


Effects of therapy with a free-standing robotic exoskeleton on motor function and other health indicators in people with severe mobility impairment due to chronic stroke: A quasi-controlled study

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Abstract

Introduction: Robotic exoskeletons facilitate therapy in upright postures. This study aimed to evaluate potential health-related effects of this therapy for people with severe mobility impairment due to chronic stroke.

Methods: This quasi-controlled trial with 12 weeks of twice weekly therapy in a free-standing exoskeleton, and 12 weeks follow up, included people dependent for mobility, with stroke at least 3 months prior. The primary outcome was lower limb motor function. A battery of secondary outcomes was evaluated.

Results: Nine participants were enrolled. There was no change in motor function. There was a significant between phase difference in level of independence with activities of daily living (median post-intervention change = 5, IQR = 0, 10, $p = 0.01$), and grip strength (affected limb) (median post-intervention change = 1, IQR = 0, 2, $p = 0.03$). A significant difference was found for quadriceps strength (affected limb) (median change in wait phase = 4, IQR = 2, 7.5, $p = 0.01$). Participants consistently reported positive perceptions of the therapy.

Conclusions: Therapy with a free-standing exoskeleton is acceptable to participants and can facilitate improvements in level of independence and grip strength. Restrictions regarding eligibility to use the device, may reduce the clinical application of this therapy for people with stroke.

Keywords

free-standing, neurorehabilitation, rehabilitation devices, robotic exoskeleton, stroke

Introduction

Stroke is a leading cause of disability in Australia, with an estimated 475,000 people living with the effects of stroke.¹ Of these, 65% are left with severe disability, affecting their capacity to independently carry out activities of daily living.² There is extensive evidence that severe mobility impairment,³ reduced functional ability^{4–6} and diminished quality of life (QoL) contribute to post-stroke morbidity, with many people dependent on the assistance of aids, including wheelchairs.

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Comprehensive rehabilitation is the mainstay of management for these individuals to try and counter these associated morbidities. It is thought to be necessary for this therapy to be task specific, highly repetitious, and of high intensity to allow the neural system to form complex pathways for tasks important to the individual.^{7,8} However, individuals with severe mobility impairment can be limited in their ability to perform large volumes of intensive therapy due to their dependence on others to attain upright posture. Recent advances in technology, particularly robotics, have the potential to reduce this barrier by facilitating standing postures and allowing greater volumes of practice in these positions, with less manual assistance from therapists.

The emergence of lower limb exoskeletons in rehabilitation began by pairing robotics with treadmills, with devices such as the Lokomat⁹. Despite extensive research, evidence regarding the superiority of this type of therapy over traditional methods has not been established.^{10,11} This is in part largely due to the lack of translation from treadmill gait to overground walking.¹² This precipitated the development of overground exoskeletons of which there is a wide range with various features. Devices may be machine or user-initiated, have single or multiple actuated joints, and be used as either a single or double leg support.¹³

Research has shown that the use of exoskeletons in stroke rehabilitation appears to be feasible¹⁴⁻¹⁸ and safe.^{19,20} There was some evidence of improvement in gait and balance outcomes in a 2018 systematic review,²⁰ however these improvements were not significantly better than with routine therapy, and the varied devices and diverse patient characteristics included in the review limit interpretation of the findings.²⁰ To date, most of the literature has focused on gait parameters rather than other rehabilitation outcome measures such as motor function, mood, levels of independence and quality of life,^{20,21} which may be more meaningful to those with severe mobility impairment and warrant further investigation.

Currently, overground robotic exoskeletons require the user to stabilize themselves in an upright position using a walking aid. The exception to this is the Rex Bionics device (Auckland, NZ), which is free-standing and fully supportive.²² It places the user in the most natural standing position of the currently available exoskeletons, without the user needing to lean on a walking aid for support. To date there has been no published research evaluating the effectiveness of exercise therapy provided using this device. It is thus appropriate and timely to investigate the potential merits of the use of this free-standing exoskeleton in the rehabilitation of individuals with stroke. The primary aim of this study was to establish the potential benefits of therapy delivered using the exoskeleton for improving lower limb motor function such as transfers, sitting balance and

mobility, in people with stroke, using the REX exoskeleton. Secondary aims included investigating other health-related benefits such as mood and QoL, and acceptability of therapy with this device. More specifically, we aimed to determine if:

1. Therapy facilitated by a free-standing exoskeleton improves lower limb motor function in people with severe mobility impairment due to chronic stroke.
2. Therapy facilitated by a free-standing exoskeleton has other health-related benefits, in people with severe mobility impairment due to chronic stroke.
3. This treatment modality is acceptable to people with severe mobility impairment due to chronic stroke.

