THE ASSOCIATION BETWEEN LOWER EXTREMITY MOVEMENT PATTERNS AND PHYSICAL FUNCTION IN PEOPLE WITH KNEE OSTEOARTHITIS

by

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Purpose: Explore the association between movement pattern variables and physical function (PF), compare movement pattern changes between standard and agility/perturbation training and explore the association of movement pattern changes with PF changes after an exercise program.

Methods: Baseline evaluation was performed to collect subject characteristics, self-reported and performance-based PF followed by motion analysis and electromyography tests performed during gait and step down tasks. Subjects randomized into standard or agility/perturbation groups underwent 12 training-sessions. Post-treatment evaluation was performed at 2 months.

Analyses: All analyses were performed for gait and step down task separately. At baseline stepwise multiple regression analyses were performed to explore the association of lower extremity kinematics and co-contraction with the Western Ontario and McMaster Universities Osteoarthritis Index -PF subscale (WOMAC-PF) and the Get up and Go test (GUG) separately. At post-treatment, comparisons of the changes in lower extremity kinematics and changes in co-contraction patterns between subjects who received standard versus agility/perturbation training were performed. Following, stepwise multiple regression analyses were performed to explore the association of changes in lower extremity kinematics and changes in co-contraction with changes in WOMAC-PF and changes in GUG.

Results: At baseline results indicated that increased co-contraction during gait and step down were associated with poorer PF. The increased co-contraction of lateral muscle couples during gait was probably an attempt to control knee loading. The increased co-contraction of lateral and medial muscle couples during the step down was likely an attempt to avoid pain and instability as well as control loading at the knee. At post-treatment there was no difference in movement patterns changes between the two exercise groups. Increased co-contraction during gait was associated with improvement in GUG whereas during step down increased co-contraction was associated with worsening in WOMAC-PF. At both time points the observed associations of co-contraction with PF were likely a response to the unique constraints imposed by gait and the step down. We believe in order to improve patterns of movement and thereby improve PF in this population, rehabilitation programs may need to focus on specific practice of tasks which are difficult to people with knee osteoarthritis.

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When someone goes on a long journey such as the PhD degree one thing is certain, you will not walk alone. Several people along the way made this journey possible and many other people walked on this road with me. My dissertation committee was invariably with me every step of the way. My mentors taught me hard work, perseverance and gave me the guidance to finish the journey. At the same time they also taught me life lessons such as patience, kindness and understanding. I will cherish the memories of all the time spent with each and every one of them.

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1 INTRODUCTION

1.1 STATEMENT OF THE PROBLEM

Knee osteoarthritis (KOA) is a debilitating degenerative disease that decreases the physical function status of the population affected by it.[1-4] A common characteristic of people with KOA is decreased range of motion and increased co-contraction activation patterns of key lower extremity muscles during ambulation.[2,4-6] Even though physical function and characteristics of gait such as range of motion (ROM), ground reaction forces (GRFs) and joint moments have been extensively studied in people with KOA,[5,7-9] the association between function and these biomechanical factors is uncertain. We believe that among these gait variables, decreased ROM and/or increased co-contraction activation patterns may affect physical function in individuals with KOA.

Bernstein proposed that a stiffened pattern of movement is a strategy used at the initial stages of learning how to solve a new motor problem.[10] The movement pattern adopted by people with KOA (i.e. decreased ROM and increased muscle co-contraction) may be an attempt to simplify and control movement and maybe control pain under the new condition of a degenerated knee joint. Detection of this stiffened pattern of movement may be important for guiding exercise treatment of people affected by KOA. Treatments targeting the release of the stiffness may result in better physical function. People with stiffened patterns of gait may benefit from movement enrichment programs by increasing the available motions and decreasing muscle co-contraction. Standard physical therapy programs have been shown to improve physical function in individuals with KOA.[11] We believe that a movement enrichment program that includes agility and perturbation training will promote reduction of the stiffness during gait and may promote improvement in physical function beyond what standard exercise will predict in this population.

The overall aim of this study is to explore the association of changes in lower extremity joint kinematics and muscle co-contraction with changes in physical function in people with KOA who undergo exercise treatment.

1.2 AIMS AND HYPOTHESIS

1.2.1 Specific Aim 1

Explore the association between baseline measures of physical function with lower extremity joint kinematics of hip, knee and ankle and muscle co-contraction in people with KOA during the loading phase of gait and of a step down task.

1.2.1.1 Hypothesis 1

We hypothesize that people with KOA who exhibit lower levels of physical function will have decreased lower extremity joint excursions and increased co-contraction during the loading phase of gait and of a step down task.

1.2.2 Specific Aim 2

Compare the changes in lower extremity kinematics and muscle co-contraction patterns between subjects who receive standard rehabilitation and subjects who receive agility and perturbation training in addition to the standard exercise program.

1.2.2.1 Hypothesis 2

We hypothesize that people who undergo agility and perturbation training will have greater increases in lower extremity joint motion excursions and greater decreases in co-contraction during functional task performance after training than people who undergo a standard exercise program.

1.2.3 Specific Aim 3

Explore the association of changes in lower extremity joint kinematics and changes muscle co-contraction with changes in measures of physical function in people with KOA who undergo exercise treatment.

1.2.3.1 Hypothesis 3

We hypothesize that increase in lower extremity joint excursions and decrease in co-contraction of the lower extremity muscles will be associated with increase in physical function after an exercise program.

1.3 BACKGROUND

1.3.1 ALTERATIONS OF GAIT IN KOA

Knee Osteoarthritis (KOA) is a condition that can alter normal lower extremity biomechanics.[4,7] Several studies reported that individuals who have KOA adopt different gait patterns than age and gender matched controls.[4,7] Among the common gait alterations there are decreased knee excursion,[5] altered GRFs[12] and higher muscle activation patterns of lower extremity muscles.[2,4,6] These alterations may be due to a variety of impairments such as status of the articular surface of the knee, pain intensity,[12,13] knee instability, joint effusion[12] and decreased muscle strength.[5]

Decreased ROM combined with increased co-contraction of key lower extremity muscle couples may produce higher compressive loads at the joints and consequently may facilitate the progression of KOA.[4] The combination of these two gait changes may characterize the typical stiffening strategy adopted by this population during gait. A similar pattern of joint stiffening during gait has been described in individuals with anterior cruciate ligament rupture by Chmielewski et al.[14] The description of this pattern includes reduced knee motion, reduced internal knee moment, greater hip and less knee extensor moment contribution towards support moment, delayed peak hamstring muscle activation, and generalized co-contraction of the muscles that cross the knee. Another similarity between these two populations is the complaint of knee instability.[1,14] Fitzgerald et al reported that 63% of the individuals with KOA had complaints of knee instability episodes such as giving way, buckling or shifting of the knee during activities of daily living (ADLs) and 44% reported that these instability episodes affected their ability to function.[1] According to Childs et al, people with KOA may rely on this primitive pattern of stiffness to avoid knee joint instability and/or pain during ambulation.[4] Chmielewski et al also believe that people with ACL deficient knees use stiffening of the knee joint as an alternative mechanism to increase stabilization. Although in both populations this strategy may be used with the intent of simplifying movement, in the long term it may contribute to a decline in level of physical function and perhaps to the progression knee osteoarthritis disease.[4,14]

1.3.2 THE STIFFENED STRATEGY IS A PRIMITIVE MOVEMENT STRATEGY

In 1967, the work of Nicolai Bernstein was translated and published in English which gave many scientists access to his point of view on motor learning. Bernstein suggested that solving the motor learning process would lead to understanding of the coordination of the human motor control apparatus.[10] Degrees of freedom may be simply described as the number of planes a rigid body can move in; a uniaxial joint that has one plane of movement thus has 1 degree of freedom. However, the human body has to manage an enormous number of degrees of freedom due to the complex system of bony segments, linked by joints and layers of musculature, which allows movement in a variety of different planes.[10] The variety of muscles and motor units moving a bony segment increases greatly the number of degrees of freedom of a given joint and even more if a whole limb is taken into consideration.[15]

Bernstein proposed that the development of skilled movement could be divided into three stages. Initially, in solving a new unfamiliar motor problem, the learner is required to assemble and reorganize the control over all possible movement.[10] This phase is frequently referred to as “freezing the degrees of freedom”.[16-19] For this study we will refer to it as a stiffened pattern of movement. In the second stage, with practice of the new movement there is a gradual release of the stiffened pattern of movement and this f reed movement is incorporated into a more economical task specific coordinative structure.[16,17,19] In the third stage, the passive forces that occur during the movement are used to their fullest extent to enhance the efficiency of the active forces in a finely tuned coordinative system.[16,19]

There are two strategies used to stiffen the available movement. One of them implies keeping the whole body or the joint angles fixed and rigidly held in order to operate as a single unit.[16,18,19] For example, in a skiing task a novice locks the hip and knee joints in order to reduce the movement in these joints and as an attempt to maintain standing balance while on the ski apparatus. The second strategy involves introducing nonflexible couplings between multiple degrees of freedom promoting the phase locked joints to move in close relationship. An example of this second strategy is co-contraction of agonist and antagonist muscle couples such as biceps/ triceps and wrist flexors/ extensors during a dart throwing activity in an attempt to increase accuracy by inducing the joints to move in close relationship. The combination of these two strategies simplifies the given task by only requiring a specific ensemble to be actively controlled.[16,19]

The strategies used during gait in individuals who have KOA and the strategies used to stiffen the movement pattern while learning a novel skill appear to be similar. Reduced ROM and strong muscles couplings are common to both situations.[2,4,15,16,19] The pattern that we have been referring to as a stiffened pattern during gait may reflect an attempt of these individuals to solve the coordination problem imposed by a degenerated knee joint. Gait and ascending or descending steps are not novel skills. Actually these activities have been described as the most common ambulatory activities of daily living (ADLs). [20] People with KOA have been dealing with walking and managing steps since they were toddlers. However, since there is increasing pain and deterioration of the cartilage and most likely other structures in their knees, these individuals have to adjust the performance of such basic activities under this new structural and physiological environment. In the motor behavior literature, several studies have reported similar patterns of stiffness during performance of various tasks in which there is a combination of decreased ROM and strong muscle couplings. These reports are based on scenarios such as learning novel skills or learning to perform a skill with the non-dominant limb.[16,18,19,21]

Several studies have reported on experiments assessing the stiffened patterns of movements while performing upper extremity tasks. Steenbergen et al observed the ability to achieve coordination during a hand grip task in 7 right-handed subjects.[19] A 3-D motion analysis was performed while subjects performed a task in which they had to move a cup, either empty or full, consecutively through to several target locations. Initially, the subjects had to move the cup from the original resting position on the first plate to a second plate, positioned 30 cm in front of the starting position along the midline of the body. Next, the cup had to be moved from the second plate to the third which was placed 20 cm to the left of the cup location in the right hand conditions or 20 cm to the right of the cup in left hand conditions. There were four conditions performed; cup empty/ right hand, cup full/ right hand, cup empty/ left hand and cup full/ left hand. The authors hypothesized that the least constrained task (empty cup/ right hand) would demonstrate minimal amount of individual joint stiffening and independent control of joint angles, whereas the cup full/left hand would require tight joint couplings or fixed limb segments movements.[19]

The results demonstrated that the movement times were longer for the full cup conditions and for the left hand conditions.[19] The peak velocity was reached later for the conditions in which the cup was full and the magnitude of peak velocity decreased in the same condition.

Subjects reached the maximum hand opening relatively sooner when more precision was required, and this effect was stronger for the left hand. The authors stated that it is evident that joint freezing was implemented as a means of solving a complex movement problem. In both shoulder and elbow joint, angular displacements in the second half of the hand transport phase were reduced to a minimum, implying stiffening of the joints in this phase for all four conditions. However, the decrease of angular change started earlier and was more noticeable in the full cup conditions.[19] Although the sample size was small, this study provides some support to the "stiffened pattern of movement" while learning a novel task. However, practice of the skilled movement was not a component in the design of the study. Consequently, it does not provide relevant information related to the release of the stiffening phase.

McDonald et al believed that one of the confounding problems of previous studies that attempted to observe changes in coordination control patterns is that the findings appear to be very task dependent.[21] In other words, the kinematic parameters such as joint movements that remain invariant in different experiment protocols are dependent to a large degree on the constraints imposed by the task. For example, a writing task versus a dart throwing task has different constraints because of its nature. Even though the writing task does influence all upper extremity joints, the main action occurs at the level of the wrist. In contrast, in dart throwing, although the wrist has a critical role for precision of this task, the shoulder and elbow joints also have important roles in the performance this task. In summary, different tasks do have variable constraints and they need to be taken into consideration in this field of study. For these reasons, McDonald et al reported a series of cases in which their objective was to observe the effects of practice on kinematic variables of a throwing task. Five male subjects were recruited for this study.[21] All of the subjects were proficient in throwing darts to a target board and were right hand dominant. A motion analysis of the upper extremity was performed in 3-D using a Selspot camera system and light-emitting diodes (LEDs) on upper extremity bone landmarks. They had practice sessions during 10-14 days, in which the dominant arm was allowed to perform 2 sessions of 250 trials and the non-dominant arm was allowed to perform 5 sessions of 250 practice trials. The first 10 trials of the first session for each condition were recorded. For the dominant arm condition the last 10 trials of the second session were recorded and for the non-dominant arm the last 10 trials of the 5th practice session were also recorded.[21]

Four different performance measures were generated: joint-space data, hand trajectory data, position of the hand at point of dart release and task scores. These four measures were evaluated with respect to limb condition (dominant and non-dominant) and practice phase (pre and post practice). The joint-space correlations on the dominant side between wrist-elbow and wrist-shoulder joints had a significant absolute value reduction with practice when compared to the elbow-shoulder correlation, whereas the non-dominant limb kept high cross correlations between wrist, elbow and shoulder angles during the practice period.[21] Regarding the angular velocity correlations the non-dominant limb showed higher correlations between all joints. The elbow-shoulder joints were the most highly correlated in both limb conditions. The within subjects standard deviations of angular displacement mean were greater in the non-dominant limb, but no change with practice was observed. Resultant trajectories were found to be highly consistent as well as the within subject cross correlations between limb conditions and phase of training. The resultant trajectory means showed low standard deviations, indicated highly stable locations for these trajectories. Release point and scoring results did not change with practice.[21]

The authors concluded that the non-dominant limb demonstrated a coordination mode typical of Bernstein's unpracticed performer, in that there was an increase in stiffness through constraining the limb to act as a functional unit. This interpretation is supported by the high cross-correlations of angular displacement and angular velocity in the non-dominant limb. These greater cross correlations in the non-dominant arm suggest that in a relatively unpracticed condition, the motion at the different joints is not coordinated independently, but rather as a fixed unit. However, with respect to the performance scores post-practice, even though both arms showed improvement their performance scores this improvement was not statistically significant.[21] Perhaps for a complex task such as dart throwing the amount of practice was not enough to promote clear changes in performance. The authors concluded that both movement variability and changes in the mode of coordination can be affected by practice. It possible that with greater amount of practice a statistically significant improvement could have been observed indicating that practice might induce change in coordination control.

Newell and van Emmerik published a study focusing on coordination acquisition during an upper extremity activity.[18] They performed a qualitative and quantitative analysis of their 3-D (3 dimension) motion analysis during the performance of two writing tasks. The subjects had to repetitively write cursive *e*'s and write their own signatures with the dominant arm and the non-dominant arm. There were 5 right handed subjects and 5 left handed subjects recruited. Practice trials were performed by 3 out of the 5 right handed subjects with their non-dominant arm. Data were collected at the end of the practice trial. This descriptive analysis of subjects learning to write provides some evidence to support Bernstein's suggestion that skill acquisition reflects the mastery of redundant available motion. For right handed subjects, the correlation of joint motions in the non-dominant limb was significantly higher than those in the dominant limb.[18] This result illustrates the initial stages of motor learning proposed by Bernstein in which the performer has to initially stiffen the movement pattern by "locking" the joints and, hence reverting to a more primitive pattern of movement in which there is less motion of the upper extremity and having the limb segments moving all together as a unit. However, the results of this study did not support the following phase of the theory in which with practice there should be a release of the stiffened pattern of movement and consequently the limb segments would start to move with more independence from each other. At the end it was observed that the patterns of kinematic linkage of the non-dominant arm displayed a high degree of similarity with those obtained in the early phase of practice with the same arm. The authors suggested that the acquisition of structure of motion may take much more practice than has been typically applied in experimental studies of skill acquisition.[18]

The literature is sparse regarding experiments assessing the stiffened pattern of movement and its progression to less stiff patterns of movements. A review of a two studies that performed these assessments on lower extremity follows. Anderson and Sidaway performed an experiment on a series of cases, 5 experimental subjects and 3 control subjects, in which kinematic data was collected during the performance of a soccer kick task.[17] The 5 individuals in the experimental group were right foot dominant and had never received any formal soccer training or participated in any organized soccer games. The 3 subjects selected to be controls in this study were collegiate soccer players and were asked to perform the soccer kick task to determine the amount of improvement the novice players had gone through. The task was a right-footed soccer kick in which the primary goal was to maximize ball velocity although they should try to hit the target area. Two dimension video data were recorded prior to and after 10 weeks of practice.[17] Intra-class correlation coefficients were calculated on 3 pre-training and 3 post-training trials and showed that the dependent variables reliably assessed performance (.75 to .99). The authors believe there were considerable changes in the performance of the experimental group, although their posttest means were not close to the means of the expert group. For the experimental subjects the mean of Maximum Foot Linear Velocity increased from a 14.9 m/s pre-training to a 21.9 m/s post-training (expert mean= 25.6m/s). In addition, the experimental subjects showed an increase in mean Maximum Knee Angular Velocity from 1145 deg/s to 1287 deg/s (expert mean = 1493 deg/s). An increase in joint ROM was seen at the knee and hip joints. The knee had a mean excursion of 90.5 deg before training and a mean excursion of 103.6 deg after training (expert mean = 120.7 deg). The hip also improved from an initial mean excursion of 86.3 deg to 103.4 deg after training (expert mean = 134.9 deg). Even though novice players improved in these four parameters, based on their reported results Maximum Foot Linear Velocity and Hip Excursion were significantly different from the experts after practice. On the other hand, Maximum Knee Angular Velocity and Knee excursion were not statistically different from the experts after practice. Their conclusion was that the performance improvement was due to a change in coordination rather than simply an increase in a speed of the movement pattern. The findings of this study also provide some support to Bernstein's ideas on the acquisition of skilled movement behavior.[17]

Similar results were obtained by Vereijken et al on motor control improvement during the performance of a lower extremity activity.[16] They recruited 5 male subjects that had no prior experience with skiing or with a ski apparatus. These subjects had to learn how to perform slalom-like ski movement on a ski apparatus. The instructions given were to learn to perform large amplitude, high-frequency side to side movements on the apparatus while having their hands behind their backs at all times. A motion analysis was done and the kinematic variables were recorded with the use of 11 light-emitting diodes (LEDs). The LEDs were placed on both shoulders, hips, knees, ankles and tip of the shoes. One hundred and forty trials of 1 min duration each were performed and spread over 7 consecutive days. Thirty four trials, divided over the total practice period, the initial 30 seconds of data were recorded. The kinematic variables taken into account were amplitude and frequency of platform movement, in addition to hip, knee and ankle angles.[16] Their results showed gradual improvement of the amplitude and frequency after the first day of training. The small ranges of angular motion and small standard deviations demonstrated that these joints were rigidly fixed at the beginning of practice. Later in practice there was an increase in mean joint motion and increase of the respective standard deviations. The magnitude of the cross correlations between joints ranged from moderate to high in early practice. These results associated with the small ranges of angular motion suggest that the strategy used was to restrict motion and create dependence between joints. An increase in angular motion and an overall systematic decrease in the cross correlations between joints were observed with practice indicating freeing of the initial stiffened pattern of movement. The authors suggest that gradual decrease in couplings between body angles might continue to gradually reduce if the practice period was longer. They also concluded that an increase in time of practice was needed which is similar to the claims by Anderson and Sidaway.[16] Even though the authors failed to demonstrate statistical significance in this analysis it possible that the small sample size might have been the reason for this result.

As can be observed by this review of the literature, not all the components of Bernstein's theory have been extensively studied. All of the reported studies focused on the first phase of Bernstein's theory; however their sample sizes were extremely small and biases such as no control group may have influenced the results. In addition, not all of the studies listed above explored the effect of practicing the new movement component which may lead to the release of the stiffened pattern of movement. The studies that did include practice did not find statistical significance. In these instances, the authors suggested that longer periods of practice may be required in order to find statistical significance.[17,18] Their conclusion may be true; however it is possible that bigger sample sizes would have been enough to demonstrate statistical significance of these results. A better designed study with an adequate sample size and sufficient practice training period may show evidence to support the stiffening and its release as suggested in Bernstein's theory.

