Multicenter Evaluation of Electrical Stimulation Systems for Walking

Marguerite Wieler, PT, Richard B. Stein, DPhil, Michel Ladouceur, PhD, Maura Whittaker, PT, Andrew W. Smith, PhD, Saad Naaman, MD, Hugues Barbeau, PhD, Joanne Bugaresti, MD, Elaine Aimone, PT


Objective: To test the long-term benefits of several noninvasive systems for functional electrical stimulation (FES) during walking.

Design: Forty subjects (average years since injury, 5.4) were studied in four centers for an average time of 1 year. Gait parameters were tested for all subjects with and without FES. Thus, subjects served as their own controls, since the specific effect of using FES could be separated from improvements resulting from other factors (eg, training).

Setting: Subjects used the devices in the community, but were tested in a university or hospital setting.

Patients: Subjects with spinal cord injury (n = 31) were compared to subjects with cerebral damage (n = 9).

Main Outcome Measures: Gait parameters (speed, cycle time, stride length). Acceptance was studied by means of a questionnaire.

Results: Some initial improvement in walking speed (average increase of >20%) occurred, and continuing gains were seen (average total improvement, 45%). The largest relative gains were seen in the slowest walkers (speeds of <0.3m/sec). Acceptance of the FES systems was good and improved systems have been developed using feedback from the subjects.

Conclusions: Based on the improvements in speed and the acceptance of these FES systems, a greatly increased role for FES in treating gait disorders is suggested.

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MORE THAN 30 YEARS ago, Liberson and colleagues introduced single-channel electrical stimulation in stroke patients to prevent foot drop (ie, the foot drops or drags on the ground during the swing phase of walking because of lack of voluntary ankle dorsiflexion). The technique is now generally known as functional electrical stimulation (FES), because stimulation replaces or assists a functional movement that is lost after injury to or diseases of the central nervous system. FES can be distinguished from therapeutic electrical stimulation, which is applied to strengthen muscles weakened, for example, by disuse. Clinical use of FES is increasing; it is currently being used to restore and augment respiration, bladder, bowel, and sexual function, hand grasp, and standing and walking. Many applications require surgical implantation of electrodes; others are noninvasive, with electrodes applied to the skin’s surface. Several studies have reviewed the use of FES in its original application, foot drop, including one study of more than 1,500 hemiparetic patients. FES has also been applied to persons who have a spinal cord injury (SCI) or have lost supraspinal control of α-motoneurons for other reasons. At least four channels of stimulation are required for walking after complete SCI and more channels of stimulation may be needed for greater speed and better quality of gait (ie, trunk stabilization) or other functions such as climbing stairs. Systems with more than 4 to 6 channels of surface electrodes are complex enough that they have only been tested on a research basis.

Graupe and Koln applied a commercially available system, Parastepa to more than 100 SCI subjects. Solomonow and associates tested FES with a reciprocal gait orthosis (RGO) on 70 SCI subjects. Some subjects did very well, but most did not use such a system in place of a wheelchair. Energy consumption is high with FES alone and subjects tire easily. Bracing can reduce the energy cost somewhat and can improve endurance, but is often bulky and inconvenient to use for long periods.

Simpler systems suffice for SCI subjects where some function remains (ie, the injury is incomplete). In a previous study 10 subjects with incomplete SCI showed a significant increase in walking speed. The benefits were sufficient to initiate a multicenter trial across Canada. The trial was undertaken because (1) the earlier study had a small sample, (2) FES systems were untested in other clinical centers with less experience using FES, (3) the long-term effects on function were unknown, and (4) further insight was needed into the reasons why specific FES systems were accepted or rejected.

SCI occurs at a variety of levels and with varying degrees of sensory and motor preservation. Since our rationale was to determine which types of patients would benefit most and who would use these systems in daily life, we purposely accepted people with a wide range of initial walking speeds. Also, since some subjects were followed for several years, it was not practical to enroll a very large number of people in the study. Therefore, each subject was tested in each session with and without FES. Subjects, in effect, served as their own controls since therapeutic effects from various sources (eg, electrical stimulation, training and increased amount of walking) could be separated from the specific benefits of FES.

Overall, the goals of the present study were to (1) evaluate simple, surface FES systems for walking, (2) study their acceptance by subjects with an incomplete SCI compared to...
subject with cerebral impairment caused by stroke or head injury. (3) assess limitations to widespread acceptance of the FES devices, and (4) develop improved systems that might overcome these limitations. Brief accounts of some results have been presented previously.16,17

METHODS

Subject Population

Forty subjects used FES-assisted walking for at least 3 months and many have continued for several years. Seven other subjects began the training, but discontinued participation before enough data were obtained for analysis. Of the 40 subjects that continued, 31 had an incomplete SCI. Eight others had cerebral impairment from stroke and 1 from head injury; these 9, however, presented clinically with motor deficits similar to the SCI subjects. The distribution of lesion levels (fig 1A) is similar to that found in the general SCI population,16 excluding lumbosacral levels of injury, to ensure that leg muscles of interest were neither denervated nor receiving normal descending input. The numbers of subjects from the four centers were: Edmonton, 14; Montreal, 14; Vancouver, 7; and Toronto, 5.

All subjects were older than 17yrs and gave informed consent to participate in the study. They were assessed clinically for range of motion (active and passive), sensation, and voluntary muscle strength (measured manually). Patients were excluded if they had symptomatic cardiovascular diseases, extreme spasticity, or problems with pressure sores. Adequate cognitive ability was required for subjects to give informed consent, as approved by the human ethics committees at the participating institutions. Although there was some overlap in the distribution of ages at the start of FES, the cerebral impairment group was much older, 57 ± 4yrs (mean ± SE), than the SCI group, 36 ± 2yrs (fig 1B). The cerebral impairment group was also seen sooner after injury, 3 ± 1yrs, than was the SCI group, 6 ± 1yrs (fig 1C). All but two subjects entered the study more than a year after injury, so neurological recovery had stabilized and was not expected to change significantly.

All subjects had difficulty walking because of muscle paresis/paralysis following injury to the spinal cord or brain. All could stand and, with one exception, could walk to some extent without FES. There were also a wide range of residual motor ability in the upper extremity of subjects. Figure 1D shows the distribution of initial walking speeds without FES; these are average values for all measurements, typically taken over the first month or two after beginning the program (3.4 ± 0.5 m/s).

Stimulation

Stimulation was with 1 to 4 channels of stimulation, using either the Unistim® or WalkAide® (1-channel) devices or the Quadstim® (4-channel) device. The Unistim and Quadstim devices were based on designs developed at the Jozef Stefan Institute, Belgrade, Yugoslavia,19 but were produced in Edmonton with some improvements. The Unistim device employed a hand switch to turn stimulation on and off. With the Quadstim device, flexors were stimulated when a hand switch was pressed and extensors were stimulated when it was not. When stimulation of both legs was needed, two hand switches were provided.

The WalkAide, designed to overcome problems associated with earlier devices, featured an inbuilt sensor that measures the tilt of the shank with respect to gravity.20 Either the tilt sensor or traditional foot and hand switches can be used to control stimulation. The stimulus is turned on near the end of the stance phase when the lower leg is tilted back (behind the body), and turned off near the beginning of the next stance phase when the lower leg is tilted forward (in front of the body). Nine subjects used prototypes of the WalkAide that were developed at the University of Alberta. All devices were approved by the Canadian Standards Association.

Subjects presenting mainly with foot drop had stimulation applied to the common peroneal nerve. If the resultant ankle dorsiflexion was insufficient, then the stimulus was increased in some subjects to elicit a flexor reflex and activate hip and knee flexors. A few subjects also had stimulation to the hamstrings to increase knee flexion. If subjects showed knee or ankle instability during stance, stimulation of the quadriceps muscles or the tibial nerve was added. For instability around the hip/pelvis, gluteus medius could be stimulated. Subjects used Multiweek self-adhesive, surface electrodes or the equivalent for stimulation. Stimulation of the quadriceps muscles or other large muscles (gluteals, hamstrings) was with rectangular electrodes (3.5cm × 8.5cm), but the active electrode over the common peroneal nerve was circular (3cm in diameter). The type of stimulation used for each subject was left to the judgment of clinicians at each of the centers. No stimulation-induced complications requiring medical attention, such as burns, falls, or fractures, occurred at any of the centers. A few subjects showed minor skin irritation transiently.

Gait Analysis

Gait was analyzed using a video camera (plus additional systems in some centers), while subjects walked rapidly, but safely, with and without FES. Subjects using more than one type of walking aid or brace were studied with each assistive device. Typically, four trials of >5m of walking were inter-
leaved to minimize the effects of fatigue. Subjects began walking before the beginning of the walkway and continued beyond the walkway. Time was superimposed on the video. The time of crossing the 0 and 5m marks was measured from the video and used to compute velocity. Stride length and cycle time were measured from all complete steps within the 5m walkway.

Availability for gait analysis varied with family and employment situations and distance from the participating centers (some lived >500km away). Some subjects of particular interest were recorded many times over more than 3 years to study the full time course of the changes. For general comparisons, initial and final values were used. Where several sessions were available after a stable final speed was reached, results were averaged (51 ± 5wks). Averaging increases accuracy, but may underestimate the overall changes, since substantial improvement can take place within the averaged periods (fig 2). The trials could not be done in a blinded fashion, since most subjects felt the stimulus clearly and it was obvious to the person making the gait measurements whether foot drop, for example, was present or absent.

Walking speed (m/sec), stride length (m) and cycle time (sec) were measured over all 5m segments for the more affected leg. Changes over time were fitted with a curve of the form \( y = a + b \exp (ct) \), where parameters \( a \), \( b \), and \( c \) were chosen using a nonlinear algorithm.

### RESULTS

#### Speed

Dramatic, long-term changes were observed in a subject (fig 2A), who used a single channel FES system stimulating the common peroneal nerve for over 3 years. His walking speed was initially less than 0.2m/sec without FES and showed little increase when he first tried FES 4.5yrs after his C5/C6 injury. He continued to improve toward an asymptote near 0.8m/sec, a fourfold increase. After a few weeks he switched from a walker to Canadian crutches and abandoned the use of a wheelchair almost completely. Later, he tried canes, which he likes, although his speed is slower. His speed also increased without FES, presumably because of the increased strength from stimulating the dorsiflexor muscles and increased conditioning and coordination from walking more. Originally, he took nearly a minute to walk 10m; he improved to cover this distance in less than 15sec. Five of 40 subjects progressed qualitatively in their normal mode of locomotion (from wheelchair to crutches, crutches to canes, etc). Figure 2B shows a more typical subject who continued with the same walking aid. He increased his speed both with and without FES over a period of several months.

The total change in walking speeds for all subjects (fig 3) is the final value with FES minus the initial value without FES. However, some changes may be due to the training and attention that subjects received by participating, rather than a direct effect of FES. This training effect could be assessed by comparing the initial and final speeds without FES. The values were quite variable, so subjects were divided into five groups (quintiles) based on their initial speed without FES (fig 3). Subjects typically increased their speed 0.1 to 0.2m/sec (14 ± 0.3m/sec [mean ± SE]) from an initial speed of 0.16 ± 0.06m/sec. The training effect accounted for more than half of the increase, 10 ± 0.3m/sec, but was not evenly distributed among the quintiles. For example, the fastest group (>1m/sec) showed the largest absolute increase in speed, but the increase resulted entirely from training. Thus, relative rather than absolute changes in speed are more important to analyze. Four values (initial and final walking speed, with and without FES) were averaged to obtain a mean walking speed and values were then expressed relative to this mean value. Overall results and values for the SCI and cerebral impairment subjects separately show that an initial increase occurred with FES and a further increase occurred over time (fig 4). The total increase (45%) was observed in all four centers (range, 23% to 67%). SCI subjects' walking speed increased by 55% compared to 19% for those with cerebral impairment. The total change was highly significant \((p < 0.01)\). Student's paired \( t \) test for the entire population and for the SCI and cerebral impairment subjects separately. The training effect was also highly significant \((p < 0.01)\) in the total and the SCI groups, but not in the cerebral impairment group. Finally, the initial effect of FES was
ELECTRICAL STIMULATION FOR WALKING, Wieler

Fig 4. Changes in subjects' walking speeds relative to their mean speeds (a value of 1). Data are plotted for all subjects and those with spinal or cerebral injury. For each group four bars show the improvements from the initial to the final walking speeds without and with FES. Standard errors of the means are also indicated.

Initial: no FES Initial: with FES Final: no FES Final: with FES

Fig 5. Effect of FES and training on speed. The total increase in speed, relative to mean values for each subject, was greatest for those walking at the slowest speeds (>0.3m/sec). The increase for subjects who walked at high speeds was attributable to a training effect, which produced about a 20% increase for all 5 groups (8 subjects per group) divided according to their mean walking speed.

Table 1: Questionnaire Results

<table>
<thead>
<tr>
<th>Statement</th>
<th>Response Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>I can use the device easily on a regular basis.</td>
<td>53 20 20 0 7</td>
</tr>
<tr>
<td>I can walk better using FES than without stimulation.</td>
<td>70 20 10 0 0</td>
</tr>
<tr>
<td>The device helps me to do things that are important to me.</td>
<td>73 27 0 0 0</td>
</tr>
<tr>
<td>I would like to continue using FES for walking.</td>
<td>97 3 0 0 0</td>
</tr>
</tbody>
</table>

Response range, 1 (total agreement) to 5 (total disagreement). Values are reported as percentage of subjects queried (n = 30).

Fig 6. Relative stride lengths and cycle times. The increase in walking speed can mainly be attributed to an increase in stride length, rather than to a decrease in the time for a complete step cycle. Values are again shown relative to the mean for each subject, as in figure 4.

The relative benefits were confounded by the systematic differences in speed with different walking aids. Subjects who used multichannel rather than single-channel systems benefitted more with little difference in average speed, but the trend was not statistically significant.

Acceptance

At the end of the test period subjects were given the option of continuing with FES; 23 subjects continued to use FES on a regular basis, so acceptance was good. The other subjects discontinued use for a variety of reasons: unrelated medical problems (7), lack of time (4), perceived lack of progress (4), FES no longer needed because of improvements (1), or other (1). Table 1 shows the results of a short questionnaire that was answered by 30 subjects. The least positive answers were to the statement, 'I can use the device easily on a regular basis': 7% could not use the devices easily, 20% were noncommittal, 73% could use the devices easily. Over 90% agreed with the statement that they could walk better using FES. All responded that the device helped them to do important things and that they would like to continue using FES for walking.

DISCUSSION

This study is the first long-term, multicenter trial of FES for subjects with incomplete SCI. The results were encouraging with a 45% increase in walking speed, over 20% initially with the use of FES and a further 20% during the study. The subjects' SCIs or cerebral impairments occurred on average 5.4yrs before they entered the study, so significant, spontaneous increases in walking speed would not have been expected. Biofeedback has been found to facilitate stroke rehabilitation when combined with FES. Thus, participation and the added attention may
have contributed to the improvement, as well as the effects of muscle strengthening and general conditioning from walking. However, performance was assessed with and without FES in nearly every session, so the effects of training and involvement can be clearly separated from the specific effects of the stimulation. Also, the training effects would not have occurred without the device enabling them to walk better and farther.

Several subjects improved enough to switch from one aid to another (ie, from a walker to canes) or to use walking, rather than a wheelchair, as the preferred mode of locomotion. Many subjects had orthoses, such as an AFO, but rejected them for a variety of reasons (eg, discomfort, difficulty fitting into normal shoes, poor appearance). An AFO may offer some of the advantages provided by FES, but FES was found to be more acceptable to many subjects.

**SCI versus cerebral injury.** We included some cerebral impairment subjects, because simple FES systems have been applied more widely to stroke subjects and they therefore provided a good comparison to the results from persons with incomplete SCI. The two groups were quite different in respect to age and several other characteristics (fig 1). Cerebral impairment subjects increased their speed to a lesser extent (19%) than SCI subjects (55%), but the differences could be secondary to differences in walking speed. Simple FES systems were of most benefit to subjects who walked very slowly (fig 5) and our sample of stroke patients walked faster than the SCI subjects, on average. Granat6 also reported that walking walking speed improved with single-channel stimulation for subjects whose initial speeds were between 0.1 and 0.6m/sec. The reasons for the smaller improvement in subjects who walked faster initially is presumably that they already have good control over many muscle groups. Adding stimulation to one or a few muscle groups cannot substantially improve their walking speed above the improvement produced by compensating a missing movement for one over which they have voluntary control. Thus, with training those who walked fast initially were able to walk faster, but there was no specific added benefit of FES.

**Acceptance.** Overall, the responses to the questionnaire were very positive. A large majority responded that their walking was improved and that FES helped them to do things that were important to them. This was true for some subjects who showed no objective increases in speed. Granat7 found improvements in foot inversion and the symmetry of gait in a number of subjects. These parameters were not systematically measured, but could contribute to the feeling of walking better in the absence of improved speed. Many subjects reported that using FES allowed them to move their legs more easily, to do household chores, and to transfer with less effort, and that it enhanced their sense of well-being. Such changes were not captured by our objective measures. Some subjects also reported that they got less tired walking, which could correlate with the somewhat lower oxygen consumption reported elsewhere.6,15 A few subjects were tested over longer periods of walking (15min) and often showed much larger improvements than would be predicted by the increase in speed over a short runway. These issues need further study.

**Limitations.** A few subjects disagreed with the statement that the device was easy to use on a regular basis. Difficulties included a problem in finding the sites for surface stimulation, particularly over the common peroneal nerve. Problems were also reported with leads and wires connecting switches and electrodes to the stimulator. No major equipment problems occurred, and minor items, such as a broken lead or a malfunctioning switch, could be repaired easily or exchanged.

**Further development.** Based on the subjects' suggestions an improved single-channel stimulator was designed with an inbuilt sensor that measures the tilt of the shank with respect to gravity.20 The sensor signal can be used to turn the stimulator on and off, in addition to the traditional hand or foot switches, even in subjects who are walking barefoot. The stimulator, sensor and electrodes all fit in a comfortable, breathable garment contoured to fit snugly over the tibia. Positioning the electrodes with this device is much more automatic and is quicker, even for a person with only one functional arm. Initial reactions to the University-built prototypes have been very positive and a commercial version is under development.22

**CONCLUSION**

Subjects with walking speed deficits caused by SCI or cerebral damage who walk at less than 1m/sec can benefit from FES. The good acceptance of the current generation of devices and the development of more advanced, user-friendly devices suggests that FES should be applied much more in coming years to treat gait disorders.

**References**


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Suppliers
a. Sigmedics, One Northfield Plaza, Suite 410, Northfield, IL 60063.
b. Biomotion Ltd., #1503, 10010 119th Street, Edmonton, AB, Canada T5K 1Y8.
c. NeuroMotion, Suite 401, 11044 82nd Avenue, Edmonton, AB, Canada T6G 0T2.
d. Chattanooga Corporation, 4717 Adams Road, PO Box 489, Chattanooga, TN 37443.
e. leastsq, Matlab; Mathworks, Inc., 24 Prime Park Way, Natick, MA 01760.
Abstracts of the American Academy for Cerebral Palsy and Developmental Medicine 65th Annual Meeting
12–15 October 2011
Las Vegas, USA
Materials and Methods: A directional accelerometer was taped to the dorsal surface of the dominant hand to mark onset of movement. EMG data were recruited. Exclusion criteria at a large university.

Conclusions and Significance: Up to 59% of ambulant children changed their gait patterns during the preschool years. Stability of gait patterns was not established before 36 months and changes trend to an increase in severity. Stability of gait patterns has implications for the type and frequency of conservative management (including motor training, Orthoses, BoNT-A) and frequency of review required.

Table 2: Stability of gait patterns across age bands according to motor distribution.

<table>
<thead>
<tr>
<th>Age at Test (months)</th>
<th>Umbilical</th>
<th>Bilateral</th>
<th>Combined</th>
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<tbody>
<tr>
<td>24-30</td>
<td>1023 (0%)</td>
<td>1701 (60%)</td>
<td>1701 (60%)</td>
</tr>
<tr>
<td>28-36</td>
<td>1023 (0%)</td>
<td>1701 (60%)</td>
<td>1701 (60%)</td>
</tr>
<tr>
<td>34-36</td>
<td>1053 (0%)</td>
<td>1701 (60%)</td>
<td>1701 (60%)</td>
</tr>
</tbody>
</table>

Key: * indicates statistical significance.