Method

Design

This was a quasi-controlled trial. Outcome measures were taken upon study enrolment and again prior to commencing the intervention, 12 weeks later. This phase was used as a control in order to determine symptom stability, with no experimental intervention. The intervention phase commenced at week 12, for a duration of 12 weeks. There was a follow up assessment at week 36. Participants were recruited between January 2017 and June 2019, with data collection completed in February 2020. The intervention consisted of 12 weeks of twice weekly therapy using the exoskeleton in a purpose-built laboratory at the University of Newcastle, Australia. The wait phase established the level of symptom stability of each participant prior to the intervention. During the study participants were encouraged to continue with routine activities and therapy. Outcome measures were assessed at five time points: on enrolment into the study (week 0), baseline (week 12), mid intervention (week 18), post intervention (week 24), and follow up (week 36). The manuscript was written in accordance with STROBE reporting guidelines.

Ethics approval was granted in October 2016 by the Hunter New England Human Research Ethics Committee (Reference number: 16/08/17/4.06) and co-registered with the University of Newcastle (H-2016-0413). This study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12617000093381). Participants were screened for cognitive capacity to give consent, and written informed consent was obtained from all eligible participants prior to their involvement in the study.

Participants

As this was a pilot study, a convenience sample was used. We aimed to recruit all eligible and interested people in the region over a 2 year period via public promotion campaigns in social, print and news media channels. The inclusion criteria were as follows: (1) Diagnosis of stroke or traumatic brain injury at least 3 months prior to enrolment; (2) Resident of the Hunter region; (3) 18 years or older; (4) Discharged from inpatient rehabilitation programs; (5) Severe mobility impairment and reliant on wheelchair, mobility aid, or the assistance of others for standing activities, determined by a score of ≤ 4 on item five of the motor assessment scale (MAS).

The exclusion criteria were: (1) Weight >100 kg or <40 kg; height $>6'4''$ or $<4'8''$ (as per recommendations of the manufacturer); (2) Pregnancy; (3) Unstable or severe cardiac or respiratory compromise; (4) Recent fractures in lower limbs/pelvis/spine; (5) Significant cognitive impairment (Montreal Cognitive Assessment Score <19); (6) Any medical condition which may limit the ability to exercise in an upright position. This includes pressure sores in contact with the exoskeleton, lower limb heterotrophic ossification, severe lower limb muscle contracture, acute deep vein thrombosis, and hip subluxation.

Equipment: The REX exoskeleton

The REX exoskeleton is registered with the Therapeutic Goods Administration of Australia as a class one medical device approved for use in clinical settings under the supervision of a therapist trained in its use. It allows individuals to be in a fully upright, standing position to practice weight bearing activities requiring large muscle groups.²² The device can perform large volumes of specific functional movements in addition to gait training. Where possible, transfers into the device were done in standing with assistance from the therapist. Where this could not be achieved, a sling lifter was used. Participant transfers into and out of the exoskeleton were always performed with it positioned in sitting and pre-adjusted to the participants' specifications. It is adjustable in several areas to accommodate different builds and heights. Thigh length, shin length, foot length and ankle to floor height are all adjusted for each participant as required. These measurements were taken at the initial assessment for each participant and the device adjusted accordingly before each session.

Movement of the device is therapist initiated, controlled by a joystick on the right-side control arm. The device has 10 actuators which power the hip, knee and ankle on both legs.²² It does not have any biofeedback mechanism, and therefore cannot adjust movement according to the participant. The REX moves at a speed of 0.5 m/s.²³

Intervention

The intervention consisted of 24 sessions, two per week for 12 weeks. Each session involved up to half an hour of individualised, weight bearing exercise in the device, prescribed and administered by a Rex Bionics accredited physiotherapist. A combination of sit to stand practice, standing, weight shift, trunk control exercises, stepping practice, side stepping, squats and gait practice were performed. Interventions were tailored, progressed or ceased according to the individual participant's abilities, as deemed appropriate by the therapist. Blood pressure, pulse and oxygen saturation were monitored for postural hypotension or vasovagal episodes as an additional safety measure in those patients who did not routinely assume upright postures. A home exercise program was provided to complement the therapy sessions and was modified throughout the intervention phase as required.

Outcome measures

On enrolment into the study, the Montreal cognitive assessment scale (MoCA)²⁴ was administered to screen for participants' cognitive capacity to consent to the research and ability to safely participate in the therapy. Those scoring less than 19 on this measure were deemed to have severe cognitive impairment²⁴ and were therefore ineligible for the study. Demographic details such as age, gender and stroke history were recorded. Disease severity was determined using the modified Rankin scale (mRS).²⁵ These descriptive data were not re-assessed.

The primary outcome of interest was functional ability, as measured by the first five items of the MAS: supine to side-lying, supine to sitting, balanced sitting, sit to stand and walking. These scores were summed to give a total maximum score out of 30, with 30 indicating greatest functional ability. The MAS has been reported to have excellent test-retest and interrater reliability ($r = 0.98$ and $r = 0.95$ respectively)²⁶ as well as excellent concurrent validity with other measures of motor recovery in stroke populations (e.g. Fugl-Meyer total scores, $r = 0.96$)²⁷ and is a widely used measure in stroke rehabilitation.²⁶