1.3.3 RELEASE OF STIFFENED PATTERN OF MOVEMENT

In the previous section it was explained how the stiffening of movement is the first stage of the process of acquiring skill. This phase is necessary in order to achieve the movement goal, which is mastering the movement. Bernstein referred to this phase as to be "employed as the most primitive" and simplified method so later it can be replaced by more flexible, efficient and economical methods.[10] However, the progression from a stiffened pattern of movement to an unrestricted well-controlled movement is not a random occurrence. It is necessary that the individual undergoes training or practice to master the desired motor skill. The suggestion is that practice does not imply a simple repetition of a motor problem over and over again, it entails going through the "process of solving" the motor problem by techniques that were changed and refined from repetition to repetition. Therefore, practice consists of a continuing process of seeking an appropriate solution for the respective motor problem.[10]

According to Bernstein, the process of acquiring skill occurs within a circular self-regulatory system. This system is active during the performance of any given movement and at all times that the same movement is performed. Given that it is a circular servo model it is difficult to determine where the beginning and the end of the system takes place. Therefore, following the description given by Bernstein, the first component that should be taken into account is the activity itself.[10] When a movement is executed, it initiates a motor feedback input coming from the musculoskeletal structures, and initiates a sensory feedback coming from the joint receptors and other proprioceptors and Bernstein's model infers that efferent or motor feedback may accompany the sensory feedback. These two feedback inputs together provide the information of what actually happened during the movement performance. Simultaneously, there is an input signal that is originated in the commanding system. This input provides the information of what was required to happen, the ideal movement performance. The comparing system receives these "factual and required" inputs and based on the difference between them it calculates the amount of error produced by the movement. This error signal leads to changes or re-calibration of the motor program as well as creating memory of what was done wrong by recording this error signal. Following the sequence in the servo loop model, the regulator system receives these corrections enabling its control over the motor output to the muscles.[10]

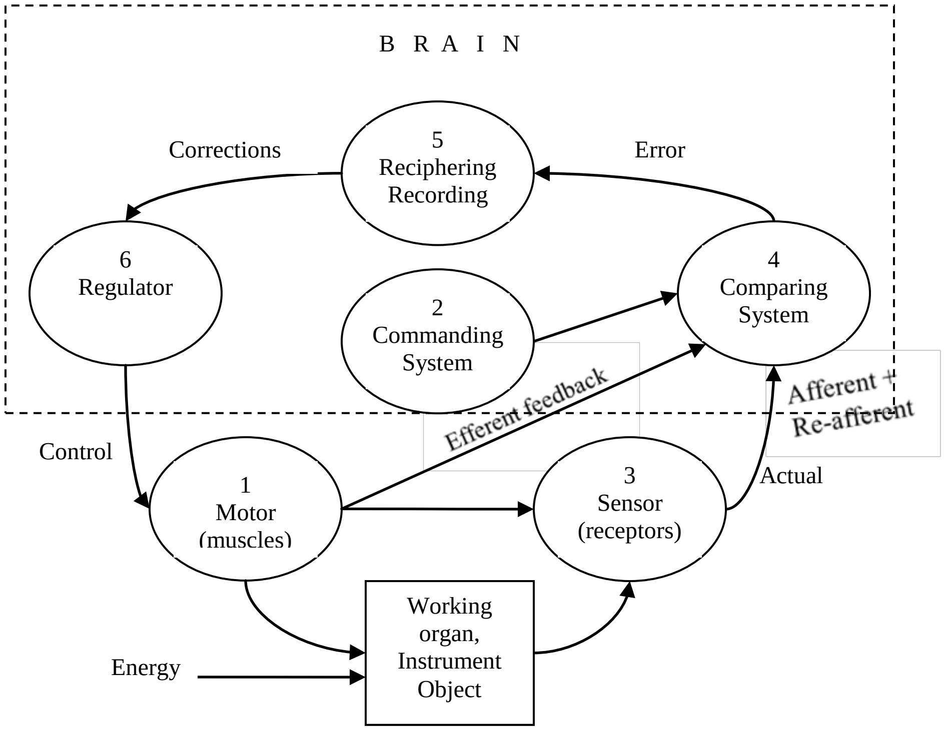


Figure 1- Bernstein's Circular Servo System [10]

Every time a movement is performed this self-regulated system will be activated. Each time movement performance will be different based on the corrections created by the previous cycles and also based on the vast memory of the errors that had previously occurred. This memory assists so that these errors are not repeated and therefore, quality of the movement performance is enhanced. Therefore, with practice the movement performance will get closer and closer to the ideal performance.[10]

There is substantial evidence in the neuroscience literature that practice of new motor skills improves performance and leads to positive structural change in the motor cortex and other components in the motor system.

1.3.4 STRUCTURAL CHANGES TO THE MOTOR CORTEX

Thus far, motor skill acquisition has been extensively studied in animal models more than in human models due to the difficulty of using invasive methods in human subjects. The following review of the literature will show the structural changes observed in motor cortex of animals due to practice of novel skill and exposure to challenging environments. These changes in motor cortex coincide with changes observed in motor behavior during the performance of novel tasks in these animal models. Even though one may argue that animal models may not transfer to human models to the full extent, these data offer a strong argument that it is likely that similar structural reorganization of the motor cortex may also happen in humans. Therefore, animal data may be used to support the need to modify standard physical therapy treatments into more challenging and skilled oriented treatments in order to achieve similar changes.

At present, it is well documented and clear that the motor cortex of adult mammals is capable of rapid widespread functional reorganization, suggesting that the circuitry underlying the cortical representations is inherently plastic.[22,23] In addition, it is well established that the reorganization of the somatosensory cortex can be induced by pathological disturbances but it also can be selectively altered by behavioral experiences.[22,24] In order to understand these structural changes it is important to understand the structural and morphological underlying synaptic plasticity. Dendritic spines appear to be a major the substrate of this plasticity. These tiny dendritic protrusions receive the majority of excitatory synapses.[25] According to Kasai, dendritic spines structure-stability-function relationships suggest that large spines are ‘memory spines’ and the small ones are ‘learning spines’. Large spines are stable and maintain strong synaptic connections. Small spines are unstable and are mostly responsible for the acquisition of memory.[26] Motility is another typical characteristic of dendritic spines. These structures have the ability to expand or retract and morph, always seeking for strong synaptic connections. Motility is required for synapse formation and its turnover would last throughout the lifetime of the organism, never stopping completely, but decreasing with age.[27] Spine sprouting and retraction are associated with synapse formation and with synapse elimination respectively. The balance between formation and elimination of spines explains the constant synaptic densities rather than lack of synaptogenesis. The turnover of spines is increased by sensory deprivation and experience-dependent “rewiring of the brain” may be caused by altering synaptic connectivity.[25]

There is substantial evidence of learning-dependent alterations in both neuron morphology and regional brain function.[28] In 1990, Black et al developed a study in which 38 hooded female rats were housed individually for 30 days in one of four experimental groups. Rats in the acrobatic group (AC) were given increasingly longer and difficult trials consisting of elevated paths, rope bridges and other obstacles of the same type. Initially, the rats needed considerable amount of time to overcome the obstacles. By the last week of training there was a significant decrease in the time needed to overcome more difficult obstacles reflecting a substantial amount of motor learning. Rats in a forced exercise (FX) control group walked at 10m/min on a treadmill initially and progressed to a longer periods until they reached the 1 hour daily mark. All FX rats were able to master walking on the treadmill by the first day, which was evidence that the amount of learning in this task was small.[28] There was a third group, voluntary exercise (VX) group that had access to a running wheel. The number of wheel rotations was recorded daily. Within 3 days the rats were able to master the simple balancing and coordination required to run in a wheel. The fourth group was the inactive condition (IC) that did not have opportunities for learning or exercise since they were kept in regular laboratory cages. The IC and VX groups were used as controls for the AC and FX groups. By the end of 30 days the rats in the AC group walked 0.9 Km slowly, in the FX group the rats walked 10.8 Km at a trot, the VX rats had run 19 Km with a standard deviation of 4 Km and the IC group had performed zero exercise. The AC group did not show significant difference in capillary density in relation to the other groups, but the VX and the FX groups had a higher capillary density than the AC and IC groups. In addition, the AC group had 25% more synapses per Purkinje cell, at the Cerebellum, than the other groups.[28] Therefore, the authors concluded that the acrobatic training effect was to increase the amount of synapses while vascular density remained the same and that the two exercise groups' effects were to increase the blood vessels density without changes in numbers of synapses. When there is a need for skilled movements, synaptic connections change. When there is a need for extensive repetition of simple, well practice movements, the vascular density is enhanced to supply the increased metabolic load due to higher sustained levels of neuronal activity.[28]

Following the same line of experiments Nudo et al developed a study to determine the different effects of skill acquisition and functional organization in primate motor cortex.[22] The squirrel monkeys used in the experiment were trained to retrieve food treats from either the smallest or the largest well. Both groups had the same amount of motor use of their finger flexors during training. The group trained to retrieve food from the small well showed an improvement in motor skill and significant changes in the post-training motor maps. The group retrieving food from the large well had almost perfect performance throughout the task resulting in no evident change in motor skill and few changes in motor maps. The authors reached similar conclusions as Black and colleagues[28] in the study reported previously. The results suggest that functional mapping of the motor cortex is altered by learning of new motor skill rather than by repetitive motor use alone.[22]

Remple et al performed an experiment with 24 hooded rats that were randomly assigned to three groups.[29] The groups were the Power Reaching Condition (PRC), the Control Reaching Condition (CPC) and the Non-Reaching Condition (NRC). During the pre-training period, the rats were required to reach through a slot in front of the cage to obtain a strand of dried pasta. Each rat finished the training period after performing 25 successful reaches within 30 min for 2 consecutive days. In the PRC (n=8) the bundles of dried pasta were taped together in order to prevent the rats from grasping individual strands. This group trained 3x/ week, for 4 weeks, on progressively increasing the bundle size until the rat could not break the bundle after 20 attempts. Taking out one strand from the number that the rat failed to break defined the maximum bundle size (MBS).[29] These rats were trained to increase their strength based on the MBS until they were able to break the MBS 10 times. Then a new measurement of MBS was taken and the same progression was applied. The last measurement of MBS was taken at the 30 days of training. The CRC group (n=8) controlled for the increase in forelimb use and for the skilled movement performed by the PRC group. The CRC rats were trained to break one strand of dried pasta 10 times per training. The training sessions were done on the same days as the PRC. The MBS of this group was also accessed at the end of 30 days of training. The rats in the NRC group were kept in their cages during the experiment period and did not receive any kind of training.[29]

The results showed significant improvement in strength of the PRC group from the pre-training period and that their strength improvements were greater than the CRC group.[29] The accuracy of reaching for PRC and CRC groups improved significantly throughout training. Post hoc analysis showed the PRC and CRC groups had significantly greater percentage of forelimb representations in the motor cortex than the NRC group. In comparison to the non-reaching group, the rats trained to progressively retrieve larger bundles of pasta did not differ significantly in motor map representation from the group that had to reach and break only one pasta strand. This study shows the motor mapping in the motor cortex is responsive to skill learning rather than strength training.[29] This result supports the idea that the motor cortex is organized to coordinate movement and that novel action patterns promote changes in cortical mapping representations.

Kleim et al randomly assigned 12 hooded rats to either a skilled reaching condition (SRC, n= 6) or an unskilled reaching condition (URC, n= 6) to study motor dependent motor plasticity.[23] The URC cage had a lever that when pressed dispensed food pellets into a receptacle and the rat had to retrieve the food with their tongue and mouth. The SRC rats, one day prior to training, were encouraged to reach through the slot to obtain food pellets from a circular stationary table outside of their cage. During the first 5 days of training, the table was moved 1 cm away to force the rats to have to grasp the pellets instead of scrape them into the cage. From day 6 to 10, 16 pellets were placed around the edge of the slowly rotating table. The results showed that the URC performed 400 bar presses during each of the 10 24hour training sessions. The SRC group's performance progressively improved with training.[23] The mapping of movement representations varied as a function of training condition. The SRC showed an increase in the representation of the digit and wrist areas when compared to the URC group. In addition, the SRC rats had a significantly greater volume of neuropil (network of axons and dendrites that surrounds the cell bodies) per layer 5 neuron than the URC group. To maintain the synapse density and simultaneously to increase the volume of neuropil per neuron resulted in significant increase in number of synapses/ neuron in the SRC.[23] This experiment is in agreement with the previously reported studies that learning-dependent synaptogenesis and functional reorganization are localized in motor cortex areas that mediate learned behavior. This study also suggest that synapse formation promotes changes in cortical circuitry and that motor cortex reorganization occurs in response to skilled movements rather than simply by increased limb use.[23]

This literature supports the idea that standard therapy with repetitive exercises, muscle flexibility, strength and aerobic training may not be enough to accomplish the structural motor cortex and/or cerebellar changes that are necessary to deal with the challenges of everyday life. Coping with the obstacles that are imposed everyday on individuals that have KOA require solving motor coordination problems. We believe that once these people are provided with an enriched treatment environment where they will be challenged to learn novel skilled movements and solve motor control problems, motor cortex mapping changes will occur. Even though the previously reported experiments were not performed in humans according to the findings discussed above and following, there is a strong suggestion that the inherent plasticity of the motor control system can be used to achieve better results in therapy.

1.3.5 AGILITY AND PERTURBATION TRAINING

A treatment program that exposes individuals to the movement problems and challenges that they will encounter during activities of daily living may be required in order to obtain the necessary structural and functional motor cortex changes as well as cerebellar plasticity in individuals with KOA. Lewek et al suggests that rehabilitation in this population may be more effective if neuromuscular strategies are introduced into the treatment.[30] In 2002, Fitzgerald and colleagues published a case report in which a patient with KOA had undergone agility and perturbation training.[31]This treatment is commonly seen in rehabilitation of Anterior Cruciate Ligament rupture patients.[14] By the end of the therapy sessions the patient reported no longer having pain with walking and did not need to use the handrail while going up and down stairs. The patient returned to playing golf without complaints of pain or knee instability.[31]

Agility and perturbation training exposes subjects to motor challenges that otherwise might not be experienced by these people. This therapeutic exposure to challenging environments may help this population to develop appropriate motor skills to deal with destabilizing loading forces encountered during activities of daily living.[31]Any treatment program, either standard treatment of OA or agility and perturbation training will activate the self regulatory system explained by Bernstein. However, we believe that the agility and perturbation exercises will provide the required motor and the sensory feedback to diminish the amount of error produced every time the loop is activated during each specific task. During the perturbation training on the roller board, for example, the patient is instructed on how to respond to the destabilizing forces without moving the board. At this time, the patient is having sensory and motor feedback because he/she is acting against these forces and the patient is also receiving verbal feedback from the therapist who is telling the patient how to improve the responses. The therapist is providing feedback of what is the ideal performance. Details of this training program have been described in a previous publication.[32] Pictures of the agility and perturbation activities are shown in Appendix A.

According to Bernstein, every time the exercises are performed the patient is creating a memory of errors that should not be performed again and is also making corrections in the program to improve the motor output.[10] As described previously, to acquire skill and actually have mapping changes in the motor cortex, a treatment that provides the people with the tools to successfully accomplish this goal might be necessary. Therefore, we believed the versatile and enriched environment used during the agility and perturbation training program would give people the opportunity to experience motor challenges and more importantly, go through the process of solving motor coordination problems. In addition, we believed that after treatment subjects that received agility and perturbation training would show changes in lower extremity kinematics and changes in co-contraction during gait and step down performance. For example, we expected to observe at baseline lower values in joint excursion to be associated with high co-contractions of lower extremity muscle couples. These two variables together have been suggested to represent the stiffened pattern of movement typically seen in people who have KOA.[4,33,34] At post-treatment, we expected to see an increase in joint excursion and a decrease in the co-contraction of lower extremity muscle couples. These changes might indicate less stiffness during gait and during a step down task, which might be representative of the release of the stiffened pattern of movement due to skill acquisition. It seems logical to assume that rehabilitation programs for people with KOA will promote changes around the knee, because the exercises are targeting this area. However, the agility and perturbation training targets the entire lower extremity structure and muscles. While performing these activities subjects will utilize not only the musculoskeletal system but also the sensorimotor system. Therefore, with the use of agility and perturbation training it was expected to observe changes within the whole limb, not only at the knee but at the hip and ankle also.

1.4 PHASES OF THIS STUDY

The first phase of this study was to determine at baseline the association of decreased lower extremity joint excursion and increase co-contraction of key lower extremity muscle couples with the level of physical function in people with KOA. This phase of the study is reported in Chapter II. The second phase of this study was to compare the changes in lower extremity kinematics and muscle co-contraction patterns between subjects who receive standard rehabilitation and subjects who receive agility and perturbation training in addition to the standard, impairment-based exercise program. In addition, the second phase of this study was to explore the association of changes in lower extremity joint kinematics and changes in level of co-contraction of lower extremity muscle couples with changes in physical function in people with KOA after an exercise program. The second phase of this study is reported in Chapter III. In Chapter IV we outline the significance of our study and discuss directions of future research.

2 THE ASSOCIATION BETWEEN LOWER EXTREMITY MOVEMENT PATTERNS AND PHYSICAL FUNCTION IN PEOPLE WITH KNEE OSTEOARTHRITIS

2.1 INTRODUCTION

Knee Osteoarthritis (KOA) is a debilitating, degenerative disease that decreases the physical function (PF) status of people affected by it.[1-4] Level of physical function can be affected by a variety of factors such as age, body mass index (BMI), psychosocial characteristics, pain and activity level, knee alignment and instability, quadriceps strength and activation failure.[35-37] Establishing and understanding how these factors contribute to the decline in physical function is important in the development of better treatments that can effectively reduce disability in people with KOA.

It is well-known that people with KOA ambulate with altered lower extremity biomechanics when compared to healthy controls.[4,7,38,39] Among the common gait alterations are decreased knee excursion,[4,5] and increased co-contraction of lower extremity muscles.[2,4,6,34,38-40] The combination of decreased knee excursion and increased co-contraction may create the typical stiffened pattern of movement seen in this population.[4,33] This stiffened gait pattern has been suggested to be an attempt to reduce joint load[9,41], level of pain and knee instability.[4,42] However, even though this stiffened pattern of movement may be a compensatory strategy for people with KOA to keep performing their activities of daily living (ADLs), concerns have been raised that in the long term it might contribute to functional decline and progression of the disease.[4,30]

A similar combination of reduced joint excursion and increased muscle co-contraction has been described as an attempt by the neuromuscular system to gain control over movement.[16,19] The rationale is that with healthy joints this strategy is used to facilitate motor skill acquisition. When learning a new motor skill the neuromuscular system uses this stiffened movement strategy to simplify and solve the new motor problem.[10,16,18,43] It appears that the stiffened pattern of movement adopted by people with KOA and by healthy individuals when learning a new motor skill are similar taking into consideration the presence of reduced joint excursion and increased co-contraction of the surrounding muscles in both instances.[2,4,15,16,19] If this assumption holds true then the stiffened pattern of movement seen in people with KOA may reflect an attempt by the neuromuscular system to solve the motor problem when facing certain ADLSs.

Walking, and ascending and descending stairs are described as the most commonly encountered walking ADLs. [20] Thereby, these activities cannot be described as novel skills for individuals affected by KOA. However, people with KOA have to walk and manage steps under sensory and motor impairments, such as decreased joint position sense[44], decreased quadriceps strength[11,44], pain[45], knee joint instability[1,46] and joint narrowing[47], altered muscle activation patterns[4,33,38,48] and increased loads on the medial compartment[9,47,49-51]. Therefore, it is likely that the structural and physiological conditions imposed by the degenerated knee joint may create a novel condition in which these individuals have to relearn how to perform such basic tasks.

Decreased knee excursion and altered patterns of muscle activation have been extensively described in people with KOA during walking and it has been described also in a few studies during a step down task. In addition, muscle electric activity has been suggested to potentially be a better predictor of physical function in people with KOA than muscle strength.[35,42]Understanding how these biomechanical factors relate to each other and how they relate to physical function will be an important contribution to the development of movement enriched rehabilitations programs as suggested by Sharma.[35]

The purpose of our study was to explore the association of lower extremity kinematics and muscle activation patterns with physical function during walking and going down a step. Furthermore, we explored if the combination of a stiffened knee and increased co-contraction during these activities predicted level of physical function in people with KOA. For both questions we hypothesized that the stiffened pattern of movement created by decreased motion and increased co-contraction during gait and step down would be associated with poorer physical function in people with KOA.

2.2 PATIENTS AND METHODS

2.2.1 Subjects

The data reported here is part of a larger randomized clinical trial comparing 2 rehabilitation programs for people with KOA.[52] One hundred forty-two subjects participated in the present cross-sectional study reported here. Subjects were included in the study if they were ≥40 years of age, met the 1986 American College of Rheumatology clinical criteria for KOA [53], and had a grade ≥2 Kellgren/Lawrence radiographic changes in the tibiofemoral joint.[54] Subjects were excluded from the study if they had conditions that would place them at risk for injury during the exercise training program (e.g., required an assistive device for ambulation, had a history of ≥2 falls in the previous year, or were unable to ambulate 100 feet independently), had undergone total knee arthroplasty, exhibited uncontrolled hypertension, had history of cardiovascular disease, had history of neurologic disorders that affect lower extremity function (e.g., stroke, peripheral neuropathy), reported vision problems that affected performance of basic mobility tasks. All subjects signed an informed consent form approved by the University of Pittsburgh Institutional Review Board prior to participation in the study.

2.2.2 Measures

Physical Function. Physical Function was assessed by a performance-based test and a self-report questionnaire. The Get up and Go test (GUG) was used to test performance-based physical function. It measures the time a subject takes to get up from a standard-height chair and walk 50 ft on a level and unobstructed corridor as fast as possible.[44] A stopwatch was used to measure the time from the command “go” until subjects crossed the finish line. A longer time to complete the GUG represents greater functional limitations. This test has been shown to have a good intra-rater (ICC = .95) and inter-rater (ICC = .98) reliability.[1,55] The Western Ontario and McMaster Universities Osteoarthritis Index -physical function subscale (WOMAC-PF) was used as the self-reported measure of physical function. The WOMAC-PF has 17 items (each item is scored on a 5-point Likert scale from 0 to 4), and a total score of up to 68 points. Higher scores indicate worse function. Reliability and validity of the WOMAC has been established.[56,57]

Motion Analysis Procedures. Subjects walked along an 8.5m long vinyl-tiled walkway. An eight camera Vicon® (Vicon Peak–UK) 612 motion measurement system recorded three-dimensional motion data at a sampling rate of 120 Hz from the Plug-In-Gait maker set. Ground reaction forces were measured on two Bertec® (Bertec Corporation, OH, USA) force plates embedded into the walkway. The forces were recorded at a sampling rate of 1080 Hz and synchronized with the motion data. Five walking trials at self-selected walking speed were collected and averaged, where subjects contacted the force platforms without targeting. Five trials were collected with subjects stepping down from a platform 18 cm high onto the force plate leading with their most affected limb. Marker trajectories and ground reaction force data were low-pass filtered (Butterworth fourth order, zero phase lag) at 6 and 40 Hz, respectively. Data were analyzed using MatLab™ version 7.0 (The Mathworks, Inc, Natick, MA, USA). Mean joint excursions of hip, knee and ankle in the sagittal plane were calculated during the loading phase i.e. from heel strike to the first peak of vertical ground reaction force on both gait and step down conditions.

