Original Research

Locomotor Training and Strength and Balance Exercises for Walking Recovery After Stroke: Response to Number of Training Sessions

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Background. Evidence-based guidelines are needed to inform rehabilitation practice, including the effect of number of exercise training sessions on recovery of walking ability after stroke.

Objective. The objective of this study was to determine the response to increasing number of training sessions of 2 interventions—locomotor training and strength and balance exercises—on poststroke walking recovery.

Design. This is a secondary analysis of the Locomotor Experience Applied Post-Stroke (LEAPS) randomized controlled trial.

Setting. Six rehabilitation sites in California and Florida and participants' homes were used.

Participants. Participants were adults who dwelled in the community (N=347), had had a stroke, were able to walk at least 3 m (10 ft) with assistance, and had completed the required number of intervention sessions.

Intervention. Participants received 36 sessions (3 times per week for 12 weeks), 90 minutes in duration, of locomotor training (gait training on a treadmill with body-weight support and overground training) or strength and balance training.

Measurements. Walking speed, as measured by the 10-Meter Walk Test, and 6-minute walking distance were assessed before training and following 12, 24, and 36 intervention sessions.

Results. Participants at 2 and 6 months after stroke gained in gait speed and walking endurance after up to 36 sessions of treatment, but the rate of gain diminished steadily and, on average, was very low during the 25- to 36-session epoch, regardless of treatment type or severity of impairment.

Limitations. Results may not generalize to people who are unable to initiate a step at 2 months after stroke or people with severe cardiac disease.

Conclusions. In general, people who dwelled in the community showed improvements in gait speed and walking distance with up to 36 sessions of locomotor training or strength and balance exercises at both 2 and 6 months after stroke. However, gains beyond 24 sessions tended to be very modest. The tracking of individual response trajectories is imperative in planning treatment.

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Dose is a critical parameter contributing to the effectiveness of therapeutic interventions for motor and behavioral recovery after stroke.[1-4] Exercise parameters that contribute to a dose-response relationship in physical rehabilitation consist of frequency (number of training sessions per week), intensity (cardiopulmonary workload), duration (total number of treatment sessions) and type.[5] The National Center for Medical Rehabilitation Research claimed an essential need for evidence-based guidelines to inform rehabilitation practice relative to intervention timing, intensity, and duration for people after stroke.[6] More recently, a Cochrane review called for research to specifically investigate the effects of different durations of gait training employing treadmill with body-weight support on walking recovery after stroke.[7]

Intervention response must be examined in the context of relevant and functionally important outcomes. Gait speed is regarded as a significant, sensitive, and reliable marker of deficit severity and functional community walking ability.[8-13] Additionally, although stroke survivors often achieve sufficient recovery to perform some limited walking, the ability to walk longer distances, as needed for community ambulation, often remains compromised. Therefore, walking distance is also an important and functionally relevant outcome measure to assess when examining the dose-response relationship. Thirdly, as a return to home and community ambulation is a primary rehabilitation goal for many survivors after stroke,[14] recording steps taken outside of the clinic or laboratory setting is informative to determine if gait speed and endurance improvements are translated into a patient's daily life.

The design of the multisite, Phase III Locomotor Experience Applied Post-Stroke (LEAPS) randomized controlled trial,[15] provides an opportunity to examine intervention response in relationship to number of intervention sessions completed. The trial's primary analysis determined that the task-specific LTP program, provided 2 or 6 months after stroke, was not superior in improving walking ability compared to the impairment-focused home exercise program (HEP).[15] Both interventions resulted in over 50% of the study population improving walking ability, defined as transitioning to a higher functional walking level based on gait speed at 1-year after stroke (eg, from severe to moderate impairment or from moderate to mild impairment). Secondary analyses of the LEAPS trial data determined that LTP and HEP were more effective than usual care physical therapy in improving walking ability at 6 months after stroke[16] and that a younger age and higher Berg Balance Scale score were predictors of response to the trial intervention.[17] The LEAPS randomized controlled trial was also designed to specifically examine the dose-response relationship, defined by number of training sessions, to successive epochs of physical therapy, from 12 to 24 to 36 cumulative sessions, on walking outcomes.

The number of training sessions for the LEAPS trial was based on preliminary work on locomotor training indicating efficacy,[18] impairment-based training indicating efficacy,[19] and relevance of frequency (eg, 3 times per week) to current clinical practice after discharge from acute rehabilitation. The relationship of number of training sessions to intervention timing (ie, point of delivery after stroke) and stroke severity is also relevant to rehabilitation effectiveness and thus to treatment planning.[20-22] Greater number of sessions may improve outcomes, but the effect of increasing the number of sessions may also depend on timing of intervention delivery and initial severity of impairment.

