UNDERSTANDING SELF-REPORTED INSTABILITY USING GAIT OUTCOMES AND WALKWAY SURFACE TRANSLATIONS IN THOSE WITH KNEE OSTEOARTHRITIS

by

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To Kayla for the unwavering love and support and
to Cecilia for reminding me that it's fun to be curious!

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ABSTRACT

Knee osteoarthritis (OA) is a progressive disease that is highlighted by debilitating symptoms that have detrimental impacts on physical activity. One such symptom is knee instability, which is self-reported in 60-80% of the OA population and 30-60% reported instability impacts activity. Self-reported instability, or sensations of buckling, shifting or giving way have been linked to poor knee joint confidence and walking difficulties. The objective of this thesis was to understand the inter-relationships that exist between knee function during gait, self-reported instability, and responses to direct and indirect walking perturbations in asymptomatic individuals and people with knee OA. Three related objectives were conducted.

For objective one, asymptomatic participants and individuals with moderate knee OA, subclassified as OA Stable and Unstable were tested in the JAR lab. Knee motion, moments and muscle activation patterns collected during treadmill walking were analyzed. Significant muscle activation magnitudes and patterns were found, identifying unique activation patterns to the OA unstable group compared to OA stable and asymptomatic groups. For the second objective, an asymptomatic group and individuals with moderate knee OA experienced unexpected direct and indirect, medial 3cm frontal plane walk surface translations of the symptomatic and asymptomatic limbs during gait. Groups responded with elevated and prolonged muscle activation patterns and no significant change in sagittal and frontal plane motion and moments. For the final objective, a preliminary analysis was completed on direct and indirect perturbation responses in an asymptomatic group, and individuals with moderate OA dichotomized into OA stable and OA unstable groups. All groups maintained joint motion and moment ranges, using elevated and prolonged muscle activation magnitudes and patterns.

These studies show that individuals who self-report instability walk with activation patterns that provide increased knee joint active stiffness. Furthermore, responses to direct and indirect perturbations in asymptomatic, moderate OA groups, and moderate OA groups dichotomized by self-reported stability increase and prolong muscle activation magnitudes patterns to provide active stiffness to maintain knee function. Responses to indirect and direct perturbations are in the direction that those with moderate OA and instability walk with day-to-day and provides information into the pathomechanics used to maintain knee function.

LIST OF ABBREVIATIONS USED

ACR	American College of Rheumatology
Ag/AgCl	Silver/Silver Chloride
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
ASYM	Asymptomatic
A/D	Analog to Digital
BMI	Body Mass Index
CMRR	Common Mode Rejection Ratio
dB	Decibels
EMG	Electromyography
GΩ	Giga-ohm
GRF	Ground Reaction Force
Hz	Hertz
ICF	International Classification of Functioning, Disability and Health
ICKAA	Initial Contact to Peak Stance Knee Adduction Angle
ICPF	Initial Contact to Peak Stance Knee Flexion
JAR	Joint Action Research
KAM	Knee Adduction Moment
KL	Kellgren-Lawrence
KOOS	Knee Injury and Osteoarthritis Outcome Score
KOS-ALDS	Knee Outcome Survey – Activities of Daily Living Scale
KOS-I	Knee Outcome Survey – Instability Question
LG	Lateral Gastrocnemius
LH	Lateral Hamstring
MDC	Minimal Detectable Change
MG	Medial Gastrocnemius
MH	Medial Hamstring
m/s	Metres per second
mm	Millimetre
MOA	Moderate Osteoarthritis
MVIC	Maximal Voluntary Isometric Contraction
N	Newton
Nm/kg	Newton metre per kilogram
OA	Osteoarthritis
OAS	Osteoarthritis Stable
OAU	Osteoarthritis Unstable
PCA	Principal Component Analysis
PFLM	Peak Stance Knee Flexion to Late Stance Flexion Minimum

pKAM	Peak Knee Adduction Moment
PP	Principal Patterns
PP-Scores	Principal Pattern Scores
ROM	Range of Motion
SD	Standard Deviation
SENIAM	Surface Electromyography for the Non-Invasive Assessment of Muscles
SPROM	Sagittal Plane Moment Range
T0	Baseline Strides
T1	Response Strides
TKA	Total Knee Arthroplasty
VL	Vastus Lateralis
VM	Vastus Medialis

GLOSSARY

DIRECT GAIT PERTURBATION

The symptomatic (ipsilateral) limb was translated and subsequent stride of the symptomatic limb (ipsilateral) was analyzed.

