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ABSTRACT

INVESTIGATING THE COMBINED EFFECTS OF WHOLE BODY VIBRATION AND VESTIBULAR STIMULATION ON SPASTICITY AND DYSTONIA IN CEREBRAL PALSY

by
Peter A Michael

This study identifies and addresses three voids and potential shortcomings associated with the classification, assessment and management of Cerebral Palsy (CP). These concerns should not undermine the significant advancement that has been made in this specific branch of rehabilitation, but addressing them is necessary. Cerebral Palsy is a group of motor impairments due to hypoxic-ischemic brain damage around the time of birth and very commonly manifests as excessive muscle tone and poor motor control. There are classifications within CP including spasticity and dystonia.

First, a level of discrepancy is present in the classification of CP between the clinical and research communities. Prior studies identify CP individuals as exhibiting varying degrees of spasticity, when in fact they often exhibit dystonia as well. Inconsistent clinical study results occur when mixed populations are unknowingly recruited. Proper classification of the type of movement disorder within CP is crucial. This study proposes the use of the Involuntary Muscle Tone (IMT) index, which is a novel measure to be computed from the pendulum knee drop (PKD) test and used to aid in proper classification. The PKD is a test of passive shank swing where the amplitudes of swing are used to observe tone present in the lower extremities, but data in this study suggests that this novel index of distance traveled can also be used as an indicator of classification.

This index also addressed the second issue, namely a lack of objective assessment that can be applied to all classifications of CP. Since it is sensitive to changes in tone, it

can serve to complement the coarse five point Modified Ashworth Scale that is commonly used. Alternate methods of analyzing the PKD include the relaxation index, which does not provide a comprehensive outcome, and an optimization model which cannot be used if the shank trajectory deviates from an ideal scenario. The IMT index is unaffected by these challenges.

Lastly, this study utilizes these tools and knowledge to investigate the reduction in tone as a result of a novel approach that incorporates Whole Body Vibration (WBV) and Vestibular Stimulation (VS) into a single session of stimulation. While they have been assessed separately as potential therapies for movement disorders, their effects on the specific classifications of CP was not well defined. Additionally, there is a lack of a controlled study that investigates the effect of a combined stimulation.

Passive parameters of knee stiffness are extracted from the PKD trajectory and include the relaxation index and the Involuntary Muscle Tone Index. Pilot data in this study supports their use, in conjunction, to describe changes in amplitude of the first swing and amount of oscillation of the leg, respectively. Active motor function was assessed via self-regulated gait and voluntary leg movements following a target. Age-matched control data showed negligible change and was used to calculate a 95% confidence interval for comparison of changes in CP data.

Analysis shows that upon receiving a single session of combined stimulation, all individuals with spastic-dystonic CP experienced a reduction in co-contraction and stiffness. Relaxation index and Involuntary Muscle Tone Index improved by as much as 53% and 89% respectively, while stride length and walk speed improved by as much as 37% and 27% respectively. Lastly, the pilot subject for the voluntary shank movement task

exhibited a 15-degree increase in tracking accuracy and range of motion as well as a 170 ms improvement in reaction time. All improvements in CP data were outside of the 95% control margin of error.

These findings may indicate that the proposed stimulation can be used as both a standalone therapeutic modality or combined with physical, occupational or robotic therapies that these subjects would have otherwise been too rigid to participate in safely. While these results are promising, a larger study with more participants is necessary.

INVESTIGATING THE COMBINED EFFECTS OF WHOLE BODY VIBRATION AND VESTIBULAR STIMULATION ON SPASTICITY AND DYSTONIA IN CEREBRAL PALSY

by
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APPROVAL PAGE

INVESTIGATING THE COMBINED EFFECTS OF WHOLE BODY VIBRATION AND VESTIBULAR STIMULATION ON SPASTICITY AND DYSTONIA IN CEREBRAL PALSY

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Be anxious for nothing, but in everything by prayer and supplication, with thanksgiving, let your requests be made known to God; and the peace of God, which surpasses all understanding, will guard your hearts and minds through Christ Jesus.
~ Philippians 4:6-7

لاَ تَهْتَمُّوا بِشَيْءٍ، بَلْ فِي كُلِّ شَيْءٍ بِالصَّلاَةِ وَالدُّعَاءِ مَعَ الشُّكْرِ، لِتُعْلَمْ طِلْبَاتُكُمْ لَدَى اللهِ.
وَسَلاَمُ اللهِ الَّذِي يَفُوقُ كُلَّ عَقْلٍ يَحْفَظُ قُلُوبَكُمْ وَأَفْكَارَكُمْ فِي الْمَسِيحِ يَسُوعَ.
فيلبي 4 : 6-7

✝

Fear not, for I am with you; Be not dismayed, for I am your God. I will strengthen you, Yes, I will help you, I will uphold you with my righteous right hand.
~ Isaiah 41:10

لاَ تَخَفْ لأَنِّي مَعَكَ. لاَ تَتَلَفَّتْ لأَنِّي إِلَهُكَ.
قَدْ أَيَّدْتُكَ وَأَعَنْتُكَ وَعَضَدْتُكَ بِيَمِينِ بِرِّي.
اشعياء 41 : 10

✝

The Lord is my light and my salvation; Whom shall I fear? The Lord is the strength of my life; Of whom shall I be afraid? When the wicked came against me to eat up my flesh, my enemies and foes, they stumbled and fell. Though an army may encamp against me, my heart shall not fear; Though war should rise against me, even then I will be confident
~ Psalm 27:1-3

اَلرَّبُّ نُورِي وَخَلاَصِي مِمَّنْ أَخَافُ؟ الرَّبُّ حِصْنُ حَيَاتِي مِمَّنْ أَرْتَعِبُ؟
عِنْدَ مَا اقْتَرَبَ إِلَيَّ الأَشْرَارُ لِيَأْكُلُوا لَحْمِي مُضَايِقِيَّ وَأَعْدَائِي
عَثَرُوا وَسَقَطُوا. إِنْ نَزَلَ عَلَيَّ جَيْشٌ لاَ يَخَافُ قَلْبِي.
إِنْ قَامَتْ عَلَيَّ حَرْبٌ فَفِي ذَلِكَ أَنَا مُطْمَئِنٌّ.
مزامير 27 : 1-3

I dedicate this degree to the people who have
encouraged and supported me on this journey.

Namely my incredible wife, Mary,
my loving parents Atif and Mary, and my dear sister Mervy,
my father and mother in law Osama and Manal Gayed,
my brother George Gayed,
and the rest of my family and friends.

Thank you all for your love!

Above all else,
Thank God!

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CHAPTER 1

BACKGROUND

1.1 Cerebral Palsy

Around the time of birth, complications may lead to cerebral ischemic brain damage. Ischemia is a condition in which the brain does not receive sufficient blood and oxygen to maintain healthy function. This hypoxic ischemic brain encephalopathy (HIE) may cause periventricular leukomalacia (PVL) and changes in the basal ganglia. The resultant brain damage may cause an inability to control muscles or coordinate movement, thereby leading to the motor control deficits commonly observed. Cerebral Palsy (CP) is one such group of movement disorders and according to the Center for Disease Control (CDC), it is the most common motor disability during childhood [1]. CP that develops prior to birth is called congenital and accounts for approximately 85% of cases, with the remained being acquired after birth due to infection or brain injury.

While the symptoms of CP can vary widely, they are primarily related to poor motor function of the upper and lower extremities; abnormal posture and dysarthric speech may also occur. It is important to note that there are several classifications of movement disorders that manifest in individuals with CP. They are: (1) spasticity, (2) dystonic, (3) a combination of dystonic and spastic or (4) ataxic [2-4]. While spasticity is present in approximately 80% of individuals with CP [1, 5, 6], it is very common that it manifests in conjunction with dystonia.

Spasticity is defined in the Journal of Pediatrics as a resistance to externally imposed movement that increases with the speed of stretch and/or the resistance to

externally imposed movements that rise rapidly above a threshold speed or joint angle [7]. In other words, spasticity can be defined as a velocity dependent hypersensitivity to joint movement [8]. Dystonia, on the other hand, is marked by uncontrolled muscle activity leading to twisting, uncomfortable posture and sometimes pain [7, 9] and is usually associated with damage to the basal ganglia. This can be observed in the individual's inability to recruit, activate and isolate individual muscle groups and results in co-contraction of the agonist and antagonist muscles. This increase in muscle tone can in turn cause poor body structure, development, limited gait and may result in the dependence on crutches or a wheelchair [10-12].

The symptoms and manifestations of CP are permanent and do not worsen over time, but usually cause problematic secondary issues that impede normal motor function. While excessive muscle tone and poor motor control are major impediments on their own, the secondary complications, especially in the developmental years, usually lead to deformations in musculoskeletal structure and require very invasive and complex surgeries for potential remediation. These secondary complications commonly include contractures. This phenomenon is the breakdown of a muscle and replacing it with connective tissue, and is triggered when a muscle remains in contraction for extended periods of time. The bone deformation and contractures contribute further to the movement disorder by hindering what is left in the way of motor control.

Currently, there are no known methods to reverse the injury or recover adequate motor control. Rather than reversing CP, therapeutic approaches have been developed and utilized widely as a means of managing the symptoms and manifestations of the disability, while attempting to minimize the adverse effects that develop as a result. Application and

success of such therapies is very dependent on the proper classification of the type of movement disorder (spastic, dystonic or a combination).

The scientific research and clinical communities are unfortunately prone to incorrectly labeling these different manifestations simply as varying degrees of spasticity [13, 14]. For example, the co-contraction "locking" of a joint that can occur in individuals with dystonia can be mistaken for excessive tone (spasticity) and it is therefore sometimes difficult for a clinician to differentiate between them. However, the distinction of the source of the tone must be made reliably as the benefits of certain therapeutic approaches differ greatly between spasticity and dystonia.

To accurately assess the feasibility of various interventions, including those implemented in this study, the distinction between these movement disorders and their classification must be maintained. Existing assessment techniques are not adequate in this respect and pose a challenge for clinicians who, while having sound judgement, are limited to subjective clinical grading scores including the Modified Ashworth Scale (MAS) [15] and Barry-Albright Dystonia Scale (BADS) [16].

Additionally, most published literature fails to recognize or maintain the difference in classification [13], and appear to be recruiting individuals with CP who experience spasticity, or broadly present with high muscle tone. This in turn may lead to confusion in the clinical evaluation of the disorders and interpretation of post- intervention results. This is a major issue that must be addressed. This proposed study, therefore, differs from previous studies that have lumped the three types of cerebral palsy together as levels of spasticity and paves the foundation for differentiating between these sub groups in future studies.

1.2 Traditional Management of Movement Disorders

With no way to reverse the brain damage and restore the affected motor control, traditional management of CP focuses on reducing the major complications of the movement disorders as well as managing pain and discomfort. This includes both invasive and non-invasive techniques mainly targeting the excessive muscle activity and the resulting increase in joint stiffness and body tone. Common techniques can be divided into several categories including pharmaceutical, surgical and non-invasive mechanical therapies, with surgical procedures being the only option with any level of permanent affect directed at motor function.

Pharmaceuticals most commonly utilized for CP are muscle relaxants, botulinum toxin and baclofen. Published literature has shown the long term effects of intrathecal baclofen on cerebral palsy [5, 17]. Murphy et al. reported significant reductions in the Ashworth scale that remained for at least 12 months [5]. Despite how remarkable these results are, there were limitations and complications due to the invasive nature of the subcutaneous pump and spinal delivery system. Botox injections, on the other hand, are administered to each muscle that is experiencing high tone or is overly active and acts by weakening that muscle, thereby decreasing the contraction. While this provides some relief, it is uncomfortable, lasts for one to six months and the resulting muscle weakness does not help with achieving motor tasks. The most temporary alternative is muscle relaxants, including tizanidine and cyclobenzaprine, which are prescribed to alleviate the discomfort of constant muscle contractions.

In severe cases, surgical options are considered and can be performed at the nerve, muscle or bone levels. While the positive effects are long lasting, there are the potential

complications associated with any surgical procedure. Such procedures include dorsal rhizotomy, tendon lengthening and osteotomies. A dorsal rhizotomy is very invasive and works by altering nerve excitability via selective severing of certain sensory nerves, thereby decreasing some of the reflexes that contribute to the spastic tone mentioned above. Tendon lengthening usually targets a contracted gastrocnemius muscle and introduces slack at the Achilles tendon in an attempt to alleviate the discomfort and complications in the lower extremities. Lastly, an osteotomy is a corrective bone surgery that is necessary if there are developmental complications or if the physician sees benefit to altering the structure of a bone or the attachment points of a tendon. For example, this would be applicable for a bowed femur, which can be corrected by sectioning and rearranging the bone into a more linear structure and allowing the body to fuse it back together.

However, the most common approaches to remediating the movement disorders are non-invasive techniques that include several types of physical and occupational therapy [18]. These include mechanical body manipulation, like stretching, various gross motor training tasks, hippotherapy, and recently, robotic therapy. These techniques are usually applied before any invasive steps are taken, and the results are usually shorter duration but do not bear the complications associated with surgery. While these approaches have been shown to improve function and aid in the management of pain, the major complication however, is qualifying for these approaches. Excessive tone and highly sensitive reflexes can sometimes lead to the inability to participate in these therapeutic modalities for the safety of the individual. This concern is especially great in robotic therapy, where the stiffness and uncontrolled muscle activity limits its administration to the affected individual and where injury can be much more severe.

1.3 Assessment of Disability and Severity

1.3.1 Modified Ashworth Scale (MAS)

Clinicians utilize a range of techniques to classify the severity of an individual's disability, but the most common and widely used scale to evaluate muscle tone abnormalities is the Modified Ashworth Scale (MAS). This is a subjective assessment of spasticity by moving the individual's limb and assigning it a value between zero and four [15]. While this assessment has claim to be reliable in determining the severity of the rigidity of a limb, it cannot differentiate between the source of the excessive tone (spasticity vs co-contraction).

Table 1.1 Modified Ashworth Scale

Grade	***Description***
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part(s) rigid in flexion or extension

Source: Bohannon and Smith, 1987

1.3.2 Barry-Albright Dystonia Scale (BADS)

The Barry-Albright Dystonia Scale [16] is the analogous scale for assessing dystonia, but is equally subjective and with only four levels between non-disabled and a nonfunctional limb in both scales, they are too coarse to be used as objective measures to distinguish changes in joint stiffness as a result of intervention.

Table 1.2 Barry-Albright Dystonia Scale

Grade	*Description*
0	Absence of lower extremity dystonia
1	Slight. Dystonia less than 10% of the time and does not interfere with normal positioning and/or functional activities
2	Mild. Dystonia less than 50% of the time and does not interfere with normal positioning and/or functional activities
3	Moderate dystonia more than 50% of the time and/or dystonia that interferes with normal positioning and/or lower extremity weight bearing or function
4	Severe dystonia more than 50% of the time and/or dystonia that prevents normal positioning and/or lower extremity weight bearing and/or function

Source: Barry and Albright, 1999

1.3.3 Pendulum Knee Drop (PKD) Assessment

Both of the abovementioned assessment techniques point to a need for an objective measure of the level of disability. The Wartenberg Pendulum Knee Drop (PKD) fills that void as an objective measure that is more sensitive to changes in knee stiffness [19]. It has been shown to be a reliable measure of tone and spasticity [20, 21] and can be used to determine the effects of an intervention. To accomplish this assessment, the shank of a seated participant is raised to extension (by the experimenter) and quickly released; the trajectory of the passive swinging of the shank is recorded. Subsequently, analysis can be done to extract several parameters that are used to quantify changes in joint characteristics. It is not recommended for this assessment to be conducted in quick succession since reflexes from one trial may affect the outcomes of subsequent trials.

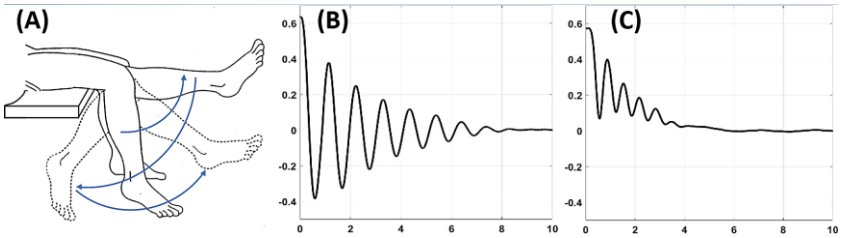


Figure 1.1 (A) administering the Pendulum Knee Drop (PKD)[20], (B) representative PKD of a non-disabled individual and (C) representative PKD of spastic CP.

This study lays the foundation for an additional use of this assessment, as a clinical classification technique to be used alongside existing methods. When this assessment is applied to a non-disabled individual, the plot of the shank trajectory resembles a damped pendulum oscillating about zero degrees (the vertical resting position). However, an individual with CP experiences stretch reflexes that do not allow the shank to swing all the way down and back past the vertical position, but rather resembles a ratcheting curve gradually approaching zero. This is typical of what we consider spastic-type CP.

Certain studies have recruited individuals with CP and referred to them as "more affected", but it is important to note that their shank trajectories appear very different from individuals with spasticity [13]. There appears to be a locking of the shank (observed in the pendulum knee drop) that is indicative of dystonia or co-contraction. This is evident when the shank does not oscillate freely, but rather exhibits some downward movement with fluctuations, but is dominated by the hanging of the limb at a specific angle, followed by a slow descent to the resting vertical position.

1.3.4 Objective Parameters Extracted from the Pendulum Knee Drop

In order to utilize the shank trajectory data to objectively determine the level of disability or observe changes before and after a therapy, there are several means of analysis. These include the relaxation index, which is a ratio of the inflection point (max position minus first inflection point) over the amplitude of the hold position (max position minus resting position). A larger range of motion during passive shank swing contributes to a larger relaxation index and is indicative of decreased muscle tone. While the pendulum knee drop test is largely overshadowed by the more popular MAS assessment, calculation of a

relaxation index allows for the use of the pendulum knee drop test to be used as a very robust objective measure in changes of passive lower extremity parameters.

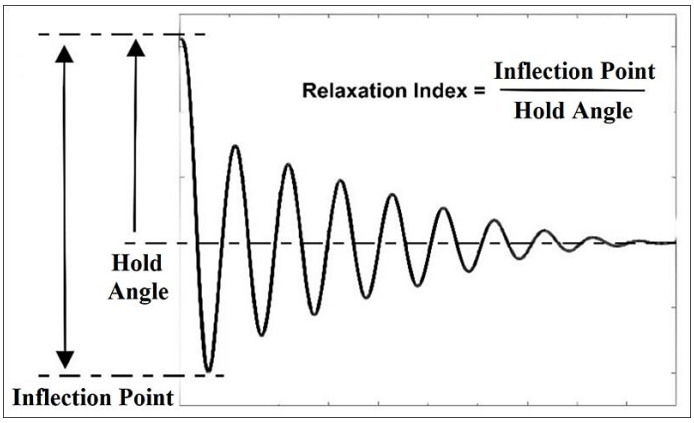


Figure 1.2 Calculating the Relaxation Index from a pendulum knee drop.

Alternatively, Simon and Foulds developed an optimization model to estimate the values of stiffness and damping about the knee joint based on the equation of a dynamic pendulum [22] with an approximation of the shank and foot mass and center of mass. It has also been modified to include the virtual trajectory which is believed to define the current position of the equilibrium to which the limb is attracted. This model can therefore be represented as:

$$I\ddot{\theta} + B(\dot{\theta} - \dot{\theta}_{VT}) + K(\theta - \theta_{VT}) = mgLsin(\theta) \quad (1.1)$$

where B is damping, K is stiffness, m is segment mass, L is segment length θ is the angle and VT represents the virtual trajectory. Preceding work in our lab has utilized this definition to develop an optimization model that can be utilized to extract the K, B and VT parameters from the recorded PKD data [22]. Unfortunately, from previous experience

utilizing this approach, it is more applicable to non-disabled and spastic trajectories, considering these two classifications resemble a damped pendulum more closely than the alternative classification of dystonic or mixed cases. It has struggled to optimize the random trajectory of a dystonic individual's leg. Previous studies from our lab attempted to overcome this by focusing on the first portion of the oscillations which appear more cyclical. While this is similar to the relaxation index and may give some insight into knee stiffness, it does not take into account the rest of the trajectory. Therefore, this study demonstrates use of a novel assessment in conjunction with the relaxation index to establish whether or not the individual has a combination of spasticity and dystonia. It also aids in the determination of an individual's potential to benefit from the proposed stimulation techniques. This assessment is a measure of the distance traveled by the shank over the duration of the leg swing during a PKD.

