NORTHWESTERN UNIVERSITY

Stepping Up to Understand Movement Challenges in Bilateral Cerebral Palsy

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ABSTRACT

Stairs and curbs often present as an exhausting environmental barrier for individuals with bilateral cerebral palsy (CP) due to their lower limb motor impairments. Indeed, performance in stair-climbing in this population has a higher correlation with disruption of mobility than walking. Community members affected by CP consider impaired mobility a high priority research area, especially given its link to serious comorbidities such as cardiovascular disease and chronic pain. Therefore, quantification of movement strategies during a step-up task in children and adolescents can offer insight into the specific impairments responsible for making stairs a barrier throughout life in CP. The results of this dissertation serve to inform intervention strategies for improving mobility and can offer a window into descending pathways influencing movement for people with bilateral CP. We first characterized the effect of load modulation on the biomechanics of a step-up task in young people without bilateral CP to build an age-appropriate model of task completion. We then compared this response to the biomechanical patterns of young individuals with bilateral CP during a step-up task with and without load modulation. Outcome measures, including frontal and sagittal plane moments in the hip, knee, and ankle, were quantified using a motion capture system in combination with force plates. Participants with bilateral CP performed similarly to their peers without bilateral CP during the step-up trials, which included increasing their extensor support moments with load but not their hip abduction moments. While participants without bilateral CP primarily used their knee and ankle to drive support moments, participants with CP increasingly depended on their hip across all load levels. Quantification of these movement strategies is a critical first step in deepening our understanding of lower limb motor impairments and the neural mechanisms behind reduced mobility in bilateral CP.

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1. INTRODUCTION

1.1. Problem Statement

Cerebral palsy (CP) is defined as a “a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain” (Rosenbaum et al., 2007). CP is the most common pediatric motor disability in the world; approximately 800,000 people in the United States live with this diagnosis. Bilateral CP specifically is caused by lesions in both brain hemispheres and often leads to a spastic diplegic (motor impairments in the lower limbs) or quadriplegic (motor impairments in the upper and lower limbs) topography. Approximately 38% of individuals with CP have diplegia, whereas approximately 23% have quadriplegia (Novak, 2014). Despite lower limb motor impairments, approximately 98% of individuals with pediatric diplegia and 24% of individuals with pediatric quadriplegia are ambulatory with and without assistive devices (Novak, 2014).

Two common lower limb motor impairments from bilateral CP are paresis (weakness) and a loss of selective voluntary motor control (SVMC). Weakness especially affects the lower limb extensors, where torque output is lower in individuals with bilateral CP compared to individuals without bilateral CP (Wiley and Damiano, 1998). Loss of SVMC is defined as the inability to independently activate the joints (Sanger et al., 2006). This motor impairment is prevalent in the knee and ankle joints in children with bilateral CP (Fowler et al., 2010). Previous literature also provides evidence pointing to abnormal coupling of the hip adductors/extensors during isometric efforts (Thelen et al., 2003) and the swing phase of stance (Fowler and Goldberg, 2009). Researchers have postulated that paresis is a direct result of damage to the corticospinal tract, which is the main motor pathway in the central nervous system responsible for limb movement, while a loss of SVMC points to upregulation of brainstem motor pathways (Cahill-Rowley and Rose, 2014; Fowler et al., 2010; Sánchez et al., 2018a; Zhou et al., 2017), which are secondary motor pathways that play a large role in posture.

Previous research in steady-state gait found that children with CP tend to depend more on their hip joint than their ankle joint during regular gait as a compensation for distal impairment (Riad et al., 2008) and show an abnormal extensor coupling pattern during the terminal swing phase of gait (Fowler and Goldberg, 2009). However, our natural environment consists of not only flat surfaces but also obstacles such as stairs and curbs. These obstacles present as an exhausting environmental barrier for individuals with bilateral CP. Indeed, in this population, performance in stair-climbing has a higher correlation with the disruption of mobility than walking (Lepage et al., 1998). Impaired mobility is further linked to serious comorbidities such as cardiovascular disease and chronic pain (Becher et al., 2020; Heyn et al., 2019; Peterson et al., 2020; Schmidt et al., 2020; van der Slot et al., 2013). As such, it is necessary to quantify movement performance during stair-climbing in individuals with bilateral CP to understand which impairments are responsible for making stairs a barrier. This quantification is especially important in the stance phase, which is the largest part of the gait cycle in children with and without CP (Brégou Bourgeois et al., 2014). When moving upwards, time in stance during the gait cycle increases compared to level-ground walking (Ma et al., 2019). Such an investigation would serve to inform current interventions, which would ultimately improve performance of this task and perhaps improve overall mobility throughout life. Most importantly, stakeholders affected by CP highly prioritize the type of research that focuses on understanding the nature of impairments affecting mobility (Gross et al., 2018; Vargus-Adams and Martin, 2009), especially in the lower limbs (Zvolanek et al., 2022).

1.2. Research Goals

The goal of this dissertation is to quantify the biomechanics of a step-up task in children with and without bilateral CP. The experimental protocol was specifically designed to provide useful information about movement in children with CP. The population of interest was the pediatric population, as 64% of individuals with bilateral CP report a decline in ambulation by the age of 25. Two lines of evidence support the exploration of movement during the initial step of stair ascent: 1) the first step requires higher joint moments (or more effort) from the lower limbs compared to subsequent steps (Wang and Gillette, 2018), which includes hip abduction and lower limb extension, and 2) this step has been shown to be a sensitive measure of movement quality in pediatric populations with neurodevelopmental disorders like CP (Stania et al., 2017). Finally, training methods such as load modulation have previously been used to discern the presence of motor impairments *and* offer a window into how descending motor pathways are working in individuals with CP. One common method during over-ground or steady-state walking is partial support of a person's body (Celestino et al., 2014; Cherng et al., 2007; Kurz et al., 2011; Phillips et al., 2007; Provost et al., 2007) or the addition of external weights (Simão et al., 2014); these approaches have been used in clinical treatment to improve the quality of gait in CP. While these methods have also been used during a step-up task, the research is extremely limited and entirely in adults (Wang and Gillette, 2018).

1.3. Research Aims

To accomplish the goal stated above, I completed the following research aims:

1) Characterized the effect of load modulation on the biomechanics of a step-up task in young people with typical development (TD). As these individuals do not have lower limb

impairments which may affect performance in a step-up task, my main hypothesis was that lower limb joint moments would increase incrementally with load.

2) Evaluated the lower limb joint moment strategies of children and adolescents with bilateral CP during a regular step-up task. My first main hypothesis was that individuals with CP would generate lower joint moments compared to children with TD, consistent with paresis of the joints. My second main hypothesis was that children with CP would depend more on the hip joint to complete the task compared to children with TD, consistent with a loss of SVMC in the knee and ankle joints.
3) Quantified the lower limb joint moment patterns of children and adolescents with bilateral CP during a step-up task with load modulation. My main hypothesis was that individuals with CP would show an increase in extension moments and a simultaneous decrease in hip abduction moments with increasing load, consistent with a loss of SVMC expressed as abnormal coupling between the hip adductors/extensors.

The overall trajectory of these aims is to first validate the experimental paradigm in children without CP and then explore performance in children with CP. Before pediatric clinicians and researchers can adapt movement in CP to achieve the best outcomes for their patients, it is imperative that they *understand* movement performance first, which is what this dissertation will accomplish.

1.4. Dissertation Outline

Chapter 2 will provide a concise review about lower extremity motor control, bilateral cerebral palsy, and the biomechanics of a step-up task. Chapter 3 will outline the motivators and barriers of cerebral palsy research participation, which influenced decisions made in the experimental design of this dissertation. Chapter 4 will use methods such as partial support of a person's body and addition of external weight to evaluate the effect of load modulation on the biomechanics of a step-up task in young people with typical development (TD). Chapter 5 will characterize lower limb joint moment strategies in adolescents with bilateral CP during a regular step-up task. Chapter 6 will quantify the same biomechanical strategies in adolescents with bilateral CP during a step-up task with load modulation. Finally, Chapter 7 will discuss the overarching results, their implications for clinical practice in CP, and future lines of inquiry.

Chapter 3 has previously been published as follows:

Zvolanek KM*, Goyal V*, Hruby A, Ingo C, Sukal-Moulton T (2022). Motivators and barriers to research participation for individuals with cerebral palsy and their families. *PLoS ONE* 17(1): e0262153. *co-first authors

2. BACKGROUND & LITERATURE REVIEW

2.1. Motor Control of the Lower Extremity

2.1.1. Motor Pathway Overview & Organization

There are two types of motor pathways that descend from the central nervous system: the lateral system (lateral corticospinal and rubrospinal tracts) and the medial system (anterior corticospinal, reticulospinal, vestibulospinal, and tectospinal tracts). The upper motor neurons of the corticospinal tract (CST) originate from pyramidal cells in the human motor cortex (**Figure 2.1**). In the mature nervous system, approximately 90% of these neurons synapse onto contralateral lower motor neurons in the spinal cord to form the lateral CST, which is responsible for limb and fine motor movements. The remaining 10% of neurons descend ipsilaterally to form the anterior CST, which controls head, neck and trunk movement.

The rubrospinal, reticulospinal, vestibulospinal, and tectospinal tracts make up the extrapyramidal pathways of the brainstem. The rubrospinal tract originates from the red nucleus of the midbrain and is typically more prominent in the fetal and neonatal brain than the adult brain (Ulfig and Chan, 2001). These pathways are responsible for mediating flexor/extensor muscle groups and have been postulated to promote synergistic movements in infants (Cahill-Rowley and Rose, 2014). The reticulospinal tract originates in the reticular formation while the vestibulospinal tract originates in the vestibular nuclei. Both pathways primarily control upright posture in the human body. Discharge patterns of reticulospinal and vestibulospinal neurons in feline hindlimb models have been related to extensor muscle activations (Drew et al., 1986; Matsuyama and Drew, 2000). These pathways have been hypothesized to play a similar role in the lower limb extensors of stroke survivors (Sánchez et al., 2018b). Finally, the tectospinal tract originates in the superior colliculus of the midbrain and is responsible for controlling head movements.

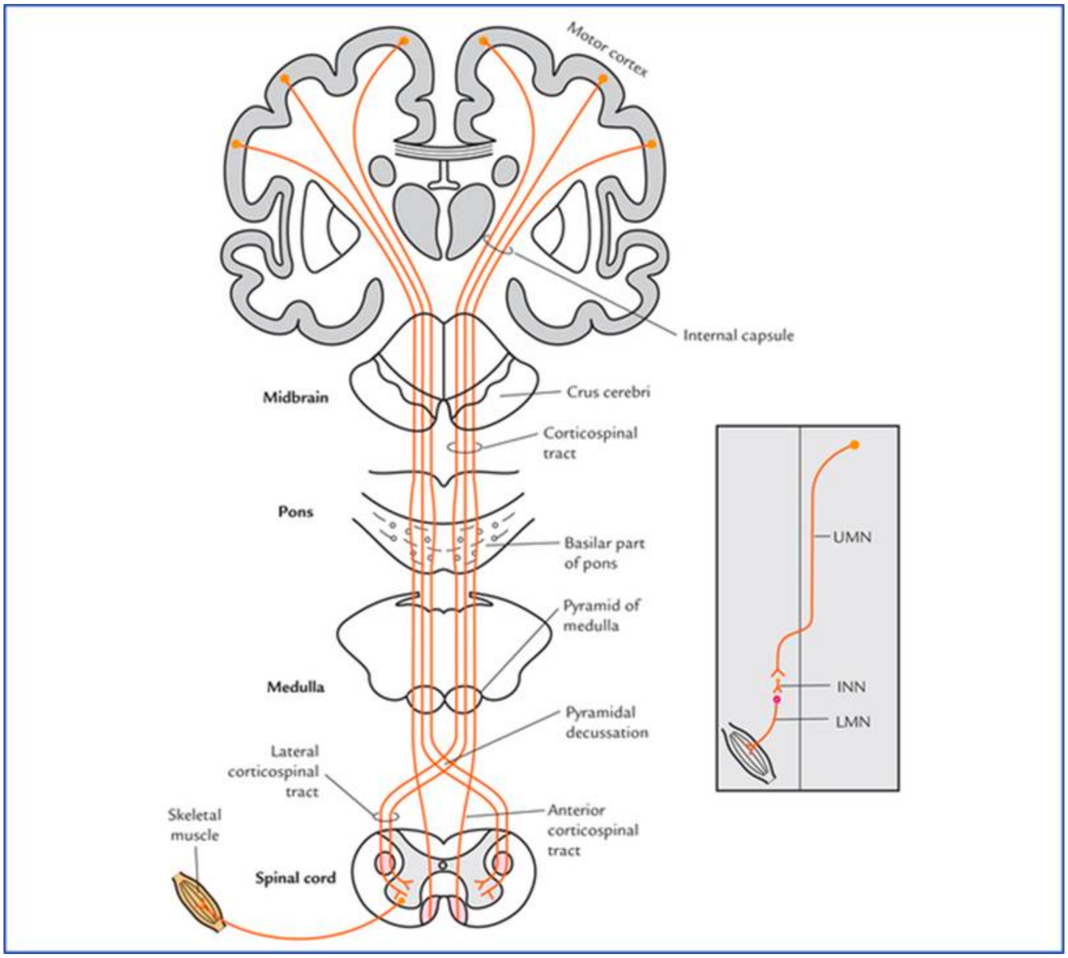

Figure 2.1. Lateral and anterior corticospinal tracts. A view of the CST as it descends from the motor cortex to synapse onto skeletal muscles. This coronal view of the brain depicts the motor cortex, which is located in the precentral gyrus of the frontal lobe. *(Figure 2.1 from the Textbook of Clinical Neuroanatomy, 2nd Edition, Chapter 17: Somatic Motor and Sensory Pathways).*

2.1.2. Development of Lower Limb Motor Pathways

Voluntary control of the lower extremity, including the hip, knee, and ankle joints, primarily comes from the CST originating from the medial portion of the motor cortex (Aicardi et al., 1992; Rech et al., 2016). The somatotopic arrangement of this section indicates that the distal lower limb joints are mapped more medially in the brain cortex compared to the proximal lower limb joints (Aicardi et al., 1992; Kapreli et al., 2007) (**Figure 2.2**).

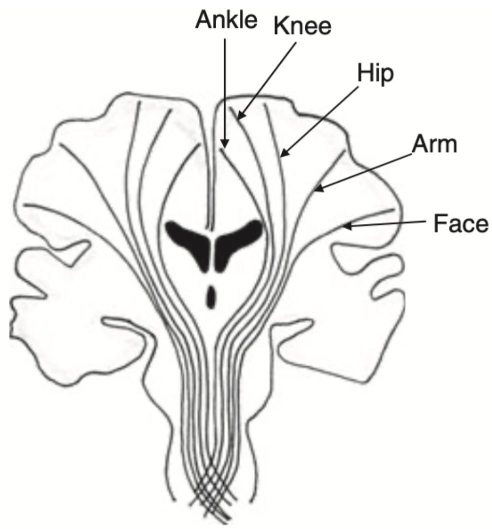

Figure 2.2. Somatotopic organization of the lower limb joints. Motor control of the lower limb joints originates from the medial motor cortex. This coronal view of the brain is through the precentral gyrus of the frontal lobe. The somatotopic arrangement shows that distal to proximal lower limb joints are mapped medial to lateral. *(Figure 2.2 from Fowler et al., 2010, adapted from Aicardi 1992).*

CST development in animal models shares some similarities with CST development in humans, especially in the timeline and manner of maturation. Corticospinal (CS) axons innervating hindlimb muscles of postnatal rats were found in the spinal gray matter by day 9, a few days after axons innervating forelimb muscles started to develop (Donatelle, 1977). In postnatal kittens, spinal motor neuron bundles to the hindlimbs start developing between day 10 and 14 and fully mature by 4-5 months, matching the observed progression of hindlimb movement after birth (Scheibel, 1970). Part of the maturation period is elimination of extra CS projections (Alisky et al., 1992) due to activity-dependent competition between terminations from the two brain hemispheres (Friel and Martin, 2007; Martin and Lee, 1999). Indeed, a variety of motor experiences are crucial to refine CS projections in cats (Martin et al., 2004). In non-human primates, magnetic stimulation can evoke electromyography (EMG) responses in lower limb muscles consistently at 5.75-months and reach maturity at 7.5-months, also after development of upper limb connections (Flament et al., 1992; Galea and Darian-Smith, 1995). This timeline is in line with the acquisition of behavioral movements such as precision grasping (Galea and Darian-Smith, 1995). Postnatal development of macaque monkeys also shows a reduction of CS projections during the maturation period (Galea and Darian-Smith, 1995).

Development of a functional CS system in humans happens prenatally, where projections reach the spinal cord at around 24 weeks post-conceptual age (Eyre, 2007; Eyre et al., 2000). Both ipsilateral and contralateral pathways to the lower limbs are present at birth (Eyre et al., 2001). Similar to cats and non-human primates, activity-dependent withdrawal of ipsilateral projections and strengthening of contralateral projections occurs throughout the first few post-natal months (Eyre, 2007; Martin, 2005). After approximately 6 months of age, ipsilateral signals have much longer onset latencies compared to contralateral signals (Eyre et al., 2001). The use of electromagnetic stimulation to assess CST integrity revealed that conduction velocity of contralateral CS pathways reach adult values by about 11 years of age (Koh and Eyre, 1988).

2.2. Typical Developmental Trajectories in Humans

2.2.1. Musculoskeletal Development of the Lower Extremity

The muscles of the lower limbs also grow and mature at the same time as neural pathways. Early muscle and bone development is optimized in-utero (Ahmad et al., 2010). Some muscle fiber diameters increase rapidly in size during this time period (Moore et al., 1971), especially between 35 weeks gestation and term (Schloon et al., 1979). Using muscle ultrasound on typical pediatric participants aged 2-16 years, researchers found significant correlations between lower limb muscle width with age, weight, and height (Lori et al., 2018). Darras et al. also found that absolute force of these muscles during isometric contractions increases with age in this population (Darras et al., 2021).

2.2.2. General Behavioral Milestones

Children meet general developmental milestones during the first few years of life, coinciding with the development of motor pathways and lower limb muscles (**Figure 2.3**). There is a transition in behaviors from a higher influence of brainstem pathways to CS control. By 2-3 months, infants kick with a variety of symmetrical movements. Infants also display primitive reflexes such as the asymmetrical tonic neck reflex, showcasing the influence of brainstem pathways in early movement. By 5-6 months, kicking becomes more asymmetrical and primitive reflexes fade away, marking a transition to increased use of CS pathways. By 7-8 months, infants typically stand using external support and are able to crawl. By 9-10 months, infants transition from standing to sitting, take forward steps, and crawl up stairs, all with minimal assistance (Berger 2007). By 11-12 months, infants begin to manage most of these movements independently.

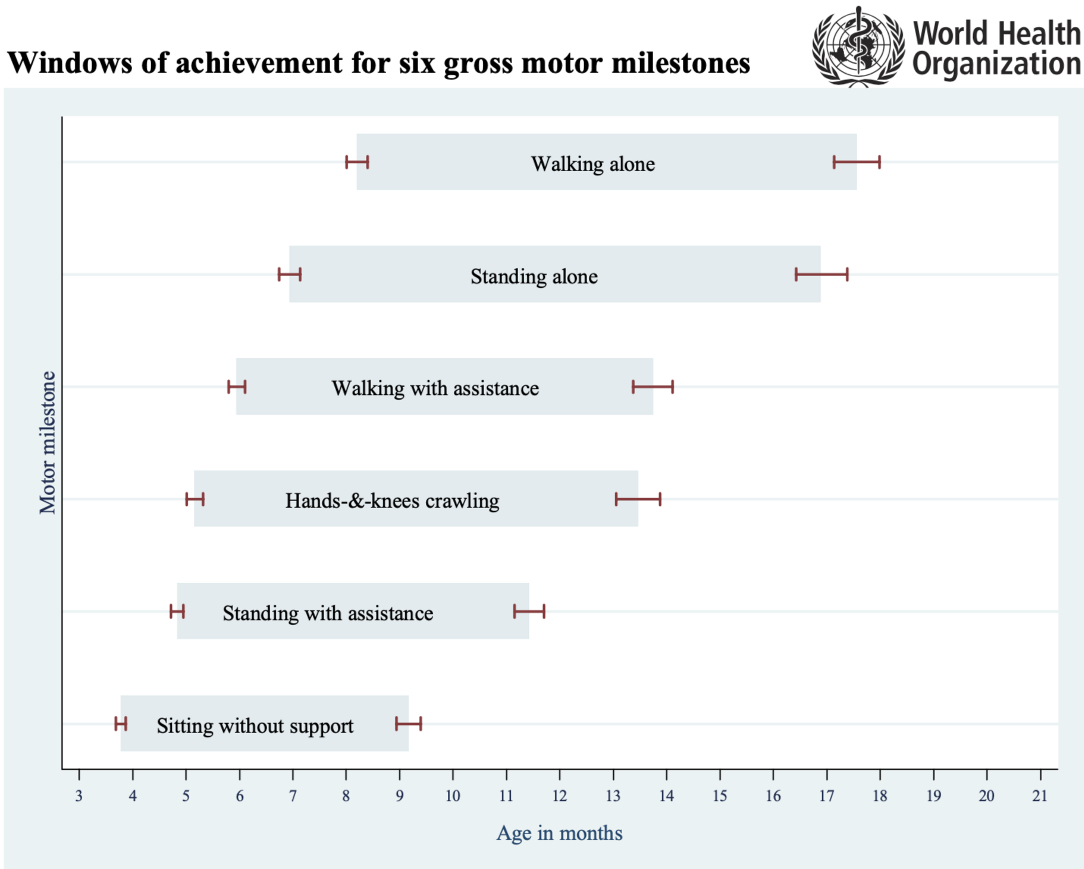

Figure 2.3. Gross motor developmental milestones. The approximate age range in months for six major gross motor developmental milestones. Gross motor skills continue to evolve throughout childhood as children learn from repeated experience. *(Figure 2.3 from WHO Motor Development Study: Windows of achievement for six gross motor development milestones, Acta Paediatrica Supplement 2006).*

Gait and balance control continue to strengthen with age. Toddlers typically develop the ability to walk up stairs between 17-22 months and run between 18-24 months. Performance in both of these activities steadily develops between 3-5 years of age (Kakebeeke et al., 2012). Improvements include walking up stairs using alternating feet and running using a heel-to-toe motion. A larger percentage of school-aged children between 6-9 years use a higher number of muscle synergies when running compared to toddlers and adults, suggesting a peak in motor exploration of this activity (Bach et al., 2021). Unsurprisingly, children with better locomotor skills also had better balance when managing perturbations (Roncesvalles et al., 2001). It is important to note that mechanisms of balance control such as torque regulation don't evolve simply because of growth and age; similar to all other motor skills, children need to learn these mechanisms through repetitive experiences (Roncesvalles et al., 2001).

2.3. Bilateral Cerebral Palsy

2.3.1. Etiology & Diagnosis

Cerebral palsy (CP) defines "a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain" (Rosenbaum et al., 2007). Spastic CP has many etiologies, including periventricular leukomalacia in preterm infants (necrosis of the white matter around the brain ventricles), hypoxia during birth (lack of oxygen to the brain), or neonatal stroke (**Figure 2.4**). Bilateral CP is one of the most common types, affecting approximately 1.9 out of 1,000 children in the US (Yeargin-Allsopp et al., 2008). Individuals with this diagnosis experience lesions in both brain hemispheres. Medial lesions may result in a diplegic motor topography affecting the lower limbs, while lesions that diffuse laterally may result in a triplegic or quadriplegic motor topography affecting the upper and lower limbs. Physicians can typically diagnose CP at around 6 months of age if a child has a noted brain injury and 1) has not met the aforementioned developmental milestones, 2) has retained early primitive reflexes, and/or 3) displays significant atypical motor function (Miller, 2005). Gross Motor Function Classification System (GMFCS) level, which stratifies children with CP based on their gross motor abilities and limitations, is determined around 2 years of age.