Electromyography Procedures. Surface electromyography (EMG) data were collected at 1080 Hz using an 8-channel Noraxon Telemyo System (Noraxon USA Inc, Scottsdale, AZ). Silver-silver chloride, pre-gelled bipolar surface electrodes (Medicotest, Inc., Rolling Meadows, IL) with an adhesive area of 3.8 cm in diameter and conductive area of 1 cm in diameter recorded EMG signals from the medial and lateral hamstrings (MH and LH), medial and lateral quadriceps (MQ and LQ), medial and lateral gastrocnemius (MG and LG), and the tibialis anterior (TA). Electrodes were oriented longitudinally in the direction of the muscle fibers on the center of the muscle belly. In order to ensure reliable placement of electrodes across subjects, measurement of subject's own length of 4 fingers breadth and 1 hand breadth were used. One hand breath was used to place the electrodes on the LQ, MG and LG. Four fingers breath were used to place the electrodes on the MQ and TA. MH and LH electrodes were placed 1/2 way of an imaginary line between the ischio tuberosity and the muscles insertion. A reference (ground) electrode was placed on the tibial crest. To reduce skin impedance and ensure proper electrode fixation, the skin at the electrode sites were lightly shaved with a standard disposable safety razor, lightly abraded with an emery board, and cleansed with 70% isopropyl alcohol. Signals were collected while muscles were resting and during maximum voluntary isometric contraction (MVIC) for data processing purposes. EMG data were rectified and smoothed using the root mean square (RMS) of a 25 ms moving window. They were then normalized by the maximum 3 second average obtained during the MVIC (NEMG). The magnitude of the co-contraction between LQ:MH, LQ:LH, MQ:MH, LQ:LG, MQ:MG, TA:LG and TA:MG was calculated using the following formula developed by Rudolph, et al:

$$\sum_{i=1}^{n}[(\text{Lower NEMG}_i/\ \text{Higher NEMG}_i * (\text{Lower NEMG}_i + \text{Higher NEMG}_i)]/n$$

where *i* is the sample number and *n* is the total number of samples in the interval. Lower NEMG is the level of activity in the less active muscle and Higher NEMG is the level of activity in the most active muscle.[58] The co-contraction indices were calculated during the loading phase i.e. from first foot contact to the first peak of vertical ground reaction force on both gait and step down conditions.

2.2.3 Statistical Analysis

Descriptive statistics, including measures of central tendency (means and medians) and dispersion (standard deviations, 25^{th} and 75^{th} percentiles) for continuous variables were calculated to summarize the data. The Kolmogorov-Smirnov test with Lilliefors' significance [59] was used to determine the normality of the data. According to the data distribution, independent samples t-test or Chi-Square were used to detect statistically significant differences ($p<0.05$) of baseline characteristics, kinematics, co-contraction indices and measurement of physical function between subjects whose data were included in regression analyses and subjects whose data were not included due to missing data values (see Figure 1 for description of missing data causes). Bivariate relationships between subject characteristics (age, gender, height and weight), kinematics, co-contraction indices and measures of physical function (GUG and WOMAC-PF) were assessed using Pearson correlation coefficients (r) for continuous data and Spearman's rank correlation coefficients (ρ) for categorical data ($p<0.05$).

For the purpose of testing if lower extremity joint kinematics and muscle couples co-contraction explain variability in physical function, a total of four stepwise multiple regression analyses were performed. Two regression analyses were performed with GUG as the dependent variable, one for gait and one for the step down task. Two other regression analyses were performed with the WOMAC-PF as the dependent variable, again, one for gait and one for the step down task. On the first step of the regression, in order to account for the effects of subject characteristics on physical function, age, gender, height and weight were entered simultaneously into the model. On the second step, variables that represent stiffened pattern of movement such as joint excursions of hip, knee and ankle, and the co-contraction index of 7 muscle couples (LQ:MH, LQ:LH, MQ:MH, LQ:LG, MQ:MG, TA:LG and TA:MG) were available for entry into the model in a stepwise manner. Due to the exploratory nature of this study and because we did not want to miss variables that could potentially contribute to the variability in change in physical function the alpha level was set at 0.1. For this reason, the probability of the F value for the regression analyses was set at 0.1 to enter the model and 0.15 for removal from the model.

In order to explore our theory that level of co-contraction might be related to physical function when people with KOA walk or step down with a stiffened knee, interaction terms between knee excursion and each muscle couple co-contraction index were created. Four separate regression models were used to predict physical function (GUG and WOMAC-PF). Initially subject characteristics were entered, followed by the main effects of knee excursion, muscle couple co-contraction index, and, then by the respective interaction term (e.g., Subject Characteristics + knee excursion + LQ:MH + knee excursion*LQ:MH = GUG). High and low values of knee joint excursion and muscle co-contraction were defined using the median of each respective variable. Alpha level was set at 0.1 in these exploratory analyses also.

2.3 RESULTS

At baseline 142 subjects with KOA completed Motion Analysis and electromyography data collection procedures. In figure 2, the flow chart delineates the number of subjects who participated in the data analyses and the number of subjects who did not participate in the data analyses due to missing data values. The reasons for missing values are also stated in the flow chart. The following results are based on 70 subjects who participated in the analyses of the gait condition and 67 subjects who participated in the analyses of the step down data. Comparisons of subject characteristics between the groups with complete versus incomplete data only showed a significant difference in age. Subjects with incomplete data were 3.1 years and 3.4 years older than the subjects with complete data for gait (p=0.04; Table 1) and for the step down (p=0.02; Table 2) conditions respectively. Subject characteristic variables demonstrated that the sample included in the statistical analysis is representative of the general population with KOA. Comparisons of kinematic and co-contraction indices between subjects with complete and incomplete data on both conditions showed a significant difference of the MQ:MG co-contraction index ($p<0.01$) during the step down task (Table 3).

2.3.1 Gait

Bivariate correlation coefficients between the subject characteristics, predictor, and criterion variables are shown in Table 4. Older subjects had slower GUG. Women and shorter subjects had slower GUG and worse WOMAC-PF. Mass was not significantly correlated to GUG or to the WOMAC-PF. Subjects who had more ROM at the hip also had more ROM at the ankle. Conversely, hip and knee joint excursion were negatively correlated, indicating that subjects who had less ROM at the knee joint had more ROM at the hip. All 7 muscle couples were positively correlated to WOMAC-PF and 4 muscle couples were positively correlated to the GUG. The positive direction of these relationships indicates that subjects with higher co-contraction indices had worse performance based and self-reported physical function.

The results of the stepwise multiple regression analyses are shown in Table 5. The regression model built to predict GUG showed that subject characteristics explained 32% of the variability in GUG ($p<0.01$). Once subject characteristics were in the model, the LQ:LG co-contraction index explained an additional 4% of the variability in GUG ($p<0.05$). The regression model predicting WOMAC-PF showed that subject characteristics explained 21% of this measure's variability ($p<0.01$). Once subject characteristics were accounted for in the model, LQ:LH co-contraction index explained an additional 6% of the variability in WOMAC-PF scores ($p<0.05$). On both regression models the beta standardized coefficient (β) of the association between the co-contraction index and the measures of physical function were positive indicating that increased co-contraction was associated with worse physical function in people with KOA.

The highest variance inflation factor (VIF) values were equal to 3.0 in both regression models, indicating no collinearity issues during the regression. Plots of the residuals showed values within 3 standard deviations. This observation indicates that linear regression assumptions were met in these analyses.[60]

The separate regression analyses exploring the association between knee joint excursion and physical function at higher (above the median) and lower (below the median) levels of co-contraction showed that the interaction between Knee Excursion * TA:LG significantly predicted GUG ($p<0.1$; Table 6). The interaction plot (Figure 2) showed that subjects with lower knee excursion and higher co-contraction of TA:LG had a slower GUG. Subjects with lower knee excursion and lower co-contraction of the TA:LG had faster GUG. While for the subjects with higher knee excursion there was no difference in GUG at either higher or lower co-contraction levels of this muscle couple.

2.3.2 Step Down

Bivariate correlation coefficients between subject characteristics, predictors and criterion variables are shown in Table 7. The significant relationships between subject characteristics and the two measures of physical function were very similar to the ones observed for the gait condition. As observed during gait, during the step down condition hip and knee joint motions were inversely related indicating that subjects who had less ROM at the knee joint had more ROM at the hip ($r = -0.42$). Hip excursion was the only kinematic variable with a significant correlation ($r = -0.25$) with an outcome measure (WOMAC-PF), indicating that less hip excursion was correlated with worse function. Similarly to gait, all 7 muscle couples were positively correlated to GUG and 5 muscle couples were positively correlated to the WOMAC-PF indicating that increased co-contraction is related to poorer physical function scores.

The regression model predicting GUG (Table 5) showed that subject characteristics explained 29% of the variability ($p<0.01$). Once subject characteristics were included in the model, LQ:LG and MQ:MH co-contraction indices explained an additional 10% ($p<0.01$) and 4% ($p=0.06$) of the variability in physical function respectively. The β coefficient of the association between GUG and LQ:LG was 0.28 and between GUG and MQ:MH it was 0.20. These positive values indicate that higher co-contraction indices of these muscle couples during the loading of the step down task were associated with slower GUG in people with KOA (Table 5).

The regression model predicting WOMAC-PF showed that subject characteristics explained 25% ($p<0.01$) of the variability. Once subject characteristics were added to the model, hip excursion during loading and MQ:MG co-contraction index explained an additional 8% ($p<0.01$) and 4% ($p=0.06$) of the variability of this self-reported measure of physical function respectively. The β coefficient for the association between hip excursion and WOMAC-PF was -0.29 indicating that decreased hip excursion during the step down task is associated with worse physical function in people with KOA. In addition, the β coefficient for the association between WOMAC-PF and MQ:MG was 0.20 indicating that higher co-contraction indices were associated with worse self-reported measure of physical function. The highest VIF values were 3.3 in both regression models. This result indicates that collinearity was not a problem. Analyses of the residual plots showed that all values were within 3 standard deviations. This observation indicates that linear regression assumptions were met during these analyses.[60]

The separate regression analyses exploring the association between knee joint excursion and physical function at higher or lower levels of co-contraction showed that the interaction between Knee Excursion * LQ:MH, Knee Excursion * TA:MG and Knee Excursion * TA:LG during the step down task significantly predicted GUG (Table 6). All 3 plots of the significant interactions showed similar results (Figures 3, 4 and 5). During the step down loading phase, people with lower knee excursion and higher co-contraction of either LQ:MH, TA:MG or TA:LG had slower GUG. Subjects with lower knee excursion and lower co-contraction of either of the 3 muscle couples had faster GUG. On the other hand, for people with greater knee excursion, the level of co-contraction did not relate to better or worse GUG.

In an attempt to further understand the results of the interaction between knee excursion and co-contraction, plots of higher TA:LG co-contraction for people with lower knee excursion were created as well as plots of lower TA:LG co-contraction for people with higher knee excursion (Appendix B). On the first scenario, for people who combine higher co-contraction and lower knee excursion during loading there is a greater variability in the co-contraction data. Visual observation indicates a consistent oscillation of the co-contraction during the loading phase. On the second scenario, for those who combine lower co-contraction and higher knee excursion during loading there is less variability in the co-contraction data. These data seems to indicate that these individuals are able to maintain a stable level of co-contraction during loading. This characteristic of higher co-contraction showing greater variability and vice-versa was observed in other muscle couples as well. These results possibly indicate a motor control problem in regulating the level of co-contraction during loading.

The same separate regression analyses were performed to predict WOMAC-PF during gait and step down. None of the interaction terms created significantly explained variability in WOMAC-PF.

2.4 DISCUSSION

After accounting for subject characteristics, we found that increased co-contraction of LQ:LG and LQ:LH during gait explained part of the variability in GUG and WOMAC-PF respectively. In addition, during the step down, increased co-contraction of LQ:LG and MQ:MH predicted GUG; and decreased hip excursion and increased MQ:MG co-contraction predicted WOMAC-PF. In general, decreased lower extremity joint kinematics did not show a significant association with the measures of physical function except for hip excursion during the step down task. We had originally hypothesized that decreased joint kinematics and increased co-contraction would concomitantly be predictors of GUG and WOMAC-PF. However, from our list of possible predictors increased co-contraction was the consistent predictor in all regression models predicting physical function.

Observation of bivariate correlations indicated that during gait, increased hip excursion was related to worse GUG and during step down, decreased hip excursion was related to worse WOMAC-PF. Even though it may seem counter intuitive that people with more hip motion would walk slower, this may be a strategy to compensate for the decreased motion of the knee joint. This theory is somewhat supported by a low but significant inverse correlation between hip and knee excursions during gait ($r = -0.26$; Table 4).The reduced motion at the knee joint might be an attempt to simplify motion in order to reduce potential pain and knee instability.[4,42] The increase in hip excursion might be an attempt to maintain mobility and compensate for the stiffening at the knee joint. This statement is in agreement with a suggestion by Messier[5] in which people with KOA may have increased the range and velocity of the hip as a compensatory mechanism to the decreased knee excursion and as an attempt to maintain walking velocity. By increasing hip motion these individuals may be able to maintain stride length and therefore have enough mobility to perform the walking task.

For both gait and step down conditions, in all regression models, subject characteristics explained from 21% to 32% of the variability in physical function. Our discussion will focus on the predictors that significantly explained variability in physical function beyond the contribution of subject characteristics. As expected, the regression models depicted similar results to the bivariate correlations. During gait, lower extremity joint kinematics did not significantly contribute to predicting either GUG or WOMAC-PF. On the other hand, increased co-contraction of LQ:LG and LQ:LH became predictors of GUG and WOMAC-PF respectively. It has been shown that increased co-contraction of muscle couples lateral to the knee is present in earlier stages of KOA when comparing people with moderate KOA, classified by presence of symptoms and radiographic changes, to healthy controls.[34] Furthermore, a difference in magnitude of lateral muscle co-contraction was not found when comparing people with severe KOA, those who are candidates to total knee replacement based on symptoms and radiographic changes, to people with moderate KOA. This result indicates that the lateral muscle co-contraction remained increased with KOA progression.[39] The conclusion drawn from these results was that increased co-contraction of lateral muscle couples might be a neuromuscular strategy adopted in early stages of KOA to constrain the detrimental effects of increased medial compartment loading which is an immediate threat to joint integrity.[34,39] Our results showed that people with poorer physical function might have adopted a similar neuromuscular strategy of increasing lateral muscle couples co-contraction potentially as an attempt to reduce medial compartment loading and thus, enable walking performance.

In the step down regression analysis with GUG as the criterion variable, the co-contraction indices of LQ:LG and MQ:MH entered the prediction model. Our results indicate that people who walked slower during the GUG had higher co-contraction of lateral and medial muscle couples surrounding the knee during a step down task. Hubley-Kosey et al found that the magnitude of co-contraction of lateral muscle couples is elevated in people with moderate and severe KOA. In addition, they reported that there is a significant increase in co-contraction of muscles located medial to the knee joint at later stages of KOA severity when compared to moderate KOA.[39-41] Their suggestion is that in addition to the attempt to unload the medial compartment by the increase in co-contraction of lateral muscles, increased co-contraction of medial muscle couples might be a strategy to reduce instability due to the increased joint narrowing seen in people with severe KOA.[39,40]. These results corroborate other reports which suggested that a prolonged activation of MG[38] and MH[40] throughout the stance phase of gait might be a mechanism to increase knee joint stability due to the increased joint space narrowing.[2,38,40]Unfortunately, all these reported results and suggestions were based on analyses of walking trials only, thereby we do not know if these assumptions hold true for a step down task. We believe the distinct pattern of response of lateral and medial muscles seen during gait and the step down are dependent on the constraints imposed by the task itself. It is known that the step down is a more stressful and demanding task than level ground walking. [61-63] Our results showed that people who walked slower during the GUG might have adopted a similar strategy during the step down as the one adopted by people with severe KOA.[39,40]. Subjects who had slower GUG also had an increase in co-contraction of lateral and medial muscle couples potentially as an attempt to increase knee stability due to the increased demand imposed by the step down task and to enable its performance. This assumption is somewhat confirmed by the observation that in our sample subjects who had slower GUG concomitant with higher co-contraction of LQ:LG or MQ:MH muscle couples tended to have more severe complaints of knee instability.

Studies have reported knee joint kinematics and kinetics during the step down task in people with KOA [4,63] but little is known on kinematics and kinetics of the hip joint during a step down task in this population. Contrary to gait, in which increased hip excursion was correlated to worse GUG, during the step down decreased hip excursion was correlated to worse WOMAC-PF (r = -0.25; Table 7). The opposite direction of the relationships between hip excursion and physical function during gait and step down may support the previous assumption that the strategy adopted by the neuromuscular system to enable performance is dependent on the unique constraints imposed by each task. This is an expected response since the step down has been shown to be a more demanding and stressful task[61-63] than gait, thereby it seems safe to assume it may also require greater skill than level walking. If these assumptions are true, instead of reducing the motion at the knee as seen during gait, the strategy used during the step down reduces motion at the hip joint. This theory can be explained to some extent by the inverse relationship (r=-0.42) observed between hip and knee excursion. This specific strategy may be necessary to maintain balance while these individuals support their body weight on a single leg by helping to maintain the center of gravity displacement [64] to a minimum and therefore enabling task performance. In other words, people with lower levels of physical function potentially would have more difficulty performing this higher skill task. Reducing hip excursion would lead to a foot placement closer to the step and consequently would decrease the displacement of their center of gravity which could improve balance. On the other hand, people who have better physical function would probably have less difficulty performing this task. Thus, people with better physical function would have greater hip excursion and consequently a bigger stride length and a greater shift of the center of gravity. These suggestions might explain the association between decreased hip excursion during the step down task and worse WOMAC-PF.

After accounting for the contribution of hip excursion, the co-contraction index of a muscle couple medial to the knee (MQ:MG) during the step down became a predictor of WOMAC-PF. This result is in agreement with our previous statement which says that during a more challenging task such as step descending, people with lower levels of physical function need to increase activation of muscle couples located medial to the knee joint in order to enhance knee stability and enable performance of the task. It has been suggested that prolonged activation of MG might have a role in stabilizing the knee in severe KOA due to the increased joint space narrowing.[38]. We believe that even though our sample was not composed of people with severe KOA only, performance of step down task requires a substantially higher level of skill and therefore requires the contribution of increased co-contraction of medial side muscle couples to provide stability during the loading. It is important to note that MQ:MG co-contraction index was significantly greater ($p<0.01$) for subjects with incomplete in comparison with those with complete data (Table 3). Although there was a significant difference, the means indicated that both groups with complete and incomplete data had higher co-contraction of MQ:MG. Also, upon visual observation of scatter plots of MQ:MG co-contraction versus GUG and versus WOMAC-PF, increased MQ:MG was correlated with worse GUG ($r=0.54$) and worse WOMAC-PF ($r=0.31$) in both groups. Thus, we believe that had the subjects with incomplete data been able to participate in the regression analyses, MQ:MG would have still been a predictor of worse physical function and perhaps it would have strengthened the relationship found.

An unexpected result was the lack of relationship between knee joint excursion and co-contraction of lower extremity muscle couples during gait and step down conditions. This result is in contrast with reports of moderate to high correlations [65] (r ranging from -.5 to -.8) between knee excursion and lower extremity muscle couples co-contraction indices in people with medial KOA and reported knee instability. These moderate to high correlations were observed during an experimental condition in which subjects had to react to a random lateral translation of a platform under their foot while walking.[42] It is likely that this lateral disturbance during walking required a much greater co-contraction of muscles surrounding the knee to control instability. Therefore, the nature of their experimental condition could have driven the correlations between knee excursion and co-contraction indices. In our study, subjects were walking straight forward at their self-selected speed and no disturbances occurred during walking, potentially requiring less co-contraction than in the group studied by Schmitt and Rudolph. In addition, about 57% of our sample reported knee instability following the criteria adopted by Schmitt and Rudolph. It has been shown that people with KOA and knee instability have poorer physical function than those who do not report instability.[1] Therefore, it is possible that our sample was less affected due to the lower frequency of reported knee instability when compared to the Schmitt and Rudolph study sample. However, in our subsample of subjects who reported knee instability, Pearson correlation coefficients did not show a significant relationship between knee excursion and co-contraction of lower extremity muscle couples. In a different report by Schmitt and Rudolph[66] , co-contraction of MQ:MH and LQ:LG predicted knee excursion during the loading phase of gait in people with exclusively medial KOA. Approximately 27% (n=19) of our sample had isolated medial KOA following the criteria adopted by Schmitt and Rudolph. Spearman Rho correlation coefficients (ρ) showed that in this subsample of 19 people with medial KOA, increased knee excursion and increased co-contraction of MQ:MH were significantly correlated (ρ=0.5, p-value= 0.01).

It is noteworthy that the relationship shown by the Spearman Rho from our data indicated that higher values in knee excursion were correlated with increased co-contraction of MQ:MH whereas, it has been suggested that increased co-contraction of lower extremity muscles couples combined with decreased excursion of the knee represent a stiffened pattern of gait in KOA.[4,33] Stiffness does not mean lack of motion, it means that a greater load is necessary in order to produce the same amount of motion. It is possible an individual with increased co-contraction and normal range of motion of the knee also has a stiffened knee. If that is the case, increased co-contraction may be the determinant factor of knee stiffness during walking. Further studies are needed to explore the association between knee joint kinematics and pattern of lower extremity muscle activation and to explore the potential ways stiffened patterns of movement may present themselves in the population affected by KOA .