1.4 Vestibular System Contribution to Muscle Tone

These objective measures are necessary to determine the effectiveness of a therapy on reductions of muscle tone, especially experimental or new exploratory treatments. In addition, to the therapies discussed above, vestibular stimulation (VS) has been linked to promising changes in knee spasticity [23-26], fine motor skills and grip strength [27]. This study builds upon the findings of recent dissertation work investigating the effects of vestibular stimulation in children with cerebral palsy [28]. The same chair stimulation apparatus was utilized to deliver 2 Hz oscillations with an amplitude of 2.5 inches to the seated subject. The target is the otolith organs of the vestibular system, which sense vertical accelerations and contribute to setting the muscle tone of the anti-gravity muscles [11, 29,

30]. Delivering these oscillations alters the firing pattern of the nerve at the base of the otoliths and thus alters muscle tone. Fifteen minutes of these high amplitude, low frequency vertical movements (referred to as vestibular stimulation) showed significant decreases in knee stiffness and damping in spastic participants, but did not contribute to the reduction of co-contraction in dystonic individuals [25]. This can be explained since vestibular stimulation increases corticospinal tract inhibition. Those who had a combination of the manifestations experienced some minor change in the shape of their pendulum knee swing, but the shank locking up due to dystonic co-contraction overshadowed the changes in all other parameters.

1.5 Whole Body Vibration Therapy

In an attempt to address that issue, a literature search showed that significant work has been done as per the applications of Whole Body Vibration (WBV) in disabled and non-disabled populations [31-33]. It is a relatively new approach in therapy, sports medicine as well as routine training. The underlying mechanism involves the activation of the muscle-tendon complex and spindle fibers. By applying high-frequency and low-amplitude vibrations to the body, the target muscles quickly lengthen and shorten. This change in length is sensed by the spindles which cause local reflexes to occur. This may prove beneficial to individuals who experience both spasticity and dystonia.

Non-disabled populations have reported some increases in muscle strength and bone density [34-36] as well as balance [36] and blood flow. It was also noted that healthy individuals do not benefit from short term stimulations, but only show improvement with prolonged exposure [37]. Similarly, disabled populations also benefitted from vibration;

Ahlborg et al. showed reductions in spasticity but not in motor function through a timed walking task in cerebral palsy adults [38]. Chan et al. reported significant improvements in the Ashworth scale as well as gait velocity in stroke patients even after a single session of training [39]. Ibrahim and Ko observed changes in walking speed and stride length [40, 41]. Lastly, Ness et al conducted a study where spinal cord injury (SCI) adults also experienced a reduction in spasticity [42]. This study in particular was of interest since it claims to target the reflex triggered muscle activity associated with SCI. It is important to note that the pendulum knee trajectory which was presented as spastic is extremely similar to the dystonic knee trajectory observed in our previous study. This was a promising observation that whole body vibration may have positive effects on dystonia when applied to our target population of dystonic-spastic CP.

1.6 Overview of Study Direction

The main goal of this work was to combine stimulations for the two sensory systems described above (muscle spindles and vestibular system) in a single session of therapy. These two stimulations are whole body vibration and vestibular stimulation, which were applied in that order. There are additional voids in movement disorders research that were identified and addressed by this study. Namely, a lack of objective measures to differentiate between the source of body stiffness or tone (spasticity vs dystonia) and the ability to use such objective measures to identify the appropriate therapy for an individual; leading to the application of vestibular stimulation for reductions in spasticity and whole body vibration for symptoms of dystonia.

By identifying the objective measures for correctly labeling the manifestations of CP, recruiting subjects is more accurate and consistent and may shed light on the reason why some studied have reported inconsistent results. Once a classification is made, an accurate therapeutic approach can be implemented; we hypothesized that the spastic-dystonic classification of movement disorders will benefit most from the proposed combination treatment of WBV and VS. Data collected was assessed using those same objective biomechanics measures of passive and active tasks, while incorporating a novel and never before used assessment of distance traveled by the shank during let swing. This will be referred to as the Involuntary Muscle Tone Index (IMT index).

Additionally, in comparison to similar work, this study utilized and explored a larger number of outcome parameters to determine the advantages of the proposed therapeutic technique. This pilot study provides insight into the benefits of the proposed combination therapy, and lays the foundation for larger studies in the future. Additionally, it identifies objective assessment parameters that may help bridge the gap between clinical assessment and research classification of movement disorders in CP.

CHAPTER 2

HYPOTHESIS AND AIMS

This study is multifaceted and serves as a pilot investigation contributing to the disabled population and the rehabilitation research communities. This study identifies and remediates recruitment and classification issues identified in similar studies, addresses the lack of robust objective clinical measures, while simultaneously investigating the effectiveness of a combination therapy that lays the groundwork for subsequent standalone and interdisciplinary studies. The therapy being investigated is a two-part intervention with two unique stimulation techniques that targeted the muscle spindles and vestibular system separately. We hypothesize that individuals with spastic-dystonic cerebral palsy will respond positively to receiving a single session of combined stimulation (Whole Body Vibration followed by Vestibular Stimulation). Specifically, we observed changes in the passive and active measures of the movement disorders:

- Participants of this study who have spastic-dystonic CP will experience an increase in relaxation index and decrease in IMT index of shank trajectory travel.
- Participants of this study who have spastic-dystonic CP will experience an increase in stride length, walking speed and step trajectory consistency.
- A single subject pilot aim will demonstrate that this combined stimulation approach improves motor function (voluntary movement error) and reaction time in individuals with spastic-dystonic CP.

2.1 Specific Aims

Specific Aim 1: To determine the effectiveness of Whole Body Vibration and Vestibular Stimulation in reducing passive manifestations of dystonia and spasticity. Assessments: passive PKD parameters including relaxation index and IMT Index. (N=7)

Hypothesis: Relaxation index will increase and Involuntary Muscle Tone Index will decrease after administration of a single session of whole body vibration immediately followed by a single session of vestibular stimulation.

Specific Aim 2: To determine the change in motor function parameters of spasticity and dystonia in individuals with CP after receiving whole body vibration and vestibular stimulation in succession. Assessment: self-regulated walking which includes walking speed, stride length and trajectory variability of gait (N=6)

Hypothesis: The subject will experience improved motor control manifested in increased walking speed, longer strides and more consistent step trajectories immediately after receiving a single session of the combined therapeutic modality.

Specific Aim 3: To determine the feasibility of utilizing goal-oriented intentional shank movements as an assessment of change in motor function in individuals with CP after receiving whole body vibration and vestibular stimulation in succession. Assessments: intentional shank movement which includes distance to target error and response time. (N=4)

Hypothesis: The subject will experience increased motor control manifested in improved shank target tracking. Data will show decreased distance-to-target error and a decrease in response time.

2.2 Specific Aim 1: Effect of Combined Therapy (WBV+VS)

This phase of the investigation quantifies the changes in passive parameters as a result of the novel combination of stimulations. By applying whole body vibration and overcoming the participant's dystonia, the therapy cannot stop there because the underlying spasticity still exists. Therefore, vestibular stimulation was applied immediately afterward to reduce the spastic muscle tone. These reductions were quantified by changes in joint properties as detected by the PKD test. We hypothesized that baseline PKD will show the shank locking up as a result of co-contraction with underlying spasticity. After WBV is administered, the trajectory will appear much more like traditional spasticity and VS will further increase the leg oscillation amplitude. These changes were quantified in the form of a relaxation index in conjunction with a measure of distance traveled by the shank, referred to as the Involuntary Muscle Tone Index. This combination is more indicative of changes to the overall trajectory of the pendulum knee drop than the relaxation index alone.

Specific aim one serves to determine the feasibility of the proposed approach. One adult subject that participated in previous studies was invited back. He was chosen based on the criteria that his previous data showed signs of dystonia. To build upon and enhance the scientific significance of the previous study, the participant received both modalities of stimulation in succession. In addition, this portion of the study included an assessment of functional changes in addition to the passive PKD assessment that was also utilized in the previous study. Therefore, the battery of tests consists of a PKD assessment followed by a static balance on a force plate.

This approach was beneficial in that this participant's ability to articulate discomfort or necessary changes was exceptional. It was therefore a tremendous resource

to understand what needed to be addressed in the study design to maximize participant comfort and safety. Additionally, equipment compatibility and unforeseen issues with user body structure and varying motor abilities could be addressed (i.e. height of stimulation chair and ability to mount and dismount unassisted).

Upon completion of this single subject pilot, three non-disabled age-matched teens received the therapy and their data assessed to serve as controls. Three age matched individuals with Cerebral Palsy were also recruited for the same protocol upon giving signed consent. The procedure is as follows:

Figure 2.1 Study design for specific aim 1.

The protocol was established based on the feedback, findings and experience with the adult subject, and necessary changes were made to the approach to provide more meaningful assessments. These changes include recruiting from a different age group, utilizing newer, more accurate and more compatible equipment, as well as rethinking motor assessments. Lastly, since the sessions ran over 3 hours, the 45-minute retention test becoming increasingly difficult to justify for the sake of the subject's comfort.

Since there are no cures for the movement disorders associated with cerebral palsy, most techniques are aimed at life-long management of the disability. Therefore, this aim targets achieving a temporary reduction in symptoms to reduce discomfort, improve mobility or enable participation in other standard of care therapeutic techniques.

2.3 Specific Aim 2: Changes in Gait Parameters After Therapy

While Specific Aim 1 provides a mathematical representation of knee trajectory and quantifies changes in joint characteristics, these changes may not always translate into meaningful functional gains. In other words, the reduction in dystonia and spasticity may be large enough to allow for physical therapists to administer traditional techniques, but may not improve the subject's walking immediately. To determine the magnitude of these effects, the subject's gait was analyzed for parameters such as step length, walking speed and consistency of step trajectory.

This approach is more thorough that the common gait assessments that are done clinically. This includes the 10-meter walk, 2-minute walk and Timed Up and Go, which are all reliable assessments that are easy to administer, but limited in the information they provide. The proposed technique of using motion capture gait allowed for extraction of specific parameters from the data in order to develop a better understanding of the aspects of motor function that are affected by the stimulation.

We hypothesized that after receiving both stimulations, the CP participants will take longer steps, walk faster and take more consistent steps. The alternative result would be no change in gait and may be due to the fact that gait is very complex set of coordinated movements and a single session may not be enough to overcome poor gait habits learned over the course of the person's lifetime.

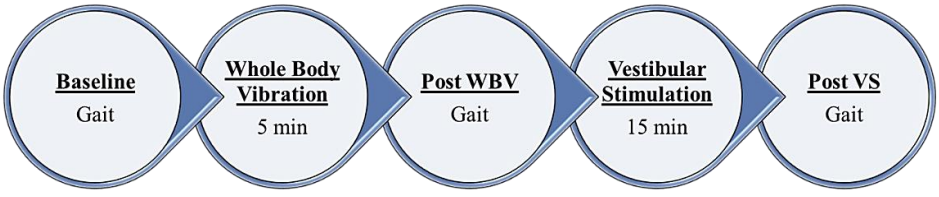


Figure 2.2 Specific Aim 2 protocol.

2.4 Specific Aim 3: Changes in Motor Function and Shank Target Tracking

Considering the complexity of gait and the number of muscle groups that are required to facilitate a change in the gait parameters (stride length and walk speed), it may be difficult to observe changes in performance due to a reduction in tone in a few muscle groups. While Specific Aim 2 is more in depth than a simple timed task by quantifying changes in the steps of a participant, this aim goes one step further and seeks to isolate a single pair of muscle groups (hamstring and quadriceps) to observe changes in motor control in a more controlled environment where other muscle groups will not mask the change.

Therefore, alterations in motor control via isolated intentional lower extremity movements were analyzed. A target bar was placed near the participant's shank and was rotated about an axis mimicking their knee. They were asked to follow along with the movement of the bar. This may give insight into their ability to accurately and effectively isolate, inhibit and control muscle groups to achieve the desired task. The distance from the target and the reaction time to achieve the task were observed. We hypothesized that the individual with CP will exhibit improved target tracking in the form of reduced distance to target as well as a decrease in their reaction time over the course of the entire movement. We did not expect to see changes in the age-matched controls.

Figure 2.3 Specific Aim 3 protocol.

2.5 Novelty and Innovation

To bring the proposed work into perspective, Table 2.1 summarizes how the therapeutic approach and assessments compare to studies of movement disorders:

Table 2.1 Comparison of Study Design to Literature

			Literature			Current Study
			Ness	Ahlborg	Androwis	Michael
Screening	Modified Ashworth			*	*	*
	PKD		*			*
Disability	CP	Spastic	*	*	*	*
		Dystonic				*
Therapy	Vestibular Stimulation				*	*
	Whole Body Vibration		*	*		*
Assessment	PKD	Relaxation Index	*			*
		Involuntary Muscle Tone Index				*
		Optimization			*	
	Active Shank Movement					*
	Walking	Speed	*	*		*
		Stride Length	*			*
		Gait Variability				*

CHAPTER 3

METHODOLOGY

3.1 Research Design Overview

Four individuals with CP and three age matched controls were recruited to participate in this study. The stimulation portion of the investigation consists of a combination of two techniques (whole body vibration and vestibular stimulation) which were applied in succession within the same session. Assessments of changes in passive and active motor function were collected before and after each stimulation. Figure 3.1 summarizes the progression of the session for each of the participants. Assessment portions are highlighted in red and the battery of tests that was administered is listed below each. The two stimulation techniques are indicated in green, no data was collected while the subject was receiving the stimulation. Data collected is indicated in blue.

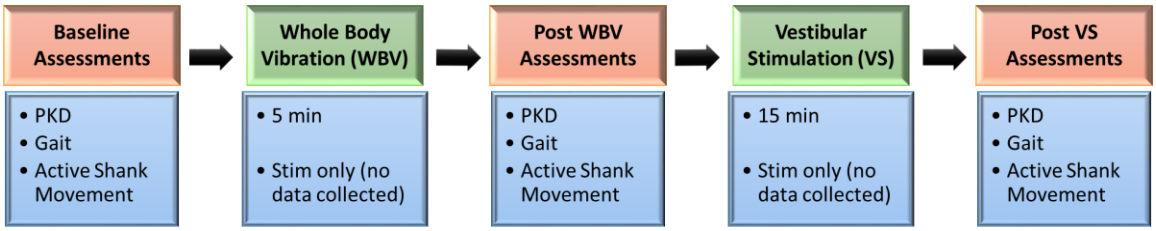


Figure 3.1 Summary of study progression.

3.2 Recruitment and Participants

This study was approved by the New Jersey Institute of Technology Institutional Review Board (IRB) under project protocol 272-16 and was renewed on a yearly basis. The approved procedure begins with informed consent for the older participant and ascent (with

parental consent) for the remainder of the subjects. It is important to note that since this study is pilot work and has never been implemented in this manner, there were approved changes made to the protocol to accommodate for unforeseen issues and concerns. The first participant was a 35-year-old male with CP who was a subject in previous studies conducted in our lab. He was a great candidate for this study considering he was dystonic-spastic, he met all inclusion criteria and agreed to provide feedback to make the study more thorough and comfortable for the young adults that would participate after him.

The six participants that were recruited after him were recommended to us by collaborating physicians who gave clearance to participate. They had an average age of 13.17 ± 0.98 years and were all accompanied by a parent or legal guardian. Three of these subjects are non-disabled controls and three showed the presence of spastic-dystonic CP.

Approved exclusion criteria apply to individuals who: 1) cannot stand on their own with minimal support, 2) have had major surgery or bone implants recently and is still recovering, 3) have spinal disk problems, 4) is prone to motion sickness, 4) is recovering from a severe leg injury, 5) weighs more than 300 lbs. or 6) are pregnant.

Table 3.1 Demographics of Participants in the Study

Study Group	Age	Gender
Control	14	F
	14	M
	12	F
Movement Disorder (CP)	35	M
	13	F
	14	F
	12	M

3.3 Protocol

Before detailing the protocol used, it is important to address the changes that were made based on our single subject pilot, discussed above. In conducting literature searches, movement disorder studies were investigating changes in either balance or gait in CP, and due to equipment constraints our initial protocol was designed to use balance as a measure of functional improvement. He was asked to stand on a force plate quietly and maintain his balance for as long as possible before needing to reach out and grab onto the surrounding support bars. When he stepped onto the force plate and let go of the safety rail, the timer began. He eventually began to sway enough and lost balance, thus reaching out and holding onto the bars, this time is recorded. The length of time he stood quietly without reaching for the bar was investigated to see if any changes in muscle activity or motor control as a result of stimulation affected his ability to maintain balance.

This assessment was done at baseline, post WBV and post VS, with each time point being repeated three times. Upon collecting and observing the data, we became skeptical that this method of investigating motor function was reliable, as discussed in later sections. After this subject had completed the session, the protocol was revised to include gait instead of balance and the revised version was also approved by NJIT's IRB committee. Figure 3.1 above represents the most recent iteration of the protocol.

The revised data collection session also began with informed consent, where all procedures and risks were verbally communicated with the participant and all equipment was demonstrated to ensure safety. The subject was then asked to provide both verbal and written consent as well as demonstrate understanding of the procedure and safety protocol. The session began by recording the subject's weight and height. Immediately afterwards,

baseline assessment was conducted, which included a battery of three measures (a pendulum knee drop, followed by self-regulated gait and lastly an active shank movement tracking a moving target).

Upon completion, the participant was prepared to begin receiving the first stimulation (whole body vibration). All wires were detached to avoid a tripping hazard and the subject was asked to stand up from the assessment chair (assistance was provided) and step onto the whole body vibration platform. Five minutes of stimulation was delivered in one minute intervals, with one minute rests in between. Immediately afterwards, they underwent the same battery of three assessments discussed above, starting with gait.

Adjacent to the vibrating platform is the vestibular stimulation chair, which is elevated and doubles for use during the pendulum knee drop assessments. Once the WBV portion of the study is completed and the post WBV gait data is collected, the participant was transferred to the vestibular chair where they were strapped in and the equipment reattached (force transducer, EMG electrodes and TrackStar). The PKD procedure was then repeated. After completion of all "Post WBV" assessment, vestibular stimulation began. This consisted of a 15-minute session where the chair and person were oscillated in the vertical direction at a rate of 2 Hz with an amplitude of 2.5 inches. This procedure is consistent with previous studies conducted in our lab [23, 25, 28, 32].

Upon completion of vestibular stimulation, the "Post VS" assessment was conducted. This PKD and active shank movement were conducted first since the subject was already in a seated position. The equipment was again detached for safety and the participant dismounted the chair and proceed to do the gait potion of the assessment. This completed the data collection session.

3.4 Equipment Used and Data Collected

3.4.1 Whole Body Vibration Platform

A platform comparable to those mentioned in a WBV literature review [43] was used. The device was purchased from DKN, a leading provider of vibrating platforms, and this specific model was their top of the line XG-10. This particular model can be programed to deliver vibrations ranging from 20 to 50 Hz with amplitudes between 2 and 4 mm. The subject received a single session of whole body vibration therapy, which consisted of five-one minute vibrations with four-one minute seated rests in between [42, 44, 45]. As discussed in similar published works, the frequency was set to 30 Hz, which provides an amplitude of 2.4 mm. To target the lower extremity muscles (hamstring and quadriceps) the subject was asked to perform a shallow squat which causes a slight activation in the thigh muscles. This is necessary for proper delivery of the stimulation as it relies on the muscle spindles being slightly contracted, where they are most susceptible to sensing and firing due to external vibrations. The vibrating platform had a chair positioned behind it to allow the participant to sit down during the prescribed rest periods without having to dismount from the platform (see Figure 3.2 below).

Figure 3.2 The XG-10 model vibrating platform (manufactured by DKN) and a representation of the whole body vibration protocol: a squatted stance during stimulation followed by seated rest (repeated five times)

3.4.2 Vestibular Stimulation Chair

The vestibular stimulation device was custom built in our lab and is pneumatically actuated [26]. The top seat portion is from a commercially available medical grade chair designed for individuals with disabilities. A very wide and sturdy metal base was fabricated (see Figure 3.3 left panel) and actuation is achieved by four heavy duty air pistons located under each corner. The pistons were driven by two MedAir brand medical grade compressors operating jointly. A combination of the pressure output and valve timing controls the rate of rise and fall of the chair and presets were developed to accommodate for each subject weight within our IRB approved range. The target frequency across all subjects was 2 Hz, since our previous studies have shown that this has the largest effect on spasticity [26, 28, 32, 46]. The subject's weight was recorded at the beginning of the session so that the appropriate changes could be made to the control code to ensure proper operation. Once the setup is complete the subject is asked to sit in the chair, and the attached harnesses were used to strap them in at the chest and hip levels. An additional leg constraint harness was built as a precaution to ensure the subject's legs were slightly extended out in front of them and did not get caught in the mechanism during the vertical oscillations.

