ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2013;94:1007-14

JOURNAL-BASED CME ARTICLE

Randomized Controlled Trial of Surface Peroneal Nerve Stimulation for Motor Relearning in Lower Limb Hemiparesis

Lynne R. Sheffler, MD,[a,b,c] Paul N. Taylor, PhD,[d] Douglas D. Gunzler, PhD,[e] Jaap H. Buurke, PhD,[f] Maarten J. IJzerman, PhD,[a,g] John Chae, MD[a,b,c,h]

From the [a]Department of Physical Medicine and Rehabilitation (PM&R), Case Western Reserve University, Cleveland, OH; [b]Cleveland Veterans Affairs Functional Electrical Stimulation (FES) Center of Excellence, Cleveland, OH; [c]Department of PM&R, MetroHealth Rehabilitation Institute of Ohio, MetroHealth Medical Center, Cleveland, OH; [d]The National Clinical FES Center, Salisbury District Hospital, Salisbury, UK; [e]Center for Health Policy Research, MetroHealth Medical Center, Cleveland, OH; [f]Roessingh Research & Development, Enschede, [g]Department of Health Technology and Services Research, University of Twente, Enschede, The Netherlands; and [h]Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH.

Statement of Need

Stroke is a leading cause of motor impairment and disability with an incidence 41 of 795,000/year and prevalence of approximately 6.4 million in the U.S. Mobility limitations associated with walking may affect up to75% of the individuals who sustain a stroke each year. Footdrop is an important post-stroke lower extremity (LE) motor impairment that contributes to mobility-related disability. The rehabilitation intervention is an ankle foot orthosis (AFO). A peroneal nerve stimulator (PNS) has been proposed as an alternative to an AFO. A PNS appears to be superior to no device in improving ambulation function.

However, data on superiority to an AFO are inconsistent. Emerging data suggest that functionally relevant, active repetitive movement strategies facilitate motor relearning following stroke. In addition to dorsiflexing the ankle during functional ambulation, daily use of a PNS may facilitate motor relearning of the lower limb such that in the long-term, neither an AFO nor a PNS is needed. In contrast, ambulation with an AFO could limit active repetitive movements at the ankle and inhibit motor relearning. To date, however, the comparative effect of a surface PNS versus usual care, including an AFO, on post-stroke motor relearning has not been evaluated in a randomized controlled trial. The primary objective of this study was to compare the effects of a PNS and usual care on lower limb motor impairment among chronic stroke survivors.

This journal-based activity has been planned and developed in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the sponsorship of Professional Education Services Group (PESG).

Accreditation Statement

PESG is accredited by the ACCME to provide continuing medical education (CME) for physicians.

Credit Designation Statement

PESG designates this Journal-based CME activity for a maximum of 2.0 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

All other health care professionals completing continuing education credit for this activity will be issued a certificate of participation.

Educational Objectives

To support the attainment of knowledge, competence, and performance, the learner should be able to achieve the following objectives:

1. List motor relearning approaches in lower limb hemiparesis.
2. Describe comparative outcomes and assessment measures.
3. Compare motor relearning effect of surface peroneal nerve stimulator (PNS) versus other options.

Planning Committee

Lynne R. Sheffler, MD, Paul N. Taylor, PhD, Douglas D. Gunzler, PhD, Jaap H. Buurke, PhD, Maarten J. IJzerman, PhD, John Chae, MD, Allen W. Heinemann, PhD, ABPP (RP), FACRM, PESG staff, ACRM Editorial Office Staff.

Faculty Profiles & Disclosure Information

As a provider accredited by the ACCME, it is the policy of PESG to require the disclosure of anyone who is in a position to control the content of an educational activity. All relevant financial relationships with any commercial interests and/or manufacturers must be disclosed to participants at the beginning of each activity. The faculty and planners of this educational activity disclose the following:

Lynne R. Sheffler, MD

Case Western Reserve University, Department of Physical Medicine and Rehabilitation (PM&R), Cleveland VA FES Center of Excellence, MetroHealth Medical Center, MetroHealth Rehabilitation Institute of Ohio, Department of PM&R, Cleveland, Ohio

No relevant financial relationships to disclose.

Paul N. Taylor, PhD

Salisbury District Hospital, The National Clinical FES Center, Salisbury, UK

Paul N. Taylor is the co-inventor of the PNS device evaluated in this study and is named on 2 patents for the device. The patents are assigned to Salisbury NHS Foundation Trust. He also holds shares in Odstock Medical Limited.

Douglas D. Gunzler, PhD

MetroHealth Medical Center, Center for Health Policy Research, Cleveland, Ohio

No relevant financial relationships to disclose.

Jaap H. Buurke, PhD

Roessingh Research & Development, Enschede, The Netherlands

No relevant financial relationships to disclose.

Maarten J. IJzerman, PhD

University of Twente, Department of Health Technology and Services Research, Enschede, The Netherlands

No relevant financial relationships to disclose.

John Chae, MD

Case Western Reserve University, Departments of PM&R and Biomedical Engineering, Cleveland VA FES Center of Excellence, MetroHealth Medical Center, MetroHealth Rehabilitation Institute of Ohio, Department of PM&R, Cleveland, Ohio

No relevant financial relationships to disclose.

Allen W. Heinemann, PhD, ABPP (RP), FACRM

Director, Center for Rehabilitation Outcomes Research, Rehabilitation Institute of Chicago, Chicago, IL

No relevant financial relationships to disclose.

PESG Staff

No relevant financial relationships to disclose.

ACRM Editorial Office Staff

No relevant financial relationships to disclose.

Resolution of Conflict of Interest

PESG has implemented a process to resolve conflict of interest for each CME activity. In order to help ensure content objectivity, independence, and fair balance, and to ensure that the content is aligned with the interest of the public, PESG has resolved the conflict by external content review.

Unapproved/Off-Label Use Disclosure

PESG requires CME faculty to disclose to the participants:

1. When products or procedures being discussed are off-label, unlabeled, experimental, and/or investigational (not U.S. Food and Drug Administration [FDA] approved); and
2. Any limitations on the information presented, such as data that are preliminary or that represent ongoing research, interim analyses, and/or unsupported opinion. Faculty may discuss information about pharmaceutical agents that is outside of FDA-approved labeling. This information is intended solely for CME and is not intended to promote off-label use of these medications. If you have questions, contact the medical affairs department of the manufacturer for the most recent prescribing information.