Although significant correlations between knee excursion and the muscle co-contraction indices were not observed and knee joint kinematics did not predict physical function, it is possible that knee excursion and muscle co-contractions may interact to have a greater impact on physical function. In order to test this theory, interaction terms between knee excursion and all the muscle couples in each biomechanical condition were entered into separate regression analyses to examine whether these interactions could have an effect on GUG and WOMAC-PF (see Statistical Analysis section). For gait, the knee excursion * TA:LG interaction term significantly predicted GUG (p=0.08; Figure 2). For the step down condition, the knee excursion

* LQ:MH (p=0.08; Figure 3), knee excursion * TA:MG (p=0.03; Figure 4), and knee excursion * TA:LG (p=0.02; Figure 5) interaction terms also significantly predicted GUG. The plots of all significant interactions depicted very similar results. During the loading phase of either condition for subjects with lower knee excursion, higher co-contraction of LQ:MH, TA:MG and TA:LG was associated with slower GUG and lower co-contraction of these muscle couples was associated with faster GUG. On the other hand, for people with greater knee excursion, the level of co-contraction did not relate to better or worse GUG.

The same separate regression analyses examining interaction effects between knee excursion and muscle co-contraction pairs were performed using the WOMAC-PF as the dependent variable. These regression analyses did not show a significant contribution of the interaction terms between knee excursion and muscle co-contraction pairs in explaining variability of the WOMAC-PF scores. A potential explanation might be that the self-report measures of physical function may be affected more by factors such as level of pain and psychosocial variables than by biomechanical variables such as knee excursion and level of co-contraction.[36]

The significant relationships of the knee excursion and muscle co-contraction interactions with the GUG, indicates that when stronger muscle co-contractions are combined with limited knee excursion, there may be a greater adverse impact on physical function, than when these variables are present in isolation or when greater amounts of knee excursion are present, regardless of the amount of muscle co-contraction. It seems there may be a sub-group of subjects with a combination of reduced knee excursion and higher muscle co-contraction that may be at risk for more difficulty with physical function. This finding may indicate that subjects may attempt to stiffen their knees in more than one way and the effect on physical functioning may depend on whether or not a strategy involving the combination of reduced knee excursion and increased co-contraction is employed.

2.5 LIMITATIONS

Our study had a number of potential limitations. Technical difficulties inherent to motion analysis and surface EMG procedures such as skin artifact due to motion of markers and electrical noise due to motion of the EMG leads respectively, reduced our original sample size substantially. However, mean comparisons between subject characteristic variables, kinematics, co-contraction indices and physical function showed that there were no differences between people who participated in the statistical analyses and those who did not due to missing data except for the MQ:MG co-contraction index. Therefore, we believe that even though missing data reduced our sample size it did not adversely affect our results.

Another potential limitation was that in order to assure subject safety during testing procedures, a strict inclusion/exclusion may have prevented us from recruiting a higher number of subjects with greater physical function limitations. If our sample had a greater number of people with more severe physical function deficits, it is possible we may have found stronger relationships between the biomechanical predictor variables and physical function. In addition to the previous limitations, it is possible that kinematics and co-contraction patterns of gait and step down were not enough to explain variability of GUG and WOMAC-PF. Perhaps performing motion analysis of other ADLs such as getting up and down from a chair and/or ascending and descending consecutive steps would have yielded greater associations between the kinematic and muscle co-contraction variables and physical function.

It should be acknowledged that subjects in our study had both medial and lateral compartment KOA and this could be a potential limitation. It is possible that specific kinematic and co-contraction variables related to medial or lateral KOA might have predicted physical function had these two groups been separated during analyses. Unfortunately, this was not planned during study design and for this reason our sample size did not allow for separate analyses. Finally, the cross-sectional nature of our design allows for discussion of the significant associations found but it precludes any conclusions regarding a causal relationship between lower extremity joint kinematics, muscle couples co-contraction and physical function.

2.6 CONCLUSION

Increased lower extremity muscle co-contraction during the loading phase of gait and the step down task was associated with worse physical function. As expected our results showed that each task generated a specific set of predictors. Due to the unique constraints imposed by each task we observed that increased co-contraction of muscle couples located lateral (gait) and located lateral and/or medial (step down) to the knee were associated with worse physical function. In addition, the analysis of the interaction between knee excursion and muscle co-contraction predicting physical function showed that higher co-contraction or lower knee excursion by themselves may not be bad for people with KOA. However, when these two biomechanical factors occurred simultaneously they had a detrimental effect on the performance of GUG. We believe that further exploration is needed to determine how rehabilitation can impact movement patterns and level of physical function of those who initially walk or step down with lower knee excursion and higher co-contraction of certain lower extremity muscle couples. Furthermore, future longitudinal studies exploring the association of changes in lower extremity joint kinematics and changes in level of co-contraction with changes in physical function are warranted.

2.7 TABLES

Table 1- Baseline Characteristics of Subjects with Complete vs Incomplete Data Included in the Gait Condition.

Variables	Subjects with Complete Data n = 70	Subjects with Incomplete Data n=63	*P* value
Age in years – Mean ± SD	62.5 ± 8.4	65.6 ± 8.7	0.04*§
Female - N (%)	45 (64.3)	37 (58.7)	0.51‡
Height in cm – Mean ± SD	169.9 ± 10.0	169.5 ± 8.5	0.72§
Weight in Kg – Mean ± SD	85.7 ± 17.9	89.6 ± 19	0.24§
GUG Test in sec **-** Mean ± SD	9.3 ± 2.0	9.7 ± 2.2	0.27§
WOMAC PF – Mean ± SD	20 ± 13	21 ± 12	0.47§

§= Tested with Independent T-test
‡= Tested with Chi-Square
*= Statistically different

Table 2 - Baseline Characteristics of Subjects with Complete vs Incomplete Data Included in the Step Down Condition.

Variables	Subjects with Complete Data n = 67	Subjects with Incomplete Data n = 62	*P* value
Age in years – Mean ± SD	62.1 ± 8.5	65.5 ± 8.1	0.02*§
Female - N (%)	45 (67.2)	35 (56.5)	0.21‡
Height in cm – Median (Min-Max)	166 (162 – 177)	170 (164 – 174)	0.60†
Weight in Kg – Mean ± SD	86.8 ± 18.1	88.1 ± 18.9	0.68§
GUG Test in sec **-** Mean ± SD	9.3 ± 2.0	9.4 ± 2.0	0.64§
WOMAC PF – Mean ± SD	20 ± 14	20 ± 11	0.92§

§= Tested with Independent T-test
‡= Tested with Chi-Square
†= Tested with Mann-Whitney U
*= Statistically different

Table 3 - Kinematic and Co-contraction indices of subjects used and not used in the Regression Analyses for gait and step down conditions.

Condition	GAIT				STEP DOWN			
Variables	Complete Data n = 70	Incomplete Data	n	*P* value	Complete Data n = 67	Incomplete Data	n	*P* value
Ankle Excursion – Mean ± SD	11.0 ± 4.4	10.0 ± 4.1	52	0.20§	29.9 ± 8.7	27.0 ± 8.3	52	0.07§
Knee Excursion – Mean ± SD	11.3 ± 4.4	11.6 ± 5.8	52	0.75§	8.9 (5.7 – 11.0)	7.8 (5.3 – 12.1)	52	0.94†
Hip Excursion – Mean ± SD	9.1 (6.7 – 12.4)	9.1 (6.2 – 11.2)	52	0.38†	6.3 ± 3.3	5.3 ± 2.6	52	0.07§
LQ:MH – Median (25^{th} -75^{th} %)	13.9 (8.3 – 22.4)	12.6 (6.9 – 26.3)	37	0.87†	16.4 (9.8 – 23.6)	19.5 (9.3 – 31.8)	30	0.21†
TA:MG – Median (25^{th} -75^{th} %)	11 (7.2 – 18.5)	13.4 (7.3 – 19.4)	50	0.45†	13.3 (7.6 – 20.6)	13.4 (7.5 – 26.1)	43	0.25†
LQ:LH – Median (25^{th} -75^{th} %)	23.5 (13.6 – 36.8)	26.9 (10.1 – 42.2)	23	0.89†	24.1 (11.9 – 34.9)	23.5 (16.6 – 32.5)	19	0.97†
MQ:MH –Median (25^{th} -75^{th} %)	13.1 (8.7 – 20.7)	14.2 (9.5 – 27.5)	25	0.50†	15.7 (10.3 – 23.6)	20.1 (10.7 – 30.6)	23	0.35†
LQ:LG – Median (25^{th} -75^{th} %)	12.9 (8.5 – 23.5)	14.5 (7.1 -28.3)	24	0.79†	24.5 (16 – 33.1)	24 (19.2 – 43.9)	22	0.35†
MQ:MG – Median (25^{th} -75^{th} %)	12.0 (8.3 – 17.4)	15.6 (10 – 25.2)	30	0.18†	23 (15.4 – 36.2)	36.1 (28 – 53.2)	25	<0.01†*
TA:LG – Median (25^{th} -75^{th} %)	12.1 (7.4 – 22.2)	14.3 (6.1 – 24.9)	32	0.87†	12.5 (7.6 – 20.7)	15 (6.5 – 27.1)	33	0.57†

§= Tested with Independent T-test
‡= Tested with Chi-Square
†= Tested with Mann-Whitney U
*= statistically different

Table 4 - Bivariate Correlations between Subject Characteristics, Kinematics, Muscle Co-contraction and Physical Function during the Gait Condition.

N=70	GUG	WOMAC-PF	Gender†	Age	Mass	Height	Ankle	Knee	Hip	LQ:MH	TA:MG	LQ:LH	MQ:MH	LQ:LG	MQ:MG	TA:LG
GUG	1	.27*	.44**	.32**	-.00	-.41**	.08	-.12	.31**	.32**	.21	.16	.27*	.25*	.15	.24*
WOMAC-PF		1	.38**	-.11	.20	-.30*	-.10	-.07	.17	.25*	.27*	.27*	.30*	.24*	.24*	.27*
Gender†			1	-.05	-.16	-.78**	.05	-.18	.41**	.43**	.40**	.04	.40**	.21	.22	.29*
Age				1	-.19	-.07	-.09	-.18	.09	.03	.09	.06	.03	-.11	.09	-.01
Mass					1	.33**	-.03	.12	.20	-.05	.03	.01	-.07	.13	.01	.09
Height						1	-.15	.10	-.34**	-.29*	-.22	-.07	-.24*	-.09	-.14	-.15
Ankle							1	-.18	.35**	-.09	-.06	-.00	-.09	.10	.01	-.02
Knee								1	-.26*	-.12	-.01	-.06	-.06	-.15	.04	-.05
Hip									1	.19	.09	.04	.10	.24*	.12	.15
LQ:MH										1	.40**	.32**	.93**	.27*	.30*	.40**
TA:MG											1	.25*	.47**	.57**	.91**	.80**
LQ:LH												1	.31**	.39**	.27*	.29*
MQ:MH													1	.22	.36**	.43**
LQ:LG														1	.63**	.77**
MQ:MG															1	.71**
TA:LG																1

†Values represent Spearman Rho; * $p<0.05$; ** $p<0.01$

Ankle; Knee; and Hip=joint excursion values.

LQ:MH= lateral quadriceps: medial hamstrings mean co-contraction index; TA:MG= tibialis anterior: medial gastrocnemius mean co-contraction index; LQ:LH= lateral quadriceps: lateral hamstring mean co-contraction index; MQ:MH= medial quadriceps: medial hamstring mean co-contraction index; LQ:LG=lateral quadriceps: lateral gastrocnemius mean co-contraction index; MQ:MG=medial quadriceps: medial gastrocnemius mean co-contraction index; TA:LG=tibialis anterior: lateral gastrocnemius mean co-contraction index.

All kinematics and EMG values were calculated during the loading phase of gait.

Table 5 – Stepwise Multiple Regression Analysis predicting GUG and Womac-PF during Gait and Step Down Conditions.

Condition	*Dependent Variable*	*Variables in Reg. Model*		*β*	*β Sig*	*Total R^2*	*Δ R^2*	*df*	*p value*
GAIT	**GUG**	Subject Characteristics	Gender	0.23	0.18	0.32	0.32	4, 65	<0.01**
			Age	0.37	0.00				
			Mass	0.14	0.22				
			Height	-0.23	0.18				
		LQ:LG		0.21	0.05	0.36	0.04	5, 64	0.05*
	WOMAC-PF	Subject Characteristics	Gender	0.20	0.27	0.21	0.21	4, 65	<0.01**
			Age	-0.08	0.45				
			Mass	0.27	0.03				
			Height	-0.23	0.22				
		LQ:LH		0.24	0.026	0.27	0.06	5, 64	0.03**
STEPDOWN	**GUG**	Subject Characteristics	Gender	0.17	0.34	0.29	0.29	4, 62	<0.01
			Age	0.27	0.01				
			Mass	0.03	0.78				
			Height	-0.22	0.22				
		LQ:LG		0.28	0.02	0.39	0.1	5, 61	<0.01**
		MQ:MH		0.20	0.06	0.43	0.04	6, 60	0.06*
	WOMAC-PF	Subject Characteristics	Gender	0.38	0.04	0.25	0.25	4, 62	<0.01**
			Age	-0.08	0.45				
			Mass	0.22	0.07				
			Height	-0.10	0.58				
		Hip Excursion		-0.29	0.01	0.33	0.08	5, 61	<0.01**
		MQ:MG		0.20	0.06	0.37	0.04	6, 60	0.06*

GUG= Get Up and Go test; **WOMAC-PF**= Western Ontario and McMaster Universities Osteoarthritis Index -physical function subscale; ***β*** **=** Beta Coefficient; ***β*** **Sig=** Beta statistical significance; **Total R^2**=Total R square value; **Δ R^2**=R square change**;** ***df*** = degrees of freedom; * $p<0.1$; ** $p<0.05$

Table 6 – Regression Analysis testing if Interaction Terms predict physical function during Gait and Step Down.

Condition	Dependent	Independent	Model 1		Model 2		Model 3		Model 4	
			Beta	Sig	Beta	Sig	Beta	Sig	Beta	Sig
GAIT	**GUG**	Gender	0.28	0.11	0.27	0.12	0.24	0.18	0.30	0.09
		Age	0.35	<0.01**	0.35	<0.01**	0.35	<0.01**	0.38	<0.01**
		Mass	0.16	0.15	0.17	0.16	0.15	0.20	0.12	0.30
		Height	-0.22	0.21	-0.23	0.22	-0.23	0.21	-0.16	0.39
		Knee Excursion			-0.01	0.94	-0.01	0.96	0.26	0.15
		TA:LG					.014	0.19	0.70	0.04*
		Knee Excursion x TA:LG							-0.63	0.08*
STEP DOWN	**GUG**	Gender	0.24	0.19	0.25	0.18	0.23	0.19	0.28	0.12
		Age	0.35	<0.01**	0.37	<0.01**	0.28	0.02**	0.28	0.01**
		Mass	0.13	0.27	0.13	0.29	0.10	0.37	0.07	0.51
		Height	-0.23	0.24	-0.22	0.27	-0.21	0.27	-0.14	0.45
		Knee Excursion			0.06	0.60	0.07	0.53	0.41	0.07*
		LQ:MH					0.29	0.08*	0.61	<0.01**
		Knee Excursion x LQ:MH							-0.47	0.08*
STEP DOWN	**GUG**	Gender	0.24	0.19	0.25	0.18	0.21	0.26	0.29	0.12
		Age	0.35	<0.01**	0.37	<0.01**	0.34	<0.01**	0.34	<0.01**
		Mass	0.13	0.27	0.13	0.29	0.13	0.27	0.05	0.66
		Height	-0.23	0.24	-0.22	0.27	-0.19	0.32	-0.07	0.71
		Knee Excursion			0.06	0.60	0.06	0.57	0.37	0.04*
		TA:GM					0.18	0.14	0.63	<0.01
		Knee Excursion x TA:MG							-0.57	0.03**
STEP DOWN	**GUG**	Gender	0.24	0.19	0.25	0.18	0.22	0.24	0.29	0.12
		Age	0.35	<0.01**	0.37	<0.01**	0.35	<0.01**	0.34	<0.01**
		Mass	0.13	0.27	0.13	0.29	0.12	0.30	0.03	0.82
		Height	-0.23	0.24	-0.22	0.27	-0.21	0.28	-0.11	0.57
		Knee Excursion			0.06	0.60	0.06	0.61	0.37	0.03*
		TA:LG					0.16	0.16	0.65	<0.01
		Knee Excursion x TA:LG							-0.62	0.02**

* p<0.1; **p<0.05

Table 7 - Bivariate Correlations between Subject Characteristics, Kinematics, Muscle Co-contraction and Physical Function during the Step Down Condition.

N=67	GUG	WOMAC-PF	Gender †	Age	Mass	Height	Ankle	Knee	Hip	LQ:MH	TA:MG	LQ:LH	MQ:MH	LQ:LG	MQ:MG	TA:LG
GUG	1	.35**	.41**	.32**	-.05	-.40**	.17	-.05	.04	.40**	.36**	.27*	.37**	.43**	.31*	.30*
WOMAC-PF		1	.43**	-.12	.23	-.30*	-.05	.08	-.25*	.18	.28*	.25*	.22	.24*	.24*	.25*
Gender†				-.08	-.15	-.76**	.31**	-.12	.26*	.11	.37**	.01	.05	.22	.09	.36**
Age				1	-.21	-.05	-.24	-.32**	.06	.28*	.18	.15	.20	.05	.24	.14
Mass					1	.33**	-.21	.13	-.23	-.01	-.14	.10	.03	.23	.03	-.06
Height						1	-.32**	.01	-.17	-.09	-.36**	-.03	-.06	-.12	-.09	-.23
Ankle							1	.22	.30*	.06	.19	-.11	.07	-.04	-.13	.01
Knee								1	-.42**	-.11	-.08	-.10	-.01	.02	-.08	-.04
Hip									1	.00	.10	-.07	-.07	.03	-.00	-.06
LQ:MH										1	.39**	.44**	.91**	.43**	.37**	.31*
TA:MG											1	.25*	.35**	.30*	.34**	.86**
LQ:LH												1	.38**	.48**	.49**	.31**
MQ:MH													1	.34**	.42**	.30*
LQ:LG														1	.48**	.36**
MQ:MG															1	.27*
TA:LG																1

†Values represent Spearman Rho; * p<0.05; **p<0.01

Ankle; Knee; and Hip=joint excursion values.

LQ:MH= lateral quadriceps: medial hamstrings co-contraction index; TA:MG= tibialis anterior: medial gastrocnemius co-contraction index; LQ:LH= lateral quadriceps: lateral hamstring co-contraction index; MQ:MH= medial quadriceps: medial hamstring co-contraction index; LQ:LG=lateral quadriceps: lateral gastrocnemius co-contraction index; MQ:MG=medial quadriceps: medial gastrocnemius co-contraction index; TA:LG=tibialis anterior: lateral gastrocnemius co-contraction index.

All kinematics and EMG values were calculated during the loading phase of gait.