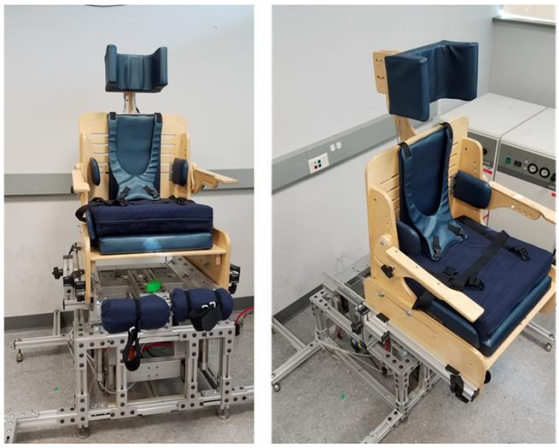


Figure 3.3 Vestibular stimulation chair in the stimulation position (left) and pulled forward for administering the PKD (right).

3.4.3 Pendulum Knee Drop

In order to properly conduct the pendulum knee drop test, the subject's feet may not touch the ground and they must be seated on a chair or table that has open space underneath for the subject's leg to swing under them without being impeded. The vestibular stimulation chair was modified to serve this purpose. The top chair portion could be pulled forward (see figure above) to enable administration of the PKD leg swing, and then pushed back onto the base during stimulation. Setup for this assessment included assisting the subject into the elevated chair, strapping them in to the harness, pulling the chair forward once they were secured, locking it in place and attaching the instruments needed to collect the data. This setup was the same for each of the three time points of collection (baseline, post whole body vibration and post vestibular stimulation).

The equipment used targeted three key features of the leg swing, namely: the location of the shank in space, the force being exerted on the shank by the experimenter and muscle activity in the hamstring and quadriceps muscles. In the earlier stages of this study, the trajectory of the shank was recorded using Ascension Technology's TrackStar system. This consists of a transmitter outputting electromagnetic signals and a receiver that senses them. The way the sensor interacts with the emitted field allows the system to calculate the location and orientation of the sensor in space with respect to the transmitter. This is a 6 degree of freedom spatial tracking system with a long track record of accuracy. However, there are three significant drawbacks: (1) it's limited to a one-meter recording volume, (2) ensuring that the transmitter is not accidentally moved and (3) the emitted electromagnetic field interferes with other equipment. It was inevitable that the transmitter would be moved while the experimenter and the subject were moving around, meaning that

the calibration protocol had to be executed before each trial was recorder. This posed an issue with length of the session overall. Through the course of this study, newer technologies became available to us and the pendulum knee drop was migrated to an infrared camera based motion tracking system. This was initially an 8 camera setup and was expanded to its current state of 16 cameras.

Additional equipment included an OptoForce 3 degree of freedom force sensor attached to the subject's shank. A housing was manufactured for the force sensor, allowing the experimenter to grab a hold of it and pull the subject's leg up using it. The force applied was recorded and was used to determine the release point at the initiation of the PKD.

Lastly, a wired Delsys electromyography (EMG) system was used to record lower extremity muscle activity, namely from the hamstring and quadriceps muscles. Disposable surface EMG electrodes were placed on each of the two muscles of interest with the reference electrode on the patella (all subjects were asked to wear shorts).

Once the setup was complete, the subject was asked to relax and not intervene in the knee swing. The force sensor was used to lift the shank to extension and released to initiate the PKD, during which, force, EMG and position data were all recorded. The trajectory data was analyzed using the relaxation index, also referred to as a first swing excursion (FSE) parameter, to measure the change in the size of the first peak from the knee drop [42].

3.4.4 Need for an Additional Objective Measure - Involuntary Muscle Tone Index

The first inflection point used by the relaxation index does not encompass all data in the PKD. Therefore, the Involuntary Muscle Tone Index is a novel assessment that was proposed and investigated to fill this void. It is an additional objective measure to be

utilized alongside the relaxation index for a complete description of the PKD trajectory and leads to the incorporation of data that may not be utilized otherwise.

The data in Figure 3.4 below demonstrates this by presenting the three main categories of PKD trajectory that are expected in the target population. Panel A is representative of the pendulum knee drop trajectory of a CP individual who exhibits both spasticity and dystonia, panel B is indicative of spastic CP and panel C is representative of an individual with unimpaired motor control.

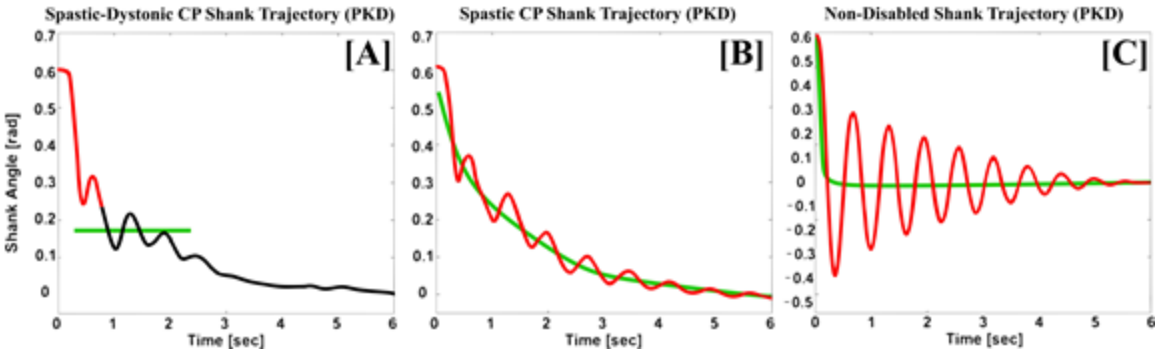


Figure 3.4 PKD shank trajectory for (A) Spastic-Dystonic CP, (B) Spastic CP and (C) Non-Disabled individuals.

Individuals with spastic-dystonic CP may exhibit co-contraction due to the dystonia (panel A) which can be identified as a short period of time where the leg locks up and oscillates about an angle greater than zero (denoted by the green horizontal line). This is followed by a slow drift down to the vertical resting position. An individual who is spastic exhibits bursts of reflexes as the leg descends during the PKD and the trajectory in panel B is very indicative of this phenomenon. Unlike the dystonic case, the oscillations appear to be centered about a second order polynomial descending towards zero (denoted by the green line). Lastly, in the case of a healthy subject (panel C) the oscillations are significantly larger and occur about an exponential curve decaying instantly to zero. This

suggests that there are no forces being exerted by muscle reflexes and that full range of motion of the leg is being used.

As discussed in chapter one, there are several mathematical ways to analyze and quantify the trajectory, but in doing so, the shortcomings of these commonly used analysis techniques is apparent. The most widely used objective measure extracted from the PKD is the relaxation index. It quantifies the amplitude of the first drop normalized to the angle from which the leg is released. While it can be applied to all three data sets, it does not encompass all the data from the shank oscillations. Alternatively, the optimization model does provide a comprehensive analysis, but can only be applied to the regions highlighted in red. Its limitation is that it relies on the trajectory resembling a damped pendulum. In the case of spastic-dystonic (which was our target population), this method provides an outcome identical to the relaxation index and offers no additional benefit. The shortcomings of these two approaches lead to the development and implementation of the Involuntary Muscle Tone Index, a new approach of extracting additional information from the remaining PKD trajectory.

3.4.5 Calculating the Involuntary Muscle Tone (IMT) Index

The Involuntary Muscle Tone (IMT) Index measures the distance traveled by the shank during critical portions of the leg swing, and accounts for both the oscillation frequency and amplitude. Visually, our ability to determine the source of tone from the PKD can be derived from the three distinct portions that exist within each shank trajectory. They are the initial drop, the oscillations phase and the rest period after the shank stops oscillating. Since the amplitude of the initial drop is accounted for by the relaxation index, the latter

two portions are the ones of interest. The figure below is representative of spastic CP and illustrates how each data set will be separated into the individual sections of interest.

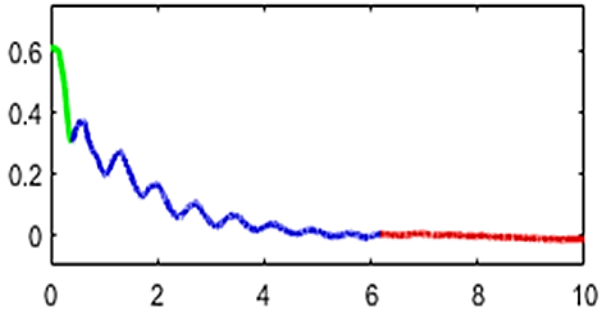


Figure 3.5 PKD trajectory of an individuals with spastic CP. Individual sections of interest are separated and colored. Initial drop in green, oscillation phase in blue and the resting phase after oscillations in red.

For this study, each IMT index was calculated utilizing ten seconds of PKD data. The onset of the drop was defined as the moment the experimenter released the shank and was determined using the reading of the force sensor used to lift the leg. A ten second window beyond this point provided ample time for the individual's shank to come to rest. Considering that each CP subject's PKD trajectory varied in shape, any offset in the resting angle (due to limited range of motion) was removed and the data was sectioned manually as seen in Figure 3.5. A Matlab code was used to compute the distance traveled during each section and the IMT index was calculated as the ratio of resting distance (blue) divided by the oscillation distance (red).

In a non-disabled individual, a majority of the distance travelled occurs during the oscillations phase, and since the shank comes to rest at zero degrees, there's very small additional change that occurs after the oscillations stop. Similarly, spasticity also exhibits this phenomenon of coming to rest at zero, but since the oscillations are smaller in amplitude, the ratio is expected to be larger than in the control group. Lastly, the trademark

characteristic of dystonic co-contraction is the locking of the limb during the oscillations, followed by the slow drift towards zero (see Figure 3.4A). This translates to a larger Involuntary Muscle Tone Index due to the contribution from the third section of the trajectory (shown in red).

Applying this to the data set in this study yielded promising results that coincided with the observations we made regarding the trajectories. The small short-lived oscillations of dystonia resulted in a larger Involuntary Muscle Tone Index when compared to the spastic trajectory. The same occurred when comparing spastic CP to non-disabled individuals. Combining this measure with the relaxation index fills a major void in conducting a complete analysis and quantifying the changes in spasticity and dystonia hypothesized in this study. Future implementations of this technique will utilize an increase in relaxation index and a decrease in Involuntary Muscle Tone Index as an indicator of the participant responding positively to the stimulation or therapeutic approach.

3.4.5 Gait

Initially, balance was used as a measure of motor functional improvement. Shortcomings of this approach (discussed in a later section) lead to the use of gait instead. Gait is a complex task, and provides multiple parameters that can be analyzed for change. This includes walking speed, stride length and smoothness of movement.

To accomplish this assessment, the infrared motion tracking camera system was utilized to track the subject's feet in space. The participant was asked to walk up and down the gait lab track while the cameras recorded their position. Recording occurred at baseline and after each of the tow stimulations to observe whether or not there is any change in motor function. This approach provides more information than the standard time up and go

and six minute walk [38, 39] tests that do not provide specific information but rather rely on a simple timed event.

Walking speed was calculated from the overall distance covered during each walk. Each subject had an average of approximately 5 round trips along the gait track. Stride length was calculated based on heel strikes. Impact with the ground signaled the start and end of each step, and the distance covered was calculated. These start and end points of each step were also used to superimpose all of the subject's step trajectories for each condition. The steps were then normalized to 100% of the gait cycle and the means and standard deviations were calculated over the course of each step. This enabled us to visualize the consistency of the subject's steps for each condition.

3.4.6 Voluntary Shank Movement

The active shank movement task is a seated assessment of intentional movements. While the complexity of gait may mask changes in lower extremity muscle activity, this task isolated for subject's ability to generate controlled movements in a meaningful manner. A rotating bar was placed alongside the seated subject's shank and its pivot point was designed to lie in line with the knee. Rotation of this target bar created an arc mimicking that of the subject's shank. The target bar and the subject's shank were both marked with infrared reflective markers and their positions in space was recorded during the course of the trial.

The experimenter moved this bar through an attainable shank range of motion, alternating flexions and extensions. The subject was asked to follow the movement of the bar as quickly and accurately as they could. This assessment was conducted at baseline, after whole body vibration and after vestibular stimulation. The measures that were

extracted are distance to target and reaction time. The difference in angle between the desired target position and the location of the subject's shank is reported as the error. In CP subjects their ability to reach full extension is limited and manifests as larger errors due to a lack of full range of motion. Therefore, a reduction in the angle error suggests an increase in the range of motion of the shank. Reaction time is calculated from the delay of subject movement with respect to the target since they were asked to move simultaneously with the target. This measure is reported in milliseconds and may signify a change in ability to generate a motor signal and execute it effectively.

CHAPTER 4

PILOT DATA NOT APPLICABLE TO AIMS

4.1 Shortcomings of Balance as a Functional Measure

During the initial phase of the study, the protocol was designed to incorporate a balance task to observe motor function changes. CP Subject 1 was recruited to participate. The assessment was conducted at baseline, then after the combined therapy (whole body vibration followed by vestibular stimulation) and an additional time after a wait period of 45 minutes. This is referred to as “retention”.

Since the goal of this study is to maximize the effects of the novel application of the two therapies, the balance testing was not included in the middle portion between the two techniques. Since it is a very involved and lengthy process where the subject must leave the area near the stimulation devices and walk over to the gait track to stand on the force plates, the best course of action was to not interrupt the stimulation and minimize the time between administering the two modalities.

Initially, the data below appeared promising in that their ability to balance increases after receiving therapy (from 8 seconds to 13 seconds) and seems to gradually be returning towards their baseline ability after 45 minutes (able to balance for 10 seconds):

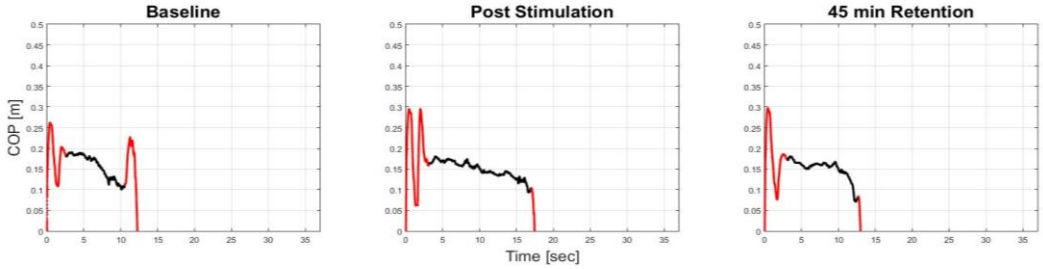


Figure 4.1 Balance task (CP Subject 1).

However, upon further inspection, there appears to be another phenomenon that overshadows this change. This may be explained by the participant using the first two balance attempts to explore techniques or becoming accustomed to balancing. By the third attempt, there is a drastic increase in their ability to stand quietly and maintain balance. This is unrelated to which phase of the study the assessment is conducted, and without the ability to determine the source of change, balance was therefore re-evaluated as a viable measure in this specific application. In future studies, and with more resources, balance measurements should be implemented with perturbation. This will enable observation of a participant's ability to react to random applications of force may be a more scientifically sound approach.

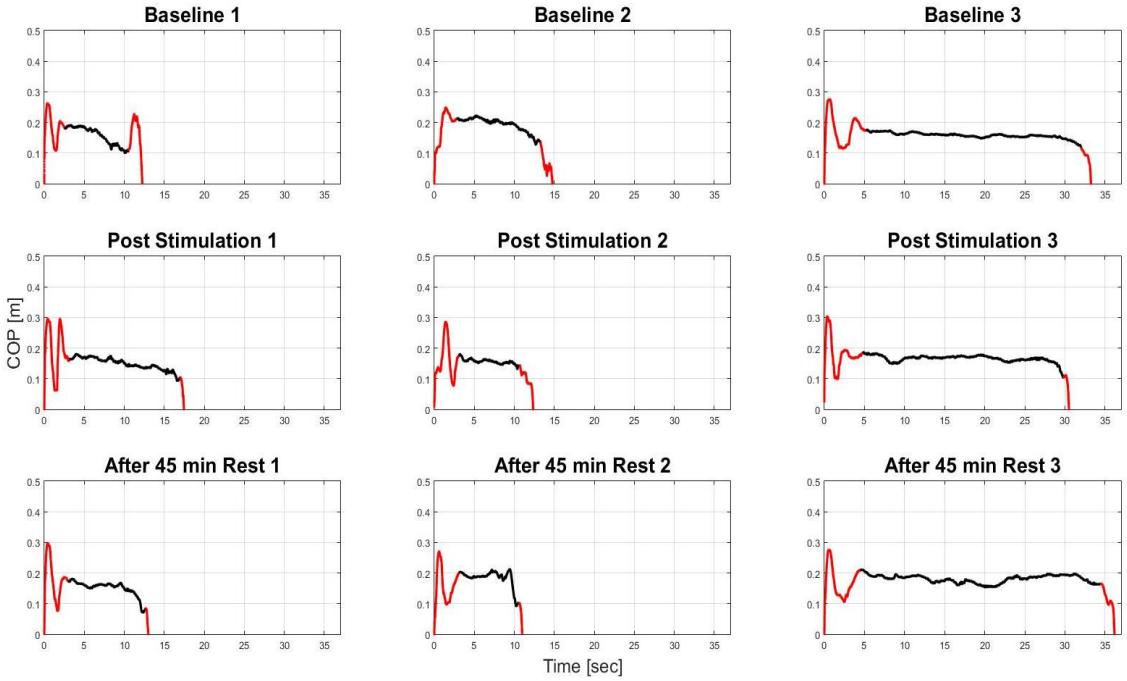


Figure 4.2 All trials of balance task (CP Subject 1).

Future data collection sessions were altered keeping this in mind. A new IRB was drafted and approved to utilize gait parameters as the measure for functional improvements in Specific Aim 2. As described above, the participant's feet were tracked in space as they walked up and down the gait track at a self-regulated speed during the allotted time.

4.2 Rare Movement Disorder, Not the Intended Target (CP Subject 2)

Subject number two is a 13-year-old female who was referred by her physician to be the first participant in the revised study. The pendulum knee drop data presented below (Figure 4.3) demonstrates a lack of oscillations that are present in both healthy participants and those with movement disorders, indicating that the knee joint is severely overdamped. Upon the completion of the study, further investigation was conducted in an attempt to understand the discrepancy. It turns out that she has Hemimegalencephaly (HME) which is a very rare condition of unknown prevalence. This condition is a result of one side of the brain being abnormally large and thereby causing manifestations of movement disorders among many other complications such as seizures and spasms. There is a lack of literature that has applied the pendulum knee drop to individuals with HME, therefore, the underlying mechanism by which an individual can exhibit such a PKD is still unclear.

Relying on the Ashworth scale alone lead her care provider to classify the participant as a candidate for this study under the impression that she presented like a traditional CP patient. While this participant appears rigid and has a gait pattern that may signify movement disorder, her pendulum knee drop does not indicate that she is the spastic-dystonic classification we sought for this study. This discrepancy in the clinical and research classifications of a patient justifies the use of PKD assessments as a recruitment

and eligibility measure in addition to its current purpose of quantifying changes post stimulation.

Her data are presented below and show no significant change across all parameters. She did not exhibit the common features associated with a CP candidate and in fact did not respond like one.