The goal of this secondary analysis is to investigate the response to number of training sessions on walking outcomes and targets 2 questions to inform rehabilitation practice. First, "Does a successively greater number of intervention sessions result in a greater improvement in walking speed and walking distance?" Second, "Does severity of initial walking impairment interact with number of sessions, such that people with greater walking impairment benefit from more sessions when comparing (a) interventions (HEP and LTP) or (b) timing of intervention delivery (E-LTP and L-LTP)?

Methods

Design Overview

The LEAPS trial was a multicenter, single-blind randomized controlled trial, with participants stratified by 2-month poststroke walking impairment (severe, <0.40 m/s; moderate, 0.40–0.79 m/s), and randomized to the E-LTP, L-LTP, or HEP groups (proportions 7:6:7). The LEAPS protocol is described at clinicaltrials.gov and has been reported previously.[23] Ethics review boards at all participating centers approved the protocol. All participants provided written informed consent. An independent medical monitor and a data safety monitoring board appointed by the National Institutes of Health oversaw the conduct, safety, and efficacy of the trial and monitored adverse events.

Setting and Participants

Participants were recruited from 6 inpatient rehabilitation sites in California and Florida. Inclusion criteria were age ≥ 18 years; stroke within 45 days and ability to be randomized at 2 months after stroke; residual paresis in the lower extremity; ability to walk 3 meters (10 ft) with no more than 1-person assistance; ability to follow a 3-step command; physician approval for participation; self-selected 10-m walking speed of less than 0.8 m/s; and living in the community at the time of randomization. The primary criteria for exclusion were dependency on assistance in activities of daily living before the stroke, exercise contraindications, preexisting neurological disorders, and inability to travel to the treatment site.[23] Although the primary LEAPS trial analysis was an intent-to-treat analysis and thus the data were imputed when necessary, the present analysis of response in relation to number of training sessions used solely the data from participants receiving the required number of sessions. Thus, only participants who received a total of 30 to 36 sessions and had walking speed measurements after 12, 24, and 30 to 36 sessions of intervention were included and defined as "completers." For the primary LEAPS analysis, a minimum of 30 sessions was

necessary for the intervention to be considered complete.

Randomization and Interventions

The LTP and HEP programs were delivered 3 times per week for 90-minute sessions over a 12- to 16-week period for a total of 30 to 36 sessions. Intervention protocols have been previously reported.[23] LTP included task-specific walking training on a treadmill with partial body weight support. The aim of the first session was to train at a maximum of 40% body-weight support, with a minimal speed of 0.89 m/s, with manual assistance as needed for proper kinematics for a total duration of 20 minutes (four 5-minute bouts) of stepping, followed by a progressive overground walking program for 15 minutes. The long-term aim of the LTP was for participants to be able to walk independently at 0% body-weight support, within a range of 0.89 m/s to 1.34 m/s with a maximum goal of independent stepping for 30 continuous minutes. Progression parameters included stepping duration, speed, weight-bearing load, and level of assistance. The home exercise programs included progressive flexibility, range of motion, upper- and lower-extremity strengthening, coordination, and static and dynamic balance exercises provided by a physical therapist in the home.

Common to both interventions was that participants were continually challenged and progressed. For LTP, at least 1 of the training parameters (stepping duration, speed, weight-bearing load or level of assistance) was progressed at each intervention session. For HEP, at least 1 of the exercises was progressed with either an increased number of repetitions or, for the strengthening exercises, level of resistance. Progression was individualized for each participant across the 36 sessions based on their initial ability and needs. Progression guidelines for both interventions were maintained throughout the course of the LEAPS trial and did not change with epoch of treatment (first, second, and third wk; 12 weeks). In addition to the LTP and HEP interventions, all participants were allowed to receive any prescribed usual and customary care during the trial intervention. Study participants were not to engage in gait training on a treadmill with body-weight support, but no other restrictions were placed on the type or amount of usual care.[24]

Outcomes and Follow-up

This secondary analysis used the LEAPS randomized controlled trial data from pretraining (2 months after stroke for E-LTP and HEP and 6 months after stroke for L-LTP), and after 12, 24, and 30 to 36 intervention sessions. Changes in 10-m walking speed[25] and distance walked in 6 minutes[26] were assessed after each successive round of 12 intervention sessions. Methods for obtaining these 2 measurements have been reported previously.[24, 27]