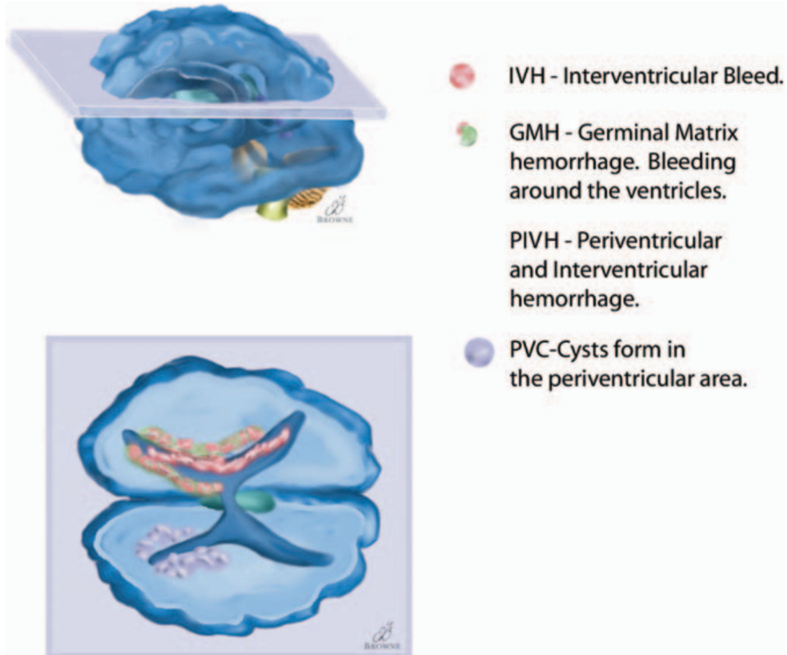

Figure 2.4. Etiologies of bilateral cerebral palsy. Bilateral CP is most typically caused by a fetal brain injury to immature blood vessels around the ventricles. An intraventricular bleed indicates bleeding in the ventricles while a germinal matrix hemorrhage indicates bleeding around the ventricles. Bleeding in both areas is a periventricular hemorrhage. These bleeds can lead to necrosis of the white matter surrounding the periventricular area, defined as periventricular leukomalacia. *(Figure 2.4 from the 2005 Cerebral Palsy textbook by Freeman Miller)*.

2.3.2. Impact on Neural and Musculoskeletal Development

A bilateral brain injury affects the typical neural and musculoskeletal development outlined in sections 2.1.2 and 2.2.1. Damage to the pyramidal tracts is postulated to make way for upregulation of extrapyramidal tracts to control the limbs, including the reticulospinal, vestibulospinal, and rubrospinal pathways (Cahill-Rowley and Rose, 2014; Sánchez et al., 2018b). In general, individuals with bilateral CP have less white matter connectivity to the lower extremity compared to the upper extremity (Samsir et al., 2018), indicating decreased corticospinal tract integrity. Neuromuscular activation to distal muscles is also reduced in children with bilateral CP compared to children without CP (Rose and McGill, 2005). Indeed, a study using transcranial magnetic stimulation to elicit evoked motor responses in the soleus muscle quantified smaller responses in adults with bilateral CP compared to adults without CP (Condliffe et al., 2019). This suggests that reduced corticospinal tract integrity largely contributes to lower limb impairments in individuals with bilateral CP.

Muscles develop rapidly in the prenatal and postnatal stages of life; as a result, postnatal care is unable to make up for the decrease of muscle cross-sectional area and bone mineral density in preterm infants compared to term-born infants (Ahmad et al., 2010). Some studies have quantified that approximately 72-85% of individuals with bilateral CP were born preterm (Ancel et al., 2006; Drljan et al., 2016). While there isn't a plethora of evidence connecting a brain injury causing CP to the occurrence of muscle damage, there are quite a number of downstream consequences to the muscles. Studies investigating lower limb muscle volumes in children with unilateral and bilateral CP have quantified decreases in muscle sizes compared to children without CP, especially in distal muscles such as the medial gastrocnemius (Barber et al., 2011; Handsfield et al., 2016). Other studies have quantified increased collagen content (Booth et al., 2001) and greater infiltration of adipose tissue in lower limb muscles (Johnson et al., 2009) in children with bilateral CP. The sum of the neural and musculoskeletal differences in individuals with bilateral CP contributes to a variety of lower limb motor impairments, which will be discussed in the following section.

2.4. Lower Limb Motor Impairments from Bilateral Cerebral Palsy

2.4.1. Paresis

Individuals with bilateral CP experience paresis (weakness) in their lower limb muscles. One study quantified significant weakness in 11 muscles in both lower limbs compared to controls (Wiley and Damiano, 1998). The extensor muscles, particularly in the distal joints, are especially weak; the ankle plantarflexors can output 33% less torque in individuals with CP compared to controls (Barber et al., 2012). This weakness has been attributed to decreased muscle size, decreased muscle activation, and increased antagonist co-activation (Barber et al., 2012; Elder et al., 2003; Stackhouse et al., 2005). Lower extremity muscle weakness can affect gait in individuals with bilateral CP. For example, weakness in the hip abductor and lower limb extensors muscles is thought to be a contributor to crouch gait in this population (Arnold et al., 2005; Steele et al., 2012). Adolescents with CP also display lower muscle endurance than adolescents without CP, making regular physical activity more difficult to engage in. Studies investigating the effects of lower extremity strength training have quantified increased gait velocity and cadence in children with CP (Damiano and Abel, 1998; Dodd et al., 2003). Qualitatively, individuals with bilateral CP report improvements in postural control, walking, and stair negotiation after strength training (McBurney et al., 2003).

2.4.2. Loss of Selective Voluntary Motor Control

The loss of selective voluntary motor control (SVMC) has been defined as "the impaired ability to isolate the activation of muscles in a selected patterns in response to demands of a voluntary posture or movement." (Sanger et al., 2006). In individuals with CP, a loss of SVMC commonly manifests in two ways: 1) greater distal joint impairment (Fowler et al., 2010; Tedroff et al., 2006) and 2) abnormal joint coupling during voluntary activations (Rose and McGill, 2005; Thelen et al., 2003; Zhou et al., 2017). During maximum voluntary contractions of distal lower limb muscles, children with CP generally activated other muscles other than the intended prime mover (Tedroff et al., 2006). In addition to distal joint impairment, previous work has shown that the lower limb extensors (hip adductors, hip extensors, knee extensors, ankle plantarflexors) are abnormally coupled in individuals with CP (Thelen et al., 2003; Zhou et al., 2017). For example, hip adductor/extensor torque coupling has been quantified during isometric knee extension efforts

(Thelen et al., 2003). Another study found that individuals with bilateral CP consistently demonstrate co-activation of the knee extensors and ankle plantarflexors (Rose et al., 1999). Overall, a loss of SVMC has been postulated to be a peripheral marker for CS damage and an upregulated use of brainstem motor pathways (Cahill-Rowley and Rose, 2014; Drew et al., 1986; Hayes Cruz and Dhaher, 2007; Matsuyama and Drew, 2000; Sánchez et al., 2018b).

Impaired SVMC negatively impacts gait performance in children with bilateral CP (Chruscikowski et al., 2017; Zhou et al., 2019). One study found that impaired SVMC predicts decreased knee extension during gait, which ultimately reduces step length and velocity (Zhou et al., 2019). The effect of this impairment has been studied extensively in the swing phase of gait: SVMC ability has been correlated with uncoupled movement of hip flexion and knee extension, foot clearance, and maximum ankle dorsiflexion angle during this phase (Fowler and Goldberg, 2009; Sardoğan et al., 2021). An extensor synergy during stance may result in equinus gait, as knee extension in this phase couples with increased ankle plantarflexion (Zhou et al., 2017). However, it is unclear if and how impaired SVMC impacts gait biomechanics during the stance phase of challenging gait tasks such as stepping up.

2.4.3. Impact of Lower Limb Motor Impairments on Quality of Life

Around 64% of individuals with pediatric diplegia who are able to independently ambulate reported a deterioration in walking skills, including a complete loss of ambulation, after the age of 25 (Jahnsen et al., 2004). This impaired mobility often leads to limited adherence to the weekly recommendations of physical activity and excessive sedentary behaviors (Heyn et al., 2019; Verschuren et al., 2016). Indeed, risk factors for cardiovascular disease increase with GMFCS level, suggesting that impaired mobility is linked to diminished cardiovascular health in this population (Heyn et al., 2019). As a result, both adolescents and young adults with bilateral CP have elevated risk factors for cardiovascular disease (Becher et al., 2020; van der Slot et al., 2013). By adulthood, those with bilateral CP are far more likely to have a cardiovascular diagnosis than those without bilateral CP (Peterson et al., 2020). In addition to cardiovascular disease risk, impaired mobility can also lead to chronic pain in this population (Schmidt et al., 2020). It is critical to learn more about the nature of the motor impairments outlined above to clarify the root cause for a lifetime of mobility, public health, and personal challenges faced by this population.

2.5. The Biomechanics of a Step-Up

2.5.1. Stepping Up in Individuals without CP

Ascending stairs is a challenging activity of daily living that requires increased effort from the lower limb joints, especially compared to level-ground walking. There are two phases of a step-up task: 1) the push-off phase, between the leading limb toe-off and initial contact where the trailing limb is in stance pushing the body up onto the step and 2) the pull-up phase, between the trailing limb toe-off and initial contact where the leading limb is in stance phase pulling the body up onto the step. The biomechanics of a step up during these two phases have been investigated in both children and adults. The lower limb abductors and extensors are activated together to maintain stability and an upright position (Lyons et al., 1983). The hip abductors contribute the most joint torque to overall abduction during this task (Novak and Brouwer, 2011), especially during the initial step of stair ascent (Wang and Gillette, 2018). The ankle and knee joints output the greatest extensor torque and power among the lower limb joints in the push-off phase and pull-up phases, respectively (Costigan et al., 2002; McFadyen and Winter, 1988; Novak and Brouwer, 2011; Protopapadaki et al., 2007; Riener et al., 2002; Strutzenberger et al., 2011). When carrying external loads during a step up, participants increased their step width (Chen and Qu, 2018) and peak vertical ground reaction forces (Wang and Gillette, 2018).

The biomechanics of a step-up task have also been investigated in other populations with neural injury, namely individuals with stroke. Previous studies have quantified decreases in peak hip abduction, knee extension, and ankle plantarflexion moments in the paretic limb of individuals with hemiparetic stroke compared to the non-paretic and control limbs (Goyal et al., 2022; Novak and Brouwer, 2013). Interestingly, researchers have also quantified increases in peak hip extension moments and sagittal plane power in both stroke limbs, likely a compensation for decreased distal joint moments (Goyal et al., 2022) (**Figure 2.5**).

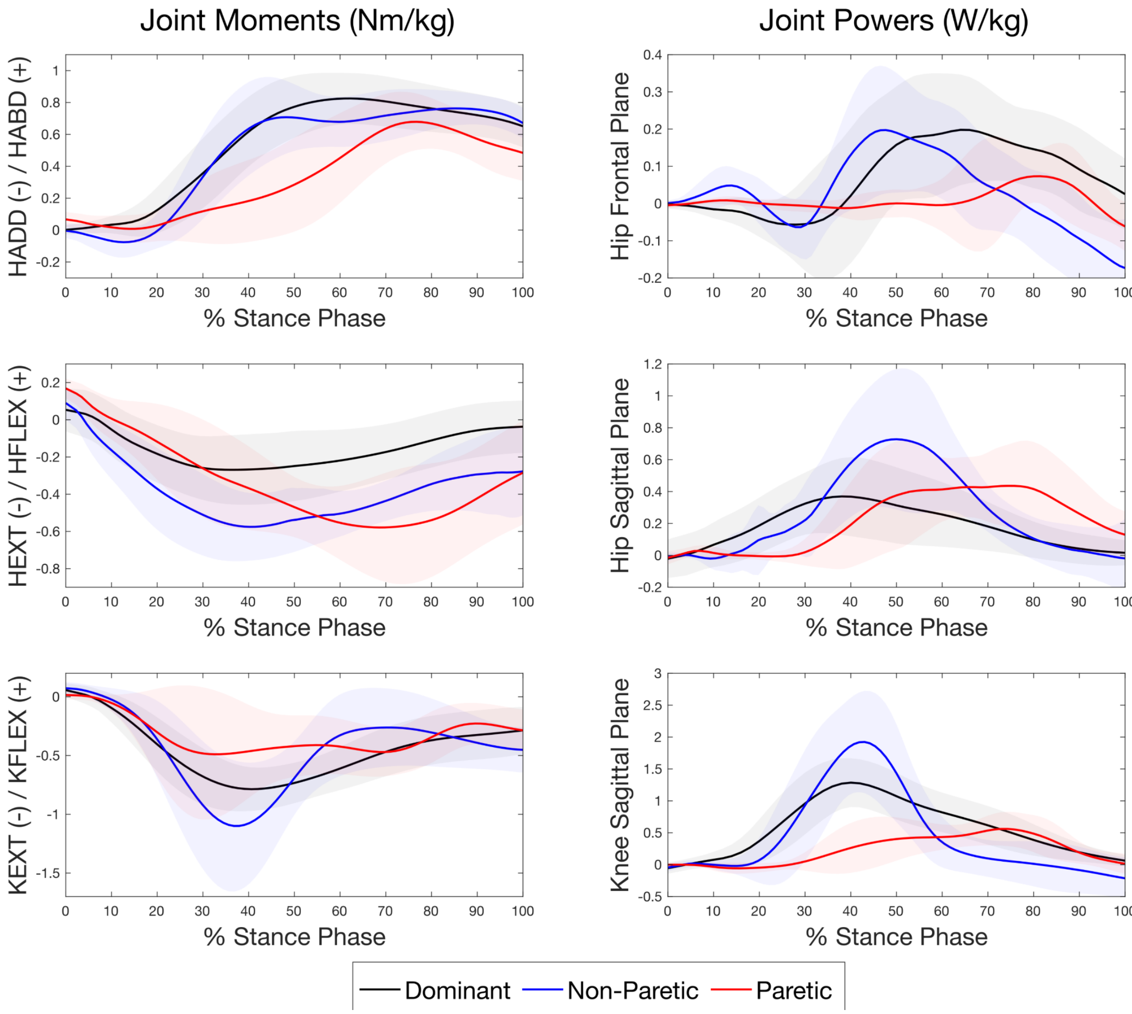

Figure 2.5. Joint kinetic profiles for individuals with and without stroke. These biomechanical measures are shown for the pull-up stance phase of a step up. The control dominant limb is in black, the stroke non-paretic limb is in blue, and the stroke paretic limb is in red. Knee extension torque and power in the paretic limb are significantly decreased compared to the non-paretic and dominant limbs, while hip extension torque and power in the paretic limb are significantly increased compared to the dominant limb. *(Figure 2.5 from Goyal et al., 2022)*.

2.5.2. Stepping Up in Individuals with CP

There is limited research quantifying joint moments during the stance phases of stepping up in this population. This is a significant gap in knowledge because 1) individuals with bilateral CP spend 74% of an inclined gait cycle in the stance phase (Ma et al., 2019) and 2) performance in stair climbing is associated with limitations to mobility, physical activity, and community participation in CP (Lepage et al., 1998). The stance requirements of a step up described in the previous section offer an optimal probe for motor impairments in individuals with CP. Progressively loading the limbs during this task can further test the limits of motor performance and offer a window into the central nervous system (Hill and Dewald, 2020; Sukal-Moulton et al., 2013, 2007). Indeed, the following chapters of this manuscript will detail research investigating the joint moments of individuals with and without bilateral CP during a step-up task with and without load modulation.

3. Motivators and barriers to research participation for individuals with cerebral palsy and their families

3.1. Abstract

Our objective was to investigate the motivators and barriers associated with the individual or family decision to participate in cerebral palsy research. Based on this information, we offer suggestions to increase the likelihood of participation in future CP studies. A digital survey was administered to stakeholders affected by cerebral palsy across the US. Our analysis focused on variables related to personal interests, travel, and study-specific elements. Statistical tests investigated the effects of responder type, cerebral palsy type, and Gross Motor Function Classification System level on travel and study-specific element variables. Recommendations were informed by responses reflecting the majority of respondents. Based on 233 responses, we found that respondents highly valued research participation (on average 88.2/100) and compensation (on average 62.3/100). Motivators included the potential for direct benefit (62.2%) and helping others (53.4%). The primary barriers to participation were schedule limitations (48.9%) and travel logistics (32.6%). Schedule limitations were especially pertinent to caregivers, while individuals with more severe cerebral palsy diagnoses reported the necessity of additional items to comfortably travel. Overall, we encourage the involvement of stakeholders affected by cerebral palsy in the research process. Researchers should consider offering flexible study times, accommodating locations, and compensation for time and travel expenses. We recommend a minimum compensation of $15/hour and a maximum time commitment of 4 hours/day to respect participants' time and increase likelihood of research participation. Future studies should track how attitudes toward research change with time and experience.

3.2. Introduction

Cerebral palsy (CP) is a broad pediatric-onset diagnosis caused by a non-progressive injury to the developing brain (Rosenbaum et al., 2007). The etiology of CP is also extremely heterogeneous, often resulting from brain injuries that occur during the early developmental period (Blair and Watson, 2006; Korzeniewski et al., 2018; Odding et al., 2006; Wimalasundera and Stevenson, 2016). Although CP is considered a pediatric-onset disorder, the associated physical and behavioral presentations are present across the lifespan and may fluctuate in severity over time. As there is currently no cure for CP, research efforts are critical for advancing our understanding of the pathophysiology and most efficacious treatments. However, the diversity of this population poses a significant recruitment challenge to researchers (Beckers et al., 2019). Limited funding for CP research also puts an added burden on researchers to be efficient with study-specific elements and recruitment, especially in the United States (Wu et al., 2015). In an attempt to address this, previous studies have surveyed individuals with CP to identify priority research areas (Gross et al., 2018; Lungu et al., 2016; Mcintyre et al., 2010). Research registries have also been established to facilitate collaboration among US institutions and to improve communication between researchers and individuals with CP (Hurley et al., 2011; Hurvitz et al., 2020). Despite these efforts, the success of CP research is dependent on the desire of individuals to participate and their ability to reasonably access the study within the limitations of their environment.

A previous study investigated the barriers to intervention-based CP research and recommended the involvement of patient populations and their families in the study development pipeline to improve recruitment (Beckers et al., 2019), an approach towards community-based participatory research. However, the study did not consider facilitators to research and only evaluated a small subset of the population interested in home-based training programs. Therefore, our objective was to sample a larger and more heterogeneous cohort of stakeholders and investigate the motivators and barriers associated with the decision to participate in CP research. We aimed to inform researchers of specific stakeholder perspectives by understanding whether factors such as Gross Motor Function Classification System (GMFCS) level, CP type, or age contribute to the decision to participate. Based on a nationwide survey, we provide recommendations for investigators to increase likelihood of recruitment and participation in future CP research.

3.3. Methods

3.3.1 Recruitment

The survey, including informed consent, was created and administered using the Research Electronic Data Capture (REDCap) platform. It was approved by the Northwestern University Institutional Review Board and remained open between May 6th and July 7th, 2020. Respondents were eligible to voluntarily participate if they resided in the United States and were either 1) caregivers of minors (under 18 years of age) with a diagnosis of CP or 2) adults with a diagnosis of CP. The survey link was shared via several platforms, including the Cerebral Palsy Research Registry (Hurley et al., 2011), ResearchMatch.org, department social media accounts, and emails to previous research participants.

3.3.2 Experimental Protocol: Qualitative Study

The digital open survey was designed to collect data about motivators and barriers of participation in CP research. The study objectives and survey questions were originally conceptualized from organic discussions among our research team. During survey development, we sought feedback from six caregivers of minors with CP and adults with CP to gather their opinions on the clarity of questions, the completeness of content, and the importance of the survey goals. The online survey (Zvolanek et al., 2021) contained optional questions in six different categories: demographics, personal interests, travel needs & preferences, study-specific elements, past research experience, and impact of COVID-19. The present analysis focused on the first four categories to summarize attitudes towards general CP research. Details of the survey development are described in further detail by Joshi et al. (Joshi et al., 2021).

3.3.3 Survey Categories

Demographics

We collected a number of variables to describe features of the respondents, listed in Table 1. In addition to CP type and GMFCS level, we asked about elements such as the time it takes for respondents to get to medical appointments and information about current and previous medical treatments common to study inclusion or exclusion criteria.

Personal Interests

All subsequent variable names are italicized in text and described in Table 2. Personal interest factors were considered intrinsic to the respondent. Respondents were asked about their perception of *research importance*, how highly they *value research participation*, and *compensation importance*, all using a visual analog scale of 0-100 to easily quantify these subjective opinions. Open-ended questions in the survey requested comment on personal goals, motivators, and barriers for participation in CP research. To gauge specific research interests, respondents were asked what *study types* and *body functions* were of high interest to them.

<u>*Travel Needs & Preferences*</u>

Respondents reported whether additional arrangements for *childcare* would be required, whether *time off work* would be required, and what *additional travel needs* would be required when leaving the house. To understand travel preferences, respondents were asked about their typical mode of *transportation* to medical appointments. We also asked participants to identify their perceived maximum *travel time for indirect benefit study*, defined as a study that is seeking to understand more about CP, and maximum *travel time for direct benefit study*, defined as a study with the potential to offer a direct benefit to the participant. Participants were asked about their overall willingness to make an extended *overnight trip* for research participation. Finally, the importance of *travel reimbursement for local study* and *travel reimbursement for distant study* was evaluated, both on a scale from 0-100.

<u>*Study-specific Elements*</u>

There were a number of variables related to explicit design of the study, which have the potential to be modified by the researcher. Respondents were asked about their most preferred study *locations* and their preferred *time of year* for study participation. Respondents' desired *compensation amount* was evaluated per hour of study participation. Respondents were also asked about the *maximum time commitment* that was reasonable for one day of participation, the *maximum study visits* they would be willing to commit, and whether they would consider participating in a *longitudinal* study.

3.3.4 Data & Statistical Analysis

IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA) was used to perform all analyses on the survey responses. Participants with missing data for a given question were excluded from analysis pertaining to that question. To summarize responses, descriptive analyses were first completed, with all percentages reported relative to the number of respondents for each question. We defined 50% as the threshold to describe the majority of survey respondents. Statistical analyses were only performed on travel and study-specific variables, as researchers can directly use this information to modify study methods during the developmental pipeline. Q-Q plots were created for quantitative variables to assess normality. Kruskal-Wallis tests, Chi-squared tests, or Kaplan-Meier survival analyses were performed on variables hypothesized to be dependent on three factors: Responder type (2 levels: adult, caregiver), CP type (4 levels: hemiplegia, diplegia, quadriplegia, other), and GMFCS level (5 levels: I, II, III, IV, V). A p-value < 0.05 was considered significant. Post hoc analyses were used to determine significant pairwise comparisons, where p-values were corrected for multiple comparisons using Bonferroni corrections. Further analyses were run to test specific hypotheses. For open-ended questions pertaining to personal interests, AH reviewed all responses, identified common themes, and categorized each response accordingly. Categorizations were reviewed and approved by KMZ and VG and summarized semi-quantitatively. For travel preferences, Wilcoxon signed-rank tests were run to determine differences between *travel time for indirect benefit* and *travel time for direct benefit* and between importance of *travel reimbursement for local study* and *travel reimbursement for distant study*.

3.4. Results

3.4.1. Demographics

In total, 255 individuals were consented and 233 (91.4% response rate) at least partially completed the survey. Respondent demographics are listed in **Table 3.1**. The survey population closely matches US census data in terms of sex, ethnicity, and race (Howden and Meyer, 2011; Humes et al., 2010; Joshi et al., 2021). The majority of participants reported no previous research experience (53.9%), a proximity to medical appointments of 1 hour or less (75.1%), and previous or ongoing physical/occupational therapy treatment for their arms (53.2%) or legs (65.7%).