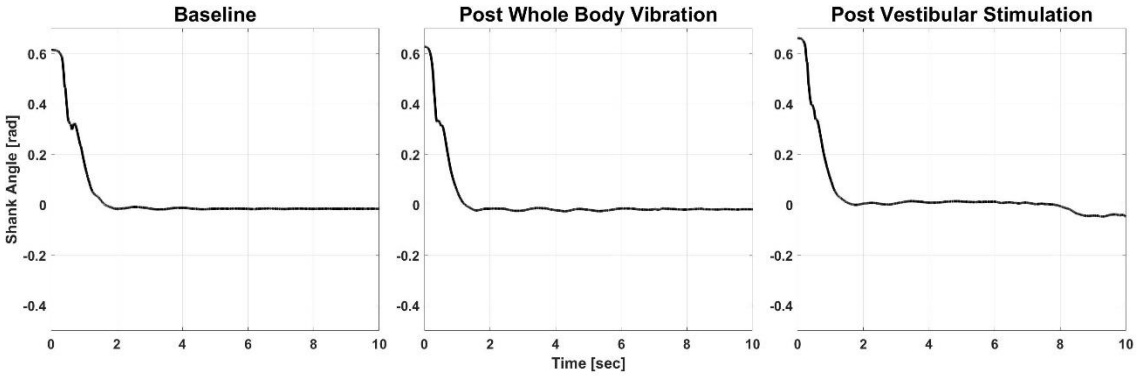


Figure 4.3 Pendulum knee drop trajectory (CP Subject 2).

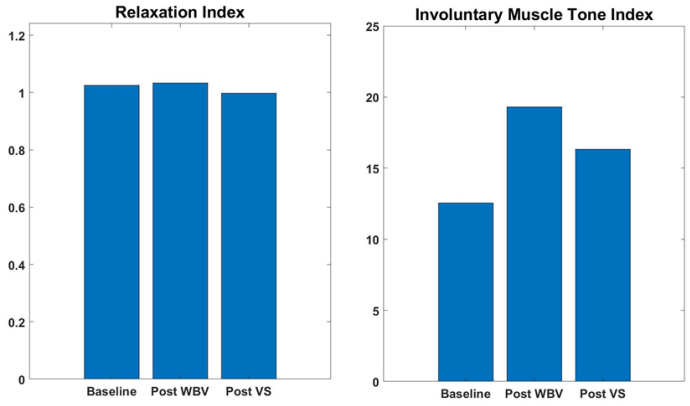


Figure 4.4 Relaxation index and Involuntary Muscle Tone Index (CP Subject 2).

A single PKD assessment was conducted at each time point and relaxation index values are 1.026 at baseline, 1.034 post WBV and 0.998 after both WBV and VS were applied, which are all approximately one (as expected with an inflection point at the resting

angle) and remain unchanged. Additionally, the Involuntary Muscle Tone Index is much larger than in both the control and the CP groups: 12.55 at baseline, 19.32 for post WBV and 16.33 post WBV and VS. This index is expected to remain below one as the distance traveled in a tradition PKD occurs mainly during the oscillation phase, which is not present in this data set. Values in such a far removed range indicate that this subject is an outlier.

Similarly, her gait data (presented below) did not demonstrate any changes or trends as a result of therapy. Her stride lengths averaged 0.538±0.0034 at baseline, 0.506±0.006 post WBV and 0.548±0.006 after both stimulations were complete. Similarly, her walking speed averages remain unchanged with means and standard error of mean at 0.413±0.0053, 0.378±0.0045 and 0.424±0.010. Both of these parameters are drastically lower than her control counterparts. This is expected considering the overdamped nature of her pendulum knee drop trajectory. This would translate into rigid lower extremities that cannot carry out the swings of gait and therefore compensates with short steps, hence the low stride length.

Walking speeds presented here are the averaged speeds of multiple walks along the gait lab track. A lack of change here as well signifies that the therapy did not have any effect on this participant, who, based on baseline PKD, would not be expected to benefit.

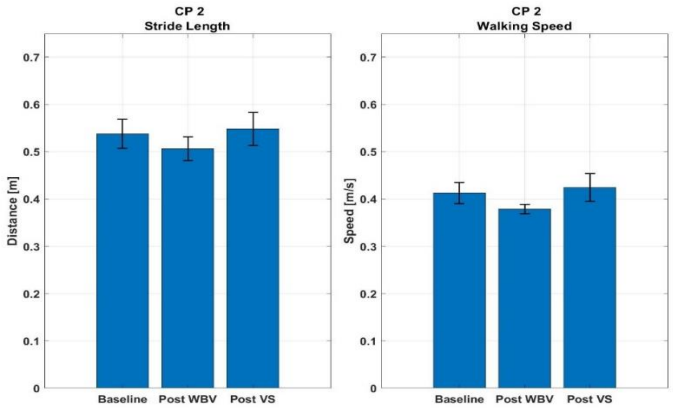


Figure 4.5 Stride length and walk speed (CP subject 2).

Lastly, step variance data show slight fluctuations in value, but are within the expected margin of error as calculated by a 90% confidence interval of control data. This coincides with the earlier findings that this subject did not experience changes in gait.

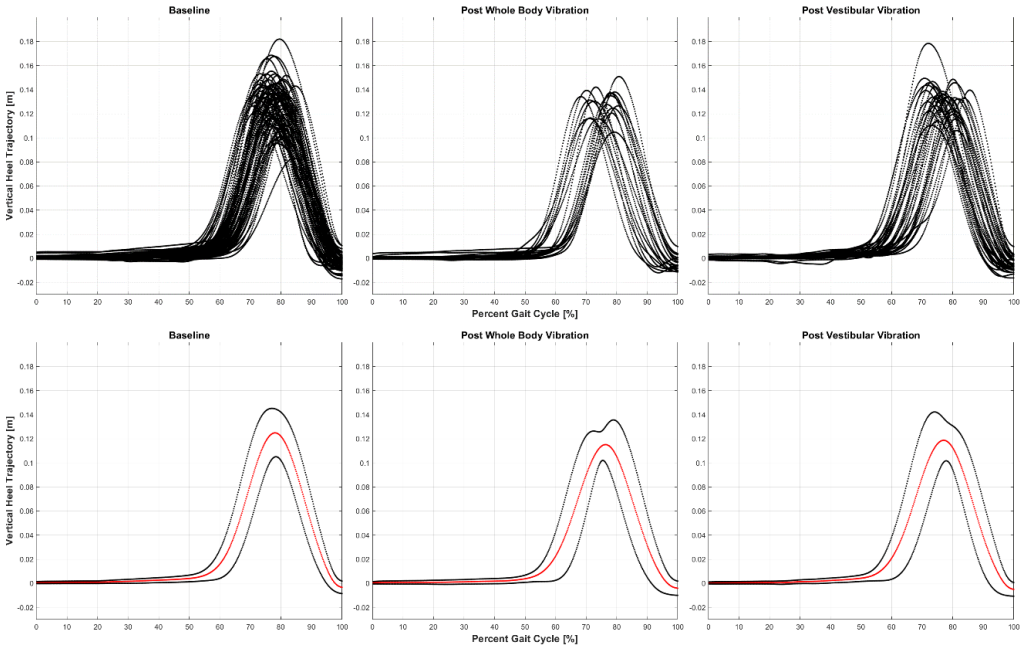


Figure 4.6 Step trajectories (upper panels), mean, mean plus and minus standard deviation (lower panels) in CP Subject 2.

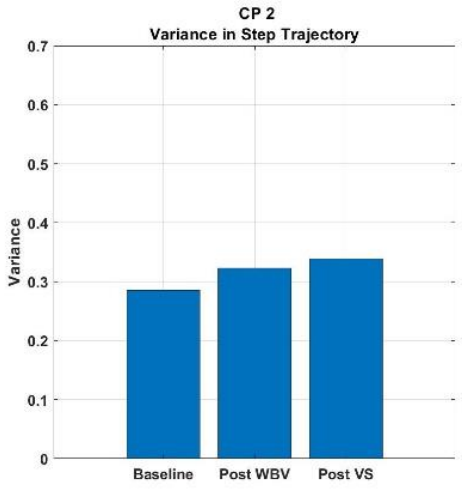


Figure 4.7 Variance of all steps in each condition (CP subject 2).

4.2.1 Pendulum Knee Drop as a Recruitment Parameter

Based on this, future work should take into account the ability to differentiate classifications of CP utilizing the PKD, and to assess whether or not an individual will qualify or benefit from either of the therapies or a combination of both. While this subject's data do not appear to support the hypothesis regarding the effectiveness of the proposed therapies for CP, it is important to note that she is not the target population, and the mechanism by which her condition factors in stimuli from the muscle spindles and vestibular systems was not the target of this study.

Her data serves a crucial purpose in the broader impact of the study and future work in this field. This outcome serves to validate the hypothesis that CP manifestations cannot be reliably classified by subjective measure alone and often prone to incorrect classification between the clinical and research communities. The remainder of subjects recruited for this study were screened for signs of dystonia and spasticity in their PKD trajectory.

CHAPTER 5

SPECIFIC AIM 1 - PASSIVE ASSESSMENT (DATA AND RESULTS)

Control data for Specific Aim 1 was collected from control subjects 1, 2 and 3. Only one data set is presented in this section as it is representative of all three subjects. Additional subject data is included in the appendix. Cerebral Palsy data from the three participants meeting the inclusion criteria is presented here. They are CP subjects 1, 3 and 4. This chapter groups the pendulum knee drop trajectories at baseline and after each of the two stimulations the participant received. Additionally, the calculated values of relaxation index and Involuntary Muscle Tone Index are presented in bar form and well as a set of three values. These values represent baseline, post WBV and post WBV+VS respectively.

5.1 Pendulum Knee Drop (PKD) - Relaxation and Involuntary Muscle Tone Index

5.1.1 Representative Age Matched Control Data (N=3)

Three aged matched teenagers were recruited to serve as the controls for this study. This data set is representative of all three and appears to show no change in trajectory.

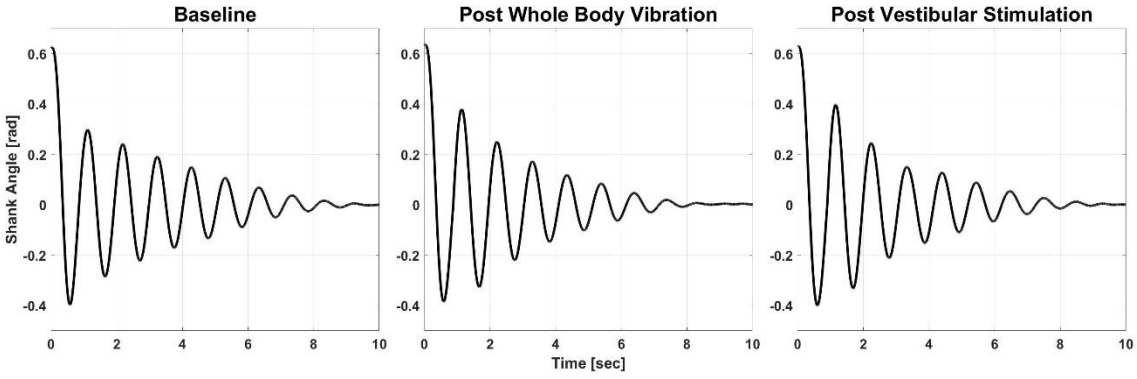


Figure 5.1 Pendulum knee drop trajectory (Control Subject 1).

While subjective measures are not the goal of this study and will not be used to draw any inferences on the effectiveness of the therapeutic technique, it is necessary to observe the shape of the pendulum knee drop and pinpoint certain regions of interest that do contain useful information regarding the validity of the data as well as the participant's motor function. In this case, it is promising to see the final resting angle reaching zero, signifying the ability to relax the knee extensor muscles and allowing the shank to rest vertically. Secondly, the shank trajectory oscillates about zero, meaning the subject's shank was acting like the expected damped pendulum and was not experiencing any unexpected factors that would alter the natural passive trajectory of the shank. Elaborating on this, it is expected that a healthy, non-spastic individual would experience an initial drop that is smaller in magnitude but opposite in sign from the initial holding position (considering that the knee joint contains connective tissue that has inherent viscosity and would dampen the drop). With that this participant exhibits all traits expected in a healthy control.

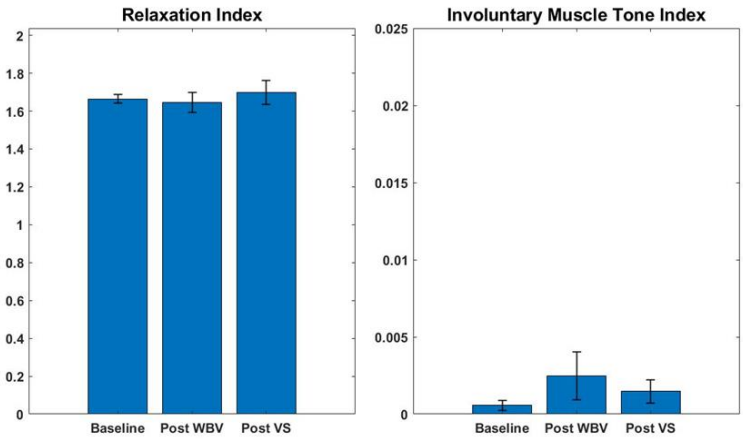


Figure 5.2 Mean relaxation index and involuntary muscle tone index of control data.

The relaxation and Involuntary Muscle Tone Index indices were calculated for baseline, post whole body vibration and post vestibular stimulation in order to quantitatively compare the observations discussed above. Controls exhibited mean

relaxation scores of 1.664, 1.646 and 1.698 at baseline, post WBV and post VS respectively. This range has been reported in other PKD studies and is a good indicator of leg oscillation unhindered by a movement disorder. As expected, within subject values did not change in all three controls, which is due to the lack of spasticity. Similarly, their Involuntary Muscle Tone Index means of 0.0005, 0.0025 and 0.00147 did not experience any major changes. Since this measure has never been implemented, we are using our own control data set to determine the range for healthy controls until a larger study is conducted. The trajectory of the three age-matched controls is very representative of the expected trajectory of healthy individuals and demonstrate a confidence threshold at 0.008, below which, the IMT Index indicates lack of a movement disorder. This index will not be used alone, but rather in conjunction with the relaxation index.

5.1.2 Cerebral Palsy Subject 1 (Pilot)

This participant does indeed qualify to participate as he exhibits dystonic tendencies as evident by the co-contraction that keeps the shank elevated for a short period of time before relaxation and the leg returning to the vertical position (see Figure 5.3, left panel).

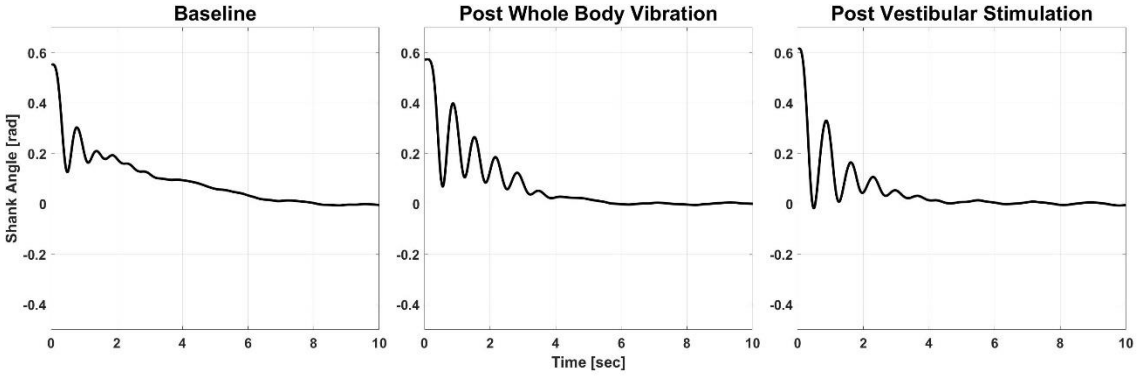


Figure 5.3 Pendulum knee drop trajectory (CP Subject 1).

Upon inspection, these graphs appear promising in that our hypothesis is supported. The participant's dystonia appears to diminish after whole body vibration and resembles the typical shank ratchet associated with spasticity. Our expectations are also met in the right panel, where the participant seems to respond well to vestibular stimulation. With the diminished co-contractions, the reduction of tone as a result of vestibular stimulation has driven the pendulum knee drop to more closely resemble that of the characteristic damped pendulum shape of a non-disabled individual. While the ideal method of assessing change is our optimization model, it relies on a pendulum test that resembles a damped pendulum, which means it works well in the spastic participants and those without disabilities. However, it cannot model trajectories where dystonic co-contraction is present. The equation of a damped pendulum cannot be applied to a shank trajectory that acts sporadically and does not oscillate about zero. Therefore, a combination of the relaxation index and the Involuntary Muscle Tone Index are necessary to fill this void and quantify changes. Relaxation index values are 0.771, 0.879 and 1.030, supporting the observation that there was compounded improvement with each therapy. Similarly, the Involuntary Muscle Tone Index confirms this improvement with values of 0.2656, 0.0445 and 0.066. This represents an 83% reduction after WBV and a 75% reduction after VS.

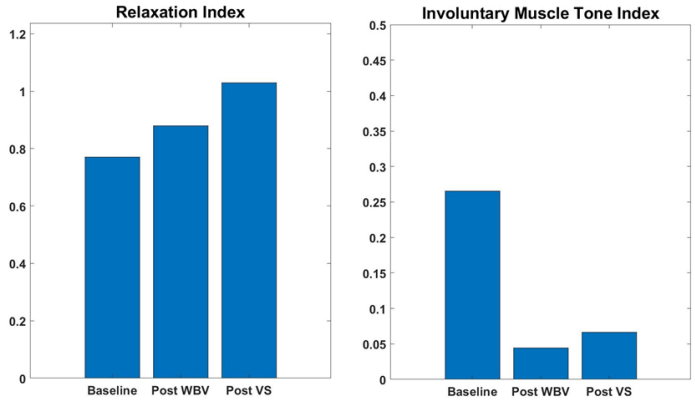


Figure 5.4 Relaxation index and Involuntary Muscle Tone Index (CP Subject 1).

5.1.3 Cerebral Palsy Subject 3

Subject number three is a 14-year-old female with CP. Her baseline PKD trajectories are indicative of the presence of dystonia and spasticity (Figure 5.7, left panel) and therefore qualifies her for the combined therapy. Her relaxation index values were equal to 0.583, 0.523 and 0.750. This is consistent with the visual appearance of the trajectories below, but more importantly demonstrates the need for an additional index to provide objective representation to the remainder of the trajectory past the first inflection point.

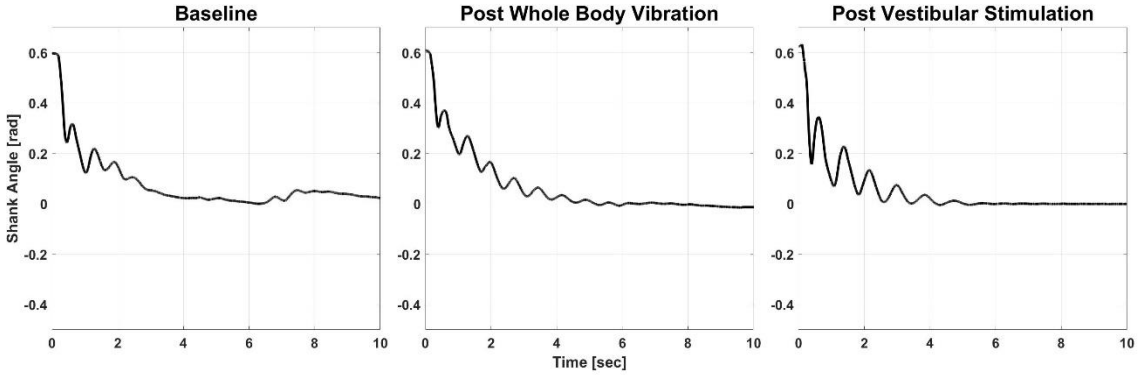


Figure 5.5 Pendulum knee drop trajectory (CP Subject 3).

In other words, the relaxation index alone may indicate that there was a negative change in PKD as a result of whole body vibration, when in fact the elimination of dystonia is demonstrated by the elimination of the shank locking observed at baseline, and replacing it with the spastic ratcheting in the Post WBV plot (middle panel). In this case, the Involuntary Muscle Tone Index shows a counteracting positive change. This can be interpreted as a change in the shape of the curve where no one factor dominates the other. The dystonia was removed, but the spasticity that remained presents with a higher inflection point but longer travel on the swing. It is not until the vestibular stimulation is applied, that this participant reflects the full effect of the therapeutic approach and supports

our hypothesis that the two overlapping conditions must be treated with targeted therapy in this specific order.