Intended Audience

This program is intended for physicians and health care professionals responsible for the comprehensive care for individuals with chronic illness and disabilities.

0003-9993/13/$36 - see front matter
http://dx.doi.org/10.1016/j.apmr.2013.01.024

Method of Participation

In order to claim credit, participants must complete the following:

1. Pre-activity self-assessment questions.
2. Read the activity.
3. Complete the CME Test and Evaluation. Participants must achieve a score of 70% on the CME Test.

Participants can complete the pre-activity self-assessment and CME Test and Evaluation online by logging on to http://acrm.cds.pesgce.com. Upon successful completion of the online tests and evaluation form, you can instantly download and print your certificate of credit.

To better define and meet the CME needs of health care professionals and enhance future CME activities, PESG will conduct an outcomes-measurement survey following the conclusion of the program. This follow-up survey is designed to measure changes to participants' practice behaviors as a result of their participation in this CME activity. You will be contacted by email 60 days following the conclusion of this activity with an outcomes measurement survey. We would greatly appreciate your participation.

CME Inquiries

For all CME certificate inquiries, please contact us at support@pesgce.com.

This continuing education activity is active starting June 1, 2013 and will expire May 31, 2014.

Estimated time to complete this activity − 2.0 hours

Abstract

Objective: To compare the motor relearning effect of a surface peroneal nerve stimulator (PNS) versus usual care on lower limb motor impairment, activity limitation, and quality of life among chronic stroke survivors.

Design: Single-blinded randomized controlled trial.

Setting: Teaching hospital of academic medical center.

Participants: Chronic stroke survivors (N = 110; >12wk poststroke) with unilateral hemiparesis and dorsiflexion strength of ≤4/5 on the Medical Research Council scale.

Interventions: Subjects were stratified by motor impairment level and then randomly assigned to ambulation training with either a surface PNS device or usual care (ankle-foot orthosis or no device) intervention. Subjects were treated for 12 weeks and followed up for 6 months posttreatment.

Main Outcome Measures: Lower limb portion of the Fugl-Meyer (FM) Assessment (motor impairment), the modified Emory Functional Ambulation Profile (mEFAP) performed without a device (functional ambulation), and the Stroke Specific Quality of Life (SSQOL) scale.

Results: There was no significant treatment group main effect or treatment group by time interaction effect on FM, mEFAP, or SSQOL raw scores ($P>.05$). The time effect was significant for the 3 raw scores ($P<.05$). However, when comparing average change scores from baseline (t1) to end of treatment (t2, 12wk), and at 12 weeks (t3) and 24 weeks (t4) after end of treatment, significant differences were noted only for the mEFAP and SSQOL scores. The change in the average scores for both mEFAP and SSQOL occurred between t1 and t2, followed by relative stability thereafter.

Conclusions: There was no evidence of a motor relearning effect on lower limb motor impairment in either the PNS or usual-care groups. However, both the PNS and usual-care groups demonstrated significant improvements in functional mobility and quality of life during the treatment period, which were maintained at 6-month follow-up.

Archives of Physical Medicine and Rehabilitation 2013;94:1007-14

Stroke is a leading cause of motor impairment and disability with an incidence of 795,000 per year and a prevalence of approximately 6.4 million in the United States.[1] Mobility limitations associated with walking may affect up to 75% of the individuals who sustain a stroke each year.[2] Footdrop, the decreased ability to dorsiflex the ankle during the swing phase of gait, is an important poststroke lower extremity (LE) motor impairment that contributes to mobility-related disability. The rehabilitation intervention considered usual care for treatment of moderate to severe poststroke dorsiflexion weakness during gait is an ankle-foot orthosis (AFO); patients with less severe dorsiflexion weakness are generally prescribed ankle-strengthening and gait-training exercises only. A peroneal nerve stimulator (PNS), which dorsiflexes the ankle during the swing phase of gait, has been proposed as an alternative to an AFO.[3-5] A PNS appears to be superior to no device in improving ambulation function.[6] However, data on superiority to an AFO are inconsistent.[6-10]

Emerging data suggest that functionally relevant, active repetitive movement strategies facilitate motor relearning after stroke.[11] Motor relearning is defined as the reacquisition of motor skills or the reduction of motor impairment after damage to the central nervous system.[12] Thus, in addition to dorsiflexing the ankle during functional ambulation, daily use of a PNS may facilitate motor relearning of the lower limb[4,5,13-21] such that in the long-term, neither an AFO nor a PNS is needed. In contrast, ambulation with an AFO could limit active repetitive movements at the ankle and inhibit motor relearning.[22,23] To date, however, the comparative effect of a surface PNS versus usual care, including an AFO, on poststroke motor relearning has not been evaluated in a randomized controlled trial.

The primary objective of this study was to compare the effects of a PNS and usual care on lower limb motor impairment among chronic stroke survivors. The secondary objective was to compare the effects of a PNS and usual care on lower limb activity limitation and overall quality of life. The demonstration of a surface PNS as an effective therapeutic intervention to facilitate motor relearning as measured on standard clinical scales could have significant impact on poststroke motor recovery, and potentially establish a new standard of care for stroke rehabilitation.

Supported by the National Institute of Child Health and Human Development (grant nos. R01HD44816, K23HD060689, and K24HD054600) and the National Institutes of Health National Center for Research Resources Clinical and Translational Science Collaborative of Cleveland (grant no. UL1RR024989).

A commercial party having a direct financial interest in the results of the research supporting this article has conferred or will confer a financial benefit on the author or 1 or more of the authors. Paul N. Taylor is the co-inventor of the PNS device evaluated in this study and is named on 2 patents for the device. The patents are assigned to Salisbury NHS Foundation Trust. He also holds shares in Odstock Medical Limited.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit on the authors or on any organization with which the authors are associated (Sheffler, Gunzler, Buurke, IJzerman, Chae).

Clinical Trial Registration Number: NCT00148343.