Table 3.1. Participant demographics

Characteristic	Respondent					
	All		Adult with		Parent of	
Sex assigned at birth						
Male	112	48.1%	31	13.3%	81	34.8
Female	120	51.5%	61	26.2%	59	25.3
Not Reported	1	0.43%	0	0.00%	1	0.43
Ethnicity						
Hispanic or Latino	23	9.87%	7	3.00%	16	6.87
Not Hispanic or Latino	204	87.6%	81	34.8%	123	52.8
Not Reported	6	2.58%	4	1.72%	2	0.86
Race						
American Indian or Alaskan Native	2	0.86%	1	0.43%	1	0.43
Asian	9	3.86%	3	1.29%	6	2.58
Black or African American	24	10.3%	10	4.29%	14	6.01
Native Hawaiian or Other Pacific	1	0.43%	0	0.00%	1	0.43
White	175	75.6%	68	29.2%	107	45.9
Two or More Races	6	2.58%	4	1.72%	2	0.86
Not Reported	16	6.87%	6	2.58%	10	4.29
Gross Motor Function Classification System						
Level I	60	25.8%	15	6.43%	45	19.3
Level II	65	27.9%	33	14.2%	32	13.7
Level III	33	14.2%	23	9.87%	10	4.29
Level IV	37	15.9%	16	6.87%	21	9.01
Level V	35	15.0%	4	1.72%	31	13.3
Not Reported	3	1.29%	1	0.43%	2	0.86
Cerebral Palsy motor topography						
Hemiplegia	72	30.9%	18	7.72%	54	23.2%
Diplegia	60	25.8%	37	15.9%	23	9.87%

Quadriplegia	76	32.6%	24	10.3%	52	22.3%
Other	19	8.15%	10	4.29%	9	3.86%
Not Reported	6	2.58%	3	1.29%	3	1.29%
Previous research experience						
Yes	101	43.3%	40	17.3%	61	26.2
No	118	50.6%	48	20.6%	70	30.0
Not Reported	14	6.01%	4	1.72%	10	4.29
Proximity to medical appointments						
Less than 30 minutes	58	24.9%	24	10.3%	34	14.6
30 minutes to 1 hour	108	46.4%	45	19.3%	63	27.0
More than 1 hour	55	23.6%	19	8.15%	36	15.5
Not Reported	12	5.15%	8	3,43%	4	1.72
Medical Treatments Received	**Body Area**					
	Arms		Legs		Spine/Trunk	
Bony surgery	4	1.72%	57	24.5%	11	4.72
Soft tissue surgery	13	5.58%	109	46.8%	1	0.43
Neural surgery	1	0.43%	6	2.58%	18	7.73
Botox or other injections	39	16.7%	72	30.9%	6	2.58
Non-injectable spasticity medication	35	15.0%	59	25.3%	31	13.3
Physical or occupational therapy	124	53.2%	153	65.7%	81	34.8
Intensive therapy programs/camps	42	18.0%	39	16.7%	20	8.58

*these demographics refer to the minor with cerebral palsy

3.4.2. Personal Interests

All subsequent variables and associated p-values are listed in **Table 3.2**. Respondents reported high mean scores for *research importance* (93.8/100), *value research participation* (88.2/100), and *compensation importance* (62.3/100). Open-ended questions revealed that the biggest personal motivators for CP research were *personal benefit* (62.2% of respondents) and *helping others* (53.4%) (**Figure 3.1A**), while the biggest personal barrier was *schedule limitations* (48.9%) (**Figure 3.1B**). With regard to research interests, the most popular *study types* were physical or occupational therapy treatments (90.8%), activity monitoring (79.1%), imaging of muscle/bone (72.4%), survey or online (71.5%), robotic games (68.9%), imaging of the brain (68.4%), and new treatments (64.9%). The most popular *body functions* of interest were the legs/feet (79.9%), muscles (79.5%), movement/fitness (79.0%), brain/nerves (76.0%), arms/hands (62.9%), and pain (50.7%) (**Figure 3.2**).

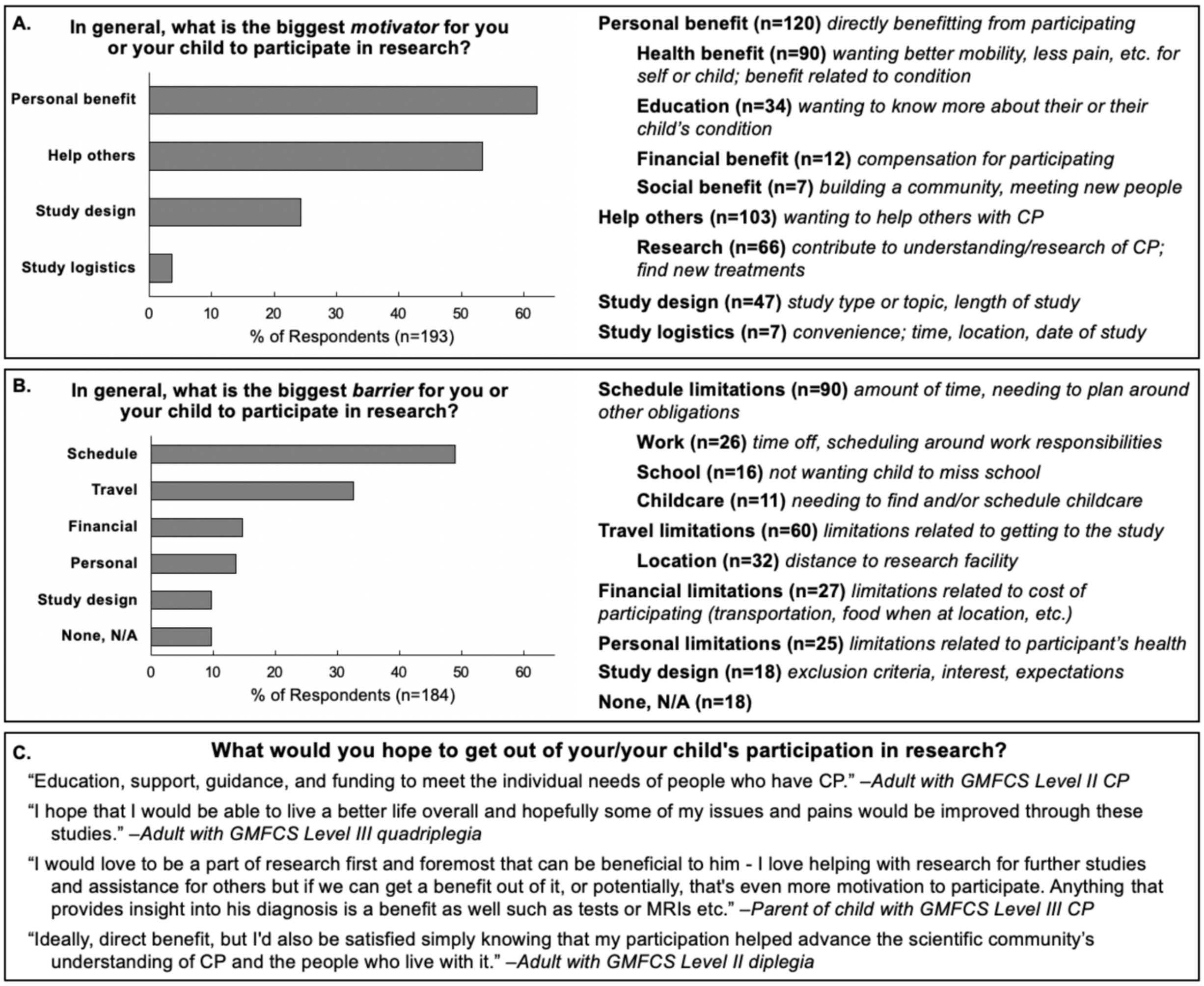

Figure 3.1. Motivators and barriers to CP research participation. Percentage of respondents who indicated (A) motivators and (B) barriers for participating in research relating to the categories shown. Indented categories are subcategories of the parent category. (C) Representative quotes indicating goals for participating in research.

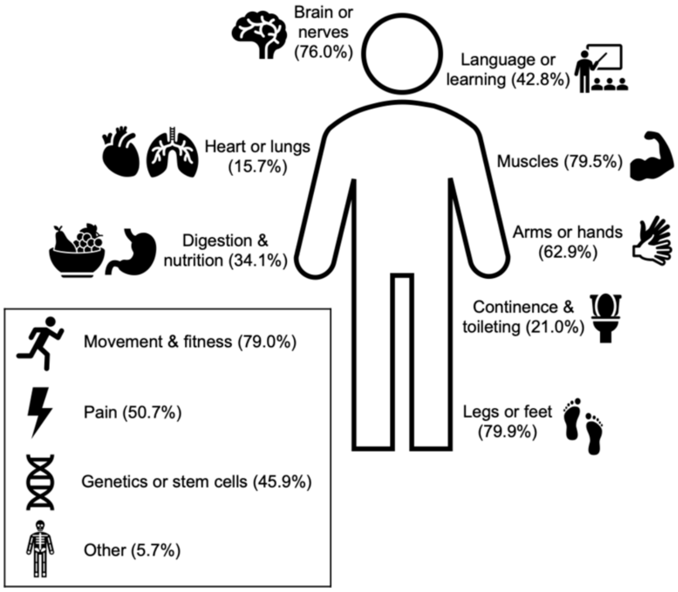

Figure 3.2. Body functions of research interest to respondents. Each of these options was offered as a checkbox for respondents to indicate if they would be interested in participating in a study that focused on these body regions/functions. Percentages are out of n = 233 respondents.

Table 3.2. Summary metrics and statistical test results

Variable	N	Summary Metrics Median (IQR) Mean (SD)	Statistical Test	p-values GMFCS Level	 CP Type	 Responder Type
Personal Interest						
Research importance: Importance of CP research (0-100)	229	99 (9) 93.8 (9.84)				
Value research participation: Value of participation in CP research (0-100)	221	97 (18) 88.2 (17.7)				

Compensation importance: Importance of compensation for study participation (0-100)	203	64 (29) 62.3 (25.7)				
Study types: Study types most likely to contact a researcher to learn more about	228	*See Results: Personal Interests*				
Body functions: Area of research focus most interested in participating or hearing more about	233	*See Figure 2A*				
Travel Needs & Preferences						
Childcare: Whether additional childcare is needed to participate	221	Yes: 75 No: 146	Chi-square	p=0.37	p=0.08	**p<0.001**
Time off work: Whether time off work is needed to participate	220	Yes: 138 No: 82	Chi-square	p=0.18	p=0.39	p=0.31
Additional travel needs: What other things need to be considered to travel to a research study	174	*See Figure 2B*				
Time			Chi-square	p=0.02	**p=0.003**	p=0.91
Breathing			Chi-square	**p=0.002**	p=0.43	p=0.70

Transition			Chi-square	p=0.02	p=0.25	**p=0.009**
Seizure			Chi-square	**p=0.001**	p=0.30	**p=0.002**
Feeding			Chi-square	**p<0.001**	**p<0.001**	**p<0.001**
Snacks			Chi-square	p=0.48	p=0.13	**p<0.001**
Medications			Chi-square	**p<0.001**	p=0.03	p=0.88
Toileting			Chi-square	**p<0.001**	**p<0.001**	**p<0.001**
Transportation			Chi-square	**p<0.001**	**p<0.001**	p=0.22
Other			Chi-square	p=0.07	p=0.61	p=0.22
Transportation: Preferred transportation method	220	*See Figure 2C*				
Drive self			Chi-square	p=0.01	**p=0.002**	**p<0.001**
Family member drives			Chi-square	p=0.97	p=0.46	p=0.06
Public transit			Chi-square	p=0.02	p=0.09	**p<0.001**

Ride service			Chi-square	p=0.17	p=0.34	**p<0.001**
Other			Chi-square	p=0.03	p=0.06	**p=0.001**
Travel time for indirect benefit study: Maximum time willing to travel from home for study without the potential for direct benefit (0.5-more than 2 hrs)	219	4 (3) 3.53 (1.40)	Chi-square	p=0.26	p=0.44	p=0.06
Travel time for direct benefit study: Maximum time willing to travel from home for study with the potential for direct benefit (0.5-more than 2 hrs)	220	5 (2) 4.13 (1.19)	Chi-square	p=0.37	p=0.15	p=0.12
Overnight trip: Willingness to make overnight or extended trip for research study	221	Yes: 110 No: 19 Maybe: 92	Chi-square	p=0.98	p=0.69	p=0.75
Travel reimbursement for a local study: Importance that cost of travel to local study is reimbursed (0-100)	203	50 (57) 49.1 (32.8)	Kruskal-Wallis	p=0.14	p=0.75	**p=0.007**
Travel reimbursement for a distant study:	205	78 (32)	Kruskal-Wallis	p=0.54	p=0.93	p=0.69

Importance that cost of travel to distant study is reimbursed (0-100)		75.3 (24.3)				
Study-specific Elements						
Locations: Preferred study location	222	*See Figure 2D*				
Current clinic			Chi-square	p=0.68	p=0.62	**p=0.03**
New clinic			Chi-square	p=0.29	**p=0.003**	p=0.94
Park			Chi-square	**p<0.001**	**p=0.01**	**p=0.02**
Lab			Chi-square	p=0.58	**p=0.003**	p=0.58
School			Chi-square	p=0.64	p=0.19	**p<0.001**
Home			Chi-square	p=0.12	p=0.95	p=0.18
Other			Chi-square	p=0.76	p=0.30	p=0.29
Time of year: Times that would be considered for research participation	127	*See Figure 2E*				

Weekends during school year			Chi-square	p=0.11	p=0.06	p=0.68
Weekdays during school year			Chi-square	p=0.06	p=0.20	**p=0.05**
Summer break			Chi-square	p=0.68	p=0.91	**p<0.001**
Spring break			Chi-square	p=0.46	p=0.61	p=0.11
Winter break			Chi-square	p=0.87	p=0.41	**p=0.002**
Non-attendance school days			Chi-square	p=0.22	p=0.15	**p=0.002**
Maximum time commitment: Amount of time in one day that is reasonable to participate in a study (0.5-8 hrs)	220	4 (3) 3.83 (1.16) *See Figure 2F*	Kruskal-Wallis	p=0.11	**p=0.003**	**p=0.002**
Maximum study visits: Maximum number of visits for one study (1-5 visits)	219	5 (2) 4.28 (1.10)	Kruskal-Wallis	p=0.62	p=0.71	p=0.21
Longitudinal: Willingness to participate in longitudinal study (Yes or No)	220	Yes: 210 No: 10	Chi-square	p=0.19	p=0.94	p=0.19

Compensation amount:	176	15 (10)	Kruskal-Wallis	p=0.71	p=0.68	p=0.94
Appropriate amount of compensation ($/hr)		16.7 (12.3)				

3.4.3. Travel Needs

Most respondents needed *time off work* (62.7%) but did not need additional arrangements for *childcare* to engage in research (66.1%). There was a significant main effect of responder type on the latter, where caregivers of minors with CP needed *childcare* more than adults with CP. When leaving their homes, the majority of respondents had *additional travel needs* such as *time* (59.2%), *transportation items* such as a wheelchair or stroller (58.0%), and *snacks* (52.9%) (**Figure 3.3A**).

Specific *additional travel needs* varied significantly based on GMFCS level, CP type, and responder type. All significant pairwise comparisons are reported in the supplemental section (**S1 Table**). There was a significant main effect of GMFCS level on *breathing items*, *seizure items*, *feeding items*, *medications*, *toileting items*, and *transportation items*. In summary, individuals classified as GMFCS level V reported needing these items more to comfortably travel. There was a significant main effect of CP type on *time*, *feeding items*, *toileting items*, and *transportation items*. In general, individuals affected by quadriplegia reported needing these items more to comfortably travel. Finally, there was a significant main effect of responder type on *transition*, *seizure items*, *feeding items*, *snacks*, and *toileting items*. Adults with CP had more concerns about *transition* to a new environment than caregivers of minors with CP. However, caregivers needed *seizure items*, *feeding items*, *snacks*, and *toileting items* for their children more than adults with CP did for themselves.

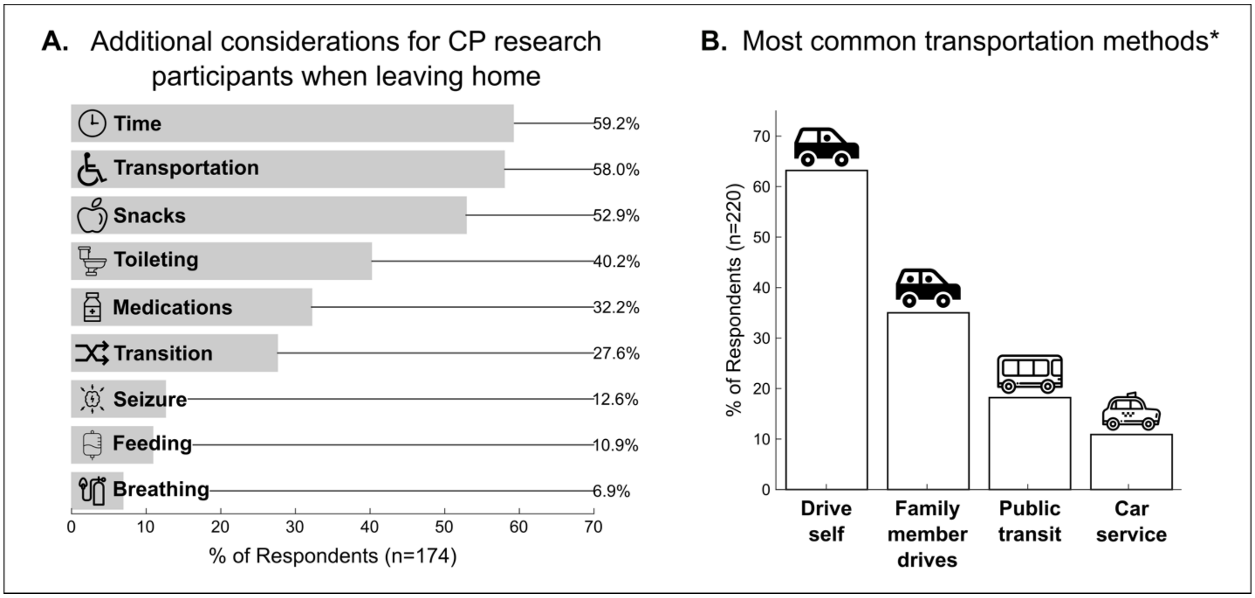

Figure 3.3. Summary of travel needs variables. (A) Summary of *additional travel needs* required to participate in CP research. The most prevalent categories were *time*, *transportation*, and *snacks*. (B) Summary of the most common *transportation* methods. Driving was the most cited mode of transportation. *6.8% of respondents selected other transportation modes.

3.4.4. Travel Preferences

The most common mode of *transportation* was by car, whether the individual drives (63.2%) or gets a ride from a family member (35.0%) (**Figure 3.3B**). There was a significant main effect of GMFCS level on *transportation* methods including *drive self*, *public transit*, and *other*, though there were no significant pairwise comparisons. There was a significant main effect of CP type on *drive self*, where respondents (both caregivers and adults with CP) affected by hemiplegia preferred to drive themselves more than those affected by diplegia or quadriplegia. There was a significant main effect of responder type on *drive self*, *public transit*, *ride service*, and *other*. Caregivers of minors with CP preferred to drive themselves more than adults with CP, whereas adults preferred public transit, ride services, or other methods of transportation.

The mean response for *travel time for indirect benefit study* was 3.53 hours, which was significantly lower ($z = -6.857$, $p < 0.001$) than the mean response for *travel time for direct benefit* *study* at 4.13 hours. Approximately half (49.8%) of respondents were willing to make an *overnight trip* for research participation. There was a significant main effect of responder type on the importance of *travel reimbursement for a local study*, where adults with CP thought reimbursement was more important than caregivers of minors with CP. The overall mean score for this variable (49.1/100) was significantly lower ($z = -9.901$, $p < 0.001$) than the mean score for the importance of *travel reimbursement for a distant study* (75.3/100).

3.4.5. Study-specific Elements

A *current clinic* (88.7%), *home* (84.7%), *lab* (73.0%), and *new clinic* (59.9%) were the most preferred *locations* for research participation (**Figure 3.4A**). There was a significant main effect of GMFCS level on *park*, where individuals who are GMFCS level I were more likely to select this location than all other levels. There was a significant main effect of CP type on *new clinic* and *lab*, where individuals affected by hemiplegia were more likely to select these locations over those affected by quadriplegia. There was a significant main effect of responder type on *current clinic*, *park*, and *school*, where caregivers of minors with CP were more likely to select these locations over adults with CP.

The majority of respondents were flexible to participate in research at any *time of year*, except for parents on *weekdays during the school year* (**Figure 3.4C**). There was a significant main effect of responder type on weekdays, where adults reported more availability compared to caregivers. There was also a significant main effect of responder type for *summer break, winter break,* and *other school holidays*, where caregivers were more willing to engage in research during these *times of year* than adults. Respondents indicated a mean *compensation amount* of $16.69/hour for participation in research. The average *maximum time commitment* was 3.83

hours/day and the average *maximum study visits* was 4.28 visits. Survival analyses on *maximum time commitment* yielded significant main effects of CP type (log rank $\chi^2(1) = 11.9$, $p = 0.001$), with no significant pairwise comparisons, and responder type (log rank $\chi^2(3) = 13.4$, $p = 0.004$). Most notably, caregiver interest dropped from 54.1% to 24.1% at a *maximum time commitment* greater than 4 hours (**Figure 3.4B**). Finally, the vast majority of respondents were willing to participate in a *longitudinal* study (95.5%).

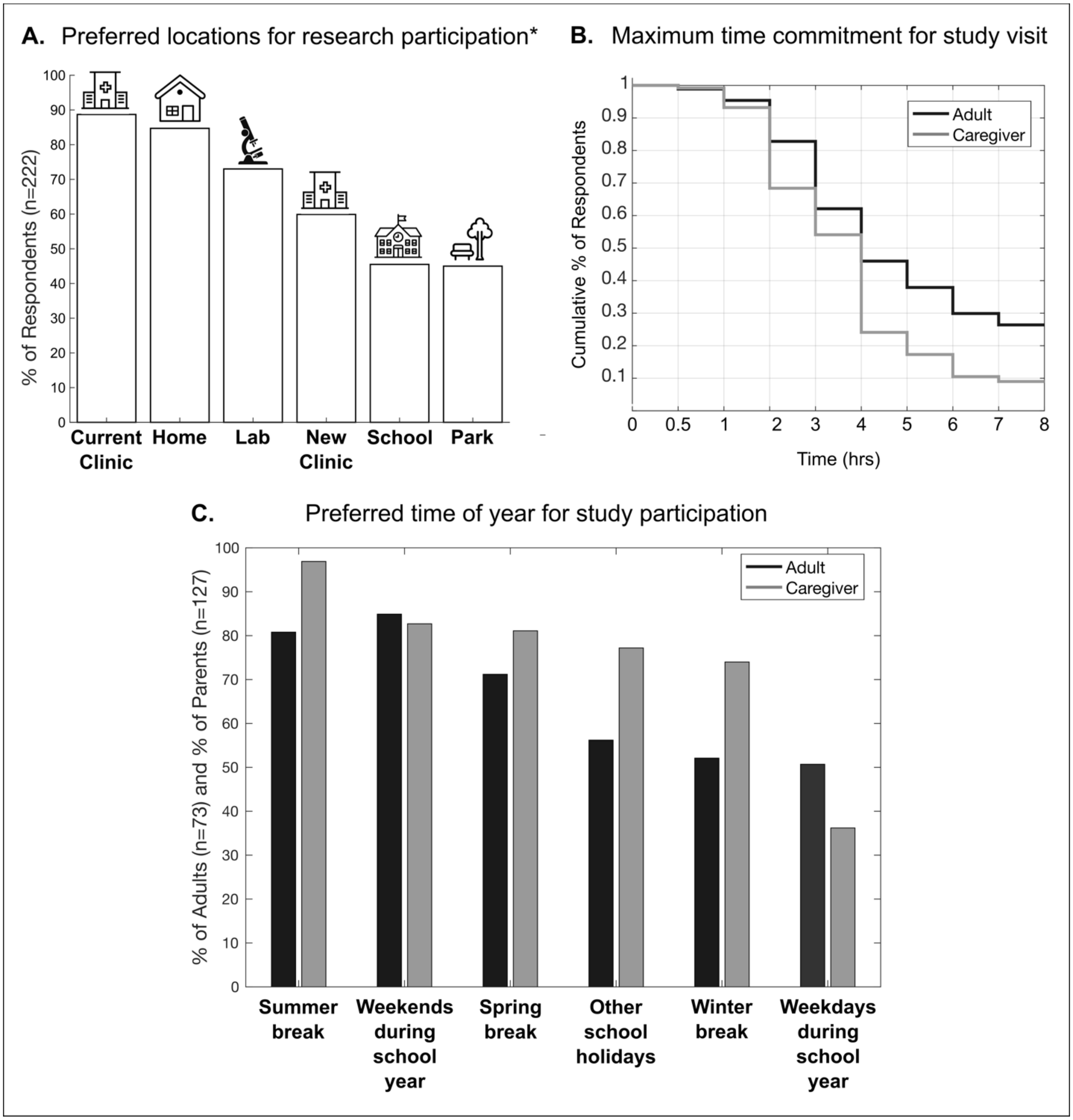

Figure 3.4. Summary of study-specific elements. (A) Summary of preferred *locations* for CP studies. *5.4% of respondents chose other locations. (B) Survival analysis for *maximum time commitment* by responder type. Less than 30% of caregivers and adults remain at 4 and 7 hours, respectively. (C) Summary of preferred *time of year* for participation by responder type.

3.5. Discussion

The purpose of this study was to determine the motivators and barriers involved in the decision to participate in CP research studies. We administered a survey to gain more insight on stakeholder perspectives, including their personal interest in research, travel needs and preferences for study participation, and study-specific elements. These results can be extrapolated into recommendations for future CP research studies to maximize participant recruitment and expedite new knowledge about CP.

Our study is one of the first to identify the personal and practical factors that influence research participation. Respondents overwhelmingly supported research and valued their own participation in research, in a wide range of topics (Figure 2A). The research areas of interest identified by our survey respondents are largely consistent with previous reports of CP research priorities (Gross et al., 2018; Shriver, 2017). Survey responses indicated that most individuals were motivated to participate by the potential for personal benefit and helping others. Where relevant, these two elements should be highlighted in recruitment materials and results should be disseminated to participants in a format that is best suited to their learning preferences (e.g. a copy of a manuscript or poster, a one-page summary, or a short video). Schedule limitations were the most prevalent barriers to research participation, especially as caregivers of minors with CP were likely to need additional childcare arrangements. Travel limitations were also a highly cited barrier to research participation. To minimize these barriers, researchers should offer flexible study times, particularly during the weekends and summer break, and/or utilize local study locations close to the home or clinics where participants are receiving care.