Data Analysis

To assess the effect of intervention group, number of training sessions (12, 24, and 36), impairment severity and their interactions, longitudinal analyses (PROC GLIMMIX in SAS) were performed on each of the outcomes (walking speed and walking distance), including a random subject effect. For each dependent variable, 12 linear contrast tests were performed to assess the effect of intervention group (comparing the HEP vs E-LTP and E-LTP vs L-LTP) by number of training sessions and impairment severity. Similarly, 18 linear contrasts were tested to assess the changes from pretraining to 12th session, 12th to 24th sessions, and 24th to 36th sessions by intervention group and severity. Lastly, 3 linear contrast tests for each of the outcomes were performed to assess the difference between the moderate and severe group on the change of each outcome values from pretraining to 12th session, 12th to 24th sessions, and 24th to 36th sessions.

To adjust for multiple testing, step-down procedures were applied to the n (=3, 12, and 18) contrast tests for each independent variable.[28] More specifically, the P values were sorted in increasing order: $P_{(1)}, \ldots, P_{(n)}$. We compared $P_{(k)}$ with .05/(n+1-k) and identified the smallest k satisfying $P_{(k)} > .05/(n+1-k)$. The first (k-1) P values were considered to be statistically significant. SAS software (SAS, Cary, North Carolina), version 9.1, was used to perform all statistical analyses.

Role of the Funding Source

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Results

From the original LEAPS randomized controlled trial cohort of 408 participants, 347 (85%) completed 30 to 36 intervention sessions and were identified as "completers." Compared to noncompleters (n=61; 15%), completers had the following baseline characteristics: fewer hospitalizations, greater proportion of large vessel distribution stroke, shorter Trail-Making Test time, better Wechsler Adult Intelligence Scale (WAIS) digit symbol subscale, lower prevalence of diabetes, lower age at stroke onset, and fewer falls. The remaining analyses were conducted on those identified as completers. The cohort was equally distributed across the 3 training groups: HEP=34.0%, E-LTP=33.7%, and L-LTP=32.3% (Tab. 1). Whereas the baseline characteristics of the 3 treatment groups were balanced in the primary LEAPS analysis,[15] in the present analysis of the completer subgroup, participants in the E-LTP group were younger, had higher NIHSS score, and had lower extremity Fugl-Meyer (LEFM) sensory and motor scores compared to the other 2 groups ($P < .05$).

Progression of the Intervention

As dictated by the study design, participants were continually challenged and progressed throughout the 36 sessions. For those in the 2 LTP groups, the training parameters of total minutes of stepping on the treadmill per session, minimum percent body-weight support

Table 1.
Summary of 2-Month Baseline Variables for LEAPS Participants (N=347) Who Completed the Intervention.

Variable		Value for Completers
Sex	Men, no. (%)	189 (54.5)
	Women, no. (%)	158 (45.5)
Age at stroke onset, y, mean (SD)		61.4 (13.0)
Race, no. (%)	Asian	46 (13.3)
	Black or African American	72 (20.7)
	White	205 (59.1)
	Other	24 (6.9)
Ethnicity, no. (%)	Hispanic or Latino	55 (15.9)
	Non-Hispanic or Latino	292 (84.1)
Education, no. (%)	<High school	74 (21.3)
	High school, GED	94 (27.1)
	>High school	179 (51.6)
Stroke characteristics Type, no. (%)	Days since stroke to randomization, mean (SD)	63.8 (8.6)
	Large vessel	146 (42.1)
	Lacuna	105 (30.3)
	Hemorrhage	63 (18.2)
	Undefined	33 (9.5)
Side, no. (%)	Left hemiparesis	156 (45.0)
	Right hemiparesis	191 (55.0)
Stroke severity (Modified Rankin Scale), no. (%)	Rankin 0 or 1	2 (0.6)
	Rankin 2	48 (13.8)
	Rankin 3	143 (41.2)
	Rankin 4	154 (44.4)
National Institutes of Health Stroke Scale score, mean (SD)		7.4 (3.8)
Comorbidity, no. (%)	Cardiovascular disease	90 (25.9)
	Hypertension	280 (80.7)
	Peripheral vascular disease	29 (8.4)
	Chronic obstructive pulmonary disease	20 (5.8)
	Arthritis/other musculoskeletal condition	121 (34.9)
	Chronic pain	67 (19.3)
	Sleep problems	81 (23.3)
	Diabetes	110 (31.7)
	Eye disease	87 (25.1)
	Neuropathy	22 (6.3)
Depression (Patient Health Questionnaire score≥10), no. (%)		55 (15.9)
Cognitive status, mean (SD)	Mini-Mental State Examination	26.1 (3.6)
	Trail Making Test part A (s)	90.1 (69.3)
	Trail Making Test part A (errors)	0.5 (1.0)
	Trail Making Test part B (s)	217.9 (106.9)
	Trail Making Test part B (errors)	1.7 (2.0)
	Trail Making Test (B – A) (s)	130.6 (87.1)
	Wechsler Adult Intelligence Scale Digit Symbol Subscale	31.9 (17.0)
Fugl-Meyer Assessment, mean (SD)	Upper extremity motor score	34.2 (20.8)
	Lower extremity motor score	24.2 (6.4)