Methods

Study design

A randomized controlled trial was performed comparing ambulation training with a surface PNS device (PNS group) to usual care (UC group). Subjects with chronic hemiparetic stroke were treated for 12 weeks (device usage period) and followed up for a total of 6 months posttreatment. Outcome assessments were performed at baseline (t1), end of the device usage period (t2), and at 12 weeks (t3) and 24 weeks (t4) posttreatment.

Participants

Subjects were recruited from a stroke rehabilitation outpatient program within a multihospital academic medical center. The institutional review boards of the involved hospitals approved the study protocol, and all participants signed informed consent. Inclusion criteria were age $\geq$18 years, $\geq$12 weeks poststroke with unilateral hemiparesis, and ankle dorsiflexion strength of $\leq$4/5 on the Medical Research Council scale. Subjects were required to ambulate $\geq$30ft without an AFO, score $\geq$24 on the Berg Balance Scale, and demonstrate correction of footdrop using a PNS without evidence of knee hyperextension during stance. Subjects were excluded for LE edema, skin breakdown, or absent sensation; serious cardiac arrhythmias, pacemakers, or other implanted electronic systems; pregnancy; uncontrolled seizure disorder; concomitant lower motor neuron dysfunction and nonstroke upper motor neuron dysfunction; uncompensated hemineglect; sensory or motor peripheral neuropathy; fixed ankle plantarflexor contracture; or LE botulinum toxin injection within the 3 months before enrollment.

Randomization procedure

Because poststroke motor outcomes may be affected by baseline motor function,[24,25] eligible subjects were first stratified on the basis of presence or absence of volitional ankle dorsiflexion before being randomly assigned to the PNS or UC group. The randomization sequence was concealed in consecutively numbered envelopes that were allocated once eligibility was determined.

Devices

The PNS device was the Odstock Dropped-Foot Stimulator,[3,5,16,a] a single-channel surface stimulator that detects heel rise at preswing via a 3-mm insole pressure-sensing footswitch. The AFO was a custom-molded, hinged AFO[b] with plantarflexion block that was fabricated using conventional techniques.

Intervention

The 12-week device usage period consisted of a functional training phase (two 1-h sessions per week $\times$ 5wk) and a postfunctional training phase (three 1-h sessions over 7wk). During the functional training phase, subjects were trained to use their devices for home and community mobility with assistive device as needed. Standard physical therapy interventions were used and individualized based on the baseline functional status of each subject. Activities included passive and active range-of-motion exercises, LE strengthening (supine and standing), standing balance activities, weight-shifting activities to the affected limb using parallel bars with transition to the least restrictive assistive device, and refinement of a reciprocal gait pattern (visual and manual cues were given). Exercises were done with multiple repetitions with an increase in difficulty and a decrease in cues, with and without the assigned device, as appropriate. A focus of the research therapy sessions was on higher-level gait activities including functionally relevant movement tasks such as stair climbing, walking on various surfaces (tile, carpet, ramps), negotiation of obstacles, community stepping (curbs), and treadmill training, as appropriate.

Subjects independently used their devices up to 8 hours per day during the device usage period once device safety was demonstrated. At each of the postfunctional training phase sessions, device function, application, and usage guidelines were reviewed with each subject to maximize device compliance. At completion of the device usage period, all subjects discontinued use of the assigned device.

List of abbreviations:

AFO	ankle-foot orthosis
FM	Fugl-Meyer
LE	lower extremity
mEFAP	modified Emory Functional Ambulation Profile
PNS	peroneal nerve stimulator
SSQOL	Stroke Specific Quality of Life
UC	usual care

Outcome assessments

The primary outcome measure was the LE portion of the Fugl-Meyer (FM) Assessment,[26-28] a valid measure of poststroke motor impairment. The FM assesses LE reflexes, flexor and extensor synergy patterns, volitional movement, and coordination and speed through a series of movement tasks, for a maximum score of 34. Secondary outcome measures were the modified Emory Functional Ambulation Profile (mEFAP) and the Stroke Specific Quality of Life (SSQOL) score. Activity limitation was assessed with the mEFAP,[29,30] a functional mobility test that measures the time (seconds) to ambulate through 5 common environmental terrains (floor, carpet, up and go, obstacles, stairs). The mEFAP score used for analysis was the sum of the 5 timed performance subscores. The SSQOL[31] is a valid, reliable measurement that assesses health-related quality of life in stroke subjects and consists of a 49-item scale (each scored 1−5) representing 12 domains, for a maximum score of 245. All subjects were assessed while not wearing the treatment device.

Statistical analysis

The study was originally designed as a 2 $\times$ 2 factorial design, with treatment group (PNS vs usual care) and dorsiflexion status (present vs absent) as between-subjects factors. Based on anticipated effect sizes on the FM derived from prior studies[32-34] and an alpha of .05, a sample size of 32 per cell or a total of 128 subjects was calculated to detect the anticipated differences between cells with 80% power. However, during subject accrual, we experienced uneven recruitment, with only 26% of subjects assigned to the dorsiflexion-absent group. Thus, the study was converted to a single-factor design (PNS vs usual care) with an anticipated difference in FM between groups of 5 points (.83 SD), which increases the power of the study to 99%. Even if the difference is as small as 3 points, the design has an 80% power to detect this difference. The stratification on dorsiflexion status was maintained during randomization to ensure an even distribution of baseline motor function. Thus, we believe this change maintains a fair comparison that is not confounded by differences in subgroups.