When scheduling participants with CP for a research study located outside of their home, travel needs for participants should be considered. To accommodate the additional time required for participants and/or their families to reach the study location, researchers should be flexible with appointment times. Indeed, utilizing flexible study protocols has previously been identified as a recommendation to improve recruitment in CP research (Beckers et al., 2019). Researchers should also consider having snacks available for participants, particularly for minors with CP. Unsurprisingly, participants classified as GMFCS level V or with a diagnosis of quadriplegia reported requiring more items in order to comfortably travel. Researchers working with these inclusion criteria might consider the home as a study location to mitigate the barrier of travel burden.

Respondents clearly noted the importance of compensation, as providing compensation to participants is consistent with appreciation of their time. In a previous study where caregivers of minors with CP were consulted on the design of randomized control trials, there was a strong preference for coverage of all treatment costs (Edwards et al., 2011). Caregivers noted that they may not be able to cover the costs themselves, the participants would be offering their time, and the study benefits were unknown (Edwards et al., 2011). From our survey responses, a minimum compensation of $15/hour and a maximum time commitment of 4 hours/day were interpreted to be respectful of the time and commitment to research participation.

In addition to financial incentives for participation, compensation for other expenses associated with travel should be considered. If a study session requires a longer duration, additional compensation can include paying for a meal. Because most respondents were willing to travel long distances for studies with and without potential for direct benefit, researchers should also consider offering travel reimbursement. This is especially important because travel limitations were a highly cited barrier to research participation. As the most preferred mode of transportation involves driving, suggestions for reimbursement include gas and parking. Flexibility around transport mode could also include fare coverage for adult participants who prefer public transit or ride services. For participants willing to make an overnight trip for a research study, researchers should consider compensating for lodging and overnight parking.

Our survey-based recommendations are centered around maximizing stakeholder participation in CP research studies. One limitation of our sample was that survey respondents were self-selected and may be biased towards research participation. Their responses may inflate measures of research importance and resource allocation (e.g. time and money), while underestimating obstacles to research participation. However, these individuals may also be more likely to respond to participant requests and therefore would be more representative of future study samples. Another limitation is that we allowed the terms "potential for direct benefit" and "indirect benefit" to be interpreted by the respondents. This does not address considerations such as the variability of perception of direct benefit (Friedman et al., 2012) and therapeutic misconceptions (Appelbaum et al., 2012). Survey responses were self-reported at one time point. Future research should determine whether attitudes towards research shift over time or are dependent on the depth of previous research experience. Finally, researchers should be informed about and supported in the engagement of the community in research. This can span a spectrum of involvement, such as one-time consultations to provide feedback on study-specific elements, formation of Community Advisory Boards, or the inclusion of community stakeholders as project investigators. Our study including stakeholders during the design phase but would have required additional funding to adequately reimburse time and efforts for larger scale engagement. As a research team, we continue to look for ways to include family stakeholders in the research process as equal partners.

We assessed the motivators and barriers to research participation from the perspectives of caregivers of minors with CP and adults with CP. By identifying these stakeholder attitudes and utilizing the information to design study protocols, individuals with CP and their families become true partners in the research that aims to benefit people like them. Researchers can best accommodate the needs of participants with CP by opting for flexible study locations, scheduling, and compensation options. We recognize that this will not be feasible for all studies but encourage researchers to consider even the smallest gestures to reduce the burden of participation.

4. LOAD MODULATION AFFECTS PEDIATRIC LOWER LIMB JOINT MOMENTS DURING A STEP-UP TASK

4.1. Abstract

Performance in a single step has been suggested to be sensitive measure of movement quality in pediatric clinical populations. Although there is less information available in children with typical development, researchers have postulated the importance of analyzing the effect of body weight modulation on the initiation of stair ascent, especially during single limb stance where upright stability is most critical. The purpose of this study was to investigate the effect of load modulation from -20% to +15% of body weight on typical pediatric lower limb joint moments during a step-up task. Fourteen participants between 5-21 years with no known history of neurological or musculoskeletal concerns were recruited to perform multiple step-up trials. Peak extensor support and hip abduction moments were identified during the push-off and pull-up stance phases. Linear regressions were used to determine the relationship between peak moments and load. Mixed effects models were used to estimate the effect of load on hip, knee, and ankle percent contributions to peak support moments. There was a positive linear relationship between peak support moments and load in both stance phases, where these moments scaled with load. There was no relationship between peak hip abduction moments and load. While the ankle and knee were the primary contributors to the support moments, the hip contributed more than expected in the pull-up phase. Clinicians can use these results to contextualize movement differences in pediatric clinical populations including cerebral palsy and highlight potential target areas for rehabilitation for populations such as adolescent athletes.

4.2. Introduction

Body weight modulation, including providing partial support of a person's body weight (Celestino et al., 2014; Cherng et al., 2007; Kurz et al., 2011; Phillips et al., 2007; Provost et al., 2007) and addition of external loads (Dodd et al., 2003; McBurney et al., 2003; Simão et al., 2014), is broadly used in research and clinical practice. This method is often adopted for individuals with neurodevelopmental disorders during steady-state gait training (Celestino et al., 2014; Cherng et al., 2007; Kurz et al., 2011; Phillips et al., 2007; Provost et al., 2007; Simão et al., 2014). The evidence is less robust for the effect of body weight modulation on the initiation of stair ascent. Researchers have postulated the importance of analyzing this specific movement because the first step up requires larger lower limb joint moments compared to subsequent steps (Wang and Gillette, 2018). This analysis may be especially important for pediatric clinical populations, for which a single step up can be a sensitive measure of movement quality (Stania et al., 2017).

The handful of studies that have investigated lower limb moments of a step-up task have all been in adults, and even fewer studies have explored the effect of load modulation (Goyal et al., 2022; Wang and Gillette, 2018). It has been confirmed that substantial hip abduction moments are necessary to maintain mediolateral stability and considerable sagittal plane extensor moments are required to keep the body upright in adults (Goyal et al., 2022; Novak and Brouwer, 2011; Wang and Gillette, 2018). There is a need for a robust model defining how these joint moments change across multiple load conditions in a typical pediatric population, especially during single limb stance where upright stability is most critical. This model would serve to contextualize movement differences in pediatric populations with neurodevelopmental disorders and highlight potential target areas for training during clinical therapy.

The purpose of this study was to investigate the effect of body weight load modulation from -20% body weight (BW) to +15% BW in 5% increments on typical pediatric lower limb joint moments during a step-up task. Based on previous literature, we hypothesized that 1) extensor support moments would incrementally increase with load during the stance phases of a step up, 2) hip abduction moments would incrementally increase with load during the stance phases of a step up, and 3) the knee and ankle joints would drive increases in extensor support moments. We also performed a secondary analysis to understand the relationship between age and leg length and the kinetic performance of a step-up task.

4.3. Methods

4.3.1. Participant Recruitment

Participants were recruited as a sample of convenience through word-of-mouth and flyers. Individuals were included in the study if they were between the ages of 5-21 years with no known history of neurological or musculoskeletal concerns that would affect their ambulation or ability to participate in the study. We sampled from a wide age range to capture step-up performance across the pediatric population. This study was approved by Northwestern University's Institutional Review Board. Participants under the age of 18 provided verbal or written assent along with parent/guardian written consent. Participants who were 18+ years provided informed written consent themselves.

4.3.2. Experimental Set-Up

Participants performed a series of trials that involved stepping up onto a raised platform. A 2x2 cluster of four force plates (AMTI, Watertown, MA) captured participant ground reaction forces at a frequency of 1000 Hz. To independently capture joint biomechanics from the right and left lower limbs, two 10.2-cm tall platforms were placed on two side-by-side anterior force plates (**Figure 4.1A**). We purposefully chose a low step height in order to replicate this experiment in the future with pediatric clinical populations, who may have a difficult time completing the protocol on a higher platform. A 10-camera motion capture system (Qualisys, Göteborg, Sweden) recorded participant kinematics at a frequency of 100 Hz using a modified Cleveland Clinic marker set (Kaufman et al., 2016). Markers were placed on thirty-four total landmarks of the trunk (sternum, C7 vertebrae, T10 vertebrae), pelvis (sacrum, bilateral posterior superior iliac spines), and lower extremities (bilateral greater trochanters, lateral femoral epicondyles, lateral malleoli, calcanei, second and fifth metatarsals, and thigh and shank four-marker clusters).

During step-up trials, participant body weight (BW) was modulated using the Zero-G Bodyweight Support System (Aretech LLC, Ashburn, VA) to subtract weight or a weighted vest to add weight. There were six total load conditions: three unweighted conditions of -20%, -15%, and -10% of BW and three weighted conditions of +5%, +10%, and +15% of BW. The weighted conditions were chosen based on loads common for children's backpacks (Bryant and Bryant, 2014; Perrone et al., 2018). Available weights included ⅓, ⅔, ½, and 1-lb bars, which were distributed evenly around the vest. The unweighted conditions represented a similar range to the weighted conditions; we did not test a -5% condition due to technical limitations of the Zero-G, which requires a minimum of 10 lbs to be removed from the user.

4.3.3. Experimental Protocol

Participants filled out the Waterloo Footedness Questionnaire – Revised (Elias et al., 1998) and completed timed single-limb stance tests to determine lower limb dominance. During the experiment, participants started in a standing position with their feet split between the two force plates posterior to the platforms (**Figure 4.1A**). Participants were instructed to step up onto the platforms at a self-selected walking speed and, after a slight pause at the top, were instructed to step back down to the starting position. Participants completed three blocks of trials, leading with either their dominant foot or their non-dominant foot. The first block was a no-load condition, where participants completed 15 steps per leading foot. The second and third blocks were randomized and consisted of either weighted or unweighted conditions. Within these blocks, the load conditions were randomized and participants completed 10 steps per leading foot. To ensure participant safety and minimize fall risk, participants were connected to an overhead trolley with a harness.

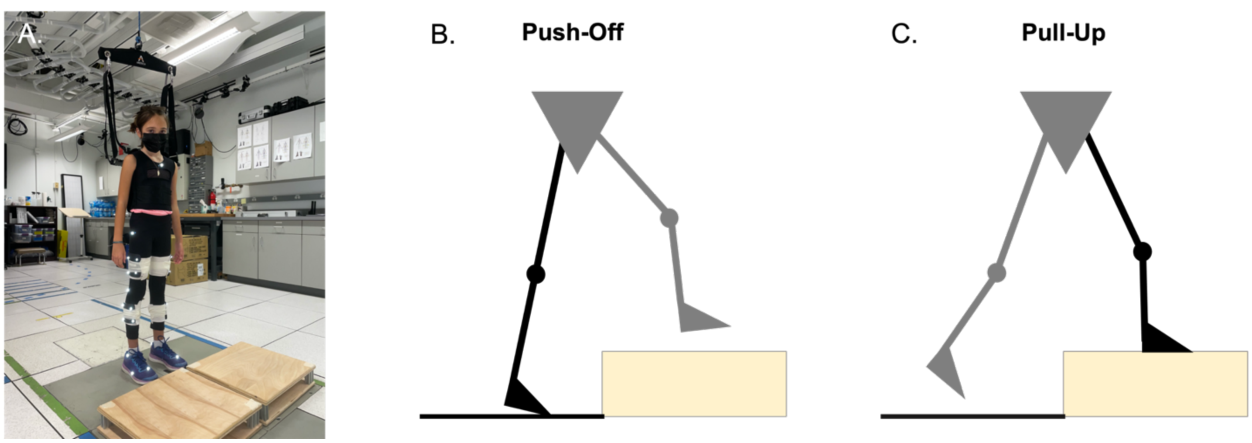

Figure 4.1. Visuals of a step-up protocol. (A) A participant, outfitted with reflective markers and a weighted vest, in the starting position behind the two raised 10.2-cm platforms. Each foot is on an independent force plate to collect information about the kinetics of both legs. Each platform is also on an independent force plate. (B) The push-off stance phase of the step-up task, between leading foot lift-off and leading foot initial contact with the step. (C) The pull-up stance phase of the step-up task, between trailing foot lift-off and trailing foot initial contact with the step.

4.3.4. Data Processing & Analysis

Data were first visually inspected in Qualisys Track Manager (Qualisys, Göteborg, Sweden) to verify that the markers were appropriately labeled. Data were then imported into Visual 3D (C-Motion, Germantown, MD). Marker and ground reaction force data were interpolated to fill in small gaps and filtered using a low-pass 4th-order Butterworth filter with a 6 Hz cutoff frequency to remove high-frequency fluctuations. We performed inverse dynamics calculations in Visual 3D to calculate hip, knee, and ankle joint moments in the sagittal and frontal plane. To account for the step height during these calculations, the two corresponding force plates were modified virtually to create raised force platforms. We used ground reaction force data to identify four gait events occurring during each step-up: leading limb lift-off, leading limb initial contact on the step, trailing limb lift-off, and trailing limb initial contact on the step.

Further processing was done in MATLAB (MathWorks, Inc., Natick, MA). We identified hip abduction and extensor support moments (the sum of hip, knee, and ankle sagittal plane moments). All joint moment data were divided by participant body weight for comparison during statistical analyses. We plotted joint moment profiles for each individual trial during two single-limb stance phases: 1) the push-off phase, between leading foot lift-off and leading foot initial contact (**Figure 4.1B**) and 2) the pull-up phase, between trailing foot lift-off and trailing foot initial contact (**Figure 4.1C**). Any trials that were two standard deviations outside of the average stance phase length were not considered for further analysis.

4.3.5. Statistical Analysis

Statistical analysis was performed in Stata IC 14.1 (StataCorp LLC, College Station, TX), and significance was set at $p<0.05$. The push-off and pull-up stance phases were considered separately in all statistical analyses. Visual inspection of the distribution of residuals was used to confirm the normality of the data. We considered the outcome measures of peak hip abduction moments, peak support moments, and individual hip, knee, and ankle percent contributions to peak support moments. The latter was calculated by dividing hip, knee, and ankle moments at the time of peak support moment by the peak support moment. For the no-load condition, we ran mixed effects models to estimate the fixed effect of the limb dominance (2 levels: dominant, non-dominant) and a random effect of participant on these outcomes. In a secondary analysis, we also ran Pearson's correlations to evaluate the strength of the relationships between peak moments and the continuous variables of age and leg length.

For the six load conditions, peak hip abduction moments and peak support moments were averaged and normalized to their average values in the no-load condition. We first ran a linear mixed effects model to determine if there were differences between the dominant and non-dominant limbs at each individual load level (interaction term). If not, the data were then combined. Linear regressions were used on these outcome measures to determine the relationship between peak moments and load. For the outcome measures of individual joint percent contributions to peak support moments, we used linear mixed effects models with two fixed effects of load (-20%, -15%, -10%, 0%, +5%, +10%, and +15% of BW) and limb (dominant, non-dominant) and a random effect of participant. Bonferroni corrections were used to correct for multiple comparisons in post-hoc analyses. In another secondary analysis, we calculated the individual slopes of peak moments vs. load for each participant. We then ran Pearson's correlations between these slopes and age and leg length.

4.4. Results

4.4.1. Participant Metrics

Fourteen individuals participated in the study (7 female). As the statistical analysis included repeated measures for each participant, the average effective sample size calculated was 25 participants. Thirteen participants were right-foot dominant and one was left-foot dominant. Participant metrics included a mean age of 12.8 ± 4.2 years, a mean weight of 53.2 ± 28.1 kg, and a mean height of 1.54 ± 0.19 m. Two participants were unable to complete the +15% load condition because the calculated BW percentage exceeded the available weights. Four participants were unable to complete the -10% condition and one participant was unable to complete the -15% condition because their weight was too low to meet the minimum weight removal requirements of the Zero-G. Profiles of other biomechanical metrics (including joint power, center of mass, and trunk kinematics) across the entire step-up task are in the Appendix (**Figure A.2-A.4**).

4.4.2. Push-Off Stance Phase

For the no-load condition, the effect of limb dominance was not significant for any outcome measures (**Figure 4.2A**). Average peak hip abduction moments were +0.730 Nm/kg and average peak support moments were -0.791 Nm/kg. There was a large ankle plantarflexion contribution of 112% to peak support moments. This served to offset a small hip flexion contribution of 3.81% and a small knee flexion contribution of 8.62%, resulting in a net extension moment.

There were no significant differences in peak moments between the dominant and non-dominant limbs at each individual load level. The linear relationship between peak hip abduction moments and load was not significant in the push-off stance phase. In contrast, the linear relationship between peak support moments and load was significant ($p<0.001$, $R^2 = 0.278$), with a coefficient of +0.817 and an intercept of +0.973 (**Figure 4.3A**). As for individual percent contributions to peak support moments, the effect of load was only significant for hip percent contributions to peak support moments ($p=0.001$). However, there were no significant pairwise comparisons (**Figure 4.4A, C, E**).

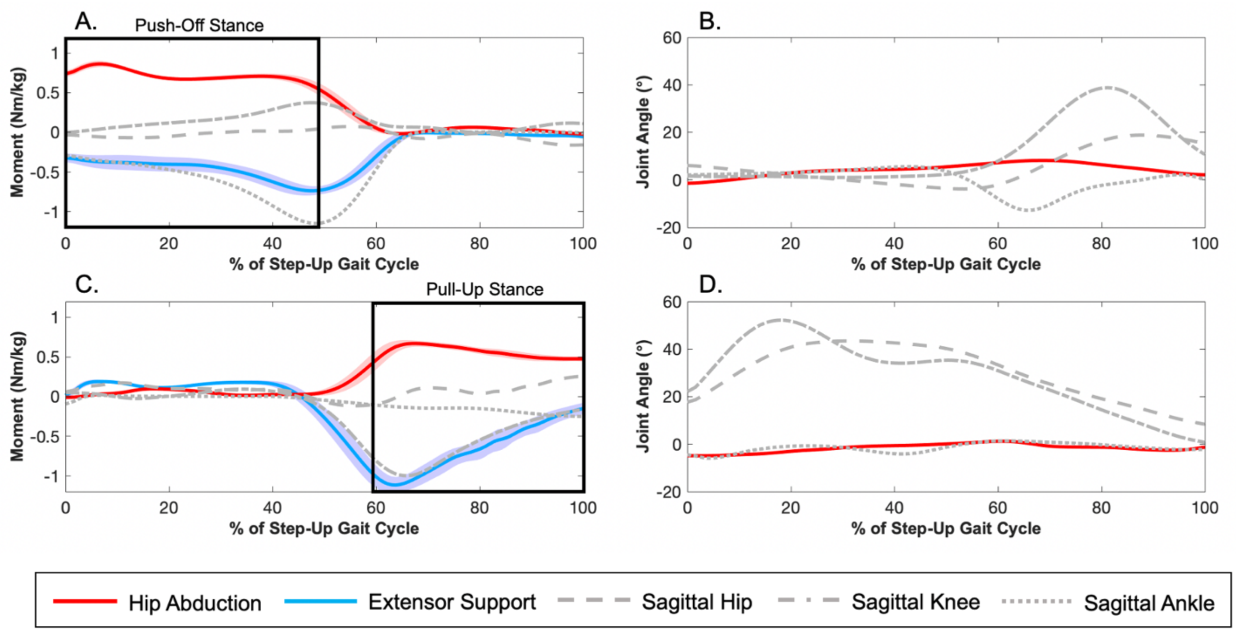

Figure 4.2. Joint biomechanical profiles of a step-up task. Representative kinetic (A and C) and kinematic (B and D) profiles from one participant during a no-load step up for the trailing leg (A and B) and the leading leg (C and D). On each x-axis, 0% corresponds to the start of a step-up trial at leading leg lift-off while 100% corresponds to the end of the trial at trailing leg initial contact with the step. On each y-axis, a positive magnitude indicates joint flexion/abduction while a negative magnitude indicates joint extension/adduction. Average hip abduction moments are in red. Individual lower limb sagittal plane moments are in gray, including the hip (gray dash), knee (gray dash-dot), and ankle (gray dot). The sum of these individual joint moments equals the extensor support moments shown in blue. Shaded regions represent one standard deviation. The black boxes on plots A and C indicate the push-off and pull-up stance phases, respectively.

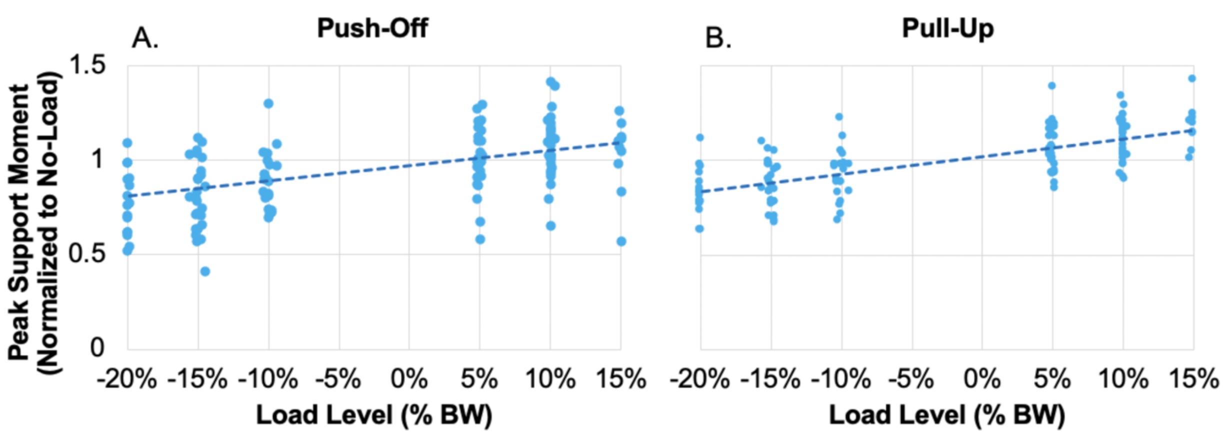

Figure 4.3. Linear regressions of peak support moments vs. load. Peak support moments vs. load for the (A) push-off and (B) pull-up stance phases. All values are divided by their respective values in the no-load condition. The linear regression for both stance phases showed a significant relationship between the two variables, with $y = 0.817x + 0.973$ for the push-off phase ($R^2 = 0.278$) and $y = 0.933x + 1.02$ for the pull-up phase ($R^2 = 0.498$).

4.4.3. Pull-Up Stance Phase

The effect of limb dominance was not significant for any outcome measures in the no-load condition (**Figure 4.2C**). Average peak hip abduction moments were +0.607 Nm/kg and average peak support moments were -1.20 Nm/kg. Average individual joint percent contributions to peak support moments were 15.9% hip extension, 66.5% knee extension, and 17.6% ankle plantarflexion.

There were no significant differences in peak moments between the dominant and non-dominant limbs at each individual load level. The linear relationship between peak hip abduction moments and load was again not significant in the pull-up stance phase. In contrast, the linear relationship between peak support moments and load was significant ($p<0.001$, $R^2 = 0.498$), with a coefficient of +0.933 and an intercept of +1.02 (**Figure 4.3B**).

The effect of load was significant for hip and knee percent contributions to peak support moments (both $p<0.001$). Pairwise comparisons revealed that hip contributions were significantly larger for +0%, +5%, +10%, and +15% compared to -20%, -15%, and -10%, while knee contributions were significantly larger for -20%, -15%, and -10% compared to +0% +5%, +10%, and +15% ($p<0.001$ for all). Despite these opposing changes, the knee remained the primary contributor to peak support moments across all load conditions (**Figure 4.4B, D, F**). The interaction between limb dominance and load was also significant for knee percent contributions ($p=0.003$). There were no significant pairwise comparisons between the dominant and non-dominant limbs at each individual load level (**Appendix Table A.1**).