2.8 FIGURES

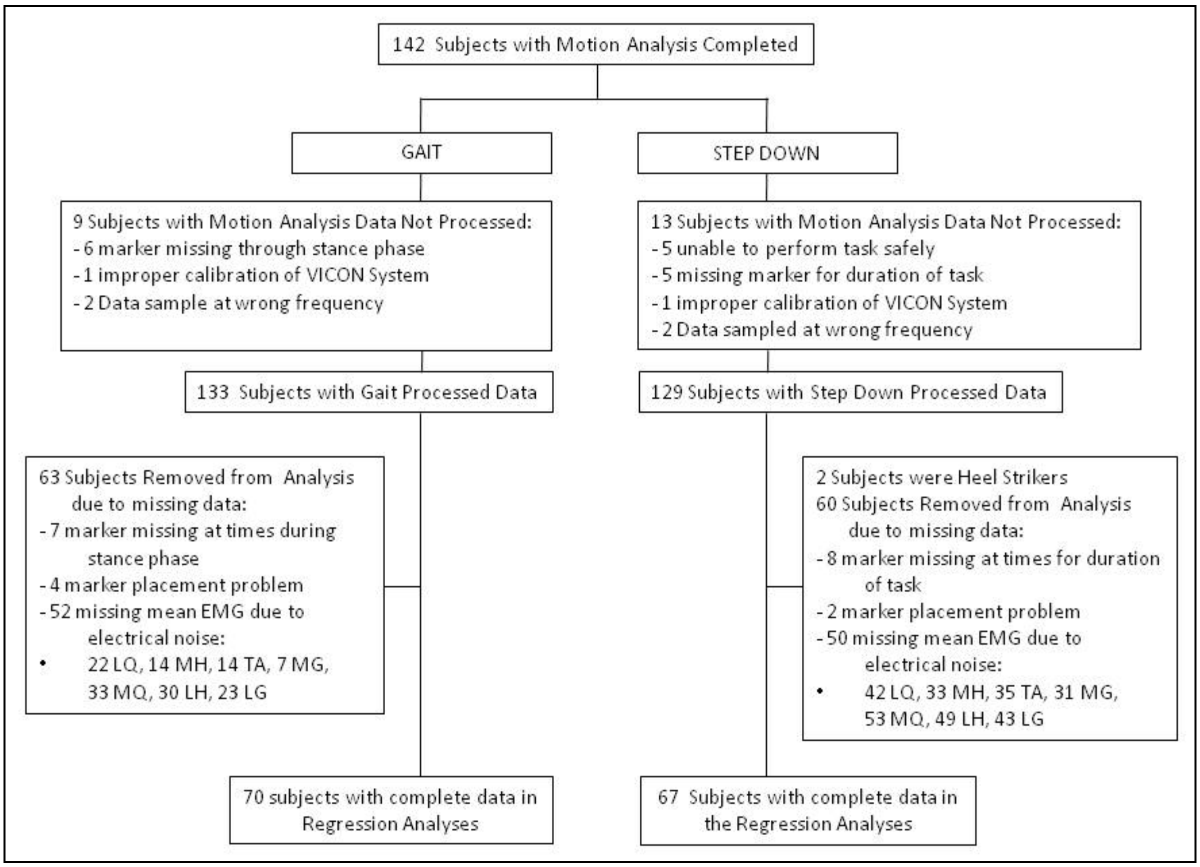


Figure 2 - Flow Chart

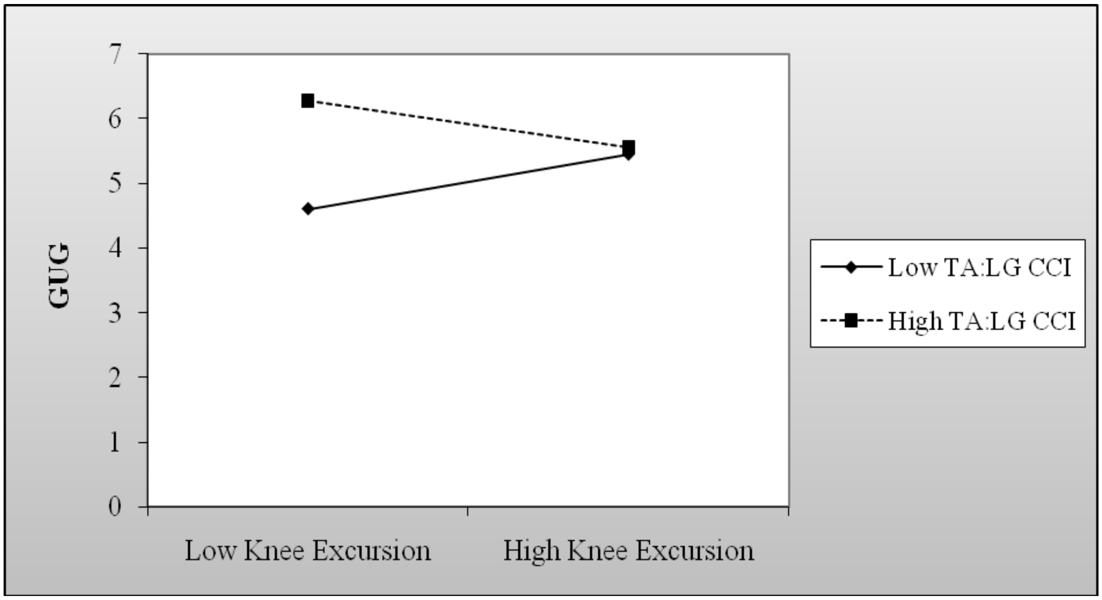


Figure 3 - Interaction Plot of Knee Excursion * TA:LG and GUG during Gait

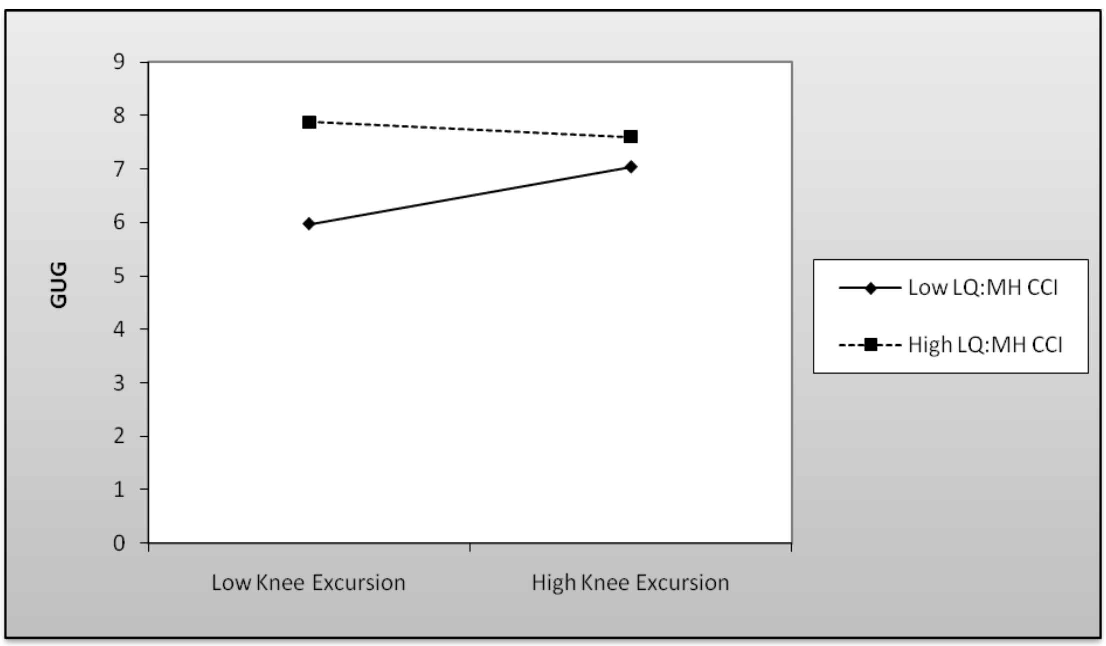


Figure 4 - Interaction Plot of Knee Excursion * LQ:MH and GUG during Step Down

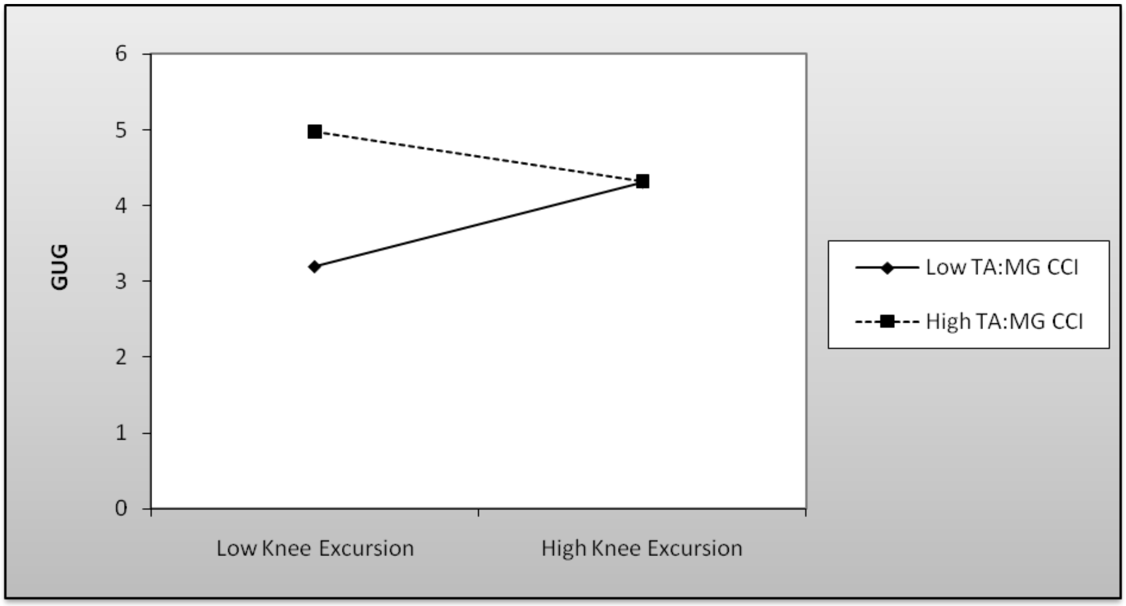


Figure 5 - Interaction Plot of Knee Excursion * TA:MG and GUG during Step Down

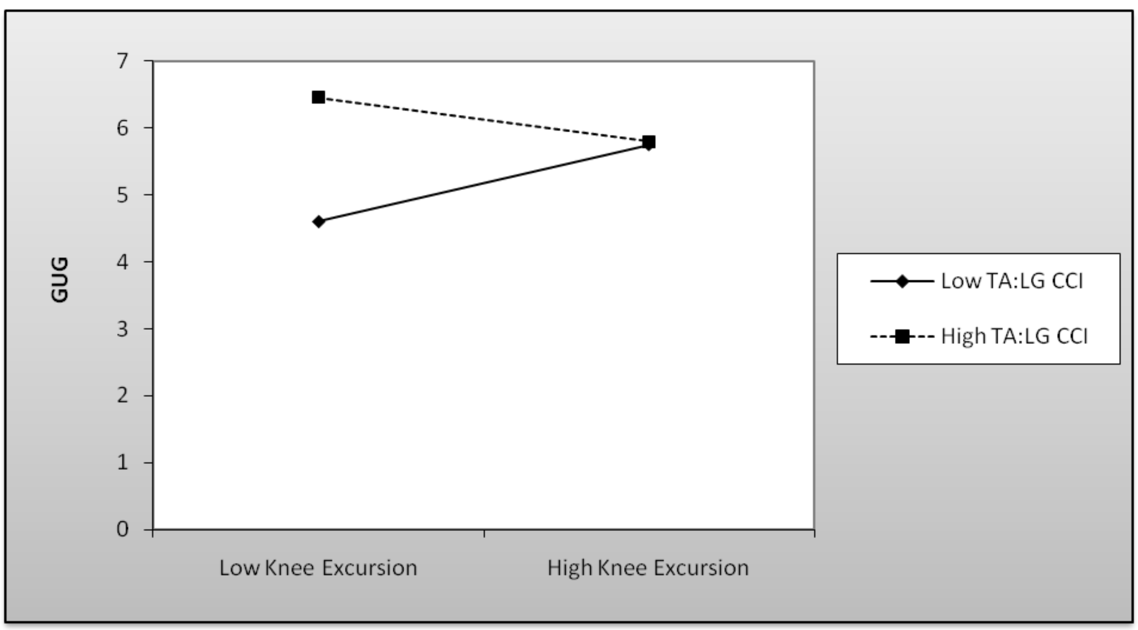


Figure 6 - Interaction Plot of Knee Excursion * TA:LG and GUG during Step Down

3 THE ASSOCIATION BETWEEN CHANGES IN LOWER EXTREMITY MOVEMENT PATTERNS AND CHANGES IN PHYSICAL FUNCTION IN PEOPLE WITH KNEE OSTEOARTHRITIS

3.1 INTRODUCTION

Knee Osteoarthritis (KOA) is a debilitating, degenerative disease that decreases the physical function (PF) status of people with the disease.[1-4] The development of rehabilitation programs that can effectively reduce disability in people with KOA depend on an understanding of factors that relate to, or mediate physical function in this population. It has been shown that people with KOA walk and step down with altered biomechanics such as reduced knee excursion[4,5,33,34,67] and higher co-contraction of key lower extremity muscle couples.[2,4,33,48] It is noteworthy that walking and ascending and descending stairs are described as the most commonly encountered ambulatory activities of daily living (ADLs).[20] Given the frequency in which these activities are performed on a daily basis it is possible that decreased knee excursion and higher co-contraction might have detrimental impact on the level of physical function in people with KOA.

Biomechanical studies in people with KOA have referred to the reduced knee excursion and increased co-contraction of lower extremity muscle couples as stiffness or as a stiffened pattern of movement.[4,33,34] Similarly, in the neuromuscular literature the combination of these two biomechanical factors, reduced joint excursions and increased co-contraction of muscle couples surrounding these joints, during motion have also been referred to as stiffness.[16,19] This stiffened pattern of movement, observed on healthy joints and surrounding muscles, is believed to be an attempt by the neuromuscular system to gain control over movement. The suggestion is that this stiffening strategy is used to facilitate learning of the new motor skill by simplifying and restricting the motion that is actively controlled. [10,16,18,43] The similar use of decreased motion and increased co-contraction, by healthy individuals learning a new motor skill and by people with KOA walking or stepping down, suggests a common strategy by the neuromuscular system to gain control over movement.[2,4,15,16,19] For the healthy individual, it may be an attempt to simplify the complexities of learning a new task. For the individual with knee OA, it may be an attempt to simplify the complexities of a task in the presence of disease related impairments such as joint pain, instability or muscle weakness.

Even though walking and managing steps cannot be described as novel skills to those affected by KOA, these people have to perform these common activities under a number of sensory and motor impairments, such as decreased joint position sense[44], decreased quadriceps strength[11,44], pain[45], knee joint instability[1,46]and altered muscle activation patterns.[4,33,38,48] Therefore, it is likely that the new structural and patho-physiological conditions imposed by the knee joint degeneration may create a novel condition in which these individuals have to adjust and adapt the performance of even the most basic tasks such as walking and managing steps. The initial stiffened pattern of movement, observed during the learning stages of a new task, might be converted to an unrestricted motion accompanied by an efficient well-coordinated pattern of muscle activation once the learning of the motor skill takes place.[10,16,17] The rationale is that skill acquisition can be achieved through continuous training and practice of the targeted task.[10] If the assumption that the neuromuscular system adopts a similar stiffening strategy either while learning a new task or performing a task under new structural and patho-physiological conditions is true, it is possible that the stiffening seen in people with KOA may also be converted into a less constricted pattern of movement. Potentially, an exercise regimen which encompasses training and practicing the targeted motor skills may promote these changes in movement pattern.

It is important to determine to what extent an exercise program can improve movement patterns in people with KOA and potentially thereby improve their level of physical function. It is possible that a standard rehabilitation program involving lower extremity muscles strengthening and stretching and aerobic exercises such as walking may promote such changes. However, we suspect that might not be the case because an impairment-based exercise program may not expose people with KOA to motor problems typically encountered during daily life. Studies have shown in animal models that aerobic and/or repetitive exercises regimens did not promote re-mapping of the motor cortex and did not improve level of performance, whereas after exposing animals to challenging environments or to tasks that required greater skill due to increased difficulty, re-mapping of the motor cortex and performance improvement were observed.[22-24,28,29] These findings suggest that an enriched movement program, in which people with KOA are exposed and challenged to learn and solve a variety of motor problems, may be necessary to release the stiffened pattern of movement typically seen in the people with KOA. The exercise program developed by Fitzgerald et al is a good example of an enriched movement program. The agility and perturbation training program involves an agility component with quick stops and starts, cutting and turning, and changes in direction and a perturbation component with balance exercises utilizing roller boards and tilt boards. Such exercises might be necessary to challenge the neuromuscular system in people affected by KOA and promote changes in the stiffened pattern of movement. We would hypothesize that once people can walk and step down with a less stiff pattern of movement it is likely that improvement in physical function might also take place. However, it is not clear whether the agility and perturbation training can induce changes in lower extremity kinematics and co-contraction, or whether any changes that might be induced actually relate to changes in physical function in people with KOA.

We believed that people who undergo agility and perturbation training would have greater increases in lower extremity joint motion excursions and greater decreases in co-contraction during functional task performance after training than people who undergo a standard, impairment-based exercise program. Therefore, the first aim of this study was to compare the changes in lower extremity kinematics and muscle co-contraction patterns between subjects who receive standard rehabilitation and subjects who receive agility and perturbation training in addition to the standard program. Furthermore, we believed there would be an association of the increase in lower extremity joint excursions and the decrease in magnitude of co-contraction with improvement in physical function in people with KOA after an exercise treatment. Therefore, the second aim of this study was to explore the association of changes in kinematics and changes in co-contraction with changes in measurements of physical function following completion of the training programs.

3.2 PATIENTS AND METHODS

3.2.1 Subjects

The data reported here are part of a larger randomized clinical trial that compared standard exercise program to agility and perturbation training in addition to standard exercise in people with KOA.[52] Subjects were included in the study if they were ≥40 years of age, met the 1986 American College of Rheumatology clinical criteria for KOA [53], and had a grade ≥2 Kellgren/Lawrence radiographic changes in the tibiofemoral joint.[54] Subjects were excluded from the study if they had conditions that would place them at risk for injury during the exercise training program (e.g., required an assistive device for ambulation, had a history of ≥2 falls in the previous year, or were unable to ambulate 100 feet independently), had undergone total knee arthroplasty, exhibited uncontrolled hypertension, had history of cardiovascular disease, had history of neurologic disorders that affect lower extremity function (e.g., stroke, peripheral neuropathy), reported vision problems that affected performance of basic mobility tasks. All subjects signed an informed consent form approved by the University of Pittsburgh Institutional Review Board prior to participation in the study.

One hundred forty two subjects underwent baseline motion analysis testing and were randomized to two groups. The standard group (STG) received a rehabilitation program composed of lower extremity stretching and muscle strengthening, and aerobic (walking) exercises. The agility and perturbation group (APG) received the standard program plus agility training (quick stops and starts, cutting and turning, and changes in direction) and perturbation training (balance exercises utilizing roller boards and tilt boards). Details of these training programs have been described in a previous publication.[32] Subjects in both groups underwent 12 supervised exercise sessions at a rate of 2 sessions per week. Post-treatment testing was performed two months after randomization. For the current study we included subjects from the main trial that had complete motion analyses data. For the gait condition, at baseline 70 subjects had complete gait data and at post-treatment testing 44 of those had complete data. For the step down condition, at baseline 67 subjects had complete data and at the post-treatment testing 34 had complete data (Figure 1).

3.2.2 Measures

Physical Function. Physical Function was assessed by a performance-based test and a self-report questionnaire. The Get up and Go (GUG) test was used to test performance-based physical function. It measures the time a subject takes to get up from a standard-height chair and walk 50 ft on a level and unobstructed corridor as fast as possible.[44] A stopwatch was used to measure the time from the command "go" until subjects crossed the finish line. A longer time to complete the Get up and Go test represents greater functional limitations. This test has been shown to have a good intra-rater (ICC = .95) and inter-rater (ICC = .98) reliability.[1,55] The Western Ontario and McMaster Universities Osteoarthritis Index -physical function subscale (WOMAC-PF) was used as the self-reported measure of physical function. The WOMAC-PF has 17 items (each item is scored on a 5-point Likert scale from 0 to 4), and a total score of up to 68 points. Higher scores indicate worse function. Reliability and validity of the WOMAC has been established.[56,57]

Motion Analysis Procedures. Subjects walked along an 8.5m long vinyl-tiled walkway. An eight camera Vicon® (Vicon Peak–UK) 612 motion measurement system recorded three-dimensional motion data at a sampling rate of 120 Hz from the Plug-In-Gait maker set. Ground reaction forces were measured on two Bertec® (Bertec Corporation, OH, USA) force plates embedded into the walkway. The forces were recorded at a sampling rate of 1080 Hz and synchronized with the motion data. Five walking trials at self-selected walking speed were collected and averaged, where subjects contacted the force platforms with their most affected limb without targeting. Five trials were collected with subjects stepping down from a platform 18 cm high onto the force plate with their most affected limb. Marker trajectories and ground reaction force data were low-pass filtered (Butterworth fourth order, zero phase lag) at 6 and 40 Hz, respectively. Data were analyzed using MatLab™ version 7.0 (The Mathworks, Inc, Natick, MA, USA). Mean lower extremity joint kinematics (hip, knee and ankle joint excursions) in the sagittal plane were calculated during the loading phase i.e. from foot contact to the first peak of vertical ground reaction force on both gait and step down conditions.

Electromyography Procedures. Surface electromyography (EMG) data was collected at 1080 Hz using an 8-channel Noraxon Telemyo System (Noraxon USA Inc, Scottsdale, AZ). Silver-silver chloride, pre-gelled bipolar surface electrodes (Medicotest, Inc., Rolling Meadows, IL) with an adhesive area of 3.8 cm in diameter and conductive area of 1 cm in diameter recorded EMG signals from the medial and lateral hamstrings (MH and LH), medial and lateral quadriceps (MQ and LQ), medial and lateral gastrocnemius (MG and LG), and the tibialis anterior (TA). Electrodes were oriented longitudinally in the direction of the muscle fibers on the center of the muscle belly. In order to ensure reliable placement of electrodes for each subject from baseline to post-treatment evaluation and across subjects, measurement of subject's own length of 4 fingers breadth and 1 hand breadth were used. One hand breath was used to place the electrodes on the LQ, MG and LG. Four fingers breath were used to place the electrodes on the MQ and TA. MH and LH electrodes were placed 1/2 way of an imaginary line between the ischio tuberosity and the muscles insertion. A reference (ground) electrode was placed on the tibial crest. To reduce skin impedance and ensure proper electrode fixation, the skin at the electrode sites were lightly shaved with a standard disposable safety razor, lightly abraded with an emery board, and cleansed with 70% isopropyl alcohol. Signals were collected while muscles were resting and during maximum voluntary isometric contraction (MVIC) for data processing purposes. EMG data were rectified and smoothed using the root mean square (RMS) of a 25 ms moving window. They were then normalized by the maximum 3 second average obtained during the MVIC (NEMG). The magnitude of the co-contraction between LQ:MH, LQ:LH, MQ:MH, LQ:LG, MQ:MG, TA:LG and TA:MG was calculated using the following formula developed by Rudolph, et al:

$$\sum_{i=1}^{n} [(\text{Lower NEMG}_i / \text{Higher NEMG}_i * (\text{Lower NEMG}_i + \text{Higher NEMG}_i)]/n$$

where *i* is the sample number and *n* is the total number of samples in the interval. Lower NEMG is the level of activity in the less active muscle and Higher NEMG is the level of activity in the most active muscle.[58] The co-contraction indices were calculated during the loading phase i.e. from first foot contact to the first peak of vertical ground reaction force on both gait and step down conditions.

3.2.3 Statistical Analysis

Change scores (post-treatment score *minus* baseline score = Δ) were calculated for each of the predictors and outcome measures. Predictor variables were change in lower extremity kinematics: Δ hip, Δ knee and Δ ankle excursions; and changes in lower extremity muscles co-contraction: Δ LQ:MH, Δ LQ:LH, Δ MQ:MH, Δ LQ:LG, Δ MQ:MG, Δ TA:LG and Δ TA:MG. Outcome variables were the change scores in GUG (Δ GUG) and in WOMAC-PF (Δ WOMAC-PF). Descriptive statistics, including measures of central tendency (means and medians) and dispersion (standard deviations, 25th and 75th percentiles) for continuous variables were calculated to summarize the data. The Kolmogorov-Smirnov test with Lilliefors' significance [59] was used to determine the normality of the data. According to the data distribution, independent samples t-test (Welch Adjustment for unequal sample sizes) or Mann-Whitney U test (continuous data) and Chi-Square (categorical data) were used to detect differences ($p<0.05$) of baseline characteristics (age, gender, height and weight) and of baseline physical function between subjects whose data were included in regression analyses and subjects who dropped out of the study before post-treatment testing. A similar statistical analysis was performed to compare subjects whose data were included in the regression analyses and subjects whose data were not included due to missing data values (see Figure 1 for description of missing data). Bivariate relationships between subject characteristics, exercise group assignment, predictor and outcome variables were assessed using Pearson correlation coefficients (r) for continuous data and Spearman's rank correlation coefficients (ρ) for categorical data ($p<0.05$). In addition, to determine if outcomes and predictor variables changed differently in the 2 exercise groups and to determine if there was a difference from baseline to post-treatment testing, a 2-way repeated measures analysis of variance (ANOVA) was performed. The main effects comparisons for group and for time and the interaction of group by time were observed. Significance level was set at 0.05.

