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Abstract

Objective

To determine whether providing a controlled resistance versus assistance to the paretic leg at the ankle during treadmill training will improve walking function in individuals poststroke.

Design

Repeated assessment of the same patients with parallel design and randomized controlled study between 2 groups.

Setting

Research units of rehabilitation hospitals.

Participants

Patients (N=30) with chronic stroke.

Intervention

Subjects were stratified based on self-selected walking speed and were randomly assigned to the resistance or assistance training group. For the resistance group, a controlled resistance load was applied to the paretic leg at the ankle to resist leg swing during treadmill walking. For the assistance group, a load that assists swing was applied.

Main Outcome Measures

Primary outcome measures were walking speed and 6-minute walking distance. Secondary measures included clinical assessments of balance, muscle tone, and quality of life. Outcome measures were evaluated before and after 6 weeks of training and at 8 weeks' follow-up, and compared within group and between the 2 groups.

Results

After 6 weeks of robotic training, walking speed significantly increased for both groups, with no significant differences in walking speed gains observed between the 2 groups. In addition, 6-minute walking distance and balance significantly improved for the assistance group but not for the resistance group.

Conclusions

Applying a controlled resistance or an assistance load to the paretic leg during treadmill training may induce improvements in walking speed in individuals poststroke. Resistance training was not superior to assistance training in improving locomotor function in individuals poststroke.

Keywords: Gait, Hemiplegia, Recovery of function, Rehabilitation, Robotics, Walking

Walking dysfunction is one of the physical limitations contributing to stroke-related disability.¹ Most stroke survivors walk with reduced walking speed² and endurance,³ as well as with residual spatial and temporal asymmetry.⁴ Walking dysfunction reduces the probability of successfully returning to work and decreases participation in community activities.⁵ As a consequence, improved walking function is a major goal of rehabilitation in individuals poststroke.

The use of body weight supported treadmill training (BWSTT) has demonstrated significant improvements in walking capability in individuals poststroke. For instance, previous studies have indicated significant improvements in gait velocity,⁶⁻⁹ endurance,¹⁰ balance,⁷ and symmetry¹¹ after BWSTT. However, BWSTT can be labor-intensive

work for physical therapists, particularly when working with patients who require substantial walking assistance after stroke.⁶

Several robotic systems have been developed for automating locomotor training.^{12,13} These robotic systems are effective in reducing therapist labor and increasing the total duration of training. However, their use has shown relatively limited functional gains for some patients¹⁴⁻¹⁶ because of the limitations of these robotic systems. For instance, the limited degrees of freedom of current robotic systems allows movement only in the sagittal plane, which may limit the natural walking pattern and affect gait dynamics.¹⁷ In addition, the fixed trajectory control strategy used in current robotic systems may encourage passive rather than active training.

Active motor training has been demonstrated to be more effective than passive training in eliciting performance improvement.¹⁸ In particular, data from hemiparetic subjects practicing upper limb movements with forces that provide passive guidance versus error enhancement indicate that greater improvements in performance are achieved when errors are magnified,¹⁹ suggesting that error-augmentation training may also be used as an effective way to improve locomotor function in individuals poststroke. Thus, we postulated that by applying a controlled resistance load to increase kinematic errors (ie, the difference between the predicted leg movement outcomes and the observed outcomes of the leg movement) of the paretic leg during treadmill walking, motor learning would be accelerated during BWSTT in individuals poststroke.

On the other hand, providing a controlled assistance load to the paretic leg may facilitate leg swing, which mimics the way that therapists provide assistance to the paretic leg during treadmill training. We postulated that providing an assistance load to the paretic leg may also improve locomotor function in individuals poststroke through a use-dependent motor learning mechanism.²⁰ To date, no randomized controlled studies have directly compared leg resistance versus assistance during BWSTT in individuals poststroke. The purpose of this study was to assess locomotor function (ie, walking speed, endurance, balance) after resistance versus assistance training in individuals poststroke. We hypothesized that subjects from both groups would show improvements in locomotor function, although

there would be greater improvements in subjects who underwent resistance training in comparison with those who underwent assistance training. Results from this study may be used to develop robotic training paradigms to improve locomotor function in individuals poststroke.