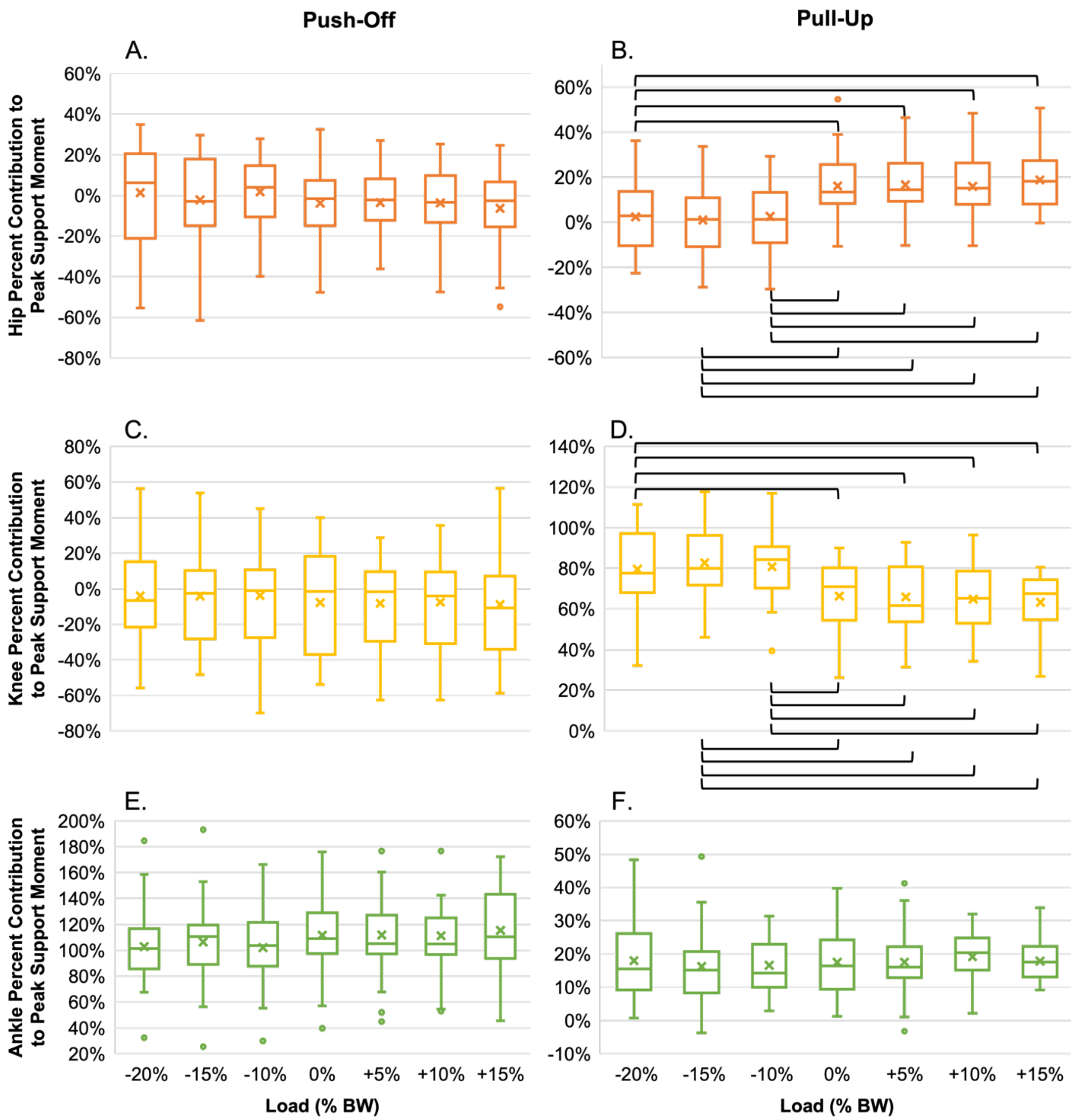

Figure 4.4. Individual joint percent contributions to peak support moments of a step-up task. Individual hip (orange), knee (yellow), and ankle (green) percent contributions to peak extensor support moment at the time of peak support moment for all loading conditions. A negative percent contribution represents a joint moment in flexion, while a positive percent contribution represents a joint moment in extension. Significant pairwise comparisons are shown by black brackets (corrected p<0.001).

4.4.4. Secondary Analysis: Age & Leg Length

As there was no significant effect of limb dominance on peak moments, the values for the dominant and non-dominant lower limbs were collapsed for the secondary analyses. For the no-load condition, Pearson's correlation analysis between peak hip abduction moments and age was significant in the push-off ($r = +0.830$, $p<0.001$) and pull-up stance phases ($r = +0.833$, $p<0.001$). This analysis was also significant between peak hip abduction moments and leg length in push-off ($r = +0.753$, $p<0.001$) and pull-up ($r = +0.770$, $p<0.001$). In summary, the magnitude of peak hip abduction increased with age and with leg length (**Figure 4.5A, B**). Pearson's correlation analysis was significant between peak support moments and age in the push-off ($r = +0.304$, $p<0.001$) and pull-up stance phases ($r = +0.358$, $p<0.001$). This analysis was also significant between peak support moments and leg length in push-off ($r = +0.265$, $p<0.001$) and pull-up ($r = +0.217$, $p<0.001$). The magnitude of peak support moment decreased with age and leg length (**Figure 4.5C, D**). For the load conditions, there were no significant correlations between the individual participant slopes of peak moments vs. load and age and leg length.

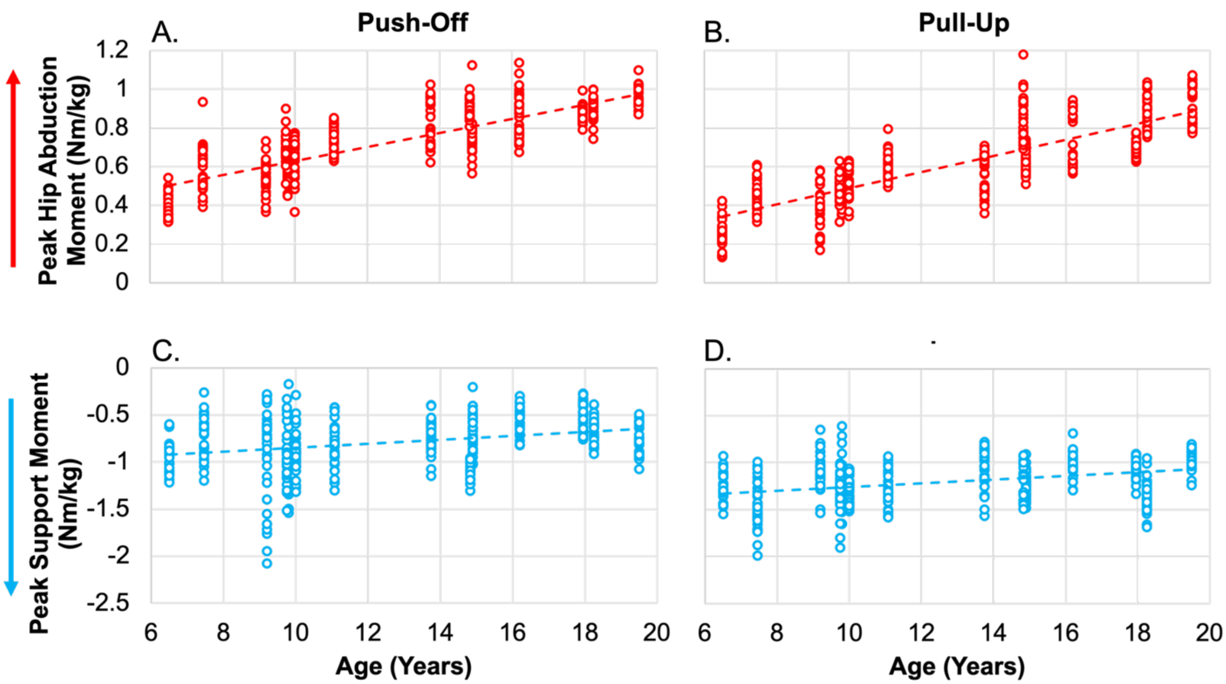

Figure 4.5. The relationship between age and peak moments of a step-up task. Peak hip abduction moments (red) and peak support moments (blue) vs. age for the no-load condition during the push-off and pull-up stance phases. Each point represents an individual no-load trial. All moment values are divided by participant weight, and arrows show the direction of increasing moment magnitude. Pearson's correlation was significant for all relationships, with r-values of (A) +0.830, (B) +0.833, (C) +0.304, and (D) +0.358. Results indicate that the magnitude of peak hip abduction increases with age, while the magnitude of peak support moment decreases with age.

4.5. Discussion

We investigated the effect of modulating body weight load from -20% to +15% on lower limb biomechanical strategies in pediatric individuals during a step-up task. There was a positive linear relationship between peak support moments and load in the push-off and pull-up stance phases, where these moments scaled with load. There was no relationship between peak hip abduction moments and load in either stance phase. While the ankle and knee were the primary contributors to the support moments, the hip contributed more than expected during weighted conditions in the pull-up phase. In a secondary analysis, we also found a significant positive correlation between peak hip abduction moments and age and leg length during the no-load condition.

Peak hip abduction moments during the no-load condition of our step-up task were similar to what has been reported in stair ascent (Novak and Brouwer, 2013, 2011; Strutzenberger et al., 2011). Our hypothesis that hip abduction moments would incrementally increase with load in both stance phases of a step-up task was not supported. Contrary to our results, significant increases in hip abduction moments between no-load and +20% of BW have been quantified during the initial step up in adults (Wang and Gillette, 2018). Hip abductor muscle activations have also been shown to significantly increase between -30% of body weight and no-load during regular gait (Mun et al., 2017). One possible explanation for our findings may be that hip abduction moments generated in the no-load condition were at a magnitude that supported mediolateral stability across all loading conditions. Alternatively, participants may have altered their stepping behavior during unweighted conditions, similar to what has been seen in adults during treadmill walking (Dragunas and Gordon, 2016). It would be interesting to use these results as a comparator to outcome measures for pediatric populations with conditions such as patellofemoral pain syndrome, where the hip abductors are weak (Xie et al., 2023).

Peak support moments during the no-load condition of our step-up task were slightly lower than what has been reported in stair ascent (Novak and Brouwer, 2013, 2011; Strutzenberger et al., 2011), most likely due to the lower step height in our study. Supporting our hypothesis, peak support moments significantly increased with load incrementally in both stance phases of a step-up task. Previous studies quantifying peak vertical ground reaction forces during the push-off and pull-up phases of stair ascent within narrow ranges of load modulation are consistent with our results (Bannwart et al., 2019; Hong and Li, 2005). This experimental paradigm may be beneficial for gait rehabilitation approaches targeting the lower limb extensors, particularly for individuals with cerebral palsy who have weak lower limb extensors (Wiley and Damiano, 1998). Hip, knee, and ankle percent contributions to peak support moments can reveal which joints are driving these changes in response to load.

The effect of load modulation on individual sagittal plane moments were expected in the push-off phase and unexpected in the pull-up phase. Similar to stair ascent, ankle plantarflexion moments contributed the most to extensor support moments in the push-off phase of a no-load step-up task (McFadyen and Winter, 1988; Nadeau et al., 2003; Novak and Brouwer, 2011; Riener et al., 2002). Our results also suggest that ankle moments scaled with peak support moments to remain the primary contributor in the push-off phase across all load conditions. Indeed, the ankle has been shown to be the most responsive joint to changes in body weight support (Goldberg and Stanhope, 2013). In contrast, the knee is primarily responsible for vertical progression of the body during stair negotiation (Costigan et al., 2002; McFadyen and Winter, 1988; Nadeau et al., 2003; Novak and Brouwer, 2011; Riener et al., 2002). This was observed in our calculated knee extension moments during the pull-up phase of a no-load step-up task. Though knee moments remained the primary contributor to peak support moments in this phase across all load conditions, these moments decreased when body weight support was removed while hip extension moments proportionally increased. This unexpected strategy may have been used to prevent overloading of the knee joint, which can operate as high as 72% of maximum capacity during regular stair climbing in young adults (Reeves et al., 2009). The hip and knee work in tandem during pull-up (Riener et al., 2002), which may explain why the redistribution of extensor moments in the weighted block is towards the hip. Using a step-up task with body weight support may be useful for clinical interventions focused on strength and control of the knee and ankle joints in pediatric populations with weaker distal joints, such as individuals with cerebral palsy (Fowler et al., 2010;

Wiley and Damiano, 1998). Alternatively, adding external loads to a step-up task may be a worthwhile approach to train the hip joint in pediatric populations such as adolescent athletes.

The magnitude of peak hip abduction moments increased with age and with leg length in both stance phases. It is possible that step width may be driving this positive correlation. Three lines of evidence support this suggestion: 1) step width increases with age in children (Gill et al., 2016), 2) wider step widths increase the mediolateral moment arm (Henderson et al., 2011), and 3) the mediolateral moment arm is positively correlated with peak hip abduction moments (Vistamehr and Neptune, 2021). In contrast, the magnitude of peak support moments slightly decreased with age and with leg length in both stance phases, indicating that younger children with shorter limbs used more relative extension moments to complete a step-up task. It's possible that younger children are still exploring how to optimize gait and therefore generating more extension than necessary to complete the task (Frost et al., 1997). For all participants, the step height was approximately 10-19% of their leg length; children with shorter lower limbs may have generated larger extension moments to complete a step up at a relatively larger step height. Age and leg length did not play a factor in the slopes of peak joint moments vs. load, suggesting that all participants had similar strategies when responding to different loads. It may be that the biomechanics of responding to load are developed at a young age and maintained through adolescence.

In summary, our study developed a model of the effect of load modulation from -20% to +15% of BW on typical pediatric lower limb joint moments during a step-up task. Limitations of the study include the resolution of load, the self-selected speed of each participant, and the placement of some reflective markers on tight-fitting clothes rather than directly on skin. One future direction is comparing this model to pediatric clinical populations to describe the possible effects of atypical development or injuries and the potential impact from interventions. Another future direction is translating the experiment to a more natural environment, which includes testing participants without a harness and varying the step height.

5. YOUNG PEOPLE WITH BILATERAL CEREBRAL PALSY USE THEIR HIP JOINT TO COMPLETE A STEP-UP TASK

5.1. Abstract

Performance in stair-climbing is largely associated with disruptions to mobility and community participation in children with cerebral palsy (CP). It is important to understand the nature of motor impairments responsible for making stairs a challenge in children with bilateral CP to clarify underlying causes of impaired mobility. In pediatric clinical populations, sensitive measurements of movement quality can be captured during the initial step of stair ascent. Thus, the purpose of this study was to quantify the lower limb joint moments of children with bilateral CP during the stance phases of a step-up task. Participants performed multiple stepping trials in a university gait laboratory. Outcome measures included extensor support moments (the sum or hip, knee, and ankle sagittal plane moments), hip abduction moments, and their timing. We recruited 7 participants per group. Surprisingly, we found that peak hip abduction and extensor support moments were not significantly lower in the CP group compared to controls. We did confirm that children with CP timed their peak moments closer together and increasingly depended on the hip joint to complete the task, especially in their more affected (MA) lower limb. Our investigation highlights some underlying causes that make stairs a challenge for the CP population and provides a possible treatment approach to strengthen lower limb muscles.

5.2. Introduction

While the majority of children with bilateral cerebral palsy (CP) are ambulatory (Novak, 2014), stairs and curbs present an exhausting environmental barrier for this population. Performance in stair-climbing is largely associated with disruptions to mobility and community participation in CP, more so than performance in walking (Lepage et al., 1998). Despite this, research investigating movement strategies during stair climbing in bilateral CP has been limited. It is important to understand what makes stairs difficult in children with bilateral CP to clarify underlying causes of impaired mobility because reduced mobility can lead to a higher risk of comorbidities such as heart disease and chronic pain in adulthood (Becher et al., 2020; Heyn et al., 2019; Peterson et al., 2020; Schmidt et al., 2020; van der Slot et al., 2013). Most importantly, community members affected by CP prioritize research focused on understanding the nature of impairments to improve overall mobility (Gross et al., 2018; Vargus-Adams and Martin, 2011, 2009), especially in the lower limbs (Zvolanek et al., 2022).

In pediatric clinical populations, sensitive measurements of movement quality can be captured during the initial step of stair ascent (Stania et al., 2017). Individuals with and without CP spend approximately 70% of an inclined gait cycle in the stance phase (Ma et al., 2019), indicating that this phase of a step-up task is worthy of investigation. Previous research in individuals with typical development has shown substantial hip abduction moments and extensor support moments, especially from the knee and ankle, to complete a step-up task (Goyal et al., 2022; Wang and Gillette, 2018, Chapter 4 of this thesis). However, bilateral lower limb motor impairments from bilateral CP can affect the biomechanics of this task. Researchers have quantified paresis, or weakness, in both the hip abductors and lower limb extensors in bilateral CP (Barber et al., 2012; Steele et al., 2012; Wiley and Damiano, 1998). Adults with stroke, who also experience paresis in the same joint directions, generated lower hip abduction, hip extension, and knee extension moments compared to adults without stroke during a step-up (Goyal et al., 2022). A reduction in selective voluntary motor control (SVMC) of distal joints such as the knee and ankle is also an often-observed motor impairment in bilateral CP (Fowler et al., 2010; Fowler and

Goldberg, 2009; Sanger et al., 2006; Zhou et al., 2017). One group of researchers found that children with CP may compensate for this coordination issue during level-ground walking by shifting kinetic output from the ankle to the hip (Riad et al., 2008). A loss of SVMC may also lead to simultaneous and coupled lower limb movements which alter timing in the gait cycle compared to children without CP (Fowler and Goldberg, 2009). In addition to the importance of this investigation in improving current interventions, understanding the nature of motor impairments can also offer insight into how the central nervous system is working (Hill and Dewald, 2020; Sánchez et al., 2018a; Sukal-Moulton et al., 2014a, 2014b, 2013; Sukal et al., 2007) during a challenging activity of daily living like a step-up task.

The purpose of this study was to quantify the lower limb joint moments of children with bilateral CP during the stance phases of a step-up task. We hypothesized that children with bilateral CP would generate lower peak hip abduction and extensor support moments compared to children with typical development (TD), and that timing of these peak moments would occur closer together in children with bilateral CP. We also hypothesized that children with bilateral CP would shift torque generation from the knee/ankle to the hip to successfully complete a step-up task.

5.3. Methods

5.3.1. Participant Recruitment

Participants with bilateral CP were recruited through the Shirley Ryan AbilityLab and the Cerebral Palsy Research Registry (Hurley et al., 2011). Inclusion criteria for these individuals were (1) between the age of 5-19 years, (2) a medical diagnosis of bilateral CP affecting the lower limbs, (3) Gross Motor Function Classification System (GMFCS) level I-III, and (4) some independent ambulatory function with ability to step up with or without assistive devices. Exclusion criteria were (1) botulinum toxin injections to lower limb muscles in the past 6 months, (2) surgeries affecting lower limb function in the past year, and (3) serious comorbidities or cognitive dysfunction that would affect ability to participate. Age and sex-matched participants without bilateral CP (typical development or TD) were recruited through word-of-mouth and flyers. This study was approved by Northwestern University's Institutional Review Board. Participants under the age of 18 provided assent in addition to informed consent from their parent/guardian, while participants 18 and older provided informed consent themselves.

5.3.2. Set-Up & Protocol

Participants performed multiple stepping trials on a 2x2 cluster of force plates (AMTI, Watertown, MA). Two 10.2-cm wooden platforms, each approximately the size of a single force plate, were placed on two side-by-side force plates to simulate a step (Figure 1A). A previous study showed that a 10.2-cm step height is both challenging and achievable for clinical populations with lower limb impairments (Goyal et al., 2022). A 10-camera motion capture system (Qualisys, Göteborg, Sweden) recorded lower limb kinematics from retro-reflective markers placed on the trunk (sternum, C7 vertebrae, T10 vertebrae), pelvis (sacrum, posterior superior iliac spines, greater trochanters), and lower extremities (lateral femoral epicondyles, lateral malleoli, calcanei, the second and fifth metatarsals, and thigh and shank four-marker clusters). Ground reaction forces and EMG signals were captured at a frequency of 1000 Hz, while kinematics were captured at a frequency of 100 Hz. Participants were also attached to a passive overhead trolley to minimize the risk of falling.

Participants started the experiment with their feet on two independent force plates posterior to the two platforms. This ensured that all ground reaction forces for the left and right lower limbs were recorded separately. Participants were then instructed to step up onto the platform at their typical walking speed. After a short pause on the step, participants were then instructed to step down and backwards onto the starting force plates. These step-up trials were repeated 5-15 times per leading foot, depending on participant fatigue and comfort. A licensed physical therapist guarded and offered support as needed for safety to participants who were GMFCS level III. In addition to the step-up trials, all participants completed timed single-limb stance tests (Newton, 1989) and the Waterloo Footedness survey (Elias et al., 1998) to identify the dominant (typical development) or less affected (bilateral CP) lower limb. Participants with bilateral CP also completed the Selective Control Assessment of the Lower Extremity (SCALE) (Fowler et al., 2009) and the locomotion ability assessment for kids (ABILOCO-Kids) (Gilles et al., 2008).

5.3.3. Data & Statistical Analysis

Qualisys Track Manager (Qualisys, Göteborg, Sweden) recorded marker and ground reaction force. Marker data were visually inspected to ensure that they were correctly labeled. All data were then exported to Visual 3D (C-Motion, Germantown, MD). The marker and ground reaction force data were first interpolated to fill in small gaps and passed through a 4th-order low-pass Butterworth filter with a 6 Hz cutoff frequency to filter out oscillations. Ground reaction force data were used to identify important gait events, including lift-off and initial contact for both lower limbs. These data were also used in combination with marker data in inverse dynamics formulas to calculate hip moments in the frontal plane and hip, knee, and ankle moments in the sagittal plane. The 10.2-cm step height was taken into account by creating a raised virtual force platform.

Joint moment data were further analyzed in MATLAB (MathWorks, Inc., Natick, MA). All joint moments were normalized to participant body weight for comparison in statistical analyses. Hip, knee, and ankle sagittal plane moments were considered separately and together, summed up to an overall extensor support moment (Novak and Brouwer, 2011). All data were plotted for each individual trial during two stance phases of the step-up trials. The push-off phase was defined when the trailing limb was in single-limb stance, between leading limb lift-off and initial contact with the step (Figure 1B). The pull-up phase was defined when the leading limb was in single-limb stance, between trailing limb lift-off and initial contact with the step (Figure 1B). For each individual participant, any step-up trial with a length outside of two standard deviations from the average were not considered in statistical analysis.

Independent two-sample t-tests were used to compare participant-specific metrics such as age, weight, and height. An ANOVA was used to compare single limb stance times between the limbs in each group (CP more affected (MA), CP less affected (LA), typical development dominant (TD)). Paired t-tests were also used to compare SCALE scores between the limbs of participants with bilateral CP. All outcome measures were considered independently for each stance phase: (1) peak hip abduction moments, (2) peak support moments, (3) individual hip, knee, and ankle percent contributions to peak support moments, (4) time duration of stance phase, and (5) time to peak moments. Individual joint percent contributions were calculated by dividing hip, knee, and ankle contributions to peak support by the overall peak support moment. Timing of peak moments were identified as a percentage of the corresponding stance phase. Chapter 4 of this thesis determined that the effect of limb dominance was not significant for children with typical development; as such, only data from their dominant limb was considered in subsequent analyses. All outcome measures were statistically compared using linear mixed effects models with one fixed effect of limb (MA, LA, TD) and a random effect of participant. All trials for each participant were input individually into the statistical models to increase the effective sample size. Significance of multiple pairwise comparisons was adjusted using Bonferroni corrections.

5.4. Results

5.4.1. Participant Summary

We recruited 7 participants in each group (**Table 5.1**). There were no significant differences in age, weight, and height between the groups. Five participants with bilateral CP were GMFCS level II and two participants were GMFCS level III. Single limb stance times between the limbs were significantly different (p=0.002), where the TD limb had a larger stance time than the LA (p=0.007) and MA limbs (p=0.004). Average SCALE scores were significantly different between the limbs of the CP group (p=0.020). Based on the data, the average effective sample size was 13 participants per group. Profiles of other biomechanical metrics (including joint power, joint kinematics, and center of mass) are in the Appendix (**Figure A.1-A.3**).

Table 5.1. Mean (SD) participant-specific metrics and clinical assessment outcomes.

	Group		
Outcome Measure	**Bilateral CP (n = 7)**		**TD (n = 7)**
Age (years)	10.5 (3.6)		10.2 (3.9)
Limb Dominance	2R / 5L		7R
Weight (kg)	38.7 (19.6)		41.7 (23.7)
Height (m)	1.40 (0.19)		1.42 (0.22)
ABILOCO-Kids (logit)	2.37 (2.45)		--
Limb	**MA**	**LA**	**TD**
Single-Limb Stance Test (s)	2.27 (2.28)*	5.25 (5.91)*	43.7 (38.2)
SCALE	3.15 (1.68)+	6.14 (3.58)	--

*p<0.05 for a significantly different from TD limb
+p<0.05 for a significantly different from CP less affected limb

5.4.2. Push-Off Stance Phase

There were no significant differences in peak hip abduction or support moments between the limbs in the push-off stance phase (**Table 5.2**). There were significant differences in hip ($p<0.001$) and ankle ($p=0.011$) percent contributions to peak support moments between the limbs (**Figure 5.1, Figure 5.2**). The MA limb had a significantly higher hip percent contribution compared to the LA and TD limbs, while the LA limb also had a significantly higher hip percent contribution compared to the TD limb ($p<0.001$ for all). In contrast, both limbs of participants with CP had lower ankle percent contributions compared to the TD limb (less affected: $p=0.016$; more affected: $p=0.003$). Raw hip, knee, and ankle contributions to peak support moments are provided in **Table 5.2**, though statistics were not run on these values.