In order to test whether changes in lower extremity kinematics and muscle co-contractions were associated with changes in physical function, a total of four stepwise multiple regression analyses were performed. Two regression analyses were performed with Δ GUG as the dependent variable, one for gait and one for step down task. Two other regression analyses were performed with the Δ WOMAC-PF as the dependent variable, again, one for gait and one for step down task. On the first step of the regressions, in order to account for the effects of subject characteristics on changes in physical function, age, gender, height and weight were entered simultaneously into the model. On the second step, in order to control for the effects of the two types of exercise interventions on the changes in physical function, group assignment was entered into the regression model. On the last step, Δ hip, Δ knee and Δ ankle excursions, and Δ LQ:MH, Δ LQ:LH, Δ MQ:MH, Δ LQ:LG, Δ MQ:MG, Δ TA:LG and Δ TA:MG were available for entry into the model in a stepwise manner. Due to the exploratory nature of this study and because we did not want to miss variables that could potentially contribute to the variability in change in physical function the alpha level was set at 0.1. For this reason, the probability of F value for the regression analyses was set at 0.1 to enter the model and 0.15 for removal from the model.

3.3 RESULTS

At baseline 70 subjects had complete data for gait and 67 subjects had complete data for the step down task. Between baseline and post-treatment testing, 9 subjects dropped out of the study. There was one outlier who had a perfect score in the WOMAC-PF indicating no functional limitation according to this measurement. Discrepancies were observed upon comparison of this subject's WOMAC-PF answers to similar questions captured by other self-reports of physical function collected for the larger trial. Therefore, it was determined that this subject did not answer the WOMAC appropriately and this subject's scores were removed from data analyses. In addition, due to missing data at the post-treatment testing, our final analyses included 44 subjects with complete data for the gait condition and 34 subjects with complete data for the step down condition. A detailed description of the number of subjects with complete gait and step down data who participated in the statistical analyses and those with missing data is shown in the flow chart (Figure 1). Baseline subject characteristics and comparisons between subjects with complete gait and step down data versus those who dropped out of the study are reported in Table 8. There were no significant differences between subjects with complete gait data and those who dropped out. For the step down group these comparisons showed that people who dropped out had a slower GUG time at baseline than those who were included in the main statistical analysis. Comparisons of baseline characteristics between those with complete data and those with missing who were not included in the main analyses are reported in Table 9. These comparisons showed that those with missing data had slower baseline GUG than subjects with complete gait and step down data. In addition, for the step down group subjects with missing data had poorer baseline WOMAC-PF scores than those with complete data.

The 2-way ANOVA comparison by group showed that lower extremity joint kinematics and co-contraction indices did not show significant change over time or by exercise group for either the gait or step down conditions (Tables 10 and 11). For the gait condition, the TA:LG co-contraction showed a statistically significant group by time interaction ($p=0.01$; Table 10). For the step down condition, the TA:MG showed a statistically significant group by time interaction ($p<0.05$; Table 11). Upon plotting the interactions we observed that subjects who received STG decreased the co-contraction of TA:LG (gait) and TA:MG (step down), and subjects who received APG increased the co-contraction of TA:LG (gait) and TA:MG (step down) after treatment. These results suggest that the changes in co-contractions were different depending on the type of intervention received. The comparison by time showed a significant improvement in WOMAC-PF score ($p<0.01$) for subjects in the gait and step down conditions, whereas the interaction of group by time did not show statistical significance in either task condition (Tables 10 and 11). These results indicate that for subjects in the gait and step down analyses improvement in WOMAC-PF was approximately the same for both STG and APG. For the subjects in the gait condition, the comparison by time showed that improvement in GUG approached significance ($p=0.053$; Table 10) but there was no significant improvement in GUG for the subjects with complete step down data (Table 11). The results of the 2-way repeated measures ANOVA with F and p values for group, time and interaction effects for the gait and step down conditions are shown in Tables 10 and 11 respectively.

3.3.1 Gait

Bivariate correlation coefficients between the subject characteristics, exercise group assignment, predictor variables and outcome variables for the gait condition are shown in Table 12. Changes in LQ:LG co-contraction was the only predictor of Δ GUG, explaining 9% of the variability in this outcome variable (Table 13). The beta coefficient of the Δ LQ:LG was $\beta= -0.30$ ($p=0.06$). This result indicates that subjects who increased the co-contraction of LQ:LG after an exercise program had greater reduction in the GUG time and subjects who decreased the co-contraction of LQ:LG had worsening of GUG. There were no changes in kinematic or co-contraction variables that were significant predictors of Δ WOMAC-PF. Subject characteristics explained approximately 21% of the variability in Δ WOMAC-PF ($p=0.06$; Table 13). The variance inflation factor (VIF) values in both regression models were under 3.8, indicating no multi-collinearity concerns. Furthermore, residual plots showed values within 3 standard deviations. This observation indicates that multiple linear regression assumptions were met in the analyses.

3.3.2 Step Down

Bivariate correlation coefficients between the subject characteristics, predictor variables and outcome variables for the step down condition are shown in Table 14. There were no changes in kinematic or co-contractions that were predictors of Δ GUG times. Change in LQ:LH co-contraction was a predictor of ΔWOMAC-PF, explaining 10% of the variability in this outcome variable ($p=0.04$). The beta coefficient of Δ LQ:LH was $\beta= 0.35$ indicating that subjects who increased the co-contraction of LQ:LH during the step down task after an exercise program had worsening of WOMAC-PF scores and subjects who decreased co-contraction of LQ:LH had improvement in WOMAC-PF (Table 13). The variance inflation factor (VIF) values in both regression models were under 3.8, indicating no multi-collinearity concerns. Furthermore, residual plots showed values within 3 standard deviations. This observation indicates that multiple linear regression assumptions were met in the analyses.

3.4 DISCUSSION

Our first aim was to compare the changes in lower extremity kinematics and muscle co-contraction patterns between subjects who receive standard rehabilitation and subjects who receive agility and perturbation training in addition to the standard program. Our results did not confirm this hypothesis. The changes in lower extremity kinematics and changes in co-contraction during the gait and the step down tasks were not different between subjects who received STG and APG as expected. Furthermore, our results did not show differences in changes of physical function between exercise groups either. However, subjects in both exercise groups showed an improvement in their WOMAC-PF scores ($p<0.01$) at post-treatment. The mean Δ WOMAC-PF was about 20% of the baseline scores, reaching the minimal clinically important difference proposed by Angst.[68] This improvement in WOMAC-PF was observed for subjects included in the gait and in the step down condition analyses.

The main effect of time for the GUG approached statistical significance ($p=0.053$; Table 10) for the people in the gait condition, but the results did not show a similar change for those subjects included in the step down task analysis (Table 11). The lack of significant improvement in GUG may be due to the higher baseline level of physical function of our sample. Due to the technical difficulties inherent in motion analysis and EMG procedures there were subjects who had missing markers or noise in the EMG data who were not included in the main analyses. These subjects with missing data had significantly slower baseline GUG times than those included in the gait and step down statistical analyses (Table 9). In addition, in order to avoid injuries during interventions and data collection procedures, exclusion criteria such as unable to ambulate 100 feet without help or interruption, more than 2 unexplained falls within the past year and use of assistive device, might have prevented recruitment of people with KOA who had more severe physical function deficits than reported in other studies. At baseline, our sample had a GUG mean of about 8.6 seconds whereas Piva et al reported 11.5 seconds for the group with KOA and 8 seconds for the matched control group.[55] This information suggests the possibility of a floor effect since subjects might have not had enough room for improvement in GUG. In addition, the fact that our sample was likely more functional than the average subjects with KOA is also confirmed by the baseline WOMAC-PF. At baseline our sample mean WOMAC-PF score was approximately 12% to 9% lower than other reports of KOA (lower scores represent better physical function).[3,69,70]

We believe this is the first longitudinal study in people with KOA to attempt to establish association between changes in patterns of movement, i.e. changes in lower extremity joint excursions and changes in co-contraction, to changes in physical function after an exercise program. For the gait condition, an increase in LQ:LG co-contraction significantly predicted improvement in GUG. On the other hand, for the step down condition an increase in LQ:LH co-contraction predicted worsening in WOMAC-PF. The direction of the relationship found for the gait condition is in contrast with our original hypothesis which stated that a decrease in co-contraction would be associated with improvement in physical function, whereas the direction of the relationship found for the step down task corroborates our hypothesis. Although these findings may seem conflicting, suggestions that Bernstein's theory of skill acquisition does not fully account for all tasks and the claims that motor learning is task dependent may help explain the disparity of our findings. .[71-74]

Some investigators believe that the initial freezing followed by freeing of movement[10] during motor learning does not apply to the development of coordination patterns of every motor task.[71-74] In support of these remarks Broderick and Newell (1999) found that when bouncing a basketball those who were more experienced in performing this task showed reduced movement variability in comparison to those with less experience.[71] Ko et al reported that in early phase of practice, cross correlations between lower extremity joints motions were low when responding to a disturbance during an upright postural task. They concluded that during initial stages of learning joint motions were more independently controlled which is in contrast with Bernstein's theory.[72] Along these findings Konczak et al observed that a reduction of sagittal shoulder motion rather than an increase in motion was associated with expert violin players.[73] They also observed that elbow ROM was not associated with amount of practice time indicating that motion at this joint did not change as a function of learning. Unfortunately wrist ROM data was not available to strengthen their findings. The general conclusion was that the movement patterns observed while learning and mastering a skill are dependent on the constraints imposed by the tasks themselves.[71-74] Furthermore, they suggested that an increase and/or decrease of motion can be observed during the early stages of learning and later when the mastering of the skill takes place. In addition to the controversy, Spencer and Thelen (1999) reported that an increase in muscle co-contraction rather than a decrease took place with practice of a reaching movement. They observed that with practice people were able to perform the reaching movement faster and thereby muscle co-contraction increased in order to control undesirable rotational torques generated during movement.[74]

In light of these findings it is possible that the increase in co-contraction of LQ:LG during gait might have been a necessary response to the constraints imposed by this task. Co-contraction is a common mechanism through which smooth controlled movement is performed. For this reason if the magnitude of co-contraction is not above the amount required for the performance of the task it should not necessarily be interpreted as a problem. We believe the LQ:LG magnitude of co-contraction was at a normal level at baseline and even with a small increase the magnitude remained at normal levels at post-treatment. To support this assumption we compared the LQ:LG magnitude of co-contraction from our sample to other samples with KOA and matched healthy controls.[2,33] In our study during gait, the magnitude of LQ:LG co-contraction was 16% at baseline and 17% at post-treatment (Figure 2). These magnitudes of LQ:LG co-contraction at both time points were similar to the magnitude reported for this muscle couple in Lewek et al (18%) and Rudolph et al 2007 (17%) in people with KOA.[2,33] In addition, these studies reported no significant difference in magnitude of LQ:LG co-contraction between people with KOA and healthy controls during walking. Although our study design did not have a healthy control group, we believe the magnitude of LQ:LG co-contraction observed in our sample is likely similar to the magnitude of this muscle couple in healthy controls as well. These comparisons led us to believe the magnitude of LQ:LG co-contraction in our sample was at a normal or appropriate level for the performance of gait. Cross-sectional studies have suggested that higher co-contraction of muscles located lateral to the knee joint might have an important role in controlling load at the knee during gait in people with KOA.[34,39] Therefore, it is possible that the small increase in LQ:LG co-contraction might be a neuromuscular response to the demands of the gait to better control loading at the knee.

Another important factor to take into consideration is the specificity of training. Both STG and APG included walking as part of the exercise programs. The regression analysis result showed that those who had a small increase in LQ:LG co-contraction also improved their GUG times. We believe the motor learning that may have taken place with practice of walking might have been transposed to the performance of the GUG because both tasks are walking based. Shemmell et al demonstrated in an isometric goal-directed torque production task that generalization of the acquired skill to unpracticed torque targets was successful. Subjects practiced at 30% of maximum voluntary contraction in 8 different torque directions. The acquired motor learning helped with accuracy and faster times to reach the torque target at lower and higher torque levels.[75] Although torque was not measured here, it is possible that the torques produced and practiced during the walking part of the exercise programs might have been transposed to the performance of the GUG test but at a higher level of effort.

The step down task is known to generate greater joint moments than level ground walking thereby, it is considered to be more physically demanding.[61,63] Taking into consideration the biomechanical differences between the two tasks, it is likely that the step down generates unique and potentially greater constraints in comparison to gait. Neither the STG nor the APG included any type of exercises that would resemble the step down task. Without practice it is reasonable to assume that the appropriate ensemble of muscle synergies to perform the step down task did not take place during the intervention period. Consequently, motor learning could not be transposed into the actual step down task performance at the post-treatment. The regression analysis result indicated that after an exercise program, a small increase in the magnitude of co-contraction of a muscle couple that had a higher magnitude at baseline (LQ:LH) was associated with worsening of WOMAC-PF.

We believe the magnitude of LQ:LH co-contraction was above the amount required to perform the step down task at baseline and with the small increase the magnitude of co-contraction became even more elevated at post-treatment. To support this assumption we compared the magnitude of LQ:LH co-contraction from our sample to another sample with KOA and matched healthy controls reported by Childs et al. In our sample during the step down task, the magnitude of the co-contraction of LQ:LH was 25% at baseline and 28% at post-treatment (Figure 3). Childs et al reported that people with KOA performed a step down task with a magnitude of LQ:LH co-contraction of 24%. In addition, they reported that this magnitude was significantly higher than in healthy controls (15%) performing this task. Similarly to gait, this comparison led us to believe that the magnitude of LQ:LH co-contraction of our sample is comparable to other people with KOA performing a step down task. Furthermore, this comparison indicates that the magnitude of LQ:LH co-contraction found in our sample during the step down task is likely elevated in comparison to healthy controls. It appears that without the specific practice of the task motor learning did not take place. It is possible that if these subjects had specifically practiced performance of a step down task, a decrease in LQ:LH co-contraction might have been observed. These results support the theory that the coordination patterns developed with learning are task constraint dependent. Gait was practiced and the change associated with improvement in GUG might have improved loading at the knee joint. On the other hand, step down was not practiced and the change associated with worsening in WOMAC-PF might have stiffened the knee joint in order to avoid pain and instability.

Contrary to the regression predicting Δ GUG during gait, changes in lower extremity kinematics or changes in co-contraction during gait were not associated with Δ WOMAC-PF. A potential explanation for this finding may be the recruitment of people with KOA with less severe deficits in physical function. It has been shown that when older adults can still perform a given task, they may fail to report subtle changes such as an adjustment on how it is performed, longer time for completion and even reduction of the frequency in which a task is performed.[76,77] It is possible that because our sample was composed of people who were able to walk without interruptions and did not use any type of assistive device, these people were not able to perceive subtle changes in their walking ability to the extent that these changes could be captured by the WOMAC-PF.

Similarly during the step down task, change in kinematics or change in co-contraction were not associated with Δ GUG, whereas increase in LQ:LH predicted worsening in WOMAC-PF. The lack of association with Δ GUG might be due to an earlier impact rehabilitation may have on how these subjects experienced the performance of the step down task versus how long biomechanical changes can be picked up by a performance-based test. It has been shown that after an intervention such as total knee replacement, self-reports detect improvement in physical function earlier than these changes can be observed in performance based tests. [78,79] It is possible that the more challenging the task the longer it would take for the neuromuscular system in older adults to show changes that could be picked up by performance-based measurement.

Furthermore, the lack of association between changes in movement pattern during the step down task with Δ GUG might be explained by the specificity of the exercises during intervention. Walking was part of both exercise programs whereas managing steps was not part of either. It is possible that the specific practice might have contributed to improvement of the walking ability which would explain the association of increase in LQ:LG co-contraction with improvement in GUG time. It is likely that in order to promote significant changes in kinematics and in co-contraction it is necessary to specifically address tasks in which people with KOA have greater difficulty. For example, if the individual with KOA has difficulty getting up from a chair he/she may need to practice techniques that specifically address this limitation.

3.5 LIMITATIONS

Our study had limitations that should be taken into consideration. Technical difficulties inherent to motion analysis and surface EMG procedures such as skin artifact due to motion of markers and electrical noise due motion of the EMG leads respectively reduced our original sample size substantially. It has been suggested that for every independent variable entered into the regression model there should be 10 subjects in the analysis.[80] The ratio of subject per independent variable in all 4 regression models ranged from 6 to 9, indicating that our sample size was less than ideal. Due to the small sample size the probability for type I error might have been enhanced.

Another potential limitation was the fact that our sample did not show as severe physical function deficits as reported in other samples with KOA. Subjects with missing data had more severe physical function deficits than those included in the analysis. We observed that the subjects with missing data had greater improvements in WOMAC-PF than those included in the analyses but this difference was not observed for the changes in GUG when same comparison was made. Therefore, had these subjects been able to be included in the main analyses the results for the regression with Δ WOMAC-PF as outcome variable could have been potentially affected. This scenario does not seem as likely for the regressions with the Δ GUG as outcome variable. However, even if these subjects had not been excluded from the analyses the overall baseline GUG and WOMAC-PF means would have still shown lower physical function deficits in comparison to other reports in KOA.[3,55,69,70] Because we excluded subjects who required assistive devices for ambulation or those who were a fall risk, we may have prevented recruitment of people with greater physical function deficits. Therefore, our results should not be generalized to people with KOA with more severe physical function deficits (e.g., those using assistive devices for ambulation or those who are at risk for falling).

3.6 CONCLUSION

Our original hypothesis that changes in kinematics and changes in co-contraction would predict change in physical function outcomes was not fully confirmed. The role of the association of changes in co-contraction with changes in physical function is not conclusive. Our results indicated that the direction of this association might be dependent upon the task constraints and on the specificity of training. A small increase in co-contraction of a muscle couple lateral to the knee joint was associated with improvement in GUG. This improvement may be due to a more effective control of joint loading provided by this muscle couple. On the other hand, the step down task was not practiced by any of the exercise groups. For this task, a small increase in co-contraction of a muscle couple that had elevated co-contraction at baseline indicated decline in WOMAC-PF. We believe that in order to improve patterns of movement in people with KOA, rehabilitation programs may need to focus on specific practice of tasks in which they have difficulty performing. Future studies including subjects with more severe physical function deficits and focusing on the specificity of training are warranted in order to establish the role of changes of patterns of movement in changes of physical function in people with KOA.

3.7 TABLES

Table 8 - Comparison of Baseline Characteristics of Subjects With Complete Data vs. Subjects Who Dropped Out for the Gait and Step Down Conditions.

Condition	**GAIT**			**STEP DOWN**		
Variables	**Complete Data n = 44**	**Drop Outs Data n = 9**	***P* value**	**Complete Data n = 34**	**Drop Outs Data n = 9**	***P* value**
Age in years – Mean ± SD	62.6 (7.5)	63.7 (8.5)	0.74§	60.6 (6.7)	63.7 (8.5)	0.34§
Female - N (%)	25 (57)	6 (67)	0.58‡	19 (56)	6 (67)	0.56‡
Height in cm – Mean ± SD	170.3 (10.6)	168.6 (11.3)	0.68§	171.7 (11.1)	168.6 (11.3)	0.47§
Weight in Kg – Mean ± SD	82.4 (15.6)	89.8 (12.6)	0.15§	83.5 (15.1)	89.8 (12.6)	0.22§
GUG Test in sec **-** Mean ± SD	8.8 (2.1)	9.9 (1.3)	0.06§	8.4 (1.5)	9.9 (1.3)	0.01§*
WOMAC PF – Mean ± SD	18 (12)	26 (19)	0.22§	17 (11)	26 (19)	0.18§

§= Independent Samples T-test (Welch Adjustment for unequal sample sizes)
‡= Tested with Chi-Square
*= Significantly different

Table 9 - Comparison of Baseline Characteristics of Subjects With Complete Data vs. Subjects With Incomplete Data for the Gait and Step Down Conditions.

Condition	**GAIT**			**STEP DOWN**		
Variables	**Complete Data n = 44**	**Incomplete Data n = 25**	***P* value**	**Complete Data n = 34**	**Incomplete Data n = 32**	***P* value**
Age in years – Mean ± SD	62.6 (7.5)	62.4 (10.1)	0.90§	60.6 (6.7)	63.8 (10.1)	0.14§
Female - N (%)	25 (57)	19 (76)	0.11‡	19 (56)	25 (78)	0.06‡
Height in cm – Mean ± SD	170.3 (10.6)	166.8 (8.8)	0.15§	171.7 (11.1)	166.7 (8.8)	0.06†
Weight in Kg – Mean ± SD	82.4 (15.6)	91.9 (20.6)	0.05§	83.5 (15.1)	90.6 (20.6)	0.12§
GUG Test in sec **-** Mean ± SD	8.8 (2.1)	10.1 (1.6)	<0.01§*	8.4 (1.5)	10.2 (2.0)	<0.01§*
WOMAC PF – Mean ± SD	18 (12)	23 (15)	0.12§	17 (11)	23 (15)	0.04§*

§= Independent Samples T-test (Welch Adjustment for unequal sample sizes)
†= Tested with Mann Whitney U test
‡= Tested with Chi-Square
*= Significantly different

Table 10 – Means and standard deviations for STG and APG at baseline and post-treatment, and results of two-way repeated measures ANOVA with F and p values by Group Effect, Time Effect (Repeated factor) and Interaction of Group by Time for Gait.

