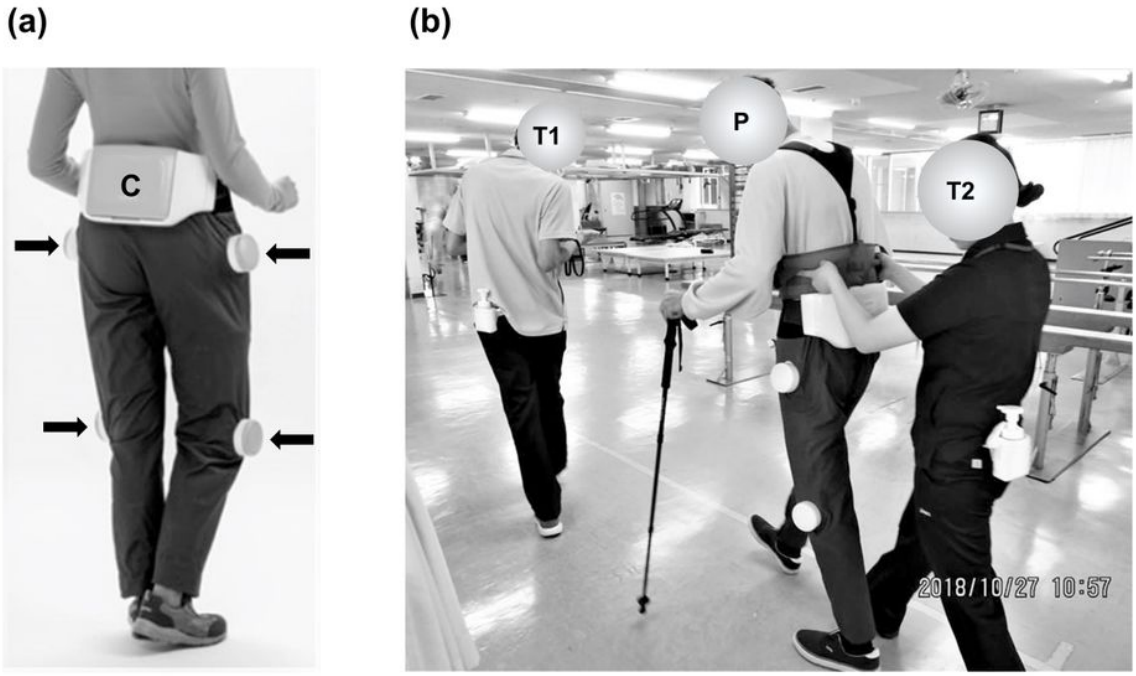

Figure 1

Appearance of the wearable curara® type 4 model (a) and gait training with curara® (b) (a) The controller box (C) and 4 actuator units (arrow) are indicated. (b) The participant (P) is accompanied by two physical therapists (T1 and T2) during gait training. Therapist T1 guides the participant and operates the mobile device to control curara® and T2 prevents the participant from falling.