Results: During bilateral shoulder flexion, EMG data revealed anticipatory activity in the dorsal muscles of the trunk and legs (IS [p<0.0001], BF [p<0.001]), suppression in the ventral muscles with posterior changes in COP. During bilateral shoulder extension, anticipatory EMG activity was seen in the ventral muscle groups (RA [p<0.001], RF [p<0.05]), suppression in the dorsal muscles and anterior changes in COP. Correlations were found between predicted APAs and scores on the GMFM (r=0.70) and PRT (r=0.78) in the children with hemiplegia, but not in children with diplegia.

Conclusions and Significance: This is the first study to use EMG to investigate APAs in children with hemiplegia and diplegia, and the first to correlate APAs with gross motor skills (GMFM) and balance (PRT). Our findings show that by age 7, children with typical motor development, diplegia and hemiplegia demonstrated the ability to generate direction specific APAs and changes in center of pressure similar to those reported in healthy adults. However, the children with CP had greater variability and decreased magnitude in their EMG activity.

F7
Anticipatory postural adjustments in children with diplegia and hemiplegia and correlations with performance measures

Objectives: To investigate anticipatory postural adjustments (APAs) in children with typical development, hemiplegia and diplegia, during bilateral shoulder flexion and extension movements performed in standing. EMG activity in muscles of the trunk and lower extremities, and anterior/posterior changes in center of pressure (COP) were studied. The GMFM and Pediatric Reach Test (PRT) were administered to the participants with CP. Objectives: (1) Children with cerebral palsy can produce direction specific APAs (EMG activation and COP displacement). (2) The APAs generated by the children with cerebral palsy will be correlated with GMFM and PRT scores.

Design: Prospective cohort study.

Participants and Setting: Children with typical development (n=9) and two groups of children with CP; diplegia (n=9) and hemiplegia (n=9), GMFCS I or II, aged 7 to 17 years were recruited. Exclusion criteria included orthopedic surgery or Botox injections within 6 months prior to recruitment. Data was collected in the motor control laboratory at a large university.

Materials and Methods: EMG electrodes were applied to the right and left trunk and lower extremity muscle groups, and participants stood on a force platform to perform bilateral shoulder flexion and extension movements. A unidirectional accelerometer was taped to the dorsal surface of the dominant hand to mark onset of movement. EMG data were filtered and aligned and integral EMGs were calculated and averaged across participants. Anticipatory changes in COP were calculated. Statistical analysis was performed using repeated measures ANOVA. Relationships between predicted APAs and scores on the GMFM and PRT were assessed using the Pearson correlation coefficient (r).

Results: During bilateral shoulder flexion, EMG data revealed anticipatory activity in the dorsal muscles of the trunk and legs (IS [p<0.0001], BF [p<0.001]), suppression in the ventral muscles with posterior changes in COP. During bilateral shoulder extension, anticipatory EMG activity was seen in the ventral muscle groups (RA [p<0.001], RF [p<0.05]), suppression in the dorsal muscles and anterior changes in COP. Correlations were found between predicted APAs and scores on the GMFM (r=0.70) and PRT (r=0.78) in the children with hemiplegia, but not in children with diplegia.

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F8
Effectiveness of a novel functional electrical stimulation device to improve unilateral footdrop in cerebral palsy

Participants and Setting: Children with typical development (n=9) and two groups of children with CP; diplegia (n=9) and hemiplegia (n=9), GMFCS I or II, aged 7 to 17 years were recruited. Exclusion criteria included orthopedic surgery or Botox injections within 6 months prior to recruitment. Data was collected in the motor control laboratory at a large university.

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Hypotheses are that the WalkAide will enhance gait performance with improved effects on gait and muscle function over time.

Design: Prospective cohort intervention study.

Participants and Setting: Participants were 17 children and adolescents with CP and unilateral footdrop (8M, 13.1±3.7y; all GMFCS I-II); four others did not complete the study. Recent lower extremity toxin injections and surgery were exclusions. The setting was a national research hospital.

Materials and Methods: 3D gait evaluations were performed at Months 0 and 3 (double baseline), 4 (after a 1-mo WalkAide weaning period), 7 (after 3mo of WalkAide use at 6h/d) and 10 (after 6mo of WalkAide use). Participants walked in barefoot (SF), shoes (SH) and WalkAide + Shoes (WA) at freely selected and fast speeds. For this analysis, repeated measures MANOVA were performed across conditions and 4 and 7 month assessments with post hoc tests as indicated (p<0.05). Outcomes included normalized gait velocity, DF mean and maximum in swing and at initial contact, and DF angular velocity. Strength and muscle ultrasound data were also collected but not included here.

Results: Mean use was 5.7 hours/day recorded by the device demonstrating excellent adherence. Significant main effect for Condition was found with WA superior to SH and BF for ankle kinematic values at both speeds and times, except DF at initial contact for fast speed which was significant only at 7 months. There were no differences between BF and SH. Walking velocity was greater for WA versus BF but not SH at both times for self-selected, and at 7 months for fast speed. No main effect was seen for Time, but Condition x Time interaction was significant for DF maximum and initial contact with WA showing improved DF over time (Figure 1a,b).

Conclusions and Significance: Participants tolerated the WalkAide well, walked faster compared to barefoot, and demonstrated improved DF as compared to SH and BF by 7 months in all cases. Interactions suggest that patients may continue to improve with continued FES use which is not an anticipated outcome for traditional orthoses. Understanding the underlying mechanisms for this improvement over time (e.g. neural or muscle plasticity) requires further investigation.

To change or not to change: application of minimum clinically important difference (MCID) for children with cerebral palsy

AM BAGLEY, GE GORTON, DJ OEFFINGER

Background and Objectives: Identifying characteristics that could predict positive or negative changes related to desired functional outcomes in children with cerebral palsy (CP) would be clinically useful. Previously, we defined responsiveness of commonly used outcome measures as minimum clinically important differences (MCIDs) [1]. The purpose of this work was to apply positive and negative MCID thresholds to a longitudinal dataset to identify groups of participants who changed Gross Motor Function Measure (GMFM66) score over the course of a year, and to compare baseline characteristics among the positive change (POS), negative change (NEG), and no change groups (NULL).

Design: Multi-center prospective cohort; convenience sample from seven pediatric centers.

Participants and Setting: Two hundred and twenty-eight children with CP (90 GMFCS Level I, 91 Level II, 47 Level III; 148 male, 80 female; mean age 12.9y) completed assessments at baseline and 12 months later (mean 13.5±2.3) GMFM66, 1 minute walk test (IMWT), timed up and go, gait analysis, and Pediatric Outcomes Data Collection Instrument (PODCI) were performed.

Materials and Methods: MCIDs for GMFM66 scores based on a medium effect size were calculated for each GMFCS
Foot drop is the inability to voluntarily dorsiflex the ankle during the swing phase of gait. Foot drop decreases gait quality, limits mobility, increases fall risk, and greatly increases energy expenditure during walking. Traditionally, foot drop is treated with passive dorsiflexion support by an ankle foot orthosis (AFO) but today, functional electrical stimulation (FES) devices are available to promote comfortable, effective active dorsiflexion during gait for patients with central nervous system (CNS) causes of foot drop. The WalkAide® FES System’s unique control system, with tilt sensors to trigger electrical stimulation during the swing phase, can help normalise gait and thus optimise safety, cosmesis and energy efficiency in people with stroke, multiple sclerosis, cerebral palsy and a wide range of other CNS disorders.

Causes of Foot Drop
Foot drop is usually caused by damage to areas of the nervous system that control ankle dorsiflexion. Foot drop may be caused by central or peripheral nerve dysfunction and is common in patients with a wide variety of neurological diagnoses including stroke, multiple sclerosis (MS), traumatic brain injury (TBI), spinal cord injury (SCI), cerebral palsy (CP) and peripheral neuropathy.

Treatment of Foot Drop
Traditionally, foot drop of all aetiologies is treated with bracing using an ankle foot orthosis (AFO) (see Figure 1A). An AFO is a device usually made of plastic, which wraps under the foot and behind the calf to passively assist ankle dorsiflexion. AFOs are simple devices that are widely available at relatively low cost, but they have a number of disadvantages and limitations. The passive dorsiflexion assistance they provide does not promote active use of remaining or recovering dorsiflexion function and also limits ankle range of motion. In addition, AFOs can be uncomfortable, bulky and, if poorly fitted, produce areas of pressure and tissue breakdown. Many patients find AFOs so uncomfortable or unsightly that they do not use them. Therefore, research has focused on developing alternative ways to treat foot drop. One of the most effective treatments for foot drop is functional electrical stimulation (FES, see Figure 1B).

Who Can Use the WalkAide® Functional Electrical Stimulation System for Foot Drop?
FES is a new approach to treating foot drop. FES uses a low-level electrical current to stimulate peripheral motor nerves to produce active muscle contractions that promote functional movement. FES for foot drop involves stimulating the peroneal nerve to produce active dorsiflexion during the swing phase of gait. FES can be used to treat foot drop when the CNS is damaged and the peripheral nerves, neuromuscular junction and muscles are intact. Therefore, FES is particularly effective for treating foot drop caused by CNS disorders such as stroke, MS, TBI, incomplete SCI and CP as well as other, less common CNS disorders.

How the WalkAide Functional Electrical Stimulation System Treats Foot Drop
The WalkAide® FES System is a non-invasive, self-contained device designed specifically to provide comfortable and effective transcutaneous stimulation to the peroneal nerve to improve dorsiflexion during the swing phase of gait. The WalkAide FES System is contained in a cuff worn around the proximal leg just below...
the knee (see Figure 1B). The device includes tilt sensors, with accelerometers and inclinometers to measure the speed and position of the lower leg to trigger stimulation, and a pulse generator and self-adhesive electrodes to deliver the electrical current. The entire device is powered by a single AA battery. With the WalkAide, low intensity pulses of electrical current, of sufficient duration and amplitude to produce action potentials in peripheral nerves, are delivered from the generator to transcutaneous self-adhesive electrodes placed over the common peroneal nerve near the fibular head (see Figure 2). The stimulated action potentials are transmitted orthodromically to the superficial and deep peroneal nerves, and thence to the neuromuscular junctions of the muscles of the lateral and anterior compartment of the leg. This causes acetylcholine release at the neuromuscular junctions and muscle contractions to produce active ankle dorsiflexion. The tilt sensors trigger the electrical current pulses to start just as the patient enters the swing phase of gait and to end when swing ends. This produces dorsiflexion throughout swing phase, minimising or entirely eliminating foot drop and normalising the gait pattern.

Features and Advantages of the WalkAide Functional Electrical Stimulation System

FES has a number of advantages over an AFO for treatment of foot drop (see Table 1). The active contraction produced by FES can help to prevent the muscle atrophy and range of motion loss associated with passive support offered by an AFO. In addition, the active muscle contractions and joint motion stimulate muscle spindles, Golgi tendon organs and joint proprioceptors, increasing sensory awareness and input to the CNS. This sensory input improves motor output, including the quality and control of movement patterns, the degree of reflex activity and the balance of muscle tone. The repetitive active movement stimulated by FES-facilitated gait also contributes to motor learning and neuroplastic changes in the CNS. By establishing and promoting active motion in patients with foot drop, FES fosters long-term improvements in motor control, balance of muscle activation and quality and efficiency of gait. Unique features of the WalkAide FES System make it particularly well suited to the treatment of foot drop. The WalkAide is the only device on the market that uses tilt sensors to detect the angular velocity of the leg during gait and to use this information to determine when to trigger stimulation, and thus muscle contraction, during the gait cycle. Most other devices use a heel-sensor-triggered switch to detect the beginning and end of swing phase. Since heel switch devices stimulate whenever the heel is off the ground, stimulation may occur when the heel, but not the toes, are raised. This can promote inefficient walking...
patterns including steppe gait and stiff legged walking with hip circumduction and vaulting. By triggering stimulation specifically in response to leg movement in the sagittal plane, the WalkAide stimulates dorsiflexion when the patient swings their leg straight through in the sagittal plane. This unique tilt sensor triggered stimulation promotes normal gait not only by stimulating optimal timing of ankle dorsiflexion during gait but also by helping the patient decrease compensatory motions and improve voluntary motor control at the hip and knee. All of these features contribute to the WalkAide allowing the person with foot drop to walk faster, more safely and with reduced energy consumption.11,16,47

The WalkAide FES System can also be precisely tailored to each individual’s gait pattern and can adapt to a range of patient-initiated changes in gait. It alters the timing of the stimulation if walking speed direction or step length, change. It also adapts to changes produced by different gait tasks, such as walking up or down stairs or inclines or walking on rough terrain. Having a tilt sensor on the leg rather than a heel switch also allows the patient to use the WalkAide with a wide variety of footwear, or even to walk barefoot (see Figure 3). All of these features give the patient improved function during a wide range of activities of daily living and improve quality of life. The unique design and construction of the WalkAide System further contribute to its utility. The entire device is essentially contained in one component. The unit attaches to a lightweight cuff strapped around the leg that can be accurately placed and fully operated with one hand. The cuff is fully washable and the device is powered by a single AA battery that lasts for up to one month of use. The WalkAide System offers you and your patients the latest advance in the treatment of foot drop. It is the most physiologic and effective approach for optimising gait mechanics and efficiency in patients with foot drop, allowing them to walk quickly, efficiently, and safely in the widest range of conditions.
Does Functional Electrical Stimulation for Foot Drop Strengthen Corticospinal Connections?

Dirk G. Everaert, PhD,1 Aiko K. Thompson, PhD,1,2 Su Ling Chong,1 and Richard B. Stein, DPhil1

Abstract

Background. Long-term use of a foot-drop stimulator applying functional electrical stimulation (FES) to the common peroneal nerve improves walking performance even when the stimulator is off. This “therapeutic” effect might result from neuroplastic changes. Objective. To determine the effect of long-term use of a foot-drop stimulator on residual corticospinal connections in people with central nervous system disorders. Methods. Ten people with nonprogressive disorders (eg, stroke) and 26 with progressive disorders (eg, multiple sclerosis) used a foot-drop stimulator for 3 to 12 months while walking in the community. Walking performance and electrophysiological variables were measured before and after FES use. From the surface electromyogram of the tibialis anterior muscle, we measured the following: (1) motor-evoked potential (MEP) from transcranial magnetic stimulation over the motor cortex, (2) maximum voluntary contraction (MVC), and (3) maximum motor wave (M_max) from stimulating the common peroneal nerve. Results. After using FES, MEP and MVC increased significantly by comparable amounts, 50% and 48%, respectively, in the nonprogressive group and 27% and 17% in the progressive group; the changes were positively correlated (R^2 = .35; P < .001). Walking speed increased with the stimulator off (therapeutic effect) by 24% (P = .008) and 7% (P = .014) in the nonprogressive and progressive groups, respectively. The changes in M_max were small and not correlated with changes in MEP. Conclusions. The large increases in MVC and MEP suggest that regular use of a foot-drop stimulator strengthens activation of motor cortical areas and their residual descending connections, which may explain the therapeutic effect on walking speed.

Keywords

neuroplasticity, transcranial magnetic stimulation (TMS), multiple sclerosis, stroke, electromyogram (EMG), foot drop

Introduction

Since Liberson et al1 applied the first foot-drop stimulator in 1961, electrical stimulation has been used to dorsiflex the ankle during the swing phase of the gait cycle in people with limited active ankle dorsiflexion. Liberson et al found that the foot-drop stimulator had an immediate beneficial effect on walking in some people, similar to the effects of an ankle-foot orthosis. The immediate improvement in walking performance is now often referred to as an orthotic effect. They also noted that the improvement could continue for some time after the stimulation was turned off, which they referred to as a carryover effect. Regular use of functional electrical stimulation (FES) for foot drop leads to a longer-lasting improvement after the stimulation is turned off. This therapeutic or training effect has been noted often2-5 and can last for days or weeks. What is being trained and how the training occurs is not clear. Muscles, spinal circuits generating the walking pattern, and/or residual, descending corticospinal pathways could all be strengthened.

Some support for the idea that corticospinal connectivity improves with long-term FES use comes from studies that have used transcranial magnetic stimulation (TMS). During the past 30 years, TMS has become increasingly popular for measuring corticospinal connections.6,7 TMS produces little discomfort and stimulates cortical circuits that then activate pyramidal neurons synaptically in the motor cortex. Several studies have documented that short-term electrical stimulation of peripheral nerves increases the motor-evoked potential (MEP) in response to TMS over the leg area of the motor cortex.8-10 Thompson and Stein10 showed that in healthy people, FES alone in quietly seated people or FES timed to the swing phase of walking caused increased
corticospinal excitability within 30 minutes and that this excitability remained high for at least 30 minutes after the end of nerve stimulation. In contrast, 30 minutes of walking on a treadmill did not increase corticospinal excitability. Thomas and Gorassini reported an increased response to TMS (46%) after 3 to 5 months of intensive treadmill training in patients with incomplete spinal cord injury (SCI). In the companion article, we found that people with various central nervous system (CNS) disorders experienced a therapeutic effect when they used prototypes of a new foot-drop stimulator (WalkAide, Innovative Neurotronics Inc, Austin, TX) for 3 months or more. Those with generally nonprogressive disorders such as a stroke or SCI had a 17.8% increase in walking speed after 3 months and 28% after 11 months (P < .001, measured with the stimulator turned off). The increases in speed for those with progressive disorders such as multiple sclerosis (MS), were 9.1% (P = .004) and 7.9% (P = .12), respectively.

We were interested in investigating whether there were common corticospinal mechanisms underlying the improvements in walking performance after FES use in people who have foot drop arising from different CNS disorders. To analyze possible mechanisms, we used TMS and other electrophysiological techniques. We tested people with nonprogressive and progressive conditions before and after 3 to 12 months of using a foot-drop stimulator while walking in the community. We hypothesized that long-term FES use would strengthen the residual descending connections from motor-related areas of the cortex. Changes in corticospinal excitability were determined by measuring MEPs in the ankle dorsiflexor muscles resulting from transcranial magnetic stimuli.

Methods
Participants

The participants for this study were a subset of the larger group that participated in the multicenter trial (WalkAide trial) studying the effects of a foot-drop stimulator on walking performance as described in the accompanying article. Only those from the Edmonton center were recruited for this part of the study because the TMS and other electrophysiological test equipment were not available in the other centers. Furthermore, only those who entered the trial after approval was obtained for the TMS (April 2002) were included. Participants had a foot drop resulting from progressive and nonprogressive CNS disorders and were in a chronic stage, that is, at least 6 months after the injury or incident. Inclusion focused on the dysfunction related to foot drop, rather than on specific diagnosis; therefore, people with various disorders causing a foot drop were included. The basic inclusion criteria for the WalkAide trial are presented in detail in the companion article. Patients were excluded if they had contraindications for TMS according to the NIH guidelines (eg, history of epilepsy, metal in the head other than dental fillings, etc). Furthermore, 3 people were excluded who had no measurable MEPs at the start of the trial, even with maximum TMS output.

Study Design

Participants gave their written, informed consent to participate in the trial in accordance with the requirements of the human ethics committee of the University of Alberta. They were fitted with a WalkAide foot-drop stimulator, which they used on a daily basis at home and for walking in the community. The participants decided how much they would use the WalkAide, but use was recorded by the device and later analyzed. In those with bilateral foot drop, the stimulator was only applied to the more affected limb.

Before the participants started using the WalkAide at home, data were collected for walking performance and the electrophysiological measures. All participants came back for testing after 3 months of WalkAide use. Those who were willing and able to participate in a longer follow-up were tested again at 6 months and at about 12 months, when possible.

Foot-Drop Stimulator and Walking Speed

Full details on the WalkAide and walking test were presented in the companion article. The WalkAide stimulates the common peroneal nerve to dorsiflex the ankle during the swing phase of the gait cycle. Briefly, it consists of a stimulator unit mounted on a cuff that fits around the upper part of the shank and calf. Two electrodes are attached to the inside of the cuff with Velcro. The cuff has a molded hard plastic insert that facilitates proper positioning of the electrodes over the nerve and tibialis anterior (TA) muscle. The WalkAide uses either a tilt sensor or a heel sensor to control the stimulation timing. For all participants in this trial, good control of the timing of stimulation was obtained with the tilt sensor. The tilt sensor is the preferred trigger mode because it is integrated in the unit and thus eliminates the need for an external heel sensor.