A battery of validated secondary outcome measures was included to comprehensively evaluate all the potential effects of the intervention. Each assessment was conducted in a standardised order and according to published guidelines to maximise reliability. Grip and quadriceps strength were assessed using dynamometers and recorded as kilograms of force. Grip strength was measured as it is an indicator of overall health and frailty.²⁸ Balance was assessed using the five times sit to stand test (FTSST),²⁹ recorded as the time taken to perform the task, and the functional reach test (FR).³⁰ The unaffected or least affected arm was assessed in functional reach to ensure balance

was accurately evaluated and not impacted by reduced upper limb function on the affected side.³¹

Independence with activities of daily living (ADLs) was measured using the Barthel index which is a valid measure of physical disability.³² The index contains 10 common tasks where the patient is given a score based on their ability to perform each task. Total scores range between 0 and 100, with lower scores indicating higher levels of disability. The hospital anxiety and depression scale (HADS) was used to assess mood on a scale of 0–42, with 42 being the worst outcome.³³ Fatigue was measured using the fatigue assessment scale (FAS) on a 50-point scale, with 50 representing the most fatigued.³⁴ Self-reported health status was assessed using the short form 8 (SF8) which measures eight domains of health including physical functioning, and role limitations due to physical health. We allocated a number to each answer with the lower score being more positive. The total score was out of 42, with 42 indicating the most negative outcome.³⁵

Participant acceptability of the intervention was assessed via a survey, designed by this research team (see [Appendix 1](#)), which contained 18 questions in total. 16 closed questions related to safety, comfort, likability, and useability

of the device, were scored on 5-point Likert scales, adding to a total of 80 points, with a higher score indicating more favourable responses. Two open questions asked for participants' views on liked and disliked features of the intervention. Information about the use of paid care and support equipment was also collected. Documentation of adverse events occurring during the therapy sessions and throughout the duration of the program, compliance and drop-outs, and a participation log were kept by the therapist.

Data collection and analysis

All outcomes were assessed for changes between each of the time points and were reported as medians and interquartile ranges (IQR). A time series analysis was conducted using the Friedman test, to evaluate differences between time points. All missing data were managed with intention to treat analysis by inputting the last measure and carrying it forward. Qualitative data were categorised according to themes. Statistical significance was set at <0.05 . All analyses were conducted using Stata 14.2 statistical analysis software.³⁶

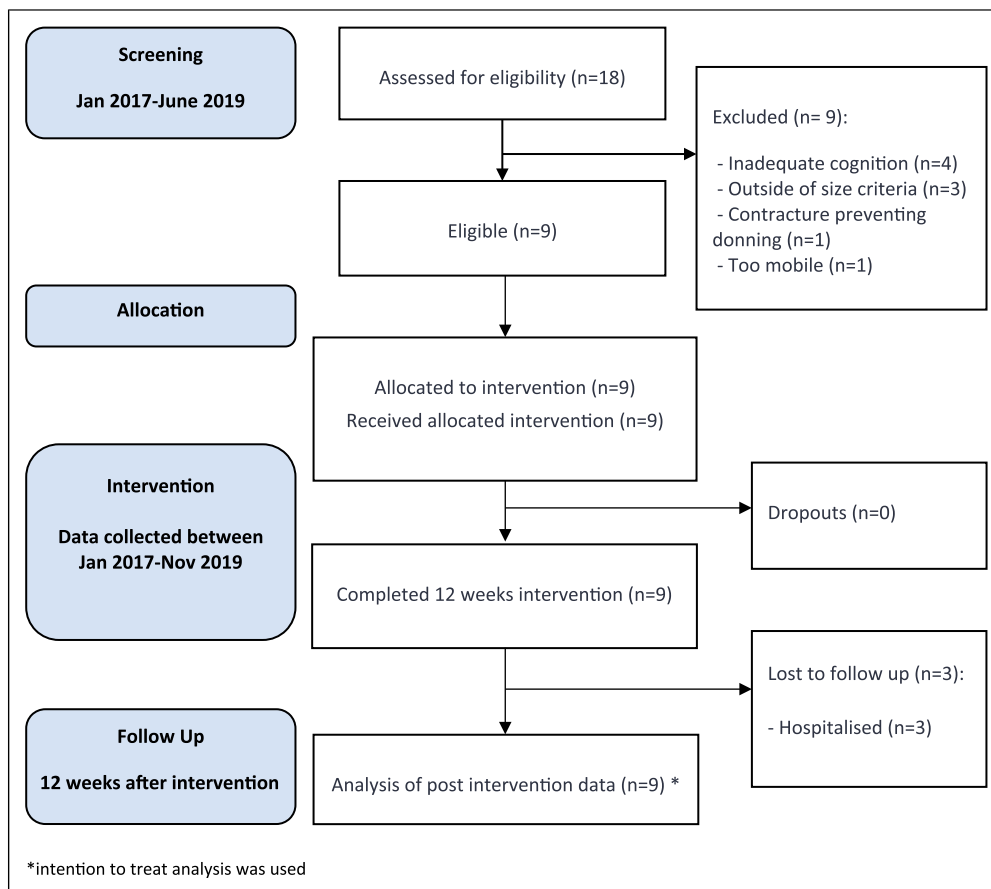


Figure 1. Flow of participants through the study.