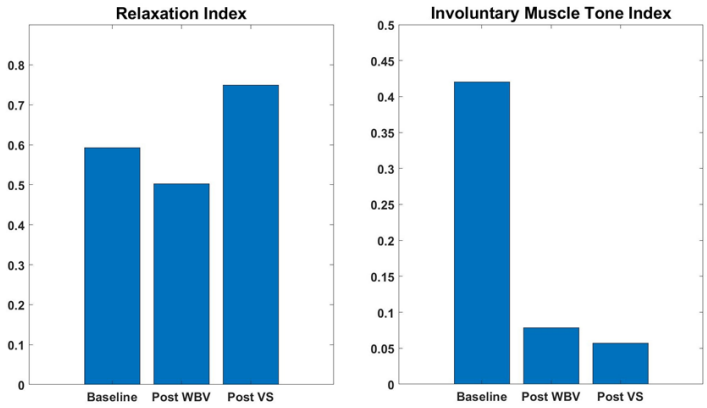


Figure 5.6 Relaxation index and Involuntary Muscle Tone Index (CP Subject 3).

Upon decrease of dystonia with WBV, the underlying spasticity can be targeted and decreased. The resulting Involuntary Muscle Tone Index values are 0.421, 0.0786 and 0.057, representing an 81% and 86% reduction respectively. The largest improvement in both indices was observed at the end of the combined therapies. These data are promising and show a reduction in both dystonia and spasticity. The random movements and shank lock in the baseline have diminished and the leg oscillations are much more consistent and occur with larger amplitudes, indicating a reduction in damping.

5.1.4 Cerebral Palsy Subjects 4

Subject number four is a 12-year-old male with CP. Their data presents most similarly to that of subject three, and interestingly exhibits the inverse issue where only one index does not describe all observed changes. As seen in the PKD trajectory, a larger relaxation index after the first therapy is promising, and the remainder of the trajectory has changed due to elimination of dystonia. This is represented by the decrease in the Involuntary Muscle Tone Index.

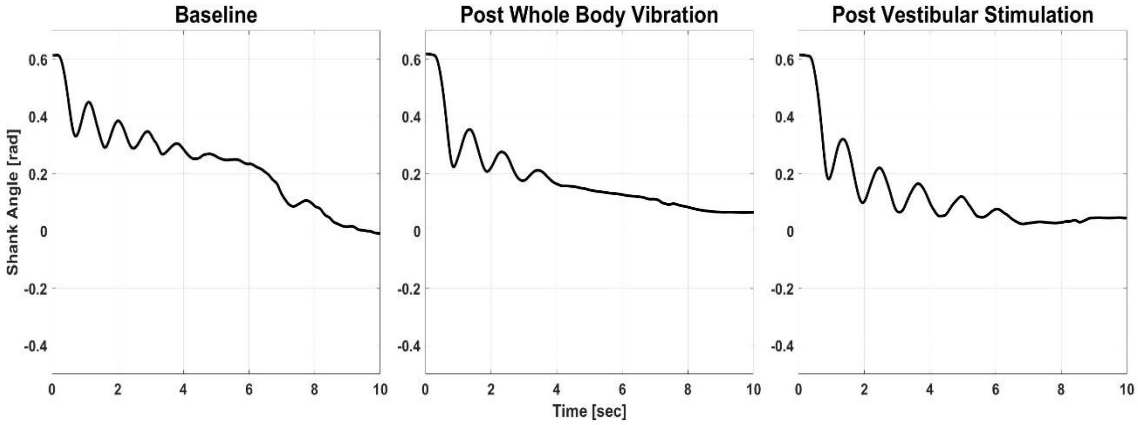


Figure 5.7 Pendulum knee drop trajectory (CP Subject 4).

The relaxation index for these data are 0.461, 0.638 and 0.707, demonstrating a steady increase in the magnitude of inflection point as the therapies compound. The Involuntary Muscle Tone Index has values of 0.423, 0.2108 and 0.045. This represents a reduction of 50% and 89% respectively. The gradual decline can be interpreted as the change from one classification of CP to another, while the combination of the two therapies shows the largest improvement in both measures.

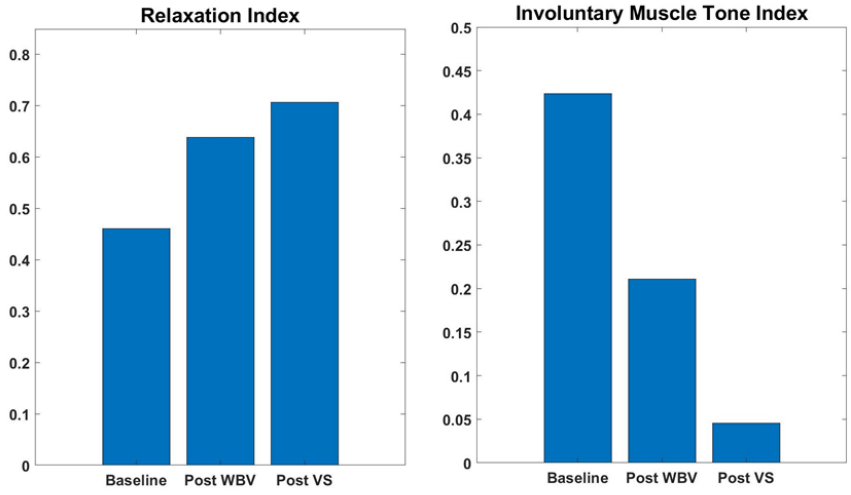


Figure 5.8 Relaxation index and Involuntary Muscle Tone Index (CP Subject 4).

5.1.5 Overall PKD Results

The table below summarizes the changes in passive joint parameters as a result of the combined therapy.

Table 5.1 Summary of Relaxation Index and Involuntary Muscle Tone Index Data

	Relaxation Index			Involuntary Muscle Tone Index		
Subject	**Baseline**	**Post WBV (Δ baseline)**	**Post VS (Δ baseline)**	**Baseline**	**Post WBV (Δ baseline)**	**Post VS (Δ baseline)**
Control 1	1.639	1.609 (-1.82 %)	1.633 (-0.37 %)	0.0007	0.0041 (0.0034)	0.0006 (-0.0001)
Control 2	1.676	1.622 (-3.23 %)	1.703 (1.62 %)	0.0008	0.0008 (0.00)	0.0022 (0.0014)
Control 3	1.678	1.707 (1.72 %)	1.758 (4.73 %)	0.0002	0.0026 (0.0024)	0.0016 (0.0014)
CP 1	0.771	0.879 (14.01 %)	1.030 (33.59 %)	0.2656	0.0445 (-0.2211)	0.066 (-0.1996)
CP 3	0.583	0.523 (-10.35 %)	0.750 (28.62 %)	0.421	0.0786 (-0.3424)	0.0572 (-0.3638)
CP 4	0.461	0.638 (38.44 %)	0.707 (53.40 %)	0.423	0.2108 (-0.2122)	0.045 (-0.378)

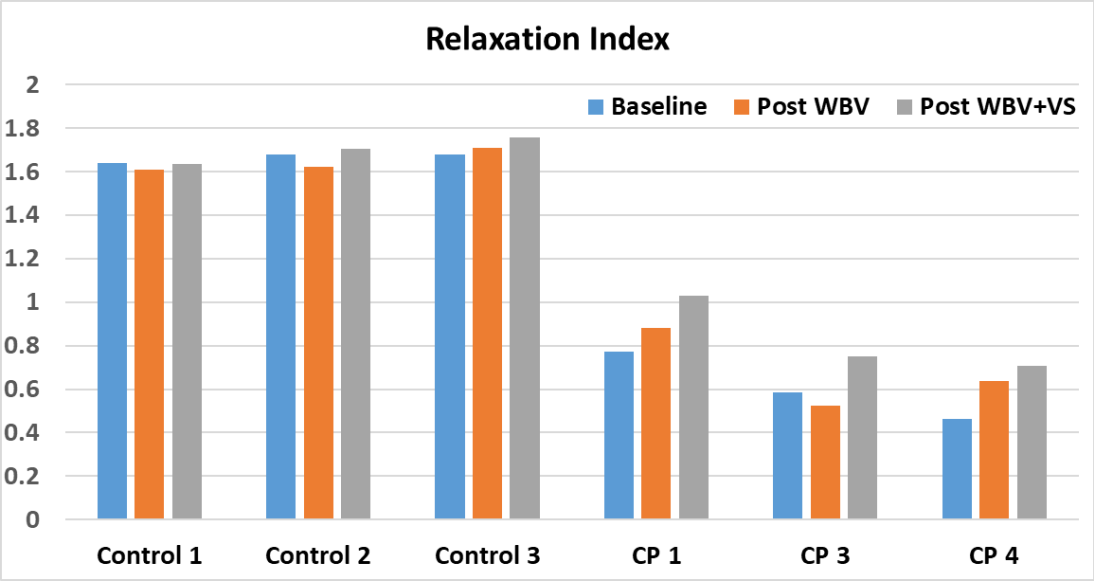


Figure 5.9 Summarized relaxation index data.

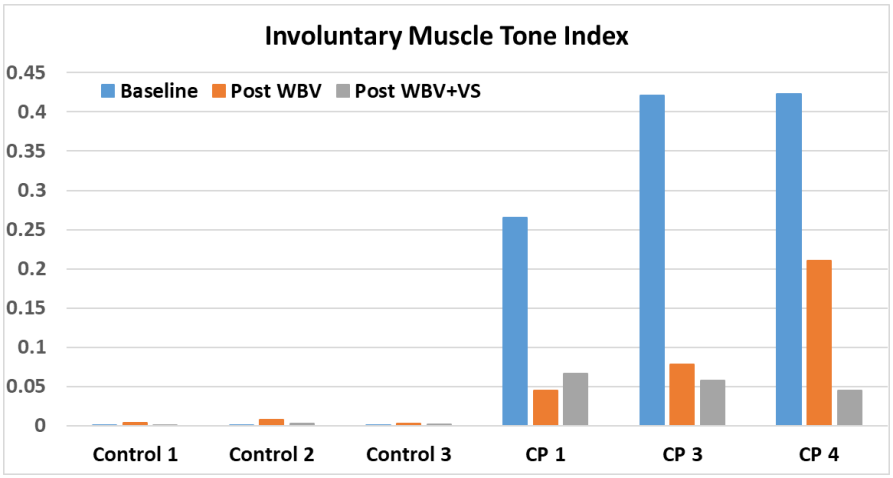


Figure 5.10 Summarized Involuntary Muscle Tone Index.

From these bar plots, healthy subjects experience higher relaxation index and a much smaller IMT index that their CP counterparts. To validate this, a 95% margin of error was calculated based on the control data at the baseline, WBV and VS time points. This is indicated by the black bars below. This shows that the control data confidence range is significantly different from the data observed in CP and it is unlikely that the values observed in the two groups can be caused by noise levels.

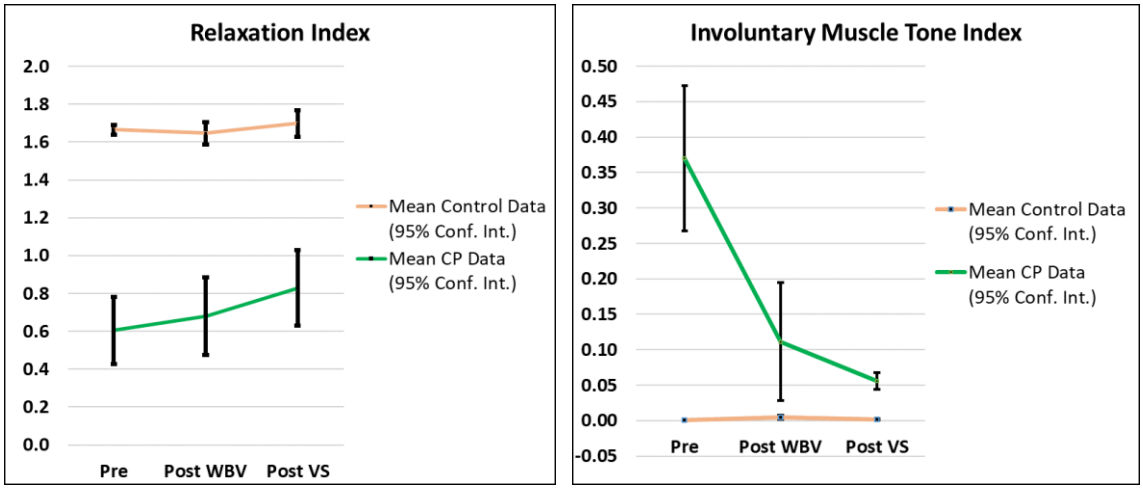


Figure 5.11 Mean Relaxation Index and Involuntary Muscle Tone Index with bounding 95% confidence interval range in CP and age-matched controls.

From these data, healthy controls experienced changes in the range of 0 to 10% and can be attributed to inherent noise in the data. It is important to note the dramatic changes observed in individuals with CP, up to an 89% improvement. To validate this, 95% confidence intervals were calculated based on the changes in control data to determine the amount of potential noise and see if the changes observed in CP are meaningful.

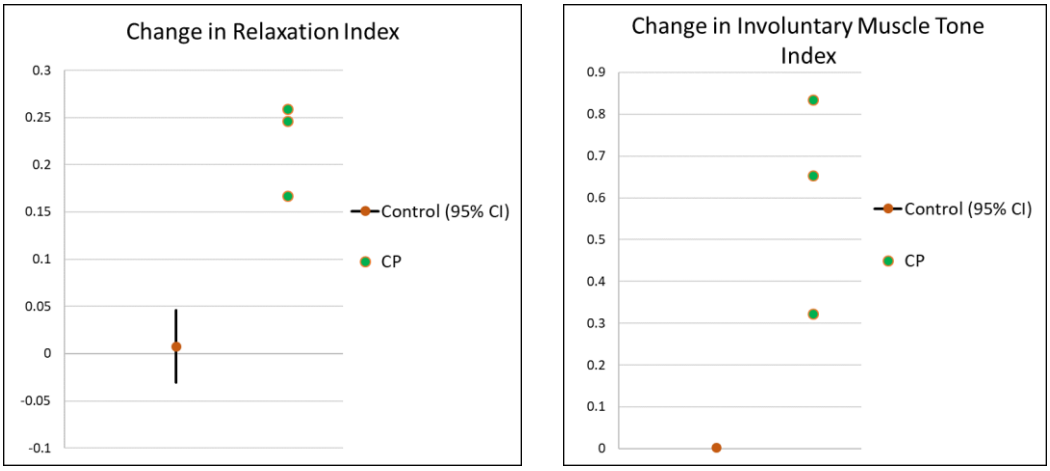


Figure 5.12 Changes in CP relaxation index (left panel) and Involuntary Muscle Tone Index (right panel) vs 95% confidence interval of change in control subjects.

The plots in Figure 5.12 show the mean change in all control subjects after stimulation as an orange data point. The 95% confidence interval of that change is represented by the black vertical line. The changes observed in each of the CP subjects are represented by the green data points. From these two plots we can deduce that the dramatic changes observed in the CP subjects lie outside of the 95% confidence interval based on our control population. This means that both parameters detected changes at levels well outside of the likely noise range and that the observed improvements are a result of the stimulation technique.

CHAPTER 6

SPECIFIC AIM 2 – FUNCTIONAL ASSESSMENT DATA AND RESULTS

6.1 Changes in Stride Length and Walk Speed

Gait data was collected from all three control subjects as well as CP subjects 3 and 4. While the intention was to have 3 CP subjects for this aim, chapter 4 presents the data from CP subject 2 and discusses why she is not a candidate for inclusion and analysis with the other CP subjects presented here.

6.1.1 Representative Data of Age Matched Controls (N=3)

Walking data were very consistent within each of the three control participants and the set below is representative of the outcomes from all three controls. Stride lengths were 0.964±0.01 at baseline, 0.998±0.0085 after whole body vibration and 0.991±0.007 after both stimulations, and did not show much variation. Likewise, self-regulated walking speeds of 0.860±0.01, 0.872±0.005 and 0.852±0.008 demonstrated a similar trend of consistency. Therefore, the healthy individuals did not experience any improvement or disruption in their normal gait patterns, as evident by the extracted parameters.

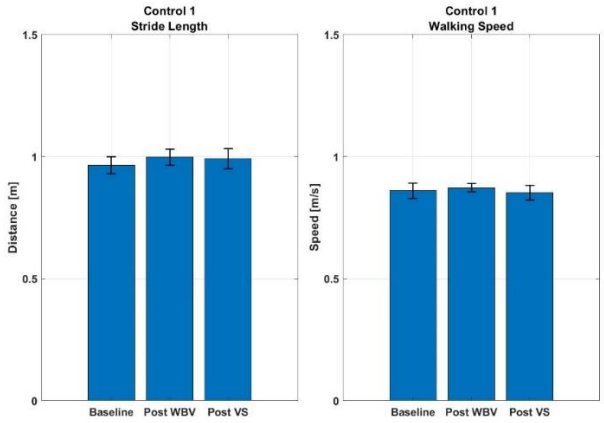


Figure 6.1 Representative mean stride length and walk speed (Control Subject 1).

6.1.2 Stride Length and Walk Speed of CP Subject 3

From the data in specific aim one, this subject responded very well to the therapy and demonstrated large reductions in dystonia and spasticity. To observe how well these changes translated to functional improvements, they were asked to perform the abovementioned self-regulated walking task. There were no targets or obstacles and the participant was blinded to the outcome measures we would extract in post processing. This subject's mean strides were 0.725±0.012, 1.096±0.014 and 0.994±0.007 meters. These improvements in stride length are well outside of the 95% margin of error determined from control data and are therefore promising. Similarly, walking speed appears to have also improved proportionally with values of 0.786±0.018, 1.083±0.013 and 0.997±0.009 meters/sec. Further observation suggests that this participant benefitted more from whole body vibration and therefore the major hindrance to their gait is dystonia. A remediation of which resulted in a 51.1 and 37.9 percent increase in gait parameters that are useful in daily living and that can lead to a larger impact if paired with alternative approaches of compounding therapies immediately after administration of the protocol in this study.

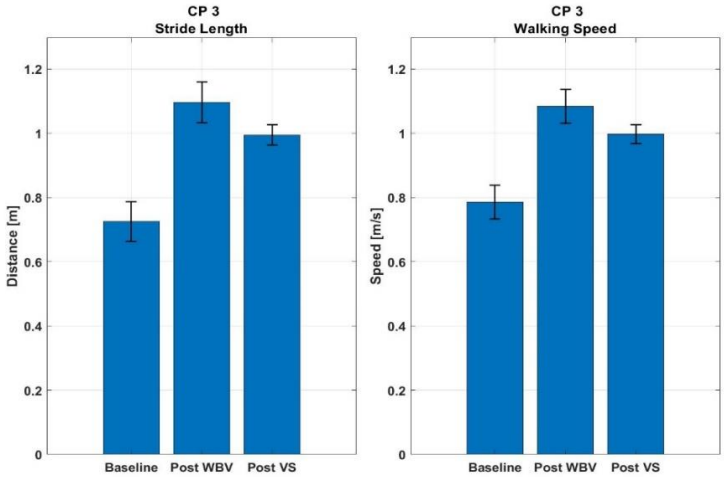


Figure 6.2 Mean stride length and walk speed (CP Subject 3).

6.1.3 Stride Length and Walk Speed of CP Subject 4

This subject also showed promising response to the therapy in passive parameters during specific aim 1. Interestingly, these drastic changes do not manifest as equally large changes in gait parameters. While it is promising to see these improvements, it is still reasonable to expect that it will take more than a single session of therapy to elicit larger changes. Nonetheless, his stride lengths were 0.526±0.007, 0.600±0.005 and 0.607±0.006 meters. Similarly, walk speed values were 0.287±0.017, 0.339±0.011 and 0.336±0.013 meters/sec. These values represent a 14 and 18 percent improvement with an upward trend toward improvements in both parameters. It is important to note that gait is a very complex set of coordinated movements that span beyond the muscle groups of the lower extremities. It is therefore very likely, and almost expected that sudden changes in muscle tone and firing patterns may lead to an adjustment period where the participant is not realizing the improvement to its full potential. The proposed methodology to test this would be to conduct a multi-session treatment that incorporates targeted training for these parameters.