Walking speed was measured with a 4-minute walking test around a 10-m figure of 8. During the 4-minute test, the physiological cost index (PCI) was also determined as a measure of effort. During each test session, the figure-8 test was performed twice, once with the stimulator turned on (FES On) and once with the stimulator off (FES Off). For this study, we calculated the changes in walking speed over time with FES Off (speed after N months FES use – baseline speed), previously defined as the therapeutic effect of the foot-drop stimulator. The therapeutic effect reflects the
improvements in walking related to physiological factors, whereas the so-called orthotic effect (speed with FES On vs Off) reflects improvements caused by biomechanical factors. We excluded the orthotic effect of the stimulator when comparing changes in speed with the changes in corticospinal excitability.

**Electrophysiological Measures**

**Maximum voluntary contraction (MVC).** Participants were comfortably seated with their shank and foot in a device holding the ankle at about 100° with a strap over the midfoot. The skin was cleaned with alcohol and dried before placing the electromyogram (EMG) electrodes. Self-adhesive Ag-AgCl electrodes (3.5 × 2.2 cm²; Vermont Medical Inc, Bellow Falls, VT) were placed about 2 cm apart over the belly of the TA muscle at about a third of the distance between the knee and the ankle. The EMG from the TA muscle of the more affected leg was rectified and smoothed with a 3-Hz first-order low-pass filter. The MVC was defined as the highest EMG reached during contractions of 2 to 4 s. Values for 3 separate contractions were averaged with a few seconds rest between measurements. MVC is usually measured as a force, but the force can be generated by a number of muscles. Use of EMG limits the measurement to the muscles being stimulated with FES and tested with TMS, which seemed more appropriate in the present study.

**Maximum motor wave (M_{mmax}).** The common peroneal nerve was stimulated (Grass SD-9 stimulator, AstroMed Inc, West Warwick RI) as it passes by the head of the fibula. The cathode was placed over a low-threshold point along the nerve, and the anode was placed 2 to 3 cm more distal and anterior over the TA muscle. The stimuli were applied every 2 to 4 s, and the responses to 4 stimuli were averaged at each intensity. The stimulus duration was 1 ms, and the intensity was increased in increments of 10% to 20% until further increase in the stimulus did not increase the motor wave (M-wave) for the TA muscle. M_{mmax} was defined as the peak-to-peak amplitude of the maximum M-wave.

**Motor-evoked potentials.** An MES-10 stimulator (Cadwell, Kennewick, WA) was used to deliver magnetic stimuli with a double-D coil having a radius of 8 cm. The intervals between stimuli varied randomly between 2.5 and 5 s, so participants could not anticipate the time of stimulation. The coil was placed over the leg area of the motor cortex (see the description of the procedure for details). MEPs were recorded from the TA muscle while the participants contracted the TA to a level that was 15% to 20% of MVC, as displayed on an oscilloscope. Because the MVC of many participants changed over the course of the trial, and MEPs are sensitive to the background level, we tried to match the background contraction to 15% to 20% of the baseline MVC before FES use during all subsequent recordings.

van Hedel et al. found that the highest test–retest reliability for MEPs in the TA muscle was obtained when controls and participants with incomplete SCI contracted at 20% to 40% of MVC. We used the lower end of this range to minimize fatigue. We did not measure MEPs at rest (without background contraction), because some participants had no resting MEP at all, and in many participants, we could not measure a 50-μV response that is sometimes used as a criterion to determine the TMS threshold for a resting MEP in the TA muscle.

The MEPs were averaged per set of 4 stimuli (see below) using a custom-written program in MATLAB (MathWorks, Natick, MA). The MEPs were quantified by means of the peak-to-peak value for each average (ppMEP) and the mean-rectified value (mrMEP) calculated as the average potential over a time window in which the response was higher than background (see vertical dashed lines in Figure 1). The window was fixed for all trials for the same participant during all follow-ups. Background was calculated as the
mean-rectified TA EMG for 40 ms before the stimulus, and this value was subtracted from the mrMEP.

**TMS Procedure**

To find the position with the maximum response to TMS or the “hot spot” for the TA muscle, the coil was initially placed at 1 cm lateral and 1 cm posterior to the vertex of the head, that is, the typical location for TA. Then, the coil was moved in centimeter increments to probe for locations with higher responses. Next, MEPs were measured at the hot spot to construct an input–output curve: 4 TMS stimuli were delivered at each of several intensities typically ranging from 60% to 90% of the maximum stimulator output. An example of a typical input–output curve is shown in Figure 2.

Next, a mapping of the MEPs was done. For this purpose, a transparent centimeter grid was lined up with the vertex of the head, and 4 TMS stimuli were delivered at each of 25 positions ranging from the midline to 3 cm lateral and from 3 cm anterior to 3 cm posterior to the vertex. This provided an MEP map of cortical regions that produced a response in the TA muscle. A stimulus level that produced 50% to 70% of the maximum MEP was used for mapping. The appropriate stimulator level was determined by increasing or decreasing the level until 50% to 70% of the maximum response was obtained, typically about 80% of maximum stimulator output. The same stimulus level was used both before and after FES use.

It took approximately 6 minutes to deliver the 100 stimuli for a complete map. Some participants could not maintain a contraction of 15% to 20% of MVC for this length of time, so rest breaks were given as needed. We limited the number of stimuli per point to 4 because fatigue is common in MS and some other CNS conditions. Although more stimuli might be desirable to reduce variability in the data, many participants would not have been able to maintain a contraction long enough. After the mapping, an input–output curve was repeated at the original hot spot. If the mapping revealed another location with high output, an input–output curve was also measured at that location.

**Data Analysis**

MEPs tend to be variable when repeated within the same recording session and between recordings on different days. Therefore, we calculated a maximum MEP (\(\text{MEP}_{\text{max}}\)) by averaging the mrMEPs of the 4 positions with the highest values from the mapping procedure together with the maximum values from the input–output curves. Thus, the \(\text{MEP}_{\text{max}}\) for each participant was based on at least 20 MEPs in total (4 at 4 locations and 4 at maximum intensity). Because the electrophysiological and walking measures differed widely between participants, most of the analysis was done on ratios dividing values after and before WalkAide use. For those with several follow-up sessions (eg, after 3 and 6 or 12 months of WalkAide use), we used the data from the session during which the background level of TA EMG best matched the level of the baseline session. Distributions of ratios tend to be skewed, because decreases are limited to between 1 and 0, whereas increases can range from 1 to infinity. Most mean values presented are geometric means (which are based on log ratios), because they are less influenced by outliers than the traditional arithmetic mean. Statistical testing was performed on log-transformed data because log ratios are more normally distributed. Regular and paired Student t tests were used to test for differences between groups and time points, respectively.

**Results**

**Participants**

Twenty-six participants with progressive CNS disorders (24 with MS and 2 with familial spastic paraparesis) met the inclusion criteria, as did 10 participants with generally nonprogressive disorders (6 with stroke, 2 with incomplete SCI, 1 with traumatic brain injury, and 1 with foot drop arising from surgical complications). The accompanying article showed that pooling of the different nonprogressive conditions was justified because there were no differences in walking performance at any of the time points between the conditions. Mean ages (± standard deviation) for the nonprogressive and progressive groups were 54.0 ± 15.5 years and 54.2 ± 9.2 years, respectively. Patients in the nonprogressive group had their condition on average for 13.7 years (range, 0.7-39 years) and those the progressive group for
11.8 years (range, 2-25 years). The mean time between the before and after test session was 6.5 months (range, 3-12 months) for the nonprogressive group and 5.2 months (range, 3-12 months) for the progressive group. None of these differences was statistically significant.

**MEP Changes in Selected Participants**

Figure 1 shows data from 2 participants with MS who had remarkable increases in their MEPs after WalkAide use. The top part of the figure shows more than 60 superimposed raw responses from the mapping procedure before (A) and after (B) 6 months of FES use for 1 participant. The raw traces show the TMS stimulus artifact at 0 ms followed by increased EMG activity after a delay of about 40 ms. The raw traces show occasional activity of larger motor units after FES use (large oscillations) that were not present before. The large motor units were active during background contraction but seemed more frequent after the TMS pulses. The middle part of Figure 1 (C and D) shows the mean-rectified responses for the same data. The burst of increased activity in the window from 40 to 75 ms, as indicated by the vertical dashed lines, is much larger after 6 months of FES (D) than before (C). However, for this participant, the level of background contraction was slightly higher for the retest (D). The time window of the MEP was the same before and after FES use. The bottom part of Figure 1 (E and F) shows data from another participant with MS. In this example, the participant maintained a slightly lower background for the retest after 6 months, but the MEP was still greatly increased.

Figure 2 shows an example of typical input/output curves for the MEPs elicited in a person with a stroke. Each value is the mean ± standard error of the mean (SEM) of 4 stimuli applied at each stimulation level. The mrMEP values are generally much smaller than the peak-to-peak values. To compare both, the mean-rectified values were scaled by a factor of 5. As previously documented,9,17 the stimulus–response relationship typically follows a sigmoidal curve. For this participant, the response reached a plateau at 80% to 90% of TMS output. The goodness of fit was not important for our study because we only wanted to verify that the plateau was reached and maximum MEPs were measured. The maximum peak-to-peak MEP for this stroke participant was much smaller (about 0.2 mV) than the values of 1 to 3 mV typically obtained for controls.9

Figure 3 shows a map of the MEPs that were elicited by stimulation over different points of the cortex for the same participant as in the upper parts of Figure 1. Figures 3A (smoothed surface plot) and 3B (actual values) show the map before WalkAide use. The values were generally below 0.1 mV, and there was a valley where a peak is normally expected for the leg area at approximately 1 cm lateral and 1 cm posterior to the vertex.8,9 After 6 months of WalkAide use, a central valley remained, but much larger responses were measured somewhat medial and anterior to this valley (Figures 3C and 3D). The presence of a valley with a rim of more functional tissue was observed quite commonly, but the areas that showed increased MEPs after FES use varied between participants (see also Stein et al3).

**Changes in MEPmax and MVC**

Figure 4 and Table 1 show the changes in physiological, functional, and control variables after WalkAide use. The mean increase (± SEM) in mean-rectified MEPmax after WalkAide use was 48% ± 17% (ratio after/before = 1.48;  

\[ P = .003 \]

for the nonprogressive group (from 41 to 60 µV) and 17% ± 11% (ratio after/before = 1.17;  

\[ P = .046 \]

for the progressive group (from 22 to 26 µV). Out of 36 participants, 19 (53%) had an increase in MEPmax of greater than 20%, and 11 participants (31%) had an increase greater than 40%. Whereas the nonprogressive group had significantly higher MEPmax values before and after FES use (  

\[ P = .033 \] and  

\[ P = .020 \], respectively) than the progressive group, the changes
The differential increase in MVC and MEPmax after WalkAide use was more substantial for the progressive group than for the nonprogressive group (Table 1). The mean increases in MVC after WalkAide use were similar to the MEPmax increases: 50% ± 20% (P = .008) for the nonprogressive group (from 55 to 82 μV), and 27% ± 18% (P = .013) for the progressive group (from 61 to 77 μV). The MVCs were not significantly different between the 2 groups (before, P = .70; after, P = .68; Table 1) and nor were the MVC changes (P = .31; Figure 4).

Figure 5 shows the relationship between MEPmax and MVC and their changes for all participants combined (nonprogressive and progressive group). There was a significant positive correlation between MEP and MVC (R² = .46; P < .001; Figure 5A). More important, whereas we already mentioned similar mean increases for MEPmax and MVC, Figure 5B shows a significant positive correlation between the MEPmax changes and MVC changes (i.e., the ratios; R² = .35; P < .001), indicating that those with greater increases in MEPmax after WalkAide use also had greater increases in MVC.

Changes in Walking Speed

The improvement in MVC and MEPmax carried over to walking speed. The mean increase (±SEM) in walking speed after WalkAide use, measured with FES Off (i.e., the therapeutic effect over time without the orthotic effect; see the Methods section) in the nonprogressive group was 24% ± 8% (P = .008), which is about half the increases in MEPmax and MVC. In the progressive group, the increase in walking speed was 7% ± 3% (P = .014), which is 41% of the change in MEPmax and 26% of the MVC change. Analysis of the PCI data showed that the increases in walking speed after WalkAide use were similar to the MEPmax increases: 50% ± 20% (P = .008) for the nonprogressive group (from 55 to 82 μV), and 27% ± 18% (P = .013) for the progressive group (from 61 to 77 μV). The MVCs were not significantly different between the 2 groups (before, P = .70; after, P = .68; Table 1) and nor were the MVC changes (P = .31; Figure 4).

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Changes in Walking Speed

The improvement in MVC and MEPmax carried over to walking speed. The mean increase (±SEM) in walking speed after WalkAide use, measured with FES Off (i.e., the therapeutic effect over time without the orthotic effect; see the Methods section) in the nonprogressive group was 24% ± 8% (P = .008), which is about half the increases in MEPmax and MVC. In the progressive group, the increase in walking speed was 7% ± 3% (P = .014), which is 41% of the change in MEPmax and 26% of the MVC change. Analysis of the PCI data showed that the increases in walking speed after WalkAide use were similar to the MEPmax increases: 50% ± 20% (P = .008) for the nonprogressive group (from 55 to 82 μV), and 27% ± 18% (P = .013) for the progressive group (from 61 to 77 μV). The MVCs were not significantly different between the 2 groups (before, P = .70; after, P = .68; Table 1) and nor were the MVC changes (P = .31; Figure 4).

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speed were not because of an increased effort (ie, because the participants were trying harder). The mean PCI changes (measured with FES Off) were negative in both groups (although not significantly), suggesting that the participants were walking with less effort after WalkAide use. The mean decreases were, respectively, 4% ± 8% (P = .69) and 3% ± 5% (P = .44) for the nonprogressive and progressive groups.

Changes in M_{max} and Background Activity

The M_{max} and background activity were also measured. The increases in MEP_{max}, MVC, and walking speed could possibly be caused by increases in muscle size, rather than cortical or spinal changes. Therefore, we measured the change in M_{max} before and after WalkAide use. The mean increase (± SEM) in M_{max} was significant (12% ± 4%; P = .018; Figure 4) in the nonprogressive group (from 2.38 to 2.66 mV; Table 1) but not significant (6% ± 10%; P = .52) in the progressive group (from 2.53 to 2.67 mV). The M_{max} increases indicate that both groups may have had some hypertrophy of the TA muscle. However, the increases in M_{max} were much smaller and not correlated with the changes in the MVC and MEP_{max} (R^2 = .086 and .022, respectively).

Furthermore, the measured increases in MEP_{max} could also be secondary to an increase in the participant’s voluntary background contraction because a higher level of background contraction results in higher MEPs. The mean changes in level of background contraction were very small and not significant: 2% ± 6% (P = .78) for the nonprogressive group and 3% ± 1.5% (P = .06) for the progressive group.

Discussion

The most interesting finding in this study was that use of a foot-drop stimulator for several months resulted in large, correlated increases in the MVC and the MEP elicited by stimulating the leg area of the motor cortex and related areas. A marked increase in voluntary contraction and MEPs in a few months as a result of using a FES device is remarkable considering that one group had been stable (nonprogressive) and the other slowly declining (progressive) for many years. Because of the chronic condition of the participants, the changes were unlikely to be a result of spontaneous recovery. The increases in MVC and MEP indicated that the participants had better voluntary control over the TA muscle. Therefore, the increases in walking speed probably resulted from the improved voluntary control. The changes in walking speed were smaller than the physiological changes, but this is not surprising because walking involves more muscle groups than just the ankle dorsiflexors. Other muscles, such as the ankle plantar flexors that are not being stimulated by the foot-drop stimulator, did not change. Therefore, strengthening the voluntary control of only the ankle dorsiflexor muscles would be expected to have a small effect on the overall walking speed. Possible explanations for the physiological changes are explored further in the following sections.

Changes in Background Contraction, Muscle Size, and Walking Activity

The MEPs were measured while the participants were asked to maintain a target level of voluntary contraction in the TA muscle as shown on an oscilloscope (see the Methods section). Without a voluntary contraction, the responses were small or absent in many participants. Because the magnitude of the MEP is quite dependent on the background level,19 the levels were carefully matched before and after using FES. The level of background contraction was well matched with only a 2% to 3% increase on average during retesting, and this change was not statistically significant. Thus, the large, significant increases in MEP_{max} of about 30% to 50%
after WalkAide use are unlikely to result from changes in background contraction. Changes in MVC and MEP could also result from an increase in muscle mass, that is, hypertrophy caused by training. As $M_{\text{max}}$ is related to muscle mass, the relatively small increases of 6% to 12% in $M_{\text{max}}$ indicated that muscle hypertrophy was probably not the major cause of the larger changes in $\text{MEP}_{\text{max}}$.

An alternative explanation is that the MEP and MVC increases did not result directly from the FES but arose just from walking more. The amount that participants walked on a daily basis was not controlled but was measured by the WalkAide device. The participants of the TMS study were already community ambulators, walking 1850 steps/day on average before WalkAide use, and they increased their walking to about 2100 steps/day during the study. We have previously shown that walking activity in itself (normal participants walking for 30 minutes on a treadmill without FES) does not cause an increase but rather a slight decrease in MEPS to the TA muscle. Thus, the extra activity of 250 steps/day was unlikely to cause the large increases in $\text{MEP}_{\text{max}}$ and MVC.

### Changes in Spinal Circuits

Yet another possible reason for the changes in electrophysiological and functional measures is some alteration in spinal circuits. We recently showed that patients with foot drop caused by CNS disorders had increased H-reflexes in the soleus muscle. The enhanced soleus reflex may be a contributing factor to foot drop because it produces increased resistance to ankle dorsiflexion. Chen et al. were able to condition the H-reflex, the electrical analog of the stretch reflex, up or down in spinal animals. However, Thompson et al. found no significant decrease in the soleus H-reflex after use of the foot-drop stimulator, so the soleus H-reflex does not seem to be related to the functional changes observed here.

Reduced disynaptic inhibition of the soleus muscle has also been reported in various CNS conditions. Because of lack of inhibition, the antagonist calf muscles may not be turned off with TA activity during the swing phase, which may also contribute to foot drop. Thompson et al. found that reciprocal inhibition of the soleus muscle was significantly reduced after but not before using FES, which would also not contribute to a functional improvement in foot drop. Finally, reciprocal inhibition of the TA muscle is abolished in participants with nonprogressive disorders but not in those with progressive disorders and returns after FES use in these participants. The restored inhibition is in the opposite direction to that expected with an increase in the TA MEP. Thus, there are numerous changes in spinal circuitry, but they don’t seem to account for the increased MEPS to the TA muscle in the current study.

### Possible Mechanisms for the Changes in Corticospinal Excitability

We concluded that the most likely explanation for the large increase in MEPS is that the activation of motor-related areas of the cortex and their residual corticospinal pathways has been strengthened. Analysis of the MEP mapping data showed that the patients often had lower MEPS focused over the leg area, which means that the cortical damage was quite selective in conditions such as stroke and MS. After use of the foot-drop stimulator, increased MEPS were generally measured at locations adjacent to tissue damaged by the disease process (see Figure 3). This shift in locations with high output indicates that adjacent areas may “take over” to some extent from the damaged leg area. The mechanism for this shift is not known but probably involves coupling of sensory signals from the electrical stimulation and from the walking movements with motor signals (eg, from descending commands). This coupling might lead to Hebbian learning, perhaps through long-term potentiation.

Which combinations of sensory-motor signals are most effective to promote plasticity is not clear, and different signals may have different roles. Voluntary activation or repetitive electrical stimulation of nerves in a limb may produce large, transient changes (minutes to hours) in MEPS. Our participants used FES during walking on a daily basis, which may have produced accumulating effects that developed over a few days or months. In resistance training of the TA muscle in able-bodied persons, MVC increased faster in the first couple of weeks than could be accounted for by protein synthesis in the muscle. This increase was associated with an increased MEP with no change in the M-wave. Thus, our data and other recent studies support the hypothesis proposed in the Introduction section that repetitive daily stimulation makes the transient changes in MEPS longer lasting and more stable. Long-term potentiation of neural pathways, which might be an underlying mechanism, has been described with different time courses, depending on whether protein synthesis and/or gene expression are activated.

Some anecdotal observations in our patients further support the hypothesis. Several participants reached the point where their voluntary dorsiflexion was sufficient, so that they didn’t need the foot-drop stimulator after the trial. Others found that their voluntary control weakened again if they didn’t use FES. Some reported that using the stimulator every few days, particularly when they were planning to do a lot of walking, was sufficient to maintain function.

