

Therapeutic Effect of an Implantable Peroneal Nerve Stimulator in Subjects With Chronic Stroke and Footdrop: A Randomized Controlled Trial

Anke IR Kottink, Hermie J Hermens, Anand V Nene, Martin J Tenniglo, Catharina G Groothuis-Oudshoorn, Maarten J IJzerman

Background and Purpose

Footdrop, characterized by a person's inability to raise the foot at the ankle, is a common problem in patients with stroke. A randomized controlled trial was performed to determine the therapeutic effect of using a new implantable, 2-channel peroneal nerve stimulator for 6 months versus an ankle-foot orthosis (AFO).

Subjects

Twenty-nine patients with chronic stroke and footdrop participated in the study. The mean time from stroke was 7.3 years (SD=7.3), and all subjects were community ambulators.

Methods

The study used a randomized controlled trial design. The functional electrical stimulation (FES) group received the implantable stimulation system for correction of their footdrop. The control group continued using their conventional walking device (ie, AFO, orthopedic shoes, or no walking device). All subjects were measured at baseline and at weeks 4, 8, 12, and 26 in the gait laboratory. The therapeutic effect of FES on the maximum value of the root mean square (RMSmax) of the tibialis anterior (TA) muscle with both flexed and extended knees and walking speed were selected as the primary outcome measures. The RMSmax of the peroneus longus (PL), gastrocnemius (GS), and soleus (SL) muscles with both flexed and extended knees and muscle activity of the TA muscle of the affected leg during the swing phase of gait were selected as secondary outcome measures.

Results

A significantly higher RMSmax of the TA muscle with extended knee was found after using FES. No change in walking speed was found when the stimulator was not switched on. A significantly increased RMSmax of the GS muscle with both flexed and extended knees was found after using FES.

Discussion and Conclusion

Functionally, no therapeutic effect of implantable peroneal nerve stimulation was found. However, the significantly increased voluntary muscle output of the TA and GS muscles after the use of FES suggests that there was a certain extent of plasticity in the subjects in this study.

AIR Kottink, MSc, is Human Movement Scientist, Roessingh Research and Development, PO Box 310, 7500 AH, Enschede, the Netherlands. Address all correspondence to Ms Kottink at: a.kottink@rrd.nl.

HJ Hermens, PhD, is Clustermanager, Roessingh Research and Development, and Professor of Neuromuscular Control and Professor of Remote Monitoring and Treatment, Institute for Biomedical Technology, University of Twente, Enschede, the Netherlands.

AV Nene, MD, PhD, is Senior Researcher, Roessingh Research and Development, and Rehabilitation Doctor, Roessingh Rehabilitation Center, Enschede, the Netherlands.

MJ Tenniglo, PT, is Physiotherapist, Roessingh Rehabilitation Center.

CG Groothuis-Oudshoorn, PhD, is Biostatistician, Roessingh Research and Development.

MJ IJzerman, PT, PhD, is Chair, Clinical Epidemiology and Health Technology Assessment, Institute for Biomedical Technology, University of Twente.

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In most countries, patients with ankle dorsiflexor paresis, called “footdrop,” are provided with an ankle-foot orthosis (AFO). An AFO provides mediolateral stability at the ankle during the stance phase of gait and improves the swing phase of the paretic leg by facilitating toe clearance and promoting heel-strike.¹ Advantages of an AFO are that it is easy for the patient to apply, it provides consistent and stable support, and it is a relatively inexpensive device. A disadvantage is the limitation in mobility of the ankle joint during ambulation, which may inhibit recovery in the long term. In addition, patients often find AFOs to be uncomfortable or ineffective.² Beckerman et al³ reported that half of their patients were not adherent in wearing an AFO and that two thirds of their patients were not satisfied with the use of an AFO, as measured with the Sickness Impact Profile. Literature about AFOs is not conclusive, and the effect of an AFO on daily activities remains unknown.⁴

Functional electrical stimulation (FES) may be an alternative approach to correcting footdrop that works by stimulating the peroneal nerve during the swing phase of the gait cycle. Liberson and colleagues⁵ were the first investigators who reported on the application of FES in patients with footdrop as a consequence of stroke. They noted that some patients with stroke continued to dorsiflex the foot while walking after stimulation was stopped. This effect also was reported by other investigators.⁶⁻⁸ These results suggest that, as a consequence of walking with FES, plastic changes occur in the nervous system. Different names have been used in the literature to describe this phenomenon (ie, “carryover effect,” “therapeutic effect,” and “motor re-learning effect”). The definition given by Waters for this phenomenon is “a temporary increase in vol-

untary control observed immediately after electrical stimulation.”^{9(pp975-976)}

Recently, a meta-analysis was published by Robbins et al¹⁰ on the therapeutic effect of FES with surface electrodes on gait speed in patients with stroke. Three controlled studies examining the effect of peroneal nerve stimulation¹¹⁻¹³ were included in the meta-analysis. By using a fixed-effects model, a mean difference of 0.18 m/s was found ($P<.01$), indicating that FES can produce significant sustained improvements in gait speed even after the stimulator is turned off. An earlier, more descriptive review by Burrige et al¹⁴ examined both the orthotic and therapeutic effects of surface electrodes using single or dual channels of stimulation as an intervention for footdrop. A carryover effect was found in some of the studies⁶⁻⁸ included in their review. The underlying mechanism and the duration and extent of the effects were not specified, and the type of patient who might benefit from this intervention could not be identified. Their conclusion was that more work is needed to be able to answer these questions.

Surface-based FES is a common approach in the clinical setting, but there are several problems with this approach, especially difficulty positioning the electrode accurately with one hand and skin allergies.² Assuming that footdrop requires a permanent solution, an implantable system might be considered. Potential advantages of an implantable system include stability of electrode position, easier donning and doffing of the system, and reduced pain and skin irritation.