(Continued)

Table 1.
Continued.

Variable		Value for Completers
	Motor score	58.3 (25.6)
	Sensation score	19.4 (6.0)
Intervention group, no. (%)	Early locomotor training program	117 (33.7)
	Home exercise program	118 (34.0)
	Late locomotor training program (usual care)	112 (32.3)
Severity, no. (%)	Severe	182 (52.4)
	Moderate	165 (47.6)
Step Activity Monitor total steps, median (25th percentile–75th percentile)		1,774 (736–3,615)
Exercise Tolerance Test, mean (SD)	Exercise duration, min	6.0 (2.3)
	Borg Exertion Scale rating	16.1 (3.7)
Berg Balance Scale score, mean (SD)		36.1 (14.0)
Activities-Specific Balance Confidence Scale score, mean (SD)		45.4 (23.9)
Body mass index, mean (SD)		27.5 (5.5)
Fallers, no. (%)	No fall	140 (40.3)
	Single fall	82 (23.6)
	Multiple falls/injurious fall	125 (36.0)
Hospitalization, no. (%)	Yes	98 (28.2)
	No	249 (71.8)

achieved per session, maximum training speed achieved per session, and amount of time spent in overground training per session progressed throughout the intervention period with no plateau. There was a statistically significant difference in all training parameters between sessions 13 to 24 and sessions 25 to 36 ($P < .05$; Tab. 2). Participants in the HEP group were also continually progressed in resistance applied and repetitions completed. Participants progressed from completing limb exercises with gravity reduced, to against gravity, to using resistance bands. They progressed in standing balance exercises from shoulder-width stance, to staggered stance, with eyes open to eyes closed.

Walking Speed Across Session Intervals

Walking speed improved significantly following the initial 12 sessions compared to pretraining within each training group (E-LTP, HEP, and L-LTP) and severity level (moderate and severe). Further significant improvement in walking speed resulted from the second set of 12 sessions (24 total) for all groups except those in the L-LTP group with moderate severity. Walking speed improvement at session 36, relative to walking speed after 24 sessions, was restricted to the E-LTP severe and the L-LTP moderate and severe groups (Tab. 3; Fig. 1). Weak responses during the 24- to 36-session epoch could reflect a reduced number of sessions (30–35) for some participants during this epoch. A regression analysis to determine the effect of additional training sessions after 30 on change in gait speed, including all participants, showed that each session was associated with a 0.011 m/s walking speed change (P=.003).

Walking Distance Across Session Intervals

We observed similar results for walking distance as for speed. Walking distance improved significantly following the initial 12 sessions compared to pretraining within each training group (E-LTP, HEP, and L-LTP) and severity level (moderate and severe). Further significant improvement in walking distance resulted following the second set of 12 sessions (24 total) for all groups except those in the L-LTP group with moderate severity. The improvement in walking distance achieved with 25 to 36 sessions, compared to walking distance at the end of 24 sessions, was only observed in E-LTP severe, HEP moderate, and L-LTP moderate groups (Tab. 3; Fig. 2).

Discussion

We investigated the impact of number of sessions of 2 different exercise interventions in which content and timing of therapy were controlled in a systematic way.[29] This secondary analysis from the completed LEAPS randomized controlled trial examined the immediate relationship between number of training sessions and walking outcomes over 3 successive epochs of 12 intervention sessions (after 12 sessions (18 hours of treatment), 24 sessions (36 hours of treatment), and 30 to 36 sessions (45-54 hours

Table 2.
Progression of Training Parameters of Locomotor Training Program Across Intervention Epochs