Although the increases in the MVC and MEP were smaller in the progressive group, the differences between groups were not statistically significant. Our study included people who had a stroke as well as people with MS, who showed dramatic increases in MEPS (see Figures 1 and 3),
suggesting that the same plastic changes were operative in participants with progressive disorders as in those with non-progressive disorders. The improvements in MVC and MEP that were observed in those with progressive disorders are probably not maintained indefinitely. We do not claim that stimulation can prevent the inevitable consequences of a disease such as MS. However, this article and the accompanying one provide strong evidence that using a foot-drop stimulator can maintain walking speed and strengthen residual neural connections in people with secondary progressive MS as well as in those with nonprogressive disorders.

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References


Using FES for Foot Drop Strengthens Cortico-Spinal Connections

Stein RB 1, Everaert D 1, Chong SL 1 Thompson AK 2

1 Centre for Neuroscience and Department of Physiology, University of Alberta, Edmonton, Canada
2 Wadsworth Center, N.Y. State Department of Health, Albany NY, USA
Richard.Stein@UAlberta.ca.

Abstract

Thirty subjects with foot drop were studied before and after use of the WalkAide foot drop stimulator for 3-12 months. We measured: maximum voluntary contraction (MVC) as mean rectified EMG in tibialis anterior (TA) and soleus muscles, maximum M-wave from stimulating nerves to these muscles, motor evoked potentials (MEP) from motor cortical stimulation, walking speed and physiological cost index (PCI). MVC (40%), MEP (25%), velocity with FES (20%) all increased very significantly (p<0.001). Velocity without FES also increased (10%) and PCI (effort) decreased significantly (10%, p<0.05). Mmax did not change significantly in the whole population. The large increases in MVC and MEP suggest that regular use of FES strengthens residual, descending connections including those from motor cortex. The strengthened connections may also account for the well known carry-over effect that allows increased walking speed even without FES.

1 Introduction

In their initial report on the use of electrical stimulation to treat the common condition of foot drop, Liberson et al. [1] noted that some people who used the stimulation improved their walking function even after the stimulation was turned off. This “carry-over” effect has been noted many times subsequently and may have a time course from minutes to weeks. The term “training effect” is probably better, since the increase results from using the stimulation for a period of time. What is being trained and how the training occurs is not clear. Muscles, spinal circuits generating the walking pattern and/or residual, descending pathways could all be strengthened. In this paper we studied the possible role of residual, descending connections on the training effect in subjects who have used a recently developed foot drop stimulator (WalkAide) for 3 months or more. The WalkAide is now available commercially from Innovative Neurotronics, Inc. (Austin TX). We hypothesized that repeated, daily use of FES would strengthen cortico-spinal pathways and that the strengthening might persist after long-term use.

2 Methods

Subjects were assessed for the use of the WalkAide foot drop stimulator. Subjects who met the inclusion and exclusion criteria [2] and gave their written, informed consent did a number of tests before they took the device home and repeated the tests after 3-12 months of using the WalkAide. These tests included: 1) MVC, measured as the rectified and filtered EMG (3 Hz RC low-pass filter) from the TA and soleus muscles; 2) Maximum M-wave. For TA muscle the common peroneal nerve was stimulated as it passes the head of the fibula. The stimulus intensity was increased until the motor response reached a maximum value. For the soleus muscle the tibial nerve was stimulated in the popliteal fossa and the intensity was again increased until the response reached a maximum value; 3) Trans-cranial Magnetic Stimulation (TMS). Subjects contracted to a level of 15-20% of MVC. An MES-10 stimulator (Cadwell, Kennewick WA) was used with a double-D coil having radii of 8 cm. Input-output curves and mapping were done as described previously [2]. We measured peak-to-peak and mean rectified values with respect to a baseline EMG level in the 40 ms prior to the stimulus; 4) Walking speed was tested on a monthly basis both with and without FES over a straight 10 m distance and around a 10 m figure-of-eight for 4 minutes [2]. 5) PCI, which gives a measure of effort, was calculated as a change in heart rate to walk a given distance during the 4 min. walking trials [2].

3 Results

People with a variety of CNS disorders that cause foot drop can benefit from FES. Therefore, we accepted people with various conditions into the trial, but did categorize them...
into generally progressive (n= 20; multiple sclerosis, hereditary progressive paraparesis, etc.) and generally non-progressive (n=10; stroke spinal cord injury, head injury, etc.) conditions. Since the effects might be more variable in the progressive group, more subjects were enrolled with progressive disorders. Most multiple sclerosis patients enrolled were judged to be slowly progressive (not subject to acute attacks and partial recoveries) by a neurologist (K. Warren) who specializes in this disease. The mean ages of the subjects and the times since onset of the conditions were similar.

Figure 1 shows that there are highly significant increases in many variables. The MEP and the MVC increased similarly for the non-progressive group. For the progressive group the increase (23%) was intermediate between the increases in MVC and walking speed. The increases for both groups were statistically significant (p<0.05), but not significantly different from one another. Although the walking speed increased, the effort (PCI) to walk a given distance decreased by ~10%.

**4 Discussion and Conclusions**

Most of the measures recorded increased substantially. The largest increase and most interesting finding in this study was that the use of FES for 3 months or more produced large increases in maximum voluntary contraction (MVC) and in motor evoked potentials (MEPs) evoked by stimulating the leg area of the motor cortex. The increases could perhaps be due to increasing the size and strength of the muscle, rather than cortical or spinal changes. Therefore, we measured the change in the maximum M-wave before and after the use of the WalkAide. It increased a small amount (about 10%), presumably from some hypertrophy of the muscle. However, the increase was much smaller than for the change in MVC and the MEP. The difference was significant for the non-progressive group (p<0.05); there was greater variability in the progressive group, and the difference did not reach statistical significance.

The increase in MEP could also be secondary to an increase in the background voluntary contractions that the subjects generated, which is known to affect the MEP [3]. Without a voluntary contraction the responses were small or absent in many subjects, so subjects were given a target level to maintain (see Methods). Although we tried to match the levels before and after, the background levels were about 15% higher after using the FES. However, the 40% increase in the MEP amplitude is more than can be attributed to the 15% increase in background. This increase was significant for the progressive group and the whole group, but did not reach significance with the smaller size of the non-progressive group. Actually, subjects exerted less effort to maintain the background after FES, since it was now a smaller fraction of the MVC. The effects of Mmax and background activity are not additive. A larger Mmax would affect both the MEP and the background activity, so the differential increase can be explained most easily in terms of strengthened cortico-spinal connections.

Another possibility is that the increases are due to changes in spinal circuits. We have also studied spinal reflexes in these subjects and observed some changes (unpublished observations). However, the present findings can not easily be attributed to changes at the spinal level [4].
How can FES strengthen residual cortico-spinal connections? The mechanism is not known but probably involves coupling of sensory signals from the stimulation and from the walking movements with motor signals (e.g., from Renshaw cells) and descending commands. Use or repetitive stimulation of a limb produces large, transient changes (minutes to hours) in MEPs [5, 6]. Since the subjects mainly used FES on a daily basis, accumulating effects may develop in months or even days [7]. Thus, the data are consistent with, but can not prove the hypothesis in the Introduction, namely that repetitive daily use makes the transient changes in cortical excitability longer lasting and more stable. Several subjects reached the point where the voluntary dorsiflexion was sufficient that they didn’t need the foot-drop stimulator after the trial. If they didn’t use it, others found that their voluntary control weakened. They reported that using the stimulator every few days, particularly when they were planning to do a lot of walking, was sufficient to maintain function.

We were surprised that the increases were almost as large in the progressive group as in the non-progressive group. Any differences that appear between the two groups in Fig. 1 were not statistically significant. However, the progressive subjects with MS were selected to have a slowly progressive form, rather than the recurring/remitting form. Inclusion of the latter form of MS would have made it very difficult to determine trends. The improvements were observed over 3-12 months, but would probably not be maintained indefinitely. We do not claim that stimulation can prevent the inevitable consequences of a disease such as MS. Indeed, two subjects with MS and one with spinal cord injury had to be excluded because their condition worsened dramatically during the period of study. Nonetheless, the progressive subjects were particularly enthusiastic about using the foot-drop stimulator. In part, this may result from the very negative prognosis of a progressive disorder such as MS. Any improvement, even if only for a limited period of time, is most welcome. If progressive subjects can remain ambulatory in their own home and not become dependent on wheelchairs and/or assisted living facilities for a few more years, this can significantly reduce health care and social service expenditures.

References

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Long-Term Therapeutic and Orthotic Effects of a Foot Drop Stimulator on Walking Performance in Progressive and Nonprogressive Neurological Disorders

Richard B. Stein, DPhil,1 Dirk G. Everaert, PhD,1 Aiko K. Thompson, PhD,1,2 Su Ling Chong,1 Maura Whittaker, MBA,3 Jenny Robertson,3 and Gerald Kuether, MD4

Abstract

Background. Stimulators applying functional electrical stimulation (FES) to the common peroneal nerve improve walking with a foot drop, which occurs in several disorders. Objective. To compare the orthotic and therapeutic effects of a foot drop stimulator on walking performance of subjects with chronic nonprogressive (e.g., stroke) and progressive (e.g., multiple sclerosis) disorders. Methods. Subjects with nonprogressive (41) and progressive (32) conditions used a foot drop stimulator for 3 to 12 months while walking in the community. Walking speed was measured with a 10-m test and a 4-minute figure-8 test; physiological cost index (PCI) and device usage were also measured. The subjects were tested with FES on and off (orthotic effect) before and after (therapeutic effect) stimulator use. Results. After 3 months of FES use, the nonprogressive and progressive groups had a similar, significant orthotic effect (5.0% and 5.7%, respectively, \( P < .003 \); percentage change in mean values) and therapeutic effect with FES off (17.8% and 9.1%, respectively, \( P < .005 \)) on figure-8 walking speed. Overall, PCI showed a decreasing trend (\( P = .031 \)). The therapeutic effect on figure-8 speed diverged later between both groups to 28.0% (\( P < .001 \)) and 7.9% at 11 months. The combined therapeutic plus orthotic effect on figure-8 speed at 11 months was, respectively, 37.8% (\( P < .001 \)) and 13.1% (\( P = .012 \)) and PCI decreased 18.2% (\( P = .038 \)) and 6.5%, respectively. Conclusions. Subjects with progressive and nonprogressive disorders had an orthotic benefit from FES up to 11 months. The therapeutic effect increased for 11 months in nonprogressive disorders but only for 3 months in progressive disorders. The combined effect remained significant and clinically relevant.

Keywords

stroke, multiple sclerosis, spinal cord injury, drop foot

Introduction

Foot drop is a common symptom in various disorders of the central nervous system (CNS), such as stroke, multiple sclerosis (MS), and incomplete spinal cord injury (SCI). Foot drop results from weakness or lack of voluntary control in the ankle and toe dorsiflexor muscles. Concomitant spasticity of antagonistic calf muscles may further limit ankle dorsiflexion, and often synergistic knee and hip flexor muscles are weak. As a result, the foot drops and the toes may not clear the floor during the swing phase of walking.1-3 Disruption of the normal gait pattern may reduce walking speed, decrease walking endurance, and cause trips and falls. The conventional approach to treating foot drop has been the application of an ankle–foot orthosis (AFO). An AFO holds the ankle passively at about 90° and prevents the foot from dropping during the swing phase. Although an AFO mitigates some of the walking difficulty, it may not provide enough assistance, especially when the hip flexors are also weak.4 As an AFO passively limits ankle movement, it may stiffen the ankle joint and result in contractures of the plantar flexors. In addition, AFOs may have practical drawbacks because of size and weight and are not cosmetically appealing. Two different sizes of shoes may be needed.
An alternative approach is to apply functional electrical stimulation (FES) to the common peroneal (CP) nerve during the swing phase of the gait cycle. Through electrical stimulation the ankle can be flexed beyond 90°, which helps the toes to clear the floor during the initiation of the swing phase. Depending on the placement of the electrodes, ankle dorsiflexion will be associated with more or less eversion. The added eversion in the swing phase increases ankle stability during the next foot contact, as people with a foot drop often tend to invert and land on the lateral border of the foot. In addition, the stimulation may inhibit antagonists such as the calf muscles and assist flexion at other joints through a flexor reflex (withdrawal reflex). The clinical benefits of FES devices to enhance gait can be evaluated by comparing walking speed or other gait parameters with and without nerve stimulation. The immediate change in gait with FES on, compared with FES off, is sometimes referred to as the orthotic effect, because FES mimics the effect of an AFO in helping to clear the foot over the ground.

In addition to the orthotic effect, which is related to improved biomechanics of walking, foot drop stimulators also seem to have a physiological effect on voluntary ankle movement. Since Liberson et al first applied FES, several studies have noted that some hemiplegic subjects who used electrical stimulation improved their walking function, even after the stimulation was turned off. This phenomenon received the name carryover effect, because it was initially reported as a short-lasting (minutes) effect of the electrical stimulation. Subsequent studies have shown that the so-called carryover effect may increase over time with long-term and repeated use. In more recent studies, the change in walking performance over time, measured while FES is off, has been referred to as a therapeutic effect, a term that seems more appropriate for the changes associated with long-term FES use. The total effect of the FES is the sum of the orthotic and therapeutic effects. There have been a number of studies on the effects of peroneal nerve stimulators, mainly on people with stroke, and some of the results have been summarized in 3 review articles. All studies found an orthotic effect of using a foot drop stimulator. Studies on people with stroke generally described a therapeutic effect, but 2 randomized control trials did not confirm this result. In contrast, the occurrence of a therapeutic effect in chronic progressive diseases, such as MS, remains obscure. Taylor et al found no therapeutic effect for the MS group as a whole, although 3 out of 21 subjects showed a clinically relevant therapeutic effect. We previously reported results from 26 subjects with mainly nonprogressive disorders. In that earlier study differences between nonprogressive and progressive groups could not be analyzed because there were too few subjects with progressive disorders. Therefore, we subsequently enrolled more subjects, most of whom had progressive disorders. All subjects had their conditions for at least 6 months, so no spontaneous recovery without using FES was expected. The present study includes the 26 subjects from the preliminary study mentioned above.

The study on these chronic subjects was designed to answer several questions:

1. Do people with generally nonprogressive conditions experience a therapeutic effect, whereas people with progressive conditions only have an orthotic effect? This question is important because the therapeutic effect of FES may be an indication of plasticity in the CNS and lead to long-term improvement in the motor capacity of the affected limb.

2. What is the time course of the orthotic and therapeutic changes? Most previous studies only examined a single time point before and between 3 and 6.5 months after starting FES. In a progressive disorder there may be a therapeutic benefit at one time that disappears as the progression of the disease continues, so studying the full time course is required.

3. All subjects used a prototype of a new foot drop stimulator with an integrated tilt sensor that is now available commercially (WalkAide; Innovative Neurotronics, Austin, TX). Previous studies from other groups used devices with heel switch control. How successful is the tilt sensor in obtaining adequate control of the timing of stimulation? In this article, we describe the changes in walking performance in relation to these questions. A companion article focuses on possible central mechanisms underlying the therapeutic effect by testing corticospinal excitability using transcranial magnetic stimulation before and after using the foot drop stimulator.

**Methods**

**Subjects**

Subjects were included who had a foot drop resulting from progressive and nonprogressive CNS disorders and were in a chronic stage, that is, at least 6 months after the onset of the disorder. A test–retest design was used, wherein each subject is measured with and without a foot drop stimulator at various intervals to allow the magnitude of the therapeutic and orthotic effects to be calculated separately. As described in the Introduction, the difference (FES On – FES Off) at a given time is referred to as an orthotic effect. The difference between FES Off before and after a period of FES use is referred to as a therapeutic effect.
Inclusion focused on the dysfunction related to foot drop rather than on specific diagnosis; therefore, people with various disorders causing a foot drop were included: for example, stroke, incomplete SCI, brain injury, and MS. Additional criteria for inclusion in the trial were (1) adults aged 18 years or older; (2) inadequate dorsiflexion during the swing phase of gait, resulting in inadequate limb clearance; (3) medical referral to participate; (4) adequate cognitive and communication function to give informed consent, understand the training instructions, use the device, and give feedback; (5) ability to ambulate at least 10 m with or without a portable assistive device (eg, walker, crutch, cane, but no parallel bars). Exclusion criteria were (1) lower motor neuron injury with inadequate response to stimulation; (2) history of falls greater than once a week; (3) severe cardiac disease such as myocardial infarction, congestive heart failure, or a demand pacemaker; (4) fixed ankle contractures of >5° of plantar flexion with knee extended; (5) ambulation velocity greater than 1.2 m/s; (6) unable to operate the device safely; and (7) comorbid conditions unlikely to survive 1 year.

Subjects were mainly recruited from 3 participating centers (Edmonton and Vancouver in Canada and Hannover, Germany). One subject was recruited by Dr Joyce Fung (McGill University, Montreal, Canada) and one by Drs Kimito Momose and Kouji Ihashi (Yamagata Prefectural University of Health Science, Yamagata, Japan). Data were collected over a 6-year period between April 2002 and May 2008.

**Study Design**

Subjects gave their written, informed consent to participate in the trial in accordance with the human ethics committees of the participating institutions. During the first session, subjects were fitted with a WalkAide foot drop stimulator, and baseline walking data were collected. The subjects usually came back on a second day for training on how to use the WalkAide. Then, they took the WalkAide and started using it on a daily basis at home and for walking in the community. All subjects came back for testing after 1, 2, and 3 months. After 3 months most subjects wanted to continue to use the WalkAide. However, because of the costs, distances involved (some subjects lived up to 2000 km from the participating centers), and availability of devices, some subjects could not continue for longer periods of time. Those who could continue were tested at 6 months and, where possible, at about 12 months. Throughout their participation in the trial, the use of medications relevant to foot drop (eg, antispasticity drugs) was documented. The subjects were asked to maintain their medications constant, as far as possible, and not to start other therapies such as botulinum toxin (Botox).

**WalkAide Foot Drop Stimulator**

The WalkAide consists of a single-channel stimulator mounted on a cuff that fits around the upper part of the shank and calf. Two round, hydrogel electrodes (diameter 3.2 cm) are attached to the inside of the cuff with Velcro. The active electrode is typically positioned over the CP nerve just distal and dorsal to the head of the fibula, whereas the indifferent electrode is placed over the tibialis anterior muscle belly. Precise positioning of the electrodes usually results in adequate ankle movement balancing dorsiflexion with eversion. The lightweight cuff is only 5.5 cm high and is designed to provide optimal stability with minimal amount of skin coverage to increase wearing comfort over long periods of time. The cuff has a molded hard plastic insert, which facilitates proper positioning of the electrodes over the nerve and muscle from day to day.

To synchronize the stimulation with the swing phase of the gait cycle, the WalkAide uses a tilt sensor or a heel sensor. Thresholds for these sensors and other timing parameters are selected during an initial setup process during which the WalkAide is connected to a computer running custom-made software. During the setup process, a therapist controls the timing of the stimulation delivered by the WalkAide by operating a hand switch, while the subject walks at a comfortable pace. At the same time, the signals from the heel and tilt sensors are recorded by the computer. Optimizing routines are used to match the timing based on the tilt signal with the stimulation periods indicated by the heel signal or manual switch. If necessary, the thresholds and timing parameters can be adjusted manually to fine-tune the timing. After the optimal parameters have been downloaded into the WalkAide, one or more sets of data are collected with the patient walking at varying speeds, showing the continuous heel and tilt signal data and the periods where the stimulator was on. The accuracy of the tilt-based timing can be assessed graphically by looking at the overlap of the “On” periods indicated by the 3 trigger modes (tilt, heel, manual) and by comparing the “On” periods with the continuous heel and tilt signal. The parameter settings for the tilt sensor are deemed satisfactory when there are no missing or extra triggers during normal walking, that is, the device fires one stimulus train for each step. Furthermore, the start and duration of the “On” periods correspond with the other trigger modes (heel and hand switch).

**Walking Performance**

The primary outcome measures were walking speed and physiological cost index (PCI), which is a commonly used measure of walking effort. Walking speed was measured with a 10-m straight-line test. A 4-minute test around a 10-m figure-8 evaluated speed at a longer distance that...
included turns, and the concomitant effort expended. The subjects were asked to walk at their maximal safe speed for both walking tests. For the straight-line test, the time was measured for the subjects to cross 2 lines on the floor separated by 10 m, with 2 m at either end for acceleration to and deceleration from a steady walking speed. For the figure-8 test, the total distance walked in 4 minutes was measured. Both walking tests were performed with and without the stimulator turned on, which we refer to as FES On and FES Off. Each test session was started with the straight-line test that was performed twice with FES On and twice with FES Off, in a fixed order: Off–On–On–Off or On–Off–Off–On. Baseline testing was performed in the first order, but on successive visits the order was switched to minimize the effect of fatigue. The figure-8 tests were performed next, with FES Off first at baseline. The order of FES On and FES Off was also alternated for the figure-8 tests on successive visits. Subjects could not be blinded to whether the stimulation was on or off, because they could feel the stimulus and see their foot move. Similarly, the people measuring walking performance could not be blinded, because they too could observe the movements evoked by FES.

