University of Cincinnati

Date: 10/30/2014

I, Amy F Bailes, hereby submit this original work as part of the requirements for the degree of Doctor of Philosophy in Epidemiology (Environmental Health).

It is entitled: Effects of Functional Electrical Stimulation Neuroprosthesis in Children with Hemiplegic Cerebral Palsy

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Effects of Functional Electrical Stimulation Neuroprosthesis in Children with Hemiplegic Cerebral Palsy

A dissertation submitted to the Graduate School of the University of Cincinnati
In partial fulfillment of the requirements for the degree of

Doctor of Philosophy (Ph.D.)

In the Division of Epidemiology
Of the Department of Environmental Health
Of the College of Medicine
2014

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Abstract

Background: Studies examining the effects of FES neuroprosthesis in children with hemiplegia are limited and only examine its effects on body structure and function (BSF) outcomes. Unstudied, but of importance, are the effects of this novel intervention on activities and participation (AP) outcomes in children with hemiplegic cerebral palsy (CP). The purpose of this study was to evaluate the effects of FES neuroprosthesis use across the International Classification of Function (ICF) categories of BSF and AP. Specifically assessed were effects on ankle motion, overall gait pathology, walking endurance, oxygen cost, stair climbing ability and obstacle course negotiation.

Methods: Using a two factor repeated measures design, eleven children with hemiplegic CP (mean age 9 years 11 months) were evaluated before and after participation in an intervention consisting of FES neuroprosthesis daily use. A comprehensive set of outcomes spanning the ICF categories of BSF and AP were collected with the FES turned off (Stim Off) and repeated with the FES turned on (Stim On) at baseline and post assessment. Further performance and satisfaction with individualized goals, and safety and satisfaction with the device were assessed. Pairwise comparisons of interest were: Baseline_{Stim On} - Baseline_{Stim Off} (immediate orthotic effect), Post_{Stim Off} - Baseline_{Stim Off} (therapeutic effect) and Post_{Stim On} - Baseline_{Stim Off} (total effect).

Results: Statistically significant improvement on BSF measures were observed for a total effect of FES neuroprosthesis use on average dorsiflexion at initial contact $df_{initial}$ (adjusted $p = 0.01$) walking speed (adjusted $p = 0.006$), and walking endurance (adjusted $p = 0.005$), but not on peak dorsiflexion during swing ($df_{swing}$), overall gait pathology, oxygen cost, stride length or cadence. Although not statistically significant, large effect sizes were observed for a total effect on $df_{swing}$ ($d = .89$) and for a therapeutic effect on walking endurance ($d = 0.92$). Statistically significant
improvement on AP measures were observed for a *therapeutic effect* on the number of steps to complete an obstacle course (p=0.004) but not on stair climbing ability. Although not statistically significant a large effect size was observed for a *total effect* of device use on the number of steps off the obstacle course path (d=0.83). Further, participants reported a statistically significant improvement in performance (p=0.0006) and satisfaction (p=0.0007) with individualized goals, a reduced frequency of trips after the intervention (p=0.008) and high satisfaction with the device.

**Conclusions:** Results from this study support previous studies of FES neuroprosthesis effects on BSF outcomes, and add to the literature in supporting positive effects on AP outcomes. Further, satisfaction is high when using the device with a high level of regular support and communication with therapists trained in using the device. These results should be interpreted with caution because of the limitations including a small sample size, lack of control group, selection bias, and lack of blinding of the assessor. Further studies of this intervention should be performed with larger samples of children over longer intervention periods, combined with other interventions, and compare FES neuroprosthesis to ankle foot orthosis (AFO) use in children with hemiplegic CP.
Acknowledgements

I am grateful for the funding sources that have supported my coursework and research during this process. Specifically, to the Foundation for Physical Therapy Promotion of Doctoral Studies scholarship awards (2009-2012) and the Pedal with Pete Foundation. The project described was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health, under Award Number UL1TR000077. (REDCap) The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Thank you to Keith McBride and Bioness Inc. (Valencia, CA, USA) for donating L300 devices for use in the study.

There are many people that I am indebted to for the completion of this dissertation. First and foremost I would like to thank my committee and my “village”. I am grateful for Dr. Dunning PT PhD. who has challenged me to become a critical thinker, Dr. Haynes, who met with me at the very beginning of this journey and was open to a program meaningful to physical therapy research, Dr. Succop who was always willing to answer any statistics questions no matter how basic and Dr. Long for expanding my comfort level with technology.

I would also like to thank the students and staff within the Environmental health program who guided me along the way and provided hours of free advice, Becky Reder, who does not believe in “can’t”, and Sheila Mun-Bryce whose memory continues to be a source of mentorship to me. I am also grateful to Mike Clay and Melissa Tremper for honoring the protocol and providing the PT expertise for the study intervention visits, to Cailee Caldwell for providing biomechanical expertise in the motion analysis lab and to Matt Fenchel for providing REDCap and statistical guidance. Thank you to the Research Team within the Division of Occupational Therapy and Physical Therapy for supporting me during this long process. To Dr. Mary Gannotti who mentors me from afar, thank you for your optimism and determination they are contagious. To Ashley Neff, Alicia Brummett, Scott Dean, and Jillian Moulton who did a lot of behind the scenes work to keep the research process going, I thank you.

To my extended family and friends that always encourage me to keep going, tolerate my piles of paper at home, and understand my declines of social gatherings. I am lucky to have you all in my cheering section and as editors when needed.

To my husband Michael, thank you for your endless support and encouragement. Thank you to Anna and Tali Bailes, for 1) always, 2) always, and 3) always inspiring me to become a better person. I have enjoyed watching you grow up during this process and hope that you someday appreciate me pursuing one of my dreams.

To Boo and Sophie Bailes for always keeping me company under the dining room table whether I am doing homework or writing and only making noise when you really thought you could catch that squirrel.

Finally and most importantly I am grateful to the families and children who participated and remain committed to improving the lives of individuals with cerebral palsy.
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Abbreviations

CP: Cerebral Palsy

ICF: International Classification of Function

BSF: Body Structure and Function

AFO: Ankle foot orthosis

FES: Functional Electrical Stimulation

3DGA: Three dimensional gait analysis

Stim On: The device is on the leg and the stimulation is on.

Stim Off: The device is on the leg but the stimulation is turned off.

d_{\text{swing}}: \text{average peak dorsiflexion during swing}

d_{\text{initial}}: \text{average dorsiflexion at initial contact}

GDI: Gait deviation index used to measure overall gait pathology

NNCOST: Net Nondimensional energy cost a measure of oxygen cost

6MWT: Six minute walk test used to measure walking endurance

TUDS: Timed up and down stairs

SWOC: Standardized walking obstacle course

COPM: Canadian Occupational Performance Measure used to measure individualized goals
Chapter 1: Introduction, Hypothesis and Specific Aims

Introduction

Cerebral palsy (CP) describes a group of permanent disorders of movement and posture that are attributed to non-progressive disturbances in the developing brain\(^1\) with a stable prevalence rate of 3.1-3.6 per 1000 since 1996.\(^2\) CP ranks as the second most prevalent early-onset neurological disorder, trailing only autism\(^3\) and results in a wide range of functional limitations ranging from ambulating with minor difficulties to not being able to ambulate at all. In 2001, the United Cerebral Palsy foundation estimated that approximately 10,000 babies born in a year will develop CP and that 764,000 children and adults have CP.\(^4\) The CDC estimated the lifetime cost in 2003 dollars to total 11.5 billion for all people born in 2000 who have CP.\(^5\) Costs to society, the individual, and families will continue to rise with increasing costs of health care and population growth.

Hemiplegia (affecting one side of the body) accounts for 22.6 - 40% of all cases of CP.\(^6-10\) Further, preliminary findings with recent neuroimaging techniques suggest the incidence of hemiplegia is increasing.\(^11\) The most common gait impediment for children with hemiplegic CP is foot drop or poor foot clearance during swing phase and diminished heel strike on their affected side, which may limit their higher-level ambulation and balance skills.\(^12\)

Cerebral palsy (CP) is the most frequent neurological diagnosis seen by pediatric physical therapists.\(^13\) Physical therapists play an important role in treating individuals with CP throughout their lifespan and aid in making decisions about medical interventions including bracing, surgery and spasticity management.\(^13\) Therapy interventions can be categorized as child-active rehabilitation approaches, compensatory and environmental adaptation approaches and health and secondary prevention approaches.\(^14\) All approaches play an important role, however more
recent evidence for cortical neuroplasticity in children with CP\textsuperscript{15-20} supports child active approaches that focus on task specific practice and massed practice as best practice.\textsuperscript{14}

The World Health Organization’s (WHO) International Classification of Functioning, Disability and Health (ICF) framework (Figure 1) which was introduced in 2001 provides an integrated and universal language for measuring health and disability that has been applied across rehabilitation studies and disciplines.\textsuperscript{21} The ICF framework reflects a dynamic interaction between person and environment with a move toward the identification of participation as an important outcome of health.\textsuperscript{22}

The ICF provides the following definitions:\textsuperscript{21}

- **Body functions**: The physiological functions of body systems
- **Body structures**: Anatomical parts of the body such as organs, limbs and their components
- **Impairment**: Problems in body function or structure such as a significant deviation or loss
- **Activity**: Execution of a task or action by an individual
- **Participation**: Involvement in a life situation
- **Activity limitations**: Difficulties an individual may have in executing activities
- **Participation restrictions**: Problems an individual may experience in involvement in life situations
- **Environmental factors**: The physical, social and attitudinal environment in which people live and conduct their lives
- **Personal factors**: The particular background of an individual’s life and living composed of attitudes and features that are not part of a health condition or health state
The ICF has clarified the way clinicians consider intervention options for individuals with CP, which has resulted in a shift of clinical research focus from body structure and function to an increased emphasis on outcomes related to activity and participation. The ICF framework has been used extensively in pediatric rehabilitation literature. Outcomes used to measure intervention effectiveness need to be multidimensional to encompass the impact of what clinicians offer at different levels of the ICF.

The current physical therapy treatment for hemiplegia involves wearing an ankle foot orthosis (AFO). AFO’s limit active movement and may hinder motor learning, further contributing to the muscle weakness in CP. In addition, older children are often unwilling to wear an AFO due to the bulk and discomfort. Functional electrical stimulation (FES) neuroprostheses provide an alternative to AFOs for foot drop and have been shown to increase neuroplasticity, function and quality of life in adults with hemiplegia. Studies of FES neuroprosthesis in children are limited and unclear. To date there have been 3 trials, one in the US, one in Israel, and one in Australia using FES neuroprosthesis in children with hemiplegic CP all of which measure outcomes only in the body structure and function (BSF) domain of the ICF. The most rigorous was a sample of 21 individuals enrolled at the NIH to participate in a 10-month study of the effects of FES neuroprosthesis that included a total of 5 assessments (baseline before receiving the device, at receipt of device, after 4 week accommodation phase, after 3 months of daily use, and after 3 more months during which the individual was given a choice to wear the device). Improved gait kinematics, muscle size, and muscle control were reported in these individuals. One study with a smaller sample of five individuals also reported improved gait kinematics. Using less standardized measures Pool reported improvements in ankle range of motion, muscle control, strength, and reductions
in spasticity and falls. However, statistical flaws in Pool’s study limit the interpretation of the results.\textsuperscript{40}

The effects of FES neuroprosthesis use on oxygen cost, walking endurance or across the ICF domains of activity and participation have not been investigated in children. The use of new technology not only requires understanding the changes it imposes on body structures and function, but practitioners also need to understand how such changes affect a child’s functional performance and participation in meaningful activities.\textsuperscript{41} More studies are warranted using this technology before it is regularly recommended for home use in this population.

**The purpose of this study** was to evaluate the effects of an FES neuroprosthesis across the ICF domains of BSF, as well as in activity and participation in children with hemiplegic CP. The effects of the FES neuroprosthesis can be described in several ways as illustrated in Figure 2. The **immediate orthotic effect** indicates changes that occur when initially wearing the device. A **training effect**, beyond the immediate effect, may occur as the patient uses the device. The **therapeutic effect** indicates improvements seen over time without wearing the device and may result from neural plasticity or strengthening of the involved extremity. The **total effect** indicates changes over time that includes both the immediate orthotic and training effects. This study will investigate the immediate orthotic effect, the therapeutic effect and the total effect.

**Overall Hypothesis:**

*In children with hemiplegic CP, an intervention using the FES neuroprosthesis will result in significant improvements across the ICF domains of BSF and AP. Further, overall satisfaction with the device will be high.* To test this hypothesis the following aims will be accomplished:
Specific Aims:

Specific Aim 1: Determine the immediate orthotic, therapeutic and total effects of FES neuroprosthesis use on body structure and function outcomes specifically ankle dorsiflexion during swing, ankle dorsiflexion at initial contact, overall gait pathology, oxygen cost, and walking endurance.

Specific Aim 2: Evaluate changes in activity and participation outcomes specifically stair climbing, obstacle course negotiation and individualized goals of activity and participation.

Specific Aim 3: Evaluate satisfaction, trips and falls, and adverse events in children with hemiplegic CP using the FES neuroprosthesis device.

Background

The brain reorganizes after task specific and massed practice, including in individuals with cerebral palsy. Studies of task specific training \(^{42,43-45}\) and massed practice \(^{46,47}\) show positive results on clinical outcome measures in children with CP. In addition, evidence from neuroimaging techniques is building for cortical neuroplastic potential in children with hemiplegia after task specific repetitive training.\(^{15-20}\) The FES neuroprosthesis offers task specific massed practice through daily continuous use during waking hours. Therefore, in addition to being a neuroprosthesis, the device may promote functional improvement through cortical neuroplasticity.

There is evidence to support the use of FES in adults with chronic hemiplegia due to stroke. The goal of FES is to improve muscle function during the time at which the muscle would normally be active. Studies of FES neuroprosthesis in adults with chronic hemiplegia have demonstrated significant orthotic effects, while the unit is on consisting of improvements in gait,\(^{31,32,48-50}\) social participation,\(^{48}\) balance,\(^{31}\) and functional activities.\(^{50}\) In addition, studies
report positive therapeutic effects that continue after the unit is turned off, suggesting maintained improvement and functional recovery in adults. More recently a multicenter randomized trial comparing an FES neuroprosthesis and AFO for foot drop in adults after stroke was published. Using either an FES or AFO for 30 weeks resulted in clinically and statistically significant improvement in gait speed and other functional outcomes. However the trajectory of change in gait speed appeared to continue after 30 weeks in the FES group vs the AFO group where it appears to plateau. User satisfaction was higher in the FES group.

**Studies of FES neuroprosthesis in children with CP are limited and unclear.** Past studies of FES in children with CP have reported beneficial effects in gait parameters including improved dorsiflexion, improved gait speed, and reduced asymmetry. However these studies used a large stimulator with external wires that were reported to be difficult to manage, with one third of participants reporting problems with compliance and the need for the caregiver to repeatedly remove and re-attach electrodes. The innovative technology in this study incorporates a radio frequency connection that eliminates the need for external wires or daily relocating of the electrodes to obtain ideal muscle stimulation. The reduced need for external wires and repositioning of electrodes is likely to increase feasibility and use of the device in this population.

To date there have been three trials reporting the effects of FES neuroprosthesis use in children with hemiplegia. A sample of 21 patients were enrolled at the NIH to participate in a 10 month study of the effects of FES neuroprosthesis use that included a total of 5 assessments (baseline before receiving device, at receipt of device, after 4 week accommodation phase, after 3 months of daily use, and after 3 more months during which time the individual was given a choice to wear the device). Prosser reports on the orthotic effects of the device in 19
participants (mean age 12 years 11 months) with statistically significant improvement in dorsiflexion in swing and initial heel contact with no change in walking speed cadence and step length. Damiano\(^{37}\) reports on 14 of those from the initial cohort (mean age 14.1 years) with complete ultrasound data over the 5 assessments that muscle size significantly increased demonstrating use dependent plasticity and function after 4 months. Muscle size increase by ultrasound was maintained at follow up (after period of choice to wear) despite a reported decrease in wear time of the FES unit, but barefoot ankle motion returned to baseline indicating no sustained therapeutic effect on ankle control.