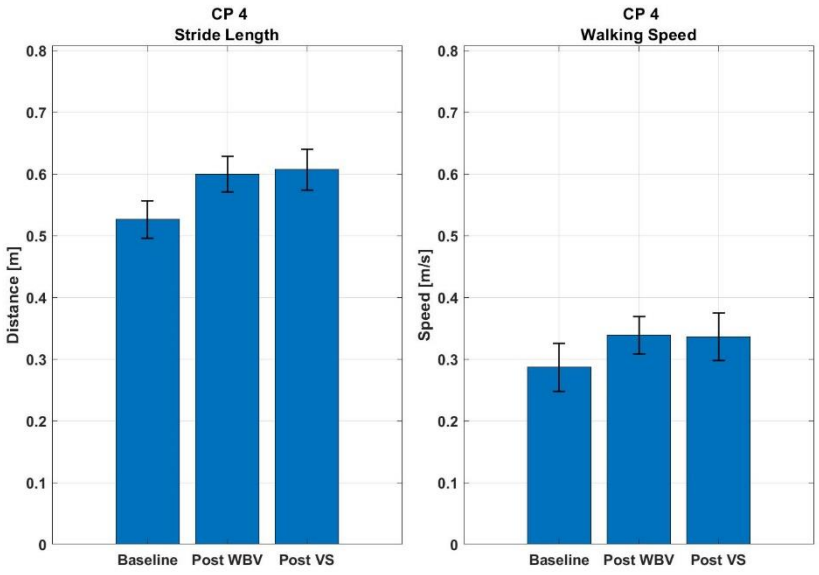


Figure 6.3 Mean stride length and walk speed (CP Subject 4).

6.1.4 Overall Stride Length and Walk Speed Results

The following table summarizes the stride length and walk speed data for all subjects. It is interesting to note the scale of change in each of the two groups (control and CP). The two subsequent bar plots demonstrate this tabulated data across all subjects.

Table 6.1 Overall Stride Length and Walk Speed Data

	Stride Length			Walk Speed		
Subject	**Baseline**	**Post WBV (Δ %)**	**Post VS (Δ %)**	**Baseline**	**Post WBV (Δ %)**	**Post VS (Δ %)**
Control 1	0.964±0.01	0.998±0.009 (3.51 %)	0.991±0.007 (2.85 %)	0.860±0.01	0.872±0.005 (1.43 %)	0.852±0.008 (-0.94 %)
Control 2	1.200±0.011	1.202±0.005 (0.13%)	1.193±0.009 (-0.66 %)	0.827±0.012	0.894±0.01 (8.14 %)	0.867±0.008 (4.84 %)
Control 3	1.384±0.007	1.314±0.004 (-5.07 %)	1.400±0.005 (1.19 %)	1.160±0.006	1.044±0.003 (-9.98 %)	1.126±0.004 (-2.91 %)
CP 3	0.725±0.012	1.096±0.014 (51.13 %)	0.994±0.007 (37.07 %)	0.786±0.018	1.083±0.013 (37.90 %)	0.997±0.009 (26.90 %)
CP 4	0.526±0.007	0.600±0.005 (14.02 %)	0.607±0.006 (15.35 %)	0.287±0.017	0.339±0.011 (18.16 %)	0.336±0.013 (17.25 %)

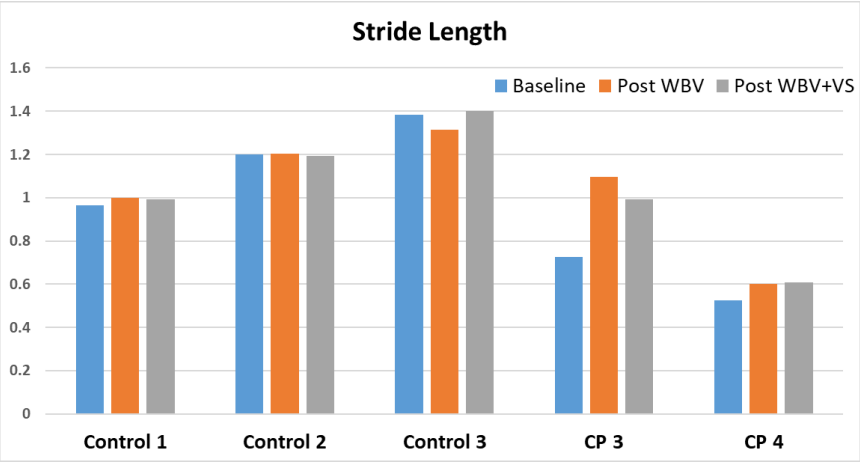


Figure 6.4 Mean stride length data for control and CP subjects.

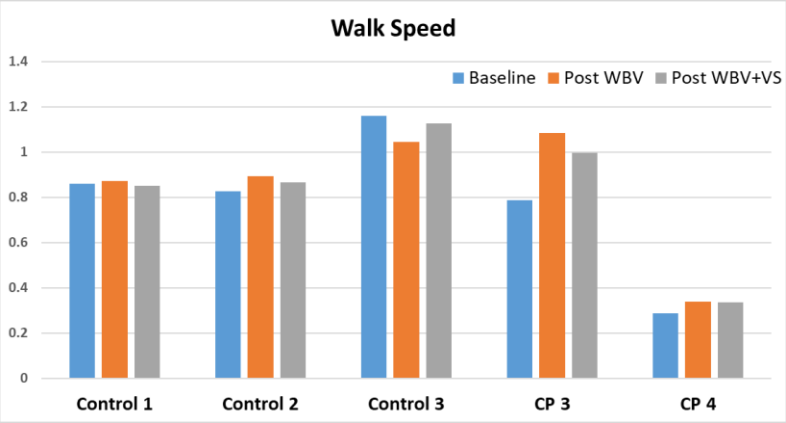


Figure 6.5 Mean walking speed data for control and CP subjects.

The data shows that while control subjects did experience small fluctuations (10% maximum) in both parameters, the CP subjects experienced improvements that are outside of the control confidence interval (Figure 6.6) It is important to note that the CP subjects that responded well in specific aim 1 (CP subjects 3 and 4) did so again here and experienced changes in the range of 15 to 50% from their baseline values. The 95% confidence interval presented below suggests that these changes are outside of the range of noise from our control group. It is promising to see such an effect size after only a single session of this proposed therapy.

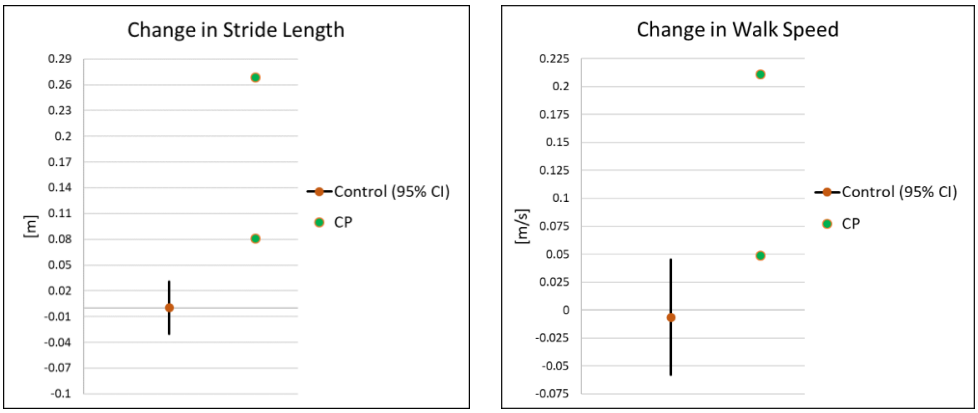


Figure 6.6 Changes in CP stride length and walking speed vs 95% confidence interval of change in control subject.

6.2 Consistency of Gait Trajectory

Variance in the step trajectory signifies how consistently the individual was stepping. As this data is normalized to percent of gait cycle, it is isolating for trajectory shape alone, while the stride length has already been extracted and discussed above.

6.2.1 Representative Control Data

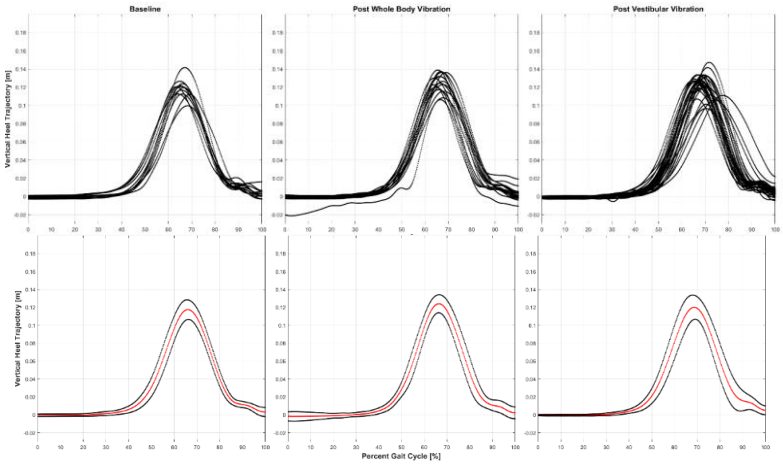


Figure 6.7 Step trajectories (upper panels), mean, mean plus and minus standard deviation (lower panels) in Control Subject 1.

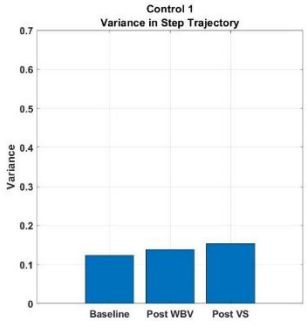


Figure 6.8 Variance of all steps in each condition (Control Subject 1).

The representative control data shows negligible change in variance due to whole body vibration and vestibular stimulation. Overall these minimal fluctuations are likely due to the subjects having consistent initial step trajectory, thereby already having very small room for improvement.

6.2.2 CP Subject 3 Data

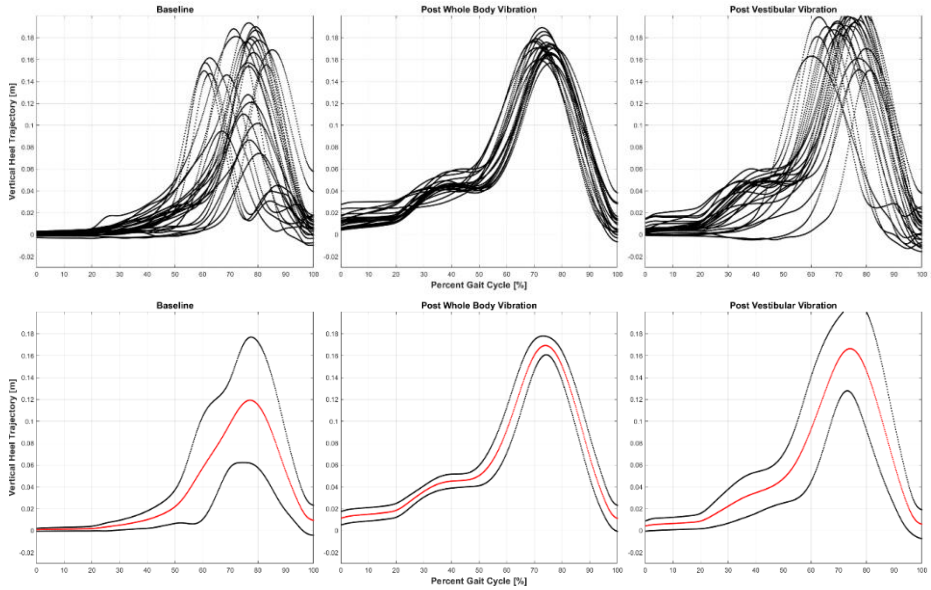


Figure 6.9 Step trajectories (upper panels), mean, mean plus and minus standard deviation (lower panels) in CP Subject 3.

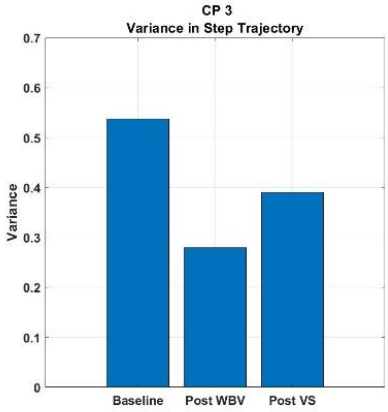


Figure 6.10 Variance of all steps in each condition (CP Subject 3).

CP subject 3, who showed a promising response to the therapy in the previous assessment measures also experienced a drastic improvement in step variance between baseline to post whole body vibration. These variance values are 0.429, 0.338, and 0.283, marking nearly a 48% improvement. The subject appears to have started a regression towards baseline, but even after vestibular stimulation, they exhibit a 27.4% improvement.

6.2.3 CP Subject 4 Data

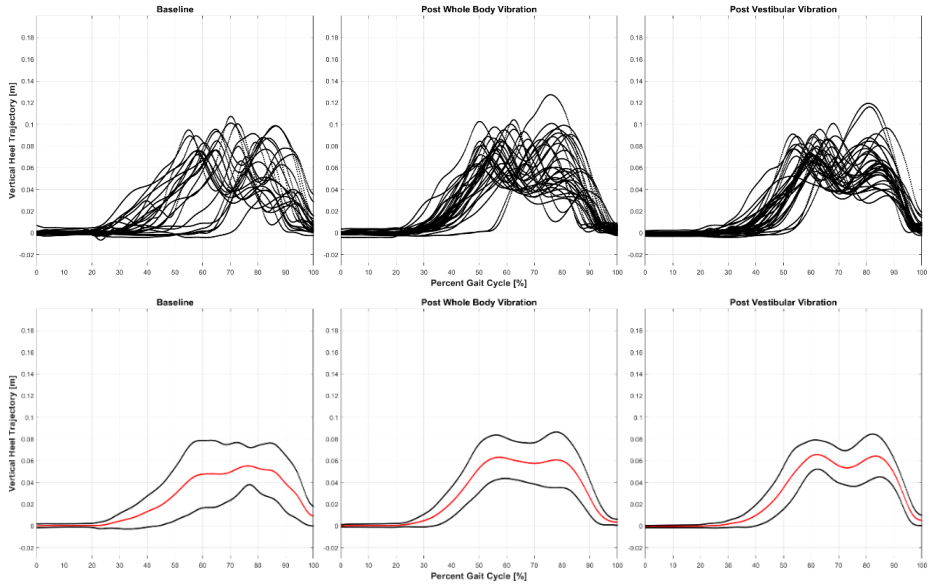


Figure 6.11 Step trajectories (upper panels), mean, mean plus and minus standard deviation (lower panels) in CP Subject 4.

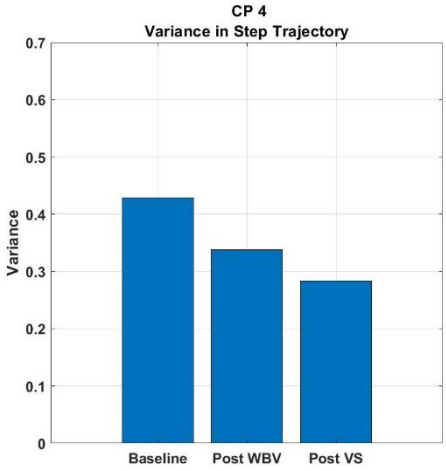


Figure 6.12 Variance of all steps in each condition (CP Ssubject 4).

CP subject 4 experienced large variance in step trajectory at baseline. This was decreased by 21% as a result of whole body vibration. There was a compounded benefit of an additional 12.8% due to the vestibular stimulation applied immediately after. Therefore, a singles session has resulted in an overall improvement of 33.9%.

Table 6.2 Overall Step Variability Data

Subject	Step Variance		
	Baseline	**Post WBV (Δ %)**	**Post VS (Δ %)**
Control 1	0.123	0.133 (8.03 %)	0.139 (13.01 %)
Control 2	0.189	0.184 (-2.86 %)	0.168 (-11.08 %)
Control 3	0.183	0.174 (-5.06 %)	0.174 (-4.74 %)
CP 3	0.537	0.280 (-47.88 %)	0.390 (-27.41 %)
CP 4	0.429	0.338 (-21.17 %)	0.284 (-33.92 %)

From the above table summarizing step variance and the changes that come about as a result of the therapy, it appears that those individuals who exhibited an improvement in passive parameters as well as gait performance, had similar outcomes here (namely CP subjects 3 and 4).

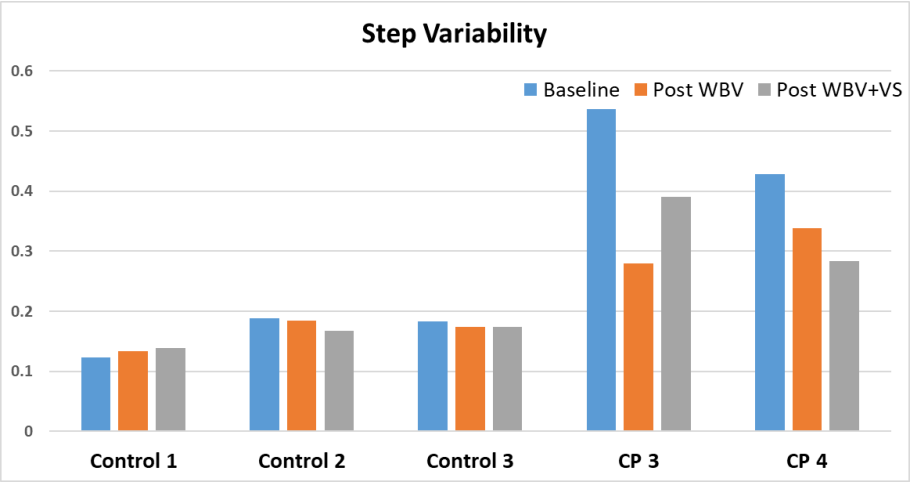


Figure 6.13 Step trajectory variability data for all subjects.

The two CP subjects experienced improvements between 21 and 48%, which is much larger than the minor fluctuations that appear in the control data sets, which do not exceed 13%. To validate this, the 95% confidence interval was calculated on all control data before and after the stimulations to determine the underlying level of noise.

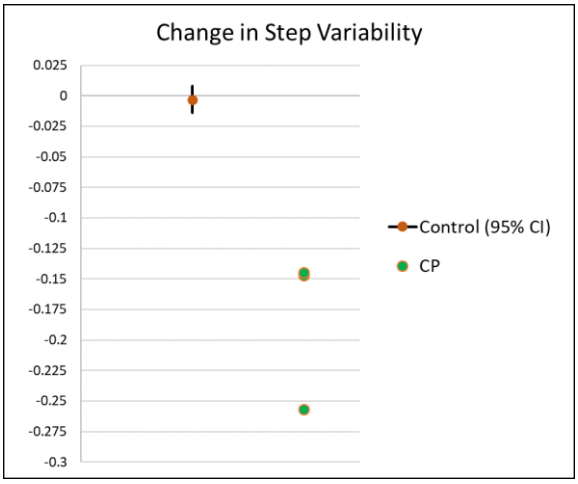


Figure 6.14 Changes in CP step trajectory variability vs 95% confidence interval of changes in control subjects.

Step variability remained the same, on average (as evident by the orange data point near zero, and the confidence interval is represented by the black vertical line. The green data points show that the improvements observed in the CP subjects lies well outside of that confidence interval and are likely to be a result of the stimulations. Therefore, we can conclude that in these pilot subjects, there is a marked increase in walk speed as a result of steps that are not only longer, but that have also become much more consistent after application of this therapy.

CHAPTER 7

SPECIFIC AIM 3 – ACTIVE SHANK MOVEMENT DATA AND RESULTS

7.1 Motor Control - Active Shank Target Tracking

This aim seeks to determine changes in motor function at the specific joint level as opposed to the holistic view of Aim 2. By targeting the shank and the agonist and antagonist of the knee joint, we can determine if the changes to passive stiffness and dystonia have manifested into any improvement in the subject's ability to generate a fast and accurate movement. This measure is crucial to the overall outcome of this study, in that an improvement in motor control is promising for the multi-session studies as well as using this therapy as a pre-treatment to other traditional and robust physical therapy approaches.

7.1.1 Representative of Age Matched Controls (N=3)

These results are representative of the control subjects, and do not show any change in response to the therapy. The control data show consistent ability to track the target with their shank to within 10 degrees and with an average response time of 0.2 seconds. These values are consistent with approximate reaction times for a healthy individual.