There were significant differences in time duration of the push-off stance phase ($p=0.005$), where the LA limb spent more time in the stance phase than the MA ($p=0.001$) (**Table 5.2**). There were also significant differences in timing of peak moments between the limbs (both $p<0.001$). Both limbs of participants with CP reached a peak hip abduction moment later compared to the control limb (LA: $p<0.001$; MA: $p=0.004$) and reached a peak support moment earlier compared to the TD limb (LA: $p<0.001$; MA: $p<0.001$).

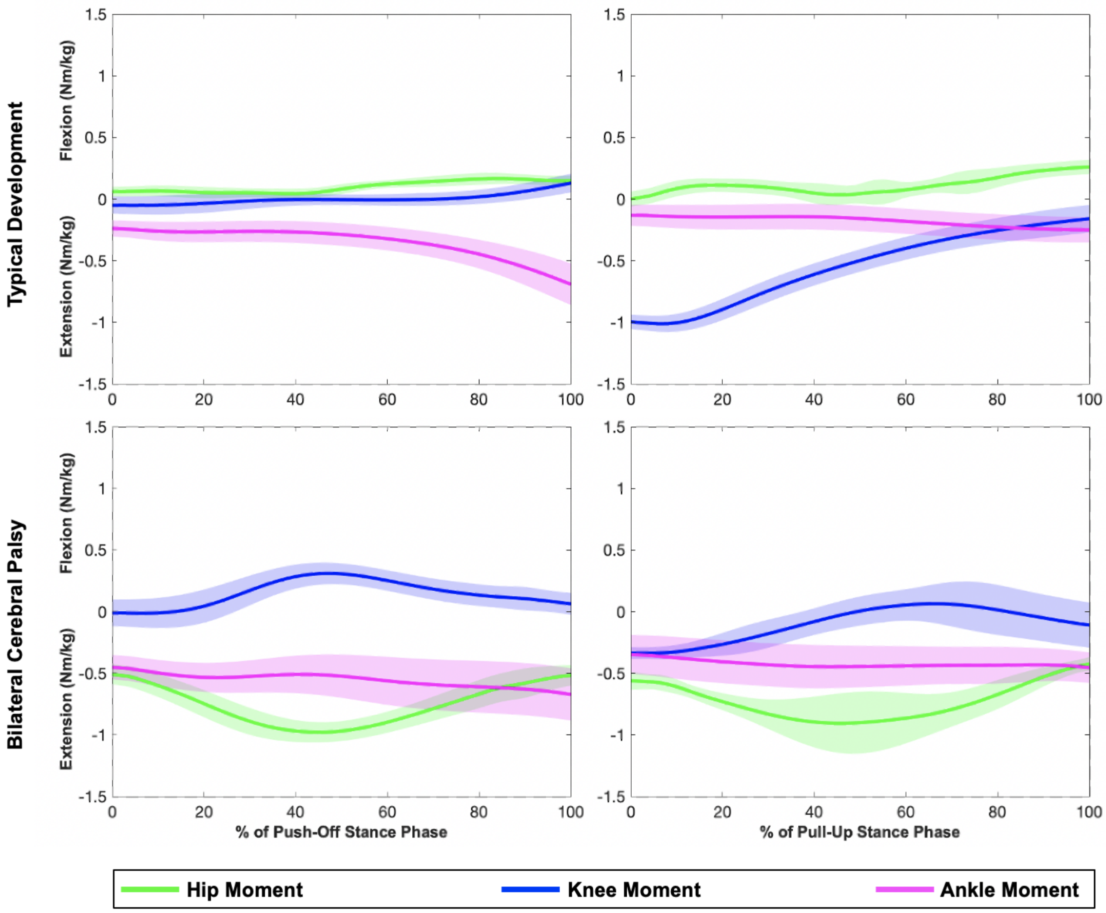

Figure 5.1. Representative joint moment profiles of a step-up task from the CP and TD groups. Representative plots of hip, knee, and ankle sagittal plane moments during the push-off (left) and pull-up (right) stance phases of a step-up task. The top row displays joint moments from an individual in the TD group, while the bottom row displays joint moments from an individual in the bilateral CP group (MA limb). Shaded regions represent one standard deviation. Compared to the individual with TD, the individual with CP generated larger hip extension moments.

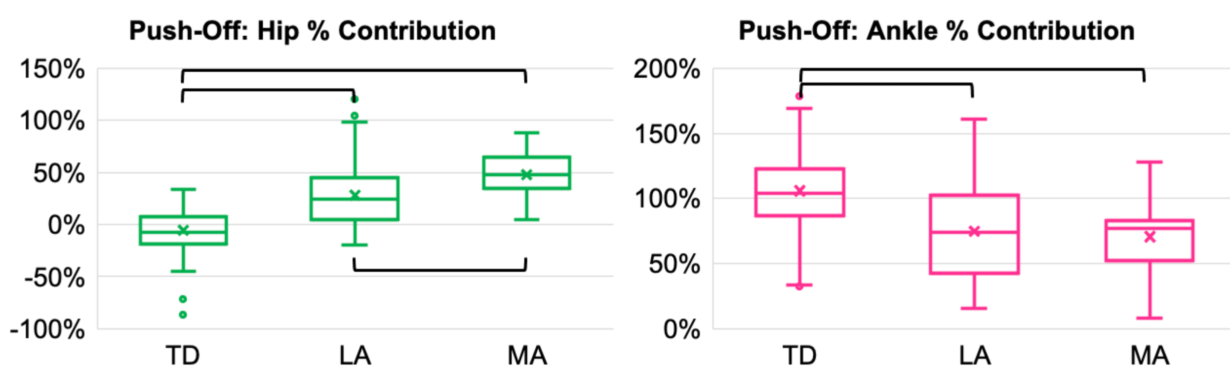

Figure 5.2. Significant joint contributions to peak support moments in the push-off phase. Hip and ankle percent contributions during the push-off stance phase of a step-up task for each lower limb (TD = typical development, LA = bilateral CP less affected, MA = bilateral CP more affected). Significant pairwise comparisons are shown by the black brackets (corrected $p<0.017$).

Table 5.2. Mean (SD) outcome measures for the push-off stance phase of a step-up task. For individual percent contributions to peak extensor support moment, a negative percentage indicates a joint flexion contribution. MA = more affected limb of participants with bilateral CP, LA = less affected limb or participants with bilateral CP, TD = dominant limb of participants with typical development.

Push-Off Stance Phase			
	Group		
Metric	**Bilateral Cerebral Palsy**		**Typical**
Joint Moment (Nm/kg)	**MA**	**LA**	**TD**
Peak Hip Abduction	0.598 (0.206)	0.552 (0.188)	0.658 (0.178)
Peak Extensor Support	-1.08 (0.227)	-1.08 (0.321)	-0.887 (0.333)
Individual Joint Moments at the Time of Peak Support Moments (Nm/kg)	**MA**	**LA**	**TD**
Hip	-0.531 (0.257)	-0.270 (0.255)	0.015 (0.143)
Knee	0.201 (0.241)	-0.046 (0.387)	0.017 (0.261)
Ankle	-0.751 (0.288)	-0.765 (0.359)	-0.873 (0.278)
Individual Percent Contributions to Peak Support Moments (%)	**MA**	**LA**	**TD**
Hip	48.0 (20.3)*$^{+}$	28.4 (28.7)*	-5.86 (20.9)
Knee	-18.6 (22.3)	-2.96 (42.9)	0.017 (33.7)
Ankle	70.6 (27.8)*	74.6 (37.4)*	106 (30.8)
Temporal	**MA**	**LA**	**TD**
Average stance time (s)	0.533 (0.107)$^{+}$	0.604 (0.155)	0.513 (0.092)
Time of Peak Hip Abduction	22.6 (0.092)*	25.4 (0.124)*	16.4 (0.089)
Time of Peak Support (% of	57.6 (36.4)*	57.8 (36.2)*	94.1 (0.181)

*$p<0.05$ for a significantly different from TD limb

$^{+}p<0.05$ for a significantly different from CP less affected limb

5.4.3. Pull-Up Stance Phase

There were significant differences in peak support moments (p<0.001) between the limbs in the pull-up stance phase (**Table 5.3**). Both the limbs of participants with CP generated higher peak support moments compared to the TD limb (LA: p=0.016; MA: p=0.001). There were also significant differences in hip and knee percent contributions to peak support moments between the limbs (both p<0.001) (**Figure 5.1, Figure 5.3**). The MA limb had a significantly higher hip percent contribution compared to the LA and TD limbs (both p<0.001). In contrast, the MA had a significantly lower knee percent contribution compared to the LA and TD limbs (both p<0.001), while the LA limb also had a significantly lower knee percent contribution compared to the TD limb (p=0.003). Raw hip, knee, and ankle contributions to peak support moments are provided in **Table 5.3**, though statistics were not run on these values.

There were no significant differences in the time duration of the pull-up stance phase between the limbs, though there was a significant difference in time of peak support moment (p=0.042) (**Table 5.3**). The MA limb reached a peak support moment later compared to the LA (p=0.020) and TD limbs (p=0.012).

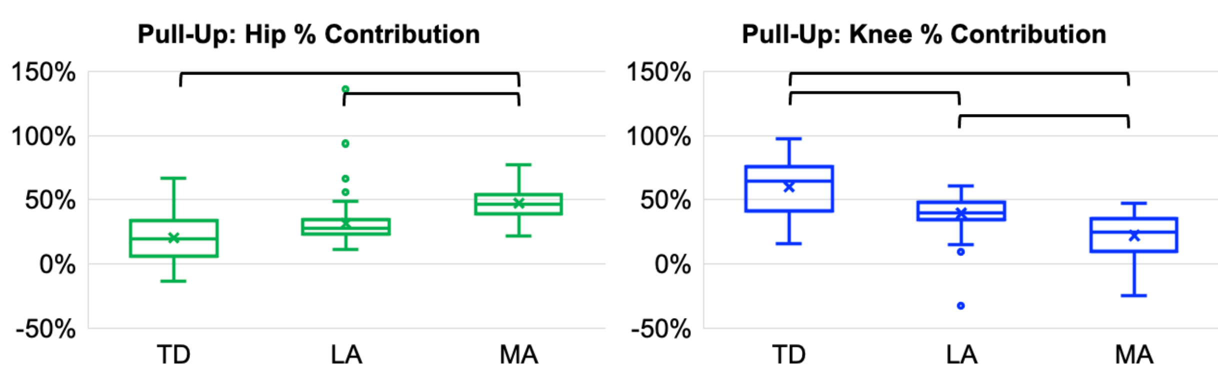

Figure 5.3. Significant joint contributions to peak support moments in the pull-up phase. Hip and knee percent contributions during the pull-up stance phase of a step-up task for each lower limb (TD = typical development, LA = bilateral CP less affected, MA = bilateral CP more affected). Significant pairwise comparisons are shown by the black brackets (corrected p<0.017).

Table 5.3. Mean (SD) outcome measures for the pull-up stance phase of a step-up task. MA = more affected limb of participants with bilateral CP, LA = less affected limb or participants with bilateral CP, TD = dominant limb of participants with typical development.

Pull-Up Stance Phase			
	Group		
Metric	**Bilateral Cerebral Palsy**		**Typical**
Joint Moment (Nm/kg)	**MA**	**LA**	**TD**
Peak Hip Abduction	0.553 (0.264)	0.573 (0.214)	0.520 (0.192)
Peak Extensor Support	-1.55 (0.219)*	-1.66 (0.405)*	-1.23 (0.180)
Individual Joint Moments at the Time of Peak Support Moments (Nm/kg)	**MA**	**LA**	**TD**
Hip	-0.726 (0.189)	-0.501 (0.183)	-0.292 (0.226)
Knee	-0.352 (0.260)	-0.666 (0.246)	-0.657 (0.253)
Ankle	-0.469 (0.216)	-0.494 (0.230)	-0.225 (0.184)
Individual Percent Contributions to Peak Support Moments (%)	**MA**	**LA**	**TD**
Hip	47.2 (11.4)*+	31.5 (17.0)	20.2 (17.0)
Knee	22.3 (16.0)*+	39.4 (13.4)*	60.3 (19.6)
Ankle	30.6 (14.3)	29.1 (12.8)	19.5 (14.9)
Temporal	**MA**	**LA**	**TD**
Average stance time (s)	0.479 (0.106)	0.539 (0.240)	0.470 (0.083)
Time of Peak Hip Abduction	51.9 (22.5)	42.4 (23.3)	45.3 (31.3)
Time of Peak Support (% of	17.1 (15.2)*+	10.4 (7.15)	7.03 (4.70)

*p<0.05 for a significantly different from TD limb
+p<0.05 for a significantly different from less affected limb

5.5. Discussion

The present study quantified differences in the lower limb joint moment strategies of a step-up task between children with and without bilateral CP. While there were only small differences in peak moments between the CP and TD groups, there were significant differences in timing of these moments during each stance phase of a step-up task. We also quantified an increased dependence on the hip joint to keep the body upright during a step up with an associated decreased use of the knee and ankle joints in the CP group, especially in the MA limb. These results can further help us narrow down target areas to improve movement quality in bilateral CP.

Our first hypothesis that peak hip abduction and extensor support moments of a step-up task would be lower in children with bilateral CP was surprisingly not confirmed. Given that step initiation requires larger frontal plane moments compared to subsequent steps (Wang and Gillette, 2018), our results suggest that this step-up task can be used as a strengthening activity for individuals with CP because it provides a functional load to the hip abductor muscles. Children with bilateral CP unexpectedly generated significantly larger peak support moments in the pull-up phase compared to controls, reflective of the high demand from the lower limb extensors required by this phase of stair ascent (Novak and Brouwer, 2011; Reeves et al., 2009; Riener et al., 2002; Strutzenberger et al., 2011). Despite extensor muscle weakness in the hip, knee, and ankle (Wiley and Damiano, 1998), children with CP in our study were successful in completing the step-up task, meaning that they were able to meet the minimum support moment threshold. However, the greater effort output by the extensors during the pull-up phase may be part of an alternative and inefficient strategy to step up, similar to that which has been quantified in other clinical populations and older adults (Brown et al., 2016; Reeves et al., 2009).

Indeed, children with bilateral CP used their hip extensors more and their knee and ankle extensors less compared to controls when stepping up, which confirms our original hypothesis. This strategy is especially prevalent in the MA limb. Previous research has quantified a similar shift in children with hemiparetic CP during gait (Riad et al., 2008) and adults with hemiparetic stroke during stair ascent (Goyal et al., 2022), possibly as a compensation for distal weakness in the paretic limb. However, weakness may not be the only impairment affecting the distal joints in children with bilateral CP. Recall that in the TD group, the ankle contributes the most to support moments in the push-off phase while the knee contributes the most to support moments in the pull-up phase. In the CP group, while the ankle joint did not produce equally enough plantarflexion during the push-off phase (see **Table 5.2**: Individual Joint Moments & Percent Contributions to Peak Support Moments), it did during the pull-up phase of a step-up task. This change in pattern and capacity between two different contexts, which in this case are the two stance phases, suggests that a loss of SVMC in the distal joints (Sanger et al., 2006) may primarily be responsible for the shift in hip dependence during a step up (**Figure 5.4**).

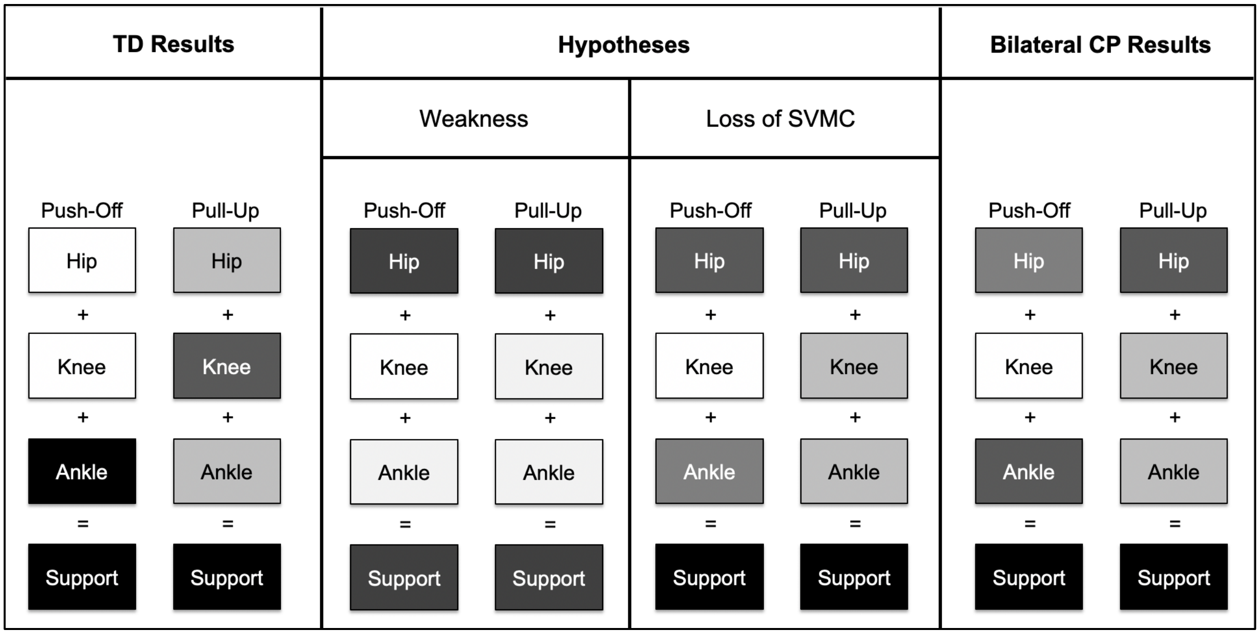

Figure 5.4. A concept map of hypothesized contributions to support moments and results. This figure depicts a concept map of contributions to extensor support moments from the hip, knee, and ankle joints. A darker shade of an individual joint indicates a larger contribution to support moment. In the TD group, the ankle joint had the largest contribution to support moments in the push-off phase while the knee had the largest contribution to support moments in the pull-up phase. If distal joint weakness was the primary impairment affecting gait in children with bilateral CP, we hypothesize that the hip joint compensates for low knee and ankle joint contributions in both stance phases. We might also hypothesize that overall support moments would be lower in the bilateral CP group compared to the TD group. However, if a loss of SVMC was the primary impairment affecting gait, we hypothesize that 1) hip contribution increases as compensation for decreased contribution from the ankle joint only in the push-off phase and 2) hip contribution increases as compensation from decreased contribution from the knee joint only in the pull-up phase. Indeed, the results from the bilateral CP group point towards a loss of SVMC, as there was a pattern change between the two different stance phases rather than an overall decrease in contributions from both the knee and ankle joints in both stance phases.

The ability to independently activate the joints is significantly reduced in the knee and ankle compared to the hip (Fowler et al., 2010) and has been correlated with abnormal gait patterns in CP (Chruscikowski et al., 2017; Zhou et al., 2019). Researchers have hypothesized that a loss of SVMC is due to corticospinal tract damage and compensatory use of brainstem motor pathways, including the rubrospinal, reticulospinal, and vestibulospinal tracts (Cahill-Rowley and Rose, 2014; Fowler et al., 2010; Sánchez et al., 2018a; Zhou et al., 2017). In general, the brainstem motor pathways have connections to the hip joint for postural control. Stimulations to activate the human vestibular system have induced activity in hip extensor muscles such as the gluteus medius and biceps femoris (Ali et al., 2003), which might explain the notable hip extension activity in the CP group during a step-up task. Future interventions to improve mobility in CP may benefit from focusing on strengthening the hip joint (Riad et al., 2008) to optimize its function as compensation for distal joint impairment. In addition, a focus on improving distal SVMC ability during early intervention in bilateral CP (Riad et al., 2008; Sargent et al., 2020) may improve efficiency of their mobility and limit the need for dependence on the hip joint during gait and stairs.

Increased dependence on the hip extensors may also explain why timing of peak hip abduction moments and support moments were closer together in both limbs of participants with CP compared to the TD limb. During stair ascent, the gluteus maximus muscle plays a role in both hip extension and hip abduction (Lyons et al., 1983). We postulate that this muscle played a larger role in contributing to overall extension in our participants with bilateral CP, and therefore influenced the timing of both peak moments. In addition to closer peak moments, timing of the first peak moment in each stance phase occurred later in the CP limbs compared to the control limb. As the rate of force development is significantly lower in children with bilateral CP compared to children with TD during isometric conditions (Moreau et al., 2012), it may be inferred that the ability to rapidly generate torque in dynamic conditions is also impeded. This delay also suggests an increased use of brainstem motor pathways, as multiple synapses increases the central motor conduction time compared to the corticospinal pathways (Eyre et al., 2001; Lemon, 2008).

In this study, we quantified the differences in lower limb joint moments between children with and without bilateral CP during a functional step-up task. Limitations of the study include instructing participants to move at a self-selected speed, which was mitigated through normalization of the stance phases, and the low sample size in each group, though the effective sample size was increased using repeated measures in statistical analyses. Our investigation highlights some underlying causes that make stairs a challenge for the CP population and provides a possible treatment approach to strengthen lower limb muscles. Rehabilitation focused on optimizing use of the hip extensors and improving distal joint coordination may lead to better outcomes for children with bilateral CP.

6. Young people with bilateral CP may work outside of a stereotypical extensor coupling to complete a step-up task

6.1. Abstract

A loss of selective voluntary motor control (SVMC) has been postulated to affect performance of a step-up task in children with bilateral cerebral palsy (CP). Another characteristic of loss of SVMC in the lower limbs is the abnormal coupling between the hip adductors, hip extensors, knee extensors, and ankle plantarflexors. Research investigating this coupling during the stance phases of a step-up task has been limited and would greatly benefit our understanding of movement performance in children with bilateral CP. We recruited participants with bilateral CP and typical development (TD) to complete a series of step-up trials with load modulation from -20% to +15% in 5% increments. We first determined the effect of load modulation on peak extensor support and hip abduction moments in both groups during the push-off and pull-up stance phases. We also looked into the effect of load modulation on hip, knee, and ankle percent contributions to peak support moments. Participants with CP did not display abnormal coupling between the hip adductors and lower limb extensors, perhaps working outside of this characteristic loss of SVMC to meet the demands of the task. We also found that at each load level, individuals with CP consistently depend heavily on the hip joint to keep themselves upright. These findings perhaps further reinforce the nature and underlying causes of impairment in bilateral CP, including upregulation of brainstem pathways as compensation for corticospinal pathway damage. In addition, our protocol may be an effective intervention for hip strengthening and lower limb coordination by working within motor constraints to improve gait.

6.2. Introduction

A loss of selective voluntary motor control (SVMC) in the distal lower limb joints has been postulated to affect performance of a step-up task in children with bilateral cerebral palsy (CP) (Chapter 5 of this thesis). Another characteristic of loss of SVMC in the lower limbs of individuals with nervous system injury is the abnormal coupling between the hip adductors, hip extensors, knee extensors, and ankle plantarflexors. Aspects of this atypical coupling have been quantified in isometric postures mimicking gait (Hayes Cruz and Dhaher, 2007; Sánchez et al., 2018a; Thelen et al., 2003) and the swing phase (Fowler and Goldberg, 2009; Zhou et al., 2017). However, research investigating this coupling during the stance phase of a dynamic gait task has been limited and would greatly benefit our understanding of stance phase performance in children with CP. The initial step of stair ascent is an optimal probe for this purpose, as this task 1) requires a combination of substantial hip abduction moments and extension moments (Goyal et al., 2022; Lyons et al., 1983; Novak and Brouwer, 2011; Wang and Gillette, 2018) and 2) is considered a sensitive measure of movement performance in pediatric populations with neurodevelopmental disorders (Stania et al., 2017).

Previous studies have used load modulation to quantify abnormal coupling (Hayes Cruz and Dhaher, 2007; Hill and Dewald, 2020; Sánchez et al., 2018a; Sukal-Moulton et al., 2013; Sukal et al., 2007) in populations with neurological injury. For example, Hill et al. progressively unweighted the shoulder abductors and measured reach distance to quantify an atypical flexor coupling (Hill and Dewald, 2020). Two commonly-used load modulation techniques used during gait training are support of a person's body weight (Celestino et al., 2014; Cherng et al., 2007; Kurz et al., 2011; Phillips et al., 2007; Provost et al., 2007) and the addition of external loads (Simão et al., 2014; Chapter 4 of this thesis). When combining a step-up task with load modulation between -20% to 15% body weight (BW), young people with typical development (TD) showed an incremental increase in peak extensor support moments with load but no change in peak hip abduction moments (Chapter 4 of this thesis), a strategy that may be impacted in individuals with CP. The presence of abnormal coupling also has implications for the descending motor pathways used to complete a step-up task; multiple studies have linked this coupling to compensatory use of brainstem pathways (Cahill-Rowley and Rose, 2014; Hayes Cruz and Dhaher, 2007; Hill and Dewald, 2020; Sánchez et al., 2018a; Sukal-Moulton et al., 2013; Zhou et al., 2017).