Danino\(^{38}\) compared three different overall gait pathology scoring methods in five patients with hemiplegia (mean age 16.5 years) at one time point after accommodation to wearing the unit, under two conditions; the unit turned off then turned on. Two of the three scoring methods demonstrated statistically significant improvements for the affected leg in the turned on condition. Also at 1 year, these individuals expressed high satisfaction and continued to use the device.

Pool and colleagues\(^{39}\) report a multiple single subject ABA design in 12 children (mean age, 9 years 2 months) in which participants wore an FES device daily for 8 weeks during phase B. They report improved ankle range, selective motor control, strength, reduced spasticity, toe drag and falls during the intervention phase. However a study commentary\(^{40}\) points out their improper use of statistical analyses and unstable baseline data which suggests their reported differences as being due to chance.

**Preliminary work:**

In addition to the above trials our team collected preliminary data\(^{54}\) comparing performance on functional measures and oxygen consumption with the FES neuroprosthesis unit.
turned off (Stim Off) followed by the unit turned on (Stim On) in five children with hemiplegia. Our findings demonstrate improved distance traveled in one minute in the Stim On condition for three of five participants, but greater net nondimentional oxygen cost (NNCost) during the one-minute walk test. Of interest was the improvement in stair climbing in one participant, who had been using the device the longest without any concurrent AFO use. This may suggest an improvement in stair-climbing function associated with FES use that is acquired over time. This preliminary work was utilized to secure $30,000 from the Pedal with Pete Foundation to carry out this dissertation research.

**Significance/relevance to environmental health:**

Environmental health encompasses physical, chemical, and biological factors external to a person that can affect health and targets disease prevention and the creation of health-supportive environments. Susceptible groups, including individuals with disabilities, require specific attention to minimize the risks they face. Occupation is a unique and important aspect of environmental health. A child’s role or occupation includes playing, learning, participating as a family member and as a friend, and exploring future roles. Literature suggests that children and youth with CP are limited in their fulfillment of occupational roles. Therefore this study is significant in that it exposes children with hemiplegia to a novel intervention that is likely to have a positive effect on their ability to perform their “job” to learn, play, participate in their social roles and explore future roles.

Cerebral palsy is the most common motor disability in childhood in the US affecting about 1 in 323 children. Cincinnati Children’s Hospital Medical Center serves over 1600 children with CP annually. A three-year review (2009-2011) of the electronic records from the
Division of Occupational Therapy and Physical Therapy (OTPT) revealed approximately 250 individuals with hemiplegia, demonstrating the wide application of this intervention. This study provides information critical for adapting current adult treatment strategies to children and will likely lead to advances in therapeutic rehabilitation. This study makes an innovative contribution to the literature by adding to the existing knowledge about this technology across previously unstudied ICF domains addressing a child’s ability to perform activities and participate in their occupational role within their family and community. Information from this study will also be valuable in powering future studies and obtaining funding for a comparative effectiveness trial to compare this intervention to the standard care of AFO in this population.
**Figure 2** Comparison Effects (reprinted with permission from Open Access Journal of Clinical Trials 01/2013; 5:39-49: "The Functional Ambulation: Standard Treatment vs. Electrical Stimulation Therapy (FASTEST) trial for stroke: Study design and protocol.")

<table>
<thead>
<tr>
<th>Baseline assessment</th>
<th>Post assessment</th>
</tr>
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<tbody>
<tr>
<td><strong>FES unit turned OFF</strong></td>
<td><strong>FES unit turned OFF</strong></td>
</tr>
<tr>
<td><strong>Immediate orthotic effect</strong></td>
<td><strong>Total effect</strong></td>
</tr>
<tr>
<td><strong>FES unit turned ON</strong></td>
<td><strong>Orthotic training effect</strong></td>
</tr>
<tr>
<td><strong>Therapeutic effect</strong></td>
<td><strong>Treatment time</strong></td>
</tr>
</tbody>
</table>
Chapter 2: Effects of FES Neuroprosthesis Use on Body Structure and Function Outcomes in Children with Hemiplegic Cerebral Palsy
Introduction

Cerebral palsy (CP) describes a group of permanent disorders of movement and posture that are attributed to non-progressive disturbances in the developing brain\(^1\) with a stable prevalence rate of 3.1-3.6 per 1000 since 1996.\(^2\) CP ranks as the second most prevalent early-onset neurological disorder, trailing only autism \(^3\) and results in a wide range of functional limitations ranging from ambulating with minor difficulties to not being able to ambulate at all. Those who do ambulate, experience higher energy costs with greater variability and reduced walking endurance than typically developing children.\(^64,65,66-68\) Further, high energy cost is correlated with activity limitations\(^69\) and can lead to reduced walking with age.\(^70\)

Hemiplegia (affecting one side of the body) accounts for 22.6 - 40% of all cases of CP.\(^6-10\) Further, preliminary findings with recent neuroimaging techniques suggest the incidence of hemiplegia is increasing.\(^11\) The most common gait impediment for children with hemiplegic CP is foot drop or poor foot clearance during swing phase and diminished heel strike on their affected side, which may limit their higher-level ambulation and balance skills.\(^12\)

The current treatment for hemiplegia involves wearing an ankle foot orthosis (AFO). AFO’s limit active movement, potentially hinder motor learning, and contribute to the muscle weakness in CP. In addition, older children are often unwilling to wear an AFO due to the bulk and discomfort. Functional electrical stimulation (FES) neuroprostheses provide an alternative to AFOs for foot drop and have been shown to increase neuroplasticity, function and quality of life in adults with hemiplegia.\(^28-36\) Only one study\(^36\) compared the FES neuroprosthesis use to wearing an AFO and found no difference in gait outcomes, but higher user satisfaction in the FES group.
Studies of FES neuroprosthesis use in children are few in number and have limitations. To date there have been three cohorts of children with hemiplegia studied, one in the US,\textsuperscript{12,37} one in Israel,\textsuperscript{38} and one in Australia\textsuperscript{39} using FES neuroprosthesis in a total of 36 children with hemiplegic CP. These studies measured outcomes only in the body structure and function (BSF) domain of the International Classification of Function (ICF).\textsuperscript{21} Specifically they report improvements in ankle range of motion,\textsuperscript{39} gait kinematics,\textsuperscript{12,37,38} muscle size,\textsuperscript{37} muscle control,\textsuperscript{37,39} strength\textsuperscript{39} and reduced spasticity.\textsuperscript{39} Interpretation of Pool’s\textsuperscript{39} results are limited due to statistical flaws.\textsuperscript{40} Generalizability of Danino’s\textsuperscript{38} findings are limited due to the small sample size. None of the prior studies evaluated FES neuroprosthesis use on oxygen cost or walking endurance. Clearly more studies are warranted using this technology before it is regularly recommended for home use in this population.

The effects of the FES neuroprosthesis can be described in several ways. The immediate orthotic effect indicates changes that occur when initially wearing the device. A training effect beyond the immediate effect may occur as the patient uses the device. The therapeutic effect indicates improvements seen over time without wearing the device and may result from neural plasticity or strengthening of the involved extremity. The total effect indicates changes over time that includes both the immediate orthotic and training effects. The study summarized in this dissertation investigates the immediate orthotic effect, the therapeutic effect and the total effect of FES neuroprosthesis use in children with hemiplegic CP.

The purpose of this study is to evaluate the effects of FES neuroprosthesis use on BSF outcomes specifically ankle motion, overall gait pathology, walking endurance and oxygen cost in children with hemiplegic cerebral palsy. We hypothesized that FES would improve peak ankle
dorsiflexion in swing, ankle dorsiflexion at initial contact, overall gait pathology, walking endurance and oxygen cost.

**Methods**

This study was reviewed and approved by the IRB at Cincinnati Children’s Hospital Medical Center. Written parental permissions were obtained prior to participation in addition to assent of the participant in the cases where the participant was 11 years or older.

**Study Design:** This study used a two factor repeated measures design that evaluated individuals before and after participation in an intervention consisting of FES neuroprosthesis daily use. The protocol included a screening visit (visit 0), baseline assessment (visit 1), a four week accommodation period which included seven one hour PT sessions to acclimate to wearing the FES unit (visits 2-8), monthly one hour PT well check visits (visits 9-10) during 12 weeks of daily use and a post assessment (visit 11). See Figure 1 for timeline of visits. All assessments were administered with the unit turned off (Stim Off) and then were repeated with the unit turned on (Stim On) at baseline and post assessment. No additional therapy was provided during the study protocol. This dissertation study collected outcome measures across the ICF categories of BSF, activities and participation in addition to safety and satisfaction information. Included in this chapter are the outcomes related to BSF. Results on activity and participation outcomes, in addition to safety and satisfaction will be reported in a subsequent chapter.

**Participants:** Sample size was estimated using Power and Sample Size v3.0 software (Vanderbilt University). Sample size was calculated for the primary hypothesis based on a paired t test for one group using the main outcome variable of peak ankle dorsiflexion in swing. Previously published data indicate that in a non-FES condition, children with hemiplegia demonstrate peak ankle dorsiflexion during swing of 0.7±3.8°. Further, a 2.6° difference between
stimulation and no stimulation conditions was measured after 1 month of FES neuroprosthesis use, and a 3.8° difference between conditions was measured after 3 months of use.\textsuperscript{12} Using this 3-month mean difference of 3.8±3.8°, the sample size estimation found a sample size of 10 subjects necessary to reject the null hypothesis of zero change in peak ankle dorsiflexion during swing\textsuperscript{(power= 0.8, Type I error(α)=0.05)}. We anticipated screening 15 individuals to account for failed screenings and participant dropout.

Treating therapists at the outpatient PT clinical sites, as well as clinicians in the institution’s multidisciplinary CP clinic identified children between 6-17 years with hemiplegic CP, GMFCS\textsuperscript{71} I or II with foot drop during gait particularly absence of initial heel contact without wearing an AFO. Identified families were asked permission for the study team to contact them. Families also contacted the PI directly upon learning about the study from their treating clinician or by other means. Recruitment methods included general advertising, social, print and web-based tactics. Exclusion criteria were passive range of motion less than 0 degrees dorsiflexion with the knee extended, any metal implants containing electrical circuitry, continuous regular use of neuroprosthesis stimulation previous to study enrollment, previous orthopedic procedure involving tibialis anterior muscle at any time, previous orthopedic procedure to affected limb in the last year, botulinum toxin administered within the past 3 months, or plans for such treatment during the course of the study and any condition that the principal investigator thought would limit ambulatory progress (e.g. arthritis, uncontrolled seizures).

\textbf{Intervention} The Ness L300 Foot Drop System manufactured by Bioness Inc. (Valencia CA, USA) is a small device that delivers surface electrical stimulation to the common fibular peroneal nerve which innervates the tibialis anterior and other ankle dorsiflexors. The L300
consists of an in-shoe pressure sensor, a control unit and an orthotic cuff that holds two stimulation surface electrodes (Figure 2). The electrodes are positioned to produce dorsiflexion and slight eversion. Once the optimal electrode placement is determined, the orthotic cuff holds the electrodes in place reducing the need for daily placement and increasing the reliability of electrode placement for home use. Stimulation parameters are set by the clinician using a PDA clinician’s programmer to elicit the most effective contraction during ambulation. The device can deliver stimulation in two modes; training mode which is cyclic stimulation when the individual is not walking, or gait mode which is activated through the in shoe gait sensor while the individual is walking. Education on the use and maintenance was provided throughout the four week accommodation period. During the accommodation period the individual used the unit in training mode while seated for cyclic stimulation for 15 minutes a day for the first week, followed by 20 minutes a day to gradually strengthen and condition the muscles for use. Also during the four week accommodation period participants were instructed to gradually increase wear time with the unit in gait mode when active from 15 minutes each day to all day use. Skin care guidelines were reviewed and provided to the family during the initial fitting. At the end of the four week accommodation period participants were instructed to discontinue using the device in training mode and to wear it for at least 6 hours a day in gait mode during their typical daily activities. No additional physical therapy was provided during the intervention.

Individualized adjustments and reevaluation of the settings and electrode placement took place at each visit, as well as family support and communication with the study team to increase tolerance to using the device. Participants experiencing problems were encouraged to return for assistance or discuss the issue over the phone with study staff outside of the scheduled visits. The average number of steps per day and average number of minutes walking while wearing the
device was recorded by the device. In addition the family was asked to keep a daily log of use, noting hours of use each day, problems or concerns.

**Outcome Measures**

Peak ankle dorsiflexion in swing ($df_{\text{swing}}$ degrees) ankle dorsiflexion at initial contact ($df_{\text{initial}}$ degrees), and overall gait pathology as estimated by the gait deviation index\textsuperscript{72} ($GDI$, unitless) were calculated via instrumented three dimensional gait analysis (3DGA) utilizing the 12-camera Raptor4 Digital System (Motion Analysis Corporation; Santa Rosa, CA, USA) and four 6-DOF force plates (AMTI; Watertown, MA, USA). A modified Helen-Hayes maker set was utilized for data capture. Foot markers were placed on the shoes by palpating the metatarsal heads through the shoes for the three toe makers (on the lateral borders of the $1^{\text{st}}$ and $5^{\text{th}}$ heads and in between the $2^{\text{nd}}$ and $3^{\text{rd}}$ head) and then aligning the heel marker on with the posterior calcaneal tuberosity. Markers remained in place for both Stim Off and Stim On conditions. Each participant was instructed to walk over ground at a self-selected speed for approximately ten passes over the force plates. The last five gait cycles for each side were extracted for analysis. Temporal-spatial measurements were also collected via 3DGA.

The Gait Deviation Index ($GDI$)\textsuperscript{72} is a new measure of overall gait pathology with established validity in CP which uses 15 gait features obtained from 3DGA incorporating pelvis, hip, knee and ankle kinematics to create one scaled score. It measures a scaled distance away from the average typically developing gait resulting in a single number that can be interpreted as follows: $GDI \geq 100$ indicates the absence of gait pathology. Every 10 points that the $GDI$ falls below 100 corresponds one standard deviation away from the TD mean. The $GDI$ has been able
to distinguish between the affected and unaffected limb in individuals with hemiplegia.\textsuperscript{72} We calculated the GDI of the affected leg for analysis in this study.

**Walking endurance** was assessed with the Six Minute Walk Test(\textit{6MWT}) which is a self-paced submaximal test that assesses functional capacity for walking a prolonged distance.\textsuperscript{73} It demonstrates good to excellent reliability in children with CP.\textsuperscript{74} The 6MWT was administered in the OTPT division in a rectangular hallway that measures 160.75 feet (49 meters); orange cones were placed at each corner to provide visual goals of the route. Children were instructed to walk as many laps as possible in 6 minutes without running. A practice trial was not provided because of concern for fatigue\textsuperscript{73} and other evidence that a practice trial does not enhance reliability.\textsuperscript{75} The primary investigator (PI) walked behind the participant with a measuring wheel to mark distance and provided standardized encouragement at each minute completed (i.e. “You have gone 1 minute, you have 5 more to go, keep up the good work”). The distance covered in feet over a 6-minute timespan was recorded and treated as a continuous variable.