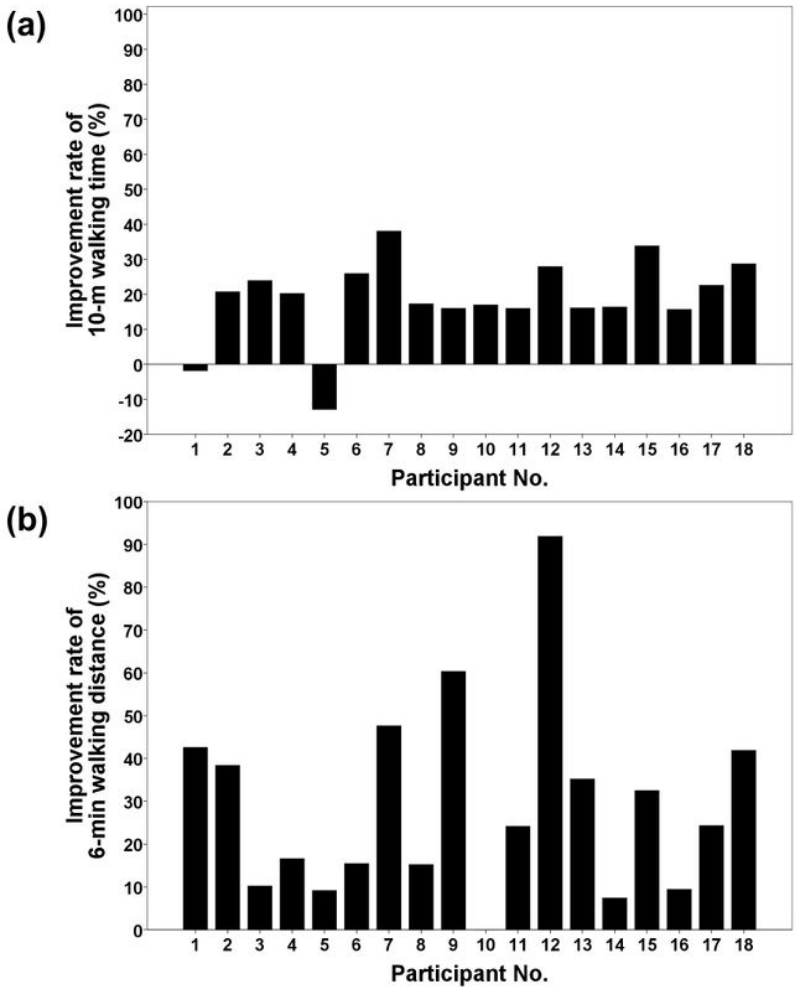

Figure 2

Results of the main outcome measures (a) The improvement rate of the 10-m walking time. (b) The improvement rate of the 6-min walking distance.

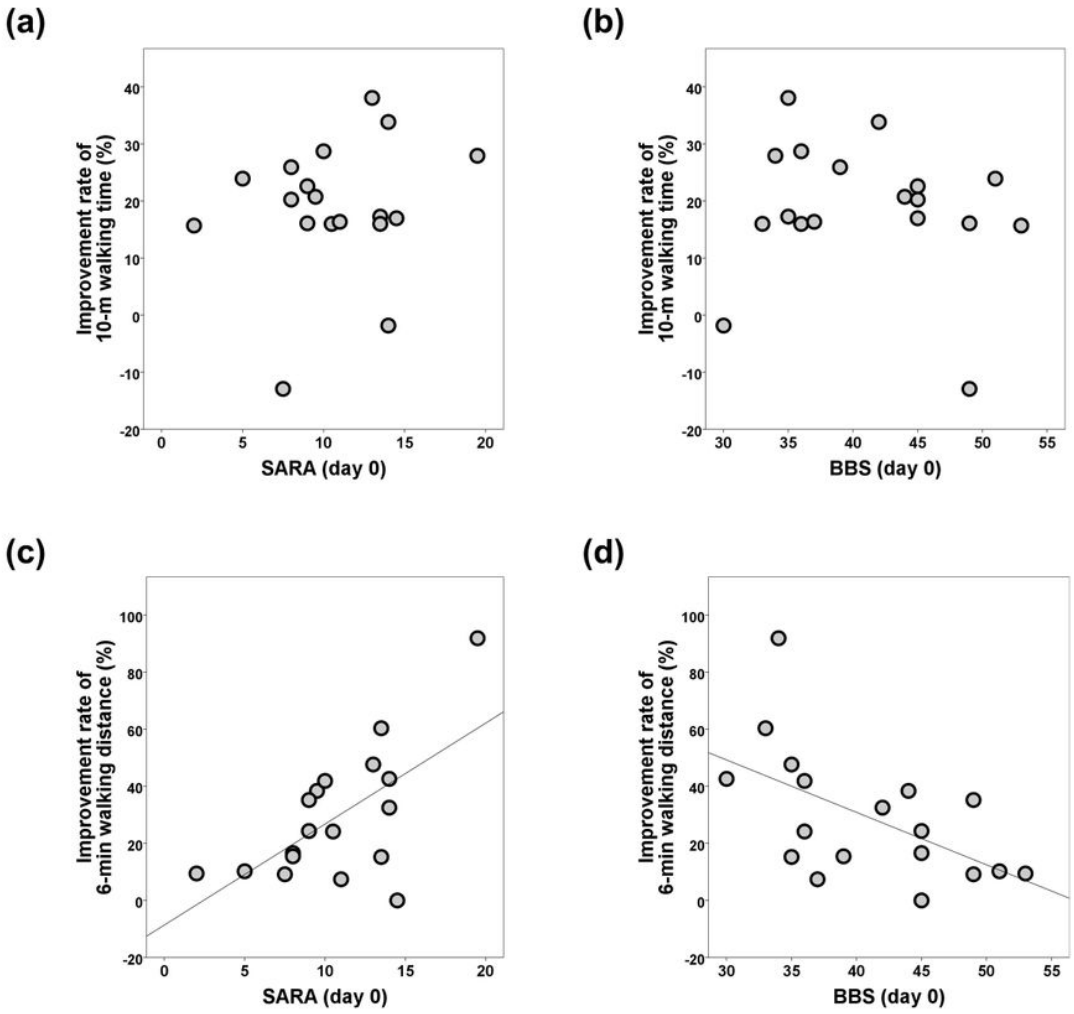

Figure 3

Correlation of the SARA (a, c) and BBS (b, d) scores with the main outcome measures The improvement rate of the 6-min walking distance, but not that of the 10-m walking time, is correlated to the SARA and BBS scores at baseline (day 0).