Parameter	Summary Statistics, Average ± SD (Range)			Difference Between Sessions 13–24 and Sessions 25–36	
	Sessions 1–12	Sessions 13–24	Sessions 25–36	Model-Based Estimate	*P* Value From Mixed Model
Total minutes of training on treadmill/session	19.0 ± 6.0 (0.7–60.1)	22.1 ± 5.4 (0.3–35.0)	23.0 ± 5.5 (0.2–37.7)	−0.55	.001
Minimum BWS%[a] achieved/session	25.4 ± 8.6 (0.0–55.0)	17.5 ± 9.3 (0.0–65.0)	12.1 ± 8.8 (0.0–45.0)	5.17	<.0001
Maximum training speed achieved/session (mph)	1.84 ± 0.78 (0.40–40.0)	2.06 ± 0.59 (0.50–20.0)	2.12 ± 0.43 (0.50–11.7)	−0.04	.018
Total minutes of training overground/session	16.1 ± 6.7 (1.0–113.0)	16.7 ± 6.6 (1.0–74.0)	17.5 ± 7.5 (1.0–84.0)	−0.87	.001
Average heart rate as a percentage of age-predicted maximum	56.3 ± 10.9	57.1 ± 10.8	57.2 ± 10.8	−0.47	.059

[a] BWS%=body-weight support percentage.

Table 3.
Improvements Across Training Time Periods for the 2 Outcome Variables[a]

Outcome	Group	Severity	Pretraining–12th Session		Sessions 13–24		Sessions 25–36	
			Mean±SD	*P*	Mean±SD	*P*	Mean±SD	*P*
Walking speed (m/s)	E-LTP	Severe	0.12±0.13	**<.0001**	0.07±0.13	<.0001*	0.04±0.08	**<.0001**
		Moderate	0.20±0.15	**<.0001**	0.11±0.13	<.0001*	0.03±0.09	.024
	HEP	Severe	0.11±0.16	**<.0001**	0.07±0.10	<.0001*	0.02±0.12	.008
		Moderate	0.13±0.16	**<.0001**	0.07±0.13	<.0001*	0.01±0.14	.025
	L-LTP	Severe	0.06±0.09	**<.0001**	0.05±0.12	.0001*	0.03±0.10	**.001**
		Moderate	0.11±0.13	**<.0001**	0.03±0.11	.092	0.04±0.13	**<.0001**
Walking distance (m)	E-LTP	Severe	33.6±41.7	**<.0001**	23.6±35.5	<.0001*	12.7±24.5	**<.0001**
		Moderate	54.7±43.2	**<.0001**	38.3±44.1	<.0001*	12.5±36.4	.006
	HEP	Severe	37.0±45.8	**<.0001**	24.2±27.3	<.0001*	3.5±47.6	.074
		Moderate	44.9±47.8	**<.0001**	17.9±37.9	.001*	13.8±46.3	**<.0001**
	L-LTP	Severe	19.8±26.4	**<.0001**	23.4±42.1	<.0001*	4.6±36.5	.014
		Moderate	29.0±33.8	**<.0001**	11.0±36.0	.016	11.1±30.3	**.003**

[a] *P* values of the 18 contrast *t* tests for each outcome were adjusted with a step-down procedure. The significant findings are shown in bold type.

of treatment)), compared across intervention type and level of walking severity.

We found that, at both 2 and 6 months after stroke, participants benefited from up to 24 sessions of locomotor training or strength and balance exercises with the single exception of the L-LTP moderate group, which failed to show significant gains in gait speed during the second 12 treatment epoch. Significant improvements were observed with greater than 24 sessions in severely impaired participants receiving LTP at 2 months after stroke and in both L-LTP groups.

Although participants in all groups continued to increase walking speed with further treatment, up to and including 36 sessions, our data revealed progressively diminishing returns, best illustrated in Figure 2. Walking speed gains during the 25- to 36-session epoch were statistically significant only for the E-LTP severe group and for the L-LTP moderate and severe groups (Tab. 3). These findings for walking speed were substantially paralleled by those for walking distance (Tab. 3, Fig. 2). The

