# SOMATOSENSORY DEFICITS AFFECT BALANCE AND MOTOR FUNCTION IN CHILDREN WITH CEREBRAL PALSY. STOCHASTIC RESONANCE STIMULATION CAN MODULATE SOMATOSENSATION TO ENHANCE BALANCE.

by

Anastasia Zarkou

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biomechanics and Movement Science

Summer 2017

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## ACKNOWLEDGMENTS

It is hard to believe that this journey is finally coming to an end. It feels like yesterday when I first visited the University of Delaware and kept thinking while walking through the campus how lucky I was that I was able to fulfil one of my dreams. Looking back, I can now say with certainty that I couldn't have completed my Ph.D. without the support of my professors, colleagues, friends, and family; especially during the times when I was feeling nostalgic for Greece.

Foremost, I would like to thank my advisor, Dr. Samuel Lee, for giving me the opportunity to pursue my own research ideas while sharing his time and expertise in helping me to successfully accomplish them. Thank you Dr. Lee for helping me grow into a better researcher with confidence. I am grateful to my dissertation committee members for their support: Dr. Galloway, thank you for your inspirational lectures and constructive critique on my work. Dr. Modlesky, thank you for your earnest feedback and for sharing your knowledge on Cerebral Palsy. Dr. Prosser, thank you for your support in my academic and non-academic life. Your invaluable guidance and encouragement was critical in completing this dissertation. I would also like to express my deep appreciation to Dr. Jeka for embracing me as an "unofficial" member of his team. Finally, Dr. Binder-Macleod thank you for always being available, for your constructive feedback and career development advice.

I am truly grateful of being a member of the BIOMs community. A special thank you to my lab mates from both the Lee and Jeka Labs: Ahad Behboodi, Henry Wright, James Alesi, Melissa Torres, Dr. Hwang, and Peter Agada. I would like to

particularly thank Dr. Nicole Zahradka for being a great friend and colleague. This work would have never been completed without the support of our lovely participants and their families. Their kind words fueled my motivation. Finally, I am thankful to my dear friends: Zoi, Chrissa, Maria, and Sofia for their encouragement.

I dedicate this dissertation to my beloved parents, Ioanni and Dafni, and my sister, Thelxi, who patiently stayed by my side all these years, believing in me and endlessly encouraging me in every step of this journey. To my two baby nieces, Nefeli and Irida, who brighten up my life. Last but not least, to Dr. Michail Vafeiadis, who throughout my Ph.D. life in the United States was my friend, my hope, my smile, my love …and now my husband.

For all the people who follow their dreams:

**Ihtaka** by C. P. Cavafy

"As you set out for Ithaka,
Hope your road is long one, full of adventure, full of discovery…
…Keep Ithaka always in your mind, arriving there is what you're destined for…
…Ithaka gave you the marvelous journey…
…Wise as you will have become, so full of experience, you'll have understood
by then what these Ithakas mean."

(*Collected Poems: Princeton University Press, 1975)*

A special thanks to the Onassis Foundation that partially supported my dissertation work. This research was supported by Shriners Hospitals for Children- Philadelphia under the grant: #22173 PHI.

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## ABSTRACT

Traditional rehabilitation and motor learning approaches in Cerebral Palsy (CP) are generally motor-centric focusing on how to improve musculoskeletal and motor impairments, and are marginally effective. Less attention has been paid to deficits in sensory processing that could potentially shape motor behavior, especially in relation to dynamic control of upright stance. Recent neuroimaging evidence on disrupted thalamocortical connections and aberrant somatosensory cortical activation supports the presence of sensory dysfunction in children with CP. Yet, limited research has thus far explored somatosensory deficits in lower extremities (LE) and how they influence motor ability in CP. Additionally, there is not a universally accepted framework for the diagnosis and treatment of sensory information and processing impairments in this population. Hence, the purpose of this dissertation was to identify distal LE somatosensation deficits, delineate their relationship with balance and motor function, and investigate if they can be modulated by utilizing Stochastic Resonance (SR) stimulation to enhance balance control in CP. Our results indicated that children with spastic diplegia exhibited diminished plantar cutaneous and ankle proprioceptive ability that may influence their balance and motor control; therefore, contributing to their poor functional performance. Applying SR stimulation in the LE during quiet stance resulted in decreased postural sway suggesting enhanced stability and, thus, SR may be used as a therapeutic tool to improve balance performance by up-regulating somatosensory information in CP. From a clinical standpoint, these findings could lead to an improved therapeutic management in CP by: 1)

recommending the use of an easy to administer and cost effective battery of sensory tests in daily practice to identify individuals with somatosensory impairments, 2) assisting clinicians to design more effective subject-specific plans by targeting not only motor but also sensory deficits, and 3) introducing SR stimulation as a novel sensory-oriented method for somatosensory facilitation and training balance control in CP. Specifically, combining afferent SR stimulation while performing daily activities may promote neuroplasticity and, as a result enhance motor and sensory function compared to traditional motor-centric protocols.

# Chapter 1

# INTRODUCTION

## 1.1 Background and Significance

### Cerebral Palsy

Cerebral Palsy (CP) is the most common pediatric neurological condition that results in physical disability and has been associated with decreased health-related quality of life[1] and high economic cost[2]. According to the United Cerebral Palsy, approximately 764,000 individuals with CP live in the United States[3] and its prevalence ranges from 2 to 3.9 per 1000 live births[4–6]. CP is 30% higher in males than females with an overall ratio of 1.5: 1 (boys: girls)[7], as well as higher for black than non-Hispanic children[5,7]. A traditional classification of CP is based on the type of muscle tone disorder (spastic, dyskinetic, or ataxic) and impairment location (hemiplegia, diplegia, or tetraplegia). Spastic CP, the most common subtype, represents 77- 81% of the population[5–7], with bilateral CP being more prominent[5,7].

Children with CP present a wide range of motor disability patterns that affect their physical activity and create barriers to social participation, an important factor of their well-being (i.e. World Health Organization's International Classification of Functioning, Disability, and Health (WHO- ICF) model of disability). Although the injury to the developing brain is not progressive, it results in motor and postural impairments that are progressive throughout their lifetime[8] and related with reduced ambulatory ability[9] and poor balance performance[10–12].

**Postural Control in CP**

Normal postural control has been characterized as a complex motor skill that requires the interaction of motor, sensory and cognitive systems to control a body's position in space for the purposes of orientation and stability[13,14]. Multiple physiological systems contribute to maintaining upright stance (**Figure 1.1**), while the control of posture depends on the active interaction between the individual, the performed task and the environment[14]. In contrast to normal postural responses, CP postural control characteristics include: descending pattern of muscle recruitment (proximal to distal strategy)[15], reverse order of muscle activation (antagonist followed by agonist activation)[15,16], compensatory agonist/antagonist coactivation[14], inability to quickly modulate postural responses to adapt to perturbations[14], and presence of sensory deficits[17–22]. All of these factors affect the ability of individuals with CP to maintain their standing balance.


**Figure 1.1** This model represents the underlying systems that contribute to postural control. Adapted by Horak et al. (2009)[23].

Flexible postural control and motor planning require organizing and integrating sensory inputs to efficiently coordinate motor actions[13,14,23]. Based on the sensory weighting theory of postural control, information from the visual, vestibular, and somatosensory systems are regulated dynamically to adapt in a constant changing environment[14,24]. For example, when vision is occluded the central nervous system (CNS) depends on somatosensory cues to maintain the upright stance in a firm surface, whereas while standing upon a compliant surface the CNS relies predominantly on vestibular cues for stability. Impairments in any of the sensory systems (e.g. somatosensory) would alter the reweighting process, as information from the intact system (e.g. visual or vestibular) compensates by upregulating feedback during balance tasks; regardless of the type of support surface or the visual feedback condition[24]. Therefore, deficits in at least one of the aforementioned sensory systems likely contribute to the poor postural and balance control exhibited by individuals with CP.

**Sensory Impairments in CP**

The reclassification of CP acknowledges the contribution of impaired sensation in motor performance[8]. In this context, Hoon et al. (2009) proposed a theoretical model that emphasized the influence of thalamocortical (i.e. sensory) pathway disruptions on motor impairments in individuals with spastic CP (**Figure 1.2**)[25]. Specifically, by using diffusion tensor imaging (DTI), they demonstrated a more severe injury in the sensory white matter tracts than in the motor (i.e. corticospinal) tracts of children with periventricular leukomalacia[25]. Interestingly, Hoon and colleagues found that only the sensory pathway injury, not the motor pathway injury,

was significantly related with mobility, strength, touch threshold, and proprioception measures[25]; supporting the important role of sensory information on motor function. Numerous imaging studies have provided evidence on sensory dysfunction in CP[25–29]. Specifically, the reported thalamocortical connection injury[25,28] may result in abnormal or limited transmission of afferent information to the cortex contributing to the abnormal activation of the somatosensory cortical areas[26,27] and thus, influencing the sensorimotor cortical connectivity[29]. The impaired transmission and processing of afferent information, therefore, would negatively affect motor performance in CP. For example, diminished and desynchronized neural activity in somatosensory cortices has been correlated with walking and ankle strength deficits[27], as well as with impaired feedback[26] and feedforward mechanisms[30]; suggesting that poor processing and integration of somatosensory information can lead to diminished postural and motor control in CP.

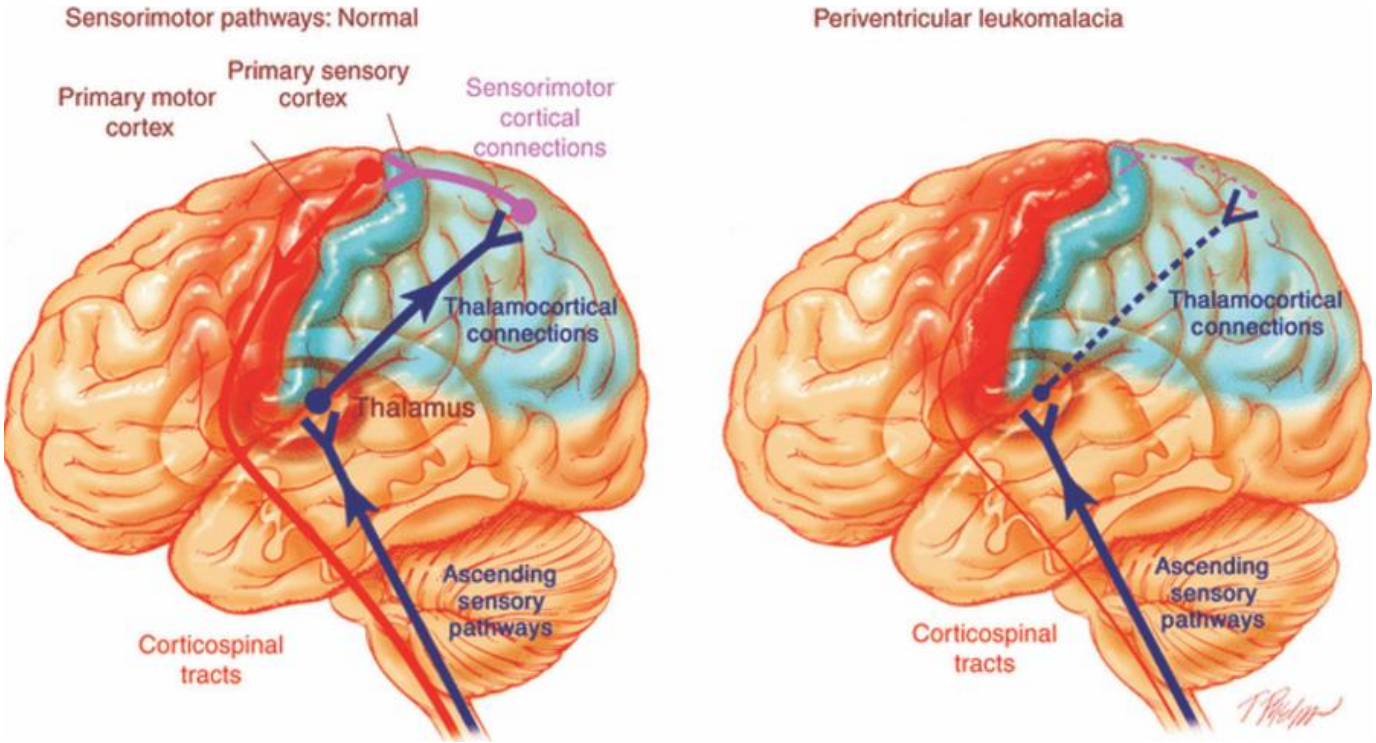


**Figure 1.2** Schematic illustration of the simplified theoretical model of motor impairment associated with sensory and motor white matter pathway injury. On the left, a TD brain is presented with the sensorimotor pathways intact. In the CP model (image on the right), the dotted blue line shows the disrupted thalamocortical connections that potentially contribute to the aberrant sensorimotor cortical connectivity (dotted purple line) and, thus, further accentuate the injury in the corticospinal tracts (thin red line). Adapted by Hoon et al. (2009)[25].

Likewise, clinical studies reported that children with CP have somatosensory impairments in light touch pressure[17,18,22,31], two-point discrimination[17,18,31,32], stereognosis[17,18,31,32], vibration[22], and proprioception[22,31,33] . Most of the literature has focused on the upper extremity (UE) somatosensory deficits[17,18,31,32] in approximately 75% - 90% of the CP population[17,34]. A series of studies by Auld and colleagues utilized a battery of sensory tests, after validating its reproducibility[19], to assess UE tactile ability in unilateral CP[17,18]. Their findings confirmed that children with hemiplegia have poor tactile function in the impaired hand, but also simultaneous dysfunction in the unimpaired hand compared to a group of typically developing (TD) children[17]. In addition, these deficits influenced their unimanual and bimanual performance even when proprioceptive and visual information were available, thus illustrating the important role of tactile ability in motor performance[18]. As such, the authors highlighted the importance of using a clinical sensory evaluation in clinic and research settings to guide rehabilitation interventions[17], especially since sensory examinations are often excluded in daily practice to save time or to focus on the more obvious motor deficits in CP[22].

**Lower Extremity Somatosensation in CP**

Somatosensory feedback from the lower extremities (LE), including both tactile and proprioceptive information, is crucial for balance control[35–37]. Cutaneous receptors from the sole of the foot provide tactile inputs on spatial and temporal plantar pressure distribution[35]. Joint position sense and kinesthesia primarily depend on proprioceptive information provided by the muscle spindles, Golgi tendons, and joint receptors[38]. Together, the interplay of the aforementioned somatosensory signals allows for a stable posture[37] and gait[39] by triggering appropriate postural responses.

Loss of plantar sensation can exacerbate proprioceptive deficits and result in increased postural sway velocity and decreased balance ability when local anesthetic injections are administered in the plantar side of the feet of healthy individuals[40]. Additionally, individuals with peripheral nervous system disorders[41] and multiple sclerosis[42] exhibit poor foot and ankle tactile and proprioceptive ability that negatively affects their standing balance. Although recent imaging studies have indicated aberrant activity of somatosensory cortices representing the foot in CP[26,43,44], the somatosensory deficits in this population are not well defined.

Only a few studies have investigated lower extremity (LE) somatosensation in CP and found diminished pain, scratch sensation, and joint position sense in the knee[22] and hip joints[33]. Hip proprioceptive deficits in unilateral and bilateral CP contributed to increased postural sway and decreased gait velocity, indicating the strong relationship of LE somatosensation with balance and mobility[45]. Although distal LE impairments are more prominent and severe than proximal impairments in spastic diplegia[46], there is lack of information on foot and ankle somatosensory function in CP. Previous work provided evidence on the relationship between the somatosensory cortical response to foot tactile stimulation and mobility[43]. However, the contribution of plantar cutaneous afferents and proprioceptive information of ankle joints to balance control and motor performance in CP still remains unclear.

Altogether, quantifying foot and ankle tactile and proprioceptive deficits may provide insights about the nature and extent of somatosensory impairments in CP and potentially assist in developing a comprehensive LE sensory test battery that will lead to improved identification of body function impairments. Moreover, characterizing the relationship between distal LE somatosensation and motor function may provide the

foundation for designing more effective training programs since it has been suggested that new sensory-oriented therapeutic approaches can potentially improve the structural integrity of motor and sensory pathways in CP[47].

**Modulating distal LE somatosensation to enhance balance in CP**

Stochastic resonance stimulation (SR) may be an effective stimulus to upregulate afferent input in individuals with CP to improve postural control. SR stimulation is a type of subsensory random noise that improves a nonlinear system's sensitivity and, in turn, increases a weak signal's detectability[48,49]. Two different types of SR have been reported in the literature: mechanical (i.e. subsensory vibratory noise)[50–53] and electrical (i.e. subsensory electrical noise)[50,54–60]. Both SR types have been found to improve postural control when applied to the sole of the feet[50,51], knee joint[50,61], mastoid processes[57,58,62], shank muscles[54,55,58–60], and ankle joint ligaments[58,60].

One potential neurophysiological mechanism describing the SR phenomenon at the sensory receptor level is that the applied subthreshold electrical noise increases the receptor's excitability, which, in turn, makes the sensory neuron more likely to fire an action potential and, thus, allows the detectability of a weak afferent signal[50]. Moreover, SR is not only present in the peripheral receptor level but in the neuronal pathways of CNS as well[63,64]. For instance, Iliopoulos et al (2014) applied an unperceivable tactile stimulus and SR electrical noise into two distinct peripheral receptors (**Figure 1.3: B**)[64]. It is likely that these two signals converged in the CNS resulting in increased detectability of the weak tactile input[64]. Another interesting characteristic of SR is the inverted U-shaped relationship between signal's detectability and noise's intensity suggesting that an optimal level of noise is needed

to enhance signal detection[48,49,63,64] and, therefore, an optimization procedure should be followed to identify the subject- specific optimal SR intensity for SR testing[52,55,57,62].

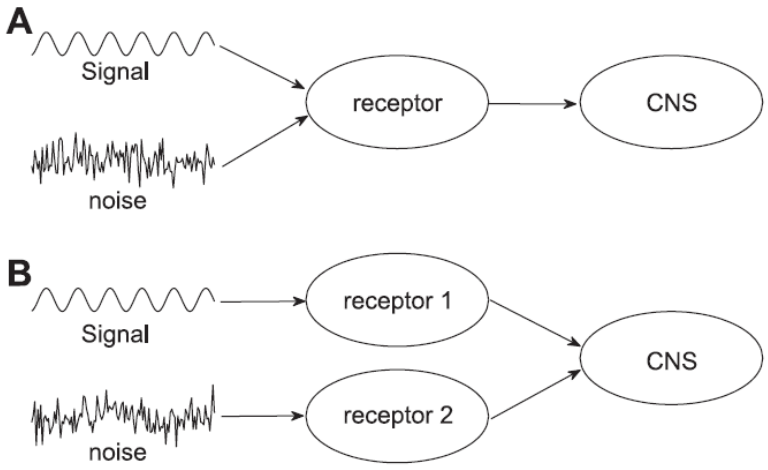


**Figure 1.3** To identify if SR is occurring not only in the peripheral but also in the central nervous system, a double receptor design (B) should be utilized. Compared to a single receptor design (A), in the double receptor design (B) the unperceivable afferent signal and SR noise are introduced in two different receptors and, therefore, any beneficial effect of SR could be attributed to the interaction of the signal and the noise in the CNS. Adapted by Aihara et al. (2010)[63].

SR has been used to enhance balance in healthy adults[50,54,56–58], older people[50,51], individuals with functional ankle instability[59,60,65], and patients with diabetic neuropathy and stroke[66] by improving sensory signal strength in the somatosensory[50,58,60,61,66] and vestibular[57,58,62] systems. Recent evidence indicated that therapeutic interventions using SR stimulation have ameliorated proprioceptive deficits[65] and balance disturbances earlier and to a greater extent than traditional

rehabilitation in individuals with ankle instability[67]. Despite the potential promise of SR in improving postural control, its use in CP population is novel. If SR stimulation can, indeed, modulate sensory deficits to improve postural control, it can be a promising tool that, upon further development, could be used as part of future therapeutic interventions for the treatment of balance deficits in children with CP.

**Dissertation's Overall Goal**

Balance impairments in CP have been associated with poor functional mobility[14], increased risk for falls and higher levels of caregiver dependence[10], consequently affecting the overall quality of life of children with CP. Currently, rehabilitation interventions in CP focus on improving functional performance and decreasing motor deficits[68–71] but with limited consideration of sensory impairments whose deficits affect motor and balance control. Since sensory information and integration are key components of postural control, therapeutic plans should include the assessment of the sensory modalities and facilitation as part of the everyday treatment procedure. This series of studies is the first to determine the presence of foot and ankle somatosensory deficits in children with CP and delineate their relationship with balance and motor function. Additionally, to modulate distal LE somatosensation, electrical SR stimulation is used to enhance an afferent signal's detectability and improve balance performance in this population. The overall goal of this work is to provide important insights to inform clinicians on the assessment and treatment of distal LE somatosensory impairments to improve overall functionality in children and adolescents with CP.

## 1.2 Specific Aims and Hypotheses

Traditional rehabilitation and motor learning approaches in CP are generally motor-centric, focusing on techniques to improve musculoskeletal and motor impairments. Less attention has been paid to deficits in sensory processing that could potentially shape motor behavior, specifically in relation to dynamic control of upright stance. Recent neuroimaging studies in individuals with CP reported aberrant somatosensory cortical activation and severe injury not only in the descending corticospinal connections related to motor function, but also in thalamocortical sensory pathways. These findings suggest an essential link between the sensory and motor areas on motor performance. Although previously investigated in other populations, the relationship between foot and ankle somatosensory ability on balance and motor function has not been studied in children with CP.

Approaches to improve distal somatosensation, like SR stimulation, have been used to enhance balance in older adults and in individuals with peripheral neuropathy, functional ankle instability, and stroke. In particular, SR stimulation has been shown to reduce postural sway in individuals with sensory deficits by improving the detection and transmission of afferent information. SR is an inherent phenomenon in which a random subsensory noise improves a nonlinear system's sensitivity to differentiate a weak somatosensory signal and thereby potentially enhances essential sensory information processing for self-orientation and equilibrium control of upright stance. Despite the potential promise of SR in improving balance performance, its application in individuals with CP is novel.

The purpose of this dissertation is to determine the presence of foot and ankle somatosensory deficits in children with CP and delineate their relationship with motor function. SR stimulation will be used to modulate somatosensory information to

enhance balance control, which may positively influence functional performance and the overall quality of life of individuals with CP.

**Aim 1: To compare foot and ankle somatosensory ability between children and adolescents with CP and their typically developing (TD) peers.**

A battery of sensory tests, traditionally used in clinical settings, will be used to assess foot and ankle somatosensory ability (light touch-pressure, two-point discrimination, vibration, joint position sense, and kinesthesia) in individuals with CP and their TD peers. The scores for all the somatosensory measures will be documented and compared between the CP and TD groups.

**Hypothesis 1.1:** Individuals with CP will demonstrate diminished tactile ability (light touch-pressure, two-point discrimination, and vibration sensation) compared to their TD peers.

**Hypothesis 1.2:** Individuals with CP will demonstrate diminished proprioceptive ability (joint-position sense and kinesthesia) compared to their TD peers.

**Aim 2: To investigate the relationships between foot and ankle somatosensory ability with postural control, balance performance, gross motor and walking ability, functional mobility, and strength in children and adolescents with CP.**

A battery of sensory tests as described in Aim 1 will assess somatosensory ability. Postural control and balance performance will be assessed by using the Balance Evaluation System Test (BESTest) as well as Center of Pressure (COP) measures. Gross motor ability will be evaluated with the Gross Motor Functional

Measure (GMFM-66-IS). Spatiotemporal gait characteristics will be used to describe walking ability. Functional mobility will be assessed by performing the Timed Up and Go (TUG), and 6-Min Walk (6MWT) Tests. The strength of the ankle plantar flexors will be measured by testing the maximum volitional isometric contraction (MVIC). Correlation analysis will be performed to define the relationships between each of the tested somatosensory modalities with the examined balance and motor variables.

**Hypothesis 2.1**: Foot and ankle somatosensory ability will be related to postural control, balance performance, gross motor and walking ability, functional mobility, and strength in individuals with CP.

**Aim 3: To investigate the immediate effect of somatosensory SR electrical stimulation on balance performance in children and adolescents with CP and their TD peers.**

Somatosensory SR electrical stimulation will be applied to the muscles and ligaments of the ankle joints during quite upright stance with and without visual feedback. Balance performance will be evaluated by using the COP measures. To investigate the effects of SR on children with CP, the COP measures will be compared between the SR stimulation and the control-no stimulation "sham"-conditions. Lastly, we will compare the improvements in the COP measures due to the application of SR between the CP and TD group, to examine which group can benefit more by SR stimulation.

**Hypothesis 3.1**: Somatosensory SR electrical stimulation will enhance balance performance in individuals with CP compared to a sham control condition without SR stimulation.

**Hypothesis 3.2**: Individuals with CP will demonstrate greater improvements in their balance performance when somatosensory SR electrical stimulation is applied compared to their TD peers.

# Chapter 2

# FOOT AND ANKLE SOMATOSENSORY DEFICITS IN CHILDREN WITH CEREBRAL PALSY

## 2.1 Abstract

Upper extremity somatosensory deficits are prevalent in individuals with cerebral palsy (CP). However, there are only limited information on lower extremities' (LE) somatosensation in CP, despite its prominent role in postural control and motor performance. Thus, the objective of this study was to investigate the foot and ankle tactile and proprioceptive ability in children with cerebral palsy (CP) by using a simple and cost-effective battery of clinical sensory tests and compare their results to typically developing (TD) age-matched individuals.

Ten children with CP (mean age 15y 5mo [SD 2y 9mo]; spastic diplegia; GMFCS I- III) and 11 TD peers (mean age 15y 10mo [SD 2y 2mo]) participated in the study. Light-touch pressure and two-point discrimination were assessed in the plantar side of the foot by using a monofilament kit and an aesthesiometer, respectively. The duration of vibration sensation at the first metatarsal head and medial malleolus was also recorded. Finally, the error in joint position sense and kinesthesia of the ankle were tested.

Our findings indicated diminished tactile and proprioceptive ability in the CP group. In particular, plantar light touch pressure and two-point discrimination, and ankle joint position sense were significantly reduced in children with spastic diplegia compared to the TD control group. These findings suggest that children with CP have

foot and ankle tactile and proprioceptive deficits. Assessment of LE somatosensory ability should be included in the clinical practice as it can guide clinicians in designing more effective treatment protocols to improve functionality in CP.

## 2.2 Introduction

Cerebral Palsy (CP) is the most common pediatric neurological condition that results in physical disability, and is caused by a static lesion in the developing fetal or infant brain[8]. The most prevalent type of brain injury in CP is periventricular leukomalacia, a condition associated with corticospinal pathway injury that is thought to be the primary cause of motor deficits in this population[25,72]. Traditional rehabilitation and motor learning approaches in CP are generally motor-centric, focusing on techniques to ameliorate musculoskeletal and motor impairments. Less attention has been paid to deficits in sensory systems that could negatively influence the feedback and feedforward control mechanisms and therefore potentially shape motor behavior. In fact, there is recent evidence of disrupted thalamocortical connections[25,28,73] which may alter the somatotopic representation[28], and result to aberrant somatosensory cortical activity and synchrony[26,43], suggesting sensory processing dysfunction in children with CP. Additionally, Hoon and colleagues (2009) reported that a more severe injury in the thalamocortical pathways was associated not just with greater sensory, but greater motor impairments as well, whereas injury in the corticospinal pathways was not correlated with either in this population. Hence, they proposed a theoretical model of motor impairment associated with the sensorimotor pathway injury in individuals with spastic CP (**Figure 1.2; Chapter 1**) [25].

Sensory deficits have been attributed primarily to the immature brain injury and secondarily as a result of motor impairments[74]. Particularly, reduced physical activity may limit opportunities for learning and perceptual development experience in CP[8,74]. In addition, recent studies have reported somatosensory impairments in light touch pressure[17,18,22,31], two-point discrimination[17,18,31,32], stereognosis[17,18,31,32], vibration[22], and proprioception[22,31,33]. Many of those studies reported tactile

deficits[17,18,31,32,34] that have been associated with unimanual and bimanual performance[17,18] and precision grip tasks[34] in the affected hand of individuals with unilateral CP, suggesting an essential link between somatosensory information and motor performance in upper extremities (UEs). Auld et al. proposed the use of a comprehensive test battery of sensory assessments to investigate tactile function in children with hemiplegia[17,18]. Their findings revealed that approximately 75% of this population present tactile dysfunction and highlighted the importance of using a clinical sensory evaluation in an effort to guide rehabilitation interventions[17]. Moreover, an UE clinical sensory battery has been suggested as a valuable tool in identifying sensory deficits in children with mild sensory impairment[31] in clinic and research settings.

Only a few studies heretofore have examined lower extremity (LE) somatosensation deficits in CP[22,33]. The feasibility of performing LE somatosensory assessments in children with spastic diplegia of at least 5 years of age has been validated by McLaughlin and colleagues (2005)[22]. In this study, it was demonstrated that pain, position sense, and direction of scratch are diminished in a group with CP[22]. Each of the tested sensory modalities, however, were only documented with a "pass or fail" score (based on the participant's correct or incorrect identification of each sensory stimuli) and therefore lack important information on the magnitude of the deficit[22]. Additionally, Wingert et al. reported transverse plane (internal/ external rotation) hip proprioception deficits in unilateral and bilateral CP[33]. Less consideration has been given to investigation of ankle proprioception as well as plantar cutaneous afferent feedback deficits in CP population, despite distal LE impairments being more

prevalent and more severe than proximal impairments in spastic diplegic CP[46] and have been moderately related to gross motor function[75].

Plantar cutaneous somatosensation provides important information in maintaining balance during dynamic tasks like gait[76] and it is site-specific[77] as different areas of the foot sole provide inputs to CNS regarding the body position to elicit the proper motor response to perturbations[37]. Numerous glabrous mechanoreceptors are located at the plantar side of the foot, which is the boundary between the body and the ground during upright position, and has been characterized as a "dynamometric map" that can detect the foot pressure distribution during static and dynamic loading conditions[37]. The fast and slow adapting cutaneous receptors (i.e. Ruffini endings, Merkel's cells, Meissner's Pacinian corpuscles)[38] are not only sensitive to the movement of the center of pressure (COP) but can potentially elicit reflex correcting responses to enhance balance[35]. Furthermore, afferent tactile inputs are integrated with proprioceptive information from the ankle joint to provide feedback to CNS for the body position in respect with the supporting surface. Proprioceptive receptors, such as muscle spindles, joint afferents, and Golgi tendon organs, contribute to joint position sense and kinesthesia[38]. Despite the prominent role of LE somatosensation (tactile and proprioceptive inputs) in controlling the upright stance during standing, walking, and performing functional activities, sensory assessments are often excluded in clinical practice to save time, or to focus on the more obvious motor deficits[22].

Quantifying the nature and extent of somatosensory impairments in CP could potentially assist in developing a comprehensive LE sensory test battery that will lead to improved identification of body function impairments, and in turn guide therapeutic

management in CP. In the present study, we investigated the magnitude of foot and ankle tactile and proprioceptive deficits in children with spastic diplegia and compared their results to typically developing (TD) age-matched peers (Aim 1). We hypothesized that somatosensory ability (light touch-pressure, two-point discrimination, vibration, joint position sense, and kinesthesia) would be diminished in the CP compared to TD group (Hypotheses 1.1 and 1.2).

## 2.3 Methods

### 2.3.1 Participants

Ambulatory individuals with spastic diplegic CP aged 8-18 years old and age-matched healthy subjects participated in this study. Participants with CP were recruited through the outpatient CP clinic at Shriners Hospital for Children (SHC) in Philadelphia and other means of contact such as: recruitment letters, flyers/advertisements, and also via professional contacts and local referral sources. Healthy volunteers were recruited from subjects' siblings and friends and from the community through advertisement. Before participation, potential subjects were screened by a physical therapist or an orthopedic surgeon to determine eligibility. Individuals with CP were classified as levels I - III on the Gross Motor Functional Classification Scale (GMFCS), and were able to stand without assistance for at least 2 m and follow multiple commands. The exclusion criteria for the CP group included: receipt of botulinum toxin injection in the last 6 months, severe LE spasticity (e.g. a score of 4 on the modified Ashworth Scale), and a previous selective dorsal root rhizotomy. Participants also had to report no history of: LE surgery, fracture, or trauma a year prior to participation, LE joint instability, uncorrected visual

impairments, or marked hearing and vestibular deficits. Finally, all the subjects were screened for scoliosis by visual inspection and scoliometer measures as well as for pregnancy (if female and after menarche) and were excluded from the study if found positive.

Parents or legal guardians signed informed consents and participants under 18 years of age signed informed assent documents prior to participation. Eighteen year old subjects signed their own informed consent. The study was approved by the IRB of Temple University (for SHC) and the University of Delaware.

### 2.3.2 Experimental Procedures

Following the screening and informed consent/ assent procedures, each participant underwent a comprehensive foot and ankle somatosensory clinical test battery. These tests assessed tactile and proprioceptive function. For light touch-pressure, two-point discrimination, vibration sensation, and joint position sense assessments, each subject laid down comfortably on the exam table. Kinesthesia was tested in the seated position. Before proceeding with the testing session, participants performed a practice trial with visual feedback for each test to assure understanding of instructions. Actual tests were performed in random order without visual feedback, and took approximately one hour to complete.

**Somatosensory Ability**

*Light touch pressure.* Light-touch sensation (tactile registration) was assessed on the plantar surface of each foot by using the 6-item Monofilaments kit (Baseline®, White Plains, New York, USA) at the first metatarsal head, fifth metatarsal head, and heel[40,42,77]. Generally, each monofilament is of different diameter and buckles when a specific force is applied on the skin. The test was performed by touching the skin with

a monofilament in a perpendicular orientation three times in each area and in a random order (including 3 sham trials per area). Filaments were pressed slowly until they buckled and held steady for 1.5 sec[78]. Prior studies suggested to record an affirmative response as one out of three trials when light touch is being evaluated[17,42], however, in this study we wanted to decrease the possibility of a false positive response. Therefore, a response was considered as affirmative if the subject identified two out of the three trials in each corresponding monofilament and location. The procedure started with the largest filament (6.65 monofilament level) to ensure the participant's ability to identify the applied stimulus. If it was correctly identified in all sites, we then proceeded by applying the smallest monofilament (2.83 monofilament level), and progressively applied thicker filaments until the threshold was reached. Light touch pressure threshold was recorded as the lowest monofilament value at which the participant was in position to correctly identify the stimulus twice for each location and limb.

*Two-point discrimination.* Two-point discrimination was assessed on the plantar side of the foot by using an aesthesiometer (Baseline®, White Plains, New York, USA) on the forefoot and heel[40,42]. Three trials per condition (two-point stimuli, one-point stimulus, no stimulus-sham-trial) and location were performed randomly, and the individual was asked to identify the number of stimuli (i.e., two, one, or none). The tested distance between the two-point stimuli was predefined in a range from 10 to 50 mm for the purposes of this study. The procedure began by testing the largest distance (50 mm) to ensure the subject's ability to detect the two different stimuli. If the subject correctly identified two out of the three trials per site, we then proceeded with the smallest tested distance (10 mm) and increased the distance by 5 mm

increments up to 45 mm until the threshold was reached. The two-point discrimination threshold was defined as the minimum distance in mm between two stimulus points, that were correctly identified as distinct points twice for each area[17,40,42].

*Vibration sensation.* The vibration sensation was evaluated by using a 128 Hz tuning fork (Rydel- Seiffer graduated tuning fork, Martin Tuttlingen, Germany) over the first metatarsal head and medial malleolus bilaterally[22,42,79]. A 128 Hz tuning fork has been suggested as a more sensitive clinical tool for measuring abnormal vibratory sense compared to tuning forks of other frequencies[79]. The duration of the vibration stimulus was recorded by a chronometer, starting from the activation time of the tuning fork until the participant reported that he/she could not feel it[79]. The average time (s) of the three trials for each site was used for analysis[42].

*Joint position sense.* For this assessment, the participant laid prone on the exam table. A digital goniometer (Medigauge, Westford, MA) was attached to the shank and foot of each participant by using a self-adherent elastic wrap (CoFlex, Andover Healthcare Inc., Salisbury, CA) by a physical therapist. The axis of rotation of the goniometer was aligned with the ankle joint center. The goniometer was used to measure the angle displacement during testing. The initial position of testing required each participant's knee joint of the tested leg in $90^0$ degrees of flexion and the ankle joint in neutral position ($0^0$ degrees dorsiflexion). The tested foot was passively moved by a physical therapist to a specific joint angle, remained in this position for 3 s, and returned in the neutral position. Then, the subject was instructed to actively reproduce the position as accurately as possible and maintain that position for 3-5 s. The procedure was repeated 3 times per side (left and right). The magnitude of error

between the performance and target joint angle was recorded at the nearest degree for each trial[33]. The average of 3 trials for each ankle joint was computed for analysis.

*Kinesthesia.* While the participant was seated without view of the tested foot, the tested foot was grasped on its lateral and medial edges between the thumb and the index fingers by a physical therapist[80]. The ankle joint was passively plantarflexed or dorsiflexed in a random order. Participants were asked to instantly report the direction of the displacement of the ankle joint[33]. Performance accuracy was determined as the number of correct responses out of 10 trials (5 in each direction) and was converted to a percent value.

### 2.3.3 Statistical Analysis

All data were analyzed by using SPSS (version 23; SPSS Inc., Chicago. IL, USA). Data normality was examined by visual inspection of Q-Q plots and by conducting the Shapiro-Wilk test. Demographic data (age, height, weight, BMI) were normally distributed and therefore analyzed with two-tailed independent samples t-tests. To investigate for sex differences, a Fisher's exact test of independence was performed. The distribution of the light touch pressure, two-point discrimination, vibration, and kinesthesia data deviated from normality and comparisons between the CP and TD groups were made using Mann-Whitney U test. Joint position sense comparisons were made by using an independent sample t-test. Given our a priori hypotheses, all the performed tests for the somatosensory assessments were one-tailed and the statistical significance was set at $p < 0.05$. Finally, mean and standard deviations were calculated for the demographic characteristics of the participants, whereas median and interquartile ranges were computed for the somatosensory

assessments. For the normally distributed joint position sense error data, mean and 95% confidence intervals (CI) were also calculated.

## 2.4 Results

Ten children with CP and eleven age-matched TD subjects participated in this pilot study to investigate the presence of foot and ankle tactile and proprioceptive deficits. The demographic characteristics are presented in **Table 2.1**. Age, sex, height, weight, and BMI were not significantly different between the two groups ($p > 0.05$).

**Table 2.1**: Demographic characteristics of children with CP and their TD peers. Means and standard deviations (in parentheses) are presented in the table.

| | **CP group (n=10)** | **TD group (n=11)** |
|---|---|---|
| **Age** (years, months) | 15 y 5 mo (2y 9 mo) | 15 y 10 mo (2 y 2 mo) |
| **Sex** (male/ female) | 9/ 1 | 6/ 5 |
| **GMFCS** (level) | I: 4; II: 3; III: 3 | - |
| **Height** (cm) | 162.16 (12.46) | 167.16 (15.84) |
| **Weight** (kg) | 62 (30) | 62.7 (24.3) |
| **BMI** ($kg/m^2$) | 22.6 (7.8) | 21.7 (5.15) |

Preliminary analysis of our data revealed no statistically significant differences between the left and right limbs for all the examined foot and ankle somatosensory assessment scores and therefore, left and right measures were pooled together and averaged by testing site for the analysis. **Table 2.2** shows median and interquartile range values for all foot and ankle somatosensory scores except joint position sense error values that are presented with mean and 95% CI. The group with CP demonstrated increased scores in all of the somatosensory assessments except kinesthesia compared to the TD group suggesting sensory impairments.

**Table 2.2**: Somatosensory assessment scores (median & interquartile range (IQR)) in children with CP and children with TD. Ankle joint position sense error data were normally distributed and presented as means with ± 95% confidence intervals indicated in parentheses. Asterisks correspond to significant differences between the CP and TD groups.

| **Sensory Assessments** | **CP Group** Median (IQR) | **TD Group** Median (IQR) |
|---|---|---|
| **Light-Touch Pressure** (level) | | |
| 1st Metatarsal | 4.31 (4.14 - 4.61)** | 3.96 (3.61 - 3.96) |
| 5th Metatarsal | 4.31 (4.14 - 4.9)* | 3.61 (3.61 - 4.31) |
| Heel | 4.38 (4.22 - 5.18) | 4.31 (3.96 - 4.31) |
| **Two-point Discrimination** (mm) | | |
| Forefoot | 17.5 (13.75 - 21.25)** | 12.5 (10 - 12.5) |
| Heel | 17.5 (16.88 - 25.63)*** | 12.5 (10 - 15) |
| **Vibration Sensation** (s) | | |
| 1st Metatarsal | 15.5 (14.46 - 20.58) | 15 (11.83 - 18.5) |
| Medial Malleolus | 16.17 (11.09 - 19.25) | 14 (9.83 - 15) |
| **Joint Position Sense** (degrees) | | |
| Ankle | 4.5 (2.45 - 5.96)* | 2.83 (1.76 - 3.85) |
| **Kinesthesia** (%) | | |
| Ankle | 100 (97.92 - 100) | 100 (100 - 100) |

*p < 0.05; ** p< 0.01; *** p< 0.001

In particular, light touch-pressure thresholds were significantly higher for individuals with CP at the first and fifth metatarsal head of the plantar side of the feet than for TD participants (first metatarsal: U= 21, Z= -2.48, p= 0.008; fifth metatarsal: U= 26, Z= -2.19, p= 0.02; **Figure 2.1**). At the heel site, there was no difference between subjects with CP and controls (U= 35.5, Z= -1.42, p= 0.09).

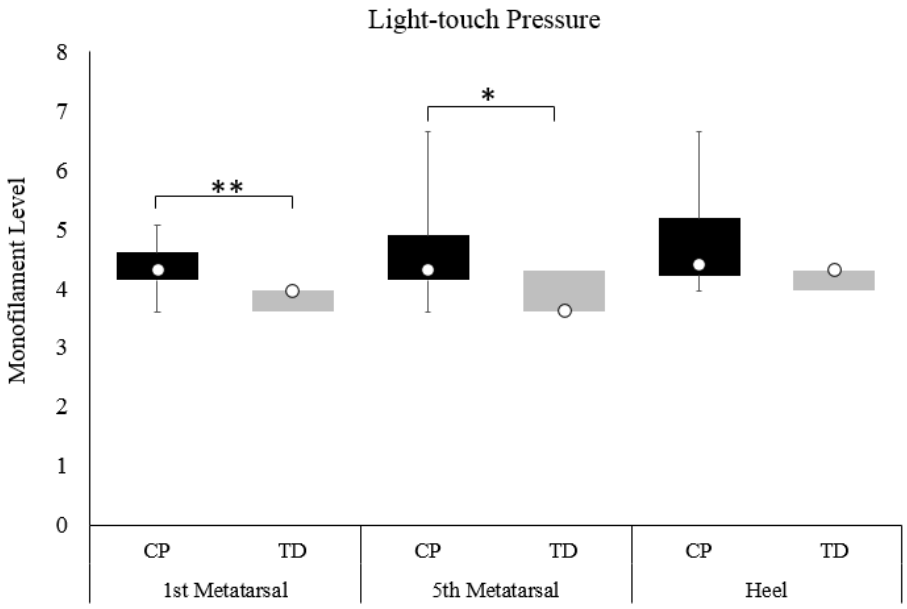


**Figure 2.1**: Box plots of the light-touch pressure thresholds at the first metatarsal head, fifth metatarsal head, and heel application sites for children with CP and TD children. The white dots within the boxes correspond to the groups' median, the boxes indicate the first and third quartile, and the whiskers the 95% confidence intervals around the median. In the TD group (grey box-plots), the 95% confidence intervals are within the interquartile range; therefore, no whiskers are shown. Asterisks correspond to significant differences between the groups (* $p < 0.05$; ** $p < 0.01$).

A Mann-Whitney test indicated that the distance between the two perceived points for the two-point discrimination sensation was greater for children with CP (Median= 17.5mm) than their TD peers (Median= 12.5mm) for both forefoot and heel sites (**Figure 2.2**; $p < 0.01$). Therefore, children with CP first identified two applied stimuli as distinct when they were separated by a larger distance compared to the TD group.

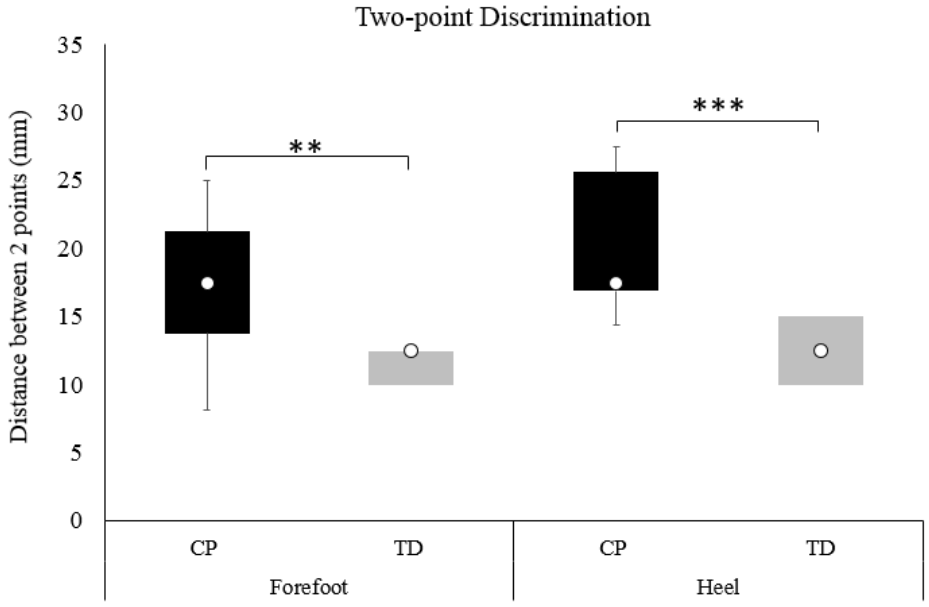


**Figure 2.2**: Box plots of the two-point discrimination thresholds at the forefoot and heel application sites for children with CP and TD children. The white dots within the boxes correspond to the groups' median, the boxes indicate the first and third quartile, and the whiskers the 95% confidence interval of the median. In the TD group (grey box-plots), the 95% confidence intervals are within the interquartile range; therefore, no whiskers are shown. Asterisks correspond to significant differences between the groups (** $p < 0.01$; *** $p < 0.001$).

Individuals with CP perceived the vibration stimulus for a longer period compared to the TD participants at the first metatarsal and medial malleolus tested sites but this difference was not significant (**Figure 2.3**).

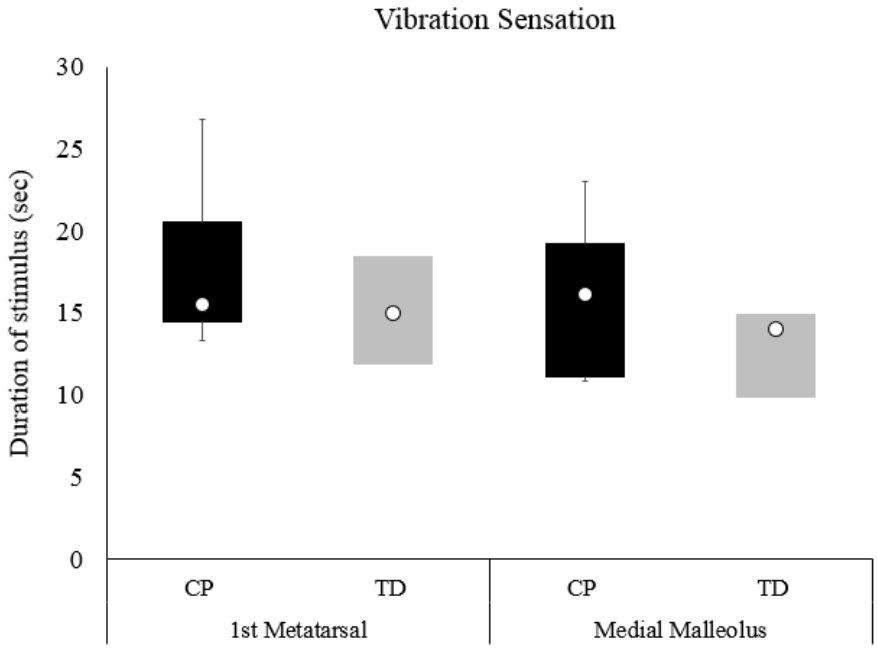


**Figure 2.3**: Box plots of the vibration scores at first metatarsal and medial malleolus for children with CP and TD children. The white dots within the boxes correspond to the groups' median, the boxes indicate the first and third quartile, and the whiskers the 95% confidence intervals around the median. In the TD group (grey box-plots), the 95% confidence intervals are within the interquartile range; therefore, no whiskers are shown.

An independent samples t-test was conducted to compare ankle joint position sense error for CP and TD individuals. There was a significant difference in the scores for CP (M= 4.2, 95%CI= 1.75) and TD (M= 2.8, 95%CI= 1.05) groups; t (18) = 2, p= 0.03 (**Figure 2.4**). These results suggest that the group with CP made larger errors in reproducing the targeted ankle angle than the controls. On the kinesthesia test, no difference was found between the two tested groups as participants performed equally well and accurately detected the passive ankle movement direction.

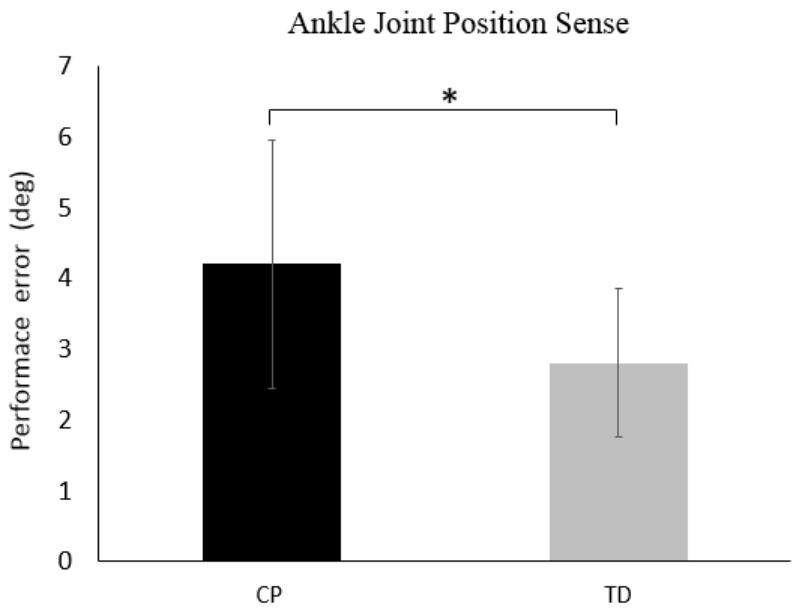


**Figure 2.4**: Means (± 95% confidence intervals) of ankle joint position sense error for children with CP and their TD peers. Asterisk indicates significant difference between the groups (* $p < 0.05$).

## 2.5 Discussion

The main objective of this study was to explore the magnitude of foot and ankle somatosensory deficits in children with CP compared to TD controls. Our findings indicated diminished tactile and proprioceptive ability in the CP group. In particular, plantar light touch pressure and two-point discrimination, and ankle joint position sense were significantly impaired in children with spastic diplegia. Appropriate somatosensory feedback is a critical component for refined motor performance, thus sensory assessment in CP may help define individual-specific deficits and lead to more effective clinical treatment approaches.

This study is the first to demonstrate that children with spastic diplegia have higher plantar cutaneous thresholds suggesting foot tactile impairments relative to

their age-matched TD peers. Similarly, increased foot tactile sensation thresholds have been reported in individuals with peripheral nervous system disorders[41,81] and multiple sclerosis[42] and have been related to impaired balance control. Our results showed diminished light touch pressure ability in the forefoot site and decreased two-point discrimination in both the forefoot and heel sites of the foot. Forefoot and heel plantar sites represent the anterior and posterior supporting zones of the foot that are crucial during upright stance[37]. In particular, the forefoot area contributes to the forward propulsion during push-off phase of gait, while the heel area provides important neural input regarding the initiation of the stance phase of gait[14]. Decreased plantar cutaneous information in these areas has been associated with increased postural sway during unperturbed stance[40] and altered kinematics and muscle activation patterns during gait[39]. We speculate, therefore, that poor postural control performance in children with CP can partially be attributed to their foot tactile deficits.

Another interesting finding from this study is that all participants with CP were able to perceive the vibration stimulus at the first metatarsal and medial malleolus sites and did not perform differently compared to the control group. Previous research suggested that children with CP were not able to correctly identify the vibration stimulus in their LE[22]. In particular, McLaughlin et al., classified a testing trial as successful when the participant reported the cessation of the vibration stimulus at or close to when the examiner could not detect the stimulus[22]. In an effort to be more accurate in quantifying vibration sensation, the duration of the perceived stimulus was recorded in this study and, although not significant, it was longer in the CP group compared to controls. Higher vibration perception thresholds have been reported in subjects with knee osteoarthritis[82] and diabetic polyneuropathy[83] suggesting sensory

impairments in the LEs with increased risk of falls and fall related injuries[84]. In contrast, children with an idiopathic toe walking gait showed increased sensitivity in vibration perception at the right hallux due to sensory processing deficits that potentially resulted to the toe walking pattern[85]. Vibration sensation should therefore be explored further in CP, which will give a clearer understanding of vibratory function and how its deficits may affect motor performance.

The children with spastic diplegia presented significantly larger error in reproducing the target ankle position in sagittal plane compared to the TD participants, even though the mean error difference between groups was only 1.7 degrees. Hip joint position sense errors of similar magnitude, in the transverse plane, were significantly correlated with increased center of pressure and center of mass sway during quiet stance and decreased gait velocity in CP[45]. Interestingly, when kinesthesia was examined we did not find any differences between the CP and TD groups. Previous studies have reported joint position sense deficits in the hip and knee joints[22,33] while hip's joint kinesthesia was not affected in spastic diplegia[33]. One potential reason is that detecting the direction of movement, as required by the kinesthesia test, is a simpler task compared to the joint position test for individuals with CP that are able to stand independently[33]. Another possible explanation is that the kinesthesia testing was not sensitive enough to detect possible impairments in the CP group. In particular, we hypothesize that despite of grasping the foot on its medial and lateral edges to passively move it during testing, sensory inputs from the tactile pressure receptors in these areas, although minimal, may have contributed to the participants' ability to detect the direction of movement. Overall, the joint position sense test may be a better

method to detect proprioceptive deficits in children with CP that have mild to moderate motor impairments in clinical settings.

Somatosensory feedback, including both tactile and proprioceptive information, is crucial for balance control[35–37] and based on our clinical findings children with spastic diplegia exhibit diminished foot and ankle somatosensory ability. Cutaneous receptors from the sole of the foot provide tactile inputs for spatial and temporal information regarding the pressure distribution on the plantar side of the feet and specifically signal the foot's contact with the ground[35]; thus, their role is essential to trigger appropriate compensatory postural responses to external perturbations[37]. A stable standing position mainly depends on ankle joint proprioceptive information, primarily from muscle spindles, regarding the changes in joint angle[36]. In addition, Golgi tendons' inputs contribute to balance control by indicating the changes in lower leg muscles' tension[38]. The interplay of the aforementioned somatosensory signals allows for a stable posture[37] and gait[39]; hence, the observed deficits in individuals with spastic diplegia can largely affect their balance and result in poor performance during functional activities[14], increased risk for falls and higher levels of caregiver dependence[10].

Our results support the notion that children with CP have somatosensory deficits in their LEs[22,33]. This is in line with previous research that showed that when a tactile stimulation was applied on the plantar side of the foot it resulted to diminished cortical activation[43] and asynchronous cortical response of the neural population[26] in somatosensory areas representing the foot in CP. The aberrant somatosensory cortical responses can potentially be attributed to the disrupted thalamocortical fibers that connect the thalamus with the postcentral gyrus[28] as they do

not allow the proper progression of sensory afferent signals to the cortex. Additionally, as a compensation mechanism for the diminished thalamocortical inputs, the intracortical connections among different somatosensory cortex subdivisions become more dominant thus resulting in an expanded functional connectivity map[29]. These functionally connected brain networks, however, may be related to the abnormal processing of somatosensory information as they do not allow the distinction between the different peripheral sensory inputs by the appropriate cortical areas[29]. Consequently, there is an aberrant connectivity between the sensory and motor areas[29] that may further accentuate the injury in the corticospinal (motor) pathways in spastic diplegia[25] and result in the manifested motor impairments and the concomitant limited environmental exploration. The decreased motor and sensory experience early in life may influence somatosensory perception, which plays a main role in the development of the gross and fine motor skills[86]. As such, somatosensory deficits in CP may negatively influence motor control by interfering with the acquisition of feedforward anticipatory strategies and feedback mechanisms that enable modification of the intended behavior in response to perturbations. Thus, without improvement in sensory processing and lack of experience in movement skills, larger changes in functional organization of motor and sensory-related cortical areas may take place and result in greater motor deficits in CP.

We note that the current study is of a small sample size; however, despite the small number of participants, we were able to demonstrate significant differences between the CP and TD groups in several of the somatosensory measures. We hypothesize that contributing factors for the observing significant differences may be the inclusion of individuals with only spastic diplegia with mild to moderate motor

impairments (GMFCS level I-III) and that the demographic characteristics for the CP and control groups were well matched.

One limitation of our study involves the way that the proprioceptive tests were performed. During the joint position assessment, a digital goniometer was used by a physical therapist to evaluate the participants' joint position performance error. However, using a goniometer has been proved to introduce variability in joint angle measurements in ambulatory children with spastic CP[87]. To improve the accuracy of our measurements, the same physical therapist performed three consecutive trials of the ankle joint position test and recorded the averaged performance error for each subject. Additionally, the recorded value for the groups' means was above the limits of 2.4 degrees of the reported goniometric measurement error for the ankle joint[87]. Finally, the kinesthesia test, as previously mentioned, was not sensitive enough to detect proprioceptive deficits.

## 2.6 Conclusion

Using a simple and cost-effective battery of sensory tests in daily clinical practice may allow for the characterization of somatosensory deficits in CP. In particular, ambulatory children with spastic diplegia exhibited decreased foot tactile and ankle proprioceptive ability compared to their age-matched TD peers. These findings corroborate the notion that somatosensory impairments are prominent in CP not only in their UE but in the LE as well, and may be associated with decreased postural control performance[45]. These deficits have been attributed primarily to the immature brain injury and secondary as a result of limited motor learning and sensory perceptual development experience[8] that, in turn, further contribute to the sensory processing impairments by altering the brain's functional connectivity and

reorganizing sensory cortical areas. To break this cycle, rehabilitation protocols in CP that have traditionally included only motor learning strategies and were marginally effective[88] should include sensory facilitation techniques as well; especially in light of evidence regarding structural integrity improvements in white-matter pathways following an intensive training protocol[47].

# Chapter 3

# FOOT AND ANKLE SOMATOSENSORY DEFICITS AFFECT BALANCE AND MOTOR FUNCTION IN INDIVIDUALS WITH CEREBRAL PALSY

## 3.1 Abstract

Recent evidence on disrupted thalamocortical connections and aberrant somatosensory cortical activation supports the presence of sensory dysfunction in individuals with cerebral palsy (CP). Upper-limb tactile impairments are related to manual function deficits and highlight the important link between sensory function and motor performance. Yet, limited research has thus far explored sensory deficits in lower extremities (LE) and their association with balance and motor function. Hence, this study aimed to investigate the relationship between foot and ankle somatosensory ability and functional performance in children with bilateral spastic CP.

A total of 10 children with CP (spastic diplegia; median age: 16y; range: 9-18y; GMFCS level I= 4; level II= 3; level III= 3) participated in this pilot study. All data were collected at the Shriners Hospital for Children, Philadelphia. Duration of vibration sensation, threshold of light-touch pressure, two-point discriminatory ability of the plantar side of the foot, and error in joint-position sense of the ankle were assessed. Balance was tested by the Balance Evaluation System Test (BESTest) and postural sway measures during a standing task. Motor performance was evaluated by using a battery of clinical assessments tools. In particular, gross motor ability was evaluated using the Gross Motor Function Measure (GMFM-66-IS). Spatiotemporal gait characteristics (velocity, step length) were used to determine walking ability.

Functional mobility was tested with the Timed Up and Go (TUG) and 6 Min Walk (6MWT) tests. Finally, a computerized isokinetic dynamometer was used to quantify isometric muscle strength of the ankle plantarflexor muscles.

Vibration and two-point discrimination were strongly related to balance performance. For ankle joint position sense, the larger the proprioception errors the lower the participants scored in the Postural Responses subdomain of the BESTest (rho= -0.7, p= 0.02). Vibration sensation of the first metatarsal head demonstrated a significantly strong relationship with motor performance as measured by GMFM-66-IS, spatiotemporal gait parameters, TUG, and ankle plantarflexors strength test (rho= -0.59 to -0.78, $p < 0.05$). Light touch pressure measure was strongly associated only with the 6MWT.

Foot and ankle somatosensation was strongly related to balance and motor function in individuals with CP. Vibration and two-point discrimination sensation in the LEs, in particular, may influence balance and motor performance in children with spastic diplegia. These findings emphasize the importance of developing a thorough LE sensory test battery that can guide traditional treatment protocols toward a more holistic therapeutic approach by combining both motor and sensory rehabilitative strategies to improve motor function in CP.

*Note: This work was presented in the 70$^{th}$ Annual Meeting of the AACPDM (Appendix D).* [89]

## 3.2 Introduction

Sensory inputs are crucial for the developing nervous system as they allow for the proper synaptic organization of the brain. In particular, somatosensory information is important for motor learning in early stages of development and provides the foundation for the acquisition of more complex behavioral skills[32,86]. Somatosensory perception is essential for the execution of coordinated movements by contributing to the formulation of the desired motor plan and providing appropriate feedback during the execution of the motor plan to correct potential performance errors[90,91]. Abnormal somatosensory processing has been associated with communication, motor, and social skill deficits in a range of neurodevelopmental disorders like cerebral palsy (CP)[86]. Even though CP has been traditionally characterized as a developmental disorder of movement and posture, the reclassification of CP acknowledges coexistent sensory information and sensory processing deficits associated with this pathology[8].

Sensory deficits in CP have been primarily attributed to the injury of the immature brain and, secondarily, arise as a result of limited learning experience[8,74] because motor impairments may not allow environmental exploration; a crucial element in development. Numerous imaging studies showed thalamocortical pathway disruption and aberrant somatosensory cortical activation in children with spastic CP[26,28,29,43], suggesting sensory processing dysfunction in this population. For example, injury of the posterior (sensory) thalamic radiations in white mater[25,28] may result in abnormal or limited transmission of afferent information to parietal and frontal cortex and subsequently contribute to motor disorders of spastic diplegia[33]. Sensory tract injury and decreased neural activity in somatosensory cortices have been also correlated with walking and strength deficits in CP[28,43]. Additionally, the amount of error in ankle force performance has been related to the desynchronization of

neuronal discharges in the somatosensory cortices[26], suggesting that impaired feedback mechanisms in this population can affect the skeletal musculature's ability to adapt in a changing environment. Furthermore, abnormal sensorimotor oscillatory activity during a knee extension task has shown that children with CP may have anticipatory feedforward control deficits, as their limited environmental exploration early in life does not allow them to develop appropriate internal models for a successful motor response[30]. Altogether, the aforementioned findings suggest that the sensory processing deficits associated with this pathology may lead to impaired motor planning and diminished postural control.

Clinical studies have reported somatosensory impairments in upper extremities[17,18,20,21,31] affecting up to 90% of children with hemiplegia[34]. Most of these studies reported tactile deficits that have been associated with poor unimanual and bimanual motor performance[17,18] and inability to characterize an object by its properties (i.e. weight, texture, shape etc.)[17]. Additionally, impaired somatosensory integration has negatively influenced feedforward motor control mechanisms during precision grip tasks even in cases where only one hand was primarily affected as in unilateral CP[34]. By using a fingertip force paradigm, Gordon et al. (1999) showed that children with hemiplegia presented anticipatory control deficits in the affected hand due to disrupted sensory information[92,93]. In a systematic review on precision grip and sensory impairments in CP, the authors concluded that the relationship between sensory dysfunction and prehension deficits needs to be delineated to improve the design of more focused and effective neurorehabilitation approaches for manual function[34].

Studies have also found that children with CP exhibit lower extremity (LE) somatosensation deficits[22,33]. Specifically, impairments in pain[22], position sense of knee[22] and hip[33], and direction of scratch[22] have been reported in spastic CP. Similarly, Aim's 1 findings showed that plantar light touch pressure and two-point discrimination, and ankle joint position sense were significantly impaired in children with spastic diplegic CP compared to their typically developing (TD) peers by using a simple battery of clinical sensory tests (Chapter 2). Kurz and colleagues (2015) provided evidence on the relationship between somatosensory cortical activation and mobility as they showed that an abnormal cortical response to plantar tactile stimulation may negatively affect walking ability and plantarflexors' strength in this population[43]. Additionally, hip proprioception deficits in children with unilateral and bilateral CP have been linked to increased postural sway and decreased gait velocity, even when visual information was upregulated[45]. Overall, deficits in sensory information and processing contribute in motor impairments; however, for individuals with CP the relationship between foot and ankle somatosensory ability and balance performance is not clear. This chapter, therefore, delineates the contribution of decreased plantar cutaneous feedback and inaccurate ankle proprioceptive input on balance control and motor performance in this population (Aim 2). Balance control was assessed by using the Balance Evaluation System Test (BESTest) as well as Center of Pressure (COP)-based measures during a standing balance test. Motor performance was evaluated by completing the following clinical tests: Gross Motor Functional Measure (GMFM-66-IS) to assess gross motor ability, spatiotemporal gait characteristics to describe walking ability, Time Up and Go (TUG), and 6-Min Walk Tests (6MWT) to assess functional mobility, and strength testing of the ankle plantar

flexors. In this study, impaired balance and motor function was expected to be related with poor somatosensory ability in children with CP (Hypothesis 2.1). The findings of this study will shed light on how to design more effective sensory-oriented rehabilitative protocols in CP.

## 3.3 Methods

### 3.3.1 Participants

The protocol was approved by the Institutional Review Board (IRB) of Temple University and the University of Delaware. Informed parental consent and child assent or consent forms were obtained prior to participation. Ten ambulatory individuals with spastic diplegia, who were able to stand without any assistive device, were recruited from the outpatient CP clinic at Shriners Hospital for Children in Philadelphia, PA, USA. All the participants were able to follow multiple step commands to complete the somatosensory assessments and clinical measures. Individuals with a history of selective dorsal rhizotomy, a score of 4 on the modified Ashworth scale, severe scoliosis (primary curve > $40^0$), LE joint instability, and marked visual, hearing, and vestibular deficits were excluded from the study. Additional exclusion criteria were: LE orthopaedic surgery or fracture in the year prior participation, botulinum toxin injections within the past 6 months, and pregnancy if the participant was female.

### 3.3.2 Experimental Procedures

**Somatosensory Ability**

All the children completed a comprehensive clinical evaluation to document their foot and ankle somatosensory ability. *Light-touch pressure* sensation was assessed by using the 6-item Monofilaments kit (Baseline®, White Plains, New York,

USA) at the first and fifth metatarsal heads and heel of the plantar side of each foot[40,42,77]. Light touch pressure threshold was defined as the thinner monofilament value the participant correctly identified twice out of three trials for each application site. *Two-point discrimination* was assessed by using an aesthesiometer (Baseline®, White Plains, New York, USA) on the forefoot and heel of the plantar side of each foot[40,42] and scored as the minimum distance, in mm, between two stimulus points[17,40,42], which were correctly identified as distinct points twice out of three trials for each site. *Vibration sensation* was evaluated by using a 128 Hz tuning fork (Rydel-Seiffer graduated tuning fork, Martin Tuttlingen, Germany) at the first metatarsal head and medial malleolus bilaterally[22,42]. The duration of the perceived vibration stimulus (average of 3 trials) for each site was recorded. For the ankle *joint position sense* assessment, the participant was instructed to actively reproduce, as accurately as possible, a target joint angle position for each leg. The magnitude of error between the performance and target joint angle was recorded to the nearest degree (average of 3 trials) for each ankle[33,45]. To assess *kinesthesia* for the ankle joint, participants were asked to instantly report the direction of the displacement as their ankle joint was passively dorsi- or plantarflexed[33]. Performance accuracy was determined as the number of correct responses out of 10 trials[33].

All the aforementioned testing procedures were performed in random order, without visual feedback, and the total testing duration was approximately one hour (see Chapter 2: Method section for detailed description for all the sensory tests). To determine an individual's threshold for each somatosensory test (overall score) and each site of sensory stimulus's application (site-specific score), the average of the combined left and right side scores were computed. In addition, the overall score for

each somatosensory test was calculated by averaging the values of all the application sites for every somatosensory modality. Both overall and site-specific scores were used in the analysis.

**Balance Performance**

*Postural Control.* The Balance Evaluation Systems Test (BESTest) is a 36-item physical performance scale and was employed to assess balance in the following postural control domains: 1) Biomechanical Constraints, 2) Stability limits/verticality, 3) Anticipatory Postural Adjustments, 4) Postural Responses, 5) Sensory Orientation, 6) Stability in Gait[23] (see Appendix A). Each item was assessed on a four-point scale and percentage scores were calculated for each domain with higher scores suggesting better balance performance. An overall BESTest score was also computed. The BESTest can discriminate postural control abilities in children with TD with high reproducibility[94] and has been used previously in children with CP to evaluate balance after the completion of a treadmill training protocol[95].

*Standing Balance.* Standing balance was assessed by postural sway measures (COP-based measures). Participants stood barefoot on 2 force plates with their feet in neutral position – the distance between heels was approximately 11% of each subject's height and at a $14^0$ degrees angle between each foot and the midline[24]. Tape traces of the feet on the force plates were used to ensure consistent positioning between trials. The children were instructed to stay as motionless and upright as possible and were asked to keep their gaze straight ahead at the eye level. The duration of each trial was 25s for a total of 2 trials and the resting interval between trials depended on each participant's comfort and fatigue level. Finally, an overhead harness system was used to prevent falls during each trial.

For kinetic assessment of balance, two AMTI force plates (OR6-7-1000, Advanced Mechanical Technology Inc., Watertown, MA) were used. The force plate data were collected by using Vicon Nexus software (v1.8.5) at 100 Hz sampling rate and filtered with a fourth-order, zero phase response, low-pass Butterworth filter with a cutoff frequency of 5 Hz[52,96]. Then, the resultant COP velocity (COPV) and 95% COP Confidence ellipse area (COPA) were computed and used for further analysis[96].

**Motor Performance**

*Gross Motor Ability.* The Gross Motor Function Measure Item Set (GMFM-66-IS; see Appendix B), the abbreviated version of Gross Motor Function Measure 66 (GMFM-66), is a standardized instrument designed to measure change in gross motor function in children with CP[97]. For GMFM-66-IS, an algorithm of 3 decision items from GMFM-66 (items 23, 67, and 85) was used to define which of the four available item sets can be administered[97] to represent more accurately each child's function level. It has been reported that there is no systematic difference between different item sets[97] with high levels of validity and reliability (ICC > 0.98)[98]. For the purposes of this study, the item sets 3 (n= 39 items) and 4 (n= 22 items) were used since our participants had only mild mobility impairments (GMFCS I- III; they were able to stand without assistive device). Each item was graded on a four-point scale ranging from 0 (does not initiate the required task) to 3 (completes the required task) and was scored by a physical therapist using GMAE software.

*Walking Ability.* Spatiotemporal characteristics of gait were evaluated while children walked on an instrumented walkway (GAITRite®, CIR Systems Inc., Franklin, NJ). The GAITRite mat was positioned on the floor and participants started walking 1.2 m before the beginning of the mat (acceleration walkway) and continued

walking 1.2 m after reaching the end of the mat (deceleration walkway). Subjects were tested in bare feet walking at their fast speed and without using any assistive device. Two to 6 trials were collected depending on participants' number of steps per trial (i.e. at least 16 steps per condition). To be a valid walking pass, trials had to consist of at least 4 consecutive footfalls on the instrumented walkway. The first four gait cycles for each side (right and left) were used for further analysis; thus, collecting a total of 8 strides allowed for reliable estimation of gait parameters in children with CP (GMFCS I-III)[99]. The following spatiotemporal parameters were collected: gait speed, and step length and normalized to height (Non-Dimensional approach)[100]. All values from the selected gait cycles were averaged for each variable of interest.

*Functional Mobility.* The Timed Up and Go (TUG) test quantifies functional mobility. Children rose from a seated positon, walked 3 meters, turned around, and walked back to the chair and sat down as quickly and safely as possible[101]. The test was repeated three times and the average time was recorded. Participants performed the test barefoot without using an assistive device. The 6-Minute Walk (6MWT) assessed participants' walking aerobic capacity[102,103]. Each subject was asked to ambulate around a fixed course as safely and quickly as possible. The distance that the individual was able to traverse in the allotted time was recorded. Only one individual with CP needed to use his walker to complete the test.

***Strength.*** The Maximum Volitional Isometric Contraction (MVIC) of triceps surae, bilaterally, was assessed by a computerized controlled dynamometer (KinCom II, Chattecx Corporation, Chattanooga, TN). Children were positioned in the dynamometer for triceps surae testing as previously described in the literature[104]. A total of 3 trials for each side were collected with a 3-min resting period between trials.

During each trial, visual feedback and enthusiastic verbal encouragement were provided to participants. The peak MVIC value was normalized with each subject's body weight and then the left and right MVIC were averaged and used for subsequent analysis.

### 3.3.3 Statistical Analysis

Median and interquartile ranges (IQR) were computed for the demographic characteristics and the sensory and motor function clinical assessments. Spearman rank correlation coefficients were calculated to determine the relationships between somatosensory ability and the respective clinical measures that assess balance and motor performance. According to Cohen's standards, rho coefficients greater than 0.5 indicate strong relationships, 0.3-0.5 moderate relationships, and 0.1-0.3 weak relationships[105]. Statistical significance was set at $p < 0.05$. The SPSS (version 23; SPSS Inc, Chicago. IL, USA) statistical software was used for the analysis.

## 3.4 Results

A total of 10 children with CP participated in this study. The median group values for age, height, and weight were 15y 6 m, 165.8cm, and 58.25kg respectively. The demographic characteristics of each individual are presented in **Table 3.1**.

**Table 3.1:** Participants' demographic information. All the children had spastic diplegic CP.

| | Age | Sex | GMFCS[#] | Height | Weight |
|---|---|---|---|---|---|
| 1 | 9y 1m | M | I | 142cm | 33kg |
| 2 | 17y 8m | M | II | 182.5cm | 127kg |
| 3 | 18y 0m | M | I | 158.5cm | 58.3kg |
| 4 | 15y 7m | M | III | 164.6cm | 49.1kg |
| 5 | 13y 1m | M | I | 146cm | 30.2kg |
| 6 | 18y 6m | M | II | 170cm | 66kg |
| 7 | 18y 6m | M | I | 170cm | 58.2kg |
| 8 | 15y 2m | M | III | 169cm | 98.9kg |
| 9 | 15y 6m | M | III | 167cm | 59.3kg |
| 10 | 13y 5m | F | II | 152cm | 40kg |

[#]Gross Motor Function Classification Scale

Children with CP were able to detect accurately the direction of movement during the kinesthesia assessment (Median: 100%, IQR: 97.92- 100%). In Chapter 2, we concluded that this test might be too simple for individuals with CP who have mild to moderate motor impairments and is not sensitive enough to detect proprioceptive deficits. Therefore, the kinesthesia test was not included in the analysis as all the participants scored close to 100% and a correlation analysis would have demonstrated a ceiling effect, hence making it difficult to assess its relationship with motor and balance performance. For the rest of the foot and ankle somatosensory tests and motor function clinical measures, the median and IQR values are presented in **Table 3.2**.

**Table 3.2:** Median and Interquartile Range (IQR) values for somatosensory and motor ability assessments in children with CP.

| Sensory Assessments | Median (IQR) | Motor Ability Assessments | Median (IQR) |
|---|---|---|---|
| **Light Touch Pressure** (level) | | **Postural Control** (%) | |
| 1st Metatarsal | 4.31 (4.14- 4.61) | BESTest *Overall* | 62.96 (40.28- 83.10) |
| 5th Metatarsal | 4.31 (4.14- 4.9) | BESTest 1 *Biomechanical Constraints* | 56.67 (33.33- 81.67) |
| Heel | 4.38 (4.22- 5.18) | BESTest 2 *Stability limits/ verticality* | 78.57 (63.10- 85.71) |
| Overall | 4.33 (4.14- 4.79) | BESTest 3 *Anticipatory Postural Adjustments* | 52.78 (48.61- 91.67) |
| **Two-point Discrimination** (mm) | | BESTest 4 *Postural Responses* | 30.55 (19.44- 55.55) |
| Forefoot | 17.5 (13.75- 21.25) | BESTest 5 *Sensory Orientation* | 76.67 (48.33- 100.00) |
| Heel | 17.5 (16.88- 25.63) | BESTest 6 *Stability in Gait* | 64.29 (28.57- 95.24) |
| Overall | 17.5 (16.56- 21.56) | **Balance Performance** | |
| **Vibration** (s) | | COPV (mm/s) | 5.55 (4.16- 7.25) |
| 1st Metatarsal | 15.5 (14.46- 20.58) | COPA ($mm^2$) | 81.10 (15.49- 109.39) |
| Medial Malleolus | 16.17 (11.09- 19.25) | **Gross Motor Ability** (%) | |
| Overall | 16.79 (12.83- 19.19) | GMFM-66-IS | 75.00 (68.78- 89.03) |
| **Joint Position Sense** (degrees) | | **Walking Ability** (ND) | |
| Ankle | 4.5 (3.10- 5.17) | Velocity | 0.33 (0.26- 0.36) |
| | | Step Length | 0.35 (0.31- 0.37) |
| | | **Functional Ability** | |
| | | TUG (s) | 7.84 (5.93- 12.10) |
| | | 6MWT (m) | 467.72 (381.10-534.31) |
| | | **Strength** | |
| | | MVIC (N/ Kg) | 4.69 (2.04- 6.83) |

**Relationships between Somatosensation and Balance Ability**

Spearman rho correlation coefficients, presented in **Table 3.3**, were computed to assess the relationship between somatosensory ability (Overall Scores) and balance performance. Two-point discrimination was strongly related with the BESTest score in all subdomains (rho= -0.57 to -0.86, p< 0.05) - except the *Anticipatory Postural Adjustments* subdomain- and the 95% eclipse area of the COP (rho= 0.86, p= 0.001). A strong relationship was also revealed between vibration sensation and the *Stability Limits/Verticality* subdomain of BESTest (rho= -0.56, p= 0.04) and COP velocity and area measures (COPV: rho= 0.69, p= 0.01; COPA: rho= 0.73, p= 0.01). Scatterplots partially summarize these results (**Figure 3.1**).

**Table 3.3:** Spearman's rank correlations between the somatosensory ability thresholds and balance control scores in children with CP. Asterisks indicate significant relationships (*p< 0.05; **p< 0.01).

| | Somatosensory Ability Measures | | | |
|---|---|---|---|---|
| | Light Touch Pressure | Two–point Discrimination | Vibration | JPS[#] |
| **Postural Control** | | | | |
| BESTest *Overall* | .12 | -.64* | -.31 | -.28 |
| BESTest 1 *Biomechanical Constraints* | .07 | -.62* | -.12 | -.19 |
| BESTest 2 *Stability limits/ verticality* | .36 | -.83** | -.56* | -.34 |
| BESTest 3 *Anticipatory Postural Adjustments* | .00 | -.48 | -.39 | .00 |
| BESTest 4 *Postural Responses* | .38 | -.57* | -.26 | -.70* |
| BESTest 5 *Sensory Orientation* | .12 | -.58* | -.14 | -.52 |
| BESTest 6 *Stability in Gait* | .05 | -.69* | -.52 | -.11 |
| **Balance Performance** | | | | |
| COPA | -.41 | .86** | .73** | .23 |
| COPV | .10 | .45 | .69* | -.09 |

[#]JPS: Joint Position Sense

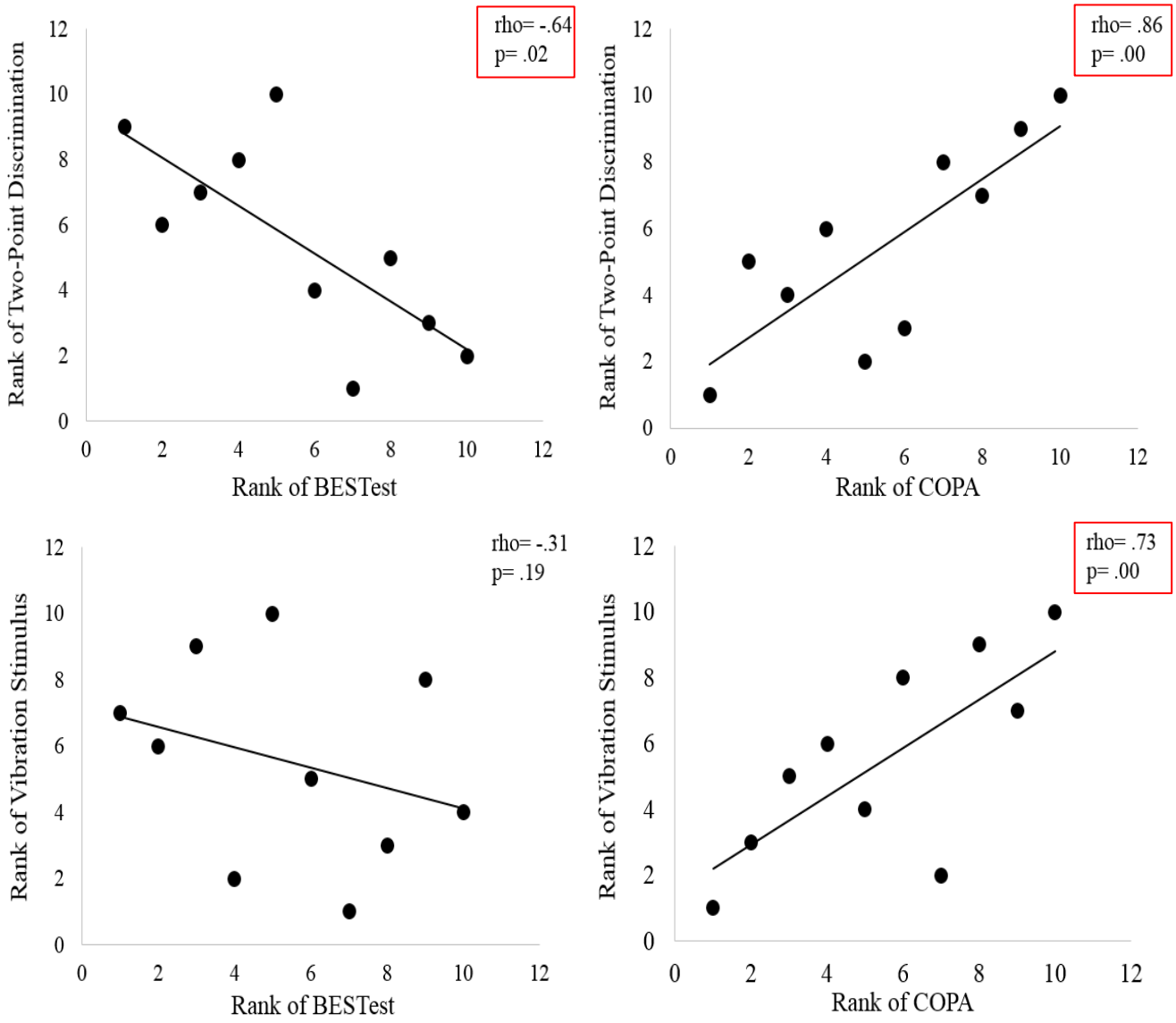


**Figure 3.1:** Scatter plots of the relationships between two-point discrimination and vibration senses and balance ability using Spearman's rank correlations in the children with CP. Each data point reflects a participant.

Ankle joint position sense was significantly associated with the *Postural Responses* subdomain of BESTest (**Figure 3.2**: rho= -0.70, p= 0.02). For all the aforementioned relationships, the rho coefficients' negative value indicated that the

higher the somatosensory assessment thresholds indicating greater impairment, the lower participants' score in the BESTest; whereas, the positive value suggested that the higher the somatosensory thresholds the larger the postural sway measures during the standing balance test.

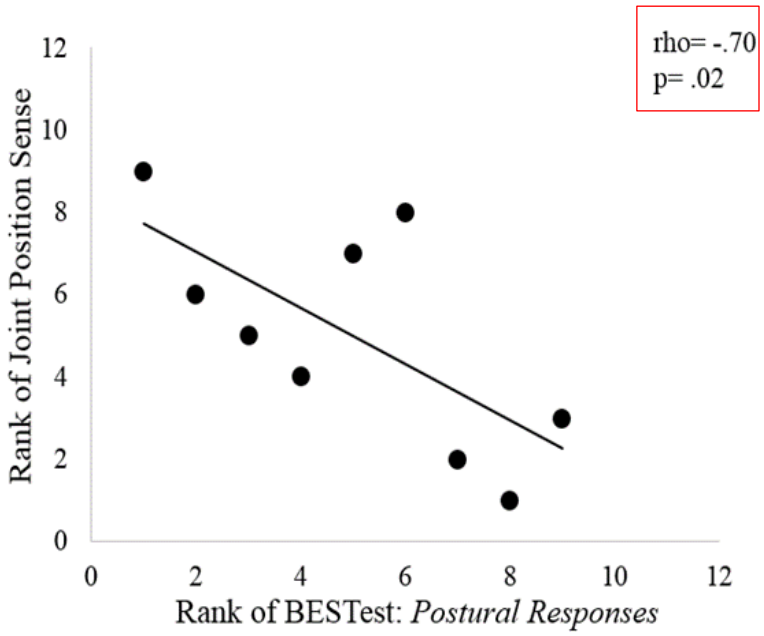


**Figure 3.2:** Scatter plot of the rank of the BESTest score in the 4th Subdomain (postural responses) and the rank of the ankle joint position sense in the children with CP. Each data point reflects a participant.

Spearman rho correlation coefficients were also computed to characterize the relationships between the site-specific scores of the somatosensory tests and the balance clinical measures (**Table 3.4**). In particular, there was a negative correlation between the two-point discrimination in the forefoot area with two of the subdomains of the BESTest (Stability Limits/ Verticality: rho= -0.68, p= 0.01; Stability in Gait: rho= -0.58, p= 0.04). Similarly, two-point discrimination in the heel area was strongly

related with three of the subdomains and the overall score of BESTest (rho= -0.62 to -0.65, $p< 0.05$). Vibration sensation in the first metatarsal site demonstrated a strong negative relationship with the overall BESTest score (rho= -0.60, p= 0.03) and the score in: Stability Limits/Verticality, Postural Responses, and Stability in Gait subdomains of BESTest (rho= -0.62 to -0.70, $p< 0.05$). These correlations suggested that the higher the two-point discrimination thresholds and the longer the vibration stimulus was perceived the poorer the participants performed in the BESTest, indicating impaired postural control in these individuals (**Table 3.4**).

Two-point discrimination in the forefoot and heel sites and vibration sensation in the first metatarsal site showed a strong positive relationship with the COP sway area (rho= 0.72 to 0.77, $p< 0.01$). Additionally, increased two-point discrimination thresholds and longer vibration perception in the forefoot and medial malleolus areas, respectively, were significantly associated with increased velocity of COP sway (rho= 0.65, p= 0.02 and rho= 0.77, p= 0.00). Finally, none to weak relationships were found between site-specific scores for light touch pressure and the balance performance measures, hence, this data are not presented in **Table 3.4**.

**Table 3.4:** Spearman's rank correlations between two-point discrimination and vibration senses, at different application sites, and balance ability measures for the children with CP. Asterisks indicate significant relationships (*p< 0.05; **p< 0.01).

| | Two-point Discrimination | | Vibration | |
|---|---|---|---|---|
| | Forefoot | Heel | 1st Metatarsal | Medial Malleolus |
| **Postural Control** | | | | |
| BESTest *Overall* | -.45 | -.54 | -.60* | -.05 |
| BESTest 1 *Biomechanical Constraints* | -.29 | -.62* | -.54 | .13 |
| BESTest 2 *Stability limits/ verticality* | -.68* | -.65* | -.69* | -.15 |
| BESTest 3 *Anticipatory Postural Adjustments* | -.35 | -.29 | -.54 | -.22 |
| BESTest 4 *Postural Responses* | -.33 | -.64* | -.70* | .07 |
| BESTest 5 *Sensory Orientation* | -.31 | -.53 | -.51 | .21 |
| BESTest 6 *Stability in Gait* | -.58* | -.47 | -.62* | -.24 |
| **Balance Performance** | | | | |
| COPA | .72** | .74** | .77** | .46 |
| COPV | .65* | .33 | .34 | .77** |

**Relationships between Somatosensation and Motor Ability**

Children with higher light touch pressure thresholds in their plantar side of the foot (overall score) were more likely to cover a shorter distance during the 6MWT, as indicated by the negative rho coefficient of -0.55 (**Figure 3.3**). Additionally, only vibration sensation of the first metatarsal head demonstrated a significantly strong relationship with motor performance as measured by GMFM-66-IS, spatiotemporal gait parameters, TUG, and plantaflexor strength (**Figure 3.4**). Particularly, the longer the participants were able to perceive the vibration stimulus in the first metatarsal area the more likely they were to have limitations in gross motor function (rho= -0.63, p= 0.03), and walking ability (gait velocity: rho= -0.78, p= 0.00; step length: rho= -0.59, p= 0.04), functionality (TUG: rho= 0.66, p= 0.02), and plantarflexors' strength (rho= -

0.61, p=0.03). The rest of the somatosensory site-specific scores were weakly to moderately associated with motor function tests, and these relationships were not statistically significant.

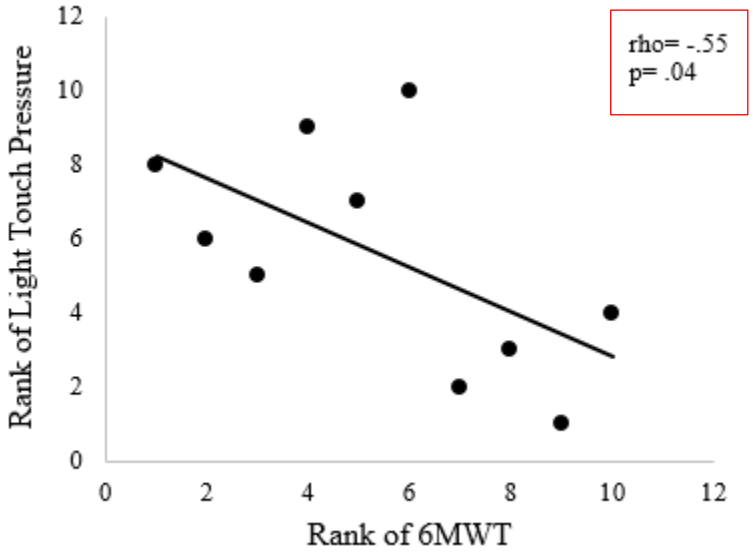


**Figure 3.3:** Scatter plot of the rank of the 6MWT and the rank of the light touch pressure in the children with CP. Each data point reflects a participant.

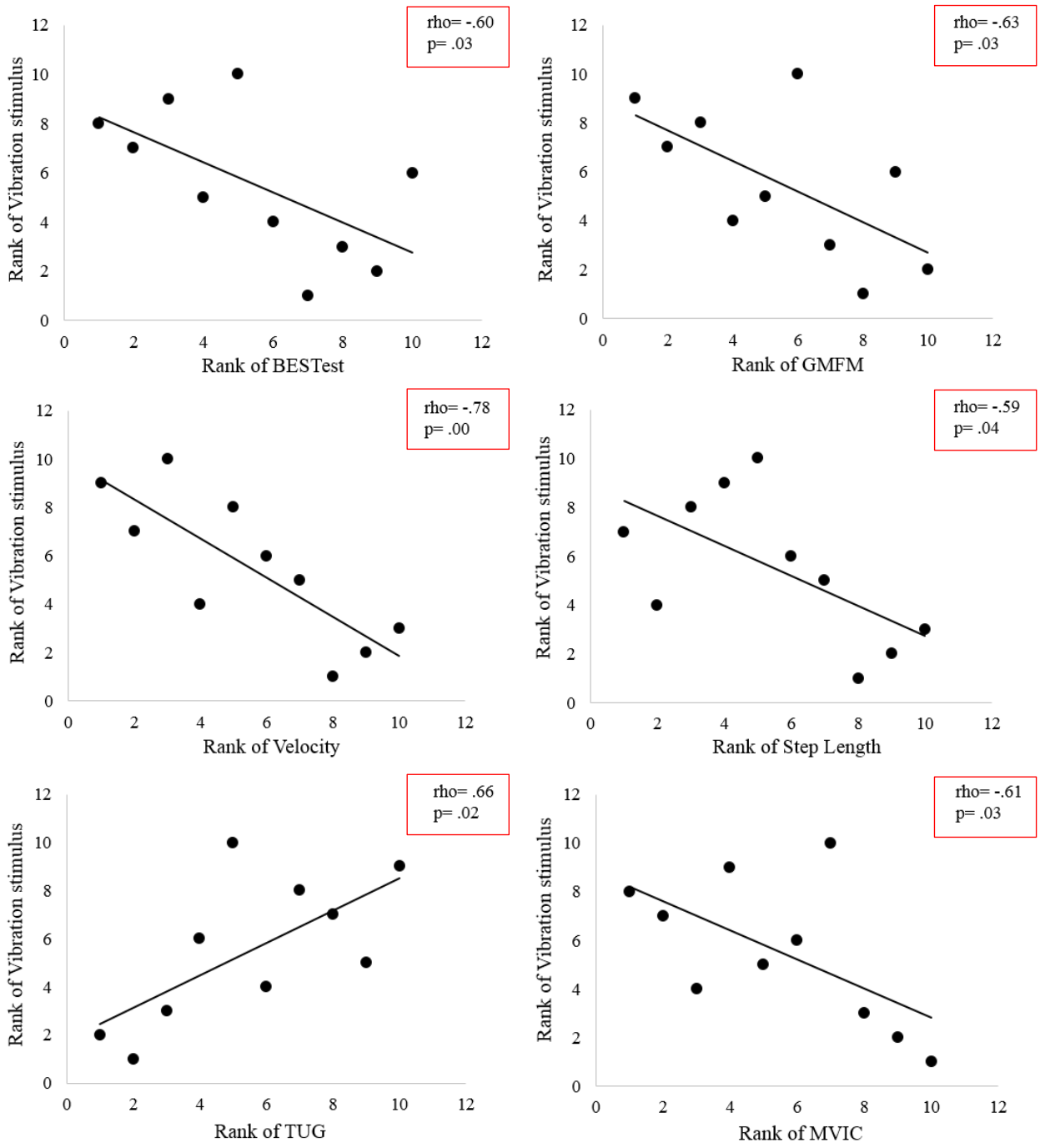


**Figure 3.4:** Scatter plots of the Spearman's rank correlations between the rank of the vibration stimulus when applied in the first metatarsal area and the rank of motor performance variables for children with CP.

## 3.5 Discussion

This study investigated the relationship between foot and ankle somatosensory ability and motor function in individuals with spastic diplegic CP. Our results demonstrated that foot and ankle somatosensation is strongly related to standing balance and motor performance; thus, supporting the notion that plantar cutaneous and ankle proprioceptive deficits may contribute to the postural control and mobility impairments in this population. These clinical findings emphasized the importance of developing a thorough LE sensory test battery that can identify subject-specific sensory deficits and, therefore, guide traditional treatment protocols toward a more comprehensive therapeutic approach by combining motor and sensory rehabilitative strategies to improve motor function in CP.

**Relationship between Somatosensation and Balance Ability**

Flexible postural control and motor planning require organizing and integrating visual, vestibular, and somatosensory inputs to efficiently coordinate motor actions[14]. Impairments in at least one of the aforementioned sensory systems could be a contributing factor in the poor balance control exhibited by individuals with CP. Postural control deficits in this population have been attributed to biomechanical changes in postural alignment and also to central nervous system (CNS) and sensory processing impairments[28,43,106]. This study's results showed that LE somatosensory ability is strongly related to balance performance in CP and, therefore, deficits in the plantar cutaneous and ankle proprioceptive ability may partially contribute to balance deficits.

Among the tested somatosensory modalities, two-point discrimination in the plantar side of the foot were significantly associated with all but one of the subdomains of BESTest and the area of COP sway during quiet stance. Specifically,

the larger the distance between the two applied stimuli that were perceived as distinct by the participants, the poorer they performed in five different underlying systems that contributed to postural control, suggesting generalized balance problems in CP. When we investigated the site-specific scores for two-point discrimination, both the forefoot and heel areas contributed to the observed poor balance performance. These findings indicated that limited spatial and temporal tactile information from the anterior and posterior supporting zones of the foot (i.e. forefoot and heel areas)[37] may result in inability to trigger the appropriate compensatory responses to maintain a stable upright stance in CP.

Vibration sensation in the first metatarsal area showed significant relationships with 3 subcategories of BESTest and the area of COP sway. These findings suggested that when a child was able to perceive vibration sensation for a longer period of time, they showed decreased functional stability limits, impaired compensatory postural responses, and dynamic & static stability deficits. Previous research in vibration sensation reported that children with CP were not able to properly identify a vibration stimulus in their LE[22]. In Chapter 2, we showed that children with CP, although they did not perform significantly different compared to controls, perceived the vibration stimulus for a longer period. Conversely, for individuals with multiple sclerosis[42] the duration of the perceived vibration is shorter compared to healthy adults and this has been attributed to spinal dorsal column abnormalities associated with this pathology[107]. Temlett (2009) showed that the duration of the vibration sensation also declines with age due to the nerve fibers degeneration and deterioration of Pacinian corpuscles, which are the primary mechanoreceptors of vibration sensation[108]. In this study, the recorded longer period of vibration sensation in CP may have indicated

aberrant and prolonged processing and integration of the afferent vibratory input by the CNS that resulted in impaired balance control. This corroborates brain imaging findings proposing that sensory processing deficits contribute to the motor planning and execution impairments in spastic diplegia[26,29,30,43].

Ankle joint position sense errors were significantly related with the *Postural Responses* subdomain of BESTest. In particular, for this category's balance tasks, participants were required to regain their equilibrium with and without taking a step following perturbations in different directions (i.e. forward, backward, or lateral) induced by the examiner's hands[23]. Children with CP were unable to elicit an appropriate postural response to unexpected perturbations, receiving a median group score of 30.55 out of the maximum 100. The lower they scored in this subdomain, they presented larger errors in reproducing the target ankle position during the joint position sense test. These findings potentially reflected that ankle proprioceptive deficits did not allow for proper sensory feedback during the execution of the motor response and, therefore, children with CP were unable to regain equilibrium during a challenging balance task. Similarly, Damiano et al. (2013) reported that increased hip proprioception errors were significantly related to increased postural sway during quiet stance and decreased gait velocity in CP[45]. Overall, the findings suggested that evaluation of proprioception should be incorporated into LE sensory battery tests, especially in light of the evidence that proprioceptive deficits can be exacerbated by the loss of plantar cutaneous inputs affecting balance stability[40].

**Relationship between Somatosensation and Motor ability**

In Chapter 2, we showed that light touch pressure thresholds significantly increased in individuals with CP compared to their age-matched typically developing

peers. Despite that higher light touch pressure thresholds have been associated with poor balance performance in older adults[77], individuals with multiple sclerosis[42], and peripheral neuropathy[41,81], this study demonstrated that the only significant relationship in children with CP was between light touch pressure and the 6MWT and was not associated with balance measures. Specifically, higher light touch pressure thresholds were significantly related with shorter distances covered over a 6 m period. A possible explanation is that during dynamic activities like gait, in which the loading response may be equivalent to several times the body weight of the individual, the plantar mechanoreceptors' thresholds are more likely to be reached compared to simpler balance tasks that involve lower levels of plantar pressure, such as the ones that occur during postural shifts to maintain standing balance[77]. Therefore, the impact of the plantar light touch pressure deficits on postural stability in CP might be more evident during a prolonged walking task, like the 6MWT. Further research is needed to delineate the reweighting of plantar somatosensory cues and how it affects motor function not only during static but also dynamic and prolonged activities.

Interestingly, vibration sensation at the first metatarsal head was the only sensory modality that was significantly related with the majority of the clinical motor assessments. Specifically, longer duration of the vibration perception was significantly related with impaired gross motor and walking ability, functional mobility, and plantarflexors' strength. These results implied that vibratory information, as provided by the stimulation of Pacinian corpuscles that are located at both the subcutaneous tissue, bony periosteum, and joint ligaments[108], are crucial for static and dynamic postural control. Specifically, loading of first metatarsal head area contributed to forward propulsion during push-off phase of gait[14] and decreased sensory inputs from

this area have been associated with decreased score in the Berg Balance Scale and walking speed[77]. Finally, our findings showed that distal vibration impairments are more prominent compared to proximal ones (i.e. first metatarsal head vs. medial malleolus sites) and can affect the overall functional level in this population. Altogether, this study provided evidence of increased distal deficits of lower extremities not only in the motor[46], but in the sensory domain as well.

This work highlighted the strong relationship between somatosensory ability and variables of balance and motor performance in CP despite having a small sample size. These observations may imply that somatosensory dysfunction is highly pervasive in children with CP, however, we still urge caution in interpreting these results because of our small sample size. Furthermore, we acknowledge the fact that musculoskeletal deficits, in addition to poor somatosensory ability, can contribute to the noted motor impairments witnessed in children with CP as this pathology is multifactorial. Finally, over the course of the past decade, neuroimaging evidence has supported the existence of somatosensory processing deficits and abnormal sensorimotor connectivity in this population[26,28,29,43], however, there is limited research on the clinically detectable LE somatosensory impairments. Combining brain-imaging techniques with our clinical assessment methods might have further strengthened the results of this study.

### 3.6 Conclusion

Somatosensory system is essential to motor control by providing information for the formulation of the appropriate feedforward anticipatory strategy and for the regulation of the feedback mechanism, which allows the correction of performance errors during the execution of a motor plan[90,91]; hence, impairments in this system may

impact motor behavior. In support of prior imaging work[26,28–30,43], our clinical findings suggested that sensory processing dysfunction partially contributed to the motor planning and execution impairments that affect postural control and motor function in CP. Specifically, we provided evidence that somatosensory deficits in the LEs, specifically two-point discrimination and vibration sensation, appear to strongly influence balance and motor performance in children with spastic diplegia. Therefore, addressing the reported somatosensory impairments may contribute to postural stability and functional mobility improvements in this population.

Our research proposed that using a simple battery of clinical tests to assess somatosensation allows for the identification of tactile and proprioceptive deficits and, therefore, provides important information for clinical care in CP. Further research is required to investigate the minimum necessary number of somatosensory assessments that should be included in the clinical practice. A short screening tool that includes modality and site-specific tests besides being administered in a timely manner can potentially identify motor function declines in CP. In addition, it can guide traditional treatment protocols toward a more holistic therapeutic approach by combining motor and sensory rehabilitative strategies to improve overall functionality and quality of life in CP.

# Chapter 4

# STOCHASTIC RESONANCE STIMULATION IMPROVES BALANCE IN CHILDREN WITH CEREBRAL PALSY

## 4.1 Abstract

Stochastic Resonance (SR) Stimulation has been used to enhance balance in populations with sensory deficits by improving the detection and transmission of afferent information. Despite the potential promise of SR in improving postural control, its use in individuals with cerebral palsy (CP) is novel. The objective of this study was to investigate the immediate effects of electrical SR stimulation when applied in the ankle muscles and ligaments on postural stability in children with CP. Additionally, we examined if individuals with CP can benefit more from the application of SR compared to their healthy controls.

Ten children with spastic diplegia (GMFCS level I- III), able to stand independently, and ten age-matched typical developing (TD) peers participated in this study. The sensory SR thresholds were determined for each individual. The control condition and four stimulation intensities (25%, 50%, 75%, 90% of the sensory SR threshold), randomly ordered, were tested while each participant stood motionless on top of 2 force plates for 25s with their eyes open and closed. The differences between the resultant center of pressure velocity (COPVr) of the 4 SR stimulation conditions over the control condition were calculated. The intensity that produced the greatest balance improvements (i.e. reduction in COPVr) was defined as the optimal SR intensity level for each individual and subsequently used for the analysis for each

visual feedback condition. Then, the COPV in the anteroposterior (A/P) and medial-lateral (M/L) directions, 95% COP confidence ellipse area (COPA), and root mean square (RMS) A/P and M/L distance of COP displacement for the optimal and control SR conditions were computed and compared.

For both groups, SR significantly enhanced stability as measured by the reduction in COPVr, COPV in A/P direction, and COPA measures compared to the control condition for visual feedback condition ($p< 0.05$). In the absence of visual information, SR significantly decreased COPV only in M/L direction. Mean COPA, RMS A/P and M/L values decreased, but changes were not statistically significant. Additionally, children with CP demonstrated greater improvements in their balance performance compared to their TD peers in all the COP measures but the RMS in M/L direction during the eyes open condition. When visual feedback was not provided, the only significant difference between groups was in the COPV in M/L direction measure.

SR stimulation may have the potential to be used as a therapeutic tool to improve balance performance by upregulating somatosensory information in individuals with CP. Applying subject-specific SR stimulation intensities is recommended to maximize balance improvements. Additionally, individuals with somatosensory deficits, like children with CP, can benefit more by the application of SR. Overall, balance rehabilitation interventions in CP might be more effective if sensory facilitation methods, like SR, are utilized by the clinicians.

*Note: This work was partially presented in the Pediatric Section of the Combined Section Meeting APTA 2017 (Appendix E).*[109]

## 4.2 Introduction

Control of human upright posture during standing and walking is critical for performing functional activities and requires the integration of sensory inputs from visual, vestibular, and somatosensory systems[14]. All these modalities are regulated dynamically and modified based on the individual, the performed task and the environmental conditions in a process also known as sensory reweighting[14]. For instance, the somatosensory system is predominant for maintaining balance on a static surface when vision is unavailable, whereas in a compliant surface the central nervous system (CNS) depends upon vestibular cues to regulate upright stance. Sensory impairments can influence postural control by either affecting sensory feedback during the execution of a motor response in a continuous changing environment or by experiencing difficulties in developing and pre-selecting the desired motor plan based on previous experience[14,30,110]. Therefore, the observed sensory dysfunction in approximately 90% of children with CP[34] may partially contribute to poor feedback and feedforward motor control[30], resulting in functional constraints associated with this pathology.

The development of movement and posture in CP is primarily affected by a static lesion that occurs in the developing fetal or infant brain[8]. Although the brain injury is not progressive, it results in motor and functional impairments that are progressive through lifetime and related with reduced ambulatory ability[9] and poor balance performance[10–12]. In particular, postural instability has the most significant contribution to the model of primary impairments (i.e. related to the brain injury) compared to the muscle tone and motor coordination deficits in this population[111]. In contrast to normal postural responses, CP postural control characteristics include: descending pattern of muscle recruitment (proximal to distal strategy)[15], reverse order

of muscle activation (antagonist followed by agonist activation)[15,16], compensatory agonist/ antagonist coactivation[14], and inability to quickly modulate postural responses[14] and adapt to perturbations. Sensory deficits are also prevalent in individuals with CP[17–19,21,22,33], and can largely affect postural control and consequently balance. Furthermore, balance deficits in this population are associated with inability to successfully perform functional activities[14], increased risk for falls and higher levels of caregiver dependence[10], and can potentially lead to decreased chances for environmental exploration and social participation.

Postural control deficits in CP have been attributed in biomechanical changes in postural alignment and also in CNS and sensory processing impairments[106]. Disrupted thalamocortical networks[25,28] and impaired somatosensory cortical activation[26,29,43] may affect motor behavior. This is consistent with our clinical findings on the relationship between plantar cutaneous and ankle proprioceptive impairments and motor deficits in CP (Chapter 3). Specifically, we provided evidence that aberrant plantar two-point discrimination, vibration sensation on the first metatarsal head, and ankle joint position sense were related with poor performance in the majority of the underlying systems that contribute to postural control as measured by BESTest and postural sway measures. Damiano et al. (2013) showed significantly moderate to strong relationships between hip proprioceptive deficits in the transverse plane and balance parameters as measured during quiet bipedal stance with eyes open and eyes closed[45]. Altogether, these findings revealed the important link between lower extremities (LE) somatosensation with balance and motor ability, as somatosensory impairments affect both motor and balance control in individuals with

CP. Therefore, the assessment and facilitation of LE somatosensory information should be part of the everyday treatment procedure in this population.

Over the last decade, there is an increasing number of interventions targeting postural control and balance in children with CP[112]. A systematic review on postural control interventions identified only five training protocols that are potentially effective, based on a moderate level of evidence, and all of them are mainly motor-centric with the exception of hippotherapy which involves the provision of both sensory and motor cues through the horse's movement[112]. Yet, this treatment is expensive and of limited availability[113]. The need for further sensory-oriented rehabilitation approaches has been previously highlighted in the literature[27,44,45], especially in light of evidence of plasticity in the white matter pathways following a combined therapy[47] and the potential of beneficial structural changes in the primary somatosensory cortex following somatosensory therapy in individuals with CP[78].

A promising sensory-centric therapeutic approach involves the modulation of somatosensory information by using a sub-sensory stochastic resonance (SR) stimulation to enhance balance control of upright stance. The phenomenon of SR, where random noise improves a nonlinear system's sensitivity to differentiate a weak signal, has been observed in various biological systems[48,49]. Furthermore, studies demonstrated that either mechanical or electrical SR stimulation can be used to enhance balance in: healthy adults[50,54–58], older people[50,51], individuals with functional ankle instability[59,65,67] and knee osteoarthritis[61], and patients with diabetic neuropathy and stroke[66] by improving the sensory signal's strength in the somatosensory[50,58,59,61,66,67] and vestibular[57,58,62] systems. Recent evidence indicated that therapeutic interventions using electrical SR stimulation has ameliorated

proprioceptive deficits[65] and balance disturbances earlier and to a greater extent than traditional rehabilitation in individuals with ankle instability[114]. Conversely, a study by Kyvelidou and colleagues (2017) concluded that mechanical SR did not improve the development of sitting behavior when combined with a perceptual-motor intervention in children with CP between the ages of 2 to 6 years[53]. In this study, however, the intensity of the mechanical SR was determined upon the facial expressions of each participant (i.e. a therapist adjusted the amplitude of the vibratory tractors until the SR stimulus was not noticeable on the child's facial expressions) potentially resulting in using inappropriate levels of SR noise that were not beneficial in advancing sitting postural control[53]. Therefore, an optimal amount of SR stimulation is necessary to improve balance performance[49,52,57,62] and should be subject- specific as each individual might benefit more by different SR intensity levels[52,62].

In the present study, we investigated the immediate effects of SR electrical stimulation on balance performance in children and adolescents with CP and their typically developing (TD) peers (Aim 3). To ensure appropriate levels of SR stimulation during the balance task, we included in our experimental design a procedure to identify each participant's SR sensory threshold followed by an optimization protocol to define the subject-specific optimal SR intensity[52]. We hypothesized that the application of SR would enhance balance control during quiet stance compared to a sham condition in individuals with CP (Hypothesis 3.1). A secondary hypothesis was that the CP group would demonstrate greater improvements in balance performance compared to the TD group when somatosensory SR stimulation would be applied (Hypothesis 3.2).

## 4.3 Methods

### 4.3.1 Participants

Ten individuals with CP and 10 age-matched TD peers between the ages of 8-18 years participated in this study. Children with CP were able to stand independently for at least 2 min (GMFCS I- III) and had a diagnosis of spastic diplegia. The inclusion and exclusion criteria are presented in **Table 4.1**. The protocol of this study was approved by the Institution Review Board of Temple University (for Shriners Hospital for Children, Philadelphia) and the University of Delaware. All the participants and their legal guardians signed the approved assent and consent documents, respectively.

**Table 4.1:** Inclusion and Exclusion criteria for participation in the study. Asterisk indicates the eligibility criteria that should be met only by children with CP.

| Inclusion | Exclusion |
|---|---|
| • Age 8 - 18 years<br>• The diagnosis of spastic diplegic CP*<br>• Levels I-III GMFCS classification*<br>• Ability to stand independently (i.e. without using any assistive device)<br>• Visual, perceptual, and cognitive/ communication skills to follow multiple step commands<br>• Seizure-free or well controlled seizures<br>• Ability to communicate pain or discomfort during testing procedures<br>• Willingness to participate in testing<br>• Ability to obtain Parental/guardian consent and child assent/consent | • Diagnosis of athetoid, ataxic or quadriplegic CP*<br>• Significant scoliosis with primary curve > 40°<br>• Lower extremity surgery or fractures in the year prior testing<br>• Joint instability or dislocation in the lower extremities<br>• A history of selective dorsal root rhizotomy*<br>• Botulinum toxin injections in the lower extremities within the past 6 months*<br>• Marked visual, hearing, vestibular deficits<br>• Implanted medical device that may be contraindicated with application of SR stimulation<br>• Severe spasticity of any lower extremity muscle (eg. a score of 4 on the Modified Ashworth Scale)*<br>• Pregnancy |

### 4.3.2 Experimental Procedures.

***SR stimulation***. Our SR Stimulation System was consisted of four linear isolated stimulators (STMISOLA, Biopac Systems, Inc., Goleta, California, USA). The SR signal (Gaussian White Noise, zero mean, standard deviation 0.05) was generated by a custom LabView program to trigger each Biopac stimulator via a 16 bit PCI 6733 National Instruments multifunction data acquisition card (**Figure 4.1**). Self-

adhesive electrodes, 5 x 5 cm, were placed over the lateral soleus, peroneus longus, and tibialis anterior muscles and anterior talofibular and deltoid ankle ligaments of each leg[58,65,67] after the skin was cleaned and dried. Flexible non-adhesive wrap (CoFlex, Andover Healthcare Inc., Salisbury, CA) was used to tightly secure the electrodes. The maximum current output, controlled by our LabView program, was limited to 5 mA.

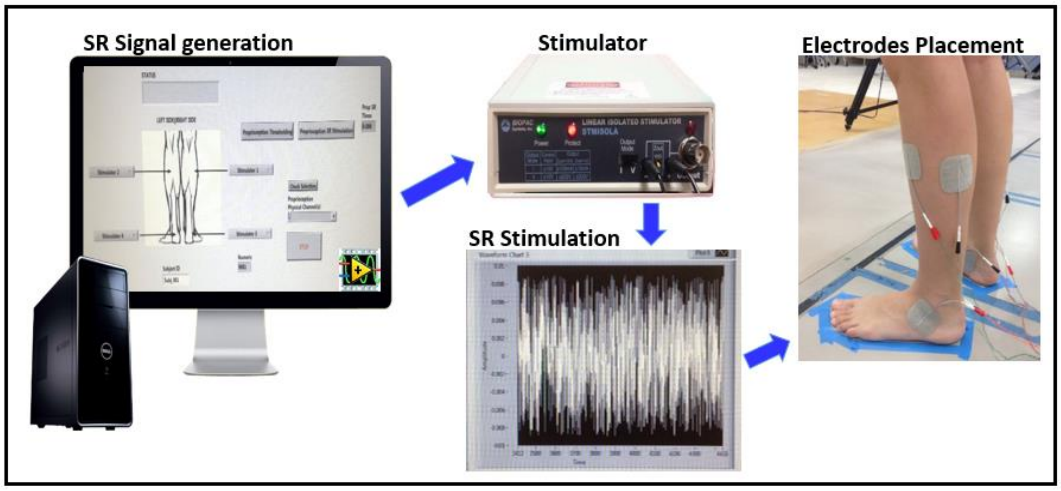


**Figure 4.1:** Schematic illustration of the SR Stimulation System. Our system consisted of a computer and 4 stimulators. The SR signal was generated by a custom LabView control program to trigger the stimulators that subsequently delivered electrical SR stimulation in the muscles and ligaments of the ankle joints.

***SR Sensory Threshold***. To determine the SR optimal intensity for each individual, we verified each subject's sensory threshold (i.e., the level of stimulation required for an individual to just detect a tingling sensation on the stimulus sites)[52,55,58]. During the thresholding procedure, each subject was required to stand on

both feet with their eyes closed, and the SR electrical stimulus amplitude was increased in 0.001 mA increments, initialized at zero, until the subject reported feeling the stimulation (SR sensory threshold). This threshold was verified if the subject could no longer perceive the stimulus when the intensity was decremented. This procedure was repeated four times and the lowest value indicated the subject's sensory threshold and was recorded for subsequent reference.

***SR experimental protocol***. To investigate the effects of electrical SR stimulation in balance, four different stimulation intensities: 25%, 50%, 75%, and 90% of the subject-specific sensory threshold and a sham, no stimulation, control condition were used[52,58]. Following the thresholding process, participants stood barefoot on 2 AMTI force plates (Advanced Mechanical Technology Inc.) in a standardized way as previously described (Chapter 3; Method Section: Standing Balance). For each trial, they were instructed to maintain a still and upright posture for 25 s while having their eyes open (EO) or closed (EC). During the eyes open condition, they were advised to keep their gaze straight ahead at the eye level, whereas during the eyes closed condition a sleeping mask was used to cover the eyes. For each stimulation intensity and visual feedback condition, two trials were performed. The control conditions were tested first and then the stimulation trials were performed in random order. Two additional control condition trials were performed at the end of the testing procedure to examine for learning or fatigue effects. The resting interval between trials depended on each participant's comfort and fatigue level. Finally, an overhead harness system was used to prevent falls during each trial (**Figure 4.2**).


**Figure 4.2:** A child with CP while standing on top of the force plates. SR stimulation is applied.

All the force plate data were collected using Vicon Nexus software (v1.8.5) at 100 Hz sampling rate. Also, to avoid any transient effects due to the addition of SR stimulation[115], only the last 20 s of each trial were filtered with a fourth-order, zero phase response, low-pass Butterworth filter with a cutoff frequency of 5 Hz[52,96] and used for further analysis. The differences between the resultant center of pressure velocity (COPVr) of the 4 SR stimulation conditions over the control condition were calculated. The intensity that produced the greatest balance improvements (i.e. reduction in COPVr) was defined as the optimal SR intensity for each individual and was subsequently used for the analysis[52]. Then, the COPV in A/P and M/L directions, COPA, and RMS A/P and M/L distance of COP displacement for the optimal SR stimulation and control conditions were computed. These COP-based measures have

been previously used to determine the effect of SR stimulation during upright stance in individuals with functional ankle instability[52].

### 4.3.3 Statistical Analysis.

All data were analyzed using SPSS (version 23; SPSS Inc., Chicago. IL, USA) with the level of significance set at $p< 0.05$. Initially, the data were examined for normality using Shapiro-Will test and Q-plots. All the data were normally distributed except the COPA measures that were transformed with a square root transformation before proceeding with the analysis. Independent samples t-tests were performed to examine if there were significant differences between groups in age, height, weight, and BMI. A Fisher's exact test determined if there were sex differences. To rule out learning or fatigue effects, paired t-tests were computed on the COPVr of the initial and last control (no stimulation) trials for EO and EC conditions. To investigate the effects of SR stimulation in CP population (Hypothesis 3.1), all the COP measures were examined separately by a two-way repeated measures ANOVA with 2 within factors (intensity: optimal SR stimulation, control condition; visual stimuli: EO, EC). Based on our a priori hypothesis 3.1, paired t-tests for planned comparisons were performed between the optimal SR stimulation and control conditions when a significant main effect for intensity condition was found.

To investigate if children with CP demonstrated greater improvements in their balance performance when SR stimulation was applied compared to their TD peers (Hypothesis 3.2), the differences between the COP measures of the optimal stimulation intensity over the control condition were computed, square root transformed, and subsequently used for the analysis. Separate 2 x 2 mixed model repeated measures ANOVA with visual stimuli (EO, EC) as the within-subjects factor

and group (CP, TD) as the between-subjects factor were conducted for the COP measures. Planned comparisons (unpaired t-tests) were performed between the CP and TD groups for each visual feedback condition when a significant group effect was found. Finally, mean and standard errors were calculated for the demographic data and all the COP variables of interest.

## 4.4 Results

All children completed the experimental process, however, due to technical problems during the collection of the kinetic data, only the data of 18 participants (9 CP and 9 TD children) were analyzed. No significant differences were found for age, sex, height, weight, and BMI between the CP and the TD groups (**Table 4.2**).

**Table 4.2:** Demographic characteristics of children with cerebral palsy and their typical developing peers. Means and standard errors (in parentheses) are presented in the table.

| | **CP group (n=9)** | **TD group (n=9)** |
|---|---|---|
| **Age** (years, months) | 15 y 5 mo (1y 0.9 mo) | 15 y 6 mo (0.8 y 1.3 mo) |
| **Sex** (male/ female) | 8/ 1 | 5/ 4 |
| **GMFCS** (level) | I: 3; II: 3; III: 3 | - |
| **Height** (cm) | 164 (3.9) | 164.9 (5.4) |
| **Weight** (kg) | 66 (9.9) | 60.4 (8.4) |
| **BMI** ($kg/m^2$) | 23.5 (2.6) | 21.5 (1.8) |

Paired sample t-tests on the initial and the last control – no stimulation-conditions for the COPVr measure showed no significant differences and thus, ruled out any fatigue, learning or carry over effects of SR stimulation (EO: $t(17)= 1.4$, $p=$

0.18; EC: $t(17)= 0.76$, $p= 0.46$). Therefore, improvements in balance were attributed to the application of electrical SR stimulation during the specific test conditions.

For Hypothesis 3.1, separate 2 (intensity) X 2 (visual feedback) repeated measures ANOVAs were conducted to examine the effectiveness of SR on balance in children with CP (**Table 4.3**). A main effect was obtained for intensity, with participants demonstrating decreased COPV in A/P and M/L directions, COPVr, and COPA measures when SR stimulation was applied ($p< 0.05$). Additionally, a main effect was found for visual feedback condition only for the COPV in M/L direction indicating that when participants with CP had their eyes closed they exhibited higher COP velocity in the frontal plane ($F(1,8)= 5.61$, $p= 0.04$, partial $\eta^2 = 0.41$). Finally, we did not find any main effects for the RMS measures or a significant intensity X visual feedback interaction for all the tested COP measures.

**Figure 4.3** shows means and standards errors for all the COP measures for both eyes open and eyes closed conditions. Specifically, children with CP improved their balance with the addition of the optimal SR stimulation compared to the control condition for all measures. These improvements were significant only for the COPV in A/P direction, COPVr and COPA measures for the eyes open condition and for the COPV in M/L direction and COPVr measures for the eyes closed condition.

**Table 4.3:** Main effects of intensity (control vs. SR stimulation) and visual feedback (eyes open vs. eyes closed) for the COP measures in children with CP.

| | Repeated Measures Two-way ANOVA | | | | | |
|---|---|---|---|---|---|---|
| | Main Effect: Intensity | | | Main Effect: Visual Feedback | | |
| | F value | P value | Partial $\eta^2$ | F value | P value | Partial $\eta^2$ |
| **COPV A/P** (mm/s) | F (1,8)= 5.56 | p= 0.04 | 0.41 | F (1,8)= 0.01 | p= 0.9 | 0.00 |
| **COPV M/L** (mm/s) | F (1,8)= 7.54 | p= 0.02 | 0.48 | F (1,8)= 5.61 | p= 0.04 | 0.41 |
| **COPVr** (mm/ s) | F (1,8)= 9.75 | p= 0.01 | 0.55 | F (1,8)= 0.62 | p= 0.45 | 0.72 |
| **COPA** ($mm^2$) | F (1,8)= 6.59 | p= 0.03 | 0.45 | F (1,8)= 0.00 | p= 0.99 | 0.00 |
| **RMS A/P** (mm) | F (1,8)= 1.95 | p= 0.20 | 0.19 | F (1,8)= 0.19 | p= 0.67 | 0.02 |
| **RMS M/L** (mm) | F (1,8)= 4.35 | p= 0.07 | 0.35 | F (1,8)= 0.58 | p= 0.47 | 0.07 |

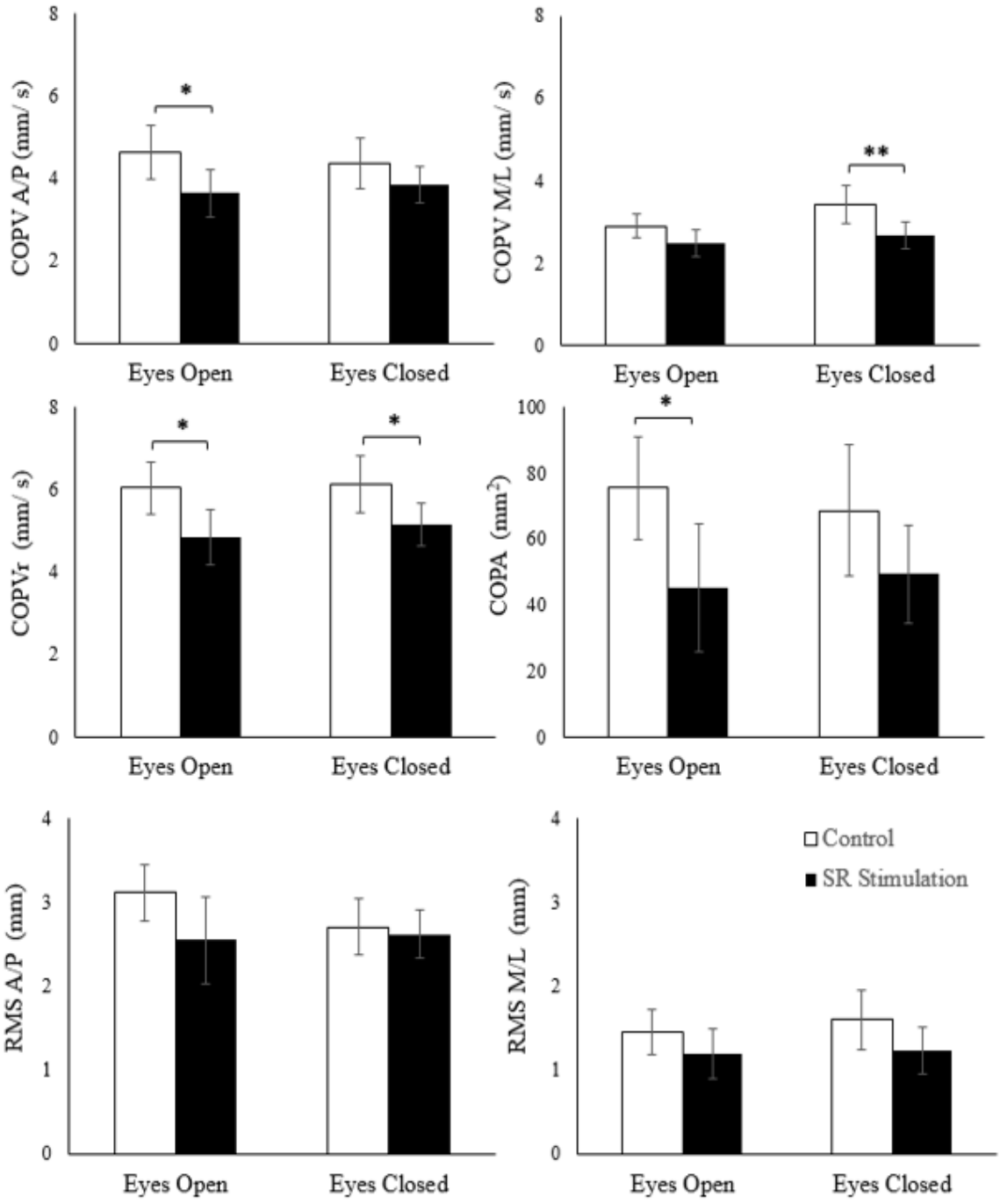


**Figure 4.3:** COP measures during upright quiet stance in children with CP with their eyes open and closed. White bars represent the control-no stimulation-condition and the black bars the optimal SR stimulation condition. Error bars represent standard errors, * $p < 0.05$, ** $p < 0.01$

For our second hypothesis, we investigated if children with CP demonstrated greater balance improvements due to the application of SR than their TD peers. In **Figure 4.4**, representative stabilograms for a child with CP and a child with TD showed COP sway traces during quiet stance for both the SR stimulation and control conditions. The graphs showed that the addition of an optimal SR noise decreased the area of the COP sway for both participants indicating improved postural stability; and this decrease was larger for the child with CP.

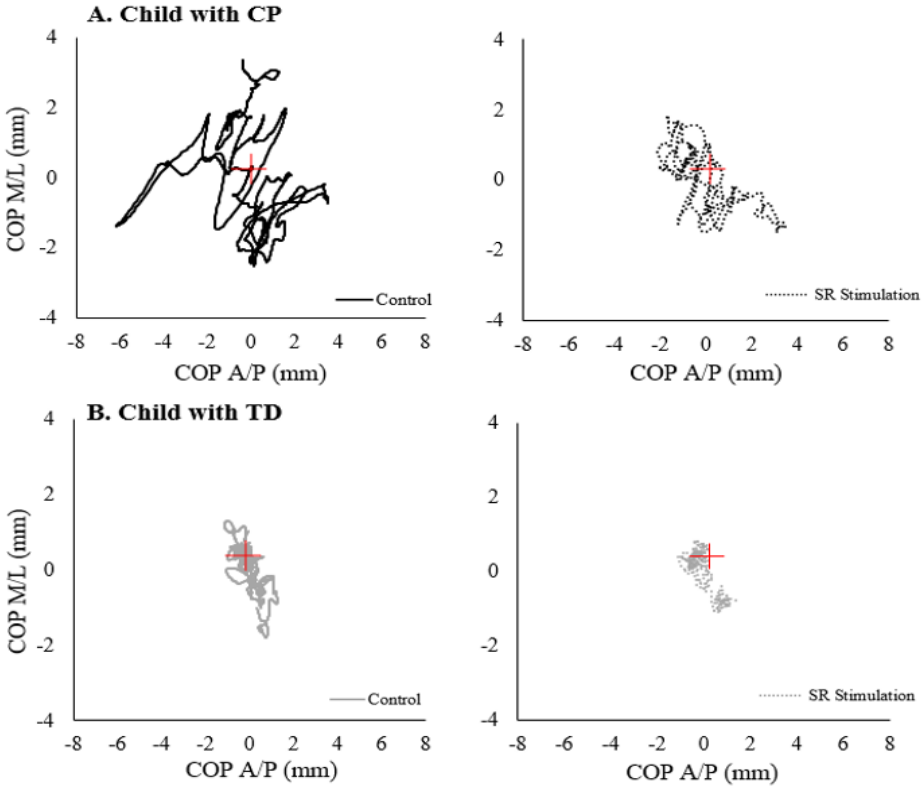


**Figure 4.4:** Representative data from a child with CP (A) and a TD individual (B), showing COP stabilograms during quiet stance with their eyes open. Two experimental condition are shown for: control-no stimulation-condition (solid line), and SR Optimal Stimulation condition (dotted line).

Separate 2 (intensity) X 2 (group) mixed model repeated measures ANOVAs, with intensity as a within factor was conducted for all the variables of interest. A significant main effect was found for group in COPVr ($F(1,16)= 5.27$, $p= 0.03$, partial $\eta^2 = 0.25$), COPV in M/L direction ($F(1,16)= 7.37$, $p= 0.01$, partial $\eta^2 = 0.32$), and COPA ($F(1,16)= 8.52$, $p= 0.01$, partial $\eta^2 = 0.35$). Additionally, a marginally significant main effect for group was found for COPV ($F(1,16)= 3.78$, $p= 0.07$, partial $\eta^2 = 0.19$) and RMS ($F(1,16)= 3.9$, $p= 0.06$, partial $\eta^2= 0.20$) in A/P direction. These results indicated that the CP group benefited more from the application of SR during upright stance. Furthermore, the planned comparisons suggested that children with CP significantly improved balance compared to the control group when visual information was provided (**Table 4.4**). For the eyes closed condition, the CP group showed significantly greater balance performance with the SR noise compared to controls only for the COPV in M/L direction (**Table 4.4**).

**Table 4.4:** Mean ± SE for the differences between the COP measures of the optimal SR stimulation intensity over the control condition for children with CP and their TD peers. The negative sign indicates that the addition of SR resulted in decreased COP measures suggesting balance improvements. Asterisks denote significant differences between groups for each visual feedback condition (* $p < .05$; ** $p < .01$).

| | **Eyes Open** | | **Eyes Closed** | |
|---|---|---|---|---|
| | *CP Group* | *TD Group* | *CP Group* | *TD Group* |
| **COPVr** (mm/ s) | -1.20± 0.47* | -0.17± 0.16 | -0.99± 0.44 | -0.34± 0.28 |
| **COPV A/P** (mm/s) | -0.99± 0.40* | 0.05± 0.29 | -0.54± 0.38 | 0.01± 0.28 |
| **COPV M/L** (mm/s) | -0.42± 0.32** | 0.20± 0.20 | -0.75± 0.24* | 0.14± 0.33 |
| **COPA** ($mm^2$) | -30.25± 18.84** | -0.12± 2.9 | -19.34± 15.13 | 0.54± 5.02 |
| **RMS A/P** (mm) | -0.56± 0.30** | -0.08 ± 0.17 | -0.09± 0.29 | 0.18± 0.20 |
| **RMS M/L** (mm) | -0.26± 0.27 | 0.13± 0.09 | -0.36± 0.20 | -0.01± 0.16 |

## 4.5 Discussion

In this study, we investigated the immediate effects of SR stimulation during quiet stance in individuals with CP and their TD peers. Specifically, we showed that applying a subsensory SR noise in the muscles and ligaments of the ankle joints during quiet stance resulted in decreased COP sway compared to the control-no stimulation-condition in the CP group. Additionally, we demonstrated that the improvements in balance performance (i.e. reductions in the COP measures) due to the application of SR were significantly greater in the CP group than the TD group. Overall, the detected balance improvements were potentially due to the upregulation of the afferent somatosensory inputs, as the SR stimulation increased their detectability by the CNS. These findings suggested that SR stimulation is a promising

tool that, upon further development, can be used as part of future therapeutic interventions for the treatment of balance deficits in children with CP.

Previous studies showed that applying SR noise in the lower extremities can decrease postural sway and improve balance in populations with somatosensory deficits[50,52,61,65–67,116]. Likewise, we demonstrated that children with CP, who exhibit foot and ankle somatosensory deficits, can benefit from the application of electrical SR noise in the lower extremities during standing. One potential neurophysiological mechanism that describes electrical SR is that the subthreshold electrical noise signals cause small changes in receptor transmembrane potentials, which, in turn, make the sensory neuron more likely to fire an action potential in the presence of a weak stimulus[50,66]. We speculated that the optimal level of electrical SR noise enhanced the excitability of the muscle spindles located in the tibialis anterior, peroneus longus, and lateral soleus and the joint receptors in the anterior talofibular and deltoid ankle ligaments. This resulted in lower proprioceptive receptors thresholds and, thus, increased detectability of afferent signals by CNS. Integration of these inputs by CNS allowed for improved postural reflexes and subsequently balance function in CP, as a stable standing position mainly depended on ankle joint proprioception[36].

Plantar cutaneous information is also essential in triggering appropriate compensatory postural responses[37] during upright stance. In Aims 1 & 2 (Chapter 2 and 3), we showed that children with CP exhibited increased plantar tactile thresholds that were significantly related to balance impairments. In Aim 3, based on the notion that the SR phenomenon is also present in the neuronal networks of the CNS[63,64,117], we used SR stimulation on the muscles and ligaments of the ankle joints to potentially modulate the diminished plantar cutaneous inputs. To investigate if SR is occurring in

the CNS, a double receptor experimental design (see **Figure 1.3**)[63] has been utilized by Iliopoulos and his team. Specifically, their findings demonstrated enhanced perception of near-threshold electrical pulses when applied to the index finger while SR noise was applied to the middle finger[64]. Particularly, introducing two distinct signals in two different peripheral pathways (i.e. electrical pulses to index and noise to middle finger) suggested that the interaction of these 2 signals occurred in the CNS; providing evidence of SR behavior not only in the peripheral (i.e. sensory receptors) but in the CNS as well[64]. Therefore, we speculated that the application of SR noise increased the detectability of the ankle's proprioceptive (i.e. peripheral SR) and the plantar cutaneous signals (i.e. central SR) to improve balance performance in children with CP.

Our results demonstrated that the application of SR resulted in significant balance improvements in individuals with CP primarily in the eyes open condition. Due to their inherent somatosensory impairments, it is possible that children with CP relied more on their visual input to maintain a stable upright stance. This is not surprising since previous research showed visual dependency as a compensatory strategy for proprioceptive deficits in CP[33]. Conversely, children with CP showed similar postural sway increments when vision was occluded as the control group, indicating that they did not have to depend more on visual feedback to maintain upright stance[118]. In our study, we speculated that the upregulated somatosensory information, due to the addition of the SR noise, and along with the visual information, provided enhanced sensory inputs and processing that resulted in improved balance control compared to the eyes closed condition. These findings suggested that incorporating visual feedback strategies, for example by using mirrors

or playing virtual reality games during a balance training protocol, is important for maximizing the benefits of the use of SR in this population.

An important characteristic of SR is the inverted U-shaped relationship between signal's detectability and the noise's intensity[48,49,63,64]. According to this relationship, there is an optimal level of noise that results in maximal detectability of a weak signal. Higher or lower levels of SR noise decrease the detection of the signal leading to degraded performance. To determine the optimal SR intensity in this study, we initially detected each individual's SR sensory threshold and then tested four different SR intensity levels (i.e. 25%, 50%, 75%, and 90% of SR threshold) to define which one of them could enhance balance performance more. Similar SR optimization protocols have been previously used for the identification of the optimal SR intensity to enhance somatosensory[52,55] and vestibular information[57,62] to improve postural stability. On the contrary, using an unreliable procedure to define the SR threshold, as previously described in the introduction section, did not produce any increase in advancing sitting behavior in children with CP[53]. Altogether, determining the subject-specific optimal SR intensity is a crucial component of SR testing to maximize somatosensory signal's detectability and to subsequently improve balance function.

Another important consideration regarding the application of SR is that the externally applied noise also depends upon the levels of the internal noise[63]. Internal SR noise is present in every level of the nervous system, from the cellular excitability to the execution of a motor task[117], and its intensity varies not only across subjects but also within the same subject[63]. Aihara et al (2010) suggested that when the internally generated noise is already at high levels, then the addition of external noise may diminish performance and vice versa[63]. In line with this notion, our findings showed

that children with CP improved their standing balance with the addition of SR compared to their TD peers. In particular, we speculated that individuals with CP had lower levels of internal noise and the application of the external SR noise facilitated the somatosensory signal detection resulting in improved balance. Moreover, the internal noise levels differed within the CP group as for each individual a different optimal SR intensity was identified. To the contrary, healthy controls potentially exhibited higher internal noise levels and applying SR on their lower extremities during quiet stance only attenuated their postural stability. Future studies should further our understanding on how CP might influence the levels of internal noise in the nervous system and the interplay between internal and external noise to enhance sensory information processing and movement.

We acknowledge that our findings were interpreted in light of the assumption that a decrease in the computed COP variables due to the application of SR indicated balance improvements. In agreement, prior studies on postural balance in CP indicated that decreased COP sway is associated with increased stability[10,12,45,118]. Specifically, children with CP usually demonstrate increased postural sway during standing compared to their TD peers in their effort to collect more somatosensory information to compensate for lower extremity somatosensory deficits (i.e. larger COP oscillation are related with ankle joint rotations and, hence, greater activation of the proprioceptive receptors) and better define their position in space[10,14]. Similarly, in this study, individuals with CP showed greater postural sway than their age-matched controls in the control-no stimulation-condition. Based on empirical data from our lab, however, some individuals with CP may utilize coactivation of the agonist and antagonist muscle groups as a compensatory strategy to maintain their upright stance

and exhibit a stiff posture. In this subgroup of individuals, decreased postural sway would suggest balance impairments and inability to adapt in a constantly changing dynamic environment. For this reason, identifying the individuals with CP that share common postural control strategies can be useful in designing appropriate treatment plans to address balance deficits.

## 4.6 Conclusion

Rehabilitation interventions in CP have thus far focused on improving motor performance but with limited consideration of somatosensory impairments, whose deficits can affect motor behavior. In addition, there is no universally-accepted framework for the identification of sensory processing impairments in children with developmental disorders, thus resulting in misdiagnosis and eventually in poor treatment[119]. Since somatosensory information is a key component of postural and motor control, more comprehensive clinical sensory assessments and more effective interventions should include sensory facilitation methods, like SR stimulation, as part of the everyday treatment procedure.

Our findings showed that SR stimulation can potentially be used as a therapeutic tool to improve balance performance by upregulating somatosensory information in children with CP. Clinicians and researchers who plan to utilize SR stimulation to modulate somatosensory input should apply subject-specific SR intensities to maximize balance improvements. Training protocols that combine afferent SR stimulation while performing daily activities may promote neuroplasticity[120] and, as a result enhance motor and sensory function compared to traditional motor-centric protocols.

# Chapter 5

# CONCLUSIONS

Traditional rehabilitation and motor learning approaches in CP are generally motor-centric, focusing on techniques to ameliorate musculoskeletal and motor impairments, and are marginally effective[88]. Less attention has been paid on the treatment of sensory deficits despite being present in 90% of this population[34] and affect their motor control[30]. Neuroimaging studies has showed abnormal somatosensory cortical activation[26,43] and injured thalamocortical pathways[25,28,73], suggesting sensory processing and integration dysfunction in children with CP. Likewise, clinical findings provided evidence on UE somatosensory impairments[17,18,21,31,32] negatively affecting manual prehension[17,18,34,92,93]. Surprisingly, little research has examined LE somatosensory deficits in CP[22,33] with no reports so far focusing on distal LE somatosensation, although its role in feedback and feedforward mechanisms that contribute to postural control is essential[90,91]. The purpose of this dissertation was to address this gap in the literature by determining the presence of foot and ankle somatosensory deficits in children with CP and delineating their relationship with balance and motor function (Aims 1 & 2). Furthermore, we investigated if SR stimulation can be used as a sensory facilitation method to modulate distal somatosensory information and enhance balance control, which may positively influence functional performance and the overall quality of life of individuals with CP (Aim 3).

In Aim 1, a simple and cost-effective battery of sensory tests was used to assess distal somatosensation in children with CP and in TD individuals. As predicted in Hypothesis 1.1, the CP group demonstrated difficulty in identifying a plantar light touch pressure stimulus compared to the TD group. Similarly, children with CP exhibited significantly higher two-point discrimination thresholds in the forefoot and heel areas of their feet than their age-matched peers. Another interesting finding, although not significant, was that participants with CP were able to perceive the vibration stimulus for a longer period than the healthy controls. Finally, the CP group demonstrated significant impairments in joint position sense but not in kinesthesia of the ankle joints, partially confirming Hypothesis 1.2. Specifically, both groups (i.e. CP and TD) received a perfect score for ankle kinesthesia indicating that this test was not sensitive enough to detect proprioceptive deficits in CP and, therefore, the ankle joint position sense test was proposed as a better method to assess proprioception. Overall, these findings corroborate the notion that children with CP experience not only UE, but also LE distal somatosensory impairments potentially due to the primary brain injury[8] and the limited learning experience as well as environmental exposure[8,74].

The reported foot and ankle somatosensory deficits can partially contribute to the motor planning and execution impairments and, thus, affect balance and motor control in CP based on Aim's 2 findings. Two-point discrimination deficits in the plantar side of the foot were significantly related with postural control. In particular, inability to perceive two applied stimuli as distinct in the forefoot and heel plantar areas resulted in generalized balance problems in this population, as these participants performed poorly in almost all of the underlying systems that play a role in postural control[23]. In addition, longer duration of the vibration perception in their first

metatarsal head was significantly related to postural disturbances and increased postural sway, potentially indicating the aberrant and prolonged processing of vibratory information by CNS. Similarly, longer perceived vibration in CP significantly affected gross motor and walking ability, functional mobility, and plantarflexors' strength; highlighting the important role of somatosensory input from the first metatarsal joint not only on the forward propulsion during gait[14], but also on the overall motor behavior. Children with CP that experienced greater impairments in ankle joint position sense also showed inability to maintain an upright stance in unexpected perturbations, demonstrating the link between ankle proprioception and feedback mechanisms. Another interesting finding was that high light touch pressure thresholds in CP were only related with smaller walking distances in a 6 m period. This possibly shows that the plantar light touch pressure deficits could only affect prolonged walking activities and not simple balance tasks in ambulatory children with CP. Altogether, this clinical evidence reinforced previous brain imaging research that associated LE somatosensory dysfunction with decreased plantarflexors strength and walking velocity[43]. Finally, our results confirmed Hypothesis 2.1, demonstrating that decreased plantar cutaneous feedback and inaccurate ankle proprioceptive input can contribute to the poor balance control and motor function affecting the overall functionality in this population.

Our approach to improve distal somatosensation involved the application of SR stimulation on the LE of children with CP and TD individuals during quiet stance (Aim 3). In the CP group, the addition of SR stimulation augmented afferent input leading to improved postural stability as measured by the decrease of the COP measures, as proposed in Hypothesis 3.1. Moreover, combined visual and SR enhanced

somatosensory information produced greater balance improvements than SR enhanced somatosensory input alone; suggesting that individuals with CP can benefit by incorporating visual feedback strategies during SR balance training protocols. In agreement with previous SR research work[52,55,57,62], our findings corroborated the important role of identifying the optimal SR intensity for each individual during SR testing to ensure somatosensory signal's detectability and maximize balance benefits. Failure to determine the subject-specific optimal SR intensity may result in degraded performance[48,49,63,64]. Finally, individuals with LE somatosensory deficits, like individuals with CP, benefited more when SR was applied to LE during a standing balance task than TD individuals, confirming Hypothesis 3.2. It is possible that children with CP had lower levels of internal noise in their nervous system compared to healthy controls and, therefore, the addition of external SR noise potentially facilitated somatosensory signal detection and subsequently balance. Future studies should focus on understanding how CP might influence the interplay between internal and external SR noise to enhance or decrease sensory information detectability and affect balance control in this population.

This dissertation work contributed to the body of literature by providing clinical evidence on foot and ankle somatosensory deficits and their influence on postural control and motor behavior in spastic diplegic CP. To the best of the author's knowledge, this was the first study that utilized electrical SR to enhance distal LE somatosensation and improve balance in this population. Although this series of studies was of small sample size, it produced significant findings regarding the assessment, impact, and improvement of the distal LE somatosensory deficits in CP. Future research could strengthen these results by including a bigger sample size and

incorporating brain imaging techniques in the experimental design to provide more insights into the effect of SR stimulation on brain reorganization and sensorimotor connectivity in CP. Lastly, from a clinical standpoint, these findings could potentially lead to improved therapeutic management in CP by: 1) suggesting the use of an easy to administer battery of sensory tests in daily practice to identify individuals with somatosensory impairments, 2) assisting clinicians to design more effective subject-specific plans by targeting not only motor but also sensory deficits in CP, and 3) proposing the use of SR stimulation for somatosensory facilitation.

**Future Directions**

Postural control and balance dysfunction have been associated with difficulties in performing daily activities and walking[121] leading to limited participation in a wide range of life domains[122]. Therefore, designing intervention protocols to improve postural control in the CP population can positively influence all three components of the WHO- ICF model of disability (i.e. body function and structure, activity, participation). Based on our findings, SR stimulation can be used as a sensory-oriented tool in improving somatosensory feedback and, thus, can be incorporated into the design of balance training programs in CP. Our future plans involve the application of SR stimulation in a fun and immersive virtual reality (VR) environment while participants play low cost VR video games. Such type of interventions can increase active participation and patients' motivation, which are key components for a successful training protocol. Finally, designing and utilizing subject-specific wearable electrode garments and footwear to apply SR during balance training or when performing daily activities can lead to augmented sensory exposure that is necessary for proper postural control responses in a challenging dynamic environment.

Especially for individuals with CP whose neurological insult took place prior to having the ability to learn flexible and stable movement, enhancing sensory experience may positively contribute to motor behavior and, hence, improve their overall quality of life.

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## Appendix A

## POSTURAL CONTROL ASSESSMENT

### BESTest
### Balance Evaluation – Systems Test
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**TEST NUMBER/SUBJECT CODE** _____ **DATE** _____

**EXAMINER NAME** _____

*EXAMINER Instructions for BESTest*

1. Subjects should be tested with flat heeled shoes or with shoes and socks off.
2. If subject must use an assistive device for an item, score that item one category lower

*Tools Required*

- Stop watch
- Measuring tape mounted on wall for Functional Reach test
- Approximately 60 cm x 60 cm (2 X 2 ft) block of 4-inch, medium-density, Tempur® foam
- 10 degree incline ramp (at least 2 x 2 ft) to stand on
- Stair step, 15 cm (6 inches) in height for alternate stair tap
- 2 stacked shoe boxes for obstacle during gait
- 2.5 Kg (5-lb) free weight for rapid arm raise
- Firm chair with arms with 3 meters in front marked with tape for Get Up and Go test
- Masking tape to mark 3 m and 6 m lengths on the floor for Get Up and Go

**SUMMARY OF PERFORMANCE: CALCULATE PERCENT SCORE**

| | | |
|---|---|---|
| **Section I:** | **_____/15 x 100 = _____** | **Biomechanical Constraints** |
| **Section II:** | **_____/21 x 100 = _____** | **Stability Limits/Verticality** |
| **Section III:** | **_____/18 x 100 = _____** | **Transitions/Anticipatory** |
| **Section IV** | **_____/18 x 100 = _____** | **Reactive** |
| **Section V:** | **_____/15 x 100 = _____** | **Sensory Orientation** |
| **Section VI:** | **_____/21 x 100 = _____** | **Stability in Gait** |
| **TOTAL:** | **_____/108 points = _____** | **Percent Total Score** |

## Balance Evaluation – Systems Test

Subjects should be tested with flat heeled shoes or shoes and socks off. If subject must use an assistive device for an item, score that item one category lower. If subject requires physical assistance to perform an item score the lowest category (0) for that item.

**I. BIOMECHANICAL CONSTRAINTS** **SECTION I: _____/15 POINTS**

1. BASE OF SUPPORT
   - (3) Normal: Both feet have normal base of support with no deformities or pain
   - (2) One foot has deformities and/or pain
   - (1) Both feet has deformities OR pain
   - (0) Both feet have deformities AND pain

2. COM ALIGNMENT
   - (3) Normal AP and ML CoM alignment and normal segmental postural alignment
   - (2) Abnormal AP OR ML CoM alignment OR abnormal segmental postural alignment
   - (1) Abnormal AP OR ML CoM alignment AND abnormal segmental postural alignment
   - (0) Abnormal AP AND ML CoM alignment

3. ANKLE STRENGTH & RANGE
   - (3) Normal: Able to stand on toes with maximal height and to stand on heels with front of feet up
   - (2) Impairment in either foot of either ankle flexors or extensors (i.e. less than maximum height)
   - (1) Impairment in two ankle groups (eg; bilateral flexors or both ankle flexors and extensors in 1 foot)
   - (0) Both flexors and extensors in both left and right ankles impaired (i.e. less than maximum height)

4. HIP/TRUNK LATERAL STRENGTH
   - (3) Normal: Abducts both hips to lift the foot off the floor for 10 s while keeping trunk vertical
   - (2) Mild: Abducts both hips to lift the foot off the floor for 10 s but without keeping trunk vertical
   - (1) Moderate: Abducts only one hip off the floor for 10 s with vertical trunk
   - (0) Severe: Cannot abduct either hip to lift a foot off the floor for 10 s with trunk vertical or without vertical

5. SIT ON FLOOR AND STANDUP *Time_____ secs*
   - (3) Normal: Independently sits on the floor and stands up
   - (2) Mild: Uses a chair to sit on floor OR to stand up
   - (1) Moderate: Uses a chair to sit on floor AND to stand up
   - (0) Severe: Cannot sit on floor or stand up, even with a chair, or refuses

**II. STABILITY LIMITS** **SECTION II: _____/21 POINTS**

6. SITTING VERTICALITY AND LATERAL LEAN

| Lean | | | Verticality | | |
|---|---|---|---|---|---|
| Left | Right | | Left | Right | |
| (3) | (3) | Maximum lean, subject moves upper shoulders beyond body midline, very stable | (3) | (3) | Realigns to vertical with very SMALL or no OVERSHOOT |
| (2) | (2) | Moderate lean, subject's upper shoulder approaches body midline or some instability | (2) | (2) | Significantly Over- or under-shoots but eventually realigns to vertical |
| (1) | (1) | Very little lean, or significant instability | (1) | (1) | Failure to realign to vertical |
| (0) | (0) | No lean or falls (exceeds limits) | (0) | (0) | Falls with the eyes closed |

7. FUNCTIONAL REACH FORWARD *Distance reached:* _____ *cm OR*_____*inches*
(3) Maximum to limits: >32 cm (12.5 in )
(2) Moderate: 16.5 cm - 32 cm (6.5 – 12.5 in)
(1) Poor: < 16.5 cm (6.5 in)
(0) No measurable lean – or must be caught

8. FUNCTIONAL REACH LATERAL *Distance reached: Left* _____ *cm (*_____*in) Right* _____ *cm (*_____*in)*

| Left | Right | |
|---|---|---|
| (3) | (3) | Maximum to limit: > 25.5 cm (10 in) |
| (2) | (2) | Moderate: 10-25.5 cm (4-10 in) |
| (1) | (1) | Poor: < 10 cm (4 in) |
| (0) | (0) | No measurable lean, or must be caught |

**III. TRANSITIONS- ANTICIPATORY POSTURAL ADJUSTMENT** **SECTION III.** _____**/18 POINTS**

9. SIT TO STAND
(3) Normal: Comes to stand without the use of hands and stabilizes independently
(2) Comes to stand on the first attempt with the use of hands
(1) Comes to stand after several attempts or requires minimal assist to stand or stabilize or requires touch of back of leg or chair
(0) Requires moderate or maximal assist to stand

10. RISE TO TOES
(3) Normal: Stable for 3 sec with good height
(2) Heels up, but not full range (smaller than when holding hands so no balance requirement) -OR- slight instability & holds for 3 sec
(1) Holds for less than 3 sec
(0) Unable

11. STAND ON ONE LEG

| Left *Time in Sec:*_____ | Right *Time in Sec:* _____ |
|---|---|
| (3) Normal: Stable for > 20 s | (3) Normal: Stable for > 20s |
| (2) Trunk motion, OR 10-20 s | (2) Trunk motion, OR 10-20 s |
| (1) Stands 2-10 s | (1) Stands 2-10s |
| (0) Unable | (0) Unable |

12. ALTERNATE STAIR TOUCHING *# of successful steps:* _____ *Time in seconds:* _____
(3) Normal: Stands independently and safely and completes 8 steps in < 10 seconds
(2) Completes 8 steps (10-20 seconds) AND/OR show instability such as inconsistent foot placement, excessive trunk motion, hesitation or arhythmical
(1) Completes < 8 steps – without minimal assistance (i.e. assistive device) OR > 20 sec for 8 steps
(0) Completes < 8 steps, even with assistive devise

13. STANDING ARM RAISE
(3) Normal: Remains stable
(2) Visible sway
(1) Steps to regain equilibrium/unable to move quickly w/o losing balance
(0) Unable, or needs assistance for stability

**IV. REACTIVE POSTURAL RESPONSE** **SECTION IV: _____/18 POINTS**

14. IN PLACE RESPONSE- FORWARD
(3) Recovers stability with ankles, no added arms or hips motion
(2) Recovers stability with arm or hip motion
(1) Takes a step to recover stability
(0) Would fall if not caught OR requires assist OR will not attempt

15. IN PLACE RESPONSE- BACKWARD
(3) Recovers stability at ankles, no added arm / hip motion
(2) Recovers stability with some arm or hip motion
(1) Takes a step to recover stability
(0) Would fall if not caught -OR- requires assistance -OR- will not attempt

16. COMPENSATORY STEPPING CORRECTION- FORWARD
(3) Recovers independently a single, large step (second realignment step is allowed)
(2) More than one step used to recover equilibrium, but recovers stability independently OR 1 step with imbalance
(1) Takes multiple steps to recover equilibrium, or needs minimum assistance to prevent a fall
(0) No step, OR would fall if not caught, OR falls spontaneously

17. COMPENSATORY STEPPING CORRECTION- BACKWARD
(3) Recovers independently a single, large step
(2) More than one step used, but stable and recovers independently OR 1 step with imbalance
(1) Takes several steps to recover equilibrium, or needs minimum assistance
(0) No step, OR would fall if not caught, OR falls spontaneously

18. COMPENSATORY STEPPING CORRECTION- LATERAL

Left
(3) Recovers independently with 1 step of normal length/width (crossover or lateral OK)
(2) Several steps used, but recovers independently
(1) Steps, but needs to be assisted to prevent a fall
(0) Falls, or cannot step

Right
(3) Recovers independently with 1 step of normal length/width (crossover or lateral OK)
(2) Several steps used, but recovers independently
(1) Steps, but needs to be assisted to prevent a fall
(0) Falls, or cannot step

**V. SENSORY ORIENTATION** **SECTION V: _____/15 POINTS**

19. SENSORY INTEGRATION FOR BALANCE (MODIFIED CTSIB)

| A -EYES OPEN, FIRM SURFACE | B -EYES CLOSED, FIRM SURFACE | C -EYES OPEN, FOAM SURFACE | D -EYES CLOSED, FOAM SURFACE |
|---|---|---|---|
| Trial 1 _____sec | Trial 1 _____sec | Trial 1 _____sec | Trial 1_____sec |
| Trial 2 _____sec | Trial 2 _____sec | Trial 2 _____sec | Trial 2 _____sec |
| (3) 30s stable | (3) 30s stable | (3) 30s stable | (3) 30s stable |
| (2) 30s unstable | (2) 30s unstable | (2) 30s unstable | (2) 30s unstable |
| (1) < 30s | (1) < 30s | (1) < 30s | (1) < 30s |
| (0) Unable | (0) Unable | (0) Unable | (0) Unable |

20. INCLINE- EYES CLOSED

Toes Up
(3) Stands independently, steady without excessive sway, holds 30 sec, and aligns with gravity
(2) Stands independently 30 SEC with greater sway than in item 19B -OR- aligns with surface
(1) Requires touch assist -OR- stands without assist for 10-20 sec
(0) Unable to stand >10 sec -OR- will not attempt independent stance

**VI. STABILITY IN GAIT** **SECTION V: _____/21 POINTS**

21. GAIT – LEVEL SURFACE *Time_____secs.*
    (3) Normal: walks 20 ft., good speed (≤ 5.5 sec), no evidence of imbalance.
    (2) Mild: 20 ft., slower speed (>5.5 sec), no evidence of imbalance.
    (1) Moderate: walks 20 ft., evidence of imbalance (wide-base, lateral trunk motion, inconsistent step path) – at any preferred speed.
    (0) Severe: cannot walk 20 ft. without assistance, or severe gait deviations OR severe imbalance

22. CHANGE IN GAIT SPEED
    (3) Normal: Significantly changes walking speed without imbalance
    (2) Mild: Unable to change walking speed without imbalance
    (1) Moderate: Changes walking speed but with signs of imbalance,
    (0) Severe: Unable to achieve significant change in speed AND signs of imbalance

23. WALK WITH HEAD TURNS – HORIZONTAL
    (3) Normal: performs head turns with no change in gait speed and good balance
    (2) Mild: performs head turns smoothly with reduction in gait speed,
    (1) Moderate: performs head turns with imbalance
    (0) Severe: performs head turns with reduced speed AND imbalance AND/OR will not move head within available range while walking.

24. WALK WITH PIVOT TURNS
    (3) Normal: Turns with feet close, FAST (< 3 steps) with good balance.
    (2) Mild: Turns with feet close SLOW (>4 steps) with good balance
    (1) Moderate: Turns with feet close at any speed with mild signs of imbalance
    (0) Severe: Cannot turn with feet close at any speed and significant imbalance.

25. STEP OVER OBSTACLES *Time_____sec*
    (3) Normal: able to step over 2 stacked shoe boxes without changing speed and with good balance
    (2) Mild: steps over 2 stacked shoe boxes but slows down, with good balance
    (1) Moderate: steps over shoe boxes with imbalance or touches box.
    (0) Severe: cannot step over shoe boxes AND slows down with imbalance or cannot perform with assistance.

26. TIMED "GET UP & GO" *Get Up & Go: Time _____sec*
    (3) Normal: Fast (<11 sec) with good balance
    (2) Mild: Slow (>11 sec with good balance)
    (1) Moderate: Fast (<11 sec) with imbalance.
    (0) Severe: Slow (>11 sec) AND imbalance.

27. Timed "Get Up & Go" With Dual Task *Dual Task: Time _____sec*
    (3) Normal: No noticeable change between sitting and standing in the rate or accuracy of backwards counting and no change in gait speed.
    (2) Mild: Noticeable slowing, hesitation or errors in counting backwards OR slow walking (10%) in dual task
    (1) Moderate: Affects on BOTH the cognitive task AND slow walking (>10%) in dual task.
    (0) Severe: Can't count backward while walking or stops walking while talking

## Appendix B

## GROSS MOTOR FUNCTIONAL MEASURE

### GMFM-66-IS (ITEM SET) [1] SCORE SHEETS FOR ITEM SETS 1, 2, 3 & 4

### FOR THE GROSS MOTOR FUNCTION MEASURE (GMFM-66)

Child's Name: _____ ID#: _____

Assessment Date: _____ year / month / day

Date of Birth: _____ year / month / day

Chronological Age: _____ year / month / day

GMFCS Level[2]:

☐ I ☐ II ☐ III ☐ IV ☐ V

Evaluator's Name: _____

Testing Condition (e.g., room, clothing, time, others present):

_____

The GMFM is a standardized observational instrument designed and validated to measure change in gross motor function over time in children with cerebral palsy. The scoring key is meant to be a general guideline. However, most of the items have specific descriptors for each score. It is imperative that the guidelines contained in the manual be used for scoring each item.

**SCORING KEY**

0 = does not initiate
1 = initiates
2 = partially completes
3 = completes
9 (or leave blank) = not tested (NT) [used for the GMAE-2 scoring*]

**It is important to differentiate a true score of "0" (child does not initiate) from an item which is Not Tested (NT) if you are interested in using the GMFM-66 Ability Estimator (GMAE) Software.**

*The GMAE-2 software is available for downloading from www.canchild.ca for those who have purchased the GMFM manual. The GMFM-66 is only valid for use with children who have cerebral palsy.

**Contact for Research Group:**
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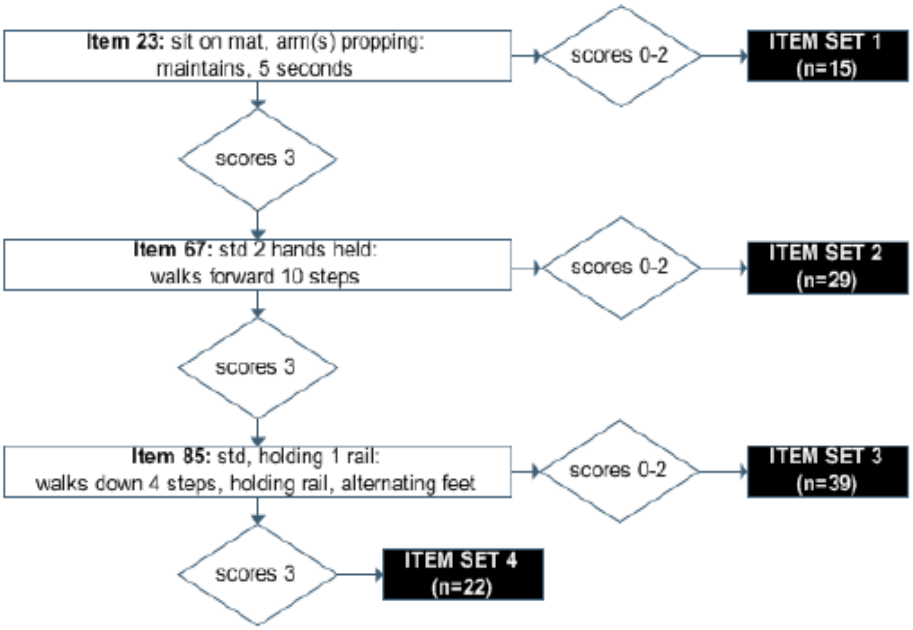
CanChild
Centre for Childhood Disability Research

[1]For an explanation of the item sets please see: Russell, D., Avery, L., Walter, S. et al. (2010). Development and validation of item sets to improve efficiency of administration of the 66 item Gross Motor Function Measure in children with cerebral palsy. *Developmental Medicine & Child Neurology*, 52(2): e48-54. EPub 2009 Oct7.

[2]GMFCS level is a rating of severity of motor function. Definitions for the GMFCS-E&R (expanded & revised) are found in Palisano, R., Rosenbaum, P., Bartlett, D., Livingston, M. (2008). Content validity of the expanded and revised Gross Motor Function Classification System. *Developmental Medicine & Child Neurology*, 50 (10), 744-50 and in the GMAE-2 scoring software. http://motorgrowth.canchild.ca/en/GMFCS/resources/GMFCS-ER.pdf

**Algorithm for Identifying Item Sets:**
*Note: Decision items are shaded in each item set




**GMFM-66 Score[1]**

| | |
|---|---|
| GMFM-66 Score = | _____ to _____ 95% Confidence Interval |
| Previous GMFM-66 Score = | _____ to _____ 95% Confidence Interval |
| Change in GMFM-66 = | |

[1]from the Gross Motor Ability Estimator (GMAE-2) Software

**GMFM ITEM SET 1** (15 items)

Check (✓) the appropriate score: If an item is not tested (NT) circle the item number in the right column.

| ITEM | A. LYING AND ROLLING | SCORE | | | | NT |
|---|---|---|---|---|---|---|
| 2. | SUP: BRINGS HANDS TO MIDLINE, FINGERS ONE WITH THE OTHER | 0☐ | 1☐ | 2☐ | 3☐ | 2. |
| 6. | SUP: REACHES OUT WITH R ARM, HAND CROSSES MIDLINE TOWARD TOY | 0☐ | 1☐ | 2☐ | 3☐ | 6. |
| 7. | SUP: REACHES OUT WITH L ARM, HAND CROSSES MIDLINE TOWARD TOY | 0☐ | 1☐ | 2☐ | 3☐ | 7. |
| 10. | PR: LIFTS HEAD UPRIGHT | 0☐ | 1☐ | 2☐ | 3☐ | 10. |
| | **B. SITTING** | | | | | |
| 18. | SUP, HANDS GRASPED BY EXAMINER: PULLS SELF TO SITTING WITH HEAD CONTROL | 0☐ | 1☐ | 2☐ | 3☐ | 18. |
| 21. | SIT ON MAT, SUPPORTED AT THORAX BY THERAPIST: LIFTS HEAD UPRIGHT, MAINTAINS 3 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 21. |
| 22. | SIT ON MAT, SUPPORTED AT THORAX BY THERAPIST: LIFTS HEAD MIDLINE, MAINTAINS 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 22. |
| 23. | SIT ON MAT, ARM(S) PROPPING: MAINTAINS, 5 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 23. |
| 24. | SIT ON MAT: MAINTAIN, ARMS FREE, 3 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 24. |
| 25. | SIT ON MAT WITH SMALL TOY IN FRONT: LEANS FORWARD, TOUCHES TOY, RE-ERECTS WITHOUT ARM PROPPING | 0☐ | 1☐ | 2☐ | 3☐ | 25. |
| 26. | SIT ON MAT: TOUCHES TOY PLACED 45° BEHIND CHILD'S R SIDE, RETURNS TO START | 0☐ | 1☐ | 2☐ | 3☐ | 26. |
| 27. | SIT ON MAT: TOUCHES TOY PLACED 45° BEHIND CHILD'S L SIDE, RETURNS TO START | 0☐ | 1☐ | 2☐ | 3☐ | 27. |
| 30. | SIT ON MAT: LOWERS TO PR WITH CONTROL | 0☐ | 1☐ | 2☐ | 3☐ | 30. |
| 34. | SIT ON BENCH: MAINTAINS, ARMS AND FEET FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 34. |
| | **C: CRAWLING & KNEELING** | | | | | |
| 39. | 4 POINT: MAINTAINS, WEIGHT ON HANDS AND KNEES, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 39. |

**GMFM ITEM SET 2** (29 items)

**Check (✓) the appropriate score:** If an item is not tested (NT) circle the item number in the right column.

| | Item | A: LYING & ROLLING | SCORE | | | | NT |
|---|---|---|---|---|---|---|---|
| * | 6. | SUP: REACHES OUT WITH R ARM, HAND CROSSES MIDLINE TOWARD TOY | 0☐ | 1☐ | 2☐ | 3☐ | 6. |
| * | 7. | SUP: REACHES OUT WITH L ARM, HAND CROSSES MIDLINE TOWARD TOY | 0☐ | 1☐ | 2☐ | 3☐ | 7. |
| | Item | B: SITTING | | | | | |
| * | 18. | SUP, HANDS GRASPED BY EXAMINER: PULLS SELF TO SITTING WITH HEAD CONTROL | 0☐ | 1☐ | 2☐ | 3☐ | 18. |
| * | 23. | SIT ON MAT, ARM(S) PROPPING: MAINTAINS, 5 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 23. |
| * | 24. | SIT ON MAT: MAINTAIN, ARMS FREE, 3 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 24. |
| * | 25. | SIT ON MAT WITH SMALL TOY IN FRONT: LEANS FORWARD, TOUCHES TOY, RE-ERECTS WITHOUT ARM PROPPING | 0☐ | 1☐ | 2☐ | 3☐ | 25. |
| * | 26. | SIT ON MAT: TOUCHES TOY PLACED 45° BEHIND CHILD'S R SIDE, RETURNS TO START | 0☐ | 1☐ | 2☐ | 3☐ | 26. |
| * | 27. | SIT ON MAT: TOUCHES TOY PLACED 45° BEHIND CHILD'S L SIDE, RETURNS TO START | 0☐ | 1☐ | 2☐ | 3☐ | 27. |
| * | 30. | SIT ON MAT: LOWERS TO PR WITH CONTROL | 0☐ | 1☐ | 2☐ | 3☐ | 30. |
| * | 31. | SIT ON MAT WITH FEET IN FRONT: ATTAINS 4 POINT OVER R SIDE | 0☐ | 1☐ | 2☐ | 3☐ | 31. |
| * | 32. | SIT ON MAT WITH FEET IN FRONT: ATTAINS 4 POINT OVER L SIDE | 0☐ | 1☐ | 2☐ | 3☐ | 32. |
| * | 34. | SIT ON BENCH: MAINTAINS, ARMS AND FEET FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 34. |
| * | 35. | STD: ATTAINS SIT ON SMALL BENCH | 0☐ | 1☐ | 2☐ | 3☐ | 35. |
| * | 36. | ON THE FLOOR: ATTAINS SIT ON SMALL BENCH | 0☐ | 1☐ | 2☐ | 3☐ | 36. |
| | Item | C: CRAWLING & KNEELING | | | | | |
| * | 39. | 4 POINT: MAINTAINS, WEIGHT ON HANDS AND KNEES, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 39. |
| * | 40. | 4 POINT: ATTAINS SIT ARMS FREE | 0☐ | 1☐ | 2☐ | 3☐ | 40. |
| * | 41. | PR: ATTAINS 4 POINT, WEIGHT ON HANDS AND KNEES | 0☐ | 1☐ | 2☐ | 3☐ | 41. |
| * | 42. | 4 POINT: REACHES FORWARD WITH R ARM, HAND ABOVE SHOULDER LEVEL | 0☐ | 1☐ | 2☐ | 3☐ | 42. |
| * | 43. | 4 POINT: REACHES FORWARD WITH L ARM, HAND ABOVE SHOULDER LEVEL | 0☐ | 1☐ | 2☐ | 3☐ | 43. |
| * | 44. | 4 POINT: CRAWLS OR HITCHES FORWARD 1.8m (6') | 0☐ | 1☐ | 2☐ | 3☐ | 44. |
| * | 45. | 4 POINT: CRAWLS RECIPROCALLY FORWARD 1.8m (6') | 0☐ | 1☐ | 2☐ | 3☐ | 45. |
| * | 46. | 4 POINT: CRAWLS UP 4 STEPS ON HANDS AND KNEES/FEET | 0☐ | 1☐ | 2☐ | 3☐ | 46. |
| * | 48. | SIT ON MAT: ATTAINS HIGH KN USING ARMS, MAINTAINS, ARMS FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 48. |
| | Item | D: STANDING | | | | | |
| * | 52. | ON THE FLOOR: PULLS TO STD AT LARGE BENCH | 0☐ | 1☐ | 2☐ | 3☐ | 52. |
| | Item | E: WALKING, RUNNING & JUMPING | | | | | |
| * | 65. | STD, 2 HANDS ON LARGE BENCH: CRUISES 5 STEPS TO R | 0☐ | 1☐ | 2☐ | 3☐ | 65. |
| * | 66. | STD, 2 HANDS ON LARGE BENCH: CRUISES 5 STEPS TO L | 0☐ | 1☐ | 2☐ | 3☐ | 66. |
| * | 67. | STD, 2 HANDS HELD: WALKS FORWARD 10 STEPS | 0☐ | 1☐ | 2☐ | 3☐ | 67. |
| * | 68. | STD, 1 HAND HELD: WALKS FORWARD 10 STEPS | 0☐ | 1☐ | 2☐ | 3☐ | 68. |
| * | 69. | STD: WALKS FORWARD 10 STEPS | 0☐ | 1☐ | 2☐ | 3☐ | 69. |

**GMFM ITEM SET 3** (39 items)

**Check (✓) the appropriate score:** If an item is not tested (NT) circle the item number in the right column.

| | Item | B: SITTING | SCORE | | | | NT |
|---|---|---|---|---|---|---|---|
| * | 23. | SIT ON MAT, ARM(S) PROPPING: MAINTAINS, 5 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 23. |
| * | 25. | SIT ON MAT WITH SMALL TOY IN FRONT: LEANS FORWARD, TOUCHES TOY, RE-ERECTS WITHOUT ARM PROPPING | 0☐ | 1☐ | 2☐ | 3☐ | 25. |
| * | 30. | SIT ON MAT: LOWERS TO PR WITH CONTROL | 0☐ | 1☐ | 2☐ | 3☐ | 30. |
| * | 31. | SIT ON MAT WITH FEET IN FRONT: ATTAINS 4 POINT OVER R SIDE | 0☐ | 1☐ | 2☐ | 3☐ | 31. |
| * | 32. | SIT ON MAT WITH FEET IN FRONT: ATTAINS 4 POINT OVER L SIDE | 0☐ | 1☐ | 2☐ | 3☐ | 32. |
| * | 34. | SIT ON BENCH: MAINTAINS, ARMS AND FEET FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 34. |
| * | 35. | STD: ATTAINS SIT ON SMALL BENCH | 0☐ | 1☐ | 2☐ | 3☐ | 35. |
| * | 36. | ON THE FLOOR: ATTAINS SIT ON SMALL BENCH | 0☐ | 1☐ | 2☐ | 3☐ | 36. |
| * | 37. | ON THE FLOOR: ATTAINS SIT ON LARGE BENCH | 0☐ | 1☐ | 2☐ | 3☐ | 37. |
| | **Item** | **C: CRAWLING & KNEELING** | | | | | |
| * | 39. | 4 POINT: MAINTAINS, WEIGHT ON HANDS AND KNEES, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 39. |
| * | 40. | 4 POINT: ATTAINS SIT ARMS FREE | 0☐ | 1☐ | 2☐ | 3☐ | 40. |
| * | 42. | 4 POINT: REACHES FORWARD WITH R ARM, HAND ABOVE SHOULDER LEVEL | 0☐ | 1☐ | 2☐ | 3☐ | 42. |
| * | 43. | 4 POINT: REACHES FORWARD WITH L ARM, HAND ABOVE SHOULDER LEVEL | 0☐ | 1☐ | 2☐ | 3☐ | 43. |
| * | 45. | 4 POINT: CRAWLS RECIPROCALLY FORWARD 1.8m (6') | 0☐ | 1☐ | 2☐ | 3☐ | 45. |
| * | 46. | 4 POINT: CRAWLS UP 4 STEPS ON HANDS AND KNEES/FEET | 0☐ | 1☐ | 2☐ | 3☐ | 46. |
| * | 48. | SIT ON MAT: ATTAINS HIGH KN USING ARMS, MAINTAINS, ARMS FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 48. |
| * | 51. | HIGH KN: KN WALKS FORWARD 10 STEPS, ARMS FREE | 0☐ | 1☐ | 2☐ | 3☐ | 51. |
| | **Item** | **D: STANDING** | | | | | |
| * | 52. | ON THE FLOOR: PULLS TO STD AT LARGE BENCH | 0☐ | 1☐ | 2☐ | 3☐ | 52. |
| * | 53. | STD: MAINTAINS, ARMS FREE, 3 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 53. |
| * | 54. | STD: HOLDING ON TO LARGE BENCH WITH ONE HAND, LIFTS R FOOT, 3 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 54. |
| * | 55. | STD: HOLDING ON TO LARGE BENCH WITH ONE HAND, LIFTS L FOOT, 3 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 55. |
| * | 56. | STD: MAINTAINS, ARMS FREE, 20 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 56. |
| * | 57. | STD: LIFTS L FOOT, ARMS FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 57. |
| * | 58. | STD: LIFTS R FOOT, ARMS FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 58. |
| * | 59. | SIT ON SMALL BENCH: ATTAINS STD WITHOUT USING ARMS | 0☐ | 1☐ | 2☐ | 3☐ | 59. |
| * | 64. | STD: PICKS UP OBJECT FROM FLOOR, ARMS FREE, RETURNS TO STAND | 0☐ | 1☐ | 2☐ | 3☐ | 64. |
| | **Item** | **E: WALKING, RUNNING & JUMPING** | | | | | |
| * | 65. | STD, 2 HANDS ON LARGE BENCH: CRUISES 5 STEPS TO R | 0☐ | 1☐ | 2☐ | 3☐ | 65. |
| * | 66. | STD, 2 HANDS ON LARGE BENCH: CRUISES 5 STEPS TO L | 0☐ | 1☐ | 2☐ | 3☐ | 66. |
| * | 67. | STD, 2 HANDS HELD: WALKS FORWARD 10 STEPS | 0☐ | 1☐ | 2☐ | 3☐ | 67. |
| * | 68. | STD, 1 HAND HELD: WALKS FORWARD 10 STEPS | 0☐ | 1☐ | 2☐ | 3☐ | 68. |
| * | 69. | STD: WALKS FORWARD 10 STEPS | 0☐ | 1☐ | 2☐ | 3☐ | 69. |
| * | 70. | STD: WALKS FORWARD 10 STEPS, STOPS, TURNS 180□, RETURNS | 0☐ | 1☐ | 2☐ | 3☐ | 70. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| * | 71. | STD: WALKS BACKWARD 10 STEPS..... | 0☐ | 1☐ | 2☐ | 3☐ | 71. |
| * | 72. | STD: WALKS FORWARD 10 STEPS, CARRYING A LARGE OBJECT WITH 2 HANDS | 0☐ | 1☐ | 2☐ | 3☐ | 72. |
| * | 77. | STD: RUNS 4.5m (15'), STOPS & RETURNS..... | 0☐ | 1☐ | 2☐ | 3☐ | 77. |
| * | 78. | STD: KICKS BALL WITH R FOOT ..... | 0☐ | 1☐ | 2☐ | 3☐ | 78. |
| * | 79. | STD: KICKS BALL WITH L FOOT..... | 0☐ | 1☐ | 2☐ | 3☐ | 79. |
| * | 80. | STD: JUMPS 30cm (12") HIGH, BOTH FEET SIMULTANEOUSLY ..... | 0☐ | 1☐ | 2☐ | 3☐ | 80. |
| * | 85. | STD, HOLDING 1 RAIL: WALKS DOWN 4 STEPS, HOLDING 1 RAIL, ALTERNATING FEET..... | 0☐ | 1☐ | 2☐ | 3☐ | 85. |

**GMFM ITEM SET 4** (22 items)

**Check (✓) the appropriate score:** If an item is not tested (NT) circle the item number in the right column.

| | Item | B: SITTING | SCORE | | | | NT |
|---|---|---|---|---|---|---|---|
| * | 23. | SIT ON MAT, ARM(S) PROPPING: MAINTAINS, 5 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 23. |
| | Item | D: STANDING | | | | | |
| * | 57. | STD: LIFTS L FOOT, ARMS FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 57. |
| * | 58. | STD: LIFTS R FOOT, ARMS FREE, 10 SECONDS | 0☐ | 1☐ | 2☐ | 3☐ | 58. |
| * | 60. | HIGH KN: ATTAINS STD THROUGH HALF KN ON R KNEE, WITHOUT USING ARMS | 0☐ | 1☐ | 2☐ | 3☐ | 60. |
| * | 61. | HIGH KN: ATTAINS STD THROUGH HALF KN ON L KNEE, WITHOUT USING ARMS | 0☐ | 1☐ | 2☐ | 3☐ | 61. |
| * | 62. | STD: LOWERS TO SIT ON FLOOR WITH CONTROL, ARMS FREE | 0☐ | 1☐ | 2☐ | 3☐ | 62. |
| * | 63. | STD: ATTAINS SQUAT, ARMS FREE | 0☐ | 1☐ | 2☐ | 3☐ | 63. |
| | Item | E: WALKING, RUNNING & JUMPING | | | | | |
| * | 67. | STD, 2 HANDS HELD: WALKS FORWARD 10 STEPS | 0☐ | 1☐ | 2☐ | 3☐ | 67. |
| * | 73. | STD: WALKS FORWARD 10 CONSECUTIVE STEPS BETWEEN PARALLEL LINES 20cm (8") APART | 0☐ | 1☐ | 2☐ | 3☐ | 73. |
| * | 74. | STD: WALKS FORWARD 10 CONSECUTIVE STEPS ON A STRAIGHT LINE 2cm (3/4") WIDE | 0☐ | 1☐ | 2☐ | 3☐ | 74. |
| * | 75. | STD: STEPS OVER STICK AT KNEE LEVEL, R FOOT LEADING | 0☐ | 1☐ | 2☐ | 3☐ | 75. |
| * | 76. | STD: STEPS OVER STICK AT KNEE LEVEL, L FOOT LEADING | 0☐ | 1☐ | 2☐ | 3☐ | 76. |
| * | 77. | STD: RUNS 4.5m (15'), STOPS & RETURNS | 0☐ | 1☐ | 2☐ | 3☐ | 77. |
| * | 80. | STD: JUMPS 30cm (12") HIGH, BOTH FEET SIMULTANEOUSLY | 0☐ | 1☐ | 2☐ | 3☐ | 80. |
| * | 81. | STD: JUMPS FORWARD 30 cm (12"), BOTH FEET SIMULTANEOUSLY | 0☐ | 1☐ | 2☐ | 3☐ | 81. |
| * | 82. | STD ON R FOOT: HOPS ON R FOOT 10 TIMES WITHIN A 60cm (24") CIRCLE | 0☐ | 1☐ | 2☐ | 3☐ | 82. |
| * | 83. | STD ON L FOOT: HOPS ON L FOOT 10 TIMES WITHIN A 60cm (24") CIRCLE | 0☐ | 1☐ | 2☐ | 3☐ | 83. |
| * | 84. | STD, HOLDING 1 RAIL: WALKS UP 4 STEPS, HOLDING 1 RAIL, ALTERNATING FEET | 0☐ | 1☐ | 2☐ | 3☐ | 84. |
| * | 85. | STD, HOLDING 1 RAIL: WALKS DOWN 4 STEPS, HOLDING 1 RAIL, ALTERNATING FEET | 0☐ | 1☐ | 2☐ | 3☐ | 85. |
| * | 86. | STD: WALKS UP 4 STEPS, ALTERNATING FEET | 0☐ | 1☐ | 2☐ | 3☐ | 86. |
| * | 87. | STD: WALKS DOWN 4 STEPS, ALTERNATING FEET | 0☐ | 1☐ | 2☐ | 3☐ | 87. |
| * | 88. | STD ON 15cm (6") STEP: JUMPS OFF, BOTH FEET SIMULTANEOUSLY | 0☐ | 1☐ | 2☐ | 3☐ | 88. |

# Appendix C

## INSTITUTIONAL REVIEW BOARD APPROVAL LETTER

RESEARCH OFFICE

210 Hullihen Hall
University of Delaware
Newark, Delaware 19716-1551
*Ph:* 302/831-2136
*Fax:* 302/831-2828

| | |
|---|---|
| DATE: | April 6, 2017 |
| TO: | John Jeka |
| FROM: | University of Delaware IRB |
| STUDY TITLE: | [613523-4] "Sensor Fusion for Balance Control in Children with Cerebral Palsy" |
| SUBMISSION TYPE: | Continuing Review/Progress Report |
| ACTION: | APPROVED |
| APPROVAL DATE: | April 6, 2017 |
| EXPIRATION DATE: | March 17, 2018 |
| REVIEW TYPE: | Administrative Review |
| REVIEW CATEGORY: | *Temple IRB is the IRB of Record* |

Thank you for your submission of Continuing Review/Progress Report materials for this research study. The University of Delaware IRB (HUMANS) has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Administrative Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

If you have any questions, please contact Nicole Farnese-McFarlane at (302) 831-1119 or nicolefm@udel.edu. Please include your study title and reference number in all correspondence with this office.

## Appendix D

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