The purpose of this study was to evaluate the effect of load modulation on the biomechanics of a step-up task in children and adolescents with bilateral CP. The primary hypotheses were that 1) extensor support moments would incrementally increase with load and 2) hip abduction moments would incrementally decrease with load in the CP group, consistent with a loss of SVMC expressed as abnormal extensor coupling. We also hypothesized individuals with bilateral CP would continue to exhibit a distal loss of SVMC throughout all load conditions by 1) increasing hip contributions to support moments in both stance phases, 2) decreasing ankle contributions in the push-off phase, and 3) decreasing knee contributions in the pull-up phase.

6.3. Methods

6.3.1. Participant Recruitment

Recruitment and overall experimental set-up, protocol, and analysis have been described in Chapters 4 and 5 of this thesis. In brief, we recruited participants through the Shirley Ryan Ability Lab, the Cerebral Palsy Research Registry (Hurley et al., 2011), word-of-mouth, and promotional flyers. Participants with bilateral CP were included in the study if they (1) were between 5-19 years, (2) had a medical diagnosis of bilateral CP affecting the lower limbs, (3) were classified in the Gross Motor Function Classification System (GMFCS) level I-III, and (4) were able to step up with or without assistance. They were excluded if they (1) received botulinum toxin injections to the lower limb muscles in the past 6 months, (2) underwent any surgery affecting lower limb function in the past year, or (3) had any co-occurring conditions that would affect ability to participate. Northwestern University's Institutional Review Board approved this study. Participants 18 years and older provided informed consent themselves, while participants under 18 years provided assent along with parent/guardian informed consent.

6.3.2. Experimental Set-Up

All participants were instructed to perform multiple step-ups onto a raised platform in a university gait laboratory. Two measurement tools were used to record data from the trials: a 2x2 cluster of in-ground force plates (AMTI, Watertown, MA) and a 10-camera motion capture system (Qualisys, Göteborg, Sweden). Two 10.2-cm raised platforms were placed on side-by-side anterior force plates to simulate a step. This lower step height has proven to be sufficiently challenging and achievable for participants with neurological injury (Goyal et al., 2022; Chapter 5 of this thesis). Ground reaction forces were recorded from the force plates at a frequency of 1000 Hz. Gait kinematics were recorded from the motion capture system at a frequency of 100 Hz using a modified Cleveland Clinic marker set (Kaufman et al., 2016). Markers were placed on landmarks of the trunk (sternum, C7 vertebrae, T10 vertebrae), pelvis (sacrum, bilateral posterior superior iliac spines), and lower extremities (bilateral greater trochanters, lateral femoral epicondyles, lateral malleoli, calcanei, second and fifth metatarsals, and thigh and shank four-marker clusters). For safety reasons, all participants were connected to a passive trolley throughout the experiment.

Participants' body weight (BW) was modulated using the Zero-G Bodyweight support system (Aretech LLC, Ashburn, VA) to subtract -20%, -15%, and -10% BW and a weighted vest to add +5%, +10%, and +15% BW. We chose the weighted conditions to best represent what children typically carry in their backpacks (Bryant and Bryant, 2014; Perrone et al., 2018). Weights of ⅓, ½, ⅔, and 1-lb were distributed evenly around the vest to meet the weighted conditions. We chose the unweighted conditions to mirror the weighted conditions, though a -5% BW condition could not be tested due to the technical limitations of the Zero-G.

6.3.3. Experimental Protocol

To identify which lower limb was dominant (typical development or TD group) or less affected (bilateral CP group), all participants completed timed single-limb stance tests and the Waterloo Footedness survey (Elias et al., 1998). Participants with bilateral CP also completed additional clinical assessments to determine impairment level, including the Selective Control Assessment of the Lower Extremity (SCALE) (Fowler et al., 2009) and the locomotion ability assessment for kids (ABILOCO-Kids) (Gilles et al., 2008).

All participants started the step-up trials with their feet on two side-by-side force plates posterior to the raised platforms. With this set up, ground reaction forces from the left and right feet were always recorded separately. Participants were then instructed to step up onto the raised platform at a self-selected walking speed with either their dominant/less affected foot or their non-dominant/more affected foot. Once both feet were on the raised platforms, participants were then instructed to step back into the starting position. The first pair of trials was always the no-load condition, where participants completed 5-15 steps per leading foot. The next two blocks of trials were randomized as either the unweighted or weighted conditions. Within these blocks, the loading conditions were also randomized and participants completed 5-10 steps per leading foot. To ensure that participants with bilateral CP felt safe and comfortable during the experimental protocol, a licensed physical therapist was available to guard and provide external support intermittently as needed.

6.3.4. Data Analysis

First, data were examined in Qualisys Track Manager (Qualisys, Göteborg, Sweden) to ensure that markers were correctly labeled. Second, data were imported into Visual 3D (C-Motion, Germantown, MD) to calculate hip abduction and lower limb extension moments using inverse dynamics. Marker and ground reaction force data were interpolated to close small gaps and filtered using a low-pass 4th-order Butterworth filter with a cutoff frequency of 6 Hz to eliminate high frequency spikes. The two anterior force plates were also modified to create a virtual force platform simulating the two steps. The four gait events per stepping trial (leading limb lift-off, leading limb initial contact on the step, trailing limb lift-off, and trailing limb initial contact on the step) were identified using ground reaction force data. All data were then imported into MATLAB (MathWorks, Inc., Natick, MA) to identify peak support (the sum of hip, knee, and ankle sagittal plane moments) and hip abduction moments in the push-off and pull-up stance phases. Any trials that were two standard deviations outside of the average stance phase were not considered in statistical analyses. In addition, all moments were normalized to participant weight.

6.3.5. Statistical Analysis

Statistical analysis was performed in Stata IC 14.1 (StataCorp LLC, College Station, TX) with significance set to $p<0.05$. All analyses were separate for the push-off and pull-up stance phases. Normality of the data was confirmed via distribution of the residuals. The first set of outcome measures were peak support and peak hip abduction moments. We ran a regression analysis between peak moments and load for each lower limb (typical development dominant (TD), bilateral CP less affected (LA), bilateral CP more affected (MA)). If the regressions were significant, we then determined if the coefficients were significantly different from each other. The second set of outcome measures were hip, knee, and ankle percent contributions to peak support moments. These values were calculated by dividing the hip, knee, and ankle sagittal plane segment of support moment by the total support moment. Mixed effects models were used on these individual percent contributions to estimate the fixed effects of load (7 levels: -20%, -15%, -10%, 0%, +5%, +10%, +15% BW), limb (TD, LA, MA), and their interaction with an added random effect of participant. We primarily focused our results on the interaction term, specifically comparisons between the limbs at each individual load level (other than the no-load condition, which is reported in Chapter 5 of this thesis) and between all the load levels within each limb. The p-values for all pairwise comparisons were corrected using Bonferroni corrections.

6.4. Results

6.4.1. Summary of Participants

Seven participants were recruited for each group (**Table 6.1**). As described in Chapter 5 of this manuscript, there were no significant differences between the groups in age, weight, and height. There were significant differences in single limb stance times (p=0.001), where the TD limb had a longer stance time than the LA (p=0.007) and MA limbs (p=0.004). In the bilateral CP group, 5 participants were GMFCS level II and 2 participants were GMFCS level III, and the LA limb had a significantly higher SCALE score than the MA limb (p=0.020). There were 10 missing data points across the analyses either due to technical limitations of the Zero-G or discomfort with external loads: 6 from the CP group (n = 2: -15%, -10%, +5%; n = 1: +10%, +15%) and 4 from the TD group (n = 2: -10%; n = 1: +15%).

Table 6.1. Mean (SD) participant-specific metrics and clinical assessment outcomes.

Outcome Measure	Group		
	Bilateral CP (n = 7)		TD (n = 7)
Age (years)	10.5 (3.6)		10.2 (3.9)
Limb Dominance	2R / 5L		7R
Weight (kg)	38.7 (19.6)		41.7 (23.7)
Height (m)	1.40 (0.19)		1.42 (0.22)
ABILOCO-Kids	2.37 (2.45)		--
Limb	**MA**	**LA**	**TD**
Single-Limb Stance Time (s)	2.27 (2.28)*	5.25 (5.91)*	43.7 (38.2)
SCALE	3.15 (1.68)$^{+}$	6.14 (3.58)	--

*p<0.05 for a significantly different from TD limb
$^{+}$p<0.05 for a significantly different from CP less affected limb

6.4.2. Push-Off Stance Phase

The regressions for peak support moment vs. load were significant for all lower limbs (**Figure 6.1**); however, the regressions for peak hip abduction moment vs. load were not significant for any limb (**Table 6.2**). Comparisons of the coefficients for peak support moment vs. load revealed no significant differences between the limbs.

For hip percent contribution to peak support moment, the MA limb had a significantly higher contribution than the LA and TD limbs at each individual load level (all p<0.017), while the LA limb also had a significantly higher contribution than the TD limb (all p<0.017) (Figure 2). For ankle percent contribution to peak support moment, the MA limb had a significantly lower contribution than the TD limb at each individual load level (all p<0.017), while the LA limb also had a significantly lower contribution than the TD limb at the -20% and -10% BW levels (all p<0.017). Despite these differences, the ankle remained the primary contributor to peak support moments in the push-off phase across all load levels (**Figure 6.2**).

There were no significant differences in knee percent contribution to peak support moment between the limbs at each individual load level. There were also no significant differences in hip, knee, or ankle percent contributions between the load levels within the MA, LA, and TD limbs.

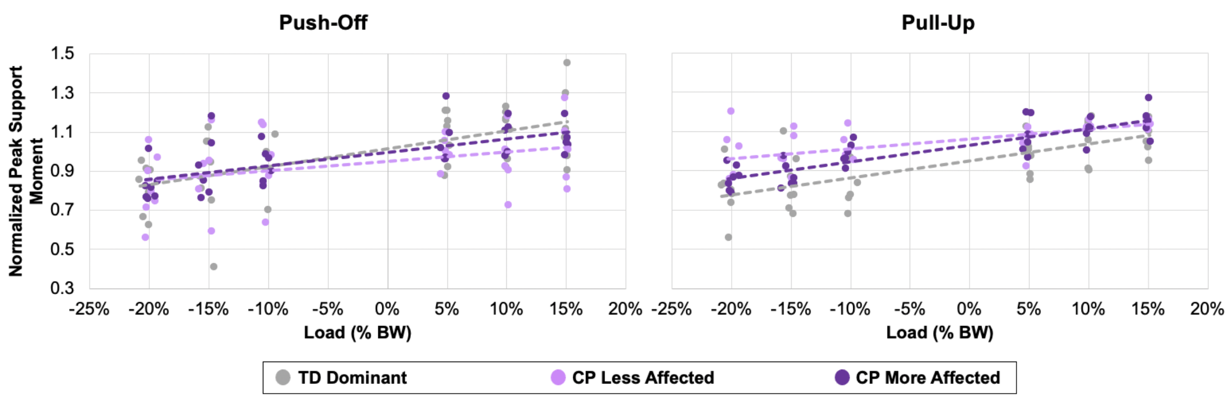

Figure 6.1. Linear regressions for peak support moments vs. load in CP & TD. Linear regressions for Peak Support Moment vs. Load for the TD Dominant (gray), CP Less Affected (light purple), and CP More Affected (dark purple) limbs. Peak moments are normalized to their value in the no-load condition. All regression metrics are outlined in Table 2.

Table 6.2. Mean (SE) metrics from the linear regressions for both stance phases.

Regression Metric	Group		
	Bilateral CP		TD
Push-Off Stance Phase	**More Affected**	**Less Affected**	**Dominant**
Coefficient	0.685 (0.138)	0.479 (0.208)	0.918 (0.194)
Constant	0.996 (0.019)	0.949 (0.028)	1.01 (0.03)
R^2-value	0.429	0.138	0.376
P-value	<0.001	0.028	<0.001
Pull-Up Stance Phase	**More Affected**	**Less Affected**	**Dominant**
Coefficient	0.835 (0.090)$^+$	0.491 (0.103)	0.863 (0.139)
Constant	1.03 (0.01)	1.06 (0.01)	0.951 (0.019)
R^2-value	0.723	0.406	0.511
P-value	<0.001	<0.001	<0.001

$^+$p<0.05 for a significantly different from CP less affected limb

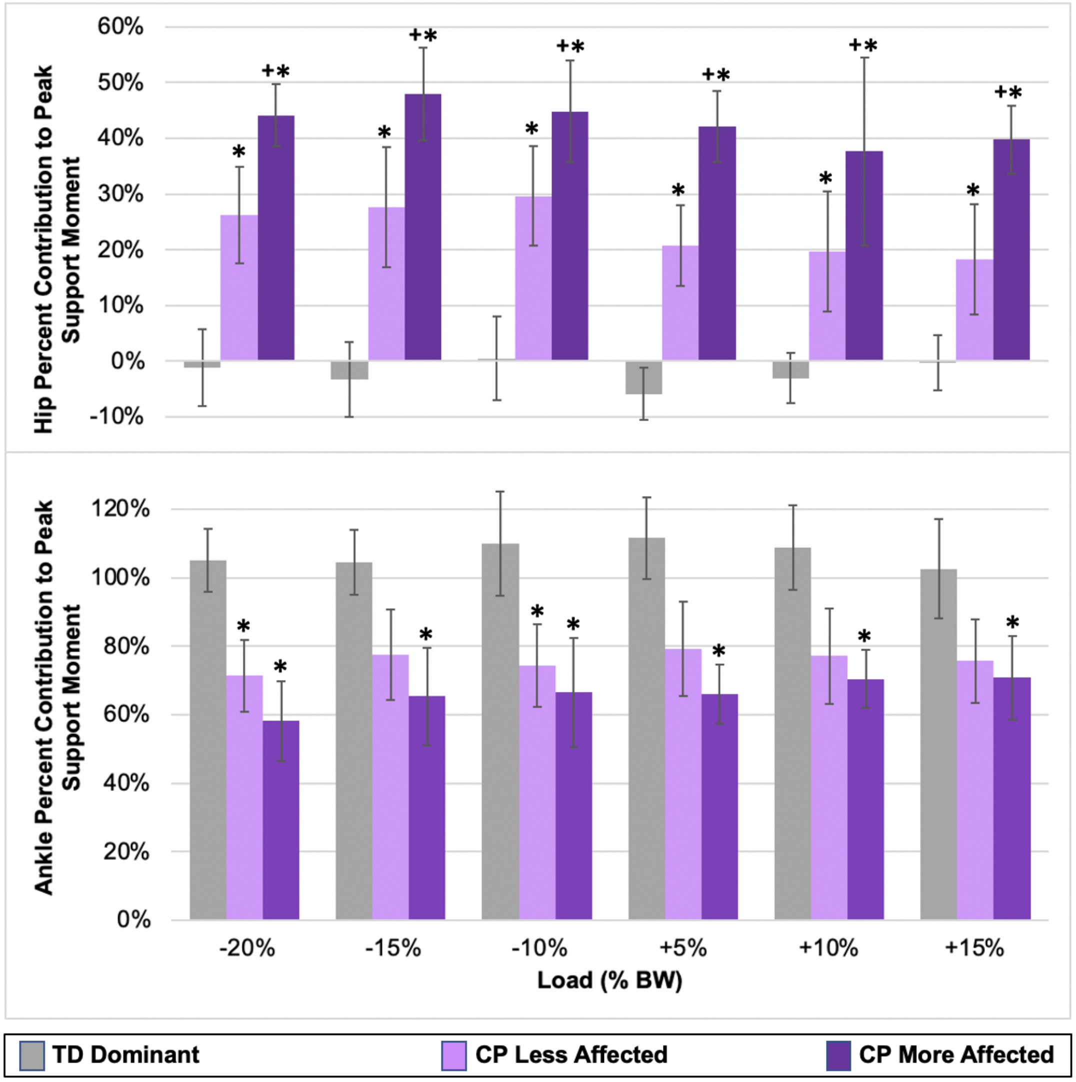

Figure 6.2. Significant joint contributions to peak support moments in push-off across loads. Hip (top) and ankle (bottom) percent contributions to peak support moments in the push-off stance phase. The CP MA limb had a significantly higher hip percent contribution (top) and significantly lower ankle percent contribution (bottom) compared to the TD limb at each load level. Despite these shifts, the ankle remained the primary contributor (highest percentage) to peak support moment in the push-off phase at all load levels. Error bars reflect standard error.
*p<0.05 for a significantly different from TD limb
+p<0.05 for a significantly different from CP less affected limb

6.4.3. Pull-Up Stance Phase

The regressions for peak support moment vs. load were significant for all lower limbs (**Figure 6.1**); however, the regressions for peak hip abduction moment vs. load were not significant for any limb (**Table 6.2**). Comparisons of the coefficients for peak support moment vs. load revealed that only the coefficient for the LA limb was significantly lower than the MA limb ($p=0.009$).

For hip percent contribution to peak support moment, the MA limb had a significantly higher contribution than the LA and TD limbs at each individual load level (all $p<0.017$) (**Figure 6.3**). Within the TD limb, significant differences between the load levels were similar to those reported in Chapter 4 of this thesis, where +5%, +10% > -10%, -15%, -20% and +15% > -10%, -15% (all $p<0.002$). Within the LA limb, the only significant difference in hip percent contribution was between +5% > -10% ($p=0.002$). Within the MA limb, the only significant differences in hip contributions were between 0%, +5%, and +15% > -20% (all $p<0.001$).

For knee percent contribution to peak support moment, the MA limb had a significantly lower contribution than the LA and TD limbs at each individual load level (all $p<0.017$), while the LA limb also had a significantly lower contribution than the TD limb (all $p<0.017$) (**Figure 6.3**). For the TD limb, significant differences between the load levels were similar to those reported in Chapter 4, where +10% > -10%, -15%, -20% and +5%, +15% > -10%, -15% (all $p<0.001$). For the LA limb, the only significant difference in knee percent contribution was between +15% > +5% ($p<0.001$). For the MA limb, the only significant difference in knee contributions was between -20% > 0% ($p<0.001$). There were no significant differences in ankle percent contribution to peak support moment for any relevant pairwise comparisons.

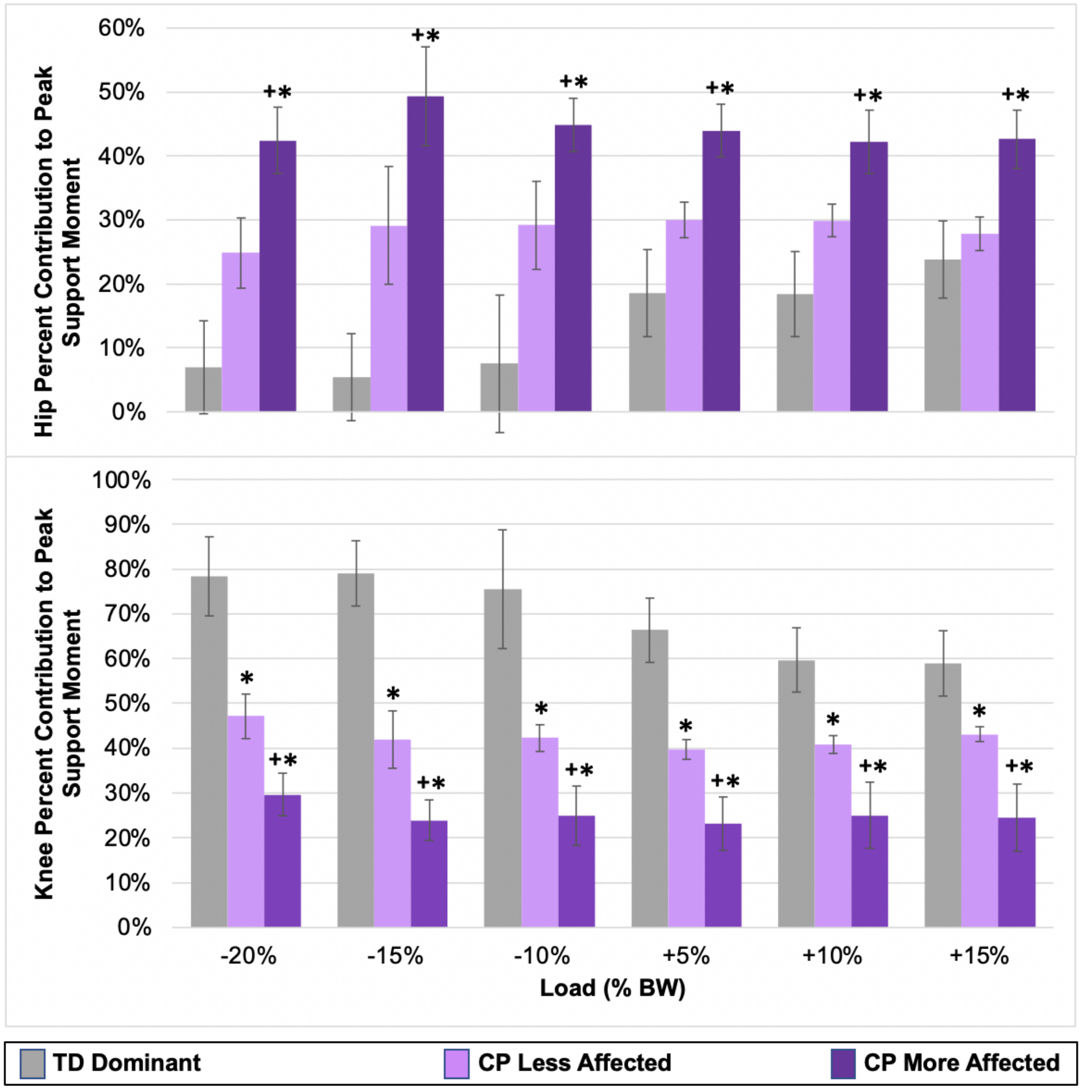

Figure 6.3. Significant joint contributions to peak support moments in pull-up across loads. Hip (top) and knee (bottom) percent contributions to peak support moments in the pull-up stance phase. The CP MA limb had a significantly higher hip percent contribution (top) and significantly lower ankle percent contribution (bottom) compared to the TD and CP MA limbs at each load level. Error bars reflect standard error.
*p<0.05 for a significantly different from TD limb
+p<0.05 for a significantly different from CP less affected limb

6.5. Discussion

This study explored the effect of load modulation from -20% to +15% on lower extremity joint moments of a step-up task in individuals with bilateral CP. While the linear relationship between peak moments and load was significant for extensor support moments in the lower limbs of both the TD and CP groups, the coefficients of these relationships were not significantly different between the two groups. We also found that at each load level, individuals with CP consistently depend heavily on the hip joint to keep themselves upright, especially in the MA limb. These findings perhaps further reinforce the nature and underlying causes of impairment in bilateral CP briefly discussed in Chapter 5 of this thesis.

While we confirmed the hypothesis that extensor support moments would increase with load in both groups, we surprisingly found that hip abduction moments did not decrease with load in individuals with bilateral CP. This result is contrary to the hypothesized abnormal coupling between the hip adductors and lower limb extensors thought to be associated with damage to corticospinal pathways and upregulation of brainstem pathways such as the vestibulospinal or rubrospinal tracts (Cahill-Rowley and Rose, 2014; Fowler et al., 2010; Sánchez et al., 2018a; Zhou et al., 2017). Our participants with bilateral CP may have experienced some amount of this stereotypical coupling, but worked outside of it to meet the demands of the task (Goyal et al., 2022; Lyons et al., 1983; Novak and Brouwer, 2011; Wang and Gillette, 2018). For example, it's possible that excitation of the hip adductors increased with load from abnormal coupling (Thelen et al., 2003); however, the hip abductors were able to overcome this antagonist activation to net a hip abduction moment. This suggests that load modulation combined with a step-up task may be a useful method to train lower limb coordination, both biomechanically and neurally.

It may be possible that individuals with a higher level of impairment are more affected by abnormal adductor/extensor coupling. In fact, previous research has shown that lower limb motor control strategy in children with CP is dependent on impairment level (Goudriaan et al., 2022). Evidence of lower SVMC was seen in our sample: participants who were GMFCS level III had lower average SCALE scores than participants who were GMFCS II. When separating the joint moment data by GMFCS level, we observed that individuals who were GMFCS level III did show a decrease in peak hip abduction moments with increasing load. However, our sample only includes 2 individuals at GMFCS III and a larger sample size is needed to confirm this theory and establish a continuum of the relationship between SVMC and functional performance (Chruscikowski et al., 2017).