To calculate PCI, heart rate was registered with a Polar monitor every 15 seconds during the 4-minute figure-8 test, as well as 2 minutes before, and up to 4 minutes after. PCI is calculated as the difference between resting heart rate and active heart rate during walking (in beats/min), divided by the average walking speed (m/min) over the 4-minute walking period. The active heart rate was calculated as the average rate during the last 2 minutes of walking. The resting heart rate was calculated as the mean of the 2-minute rest period before the walking and the last 2 minutes of the rest period after walking. As the PCI calculations are sensitive to changes in resting heart rate, a number of precautions were taken to ensure reliable resting values. Sufficient time was given to the subjects to make sure their heart rate settled down before the start of testing. The subjects sat in a comfortable chair with an arm rest and were asked to relax, and talking was avoided. Heart rate was monitored continually, and the actual recording of the initial resting values was only started when a stable heart rate was reached. The heart rate after walking typically reached pre-walking resting values after 2 minutes of resting and was monitored for another 2 minutes. If necessary, the period was extended until the basal level from before walking was reached. Thus, the subjects were always at a resting heart rate before starting the next figure-8 test. The PCI may not be a good measure of effort in patients receiving medication that controls heart rate. However, we included all subjects in our PCI data, including the patients with known use of such medications, as analysis of their PCI data showed that their heart rates were still responsive to the periods of walking and rest.

Although the PCI is commonly used as a measure of effort in walking, it is not as reliable or sensitive as oxygen consumption measurements \( (V_{O_2}) \) as a measure of energy consumption.\(^{21-23}\) Equipment to measure \( V_{O_2} \) was not available at most of the centers, and the requirement for a large number of repeated measures meant that PCI was the only feasible method.

**WalkAide Usage**

In addition to walking performance, data were collected on usage of the WalkAide. The WalkAide keeps track of the number of hours per day that the device is on and the number of stimulus trains delivered per day. As each stimulus train normally represents 1 step, the device measures the number of steps taken with the device on a daily basis. The usage data were downloaded from the device each time the subject came in for testing. There was considerable day-to-day variability because some subjects did not wear the device on some days. Therefore, straight lines that minimized the least square error were fitted to the data over a period of about 100 days. Initial and final values for the percentage of days the WalkAide was used (per bin of 10 days), and for the number of hours/day and steps/day on the days it was used, were calculated from the fitted line at 0 and 100 days.

**Data Analysis**

All walking variables were analyzed for the effect of 3 factors, that is, Time, FES, and Group. The factor Time refers to the assessments from baseline (Time 0) up to 11 months. The factor FES refers to the data with FES On and Off. Group refers to the progressive and nonprogressive subject groups. To compare with other studies we defined 3 change scores for the different variables. Changes comparing FES On and Off at a given time are referred to as the orthotic effect. Changes over time (values at Time X – Time 0) are referred to as the therapeutic effect. We calculated the therapeutic effect for both the FES On and FES Off conditions. Finally, the combined orthotic and therapeutic effect, briefly referred to as the combined effect, was calculated as (values at Time X with FES On) – (values at Time 0 with FES Off).

Statistical analysis was performed using software from SPSS Inc (Chicago, IL). Generally, a 3-way ANOVA with 2 repeated factors (Time and FES) and 1 group factor (Group) was performed first to examine the main effects and interactions. When necessary, 2-way or 1-way independent or repeated-measures ANOVAs were performed afterward for more specific comparisons. For each ANOVA, sphericity was assessed using Mauchly’s test. When the condition of sphericity was not met \( (P < .05) \), Greenhouse–Geisser or Huynh–Feldt corrected statistics were used if the estimate of sphericity (epsilon) was respectively <.75 or >.75.
multiple comparisons, Bonferroni or Sidak corrected post hoc tests were used. For 1-way independent ANOVAs, the Brown–Forsythe corrected statistics were used when the homogeneity of variances criterion was violated, and Hochberg’s GT2 procedure was used for the post hoc tests when sample sizes were very different. Full statistical details are presented in this article only once. F values and degrees of freedom for the ANOVAs are omitted in the text when they are given in the figures and tables. P values > .05 are reported in the text as NS (nonsignificant) when available as a number in figures and tables.

Results

Subjects

Descriptive statistics of the progressive and nonprogressive groups are given in Table 1 for the 73 subjects who completed at least 3 months of the study. Eleven other subjects dropped out of the study. Four subjects dropped out because of medical reasons (not related to the WalkAide) and 1 was too busy and could not make the time commitment. Two subjects gave up after, respectively, 1 and 2 months because they did not like the WalkAide or did not get enough benefit from it, and another subject dropped out after 2 months because of skin irritation under the electrodes. Within the nonprogressive group (n = 41), the largest number had a cerebrovascular accident (CVA, 26). Others had foot drop from an SCI (9), surgical complications (3), head injury (2), and cerebral palsy (1). The progressive group (n = 32) consisted of 31 subjects diagnosed with secondary progressive MS (rather than the relapsing–remitting form) and 1 with familial spastic paraparesis. The nonprogressive and progressive groups did not differ significantly in age or time since onset. The means ± standard deviations (SD) were, respectively, 52.0 ± 16.0 and 54.2 ± 9.8 years for age (F(1, 67.5) = 0.56; P = .46) and 10.7 ± 11.7 and 11.5 ± 8.6 years for time since onset of disease (F(1, 71) = 0.18; P = .73). All subjects lived independently at home, alone or with their family, and were able to walk in the community without assistance from other people. Some walked without aides; others used aides such as a cane, 2 elbow crutches, and 3 or 4 wheeled walkers, and a few with higher level of disability used a motorized scooter for longer distances.

To justify the pooling of the walking data for the subjects with CVA, SCI, and other conditions, we checked for differences between these subgroups in the nonprogressive group. Pooling was justified as 2-way mixed ANOVAs (FES × Condition) revealed no significant differences in any of the walking variables (figure-8 speed, straight-line speed, and PCI) between the subjects with CVA, SCI, and other conditions at baseline and 1, 2, and 3 months follow-up. The 1 subject with familial paraparesis was pooled together with the MS subjects into the progressive group.

Tilt Versus Heel Sensor Control

For 72 out of the 73 subjects, the tilt sensor was adequate to obtain good timing of the stimulation, according to the criteria explained in the Methods. Only 1 subject used the heel switch because he had a very stiff-legged gait, taking small steps with insufficient modulation in tilt to reliably trigger stimulation. Two others used a heel switch initially for the same reason, but then switched to a tilt sensor after a few weeks, as their walking pattern improved.

Walking Speed: 3-Month Follow-up

Figure 1 shows the changes in walking performance over the first 3 months with FES On and Off for the progressive and nonprogressive groups. Figure 1A shows figure-8 walking speed for 40 nonprogressive and 32 progressive subjects.

| Table 1. Subject Characteristics for Nonprogressive and Progressive Groups |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                | n       | Age (Years) | Since Onset (Years) | Male (%) | 10-m Speed (m/s) | Figure-8 Speed (m/s) | PCI (Beats/m) |
| Nonprogressive |         |            |                     |          |                 |                    |               |
| CVA            | 26      | 58.8 ± 14.6| 7.5 ± 8.7           | 54       | 0.64 ± 0.26     | 0.47 ± 0.17        | 0.71 ± 0.39   |
| SCI            | 9       | 45.1 ± 9.2 | 21.1 ± 15.3         | 89       | 0.82 ± 0.36     | 0.48 ± 0.22        | 1.33 ± 0.73   |
| Other          | 6       | 32.7 ± 8.5 | 8.9 ± 9.3           | 50       | 0.66 ± 0.43     | 0.48 ± 0.30        | 1.23 ± 0.87   |
| Total          | 41      | 52.0 ± 16.0| 10.7 ± 11.7         | 61       | 0.68 ± 0.31     | 0.48 ± 0.20        | 0.92 ± 0.61   |
| Progressive   |         |            |                     |          |                 |                    |               |
| MS             | 31      | 54.2 ± 9.9 | 11.5 ± 8.7          | 52       | 0.80 ± 0.36     | 0.54 ± 0.23        | 0.80 ± 0.44   |
| FP             | 1       | 54.0       | 12.0                | 100      | 0.30            | 0.21               | 1.04          |
| Total          | 32      | 54.2 ± 9.8 | 11.5 ± 8.6          | 53       | 0.78 ± 0.36     | 0.53 ± 0.23        | 0.80 ± 0.44   |

Abbreviations: PCI, physiological cost index; CVA, cerebral vascular accident (stroke); SCI, spinal cord injury (complete); MS, multiple sclerosis (secondary progressive); FP, familial spastic paraparesis; FES, functional electrical stimulation.

aOther causes of foot drop in the nonprogressive group were surgical complication (3), head injury (2), and cerebral palsy (1). Onset indicates time since onset of injury or disease. Speed indicates walking speed measured with 10-m straight-line test and 4-minute figure-8 test at baseline with FES Off. PCI also measured at baseline with FES Off. All values are mean ± standard deviation.
Figure 1. Speed increases and physiological cost decreases after functional electrical stimulation (FES) use. Walking performance before and after 1, 2, and 3 months of using the foot drop stimulator for the whole group (40 nonprogressive and 32 progressive subjects). Number of subjects varied between outcome measures because of missing values. Mean values are shown for measurements taken with FES On and Off at each time point for the nonprogressive and progressive groups. (A) 4-Minute figure-8 walking speed. (B) 10-m straight-line walking speed. (C) Physiological cost index (PCI). The tables give the results of a 3-way ANOVA (Time × FES × Group) for each variable. The factor Time refers to the measurements at 0, 1, 2, and 3 months; the factor FES refers to the measurements with FES On and Off. Significant effects with \( P < .05 \) are shown in italics. Changes over time are referred to as therapeutic effect; changes with FES On compared with FES Off are referred to as orthotic effect.

Three-way mixed ANOVAs (Time × FES × Group) revealed a significant main effect of FES (\( P < .001 \)) and Time (\( P < .001 \)) on figure-8 walking speed without any interactions between Time, Group, and FES (Time × Group, FES × Group, Time × FES, all NS). This indicates that, on average, all subjects walked significantly faster with FES On than with FES Off (ie, orthotic effect) and that the orthotic benefit was similar in the nonprogressive and progressive groups. The mean absolute walking speeds (m/s) and percentage changes in mean speed are given in Table 2. The nonprogressive group had a 5% orthotic benefit on figure-8 speed at baseline and at 3 months (Table 2). In the progressive group, the orthotic benefit was 2.3% at baseline and 5.7% at 3 months.

In addition to the immediate orthotic effect of FES, prolonged use of the WalkAide also had a therapeutic effect,
Table 2. Walking Performance Over 3 Months and 11 Months\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>FES Off</th>
<th>FES On</th>
<th>Orthotic Effect</th>
<th>Therapeutic Effect</th>
<th>Combined</th>
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<tr>
<td></td>
<td>0 Months</td>
<td>3 Months</td>
<td>0 Months</td>
<td>3 Months</td>
<td>0 Months</td>
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<tr>
<td><strong>3-Month Follow-up</strong></td>
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<tr>
<td>Figure 8 (m/s)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Nonprogressive</td>
<td>40</td>
<td>0.48 ± 0.032</td>
<td>0.56 ± 0.043</td>
<td>0.50 ± 0.033</td>
<td>0.59 ± 0.044</td>
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<tr>
<td>Progressive</td>
<td>32</td>
<td>0.53 ± 0.041</td>
<td>0.58 ± 0.047</td>
<td>0.54 ± 0.040</td>
<td>0.61 ± 0.046</td>
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<tr>
<td>10-m test (m/s)</td>
<td></td>
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<tr>
<td>Nonprogressive</td>
<td>32</td>
<td>0.68 ± 0.055</td>
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<td>0.71 ± 0.054</td>
<td>0.80 ± 0.065</td>
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<tr>
<td>Progressive</td>
<td>30</td>
<td>0.78 ± 0.066</td>
<td>0.82 ± 0.072</td>
<td>0.81 ± 0.072</td>
<td>0.88 ± 0.070</td>
</tr>
<tr>
<td>PCI (beats/m)</td>
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<td></td>
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<tr>
<td>Nonprogressive</td>
<td>38</td>
<td>0.92 ± 0.10</td>
<td>0.86 ± 0.10</td>
<td>0.92 ± 0.10</td>
<td>0.86 ± 0.10</td>
</tr>
<tr>
<td>Progressive</td>
<td>32</td>
<td>0.80 ± 0.08</td>
<td>0.78 ± 0.08</td>
<td>0.80 ± 0.08</td>
<td>0.73 ± 0.05</td>
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<tr>
<td><strong>11-Month Follow-up</strong></td>
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<tr>
<td>Figure 8 (m/s)</td>
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<tr>
<td>Nonprogressive</td>
<td>14</td>
<td>0.54 ± 0.071</td>
<td>0.69 ± 0.089</td>
<td>0.59 ± 0.071</td>
<td>0.74 ± 0.096</td>
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<tr>
<td>Progressive</td>
<td>19</td>
<td>0.55 ± 0.053</td>
<td>0.59 ± 0.070</td>
<td>0.57 ± 0.054</td>
<td>0.62 ± 0.069</td>
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<td>10-m test (m/s)</td>
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<tr>
<td>Nonprogressive</td>
<td>13</td>
<td>0.77 ± 0.102</td>
<td>0.96 ± 0.119</td>
<td>0.82 ± 0.100</td>
<td>1.02 ± 0.131</td>
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<tr>
<td>Progressive</td>
<td>20</td>
<td>0.78 ± 0.077</td>
<td>0.82 ± 0.096</td>
<td>0.81 ± 0.082</td>
<td>0.86 ± 0.092</td>
</tr>
<tr>
<td>PCI (beats/m)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonprogressive</td>
<td>13</td>
<td>0.86 ± 0.17</td>
<td>0.72 ± 0.11</td>
<td>0.87 ± 0.19</td>
<td>0.70 ± 0.12</td>
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<tr>
<td>Progressive</td>
<td>18</td>
<td>0.78 ± 0.09</td>
<td>0.79 ± 0.09</td>
<td>0.75 ± 0.09</td>
<td>0.73 ± 0.10</td>
</tr>
</tbody>
</table>

Abbreviations: FES, functional electrical stimulation; PCI, physiological cost index.

\(^a\) Results for walking speed measured with the 4-minute figure-8 and 10-m straight-line test and PCI. The group with 11-month follow-up (14 nonprogressive and 20 progressive subjects) is a subset of the group with 3-month follow-up (41 nonprogressive and 32 progressive subjects). The number of subjects varied somewhat between outcome measures because of missing values. Values (mean ± standard error of mean) are given at baseline (0 months) and endpoint for each group (3 and 11 months) with FES On and FES Off. The orthotic, therapeutic, and combined effects are percentage changes of the mean values calculated as follow: Orthotic effect = 100 × (FES On – FES Off)/FES Off; Therapeutic effect = 100 × (N Months – 0 Months)/0 Months; Combined effect = 100 × (N Months FES On – 0 Months FES Off)/(0 Months FES Off). N indicates number of subjects; Off means FES Off; On means FES On; Combined indicates Combined effect.
that is, figure-8 walking speed increased over time (main Time effect mentioned above). The therapeutic effect over the first 3 months was similar for FES On and Off (Time × FES, NS). Mean walking speed with FES On after 3 months was increased by 17.8% (from 0.50 to 0.59 m/s) in the nonprogressive group and by 12.6% (from 0.54 to 0.61 m/s) in the progressive group. The therapeutic effect at 3 months measured with FES Off was also 17.8% for the nonprogressive group and 9.1% for the progressive group. Although the increase in mean speed after 3 months was greater in the nonprogressive group than in the progressive group (especially with FES Off where the effect was nearly double), the 3-way ANOVA over all time points did not show a significant Time × Group interaction effect ($P = .23$) or a main Group effect ($P = .66$). The nonprogressive group had the largest increase in speed after 1 month of use (12% average for FES On and Off combined), whereas the increase was more gradual in the progressive group. However, Bonferroni corrected post hoc tests (for FES On/Off combined) showed that the therapeutic effect was already significant after 1 month use for both groups (nonprogressive $P < .001$; progressive $P = .039$).

Figure 1B shows walking speed for the 10-m straight-line test, which was available for 32 nonprogressive and 30 progressive subjects. The overall effects were similar to those for the figure-8 test. There was a significant orthotic effect (FES, $P < .001$) and therapeutic effect (Time, $P < .001$) on straight-line walking speed, with no interactions between Time, FES, and Group. The orthotic effect on straight-line walking speed at baseline and 3 months was, respectively, 4.3% and 5.9% in the nonprogressive group and 3.9% and 6.7% in the progressive group. The therapeutic effect with FES Off and On was, respectively, 12.0% and 13.7% for the nonprogressive group and 5.3% and 8.1% for the progressive group. Sidak corrected post hoc tests showed that the increase in speed with respect to baseline only became significant after 2 months (FES On/Off and both groups combined).

In Figure 2A, straight-line speed was plotted against figure-8 speed, measured at 3 months with FES Off, for 30 nonprogressive and 30 progressive subjects. Both speeds were highly correlated ($r^2 = .89; P < .001$), and the best-fitting linear regression line had a slope of .73, indicating that figure-8 speed was about 30% slower on average. The slopes were similar in both the nonprogressive and progressive groups, respectively, .75 ($r^2 = .87$) and .71 ($r^2 = .91$). Data would fall on the dashed unity line if the speeds were the same. However, between-subject variability was large, and the ratio of figure-8 to straight-line speed ranged from .5 to 1.0. Because the subjects were asked to walk at the maximal safe speed that they could maintain for both tests, the slower walking speeds obtained for the figure-8 tests may be attributed to the fact that the longer test requires endurance and the agility to make turns.

On average, the orthotic benefits for the straight-line and figure-8 speeds were comparable, whereas the therapeutic and combined effects were slightly higher for the figure-8 test (Table 2). To verify the trends in the mean values reported in Table 2, we plotted the change in straight-line speed against the change in figure-8 speed for all subjects (combined effects at 3 months, see Figure 2B). Changes in speed on both tests were highly correlated overall ($r^2 = .58; P < .001$), for the nonprogressive group ($r^2 = .64; P < .001$) and for the progressive group ($r^2 = .49; P < .001$). Figure 2B shows that the corresponding linear regression line ($y = 0.57x + 9.39$) does not go through the origin, which means that a simple multiplication factor is not sufficient to describe the relationship between the changes on both tests. Further analysis showed that the people with a 0% to 10% increase...
on the 10-m test had an increase on the figure-8 test that
was on average about 3 times larger (mean ratio 3.2). People
with a 10% to 20% increase on the 10-m test had a similar
increase on the figure-8 (mean ratio 1.2), whereas people
with 10-m test increases greater than 20% had relatively
smaller figure-8 increases (mean ratio 0.8).

**Walking Speed: I I-Month Follow-up**

Within the nonprogressive and progressive groups, respec-
tively, 31 and 29 subjects continued the trial up to 6 months
(mean 5.5 months) and 14 and 19 subjects up to 11 months
(mean 10.8 months). External factors influenced who could
continue and the exact timing of the visits (see Study Design
in Methods). To make sure there were no performance dif-
fferences between the subjects who stopped using FES after
3 months and those who continued up to 6 and 11 months,
we performed 2-way mixed ANOVAs for figure-8 speed
with FES Off combining the first 4 time points (baseline, 1,
2, 3 months) and 3 subgroups with different lengths of
follow-up (up to 3, 6, and 11 months). The statistics indi-
cated that the subjects who continued to use the WalkAide
longer were not necessarily those who benefited most over
time (Time × Follow-up-length: nonprogressive, F(4.9, 91) =
1.2, \( P = .31 \); progressive, F(4.58, 66) = .29, \( P = .91 \)) or
walked faster (or slower) to begin with (Follow-up-length:
nonprogressive, F(2, 37) = 1.5, \( P = .23 \); progressive sub-
jects, F(2, 29) = .19, \( P = .82 \)). The effects were similar for
figure-8 speed with FES On. Analysis of the PCI data also
showed similar results, that is, no interaction effect between
Time and Follow-up-length and no difference between the
groups with different Follow-up periods.