Results

Participants

Of eighteen potential candidates referred for assessment, nine participants were recruited. The main reasons for exclusion were inadequate cognition ($n=4$), and not meeting the size criteria for the exoskeleton ($n=3$) (see [Figure 1](#) for the flow of participants through the study). There was 100% completion of the 24 intervention sessions, but due to hospitalisation, three could not attend their 12 weeks follow up evaluation.

The median age of participants was 55 years (IQR = 48, 71), and there was a ratio of seven males to two females. Eight participants could transfer into the device from a standing position with assistance; the remaining participant required the use of the mechanical hoist for transfers. The median time since stroke was 1 year (IQR = 0.58, 1.42) and most participants had moderate to moderately severe disability³⁷ (median mRS = 4/5, IQR = 3, 4). The median MoCA score upon enrolment was 25/30 (IQR = 22, 25) (see [Table 1](#) for a summary of demographic data). The median time taken to complete the 24 sessions was 14 weeks (IQR = 12.7, 16), with variation due to participant or researcher illness, public holidays, and operational issues with the device. There were no adverse events throughout the study.

Motor function

Baseline MAS scores ranged from 4-26, and in the enrolment-pre-intervention period (0-12 weeks) there was a median change of 0 (IQR = -2, 3). There was an overall pre-post-intervention (12-24 weeks) median improvement of one on the summed MAS items (IQR = 0, 1; [Figure 2](#);

[Table 2](#)). In all but one participant, improvement occurred in the first half of the intervention phase (12-18 weeks) (median change = 1, IQR = 0, 2), rather than the second half (18-24 weeks) (median change = 0, IQR = -1, 1). The differences between change scores in each study phase were not statistically significant ($n = 9$, $p = 0.08$). As demonstrated in [Figure 2](#), five of the nine participants had a change in the MAS, while the other four did not. Four of the five had the lowest MAS scores upon enrolment (≤ 17), and further analysis revealed a median change of two for those participants (IQR = 1, 3.75) compared to the five with higher baseline MAS scores (median change = 0, IQR = 0, 0; [Figure 2](#)). No change in the median MAS score was seen during the follow up phase (24-36 weeks) (median change = 0, IQR = 0, 0).

Other impairment-based outcomes

The nine participants were able to complete all the included outcome measures, except for FTSST ($n=7$) and FR ($n=7$), as two participants were unable to complete those tests without physical assistance. Changes were inconsistent both between participants and across time points for the FR, FTSST, grip strength (unaffected limbs) and strength in the unaffected quadriceps (see [Table 2](#) for a summary of impairment-based outcomes). A statistically significant difference was found between time points for grip strength (affected limb) ($p = 0.03$) with the greatest improvement found from 12-24 weeks (median change = 1 kg, IQR = 0, 2). There was a statistically significant difference between time points for the affected quadriceps ($p = 0.01$), with improvements found from 0-12 weeks (median change = 4 kg, IQR = 2, 7.5) and 24-36 weeks (median change = 3 kg, IQR = 0, 4).

Table 1. Baseline characteristics of participants.

Participant	Sex	Age	Time since diagnosis (years)	Stroke region	Level of disability (modified rankin score)	Mobility status	Enrolment motor assessment scale score (/30)
1	M	48	0.5	Non-dominant	4	Quad stick	14
2	M	74	0.6	Non-dominant	4	Quad stick	18
3	M	55	6	Dominant	3	Quad stick	17
4	M	67	1	Non-dominant	3	Quad stick	19
5	M	53	1.4	Non-dominant	3	Quad stick	19
6	M	76	7	Both hemispheres	3	4 wheeled frame	24
7	F	43	1	Dominant	4	4 wheeled frame	26
8	M	71	0.4	Non-dominant	4	Quad stick	14
9	F	45	1.2	Brainstem	5	Sling lifter	4
Median (IQR)	—	55 (48, 71)	1 (0.6, 1.4)	—	4 (3, 4)	—	25 (22, 25)

Legend: M—Male, F—Female, IQR—interquartile range.

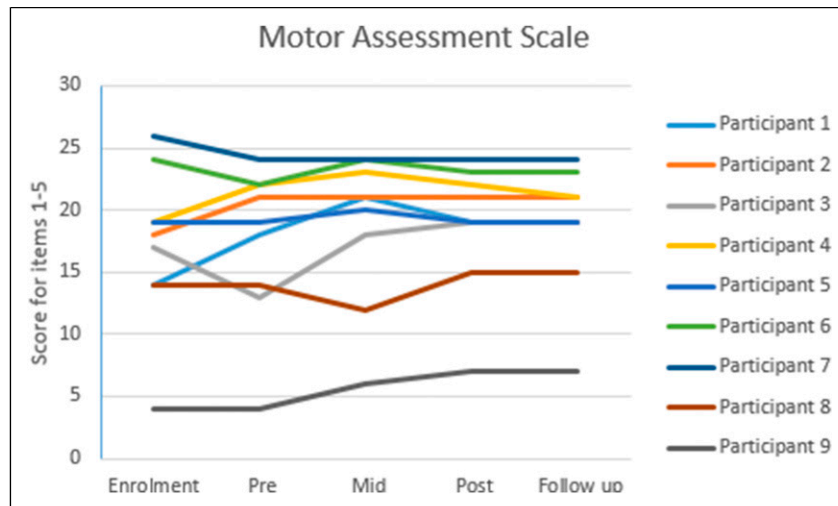


Figure 2. Motor assessment scale scores throughout the study for each participant.