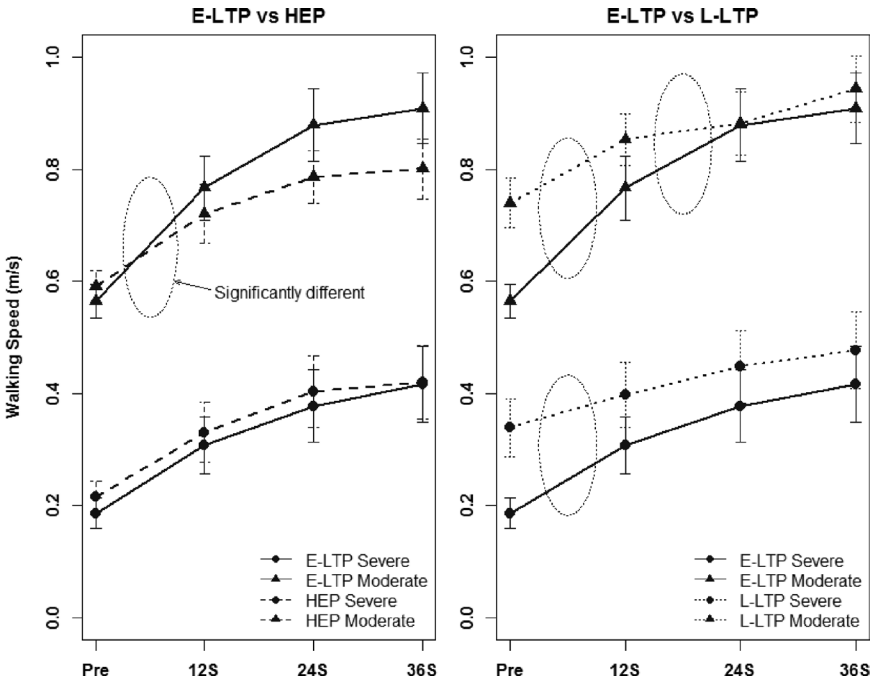

Figure 1.
Walking speed (m/s) improvements by sessions, training groups, and severity, comparing E-LTP to HEP and E-LTP to L-LTP. E-LTP=early locomotor training program, HEP=home exercise program, L-LTP=late locomotor training program, S=sessions. Gains across different groups are compared, and the significant findings are marked by ellipses.

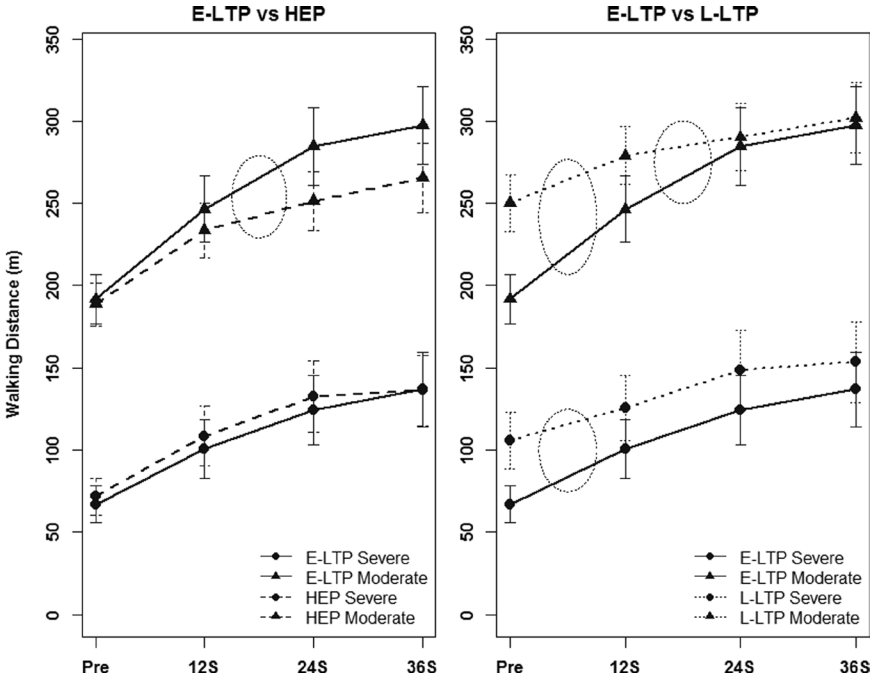

Figure 2.
Improvements in walking distance (m) by sessions, training groups, and severity, comparing E-LTP to HEP and E-LTP to L-LTP. E-LTP=early locomotor training program, HEP=home exercise program, L-LTP=late locomotor training program, S=sessions. Gains across different groups are compared, and the significant findings are marked by ellipses.

results of the regression analysis of gait speed on number of training sessions in the 30 to 36 month epoch suggest that, while additional sessions might, on average, elicit further increases in walking speed, the calculated gain of 0.066 m/s achieved, on average, over 6 sessions would still fall well below the minimal clinically important difference of 0.16 m/s we previously established.[30]

Training parameters were progressed throughout the 36 intervention sessions (Tab. 2). Although the severely impaired group receiving E-LTP were likely to be particularly challenged during the last 12 sessions of treatment, by virtue of the severity of their impairment, their mean absolute gain in walking speed during these sessions, although statistically significant, was only 0.04 m/s (Tab. 3). Thus, the attenuation of therapy effect over the 24- to 36-session epoch seems unlikely be explainable on the basis of a training plateau.