INDIRECT GAIT PERTURBATION

The asymptomatic limb (contralateral) was translated and the landing stride on the symptomatic limb (ipsilateral) was analyzed.

OA STABLE GROUP

Self-reports “I do not have the symptom” to the question “To what degree does giving way, buckling or shifting of your knee affect your daily activity level?” Adopted from Irrgang et al [224].

OA UNSTABLE GROUP

Self-reports “This symptom affects my activity slightly, moderately or severely” to the question “To what degree does giving way, buckling or shifting of your knee affect your daily activity level?” Adopted from Irrgang et al [224].

SELF-REPORTED KNEE INSTABILITY

A sudden loss of postural support during weight bearing as a result of buckling shifting or giving way of the knee joint. Adopted from Fitzgerald et al [25].

STABILITY

The way a system behaves following a perturbation, and if the state of that system remains within specific boundaries of control. Adopted from Grenier and McGill [258].

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CHAPTER 1: INTRODUCTION

In 2014, osteoarthritis (OA) was ranked the third most rapidly rising condition associated with disability worldwide [1] and it is estimated that 1 in 4 Canadians will be diagnosed with OA in the next 20 years [2]. The disease is highlighted by debilitating symptoms that have detrimental impacts on physical activity, retaining employment, and maintaining quality of life [3, 4]. This creates economic and societal burdens on health systems and individuals. Persons with lower extremity OA consume health care resources at twice the rate [5], are 40-50% more likely to utilize disability pension [6], are 14% more likely to retire early [7] and incur 2-3x more health care costs compared to asymptomatic peers [8]. The impact of this increased workload will be felt by primary health care providers, who have struggled to manage OA [9]. Clinical practice guidelines recommend weight management, education and physical activity [10], yet general practitioners understate nutrition and physical activity messaging and overprescribe pharmaceutical and surgical treatment options [11, 12]. The heterogenous presentation of OA complicates clinical decision making but one thing is clear, we have to keep people with OA physically active, to prevent not only the detriments of OA, but also the impact of this disease on the health of individuals [13-15].

OA is highly debilitating when impacting the lower extremity [16] and in particular the knee joint, as knee joint function is essential to many everyday activities (i.e. walking, sitting, standing, etc.). Knee OA arises from a complex interplay between metabolic, genetic, biochemical and/or biomechanical features [17, 18], that have resulted in knee

OA becoming the leading cause of morbidity in older adults [19]. Knee OA is characterized by loss of articular cartilage [20], altered structure and remodeling of subchondral bone [21], development of osteophytes [22], ligamentous laxity [23] and meniscal damage [24]. These whole joint structural changes are accompanied by the development of a wide spectrum of acute and chronic, physical and emotional symptoms. Knee joint instability [25-28], inflammation and/or effusion [29, 30], reduced range of motion (ROM) [31-33], increased loading [34-36], reduced quality of life [4, 37, 38], depression [39-41], pain [42-45], muscle weakness/strength deficits [46-48], and physical limitations [49-51] are commonly presented in those with knee OA. Due to an interaction among varying physical OA symptoms, individuals develop a lack of confidence [52, 53] in their joint's ability to support them during weight bearing activities [54], resulting in decreased physical activity, increased sedentary behaviours and reduced physical function [50].

Walking analyses have been used more frequently over the past two decades to investigate the relationship between joint impairments and activity limitations associated with knee OA [43, 55-58]. Results have shown that individuals with medial compartment knee OA walk with a less dynamic, or "stiffer" walking pattern compared asymptomatic older adults [31, 33, 59, 60], defined by less sagittal plane knee joint ROM during stance and less dynamic flexion-extension moments [33, 59-61], and occurs during over ground and treadmill walking. The stiffening or stabilizing strategy is often accompanied by altered muscle activation magnitudes and patterns and/or co-activation [31, 61-63], thought to provide the knee with increased active stiffness [64, 65]. The question remains

as to why individuals with knee OA are adopting these walking patterns, particularly given the reports of poor knee confidence during weight-bearing activities [52, 53].