Other health-related outcomes

A statistically significant difference was found between time points for independence with ADLs ($p = 0.01$), with the only change found between 12–24 weeks (median change = 5, IQR = 0, 10; Figure 3). No further statistically significant changes were demonstrated. There were positive trends in both mood and fatigue during the intervention phase (12–24 weeks) which were not seen in the wait (0–12 weeks) or follow up (24–36 weeks) phases. The use of anti-fatigue and anti-depressant medication in some participants may have confounded these results. There was also a positive, but not statistically significant, trend in the wait phase (0–12 weeks) for health-related QoL. See Table 3 for a summary of other health-related outcomes.

Use of services and equipment

All nine participants used formal care services to support them at home. Over the course of the intervention phase (12–24 weeks), one participant decreased and then ceased use of a mechanical sling lifter, and increased use of a stand-assist device. The same participant also decreased reliance on support services, no longer requiring 24-h care. Due to a change in home circumstances, another participant started having increased support over the weekends during the intervention phase.

Acceptability

Participants were generally positive about the therapy they received in the device. Positive responses were grouped into physical benefits, including the

experience of more ‘normal’ movement, and experiences different to those in conventional physiotherapy; and emotional and cognitive benefits such as confidence, motivation and improved focus. The disliked features of the therapy were separated into device specific comments such as the slowness and robotic nature of the movement; and comments relating to the dosage of the intervention. See Table 4 for responses to open survey questions. Participants responded to survey questions with a median score of 69/80 (IQR 63, 72) at the beginning of the intervention phase (week 12), and 74 (IQR 56, 77) when asked the questions again at the end of the intervention phase (week 24). There was no change in this score at follow up (week 36). When asked at the end of the intervention “Given the opportunity, would you like to continue receiving therapy in the device?”, participants scored a median of 4/5 (IQR = 3, 5) where one was “definitely not”, and five was “definitely”. Across all survey domains, the median score was at least 80% of the maximum. The lowest scoring domain was ‘comfort’, with a median score of 20/25 throughout the intervention phase. See Table 5 for a summary of scores for each survey domain.

Device performance

Throughout the study, there were eight occasions where faults with the device required engineering intervention. The most common issue was hip actuators requiring replacement (five times). Other issues included loose

Table 2. Impairment based outcomes.

Outcome	Enrolment - pre-intervention (0–12 weeks)		Pre – mid-intervention (12–18 weeks)		Mid – post-intervention (18–24 weeks)		Pre-post intervention (12–24 weeks)		Follow up (24–36 weeks)		Analysis	
	Median (IQR)	I (0, 3)	Median (IQR)	I (0, 2)	Median (IQR)	I (-1, 1)	Median (IQR)	I (0, 1)	Median (IQR)	I (0, 0)	Q statistic	p value
Motor assessment scale (n=9)	3.5 (-3.5, 3.5)		0.5 (0, 3)		-1 (-3.5, 0)		0 (-1, 3.5)		0 (0, 3)		8.20	0.08
Functional reach: Unaffected limb (n=7)	-4.11 (-7.56, -0.33)		1.1 (-4.89, 8.02)		-0.92 (-6.7, 1.5)		-0.55 (-3.04, 0.38)		3.21 (0, 4.91)		7.30	0.12
5x sit to stand (n=7)	0 (-0.5, 1)		0 (0.5, 2)		0 (-0.5, 0.5)		1 (0, 2)		0.5 (0, 1)		10.88	0.03**
Grip strength: Affected limb (n=9)	0 (1, 4)		-1 (-3, 2)		0 (-4, 3)		0 (-2, 2)		0 (0, 2)		0.42	0.98
Grip strength: Unaffected limb (n=9)	4 (2, 7.5)		0 (-1, 4)		-2 (-6, 0)		-2 (-3, 2)		1 (0, 4)		12.35	0.01**
Quadriceps strength: Affected limb (n=9)	-1 (-2, 5)		0 (-1, 2)		1 (-4, 4)		0 (-4, 4)		0 (0, 4)		1.80	0.77
Quadriceps strength: Unaffected limb (n=9)												

IQR=interquartile range; ** - statistically significant.