VARIABLES	Mean ± standard deviation per exercise group				Two-way Repeated Measures ANOVA Results					
	STG		APG		Group Effect		Time Effect		Group x Time Effect	
	Baseline	Post-treatment	Baseline	Post-treatment	F	p	F	p	F	p
GUG	9.1 ± 2.6	8.6 ± 2.1	8.6 ± 1.5	8.3 ± 1.4	0.49	0.48	3.95	0.053	0.29	0.59
WOMAC-PF	19.2 ± 13.2	14.8 ± 11.8	15.6 ± 9.5	13.5 ± 8.4	0.60	0.44	9.60	<0.01*	1.18	0.28
Ankle	10.7 ± 4.6	9.2 ± 3.2	12.2 ± 4.7	12.0 ± 5.0	3.25	0.08	2.00	0.16	1.25	0.27
Knee	11.4 ± 4.6	11.0 ± 4.8	10.6 ± 4.6	9.8 ± 3.7	0.68	0.41	1.10	0.30	0.14	0.71
Hip	10.1 ± 4.3	9.5 ± 3.5	9.2 ± 5.7	8.5 ± 3.8	0.71	0.40	1.19	0.28	0.00	0.97
LQ:MH	15.4 ± 10.3	16.1 ± 9.9	12.6 ± 6.8	15.1 ± 9.0	0.64	0.43	1.23	0.27	0.35	0.55
TA:MG	14.8 ± 17.1	16.6 ± 17.9	13.6 ± 11.5	12.0 ± 7.3	0.48	0.49	0.00	0.96	1.55	0.22
LQ:LH	24.8 ± 17.6	27.8 ± 18.5	24.4 ± 15.3	26.4 ± 14.7	0.04	0.84	1.27	0.26	0.06	0.81
MQ:MH	16.6 ± 12.2	15.1 ± 11.4	12.4 ± 6.3	14.9 ± 9.9	0.66	0.42	0.10	0.75	1.56	0.22
LQ:LG	16.3 ± 12.1	16.2 ± 12.5	15.7 ± 13.4	18.4 ± 16.0	0.04	0.84	1.41	0.24	1.80	0.20
MQ:MG	15.5 ± 16.5	16.2 ± 18.0	15.5 ± 11.1	13.7 ± 7.2	0.09	0.80	0.16	0.69	0.75	0.40
TA:LG	18.1 ± 16.3	15.2 ± 11.5	12.9 ± 10.4	16.0 ± 15.5	0.29	0.59	0.00	0.94	7.25	0.01*

*= statistically significant

Ankle; Knee; and Hip= joint excursion values

Table 11– Means and standard deviations for STG and APG at baseline and post-treatment, and results of two-way repeated measures ANOVA with F and p values by Group Effect, Time Effect (Repeated factor) and Interaction of Group by Time for Step Down.

VARIABLES	Mean ± standard deviation per exercise group				Two-way Repeated Measures ANOVA Results					
	STG		APG		Group Effect		Time Effect		Group x Time Effect	
	Baseline	Post-treatment	Baseline	Post-treatment	F	p	F	p	F	p
GUG	8.4 ± 1.6	8.2 ± 1.5	8.4 ± 1.6	8.2 ± 1.3	0.00	0.97	1.60	0.21	0.00	0.98
WOMAC-PF	17.3 ± 12.1	12.6 ± 12.0	16.3 ± 11.2	14.2 ± 9.2	0.01	0.94	8.75	<0.01*	1.36	0.25
Ankle	30.0 ± 9.6	31.3 ± 10.9	30.0 ± 8.0	30.5 ± 10.4	0.01	0.91	0.37	0.55	0.06	0.81
Knee	10.9 ± 4.5	10.7 ± 4.1	8.2 ± 5.0	9.9 ± 6.7	0.98	0.33	1.85	0.18	2.38	0.13
Hip	7.3 ± 2.5	6.8 ± 2.9	6.6 ± 3.9	7.1 ± 4.2	0.02	0.88	0.000	0.99	1.05	0.31
LQ:MH	14.8 ± 9.7	15.7 ± 9.2	17.2 ± 9.0	20.3 ± 11.7	1.34	0.25	1.37	0.25	0.42	0.52
TA:MG	14.5 ± 9.7	11.1 ± 7.0	11.4 ± 7.2	14.4 ± 11.2	0.00	0.96	0.03	0.85	10.77	<0.01*
LQ:LH	20.6 ± 16.1	23.7 ± 17.7	28.3 ± 15.8	32.4 ± 18.0	2.23	0.14	3.20	0.08	0.07	0.79
MQ:MH	15.2 ± 9.4	15.1 ± 10.9	17.2 ± 9.2	20.6 ± 12.2	1.41	0.24	0.83	0.37	0.98	0.33
LQ:LG	19.5 ± 9.0	22.6 ± 10.6	25.5 ± 14.3	27.2 ± 15.6	1.62	0.21	2.32	0.14	0.18	0.67
MQ:MG	20.5 ± 11.7	23.9 ± 19.6	25.8 ± 13.2	28.6 ± 12.4	1.44	0.24	1.40	0.24	0.01	0.91
TA:LG	14..3 ± 10.0	12.9 ± 9.1	10.9 ± 6.8	13.8 ± 10.6	0.18	0.67	0.41	0.53	3.43	0.07

*= statistically significant

Ankle; Knee; and Hip= joint excursion values

Table 12 - Bivariate Correlation Table of Subjects Whose Data Was Used in Regression Analyses for the Gait condition.

GAIT	Δ GUG	Δ WOMAC-PF	Arm†	Gender†	Age	Mass	Height	Δ Ankle	Δ Knee	Δ Hip	Δ VL:HM	Δ TA:GM	Δ VL:HL	Δ QM:HM	Δ VL:GL	Δ QM:GM	Δ TA:GL
Δ GUG	1	0.13	0.08	-0.06	-0.23	0.08	0.11	0.05	-0.14	-0.07	0.08	-0.13	0.07	0.05	-0.28	-0.18	-0.06
Δ WOMAC-PF		1	0.18	-0.21	0.06	-0.14	0.23	0.32*	0.15	0.17	-0.07	-0.05	0.16	0.11	-0.13	0.09	0.11
Arm†			1	-0.22	-0.24	0.05	0.10	0.12	-0.01	0.04	0.00	-0.04	-0.06	0.05	0.19	-0.04	0.36*
Gender†				1	0.12	-0.42	-0.82**	0.02	-0.09	-0.12	-0.01	0.05	-0.08	-0.11	0.12	0.1	0.01
Age					1	-0.02	-0.21	0.14	-0.01	-0.05	0.01	0.12	-0.11	0.12	0.01	0.11	-0.03
Mass						1	0.58**	-0.05	-0.08	-0.03	0.23	-0.09	-0.11	0.16	-0.08	-0.14	-0.05
Height							1	0.02	0.10	0.16	0.13	-0.08	-0.04	0.07	-0.17	-0.11	-0.06
Δ Ankle								1	0.12	0.02	0.07	-0.12	0.35*	0.27	0.29	0.17	-0.05
Δ Knee									1	-0.04	-0.04	-0.13	-0.19	-0.05	0.08	-0.06	-0.20
Δ Hip										1	-0.26	-0.09	-0.11	-0.13	-0.07	-0.04	0.07
Δ VL:HM											1	-0.08	0.00	-0.81**	0.06	-0.07	0.20
Δ TA:GM												1	0.08	-0.15	0.16	0.84	0.12
Δ VL:HS													1	0.03	0.15	0.28	-0.23
Δ QM:HM														1	0.23	0.01	0.28
Δ VL:GL															1	0.29	0.41**
Δ QM:GM																1	-0.01
Δ TA:GL																	1

†Values represent Spearman Rho; Δ= Change score * $p<0.05$; ** $p<0.01$
Ankle; Knee; and Hip=joint excursion values.
LQ:MH= lateral quadriceps: medial hamstrings co-contraction index; TA:MG= tibialis anterior: medial gastrocnemius co-contraction index; LQ:LH= lateral quadriceps: lateral hamstring co-contraction index; MQ:MH= medial quadriceps: medial hamstring co-contraction index; LQ:LG=lateral quadriceps: lateral gastrocnemius co-contraction index; MQ:MG=medial quadriceps: medial gastrocnemius co-contraction index; TA:LG=tibialis anterior: lateral gastrocnemius co-contraction index.
All kinematics and EMG values were calculated during the loading phase of gait.

Table 13 – Stepwise Multiple Regression Analyses predicting Δ GUG and Δ Womac-PF during Gait and Step Down Conditions.

Condition	*Dependent Variable*	*Variables in Reg. Model*		*Final Model*		*R^2 Total*	*R^2 Change*	*df*	*p-values*
				β	***β Sig***				
GAIT	**Δ GUG**	Subject Characteristics	Gender	0.17	0.52	0.06	0.06	4, 39	0.62
			Age	-0.20	0.24				
			Mass	0.12	0.68				
			Height	0.03	0.86				
		Group		0.12	0.47	0.06	0.00	5, 38	0.77
		Δ LQ:LG		-0.30	0.06*	0.15	0.09	6, 37	0.06*
	Δ WOMAC-PF	Subject Characteristics	Gender	-0.02	0.93	0.21	0.21	4, 39	0.06*
			Age	0.22	0.16				
			Mass	-0.47	0.01*				
			Height	0.53	0.06*				
		Group		0.22	0.16	0.25	0.04	5, 38	0.16
STEP DOWN	**Δ GUG**	Subject Characteristics	Gender	0.55	0.13	0.09	0.09	4, 29	0.60
			Age	-0.16	0.39				
			Mass	0.39	0.32				
			Height	0.01	0.96				
		Group		0.14	0.51	0.10	0.01	5, 28	0.51
	Δ WOMAC-PF	Subject Characteristics	Gender	0.42	0.17	0.13	0.13	4, 29	0.39
			Age	0.22	0.19				
			Mass	-0.34	0.11				
			Height	0.95	0.01*				
		Group		0.41	0.03*	0.27	0.14	5, 28	0.03*
		Δ LQ:LH		0.35	0.04*	0.37	0.10	6, 27	0.04*

Δ= Change Score; **GUG=** Get Up and Go test; **WOMAC-PF**= Western Ontario and McMaster Universities Osteoarthritis Index -physical function subscale; ***β*** **=** Beta Coefficient; ***β*** **Sig=** Beta statistical significance; **Total R^2**=Total R square value; **Δ R^2**=R square change**;** ***df*** = degrees of freedom; * p<0.1;

Table 14 - Bivariate Correlation Table of Subjects Whose Data Was Used in Regression Analyses for the Step Down Condition.

STEP DOWN	Δ GUG	Δ WOMAC -PF	Arm†	Gender†	Age	Mass	Height	Δ Ankle	Δ Knee	Δ Hip	Δ VL:HM	Δ TA:GM	Δ VL:HL	Δ QM:HM	Δ VL:GL	Δ QM:GM	Δ TA:GL
Δ GUG	1	0.09	0.00	0.18	-0.13	-0.05	-0.06	0.23	0.05	-0.09	0.08	-0.05	-0.20	0.02	0.02	-0.08	-0.17
Δ WOMAC-PF		1	0.18	-0.13	0.07	0.01	0.27	-0.09	0.18	0.03	-0.19	0.03	0.26	-0.08	0.26	0.02	0.39*
Arm†			1	-0.19	0.00	0.15	-0.05	-0.06	0.30	0.15	0.11	0.55**	0.09	0.17	-0.08	-0.06	0.26
Gender†				1	0.10	-0.55**	-0.85**	-0.15	-0.06	-0.19	-0.06	-0.17	0.06	0.01	0.17	-0.03	0.05
Age					1	0.11	-0.06	-0.05	0.06	-0.14	-0.11	0.11	-0.26	0.06	-0.12	-0.17	0.27
Mass						1	0.62**	0.28	0.13	0.01	0.03	0.15	-0.27	0.08	-0.32	-0.22	-0.19
Height							1	0.16	-0.02	0.01	0.08	0.01	-0.22	-0.01	-0.21	-0.17	-0.16
Δ Ankle								1	0.48**	0.24	-0.10	-0.09	-0.13	0.00	0.08	0.14	-0.14
Δ Knee									1	0.09	-0.31	0.11	-0.15	-0.18	-0.05	-0.17	0.16
Δ Hip										1	-0.01	0.07	-0.29	0.02	0.49**	0.05	0.07
Δ VL:HM											1	0.29	-0.13	0.87**	-0.13	0.14	0.11
Δ TA:GM												1	-0.18	0.40*	-0.09	0.04	0.63**
Δ VL:HS													1	-0.12	0.26	0.40*	0.07
Δ QM:HM														1	-0.11	0.33	0.31
Δ VL:GL															1	0.31	0.20
Δ QM:GM																1	0.17
Δ TA:GL																	1

†Values represent Spearman Rho; Δ= Change score * $p<0.05$; ** $p<0.01$

Ankle; Knee; and Hip=joint excursion values.

LQ:MH= lateral quadriceps: medial hamstrings co-contraction index; TA:MG= tibialis anterior: medial gastrocnemius co-contraction index; LQ:LH= lateral quadriceps: lateral hamstring co-contraction index; MQ:MH= medial quadriceps: medial hamstring co-contraction index; LQ:LG=lateral quadriceps: lateral gastrocnemius co-contraction index; MQ:MG=medial quadriceps: medial gastrocnemius co-contraction index; TA:LG=tibialis anterior: lateral gastrocnemius co-contraction index.

All kinematics and EMG values were calculated during the loading phase of gait.

3.8 FIGURES

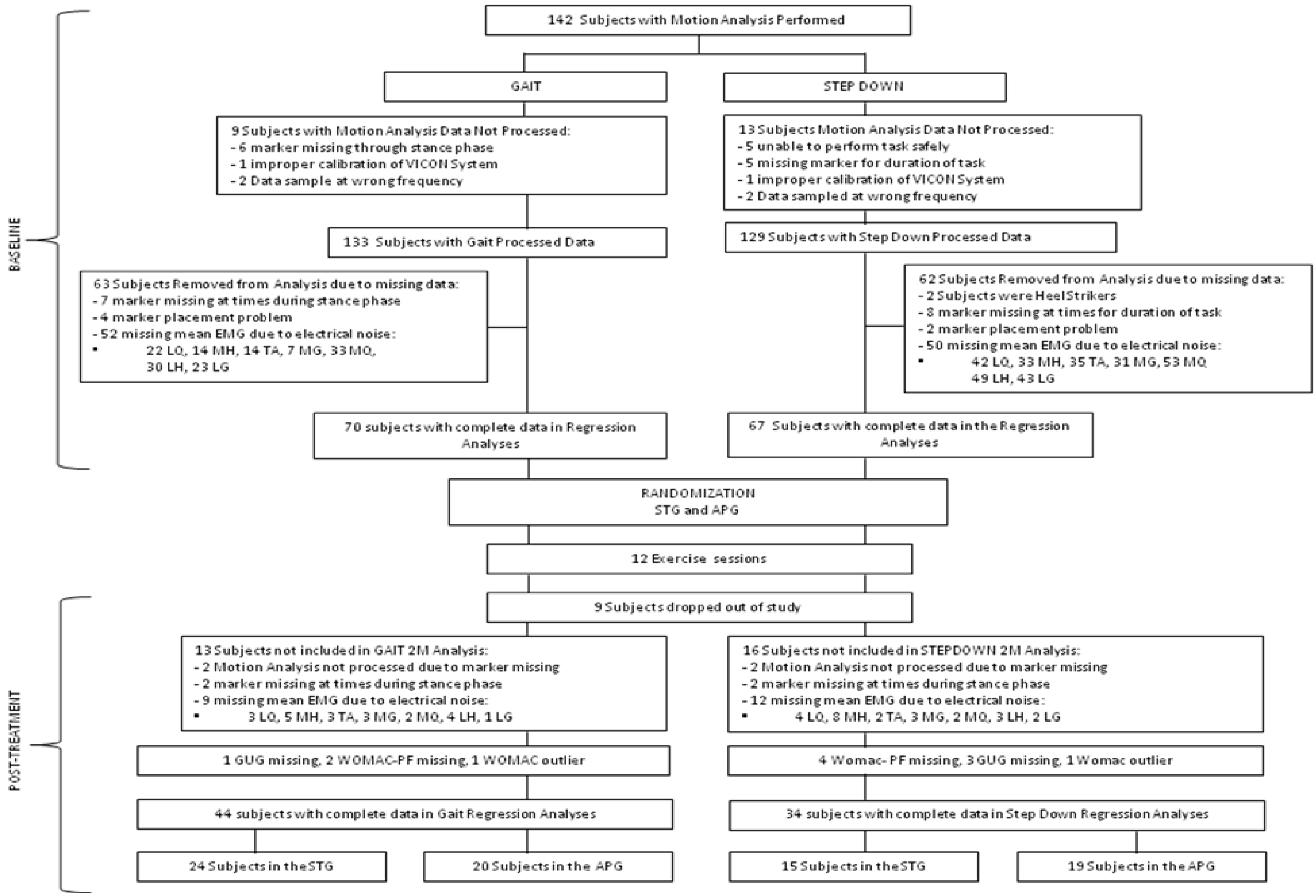


Figure 7 - Baseline and Post-treatment Flow Chart

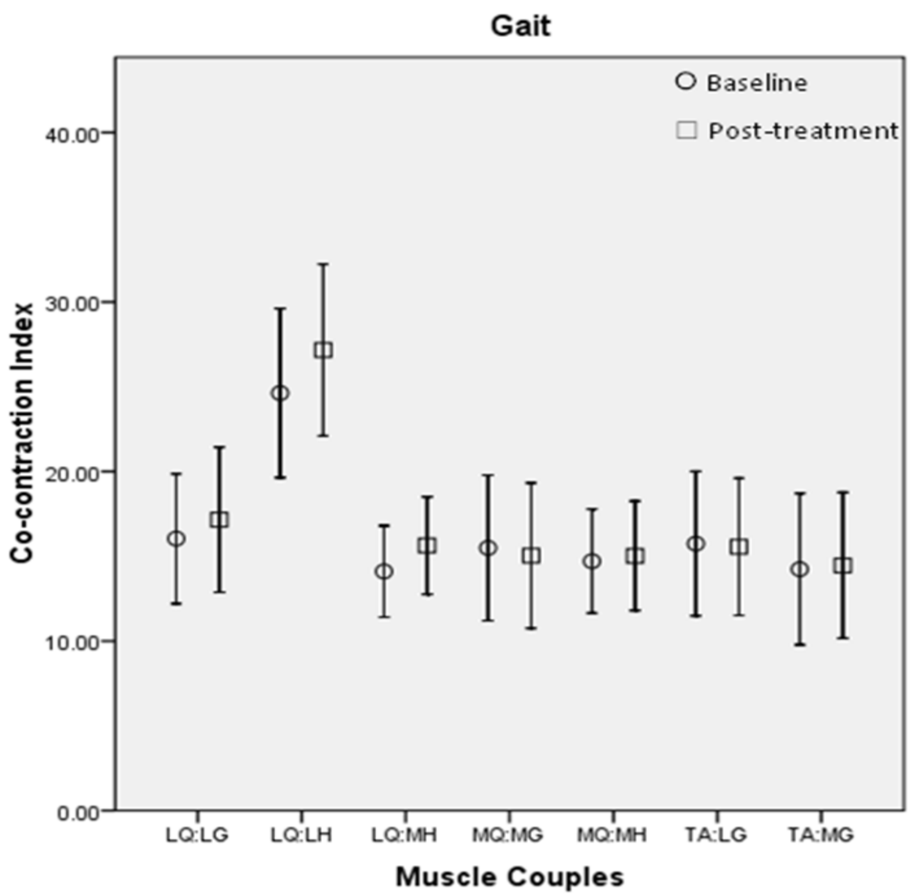


Figure 8 - Baseline and Post-treatment Means and 95% Confidence Interval of Muscle Couples Co-contraction Indices during Gait.

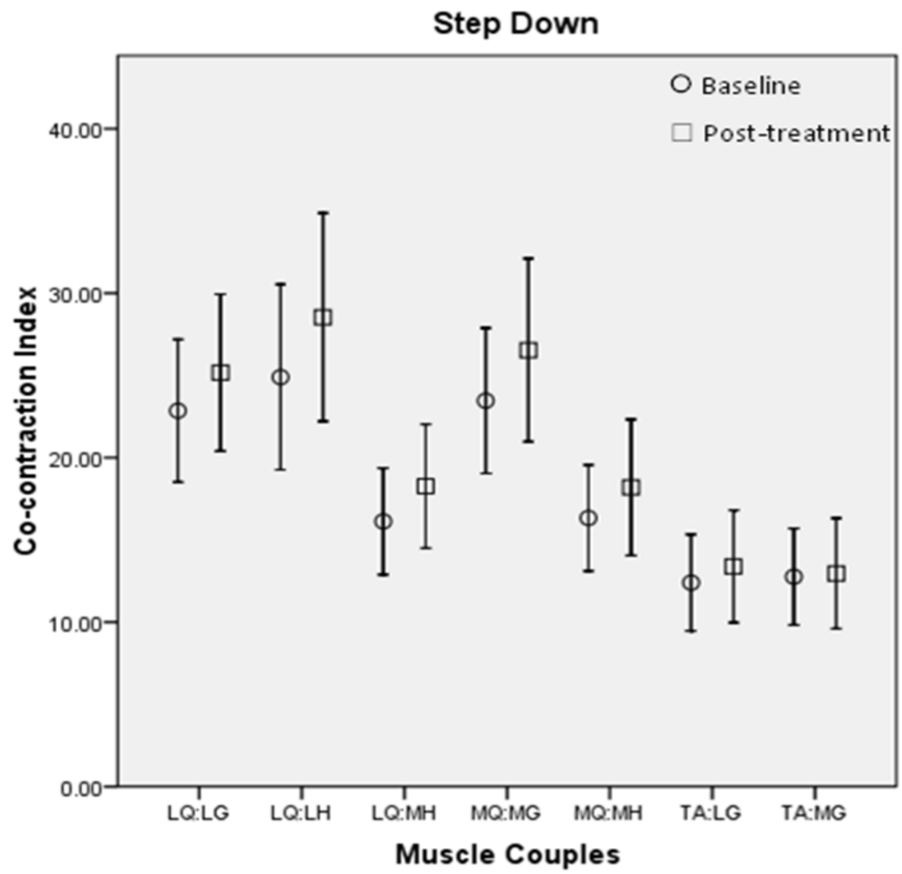


Figure 9 - Baseline and Post-treatment Means and 95% Confidence Interval of Muscle Couples Co-contraction Indices during Step Down.

