

Walking Speed, Gait Asymmetry, and Motor Variability

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Thesis submitted to the faculty of the Virginia Polytechnic Institute and State University in
partial fulfillment of the requirements for the degree of

Master of Science
In
Biomedical Engineering

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February 6, 2018
Blacksburg, Virginia

Keywords: Asymmetry, Variability, Gait, Walking speed, Correlation

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ABSTRACT

Study design is among the most fundamental factors influencing collection and interpretation of data. The purpose of this study is to understand the effect of design choices by evaluating gait mechanics in healthy control participants using three primary objectives: 1) determine the repeatability of marker placement, 2) determine the effect of set versus self-selected walking speed, and 3) examine the correlation between gait asymmetry and motor variability.

Ten and fifty-one healthy control participants were recruited for aim 1 and aims 2/3, respectively. Reflective markers were placed on lower-extremity bony landmarks and participants walked on an instrumented treadmill while 3D motion capture data was collected. For aim 1, this procedure was repeated at two time points 30 minutes apart. For aims 2 and 3, participants completed set and self-selected speed trials. JMP Pro 13 was used to compare joint kinetics and gait kinematics for all aims.

Marker placement was repeatable between time points. Participants walked slower in the self-selected walking speed trial, which resulted in both kinematic and kinetic gait mechanics alterations. Gait asymmetry was significantly correlated with motor variability for both spatial and temporal measures.

Current study findings reiterate the importance of walking speed when evaluating gait symmetry, joint kinetics, and kinematics. The decision regarding whether to utilize a set or self-selected speed condition within a study design should be made based on whether the measures of interest are independent of walking speed. Gait asymmetry and motor variability are related and should not be treated as independent components of gait.

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GENERAL AUDIENCE ABSTRACT

This study aims to evaluate gait (walking) mechanics in healthy young adults by evaluating the impact of multiple study design choices and relationships between different aspects of gait. Loading and movement data was collected from a total of sixty-one participants. This data was then used to calculate several gait measures including symmetry between limbs, joint ranges of motion, and variability of movement. The potential impact of study design choices including setting walking speed for all participants and evaluating loading asymmetry and movement variability independently are discussed based on the findings of the current study.

Acknowledgements

I would like to thank Dr. Robin Queen, my research advisor and faculty mentor for all of her support in completing this study.

I would also like to Dr. Divya Srinivasan and Dr. Matthew McCullough for all of the valuable feedback and assistance in this project.

I would like to thank the research team for their assistance in data collection and processing.

Lastly, I would like to thank my family and friends for all of their continued support and encouragement.

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1. Introduction

1.1 Walking Speed

The effect of walking speed on both gait parameters and long-term outcomes has been well established in both healthy and pathologic populations including patients with osteoarthritis, stroke, and amnesia [1-21]. In healthy children, gait kinetics, kinematics, EMG activation, and spatio-temporal parameters are all affected by walking speed [4]. Likewise, many gait parameters are affected by walking speed in healthy adults, including most spatio-temporal parameters, hip flexion, hip extension, knee flexion, vertical ground reaction forces, and EMG activation, among others [1-3]. Additional effects of walking speed on gait stability [6, 8], stride-to-stride variability [9, 22], gait symmetry [10], muscle activity [5, 11-13], and joint contributions [7, 13] have also been found.

Walking speed not only affects gait patterns, but also long-term outcomes and survival, making it a measure of critical importance, especially in older adult populations. In older adults, walking speed is correlated with functional ability, stability, confidence, mortality, length of hospital stay, risk of stroke, and risk of dementia [23-28]. Due to its ability to act as a general indicator of health decline and mortality risk, walking speed has been described as “almost the perfect measure” and “the sixth vital sign” by Fritz et al [23]. Not surprisingly, walking speed has been studied heavily in pathologic populations, especially those mostly affecting older adults. Joint contributions, gait kinetics, and gait kinematics are all affected by walking speed in knee osteoarthritis patients [14-18]. Similarly, gait kinetics and kinematics are affected by walking speed in stroke patients [19, 20] and cognitive function is affected by walking speed in elderly adults with amnesia [21].

Based on these findings, walking speed is an important factor to consider when performing

biomechanical analyses in any population. Depending on the experimental setup, effects of walking speed can be accounted for differently. In over-ground studies, walking speed must be measured during testing and included as a factor in analyses. Similarly, in treadmill studies, one option for accounting for walking speed is to determine the participant's self-selected comfortable walking speed and then adjust walking speed accordingly to match this self-selected speed. Another method used in treadmill studies, however, is setting walking speed at a single value for all participants. One consequence of this setup is that the set walking speed may be different from the participants' comfortable walking speed. Based on the numerous studies finding that walking speed affects gait mechanics, any difference between the participant's self-selected comfortable walking speed and the set walking speed for all participants could affect results.

Several studies have investigated the differences between over-ground and treadmill walking, with some finding differences [29-31] and others finding them to be similar [32, 33]. While walking at different speeds and treadmill versus over-ground walking have both been evaluated in the literature, the effect of setting walking speed on a treadmill has not yet been directly studied.

1.2 Gait Asymmetry

1.2.1 Previous Literature

Gait symmetry is a complex and controversial phenomenon. Gait is often assumed to be symmetrical, which was reinforced by several investigations in the 1980s and 1990s. Studies by Hamill, Menard, and Hannah found no significant limb asymmetry at the hip and knee joints during natural walking, along with no asymmetries due to limb preference [34-36]. Despite these findings, many other investigators have found significant limb asymmetry [37-61] and the existence of limb

asymmetry in at least some pathologic populations has also been reported [62-66]. Still, there is some controversy on the presence of limb asymmetry, especially in healthy populations.

Causes of limb asymmetry in healthy populations are unclear. As an explanation, some investigators have suggested a theory of functional asymmetry [58, 67-72], which is defined as a consistent task discrepancy between non-dominant and dominant lower limbs [59], resulting in asymmetry even in the absence of pathology. Under this theory, the non-dominant limb acts to provide support and contributes more to the vertical acceleration during walking, while the dominant limb acts to provide propulsion and contributes more toward the forward acceleration during walking [67, 69]. Therefore, limb asymmetry in gait is not necessarily a function of pathology but is a function of complementary functions performed by the different limbs [69, 71]. Sadeghi et al provided evidence supporting this theory by identifying greater power generation on the dominant limb greater power and energy absorption on the non-dominant limb [58]. Additionally, the greater dominant limb power found at the ankle, knee, and hip was concentrated to the push-off or propulsion period while the power and energy absorption of the non-dominant limb was spread throughout the stance phase. Based on these results, Sadeghi et al concluded that the main functions of the dominant and non-dominant limbs were propulsion and support, respectively [58].

Although the theory of functional asymmetry has been embraced by some [58, 67-72], not all studies have found supporting evidence [60, 73]. Rice and Seeley found limited affirmation of the functional asymmetry theory in a study finding that walking speed affects limb asymmetry [60]. Participants walked at 9 different speeds and the propulsion and support impulses, indicative of contribution to propulsion and support respectively, were calculated for each limb. The support impulse was greater on the dominant limb, which disagrees with the functional asymmetry theory,

in 3 of the 9 speeds. Evidence supporting the theory was only found in the fastest of the included 9 walking speeds, with the propulsion impulse being greater on the dominant limb [60]. Similarly, a study by Seeley et al evaluated propulsion and support impulses at slow, regular, and fast walking speeds [73]. Impulses between limbs were generally symmetrical with greater propulsion impulse in the dominant limb only being found at the fast walking speed. These results describe a relationship between walking speed and limb asymmetry and refute the general theory of functional asymmetry which does not include walking speed as a factor.

Limb asymmetry during locomotion continues to be a topic of controversy with results varying widely between studies. Lathrop-Lambach, Hammill, Dellagrana, Burnett, Lythgo, Schot, and Herzog all investigated limb asymmetry in healthy asymptomatic participants [34, 37, 52, 54-56, 74, 75], but did not all find similar trends. One possible factor contributing to these differences is the task during which the symmetry data was collected. Lathrop-Lambach and Lythgo both studied symmetry during walking and were able to establish the presence of limb asymmetry in lower limb joint moments and spatiotemporal variables, respectively [52, 54, 55]. Dellagrana and Schot were additionally able to identify limb asymmetries during quadriceps and hamstrings contractions and drop landings, respectively [56, 74]. However, both Hamill and Burnett also evaluated symmetry during walking and found no significant limb asymmetries, so other factors and design aspects likely caused differences in results as well [34, 75].

Another factor that differed significantly between studies is the number of included participants. Lanthrop-Lambach and Lythgo both included participant population sizes of over 150, while Hammill and Burnett, who did not see any limb asymmetry, included 10 and 35 participants, respectively [34, 52, 54, 55, 75]. Therefore, it is possible that the higher sample size included by Lanthrop-Lambach and Lythgo allowed for identification of significant asymmetries.

Herzog et al found difficulties in concluding symmetric or asymmetric gait due to extremely high variation within variables [37]. Based on these results, another possible reason for varying results between similar studies is the high degree of variability within the participant population. However, this possibility is complicated by the fact that Giakas only found high variability in medial-lateral components of several variables and found acceptable variability in other components [50]. Limb-asymmetry likely results from a complex set of factors and further investigation is needed to better understand the presence or absence of gait asymmetry in healthy populations.

One athletic area in which limb asymmetry during gait is of particular interest is running since asymmetry is commonly associated with running-related injuries [76]. In female runners who had previously sustained stress fractures, braking force, vertical impact ground reaction force, and peak shock were found to be higher in the affected limb than in the unaffected limb [77]; this finding was coupled with the observation that previously injured female runners seemed to have elevated lateral ground reaction forces and loading rates bilaterally compared to the never-injured control group. Based on these results, elevated loading rates, elevated ground reaction forces, and asymmetry between limbs would lead to higher single-side injury risk and susceptibility [77].

Ciacchi used kinematic asymmetry between limbs in sub-elite male sprinters to evaluate risk of hamstring injury [78]. Sprinters with no history of hamstring sprain exhibited a high level of symmetry during sprinting, while those with a history of previous hamstring sprain surpassed thresholds for asymmetry during the same task. Rauh et al studied the effects of Q-angle on lower extremity injury risk in cross country runners; results showed increased risk for runners with large or asymmetric Q-angles [79].

Although some degree of asymmetry is arguably present in both previously injured and non-injured runners, significant differences can be observed between the levels of asymmetry between the groups. A prospective cohort study by Bredeweg, Buist, and Kluitenberg followed 210 novice male and female runners over 9 weeks; at the end of this period, 34 runners has sustained a running-related injury [80]. Variability in degree of symmetry was high both at the beginning and end of the 9-week period among participants. Still, the symmetry angle of the impact peak observed in injured runners was significantly lower when compared to that of non-injured runners, indicating higher degrees of asymmetry in participants incurring a running-related injury.

Although many studies have investigated the effect of limb asymmetries on lower-limb injury risk, the relationship between asymmetry and injury risk has not been definitively established. Several studies have suggested ties between the two, but others have interacting factors and warn that caution should be used when examining asymmetry and lower-limb injury risk as a related pair. A review conducted by Carpes et al found environment, terrain, walking or running speed, movement intensity, and movement duration to all significantly affect asymmetries during running and cycling [81]. The effects of as many additional factors as possible should be considered when drawing conclusions about the relationship between asymmetry and lower-limb injury risk.

The relationship between limb dominance, defined as the preferential use of one limb in voluntary motor acts [59], and limb asymmetry has also been studied by multiple investigators. Hamill [34], Burnie [82], and Hewison et al [83] found a significant relationship between dominant limb and asymmetry observed in ground reaction forces, peak torque, and temporal and kinematic data, respectively. After finding similar results, Gundersen et al [38] concluded that gait asymmetry could not be used as a predictive measure of limb dominance. Contrary to Hamill, Burnie, Hewison, and Gunderson finding no relationship between limb dominance and limb

asymmetry, several investigators have found a significant relationship [39, 45, 47, 51, 59, 63, 67, 68, 70, 84-86]. In addition to general relationships between limb dominance and asymmetry found by investigators such as Arsenault, Vanden-Abeelee, Arsenault, Ounpuu, and Singh, dominant limb has been suggested to have a supporting function [67] with differing EMG profiles during plantar flexion in walking between limbs [86]. This relationship is still in need of further investigation, especially since no single method for identification of dominant limb is used by all investigators.

1.2.2 Limb Asymmetry Measures

Although the presence of limb asymmetry has been widely studied, no consensus has been formed on a single measure of limb asymmetry during gait. Perhaps the most commonly used method is calculation of the limb symmetry index, which was first used by Robinson et al [87]. The limb symmetry index compares right and left limbs measures of a specific variable, with a symmetry index value closer to 0 symbolizing greater symmetry. While this method is commonly used, Robinson's symmetry index calculation compares differences between limbs to the average. If large asymmetries are present, this limitation can prevent either limb from being represented [59]. Due to this limitation, many other methods have been suggested or adapted for quantification of gait asymmetry.

Crenshaw and Richards, Kutilek et al, and Shorter et al all proposed new methods for quantifying gait asymmetry [61, 88, 89]. The method proposed by Crenshaw and Richards involves calculating 5 measures to assess joint symmetry: trend symmetry, phase shift, range amplitude ratio, range offset, and trend symmetry accounting for phasing differences [88]. While this method does allow for comparison of the entire waveform instead of a specific set of points or average values, the method cannot be used for discrete data points, including spatiotemporal

variables [88]. Kutilek et al's method, alternately, uses bilateral angle-angle diagrams to quantify the degree of asymmetry [61]. This method allows for direct comparison of joint angles between limbs over the entire waveform and avoids the use of symmetry indices or ratios that utilize only discrete data points. One main limitation of this method, however, is that these diagrams are sensitive to signal synchronization precision and signal quality [61]. The approach proposed by Shorter et al used a regions of deviation analysis comparing movement in braced conditions, which simulated asymmetric gait, and unbraced conditions, which simulated normative gait, within participants [89]. Similarly to the methods proposed by Crenshaw et al and Kutilek et al, Shorter's method allows for assessment of symmetry over the entire gait cycle or waveform. However, Shorter's method requires comparison to a set of data assumed to have no asymmetry [89].

In addition to new methods for quantifying gait asymmetry being proposed, new indices defining limb asymmetry have also been suggested. As previously discussed, the most widely used gait symmetry index was defined by Robinson et al and is termed the limb symmetry index (LSI) [87]. The LSI effectively quantifies the degree of difference between limbs but only reflects symmetry within a single variable. Exell et al developed a composite scoring method incorporating symmetry angles, measures of inter-limb symmetry previously proposed by Zifchock et al [90], of multiple kinematic and kinetic variables into a single score [91]. This method also excludes any variables with inter-limb variability that is not significantly larger than intra-limb variability, meaning the resulting metric only includes variables where significant differences will only be indicative of limb asymmetry. One limitation to Exell's method, however, is that absolute asymmetry values were used for each variable, making the asymmetry values less comparable between variables [91].

Another conceptually similar symmetry index is the global gait asymmetry index proposed by Cabral et al [92]. Cabral et al discusses limitations of the limb symmetry index such as the potential for artificial inflation and variation in the choice of reference value based on the question of interest. These limitations in addition to the fact that a symmetry index is only applicable for a single variable make the use of a symmetry index during biofeedback less effective. Therefore, Cabral et al developed the global gait asymmetry (GGA) metric which considers movement in the sagittal, frontal, and transverse planes and can be efficiently calculated for gait biofeedback. The lack of normalization and the inability to determine the direction of asymmetry in Cabral's score are still limitations of this newer method. Several other measures and methods of measuring limb asymmetry have been proposed and are used for various research applications as well [93-95].

1.3 Gait Variability

1.3.1 Overview

Variability in movement patterns is a topic of significant debate, with several studies drawing seemingly contradictory conclusions about the role of variability in motor control. The reigning theory for decades conceptualized any variability as statistical error [96]. In this theory, every movement is dictated by two aspects: the intended action (the plan) and other parameters that can be varied to produce an effect of flexibility and adaptability in response to environmental fluctuations [97]. The desired action is perfectly reproducible performance and motor variability is considered error resulting from the central nervous system's inability to precisely reproduce motor actions [98, 99]. In other words, motor variability is harmful and decreases performance accuracy [100, 101]. High degrees of motor variability, therefore, are often associated with gait instability, novice expertise level, and falls in elderly populations, among others [102, 103].

While this theory includes variability in performance, it does not encapsulate the control mechanisms underlying movements and actions. Another approach began to emerge as researchers increasingly found evidence of both positive and negative roles of motor variability. This new approach, referred to under the umbrella term “complex systems science” [96], is formed on the idea that motor control is a complex system of dynamically interrelated elements [104]. Variability is considered a key aspect of adaptability [105] and, therefore, has a function and significant role in motor control. The complex systems science perspective emphasizes the role of variability in motor control and development of expertise.

The term “variability” is defined by Newell and Slifkin as “the variance of movements generated by an individual under the same task conditions” [96]. The term can be broken down into 3 categories: 1) intra-trial, 2) inter-trial, and 3) inter-participant variability, each of which may require different context-dependent measurement methods [102]. Two commonly-utilized methods are time-continuous data analysis for intra-participant variability and discrete data analysis for inter-trial or inter-participant variability [102].

1.3.2 Previous Literature

One of the areas of research resulting in significant controversy is the role of variability in motor control, as described above. Researchers have increasingly found evidence supporting the theory that variability can both serve to increase flexibility and adaptability of the motor system and be a result of pathology. Heiderscheit describes negative motor variability as being associated with task outcome measures such as stride characteristics and adaptive variability as being associated with joint coordination patterns [106]. Agreeing with Heiderscheit’s conclusions,

Gabell and Maki also found increased variability in temporal variables to be predictive of fall risk [103, 107].

Gabell and Nayak also suggested two independent operating mechanistic groups: gait-patterning mechanisms, which include variations in step length and stride time, and balance-control mechanisms, which include variations in stride width and double-support time. Results show more consistency in gait-patterning mechanisms than in balance-control mechanisms, regardless of age; Gabell and Nayak concluded that increased gait variability is not a normal result of aging but that deficits in the balance-controlling mechanisms of gait may be impaired as a result of pathology. Two studies by Hausdorff et al provided supporting evidence for this theory of stride characteristic variability being indicative of pathology and gait instability by finding increased variability of temporal gait parameters in elderly fallers both when compared to young adults and elderly non-fallers [108, 109].

Heiderscheit also introduces variabilities seen in pathology, specifically neuromuscular pathology [106]. Increases in variability of stride characteristics have been seen in patients with Huntington's disease, Parkinson's disease, cerebellar ataxia, subcortical arteriosclerotic encephalopathy, pediatric spastic cerebral palsy, and congestive heart failure, among others [110-114]. Conversely, decreases in variability of joint coordination patterns have been found in patients with Parkinson's disease, patellofemoral pain, and spastic hemiplegic cerebral palsy, and cardiac pathologies [106, 115-118]. Ongoing investigations in the Kevin P. Granata Biomechanics Lab have found no differences in variability of stride, swing, stance, and or double support time between limbs in ankle osteoarthritis patients; a sex-specific difference in variability was found in stride, swing, stance, and double support time, however (abstract in review). This stark difference in the manifestation of pathology through variation in gait parameters suggests that joint

coordination variation may be advantageous for motor control and that stride characteristic variability is indicative of detrimental motor control. The former, based on the complex systems science perspective, contributes to the increased adaptability of the system, which is why decreases are seen in pathology. The latter may contribute to gait instability, which is why increases are seen in pathology.

Several other investigators observed positive effects of variability, reinforcing the theory of movement variability playing a crucial role in neuromuscular control. Joint coordination variability has been suggested to increase system flexibility and adaptability, helping to produce efficient movement patterns [119]. Increased variability across individuals and tasks has been associated with faster learning capabilities in both reward-based and error-based learning protocols [120, 121]. Wu et al discusses two phases of learning: exploration, referring to gaining knowledge about an environment or task, and exploitation, referring to the utilization of this knowledge to successfully complete a task [121]. A high level of motor variability in the exploration phase enables the body to test different movement patterns in order to find the most efficient solution. This exploratory phase also provides the system with flexible options that allow for quick movement alterations based on environmental fluctuations. Following this highly variable phase, the body has an understanding of the environmental surroundings and motor variability drops during the exploitation phase, where movements become more consistent.

In addition to the effects of variability on learning rate, Wu et al also describes the effect of variability on the manifestation of pathology on movement patterns [121]. In neuromuscular pathology, there is some restriction of viable movement pattern options; some causes of these restrictions may include pain reduction, decreased muscle function, and damaged neurons. Since fewer pathways are available, less variability exists in initial learning, the exploratory learning

phase is dampened, and the system is left with pathologic patterns instead of efficient healthy patterns. After the exploratory phase, a system with pathology experiences more internal fluctuations and is less able to minimize variability in a movement pattern, even over time; this inability is evidenced by the higher motor variability found in pathologic stride characteristics, for example.

Similar to some discussions by Wu et al about learning rate being task-dependent, Springer et al further tests the effect of task on movement variability by evaluating dual-tasking in healthy young adults, healthy older adults, and older adults who have experienced falls [122]. Executive function, referring to the cognitive process directing goal-achievement and balancing multiple tasks simultaneously [123], was also evaluated in this study. While dual-tasking did not affect swing time variability in healthy young and older adults, older fallers saw an increase in swing time variability. Executive function was also compromised in the older adults in response to dual-tasking, suggesting gait destabilization in elderly fallers compared to healthy young and older adults.

Other factors such as walking speed, which relates to increases in both stride length and stride time variability, play a role in understanding motor variability [106, 124, 125]. In addition to spatial-temporal variability, which has been the focus of significant gait variability literature due to its suggested indication of stability, kinetic and kinematic variability has also been investigated. Winter et al found little variability in kinematics and ground reaction forces during gait, but found substantial variation in knee and hip kinetics [125]; the variability observed was not random but strongly co-varied with knee and hip movements. Gait variability is still a growing field and presents a complex interconnection between motor learning, efficient movement, and pathology.

1.3.3 Variability Measures

In time-continuous data analysis, both linear and non-linear measures can be used to quantify stride-to-stride variability. The most commonly used linear variability measures are standard deviation (SD) and coefficient of variation (CV). The simpler of these measures, SD, is the variation from the mean of a time series or distribution [126]. Standard deviation can be used to discern skewness of a data set and can give valuable information about the distribution of one or more variables. However, this measure weighs extreme values more heavily than those closer to the mean. Standard deviation also assumes normally distributed data, which may require manipulation of raw data by transformation or may not even be possible to obtain for all data sets.

The related measure coefficient of variation (CV) is the ratio of standard deviation to the mean [126]. Since the coefficient of variation is expressed as a percentage, it is easy to evaluate and interpret relative to the data set. Conversely, the significance of a specific standard deviation value is dependent on also knowing the mean and distribution of the data. Coefficients of variation also enable evaluation of variability across multiple variables. The main limitation of this measure is in data sets where the mean is close to zero or where there are both positive and negative values. The calculation of coefficient of variation involves dividing by the mean, resulting in artificially inflated results when the mean is close to zero.

Entropy, another measure used in time-continuous data analysis, describes the amount of disorder in a system by reflecting the ability to predict the next data point based on the current data point [127]. Approximate entropy (ApEn), developed by Pincus [128], describes the predictability of time-series data based on previous points using a continuous data set [102, 129]. If a system has an ApEn close to 1, there is a low degree of disorder and the system is considered highly stable, as reflected by easy predictability of the next point based on the previous point. If a system has an

ApEn closer to 2, however, there is a high degree of disorder, the system is considered unstable, and the value of the next point is unpredictable based on the previous point. Limitations of using ApEn include bias in the estimation due to self-matching of the vectors used in the calculation and sensitivity to the set tolerance threshold have been addressed with the introduction of other entropy measures such as sample and fuzzy entropy, among others [129].

Recurrence quantification analysis (RQA) is based on the use of recurrence plots and is used to visualize dynamic changes and repetitions within a complex system over time [130, 131]. This nonlinear method has been used in several disciplines such as psychology and climate change, but has rarely been used in studying movement variability due to the high number of input parameters required. RQA, as opposed to several other variability measures, is able to give information on the nature of the variability instead of only on the total amount of variability. However, in order for this to be done appropriately, several input parameters are required to provide more information about the data set and system. Therefore, this method has not been used as extensively in biomechanics research. However, if sufficient information is available for RQA input, this method can reveal additional information not brought out by standard deviation or entropy calculations.

One other time-continuous analysis method is the calculation of the largest lyapunov exponent (LLE), which describes how quickly points within a system deviate from a predetermined point of system stability. The higher this measure becomes, the faster divergence from the point of stability, signifying chaos within the system; conversely, an LLE value close to zero signifies a stable system. Due to its focus on assessing stability of a system, LLE calculation has been used to directly measure movement stability [132].

Each of the above-mentioned techniques, with the exception of recurrence quantification analysis, only requires time series data as would normally be collected in biomechanics studies.

Using both linear and non-linear techniques such as those described above, studies examining movement variability in both healthy and pathologic populations have been able to begin elucidating the role of variability in motor control, possible causes of movement variability, and related interconnected factors affecting variability.

1.4 Purpose

The purpose of this study is to evaluate gait mechanics in healthy control participants when walking on a treadmill. This study has three primary objectives: 1) determine the between-time repeatability of marker placement for biomechanical assessment, 2) determine the effect of setting walking speed during biomechanical assessment versus allowing participants to self-select a comfortable walking speed, and 3) examine the within-participant correlation between gait asymmetry and motor variability in a healthy control population.

Specific Aim 1: To determine the between-time repeatability of marker placement during the biomechanical assessment.

Specific Aim 2: To determine the effect of setting a defined walking speed during biomechanical assessment versus allowing participants to self-select a comfortable walking speed.

Hypothesis: Comfortable self-selected walking speeds will vary significantly from the defined set walking speed of 3.5 mph (1.5 m/s) and that gait asymmetry will be significantly different between the set-speed and self-selected speed conditions.

Specific Aim 3: To examine the within-participant correlation between gait asymmetry and motor variability in a healthy control population.

Hypothesis: Increases in gait asymmetry will be related to increases in gait variability during treadmill walking.

Many factors have been found to affect gait variability including walking speed, age, and pathology. Variability of gait parameters such as stride length, stride time, and stance phase percentage have also been shown to be lower in treadmill walking relative to over-ground walking despite participants walking at their preferred walking speed in both conditions. Although several factors have been associated with changes in gait variability, none have been able to fully explain the degree of gait variability; there are additional factors associated with variability during gait that are not currently understood.

While both gait variability and asymmetry have been evaluated concerning injury risk and pathology, the direct relationship between gait variability and asymmetry has not yet been studied. Examining the correlation between gait asymmetry and motor variability may help to better understand sources of variability and to inform potential interventions altering motor variability.

2. Methods

2.1 Overview

The repeatability study in Aim 1 tested between-time repeatability of marker placement. For Aims 2 and 3, participants participated in 2 five minute walking trials; the first trial was at a set speed of 1.5 m/s and the second was at their self-selected comfortable walking speed. Gait mechanics were compared when walking speed is set versus self-selected to address Aim 2. Movement and limb loading asymmetry, along with stride-to-stride motor variability, were calculated from this biomechanical assessment to perform a within-participant analysis of the correlation between gait asymmetry and motor variability, addressing Aim 3.

2.2 IRB Approval

The Edward Via College of Osteopathic Medicine (VCOM) IRB has approved this study. In compliance with federal regulations, any injuries, adverse events, or unanticipated events were appropriately reported to the VCOM IRB.

2.3 Participant Population

2.3.1 Aim 1

A study population of ten recreationally active adults between the ages of 18 and 35 were recruited from the local community. An effort was made to maintain equal numbers of males and females, but this equal ratio was not strictly maintained.

2.3.2 Aims 2 and 3

A study population of fifty-one recreationally active adults between the ages of 18 and 35 were recruited from the local community to participate in this study. Recruitment aimed for

approximately equal numbers of men and women. Exclusion criteria included a history of major lower extremity surgery, currently being under the care of a medical professional for any musculoskeletal disease or injury, and any lower extremity injury in the past 3 months that limited physical activity for more than 1 day. Each participant signed informed consent prior to study initiation.

2.4 Repeatability Study

The marker placement repeatability pilot study was performed prior to the initiation of the larger study to assess the walking speed and variability questions in Aims 2 and 3. To evaluate between-time repeatability of marker placement, movement patterns were evaluated using an 8-camera Miquis M1 motion capture system (Qualisys, Gothenburg, Switzerland) at a sampling rate of 120Hz. Participants were asked to wear attire provided by the lab, which included form fitting shorts, a shirt, and Nike Air Pegasus Zoom 34 neutral cushioning athletic running shoes to control effects of clothing and footwear on gait mechanics. Reflective markers were placed bilaterally on lower extremity bony landmarks at the start of the assessment to track motion of the body segments during walking as shown in Figure 1.

Markers were placed bilaterally on the 1st and 5th metatarsal head, medial and lateral malleolus, superior, inferior, and lateral calcaneus, medial and lateral femoral condyle, anterior superior iliac spine (ASIS), iliac crest, greater trochanter, posterior superior

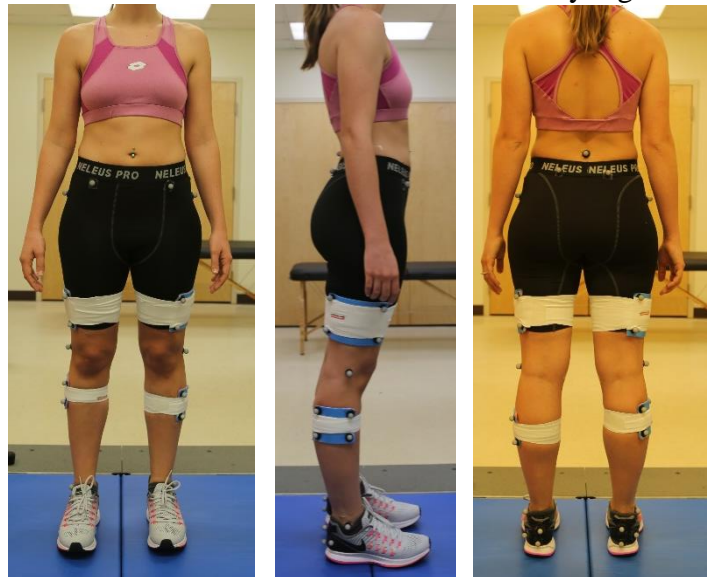


Figure 1: Lower extremity marker set used during biomechanical testing

iliac spine (PSIS), and L4/L5 vertebrae. After collecting a static trial, the bilateral markers on the 1st and 5th metatarsal heads, medial malleolus, medial femoral condyle, and iliac crest were removed to allow participants to move more naturally while walking.

Participants completed two walking trials with each trial lasting three minutes in duration. During each trial, participants walked continuously at a 1.5m/s. Joint angles were continuously recorded from the motion capture system. To allow participants to develop a consistent cadence, the first and last thirty seconds were not assessed. All markers were removed after the first walking trial. Following a period of 30 minutes, markers were re-applied and the second identical walking trial was completed. The following variables were calculated for this repeatability study: peak angles for hip flexion, extension, abduction, adduction; peak angles for knee flexion, extension, valgus, varus; peak angles for ankle dorsiflexion and plantar flexion.

2.5 Biomechanical Assessment (Aims 2 and 3)

Biomechanical assessments were performed in the Granata Treadmill Lab to assess both movement and loading asymmetry using a 3D motion capture and an instrumented treadmill. An 8-camera Miquis M1 system (Qualisys, Gothenburg, Switzerland) was used to collect motion capture data at a sampling rate of 120Hz, while a fore-aft split belt instrumented treadmill (AMTI, Watertown, Massachusetts) was used to collect loading data at 1440Hz. The motion capture system was synchronized with the treadmill, and the setup was calibrated at the start of each testing day.

Participants wore form fitting shorts, a shirt, and Nike Zoom neutral cushioning athletic running shoes, all of which were provided by the lab to control effects of clothing on gait mechanics. Footwear affects spatial-temporal gait parameters, lower extremity muscle activity, gait kinematics, and joint kinetics [133-137]; to control for this effect, footwear was standardized

to the Nike Zoom neutral cushioning athletic running shoe. Reflective markers were placed bilaterally on lower extremity bony landmarks prior to start of testing to track motion of the body segments during walking as shown in Figure 1. Markers will be placed bilaterally on the 1st and 5th metatarsal head, medial and lateral malleolus, superior, inferior, and lateral calcaneus, medial and lateral femoral condyle, anterior superior iliac spine (ASIS), iliac crest, greater trochanter, posterior superior iliac spine (PSIS), and L4/L5 vertebrae. A static trial was collected to compute segment lengths, joint centers, and bony structure for reference in later calculations; this reference trial is necessary for later calculations of joint kinetics and kinematics. The participant's weight was also pulled from the static trial. After collecting the static trial, bilateral markers on the 1st and 5th metatarsal heads, medial malleolus, medial femoral condyle, and iliac crest were removed since these markers were not used in joint kinetics or gait kinematics calculations; removal of these markers also allowed participants to walk more naturally.

Participants completed 2 five minute walking trials. During the first 5 minute walking trial, the participant walked continuously at a set speed of 1.5 m/s. Between walking trials, participants took a 5 minute rest. During the second walking trial, each participant walked at his/her self-selected comfortable walking speed, which was set at the start of the trial and will be held constant throughout the trial. To determine this comfortable walking speed, the speed of the treadmill was slowly increased until the participant indicated they are comfortable. Since walking speed affects gait mechanics and is affected by age [1, 10, 16], the effect of setting walking speed was investigated in Aim 2. Marker trajectories, joint angles and ground reaction forces were continuously recorded from the motion capture system and the instrumented treadmill, respectively, from minute 1 to minute 4; to ensure that participants develop a consistent cadence, the first minute and last minute were excluded. Marker trajectories were used to calculate spatial

and temporal gait parameters. Joint angles and ground reaction forces were used to calculate peak angle, symmetry, impulse, and range of motion measures.

2.6 Data Processing

The biomechanical analysis provided kinematic and kinetic data addressing each aim by determining 1) the between-time repeatability of marker placement, 2) the effect of setting walking speed versus allowing participants to self-select a comfortable walking speed, and 3) the within-participant correlation between gait asymmetry and motor variability in a healthy control population. All biomechanical time-series data were calculated using Visual 3D software (C-Motion, Bethesda, Maryland). Joint angles were calculated as Cardan angles between segments with an order of rotation of flexion-extension, abduction-adduction, and internal rotation-external rotation; this order correspond to the x, y, and z axes, respectively. Joint moments at the ankle, knee, and hip joints were calculated using inverse dynamics and were expressed as internal moments.

All ground reaction forces were normalized to body mass. This normalization technique has been used in related gait mechanics literature [18, 109, 125, 138]. Analysis was performed for the full gait cycle, defined from heel strike on one foot to heel strike on that foot again. Previously published custom Matlab scripts [139-141], were used to extract data for both primary and secondary outcome variables, described in the respective sections below (MathWorks Inc, Natick, Massachusetts).

2.6.1 Repeatability Study

The primary measure, peak knee flexion angle, was compared on each limb and at each time point during the repeatability study to ensure consistent marker placement. The following

secondary measures were also compared: peak hip flexion angle, peak hip extension angle, peak hip abduction angle, peak hip adduction angle, peak knee flexion angle, peak knee extension angle, peak knee valgus angle, peak knee varus angle, peak ankle plantarflexion angle, and peak angle dorsiflexion angle. These measures were selected because they characterize how the skeleton is reconstructed and are used to compute both joint kinetics and kinematics. Therefore, if these measures are consistent, the basis used for skeleton reconstruction and variable calculation is also consistent and repeatable.

2.6.2 Effect of Set Walking Speed (Aim 2)

Based on previously performed symmetry studies, the primary outcome variable for Aim 2 was peak vertical ground reaction force symmetry. Previous ground reaction force symmetry data by Herzog et al [37] was used to complete the power analysis for study Aims 2 and 3; the effect size, alpha level, and power were set at one standard deviation (3.8%), 0.05, and 0.8, respectively. This analysis showed a minimum of 34 participants necessary and to ensure sufficient power 50 participants were included in the study population. Symmetry between limbs was defined using the limb symmetry index (LSI) [37]:

$$\text{LSI} = \frac{X_R - X_L}{0.5 * (X_R + X_L)} * 100\% \quad (1)$$

where X_R and X_L denote data for the right and left limbs, respectively. The LSI provides a directional indication of asymmetry with 0% representing perfect symmetry; a positive LSI indicates the value is higher on the right side while a negative LSI indicates the value is higher on the left side. The direction of asymmetry was not important to the research questions in this study, however, so the absolute value of the LSI was used in analysis. The LSI can also present skewed information if the value of the measure is negative on one limb and positive on the other. This case

would result in a denominator approaching zero, inflating LSI values. However, this possibility was not expected in this case since only healthy control participants were included. A LSI of 10% or below was considered symmetrical while any value exceeding 10% will be considered asymmetrical [142, 143]. For each walking speed trial, these symmetry indices were calculated between successive steps and then averaged across step pairs throughout the entire trial. For each participant, the average LSI in the set-speed walking trial was compared to the LSI in the self-selected speed walking trial. The following secondary variables were also included in this analysis: vertical ground reaction force impulse, sagittal plane hip, knee, and ankle range of motion, and peak knee flexion angle. These measures were selected because they are measured and reported in a wide variety of gait mechanics studies more commonly than frontal plane kinematics and spatial and temporal measures. Any findings in this study aim would, therefore, be more broadly applicable.

2.6.3 Correlation between Gait Asymmetry and Motor Variability (Aim 3)

Step length, single support time (% stride), and swing time (% stride) asymmetry were assessed between limbs. Correlations between these asymmetry metrics on step length, stride length, step width, stride time, single and double support time (% stride), and swing time (% stride) stride-to-stride variability were determined.

2.7 Statistical Analysis

Statistics for all aims were run using JMP Pro 13 (SAS, Cary, NC). To determine the repeatability of marker placement (Aim 1), an intra-class correlation coefficient (ICC) was calculated for each variable. An ICC of absolute single-rater reliability based on a one-way random

effects model was used, defined as ICC(1,1) by Shrout and Fleiss [144] and ICC(1) by McGraw and Wong [145]. This ICC form computes the ratio of between-subjects variance to the sum of within-subject and between-time variance; the equation used to calculate this ICC is shown in Equation 2. ICC values above 0.8 were considered “excellent”, values between 0.6 and 0.8 were considered “fair”, and those below 0.6 were considered “poor” [146]. “Good” and “fair” ICC values were indicative of acceptable repeatability.

$$ICC = \frac{\sigma_y^2}{\sigma_y^2 + \sigma_\varepsilon^2} \quad (2)$$

where $\sigma_y^2 = \text{between} - \text{subject variance}$ and $\sigma_\varepsilon^2 = \text{between} - \text{time variance}$

To determine the effect of setting walking speed (Aim 2), the distribution of each parameter was checked for normality. All parameters were found to be normally distributed after evaluating the histograms and Q-Q plots, so paired t-tests were performed for each measure. An alpha level of 0.05 indicated statistical significance.

To evaluate the linear relationship between gait asymmetry and motor variability (Aim 3), Pearson’s correlations between each pair of asymmetry and variability metrics were calculated. Pearson’s correlations were chosen over Spearman correlations because the direct linear relationship between raw gait asymmetry and motor variability measures was of interest instead of ranked values. An alpha level of 0.05 indicated significance and correlation coefficients (R values) of below 0.34, 0.37-0.67, 0.67-0.9, and above 0.9 indicated poor, moderate, high, and very high correlations respectively [147]. This process was repeated for each of the eleven variability outcome measures.

3. Results

3.1 Repeatability Study

A study population of ten recreationally active adults between the ages of 18 and 35 were included [height: 1.76m (0.12), weight: 80.00 kg (13.27), men (n = 5), women (n = 5)]. This study aim evaluated between-time repeatability of marker placement. The ICCs for this analysis, shown in Table 1 below, were all acceptable; therefore, marker placement was repeatable. Examples of plots comparing joint kinematics between time points is shown in Figure 2.

Table 1: Intra-class correlation coefficients of peak angles on the left limb calculated at 2 time points approximately 30 minutes apart. † “good” correlation, ‡ fair correlation

Variable	ICC	Variable	ICC
Hip Flexion	0.949 †	Knee Extension	0.976 †
Hip Extension	1 †	Knee Valgus	0.887 †
Hip Abduction	0.9593 †	Knee Varus	1 †
Hip Adduction	1 †	Ankle Plantarflexion	0.983 †
Knee Flexion	0.995 †	Ankle Dorsiflexion	1 †

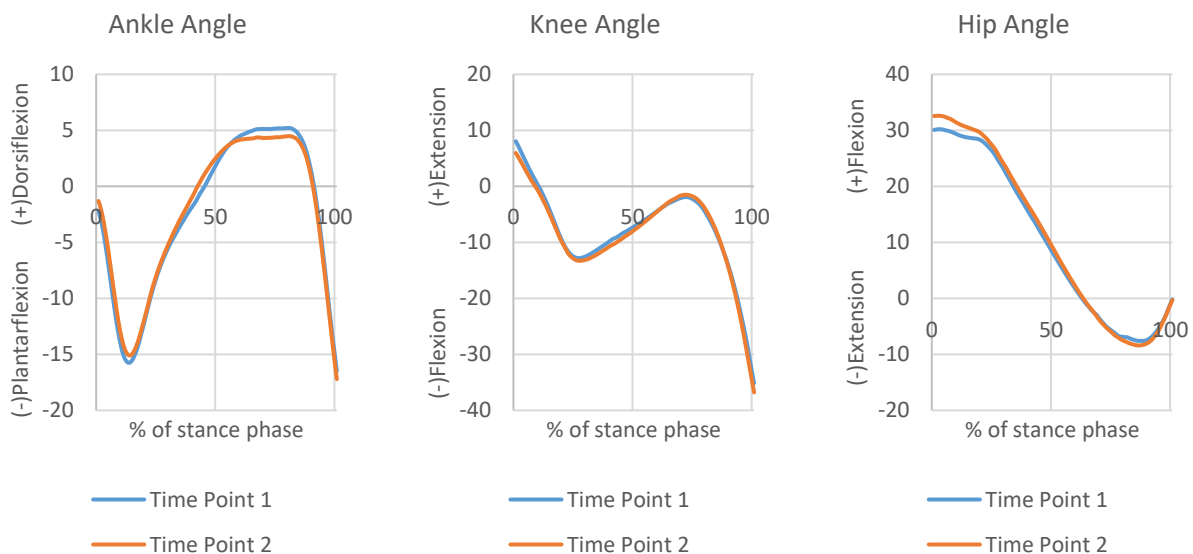


Figure 2: Representative sagittal plane gait kinematics plots between testing time points for a single participant.

3.2 Effect of Set Walking Speed (Aim 2)

A study population of fifty-one participants were recruited for this study. One participant was discovered to have not met inclusion criteria after testing; therefore, the data for that participant was excluded. During data processing, the static reference trial was unusable for one participant; one marker was not placed during data collection, and data was corrupted and unable for another participant. A fourth participant was determined to be an outlier during data analysis; therefore, only data from 47 participants was usable. Participant demographic information can be found in Table 2. Although the Shapiro-Wilk test determined all variables in this analysis to be non-normally distributed, the variables followed the expectations of normally-distributed data based on visual examination of the histograms and Q-Q plots. For this reason, parametric paired-t-test were run for each variable comparing the two walking speeds (set and self-selected). The histograms and Q-Q plots for each measure in this analysis are shown in Figure 3. Walking speed was significantly different between set and self-selected (SS) conditions (set: 1.56 m/s, SS: 1.38 m/s, $p < 0.001$). Vertical ground reaction force symmetry, vertical ground reaction force impulse, peak knee flexion angle, and knee range of motion on the dominant limb were different between set and self-selected speed conditions. Vertical ground reaction force symmetry and impulse were higher in the set speed condition. Peak knee flexion angle and knee range of motion on the

*Table 2: Participant Demographics for Aims 2 and 3. * = Self-selected speed is significantly different than the set speed of 1.5 m/s. The p-values shown reflect differences between men and women for each demographic measure.*

	Age	Height (m)	Weight (kg)	Self-selected Speed (m/s)
Men (n = 23)	24.17 (4.84)	1.80 (0.07)	78.81 (14.76)	1.40 (0.34) *
Women (n = 24)	24.54 (2.50)	1.70 (0.05)	66.90 (9.44)	1.36 (0.28) *
p-value	0.620	<0.001	<0.001	0.611

dominant limb were higher in the self-selected speed condition. Sagittal plane hip, knee, and ankle range of motions other than knee range of motion on the dominant limb were unaffected by the speed condition. Average and standard deviations, along with p-values comparing between set and self-selected speed conditions can be found in Table 3.

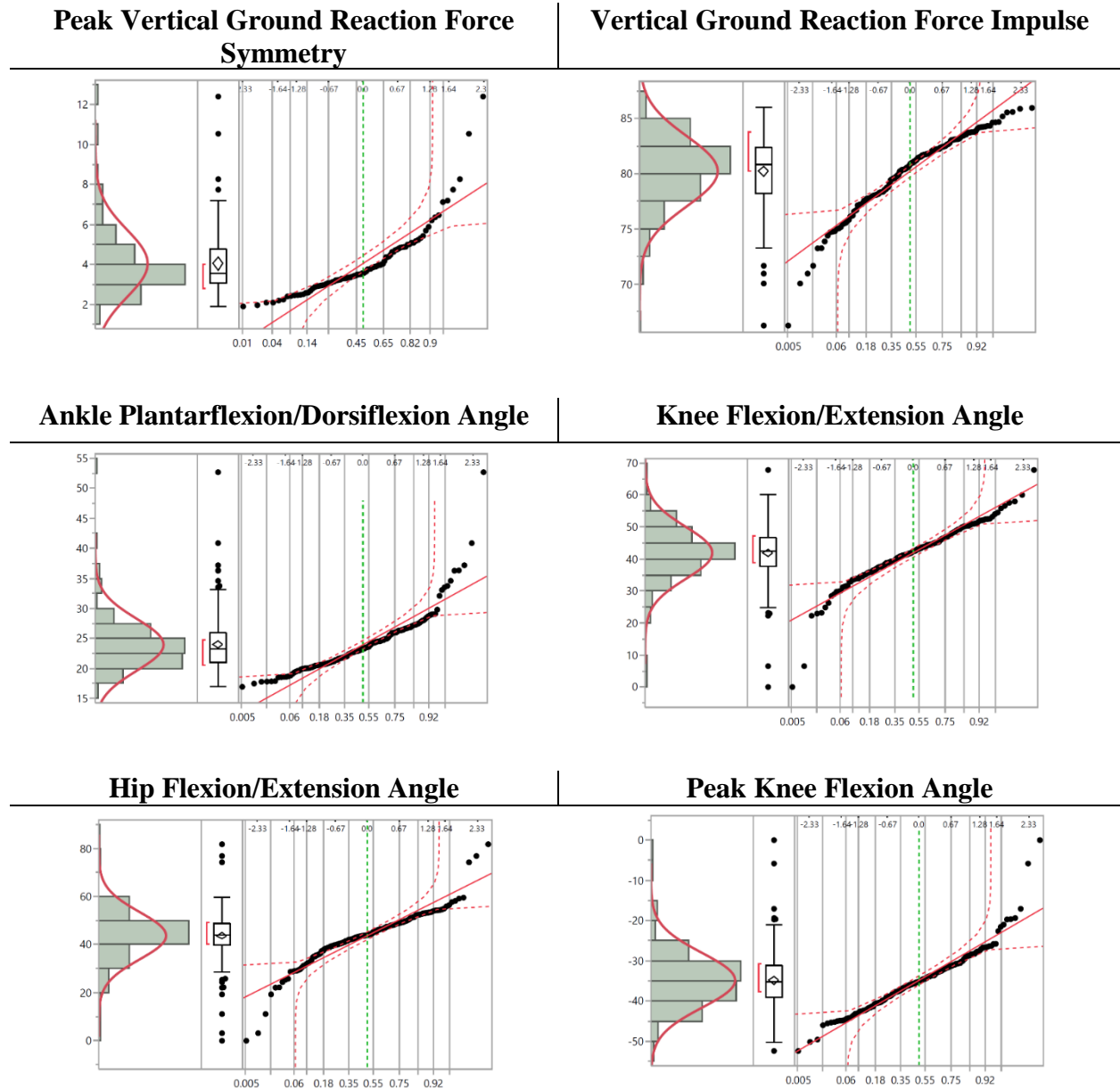


Figure 3: Histograms and Q-Q plots for each measure of interest. These plots were visually inspected and determined to follow requirements for the use of parametric statistics.

Table 3: Average, standard deviation, and p-values for effect of speed condition. † : $p < 0.05$

Variable	Average (SD)	p-value
Peak vGRF Asymmetry	Set: 4.30 (1.52) SS: 3.85 (1.83)	0.025 †
vGRF Impulse – D	Set: 81.05 (2.35) SS: 79.62 (3.53)	0.008 †
vGRF Impulse – ND	Set: 81.06 (2.08) SS: 79.00 (3.98)	0.006 †
Ankle Plantarflexion/Dorsiflexion - D	Set: 23.81 (4.46) SS: 24.22 (5.20)	0.474
Ankle Plantarflexion/Dorsiflexion - ND	Set: 24.05 (3.73) SS: 24.07 (3.91)	0.976
Knee Flexion/Extension - D	Set: 42.03 (6.16) SS: 44.24 (7.14)	0.014 †
Knee Flexion/Extension - ND	Set: 39.56 (8.93) SS: 42.72 (8.12)	0.077
Hip Flexion/Extension - D	Set: 45.35 (9.11) SS: 42.12 (10.75)	0.054
Hip Flexion/Extension - ND	Set: 45.13 (9.40) SS: 42.10 (10.08)	0.123
Peak Knee Flexion Angle – D	Set: 34.74 (5.26) SS: 36.35 (5.84)	0.012 †
Peak Knee Flexion Angle – ND	Set: 33.15 (8.16) SS: 35.68 (6.32)	0.037 †

3.3 Correlation between Gait Asymmetry and Motor Variability

A study population of fifty-one participants were recruited for this study. One participant was discovered to have not met inclusion criteria after testing; therefore, the data for that participant

was excluded. During data processing, the static reference trial was unusable for one participant; one marker was not placed during data collection, and data was corrupted and unable for another participant. A fourth participant was determined to be an outlier during data analysis; therefore, only data from 47 participants was usable. Participant demographic information can be found in Table 2. Since there was a significant difference in walking speed and differences in gait mechanics were found between set and self-selected speed conditions, the analysis for this study aim was performed for only the set speed condition. Correlation coefficients and corresponding p-values

Table 4: R (Correlation Coefficient) and correlation p-values for each set of asymmetry and variability measures in the set speed condition. Measures of interest listed horizontally and vertically are of gait asymmetry and motor variability, respectively. [†] $|R| > 0.9$ (very high). [‡] $0.9 > |R| > 0.67$ (high). [€] $0.67 > |R| > 0.34$ (moderate). [¥] $|R| < 0.34$ (poor). [§] $p < 0.05$.

Measures of Interest	Step Length LSI		Swing Time LSI		Single Support Time LSI	
	R	p-value	R	p-value	R	p-value
Step Length - D	-0.588	<0.001	0.162	0.262	0.044	0.761
Step Length – ND	-0.566	<0.001	0.237	0.097	0.107	0.460
Stride Length – D	0.186	0.195	-0.023	0.876	0.241	0.093
Stride Length – ND	0.198	0.168	-0.065	0.652	0.217	0.130
Stride Time – D	-0.237	0.098	0.824	<0.001	0.115	0.425
Stride Time – ND	-0.234	0.101	0.825	<0.001	0.116	0.421
Single and Double Support Time - D	-0.226	0.115	0.933	<0.001	0.295	0.038
Single and Double Support Time - ND	-0.248	0.082	0.931	<0.001	0.291	0.040
Swing Time – D	-0.165	0.252	0.844	<0.001	0.138	0.338
Swing Time – ND	-0.189	0.188	0.901	<0.001	0.173	0.230
Step Width	-0.387	0.006	0.275	0.053	0.185	0.199

for each pair of asymmetry and variability metrics are reported in Table 4. Stride length variability was not related to any of the asymmetry measures. All other variability metrics were significantly related to at least one asymmetry measure. The strongest relationships existed between temporal variability measures and swing time asymmetry. Increases in swing time asymmetry and, to a lesser degree, single support time asymmetry were related to increases in variability of stride, swing, and single and double support times. The correlation between support time variability and single support time asymmetry was poor but still statistically significant. Increases in step length asymmetry significantly inversely correlated to decreases in step length and step width, but these relationships were not as strong as those observed between temporal variability measures and swing time asymmetry. Spatial and temporal asymmetry were only significantly related to spatial and temporal variability, respectively. Temporal relationships were stronger than spatial relationships.

4. Discussion

In the evaluation of marker placement, all ICCs were acceptable; therefore, marker placement was determined to be repeatable. The results of this study indicate that setting a constant walking speed for all participants leads to significant kinetic and kinematic differences in gait mechanics. Therefore, which of these study designs is used should be chosen intentionally depending on whether the particular measures of interest are affected by walking speed. The direct relationship between temporal asymmetry and variability along with the inverse relationship between spatial asymmetry and variability were also shown in this study. Gait asymmetry is related to motor variability, but this relationship varies between temporal and spatial measures. The high degree of temporal variability explained by temporal asymmetry suggests that temporal asymmetry is a strong explanatory variable of temporal variability.

The results of the reliability analysis indicated that in a new investigator, markers were reliable placed between time points approximately 30 minutes apart. Repeatable marker placement is essential in gait mechanics research since inconsistent marker placement can impact results and skew study data. For this reason, the skill is one of the first that new investigators in the field need to master prior to data collection that will be completed between days or between conditions in which markers may need to be removed and reattached. The results of this study demonstrate that this new investigator is able to place lower-extremity markers with high repeatability. Despite being carried out with a relatively small number of participants, the population contained a wide variety of body sizes and shapes. The ease of marker placement can vary depending on body shape and fat deposition. Therefore, the repeatability shown in this study are given increased strength due to the variety of individuals who were included in the participant sample. The repeatability

found in this study aim will be particularly important in future between-time or between-day studies.

One limitation of this study aim was that the upper body was not included. Including the upper extremity would have increased testing and data processing time, and upper extremity data was not of primary interest in this study since the new investigator has a current focus on lower extremity mechanics. Due to the limited motion capture data collection space, including the upper extremity would have required positioning the cameras at angles that would make unique identification of the heel markers more difficult. If the new investigator were to conduct an upper extremity biomechanics study, another similar upper extremity marker placement repeatability study would be necessary prior to study initiation. However, as long as lower-extremity biomechanics are the focus, the repeatability reported in this study would be sufficient for the investigator to proceed with data collection.

The set speed was significantly different than the self-selected speed of the study participants (set: 1.56m/s, SS: 1.38m/s, $p < 0.001$). Previous studies have found average walking speeds closer to 1m/s in older adult populations [148, 149], but previous investigations in the 18-35 age population found average speeds between 1.2m/s and 1.5m/s [150-156]. The set speed condition for this study was toward the top of that range which may have been more of a “fast” walking speed for some participants. Effects of walking speed on several gait parameters including peak knee flexion moment, vertical ground reaction force, lower extremity joint moments and powers, lower extremity joint kinematics, muscle activity, and spatial-temporal parameters have also been previously observed [1, 3, 4, 18, 157-162]. Since walking speed was different between speed conditions, some measures of interest were expected to change. The results of this study agree well with previous literature and support this hypothesis. Vertical ground reaction force

asymmetry was higher in the set speed condition, in which the walking speed was higher. Previous studies investigating the effect of walking speed on vertical ground reaction force symmetry have been performed in children, amputees, and after stroke [163-165]. Several other studies have established the effect of walking speed on vertical ground reaction force amplitude [2, 5, 10, 166]. However, to date there has not been a study evaluating the effect of walking speed on vertical ground reaction force symmetry index in healthy adults; the effect found in this study fills that gap in the literature. Along with vertical ground reaction force symmetry, impulse also increased with walking speed in the set speed condition. Since impulse is calculated as the area under the vertical ground reaction force curve, this result is likely due to the higher peak vertical ground reaction force increasing this total area. The only result found in this study that disagreed with previous literature was in the effect of walking speed on knee range of motion on the dominant limb. A previous study by Chiu et al found no differences in lower extremity joint ranges of motion with increased walking speed [5]. However, this difference in joint range of motion may be driven by the significant differences in peak knee flexion angle. Although approaching significance, this effect was not seen on the non-dominant limb, possibly due to higher variances compared to the dominant limb which could prevent significant effects from being found. The current study found no other differences in hip, knee, and ankle range of motion on either limb between speed conditions which agrees with prior literature [5]. It is possible that the change in walking speed did not cause proportional differences in the opposite peaks of each joint angle. Therefore, the range of motion at each lower extremity joint was not significantly affected by the change in walking speed.

There are multiple limitations that should be noted with this study aim. The first limitation is that the order in which the set and self-selected speed walking trials was performed was not

randomized; all participants completed the set speed trial followed by the self-selected speed trial. Between trials, participants were given a five-minute rest break to prevent fatigue, but this lack of randomization could have resulted in ordering effects on the results. This lack of random ordering is a flaw of the current study design and could have prevented additional significant results from being detected. Another limitation of this study was the method used to identify the participant's self-selected speed. The treadmill was started at 1mph and the speed was slowly increased until the participant identified their walking speed as “comfortable”. Using methods such as that described by Dingwell et al. to identify self-selected speed may be more able to identify self-selected speed [167]. The technique developed by Dingwell involves starting at a slow speed and slowly increasing speed until the participant identifies that their walking speed is faster than preferred. The speed is then decreased until the participant identifies that their walking speed is slower than preferred. This process is repeated until three sets of “faster” and “slower” walking speeds are determined; these speeds are averaged to identify the participant’s preferred walking speed [167]. A third limitation of this study is that the effect of setting walking speed is difficult to separate from the effect of faster walking speed since walking speed also changed between speed conditions. This limitation is particularly important due to the two previously described limitations; since order of conditions was not randomized and there is question as to whether participants’ self-selected speed was truly identified, the effects seen in this study aim may be attributable more to changes in walking speed between conditions than to a set speed design. In order to be able to separate these effects, the previous limitations of potential order effects and self-selected speed identification would need to be addressed.

Set walking speed was significantly different than self-selected walking speed identified by increasing treadmill speed until participants indicated that they were at a comfortable speed.

This change in walking speed between conditions led to kinetic and kinematic gait changes between conditions with almost all results agreeing with previous literature. These results provide evidence on the effect of walking speed on the symmetry index of vertical ground reaction in this healthy young population. As noted by previous investigators, walking speed is an important aspect of gait to consider when evaluating symmetry, joint kinetics, and kinematics during gait with any population. Participants self-selecting walking speed allows participants to all walk at their comfortable speed, making the results more indicative of normal walking across all subjects; this method also does not bias the walking speed against shorter and taller participants. However, allowing participants to self-select their speed introduces walking speed as a necessary covariate in analysis. Setting walking speed for all participants removes the additional factor of walking speed in study analysis, but there will still be an effect of differences in preferred walking speed; that limitation could make finding significant results more difficult. Setting walking speed may be a simple and viable option if the measures of interest act independently of walking speed. If this is not the case, either the self-selected speed design should be used or preferred walking speed should be accounted for in some way.

Motor variability has been heavily studied in prior literature, both being described as noise in the motor control system [96, 98-101] and a functional adaptation to increase adaptability and flexibility of the system [168]. Changes in motor variability have been associated with fall risk, fatigue, musculoskeletal injury, pain, walking speed, and spatial-temporal gait alterations [22, 109, 116, 167, 169-176]. Factors including age, pathology, and sex have been shown to affect motor variability [9, 110, 177-179], but its role in essential everyday activities such as walking are still not fully understood. The current study found relationships between asymmetry and both temporal and spatial variability. These relationships not only existed but several showed high correlations,

particularly those including temporal variability measures. Although these results indicate that there is a relationship between gait asymmetry and motor variability, they do not provide enough information to know which is the driving factor. There is currently no feasible way to expand this relationship to establish causality since that would require directly manipulating gait asymmetry and motor variability. Asymmetry and variability are similar in that they can indicate both pathology and function; the context of the observed asymmetry and variability is crucial. Under the functional asymmetry theory, lower-extremity asymmetries may exist where one limb is utilized more for propulsion and strength while the other functions more to ensure balance and stability [58, 180]; sports favoring one limb such as soccer provide an example of when a functional asymmetry may exist. In this context, the results of the current study suggest that increased temporal variability and possibly decreased spatial variability may be observed in association with functional gait asymmetries. The possibility that altered motor variability may actually be individual adaptation responses to optimize functionality has been introduced [100, 181-183]; increased variability is not necessarily indicative of pathology [182]. Therefore, when functional asymmetries are present, associated variability alterations may suggest increases in adaptability that serve as functional compensatory mechanisms. Although many compensatory variability responses observed have been in joint coordination of movement patterns [106, 119, 184], similar compensatory variability may be present in temporal and spatial components of gait. However, these same observations in older adults with lower extremity pathology may indicate decreased motor control and compromised balance instead of a functional asymmetry. The context and population are essential to consider when interpreting the potential meaning of the relationships between asymmetry and variability found in this study.

One significant limitation of this study was that relationships between asymmetry and variability were only explored for spatial and temporal parameters. Furthermore, only one spatial and two temporal asymmetry measures were included in the analysis. The decision to focus on spatial and temporal gait measures was made based on a similar focus in gait variability literature evaluating injury risk and function of motor variability. Future studies could investigate possible relationships between additional spatial and temporal gait parameters and expand to include kinetic and other kinematic measures. Another limitation of this study was the entire population being healthy young adults. Since much of the motor variability literature focuses on older adults and control mechanisms, this lack of age diversity limits the power of relating these study results back to all relevant populations including older adults or adults with pathology.

The results of this study contribute to our understanding of the relationship between gait asymmetry and motor variability. Regardless of the mix in strength of results found in the current study between temporal and spatial measures, the determined relationship between gait asymmetry and motor variability is valuable. This link provides another avenue to better understand the role of motor variability in gait. With full context in mind, this relationship provides a powerful tool bridging the gap between two important aspects of gait mechanics. Changes in motor variability observed in different speed, task, and pathology conditions may be associated with changes in gait asymmetry. Knowing that increases in motor variability have often been related to increased fall risk in older adults, gait retraining focusing on altering gait asymmetry may be a useful intervention to decrease fall risk in that population. In young adults, this relationship could also aid in further investigations of whether functional asymmetry and compensatory variability are actually related phenomena. Based on these results, gait asymmetry and motor variability should be investigated in tandem and should not be thought of independently.

5. Conclusion

A new investigator's ability to place markers consistently was demonstrated. This skill is essential in between-time and between-day repeated measures studies to ensure that inconsistent marker placement will not impact study results. Current study findings reiterated the importance of walking speed when evaluating gait symmetry, joint kinetics, and kinematics. Despite a relatively small change in walking speed between conditions, increased walking speed resulted in both kinetic and kinematic gait mechanics differences. The decision regarding whether to utilize a set or self-selected speed condition within a study design should be made based on whether the measures of interest are independent of walking speed. Using either condition, the effect of differences in preferred walking speed should be kept in mind in the interpretation of results. Gait asymmetry and motor variability are directly related in the case of temporal measures and inversely related for spatial measures. These relationships could be used in the development of future gait retraining interventions to decrease fall risk or promote more symmetrical loading following musculoskeletal injury or surgery.

6. References

1. Kirtley, C., M.W. Whittle, and R.J. Jefferson, *Influence of walking speed on gait parameters*. J Biomed Eng, 1985. **7**(4): p. 282-8.
2. Chung, M.-J. and M.-J.J. Wang, *The change of gait parameters during walking at different percentage of preferred walking speed for healthy adults aged 20–60 years*. Gait & Posture, 2010. **31**(1): p. 131-135.
3. Murray, M.P., et al., *Comparison of free and fast speed walking patterns of normal men*. Am J Phys Med, 1966. **45**(1): p. 8-23.
4. Schwartz, M.H., A. Rozumalski, and J.P. Trost, *The effect of walking speed on the gait of typically developing children*. Journal of Biomechanics, 2008. **41**(8): p. 1639-1650.
5. Chiu, M.C. and M.J. Wang, *The effect of gait speed and gender on perceived exertion, muscle activity, joint motion of lower extremity, ground reaction force and heart rate during normal walking*. Gait Posture, 2007. **25**(3): p. 385-92.
6. Chiu, M.C., H.C. Wu, and L.Y. Chang, *Gait speed and gender effects on center of pressure progression during normal walking*. Gait Posture, 2013. **37**(1): p. 43-8.
7. Chiu, S.L. and L.S. Chou, *Effect of walking speed on inter-joint coordination differs between young and elderly adults*. J Biomech, 2012. **45**(2): p. 275-80.
8. Kang, H.G. and J.B. Dingwell, *Effects of walking speed, strength and range of motion on gait stability in healthy older adults*. J Biomech, 2008. **41**(14): p. 2899-905.
9. Kang, H.G. and J.B. Dingwell, *Separating the effects of age and walking speed on gait variability*. Gait Posture, 2008. **27**(4): p. 572-7.
10. Crowe, A., et al., *The influence of walking speed on parameters of gait symmetry determined from ground reaction forces*. Human Movement Science, 1996. **15**(3): p. 347-367.
11. den Otter, A.R., et al., *Speed related changes in muscle activity from normal to very slow walking speeds*. Gait Posture, 2004. **19**(3): p. 270-8.
12. Neptune, R.R., K. Sasaki, and S.A. Kautz, *The effect of walking speed on muscle function and mechanical energetics*. Gait Posture, 2008. **28**(1): p. 135-43.
13. Chen, I.H., K.N. Kuo, and T.P. Andriacchi, *The influence of walking speed on mechanical joint power during gait*. Gait & Posture, 1997. **6**(3): p. 171-176.
14. Zeni, J.A., Jr. and J.S. Higginson, *Differences in gait parameters between healthy subjects and persons with moderate and severe knee osteoarthritis: a result of altered walking speed?* Clin Biomech (Bristol, Avon), 2009. **24**(4): p. 372-8.
15. Landry, S.C., et al., *Knee biomechanics of moderate OA patients measured during gait at a self-selected and fast walking speed*. J Biomech, 2007. **40**(8): p. 1754-61.
16. Bejek, Z., et al., *The influence of walking speed on gait parameters in healthy people and in patients with osteoarthritis*. Knee Surg Sports Traumatol Arthrosc, 2006. **14**(7): p. 612-22.
17. Mockel, G., et al., *The influence of walking speed on kinetic and kinematic parameters in patients with osteoarthritis of the hip using a force-instrumented treadmill and standardised gait speeds*. Arch Orthop Trauma Surg, 2003. **123**(6): p. 278-82.
18. Andriacchi, T.P., J.A. Ogle, and J.O. Galante, *Walking speed as a basis for normal and abnormal gait measurements*. J Biomech, 1977. **10**(4): p. 261-8.
19. Wagenaar, R.C. and W.J. Beek, *Hemiplegic gait: a kinematic analysis using walking speed as a basis*. J Biomech, 1992. **25**(9): p. 1007-15.

20. Kim, C.M. and J.J. Eng, *Magnitude and pattern of 3D kinematic and kinetic gait profiles in persons with stroke: relationship to walking speed*. *Gait Posture*, 2004. **20**(2): p. 140-6.
21. Doi, T., et al., *Cognitive function and gait speed under normal and dual-task walking among older adults with mild cognitive impairment*. *BMC Neurol*, 2014. **14**: p. 67.
22. Jordan, K., J.H. Challis, and K.M. Newell, *Walking speed influences on gait cycle variability*. *Gait Posture*, 2007. **26**(1): p. 128-34.
23. Fritz, S. and M. Lusardi, *White paper: "walking speed: the sixth vital sign"*. *J Geriatr Phys Ther*, 2009. **32**(2): p. 46-9.
24. Rabadi, M.H. and A. Blau, *Admission ambulation velocity predicts length of stay and discharge disposition following stroke in an acute rehabilitation hospital*. *Neurorehabil Neural Repair*, 2005. **19**(1): p. 20-6.
25. Ostir, G.V., et al., *Measures of lower body function and risk of mortality over 7 years of follow-up*. *Am J Epidemiol*, 2007. **166**(5): p. 599-605.
26. McGinn, A.P., et al., *Walking speed and risk of incident ischemic stroke among postmenopausal women*. *Stroke*, 2008. **39**(4): p. 1233-9.
27. Waite, L.M., et al., *Gait slowing as a predictor of incident dementia: 6-year longitudinal data from the Sydney Older Persons Study*. *J Neurol Sci*, 2005. **229-230**: p. 89-93.
28. Yoward, L.S., P. Doherty, and C. Boyes, *A survey of outcome measurement of balance, walking and gait amongst physiotherapists working in neurology in the UK*. *Physiotherapy*, 2008. **94**(2): p. 125-132.
29. Alton, F., et al., *A kinematic comparison of overground and treadmill walking*. *Clin Biomech (Bristol, Avon)*, 1998. **13**(6): p. 434-440.
30. Lee, S.J. and J. Hidler, *Biomechanics of overground vs. treadmill walking in healthy individuals*. *J Appl Physiol (1985)*, 2008. **104**(3): p. 747-55.
31. Stolze, H., et al., *Gait analysis during treadmill and overground locomotion in children and adults*. *Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control*, 1997. **105**(6): p. 490-497.
32. Riley, P.O., et al., *A kinematic and kinetic comparison of overground and treadmill walking in healthy subjects*. *Gait Posture*, 2007. **26**(1): p. 17-24.
33. Parvataneni, K., et al., *Kinematic, kinetic and metabolic parameters of treadmill versus overground walking in healthy older adults*. *Clin Biomech (Bristol, Avon)*, 2009. **24**(1): p. 95-100.
34. Hamill, J., B. Bates, and K. Knutzen, *Ground reaction force symmetry during walking and running*. *Research Quarterly for Exercise and Sport*, 1984. **55**(3): p. 289-293.
35. Menard, M.R., et al., *Comparative biomechanical analysis of energy-storing prosthetic feet*. *Arch Phys Med Rehabil*, 1992. **73**(5): p. 451-8.
36. Hannah, R.E., J.B. Morrison, and A.E. Chapman, *Kinematic symmetry of the lower limbs*. *Arch Phys Med Rehabil*, 1984. **65**(4): p. 155-8.
37. Herzog, W., et al., *Asymmetries in ground reaction force patterns in normal human gait*. *Med Sci Sports Exerc*, 1989. **21**(1): p. 110-4.
38. Gundersen, L.A., et al., *Bilateral analysis of the knee and ankle during gait: an examination of the relationship between lateral dominance and symmetry*. *Phys Ther*, 1989. **69**(8): p. 640-50.
39. Singh, I., *Functional asymmetry in the lower limbs*. *Acta Anat (Basel)*, 1970. **77**(1): p. 131-8.

40. Du Chatinier, K. and R.H. Rozendal, *Temporal symmetry of gait of selected normal human subjects*. Proc K Ned Akad Wet C, 1970. **73**(4): p. 353-61.
41. Allard, P., et al., *Simultaneous bilateral 3-D able-bodied gait*. Human Movement Science, 1996. **15**(3): p. 327-346.
42. Chodera, J. and R. Levell, *Footprint patterns during walking*. Perspectives in biomedical engineering, 1973: p. 81-90.
43. Chodera, J.D., *Analysis of gait from footprints*. Physiotherapy, 1974. **60**(6): p. 179-81.
44. Stefanyshyn, D.J. and J.R. Engsborg, *Right to left differences in the ankle joint complex range of motion*. Med Sci Sports Exerc, 1994. **26**(5): p. 551-5.
45. Rosenrot, P. *Asymmetry of gait and the relationship to lower limb dominance*. in *Proc Conf Human Locomotion*. 1980.
46. Rosenrot, P., J. Wall, and J. Charteris, *The relationship between velocity, stride time, support time and swing time during normal walking*. J Hum Mov Stud, 1980. **6**: p. 323-335.
47. Wheelwright, E.F., et al., *Temporal and spatial parameters of gait in children. I: Normal control data*. Dev Med Child Neurol, 1993. **35**(2): p. 102-13.
48. Damholt, V. and N.B. Termansen, *Asymmetry of plantar flexion strength in the foot*. Acta Orthop Scand, 1978. **49**(2): p. 215-9.
49. Crowe, A., et al., *Characterization of gait of young adult females by means of body centre of mass oscillations derived from ground reaction forces*. Gait & Posture, 1993. **1**(1): p. 61-68.
50. Giakas, G., et al., *Comparison of gait patterns between healthy and scoliotic patients using time and frequency domain analysis of ground reaction forces*. Spine (Phila Pa 1976), 1996. **21**(19): p. 2235-42.
51. Ounpuu, S. and D.A. Winter, *Bilateral electromyographical analysis of the lower limbs during walking in normal adults*. Electroencephalogr Clin Neurophysiol, 1989. **72**(5): p. 429-38.
52. Lathrop-Lambach, R.L., et al., *Evidence for joint moment asymmetry in healthy populations during gait*. Gait Posture, 2014. **40**(4): p. 526-31.
53. Haddad, J.M., et al., *Adaptations in interlimb and intralimb coordination to asymmetrical loading in human walking*. Gait Posture, 2006. **23**(4): p. 429-34.
54. Lythgo, N., C. Wilson, and M. Galea, *Basic gait and symmetry measures for primary school-aged children and young adults. II: walking at slow, free and fast speed*. Gait Posture, 2011. **33**(1): p. 29-35.
55. Lythgo, N., C. Wilson, and M. Galea, *Basic gait and symmetry measures for primary school-aged children and young adults whilst walking barefoot and with shoes*. Gait Posture, 2009. **30**(4): p. 502-6.
56. Dellagrana, R.A., et al., *Evidence for Isokinetic Knee Torque Asymmetries in Male Long Distance-Trained Runners*. Int J Sports Phys Ther, 2015. **10**(4): p. 514-9.
57. Sadeghi, H., *Local or global asymmetry in gait of people without impairments*. Gait Posture, 2003. **17**(3): p. 197-204.
58. Sadeghi, H., P. Allard, and M. Duhaime, *Functional gait asymmetry in able-bodied subjects*. Human Movement Science, 1997. **16**(2): p. 243-258.
59. Sadeghi, H., et al., *Symmetry and limb dominance in able-bodied gait: a review*. Gait Posture, 2000. **12**(1): p. 34-45.

60. Rice, J. and M.K. Seeley, *An investigation of lower-extremity functional asymmetry for non-preferred able-bodied walking speeds*. Int J Exerc Sci, 2010. **3**(4): p. 182-188.
61. Kutilek, P., et al., *Kinematic quantification of gait asymmetry based on characteristics of angle-angle diagrams*. Acta Polytechnica Hungarica, 2014. **11**(5).
62. Skinner, H.B. and D.J. Effeney, *Gait analysis in amputees*. American Journal of Physical Medicine & Rehabilitation, 1985. **64**(2): p. 82-89.
63. DeVita, P., D. Hong, and J. Hamill, *Effects of asymmetric load carrying on the biomechanics of walking*. J Biomech, 1991. **24**(12): p. 1119-29.
64. Titianova, E.B. and I.M. Tarkka, *Asymmetry in walking performance and postural sway in patients with chronic unilateral cerebral infarction*. J Rehabil Res Dev, 1995. **32**(3): p. 236-44.
65. Kaufman, K.R., L.S. Miller, and D.H. Sutherland, *Gait asymmetry in patients with limb-length inequality*. J Pediatr Orthop, 1996. **16**(2): p. 144-50.
66. Griffin, M., S. Olney, and I. McBride, *Role of symmetry in gait performance of stroke subjects with hemiplegia*. Gait & Posture, 1995. **3**(3): p. 132-142.
67. HIRASAWA, Y., *An observation on standing ability of Japanese males and females*. Journal of the Anthropological Society of Nippon, 1979. **87**(2): p. 81-92.
68. Vanden-Abeelee, J., *Comments on the functional asymmetries of the lower extremities*. Cortex, 1980. **16**(2): p. 325-329.
69. Hirasawa, Y., *Left leg supporting human straight (bipedal) standing*. Saiensu, 1981. **6**: p. 32-44.
70. Matsusaka, N., et al., *Relationship between right and left leg in human gait from a viewpoint of balance control*. Biomechanics IX-A, 1985: p. 427-430.
71. Hirokawa, S., *Normal gait characteristics under temporal and distance constraints*. J Biomed Eng, 1989. **11**(6): p. 449-56.
72. Sadeghi, H., et al., *Lower limb muscle power relationships in bilateral able-bodied gait*. Am J Phys Med Rehabil, 2001. **80**(11): p. 821-30.
73. Seeley, M.K., B.R. Umberger, and R. Shapiro, *A test of the functional asymmetry hypothesis in walking*. Gait Posture, 2008. **28**(1): p. 24-8.
74. Schot, P.K., B.T. Bates, and J.S. Dufek, *Bilateral performance symmetry during drop landing: a kinetic analysis*. Med Sci Sports Exerc, 1994. **26**(9): p. 1153-9.
75. Burnett, D.R., et al., *Symmetry of ground reaction forces and muscle activity in asymptomatic subjects during walking, sit-to-stand, and stand-to-sit tasks*. J Electromyogr Kinesiol, 2011. **21**(4): p. 610-5.
76. Cavanagh, P.R., *The biomechanics of lower extremity action in distance running*. Foot & ankle, 1987. **7**(4): p. 197-217.
77. Zifchock, R.A., I. Davis, and J. Hamill, *Kinetic asymmetry in female runners with and without retrospective tibial stress fractures*. Journal of biomechanics, 2006. **39**(15): p. 2792-2797.
78. Ciacci, S., et al., *Assessment of kinematic asymmetry for reduction of hamstring injury risk*. International Journal of Athletic Therapy and Training, 2013. **18**(6): p. 18-23.
79. Rauh, M.J., et al., *Quadriceps angle and risk of injury among high school cross-country runners*. journal of orthopaedic & sports physical therapy, 2007. **37**(12): p. 725-733.
80. Bredeweg, S., I. Buist, and B. Kluitenberg, *Differences in kinetic asymmetry between injured and noninjured novice runners: a prospective cohort study*. Gait & posture, 2013. **38**(4): p. 847-852.

81. Carpes, F.P., C.B. Mota, and I.E. Faria, *On the bilateral asymmetry during running and cycling - a review considering leg preference*. Phys Ther Sport, 2010. **11**(4): p. 136-42.
82. Burnie, J. and D.A. Brodie, *Isokinetic measurement in preadolescent males*. Int J Sports Med, 1986. **7**(4): p. 205-9.
83. Baker, P.A. and S.R. Hewison, *Gait recovery pattern of unilateral lower limb amputees during rehabilitation*. Prosthet Orthot Int, 1990. **14**(2): p. 80-4.
84. Arsenault, A., D. Winter, and R. Marteniuk, *Is there a 'normal' profile of EMG activity in gait?* Medical and Biological Engineering and Computing, 1986. **24**(4): p. 337-343.
85. Arsenault, A.B., D.A. Winter, and R.G. Marteniuk, *Bilateralism of EMG profiles in human locomotion*. Am J Phys Med, 1986. **65**(1): p. 1-16.
86. Ounpuu, S., *Bilateral analysis of the lower limbs during walking in normal individuals*. 1987.
87. Robinson, R., W. Herzog, and B. Nigg, *Use of force platform variables to quantify the effects of chiropractic manipulation on gait symmetry*. Journal of manipulative and physiological therapeutics, 1987. **10**(4): p. 172-176.
88. Crenshaw, S.J. and J.G. Richards, *A method for analyzing joint symmetry and normalcy, with an application to analyzing gait*. Gait Posture, 2006. **24**(4): p. 515-21.
89. Shorter, K.A., et al., *A new approach to detecting asymmetries in gait*. Clin Biomech (Bristol, Avon), 2008. **23**(4): p. 459-67.
90. Zifchock, R.A., et al., *The symmetry angle: a novel, robust method of quantifying asymmetry*. Gait & posture, 2008. **27**(4): p. 622-627.
91. Exell, T.A., et al., *Gait asymmetry: composite scores for mechanical analyses of sprint running*. J Biomech, 2012. **45**(6): p. 1108-11.
92. Cabral, S., et al., *A Global Gait Asymmetry Index*. J Appl Biomech, 2016. **32**(2): p. 171-7.
93. Dewar, M.E. and G. Judge, *Temporal asymmetry as a gait quality indicator*. Medical and Biological Engineering and Computing, 1980. **18**(5): p. 689-693.
94. Gouwanda, D. and S.A. Senanayake, *Identifying gait asymmetry using gyroscopes—A cross-correlation and Normalized Symmetry Index approach*. Journal of Biomechanics, 2011. **44**(5): p. 972-978.
95. Jiang, S., et al. *Primary Exploration on the Symmetry of Human Walking*. in *Computer and Information Technology, 2009. CIT'09. Ninth IEEE International Conference on*. 2009. IEEE.
96. Newell, K.M. and A.B. Slifkin, *The nature of movement variability*. Motor behavior and human skill: A multidisciplinary perspective, 1998: p. 143-160.
97. Schmidt, R.A., *A schema theory of discrete motor skill learning*. Psychological review, 1975. **82**(4): p. 225.
98. Stergiou, N. and L.M. Decker, *Human movement variability, nonlinear dynamics, and pathology: is there a connection?* Human movement science, 2011. **30**(5): p. 869-888.
99. Schmidt, R.A., *Motor schema theory after 27 years: reflections and implications for a new theory*. Research quarterly for exercise and sport, 2003. **74**(4): p. 366-375.
100. Davids, K., et al., *Movement systems as dynamical systems: the functional role of variability and its implications for sports medicine*. Sports Med, 2003. **33**(4): p. 245-60.
101. Newell, K.M., *Motor skill acquisition*. Annu Rev Psychol, 1991. **42**: p. 213-37.
102. Komar, J., L. Seifert, and R. Thouvarecq, *What variability tells us about motor expertise: measurements and perspectives from a complex system approach*. Movement & Sport Sciences, 2015(3): p. 65-77.

103. Maki, B.E., *Gait changes in older adults: predictors of falls or indicators of fear?* Journal of the American geriatrics society, 1997. **45**(3): p. 313-320.
104. Rosnay, J.d., *Le macroscope. Vers une vision globale.* Paris: Seuil, 1975.
105. Seifert, L., C. Button, and K. Davids, *Key properties of expert movement systems in sport : an ecological dynamics perspective.* Sports Med, 2013. **43**(3): p. 167-78.
106. Heiderscheit, B.C., *Movement variability as a clinical measure for locomotion.* Journal of Applied Biomechanics, 2000. **16**(4): p. 419-427.
107. Gabell, A. and U.S. Nayak, *The effect of age on variability in gait.* J Gerontol, 1984. **39**(6): p. 662-6.
108. Hausdorff, J.M., et al., *Increased gait unsteadiness in community-dwelling elderly fallers.* Arch Phys Med Rehabil, 1997. **78**(3): p. 278-83.
109. Hausdorff, J.M., D.A. Rios, and H.K. Edelberg, *Gait variability and fall risk in community-living older adults: a 1-year prospective study.* Arch Phys Med Rehabil, 2001. **82**(8): p. 1050-6.
110. Hausdorff, J.M., et al., *Gait variability and basal ganglia disorders: stride-to-stride variations of gait cycle timing in Parkinson's disease and Huntington's disease.* Mov Disord, 1998. **13**(3): p. 428-37.
111. Hausdorff, J.M., et al., *Increased walking variability in elderly persons with congestive heart failure.* J Am Geriatr Soc, 1994. **42**(10): p. 1056-61.
112. Palliyath, S., et al., *Gait in patients with cerebellar ataxia.* Movement disorders, 1998. **13**(6): p. 958-964.
113. Ebersbach, G., et al., *Comparative analysis of gait in Parkinson's disease, cerebellar ataxia and subcortical arteriosclerotic encephalopathy.* Brain, 1999. **122** (Pt 7): p. 1349-55.
114. Steinwender, G., et al., *Intrasubject repeatability of gait analysis data in normal and spastic children.* Clin Biomech (Bristol, Avon), 2000. **15**(2): p. 134-9.
115. Van Emmerik, R.E., et al., *Identification of axial rigidity during locomotion in Parkinson disease.* Arch Phys Med Rehabil, 1999. **80**(2): p. 186-91.
116. Hamill, J., et al., *A dynamical systems approach to lower extremity running injuries.* Clin Biomech (Bristol, Avon), 1999. **14**(5): p. 297-308.
117. Jeng, S.-F., et al., *Self-optimization of walking in nondisabled children and children with spastic hemiplegic cerebral palsy.* Journal of Motor Behavior, 1996. **28**(1): p. 15-27.
118. Kleiger, R.E., et al., *Decreased heart rate variability and its association with increased mortality after acute myocardial infarction.* The American journal of cardiology, 1987. **59**(4): p. 256-262.
119. Clark, J.E. and S.J. Phillips, *A longitudinal study of intralimb coordination in the first year of independent walking: a dynamical systems analysis.* Child Dev, 1993. **64**(4): p. 1143-57.
120. Herzfeld, D.J. and R. Shadmehr, *Motor variability is not noise, but grist for the learning mill.* nature neuroscience, 2014. **17**(2): p. 149-150.
121. Wu, H.G., et al., *Temporal structure of motor variability is dynamically regulated and predicts motor learning ability.* Nat Neurosci, 2014. **17**(2): p. 312-21.
122. Springer, S., et al., *Dual-tasking effects on gait variability: The role of aging, falls, and executive function.* Movement Disorders, 2006. **21**(7): p. 950-957.
123. Royall, D.R., et al., *Executive control function: a review of its promise and challenges for clinical research. A report from the Committee on Research of the American*

- Neuropsychiatric Association. The Journal of neuropsychiatry and clinical neurosciences*, 2002. **14**(4): p. 377-405.
124. Beauchet, O., et al., *Gait variability among healthy adults: low and high stride-to-stride variability are both a reflection of gait stability*. *Gerontology*, 2009. **55**(6): p. 702-706.
 125. Winter, D.A., *Kinematic and kinetic patterns in human gait: variability and compensating effects*. *Human Movement Science*, 1984. **3**(1): p. 51-76.
 126. Hamacher, D., et al., *Kinematic measures for assessing gait stability in elderly individuals: a systematic review*. *J R Soc Interface*, 2011. **8**(65): p. 1682-98.
 127. Kantz, H. and T. Schreiber, *Nonlinear time series analysis*. Vol. 7. 2004: Cambridge university press.
 128. Pincus, S.M., *Approximate entropy as a measure of system complexity*. *Proceedings of the National Academy of Sciences*, 1991. **88**(6): p. 2297-2301.
 129. Bravi, A., A. Longtin, and A.J. Seely, *Review and classification of variability analysis techniques with clinical applications*. *Biomed Eng Online*, 2011. **10**: p. 90.
 130. Webber, C.L., Jr. and J.P. Zbilut, *Dynamical assessment of physiological systems and states using recurrence plot strategies*. *J Appl Physiol* (1985), 1994. **76**(2): p. 965-73.
 131. Zbilut, J.P. and C.L. Webber, *Embeddings and delays as derived from quantification of recurrence plots*. *Physics letters A*, 1992. **171**(3-4): p. 199-203.
 132. Dingwell, J.B. and J.P. Cusumano, *Nonlinear time series analysis of normal and pathological human walking*. *Chaos*, 2000. **10**(4): p. 848-863.
 133. Arnadottir, S.A. and V.S. Mercer, *Effects of footwear on measurements of balance and gait in women between the ages of 65 and 93 years*. *Phys Ther*, 2000. **80**(1): p. 17-27.
 134. Menant, J.C., et al., *Effects of walking surfaces and footwear on temporo-spatial gait parameters in young and older people*. *Gait Posture*, 2009. **29**(3): p. 392-7.
 135. Morio, C., et al., *The influence of footwear on foot motion during walking and running*. *J Biomech*, 2009. **42**(13): p. 2081-8.
 136. Nurse, M.A., et al., *Changing the texture of footwear can alter gait patterns*. *J Electromyogr Kinesiol*, 2005. **15**(5): p. 496-506.
 137. Butler, R.J., M.E. Russell, and R. Queen, *Effect of soccer footwear on landing mechanics*. *Scand J Med Sci Sports*, 2014. **24**(1): p. 129-35.
 138. Messier, S.P., et al., *Osteoarthritis of the knee: effects on gait, strength, and flexibility*. *Arch Phys Med Rehabil*, 1992. **73**(1): p. 29-36.
 139. Butler, R.J., et al., *Changes in landing mechanics in patients following anterior cruciate ligament reconstruction when wearing an extension constraint knee brace*. *Sports health*, 2014. **6**(3): p. 203-209.
 140. Dai, B., et al., *Using ground reaction force to predict knee kinetic asymmetry following anterior cruciate ligament reconstruction*. *Scandinavian journal of medicine & science in sports*, 2014. **24**(6): p. 974-981.
 141. Dai, B., et al., *Anterior cruciate ligament reconstruction in adolescent patients: limb asymmetry and functional knee bracing*. *The American journal of sports medicine*, 2012. **40**(12): p. 2756-2763.
 142. Schmitt, L.C., M.V. Paterno, and T.E. Hewett, *The impact of quadriceps femoris strength asymmetry on functional performance at return to sport following anterior cruciate ligament reconstruction*. *J Orthop Sports Phys Ther*, 2012. **42**(9): p. 750-9.
 143. Kvist, J., *Rehabilitation following anterior cruciate ligament injury: current recommendations for sports participation*. *Sports Med*, 2004. **34**(4): p. 269-80.

144. Shrout, P.E. and J.L. Fleiss, *Intraclass correlations: uses in assessing rater reliability*. Psychological bulletin, 1979. **86**(2): p. 420.
145. McGraw, K.O. and S.P. Wong, *Forming inferences about some intraclass correlation coefficients*. Psychological methods, 1996. **1**(1): p. 30.
146. Bautmans, I., et al., *Reliability and clinical correlates of 3D-accelerometry based gait analysis outcomes according to age and fall-risk*. Gait Posture, 2011. **33**(3): p. 366-72.
147. Taylor, R., *Interpretation of the correlation coefficient: a basic review*. Journal of diagnostic medical sonography, 1990. **6**(1): p. 35-39.
148. Aoyagi, K., et al., *Comparison of performance-based measures among native Japanese, Japanese-Americans in Hawaii and Caucasian women in the United States, ages 65 years and over: a cross-sectional study*. BMC geriatrics, 2001. **1**(1): p. 3.
149. Fitzpatrick, A.L., et al., *Associations of gait speed and other measures of physical function with cognition in a healthy cohort of elderly persons*. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 2007. **62**(11): p. 1244-1251.
150. Al-Obaidi, S., et al., *Basic gait parameters: A comparison of reference data for normal subjects 20 to 29 years of age from Kuwait and Scandinavia*. Journal of rehabilitation research and development, 2003. **40**(4): p. 361.
151. Bohannon, R.W., *Comfortable and maximum walking speed of adults aged 20—79 years: reference values and determinants*. Age and ageing, 1997. **26**(1): p. 15-19.
152. Goble, D., G. Marino, and J. Potvin, *The influence of horizontal velocity on interlimb symmetry in normal walking*. Human Movement Science, 2003. **22**(3): p. 271-283.
153. Hollman, J.H., et al., *Age-related differences in spatiotemporal markers of gait stability during dual task walking*. Gait Posture, 2007. **26**(1): p. 113-9.
154. Laufer, Y., *Age and gender-related changes in the temporal-spatial characteristics of forwards and backwards gaits*. Physiotherapy Research International, 2003. **8**(3): p. 131-142.
155. Mills, P.M. and R.S. Barrett, *Swing phase mechanics of healthy young and elderly men*. Human movement science, 2001. **20**(4): p. 427-446.
156. Oberg, T., A. Karsznia, and K. Oberg, *Basic gait parameters: reference data for normal subjects, 10-79 years of age*. Journal of rehabilitation research and development, 1993. **30**(2): p. 210.
157. Shiavi, R. and P. Griffin, *Changes in electromyographic gait patterns of calf muscles with walking speed*. IEEE Transactions on Biomedical Engineering, 1983(1): p. 73-76.
158. Detrembleur, C., P. Willems, and L. Plaghki, *Does walking speed influence the time pattern of muscle activation in normal children?* Dev Med Child Neurol, 1997. **39**(12): p. 803-7.
159. Stansfield, B.W., et al., *Normalized speed, not age, characterizes ground reaction force patterns in 5-to 12-year-old children walking at self-selected speeds*. Journal of Pediatric Orthopaedics, 2001. **21**(3): p. 395-402.
160. Hof, A.L., et al., *Speed dependence of averaged EMG profiles in walking*. Gait Posture, 2002. **16**(1): p. 78-86.
161. Grieve, D. and R.J. Gear, *The relationships between length of stride, step frequency, time of swing and speed of walking for children and adults*. Ergonomics, 1966. **9**(5): p. 379-399.
162. Diop, M., et al., *Influence of speed variation and age on ground reaction forces and stride parameters of children's normal gait*. Int J Sports Med, 2005. **26**(8): p. 682-7.

163. Nolan, L., et al., *Adjustments in gait symmetry with walking speed in trans-femoral and trans-tibial amputees*. *Gait Posture*, 2003. **17**(2): p. 142-51.
164. Kim, C.M. and J.J. Eng, *Symmetry in vertical ground reaction force is accompanied by symmetry in temporal but not distance variables of gait in persons with stroke*. *Gait Posture*, 2003. **18**(1): p. 23-8.
165. Diopa, M., et al., *Influence of speed variation and age on the asymmetry of ground reaction forces and stride parameters of normal gait in children*. *J Pediatr Orthop B*, 2004. **13**(5): p. 308-14.
166. Keller, T.S., et al., *Relationship between vertical ground reaction force and speed during walking, slow jogging, and running*. *Clinical biomechanics*, 1996. **11**(5): p. 253-259.
167. Dingwell, J.B. and L.C. Marin, *Kinematic variability and local dynamic stability of upper body motions when walking at different speeds*. *J Biomech*, 2006. **39**(3): p. 444-52.
168. Bartlett, R., J. Wheat, and M. Robins, *Is movement variability important for sports biomechanists?* *Sports biomechanics*, 2007. **6**(2): p. 224-243.
169. Maki, B.E., *Gait changes in older adults: predictors of falls or indicators of fear*. *J Am Geriatr Soc*, 1997. **45**(3): p. 313-20.
170. Nakamura, T., K. Meguro, and H. Sasaki, *Relationship between falls and stride length variability in senile dementia of the Alzheimer type*. *Gerontology*, 1996. **42**(2): p. 108-113.
171. Selen, L.P., P.J. Beek, and J.H. van Dieen, *Fatigue-induced changes of impedance and performance in target tracking*. *Exp Brain Res*, 2007. **181**(1): p. 99-108.
172. Cignetti, F., F. Schena, and A. Rouard, *Effects of fatigue on inter-cycle variability in cross-country skiing*. *J Biomech*, 2009. **42**(10): p. 1452-9.
173. Georgoulis, A.D., et al., *A novel approach to measure variability in the anterior cruciate ligament deficient knee during walking: the use of the approximate entropy in orthopaedics*. *J Clin Monit Comput*, 2006. **20**(1): p. 11-8.
174. Lomond, K.V. and J.N. Cote, *Movement timing and reach to reach variability during a repetitive reaching task in persons with chronic neck/shoulder pain and healthy subjects*. *Exp Brain Res*, 2010. **206**(3): p. 271-82.
175. Gates, D.H. and J.B. Dingwell, *The effects of neuromuscular fatigue on task performance during repetitive goal-directed movements*. *Exp Brain Res*, 2008. **187**(4): p. 573-85.
176. Jordan, K. and K.M. Newell, *The structure of variability in human walking and running is speed-dependent*. *Exerc Sport Sci Rev*, 2008. **36**(4): p. 200-4.
177. Buzzi, U.H., et al., *Nonlinear dynamics indicates aging affects variability during gait*. *Clinical biomechanics*, 2003. **18**(5): p. 435-443.
178. Barrett, R., M.V. Noordegraaf, and S. Morrison, *Gender differences in the variability of lower extremity kinematics during treadmill locomotion*. *J Mot Behav*, 2008. **40**(1): p. 62-70.
179. Morris, M.E., et al., *The biomechanics and motor control of gait in Parkinson disease*. *Clin Biomech (Bristol, Avon)*, 2001. **16**(6): p. 459-70.
180. Sadeghi, H., et al., *Symmetry and limb dominance in able-bodied gait: a review*. *Gait & posture*, 2000. **12**(1): p. 34-45.
181. Glazier, P.S. and K. Davids, *Constraints on the complete optimization of human motion*. *Sports Med*, 2009. **39**(1): p. 15-28.
182. Latash, M.L. and J.G. Anson, *What are "normal movements" in atypical populations?* *Behavioral and brain sciences*, 1996. **19**(1): p. 55-68.

183. Davids, K., S. Bennett, and K.M. Newell, *Movement system variability*. 2006: Human kinetics.
184. Wilson, C., et al., *Coordination variability and skill development in expert triple jumpers*. *Sports Biomech*, 2008. **7**(1): p. 2-9.