**Oxygen cost** is a reliable measure of energy expenditure and was obtained using the Cosmed K4b\textsuperscript{2} (Cosmed srl; Rome, Italy) during the \textit{6MWT}. The Cosmed K4b2 is a lightweight and portable oronasal mask-based system which allows unconstrained gait and can be used in laboratory or community settings.\textsuperscript{76} Oxygen cost measures were collected during the six-minute walk test (\textit{6MWT})\textsuperscript{73} and converted to net nondimensional oxygen cost (\textit{NNcost}) following the method described and validated by Schwartz et al.\textsuperscript{77} Administration of the \textit{6MWT} with the Cosmed K4b2 provides a reproducible and valid assessment of cardiorespiratory responses and is much simpler than cycle ergometry or treadmill testing for children and adolescents with CP Level I and II.\textsuperscript{78} \textit{NNcost} has been found to be a highly reliable normalization method for measuring oxygen cost as it reduces the variability between participants of different ages,
heights, and weight while evaluating only the amount of energy used to ambulate and allows assessment over time. Its validity and repeatability have been tested in children with and without disabilities. Participants were fitted with the oronasal mask and seated for a 5 minute rest allowing the Cosmed to collect resting levels before beginning to walk for 6 minutes. Data were collected during the 5 minute seated rest and during the 6 minute walk test.

**Assessment Procedure:** Potential participants and their caregiver attended a screening visit to learn about the device and to determine if FES neuroprosthesis intervention was appropriate. Participants were then enrolled at the screening visit if they met all conditions for eligibility. Written parental permissions were obtained prior to participation in addition to assent of the participant in the cases where the child was 11 years or older. Upon enrollment, information regarding participant demographics, medications, brace wear, falls and trips experienced in the month previous to enrollment, and ankle range of motion measurements were obtained. As a measure of baseline impairment, selective control assessment lower extremity (SCALE) scores for the affected ankle were also obtained. Within two weeks of enrollment a baseline assessment was conducted. Upon arrival for testing a Polar heart rate monitor (Polar Ft1, Polar Electro) was applied around the participant’s chest and a resting heart rate was obtained. The Ness L300 unit was then donned and turned on briefly in trial mode (1-5 cycles) to ensure proper placement and adequate muscle contraction and then was turned off. After at least 15 minutes, testing began first in the Stim Off condition. The participant was provided with a 15-30 minute seated break before repeating tests in the Stim On condition (duration based on participant feedback). Heart rate was monitored and time was given between assessments in order for individual’s heart rate to return to baseline resting levels. Outcome measures of activity (standardized walking obstacle course (SWOC) and the timed up and down stairs (TUDS))
were also part of the assessment procedures, however the results on these measures are reported in a subsequent chapter of this dissertation. The outcome measures of activity were randomized along with the 6MWT for test order to eliminate the effects of testing order. With the exception of 3DGA the order of the three other outcomes administered was randomized using a computerized random numbers program. The 3DGA was not randomized to simplify testing procedures and eliminate the need to remove and reposition the markers between conditions. Specifically, the other measures were randomized with 3DGA always occurring 4th and 5th in the testing process (e.g. $SWOC_{Stim\ Off}$, $TUDS_{Stim\ Off}$, $6MWT_{Stim\ Off}$, $3DGA_{Stim\ Off}$, $3DGA_{Stim\ On}$, $TUDS_{Stim\ On}$, $6MWT_{Stim\ On}$, $SWOC_{Stim\ On}$). Testing was conducted by the PI in the outpatient division of OTPT. With the exception of three participants all testing was the same time of day at the baseline and post assessments.

**Statistical Analysis**

Study data were collected and managed using REDCap electronic data capture tools hosted at this institution. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. Data was entered into REDCap by a research assistant and verified by the PI before being downloaded and analyzed. All analyses were completed with SAS 9.3 with an alpha level of $p=0.05$. Data were examined for normality using Shapiro-Wilk and Kolmogorov-Smirnov values and by examining the residuals for each outcome variable. Descriptive statistics were used to summarize all
demographic variables and subject characteristics. A two factor repeated measures ANOVA or the non-parametric equivalent (Friedman test) was computed for each outcome variable of interest for all conditions and time. Unless otherwise specified all data was distributed normally. Multiple pairwise comparisons were made with the Tukey procedure with the alpha set at 0.05 for the three comparisons of interest:

- immediate orthotic effect \( (\text{Baseline}_{\text{Stim On}} - \text{Baseline}_{\text{Stim Off}}) \),
- therapeutic effect \( (\text{Post}_{\text{Stim Off}} - \text{Baseline}_{\text{Stim Off}}) \) and
- total effect \( (\text{Post}_{\text{Stim On}} - \text{Baseline}_{\text{Stim Off}}) \).

Effect sizes were also calculated to provide the investigator with a means of determining whether treatment differences were meaningful despite lack of statistical significance\(^{86}\) and interpreted according to Cohen\(^{87}\). 0.20 small effect, 0.50 moderate effect and 0.80 large effect.

**Results**

We had contacted or been contacted by 34 potential individuals about participating in the study. See Figure 3 for a flowchart of recruitment efforts and enrollment of 12 participants. One participant withdrew from the study at the second training visit citing concerns for using the unit while going between parents’ homes. This person’s data was not included for analysis resulting in complete data for 11 participants. Table 1 presents demographic information for participants at enrollment. Table 2 presents device stimulation parameters for each individual.

The mean age of the participants in the study was 9 years 11 months (range 6-16 years), eight were males, seven had right sided hemiplegia, and nine were classified as GMFCS Level I. Four children were not wearing daytime braces at time of enrollment, but were wearing nighttime braces. Four children were wearing daytime and not nighttime braces and three
children were wearing daytime and nighttime braces on their affected leg at the time of enrollment.

Mean and standard deviations for outcome measures across time periods are reported in Table 3. Mean differences, confidence intervals (95%) and effect sizes for comparisons of interest for each outcome are reported in Table 4.

**Average peak dorsiflexion during swing** ($df_{\text{swing}}$) Table 3-4: Two way ANOVA with repeated measures for $df_{\text{swing}}$ was statistically significant overall ($F_{3,30}=7.03$ p=0.001). Pairwise comparisons revealed no statistically significant differences for any of the comparisons of interest. Although not statistically significant, a large effect size (d=.89, mean difference 4.57, adjusted p=0.09) was observed for the total effect of the device use on $df_{\text{swing}}$. Compared to the Baseline stim off condition, participants demonstrated a decrease in $df_{\text{swing}}$ toward a more typical value in the Post Stim Off condition resulting in a negative moderate effect size (d=.50, mean difference -2.55, adjusted p=0.4) for a therapeutic effect of the device use on $df_{\text{swing}}$.

**Average dorsiflexion at initial contact** ($df_{\text{initial}}$) Table 3-4: Two way ANOVA for repeated measures for $df_{\text{initial}}$ was significant overall ($F_{3,30}=13.64$, p<.0001). Pairwise comparisons demonstrated a statistically significant total effect of device use (adjusted p=0.01) with a large effect size (d=1.03, mean difference 6.28). Small effects sizes were observed for an immediate orthotic effect (d=0.41, mean difference 2.2, adjusted p=0.25) and a therapeutic effect (d=0.34, mean difference -1.8, adjusted p=0.59) of the device use on $df_{\text{initial}}$. 
Overall gait pathology \((GDI)\) Table 3-4: Two way ANOVA with repeated measures for \(GDI\) of the affected leg revealed no statistically significant overall difference \((F_{3,30}=0.83, p=0.48)\) and small effect sizes were observed.

Stride length Table 3-4: Two way ANOVA repeated measures for stride length was not statistically significant overall \((F_{3,30}=2.56, p=0.07)\). A moderate effect size \((d=.62, \text{ mean difference } 0.08 \text{ meters})\) was observed for a total effect of device use on stride length.

Cadence Table 3-4: Two way ANOVA repeated measures for cadence was not statistically significant \((F_{3,30}=0.79, p=0.05)\). Small effect sizes were observed for cadence.

Walking speed Table 3-4: Two way ANOVA repeated measures for walking speed was not statistically significant overall \((F_{3,30}=2.68, p=0.06)\). Because the assumption of normality was not met for the \(Post_{\text{Unit Off}}\) condition, the data was also analyzed with the nonparametric Friedman test. The Friedman test revealed a statistically significant overall difference \((p=0.006)\). Pairwise comparisons revealed a statistically significant total effect \((p=0.02)\) of device use on walking speed with a moderate effect size \((d=.77, \text{ mean difference } 0.10 \text{ m/s})\). A moderate effect size was also observed \((d=.64, \text{ mean difference } 0.06 \text{ m/s}, p=0.07)\) for a therapeutic effect of device use on walking speed.

Walking endurance \((6MWT)\) Table 3-4: Two way ANOVA for repeated measures for 6MWT distance was statistically significant overall \((F_{3,30}=3.82, p=0.02)\). Pairwise comparisons demonstrated a statistically significant total effect of device use on walking endurance (adjusted \(p=0.005)\) with a large effect size \((d=1.15, \text{ mean difference } 170.45 \text{ feet})\). A large effect size on walking endurance was also found for a therapeutic effect \((d=.92, \text{ mean difference } 105.09, \text{ adjusted } p=0.07)\) on walking endurance.
**Table 3-4:** Two way ANOVA for repeated measures for NNcost was not significant overall ($F_{3,30}=1.5, p =0.23$). Small effect sizes were observed for NNcost.

**Device usage and wear time:** Technical difficulties occurred with the gait log download function of the unit and with some of the gait sensors worn in the shoe. This resulted in several days of zero use values, despite families recording use in their log. Therefore we were unable to reliably utilize the gait log data from the device to monitor and calculate wear time or number of steps per day taken with the device on. Eight of the families completed the log in enough detail to calculate wear time. The remaining 3 individuals reported wearing the device, often daily for several hours, but did not log in detail. Based on the data log completion for 8 participants we were able to calculate at an estimate of minimum wear for the study participants. Four participants documented wearing the device on average 3-6 hours per day and 4 participants documented wearing the device on average 6 or more hours per day. Three participants documented wearing the device greater than 60 days during the 12 weeks, 4 participants documented wearing the device between 30-60 days, and 1 participant documented wearing the device less than 30 days during the 12 weeks. The other participants reported wearing the device, but did not document consistently so we were unable to calculate wear time for the remaining 3 participants.

**Discussion**

Eleven children with hemiplegic CP participated in this first study to comprehensively evaluate the immediate orthotic, therapeutic and total effects of FES neuroprosthesis on BSF outcomes specifically ankle dorsiflexion during swing ($df_{sw}$), ankle dorsiflexion at initial contact ($df_{inic}$), overall gait pathology (GDI), walking endurance (6MWT) and oxygen cost (NNcost). The results from this study support the hypotheses for a statistically significant total
effect of FES neuroprosthesis use on $df_{\text{init}}$, walking speed, and walking endurance, but not on $df_{\text{swing}}$, GDI, NNcost, stride length or cadence. Although not statistically significant, large effect sizes were observed for a total effect on $df_{\text{swing}}$ (d=.89) and for a therapeutic effect on 6MWT (d=0.92). Also, moderate effect sizes were observed for a total effect on stride length (d=0.62), therapeutic effect on $df_{\text{swing}}$ (d=0.50), and a therapeutic effect on walking speed (d=0.64).

Our results did not support the hypotheses for statistically significant immediate orthotic effects or therapeutic effects from NESS L300 use on any of the outcomes measured in this study. These results suggest that one visit to trial the unit may not be sufficient to result in an orthotic effect or evaluate the potential benefits of using the device. A moderate effect size for a therapeutic effect on walking speed may suggest there is some carryover from using the device overtime that persists when the unit is not on. However, three months may not be sufficient time of device use to realize statistically significant therapeutic effects.

It is challenging to compare our study to others because of different lengths of adaptation periods and intervention phases, testing conditions, outcome measures and age of participants. There are three studies\textsuperscript{12,37-39} which have evaluated the effects of FES neuroprosthesis in children with hemiplegia. Prosser\textsuperscript{12} compared gait kinematic and temporal outcomes for 19 children (mean age 12 years 11 month) wearing their usual footwear in the FES condition to No FES condition at self-selected and fast walking speeds at three time points: baseline, after a 4 week accommodation phase and after a primary intervention period consisting of 3 months of daily use. Damiano\textsuperscript{37} reports on 14 children (mean age 14.1 years) from Prosser’s initial cohort who were followed an additional 3 months during which time individuals continued to use the device although mean daily use was less. Damiano\textsuperscript{37} assessed participants barefoot without stimulation
on to compare muscle size by ultrasound and barefoot ankle motion across time. Danino\textsuperscript{38} did not include an intervention period and compared three different overall gait pathology scoring methods at one time point with the unit turned off then turned on in 5 individuals (mean age 16.5 years) after a 6 week adaptation period (personal communication with author 9/30/14) of increasing daily use with the device. Pool\textsuperscript{39} reports a multiple single subject ABA design in 12 children (mean age, 9 years 2 months) in which participants were assessed during a 6 week pre-FES phase, an 8 week FES device daily use phase and a 6 week post-FES phase. Pool\textsuperscript{39} compared the pre-FES phase to FES intervention phase and the pre-FES to post-FES phase, using the outcomes of passive range of motion of ankle dorsiflexion measured in supine with a goniometer, the Observational Gait Scale (OGS)\textsuperscript{88} to assess gait, and a 5 point ordinal scale created by the authors to report on toe drag and falls.

\textit{Ankle Kinematics (df\textsubscript{swing} df\textsubscript{initial}):

Peak ankle dorsiflexion in swing (df\textsubscript{swing}) was assessed in three studies.\textsuperscript{12, 89,38} Prosser\textsuperscript{12} reports a statistically significant overall difference in df\textsubscript{swing} (p=0.015) between FES and no FES conditions in 19 children with hemiplegic CP (mean age 13 years 2 months) at three time points baseline, after 4 week accommodation phase and after 3 months of daily use of 1.5, 2.6 and 3.8 degrees respectively. These differences were significant at the 4 week time point and at the 3 month time point but not at baseline. (p values were not reported). We also did not find a statistically significant immediate orthotic effect (Baseline\textsubscript{Stim on} – Baseline\textsubscript{Stim off}) for df\textsubscript{swing} (mean difference .73, d= 0.13, p value=0.93) suggesting more visits are needed with the device for children to be comfortable with the stimulation before immediate orthotic effects are realized.
In our study, we also found a statistically significant overall difference in $df_{\text{swing}}$ ($p=0.001$), but this difference was not significant for any of the comparisons of interest in our study (immediate orthotic effect, therapeutic, or total effect). Because of the overall significance in $df_{\text{swing}}$ in our study, a post hoc analysis was performed for all comparisons to see where the difference existed. Post hoc analysis revealed the statistically significant difference in our study was between the $Post_{\text{Stim off}}$ (4.0 degrees) and $Post_{\text{Stim on}}$ (11.1 degrees) conditions with an adjusted $p=0.0006$. We would not consider this solely due to an orthotic effect as training effects are likely to have occurred over time.

Prosser\textsuperscript{12} showed a mean difference of 2.8 degrees in $df_{\text{swing}}$ from baseline no FES (0.7 degrees, SD 3.8) to after 3 months of use with FES on (3.5 degrees, SD 5.3). Our participants demonstrated a greater total effect with a mean difference of 4.6 degrees ($Baseline_{\text{Stim off}}$ 6.5 degrees, SD 5.8 to $Post_{\text{Stim on}}$ 11.1 degrees, SD 4.5) with larger standard deviations. The lack of statistical significance for a total effect on $df_{\text{swing}}$ in our study is likely due to the small sample size and greater variability within our sample.

Danino\textsuperscript{38} assessed peak $df_{\text{swing}}$ in 5 adolescents with hemiplegic CP (mean age 16.5 years) once after a 6 week accommodation period of increasing daily use with the device and found a mean difference of 6.2 degrees (-1.9 no FES compared to 4.2 FES) with no $p$ values reported. We did not include an assessment after the accommodation phase and therefore cannot compare our results with those of Danino.