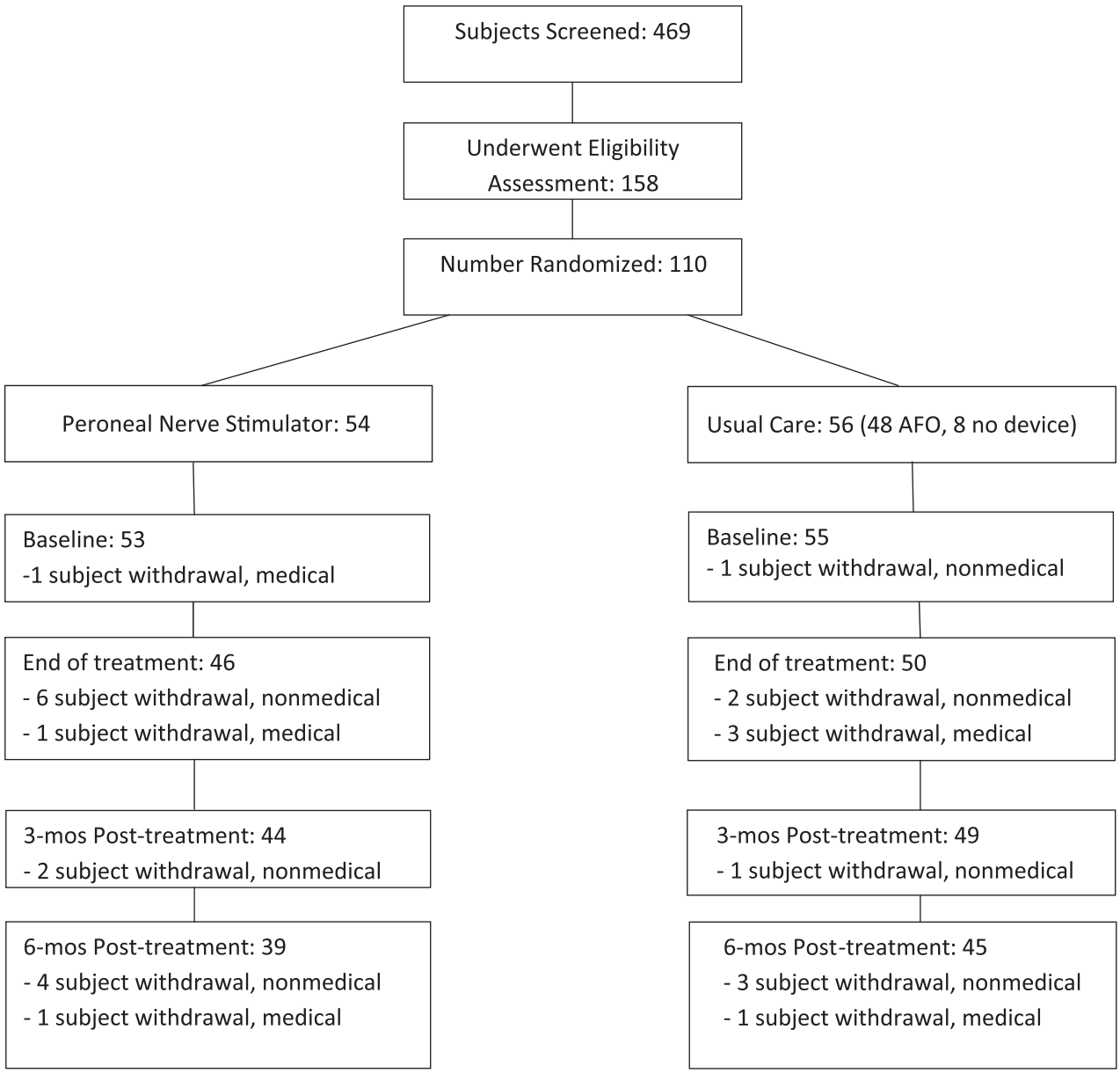

Fig 1 Participant flow diagram.

All analyses were performed as intent to treat. The Wilcoxon rank-sum test or the Fisher exact test was performed to evaluate participant baseline characteristics and baseline FM, mEFAP, and SSQOL scores between-group differences. Each outcome was modeled using a linear mixed-effects approach to evaluate the mean change in primary and secondary outcome measures with treatment group. Time was considered discrete, since measurements were made at the 4 time periods (0, 12, 24, and 36wk). However, since there was some variation in the exact date that individual measurements took place, we allowed for different growth rates for individuals by including a random intercept and slope in the models. Mixed-effects models are well suited for handling correlated repeated measurements, missing data, and dropouts in longitudinal studies.[35] In this study, the models yielded estimates of the treatment group, time, and treatment group by time effects while permitting us to control for potential confounders. We adjusted for age, sex, interval poststroke, involved hemisphere, and stroke etiology.

In order to assess the motor relearning effect of PNS on lower limb motor impairment and the impact on activity limitation, and quality of life over time, of primary interest was the 2-way interaction between treatment group and time. We used an unstructured covariance structure, which made no assumptions about the variances and covariances, and allowed for differences in variability of the measurements at each time point. Model estimation was performed via restricted maximum likelihood using PROC MIXED in SAS Version 9.2.[36,c] A P value of .05 was defined as the level of significance.

Since FM and SSQOL both have more than 11 distinct points, we approximated an interval scale in our models.[37] This approach is justified based on accepted statistical methodology and may in fact be conservative.[38,39] However, we also modeled all 3 outcomes using a more robust estimator for the SE, the EMPIRICAL option in PROC MIXED,[40] which is an asymptotically consistent "sandwich" estimator, in case parametric assumptions were violated. Further, we tested for differences between the treatment

Table 1 Baseline characteristics of treatment groups

Characteristic	PNS (n=54) (mean ± SD)	Median (1st quartile, 3rd quartile)	UC (n=56) (mean ± SD)	Median (1st quartile, 3rd quartile)	*P*
Age (y)	52.8±12.2	52.5 (44, 60)	53.2±10.1	54 (46.5, 59.5)	.84
M/F	30/24		37/19		.33
Interval post-CVA (mo)	44.7±97.5	11 (6, 49)	44.9±79.2	18.5 (8, 45.5)	.27
Etiology					.70
Embolic	13		12		
Thrombotic	17		23		
Lacunar	9		6		
Hemorrhagic	15		15		
Hemisphere					.09
Right	35		27		
Left	19		29		
DF absent/DF present	14/40		15/41		.70
FM (t1)	20.1±5.9	20 (16, 25)	20.3±6.0	21 (17, 24)	.73
mEFAP (t1)	121.5±86.6	92.6 (59.0, 138.3)	118.4±74.1	90.7 (66.1, 154.4)	.80
SSQOL (t1)	179.1±35.7	180.5 (150.5, 205.5)	175.3±40.7	180.0 (146, 210)	.81

NOTE. Values are mean ± SD, median (1st quartile, 3rd quartile), n, or as otherwise indicated.
Abbreviations: CVA, cerebrovascular accident; DF, dorsiflexion; F, female; M, male; t1, first outcome assessment (baseline).

groups at each time point using the nonparametric Wilcoxon rank-sum test with Bonferroni correction.