Methods

Participants

Screening evaluations were performed on 82 subjects, and 30 individuals with chronic hemiparetic stroke were recruited to participate in this study (tables 1 and 2). Inclusion criteria included (1) unilateral, supratentorial, ischemic, or hemorrhage stroke; (2) >6 months' duration after stroke; (3) no prior stroke; (4) self-selected walking speed \leq .99m/s; and (5) able to stand and walk (>10m) without physical assistance using assistive devices or orthoses (below knee) as needed. Exclusion criteria included (1) significant cardiorespiratory/metabolic disease and (2) score <24 on the Mini-Mental State Examination.²¹ All subjects required medical clearance for participation. All procedures were approved by the institutional review board. Written informed consent was obtained from all subjects.

Characteristics	Resistance	Assistance	P
Age (y)	53.6 \pm 8.9	57.4 \pm 9.8	.30
Sex (M/F)	9/5	9/5	.99
Race (white/other)	4/10	6/8	.16
Side of paresis (R/L)	7/7	7/7	.99
Type of stroke (ischemic/hemorrhagic)	6/6*	6/6*	.99
Time postinjury (y)	7.3 \pm 5.6	7.1 \pm 6.0	.95
Ankle-foot orthosis	7	7	.99
Assistive device	7	9	.34

NOTE. Values are mean \pm SD, n, or as otherwise indicated.

Abbreviations: F, female; L, left; M, male; R, right.

* One subject reported unknown cause of stroke and 1 reported aneurysm in resistance training group; 2 subjects reported unknown cause of stroke in assistance training group.

Table 1. Characteristics of participants

Screening Status	Number of Subjects
Screened	80
Excluded	52
	Multiple stroke (n=12)
	Brainstem lesion (n=2)
	Other diagnoses (such as brain injury or spinal cord injury) (n=7)
	Walking too quickly (ie, self-selected walking speed >1.0m/s) (n=11)
	Needed physical assistance to ambulate (n=5)
	Did not meet MMSE criteria (n=1)
	Not interested because of travel or time constraints (n=14)
Included	30
	Completed all training and test sessions (n=28)
Dropped out (n=2)	
	Poor attendance (n=1)
	Feeling "decreased balance" (n=1)

Abbreviation: MMSE, Mini-Mental State Examination.

Table 2. Subjects screened, enrolled, and tested

Of the 30 participants enrolled in the study, 2 dropped out. The remaining 28 participants completed all training and test sessions. There were no significant differences in the training parameters between the resistance and assistance training groups, except for the peak forces applied (table 3).

Training Parameters	Resistance	Assistance	P
Training time per session (min)	44±1	44±2	.70
Rating of perceived exertion (average across sessions)	11.6±2	11.7±1	.94
Training speed (m/s)			
First session	0.51±0.23	0.49±0.23	
Last session	0.69±0.24	0.66±0.28	
Average across sessions	0.62±0.06	0.59±0.05	.71
Training distance (km)			
First session	1.25±0.63	1.33±0.68	
Last session	1.91±0.69	1.82±0.84	
Average across sessions	1.70±0.64	1.62±0.74	.73
Body weight support (%)			
First session	23±3 (n=3)	31±1 (n=2)	
Last session	15±4 (n=3)	16±1 (n=2)	
Average across sessions	22±6 (n=3)	20±5 (n=2)	
Peak force of ankle resistance/assistance (N)			
First session	9.7±4.7	20.8±5.5	.000
Last session	12.6±5.3	21.7±6.3	.001
Average across session	11.5±5.0	21.7±6.7	.000

NOTE. Values are mean ± SD or as otherwise indicated.

Table 3. Training parameters of resistance versus assistance training groups

Apparatus

A custom-designed, cable-driven robotic gait training system, which has been reported previously,²² was used to provide a controlled resistance or assistance load to the paretic leg during treadmill walking (fig 1). One of the cables was attached to the paretic leg at the ankle to provide a controlled resistance or assistance load (the cable was placed posteriorly and anteriorly for resistance and assistance load, respectively) during the swing phase of gait. The load was applied from the late-stance phase to the midswing phase of gait.