In contrast to support moments, analysis of hip, knee, and ankle percent contributions to support moments across load levels within the MA and LA limbs revealed very little significant pairwise comparisons. This is also in contrast to participants with TD who did show a change in biomechanical strategy during the pull-up phase (Chapter 4 of this thesis). It is possible that loads outside of the range we tested would induce a larger change in joint biomechanics. Regardless, the lack of modulation in joint moment contribution in our results suggests that children with bilateral CP have a generic strategy to complete a step-up task. Researchers have hypothesized that individuals with CP have a simpler motor control strategy with less available variability compared to individuals with TD (Bekius et al., 2020). Contrary to our findings, many researchers have found that individuals with nervous system injury vary their motor output when experiencing load modulation (Dewald et al., 1995; Hill and Dewald, 2020; Sánchez et al., 2018a; Sukal-Moulton et al., 2013; Sukal et al., 2007). The key difference in our study is that all participants started at baseline in a standing position, already engaging their brainstem pathways to retain this posture. Responses from the reticulospinal tract after a startle are posturally dependent (Brown et al., 1991). For example, a startle in sitting produces excitation of flexion muscles, while a startle in standing produces excitation of extensor muscles (Brown et al., 1991). If participants with bilateral CP have an upregulated reticulospinal tract, then it makes sense that we see 1) an extension bias throughout the task, 2) a higher contribution to support moments from the hip, which has connections to the brainstem pathways for postural control, and 3) less output from distal muscles, which are commonly innervated by the corticospinal tract.

At each individual load level during the step-up trials, our participants with bilateral CP showed a higher dependence on the hip and a lower dependence on the knee and ankle compared to participants with TD to remain upright in extension. This confirms our secondary hypothesis and offers more evidence to support the theory that a distal loss of SVMC affects the biomechanics of a step-up task. Interestingly, the diverging results between the LA and MA limbs across all load levels highlights the role that impairment severity may play. This thought is supported by the significantly higher SCALE scores of the LA limb compared to the MA limb. Previous research has quantified SCALE scores in the left and right limbs of children with bilateral CP, but did not consider that one limb may be more affected by a loss of SVMC than the other (Fowler et al., 2010). We suggest that future research might follow the procedures of this manuscript and consistently report the lower limbs of individuals with bilateral CP by impairment level (Wiley and Damiano, 1998), similar to the way that "non-paretic" and "paretic" limbs are considered separately in individuals with hemiplegia (Hill and Dewald, 2020; Sukal-Moulton et al., 2014b, 2014a, 2013). This is critical to generalize our understanding of the nature of neural control and motor impairments in children with bilateral CP.

Our investigation into the effect of load modulation on a step-up task in individuals with bilateral CP revealed that while support moments increased with load, extension patterns in the CP group were consistent. This means that increasing body weight also increased the raw hip extension generated by our participants with CP. Because of this relationship, our protocol of increasing body weight during a step-up task may also be an effective hip strengthening intervention by working within motor constraints to improve gait (Riad et al., 2008). Selection of a load level to provide a “just right challenge” is an elegant way to train these important muscles in a salient task of daily living (Rebeiro and Polgar, 1999). Limitations of our study include the resolution of load, which was considered in the linear regression models, and the placement of some markers on clothes rather than skin. Future lines of inquiry include investigating muscle activations of the hip abductors and adductors during a step-up task and changes in step-up performance based on GMFCS level in individuals with bilateral CP.

7. CONCLUSION

7.1. Summary of Findings

The goal of this dissertation was to investigate the biomechanics of a step-up task with and without load modulation in young people with and without bilateral cerebral palsy (CP). It was important to focus on a step-up task due to the strong link between stair-climbing and impaired mobility (Lepage et al., 1998). Our findings have deepened our understanding of lower limb impairments from CP and lend insight to the neural mechanisms behind impaired mobility in this population.

In Chapter 4, we characterized the effect of load modulation from -20% to +15% of bodyweight on lower limb joint moments of a step-up task in young people with typical development (TD). Fourteen participants without CP modulated their extensor support moments incrementally with load, but not their hip abduction moments. The ankle joint primarily contributed to extension in the push-off stance phase. The knee primarily contributed to extension in the pull-up stance phase with some secondary help from the hip during weighted conditions. Overall, the step-up protocol offers a sensitive measure of movement quality and the results offer a robust model which would serve to contextualize movement differences in pediatric populations with movement challenges.

In Chapter 5, we evaluated lower limb joint moment strategies in children and adolescents with bilateral CP during a regular step-up task. Surprisingly, peak extensor support and hip abduction moments were not significantly lower in 7 individuals with bilateral CP compared to 7 individuals with TD. Instead, our participants with bilateral CP employed an alternative strategy to generate comparable support moments to complete the task– they depended more on the hip joint, especially in their more affected lower limb, to produce large extension moments in both stance phases. Increased dependence on the hip joint may have also affected timing of peak moments, which were closer together in participants with bilateral CP compared to participants with TD. The results suggest that a loss of SVMC in the knee and ankle joints may primarily be responsible for this shift in dependence. This specific motor impairment has been connected to damage to corticospinal pathways and increased use of brainstem motor pathways (Cahill-Rowley and Rose, 2014; Fowler et al., 2010).

In Chapter 6, we quantified the lower limb joint moment strategies of children and adolescents with bilateral CP during a step-up task with the same load modulation protocol described in Chapter 4. Participants with bilateral CP unexpectedly did not show a loss of SVMC expressed as abnormal coupling between the extensors and hip adductors. This negative result was surprising because abnormal adductor/extensor coupling has been linked to use of brainstem pathways (Sánchez et al., 2018a). It could be that individuals with bilateral CP had to work outside of a stereotypical coupling to meet the demands of the task, which suggests that our experimental protocol may be a useful method to train lower limb coordination. Participants with bilateral CP displayed the same biomechanical strategy described in Chapter 5 to step up across all load levels, consistent with a distal loss of SVMC. If participants with bilateral CP have an upregulated reticulospinal tract, then it makes sense that we see 1) an extension bias throughout the task (Brown et al., 1991), 2) a higher contribution to support moments from the hip, which has connections to the brainstem pathways for postural control, and 3) less output from distal muscles, which are commonly innervated by the corticospinal tract.

7.2. Future Lines of Inquiry

The results of this dissertation open up many future lines of research inquiry. Other biomechanical metrics of a step-up task, such as joint kinematics and joint power, may be useful metrics to further analyze. Another good first step is that this study should be repeated with more participants with bilateral CP who are GMFCS level III. While the functional differences between the GMFCS levels are well-defined, more nuanced differences are not. An investigation into the differences in biomechanical strategies between individuals of different GMFCS levels, particularly II & III, may uncover more specific targets for therapy for each group.

The experimental protocol outlined in this study may be a possible intervention for young people with CP. Our results indicate that a step-up task itself can help train the hip abductors and extensors. Combining the task with load modulation can strengthen the capacity of the hip extensors by working at a load that balances muscle overload and task completion. In addition, individuals with CP may benefit from a repetitive task that requires them to work outside of a stereotypical extensor/adductor coupling.

Another future direction is to investigate the biomechanics of different types of step tasks, including a lateral step, a step down, or a step during stair negotiation. These steps require different biomechanical strategies compared to a forward step. For example, load modulation may have more of an impact on hip abduction moments during a lateral step. In addition, the presence of abnormal extensor/adductor coupling may be revealed in a task with different joint moment requirements, such as a lateral step or a step down (Novak and Brouwer, 2011).

There are different forms of load modulation that can be reproduced during a step-up task or any other gait task. For example, walking with external loads strapped to the ankle may change the parameters of a step-up task. Another idea is to use three-wheel running frames to support a person's body weight during level-ground or inclined gait in natural environments. Loss of SVMC may impact performance in athletes with CP using these running frames (van der Linden et al., 2018). By quantifying gait biomechanics with and without running frames, we may begin to understand the benefits of this body weight support tool and the impact of motor impairments.

It may be prudent to directly quantify pathway integrity in individuals with bilateral CP. Though methods such as transcranial magnetic stimulation have not worked in the lower limbs due to the organization of the motor homunculus, magnetic resonance imaging may be a helpful tool in tracing descending motor pathways to the lower limbs in individuals with CP. This would give a clearer picture of the neural mechanisms underlying motor impairments in bilateral CP, which would further our understanding of this childhood diagnosis (Karbasforoushan et al., 2019).

Finally, an important future step to this research includes disseminating the results to community members affected by CP. A continuous dialogue between researchers and the CP community is key to producing research that matters. This can and will be done in multiple ways, including sending out publications and giving presentations to researchers and clinicians who would use this knowledge to benefit children with bilateral CP. This research is only a small piece of a larger puzzle; clinical research must work side-by-side with clinical practice to improve and update early interventions to target impairments such as loss of SVMC. These changes may address key action items outlined by community members affected by CP by targeting lifelong mobility in this population (Gross et al., 2018; Vargus-Adams and Martin, 2011, 2009).

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APPENDICES

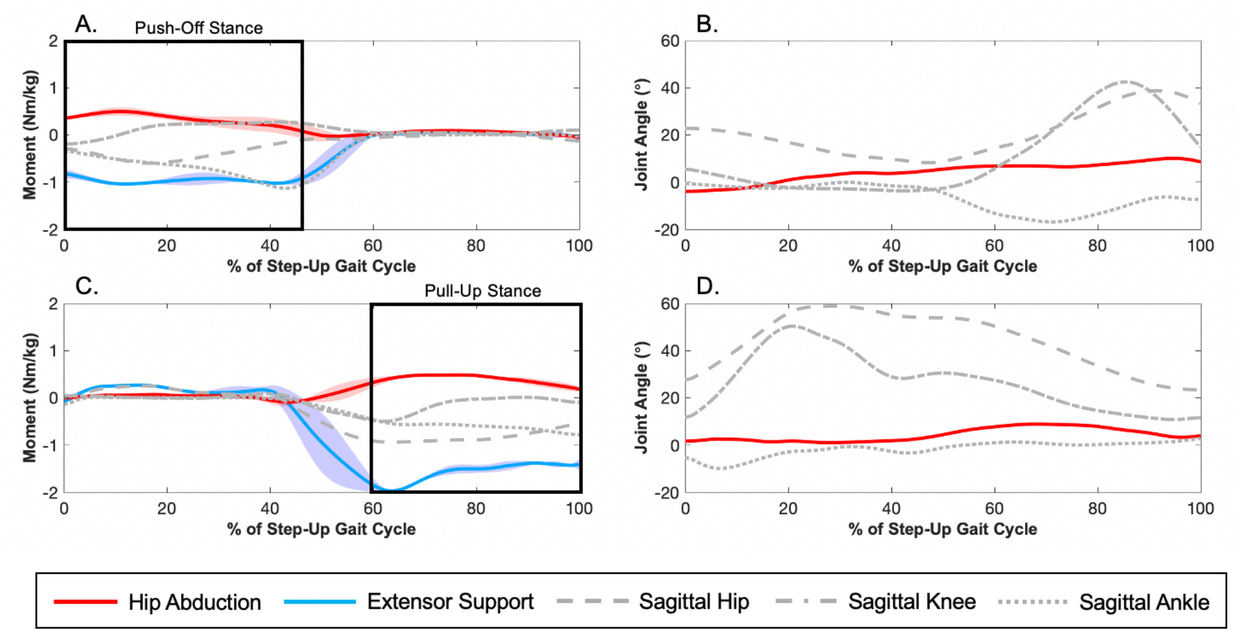

Figure A.1. Joint biomechanical profiles of a step-up task in bilateral CP. Representative kinetic (A and C) and kinematic (B and D) profiles from one participant during a no-load step up for the trailing leg (A and B) and the leading leg (C and D). On each x-axis, 0% corresponds to the start of a step-up trial at leading leg lift-off while 100% corresponds to the end of the trial at trailing leg initial contact with the step. On each y-axis, a positive magnitude indicates joint flexion/abduction while a negative magnitude indicates joint extension/adduction. Average hip abduction moments are in red. Individual lower limb sagittal plane moments are in gray, including the hip (gray dash), knee (gray dash-dot), and ankle (gray dot). The sum of these individual joint moments equals the extensor support moments shown in blue. Shaded regions represent one standard deviation. The black boxes on plots A and C indicate the push-off and pull-up stance phases, respectively.

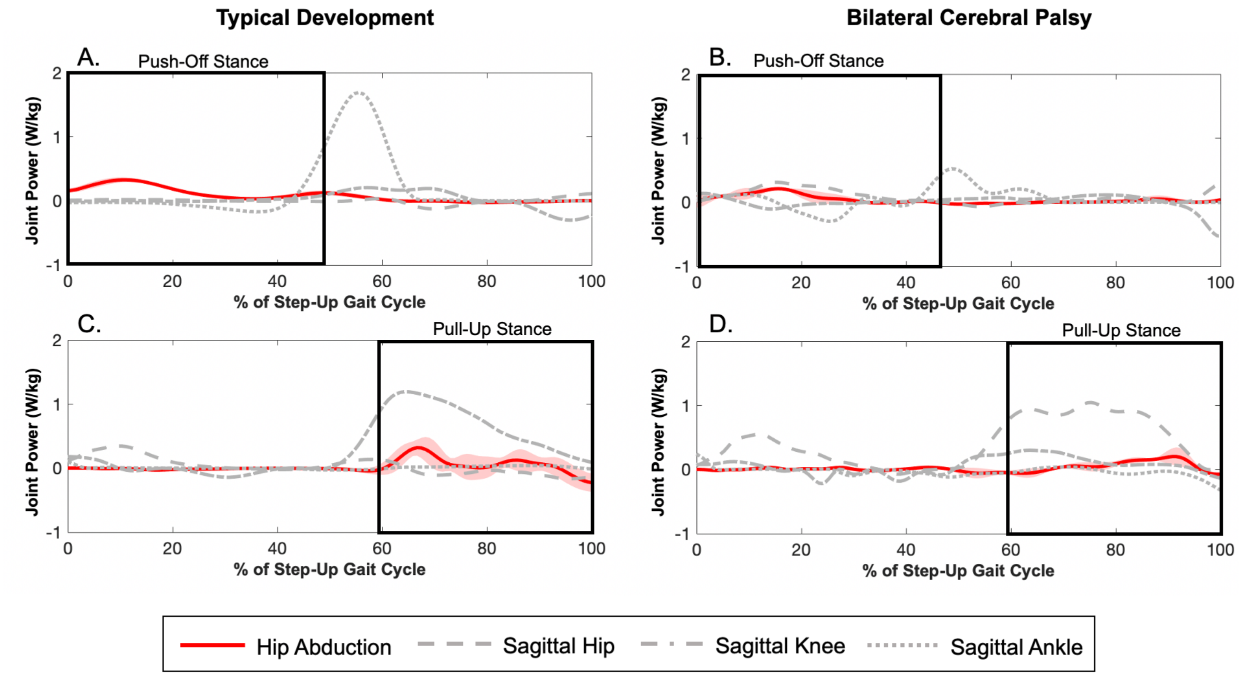

Figure A.2. Joint power profiles of a step-up task. Representative power profiles from one participant from the TD group (A and C) and the Bilateral CP group (B and D) during a no-load step up for the trailing leg (A and B) and the leading leg (C and D). On each x-axis, 0% corresponds to the start of a step-up trial at leading leg lift-off while 100% corresponds to the end of the trial at trailing leg initial contact with the step. On each y-axis, a positive magnitude indicates the generation of energy while a negative magnitude indicates the absorption of energy. Average hip abduction moments are in red. Individual lower limb sagittal plane moments are in gray, including the hip (gray dash), knee (gray dash-dot), and ankle (gray dot). Shaded regions represent one standard deviation. The black boxes on plots indicate the push-off and pull-up stance phases, respectively. In the TD group, the ankle and knee joints generate the most energy (A and C). In the CP group, power generation from the ankle joint is less in the push-off phase, while the hip joint generates the most energy in the pull-up phase (B and D).

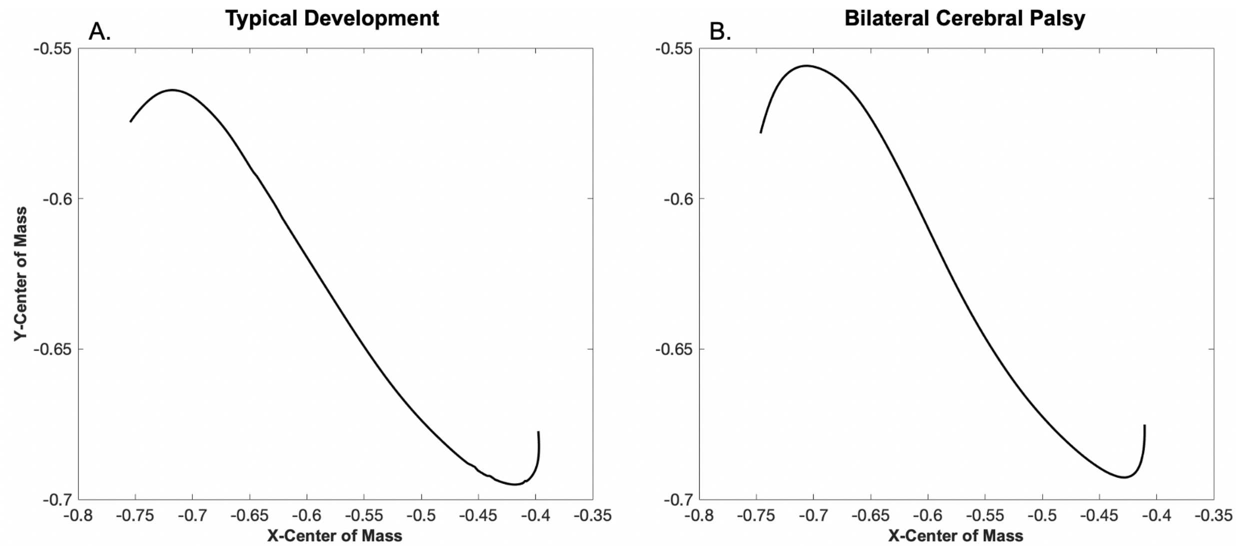

Figure A.3. Center-of-Mass (CoM) profiles of a step-up task. Representative CoM profiles from one participant from the TD group (A) and the Bilateral CP group (B) during a no-load step-up task (right leg leading). The x-axis indicates the CoM in the x-direction (towards 0 is forward onto the step) while the y-axis indicates the CoM in the y-direction (towards 0 is left side, away from 0 is right side). CoM profiles between the two groups are similar.

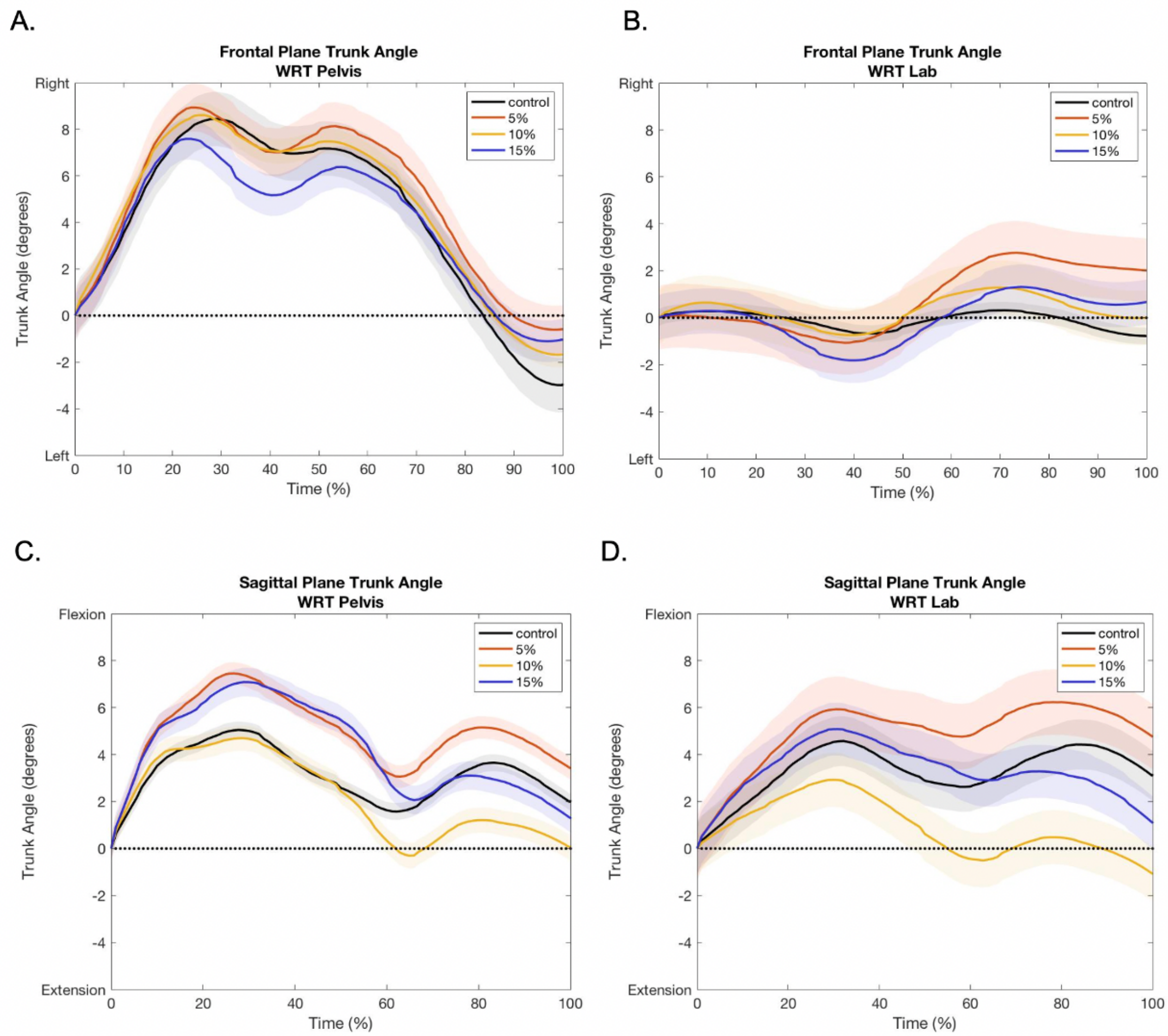

Figure A.4. Frontal and sagittal plane trunk kinematic profiles of a step-up task. Representative trunk kinematic profiles from one participant from the TD group in the frontal plane (A and B) and the sagittal plane (C and D) during a no-load step-up task, with respect to the pelvis (A and C) or the lab (B and D). On each x-axis, 0% corresponds to the start of a step-up trial at leading leg lift-off while 100% corresponds to the end of the trial at trailing leg initial contact with the step. For frontal plane plots, a positive y-axis indicates trunk lean to the right while a negative y-axis indicates trunk lean to the left. For the sagittal plane plots, a positive y-axis indicates trunk flexion while a negative y-axis indicates trunk extension. The black line represents a participant completing a no-load step-up task, while the colored lines represent a participant completing the +5% (orange), +10% (yellow), or +15% (blue) bodyweight load condition. The shaded regions indicate standard error. *(Figure A.3 from "Effects of Load Modulation on Trunk Angle of Adolescents During a Step-Up Task" by Keri Han, an Undergraduate Departmental Honors Thesis in the Department of Biomedical Engineering at Northwestern University.)*

Table A.1. Significant pairwise comparisons for a statistical analysis from Chapter 4.

Interaction between [Limb Load]	Contrast	Standard Error	Z-Score
[D +5%] vs [D -20%]	-0.101	0.023	-4.35
[D +15%] vs [D -20%]	-0.123	0.022	-5.59
[D +5%] vs [D -15%]	-0.116	0.018	-6.62
[D +10%] vs [D -15%]	-0.123	0.029	-4.19
[D +15%] vs [D -15%]	-0.138	0.021	-6.56
[ND +5%] vs [D -15%]	-0.159	0.038	-4.22
[ND +10%] vs [D -15%]	-0.172	0.038	-4.47
[ND +15%] vs [D -15%]	-0.161	0.031	-5.14
[ND +5%] vs [D -10%]	-0.120	0.025	-4.86
[D +15%] vs [D -10%]	-0.141	0.029	-4.85
[ND +15%] vs [D -10%]	-0.165	0.036	-4.53
[ND 0%] vs [ND -20%]	-0.166	0.038	-4.32
[ND +15%] vs [ND -20%]	-0.176	0.039	-4.55
[ND 0%] vs [ND -15%]	-0.184	0.027	-6.71
[ND +5%] vs [ND -15%]	-0.192	0.038	-5.02
[ND +10%] vs [ND -15%]	-0.205	0.042	-4.85
[ND +15%] vs [ND -15%]	-0.195	0.035	-5.55
[ND 0%] vs [ND -10%]	-0.119	0.028	-4.33
[ND +15%] vs [ND -10%]	-0.129	0.032	-4.09

Table A.1. Significant pairwise comparisons for the interaction term between dominance (2 levels: Dominant [D] and Non-Dominant [ND]) and load (7 levels: -20%, -15%, -10%, 0%, +5%, +10%, +15%) for the TD group, which was significant for the outcome measure of knee percent contributions to peak support moment during the pull-up stance phase of a step-up task. There were no significant comparisons between the dominant and non-dominant limbs at each individual load level.