Damiano\textsuperscript{37} reports that barefoot $df_{\text{swing}}$ increased during the three month primary intervention phase, however returned to baseline during the three month follow up period.
indicating no sustained effect on barefoot ankle motion. Our results did not support a statistically significant therapeutic effect of the device on $df_{\text{swing}}$ (mean difference -2.55 degrees, $p=0.4$). Similar to other studies,\textsuperscript{12,37-39} the intervention in this study included wearing the device during regular daily activity with the unit stimulating the muscle to produce a contraction without structured specific voluntary effort from the child. Damiano\textsuperscript{37} suggests that this method of using the FES neuroprosthesis cannot be considered task-specific practice and that using the device in training mode to augment voluntary repetitive practice of ankle dorsiflexion may be more effective in producing a therapeutic effect. Although in our study the children did use the device in training mode for 15 minutes daily during the accommodation phase, they did not continue in training mode after the accommodation phase. Future studies should include structured practice of task specific activities with the unit in training mode during the intervention phase.

Only Prosser\textsuperscript{12} reported the $df_{\text{initial}}$ and found a statistically significant overall effect of device use on $df_{\text{initial}}$ ($p=0.017$). Prosser reported the mean differences between FES and Non FES conditions in $df_{\text{initial}}$ before intervention started, after 1 month of accommodation and after 3 months of daily use of 0.4 degrees, 2.4 degrees, and 4.0 degrees respectively at self-selected walking speed. These differences were significant at the 4 week time point and at the 3 month time point but not at baseline. (P values were not reported). Our results are similar to Prosser’s and found a statistically significant overall effect on $df_{\text{initial}}$ ($p<.0001$) with post hoc analysis demonstrating a significant total effect. The children in our study demonstrated better $df_{\text{initial}}$ values at $Baseline_{\text{Stim Off}}$ (-1.5 degrees) compared to Prosser’s (-4.6 degrees), and a greater mean difference improvement (6.28 degrees) at $Post_{\text{Stim On}}$ after 3 months of use of compared to Prosser (2.9 degrees).
Our participants demonstrated higher baseline values and greater mean differences than Prosser\textsuperscript{12} and Damiano.\textsuperscript{37} One explanation for this difference could be that our sample was younger and may have greater neuroplasticity to change or that they have not developed contractures to the extent that older children may have. Further, unlike Prosser’s participants where only one was wearing an AFO at the beginning, seven of our participants were wearing an AFO which may have given them greater availability of motion. We measured baseline passive range of motion of dorsiflexion with knee extended in supine with a mean of 8.2 degrees. It is possible that children in our study had greater passive motion available than others. Other studies did not report baseline passive range of motion values of the ankle which may be a characteristic associated with outcome. Also a majority of our participants, had baseline ankle selective motor control, as measured by the SCALE,\textsuperscript{82} of 1 indicating some dorsiflexion present with a synergistic pattern of hip and knee flexion. This may account for some of the high baseline values in our sample, especially during swing, when hip and knee flexion are also occurring during the gait cycle. No other studies reported selective motor control of the ankle as measured by the SCALE which may be an important child characteristic associated with outcomes and should be measured in future studies. It is likely that some combination of these factors contribute to the differences in outcomes obtained with FES neuroprosthesis.

\textit{Overall gait pathology (GDI)}

We did not find significant differences in \textit{GDI} for the affected leg contrasting Danino’s\textsuperscript{38} findings where the \textit{GDI} of the affected leg improved after the accommodation phase comparing non FES to FES from 72.36-78.08. The mean \textit{GDI} values of the affected leg of our sample across times and conditions were 79.0, 79.6, 82.1, and 80.9 suggesting the children in our study
were higher functioning than Danino. This warrants further investigation with children functioning at various levels.

**Walking speed, Cadence and Stride Length**

Prosser and Damiano report no improvement in the spatiotemporal variables of walking speed, cadence and stride length. Although spatiotemporal variables were not in our original hypothesis we chose to evaluate them as they can explain changes in other measures (6MWT). We did find a statistically significant total effect in walking speed (p=0.02). The differences in our study may be due to the younger age or higher baseline functioning of our sample, but studies that stratify by age and baseline function would be needed to confirm this.

**Walking endurance (6MWT):**

Our study was the first to assess walking endurance in children with hemiplegia, and found a statistically significant total effect in walking endurance as measured by the 6MWT that may be explained by improvement in walking speed. However the magnitude of the difference (170.4 feet) was less than the minimal detectable change (MDC), beyond measurement variation, reported by Thompson of 206 feet in children with CP GMFCS I and II. Our participants walked shorter distances than reported for typically developing children and in the range of distances reported for children with CP at various GMFCS levels. Distance walked is difficult to compare between studies as the distance walked has been found to depend on the track length with children walking greater distances on larger tracks. For this reason we may not be able to apply Thompson’s MDC to our sample as our track measured longer at 160 feet 9 inches, than theirs at 147 feet and 7 inches.
**Oxygen cost (NNcost):**

Our study was the first to include oxygen cost as an outcome measure in individuals using FES neuroprosthesis. This is an important consideration as others report reduced energy cost for individuals with CP walking with an AFO versus barefoot.\(^92\)\(^{-94}\) Only Brehm\(^93\) measured oxygen cost similar to this study using \(NNcost\) reporting a 10.5% reduction in energy cost for those with quadriplegia but not for those with hemiplegia in the AFO condition compared to barefoot for individuals with CP mean age of 9 years at GMFCS I-III. Our participants demonstrated \(NNcost\) values across times and conditions of 0.35, 0.33, 0.31, and 0.34 which is in the range reported for other children with CP GMFCS I (0.39).\(^79\) Although we did not find statistically significant differences, the children in our study did walk farther without increased \(NNcost\) which may be considered a good outcome. It is possible, that three months is not sufficient to realize significant changes in \(NNcost\). Therefore, future studies should follow individuals over longer periods of time using the device.

**Limitations**

Despite positive findings, limitations of this study exist. Generalizability and external validity of our results are limited by the small sample size and by selection and recall bias. Selection bias may have affected the results as participants in this study likely do not broadly reflect all children with hemiplegia. Those who seek care at academic institutions are likely different than those who do not. Also, participants are more likely to come from selective families who are motivated to carry out the protocol at home. Recall bias may have affected our results as families completed the log independently at home and may not have recalled this information accurately. We were unable to blind the assessor to condition which is also a
limitation to our study. We were unable to reliably estimate dosage or wear time from the device gait log or the family log. For this reason we may not have delivered a large enough dose of the intervention to obtain significant responses. Future studies may consider other ways of determining usage of device such as regular cell phone reminders to caregivers/individuals to track use accurately or manufacturer modifications to the current system.

Conclusion

Results from this study support previous studies of FES neuroprosthesis effects on BSF outcomes. In this study statistically significant positive total effects were seen for increased ankle dorsiflexion at initial contact, walking endurance, and walking speed in children with hemiplegic CP. Moderate to large effect sizes for a total effect on $d_{\text{swing}}$ and stride length, and for a therapeutic effect on walking speed and walking endurance are positive results of this study suggesting that the FES intervention used in this study should continue to be examined in children with hemiplegia. Future studies should examine the effects over a longer period of time. Larger samples would be needed to account for the confounding effects of age, GMFCS level, and baseline characteristics such as range and selective motor control of the ankle to determine those that would benefit most from this intervention. Ideally, studies should examine all relevant effects (immediate orthotic, therapeutic and total) of using the FES neuroprosthesis device and compare FES neuroprosthesis to the standard treatment of an AFO.
Figure 1 Study Timeline

- Visit 0: within 2 weeks
- Visit 1: 4 week training period
- Visit 8: 12 week continuous use
- Visit 9
- Visit 10
- Visit 11
Figure 2 Bioness L300

Figure 3 Flowchart of Recruitment Efforts

- **Contacted**
  - N=34

- **Eligible**
  - N=12 enrolled

- **Ineligible or not interested**
  - N=22
  - Recent botox or surgery n=2
  - Not interested n=6
  - Did not meet dx criteria n=2
  - Too far away n=5
  - Lack of motion n=3
  - Does estim already n=4

- **Follow-up completed**
  - N=11

- **Withdrew from study**
  - N=1
Table 1 Participant Characteristics at Enrollment

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<td>PM Brace Wear</td>
<td>Y</td>
</tr>
<tr>
<td>Passive Ankle Dorsiflexion [deg]‡</td>
<td>+20</td>
</tr>
</tbody>
</table>

† GMFCS indicates Gross Motor Function Classification System; SCALE, Baseline ankle score of Selective Control Assessment of the Lower Extremity. AM, daytime; PM, overnight.
‡ Measured in supine with knee extended.
<table>
<thead>
<tr>
<th>Participant</th>
<th>Pulse frequency (Hz)*</th>
<th>Pulse duration/width(µs)</th>
<th>Max duration of stim (sec)</th>
<th>On ramp (ms)</th>
<th>Off ramp (ms)</th>
<th>Extended %**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35-40</td>
<td>200</td>
<td>2</td>
<td>0</td>
<td>0.2</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>200</td>
<td>3</td>
<td>0.1</td>
<td>0.1</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>200</td>
<td>4</td>
<td>0.1</td>
<td>0.1-0.3</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>200</td>
<td>4</td>
<td>0</td>
<td>0.1</td>
<td>10-30</td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>200</td>
<td>3</td>
<td>0</td>
<td>0.1-0.2</td>
<td>20-30</td>
</tr>
<tr>
<td>6</td>
<td>30-40</td>
<td>200</td>
<td>3</td>
<td>0</td>
<td>0.3</td>
<td>20-30</td>
</tr>
<tr>
<td>7</td>
<td>45</td>
<td>300</td>
<td>4</td>
<td>0</td>
<td>0.1-0.3</td>
<td>20-30</td>
</tr>
<tr>
<td>8</td>
<td>30-35</td>
<td>200</td>
<td>4-3</td>
<td>0</td>
<td>0.1-0.2</td>
<td>30</td>
</tr>
<tr>
<td>9</td>
<td>35</td>
<td>300</td>
<td>4</td>
<td>0</td>
<td>0.5-0.6</td>
<td>40-30</td>
</tr>
<tr>
<td>10</td>
<td>35-30</td>
<td>300</td>
<td>4</td>
<td>0.1</td>
<td>0.1</td>
<td>20</td>
</tr>
<tr>
<td>11</td>
<td>30-45</td>
<td>200</td>
<td>3</td>
<td>0-0.1</td>
<td>0.1</td>
<td>10-30</td>
</tr>
</tbody>
</table>

*Some participants experience a change in pulse frequency over the course of the study.

**Extended % time that the stimulation is continued after heel contact.
### Table 3  Mean Values for Each BSF Outcome n=11. Results are provided as Mean (SD); 95% CI.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Baseline</th>
<th>Post</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stim Off</td>
<td>Stim On</td>
<td>Stim Off</td>
<td>Stim on</td>
</tr>
<tr>
<td>$df_{\text{swing}}$ (degrees)</td>
<td>6.5 (5.8)</td>
<td>7.3 (5.5)</td>
<td>4.0 (4.3)</td>
<td>11.1 (4.5)</td>
</tr>
<tr>
<td></td>
<td>3.4, 9.7</td>
<td>4.1, 10.4</td>
<td>0.9, 7.1</td>
<td>8.0, 14.2</td>
</tr>
<tr>
<td>$df_{\text{initial}}$ (degrees)</td>
<td>-1.5 (6.0)</td>
<td>0.8 (4.6)</td>
<td>-3.3 (4.5)</td>
<td>4.8 (6.2)</td>
</tr>
<tr>
<td></td>
<td>-4.9,2.0</td>
<td>-2.7,4.2</td>
<td>-6.7,0.2</td>
<td>1.4,8.3</td>
</tr>
<tr>
<td>$GDI$ (unitless)</td>
<td>79.0 (7.4)</td>
<td>79.6 (8.8)</td>
<td>82.1 (9.0)</td>
<td>80.9 (8.2)</td>
</tr>
<tr>
<td></td>
<td>73.9,84.0</td>
<td>74.6,84.6</td>
<td>77.1,87.2</td>
<td>75.9,85.9</td>
</tr>
<tr>
<td>$Stride\ length$(m)</td>
<td>1.08 (0.11)</td>
<td>1.10 (0.11)</td>
<td>1.13 (0.11)</td>
<td>1.16 (0.15)</td>
</tr>
<tr>
<td></td>
<td>1.00,1.16</td>
<td>1.02,1.18</td>
<td>1.05,1.21</td>
<td>1.08,1.23</td>
</tr>
<tr>
<td>$Cadence$ (steps/min)</td>
<td>123.64 (11.93)</td>
<td>122.73 (13.26)</td>
<td>125.55 (13.79)</td>
<td>126.09 (11.89)</td>
</tr>
<tr>
<td></td>
<td>116.09,131.18</td>
<td>115.18,130.28</td>
<td>118.0,133.09</td>
<td>118.54,133.64</td>
</tr>
<tr>
<td>$Walking\ speed$ (m/s)</td>
<td>1.12 (0.13)</td>
<td>1.12 (0.13)</td>
<td>1.17 (0.09)</td>
<td>1.21 (0.12)</td>
</tr>
<tr>
<td></td>
<td>1.03,1.18</td>
<td>1.04,1.19</td>
<td>1.10,1.25</td>
<td>1.14,1.28</td>
</tr>
<tr>
<td>$6MWT$ (feet)</td>
<td>1326.5 (150.2)</td>
<td>1395.6 (149.5)</td>
<td>1431.5 (78.24)</td>
<td>1496.9 (143.9)</td>
</tr>
<tr>
<td></td>
<td>1242.0,1411.0</td>
<td>1311.1,1480.1</td>
<td>1347.1,1516.0</td>
<td>1412.4,1581.4</td>
</tr>
<tr>
<td>$NNcost$ (unitless)</td>
<td>0.35 (0.11)</td>
<td>0.33 (0.07)</td>
<td>0.31 (0.10)</td>
<td>0.34 (0.12)</td>
</tr>
<tr>
<td></td>
<td>0.29,0.42</td>
<td>0.27,0.40</td>
<td>0.24,0.37</td>
<td>0.27,0.40</td>
</tr>
</tbody>
</table>

$df_{\text{swing}}$ indicates average peak dorsiflexion during swing; $df_{\text{initial}}$ average dorsiflexion at initial contact; $GDI$, Gait Deviation Index of affected leg; $NNcost$, Net Nondimensional energy cost; 6MWT, 6 Minute walk test.
Table 4 Mean Differences and Effect Sizes for Body Structure and Function Outcomes (n=11)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Immediate orthotic effect</th>
<th>Therapeutic effect</th>
<th>Total effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean diff</td>
<td>95% CI</td>
<td>Effect size</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>Effect size</td>
<td></td>
</tr>
<tr>
<td>df&lt;sub&gt;swing&lt;/sub&gt;</td>
<td>.73</td>
<td>-2.55</td>
<td>4.57</td>
</tr>
<tr>
<td></td>
<td>-3.18, 4.63</td>
<td>-7.25, 2.16</td>
<td>-0.46, 9.6</td>
</tr>
<tr>
<td>df&lt;sub&gt;initial&lt;/sub&gt;</td>
<td>2.2</td>
<td>-1.8</td>
<td>6.28*</td>
</tr>
<tr>
<td>GDI affected leg</td>
<td>-1.20, 5.63</td>
<td>-6.2, 2.6</td>
<td>1.34, 11.22</td>
</tr>
<tr>
<td>0.66</td>
<td>3.18</td>
<td>1.92</td>
<td></td>
</tr>
<tr>
<td>0.08</td>
<td>0.39</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>Stride Length (m)</td>
<td>0.02</td>
<td>0.05</td>
<td>0.08</td>
</tr>
<tr>
<td>0.18</td>
<td>0.18</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>Cadence (steps/min)</td>
<td>-0.91</td>
<td>1.91</td>
<td>2.45</td>
</tr>
<tr>
<td>0.07</td>
<td>0.15</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>Walking Speed (m/s)</td>
<td>0.01</td>
<td>0.07</td>
<td>0.10***</td>
</tr>
<tr>
<td>0.08</td>
<td>0.64</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>6MWT (ft)</td>
<td>69.18</td>
<td>105.09</td>
<td>170.45**</td>
</tr>
<tr>
<td></td>
<td>-17.60, 155.96</td>
<td>-5.43, 215.61</td>
<td>47.47, 293.44</td>
</tr>
<tr>
<td>NNcost</td>
<td>-0.02</td>
<td>-0.05</td>
<td>-0.02</td>
</tr>
<tr>
<td>0.22</td>
<td>0.45</td>
<td>0.16</td>
<td></td>
</tr>
</tbody>
</table>