During dynamic activities, a balance of stability and mobility is established at the joint, where the passive osteoligamentous, active muscular, and neural control subsystems work cooperatively [66]. A theoretical framework, proposed for spine stability and applied to the knee, emphasizes this complex interaction between subsystems in order to maintain normal knee joint functioning [66]. Osteoligamentous structural changes (i.e. osteophytes, joint space narrowing, cartilage degradation) [67, 68] are a defining pathological feature of knee OA. In some people with knee OA, impairments also can exist in the active muscular (i.e. muscle weakness, fatigue) [69] and neural control (i.e. pain sensitization) subsystems [70]. The reciprocal relationship between subsystems proposed by Panjabi [66] suggests that altered contributions from each subsystems to balance mobility and stability to maintain knee joint function is supported by magnitudes and patterns of muscle activation found in those with knee OA [30, 43, 71-73]. Knee OA gait analyses, including biomechanics and electromyography (EMG), have provided a comprehensive understanding of joint function, however, “stability” and its interaction with mobility and physical function, has largely been understood through self-report measures.

Self-reported knee instability is defined as a sudden loss of postural support during weight bearing as a result of buckling, shifting or giving way of the knee joint [25]. Knee instability is self-reported in approximately 60-80% of those with knee OA [25, 74-76]

and 30-60% report that instability limits activity in some manner [25-27]. Instability is most often recounted during walking [54]; an increasingly difficult task for individuals with knee OA [13, 27]. Individuals reporting the symptom of instability self-impose activity limitations due to a fear of falling and poor confidence in their knee joint [50, 52], which has implications for future physical functioning [51]. To understand the impact of self-reported instability on knee joint function during walking, researchers dichotomize individuals with knee OA into unstable and stable groups [27, 77, 78]. Greater knee flexion ROM during the loading response, lower knee joint stiffness [27, 77] and increased sagittal plane motion variability [78] have been found in unstable groups. Additionally, these alterations have been found independent of clinical factors that may explain instability symptoms, including knee pain, reduced proprioception, increased laxity, varus alignment, and reduced muscle strength [76, 79] suggesting that giving way, buckling and shifting experienced in the knee may be creating a unique environment by which individuals with knee OA alter their walking mechanics.

To further understand the interactions between this clinical symptom of instability and knee function, there are two key gaps that should be addressed. First, current studies do not fully integrate EMG methods and analysis procedures with joint mechanics and clinical symptoms of instability to discern the role of the neuromuscular system to maintain knee joint function during walking in those with unstable and stable knees. Secondly, many studies to date have focused on stable walking environments; where unstable environments that challenge individuals, similar to those experienced during daily physical activities, have potential to improve understanding of how joint function is

maintained. These gaps in knowledge provides the context for which this thesis has developed; to more fully understand the utility of gait perturbations to challenge walking in individuals with knee OA and the role of the knee joint musculature to maintain joint function in those who self-report buckling, shifting and giving way that limits their physical function.

Gait perturbations have been used widely to challenge people during walking [80-87], however few studies have used gait perturbations to understand response in knee OA populations. Specifically, protocols using direct lateral translations of the symptomatic knee during initial contact have been tested [88, 89]. Kumar et al. found that both knee OA and asymptomatic groups responded with reduced knee flexion ROM and increased knee muscle activation in the first stride after the surface translation [88], whereas Schmitt and Rudolph found higher medial quadricep-hamstring co-contraction in an unstable OA group compared to a stable OA group and no differences in knee flexion ROM [89]. While groups and analysis method differed in these studies, higher muscle activation and/or co-activation [88, 89] was found after directly perturbing the symptomatic knee suggesting a response occurred in the neuromuscular system to maintain knee function in these challenged walking environments. To date, these studies provide preliminary evidence supporting the role of the musculature to maintain knee function during challenged gait in individuals with knee OA and more specifically, individuals who self-report unstable knees. Continued development of this paradigm is sought after in this thesis, building on current limitations to further elucidate the impact of knee OA on mobility and challenged walking environments.