Results

Participants and baseline characteristics

Figure 1 shows the participant flow diagram. A total of 110 or 23% of screened stroke survivors satisfied inclusion criteria and enrolled in the study. We had a lower-than-expected recruitment rate, and thus we did not reach our target enrollment of 128. Nevertheless, with the conversion of the study from a 2 × 2 factorial design to a single-factor design, 110 subjects still translates to a power of 99% to detect the anticipated difference in FM scores between groups.

Baseline characteristics of participants are shown in table 1. Forty-eight subjects (86%) randomly assigned to usual care were treated with an AFO; 8 subjects (14%) were treated with no device. Subject dropout rates at t1, t2, t3, and t4 were 2%, 13%, 15%, and 24%, respectively. The reasons for study dropout were elective subject withdrawal because of a nonmedical reason (12 subjects), a medical issue unrelated to the study device (7 subjects), subject lost to follow-up (5 subjects), and other (2 subjects).

Fugl-Meyer Assessment

There was no significant treatment group main effect ($P=.797$) or treatment group by time interaction effect ($P=.321$) on FM raw scores. The time effect was significant ($P=.007$). However, we

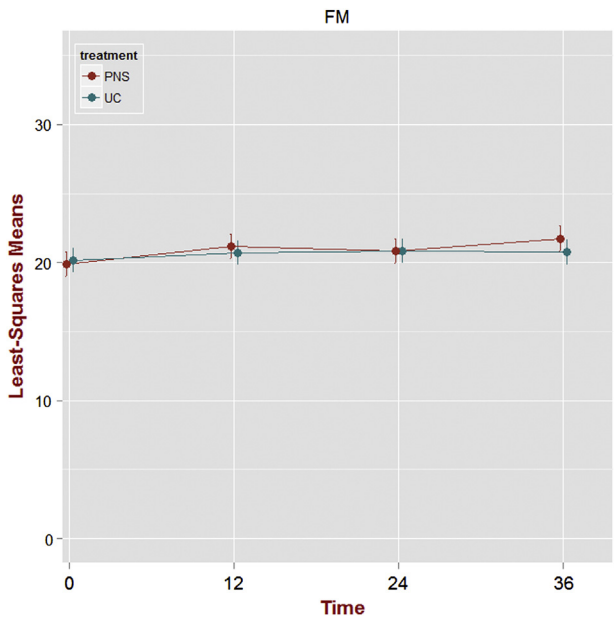

Fig 2 Plot of adjusted means over time (wk) for FM scores including SE bars.

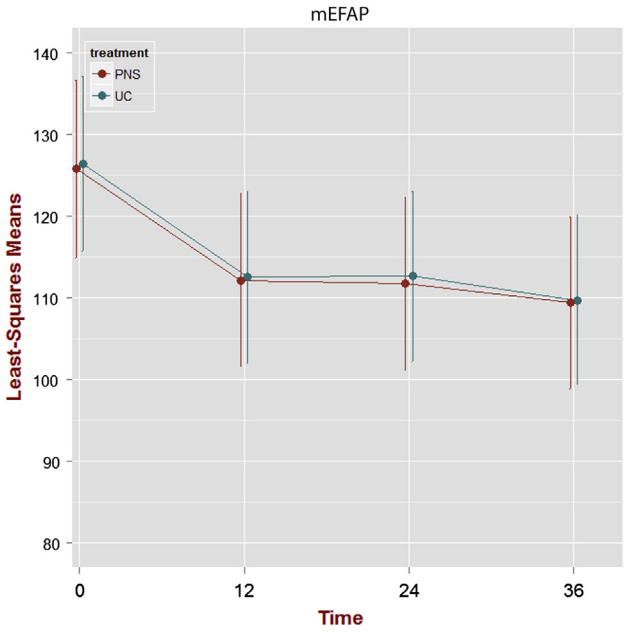

Fig 3 Plot of adjusted means over time (wk) for the mEFAP scores (s) including SE bars.

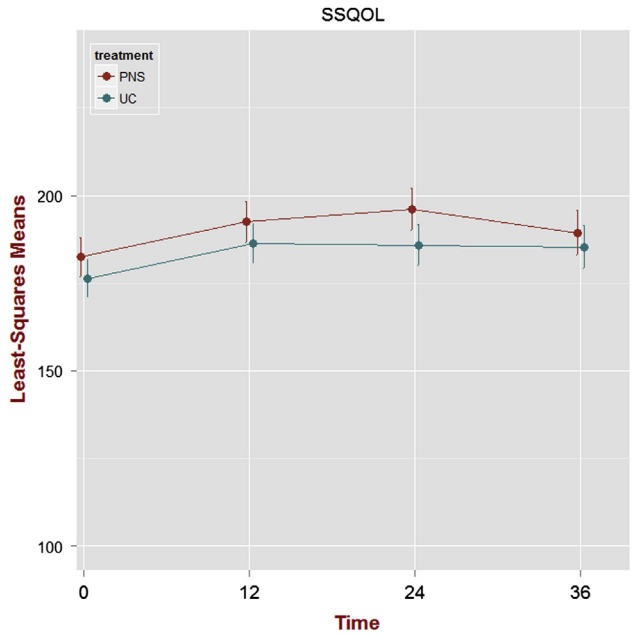

Fig 4 Plot of adjusted means over time (wk) for the SSQOL scores including SE bars.

observed no significant changes ($P>.05$) in FM score trajectories from baseline to each time point. Shown in figure 2 is a plot of adjusted means over time including SE bars for FM scores. We use least-squares means to provide a correction of the mean for missing data, estimating the marginal means for a balanced population, while adjusting for the confounders in the model.[36] The plot displays the relatively flat time effect from t1 to each subsequent time period, indicating no significant change from baseline.

Modified Emory Functional Ambulation Profile

There was no significant treatment group main effect ($P=.968$) or treatment group by time interaction effect ($P>.999$) on mEFAP raw scores. The time effect was significant ($P<.001$). Model parameter estimates of the time effect at t2, t3, and t4 were all significantly lower than the baseline (t1) estimate. Shown in figure 3 is the plot of adjusted means over time for the mEFAP scores including SE bars. Both treatment groups follow the same trajectory of a negative average change in mEFAP scores during treatment, which level off during the posttreatment period.