Statistically significant differences are in bold. Adjusted p values; *p=0.01, **p=0.005, ***p=0.02

Shaded boxes indicate moderate to large effect sizes
Chapter 3: Activity and Participation Outcomes and Satisfaction Following FES Neuroprosthesis Use in Children with Hemiplegic Cerebral Palsy: An Exploratory Study
**Introduction**

Cerebral palsy (CP) describes a group of permanent disorders of movement and posture that are attributed to non-progressive disturbances in the developing brain with a stable prevalence rate of 3.1-3.6 per 1000 since 1996.\(^2\) CP ranks as the second most prevalent early-onset neurological disorder, trailing only autism\(^3\) and results in a wide range of functional limitations ranging from ambulating with minor difficulties to not being able to ambulate at all. Children with CP are less involved in physical or skill-based community activities than are their typically developing peers.\(^{59,95}\)

Hemiplegia (affecting one side of the body) accounts for 22.6 - 40% of all cases of CP.\(^6-10\) Further, preliminary findings with recent neuroimaging techniques suggest the incidence of hemiplegia is increasing.\(^11\) The most common gait impediment for children with hemiplegic CP is foot drop or poor foot clearance during swing phase and diminished heel strike on their affected side, which may limit their higher-level ambulation and balance skills.\(^12\)

The World Health Organization’s (WHO) International Classification of Functioning, Disability and Health (ICF) framework which was introduced in 2001 provides an integrated and universal language for measuring health and disability that has been applied across rehabilitation studies and disciplines.\(^21\) It reflects interactions between a person’s health condition, body structures and functions (BSF), (such as muscle length or strength), activity (execution of a task), participation (involvement in a life situation), environmental factors (physical, social and attitudinal), and personal factors (one’s attitudes and other features that are not part of a health state). The ICF framework has been used extensively in the pediatric rehabilitation literature: as a tool for clinical reasoning,\(^24\) to identify and compare outcomes measures used in CP,\(^25\) to classify the focus of outcome studies,\(^26\) to describe the effects of children with disabilities
receiving assistive devices\textsuperscript{27} and to examine the relation between walking performance and participation in children with CP.\textsuperscript{23} Further, the ICF framework reflects a dynamic interaction between person and environment with a move toward the identification of participation as an important outcome of health.\textsuperscript{22} This has resulted in a shift of clinical research focus from body structure and function to an increased emphasis on outcomes related to activity and participation.\textsuperscript{23} Outcomes used to measure intervention effectiveness need to be multidimensional to encompass the impact of what rehabilitation specialists offer at different levels of the ICF.\textsuperscript{22}

The current treatment for hemiplegia involves wearing an ankle foot orthosis (AFO). AFO’s limit active movement and potentially hinder motor learning, and contribute to the muscle weakness in CP. In addition, older children are often unwilling to wear an AFO due to the bulk and discomfort.\textsuperscript{38} Functional electrical stimulation (FES) neuroprostheses provide an alternative to AFOs for foot drop and have been shown to increase neuroplasticity, function and quality of life in adults with hemiplegia.\textsuperscript{28-36} Only one of these studies\textsuperscript{36} compared the FES neuroprosthesis use to wearing an AFO and found no difference in gait outcomes, but higher user satisfaction in the FES group.

Studies of FES neuroprosthesis use in children are few in number and have some limitations. To date, there have been three cohorts of children with hemiplegia studied, one in the US,\textsuperscript{12,37} one in Israel,\textsuperscript{38} and one in Australia,\textsuperscript{39} using FES neuroprosthesis in a total of 36 children with hemiplegic CP. These studies have measured outcomes primarily in the body structure and function (BSF) domain of the International Classification of Function (ICF).\textsuperscript{21} Specifically they have reported improvements in ankle range of motion,\textsuperscript{39} gait kinematics,\textsuperscript{12,37,38} muscle size,\textsuperscript{37} muscle control,\textsuperscript{37,39} strength\textsuperscript{39} and reduced spasticity.\textsuperscript{39} None of the prior pediatric studies
evaluated the effects of FES neuroprosthesis use on activities or participation. Only Prosser\textsuperscript{12} included a measure of acceptability with 86% of their sample choosing to continue to use the device when given the choice after a 3 month FES phase. Only Pool\textsuperscript{39} reported on trips and falls with a reduction in both during the FES intervention phase that remained post FES intervention. None of the studies reported on adverse events. The use of new technology not only requires understanding the changes it imposes on body structures and function, but practitioners also need to understand how such changes affect a child’s functional performance and participation in meaningful activities.\textsuperscript{41} Clearly more studies are warranted using this technology before it is regularly recommended for home use in this population.

The effects of the FES neuroprosthesis can be described in several ways. The \textit{immediate orthotic effect} indicates changes that occur when initially wearing the device. A \textit{training effect} beyond the immediate effect may occur as the patient uses the device. The \textit{therapeutic effect} indicates improvements seen over time without wearing the device and may result from neural plasticity or strengthening of the involved extremity. The \textit{total effect} indicates changes over time that includes both the immediate orthotic and training effects. The study summarized in this dissertation investigates the immediate orthotic effect, the therapeutic effect and the total effect of FES neuroprosthesis use in children with hemiplegic CP.

A previous chapter of this dissertation has reported on the effects of FES neuroprosthesis on BSF outcomes. The primary goal in this chapter is to explore the immediate, therapeutic and total effects of FES neuroprosthesis use on activities and participation in children with hemiplegic CP. Specifically we will investigate changes in stair climbing ability, obstacle course negotiation and performance and satisfaction with individualized goals. Further we will examine
caregiver and client satisfaction with device use, as well as safety and adverse events associated with using the device.

**Methods**

This study was reviewed and approved by the IRB at Cincinnati Children’s Hospital and University of Cincinnati. Written parental permissions were obtained prior to participation in addition to assent of the participant in the cases where the participant was 11 or older.

**Study Design:** A two factor repeated measures design was carried out with individuals evaluated before and after an intervention consisting of FES neuroprosthesis daily use. The protocol included a screening visit (visit 0), baseline assessment (visit 1), a four week accommodation period that included seven one hour PT sessions to acclimate to wearing the FES unit (visits 2-8), monthly well check visits during the 12 week daily use (visits 9-10) and a post assessment (visit 11). A timeline of visits is provided in the previous chapter of this dissertation. All assessments were administered with the unit turned off (*Stim Off*) and then were repeated with the unit turned on (*Stim On*) at baseline and post assessment. No additional therapy was provided during the study protocol. This dissertation study is part of a larger trial collecting outcome measures across ICF categories. Included in this chapter are the outcomes related to activities and participation as well as safety and satisfaction. Results from body structure and function measures are reported in the previous chapter of this dissertation.

**Participants:** Given the exploratory nature of this study and the fact that the effects of FES neuroprosthesis use on activity and participation have not been studied previously, sample size estimation was not performed for these outcomes. Participants included the same 11 individuals enrolled in the trial evaluating the use of FES neuroprosthesis on BSF outcomes in
children with hemiplegic CP. Inclusion and exclusion characteristics have been reported in the previous chapter of this dissertation. Interested participants agreed to attend a screening and enrollment visit to make sure all conditions for eligibility were met before enrolling in the study. Written parental permissions were obtained prior to participation in addition to assent of the participant in the cases where the child was 11 years or older.

**Intervention** The Ness L300 Foot Drop System manufactured by Bioness Inc. (Valencia CA, USA) is a small device that delivers surface electrical stimulation to the common fibular/peroneal nerve which innervates the tibialis anterior and other ankle dorsiflexors. The L300 consists of an in-shoe pressure sensor, a control unit and an orthotic cuff that holds two stimulation surface electrodes. The electrodes are positioned to produce dorsiflexion and slight eversion. Once the optimal electrode placement is determined, the orthotic cuff holds the electrodes in place reducing the need for daily placement and increasing the reliability of electrode placement for home use. Stimulation parameters are set by the clinician using a PDA clinician’s programmer to elicit the most effective contraction during ambulation. The device can deliver stimulation in two modes; training mode which is cyclic stimulation when the individual is not walking, or gait mode which is activated through the in shoe gait sensor while the individual is ambulating. Education on the use and maintenance was provided throughout the four week accommodation period. During the accommodation period the individual used the unit in training mode while seated for cyclic stimulation for 15 minutes a day for the first week, followed by 20 minutes a day to gradually strengthen and condition the muscles for use. Also during the four week accommodation period, participants were instructed to gradually increase wear time with the unit in gait mode during their typical daily activities starting with 15 minutes each day to all day use. Skin care guidelines were reviewed and provided to the family during the
initial fitting. At the end of the accommodation period participants were instructed to discontinue using the device in training mode and to wear it for at least 6 hours a day in gait mode during their typical daily activities. No additional physical therapy was provided during the intervention.

Individualized adjustments and reevaluation of the settings and electrode placement occurred at each visit, as well as family support and communication with the study team to increase tolerance to using the device. Participants experiencing problems were encouraged to return for assistance or discuss the issue over the phone with study staff outside of the scheduled visits. The average number of steps per day and average number of minutes walking while wearing the device was recorded by the device and downloaded at each visit. In addition the family was asked to keep a daily log of use noting hours of use each day and documenting problems or concerns.

**Activity and Participation Outcome Measures**

Stair climbing ability was measured with the Timed Up and Down Stairs (TUDS) test which is a simple measure of functional mobility for children with ambulatory CP, that is quick, low cost, reliable\(^4\) and is reported to be a significant predictor of community mobility.\(^96\) The TUDS has been used as an outcome measure to study effectiveness of physical therapy intervention for children with CP,\(^96-99\) cancer\(^100,101\) and development delay.\(^102\) Each participant was asked to stand 30 cm from the bottom of a 12 step flight of stairs (18cm rise) and instructed to “Quickly but safely go up the stairs, turn around on the top step and come all the way down until both feet land on the landing.” Handrails were available on both sides of the staircase. Individuals faced in the direction of the movement (not to the side), and could choose any method including alternating steps, running the steps or using a handrail. The time in seconds from the “Go” cue
until the second foot returned to the landing was recorded with shorter times indicating better function.

Obstacle course negotiation was assessed with the Standardized Walking Obstacle Course (SWOC)\textsuperscript{103} which is designed to quantify ambulation in an environmental context related to challenges encountered within the home and community. Children with developmental disabilities have been reported to take significantly longer to complete the course than typically developing children.\textsuperscript{83} The SWOC requires an individual to walk on a designated path 39.5 feet long and 36 inches wide and includes negotiating three directional turns, stepping over an axillary crutch, walking across a visually stimulating mat, stepping around a trash can, walking across a shag rug and transitioning from sitting to standing and standing to sitting from a chair with armrests and a chair without armrests. See Figure 1. The SWOC was administered in the hands free condition and the study team recorded the number of seconds to complete (SWOC\text{time}), the number of steps to complete (SWOC\text{steps}), the number of stumbles or contact with obstacles on the path (SWOC\text{stumbles}) and the number of steps off the path (SWOC\text{sop}). Individuals were given a practice trial followed by two additional trials which were then averaged and recorded. The PI recorded SWOC\text{time} and SWOC\text{steps} while another study team member recorded SWOC\text{stumbles} and SWOC\text{sop}. A research assistant videotaped the three trials and the PI watched all to verify scores.

Performance and satisfaction with individualized goals was assessed with the Canadian Occupational Performance Measure (COPM)\textsuperscript{104} which is designed to evaluate performance and satisfaction with valued activities as determined by the individual.\textsuperscript{105} The COPM is a reliable, valid and responsive client-centered semi-structured interview designed to detect change in a
client's self-perception of occupational performance over time. The COPM has been used with a wide variety of clients and supports outcomes research. At the enrollment visit, the caregiver was asked to identify 2-3 goals that were important to them and that they thought the intervention might address. They were asked to score on a Likert scale 1-10 first their performance of each goal and then their satisfaction with their performance of each goal. The performance scores and satisfaction scores for each goal are summed and averaged to result in a score up to 10. The same caregiver who identified and rated the goals at the initial interview did the same at the post assessment and did not view previous results. Overall satisfaction and performance scores are generated from the COPM and were treated as continuous variables for analysis.

**Safety and Satisfaction**

*Fall and trip log:* At enrollment and at the last visit participants completed a fall log where they were asked to report first if they had experienced any falls in the last month and if so, the average number of falls in the past month followed by if they had experienced any trips and if so the average number of trips in the previous month. Circumstances regarding falls and trips were collected including any injury that received medical attention.

A user’s satisfaction questionnaire was completed by the caregiver and child (if 11 years or older) at the post assessment which included 12 questions about their overall satisfaction with the device. Responses to questions were categorical in nature with answers ranging from yes, no; to more useful, as useful, less useful; and significantly better, better, same or worse. In addition the caregiver and the client were asked if they wished to continue to use the NESS L300 at the end of the study (post assessment).
Adverse events

A log of daily use (LDU) was completed by families to provide additional information on FES neuroprosthesis use and safety. Adverse events including any skin irritation or equipment issues were documented.

Assessment Procedure

Upon enrollment, information regarding participant demographics, medications, brace wear, falls and trips experienced, range of motion and selective control assessment lower extremity (SCALE) scores for the affected ankle were obtained. Also at enrollment, individualized goals were set and scored by the caregiver using the Canadian Occupational Performance Measure (COPM). Within two weeks of enrollment a baseline assessment was conducted. Upon arrival for testing a Polar heart rate monitor (Polar Ft1, Polar Electro) was applied around the participant’s chest and a resting heart rate was obtained. The NESS L300 unit was then donned and turned on briefly in trial mode (1-5 cycles) to ensure proper placement and adequate muscle contraction and then was turned off. After at least 15 minutes, testing began in the Stim Off condition. The child was provided with a 15-30 minute seated break (duration based on participant feedback) before repeating tests in the Stim On condition. The Stim Off condition always occurred before Stim On to eliminate the possibility of carryover from the stimulation. Heart rate was monitored and time was given between assessments in order for the individual’s heart rate to return to baseline resting levels. This trial included administration of activity measures along with body structure and function measures that were reported previously. With the exception of 3DGA, the order of the outcomes administered was randomized using a computerized random numbers program to minimize the effects of testing order. The 3DGA was
not randomized to simplify testing procedures and eliminate the need to remove and reposition
the markers between conditions. Specifically the other measures were randomized with 3DGA
always occurring 4th and 5th order in the testing process (e.g. SWOC\textsubscript{Stim Off}, TUDS\textsubscript{Stim Off}, 6MWT\textsubscript{Stim Off}, 3DGA\textsubscript{Stim On}, TUDS\textsubscript{Stim On}, 6MWT\textsubscript{Stim On}, SWOC\textsubscript{Stim On}).

Testing was conducted by the PI in the outpatient division of OTPT. With the exception
of three participants all testing was the same time of day at the baseline and post assessments.