To date, no randomized clinical trial has evaluated the therapeutic effect of an implantable peroneal nerve stimulator versus an AFO on functional recovery in patients with footdrop who are in the chronic phase of

stroke. In a recent study by Kottink et al,¹⁵ a significant orthotic effect on walking speed was found in subjects who received FES, both when measured with a 6-minute walk test and when measured on a 10-m walkway.

The aim of the present study was to assess the therapeutic effect of an implantable, 2-channel peroneal nerve stimulator in comparison with that of an AFO on motor and functional recovery, as measured by 3 different outcome measures. First, the maximum value of the root mean square (RMSmax) of the tibialis anterior (TA), peroneus longus (PL), medial gastrocnemius (GS), and soleus (SL) muscles of the affected leg were measured during the performance of maximal voluntary contractions (MVCs) with the knees in both flexed and extended positions. The RMSmax reflects the capacity of the muscle output in a static test condition. Second, the amount of activity of the TA muscle of the affected leg during the swing phase of gait (RMSswing) was measured. In order to study changes in a functional status, comfortable walking speed was selected as a third outcome measure. In addition, RMSmax of the TA muscle and measurements of walking speed were correlated to investigate a positive relationship between both outcomes.

Conceptually, the repetitive stimulation of the muscles during gait for long periods of time and, consequently, the large amount of feedback to the brain might promote functional recovery. Especially in the TA muscle, increased maximal muscle activity was expected after prolonged use of FES because much higher intensity levels of stimulation for this muscle were used by our subjects when compared to the PL muscle, the other muscle that was directly stimulated. In some cases, stimulation of the PL muscle was not necessary because no inversion of

the foot was seen in these subjects during the swing phase of gait. Furthermore, we expected that the increased RMSmax of the TA muscle would result in increased walking speed when FES was switched off.

Method

Study Design

The study was conducted as a randomized controlled trial, and the CONSORT statement was used to report the trial.¹⁶ All subjects were assessed 5 times in the gait laboratory of Roessingh Research and Development, Enschede, the Netherlands. The baseline measurement took place about 4 weeks before the randomization procedure, and the follow-up measurements were performed 4, 8, 12, and 26 weeks after the surgical procedure of the FES group (see "Subjects" section for explanation of group assignments). The subjects assigned to the control group were measured in the same weeks as subjects assigned to the FES group. With the exception of RMSswing of the TA muscle, which was measured only at baseline and at week 26, the other outcomes were measured during each follow-up assessment. All measurements were performed by the same examiners (AK, MT). Ambulation activity (in meters per day) of both groups at baseline was asked by a questionnaire that was designed by Taylor and colleagues.²

The RMSmax of the TA, PL, GS, and SL muscles of the affected leg was measured during MVC while the subjects' knees were in both flexed and extended positions. While in both positions, the subjects were asked to perform an MVC in ankle dorsiflexion, plantar flexion, and eversion.

In the dynamic condition, both RMS swing of the TA muscle of the affected leg and walking speed were determined while subjects were asked to perform a 10-m walk several

Table 1.
Selection Criteria

Inclusion Criteria	Exclusion Criteria
Footdrop identified by an inability to achieve a normal heel-strike during walking	Age <18 y
First episode of hemiplegia of at least 6 mo duration as a result of a CVA ^a with stable neurological status	Passive dorsiflexion of the ankle <5° with knee in extension
Subject is an outdoor walker	Medical conditions other than CVA (ie, neurological, rheumatic, cardiovascular, or systemic disorders, including diabetes mellitus) limiting the function of walking
Able to give informed consent	Injury to deep and superficial peroneal nerve and sciatic nerve
	Any medical condition that would exclude the use of a surgical procedure or anesthetic
	Not able to don and doff the equipment
	Pregnancy

^a CVA=cardiovascular accident.

times. Walking speed was measured in 2 different conditions. All subjects started walking 4 times without using their conventional walking device (ie, AFO, orthopedic shoes, or no walking device). Thereafter, the same test was performed by both the FES and control groups while walking with their conventional walking device. The RMSswing of the TA muscle was measured only in the first test condition, when no walking device was used.

Instructing the subjects in the FES group on the proper use of the peroneal nerve stimulator and assessment of stimulation levels of the 2 output channels took place on the same day as the outcomes assessment. This was done for 2 reasons: (1) to keep the number of visits similar for both study groups so that the same amount of attention was paid to both groups and (2) to save time and travel costs in the FES group. If the subjects experienced problems, they were instructed to report them immediately so that a solution could be found as soon as possible. Blind-

ing of both the study personnel and participants was not possible because of the surgical procedures. All data were analyzed according to the intention-to-treat principle.

Subjects

Subjects were recruited in different ways. Most subjects were recruited for the study in response to an article in a local Dutch newspaper about the first results with the implantable stimulator in people who had survived a stroke. Some subjects were recruited through consultant and general practitioner referrals and in some cases on the advice of the physical therapist treating the subject. Table 1 shows the criteria for inclusion and exclusion in the study.

In total, 76 subjects were assessed for eligibility, and 47 subjects were excluded. Forty-three subjects did not fulfill the selection criteria, 3 subjects refused to participate, and 1 subject died during the period between the screening and the baseline measurement. Subjects who fulfilled the selection criteria were

Peroneal Nerve Stimulation

Table 2.