4 SIGNIFICANCE AND DIRECTION OF FUTURE RESEARCH

The development of rehabilitation programs that can effectively reduce disability in people with KOA depends on an understanding of factors that relate to, or mediate physical function in this population. Even though people with KOA have been shown to ambulate with a stiffened pattern of movement[2,4,5,33,34,48,67] it is unclear if stiffness during ambulation is associated with lower level of physical function. If this relationship is true it is important to determine if rehabilitation can change the stiffened pattern of movement and if these changes are associated with improvement in physical function. For these reasons this study explored the relationship between biomechanical variables that represent a stiffened pattern of movement (joint excursion and muscle co-contraction)[4,16,19,33,34] and physical function. In addition, this study compared the changes in pattern of movement in people with KOA who underwent standard versus agility and perturbation training and explored the association between changes in pattern of movement with changes in physical function.

At baseline, increased co-contraction consistently predicted worse level of physical function during gait and step down tasks, whereas kinematics did not seem to play as much of a role in this relationship except for hip excursion during the step down. Even though the association of increased co-contraction with poorer physical function was a common result during gait and step down, there was a noticeable distinction with regard to the location of the muscle couples selected for each task. For the gait condition, increased co-contraction of lateral muscle couples, LQ:LG and LQ:LH, were associated with poorer GUG and WOMAC-PF respectively. For the step down condition, increased co-contraction of lateral and medial muscle couples, LQ:LG and MQ:MH, predicted GUG; and increased co-contraction of a medial muscle, MQ:MG, in addition to reduced hip excursion predicted WOMAC-PF. Biomechanical studies that observed increased co-contraction of lateral muscle couples in people with moderate KOA in comparison to healthy controls[34] have suggested that this strategy may be an attempt to contain the detrimental effects of increased medial compartment loading. [34,39] It is likely that due to constraints imposed by gait such as increased medial compartment loading, people with poorer physical function might need to use a similar strategy in order to enable walking performance.

On the other hand, it seems that in order to enable step down performance the neuromuscular system might have adopted a different strategy. Because the step down task imposes more demanding constraints such as higher loads, single leg balance and greater shift of center of gravity, it is likely that the neuromuscular system has to respond with a more general increase in co-contraction strategy to control load and avoid instability and pain. Throughout stance, prolonged activation of medial side muscles such as MG[38] and MH[40] have been suggested to be a mechanism to increase knee joint stability due to the increased joint space narrowing.[2,38,40] In addition, Hubley-Kosey et al also reported that people with severe KOA showed increased co-contraction of lateral and medial muscle couples. [39-41] They suggested that in addition to the attempt to unload the medial compartment by increasing co-contraction of lateral muscles, there is an attempt to reduce instability by increasing co-contraction of medial muscles also.[39,40]. Our results indicate that people with KOA who have a lower level of physical function tend show increased co-contraction of certain muscle couples while performing ambulatory tasks. In addition, our results led us to believe that the patterns of movement that emerge when performing such tasks are potentially dictated by the unique constraints imposed by each task.

This conclusion helped us understand the post-treatment results that at first seemed conflicting. At post-treatment we observed that for the gait condition, an increase in LQ:LG co-contraction was significantly associated with improvement in GUG. On the other hand, for the step down condition an increase in LQ:LH co-contraction was associated with worsening in WOMAC-PF. Some investigators believe that Bernstein's theory of motor learning [10] does not apply to the development of coordination patterns of every motor task.[71-74] These investigators have suggested that the movement patterns observed while learning and mastering a skill are dependent on the constraints imposed by the tasks themselves.[71-74] The general belief is that either an increase and/or a decrease of motion may be observed in early stages of learning and later when the mastering of the skill takes place. In addition, it has also been shown that with practice an increase instead of a decrease in magnitude of co-contraction may be observed as a response to faster movements in an attempt to control undesirable torques.[74]

We believe that the small increase in LQ:LG co-contraction during gait might have been a necessary response to the constraints imposed by this task. Even though there was a small increase in co-contraction the magnitude remained at a level that was comparable to healthy controls during gait performance.[2,33] As has been mentioned previously, higher co-contraction of lateral muscle couples might play an important role in controlling knee medial compartment loading during gait in people with KOA.[34,39] It is likely that the small increase in LQ:LG co-contraction might have been a neuromuscular response to the demands of the gait to better control loading at the knee. This assumption is somewhat supported by the fact that walking was part of both STG and APG programs. It is likely that with practice the neuromuscular system recognized the need to increase lateral muscle co-contraction in order to better control knee loading. Shemmell et al observed that with practice of an isometric goal-directed torque production task the acquired skill was successfully generalized to the unpracticed torque targets. The acquired motor learning helped with accuracy and faster times to reach the torque target at lower and higher torque levels than the practiced ones.[75] It is possible that the motor learning that took place with walking practice was well transposed to the GUG which is a walking-based task but a higher level of effort.

For the step down condition, it is noteworthy that the magnitude of co-contraction of LQ:LH at baseline was elevated in comparison to healthy controls performing this task. [4] Therefore, the observed change increased the magnitude of co-contraction of this muscle couple to an even higher level at post-treatment. It makes sense that people who worsened their level of physical function would also increase the amount of co-contraction in order to enable performance. We believe that this increase in co-contraction, even though small, was a necessary response in an attempt to control joint loading, pain and instability during such a physically demanding task. We also believe that this increase in co-contraction was a consequence of a lack of practice. Neither the STG nor the APG included any type of exercises that would resemble the step down task. It seems safe to assume that motor learning did not take place and thereby could not be transposed into the actual step down performance at post-treatment as observed for gait. It is likely that if these subjects had specifically practiced the performance of a step down task, a decrease in LQ:LH co-contraction might have taken place and potentially might have been associated with an improvement in physical function. These results support the assumption that with practice and learning the emerging coordination patterns are task constraint dependent. We believe that in order to improve movement patterns in people with KOA, rehabilitation programs may need to focus on specific training of the tasks which people with KOA have difficulty performing. Future studies including subjects with more severe physical function deficits and with greater focus on the specificity of training are warranted in order to establish the role of changes of patterns of movement in changes of physical function in people with KOA.

At baseline, further exploration of the association of stiffened pattern of movement and physical function suggested once more that the neuromuscular system may rely on different strategies to enable movement. In a subgroup of people the significant relationships of the knee excursion and muscle co-contraction interactions with the GUG, suggested that when stronger muscle co-contractions are combined with limited knee excursion, there may be a greater adverse impact on physical function. On the other hand when these variables are present in isolation or when greater amounts of knee excursion are present, regardless of the amount of muscle co-contraction it does not seem to affect physical function as much. Ideally we would have liked to explore how this subgroup of people changed after undergoing the exercise programs. Unfortunately, due to post-treatment missing kinematics and/or EMG data it was not possible to observe changes in pattern of movement for this subgroup. We believe further exploration is necessary to establish how rehabilitation can impact movement patterns and level of physical function of those who initially walk or step down with lower knee excursion and higher co-contraction of certain lower extremity muscle couples.

Last, it is important to note that the amount of variability explained in physical function or in its change by the predictors at baseline and post-treatment was small. It is possible that other factors such as medial compartment loading, pain and knee instability, might also contribute to greater variability in physical function. Future studies are necessary to better understand how these additional factors interact with the variables that represent stiffened pattern of movement, and how they relate to physical function. At this stage, our analyses focused on determining the smallest number of factors that would explain the greatest amount of variability in physical function. In our approach, kinematic and co-contraction variables were treated individually in assessing their relationship with physical function. It is possible that this approach might have under represented the stiffened pattern of movement phenomenon. When subjects with knee OA walk or manage steps, they likely co-contract several muscle couples at once. Different people might activate different combinations of muscles couples surrounding the knee in order to stiffen it. If the patterns of recruitment of muscle couples during these activities were not consistent across subjects, treating the muscle couples individually may have cancelled out each other, and the contribution of stiffness may have been minimized. Perhaps a more comprehensive approach could better represent stiffened pattern of movement by taking into consideration the number of muscle couples that co-contract during loading. This type of approach may be more clinically relevant because it may better take into consideration how the knee functions while several muscle couples are co-contracting. For this reason we believe that an overall increased co-contraction might provide a better representation of stiffened pattern of movement and potentially explain additional variability in physical function.

In summary, the associations found between stiffened pattern of movement and physical function were not conclusive. We observed that co-contraction seems to play a consistent role in explaining variability in physical function and in its changes after an exercise treatment. In addition, our results led us to believe that neuromuscular responses might be dependent on the specific constraints imposed by each task. Specificity of training also was another factor raised by our results that perhaps should be taken into consideration when designing new rehabilitation programs for this population. Furthermore, this study helped us develop ideas on how to improve future exploration of the association between stiffened pattern of movement and physical function. Overall, we believe this project laid the groundwork for the development of more comprehensive study designs that may improve rehabilitation research in people with KOA.

APPENDIX A

EXERCISE PROGRAMS PICTURES

A.1 STANDARD PHYSICAL THERAPY

A.1.1 Stretching Exercises

Figure 10 - Supine Hamstring Stretch

Figure 12 - Prone Quadriceps Stretch

Figure 11 - Standing calf Stretch

A.1.2 Range of Motion Exercises

Start **Finish**

Figure 13 - Supine Straight Leg Raise

Start **Finish**

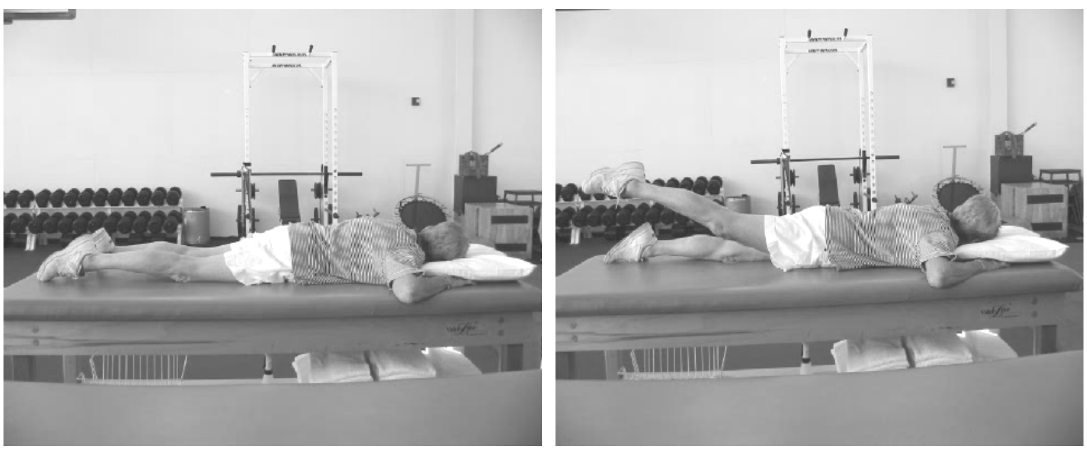


Figure 14 - Prone Straight Leg Raises

A.1.3 Strengthening Exercises

Figure 15 - Seated Knee Extension Isometrics

Figure 16 - Seated Knee Extension Isometrics

Figure 17 - Seated Leg Press

Start

Finish

Figure 18 - Standing Hamstring Curls with Cuff Weights

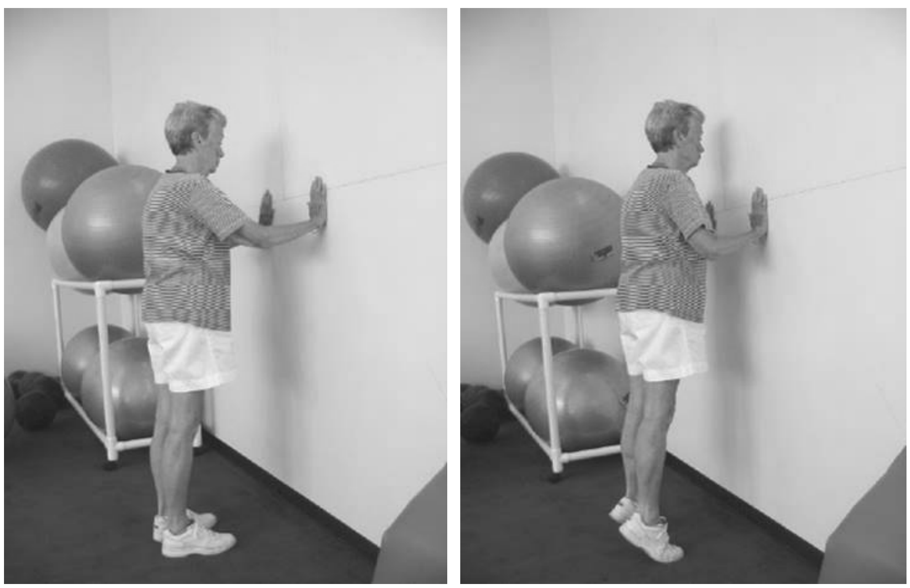


Figure 19 - Standing Calf Raises

A.2 AGILITY ACTIVITIES

A.2.1 Side Stepping

Start **Step** **End**

Figure 20 - Side Stepping

Figure 21 - Side Stepping over Obstacles

Figure 22 - Braiding Activities

Tandem Cross **Over Full Cross Over**

Figure 23 - Front cross-over steps during forward ambulation

Figure 24 - Backward cross-over steps during backward ambulation

Figure 25 - Shuttle Walking

Forward **Backward** **Left**

Right **Diagonal**

Figure 26 - Multiple changes in direction during walking on therapist command

PERTURBATION ACTIVITIES

Double Leg Support **Single Leg Support**

Figure 27 - Double leg foam balance activity

Double Leg Medial-Lateral **Double Leg with Perturbation** **Single Leg with Perturbation**

Figure 28 - Tilt board balance training Medial Lateral Perturbation

Double Leg Anterior-Posterior **Single Leg Anterior-Posterior**

Figure 29 - Tilt board balance training Anterior Posterior Perturbation

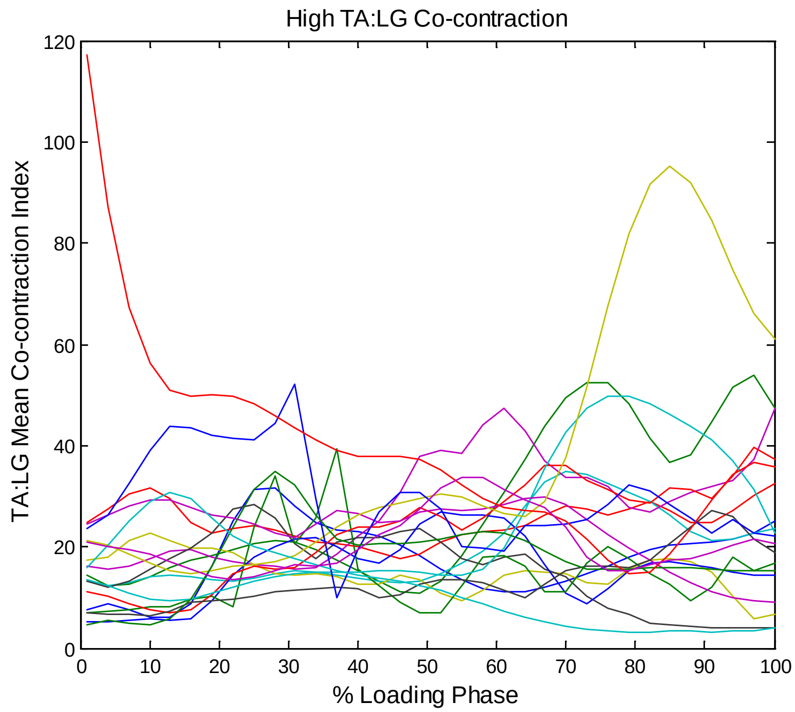
Semi-Seated Position **Standing Position**

Figure 30 - Roller board and platform perturbations

APPENDIX B

PLOTS OF CO-CONTRACTION AND KNEE EXCURSION DURING LOADING

B.1 PEOPLE WITH HIGH CO-CONTRACTION AND LOW KNEE EXCURSION.



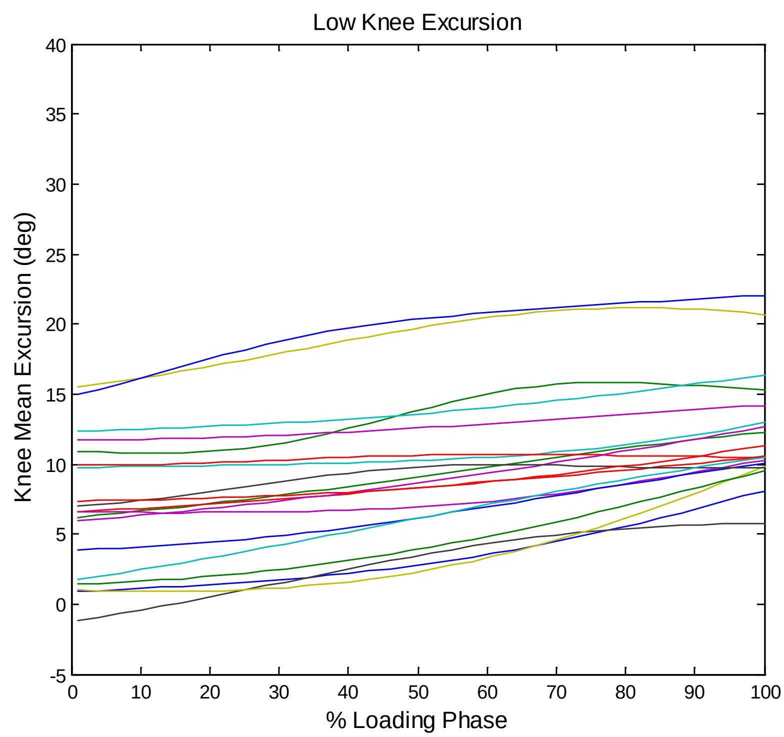


Figure 31 - Subjects with higher TA:LG co-contraction combined with lower knee excursion. For explanation see Results section of Chapter II.

B.2 PEOPLE WITH LOW CO-CONTRACTION AND HIGH KNEE EXCURSION.

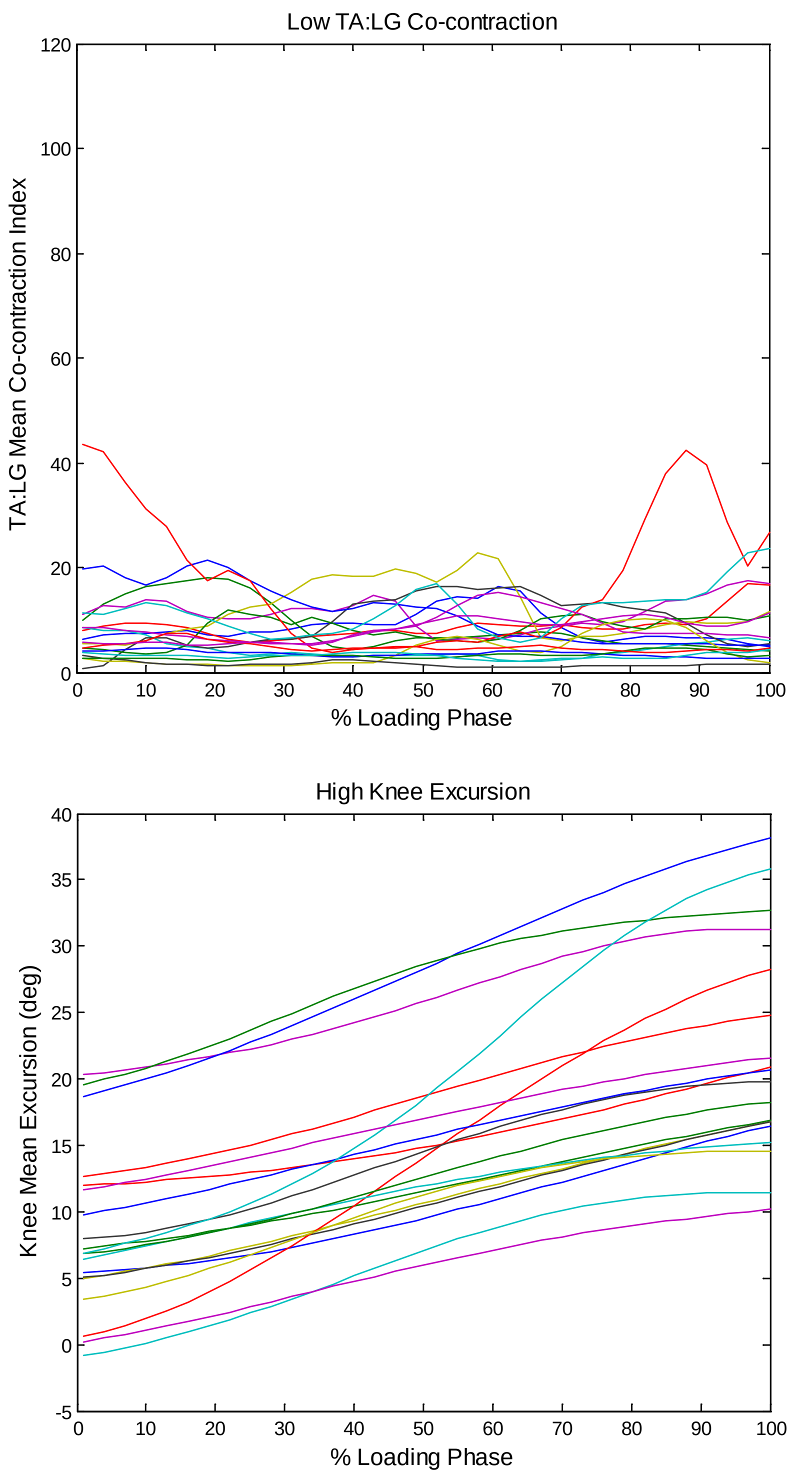


Figure 32 - Subjects with lower TA:LG co-contraction combined with higher knee excursion. For explanation see Results section of Chapter II.

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