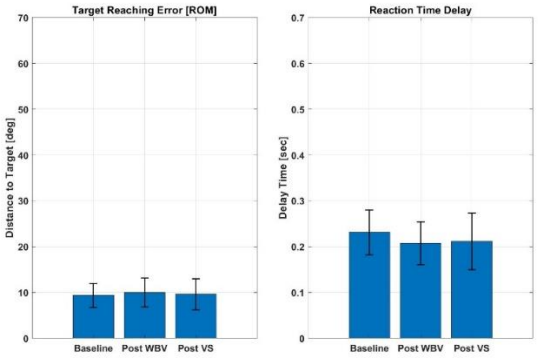


Figure 7.1 Active Tracking – Distance to target and average response time. Error bars indicate standard deviation (Control 1).

7.1.2 CP Pilot data of motor function

A single subject pilot participated in this tracking task. While their tracking error and reaction time are larger than their control counterparts, their data demonstrates an improvement as a result of the therapy. On average, this participant was 15 degrees more accurate and reacted approximately 0.15 seconds faster to the visual stimulus. An increase in tracking accuracy also suggests an increase in range of motion due to the reduced tone.

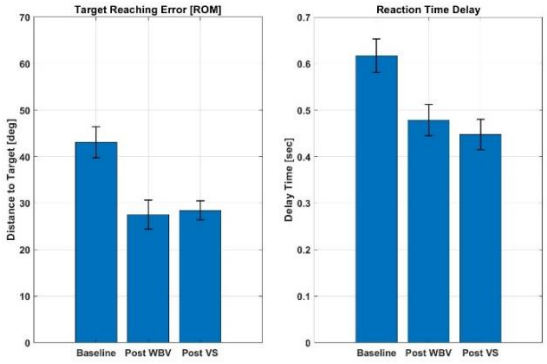


Figure 7.2 Active Tracking – Distance to target and average response time. Error bars indicate standard deviation (CP Subject 4).

Table 7.1 Overall Results (Accuracy and Response Time) of Active Shank Tracking

	Distance to Target (deg)			Time Delay – Response to Visual Stimulus (sec)		
Subject	**Baseline**	**Post WBV (Δ Degree)**	**Post VS (Δ Degree)**	**Baseline**	**Post WBV (Δ Time)**	**Post VS (Δ Time)**
Control 1	5.130±0.81	6.234±0.69 (1.10)	6.483±1.23 (1.35)	0.191±0.019	0.190±0.026 (-0.0016)	0.213±0.026 (0.02)
Control 2	11.891±0.89	14.010±0.85 (2.12)	13.150±0.98 (1.26)	0.169±0.029	0.173±0.028 (0.004)	0.199±0.023 (0.03)
Control 3	9.377±1.31	10.000±1.58 (0.62)	9.599±1.686 (0.22)	0.231±0.025	0.207±0.046 (-0.02)	0.212±0.031 (-0.02)
CP 4	43.112±1.67	27.516±1.55 (-15.60)	28.448±1.04 (-14.66)	0.617±0.018	0.479±0.016 (-0.14)	0.447±0.016 (-0.17)

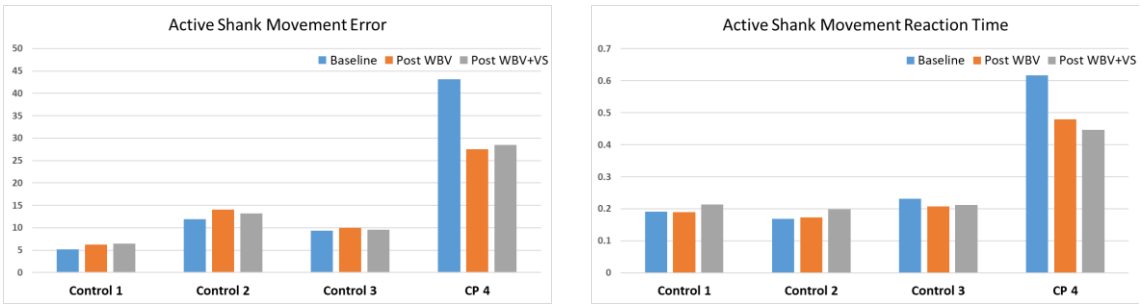


Figure 7.3 Summary of distance to target and reaction time data for all subjects.

From the summary table and Figure 7.3 above, it appears that the pilot CP subject experiences larger improvements in both tracking error and reaction time when compared with the control data that remained largely unchanged. Overall, this subject demonstrated approximately a 15-degree improvement in range of motion by being able to track the target more closely. Additionally, an improvement of 170 milliseconds observed in his reaction time, which equals approximately 27%. A 95% confidence interval was calculated based on the data from all subjects in the control group. The observed improvements are well outside of the confidence interval in both parameters. This outcome supports the hypothesis that the stimulations cause improvement in lower extremity function. This is a promising outcome, and further investigation is necessary to strengthen these findings.

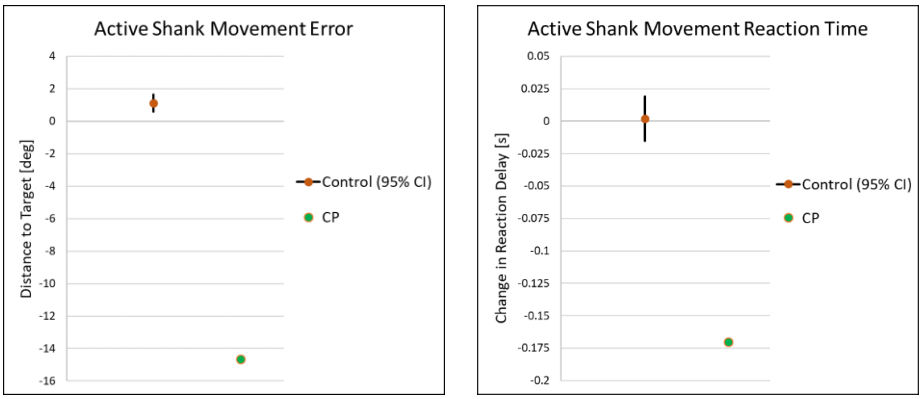


Figure 7.4 95% confidence interval of change in control data vs changes in CP movement error and reaction time.

CHAPTER 8

DISCUSSION

The most important and beneficial outcome of this work is the reduction in the severity of motor impairment in CP, with the ultimate goal being improved quality of life for individuals with movement disorders. With improved motor function comes independence, confidence and long term potential for motor learning and neural function. There is also potential for significant permanent remediation with early and continuous intervention. Additionally, this study builds upon and contributes to the scientific knowledge of the disability, as well as sheds light on certain shortcomings in therapy and literature pertaining to the management of CP. It also sets up a strong foundation and serves as the pilot work to begin filling voids in rehabilitation research for movement disorders associated with CP.

8.1 Scientific Significance

The contribution of this work to the rehabilitation research community is to shed light on potential underlying mechanisms of the disability and understanding how to identify and administer targeted interventions to overcome them. This begins with the core issue of recruiting and correctly identifying or classifying a candidate and their specific movement disorder. Current studies, including previous investigations in our lab, simply recruit based on the clinician's assessment of an individual, which is mainly based on the Modified Ashworth Scale (MAS). As discussed above, although widely used and highly regarded, the MAS is subjective and cannot reliably differentiate between spasticity and co-contraction.

This investigation sheds light on the need for objective measures to not only determine the proper classification of movement disorder (dystonia, spasticity or both), but also to determine the appropriate therapy for their specific manifestation of the disability. The proposed solution is the utilization of the PKD test and quantitatively assessing the trajectory with a combination of the relaxation index and our novel technique referred to as the Involuntary Muscle Tone Index. In conjunction, these two parameters are useful for both recruitment and for objectively determining the effect of a therapeutic approach on passive spasticity and dystonia.

The pendulum knee drop test is a reliable, repeatable and objective measure of tone. However, there is a significant amount of information that can be observed visually from the shape of the shank trajectory. Unfortunately, researchers who only report the relaxation index are leaving much of that information untapped. The approach of calculating the ratio of distance traveled by the shank helps to account for some of this information. It is not intended to be used as the sole indicator of change in the PKD, but rather as an additional parameter to quantify the changes that may be misrepresented by the relaxation index.

8.1.1 Involuntary Muscle Tone Index – An Objective Measure of Change in Tone

In this study, the Involuntary Muscle Tone Index was proposed as part of an overarching and ongoing attempt to quantify changes in the pendulum knee drop trajectory beyond that which is captured by the relaxation index. Although it was utilized on all subject data, it is most useful in the CP data where changes in tone as a result of the stimulation can be quantified. Visually, the differences in trajectory can be observed, but until now there has been a lack of objective method to describe these subjective changes.

All three spastic-dystonic CP subjects showed improvement in relaxation and IMT indices after receiving both stimulations. However, CP subject 3 is a prime example of why the IMT index is a valuable tool. While their relaxation index improved overall, there was a regression after WBV which ignores the fact that the shape of the trajectory changed (see Figure 5.5). These changes represent the shift from a spastic-dystonic PKD (evident as shank lock and a gradual drift to zero), to one that is mainly spastic, and suggests that the targeted remediation of dystonic symptoms was achieved. An 81% reduction in the Involuntary Muscle Tone Index after receiving whole body vibration suggests an improvement contradictory to the relaxation index, which fails to accurately quantify the observed changed. While the initial drop was shorter (a lower relaxation index), the rest of the shank trajectory experienced more oscillations than at baseline (a lower Involuntary Muscle Tone Index). This is therefore indicative of a change in classification.

Overall, this measure of shank travel behaves as expected based on the appearance of the trajectory, namely a control subject experiences much larger shank travel and a smaller IMT index than someone with CP (see figure 5.11). Mean of all control trials is 0.0015 while the mean of all CP trials is 0.179. Additionally, within CP, spastic trajectories manifest as smaller index values than dystonia, due to the co-contraction and lack of large oscillations. The mean of all dystonic data is 0.37 as comparted to the spastic mean of 0.056. It is important to note that, while more data is necessary to identify an exact threshold for indicating the presence and classification of disability, the confidence intervals presented above can be used as a starting point. An Involuntary Muscle Tone Index below 0.01 lies outside of the control confidence interval and may suggest a

movement disorder if paired with a relaxation index that is also below the confidence interval minimum of 1.586.

Utilizing these two measures to determine changes after stimulation showed promise and comparing the direction of change may provide meaningful insight. An increase in relaxation index and a decrease in IMT index indicates an improvement in spasticity and dystonia. A change in the same direction (i.e. a reduction in both as is the case with CP subject 3), may indicate a shift from one classification to another.

8.1.2 Involuntary Muscle Tone Index – Improved Specificity of Classification in CP

Further investigation into the use of this measure to improve the accuracy of disability classification was conducted. Figure 8.2 shows twelve data sets that have been grouped according to visual analysis of the PKD trajectory. Each column contains the 3 trajectories and a bar plot representing the Involuntary Muscle Tone Index for each colored section. The non-disabled, spastic CP and dystonic CP trajectories are grouped through use of the visual indicators discussed in chapter 3.

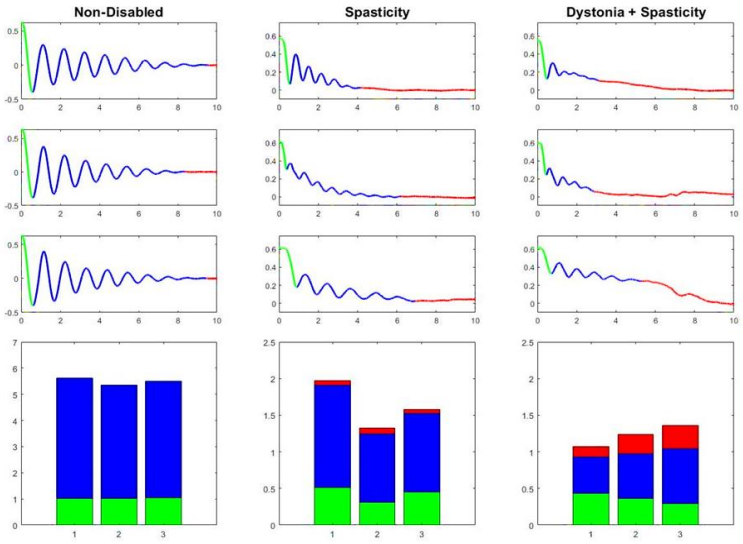


Figure 8.1 PKD trajectories grouped into classifications (non-disabled, spastic and dystonic CP). Colored bars represent each of the three trajectories in the group above it.

The trajectories were sectioned based on visual presence of oscillations and the fluctuations in the rate of change was used to validate the start and end points. Each segment's length is color coded in the stacked bar graph shown in Figure 8.2.

The IMT index was calculated for each data set and the mean of each classification group is represented in Figure 8.3. The non-disabled trajectories averaged 0.0019±0.0011, Spastic CP trajectories averaged 0.0561±0.0112 and dystonic CP averaged 0.3699±0.0521. There appear to be distinct levels along the spectrum at which each of these classifications lies and therefore the starts of a classification scale. The closer the ratio is to zero, the less likely the individual has a movement disorder, and it increases with the severity of tone.

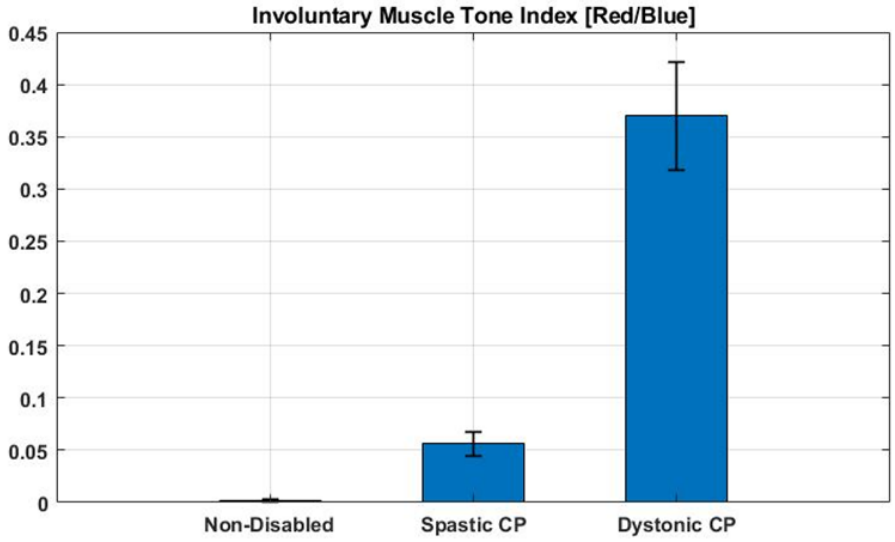


Figure 8.2 Mean Involuntary Muscle Tone Index for each classification.

The data in this study lays the foundation of a scale that will continue to be developed via the inclusion of additional data sets. With increased reliability comes the potential to implement this measure in clinical diagnoses as well as in research classification.

All data from the participants of this study suggests that the Involuntary Muscle Tone Index is a valid accompanying parameter to the relaxation index and works toward achieving the goal of quantifying the shape of a non-traditional PKD trajectory in a manner that is consistent with the visual observations we make. These observations are important to make, especially considering that the PKD can be implemented in multiple stages of a study to quantify changes in lower extremities due to therapy or application of stimulations. It is a measure that provides crucial information regarding the participant's movement disorder and how it responds to stimuli or therapy. Additional benefits derived from proper characterization of the type of CP include accurate recruitment and determination of the appropriate therapeutic approach.

While such pilot data is very promising, this study is the first of many subsequent investigations on developing additional quantitative descriptions of the shape of the PKD trajectory.

8.2 Potential Therapeutic Significance

CP has tremendous negative impact on essential daily activities and provides great demand for remediation. Efforts to reduce muscle tone and joint stiffness provide direct benefits through immediate gains in motor functions as well as indirect benefits in enabling traditional therapeutic techniques to be administered. The major aims being the prevention of further musculoskeletal damage, allowing for social and emotional development in children as well as restoring some neural function. One of the major secondary complications associated with such movement disorders is contractures. Excessive tone can cause an individual to remain in a fixed position for significant portions of their life

without stretching the affected muscle groups. This disuse triggers a remodeling process in the body through which muscle is converted to connective tissue, effectively shortening the range of motion of that muscle and amplifying the difficulty, since there in now both tone and contracture. By reducing the tone and enabling exercise or stretching, there is potential to limit or eliminate the development of contractures and ultimately significantly reducing the challenges that we face in attempting to reduce overall stiffness and improve motor function.

This study has implemented a novel therapeutic approach by combining whole body vibration and vestibular stimulation, which have been studied independently, but without the proper discrimination of the specific movement disorder of the participants. These shortcomings were addressed in this study and results show that proper application of these two therapies in succession within a single session is very promising. It is important to note that all three CP subjects exhibited signs of dystonic-spastic tone at baseline and all three responded well to the combination therapy. The improvements observed in the relaxation index and Involuntary Muscle Tone Index in CP individuals were outside of the 95% confidence interval of their age-matched control counterparts. This suggests the effect size was large enough to be a result of the stimulation, with overall improvements of 33%, 28% and 53% observed in the relaxation index for the three CP subjects, respectively. This drastic improvement in relaxation index coincided with improvements in the Involuntary Muscle Tone Index that account for changes in the complete trajectory of the shank, and the three CP subjects showed improvements of 75%, 86% and 89% respectively. The proposed therapeutic technique has therefore induced

changes in both the amplitude and duration of swing, as a direct result of a reduction in the tone and stretch reflexes that impede full range of motion swings of the shank.

This study was also designed to observe the translation of these changes in passive parameters to usable functional measures. In other words, how does a reduction in tone of a seated individual translate into improvements in the parameters of functional activities like gait? To accomplish this, gait analysis was conducted to extract key parameters like stride length, walk speed and step trajectory variability. As per the results above, two individuals with CP participated (CP subjects 3 and 4), both of whom exhibited reductions in passive tone, and did in fact perform better in the walking task as a result. Their overall walking speed improved by 26.9% and 17.3%, while their stride lengths improved by 37.1% and 15.3%, respectively. Their step trajectories also became 27.4% and 33.9% more consistent. All changes in these three gait parameters are well outside of the 95% confidence interval for expected changes in age-matched healthy controls.

Lastly, Specific aim 3 was designed to investigate these changes in motor function even further and quantifies the subject's ability to recruit, activate and isolate individual muscle groups and perform a target tracking motor assessment. Our single subject pilot (CP subject 4) showed a 14.7-degree increase in tracking accuracy and a 170 millisecond improvement in reaction time. These changes are outside of the 95% confidence interval of changes observed in the healthy counterparts. This assessment technique will be incorporated into future studies and achieving such an effect size in all aims after a single session sparks interest in multi-session studies for the future.

8.3 Limitations

There were several complications during this study that can all be used as learning experiences for future studies. The most critical factor in any human research is the availability of a subject pool to recruit from. This pilot study was conducted despite the limited funding and lack of a large number of participants that met the inclusion criteria. With such promising results, however, future studies will focus on strengthening the existing collaborations with healthcare professionals who manage significant amounts of CP patients. This will help ensure ample participants for a future large sample size study.

On the research side, several equipment related obstacles were faced. Initially, an electromagnetic transmitter and receiver were used to conduct the PKD assessment. This posed a problem with interference of noise in the EMG recording. As a result, we opted to use the motion tracking cameras to record the location of the shank during the PKD. Unfortunately, looking at the EMG data, it appears that the system is overly sensitive to wire movements and the data at the PKD drops is masked by very large spikes of saturated data with crosstalk between channels. Unfortunately, the data was unusable. Our lab has since invested in a top of the line Delsys wireless system that may help to overcome this.

The other major equipment hurdle was utilizing a small number of older motion tracking cameras to cover the entire length of the gait lab. This posed a problem in making sure all regions were visible, and distance from the camera started to become a problem. The accuracy of the data was not compromised, but makers were being lost so frequently that many data sets had to be eliminated during the analysis phase. This issue was partially remediated by adding more cameras to increase coverage, but the dead zones near the walls at the beginning and end of the gait track remained. To make matters more complicated,

the software used to collect the data attempted to stitch together marker data. Unfortunately, this software was not robust enough to detect patterns and stich the correct marker data together. Post processing of all marker data consisted of undoing the software stitching and redoing it manually. This was a labor intensive and time consuming issue that was not expected. Future studies will utilize more reliable motion tracking systems, which have been proven to contain very robust algorithms for preprocessing data sets.

While the two stimulation techniques were administered very smoothly with no adverse effects or complications, the vast number of outcome measures lead to a total session time of 3 hours. This is a very long time for an individual with a disability (especially a teenager) to be subjected to the battery of tests conducted here. Since this study was looking at numerous different aspects of disability assessment and rehabilitation, it was important to be thorough. However, future studies will be conducted by limiting the outcome measures and drastically increasing the sample size.