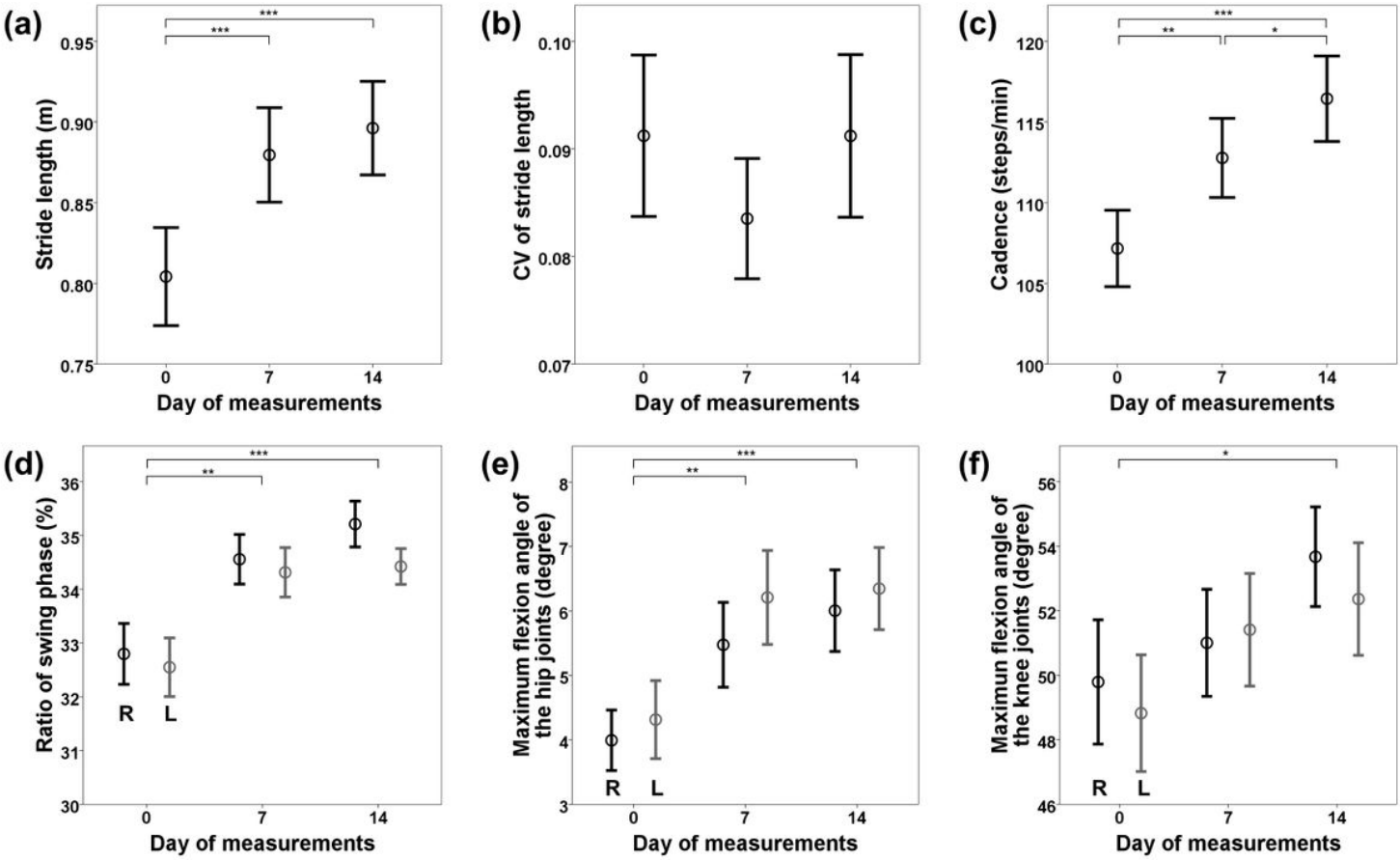

Figure 4

Distribution of gait parameters obtained by RehaGait® Circles represent mean value and bars represent 95% confidence intervals. In panels (d) to (f), black lines represent the value for the right lower limb (R) and gray lines represent the value for the left lower limb (L). (a) Stride length, (b) coefficient of variation (CV) of stride length, (c) cadence, (d) ratio of the swing phase, (e) maximum flexion angle of the hip joint, and (f) maximum flexion angle of the knee joint. *p < 0.05, **p < 0.01, ***p < 0.001.