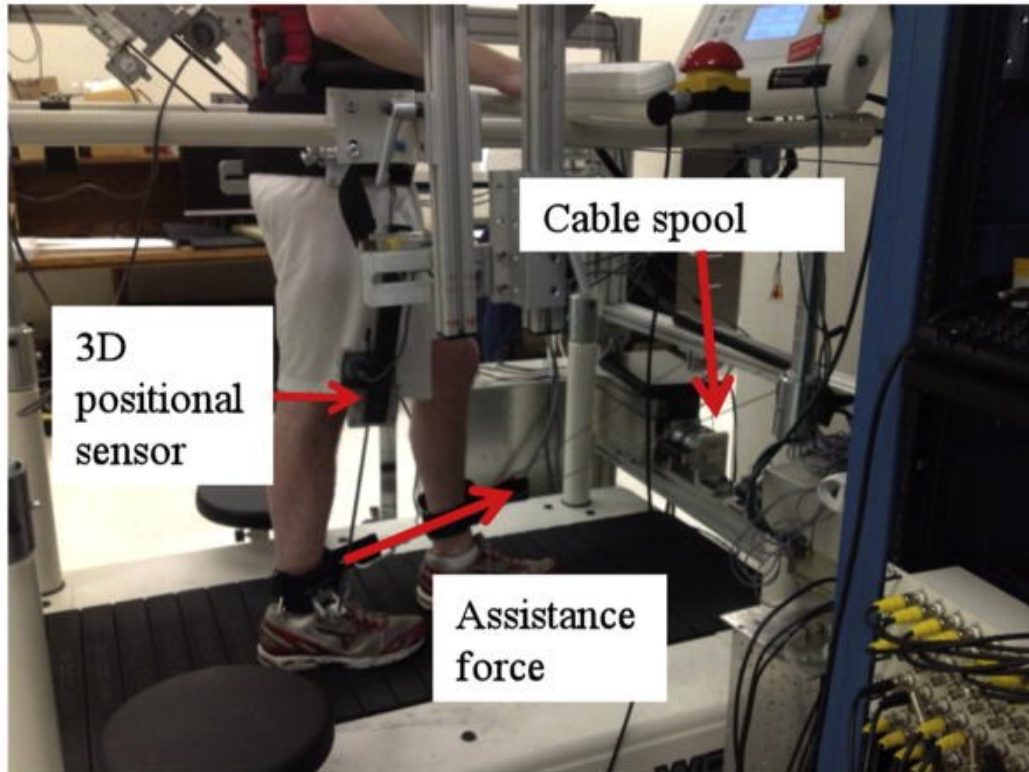


Fig 1 Experimental setup. The cable-driven robotic gait system works with the treadmill and body weight support system. Four cables driven by 4 motors, pulleys, and cable spools were used to apply controlled resistance/assistance loads to the legs. A personal computer was used to control the coordinated movement of the 4 motors. In this study, 1 cable was used to provide controlled force to the paretic leg during the swing phase of gait. Abbreviation: 3D, 3-dimensional.

Training protocol

A 6-week randomized robotic treadmill training trial was conducted by licensed physical therapists (J.M.L., J.K., J.M.) with 3 assessments of gait to determine the training effects. Subjects were blocked by gait speed into slow ($<0.5\text{m/s}$) or fast ($\geq 0.5\text{m/s}$) subgroups and were randomly assigned to either the resistance or the assistance group at the initial test. After the initial test, individuals from both groups underwent intensive robotic locomotor training on a treadmill. Subjects trained 3 times a week for 6 weeks. Each training session was 45 minutes excluding setup time. No specific feedback was provided, but verbal encouragement from therapists was provided during the course of training.

For each training session, body weight support was provided as necessary to prohibit knee buckling or toe drag during treadmill training. Treadmill speed was set at the subject's maximum comfortable walking speed of each training session. During the course of the training, the amount of the load was determined by the controller, based on the motor performance of the subject, using the control algorithm described previously.²² In brief, the assistance force provided is proportional to the kinematic errors between the measured and desired ankle horizontal position and velocity during the swing phase. The desired positions were determined from the mean recorded ankle trajectory using the position sensor for 2 healthy subjects walking on the treadmill. For subjects who were assigned to the resistance group, a controlled resistance load was applied to the paretic leg for resisting leg swing. For the assistance group, a controlled assistance load was applied to the paretic leg for assisting leg swing.

Outcome measures were assessed before training, after 6 weeks of training, and at an 8-week follow-up (F/U) examination by licensed physical therapists. Specifically, self-selected and fast overground walking velocity was collected on a 10-m instrumented walkway (GaitMat II^a), and endurance was assessed through the 6-minute timed walk.²³ Muscle tone, or spasticity, of the knee joint muscle groups was assessed using the Modified Ashworth Scale (0–4).²⁴ Balance was assessed using the Berg Balance Scale (BBS).²⁵ In addition, scores on the Activities-specific Balance Confidence (ABC) Scale²⁶ and changes in quality of life as measured by the Medical Outcomes Study 36-Item Short-Form Health Survey²⁷ were also assessed.