Sixty to 80% of people with knee OA report experiencing buckling, shifting and giving way of their knee. Using gait analyses, researchers have begun to understand knee joint function in the context of these symptoms in stable and controlled walking environments [61, 73, 90, 91]. With every step, the neuromuscular system of individuals with knee OA is responding to their structural and symptomatic knee joint environment. Occasionally these responses may be suboptimal, resulting in either sensations of or episodes of knee joint buckling, shifting or giving way. To date, while many knee OA gait research outcomes have focused on understanding the contributions of the neuromuscular system to control joint function, these studies did not differentiate whether participants report symptoms of instability or not. Additionally, challenged walking paradigms are being implemented in knee OA populations, yet how knee joint function is maintained in response to walking challenges in those with knee OA, and more specifically, those with recurrent sensations of instability, remains to be determined.

This thesis aims to fill the gap in our current understanding of knee mechanics and muscle activation patterns during gait as it pertains to self-reports of giving way, buckling, and shifting during activity in individuals with moderate knee OA (MOA). The first objective seeks to understand whether individuals with MOA classified as stable and unstable walk differently than asymptomatic (ASYM) individuals of a similar age. The second objective introduces the gait perturbation paradigm, whereby individuals with MOA and ASYM individuals experience unexpected frontal plane walking surface translations during their walking test while biomechanical and muscle activation

responses are monitored. The final objective is a preliminary analysis to dichotomize individuals with MOA into stable and unstable groups to determine whether gait perturbation responses are related to symptoms of self-reported instability. These data will provide information on the contributions of the neuromuscular system in responding to symptoms of self-reported instability, challenged walking environments, and the relationship between self-reports of instability and challenged walking responses. This information can help support individuals with knee OA in keeping active, increasing their knee confidence and maintaining health as they manage their OA.

1.1 OBJECTIVE 1

1.1.1 SUMMARY RATIONALE

In those with knee OA, 60-80% self-report knee instability and 30-60% report this symptom of instability limits their activity in some manner. These sensations can create a fear that their knee will shift, buckle or give way and if people with knee OA do not walk because of this fear, a vicious cycle of inactivity initiates and has consequences for joint and overall health. What has not been thoroughly investigated is whether individuals with MOA and self-report instability impacting activity have different walking patterns compared to those with MOA and ASYM groups with no instability. The subsystems of Panjabi's theoretical stability model experience alterations in those with knee OA, therefore the contributions of the neuromuscular subsystem, particularly in those self-reporting sensations of buckling, shifting or giving way, was the focus of Objective 1.

1.1.2 SPECIFIC OBJECTIVES

A. To determine if sagittal and frontal plane knee joint biomechanics outcome variables differ during treadmill walking in those with MOA who, using the Knee Outcome Survey Instability Question (KOS-I), self-report instability impacting activity compared to those with knee OA and ASYM groups reporting no symptoms of instability.

B. To determine if quadricep, hamstring and gastrocnemius muscle activation patterns differ during treadmill walking in those with MOA who, using the KOS-I, self-report instability impacting activity compared to those with knee OA and ASYM groups reporting no symptoms of instability.

1.2 OBJECTIVE 2

1.2.1 SUMMARY RATIONALE

Individuals with knee OA are responding to structural and symptomatic environments that result in altered knee joint function during over ground walking. Challenging walking in those with knee OA and monitoring responses could provide information on how people modify knee function outside of a controlled walking environment and the neuromuscular mechanisms that attempt to maintain joint function. Objective 2 is broken into two parts, expanding on the direct gait perturbation paradigm, where (A) individuals experience translations under the symptomatic limb (direct perturbation) while monitoring the response of the subsequent stride of the symptomatic limb and (B) individuals experience a translation under the asymptomatic limb (indirect perturbation)

while monitoring the landing stride of the symptomatic leg. A response to unexpected medial walkway surface translations involves mechanical and neuromuscular factors that have implications for improving understanding on how stability is maintained in those with MOA compared to ASYM participants.

1.2.2 SPECIFIC OBJECTIVES

A. To determine if differences between and MOA and ASYM groups are present in sagittal and frontal plane knee joint motion and moments and quadricep, hamstring, and gastrocnemius muscle activation patterns in response to direct medial 3cm midstance walking surface perturbations.

B. To determine if differences between and MOA and ASYM groups are present in sagittal and frontal plane knee joint motions and quadricep, hamstring, and gastrocnemius muscle activation patterns in response to direct medial 3cm midstance walking surface perturbations.