Characteristics of Subjects in the Functional Electrical Stimulation (FES) and Control Groups

Variable	FES Group	Control Group	P (Statistical Test)
No. of subjects (dropouts)	14 (1)	15 (3)	
Male	10	10	.78 (chi-square test)
Female	4	5	
Mean age, y (SD)	55.2 (11.36)	52.87 (9.87)	.56 (t test)
Mean time from stroke, y (SD)	9.07 (9.29)	5.67 (4.64)	.79 (Mann-Whitney test)
Physical therapy	4	3	.59 (chi-square test)
Walking distance per day			.98 (chi-square test)
10–99 m	1	1	
100–499 m	6	6	
500 m–1 km	2	3	
>1 km	5	5	
Left side affected	7	9	.89 (chi-square test)
Right side affected	7	6	

admitted to the study and 1 week after the baseline assessment were randomly allocated to either an FES group or a control group. Random allocation was performed in blocks of 2 subjects to ensure close balance of the numbers in each group. By means of a randomization list that was generated before the start of the study, it could be determined which subject of each block of 2 subjects was randomized to which treatment. The FES group received the implantable stimulator, and the control group continued using their conventional walking device for correction of their footdrop. The randomization procedure was performed by an independent individual. All subjects were allowed to continue their usual physical therapy sessions during the study, which they recorded in a diary. All subjects gave their informed consent before participating in the study.

Twenty-nine patients with footdrop due to a cerebrovascular accident (CVA) participated in the present study. Table 2 shows the characteristics of the participants. Subject characteristics were not very different between the 2 groups, with the exception of mean time after stroke,

which was longer for the FES group. At baseline, both groups also exhibited no significant difference in walking speed, indicating that the FES and control groups were matched.

The FES group consisted of 14 subjects (10 male, 4 female). Seven subjects used a plastic AFO, 3 subjects wore orthopedic shoes, and 4 subjects did not use a walking aid to correct their footdrop at the start of the study. Two of the subjects who used a plastic AFO also used a cane during walking. At the baseline measurement, 4 subjects were receiving physical therapy (3 once a week and 1 twice a week). Seven subjects were affected on the left side, and 7 subjects were affected on the right side.

The control group consisted of 15 subjects (10 male, 5 female). All subjects wore a plastic AFO, and 3 subjects also used a cane during walking. At the baseline measurement, 3 subjects were receiving physical therapy (2 once a week and 1 twice a week). Nine subjects were affected on the left side, and 6 subjects were affected on the right side.

Four subjects (1 woman in the FES group and 3 men in the control group) dropped out of the study. The implant of the subject in the FES group who dropped out showed failure after having functioned properly for about 10 weeks. Investigation of the explanted system showed that the system failure was caused by a technical defect in the epineural electrode responsible for the dorsiflexion movement. The remaining subjects of the FES group did not experience technical failure of the stimulation system and continued to use the stimulator during the entire follow-up period. In the control group, 2 subjects withdrew after the randomization procedure, and the other subject dropped out in week 11 because of psychological problems (not due to the study). Thus, for the analysis we only had 2 dropouts, both in the control group. Despite contact with them, we could not obtain the last data.

At the baseline measurement, walking speed in the FES group while subjects used their conventional walking device was calculated as the mean walking speed for the subjects who used a plastic AFO or an orthopedic shoe (n=10).

Stimulation System

The implantable, 2-channel peroneal nerve stimulator* consists of an external transmitter with a built-in antenna, a footswitch, and an implantable part consisting of the stimulator, the 2 leads, and the bipolar intraneural electrodes.^{17,18}

The transmitter uses a single 40-mm-diameter transmission coil that transmits alternately on 2 frequencies. This switching results in a pulse repetition rate of 30 Hz on each channel. The amplitudes of the monophasic pulses modulated on each carrier wave are controlled separately. The transmitter weighs approximately 0.1 kg and is attached with a strap on the lateral side of the lower leg, over the site of the implant, just below the knee. A footswitch placed under the heel of the subject's foot inside the shoe determines the on-and-off switching of the stimulation. The battery of the transmitter is charged overnight.

The implantable, 2-channel nerve stimulator is a passive device, receiving information carried by the radio frequency signals and converting them into the stimulation pulses of the desired amplitude and frequency. The receiver block is approximately 33 mm in diameter and 6 mm thick. It contains 2 independent and galvanically separate electrical circuits built upon a ceramic substrate 29 mm in diameter. The 2 circuits are tuned to operate at different frequencies (ie, 1 and 2 MHz), allowing them to be individually controlled by the transmitter. This further reduces the risk of "cross talk" between the channels. The electronic circuits of the receiver block are encapsulated in silicone rubber elastomer. One electrode is placed under the epineurium of the super-

ficial peroneal nerve (eversion), and the other electrode is placed under the epineurium of the deep peroneal nerve (dorsiflexion). The stimulation pulses have an asymmetric, biphasic charge balanced waveform.

Measurements

MVC. Bipolar surface electromyographic (sEMG) activity of the TA, PL, GS, and SL muscles was recorded during maximal ankle dorsiflexion, plantar-flexion, and eversion contractions of the affected leg of the subjects. The electrodes (Arbo, type H93SG, silver-silver chloride gel electrodes, diameter=16 mm, interelectrode space=23 mm[†]) were placed after shaving, scouring, and abrading the skin vigorously with an alcohol pad. All electrodes were placed according to international guidelines.¹⁹ A reference electrode was placed on the hand. The sEMG activity was recorded using an ambulant Porti5-16/ASD system[‡] (input impedance=10¹² Ω, gain=20, 22-bit analog-to-digital converter), which was band-pass finite impulse response filtered at 20 to 553 Hz. The RMSmax was recorded in 2 positions: with flexed and extended knees. The primary reason for this was that the subjects had to activate their muscles in and out their synergistic pattern.²⁰

First, the subjects sat on a couch in an upright position while keeping their knees in 90 degrees of flexion. They were first asked to contract the ankle dorsiflexors maximally. The investigator held the subjects' heel firmly in one hand, while using the other hand to give resistance by straightening and extending the foot.

The same test was repeated for the plantar-flexion movement. During this test, the investigator held the

subjects' heel firmly with one hand, while providing resistance with the other hand by flexing the foot. An eversion movement then was performed by the subjects. During this movement, the investigator cupped the subjects' heel in one hand and with the other hand gave resistance by grasping the distal portion of the forefoot and turning the sole of the foot toward the median plane. The subjects performed all movements 3 times for a period of 5 seconds, with a couple of seconds of rest between measurements.

Second, MVCs were performed while the subjects were lying supine on a couch. The subjects were asked again to perform maximal ankle dorsiflexion, plantar-flexion, and eversion contractions while their legs were kept in an extended position. They performed all movements 3 times for a period of 5 seconds, with a couple of seconds of rest between measurements. For each movement, a mean value was calculated by averaging the 3 values.

A customized software program was used to determine the RMSmax of the TA, PL, GS, and SL muscles. The RMSmax was calculated by taking the middle part of the electromyographic (EMG) signal to avoid start-up and slow-down effects of the MVC. Log transformation was applied to all EMG RMS data to produce a more normal distribution of values.

The same investigators measured sEMG activity during MVCs 5 times for all subjects. Because resistance was given by hand during the performance of the MVC experiment and no device was used to fix the ankle joint, intraclass correlation coefficients (ICCs) were calculated as a measure of the reliability of the MVC measurements.

[†] Tyco Healthcare Deutschland GmbH, Postfach 1217, D-93333, Neustadt/Donau, Germany.

[‡] Twente Medical Systems International BV, PO Box 6044, 7503 GA, Enschede, the Netherlands.

* Finetech Medical Ltd, 13 Tewin Ct, Welwyn Garden City, Hertfordshire, United Kingdom, AL7 1AU.

TA muscle activity during swing phase of gait. Bipolar sEMG activity of the TA muscle, the primary ankle dorsiflexor muscle, of the affected leg was recorded during the performance of a 10-m walk. The TA muscle was selected because this muscle was directly stimulated by the implantable, 2-channel peroneal nerve stimulator. Because the stimulator was active only during the swing phase of gait, as determined by a heel switch placed inside the shoe of the subjects, the RMS of the TA muscle was determined only during this phase of the gait cycle to determine a possible therapeutic effect of FES.

To be able to define the gait cycle in the EMG recordings, footswitches were used to signal heel, midfoot, and toe contacts with the floor. They consisted of an aluminium conductive sheet covering the sole of the shoe in conjunction with a conductive rubber mat. Footswitch signals were taken from both feet together with the EMG signals and, by means of a synchronization signal given during each measurement, both signals could be linked together afterward. Subjects were asked to perform the walk 4 times without using their conventional walking device. They were instructed to walk at a comfortable speed; no other instructions were given. The use of a walking stick was allowed only when needed. To keep the test conditions the same during the trial, subjects who used a walking stick at the baseline assessment also had to use a walking cane at the follow-up assessment (week 26).

A customized software program was used to determine RMSswing. For each walking session, the program automatically selected those parts of the gait cycle where the affected leg was in swing phase, from toe-off till heel-strike. The first walk was excluded from the analysis, and RMSswing was calculated by averaging

the RMS values of the remaining 3 walking sessions.

Walking speed. Walking speed was measured automatically during the 10-m walk with the VICON system,⁵ consisting of 2 infrared beams over a distance of 7.5 m. To exclude the influence of acceleration and deceleration at the beginning and end of the 10-m walk, 1.5 m was allowed at the start and finish of the test. At each assessment, both the FES group and the control group were first asked to perform the walk 4 times without the use of their conventional walking device. Next, the same procedure was accomplished with use of their conventional walking device. The subjects were instructed to walk at a comfortable walking speed; no other instructions were given. To be able to measure a possible therapeutic effect of FES, the stimulation system was not used by the FES group during the experiment. During the trial, the FES group used the stimulator only in the home environment. There was a brief resting period between walking sessions. All subjects were allowed to use a walking cane, if needed, and this was recorded. The condition during the baseline assessment was the standard for the follow-up measurements.

In both walking conditions, the first walk was excluded from analysis. For each walking condition, a mean walking speed was calculated by averaging the speeds of the 3 remaining walking sessions. To investigate the absence or presence of a therapeutic effect in the FES group, walking speed measured with and without the conventional walking device at the baseline assessment was compared with the measurements of walking speed obtained during subsequent follow-up assessments. These results were compared with the results shown by the con-

⁵ VICON-UK, 14 Minns Business Park, West Way, Oxford, United Kingdom, OX2 0JB.

trol group to examine whether a significant therapeutic effect of FES was present.

Correlation between RMSmax of the TA muscle and walking speed.

A positive relationship in the FES group was hypothesized between maximal muscle activity trained by FES and walking speed. If use of the peroneal nerve stimulator resulted in a therapeutic effect on both variables, high correlation coefficients must especially be seen in the TA muscle, since this is the muscle that was primarily stimulated. Therefore only correlations coefficients were calculated for this muscle.

Data Analysis

A power analysis was performed based on estimates that were obtained from the pooled analysis in a previous review by our group.²¹ The review intended to analyze the orthotic effect of FES on the improvement of walking in patients with footdrop following a stroke. Data on walking speed in 4 clinical articles^{11,12,22,23} were pooled to estimate a mean difference of 0.134 m/s (SD=0.124). The following numbers were used for the power analysis: in the control group, mean=0, SD=0.124; in the FES group, mean=0.134, SD=0.124; delta=0.134, alpha=0.05, power=0.8. The power calculation resulted in a number of 14 subjects in each group.

The Wilk-Shapiro test was used to test all outcome measures for normality. The RMS values were log transformed if a non-normal distribution was found. If, after log transformation, a non-normal distribution still was present, a nonparametric test was used.

MVC. A linear mixed model was used to test for differences in MVC between groups. Because a non-normal distribution was found only for the TA muscle ($P<.05$), a non-

equivalent of the linear mixed model (the nonparametric factorial model for repeated measurements described by Brunner et al²⁴) was used to analyze the RMSmax of the TA muscle. Group (FES and control), time outcome assessments (baseline and 4, 8, 12, and 26 weeks), and the interaction between group and time were entered as terms in both the parametric and nonparametric models. The interaction was used to test for differences between groups in the change in RMSmax measured over time. Differences between and within groups over the period between the baseline assessment and the follow-up assessment at week 26 were evaluated. For each muscle, the ICC of the MVC measurements within subjects was calculated using a linear mixed model, with a random intercept per subject and with time, treatment, and their interaction as fixed factors.²⁵

TA muscle activity during swing phase of gait. The RMSswing was normally distributed ($P > .05$); therefore, a paired-samples *t* test was used to compare baseline values with the values found at the week-26 follow-up assessment.

Walking speed. Differences in walking speed between groups were analyzed with a linear mixed model because walking speed was normally distributed ($P > .05$). The same terms were entered in this model in comparison with the model used for MVC. The strength of a positive relationship between the RMSmax of the TA muscle trained by FES and walking speed was tested by a Pearson correlation coefficient for each subject.

The significance level was set at $\alpha = .05$ for all tests. The linear mixed model analyses, the paired-samples *t* test, and the Pearson correlation coefficient were performed with

SPSS version 11.5 for Windows.^{||} The nonparametric factorial model for RMSmax of the TA muscle was performed with the statistical program R.²⁶

Results

MVC

Test-retest reliability. Intraclass correlation coefficients were calculated as a measure of the reliability of the MVC measurements. The ICCs for the RMSmax of the TA, PL, GS, and SL muscles over time were .77, .66, .72, and .57, respectively. The mean RMSmax of the TA, PL, GS, and SL muscles in the FES and control groups with flexed and extended knee are summarized in Figure 1.

Knee in flexion. As shown in Figures 1A and 1B, the RMSmax values of all muscles were very similar in both groups at the baseline assessment, with exception of the TA muscle, in which a higher RMSmax was found as in the control group. During the trial, the FES group showed higher RMSmax values for the TA muscle, increasing from 97 μV at the baseline assessment to 150 μV at the last follow-up assessment (Fig. 1A). The RMSmax values in the control group stayed at the same level during the trial, around 120 μV (Fig. 1B). An almost significant value was found when calculating the change in RMSmax of the TA muscle over time between groups ($P = .058$).

The RMSmax for the PL muscle stayed rather constant over time in the FES group, and the control group seemed to improve slightly during the trial, although no significantly different change in RMSmax of the PL muscle over time between groups was found ($P = .860$). The FES group showed an improvement in RMSmax of the GS muscle, from 25 to 38 μV .

^{||} SPSS Inc, 233 S Wacker Dr, Chicago, IL 60606.

A small deterioration from 22 to 17 μV in RMSmax was shown by the control group during the subsequent assessments. This resulted in a significant difference in RMSmax of the GS muscle over time between the FES and control groups ($P = .002$). Both the FES and control groups showed a rather constant RMSmax for the SL muscle, not resulting in a significantly different change between groups over time ($P = .330$).

Knee in extension. Behavior for the RMSmax of the TA muscle in the extended knee position was similar to that during the flexed knee position (Figs. 1C and 1D). The FES group showed an increase in RMSmax from 67 to 109 μV , and the RMSmax of the control group did not change during the study, staying around 81 μV . A large significant difference in the RMSmax of the TA muscle over time between groups was found ($P = .006$). The RMSmax of the PL muscle in the FES group increased slightly, from 29 to 45 μV . A small increase, from 32 to 36 μV , was found in the control group. No significantly different change over time was found in the RMSmax of the PL muscle between groups ($P = .208$). In addition, for the GS muscle, an increase in RMSmax, from 43 to 66 μV , was shown in the FES group, whereas the RMSmax of the control group did not change and stayed around 39 μV . The change in RMSmax over time between groups, therefore, was significantly different ($P = .035$). Both groups showed an RMSmax of 48 μV for the SL muscle at the baseline assessment, which stayed constant during the study in both groups. Thus, no significantly different change in RMSmax of the SL muscle was found over time between the FES and control groups ($P = .654$).

TA Muscle Activity During Swing Phase of Gait

Figure 2 shows an example of the RMSswing during a walking session of

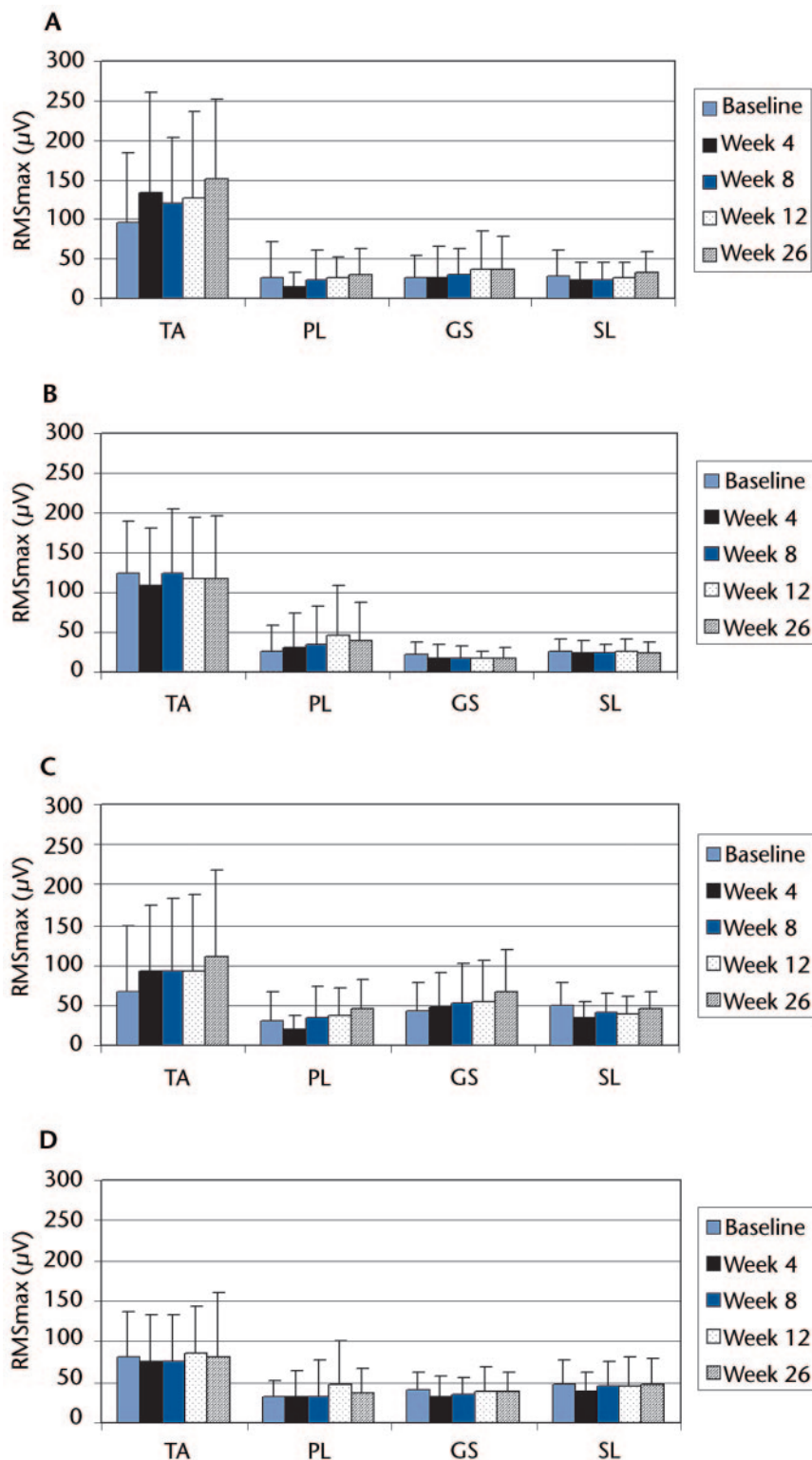


Figure 1. Mean maximal value of the root mean square (RMSmax) (in microvolts) of the tibialis anterior (TA), peroneus longus (PL), medial gastrocnemius (GS), and soleus (SL) muscles in the functional electrical stimulation (FES) group and the control group with the knee in flexion (A: FES group, B: control group) and with the knee in extension (C: FES group, D: control group), as measured by maximal voluntary contraction.

a subject with left hemiplegia. At the baseline assessment, the FES and control groups showed mean RMSswing values of 54 μV and 66 μV , respectively. During the follow-up assessment, the RMSswing in the FES group remained rather constant, showing an RMS of 58 μV ($P=.706$). In the control group, an RMSswing value of 45 μV was found, resulting in a significant decline ($P=.036$).

Walking Speed

Figure 3 shows the walking speed results of the subsequent assessments for both the FES and control groups when walking with and without a conventional walking aid. No correction for baseline was necessary in the analysis because no differences in baseline values were present between groups. Walking speed remained rather constant in both groups when no walking aid was used. The change in walking speed without a walking aid within the FES group over time, therefore, was not significantly different from that of the control group ($P=.152$). When the conventional walking aid was used, the walking speed results at the end of the study were comparable to the results at the baseline assessment in both groups. No significant difference over time was found when the 2 groups were compared with each other ($P=.238$).

Correlation Between RMSmax of the TA Muscle and Walking Speed

Table 3 shows the Pearson correlation coefficients (range and median) found for the TA muscle in both the FES and control groups. Both variables were measured in 2 conditions: RMSmax with flexed and extended knee and walking speed with and without the use of an AFO. The subjects in both groups showed large differences in correlation coefficients calculated for all conditions, as reflected by the broad ranges found for both groups. Low median correlation coefficients were shown

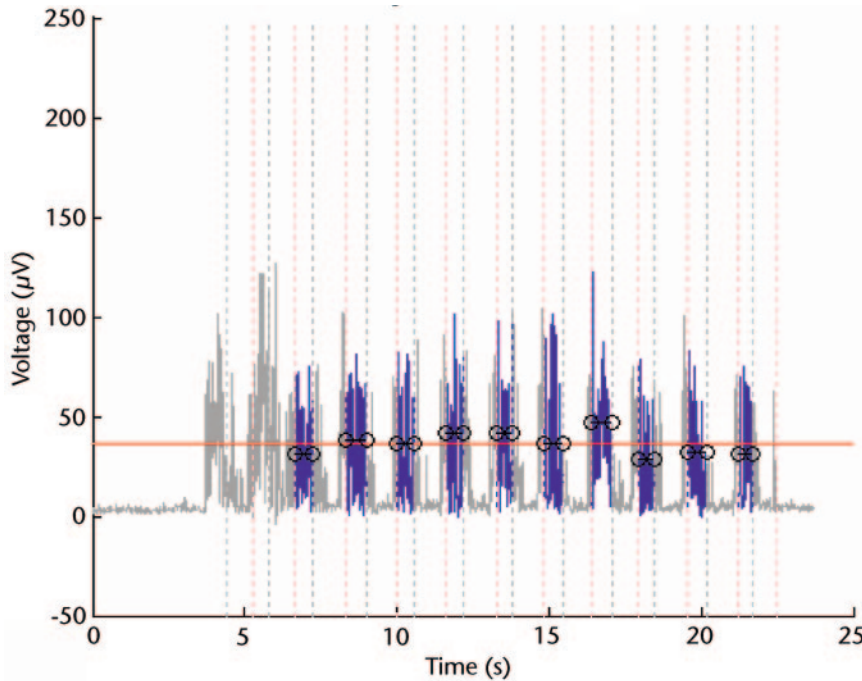


Figure 2. An example of the determination of amount of activity of the tibialis anterior (TA) muscle of the affected leg during the swing phase of gait (RMSswing) in a subject with left hemiplegia. The first dashed vertical line of the electromyographic signal represents toe-off and the second dashed vertical line represents heel-strike of the left affected leg. For every swing phase, a mean root mean square (RMS) value was calculated by the program. The horizontal line represents the mean RMS value of the TA muscle of all swing phases during a walking session.

learning for TA muscle activation. However, during the static test condition, consisting of voluntary activation of the muscles, some interesting results were found, suggesting a certain extent of plasticity in motor control.

Streiner and Norman²⁷ recommended a reliability value of .70 when a scale is used for research purposes. For both the TA and GS muscles, acceptable test-retest reliability was found for the MVC tests (.77 and .72, respectively). An ICC of .66 was found for the PL muscle, and a relatively low ICC of .57 was found for the SL muscle. The voluntary muscle output of the TA and GS muscles was increased after using the stimulation system for a period of 6 months, suggesting a training effect of FES.

The RMSmax of the TA muscle was clearly higher with flexed knee in comparison with extended knee in both groups. This typical pattern can be explained by the flexion synergy that often is seen in patients with stroke. When the hip and knee are flexed, it is easier for patients with stroke to also bring their ankle into a flexed position, resulting in a dorsiflexion movement.²⁰ Similarly, plantar flexion of the ankle must be easier to perform by patients while

by both groups between RMSmax of the TA muscle and walking speed.

Discussion

The results of the present study show that use of an implantable FES device over a 6-month period did not

result in a change in self-selected walking speed when the device was turned off in subjects with chronic stroke and footdrop. In addition, no change in TA muscle activity was observed during the swing phase of walking, indicating no task-specific

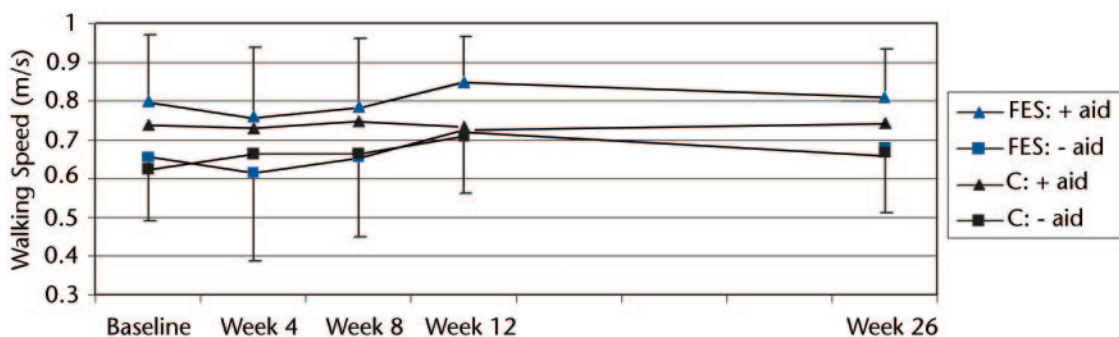


Figure 3. Mean walking speed measured in the functional electrical stimulation (FES) and control (C) groups both during walking with and without their conventional walking aid (ankle-foot orthosis, orthopedic shoes, or no assistive device). Error bars (SD) are shown only for the FES group because the error bars for the control group were very similar.

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Table 3.

Pearson Correlation Coefficients Between Maximum Value of the Root Mean Square (RMSmax) of the Tibialis Anterior Muscle, Measured With Both Flexed and Extended Knees, and Walking Speed, Measured Without and With an Ankle-Foot Orthosis (AFO) in the Functional Electrical Stimulation (FES) and Control Groups: Range (Median)

RMSmax	Walking Speed	
	Without AFO	With AFO
Knee in flexion		
FES group	-.90 to .97 (.33)	-.90 to .84 (-.07)
Control group	-.40 to .83 (.14)	-.87 to .53 (.14)
Knee in extension		
FES group	-.83 to .60 (-.20)	-.80 to .76 (.21)
Control group	-.99 to .93 (.14)	-.73 to .73 (.07)

their hip and knee are in an extended position. When examining the GS and SL results, both groups showed a higher RMSmax with extended knee. Functional electrical stimulation seemed to have the largest positive effect on maximal muscle activity produced by the TA and GS muscles at both positions.

An explanation for the increased TA muscle activity was given by Miller and Light,²⁸ who described that increased muscle activity can be accomplished in several ways, such as increasing the number of activated motor units, increasing the rate of activation, or increasing the synchronization of activation. In addition, as a result of FES training, the muscle fiber diameter may have been increased. To explain the therapeutic effect of FES on the TA muscle, Rushton²⁹ stated that the antidromic impulse in motor nerve fibers will reach the anterior horn cell. If the corticospinal-anterior horn cell synapse is a Hebb-type modifiable synapse, which means that it is strengthened by the coincidence of presynaptic and postsynaptic activity, then FES, combined with coincident voluntary effort through a damaged pyramidal motor system, could help to promote restorative synaptic modifications at the anterior horn cell level. Thus, electrical stimulation applied at rest is not expected to have any effect. Therefore, footdrop stimulation in particular, where stimulation is always applied at the time the automatic toe-

lift command is generated in the brain, might be successful in promoting functional recovery in patients. In contrast, plastic AFOs and orthopedic shoes—standard devices used for the correction of footdrop—limit the mobility of the ankle joint during ambulation and may further negatively affect recovery.

From the MVC results of the present study, it is not possible to conclude which mechanism was responsible for the increased maximal TA muscle activity. Experiments with multi-channel array electrodes may be performed in the future to assess motor control by measuring the number of motor unit action potentials (MUAPs) per second, which reflects the product of the number of motor units and their firing rate, and to examine the pattern and distribution of MUAPs following MVC more comprehensively.^{30,31} With this measurement technique, it is possible to investigate whether the increased muscle activity was caused by a local training effect of the stimulated muscle or by a change in motor control (eg, an increased number of motor units).

Yan et al³² examined the direct effect of stimulation by measuring MVC of the ankle dorsiflexors and plantar flexors to determine whether FES in combination with standard care, consisting of physical therapy and occupational therapy, was more effective in promoting motor recovery

of the lower extremity in subjects with acute stroke than placebo stimulation with standard care or standard care alone. A significantly increased MVC torque of the affected TA muscle was found, together with an improved plantarflexion torque at week 3, after stimulation of the quadriceps femoris, hamstring, TA, and GS muscles 30 minutes a day, 5 days per week, for 3 weeks.

The finding that the GS muscle, which is the antagonist of the TA muscle, also showed a significantly higher RMSmax with flexed and extended knees was not expected because this muscle was not directly stimulated. However, these results also were found by Stefanovska et al.³³ They measured maximal isometric torque during voluntary contraction in dorsiflexion and plantar flexion in patients with hemiplegia with an implanted peroneal stimulator. After 6 months of stimulation, voluntary control was improved, particularly in the stimulated TA muscle but also in the antagonistic triceps surae muscle. This increased voluntary control can be attributed to decreased tonic activity in both the TA and triceps surae muscles, another parameter measured in their study.

In contrast to our expectations, the results showed that FES used for a period of about 6 months had no therapeutic effect on walking speed.

Walking speed is an outcome measure that often is used to measure whether a therapeutic effect is present after using electrical stimulation. Recently, a mean increase of 0.18 m/s ($P < .01$) was found by Robbins et al¹⁰ in their systematic review. They reported that large effect sizes were found in FES studies examining subjects in the subacute stage of recovery, whereas relatively small effect sizes were found in FES studies examining subjects in the chronic stage of recovery. Robbins et al examined 4 FES studies^{12,13,22,34} that included patients in the chronic phase of stroke whose mean time from stroke was about 37 months. In the present study, the mean times from stroke in the FES and control groups were 109 and 68 months, respectively. The chronic status of our subjects, therefore, may be a possible explanation for our finding of no significant therapeutic effect of FES on walking speed.

A positive relationship was hypothesized between maximal TA muscle activity and walking speed in the FES group. The low median correlation coefficients found in both groups however, suggest that no relationship exists between these 2 parameters. An explanation can be found when one considers that the prime function of the TA muscle consists of lifting the foot during the swing phase of gait, which will require an amount of activity and is unlikely to be linearly related to the walking speed. More likely is that, below a certain required activity level, TA muscle activity will affect the quality of the movement and, therefore, will show some relationship with walking speed. However, when a person is able to generate this amount of activity, an increase in the activity will not affect the walking speed because it is not directly related to the propulsion of the body. For the calf muscle, for example, a positive linear relationship with walking speed

seems more plausible because of its propulsive function. Although the increased ability to voluntarily activate the TA muscle did not result in an improvement in walking speed, the higher lifting of the foot may give patients more confidence in their ability to walk without stumbling.

Study Limitations

This study had a number of limitations. The sample size was relatively small, which further limits generalizability to the broader population with stroke and placed the study at risk for false-negative results (type II error). Blinding of both the study personnel and patients was not possible because of the invasive FES treatment, which may have biased the study in favor of the FES group. Regarding the difference in AFO use between the FES and control groups, it was a coincidence that, after randomization, all control subjects used an AFO, whereas this was not the case in the FES group. There is no evidence, from the limited measurements that we made, that there were any significant differences across groups at the baseline assessment. Most subjects in the FES group had been prescribed an AFO in the past, but they rejected its use in daily practice. Differences in TA muscle activity also were observed between the groups in the baseline condition, although the differences were not statistically significant. The FES group showed lower baseline RMS values of the TA muscle while their knee was both in flexion and in extension compared with the control group.

Conclusion

Functionally, no therapeutic effect of implantable peroneal nerve stimulation was found, reflected by no change in walking speed when no stimulator was used. However, the significantly increased voluntary muscle output of the TA and GS muscles during a static task after the use of FES suggests that there is a certain

extent of plasticity in people with chronic stroke and footdrop who are community ambulators.

Ms Kottink, Dr Hermens, Dr Nene, and Dr Iljerman provided concept/idea/research design. Ms Kottink and Mr Tenniglo provided data collection. Ms Kottink, Dr Groothuis-Oudshoorn, and Dr Iljerman provided data analysis. Ms Kottink and Dr Hermens provided project management. Dr Iljerman provided fund procurement and institutional liaisons. Ms Kottink, Dr Nene, and Mr Tenniglo provided subjects. Dr Groothuis-Oudshoorn provided consultation (including review of manuscript before submission).

The experimental protocol was approved by the local medical ethics committee.

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