Stroke Specific Quality of Life

There was no significant treatment group main effect ($P=.360$) or treatment group by time interaction effect ($P=.627$) on SSQOL raw scores. The time effect was significant ($P<.001$). Model parameter estimates of the time effect at t2 to t4 were significantly higher than the baseline (t1) estimate. Shown in figure 4 is the plot of adjusted means over time for SSQOL scores including SE bars. Both treatment groups follow the same trajectory of a positive average change in SSQOL scores during treatment, which level off during the posttreatment period.

Table 2 shows the model parameter estimates, 95% confidence interval, and P value of time effect during treatment for FM, mEFAP, and SSQOL.

Table 2 Model parameter estimates, 95% CI, and P value of time effect during treatment

Outcome	Estimate	95% CI	P
FM	0.525	−0.345 to 1.396	.238
mEFAP	−13.864	−21.256 to −16.473	<.001
SSQOL	9.910	3.724 to 16.096	.002

Abbreviation: CI, confidence interval.

Robust statistical methods

We came to the same conclusions using more robust SEs in our models, in case parametric assumptions are violated. Further, none of the P values were significant for the Wilcoxon rank-sum tests for any of the 3 outcomes at any time point, even before performing Bonferroni correction, verifying that there are no significant treatment group differences at any time point.

Discussion

The primary finding of this study was that the use of a surface PNS and usual care were not associated with improvements in motor relearning among chronic stroke survivors as measured by the LE FM. In addition, the use of a PNS was no more effective than usual care in improving ambulation function (mEFAP) or quality of life (SSQOL). However, both groups had significant improvements in ambulation function and quality of life during the treatment phase, which was maintained at 6 months.

In the context of the present study, the use of a PNS and usual care among chronic stroke survivors did not facilitate LE motor relearning as indicated by change in the FM motor impairment score. The literature suggests that activity-dependent neuroplasticity requires tasks that are novel (challenging to perform), highly repetitive, functionally relevant, and cognitively engaging.[11] Data also suggest that earlier intervention is more effective than later intervention.[41] While ambulation with a PNS may be functionally relevant, the intervention specific task of ankle dorsiflexion may not be sufficiently novel and cognitively engaging. While subjects likely experienced a high number of task repetitions, we do not know the actual number of dorsiflexion repetitions. A PNS usage monitor, now routinely incorporated in commercial PNS devices, was not available at study onset. Lastly, the potential for motor relearning may be more limited in chronic stroke survivors than subacute stroke survivors.

The secondary finding of this trial was that a PNS was no more effective than usual care on functional mobility (activity limitation). However, subjects in both groups exhibited significant improvement in functional mobility during the treatment period, which was sustained throughout the follow-up period. Given that subjects were enrolled an average of 45 months poststroke and that FM scores did not improve throughout the trial, it is highly unlikely that natural recovery or an intervention-mediated reduction in motor impairment contributed to this clinical improvement. Nevertheless, it is possible that the use of a PNS conveyed focal effects not detectable by a global impairment measure such as the FM. Other PNS studies have demonstrated changes in isometric dorsiflexion/plantar flexion strength,[17] dorsiflexion torque,[18,19] maximum root mean square of the EMG signal from the tibialis anterior muscle,[21] tibialis anterior electromyographic activity,[17-19] and electromyographic cocontraction ratios.[19] However, there would be no reason to expect similar changes in the UC group. Thus, it is unlikely that theoretic focal impairment changes, not measurable by FM score, contributed to the functional improvements. An alternative explanation is that

compensatory strategies, not specific to the treatment intervention, may have been acquired during the physical therapy ambulation training and treatment period, resulting in sustained improved functional mobility. Poststroke functional improvements in the absence of clear changes in neurophysiologic parameters suggest the probable role of compensatory strategies.[42,43] In a study of poststroke gait recovery,[43] functional gait improvements, which were not associated with change in coordination patterns of muscle activation, were proposed to be related to compensatory strategies and biomechanical changes of the nonparetic LE. It is possible that both the PNS and usual-care intervention induced the same global outcomes in terms of functional ambulation and quality of life, but did so by triggering different strategies for motor relearning or different compensatory behaviors. If this is the case, 1 of the 2 treatments could produce a more effective response to facilitate long-term motor recovery. While our trial did not formally assess for compensatory strategies, all subjects additionally underwent quantitative gait analysis at each outcome assessment, and future analysis of these data will allow testing of this hypothesis.

The final finding of this trial was that although a PNS was no more effective than usual care in improving SSQOL, all subjects exhibited improved quality of life, irrespective of the study intervention. This effect was noted during the treatment period and was sustained for the duration of the trial. Given a trajectory that parallels the improvement in functional mobility, a reasonable explanation for this observation is the improvement in functional mobility. This concomitant improvement in quality of life suggests that the change in functional mobility observed in this study was clinically relevant. This finding is consistent with prior studies which have shown that multiple factors, including level of independence in activities of daily living and functional mobility, contribute significantly to quality of life after stroke.[44-49]

The present study failed to demonstrate the superiority of PNS over usual care in reducing LE motor impairment and activities limitation and improving the quality of life of chronic stroke survivors. However, an important finding of the study is that a time-limited gait rehabilitation intervention implemented on average 45 months poststroke can lead to clinically important changes in ambulation function that are maintained for at least 6 months after the end of treatment. This study adds to the growing evidence in the literature[50,51] that rehabilitation interventions in the chronic phase of stroke can be effective and clinically relevant. The study results also contribute to the ongoing debate[52] regarding the specificity of treatment on poststroke gait intervention treatment effects.