**Statistical Analysis**

Study data were collected and managed using REDCap\textsuperscript{85} (Research Electronic Data
Capture) electronic data system which is a secure, web-based application designed to support
data capture for research studies, hosted at this institution. Data was entered into REDCap by a
research assistant and verified by the PI before being downloaded and analyzed with SAS 9.3.
Normality of the data was examined with the Shapiro-Wilk and Kolmogorov-Smirnov values
and by examining the residuals for each variable. Means and 95% CIs are reported for each
outcome in Table 1. A two factor repeated measures ANOVA or the non-parametric equivalent
(Friedman test) was computed for TUDS and SWOC values. Tukey adjustment was utilized for
pairwise comparisons. When the assumption of normality was not met for any combination of
time (Baseline, Post) and condition (Stim On, Stim Off), non-parametric analyses were performed
and reported if the results differed than parametric analyses. A paired t test or the non-parametric
equivalent (Wilcoxon signed rank test) was computed for COPM performance and satisfaction
outcomes and for reported falls and trips. Effect sizes using .20 as small, .50 as moderate and .80
as large described by Cohen\textsuperscript{87} are reported for each outcome as they provide a means of
determining whether treatment differences are meaningful despite lack of statistical
significance. As this was the first time these outcomes were assessed following intervention with FES neuroprosthesis, we felt reporting effect sizes would provide more information about possible effects for the purpose of directing future research. Descriptive statistics including frequencies and proportions for categorical responses to each question on the questionnaire were calculated. Adverse events were recorded. Unless otherwise specified all data were distributed normally.

**Results**

Twelve individuals were enrolled in the study. One participant withdrew from the study at the second training visit citing concerns for using the unit while going between parents’ homes. This person’s data was not included for analysis resulting in complete data for 11 participants, mean age 9 years 11 months. Participant characteristics at enrollment have been reported in the previous chapter of this dissertation. Means and standard deviations for the outcomes across time periods are reported in Table 1. For the comparisons of interest, mean differences, confidence intervals (95%) and effect sizes for each outcome are reported in Table 2.

*TUDS Table 1-2:* A two way ANOVA for repeated measures was not statistically significant overall (F<sub>3,30</sub>=.15, p=0.93) for the *TUDS*. Eight children were consistent and did not change their use of rails across time points or conditions. The two children classified as GMFCS II used a handrail consistently while the six children classified as GMFCS I did not. Three children (GMFCS I) did vary their use of the handrail. Effect sizes were small (d=.11) for all *TUDS* comparisons.

*SWOC Table 1-2:* A two way ANOVA for repeated measures was not significant for *SWOC<sub>time</sub>* (F<sub>3,30</sub>= 0.65, p=0.59) or *SWOC<sub>steps</sub>* (F<sub>3,30</sub>=2.30, p=0.10). *SWOC<sub>steps</sub>* did not meet the
assumptions of normality in the Post Stim On condition and therefore was also analyzed non-parametrically with the Friedman test where a statistically significant therapeutic effect (d=.60 mean difference -1.68, p=0.004) was detected. A moderate effects size was also observed for a therapeutic effect of device use on SWOC\textsubscript{time} (d=.53 mean difference -.89, p=0.62).

All combinations of time and condition for SWOC\textsubscript{stumbles} and SWOC\textsubscript{sop} did not meet the assumptions of normality and were analyzed with the non-parametric Friedman test. The Friedman test for SWOC\textsubscript{stumbles} revealed no statistically significant overall difference (F\textsubscript{3,10}= 0.87, p=0.47). The Freidman test for SWOC\textsubscript{sop} revealed a statistically significant overall difference (F\textsubscript{3,10}= 3.80, p=0.03) but no statistically significant effect was found with pairwise comparisons. A moderate effect size (d=.59 mean difference -.23 p= 0.25) was found for an immediate orthotic effect of device use on SWOC\textsubscript{sop} and a large effect size (d=.83 mean difference -0.27, p= 0.13) was found for a total effect on SWOC\textsubscript{sop}.

**COPM Table 1-2:** Scores for both the COPM performance and satisfaction outcomes were distributed normally and therefore assessed with the paired t test. A statistically significant difference in COPM performance scores was found (F\textsubscript{1,10} = 23.97, p=0.0006). A statistically significant difference in COPM satisfaction scores was also found (F\textsubscript{1,10} = 23.20, p=0.0007). Large effect sizes were found for both COPM performance (d= 1.87 mean difference 2.44) and COPM satisfaction (d=2.04 mean difference 3.24).

**Safety and Satisfaction**

**Falls and Trips reported Table 1-2:** The number of falls and the number of trips were not distributed normally and were evaluated with the Wilcoxon signed rank test. There was no
statistically significant difference in falls reported at enrollment and post assessment (median difference =1, mean difference -0.36, p=0.67) A statistically significant difference was found between enrollment and post assessment in the average number of trips in the previous month (median difference 3, mean difference -2.45, p=0.01) with less trips being reported at post assessment. A large effect size (d=−1.42) was found for average trips reported in the previous month.

**Satisfaction Questionnaire** Table 3: Results from the satisfaction questionnaire are reported in Table 3. Eleven caregivers and three children completed the satisfaction questionnaire. Overall caregiver responses were positive with a majority enthusiastic (91%) about using the device and rating the L300 as more useful than other aides to assist with gait (82%), rarely needed assistance in working the L300 (55%) were satisfied with the dimensions of the device (67%), satisfied with the ease in donning/doffing the device (82%), significantly improved walking ability while using the device (64%), more confident walking with the L300 versus without it (82%) and walking on inclines and/or uneven ground (82%). All (100%) of the caregivers found the unit safe to use, would recommend a person with their child’s condition use the L300 and wanted to continue to use the L300 at the end of the study. Thirty six percent of the caregivers reported the L300 was very convenient to use during the day and 55% reported it was convenient and 9% reported that it was inconvenient. Fifty five percent reported that their child could perform the same daily tasks or activities while using the L300, 45 % reported they could perform more and 0% reported their child could perform fewer activities while using the L300 system.

The clients themselves also reported favorably, with all three reporting that they were satisfied with the dimensions, all felt they could perform the same activities while using the
device, were more confident with the L300 versus without it, found it safe, would recommend a person with their condition use it and wished to continue using the L300 at the end of the study. Two of the three individuals reported that they felt enthusiastic about continuing to use the device, found it more useful than other aids to assist their gait and felt greater confidence while walking on inclines and/or uneven surfaces. Two of the three individuals reported they were more or less satisfied with the ease of donning and doffing the L300, described the use as convenient, and felt their walking ability was better while using the L300.

Adverse Events: Skin irritation occurred in three participants. In all cases the individuals were instructed to stop wearing the L300 until the skin irritation resolved (generally within 3-7 days). Upon return to wearing the device the intensity of the stimulation was reduced and participants were instructed to gradually increase wear time of the device. One of the three switched to cloth electrodes with improved skin tolerance. The other two were already using cloth electrodes. None of the reported falls or trips during the study required medical attention. Three individuals reporting a fall and/or trip while wearing the device during the 12 week intervention period. The gait sensor malfunctioned (broken wire in 2 cases and broken clip that attaches sensor to shoe in 1 case) for three participants and a new gait sensor was provided by the manufacturer. All adverse events resolved and participants remained on the study.

Discussion

This was the first study to evaluate the effects of FES neuroprosthesis use on activity and participation outcomes in children with hemiplegic CP. The results from this study have implications for pediatric physical therapy intervention for children with hemiplegic CP but should be interpreted cautiously due to small sample size and its exploratory nature. This study demonstrated that daily use of an FES neuroprosthesis may improve performance and
satisfaction with individualized goals, result in a decrease in the reported frequency of trips and have a statistically significant therapeutic effect on the number of steps to complete a standardized obstacle course. Moderate to large effect sizes were observed for device use effects on $SWOC_{time}$, $SWOC_{steps}$, and $SWOC_{sup}$. Further, satisfaction was high with all participants wishing to continue to use the device at the end of the study.

**TUDS:** Similar to studies of other physical therapy interventions,\textsuperscript{97,98,102} we did not find a statistically significant improvement in the TUDS after an intervention. Jelsma\textsuperscript{98} found no change in TUDS scores in children with hemiplegia after participation in a Wii Fit intervention that included participation in games appropriate for improving balance and encouraging weight shift in all directions. Salem\textsuperscript{102} found no change in TUDS scores in younger children with developmental delay compared to a control group after a Wii Fit intervention. Brien\textsuperscript{97} found no change in 4 adolescents with CP, GMFCS I after an intervention consisting of virtual reality training. Our results contrast with Gorter,\textsuperscript{99} who reports an improvement in TUDS time in children with CP, GMFCS I and II, after a physical training program that addressed endurance, walking distance, walking velocity and ambulation. This suggests that we may not have seen improvement because unlike Gorter,\textsuperscript{99} our study participants were not instructed to specifically practice ambulation activities such as stairs during the intervention phase. It is also possible that more time using the device is necessary before improvements are realized.

Staircases vary between studies in the literature,\textsuperscript{84,96,102} ranging in number of stairs from 11-18. In order to compare between studies calculating seconds per step is necessary rather than seconds for the entire staircase. Gorter\textsuperscript{99} did not specify the number of steps in their staircase and therefore we are unable to directly compare our results. Typically developing children are reported to complete the TUDS in 0.58 seconds per step,\textsuperscript{84} while participants in our sample
completed the TUDS at Baseline$^{\text{No Stim}}$ in 1.3 seconds per step. Ferland$^{96}$ compared three locomotor tests in 49 children with CP GMFCS I or II, mean age (10.67 years) and found the TUDs to be a significant predictor of community mobility. Our study sample was most similar to Ferland’s in terms of GMFCS levels and mean age but their sample completed the TUDS faster (0.82 seconds) than our participants. Ferland$^{96}$ did not report the stair rise or other details about the staircase used. In our study we used a concrete stairwell (12 steps, 18cm rise) in the building. Whether the stairwell may have been uninviting or intimidating due to its size or construction materials, or for other unknown reasons our participants took longer to complete the TUDS.

It is recommended that future studies using the TUDS as an outcome measure report the number of steps in the staircase and the step rise so that comparisons between studies are possible. No participants in this study identified stairs as a goal on the COPM. However, if stair climbing is identified as a goal than intervention should target specific practice of this goal in more natural environments such as at home or school.

**SWOC:** This study was the first to utilize the SWOC to evaluate obstacle course negotiation after FES neuroprosthesis use in children with hemiplegia. We demonstrated a statistically significant therapeutic effect for $SWOC^{\text{steps}}$ (p=0.004) with an effect size of d=0.60 mean difference -1.68 indicating participants completed the SWOC Post$^{\text{Stim Off}}$ with less steps than at Baseline$^{\text{Stim Off}}$. We expected a significant total effect $SWOC^{\text{steps}}$ but two participants used several very small steps sideways as a strategy to get around the garbage can resulting in higher values and a large standard deviation. This likely explains the lack of statistical significance for a total effect of device use on $SWOC^{\text{steps}}$. Although not statistically significant
we observed a large effect size (d=0.83 mean difference -.27, p=0.13) for a total effect of device use on $SWOC_{sop}$ in our sample. In addition, we observed moderate effect sizes for a therapeutic effect of device use on $SWOC_{time}$ (d=.53 mean difference -0.89 seconds, p=0.62) in addition to an immediate orthotic effect of device use on $SWOC_{sop}$ (d=0.59 mean difference -.23, p=0.25).

These SWOC results suggest participants improved their ability to negotiate the obstacle course which is likely to have meaningful implications for children with hemiplegia in more natural environments such as in the hallways at school.

The SWOC has not been used extensively to evaluate intervention effects in children. Advantages of the SWOC are that it is inexpensive and easy to administer in the clinical environment. Two studies$^{107,108}$ found no difference in SWOC performance in children with hemiplegia after an intervention. Kott$^{107}$ found no significant difference when comparing SWOC performance with and without orthoses in children with CP GMFCS Level I and II. Zipp$^{108}$ reported no significant effects of constraint induced movement therapy on SWOC performance in children with CP, GMFCS I and II.

The SWOC can be administered in 3 conditions: walking arms free, walking carrying a tray and walking in a dimly lit environment. Our study administered the SWOC only in the arms free condition to minimize assessment burden. A significant difference in SWOC scores in children with hemiplegia walking carrying a tray compared to hands free has been reported.$^{107}$ Therefore, future studies may consider administering the SWOC in these other conditions.

**COPM**: COPM performance and satisfaction scores demonstrated statistically significant improvement at follow up. This is in agreement with other studies reporting the COPM as responsive to meaningful changes due to therapy interventions.$^{106,109,110}$ The goals
identified as important by the client or caregiver for this study reflected individual goals of participation (e.g. playing hopscotch better, improved butterfly kick resulting in fewer disqualifications during swim meets from asymmetrical kicking, and more even weight distribution on legs when playing baseball).

**Satisfaction questionnaire:** This study was the only pediatric study that collected satisfaction information in a systematic way. We used a previously used questionnaire from the adult literature.\(^{36,48}\) Similar to adults, a majority were satisfied and all wanted to continue to use the Ness L300 unit at the end of the intervention period. These results demonstrate that FES neuroprosthesis home use is feasible and that families are satisfied when frequent and close clinical support, such as in this study, is provided. When considering intervention options therapists should choose an intervention that reflects the motivation and interest of the individual.\(^{111}\) Wingstrand\(^{112}\) reports AFO wear decreases with age which is consistent with our experience with teenagers. Children especially adolescents may be more motivated to wear an FES neuroprosthesis than an AFO. In this study, two of the 3 children that were 11 years of age or older reported that they found the L300 more useful than other aids to assist their gait and function, and 1 participant reported it was as useful as other aids to assist gait. Future studies should explore the issue of preference for the neuroprosthesis or AFO.

**Adverse events:** Three participants in this study experienced skin irritation underneath the electrodes requiring them to stop wearing the device temporarily. None of the previous pediatric studies of FES neuroprosthesis\(^{12,37-39}\) report on skin related adverse events or device issues. However, a study of adults with hemiplegia using the same device\(^{36}\) as this study, did report 51 skin irritation issues accounting for 40% of study related adverse events in treatment group. Narrative comments from 3 parents in our study included frustration with the location of
the gait sensor on the side of the shoe which they felt contributed to its breakage. These results suggest that clinicians should advocate for a reasonable length of time to adapt to the unit before pursuing purchase for home use. No participant experienced a fall or trip during the study period that required medical intervention. Three participants reported falling with the device and/or tripping with the device on during the 3 month intervention period. Reducing falls and trips is a possible benefit of FES neuroprosthesis intervention\textsuperscript{37} however only Pool\textsuperscript{39} reported on falls and trips while using the device. Similar to Pool,\textsuperscript{39} our study reports a decrease in the number of trips at post intervention. However unlike Pool, we did not report a decrease in falls. Pool used a 5 point ordinal scale which may have improved the ability to detect change in reported falls and trips. Future studies should consider using a scale similar to Pool to measure trips and falls. Recall bias may have limited our ability to detect more subtle changes in falls or trips, as information about falls and trips relied on recall of participant and caregiver.

This study included several limitations. One limitation was use of a sample of convenience. Additionally, no control group was used, and the assessor was not blinded to Stim On or Stim Off condition. The chosen assessment tools may not have been sensitive to minor changes in participants’ abilities. It is possible that the intervention program was too short in duration to elicit significant changes in obstacle course negotiation and stair climbing.

Conclusion

The purpose of this exploratory study was to investigate the immediate orthotic, therapeutic and total effects of FES neuroprosthesis use on activity and participation outcomes in children with hemiplegia and to evaluate safety and satisfaction with device use. Results suggest that that FES neuroprosthesis use results in positive effects on individualized goals and self-
reported trips. Additionally it may have positive effects on obstacle course negotiation. Further, satisfaction is high when using the device with a high level of regular support and communication with therapists trained in using the device. This intervention may have greater benefits when combined with other interventions such as botulinum toxin, casting, or task specific training with the device on. Future research should continue to explore the effects of FES neuroprosthesis on activity and participation outcomes in a larger sample of individuals with hemiplegic CP with varying baseline function, over longer follow-up periods, and compare FES neuroprosthesis to AFO.
Figure 1 Standardized Walking Obstacle Course reprinted with permission from Held article 2006.
Table 1. Baseline and Post values for Outcomes. Results provided as Mean (SD); 95% CI unless noted by *

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Baseline</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stim Off</td>
<td>Stim On</td>
</tr>
<tr>
<td><strong>TUDS (s)</strong></td>
<td>15.40 (3.70)</td>
<td>15.79 (4.30)</td>
</tr>
<tr>
<td></td>
<td>13.13, 17.67</td>
<td>13.52, 18.10</td>
</tr>
<tr>
<td><strong>SWOC\textsubscript{time} (s)</strong></td>
<td>11.80 (1.86)</td>
<td>11.48 (2.00)</td>
</tr>
<tr>
<td></td>
<td>10.32, 13.27</td>
<td>10.01, 12.96</td>
</tr>
<tr>
<td><strong>SWOC\textsubscript{steps}</strong></td>
<td>20.91 (3.14)</td>
<td>20.73 (3.30)</td>
</tr>
<tr>
<td></td>
<td>18.16, 23.65</td>
<td>17.98, 23.47</td>
</tr>
<tr>
<td><strong>SWOC\textsubscript{stumbles}</strong></td>
<td>0.27 (0.61)</td>
<td>0.5 (0.74)</td>
</tr>
<tr>
<td></td>
<td>0-0*</td>
<td>0-0.5*</td>
</tr>
<tr>
<td><strong>SWOC\textsubscript{sop}</strong></td>
<td>0.36 (0.45)</td>
<td>0.14 (0.32)</td>
</tr>
<tr>
<td></td>
<td>0-1*</td>
<td>0-0*</td>
</tr>
<tr>
<td><strong>COPM performance</strong></td>
<td>4.86 (1.38)</td>
<td>7.31 (1.23)</td>
</tr>
<tr>
<td></td>
<td>3.99, 5.74</td>
<td></td>
</tr>
<tr>
<td><strong>COPM Satisfaction</strong></td>
<td>4.01 (1.63)</td>
<td>7.25 (1.55)</td>
</tr>
<tr>
<td></td>
<td>2.94, 5.08</td>
<td></td>
</tr>
<tr>
<td><strong>falls in the last month (avg)</strong></td>
<td>1.1 (1.4)</td>
<td>0.7 (1.2)</td>
</tr>
<tr>
<td></td>
<td>0-2*</td>
<td></td>
</tr>
<tr>
<td><strong>trips in the last month (avg)</strong></td>
<td>3.55 (1.7)</td>
<td>1.1(1.8)</td>
</tr>
<tr>
<td></td>
<td>2-5*</td>
<td></td>
</tr>
</tbody>
</table>

*interquartile ranges reported as these variables were not distributed normally.

TUDS indicates Timed Up and Down Stairs in seconds; SWOC\textsubscript{time}, SWOC\textsubscript{steps}, SWOC\textsubscript{stumbles}, SWOC\textsubscript{sop}

Standardized Walking Obstacle Course, COPM Canadian Occupational Performance Measure
Table 2 Mean Difference and Effect sizes for Activity and Participation Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Immediate orthotic effect</th>
<th>Therapeutic effect</th>
<th>Total effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Base on – Base off)</td>
<td>(Post off – Base Off)</td>
<td>(Post on - Base off)</td>
</tr>
<tr>
<td></td>
<td>Mean diff</td>
<td>95% CI</td>
<td>Effect size</td>
</tr>
<tr>
<td>TUDS (s)</td>
<td>.39</td>
<td>1.05, 1.84</td>
<td>-.11</td>
</tr>
<tr>
<td>SWOC &lt;sub&gt;time&lt;/sub&gt; (s)</td>
<td>-.31</td>
<td>2.21, 1.59</td>
<td>.16</td>
</tr>
<tr>
<td>SWOC &lt;sub&gt;steps&lt;/sub&gt;</td>
<td>-.18</td>
<td>1.99, 1.63</td>
<td>-.06</td>
</tr>
<tr>
<td>SWOC &lt;sub&gt;stumbles&lt;/sub&gt;</td>
<td>.23</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SWOC &lt;sub&gt;sop&lt;/sub&gt;</td>
<td>-.23</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Post Assessment – Enrollment**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean diff</th>
<th>95% CI</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPM &lt;sub&gt;Performance&lt;/sub&gt;</td>
<td>2.44</td>
<td>1.33, 3.55</td>
<td>1.87</td>
</tr>
<tr>
<td>COPM &lt;sub&gt;Satisfaction&lt;/sub&gt;</td>
<td>3.24</td>
<td>1.74, 4.74</td>
<td>2.04</td>
</tr>
<tr>
<td>falls</td>
<td>-0.4*</td>
<td>IQR -1, 1</td>
<td>-0.28</td>
</tr>
<tr>
<td>trips</td>
<td>-2.45</td>
<td>IQR 1, 5</td>
<td>-1.42</td>
</tr>
</tbody>
</table>

Bolded values indicate statically significant difference. # Friedman test (p=0.004), * Paired t test (p=0.0006) ^^ Paired t test (p=0.0007), ^ Wilcoxon Signed Rank test (p=0.01). IQR interquartile range. Shaded boxes indicate moderate to large effect sizes.
<table>
<thead>
<tr>
<th>Question</th>
<th>Caregiver responses (n=11) N (%)</th>
<th>Client responses (n=3) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How do you feel about yourself/your child continuing with use of the L300 System?</td>
<td>10 (91%)          Enthusiastic</td>
<td>2 (67)</td>
</tr>
<tr>
<td></td>
<td>1 (9%)              Indifferent</td>
<td>1 (33)</td>
</tr>
<tr>
<td></td>
<td>0                  Unenthusiastic</td>
<td>0</td>
</tr>
<tr>
<td>2. How would you rate the L300 System against other aids to assist your/your child’s gait and function?</td>
<td>9 (82)             More useful</td>
<td>2 (67)</td>
</tr>
<tr>
<td></td>
<td>2 (18)             As useful</td>
<td>1 (33)</td>
</tr>
<tr>
<td></td>
<td>0                Less useful</td>
<td>0</td>
</tr>
<tr>
<td>3. How much help did you/your child need in working the L300 System?</td>
<td>6 (55)             I rarely needed assistance</td>
<td>1 (33)</td>
</tr>
<tr>
<td></td>
<td>3 (27)             I occasionally needed assistance</td>
<td>1 (33)</td>
</tr>
<tr>
<td></td>
<td>2 (18)             I needed assistance almost each time</td>
<td>1 (33)</td>
</tr>
<tr>
<td>4. How satisfied are you with the dimensions (size, height, length, width) of the L300 System?</td>
<td>7 (67)             Satisfied</td>
<td>3 (100)</td>
</tr>
<tr>
<td></td>
<td>4 (36)             More or less satisfied</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0                Not satisfied</td>
<td>0</td>
</tr>
<tr>
<td>5. How satisfied are you child with the ease in putting on and taking off the L300 System?</td>
<td>9 (82)             Satisfied</td>
<td>1 (33)</td>
</tr>
<tr>
<td></td>
<td>2 (18)             More or less satisfied</td>
<td>2 (67)</td>
</tr>
<tr>
<td></td>
<td>0                Not satisfied</td>
<td>0</td>
</tr>
<tr>
<td>6. How would you describe using the L300 System during the day?</td>
<td>4 (36)             Very convenient</td>
<td>1 (33)</td>
</tr>
<tr>
<td></td>
<td>6 (55)             Convenient</td>
<td>2 (67)</td>
</tr>
<tr>
<td></td>
<td>1 (9)              Inconvenient</td>
<td>0</td>
</tr>
<tr>
<td>7. How would you describe your/your child’s walking ability while using the L300 System?</td>
<td>7 (64)             Significantly better</td>
<td>1 (33)</td>
</tr>
<tr>
<td></td>
<td>3 (27)             Better</td>
<td>2 (67)</td>
</tr>
<tr>
<td></td>
<td>1 (9)              Same</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0                Worse</td>
<td>0</td>
</tr>
<tr>
<td>8. While using the L300 System, has there been a change in your/your child’s ability to perform daily tasks or activities?</td>
<td>5 (45)             Can perform more activities</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>6 (55)             Can perform the same</td>
<td>3 (100)</td>
</tr>
<tr>
<td></td>
<td>0                Can perform fewer activities</td>
<td>0</td>
</tr>
<tr>
<td>9. How would you rate your/your child’s confidence in walking with the L300 System versus without it?</td>
<td>9 (82)             More confident with the L300</td>
<td>3 (100)</td>
</tr>
<tr>
<td></td>
<td>2 (18)             No difference</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0                Less confident with the L300</td>
<td>0</td>
</tr>
<tr>
<td>10. Do/does you/your child feel</td>
<td>9 (82)             Yes</td>
<td>2 (67)</td>
</tr>
</tbody>
</table>
Table 3 **Results from Satisfaction Questionnaire**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater confidence in walking on inclines and/or uneven ground while using the L300 System?</td>
<td>2(18)</td>
<td>No</td>
<td>1(33)</td>
</tr>
<tr>
<td>11. Do you find the use of the L300 System safe?</td>
<td>11(100)</td>
<td>Yes</td>
<td>3(100)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>12. Would you recommend a person with your/your child’s condition use the L300 System?</td>
<td>11(100)</td>
<td>Yes</td>
<td>3(100)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>13. Do you wish to continue to use the L300 system?</td>
<td>11(100)</td>
<td>Yes</td>
<td>3(100)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>No</td>
<td>0</td>
</tr>
</tbody>
</table>
Chapter 4 Conclusions and Future Directions

This dissertation research was focused on investigating the effects of using a novel device, FES neuroprosthesis, in children with hemiplegic CP across the ICF domains of body structures and function (BSF) and activities and participation (AP). FES neuroprosthesis intervention in children with CP is a relatively new intervention with only a few studies reporting its efficacy\textsuperscript{12,37-39} on body structure and function outcomes. Evaluating a new intervention’s effectiveness is important before interventions are widely adopted and considered standard of care. This is the first study to evaluate its effects on not only body structure and function outcomes but also activity and participation outcomes, as well as safety and satisfaction. Also, this study investigates several important effects of using the device which can be described as 1) the immediate orthotic effect which indicates change that occurs when initially wearing the device,, 2) a training effect, beyond the immediate effect, which may occur as the patient uses the device, 3) the therapeutic effect which-indicates improvements seen over time without wearing the device and may result from neural plasticity or strengthening of the involved extremity and 4) the total effect which indicates changes over time that includes both the immediate orthotic and training effects. No other pediatric study has assessed the various effects of FES neuroprosthesis device use.

Lessons Learned

At the start of this study we anticipated calling the families weekly during the 12 week home use intervention period to gather information about wear and concerns. Quickly we learned that this was going to be difficult due to family schedules and study team limitations. Therefore we adapted the study protocol to include an additional two (visits 9-10) at monthly intervals which would allow us to download the gait log from the device, have face to face discussions and address any problems with device use. Feedback was provided to the manufacturer regarding the inconsistencies downloading the
gait log for the study. Multiple phone calls occurred between study staff and manufacturer technical support to trouble shoots these difficulties.

Interventions that focus on body structure and function do not necessarily translate to improvements in activities and participation. FES neuroprosthesis primarily intervenes at the body structure and function level (ankle motion, muscle contraction, gait) but if actively used daily during meaningful activities it has the potential to affect an individual’s activity and participation. For this reason we felt it was important to evaluate activity and participation outcomes. In this study results suggest that using FES neuroprosthesis has the potential to improve obstacle negotiation, improve performance and satisfaction with individualized participation goals such as playing hopscotch, baseball, and swimming butterfly stroke. Damiano presents the opinion that wearing an FES neuroprosthesis daily does not constitute task specific active training. However, although no specific instructions were given to engage in task specific training during the intervention phase, participants were instructed to wear the unit several hours a day during normal activity. It is likely that walking and ambulation activities, as well as possibly stairs or obstacle negotiation occurred during normal daily activities. Future work might consider including additional structured task specific voluntary practice of meaningful activities which may result in greater benefit. Satisfaction with the device was high. Some participants did experience skin irritation which can be expected from ongoing electrical stimulation and should be monitored regularly. Orthotic benefits were not immediate suggesting that only after a sufficient amount of time to acclimate and trial the unit should a device be recommended to purchase for home use. Also, a high degree of clinician support and communication is helpful to work through issues with device functioning and skin irritation.

Future Directions
Future research investigating the effects of FES neuroprosthesis in this population should include following this cohort for a longer period of time. The study team was awarded a grant from the Ohio Physical Therapy Association to invite the participants back in 3 more months for another assessment time point. This process is currently underway. Future investigations should address several remaining questions while continuing to examine the immediate orthotic effect, therapeutic effect and total effect of FES neuroprosthesis use.

Confounding effects of other variables

Other factors that may influence response to the intervention include age, baseline function (range of motion and selective motor control of the ankle) and GMFCS level. A recent study\textsuperscript{112} indicates that AFO use peaks at age 5 and decreases with age which is consistent with our experiences that older children, preteens and teenagers, are often unwilling to wear an AFO. FES neuroprosthetic devices have the added attraction in that they are perceived as “cool” technology compared to AFO’s. An individual that chooses not to wear an AFO may be more likely to wear the FES neuroprosthetic device. Age is an important variable to consider also because younger children may also have less tolerance to the stimulation. In our study, participants began with greater available range of motion which may explain the greater mean differences in ankle motion that we observed while wearing the device than other studies. For this reason baseline function with regard to available motion should be considered. Selective motor control refers to the ability to selectively activate muscles without using other muscles to compensate. An individual’s ability to isolate ankle dorsiflexion muscles is likely a factor in their response to wearing the device and how much benefit to expect. Children at GMFCS Level II have more difficulty walking longer distances and with balance activities compared to GMFCS Level I.\textsuperscript{71} For this reason it is important to consider GMFCS level which may affect response to the FES neuroprosthesis intervention.
FES neuroprosthesis combined with other interventions

Although we excluded those who received other interventions near the time of study enrollment, it is likely that FES neuroprosthesis would be used in combination with other therapeutic interventions that address range of motion limitations, such as botulinum toxin, surgery or serial casting. For this reason it is important to consider evaluating FES use combined with these other interventions as it may result in even greater benefit.

Randomized controlled trial

A randomized controlled trial comparing FES neuroprosthesis use to AFO use in this population is warranted. This trial should include a crossover arm so that all could have access to the FES neuroprosthesis which would assist in study recruitment and retention. Participants that are randomized to the current standard of treatment (AFO) would be more likely to remain in the study if they were offered crossover to the FES neuroprosthesis group-the newer intervention.

Sample size calculation was estimated using Power and Sample size v3.0 software (Vanderbilt University). Sample size was calculated based on an independent t test of a continuous response variable (primary outcome $df_{initial}$) with 1 control(s) per experimental subject using $Post_{stim}$ from our study ($df_{initial}$ 4.8 degrees, standard deviation 6.2) and values of $df_{initial}$ in children with CP wearing an AFO in a previous study,$^{113}$ (2.5 degrees standard deviation 4). If the true difference in the experimental and control means is 2.3 degrees with a standard deviation of 5, we will need to study 75 experimental subjects and 75 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. Fewer subjects would be required to determine a difference in the following outcomes of interest: gait speed, $SWOC_{time}$ $SWOC_{steps}$ $SWOC_{stumbles}$ and
Allowing for a 20% drop out rate, 90 participants in each arm should be enrolled. A multi-site study would be necessary to reach the required sample size and would be costly.

**Overall summary and conclusions**

This study found that FES neuroprosthesis use resulted in positive improvements in ankle motion during gait, walking speed, walking endurance, obstacle course negotiation and performance and satisfaction with individualized goals. Furthermore, caregivers and clients were satisfied with using the device. This suggests that daily use of FES neuroprosthesis in children with hemiplegia can affect not only body structure and function but improve an individual’s ability to perform activities and participate in meaningful activities. A larger multi-site randomized controlled trial comparing FES neuroprosthesis to the standard treatment of an AFO and using a comprehensive set of assessments across the ICF is warranted in children with hemiplegic CP.
References


Bailes A. Effects of Functional Electrical Stimulation on Function and Oxygen Cost in Children with Hemiplegia. Gait and Clinical Movement Analysis Society; 2013; Cincinnati Ohio


Appendix A: Accepted abstracts


Effects of Functional Electrical Stimulation on Function and Oxygen Cost in Children with Hemiplegia

Amy F. Bailes¹, Cailee M. Caldwell¹, and Jason T. Long¹,²
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² Cincinnati Children’s Hospital Medical Center, Orthopaedic Surgery
E-mail: amy.bailes@cchmc.org

INTRODUCTION

The most common gait problem for children with hemiplegic cerebral palsy (CP) is foot drop on their affected side, which limits their higher-level ambulation and balance skills. Current treatment for hemiplegia consists of wearing an ankle foot orthosis (AFO) to prevent deformity and to improve joint alignment and biomechanics. Wearing an orthosis may limit active movement and motor learning, and contribute to muscle weakness. In addition, older children are often unwilling to wear an AFO due to the bulk and discomfort.

Functional electrical stimulation (FES) neuroprostheses have demonstrated effects on dorsiflexion during gait,¹ muscle size,² and muscle function³ in children with hemiplegic CP. However, less evidence is available regarding their effects on functional activities and oxygen cost. The purpose of this case series was to determine the effect of FES neuroprosthesis use on functional activities and oxygen cost in individuals with hemiplegic CP. Our secondary purpose was to assess the tolerance of individuals and their families to the battery of tests used in this study. Timed up and down stairs (TUDS) and the one minute walk test (1MWT) were administered to individuals during a routine clinic visit. In addition, net nondimensional oxygen cost (NNcost)⁴ was assessed with the Cosmed K4b² (COSMED srl; Rome, Italy) during the 1MWT.

CLINICAL SIGNIFICANCE

The use of new technology requires understanding the changes it imposes on body structure and function (e.g. range of motion). Practitioners also need to understand how such changes affect a child’s functional performance and resulting participation in meaningful activities.⁴

METHODS

Five children with hemiplegic CP and unilateral foot drop (ages 6-9 years; GMFCS I-II) were recruited and provided consent and assent for this study. None of the participants had received botulinum toxin within 6 months or surgery within the past year. Participants were assessed in a quiet hallway and stairwell during a regular clinic visit. Comfortable shoes and the FES unit were worn for all testing procedures; participants who normally used an AFO removed it during
testing. The TUDS and 1MWT were administered first in the No Stimulation condition (“No Stim”), followed by the Stimulation condition (“Stim”). During the 1MWT, NNcost was measured with the Cosmed K4b². Between measures; the participant was provided with a seated 5-minute rest. The caregiver provided information regarding the participant’s ability to tolerate the assessments and the caregiver’s willingness to complete the assessments in the future. The scores were compared for each assessment in each condition.

RESULTS

All participants were able to complete the assessments. Participant 4 demonstrated improvement (decreased time, 9.2%) on the TUDS in the Stim condition. All other participants demonstrated increased time (6.7-14.2%). Participants that were classified as GMFCS-I (n=3 of 5) improved their 1MWT scores in the Stim condition (increased distance 10.2-17.5%). All participants demonstrated an increase in NNcost in the Stim condition (11.1-44.4%).

DISCUSSION

Compared to previous studies, participants in this study demonstrated increased TUDS⁶ scores and decreased 1MWT⁷,⁸,⁹ distance scores in both Stim and No Stim conditions. The younger age of our participants limits our ability to compare these results to the existing literature. Increased NNcost measures in all participants suggest increased energy demand in the Stim condition. There is no clear link between magnitude of increase and any demographic parameter (length of device use, GMFCS level, etc.). The NNcost assessment was well-tolerated by all participants in both conditions, but the brief duration of testing (i.e. 1 minute) makes it difficult to compare these results to other published values. Of interest is the effect of FES use on stair climbing in Participant 4, who has been using the device the longest without any concurrent AFO use. This may suggest an improvement in stair-climbing function associated with FES use that is acquired over time.

Table 1. Subject demographics.

<table>
<thead>
<tr>
<th>Item</th>
<th>Participant</th>
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<td>-</td>
</tr>
<tr>
<td>AFO Use?</td>
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</tr>
</tbody>
</table>

Table 2. Results of assessments. NNcost is unavailable for Subject 4 due to hardware malfunction.
REFERENCES


DISCLOSURE STATEMENT

Amy Bailes and Jason Long have no conflicts of interest to disclose.
2. Poster accepted for presentation at American Physical Therapy Association
Combined Sections Meeting February 7, 2015

**Background and Purpose:** Functional electrical stimulation (FES) neuroprostheses offer an alternative to ankle foot orthoses (AFOs) for children with hemiplegia. Studies suggest FES use at the peroneal nerve improves ankle dorsiflexion\(^1\) muscle size\(^2\) and muscle control\(^3\) in children with hemiplegia. Effects on oxygen cost and functional skills have not been investigated. The purpose of this preliminary work was to evaluate prospectively the total effect of FES neuroprosthesis use (Bioness L300) on lower extremity motion patterns, oxygen cost, and functional skills, in five children with hemiplegic CP.

**Number of subjects:** Five participants with hemiplegic CP (GMFCS I-II, 4 male, 6-16yrs) participated at an outpatient pediatric hospital-based therapy clinic.

**Materials/Methods:** Participants were assessed before (baseline) and after (post) a 16-week intervention with the FES neuroprosthesis that consisted of a 4 week training period followed by 12 weeks of daily use for up to 6 hours day. No child received botulinum toxin within 6 months or surgery within the past year. Measures included peak ankle dorsiflexion in swing (\(Df\), degrees), gait deviation index (\(GDI\), unitless), net nondimensional oxygen cost (\(NNcost\), unitless) during the 6 minute walk test (\(6MWT\), feet), and the number of steps to complete the standardized walking obstacle course (\(SWOC\)). Measures were tested at baseline with no stimulation and at post with stimulation.

**Results:** All 5 participants (P1-P5) completed the protocol, with three participants demonstrating improvement in peak ankle \(Df\) in swing: P2 increased from 1.9 to 14.3 degrees; P4 increased from 4.4 to 8.7 degrees and P5 increased from 6.1 to 12 degrees. On average, \(GDI\) improved from 78.6 to 82.6, with 3 of the 5 participants demonstrating improvement. Four participants demonstrated improvements in \(NNcost\), \(6MWT\) and \(SWOC\). On average, the \(NNcost\) decreased from 0.41 to 0.32 with a range of -0.03 (P5) to -0.21 (P1). Increases in the \(6MWT\) ranged from 114 feet (P5) to 459 feet (P4), with 2 participants exceeding the minimal detectable change (MDC). The number of steps to complete the \(SWOC\) decreased in 4 of the 5 participants ranging from -1.5 steps (P4, P5) to -3 steps (P2).

**Conclusions:** In this study, positive total effects of FES neuroprosthesis use were seen in peak ankle \(Df\) in swing and \(GDI\) by 3 participants and in the \(6MWT\), \(NNcost\) and the \(SWOC\) by 4 participants. The youngest in the sample (P1), showed improvement in only 2 outcomes which may be due to a level of discomfort and the need for more training in younger children.
Clinical Relevance: FES neuroprosthesis use has the potential to improve *Df, NN cost, GDI, 6MWT* and *SWOC* in children with hemiplegia. Including measures of gait efficiency and function may provide clinicians with additional information to assist in evaluating the benefits of FES neuroprosthesis. A larger sample is needed to determine if specific child characteristics can be associated with a better response to FES neuroprosthesis. Future work should evaluate the carryover or therapeutic effect of FES neuroprosthesis use when the unit is no longer worn.

Keywords: neuroprosthesis, cerebral palsy, hemiplegia
Appendix B: Pedal with Pete Foundation Award Letter

Amy Bailes, PT, MS, PCS  
Cincinnati Children’s Hospital Medical Center  
Division of Occupational Therapy and Physical Therapy  
3333 Burnet AV  
Cincinnati, OH 45229  
513/803-0782  
Amy.bailes@cchmc.org

January 20, 2013

Dear Ms. Bailes:

On behalf of the Pedal with Pete Foundation, I am pleased to report that a grant in the amount of $30,000 will be awarded to your research at the Cincinnati Children’s Hospital Medical Center “Effects of Functional Electrical Stimulation Neuroprosthesis in Children with Hemiplegic Cerebral Palsy.” We are excited to contribute to an outstanding institution and researcher that promotes excellence in research and services for the benefit of people with cerebral palsy. Please let me know who the check should be written to and where it should be mailed.

We view this contribution as not only a donation, but also a partnership between your institution and the Pedal with Pete Foundation to help raise awareness about cerebral palsy and to improve the quality of life for persons living with cerebral palsy. Our hope would be that through increased exposure through your institution, Cincinnati Children’s Hospital Medical Center, the Pedal with Pete Foundation will generate interest to assist us in expanding our Rides to Cincinnati, and expand our mission to raise even more money for cerebral palsy research. Any suggestions or contacts (the Cincinnati Children’s, professional and CP parents’ groups) that we might follow up on would be very much appreciated as our Foundation would like to establish a Ride in Cincinnati. Pedal with Pete Foundation would love to fund more researchers at Cincinnati Children’s and continue to fulfill our mission of advancing meaningful cerebral palsy research.
In accordance with our grant request, we look forward to reviewing a semi-annual progress report that includes the amount of grant monies used to-date on the research project. This periodic progress report is important so as to allow us to report to the Foundation’s donors and to keep us appraised on the research study’s progress. Additionally, we would be very interested to hear about future research grant applications.

We are excited about this opportunity to collaborate together and hope that this alliance will increase exposure for both the Pedal-with-Pete Foundation and your research, and most importantly, result in meaningful research that leads to improving the lives of persons with cerebral palsy.

Sincerely,

Mimi Singh
Chair, Research and Education Committee
Pedal-with-Pete Foundation
Appendix C: IRB Documents

Initial IRB approval: Institutional Review Board - Federalwide Assurance #00002988

Cincinnati Children’s Hospital Med Ctr

Date: Wednesday, February 06, 2013

From: IRB Committee

To: Principal Investigator: Amy Bailes
   Occupational & Physical Therapy

Study ID: 2012-4682
Re: Study Title: Effects of functional electrical stimulation neuroprosthesis in children with hemiplegic cerebral palsy.

The above referenced protocol and all applicable additional documentation provided to the IRB were reviewed and APPROVED using an EXPEDITED review procedure in accordance with 45 CFR 46.110(b)(1)(see below) on 2/6/2013.

This study will be due for continuing review at least 30 days before: 2/5/2014.

Study Documents
Assent v.1 12.21.doc
Bailes biosketch
Bailes Pedal with Pete IRB protocol revision version 3 2.5.13docx
BailesPedal with pete
BIONESS FDA DOCS.pdf
Letter of support from OTPT Director
Long biosketch
Parental permission v.112.22.doc
protocol encounter form for pedal with pete study.doc
questionnaire Bailes pedal with pete grant
schmit biosketch
tremper biosketch

Please note the following requirements:
**Per 45 CFR 46.408** the IRB has determined that at least 1 parent(s) (or guardian) must give permission for the inclusion of a child in this research and that permission must be documented by signature on the IRB approved parental permission form.

**Per 45 CFR 46.408** the IRB has determined that documented assent must also be obtained from all child participants between 11 and 18 years of age.

**Per 45 CFR 164.508** the IRB has determined that all adult participants and/or the legally authorized representative of child participants must provide authorization for the use and/or disclosure of the protected health information in the conduct of this research.

**AMENDMENTS:** The principal investigator is responsible for notifying the IRB of any changes in the protocol, participating investigators, procedures, recruitment, consent forms, FDA status, or conflicts of interest. Approval is based on the information as submitted. New procedures cannot be initiated until IRB approval has been given. If you wish to change any aspect of this study, please submit an Amendment via ePAS to the IRB, providing a justification for each requested change.

**CONTINUING REVIEW:** The investigator is responsible for submitting a Continuing Review via ePAS to the IRB at least 30 days prior to the expiration date listed above. Please note that study procedures may only continue into the next cycle if the IRB has reviewed and granted re-approval prior to the expiration date.

**UNANTICIPATED PROBLEMS:** The investigator is responsible for reporting unanticipated problems promptly to the IRB via ePAS according to current reporting policies.

**STUDY COMPLETION:** The investigator is responsible for notifying the IRB by submitting a Request to Close via ePAS when the research, including data analysis, has completed.

**Please note:** This approval is through the IRB only. You may be responsible for reporting to other regulatory officials (e.g. VA Research and Development Office, UC Health – University Hospital). Please check with your institution and department to ensure you have met all reporting requirements.

**Statement regarding International conference on Harmonization and Good clinical Practices.** The Institutional Review Board is duly constituted (fulfilling FDA requirements for diversity), has written procedures for initial and continuing review of clinical trials: prepares written minutes of convened meetings and retains records pertaining to the review and approval process; all in compliance with requirements defined in 21 CFR Parts 50, 56 and 312 Code of Federal Regulations. This institution is in compliance with the ICH GCP as adopted by FDA/DHHS.
Thank you for your cooperation during the review process.

**Research Categories**

1. **Clinical studies of drugs and medical devices** only when condition (a) or (b) is met: (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.) (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
Most current IRB approval: Institutional Review Board - Federalwide Assurance #00002988

Cincinnati Children’s Hospital Med Ctr

Date: 1/24/2014

From: CCHMC IRB Committee

To: Principal Investigator: Amy Bailes
    Occupational & Physical Therapy

Study ID: 2012-4682
Re: Study Title: Effects of functional electrical stimulation neuroprosthesis in children with hemiplegic cerebral palsy.

The above referenced protocol and all applicable additional documentation provided to the IRB were reviewed and RE-APPROVED using an EXPEDITED review procedure set forth in 45 CFR 46.110(b)(1), Category(ies)(see below) on 1/23/2014.

This study will be due for continuing review at least 30 days before 1/22/2015

Study Documents
Assent version 3
Bailes biosketch
Bailes version 5
Bailes Pedal with pete
BIONESS FDA DOCS.pdf
FEs recruitment digital70-13 CP digital-2.pdf
FES recruitment large pad CP-LG+pad-3.pdf
FES recruitment small CP-sm3.pdf
FES recruitment_web_HemiplegicCerebralPalsy.doc
Letter of support from OTPT Director
Long biosketch
Parental permission version 3
protocol encounter form for pedal with pete study.doc
questionnaire Bailes pedal with pete grant
schmit biosketch
tremper biosketch
Continuing Review Documents:
4682 consent
Appendix D: Recruitment materials

Needed: 6 to 17 Year Olds with Hemiplegic Cerebral Palsy

This is a research study to see if wearing a device that delivers electrical stimulation to muscles, called functional electrical stimulation (FES), helps children and teens with hemiplegic cerebral palsy to walk, play and perform other functional tasks.

Those eligible to participate are children and teens 6 to 17 years old who:
- Have been diagnosed with hemiplegic cerebral palsy (meaning an arm and leg on one side of the body are affected)
- Can walk without the use of assistive devices such as a walker or cane

For more information, contact Amy Bailes at amy.bailes@echmc.org or 513-803-0782.
Appendix E: Geomapping of participants