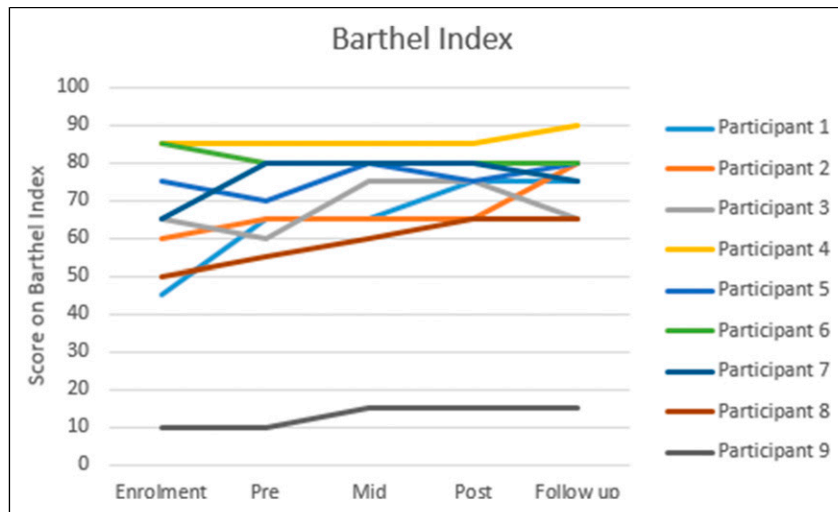


Figure 3. Barthel index scores throughout the study for each participant.

Table 3. Other health-related outcomes.

	Enrolment – pre-intervention (0–12 weeks)	Pre – mid-intervention (12–18 weeks)	Mid – post-intervention (18–24 weeks)	Pre-post intervention (12–24 weeks)<	Follow up (24–36 weeks)	Analysis	
Outcome (n=9)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Q statistic	p value
Fatigue assessment scale	1 (–1, 2)	–3 (–5, 0)	0 (–1, 2)	–1 (–3, 0)	0 (–1, 0)	5.64	0.23
Short form 8	–3 (–8, –1)	–1 (–3, 2)	1 (0, 3)	0 (–2, 2)	0 (–3, 0)	5.18	0.27
Hospital anxiety and depression scale	0 (–2, 1)	–4 (–1, 1)	0 (–5, 1)	–2 (–4, 1)	0 (–1, 0)	5.56	0.23
Barthel index	0 (–5, 5)	0 (0, 5)	0 (0, 0)	5 (0, 10)	0 (0, 5)	12.77	0.01**

IQR=interquartile range; ** - statistically significant.
Use of services and equipment.

joystick arm (compromising cabling), limbs touching each other during swing phase, ankle wiring, cracking noises, and one episode involving the thigh casing cracking.

Discussion

The results of this study have shown that there is potential for this treatment modality to benefit those with severe mobility impairment post stroke. There was post-intervention improvement in the primary outcome of motor function, particularly in those with the most severe mobility impairment at enrolment, but results were

inconsistent for other impairment-based outcomes, such as strength and balance. There were, however, some positive results in the other health-related measures of mood, fatigue and independence with ADLs, and this treatment modality is acceptable to people with stroke.

Improvements in motor function appear to be due to the intervention, with change in median scores only occurring during the intervention phase. This improvement is more apparent in those with the lowest MAS scores upon enrolment, as of the nine participants in this study, the four with the lowest MAS scores upon enrolment were the ones who gained the most during the intervention, with only one of them making any gains in the wait phase, and none

Table 4. Responses to open survey questions.

	“Liked”		“Disliked”
Physical benefits	a) Standing on right side	Device related	a) Too slow (x7) ^a
a) ‘Normal’ movement	Good for even weight-bearing to exercise Freer movement that day and the next	a) Speed b) Movement c) Size	b) Squats are too small Side steps small – would like bigger for stretch Knees didn’t bend when walking - unnatural Rigid
b) Compared to conventional physiotherapy	Increased core strength No pain Moving around Standing up straight Walking and squatting a) Whole muscles work even stomach muscles b) Provides exercise for things you wouldn’t normally do, e.g. walking backwards/sideways I could walk and stand Gave me the ability to walk and squat		c) Very big
Emotional and cognitive benefits	a) Increased confidence with balance Focus on better gait pattern and confidence with that	Design of study/dosage	Not long enough in each session Not often enough – daily sessions would be better
a) Confidence/safety	Exercise in a controlled manner		
b) Focus	b) Think about how to move		
c) Motivation/optimism	c) Positive steps forwards		
d) General	Made me feel invincible Chance to be out of my wheelchair d) Good		

Responses at both post-intervention and follow up grouped according to themes

^a - this comment was made seven times.

Table 5. Scores for each survey domain.

n=9	Pre-intervention (week 12) Median (IQR)	Mid-intervention (week 18) Median (IQR)	Post-intervention (week 24) Median (IQR)	Follow up (week 36) Median (IQR)
Perceived safety/15	13 (12, 15)	15 (13, 15)	15 (12, 15)	15 (12, 15)
Likability/20	19 (17, 20)	18 (17, 19)	18 (15, 20)	17 (15, 20)
Comfort/25	20 (18, 23)	20 (18, 21)	20 (16, 25)	23 (16, 24)
Usability/15	12 (11, 13)	13 (12, 14)	14 (11, 15)	14 (9, 15)
Continue use/5	5 (5, 5)	5 (4, 5)	4 (3, 5)	4 (4, 5)
Total score/80	69 (63, 72)	71 (64, 73)	74 (56, 77)	74 (55, 78)