Figure 3 compares changes in figure-8 walking perfor-
cance for the subjects who used the WalkAide for 11 months.
In agreement with the data for the 3-month follow-
up, the orthotic (FES, \( P < .001 \)) and therapeutic effects
(Time, \( P < .001 \)) were significant for figure-8 walking
speed. The orthotic effect was again similar for the nonpro-
gressive and progressive groups (FES × Group, NS) and
similar for all time points (Time × FES, NS). The orthotic
effects at baseline and 11 months were, respectively, 9.8% and
7.6% in the nonprogressive group and 4.3% and 4.8%
in the progressive group. In contrast to the 3-month follow-
up, the therapeutic effect over 11 months was different for
the nonprogressive and progressive groups (Time × Group,
\( P = .039 \)). Figure 3 shows how both groups increased in
walking speed over the first 3 months of WalkAide use, but
then diverged. The nonprogressive group kept improving,
whereas the progressive group reached a plateau. Although
the traces became quite separated over time, there was
no significant difference in walking speed between both
groups (main Group effect, \( P = .52 \)). The group effect was
probably not significant because of the large between-subject
variability in the data. A similar statistical analysis on the
normalized data (all values normalized to the walking speed
at Time 0 with FES Off) resulted in a highly significant main
group effect (\( P = .005 \)).

Separate 2-way ANOVAs (Time × FES) showed that the
overall therapeutic effect was significant not only for the
nonprogressive group (Time, \( P < .001 \)) but also for the pro-
gressive group (Time, \( P = .021 \)). The therapeutic effect at
11 months with FES Off and On was, respectively, 28.0% and
25.5% for the nonprogressive group and 7.9% and 8.4%
for the progressive group (Table 2). Bonferroni corrected
pairwise comparisons showed that increases compared with
baseline only became significant at 6 months (\( P = .018 \)) in
the nonprogressive group. Whereas the overall statistic
showed a therapeutic effect for the progressive group, none
of the pairwise contrasts were significant. The overall trends
for the 10-m straight-line walking speed were very similar
to the figure-8 speed in the group who used the WalkAide
for 11 months, and therefore the data were not included in
Figure 3 (orthotic effect: FES, F(1, 31) = 32.1, \( P < .001 \));
therapeutic effect: Time, F(3.05, 94.6) = 7.2, \( P < .001 \); FES
× Group, F(1, 31) = .86, \( P = .36 \); Time × FES, F(3.9, 119) = 1.1,
\( P = .36 \); Time × Group, F(3.1, 291) = 3, \( P = .034 \).

**Physiological Cost Index**

The PCI for the nonprogressive group was generally higher
(mean ± SEM, 0.92 ± 0.10 beats/m at baseline) than for the
progressive group (0.8 ± 0.08 beats/m), but 3-way mixed
ANOVA's for the 3-month follow-up data revealed that the
differences were not significant (main Group effect, NS; see
Figure 1C). There was no significant orthotic effect on
PCI (FES, NS), but there was a therapeutic effect. Overall,
the PCI significantly decreased over the first 3 months of
WalkAide use (Time, \( P = .031 \)), and the trend was similar
for the nonprogressive and progressive groups (Group ×
Time, NS). The therapeutic effect with FES Off and On
was, respectively, −6.8% and −6.6% in the nonprogressive
group and −3.0% and −8.7% in the progressive group.
The decrease in PCI over time indicates that with prolonged
WalkAide use both groups of patients used less effort while
walking faster.

In the subset of subjects with an 11-month follow-up, the
trends in PCI over time were different for the nonprogressive
(\( n = 13 \)) and progressive groups (\( n = 18 \), Time × Group,
\( P = .039 \)). Separate 2-way ANOVAs (Time × FES) per group
showed that the PCI significantly decreased over time in the
nonprogressive group (Time, \( P = .039 \)). PCI was 15.9% and
18.6% lower at 11 months compared with baseline for walk-
ing with FES Off and On, respectively. The PCI data were
less consistent over time for the progressive group and did
not show a general decreasing trend (Time, NS). Because of
the large variability between subjects, neither the pairwise
comparisons between time points nor the difference between
PCI with FES On or Off were significant.
Combined Orthotic and Therapeutic Effect on Walking Speed and PCI at 3, 6, and 11 Months

Statistical analysis for the combined effect required comparisons beyond the normal post hoc comparisons of the mixed repeated-measures ANOVAs, as it required comparison across 2 factors (Time and FES), for example, Time 0 FES Off and Time 11 FES On. Therefore, 1-factor repeated-measures ANOVAs with just Time 0 FES Off and Time End FES On in the model were performed per group to test the changes in mean values representing the combined effects.

After 3 months of WalkAide use, the combined orthotic and therapeutic effect on figure-8 speed was 23.7% for the nonprogressive group ($F(1, 39) = 34.8; P < .001$) and 15.3% for the progressive group ($F(1, 31) = 27.4; P < .001$; see Table 2). At later times the effects diverged between the nonprogressive and progressive groups, to a 29.9% and 12.5% increase respectively, at 6 months ($F(1, 29) = 38.3; P < .001$ and $F(1, 28) = 16.8, P < .001$) and 37.8% and 13.1% at 11 months ($F(1, 13) = 23.8, P < .001$ and $F(1, 18) = 7.9, P = .012$). The combined effect on PCI in the nonprogressive group increased from $-7.1\%$ ($F(1, 37) = 2.5; P = .12$) at 3 months to $-11.1\%$ ($F(1, 25) = 2.8, P = .11$) and $-18.2\%$ ($F(1, 12) = 5.4, P = .038$) at 6 and 11 months, respectively. The combined effect on PCI in the progressive group at 3, 6, and 11 months was, respectively, $-8.7\%$, $-2.4\%$, and
with the device. Time, steps/day to 2110 NS) and increased significantly over time from 1842 of steps per day of use was similar for both groups (Group, day versus 7.3 ± 0.6 h/day (Time, NS; see Table 3). The progressive group used the WalkAide during more days than the nonprogressive group, respectively, 9.2 ± 0.6 h/day versus 7.3 ± 0.6 h/day (Group, P = .038). The number of steps per day of use was similar for both groups (Group, NS) and increased significantly over time from 1842 ± 198 steps/day to 2110 ± 204 steps/day (average for both groups, Time, P = .019). A typical stride length for our population was close to 1 m, so subjects were walking about 2 km/day with the device.

### Usage

The WalkAide was used intensively from the beginning of the trial, and the number of days used did not change over time (Time, NS; see Table 3). The progressive group used the WalkAide during more days than the nonprogressive group, 85.0 ± 2.6% versus 73.4 ± 4.2% of the days (mean ± SEM, Group, P = .037). However, the number of hours per day of use increased significantly over time for both groups, on average from 7.4 ± 0.5 h/day to 9.6 ± 0.5 h/day (Time, P = .002) and was again higher for the progressive group than for the nonprogressive group, respectively, 9.2 ± 0.5 h/day versus 7.3 ± 0.6 h/day (Group, P = .038). The number of steps per day of use was similar for both groups (Group, NS) and increased significantly over time from 1842 ± 198 steps/day to 2110 ± 204 steps/day (average for both groups, Time, P = .019). A typical stride length for our population was close to 1 m, so subjects were walking about 2 km/day with the device.

### Discussion

#### Orthotic Effect

This multicenter trial showed that mean walking speed was on average 5.7% higher (ranging from 2.3% to 9.2% over all time points and for the figure-8 and 10-m test) with FES on compared with FES Off in subjects with foot drop because of various lesions of the CNS. No significant difference was observed between subjects with progressive and nonprogressive disorders or between time points. Table 4 summarizes the results for 12 studies that reported orthotic, therapeutic, or combined effects of FES on walking speed for different pathologies. The results are fairly consistent across the studies for the orthotic and combined effects. The orthotic benefit for people with a stroke ranged from 6% to 22% and for people with SCI from 7% to 21%.

Only 2 previous articles have studied the effect of a foot drop stimulator on walking performance in people with chronic progressive diseases such as MS. Taylor et al examined 21 subjects with MS and found an orthotic effect with 16% improvement in walking speed and 24% reduction in effort as measured by the PCI. Paul et al studied 12 patients with MS who had used a foot drop stimulator for at least 6 months and found an orthotic effect with a 15% increase in speed and 12% reduction in PCI. In conclusion, our results support previous studies in showing an orthotic effect in all patients, irrespective of the cause of the foot drop, and provide the additional information that the orthotic effect does not change with time over a prolonged period (11 months).

Kim et al found another interesting result, namely, that the orthotic effects of FES and a hinged AFO were similar in people with incomplete SCI when tested in a single session and that these could be combined to give a better walking performance. Despite the fact that the use of an AFO is considered to be the standard of care for correction of foot drop, only 1 study to our knowledge is available in MS that has examined the effect of an AFO on walking performance. Sheffler et al tested 15 patients with MS and found no

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### Table 3. Usage of the Foot Drop Stimulator

<table>
<thead>
<tr>
<th>Factor</th>
<th>Start</th>
<th>End</th>
<th>Overall</th>
<th>Group</th>
<th>P</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of days used</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonprogressive</td>
<td>72.0 ± 6.6</td>
<td>74.8 ± 4.7</td>
<td>73.4 ± 4.2</td>
<td>Group</td>
<td>.037</td>
<td>F(1, 36) = 4.7</td>
</tr>
<tr>
<td>Progressive</td>
<td>85.0 ± 4.1</td>
<td>84.9 ± 3.4</td>
<td>85.0 ± 2.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>80.2 ± 3.6</td>
<td>81.2 ± 2.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hours/day used</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonprogressive</td>
<td>6.5 ± 0.8</td>
<td>8.2 ± 0.8</td>
<td>7.3 ± 0.6</td>
<td>Group</td>
<td>.038</td>
<td>F(1, 36) = 4.6</td>
</tr>
<tr>
<td>Progressive</td>
<td>7.9 ± 0.7</td>
<td>10.5 ± 0.6</td>
<td>9.2 ± 0.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>7.4 ± 0.5</td>
<td>9.6 ± 0.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steps/day used</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonprogressive</td>
<td>1708 ± 299</td>
<td>2037 ± 303</td>
<td>1873 ± 225</td>
<td>Group</td>
<td>.69</td>
<td>F(1, 36) = 0.2</td>
</tr>
<tr>
<td>Progressive</td>
<td>1921 ± 264</td>
<td>2152 ± 274</td>
<td>2036 ± 189</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>1842 ± 198</td>
<td>2110 ± 204</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Usage of the stimulator in terms of percentage of days that the subjects used the foot drop stimulator over a 100-day period, hours per day that the stimulator was on, steps per day taken during the days the stimulator was used. Overall values are given in 2 directions: averages of start and end per group and averages of nonprogressive and progressive groups per time point. Values are mean ± standard error of mean. The last 3 columns show the results of a 2-way ANOVA (Time × Group) for each variable. The main Time and Group effects are shown; none of the Time × Group interactions were significant. Significant effects with P values <.05 are shown in italics.
Table 4. Overview of Studies on the Effect of FES on Walking Speed

<table>
<thead>
<tr>
<th>Study</th>
<th>Electrode</th>
<th>Stimulator</th>
<th>Design</th>
<th>Comparison</th>
<th>Condition</th>
<th>N(^a)</th>
<th>Chronicity(^e)</th>
<th>FES Use</th>
<th>Test(^f)</th>
<th>Effect on Speed (% Change)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kottink et al(^b)</td>
<td>S/S</td>
<td>ODFS</td>
<td>Pre–post</td>
<td>On/off</td>
<td>Stroke</td>
<td>16</td>
<td>3 years 7 months</td>
<td>3 months</td>
<td>10 m</td>
<td>6-22</td>
</tr>
<tr>
<td>Burridge et al(^b)</td>
<td>S</td>
<td>ODFS</td>
<td>Pre–post</td>
<td>On/off</td>
<td>Stroke</td>
<td>18</td>
<td>2.9 years</td>
<td>3 months</td>
<td>10 m</td>
<td>7</td>
</tr>
<tr>
<td>Taylor et al(^b)</td>
<td>S</td>
<td>ODFS</td>
<td>Pre–post</td>
<td>On/off</td>
<td>Stroke</td>
<td>111</td>
<td>5.4 years</td>
<td>4.5 months</td>
<td>10 m</td>
<td>12</td>
</tr>
<tr>
<td>Wieler et al(^b)</td>
<td>S</td>
<td>Unistim</td>
<td>Pre–post</td>
<td>On/off</td>
<td>SCI</td>
<td>21</td>
<td>14.6 ± 12.5 years</td>
<td>4.5 months</td>
<td>10 m</td>
<td>16</td>
</tr>
<tr>
<td>Kim et al(^b)</td>
<td>S</td>
<td>WalkAide</td>
<td>ROWS</td>
<td>Nothing,AFO/FES</td>
<td>SCI</td>
<td>19</td>
<td>11.9 ± 11.3 months</td>
<td>1 session</td>
<td>8 m/6 minutes</td>
<td>10</td>
</tr>
<tr>
<td>Sheffer et al(^b)</td>
<td>S</td>
<td>ODFS</td>
<td>ROWS</td>
<td>Nothing,AFO/FES</td>
<td>Stroke</td>
<td>14</td>
<td>2 years 7 months</td>
<td>1 session</td>
<td>5 m</td>
<td>8</td>
</tr>
<tr>
<td>Burridge et al(^b)</td>
<td>I</td>
<td>ActiGait</td>
<td>Pre–post</td>
<td>On/off</td>
<td>Stroke</td>
<td>13</td>
<td>4.9 ± 1.9 years</td>
<td>11.6 months</td>
<td>4 minutes</td>
<td>12</td>
</tr>
<tr>
<td>Kottink et al(^b)</td>
<td>I</td>
<td>STIMuSTEP</td>
<td>RCT</td>
<td>FES/AFO</td>
<td>Stroke</td>
<td>14</td>
<td>9.1 ± 9.3 years</td>
<td>6.5 months</td>
<td>10 m/6 minutes</td>
<td>23</td>
</tr>
<tr>
<td>Hausdorff(^b)</td>
<td>S</td>
<td>L300</td>
<td>Single session</td>
<td>On/off</td>
<td>MS</td>
<td>12</td>
<td>9 years 9 months</td>
<td>&gt;6 months</td>
<td>5 minutes</td>
<td>15</td>
</tr>
</tbody>
</table>

Abbreviations: FES, functional electrical stimulation; Orthot, orthotic effect = speed with FES On – FES Off; Therap, therapeutic effect = speed after – before FES use; Comb, combined effect = speed with FES On after – FES Off before; ODFS, Odstock Dropped Foot Stimulator; RCT, randomized controlled trial; ROWS, random order within subject; PT, physical therapy; AFO, ankle-foot orthosis; On/off, test with FES On and Off; MS, multiple sclerosis; SCI, spinal cord injury.

\(^a\) Only studies that reported an effect of a foot drop stimulator on walking speed were included.

\(^b\) S, surface electrodes; I, implanted electrodes.

\(^c\) Comparison indicates which comparisons were made.

\(^d\) Indicates number of subjects (for RCTs number of subjects in the FES intervention group).

\(^e\) Chronicity gives time since onset of disease or injury.

\(^f\) Test indicates whether a short-distance walking test or a longer timed test was used.

\(^g\) Actual number not in text, estimated from graph.

\(^h\) Mean time of final assessment, study also reported 90-day data.

\(^i\) Number calculated from values in tables.
significant improvement in performing timed tasks of functional ambulation with an AFO. Their results indicate that people with MS may benefit more from a foot drop stimulator than from an AFO.

**Therapeutic and Combined Effects**

In addition to the orthotic effect, an increase of walking speed even after turning the stimulation off (therapeutic effect) has been observed in several studies following the original report of Liberson et al. A meta-analysis by Robbins et al focused on this effect of electrical stimulation on walking speed in stroke patients, as presented in 8 studies. However, only 3 controlled FES studies were included in the effect model analysis, covering a total of 36 patients in the FES intervention groups (2 studies were uncontrolled trials, and 3 studies used low-level electrical stimulation during short treatment sessions without walking, ie, TENS). The mean increase in walking speed over time was 0.18 m/s (95% confidence interval = 0.08-0.28 m/s). However, the pooled therapeutic effect has to be interpreted with caution. In 2 of the 3 studies, the patients received short stimulation sessions of 10 to 60 minutes, once or twice per day, rather than using the foot drop stimulator all day while walking in the community. One of these studies actually applied the stimulation to the arm rather than the leg. Also, the duration of the trials was limited to only 3 weeks and 2 months, respectively, whereas we have shown that therapeutic changes grow over many months. Furthermore, all 3 studies only used short distance walking tests (10-20 m), which may underestimate potential changes on longer distances that are more relevant to activities of daily living (see below).

Another systematic review uses the term orthotic effect in the title but appears to be measuring what we call a combined effect. The authors report a pooled increase in walking speed for 116 subjects of 38%. However, they include studies on acute and subacute patients as well as studies that use multichannel stimulators and implanted devices. Thus, although their values show agreement with other studies including ours, the results must be treated cautiously.

A review by Burridge et al presented results of 16 articles on both the orthotic and therapeutic effects of peroneal nerve stimulation for foot drop mainly in stroke patients. However, this review was descriptive in nature, and study data were not pooled. Several more recent studies have been published subsequently and have been included in the text and in Table 4. The combined effect on walking speed ranged from 18% to 34% improvement in stroke and from 19% to 54% in SCI. In comparison, our study showed a combined effect of 38% increase in nonprogressive subjects after 11 months, which is in good agreement with previous studies. The published results are less consistent for the therapeutic effect. The 2 available randomized controlled trials in stroke subjects showed no therapeutic effect, whereas 4 uncontrolled studies showed therapeutic effects ranging from 12% to 16%. Two studies reported a 12% to 28% therapeutic effect in SCI subjects. Most studies reported the therapeutic and combined effects for a limited time and at a single time point, that is, 3, 4.5, or 6.5 months, without documenting changes over time. Our results for nonprogressive subjects are comparable with previous studies over a period of 3 months (18%), but the therapeutic effect continued to increase to 28% at 11 months. The study by Wieler et al collected data for a longer period (up to 3 years; see also Kralj et al and Swain and Taylor for longer term studies), but all data from 3 months up to 3 years were averaged. The therapeutic effect of Wieler et al (28% in SCI subjects) was the largest previously reported and is consistent with the idea that previous studies did not follow subjects long enough to observe the full therapeutic effect of using a foot drop stimulator. A more recent study by Burridge et al tested stroke patients with an ActiGait implanted stimulator up to 15 months and reported speed changes consistent with a therapeutic effect of 12% at 11.6 months (mean final assessment time).

Our results showed that the 4-minute figure-8 test and the 10-m straight-line test revealed similar trends in walking speed with regard to the factor Time and FES On or Off over a 3 and 11 month follow-up period. However, the shorter 10-m test underestimated the increases on the longer figure-8 test for people with relatively small increases or even decreases on the 10-m test (Figure 2B) and, vice versa, overestimated the figure-8 increases for people with large 10-m test increases. The reasons for these differences are not known, but the results suggest that a short walking test might not be a good predictor of the potential improvements over the longer distances that are more important for activities of daily living. Longer walking tests should be included in test protocols for assessing the effect of devices to improve walking.

**Progressive Versus Nonprogressive Disorders**

All but one previous study describing the therapeutic effect used subjects who had lesions caused by single events, such as a stroke or SCI, where no further progression of the disability was expected. Taylor et al also included subjects with MS. In contrast to stroke and SCI, no therapeutic effect was detected in the group of MS subjects as a whole. These findings suggested a potentially important difference between nonprogressive disorders such as stroke and SCI and progressive disorders such as MS.

We included several groups with nonprogressive disorders as well as a substantial number of people with MS. Although the ages and times since onset were different in
our study between the various, generally nonprogressive conditions, the walking performance was similar at all time points. This provided a justification for combining the nonprogressive subgroups. Our data also showed that the increases were not significantly different between the progressive and nonprogressive groups in the first 3 months of treatment. This suggests that the nature of the physical deficit (foot drop) was more important than the etiology in determining the early response to treatment. In contrast to the results of Taylor et al., a clear therapeutic effect was seen in the progressive group as well as the nonprogressive group during the first 3 months.