Data analysis

Data were analyzed using scores pre versus post 6 weeks of training, and pre versus 8 weeks F/U assessment. Gait speed and endurance were analyzed using repeated-measures analyses of variance (ANOVAs) for the intragroup analysis (pretraining, posttraining, and F/U). A 2-way ANOVA with main factors of treatment (resistance vs assistance) and severity of locomotor deficits (gait speed $\leq 0.5\text{m/s}$ vs $> 0.5\text{m/s}$) was used for assessing treatment and

severity on functional gains, with significance noted at $P < .05$. In addition, improvement in quality of gait (ie, step length, cadence, asymmetry of step length, single-leg support time), balance, and other clinical assessments were also analyzed using repeated-measures ANOVAs, with significance noted at $P < .05$. Bonferroni corrections were used for repeated comparisons.

Results

After 6 weeks of robotic treadmill training, overground gait speed significantly increased for subjects from the resistance group (fig 2). Specifically, self-selected and fast walking speeds significantly increased from $.53 \pm .25$ m/s to $.61 \pm .28$ m/s (ANOVA, $P = .002$; $n = 14$), and from $.72 \pm .36$ m/s to $.82 \pm .39$ m/s ($P = .001$, $n = 14$), respectively, after resistance training (see fig 2A). Further, improvements in walking speed were partially retained at F/U ($P = .03$ and $P = .002$ for self-selected and fast walk speeds, respectively). In addition, step cadence, step length of the paretic and nonparetic legs, and single-leg support time of the paretic leg significantly increased after resistance training (table 4). The 6-minute walking distance increased from 201 ± 84 m to 207 ± 80 m after resistance training, although no significant difference was noted ($P = .18$), and was 210 ± 82 m at F/U ($P = .08$) (fig 3A). BBS score also slightly increased from 44.1 ± 8.8 to 45.6 ± 9.3 after resistance training, although not significant ($P = .11$), and was 44.9 ± 9.09 at F/U ($P = .47$) (fig 3B).

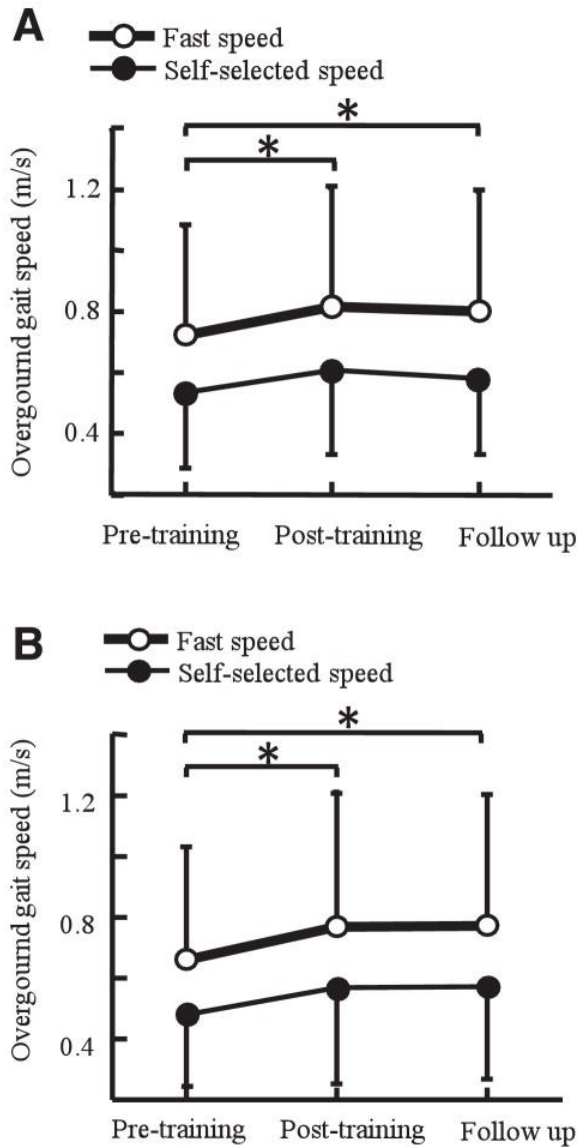


Fig 2 Self-selected and fast overground walking speed, before and after 6 weeks of robotic resistance (A) and assistance (B) treadmill training with the cable-driven robotic gait training system, and 8 weeks after the end of training. An instrumented walkway (GaitMat II) was used to measure overground gait speed. Data shown in the figure are the mean and SD of gait speed across subjects. * $P < .05$.