Study limitations

The study has a number of limitations. First, the study was changed from a 2 × 2 factorial to a single-factor design. Thus, we were not able to determine the role of baseline dorsiflexion function on study outcomes. Second, we did not reach our target recruitment. The difference of 5 points in the LE FM between groups may be too large. A smaller difference may be clinically significant, but the study lacked the power to detect this smaller effect. This concern is mitigated by the fact that while a difference of 3 to 4 points may be clinically important, figure 2 shows that the actual difference was on the order of 1 to 2 points. Third, the FM may not be sensitive to detect clinically important changes in motor impairment, as discussed above. Fourth, we do not have accurate device usage data to compare PNS to usual-care device usage. Our original study design included specific monitoring of device usage using a clinical step recorder embedded into the AFO and the device usage monitor capability of the PNS device. Unfortunately, the early iteration of the PNS devices that were purchased at initiation of this trial did not have usage monitoring capability. Future studies will need to incorporate reliable usage monitors to assess compliance and community performance. Fifth, treatment duration beyond 12 weeks or device application in the subacute poststroke period, or both, may translate into clinically important differences between groups. Finally, we had a relatively large dropout rate of 24%, which may have compromised internal validity.

Conclusions

There was no evidence of a motor relearning effect on lower limb motor impairment in either the PNS or UC groups as measured by the FM. However, even in the chronic phase of stroke, both the PNS and UC groups demonstrated significant improvements in functional mobility and quality of life that were sustained at 6 months.

Suppliers

a. Odstock Medical Ltd, The National Clinical FES Centre, Salisbury District Hospital, Salisbury Wiltshire, SP2 8BJ, United Kingdom.
b. G A Guilford & Son Ltd Orthotics and Prosthetic Center, 13515 Brookpark Rd, Cleveland, OH 44142.
c. SAS Institute Inc, 100 SAS Campus Dr, Cary, NC 27513.

Keywords

Gait; Hemiplegia; Peroneal nerve; Rehabilitation

Corresponding author

Lynne R. Sheffler, MD, Dept of Physical Medicine and Rehabilitation, Case Western Reserve University, MetroHealth Medical Center, 4229 Pearl Rd, N5-524, Cleveland, OH 44109. *E-mail address:* lsheffler@metrohealth.org.

References

1. Goldstein LB, Bushnell CD, Adams RJ, et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011;42:517-84.
2. Duncan PW, Zorowitz R, Bates B, et al. Management of adult stroke rehabilitation care: a clinical practice guideline. Stroke 2005; 36:e100-43.
3. Burridge JH, Taylor PN, Hagan SA, Wood DE, Swain ID. The effects of common peroneal stimulation on the effort and speed of walking: a randomized controlled trial with chronic hemiplegic patients. Clin Rehabil 1997;11:201-10.
4. Stein RB, Everaert DG, Thompson AK, et al. Long-term therapeutic and orthotic effects of a foot drop stimulator on walking performance in progressive and nonprogressive neurological disorders. Neurorehabil Neural Repair 2010;24:152-67.
5. Taylor PN, Burridge JH, Dunkerley AL, et al. Clinical use of the Odstock dropped foot stimulator: its effect on the speed and effort of walking. Arch Phys Med Rehabil 1999;80:1577-83.
6. Kottink AI, Oostendorp LJ, Buurke JH, Nene AV, Hermens HJ, Ijzerman MJ. The orthotic effect of functional electrical stimulation on