Higher scores indicate positivity.

changing in the follow up phase. A primary aim of this study was to address the gap in neuro-rehabilitation for the most severely mobility impaired, and this treatment modality seems to offer a potential option to this type of patient, with analysis revealing that for most participants the majority of this gain was in the first half of the intervention phase. We hypothesise that this may be due to the device providing a

new experience of movement which the participants could not have outside of the device. In the context of traditional rehabilitation this is promising, in that using this modality for a burst of therapy may be a useful adjunct to a neuro-rehabilitation program. As there is no established minimum clinically important difference (MCID) for the MAS, a median improvement of 2/30 for the most severely mobility

impaired participants, and 1/30 for the full sample, must be interpreted with caution, particularly in the absence of statistical significance, as the MAS has been shown to have greatest sensitivity for item five, walking,³⁸ and only one participant improved on this section, by one point. The remaining four sections analysed are less sensitive to change,³⁸ and meaningful changes may therefore have been missed. However, with one of these participants no longer requiring a mechanical hoist for transfers, and the group not changing significantly outside of the intervention phase, the improvement seen in this measure can be attributed to the intervention. With the improvements being maintained at follow up it could be argued that this may offer an alternative to traditional therapy for those with very limited mobility, over the short-term.

Across the remaining impairment-based outcome measures, results were inconsistent between participants and across time points. There was an improvement in grip strength in the affected limb, which may support the overall improvement in motor function, but as the change was less than 5 kg, it is unlikely to be clinically important.³⁹ Two of the exercises used in the robotic therapy sessions were sit to stand, and squats, both of which are used in traditional physiotherapy to increase quads strength. Research into the kinematics of this device has shown, however, that the device's movement does not correlate with normal human movement, which may hamper the ability of the device to influence lower limb strength.²³ The fact that our results only demonstrated improvement in strength of the affected quadriceps muscles outside of the intervention phase would support this. Due to the very supportive nature of this device, it is also likely that the device does not allow enough perturbation or trunk deviation to influence the user's balance. The results of this study for these outcomes are perhaps, therefore, not surprising.

There was post-intervention improvement in levels of independence with ADLs, and with no change outside of the intervention phase these results can be attributed to the exoskeletal therapy. Although statistically significant, the median improvement of five in the BI does not reach the 20 points change required to achieve clinical significance.³⁷ However, considering the severity of their mobility impairment, a change of five points may be meaningful to the participants. Positive changes in median scores seen during the intervention phase in fatigue and mood did not reach statistical significance and may have been confounded by the use of anti-fatigue and anti-depressant medication in two participants. Quality of life is a high priority for those with stroke,⁴⁰ and an improvement in SF-8 scores during the wait phase was consistent among all participants. As previously suggested by Lam et al.⁴¹ this reflects improved motivation in anticipation for starting the novel technology-focused therapy, particularly since with a median time since stroke of 1 year, most participants had previously undertaken

considerable amounts of rehabilitation. Interestingly these results did not then change throughout the remainder of the study. However, with inconsistency among results, lack of statistical significance, and potential confounding factors which were not controlled for, the positive findings in other health-related outcomes must be interpreted with caution.

This type of intervention is likely only appropriate for a small subset of the population of people with stroke, but for those who participated in this study, this treatment modality was accepted from the beginning of the intervention phase. Anecdotally, clinicians have anticipated that particularly older people with stroke may be anxious about using such a new and possibly confronting treatment modality, and it is possible some potential participants chose not to volunteer for the study for this reason. Although the device is large and bulky, a comment which was made by one participant, this did not appear to be a concern for any of the others. The fact that comfort was the lowest scoring survey domain is probably not surprising, given that this device requires the user to be strapped in very tightly, but must be considered given the high priority placed on comfort by users of exoskeletons.⁴² The remaining negative comments were either around speed of movement or the nature of the movement in the device but seemed to be outweighed by the positivity felt by having an opportunity to try a different type of therapy and being supported in an upright position without the risk of falling. This is a difference between the REX and all other devices and may improve accessibility of this type of therapy to those with more severe impairments post-stroke. Our findings are supported by those in a survey of people with spinal cord injury using the Ekso device,⁴³ which also found that users liked and felt benefit from this type of treatment modality. Our positive findings were reinforced by the full completion of all intervention sessions, no dropouts, and no adverse events. The loss of three participants to follow up was due to hospitalisation, unrelated to the therapy in all cases, which is not unusual with this clinical population.