Walking Improvement Beyond 6 Months After Stroke Onset

Walking speed and distance improved for all L-LTP participants through all 3 training epochs with 2 exceptions, as noted (Tab. 3). These improvements in response to an intense, progressive exercise intervention indicate that these participants had not plateaued in their recovery at 6 months after stroke, as is often reported in the stroke literature,[31] but rather remained responsive to an exercise stimulus. It should be noted that participants in the L-LTP group began the study intervention at a higher level of function compared to the E-LTP group (either because of natural recovery, usual care, or both).

Limitations

These results are limited to the 2 interventions studied in the LEAPS randomized controlled trial: locomotor training and an impairment-based program of strength and balance exercises. Additionally, the LEAPS randomized controlled trial only enrolled people who had some ability to ambulate and had passed extensive cardiac screening, including an exercise tolerance test. Of those participants who demonstrated further gains with treatment beyond 24 intervention sessions, we do not

know if more than 36 sessions would be of benefit as the study design precluded determination of a plateau. Finally, the LEAPS trial was designed as a walking recovery, not a cardiac rehabilitation trial. As such, limits were conservatively set on HR response during exercise. HR limitations approved for this protocol may have prevented participants from walking faster, longer, or with greater limb loading, which may have translated into blunted responses.

Conclusions

Understanding the optimal number of sessions of a given therapeutic intervention is critical to the implementation of evidence-based physical therapist practice. This study demonstrated that, in general, adults who dwelled in the community and had some ambulation capability showed improvements in walking recovery after up to 24 sessions of locomotor training or strength and balance exercises at both 2 and 6 months after stroke. Increasing number of treatment sessions yields steadily diminishing returns in terms of improvement in gait speed and walking distance. Even though some groups did exhibit statistically significant gains during the 25- to 36-session treatment epoch, the rate of gait speed gain between 30 and 36 treatments was such that total expected gain during this epoch would be below the minimal clinically important difference of 0.16 m/s. These results point to the imperative of tracking response to treatment over time to accurately assess when individual patients are reaching a plateau.

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Ethics Approval

Ethics review boards at all participating centers approved the protocol. All participants provided written informed consent. An independent medical monitor and a data safety monitoring board appointed by the National Institutes of Health oversaw the conduct, safety, and efficacy of the trial and monitored adverse events.

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Clinical Trial Registration

The trial was registered at ClinicalTrials.gov (registration no. NCT0024391).

Disclosures/Presentations

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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References

1 Cramer SC. Functional imaging in stroke recovery. *Stroke*. 2004;35(11 Suppl 1):2695–2698.

2 Dromerick AW, Lang CE, Birkenmeier RL, et al. Very Early Constraint-Induced Movement during Stroke Rehabilitation (VECTORS): a single-center RCT. *Neurology*. 2009;73:195–201.

3 Kwakkel G, van Peppen R, Wagenaar RC, et al. Effects of augmented exercise therapy time after stroke: a meta-analysis. *Stroke*. 2004;35:2529–2539

4 Sullivan KJ, Brown DA, Klassen T, et al. Effects of task-specific locomotor and strength training in adults who were ambulatory after stroke: results of the steps randomized clinical trial. *Phys Ther*. 2007;87:1580–1602.

5 Thompson WR, Gordon NF, Pescatello LS. *ACSM's Guidelines for Exercise Testing and Prescription*. Philadelphia, PA: Lippincott Williams & Wilkins; 2010.

6 Weinrich M, Good DC, Reding M, et al. Timing, intensity, and duration of rehabilitation for hip fracture and stroke: report of a workshop at the National Center for Medical Rehabilitation Research. *Neurorehabil Neural Repair*. 2004;18:12–28.

7 Mehrholz J, Pohl M, Elsner B. Treadmill training and body weight support for walking after stroke. *Cochrane Database Syst Rev*. 2014;(1):CD002840.

8 Harada N, Chiu V, Damron-Rodriguez J, Fowler E, Siu A, Reuben DB. Screening for balance and mobility impairment in elderly individuals living in residential care facilities. *Phys Ther*. 1995;75:462–469.

9 Kline Mangione K, Craik RL, Lopopolo R, Tomlinson JD, Brenneman SK. Predictors of gait speed in patients after hip fracture. *Physiother Can*. 2008;60:10–18.

10 Perry J, Garrett M, Gronley JK, Mulroy SJ. Classification of walking handicap in the stroke population. *Stroke*. 1995;26:982–989.

11 Steffen TM, Hacker TA, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go test, and gait speeds. *Phys Ther*. 2002;82:128–137.

12 van Iersel MB, Munneke M, Esselink RA, Benraad CE, Olde Rikkert MG. Gait velocity and the Timed-Up-and-Go test were sensitive to changes in mobility in frail elderly patients. *J Clin Epidemiol*. 2008;61:186–191.

13 Wade D. *Measurement in Neurological Rehabilitation*. Oxford, NY: University Press; 1992.

14 Combs SA, Van Puymbroeck M, Altenburger PA, Miller KK, Dierks TA, Schmid AA. Is walking faster or walking farther more important to persons with chronic stroke? *Disabil Rehabil*. 2013;35:860–867.

15 Duncan PW, Sullivan KJ, Behrman AL, et al. Body-weight-supported treadmill rehabilitation after stroke. *New Engl J Med*. 2011;364:2026–2036.

16 Nadeau SE, Wu SS, Dobkin BH, et al. Effects of task-specific and impairment-based training compared with usual care on functional walking ability after inpatient stroke rehabilitation: Leaps Trial. *Neurorehabil Neural Repair*. 2013;27:370–380.

17 Dobkin BH, Nadeau SE, Behrman AL, et al. Prediction of responders for outcome measures of locomotor Experience Applied Post Stroke trial. *J Rehabil Res Dev*. 2014;51:39–50.

18 Plummer P, Behrman AL, Duncan PW, et al. Effects of stroke severity and training duration on locomotor recovery after stroke: a pilot study. *Neurorehabil Neural Repair*. 2007;21:137–151.

19 Duncan P, Studenski S, Richards L, Gollub S, Lai SM, Reker D, et al. Randomized clinical trial of therapeutic exercise in subacute stroke. *Stroke; a journal of cerebral circulation*. 2003;34:2173-2180

20 Moore JL, Roth EJ, Killian C, Hornby TG. Locomotor training improves daily stepping activity and gait efficiency in individuals poststroke who have reached a "plateau" in recovery. *Stroke*. 2010;41:129–135.

21 Partridge C, Mackenzie M, Edwards S, et al. Is dosage of physiotherapy a critical factor in deciding patterns of recovery from stroke: a pragmatic randomized controlled trial. *Physiother Res Int*. 2000;5:230–240.

22 Richards CL, Malouin F, Wood-Dauphinee S, Williams JI, Bouchard JP, Brunet D. Task-specific physical therapy for optimization of gait recovery in acute stroke patients. *Arch Phys Med Rehabil*. 1993;74:612–620.

23 Duncan PW, Sullivan KJ, Behrman AL, et al. Protocol for the Locomotor Experience Applied Post-Stroke (LEAPS) trial: a randomized controlled trial. *BMC Neurol*. 2007;7:39.

24 Duncan PW, Sullivan KJ, Behrman AL, Azen SP, Wu SS, Nadeau SE, et al. Protocol for the locomotor experience applied post-stroke (leaps) trial: A randomized controlled trial. *BMC neurology*. 2007;7:39

25 Eng JJ, Chu KS, Dawson AS, Kim CM, Hepburn KE. Functional walk tests in individuals with stroke - relation to perceived exertion and myocardial exertion. *Stroke*. 2002;33:756-761

26 Guyatt G, Sullivan M, Thompson P, Fallen E, Pugsley S, Taylor D, et al. The 6-minute walk: A new measure of exercise capacity in patients with chronic heart failure. *Can Med Assoc J*. 1985;132:919-923

27 Barak S, Wu SS, Dai Y, Duncan PW, Behrman AL; Locomotor Experience Applied Post-Stroke Investigative Team. Adherence to accelerometry measurement of community ambulation poststroke. *Phys Ther*. 2014;94:101–110.

28 Holm S. A simple sequentially rejective multiple test procedure. *Scand J Statistics*. 1979;6:665–670.

29 Veerbeek JM, Koolstra M, Ket JC, van Wegen EE, Kwakkel G. Effects of augmented exercise therapy on outcome of gait and gait-related activities in the first 6 months after stroke: a meta-analysis. *Stroke*. 2011;42:3311–3315.

30 Tilson JK, Sullivan KJ, Cen SY, et al. Meaningful gait speed improvement during the first 60 days poststroke: minimal clinically important difference. *Phys Ther*. 2010;90:196–208.

31 Aziz NA. Long-term rehabilitation after stroke: where do we go from here? *Rev Clin Gerontol*. 2010;20:239–245.