8.4 Impact

Potential impact of this work may include increasing our understanding of CP complications and how to reverse them permanently. In the literature, non-disabled individuals increased their tone to overcome perturbations in reaching tasks. Over time, they learned to optimize that added tone while still achieving the target movement [47]. It is therefore possible that the increased tone that develops in CP is a compensatory mechanism in an attempt to overcome the lack of proper motor control. However, unlike the participants in the abovementioned study, individuals with CP do not have the positive feedback necessary to determine the correct amount of tone; it therefore continues to

increase until it becomes an inhibitor of movement. By temporarily reducing the spasticity and dystonia, the individual may be able to move successfully, which may lead to permanent reductions in the added tone as the body begins to achieve motor tasks and incorporating the missing positive feedback.

In addition, the recent increase in exoskeleton technology has provided a means for locomotion and gait training. Yet, a person who exhibits high spasticity and/or dystonia is unable to participate or benefit due to the risk of the therapist or robotic device applying force to contracted muscles or locked joints. There is an inherent risk of overextension and tearing of tissues, as well as dislocation and bone fracture.

Numerous crucial aspects of rehabilitation and CP research have been investigated with promising results, and the foundation has been laid for a larger study to investigate these findings further and identify the neurological aspects that result in the observed changes. This study and future investigations on decreasing the negative impact of the movement disorders associated with CP span beyond scientific findings and seek to impact the quality of life of individuals who are spastic and/or dystonic.

CHAPTER 9

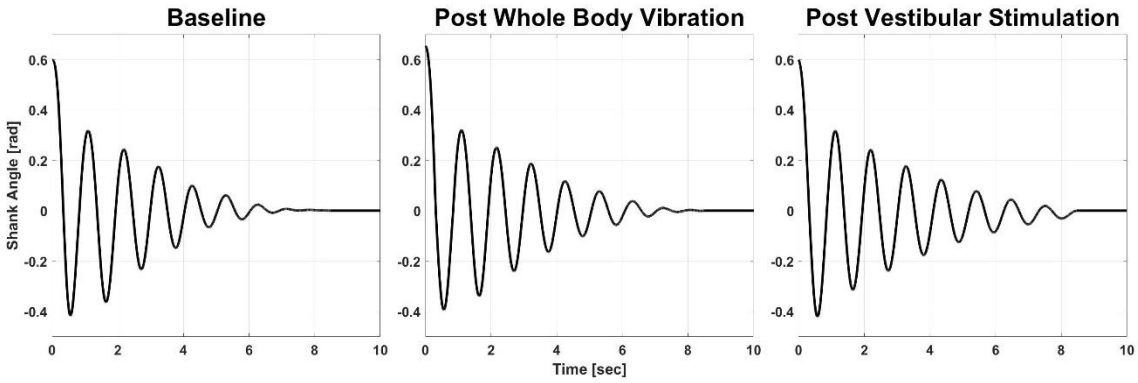
FUTURE WORK

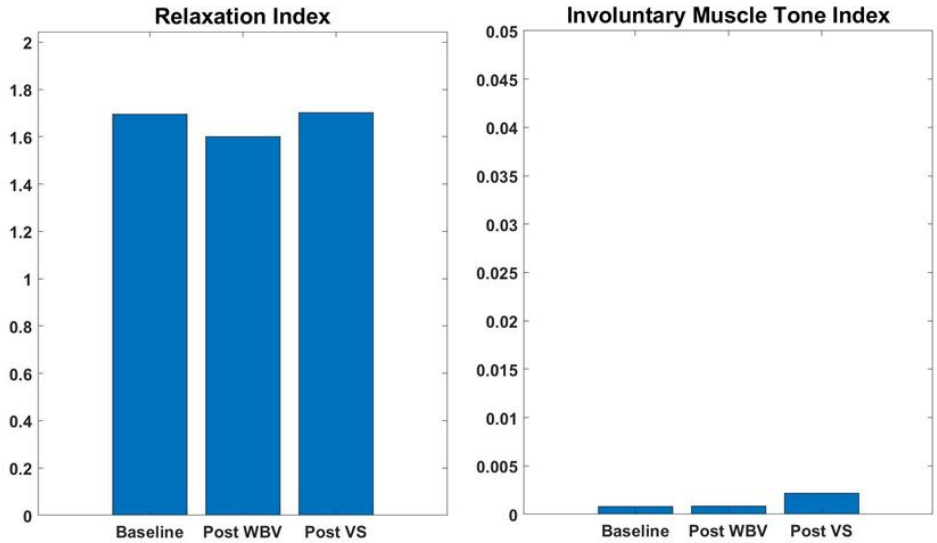
Based on these outcomes, this study lays a solid foundation for many more investigations into movement disorders associated with CP and management of these motor disabilities. Future studies will utilize the set of objective measures outlined here as well as the lessons learned to conduct a larger scale investigation utilizing the protocol established above. Additionally, a multi-session study observing the compounding and retention of improvement would give insight on the extent to which the negative implications of the movement disorder can be halted or reversed. Lastly, and most importantly, a study on extending the benefits of standard of care or other traditional therapeutics by providing a window of reduced resistance and priming the individual with a session of WBV and VS prior to the therapy. Capitalizing on this with intense training, especially during the developmental years where motor plasticity exists, may prove to have a significant compounding effect. The ability for the subject to participate in robotic therapy that they otherwise would not have been eligible for is another promising application of this work that is a foreseeable direction for this work.

APPENDIX – ADDITIONAL CONTROL DATA

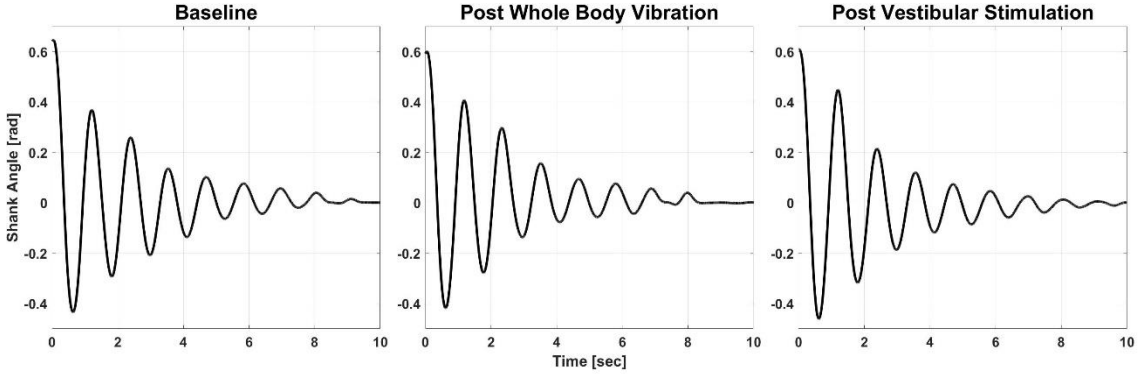
This appendix contains the plots for all control subjects referenced in the text above. This includes specific aims one, two and three for all three age-matched control participants. Data is grouped by subject in the sections below.

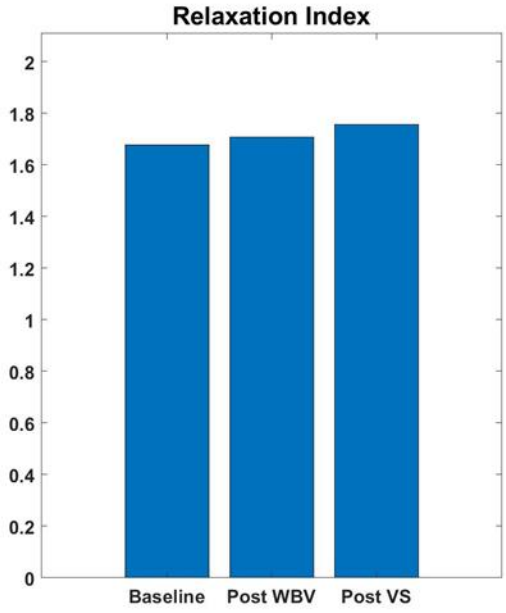
A.1 Pendulum Knee Drop Data – Control Subject 2

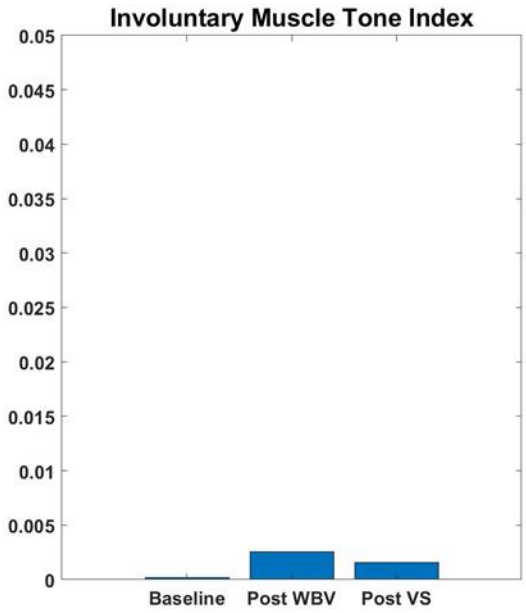




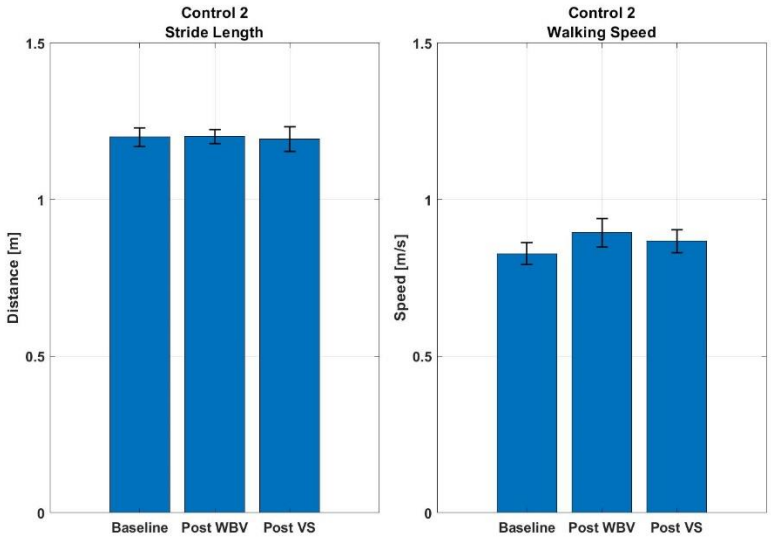
A.2 Pendulum Knee Drop Data – Control Subject 3



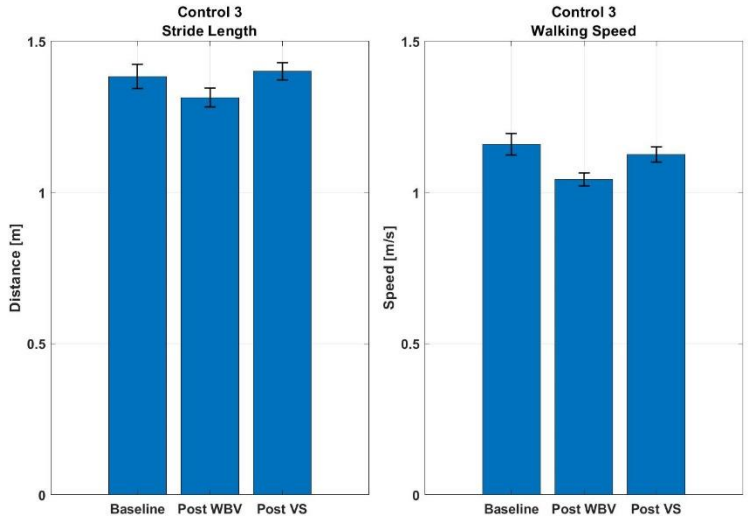




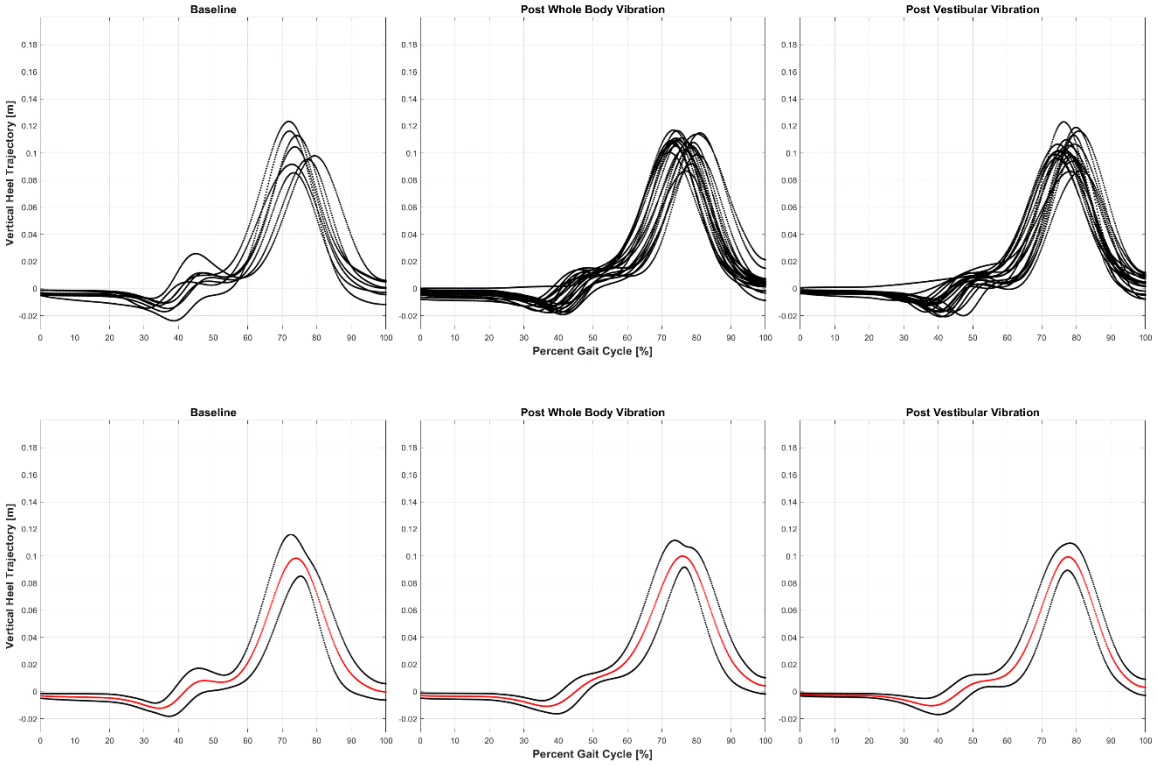
A.3 Gait Parameters (Stride Length and Walk Speed) – Control Subject 2

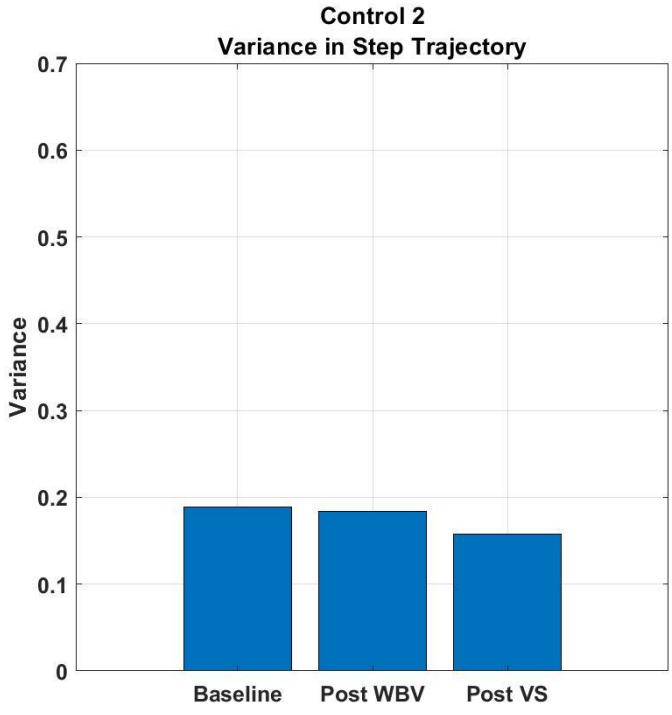


A.4 Gait Parameters (Stride Length and Walk Speed) – Control Subject 3

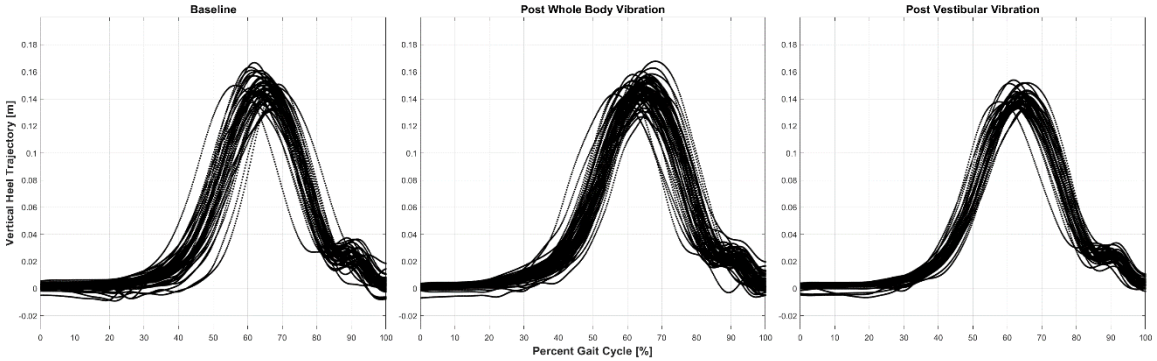


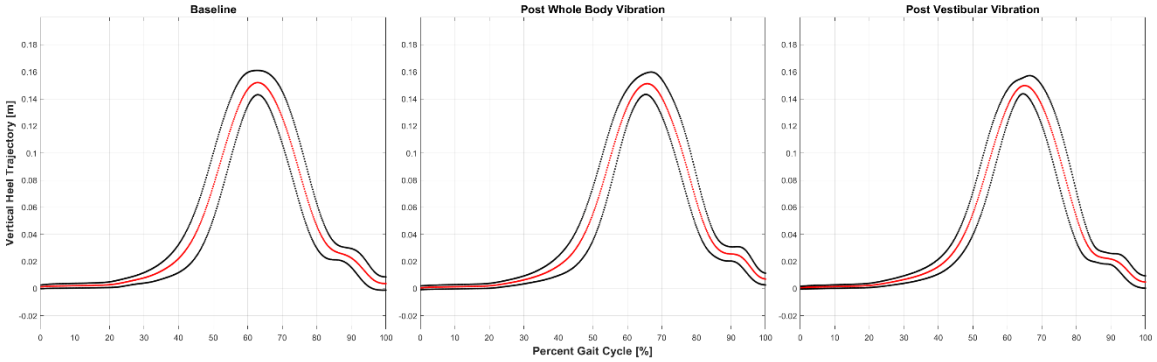
A.5 Gait Variability Data – Control Subject 2

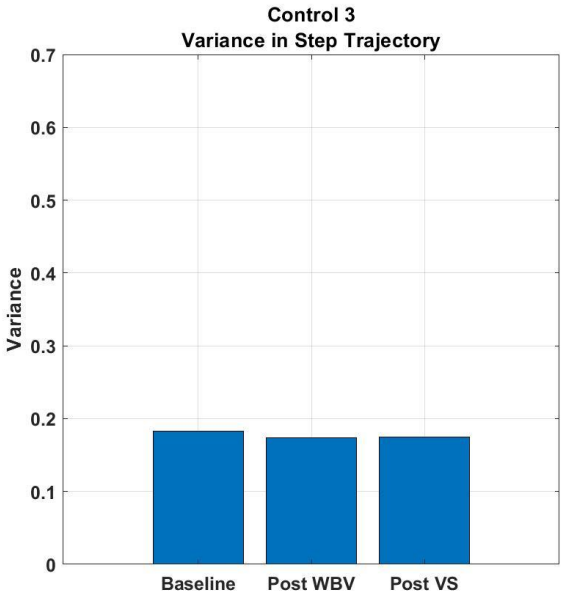




A.6 Gait Variability Data – Control Subject 3







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