This study benefitted from a long intervention phase, and 12 weeks follow up period. A wide range of commonly used, validated outcome measures were chosen, rather than just gait parameters, as previous research into the use of overground lower limb robotic exoskeletons has lacked breadth of outcome measures,²⁰ and in those with severe mobility impairment post-stroke, changes in gait are not necessarily expected. It is possible that the use of measures of gait parameters may have revealed useful findings, particularly as the most impaired participants gained the most in terms of motor function. However, with only one participant improving in the walking component of the MAS, it could be argued that the selected outcomes were an appropriate choice. Although all participants completed the intended dosage of therapy this often occurred with disruption, with the total treatment period extending beyond 12 weeks. This disruption to the delivery of the intervention

was partly due to therapist and participant illness. While this cannot be helped, future research would benefit from having more than one trained therapist to deliver the intervention. Intervention delivery was also disrupted due to the device requiring maintenance on multiple occasions. The reliability of the device is a concern in terms of adopting this modality into clinical settings. The authors suggest that improving comfort, the amount to which the device can be adjusted (better hip width, deeper and wider thigh and shin cuffs, to accommodate different sized people), device reliability (actuator durability, casing strength, reliable movement patterns), improved speed to replicate a more typical gait pattern, variable assist to encourage users to actively participate as much as possible, and a more operator friendly method to hold onto the device, would be desirable improvements to this technology. It would also be pertinent to identify the perspectives of therapists who have experience in using such devices, to determine what the barriers to implementation may be. A qualitative study with this aim has been conducted by this research team, with publication forthcoming.

This study has not been able to demonstrate that exercise with a free-standing exoskeleton is feasible in the clinical setting. Any positive findings in this study cannot be considered outside of the context of how difficult recruitment was, with 50% of potential recruits being ineligible, and a resultant small sample size despite an extensive recruitment campaign and duration, which suggests limited possible application in the clinical setting. Positive benefits may not have been seen due to possible inadequate dose of treatment, inadequate intensity of treatment, and confounding factors in a small sample study. The wait phase demonstrated that this sample was not stable in terms of motor function and other commonly used neuro-rehabilitation outcomes, which makes interpretation of post-intervention change difficult. Although the use of a home exercise program may have confounded the results, this is a typical component of all therapeutic exercise programs. As severe strokes leading to extensive cortical damage often affect language and cognition, some potential participants did not have adequate cognition to be eligible, a consideration for not just research, but also the clinical setting. The time it takes to get a participant in and out of the device varies, with the most impaired needing assistance of two or a sling lifter. This means a quick exit if a person becomes unwell or distressed is almost impossible. Having adequate cognition to be able to communicate concerns is therefore a high priority in users of this type of treatment modality and limits the clinical application further. We did not endeavor to undertake a cost-benefit analysis. However, the clinical benefit in terms of health effects needs to be evaluated in relation to the cost of delivering the therapy and is warranted in future investigations. Further research with a powered sample, a control group or crossover design and higher dosage, is needed to further explore the potential merits

of therapy with this device. Using the results from our primary outcome measure, with statistical significance set at 0.05, and a power of 0.8, a sample size of 57 would be required.

Conclusions

This study has revealed improvements in motor function, particularly in the most severely impaired participants, and in independence with ADLs, and affected limb grip strength. However, with a small sample, inconsistency in findings between and across subjects, and limited accessibility to potential users due to the necessarily strict inclusion criteria, these findings must be interpreted with caution. While we have not provided enough evidence to recommend the use of this device in clinical settings, acceptability appears high in a limited cohort of patients with severe mobility impairment due to chronic stroke. To improve clinical application, devices need to be made more accessible to patients, and reliable.

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NP.

Contributorship

NP and JM researched the literature and conceived the study. AB and NS were involved in protocol development, and gaining ethics approval, with NP and JM. CM and JG were involved in data analysis and writing the first draft of the manuscript with NP. NP was responsible for participant recruitment, and data collection. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Clinical trial registry

This study was registered with the Australian New Zealand Clinical Trials Registry, <https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372168&isClinicalTrial=False>, ACTRN12617000093381.

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Appendix I

Participant perception of therapy using HELLEN
Perceived safety.

Please rate your emotions about using HELLEN.

Anxious	1	2	3	4	5	Relaxed
Agitated	1	2	3	4	5	Calm
Pessimistic	1	2	3	4	5	Optimistic

TOTAL /15 =

Likeability.

Please rate your emotions about using HELLEN.

Dislike	1	2	3	4	5	Like
Awful	1	2	3	4	5	Pleasant
Discouraging	1	2	3	4	5	Motivating
Depressing	1	2	3	4	5	Confidence building

TOTAL /20 =

Comfort

Please rate your impression of HELLEN.

Constricted	1	2	3	4	5	Free
Uncomfortable	1	2	3	4	5	Comfortable
Cumbersome	1	2	3	4	5	Manageable
Cumbersome	1	2	3	4	5	Pain Free
Cumbersome	1	2	3	4	5	Invigorating

TOTAL /25 =

Useability.

Please rate your impression of HELLEN.

Complex to adjust	1	2	3	4	5	Easy to adjust
Of no benefit	1	2	3	4	5	Beneficial
Time intensive	1	2	3	4	5	Quick

TOTAL /25 =

Given the opportunity, would you like to continue receiving therapy in HELLEN?

Definitely not	1	2	3	4	5	Definitely not
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TOTAL /5 =

TOTAL /80 =

Please tell us what you **liked** about using HELLEN to assist your therapy

Please tell us what you **disliked** about using HELLEN to assist your therapy: