Functional electrical stimulation of the ankle dorsiflexors during walking in spastic cerebral palsy

Functional electrical stimulation of the ankle dorsiflexors during walking in spastic cerebral palsy: a systematic review

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ABBREVIATION
FES Functional electrical stimulation

AIM To assess the effect of functional electrical stimulation (FES) of ankle dorsiflexors in children and adolescents with spastic cerebral palsy (CP) during walking.
METHOD A systematic review was performed using the American Academy of Cerebral Palsy and Developmental Medicine methodology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Six databases were searched for studies applying interventions to patients aged younger than 20 years. Outcomes were classified according to the International Classification of Functioning, Disability and Health (ICF).
RESULTS Seven hundred and eighty abstracts were found, 35 articles were fully screened, and 14 articles were used for analysis. Only five articles (three studies) were of level I to III evidence. At ICF participation and activity level, there is limited evidence for a decrease in self-reported frequency of toe-drag and falls. At ICF body structure and function level, there is clear evidence (I–III) that FES increased (active) ankle dorsiflexion angle, strength, and improved selective motor control, balance, and gait kinematics, but decreased walking speed. Adverse events include skin irritation, toleration, and acceptation issues.
INTERPRETATION There are insufficient data supporting functional gain by FES on activity and participation level. However, evidence points towards a role for FES as an alternative to orthoses in children with spastic CP.

Cerebral palsy (CP) is the most common cause of motor disability in children, with an incidence of 2.11 children per 1000 births in Europe.[1] According to the current definition, CP describes a group of permanent disorders of the development of movement and posture, causing activity limitations and resulting from an injury in the developing central nervous system.[2–4]

For classifications of severity of CP, the International Classification of Functioning, Disability and Health (ICF) can be used to distinguish different levels.[5] At the level of body functions and structures, the anatomical distribution (e.g. unilateral and bilateral) and the motor abnormality (i.e. spastic, dyskinetic, or mixed) is important for this systematic review. At the level of activity and participation, the Gross Motor Function Classification System (GMFCS) is used.[6] This review focuses on walking children with spastic CP.

Spasticity and treatment options

Spasticity is defined as a velocity-dependent increase in the tonic stretch response with excessive tendon jerk reflexes; it is caused by the reduction of inhibitory impulses on lower motoneurons.[7] Spasticity often interferes with mobility, especially with walking. Spasticity of the ankle plantar-flexors, and weakness and poor selective control of the ankle dorsiflexors (such as the anterior tibial muscle), can lead to drop foot or true equinus.[8] As a result, patients with CP often have a decreased walking distance (fatigue) and increased incidence of tripping and falling. Ankle-foot orthoses are frequently used to support weakened muscles but they can restrict active motions and thereby exacerbate muscle weakness.[9]

Functional electrical stimulation

Functional electrical stimulation (FES) is defined as 'the electrical stimulation of muscles that have impaired motor control to produce a contraction to obtain functionally useful movement'.[10] Two types of FES can be distinguished: (1) direct stimulation of the anterior tibial muscle through motor points or (2) stimulation of the fibular (formerly called peroneal) nerve, namely indirect stimulation of the anterior tibial muscle, other (toe-)extensors and the

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fibular muscle group. The fibular muscle group primarily everts the foot and partly contributes to plantar-flexion.[11] FES might function as a dynamic functional orthosis.[12] The mechanism is based on depolarization of the axon by an electrical field. A bidirectional action potential, activating the motor unit, is created if the speed and intensity of the electrical field is sufficient. Direct depolarization of muscle fibres is also possible, but this requires 10 to 100 times the amount of current.[13] FES in drop foot is used to stimulate the common peroneal nerve, activating the dorsiflexor muscles of the foot during the swing phase of gait.

FES stimulus parameters

The stimulus waveform used for FES can either be monophasic or biphasic. The difference is the net movement of charged ions, which is present in monophasic but absent in biphasic waves. The biphasic waveform is preferred, because this rapid changing of stimulus polarity decreases skin irritation and increases comfort. The current amplitude is an important factor in the safety and comfort of FES. Pulse width (or phase duration) indicates the length of each phase. Either the pulse width or the amplitude should reach the threshold to create an action potential. A smaller pulse width causes less discomfort and skin irritation. The pulse rate (or frequency) of the stimulation determines the rate of nerve depolarization and influences the type of muscle contraction: twitch contractions occurring at low (1–10 pulses per second [pps or Hz]) frequency; or incomplete tetanic or fused tetanic contractions at higher frequencies (15–25 or >45–50pps). Charge per phase is calculated as the current–time integral. As the phase charge increases, more nerve fibres are excited. The interpulse interval can be constant or can be manipulated. Manipulation can sometimes lead to more force production and less fatigue, and therefore interrupted pulses are common in rehabilitation applications.

Aim of the study

This systematic review focuses on FES of the ankle dorsiflexors in children with spastic CP during walking. As previously stated, increased fatigue, falling, and tripping are the most common clinical problems. Despite several published studies on FES, consensus for clinical practice is lacking.[14] The aims of this systematic review are the following: (1) to assess the effect of FES of the ankle dorsiflexors and level of evidence on outcomes at ICF activity and participation level (e.g. fatigue, falling, and tripping) and ICF body functions and structures level (e.g. orthotic effect, gait, force, and spasticity); (2) to provide a practical guidance for stimulus parameters; and (3) to provide an overview on side effects of FES of the ankle dorsiflexors.

METHOD

This systematic review was conducted according to the American Academy of Cerebral Palsy and Developmental Medicine methodology for developing a systematic review of treatment interventions[15,16] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[17] Since human participation was not required for this study, ethical approval did not apply. For interpretation of all the results, a p-value of ≤ 0.05 was considered statistically significant.

What this paper adds

- Effects of functional electrical stimulation (FES) point towards a potential role as an alternative to orthoses for patients with spastic cerebral palsy (CP).
- Some evidence for a decrease in self-reported frequency of toe-drag and falls with the use of FES in spastic CP.
- Limited evidence for improvements in activity and participation in patients with spastic CP using FES.

Search strategy

A systematic literature search was performed using the following databases: PubMed/MEDLINE (391 articles), Embase (270 articles), the Physiotherapy Evidence Database (PEDro, 89 articles), Web of Science (308 articles), CINAHL (94 articles), and the Cochrane Library (58 articles).

The search strategy included terms describing the population ('cerebral palsy' or 'cerebral palsy' [Medical Subject Headings, MeSH]) and terms describing the intervention ('functional electrical stimulation' OR 'fes' OR 'neuroprosthesis' OR 'stimulat* foot drop' OR 'walkaide' OR 'walk aide' OR 'neurostimulat* OR 'electrical stimulation'). The searches were updated to 31 December 2015.

Operational definition of population and intervention (inclusion criteria)

We included studies that described the effects of FES intervention to the ankle dorsiflexors, producing a muscle contraction and applied during walking. This intervention had to be applied to patients with spastic CP younger than 20 years, in a GMFCS level from I to III. Studies on the described intervention applied after injection of botulinum neurotoxin A (BoNT-A) were also included but separated from the studies without BoNT-A injection. We did not exclude studies based on type of electrical stimulation before reading full texts, because of the inconsequent use of terms.

Exclusion criteria

Articles were excluded if (1) they did not report data about electrical stimulation, (2) the patients included were not diagnosed with CP, (3) the electrical stimulation intervention applied in the study was not aimed at the ankle dorsiflexors, (4) the patients were older than 20 years of age at the moment of the electrical stimulation intervention, (5) the article was not a study report, but, for example, a letter, a conference abstract, or study protocol, or (6) the article was not available in English, Dutch, or German.

If full-text reading led to the conclusion that the type of electrical stimulation studied was not FES, the article was also excluded. Articles lacking details of stimulation parameters of the FES device were excluded.

Organization of the evidence and data extraction

Grading of the articles and data extraction was independently done by two authors (IM and RJV). Table SI (online supporting information) explains the levels of evidence used in this systematic review. These levels are based on a hierarchy of the types of research design. The conduct of studies was judged using the items in Table SII (online supporting information). These first two tables are double: part (a) for group design studies and part (b) for single-subject design studies. Table SIII (online supporting information) provides a summary of all the included articles. The results of each study were classified by ICF component and included in the evidence table (Table SIV, online supporting information). Both results from level I to III studies and level IV to V studies are included because of the small amount of level I to III studies. Results with level I to III evidence are marked with an asterisk (*). The evidence tables distinguish 'orthotic' from 'therapeutic' effects of FES. Immediate correcting effects of FES therapy are labelled 'orthotic', i.e. the difference between walking with FES and walking without FES. Long-term, persisting effects are labelled 'therapeutic'. A summary of the reported adverse events is reported as Table SV (online supporting information).

RESULTS

Retrieved articles

A total of 780 articles were identified. These 780 titles and abstracts were screened by two authors. Seven hundred forty articles were excluded because of the exclusion criteria. Five articles were unavailable, even after contacting the authors. The full text of the remaining 35 articles was read and the type of electrical stimulation was determined. Subsequently, 13 articles were excluded because the applied electrical stimulation method was not FES (six studies applied neuromuscular electrical stimulation, four studies applied threshold electrical stimulation, and three applied stimulation at sensory level).[15,18–30] Two articles lacking data about FES separately to the ankle dorsiflexors were also excluded.[31,32] Five other excluded articles were reviews about FES of different muscles[14,33–36] and two articles were excluded because they did not report specific information sufficiently or were only conference abstracts instead of full-text articles.[37,38] A secondary search, consisting of checking the reference lists of the included articles, yielded one useful article.[39] Finally, 14 articles were included, which reported about 11 original studies. Two of these articles[11,40] did not describe the type of CP of the participants; for one article this problem was resolved by contacting the authors,[11] but both articles were finally included.

Patients and outcomes

In total, 127 patients received FES of the ankle dorsiflexors (14 bilaterally affected and 113 unilaterally affected). The ages of the participants ranged from 5 to 19 years and the GMFCS levels from I to III.

In three studies, percutaneous electrodes were used to provide FES. One of these three studies compared percutaneous with surface electrodes. The distinction between nerve and motor point stimulation was not clear. Most studies applied electrodes on both the nerve and the muscle belly, looking for the best response. Overall the use of tilt sensors was more common than the use of foot sensors. To control the timing of FES, seven (out of 11) studies used footswitches, and four (out of 11) used a tilt sensor. One study investigated the combination of FES with BoNT-A treatment. For details see Table SIII.

Different methods were used to measure outcomes: gait analysis, questionnaires, and clinical measurements and scales. The effect on angle of ankle dorsiflexion was investigated most frequently. A description of the results follows in the next paragraph. For detailed results see Table SIV, which provides effect, effect size, and the involved ICF component for each outcome per study. It is organized on outcome of interest and type of effect (orthotic versus therapeutic).

Reported adverse events include skin problems and acceptation issues. For details see Table SV which shows the reported information about adverse events.

To assess the effect of FES of the ankle dorsiflexors

At ICF activity and participation level

Evidence level I to III studies. Four articles with level I to III evidence reported outcomes.[10,39,41,42] Pool et al. reported a decrease in the self-reported frequency of toe-drag (statistically significant) and falls (non-significant).[41] They also reported (mostly statistically significant) improvements in self-perceived performance and satisfaction.[39] Meilahn et al. reported undertaking of a variety of physical activities while wearing the stimulator. The most frequent participation was in bicycling and running.[43] The included studies provided evidence that FES was compatible with daily life: Meilahn et al. found that, at different time points, 71% to 89% of the participants preferred FES over treatment with ankle–foot orthoses,[43] and Prosser et al. reported that 86% of the participants chose to continue FES treatment.[11] No data were available for fatigue.

Pool et al. reported an improved balance and mobility using the community-based balance and mobility score;[44] in addition, they reported improvement of dynamic stepping.[41] These outcomes were considered activity components, because of the type of measurement.[44,45] None of the included studies reported detailed results in the participation domain.

At ICF body function and structures level

Evidence level I to III studies. Four articles with level I to III evidence reported outcomes of FES therapy on the domain of body function and body structure.[10,41,42,46] Three studies reported an orthotic improvement (i.e. more dorsiflexion) in ankle dorsiflexion at two moments of the gait cycle: initial contact and peak angle in swing.[10,41,46] Van der Linden et al. reported an orthotic improvement

using the Gillette Gait Index.[10,47] They also showed a statistically significant orthotic decrease in walking speed, although others reported a non-significant increase.[10,41,46] Because walking speed was measured in laboratorial settings, it was interpreted as a body function component, because it might not be representative of the walking speed in daily life. Pool et al. reported a significant orthotic increase in step length (for the affected leg).[41] Data on ankle absorption work were not conclusive.[46] No statistically significant change in passive ankle dorsiflexion range of motion was reported.[10,41] Pool et al. reported a therapeutic increase in ankle dorsiflexion strength (both hand-held dynamometry and functional strength, measured as maximum number of heel raises) and in selective motor control.[42] They also reported a probable therapeutic decrease in gastrocnemius spasticity.[41]

Van der Linden et al. reported an increase in functional walking ability.[10,48] However, most of these results did not reach statistically significance.

Pool et al. showed a strong positive relation between ankle dorsiflexion strength and selective motor control.[42] No relation between anterior tibial or anterior compartment muscle volume and ankle dorsiflexion strength was found.[42]

Level IV to V studies. Four articles added outcomes for the angle of active ankle dorsiflexion, measured at different moments in the gait cycle (initial contact, mid-swing, or at toe-off) at different velocities (fast or normal walking speed). These outcomes showed (partly statistically significant [six out of 11 measurements]) improvement.[11,43,49,50]

Postans et al. reported a statistically significant orthotic improvement in foot contact pattern, a parameter that was not reported in level I to III studies.[49] For the therapeutic effect of FES on the foot contact pattern, no *p*-values were reported for the two measurements showing a slight trend of detoriation.[51]

Data on cadence (steps per minute) and ankle generation work were not conclusive.[11,40,52]

Pool et al. (levels IV–V) reported a non-significant change in gait pattern using the Observational Gait Scale.[9,53]

FES as add-on treatment with BoNT-A. In this systematic review, one level IV study on the effects of FES of the anterior tibial muscle after BoNT-A therapy of the antagonist (gastrocnemius muscle) was included. Van Galen et al. reported a therapeutic increase in the angle of ankle dorsiflexion at the end of the swing phase and a trend of therapeutic improvement in foot contact pattern (without *p*-values for the latter parameter).[54] The increase in active ankle dorsal flexion in the post-BoNT-A phase was not as large as in the post-FES and post-control phases. This could imply a reinforcing effect of these two treatments on each other.

What is the strength of the evidence?

Five included articles with evidence at level IV[9,11,49,51,54] hint at causal inferences, while four level V studies[40,43,50,52] only suggest the possibility of causal inferences. On the basis of the five remaining articles, which are based on two group design studies of level II[10,39,41,42] and one single-subject design study of level I,[46] it can be concluded that the outcomes are attributable to FES.

The quality of conduct of the studies mostly ranged from moderate to weak. For the level II group design studies included in this review, the quality of conduct was moderate.[10,39,41,42] In these studies the outcome assessors were not (completely) masked and only one of the studies reported a power calculation.[42] The quality of conduct of the single-subject design studies was moderate to weak, because most of the studies did not assess interrater or intrarater reliability of measures, the outcome assessors were not unaware of the phase of the study, no stability of the data was demonstrated in the baseline, the type of single-subject design study was not stated, and the authors did not apply statistical analysis. The study of Pool et al. had a strong quality of conduct.[9]

To provide a practical guidance for stimulus parameters

The parameter settings of FES showed a broad range of characteristics in the electrical field and in timing. There were no results reported on the relation between parameter setting of FES and the clinical effect. See Tables I and SIII for a summary of stimulation parameters.

What kinds and magnitudes of adverse events were documented?

Eight articles documented some information on adverse events with FES therapy.[9,10,39,41–43,49,51] Known adverse events include poor tolerance of stimulation and skin problems. Pool et al. performed (skin) checks every 1 to 2 weeks for adverse events and did not find skin problems.[9,41,42] The remainder of the studies relied on reporting of adverse events by participants or the parents, namely by questionnaires and surveys or the recording of answers by a device. Meilahn et al. reported skin irritation in 20% of the participants.[9] Postans et al. found poor tolerance of stimulation in 27% of the participants.[49]

Table I: Characteristics of functional electrical stimulation

Parameter	Characteristics
Stimulus waveform	Monophasic or biphasic
Current amplitude (calculation for biphasic waves = root-mean-square current)	20–100mA
Pulse width	3–350μs
Pulse frequency	
Twitch contractions	1–10Hz
Incomplete tetanic	15–25Hz
Fused tetanic contractions	>45–50Hz
Clinical range	16.7–50Hz
Charge per phase (current–time integral)	0.06–35mC
Interpulse interval (constant or interval)	0.2–0.3s

Since most of the included studies excluded patients with (uncontrolled) epileptic seizures and/or cardiac conditions, no evidence can be provided about the risks to these patients when using FES. Reported adverse events included embarrassment and 'not wanting to wear FES at school', besides practical issues such as improper fit and bulkiness of the cuff and problems with the electrodes and wires.[10,39,43,51]

DISCUSSION

To our knowledge, this is the first systematic review addressing the clinical application of FES of the ankle dorsiflexors at the ICF levels of activity and participation, and body structure and function.

Activity and participation level

None of the available studies really addressed the effect of FES at the activity and participation level. Of course, the decreased incidence of toe-drag and falling might indirectly point towards less interference with normal daily activities such as playing and running.[41] Decreased distance of walking as result of fatigue was not addressed in the assessed studies. Available data on walking only addressed instrumented walking in a gait laboratory. The preference of patients to continue using FES (instead of orthoses) might indirectly point towards a better acceptance in daily life.[11,43] Lastly, improvements in self-perceived performance and satisfaction were reported.[39] Nevertheless, the reported information does not make it possible to assess the effect of FES on participation.

Body and function level

One of the reasons for using FES might be as an alternative to conventional orthoses. Therefore, most studies aimed at outcome measures describing the orthotic effect of FES.

Indeed, it was consistently shown that FES increased the angle of active ankle dorsiflexion, and improved gait kinematics, selective motor control, and balance.[10,41,42] Data on the effect of FES on gait velocity were somewhat contradictory.[10,41,46] However, the main finding was a decreased or unchanged walking speed. This is in line with the results of Winter et al., who concluded that gait velocity is under control of the plantar-flexors (for push-off), hip-flexors (for pull-off), knee extensors (during late stance), and the knee flexors (during late swing).[55]

Interestingly, it was found that FES increased ankle dorsiflexion strength.[9,42] This result might be seen as a therapeutic effect of FES. In addition, these data are supported by volume increases in muscles using ultrasound and by experimental data showing FES-induced changes in muscles (morphologically and physiologically). Another body of evidence suggests modification of the afferent input of depressed body segments, thereby helping these segments in the competition for cortical representation.[13,56] This might promote adaptive changes in cortical connectivity,[57] which could be responsible for the carry-over effect.

However, it is questionable whether the improvement of strength can be generalized, since Pool et al. showed a correlation between selective motor control and force; therefore selection of patients might be important.

The effect of FES on gastrocnemius spasticity is intriguing. It can be speculated whether antagonist stimulation of the spastic muscle might inhibit the spasticity by reciprocal inhibition.[12] Consequently, the active ankle dorsiflexion angle might increase. However, this finding needs the further support of studies aimed at proving this concept.

FES and BoNT-A: synergism?

Possible mechanisms for the synergism of FES and BoNT-A are the spread of BoNT-A by activity of the muscle (induced by FES) and the reciprocal inhibition of the antagonist during activation of the agonist, as mentioned before.[58] Furthermore, the combination of BoNT-A therapy of the gastrocnemius muscle and FES of the ankle dorsiflexors tackles both the plantar-flexor spasticity and the dorsiflexor weakness, instead of concentrating on only one aspect. However, this topic needs an additional long-term prospective study to confirm these effects.

Grading of the evidence: limitations

As summarized in the Results, the level of evidence and quality of the studies in this topic are moderate. Because most (nine out of 14) of the included studies were level IV to V studies, we decided to include their results in the discussion of the parameters that were not represented in the level I to III studies.

Stimulus parameter guidance

On the basis of the existing evidence, we provide an overview of the FES parameters used (Table I). However, evidence for the relation between parameter setting and effect (orthotic and therapeutic) or side effects is currently lacking. Therefore, we are not able to provide clinical guidance for FES parameter settings.

Side effects

Part of the included studies reported information on side effects. Skin irritation and tolerance problems are most frequently reported. Decreased skin tolerance and discomfort may be more common with surface electrodes than with percutaneous electrodes.[40,59] Yet the included studies provided no evidence about this, since they all reported adverse events using surface electrodes. It is possible that a 4-week 'accommodation phase' to adapt to FES helps to increase tolerance.[11]

Patients with (uncontrolled) epileptic seizures and/or cardiac conditions were not included in the patient population. Hypothetically, the current applied by FES can travel throughout the body by way of the ionized body fluids, and subsequent side effects may occur.[12]

Despite the adverse events and some acceptation issues, the experience of patients seems to be good. This positive experience is supported by the percentage of patients continuing FES treatment (71%–89%).[11,43]

CONCLUSION AND FUTURE DIRECTION

From the current evidence, it cannot be concluded that FES (of the ankle dorsiflexors) improves functioning at the activity and participation level. However, current evidence supports the potential role of FES as an alternative to classic orthotic treatment. On the basis of the current evidence, no guideline can be provided for treatment intensity (e.g. hours per day), stimulator settings, and types of electrode. Side effects of FES are common (skin irritation) but do not seem to interfere with satisfaction and continuation, although data on side effects are limited.

Future studies should especially pay attention to the domain of activity and participation.

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SUPPORTING INFORMATION

The following additional material may be found online:

Table SIa: Levels of evidence for group design studies

Table SIb: Levels of evidence for single-subject design studies

Table SIIa: Conduct of group design studies

Table SIIb: Conduct of single subject design studies

Table SIII: Summary of studies – interventions and participants

Table SIV: Study outcomes according to the domains of the International Classification of Functioning, Disability and Health (ICF)

Table SV: Reported adverse events

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