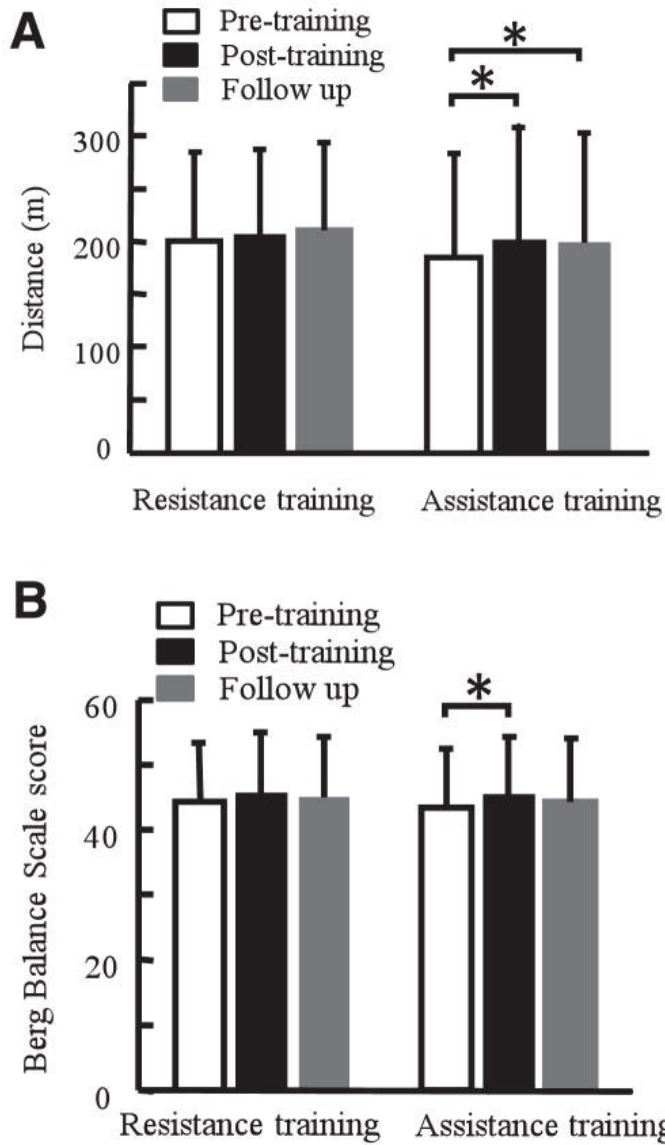


Fig 3 Six-minute walking distance (A) and BBS score (B) before and after 6 weeks of robotic resistance and assistance training, and 8 weeks after the end of training. Data shown in the figure are the mean and SD of walking distance and BBS score across subjects. * $P < .05$.

Outcome Measure	Resistance			Assistance		
	Pre	Post	F/U	Pre	Post	F/U
Single-leg support (%): SSV						
P	21.3±5.5	22.6±5.8*	22.8±5.3*	21.7±5.7	22.9±6.2*	23.8±5.6*
N	36.6±6.4	37.5±5.5	38.9±4.4*	34.0±8.0	35.2±7.7	35.3±8.2
Single-leg support (%): FV						
P	21.0±6.9	23.2±6.4	23.1±7.2	23.0±5.9	24.9±6.6*	25.3±6.3*
N	35.7±6.8	38.1±6.3	39.5±6.8	35.5±8.9	37.9±7.7	37.8±8.0
Step length: SSV (m)						
P	0.48±0.11	0.51±0.12*	0.51±0.11	0.42±0.14	0.45±0.15*	0.45±0.15*
N	0.37±0.15	0.41±0.18*	0.39±0.16	0.33±0.15	0.37±0.16*	0.37±0.17*
Step length: FV (m)						
P	0.55±0.15	0.57±0.17	0.58±0.16*	0.48±0.17	0.52±0.18*	0.52±0.18*
N	0.43±0.18	0.47±0.20*	0.47±0.19*	0.39±0.18	0.43±0.18*	0.43±0.19*
Step asymmetry: SSV	17.0±16.4	14.6±19.2	16.1±19.2	14.8±17.9	14.0±17.8	12.3±13.4
Step asymmetry: FV	15.2±16.6	12.7±16.1	13.1±18.1	14.2±18.4	14.1±18.9	11.9±14.9
Cadence (steps/min): SSV	71.3±17.1	74.7±16.8*	74.3±16.4*	71.4±17.3	76.3±22.5*	76.7±21.8*
Cadence (steps/min): FV	84.1±21.6	87.6±21.0*	86.5±21.2*	86.8±30.3	92.3±32.0*	91.1±33.0

NOTE. Values are mean ± SD.
Abbreviations: FV, faster walking velocity; N, nonparetic leg; P, paretic leg; SSV, self-selected velocity.
* $P < .05$ (within-group comparison, ANOVA).

Table 4 Selected spatial-temporal gait parameters before and after 6 weeks of robotic resistance versus assistance treadmill training, and 8 weeks after the end of training

For subjects assigned to the assistance training group, self-selected and fast walk speeds significantly increased from $.47 \pm .24$ m/s to $.56 \pm .32$ m/s ($P = .01$, $n = 14$), and from $.65 \pm .38$ m/s to $.76 \pm .45$ m/s ($P = .002$, $n = 14$), respectively, after assistance training (see fig 2B). Further, the improvements in walking speeds were partially retained at F/U ($P = .01$ and $P = .004$ for self-selected and fast walking speeds, respectively). In addition, step cadence, step length of the paretic and nonparetic legs, and single-leg support time of the paretic leg significantly increased after assistance training (see table 4). Also, the 6-minute walk distance significantly increased from 177.4 ± 99.9 m to 197.5 ± 109.5 m ($P = .002$, $n = 14$), and was partially retained at F/U (191.1 ± 108.5 m, $P = .02$), which was distinct from resistance training (see fig 3A). The BBS score significantly increased from 43.6 ± 9.0 to 45.5 ± 8.8 ($P = .02$) after assistance training, which was also distinct from resistance training, and was 44.1 ± 9.6 at F/U, although not significant ($P = .41$) (see fig 3B).

The changes in walking speed were not significant between subjects who underwent resistance versus assistance training. Specifically, the improvement in self-selected walking speed was $.07 \pm .07$ m/s and $.09 \pm .11$ m/s after resistance and assistance training, respectively, with no significant difference between the 2 groups ($P = .75$) (fig 4A). In addition, the improvement in fast walking

speed was $.10 \pm .08 \text{ m/s}$ and $.11 \pm .12 \text{ m/s}$ after resistance and assistance training, respectively, with no significant difference between the 2 groups ($P = .73$) (fig 4B). The improvement in the 6-minute walk distance tended to be greater for the assistance group than the resistance group (ie, $20 \pm 20 \text{ m}$ vs $6 \pm 16 \text{ m}$ for assistance and resistance groups, respectively), although not significant ($P = .06$). In addition, the improvement in the BBS score was 1.4 ± 3.1 and 1.9 ± 2.6 for the resistance and assistance training groups, respectively, with no significant difference between the 2 groups ($P = .63$).

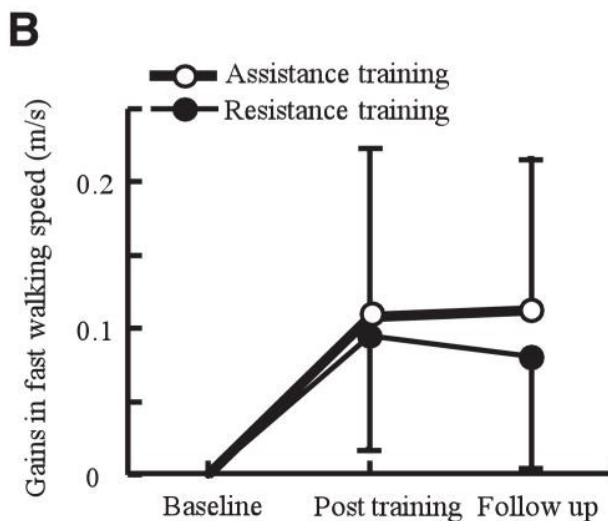
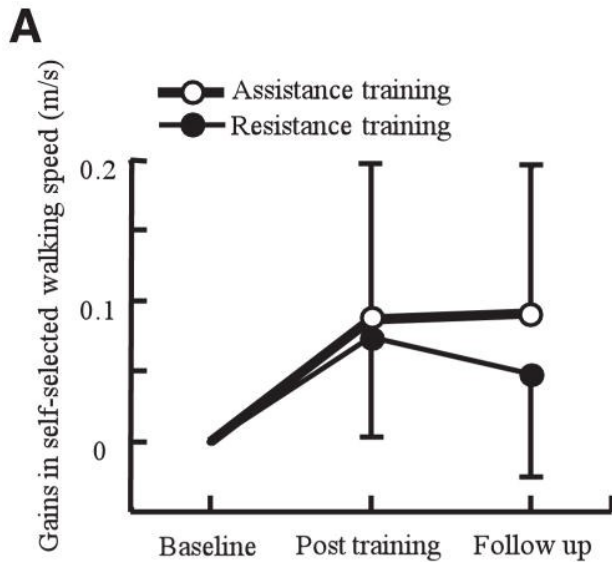


Fig 4 Improvements in self-selected (A) and fast walking (B) overground gait speed before and after 6 weeks of robotic resistance and assistance treadmill training, and 8 weeks after the end of training. Three trials were tested for each condition. The bar and error indicate the mean and SD of the functional gains in gait speed across subjects.

The walking function level has a significant impact on the improvements in walking speeds obtained after robotic training. Specifically, the improvements in self-selected walking speed were significantly greater in subjects at a high functional level (walking at speeds $>0.5\text{m/s}$) (ie, $.17\pm.09\text{m/s}$ $>.1\text{m/s}$, the minimal clinically important difference in gait speed²⁸) than for subjects at a lower functional level (walking at speeds $\leq 0.5\text{m/s}$) (ie, $.02\pm.04\text{m/s}$) after assistance training. However, there was no significant difference in the improvements in self-selected walking speed between subjects with high and low walking function after resistance training (ie, $.09\pm.07\text{m/s}$ vs $.06\pm.08\text{m/s}$ for high and low functioning subjects, respectively). There was a significant interaction between treatment group (resistance vs assistance) and severity level for self-selected walking speed ($P<.05$) but not fast walking speed ($P=.07$). ABC Scale scores significantly increased after assistance training ($P=.03$) but had no significant change after resistance training ($P=.30$). The Medical Outcomes Study 36-Item Short-Form Health Survey had no significant change after resistance or assistance training ($P=.10-.80$) (table 5).

Outcome Measure	Resistance			Assistance		
	Pre	Post	F/U	Pre	Post	F/U
ABC	73.3±24.0	75.5±19.9	73.9±25.9	74.2±15.4	78.4±13.3*	77.4±14.6
SF-36						
PCS	42.6±6.9	42.1±7.7	44.8±5.2	42.8±5.7	42.2±7.9	45.9±9.5
MCS	53.6±10.5	54.1±11.5	53.5±9.2	52.4±13.2	56.0±9.4	53.6±10.3
Modified Ashworth	1.1±0.7	1.0±0.8	0.9±0.8	0.9±0.7	0.7±0.8	0.8±0.7

NOTE. Values are mean ± SD.
Abbreviations: MCS, mental component summary; PCS, physical component summary; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey.
* $P<.05$.

Table 5 Clinical measures before and after 6 weeks of robotic resistance versus assistance treadmill training, and 8 weeks after the end of training

Discussion

Applying a controlled resistance or assistance load to the paretic leg during treadmill training using a cable-driven robotic system

significantly improved walking speed in individuals poststroke. Further, the improvements in walking speed were still partially retained at F/U, suggesting clinical significance of these robotic training paradigms. The improvements in walking speeds obtained through robotic resistance versus assistance treadmill training were comparable, although the 6-minute walking distance and the BBS and ABC Scale scores significantly improved after assistance training but not after resistance training.

Possible mechanisms of recovery after robotic training

The increase in kinematic errors produced by the resistance load may elicit an error correction process that accelerates motor learning during locomotor training in individuals poststroke. For the subjects who were assigned to the resistance training group, the resistance applied to the paretic leg produced a deviation in leg kinematics—that is, increased kinematic errors. Enhanced error has been shown to be more effective than passive guidance in improving arm performance in individuals poststroke.¹⁹ For the lower limb, a recent study²⁹ indicates that exaggerated leg asymmetry through split-belt treadmill training may result in an improvement in gait symmetry in individuals poststroke, although these aftereffects are generally short-lived after 1 session of training.

Repeated exposure to resistance training may induce a prolonged retention of aftereffect of the paretic leg in individuals poststroke. In this study, repeated exposure to a resistance load was applied to the paretic leg during 6 weeks of treadmill training. As a result, the step length of the paretic leg during overground walking increased after resistance training, suggesting that the aftereffect of an increased step length may be accumulated and transferred from one context (ie, treadmill walking) to another context (ie, overground walking) in individuals poststroke. In particular, we observed a partial retention of the increased step length of the paretic leg at F/U.

In addition, while no resistance load was applied to the nonparetic leg, the step length of the nonparetic leg also increased after resistance training. This increase may be due to the increase in single-leg stance time of the paretic leg after training (see table 4). Thus, subjects had more time to move the nonparetic leg forward to achieve

a longer step length. The increase in single-leg stance time on the paretic leg indicates an improvement in motor control of this leg during the stance phase of gait after resistance training.

On the other hand, for subjects who were assigned to the assistance training group, an assistance force provided to the paretic leg may facilitate the leg swing to induce a longer step length on the paretic side during treadmill training. The increased step length of the paretic leg may be accumulated and transferred to overground walking through 6 weeks of locomotor training, resulting in an improvement in walking function after assistance treadmill training in individuals poststroke. However, because the assistance force was applied at the paretic leg facilitating the leg to swing forward, instead of resisting the leg to induce kinematic deviation, we postulated that the motor learning mechanisms involved in robotic assistance training would be different from those involved in resistance training. A use-dependent motor learning mechanism may be involved during robotic assistance treadmill training.²⁰ The synaptic efficacy of sensorimotor pathways involved in the leg swing of the paretic leg may be enhanced by repetitive stepping assisted by the cable-driven robot.³⁰ In addition, the step length of the nonparetic leg also increased, although no assistance force was applied to the nonparetic leg during locomotor training. This may be due to the increase in single-leg stance time of the paretic leg after assistance training (see table 4).

No significant differences in improvements in walking speeds were observed between subjects who were assigned to robotic assistance versus resistance training. In addition, the 6-minute walk distance and the BBS and ABC Scale scores significantly improved after assistance training but not after resistance training, suggesting that resistance training was not superior to assistance training in improving endurance, balance, and balance confidence in individuals poststroke. A possible reason is that while the larger size of errors induced by a resistance load may accelerate motor learning, the motor memory resulted from this learning may be less retained,^{31,32} and less transferred to overground walking.³³ In addition, cognitive strategies or compensation from the nonparetic arm or leg may be used to quickly reduce errors in response to a leg resistance load, but this rapid performance improvement also vanishes quickly after that

resistance load is removed, leading to less retention of motor memory after resistance training.

Results from this current study may have some clinical applications. For instance, while most previous motor adaptation studies^{34,35} have shown that applying a force field perturbation may induce motor adaptation, which is short-lived, our study demonstrated that repeated application of a force perturbation may induce a prolonged retention of aftereffect in individuals post-stroke. Thus, a force field perturbation may be used as an adjuvant paradigm to improve locomotor function in individuals poststroke. In addition, providing a controlled assistance load to the paretic leg during treadmill training through the cable-driven robot may improve locomotor function in individuals poststroke, even for subjects of a high functional level. Thus, it seems feasible to use the cable-driven robotic gait training system to improve locomotor function in individuals poststroke.

Study limitations

The current study has several limitations. For instance, the sample size is small. In addition, the group assignment was not blinded to the physical therapists who conducted the assessment and training. Further studies with a large sample size of subjects and a comparison of the current paradigm with conventional BWSTT are warranted.

Conclusions

Applying both resistance and assistance forces at the paretic leg during treadmill training may produce improvements in walking speed in individuals poststroke, although different motor learning mechanisms may be involved. Resistance training was not superior to assistance training in improving locomotor function in individuals poststroke.

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List of abbreviations

ABC Activities-specific Balance Confidence
ANOVA analysis of variance
BBS Berg Balance Scale
BWSTT body weight-supported treadmill training
F/U follow-up

Footnotes

^aE.Q. Inc, PO Box 16, Chalfont, PA 18914-0016.

Statement of Interest

Competing financial interests. Johnson and Johnson, Lundbeck, Pfizer, GSK, Puretech Ventures, Merck, Takeda, Dainippon Sumitomo, Otsuka, Lilly, Roche, Asubio (A.A.G.). All other authors have no biomedical financial interests or potential conflicts of interest to report.

No commercial party having a direct financial interest in the results of the research supporting this article has conferred or will confer a benefit on the authors or on any organization with which the authors are associated. However, the cable-driven robotic gait training system used in the current study is a custom-designed robotic system and is not commercially available.

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