The walking speeds for the 2 groups diverged after 3 months of FES use. Whereas the nonprogressive group continued to increase speed with and without stimulation, a plateau of gait speed with a tendency to a decline in speed and a corresponding increase in the PCI occurred in the progressive group as a whole (Figure 3). Any changes toward the initial levels may be due to the progressive nature of the disease causing some of the early gains to be lost. The decrease in walking speed may also have resulted from weakening of other muscle groups that were not being stimulated. Taylor et al. studied their MS subjects at 4.5 months, whereas we saw the largest improvements at 3 months. Also, the progressive subjects with MS in our study were diagnosed as having the secondary progressive rather than the relapsing–remitting form of the disease. Taylor et al. did not include detailed clinical information on the type of MS for their subjects. If they included subjects with the relapsing–remitting form of MS, it would have made it very difficult to determine overall trends.

In response to the first question raised in the Introduction, we conclude that subjects with both progressive and nonprogressive disorders show a therapeutic effect of using foot drop stimulators. In response to the second question, an important new finding is that the benefits in the nonprogressive disorders continue to increase up to at least a year, whereas the therapeutic effects in progressive disorders appear to be largest at about 3 months and then may be offset by the progression of the disease process.

Control Methods and Usage

In all previous studies except those from our group, subjects used a heel sensor for control. In 72 of the 73 subjects, we achieved satisfactory timing of the stimulation by using the tilt sensor. The simplicity of a built-in tilt sensor and electrodes (no external wires or telemetry required) may have contributed to the extensive use of the foot drop stimulator in this study. The daily routine of putting on the WalkAide is simplified as the subjects only have to put on 1 device.

The subjects in the present study showed a remarkable compliance, using the stimulator on 80% of the days as documented by the recorded usage data (Table 3). The duration of daily stimulation and the number of steps increased in both subject groups. One reason for the high usage may be the reduced effort required for walking, as documented by the decreased PCI. In contrast to AFOs, subjects generally recognize FES as an active movement that can strengthen their muscles; this may enhance their motivation to continue and even increase use. In particular, MS subjects have been reported to be highly motivated with low dropout rates in using FES devices. In part, this may result from the negative prognosis of a progressive disorder such as MS. Any improvement in daily activities such as walking is most welcome, even if only for a limited period of time. Despite a tendency to decline after the first 3 months, the walking speed with FES was still greater after nearly a year than at the initial assessment without FES. If progressive subjects can remain ambulatory in their own home and not become dependent on wheelchairs and/or assisted living facilities, costs for health care and social services can be reduced and the quality of life can be enhanced.

Authors’ Note

The authors regret to inform that Ms Jenny Robertson is deceased. Some of the results discussed in this article were presented at the 12th Annual International FES Society Meeting, Philadelphia, November 2007, and at the Canadian Physiological Society Meeting, Lake Louise, Alberta, January 2008.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article. RBS is president of a company, Biomotion Ltd, Edmonton, Canada, that helped develop the WalkAide used in these trials and is a consultant to the current manufacturer, Innovative Neurotronics Inc.

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References


Functional Electrical Stimulation Improves Motor Recovery of the Lower Extremity and Walking Ability of Subjects With First Acute Stroke: A Randomized Placebo-Controlled Trial

Tiebin Yan, Christina W. Y. Hui-Chan and Leonard S. W. Li

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The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/cgi/content/full/36/1/80
Functional Electrical Stimulation Improves Motor Recovery of the Lower Extremity and Walking Ability of Subjects With First Acute Stroke

A Randomized Placebo-Controlled Trial

Tiebin Yan, MD, PhD; Christina W. Y. Hui-Chan, PhD; Leonard S. W. Li, MD

Background and Purpose—The effectiveness of functional electrical stimulation (FES) has been investigated in chronic hemiplegia. The present study examines whether FES, given during acute stroke, was more effective in promoting motor recovery of the lower extremity and walking ability than standard rehabilitation alone.

Methods—Forty-six subjects, 70.9 ± 8.0 years old and 9.2 ± 4.1 days after stroke, were assigned randomly to 1 of 3 groups receiving standard rehabilitation with FES or placebo stimulation or alone (control). FES was applied 30 minutes and placebo stimulation 60 minutes, 5 days per week for 3 weeks. Outcome measurements included composite spasticity score, maximum isometric voluntary contraction of ankle dorsiflexors and plantar-flexors, and walking ability. They were recorded before treatment, weekly during the 3-week treatment, and at week 8 after stroke.

Results—No significant differences were found in the baseline measurements. After 3 weeks of treatment, there was a significant reduction in the percentage of composite spasticity score, and a significant improvement in the ankle dorsiflexion torque, accompanied by an increase in agonist electromyogram and a reduction in electromyogram cocontraction ratio in the FES group, when compared with the other 2 groups (P < 0.05). All subjects in the FES group were able to walk after treatment, and 84.6% of them returned home, in comparison with the placebo (53.3%) and control (46.2%, P < 0.05) groups.

Conclusions—Fifteen sessions of FES, applied to subjects with acute stroke plus standard rehabilitation, improved their motor and walking ability to the degree that more subjects were able to return to home. (Stroke. 2005;36:80-85.)

Key Words: motor activity ■ stroke

Functional electrical stimulation (FES) has been used to treat chronic hemiplegia since the 1960s. In 1978, Stanic et al found that multichannel FES, given 10 to 60 minutes, 3 times per week for 1 month, improved gait performance in hemiplegic subjects. In 1989, Bogataj et al applied multichannel FES to activate lower limb muscles of 20 chronic hemiplegic subjects. After daily treatment 5 days per week for 1 to 3 weeks, subjects who previously were unable to walk, walked again.

In the 1990s, FES has been increasingly used to treat the lower extremity of stroke subjects. Bogataj et al compared 2 groups of stroke survivors receiving 3 weeks of FES, preceded or followed by 3 weeks of conventional therapy. Treatment was given 5 days per week for 7 to 21 days. The results showed that more subjects were able to walk and lived independently after FES.

However, most previous studies had not adopted a randomized control design. Treatment period within a study was often not standardized. Many studies failed to calculate the sample size. Subjects were mostly examined during the chronic stage. The interval to therapeutic intervention after stroke varied within each study. These observations are supported by 2 meta-analyses by Glanz et al and Chae and Yu, who reviewed articles on randomized clinical trials that assessed the efficacy of neuromuscular electrical stimulation in hemiplegia between 1966 and 1999. They found only 8 single-blinded randomized clinical trials. The initial treatment time varied from 14 to 29.2 months after stroke. Only one study had a placebo group.

Methodological issues aside, numerous studies have revealed that motor experience after brain injuries plays a major role in the subsequent physiological reorganization that occurs in the adjacent intact tissues. Repetitive execution of identical or similar movements of the limbs have been identified as crucial for motor learning and recovery in stroke subjects. Using positron emission tomography, Nelles et al and Weiller et al observed similar brain activation patterns in stroke subjects during either active or passive movements.
Their results highlighted the contribution of afferent synaptic activity to central motor control and indicated that reorganization of the sensory and motor systems occurred early after stroke.

Because FES produces functional movement, we hypothesize that the FES-induced afferent–efferent stimulation that results in limb movements plus cutaneous and proprioceptive inputs during the acute stage could be important in “reminding” subjects how to perform the movement properly. Therefore, we investigated whether FES combined with a standard rehabilitation (SR) program was more effective than SR given with placebo stimulation or alone in promoting the recovery of motor function and functional mobility during acute stroke.

Materials and Methods

Study Design

This study adopted a single-blind, stratified, randomized control design. The number of subjects was calculated a priori. According to a meta-analysis, the minimal effect size for FES in motor recovery of stroke subjects was 0.54. Thus, a sample of 33 subjects was needed to achieve 80% chance (β=0.20) of detecting 20% difference (α=0.05) in improvement among 3 treatment groups. In anticipation of possible dropout, this number was increased to 45.

After giving informed consent, subjects were allocated, in an unbiased manner by a random number produced by Jensen’s computerized method of minimization, to 1 of 3 groups receiving FES and SR, placebo stimulation and SR, or SR only (control). To minimize uneven distribution of known variables, the stratifications taken included age (45 to 59, 60 to 75, and 76 to 85), gender, type of stroke (cerebral ischemia and hemorrhage), side of hemiplegia, and muscle strength of affected hip flexors (grade of 0 to 2 to 3 according to manual muscle test). This study was approved by local ethics committees.

Subjects

Forty-six subjects with first acute stroke were recruited. Subjects were included if they had a unilateral stroke within the carotid artery system according to computerized tomography, aged 45 to 85 years old, and were independent in daily activities before stroke (Figure 1). Exclusion criteria were brain stem or cerebella lesions, medical comorbidity, receptive dysphasia, or cognitive impairment denoted by on July 10, 2007.

Intervention

All subjects received the same SR including 60 minutes each of physiotherapy based on the neurodevelopmental facilitation approach and of occupational therapy focused on activities of daily living, given once per day, 5 days per week for 3 weeks. Two dual-channel stimulators (Respond Select; Empi Inc) were connected with a program timer to form one stimulating unit for FES. Surface electrodes were applied on quadriceps, hamstring, tibialis anterior (TA), and medial gastrocnemius (MG) with subject side-lying and the affected lower extremity supported by slings. FES was delivered with 0.3-msec pulses at 30 Hz, maximum tolerance intensity (20 to 30 mA), using an activation sequence that mimicked normal gait (Figure 2). Subjects were treated within 3 days after being transferred from the acute hospital, 30 minutes per day, 5 days per week for 3 weeks. The placebo group received stimulation from an electrical stimulation device with disconnected circuit. Treatment frequency and period were identical to those of the FES group, except for the longer duration (60 minutes) thought to optimize placebo effects.

Outcome Measurements

The following measurements were recorded before treatment, weekly during the 3-week treatment in hospital, and follow-up at week 8 after stroke. To eliminate possible bias during measurements, the assessor was blinded to the nature of intervention. Composite spasticity scale (CSS) was developed by our group to more faithfully reflect the status of ankle plantar-flexor tone. It was adopted because the Ashworth scale has lower reliability and does not measure the relatively flaccid muscle tone prevalent during acute stroke. In contrast, the validity and reliability of CSS in evaluating spasticity had been demonstrated in stroke studies. Maximum isometric voluntary contraction (MVIC) of ankle dorsiflexors and plantar-flexors was measured by joint torque and surface EMG. The knee joint was fixed at 10° of flexion and the ankle in a neutral position. Two bar-shaped surface electrodes (B & L Engineering) were placed over TA and MG muscles. The electrodes were low-noise, with a pre-amplifier and a gain of 388. The input impedance was 100 megohms, the common mode rejection ratio was 95 decibels (db), and the bandwidth was 12 Hz to 3.4 KHz. During data collection, subjects were asked to contract the ankle dorsiflexors or plantar-flexors maximally for ~3 seconds. A total of 10 seconds was recorded, and 2 to 3 seconds before and 3 to 4 seconds after the contraction were taken as the baseline. Six trials were recorded under verbal encouragement, with 3 each for dorsiflexion and plantar-flexion after 2 to 3 minutes of practice. The EMG signals were sampled at 1000 Hz per channel, full-wave–rectified, and then (Butterworth) low-pass–filtered at 2.7 Hz for TA and 2 Hz for MG. The MVIC value over a 1-second window beginning from 0.5 ms before peak torque was used for normalization. The corresponding integrated EMG (IEMG) signals (mV·s) of TA and MG muscles were computed. The cocontraction ratio was calculated as the IEMG area of the antagonist over that of the agonist plus antagonist. Walking ability was assessed with the timed “Up & Go” (TUG) test when the subject could walk 7 to 8 meters without personal assistance. This test was originally designed for the elderly, but its validity and reliability had been demonstrated in Western and Chinese stroke subjects. Subjects were required to rise from a chair, walk forward 3 meters, turn, walk back, and sit down on the chair. After 1 to 2 practice runs, 3 trials were recorded. All measurement protocols had been tested for their reproducibility in our pilot study, with intraclass correlation coefficients of 0.89 to 0.98 for CSS (26 subjects), 0.73 to 0.99 for ankle dorsiflexion torque and surface EMG (19 subjects), and 0.95 to 0.99 for TUG score (37 subjects), respectively.

Statistics

Descriptive statistics were used for subjects’ relevant characteristics. Outcome measurements were analyzed with repeated measure analysis of variance using SPSS (version 10.0) to compare the main effects before, during, and after treatment, followed by post-hoc tests with Bonferroni correction to compare treatment effects among the 3 groups. For categorical variables, a χ² test was used. The significance level was set at 5% (2-tailed).

Results

No significant differences were found in the baseline values among subject groups (Tables 1 and 2), indicating that they were homogenous in these measurements before treatment.

CSS

Raw CSS scores of the affected plantar-flexors in the 3 groups were similar at the different assessment intervals (Table 2a). However, the percentage increases of CSS scores in the placebo (50.0±SD88.4%) and control groups
(64.6±64.8%) at week 3 were significantly greater than that in the FES group (30.5±35.3%) (P<0.05). In contrast, no difference was found between placebo and control groups at all times.

**MIVC**

Table 2b and 2c summarize the raw data for MIVC torque and EMG cocontraction ratio during ankle dorsiflexion in the 3 groups. When comparing the results among groups, percentage increases in MIVC torques and IEMG of the FES group were significantly larger than those of the control group from week 1 onward (P<0.01 to 0.05), and larger than the placebo group at week 3 (P=0.032) (Figure 3a and 3b). In ankle plantar-flexion, a significant effect was found only at week 3 between the FES and the other 2 groups (P<0.01, not shown). Furthermore, the EMG cocontraction ratio during dorsiflexion of the affected ankle was significantly more reduced in the FES than the other 2 groups from week 1 or 2 onward (P=0.001 to 0.042; Figure 2c).

**Walking Ability**

No differences were found in the TUG score among groups at any time (Table 2d). Before treatment, 12.2% (5/41) subjects were able to walk with a quadruped, 2 (15.4%) each in the FES and control groups and 1 (6.7%) in the placebo group. After treatment, this percentage increased markedly by week 8 in the FES group (84.6%) when compared with the placebo (60.0%) and control groups (46.2%). The χ² analysis confirmed the significant differences between the FES and the other 2 groups at week 2 or 3 and 8(P<0.05).
In addition, the mean number of days until subjects were able to start walking in the hospital was 18.1±8.4, 20.2±6.8, and 21.2±8.0, respectively, for the FES, placebo, and control groups. Although there was no significant difference among groups at the α=0.017 level, the FES group tended to walk 2 days earlier than the other 2 groups. An important finding was that more subjects receiving FES (84.6%) returned to their own home when compared with those receiving placebo stimulation (53.3%) and SR (46.2%, P<0.05; Table 1).

Discussion

Early and Intensive Intervention for Stroke Rehabilitation

Nearly all studies on the recovery of motor function in stroke survivors have found that the most rapid recovery occurs during the first few weeks after stroke.24 In a meta-analysis of 36 clinical trials in stroke rehabilitation, Ottenbacher and Jannell23 noted that early initiation of rehabilitation for stroke patients was related to improved motor and functional outcomes. Kwakkel et al24 critically reviewed 9 controlled studies involving 1051 stroke survivors who received rehabilitation programs of different intensities. They found a small but statistically significant intensity–effect relationship. These results suggested that early and intensive intervention could significantly improve motor recovery and functional outcome in stroke survivors.

In the present study, FES was applied at 8.7±5.8 days after stroke (Table 1). This was much earlier and the treatment was more intensive when compared with other studies. There was no significant difference in subjects’ characteristics before treatment (Table 1). Thus, any differences among the 3 groups could be largely attributed to the effects of intervention.

**TABLE 2. Comparison of Outcome Measurements Among the 3 Groups**

<table>
<thead>
<tr>
<th></th>
<th>FES (n=13)</th>
<th>Placebo (n=15)</th>
<th>SR (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68.2±7.7</td>
<td>73.3±8.1</td>
<td>70.4±7.6</td>
</tr>
<tr>
<td>M (%)</td>
<td>7 (53.8)</td>
<td>7 (46.7)</td>
<td>6 (46.2)</td>
</tr>
<tr>
<td>F (%)</td>
<td>6 (46.2)</td>
<td>8 (53.3)</td>
<td>7 (53.8)</td>
</tr>
<tr>
<td>Type of stroke: Ischemia</td>
<td>11</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Type of stroke: Hemorrhage</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Paretic side: L (%)</td>
<td>6 (46.2)</td>
<td>9 (60)</td>
<td>8 (61.5)</td>
</tr>
<tr>
<td>Paretic side: R (%)</td>
<td>7 (53.8)</td>
<td>6 (30)</td>
<td>5 (38.5)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>57.9±8.7</td>
<td>54.5±6.9</td>
<td>55.0±9.0</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.57±0.1</td>
<td>1.52±0.1</td>
<td>1.55±0.1</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.4±2.3</td>
<td>23.3±3.3</td>
<td>22.8±3.2</td>
</tr>
<tr>
<td>AMT, score</td>
<td>8.4±1.7</td>
<td>8.2±1.7</td>
<td>8.4±1.3</td>
</tr>
<tr>
<td>CSS, score</td>
<td>7.3±3.1</td>
<td>5.9±2.7</td>
<td>6.1±2.9</td>
</tr>
<tr>
<td>LOS at acute hospital, d</td>
<td>5.7±5.0</td>
<td>7.2±3.4</td>
<td>7.2±3.5</td>
</tr>
<tr>
<td>Initial intervention from onset, d</td>
<td>8.7±5.8</td>
<td>10.1±2.8</td>
<td>9.1±3.5</td>
</tr>
<tr>
<td>LOS at sub-acute hospital, d</td>
<td>33.5±14.0</td>
<td>34.7±10.0</td>
<td>32.7±7.9</td>
</tr>
<tr>
<td>N of subjects returning home (%)</td>
<td>11 (84.6)</td>
<td>8 (53.3)</td>
<td>6 (46.2)</td>
</tr>
</tbody>
</table>

*Values are mean±SD.*

**FES, placebo, and SR denote groups receiving functional electrical stimulation + SR, placebo stimulation + SR, and standard rehabilitation (control), respectively.**

**BMI indicates body mass index; AMT, abbreviated mental test; CSS, Composite Spasticity Scale; LOS, length of stay; M, male; F, female; L, left; R, right.**

*P=0.03 when compared with FES group.

**P=0.05 when compared with FES group.**

**P=0.01**

**P=0.05 when comparing percentage changes (not shown) for weeks 1 to 8 with week 0 within-group.**
Effects of FES on Spasticity and Motor Recovery

In this study, all 3 groups had moderate spasticity as assessed by the CSS, but the increase in the score ratio was significantly less in the FES group at week 3 (Table 2a), indicating that FES might be able to normalize muscle tone in the affected ankle plantar-flexors.

In our study, FES was delivered reciprocally to the lower limb muscles to mimic normal gait. During the phase that mimics toe-off, FES could have activated the TA motoneuronal pool antidromically in addition to directly activating the TA muscle, leading to increased contraction of the paretic TA muscle, with negligible cocontraction of the antagonist spastic plantar-flexors that tended to occur in stroke subjects. Over time, this could have led to significant improvements in the FES group, as denoted by the percentage increases in MIVC torque and IEMG of the affected TA muscle, and the percentage decrease of EMG cocontraction ratio during ankle dorsiflexion, when compared with the control group from week 1 onward, and with the placebo group from week 2 or 3 onward (Figure 3). Note that the plantar-flexion torque was also improved significantly by week 3. No significant difference was found between the placebo and control groups at any assessment interval except for the percentage decrease of EMG cocontraction ratio during week 1, thus demonstrating the general absence of any placebo effects.

Effects of FES on Early Mobility

Theoretically, there could be differences in TUG scores among the groups. However, at each assessment session, there were always new subjects who were able to walk added to each group. Hence, the scores could not be compared either within or among the groups.

Before treatment, only 12.2% (5/41) of subjects were able to walk. However, this percentage was significantly increased in the FES group, when compared with placebo and control groups, respectively, from weeks 2 and 3 onward ($P<0.05$; Table 2d). In addition, the average first walking day in hospital was $18.1\pm8.4$ days after stroke for the FES group, as compared with $20.2\pm6.8$ and $21.2\pm8.0$ days, respectively, for placebo and control groups. This means that subjects receiving FES treatment tended to walk 2 to 3 days earlier than those receiving either placebo stimulation or SR alone. Note that the length of hospital stay would not have demonstrated significant difference among groups, because subjects had to stay at the hospital until they completed the 3-week treatment even if they had reached discharge criteria. Nevertheless, their placement at discharge should have reflected treatment effects to some extent (Table 1), because the criteria for a stroke survivor to return home in Hong Kong are that the patient should be able to perform self-care and live safely at home.