the improvement of walking in stroke patients with a dropped foot: a systematic review. Artif Organs 2004;28:577-86.
7. van Swigchem R, Vloothuis J, den Boer J, Weerdesteyn V, Geurts AC. Is transcutaneous peroneal stimulation beneficial to patients with chronic stroke using an ankle-foot orthosis? A within-subjects study of patients' satisfaction, walking speed and physical activity level. J Hehabil Med 2010;42:117-21.
8. Sheffler LR, Hennessey MT, Naples GG, Chae J. Peroneal nerve stimulation versus an ankle foot orthosis for correction of footdrop in stroke: impact on functional ambulation. Neurorehabil Neural Repair 2006;20:355-60.
9. Kottink AI, Hermens HJ, Nene AV, et al. A randomized controlled trial of an implantable 2-channel peroneal nerve stimulator on walking speed and activity in poststroke hemiplegia. Arch Phys Med Rehabil 2007;88:971-8.
10. Ring H, Treger I, Gruendlinger L, Hausdorff JM. Neuroprosthesis for footdrop compared with an ankle-foot orthosis: effects on postural control during walking. J Stroke Cerebrovasc Dis 2009;18:41-7.
11. Nudo RJ. Functional and structural plasticity in motor cortex: implications for stroke recovery. Phys Med Rehabil Clin N Am 2003;14:S57-76.
12. Lee RG, van Donkelaar P. Mechanisms underlying functional recovery following stroke. Can J Neurol Sci 1995;22:257-63.
13. Sheffler LR, Hennessey MT, Naples GG, Chae J. Improvement in functional ambulation as a therapeutic effect of peroneal nerve stimulation in hemiplegia: two case reports. Neurorehabil Neural Repair 2007;21:366-9.
14. Sabut SK, Lenka PK, Kumar R, Mahadevappa M. Effect of functional electrical stimulation on the effort and walking speed, surface electromyography activity, and metabolic responses in stroke subjects. J Electromyogr Kinesiol 2010;20:1170-7.
15. Sabut SK, Sikdar C, Mondal R, Kumar R, Mahadevappa M. Restoration of gait and motor recovery by functional electrical stimulation therapy in persons with stroke. Disabil Rehabil 2010;32:1594-603.
16. Mann GE, Wright PA, Swain ID. Training effects of electrical stimulation and the conventional ankle foot orthosis in the correction of drop foot following stroke. Presented at: The First Annual Conference of FESnet 2002; Glasgow, Scotland; 2002.
17. Carnstam B, Larsson LE, Prevec TS. Improvement of gait following functional electrical stimulation. I. Investigations on changes in voluntary strength and proprioceptive reflexes. Scand J Rehabil Med 1977;9:7-13.
18. Merletti R, Zelaschi F, Latella D, Galli M, Angeli S, Sessa MB. A control study of muscle force recovery in hemiparetic patients during treatment with functional electrical stimulation. Scand J Rehabil Med 1978;10:147-54.
19. Yan T, Hui-Chan CW, Li LS. Functional electrical stimulation improves motor recovery of the lower extremity and walking ability of subjects with first acute stroke: a randomized placebo-controlled trial. Stroke 2005;36:80-5.
20. Burridge J, Taylor P, Hagan S, Swain I. Experience of clinical use of the Odstock dropped foot stimulator. Artif Organs 1997;21:254-60.
21. Kottink AI, Hermens HJ, Nene AV, Tenniglo MJ, Groothuis-Oudshoorn CG, Ijzerman MJ. Therapeutic effect of an implantable peroneal nerve stimulator in subjects with chronic stroke and footdrop: a randomized controlled trial. Phys Ther 2008;88:437-48.
22. Hesse S, Werner C, Matthias K, Stephen K, Berteanu M. Non-velocity-related effects of a rigid double-stopped ankle-foot orthosis on gait and lower limb muscle activity of hemiparetic subjects with an equinovarus deformity. Stroke 1999;30:1855-61.
23. Romkes J, Hell AK, Brunner R. Changes in muscle activity in children with hemiplegic cerebral palsy while walking with and without ankle-foot orthoses. Gait Posture 2006;24:467-74.
24. Lin KC, Huang YH, Hsieh YW, Wu CY. Potential predictors of motor and functional outcomes after distributed constraint-induced therapy for patients with stroke. Neurorehabil Neural Repair 2009;23:336-42.
25. Park SW, Wolf SL, Blanton S, Winstein C, Nichols-Larsen DS. The EXCITE Trial: predicting a clinically meaningful motor activity log outcome. Neurorehabil Neural Repair 2008;22:486-93.
26. Fugl-Meyer AR, Jaasko L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. 1. A method for evaluation of physical performance. Scand J Rehabil Med 1975;7:13-31.
27. Duncan PW, Propst M, Nelson SG. Reliability of the Fugl-Meyer assessment of sensorimotor recovery following cerebrovascular accident. Phys Ther 1983;63:1606-10.
28. Sanford J, Moreland J, Swanson LR, Stratford PW, Gowland C. Reliability of the Fugl-Meyer assessment for testing motor performance in patients following stroke. Phys Ther 1993;73:447-54.
29. Baer HR, Wolf SL. Modified Emory Functional Ambulation Profile: an outcome measure for the rehabilitation of poststroke gait dysfunction. Stroke 2001;32:973-9.
30. Liaw LJ, Hsieh CL, Lo SK, Lee S, Huang MH, Lin JH. Psychometric properties of the modified Emory Functional Ambulation Profile in stroke patients. Clin Rehabil 2006;20:429-37.
31. Williams LS, Weinberger M, Harris LE, Clark DO, Biller J. Development of a stroke-specific quality of life scale. Stroke 1999;30:1362-9.
32. Chae J, Bethoux F, Bohine T, Dobos L, Davis T, Friedl A. Neuromuscular stimulation for upper extremity motor and functional recovery in acute hemiplegia. Stroke 1998;29:975-9.
33. Francisco G, Chae J, Chawla H, et al. Electromyogram-triggered neuromuscular stimulation for improving the arm function of acute stroke survivors: a randomized pilot study. Arch Phys Med Rehabil 1998;79:570-5.
34. Duncan PW, Goldstein LB, Horner RD, Landsman PB, Samsa GP, Matchar DB. Similar motor recovery of upper and lower extremities after stroke. Stroke 1994;25:1181-8.
35. Fitzmaurice GM, Laird NM, Ware JH. Applied longitudinal analysis. New York: John Wiley and Sons; 2004.
36. Enhancements in SAS/STAT 9.2 software. Cary: SAS Institute; 2008.
37. Nunnally J, Bernstein I. Psychometric theory. 3rd ed. McGraw-Hill series in psychology. New York: McGraw-Hill Inc; 1994.
38. Johnson DR, Creech JC. Ordinal measures in multiple indicator models: a simulation study of categorization error. Am Sociol Rev 1983;48:398-407.
39. Zumbo BD, Zimmerman DW. Is the selection of statistical methods governed by level of measurement? Can Psychol 1993;34:390-400.
40. Diggle P, Liang K, Zeger S. Analysis of longitudinal data. Oxford: Oxford Science; 1994.
41. Biernaskie J, Chernenko G, Corbett D. Efficacy of rehabilitative experience declines with time after focal ischemic brain injury. J Neurosci 2004;24:1245-54.
42. Geurts AC, de Haart M, van Nes IJ, Duysens J. A review of standing balance recovery from stroke. Gait Posture 2005;22:267-81.
43. Buurke JH, Nene AV, Kwakkel G, Erren-Wolters V, Ijzerman MJ, Hermens HJ. Recovery of gait after stroke: what changes? Neurorehabil Neural Repair 2008;22:676-83.
44. Nichols-Larsen DS, Clark PC, Zeringue A, Greenspan A, Blanton S. Factors influencing stroke survivors' quality of life during subacute recovery. Stroke 2005;36:1480-4.
45. Leach MJ, Gall SL, Dewey HM, Macdonell RA, Thrift AG. Factors associated with quality of life in 7-year survivors of stroke. J Neurol Neurosurg Psychiatry 2011;82:1365-71.
46. Owolabi MO. What are the consistent predictors of generic and specific post-stroke health-related quality of life? Cerebrovasc Dis 2010;29:105-10.
47. Lynch EB, Butt Z, Heinemann A, et al. A qualitative study of quality of life after stroke: the importance of social relationships. J Rehabil Med 2008;40:518-23.
48. Patel MD, McKevitt C, Lawrence E, Rudd AG, Wolfe CD. Clinical determinants of long-term quality of life after stroke. Age Ageing 2007;36:316-22.
49. Choi-Kwon S, Choi JM, Kwon SU, Kang DW, Kim JS. Factors that affect the quality of life at 3 years post-stroke. J Clin Neurol 2006;2:34-41.
50. Wolf SL, Thompson PA, Winstein CJ, et al. The EXCITE stroke trial: comparing early and delayed constraint-induced movement therapy. Stroke 2010;41:2309-15.
51. Duncan PW, Sullivan KJ, Behrman AL, et al. Body-weight-supported treadmill rehabilitation after stroke. N Engl J Med 2011;364:2026-36.
52. Hornby TG, Straube DS, Kinnaird CR, et al. Importance of specificity, amount, and intensity of locomotor training to improve ambulatory function in patients poststroke. Top Stroke Rehabil 2011; 18:293-307.