Possible Mechanisms for the Effects of FES in Subjects With Stroke

Asanuma and Pavlides\textsuperscript{25} suggested that increase of synaptic efficacy in existing neural circuits, or formation of new synapses, may be involved in the earlier stages of motor learning. In addition, frequently repeated movements of the affected lower extremity of stroke subjects, induced by FES in this study, might reinforce network connection patterns. As Classen et al\textsuperscript{26} noted, the phenomenon of motor cortical rearrangements could be the first step in skill acquisition. Such brain plasticity could underline improvements seen in the FES group.

Generalization of the results from this study should be performed with caution because of subject selection criteria, which did not cover all stroke categories or subjects aged younger than 45 or older than 85 years. Furthermore, more significant differences might have been detected earlier if the sample size were larger.

To conclude, 15 sessions of FES, given 30 minutes per session plus SR, 5 days per week, improved motor recovery and functional mobility in acute stroke subjects, more than placebo stimulation and SR, or SR only. In fact, 84.6% of subjects who received FES and SR returned home, versus...
53.3% and 46.2%, respectively, of those receiving placebo stimulation and SR, or SR alone.

Acknowledgments
The authors thank the doctors, therapists, and nurses in the Department of Neurology, Tung Wah Hospital, Hong Kong, and the participants for their support. This study was supported by an Area of Strategic Development grant from the Hong Kong Polytechnic University to C. W. Y. Hui-Chan and a scholarship to T. Yan.

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Combined Use of Body Weight Support, Functional Electric Stimulation, and Treadmill Training to Improve Walking Ability in Individuals With Chronic Incomplete Spinal Cord Injury

*Edelle C. Field-Fote, PhD, PT*


**Objective:** To assess the effect of an intervention combining body weight support (BWS), functional electric stimulation (FES), and treadmill training on overground walking speed (OGWS), treadmill walking speed, speed and distance, and lower extremity motor scores (LEMS).

**Design:** Before and after comparison.

**Setting:** Miami Project to Cure Paralysis.

**Participants:** Nineteen subjects with American Spinal Injury Association class C injury who were at least 1 year postinjury and had asymmetrical lower extremity function.

**Intervention:** Subjects trained 1.5 hours per day, 3 days per week, for 3 months. The training consisted of body weight-supported treadmill walking assisted by electric stimulation. Stimulation was applied to common peroneal nerve of the weaker lower extremity (LE) and tuned to assist with the swing phase of the step cycle.

**Main Outcome Measures:** OGWS in the absence of both BWS and FES; LEMS, and treadmill training parameters of speed and distance.

**Results:** Over the course of training, there was a significant increase in OGWS (from .12 ± .8 m/s to .21 ± .15 m/s, p = .0008), treadmill walking speed (from .23 ± .12 m/s to .49 ± .20 m/s, p = .00003), and treadmill walking distance (from 93 ± 84 m to 243 ± 139 m, p = .000001). The median LEMS increased significantly for both the stimulated and nonstimulated leg (from 8 to 11 in the FES-assisted leg, from 15 to 18 in the nonassisted leg, p < .005 for each).

**Conclusions:** All subjects showed improvement in OGWS and overall LE strength. Further research is required to delineate the essential elements of these particular training strategies.

**Key Words:** Electric stimulation; Exercise test; Gait; Rehabilitation; Spinal cord injuries; Walking.

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**MANY INDIVIDUALS** with incomplete spinal cord injury (SCI) have the potential to walk.1-4 In recent years, numerous studies have investigated the effect of gait training in individuals with incomplete SCI to improve walking function. The experimental interventions have mainly been of 2 types: functional electric stimulation (FES)5-13 or body weight support (BWS),14-20 the latter at times in conjunction with pharmacologic agents.21-23 Results of these studies, with regard to improvement in walking ability, have been promising.

BWS assists the stance cycle of gait, allowing lower extremity (LE) loading to vary according to the capabilities of the participant and providing assistance to balance by stabilization of the trunk. Previous investigations have assessed the effects of different levels of BWS on various treadmill gait parameters including hip and knee angle displacements, mean muscle burst amplitude, and temporal gait measures. Of the BWS conditions studied, the 30% BWS condition produced the gait parameters most closely resembling those measured at 0% (full weight bearing).24 In addition, during overground walking with levels of BWS greater than 30%, subjects are unable to generate the ground reaction forces necessary to propel themselves forward (personal unpublished observation). The motorized treadmill provides rhythmic timing cues and assists with retropulsion of the stance limb, which promotes hip extension. This hip extension may be critical to the initiation of the swing phase.25,26 The swing phase of gait can be assisted with FES by using the flexion withdrawal response evoked with electric stimulation to the common peroneal nerve. This use of FES eliminates the need for manual assistance, the provision of which may impose strenuous physical demands on the therapist or trainer.

Although there have been no reports of prior investigations of the combined use of these interventions in individuals with incomplete SCI, this combined approach has considerable theoretical support,27 and as been used successfully in individuals with hemiplegia. Hesse et al28 investigated the use of multichannel electric stimulation in combination with treadmill training and BWS in 11 nonambulatory individuals with hemiparesis (9 due to cerebrovascular accident [CVA]; 5 hemorrhagic, 4 ischemic), 1 each to trauma and tumor). After the program, improvements were seen across all subjects in gait parameters such as velocity, stride length, and cadence. Although this study has interesting implications for walking in individuals with chronic incomplete SCI, there are limitations that prevent the findings from being fully applicable to that population. In addition to differences in neurologic etiology, 5 of the subjects with CVA were within 5 months postinjury, a time during which spontaneous recovery of function is to be expected.29

This investigation sought to assess changes in walking function and voluntary limb control, as well as the relationships among these variables, in individuals with chronic (defined as at least 1 year postinjury)30 incomplete SCI who are classified as American Spinal Injury Association (ASIA) class C.30 My
Table 1: Walking Mobility Criteria for Levels of Ambulation

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Physiologic ambulator</td>
<td>Endurance, strength, or level of assistance required make the ambulation not functional. May require assistance to stand. (Walks for exercise only.)</td>
</tr>
<tr>
<td>2. Limited household</td>
<td>Walks in the home but limited by endurance, strength, or safety. (Walks rarely in the home/never in community.)</td>
</tr>
<tr>
<td>ambulator</td>
<td></td>
</tr>
<tr>
<td>3. Independent household</td>
<td>Walks continuously for distances that are considered reasonable for inside the home. May require assistance with stairs inside and curbs, ramps outside the home. A wheelchair may be used outdoors. (Walks occasionally in home/rarely in community.)</td>
</tr>
<tr>
<td>ambulator</td>
<td></td>
</tr>
<tr>
<td>4. Limited community</td>
<td>Walks outside the home and can manage, doors, low curbs, and ramps. A wheelchair may be used for long distances. (Walks regularly in the home/occasionally in community.)</td>
</tr>
<tr>
<td>ambulator</td>
<td></td>
</tr>
<tr>
<td>5. Independent community</td>
<td>Walks for distances of approximately 400 meters (¼ mile) at a speed at least 50% of normal. Can manage all aspects of walking safely, including curbs, stairs, and doors. (Walks regularly in the community [rarely/never uses wheelchair].)</td>
</tr>
<tr>
<td>ambulator</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Data from Perry et al.30

The initial and final treadmill testing were adjusted to allow the subject to walking with optimal gait quality. Voluntary motor control in the LES was assessed according to ASIA standards,30 with the combined score of the hump flexor, knee extensor, ankle plantarflexor, ankle dorsiflexor, and great toe extensor comprising the lower extremity motor score (LEMS).31 A pre-training walking mobility score was established for each subject by asking subjects to rate their typical walking practice based on a modified version of the scale developed by Perry et al32 (table 1).

For the overground walking tests, subjects were strapped into a safety harness4 that was suspended from a ceiling-mounted track-and-trolley assembly. This was only for safety and no weight support was provided during the overground testing. If the subject required manual assistance to advance the weaker leg during overground walking, this assistance was provided and noted. Subjects were allowed 3 sessions to become accustomed to walking on the treadmill with the BWS and FES prior to the onset of the initial testing session.

Training

Subjects participated in a 36-session (3d/wk for 12wk) training program of BWS and FES-assisted treadmill walking. Subjects were allotted a 1.5-hour block of time during which they were permitted to determine their own walk/rest bouts. BWS was provided by a harness suspended from an overhead support. The level of BWS provided to each subject could be increased or decreased via a motorized winch and could be monitored via a light-emitting diode display. Electric stimulation (Grass S88 stimulator coupled to an SIU5 stimulus isolation unit4) to the common peroneal nerve was triggered at time of terminal stance to elicit a flexion withdrawal response to assist with stepping in the weaker limb. Stimulation parameters were: 500ms train, 50 pulses/s, 1ms pulse duration, and between 60 to 100 volts depending on subject tolerance and the level of stimulation necessary to elicit a robust flexion withdrawal reflex. Within each training session, the treadmill speed and amount of support (up to 30% BWS) provided was adjusted to allow the subject to walk optimally on the treadmill. Subjects were encouraged to walk as fast as they could while preserving good gait kinematics and were told that walking distance (time) was not important. For each walking bout, the time and distance of the walk were recorded. No attempts were made to wear the subject from use of BWS or FES over the course of training.

selection of individuals who were at least 1 year postinjury was based on literature indicating that gains in walking ability plateau by the first postinjury year.6,31 I hypothesized that with training, subjects would show an improvement in walking speed, both on the treadmill and overground, an increase in treadmill walking endurance, and an increase in LE strength.

METHODS

Subjects

Nineteen individuals (13 men, 6 women; mean age, 31.7 ± 9.4yrs) participated in this study. Thirteen subjects presented with tetraplegia, 6 with paraplegia. All subjects had ASIA class C injuries (sensory and motor function are preserved below the level of the lesion, but at least half of the muscles below the level of the lesion have a grade < 3). Median time postinjury was 56 months (range, 12–171mo). All subjects signed an informed consent consistent with University of Miami regulations for protection of human subjects.

Inclusion criteria included asymmetric LE strength with the ability: (1) to rise from sit to stand, using upper extremity assistance, and no more than moderate assistance from another person; (2) to stand upright on both legs with no more than 30% BWS, (3) with 30% BWS, to advance the stronger leg independently with the treadmill speed at 0.1 miles per hour; and (4) in the weaker leg, to display a robust flexion withdrawal reflex at tolerable levels of electric stimulation. One subject (S9) was unable to complete the final 2 weeks of the training program owing to a family emergency that arose in the 10th week of training.

Testing

Subjects were tested prior to and following participation in the training program. The primary measure of interest was overground walking speed (OGWS) in the absence of BWS and FES, which was assessed based on distance traversed in a 2-minute timed walk along an 80-foot oblong track. Subjects were allowed to use their preferred assistive device and any necessary orthotic devices, and walked at their fastest comfortable walking speed (instructed as “you will be walking for 2 minutes, walk at a quick pace, but not so fast that you will be exhausted at the end”). Subjects were also tested while walking at their fastest comfortable walking speed on a motorized treadmill during which time they were videotaped from the sagittal view (on the side of the weaker limb) for later kinematic analysis. The level of BWS and the timing of FES during
Data Analysis

Data were analyzed using Microsoft Excel 97 SR-2 Statistical Tool Pac’ and customized programs. The required level of significance for all tests was p equal to .01. Both parametric and nonparametric statistical methods were used to compare changes in walking parameters and LEMS pre- and posttraining. One-tailed, paired r tests were used to test the hypothesis that OGWS, treadmill walking speed (TWS), and treadmill walking distance increased with training. Effect size and power calculations for changes in OGWS were calculated and adjusted for repeated measures according to the technique recommended by Portney and Watkins. 33 Wilcoxon’s test, a matched-pairs, signed-rank test for ordinal data, 34 was used to compare LEMS within and between legs pre- and posttraining. Pearson’s product-moment correlation (r) was used to test the relationships among OGWS and TWS. Spearman’s rank correlation coefficient (rs), a nonparametric equivalent to the Pearson r, for correlations among ordinal data, 35 was used to assess the relationship between LEMS and the subject’s initial walking mobility scores, as well as to test the relationship between these 2 variables and OGWS.

RESULTS

Walking Parameters

Individual subject data for OGWS (tested pre-, posttraining) and TWS and treadmill distance per session are given in figure 1. The OGWS reflects the speed the subjects were able to walk independently (no BWS, no stimulation) using whatever assistive device they typically used. At the time of the initial test, 6 subjects (S1, S2, S6, S10, S12, S18) required manual assistance to advance their weaker leg; by the final test only 2 subjects continued to require this assistance (S6, S12). Treadmill speed and distance reflect subject performance under the training condition (assisted by both BWS and stimulation).

Mean OGWS (m/s) improved over the course of training (initial = 12 ± 0.8 m/s; final = 21 ± 1.5 m/s; fig 1A), as did mean TWS (initial = 23 ± 12 m/s; final = 49 ± 20 m/s; fig 1B). The OGWS and TWS increases were seen in all subjects (median change, 77% and 106%, respectively; fig 2); these changes were statistically significant (OGWS: p = .0008; TWS: p = .00003) and the effect size for OGWS was large (r = .77), yielding a statistical power of 65%. There was a good correlation between OGWS and TWS, at both the beginning (r = .71) and end (r = .82) of training, but there was no relationship between pre-post change in walking speed overground versus that on the treadmill (r = -.07).

Mean treadmill distance/session (initial = 93 ± 84 m; final = 243 ± 139 m; fig 1C) increased significantly (p = .000001). Most subjects experienced an increase in treadmill walking distance (median change, 253%); however, there were 2 subjects (S6, S14), who walked a shorter distance as the treadmill speed increased (17% and -63%, respectively). In these subjects, walking distance was sacrificed to attain faster speeds.

Prior to the onset of training, a walking mobility score was established for each subject based on his/her typical walking practice. There was a good correlation (rs = .74) between initial OGWS and mobility scores.

Lower Extremity Motor Scores

LE strength, as indicated by LEMS, increased over the course of training (fig 3). There was a median increase of 3 points in each leg (from score of 8 to score of 11 in the FES-assisted leg, from 15 to 18 in the nonassisted leg); this increase was statistically significant in each case (p < .005 for each). The difference between the FES-assisted and nonassisted leg was statistically significant (p < .005) both pre- and posttraining; this was expected given the inclusion criteria of marked asymmetry in leg strength. In 4 individuals, LEMS for 1 leg were lower after than before training, and in 3 individuals 1 leg showed no change.

A relationship was found between walking speed and strength as indicated by a moderate correlation (r = .64) between pretraining OGWS and LEMS; posttraining OGWS and LEMS showed a fair correlation (r = .39). There was little or no correlation between the change in OGWS and the change in LEMS (r = -.16). There was a moderate correlation (r = .60) between pretraining LEMS and mobility scores (as established prior to training).

Follow-Up

Because most subjects did not live locally, we were able to do only limited follow-up after posttraining assessment. Four study participants (S1, S2, S5, S11) were available for reevaluation at posttraining time intervals of 6 months to 1 year. Three of these individuals (S1, S2, S5) demonstrated OGWSs that were as good or better than that of their final evaluation. One subject (S11) did not retain the gains made during participation in the training program. However, this individual had undergone surgery (revision of cervical decompression and fusion, unrelated to participation in the study) during the poststudy year and had subsequently had a prolonged period during which she was unable to ambulate. This may account for the loss of the gains made during the training program. These findings agree with those of Wernig et al., who evaluated subjects between 6 months and 6.5 years after participation in a training program of BWS and treadmill training, and found that the vast majority maintained the gains achieved with training.

DISCUSSION

All of the subjects who participated in this study demonstrated an improvement in OGWS. All subjects had SCI of at least 1 year’s duration, and therefore I attribute the increase in walking speed to participation in the study. Walking speed has been suggested to be the critical standard of walking ability in neurologically compromised individuals. 36-38 The finding of statistical significance, together with the effect size, suggests that these are meaningful changes in OGWS. The good correlation between OGWS and TWS supports the notion that those who are able to walk fastest on the treadmill are also able to walk fastest overground. However, the lack of correlation between change in OGWS and change in TWS suggests that there is little relationship between the amount of improvement in OGWS and improvement in treadmill training speed.

The finding that LEMS correlates with walking speed agrees with prior studies by Waters et al. 39,40,41 The change in LEMS was statistically significant, but whether this change (a median of 3 points) is functionally significant is debatable. The finding that there is a moderate correlation between OGWS and mobility score and between LEMS and mobility score demonstrates that, in addition to individuals with stroke, 32 mobility scores may be applicable to ambulatory individuals with SCI. No relationship, however, was found between the change in LEMS and the change in OGWS.

The use of time-delimited walk tests is increasingly common in the rehabilitation literature 42-43 because they inherently include a reproducible measure of exercise tolerance as well as speed. The decision to use the 2-minute walk test (rather than tests of other time durations) is based on evidence that this is...
Fig 1. Initial and final values for (A) OGWS (independent: no BWS, no stimulation); (B) TWS (assisted by BWS and stimulation); and (C) TWS (assisted by BWS and stimulation). Changes in speed were in the positive direction, 2 subjects (S8, S15) had lower treadmill walking distances in the final test compared with initial values (see text).

a reliable test that compares favorably with time-delimited tests of longer durations. Also, in addition to providing a functional time period over which to calculate walking speed, preliminary work suggests that 2 minutes is the minimum time required for an individual with SCI to reach a metabolic steady-state during ambulation (Patrick L. Jacobs, PhD, exercise physiologist, written communication, Sept 1999).

Recent evidence suggests that, to maximize locomotor performance in individuals with central nervous system pathology, subjects must train at a pace that approximates normal walking speeds. None of the subjects approached normal OGWS in their independent walking by the end of the study, but 7 of the 19 subjects (37%) effectively doubled their OGWS. Cerny et al suggest that individuals with SCI who
stimulation to evoke a flexion reflex to assist with the swing phase of gait. Use of a spinal reflex to facilitate stepping has clear advantages over either multichannel stimulation or manual assistance. In addition to providing direct motor excitation to the ankle dorsiflexors, such stimulation has reduced antagonist (extensor) muscle spasticity\textsuperscript{49} (defined as a velocity-dependent increase in resistance to passive stretch)\textsuperscript{50} and modulated spinal reflex activity in a way that may be functionally beneficial.\textsuperscript{51} Although it is well recognized that sensory input is important for the modulation of the output of the locomotor generator,\textsuperscript{26} evidence also suggests that sensory input may facilitate locomotor recovery following a spinal lesion.\textsuperscript{52}

Locomotor function is affected by an individual’s muscular strength, cardiovascular endurance, and the ability of the nervous system to recruit effectively and efficiently the appropriate motoneurons. Evidence suggests that the human spinal cord contains circuitry that is capable of producing locomotor-like output.\textsuperscript{14,19,53-55} The present intervention takes advantage of spinal circuitry to assist with production of stepping (through the use of the flexion withdrawal reflex) and uses the concepts of task-oriented training. This study indicates that such a training regimen can affect important functional measures such as OGWS and LE strength in individuals with chronic SCI.

Limitations:

Subjects who participated in this study demonstrated asymmetrical LE function with severe strength deficits in at least 1 leg; because of this, these results may not be generalizable to all subjects with chronic incomplete SCI. In addition, no comparison group was used, therefore, it is possible that similar results may be obtained with only 1 form of intervention (BWS or FES) or with more conventional types of training.

Further Development

A number of subjects reported that, in addition to improvements in OGWS and LE strength, they had experienced other benefits to the training. The most commonly cited secondary benefits were improved ability to perform transfers and stair-climbing tasks, and improved standing balance. Two subjects also reported improved bowel and bladder function. Future studies should attempt to assess these functions in a standardized way before and after the subjects’ participation in the study. No adverse effects were reported.
CONCLUSIONS

Subjects with incomplete SCI, who retain some capacity for ambulation, would likely benefit from a walking program that combines BWS, FES, and treadmill training. Although the amount of improvement in walking speed (as measured by increased OGW) varies with individual participant characteristics, this training clearly has positive effects on function. Use of FES for assistance with limb advancement offers advantages over other forms of assistance. This training regimen employs the principles of task-oriented training and uses the purported locomotor-generating circuitry of the spinal cord.

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References


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