1.3 OBJECTIVE 3

1.3.1 SUMMARY RATIONALE

Objective 3 combines the rationale from previous objectives. In those with knee OA, responses to alterations in the osteoligamentous and neuromuscular subsystems may contribute to sensations or episodes of buckling, shifting or giving way during walking. Knee OA gait researchers have found that the neuromuscular subsystem alters activity in the direction of increased active stiffness to maintain knee joint function during

controlled, over ground walking. Controlled walking environments lack unexpected elements that challenge stability and where instability sensations are more likely. How individuals with self-reported unstable knees respond to challenged walking may provide an understanding neuromuscular mechanism used to maintain knee joint function. Objective 3 is a preliminary investigation, broken into two parts, where individuals with MOA, dichotomized by instability, and an ASYM group with no instability experience (A) direct perturbations and (B) indirect perturbations. Data from this preliminary analysis of responses to unexpected walkway surface translations aims to provide evidence whether mechanical and neuromuscular factors differ between those with knee OA who self-report instability that impacts activity versus those who do not.

1.3.2 SPECIFIC OBJECTIVES

A. To determine if differences between MOA participants grouped by self-reported presence of instability impacting activity and those with MOA and ASYM groups with no instability are present in sagittal and frontal plane knee joint motions and moments, and quadricep, hamstring, and gastrocnemius muscle activation patterns in response to direct medial 3cm midstance walking surface perturbations.

B. To determine if differences between MOA participants grouped by self-reported presence of instability impacting activity and those with MOA and ASYM groups with no instability are present in sagittal and frontal plane knee joint motions and

quadricep, hamstring, and gastrocnemius muscle activation patterns in response to indirect medial 3cm midstance walking surface perturbations.

1.4 THESIS STRUCTURE

Chapter 1 introduces the thesis, the topic of knee OA and the rational for studying self-reported knee instability and treadmill walking surface translations and their impacts on muscle activation patterns and sagittal and frontal plane joint biomechanics. Three main objectives are identified, and the thesis structure is outlined.

Chapter 2 provides an overview of the background literature relevant to this thesis. The literature establishes a gap in understanding the muscle activation magnitudes and patterns associated with self-reported instability and the responses to direct and indirect gait perturbations in those with knee OA. The topics reviewed include, OA burden and economic impacts, a synopsis of OA pathophysiology, an overview of OA gait mechanics, self-reported knee stability and its impacts on gait biomechanics and the current knowledge regarding challenged walking environments in knee OA.

Chapter 3 provides a description of the specific methodology used to carry out the objectives of this thesis. This chapter describes the participant selection criteria and preparation, and the methodology and considerations for outcome variables from joint motion, moments and EMG. The perturbation protocol is outlined in detail and the data processing and analyses procedures are described. A general overview of the statistical

analysis is provided, with specifics within each subsequent chapter. A sample size justification is provided.

Chapter 4 contains an original manuscript, intended for scientific publication titled, "Altered muscle activation magnitudes and patterns during gait in individuals with knee osteoarthritis self-reporting knee instability affecting activity." This manuscript addresses Objective 1 of this thesis.

Chapter 5 contains an original scientific paper titled, "Walking challenges in moderate knee osteoarthritis: a biomechanical and neuromuscular response to medial walkway surface translations" authored by Matthew Baker and co-authors Dr's William Stanish and Derek Rutherford. This manuscript addresses Objective 2A of this thesis and has been published in Human Movement Sciences 68 (2019) 102542.

Chapter 6 contains an original manuscript, intended for scientific publication titled, "Landing on the symptomatic knee after walkway surface translations of the unaffected leg: Does the neuromuscular response in those with moderate knee osteoarthritis compare to an asymptomatic cohort?" This manuscript addresses Objective 2B of this thesis.

Chapter 7 is a preliminary analysis titled, "People with knee osteoarthritis and self-reported instability have similar biomechanical and neuromuscular responses to medial walkway translations compared to osteoarthritis and asymptomatic group reporting no instability." This preliminary study addresses Objective 3A of this thesis.

Chapter 8 is a preliminary analysis titled, “Is the neuromuscular response in those with moderate knee osteoarthritis influenced by the presence of self-reported knee instability when landing with the symptomatic knee after a walkway surface translation?” This preliminary study addresses Objective 3B of this thesis.

Chapter 9 concludes the thesis by providing a general discussion of the findings among the three studies (Chapters 4-6) and two preliminary analyses (Chapter 7 and 8), concluding key results and outlining study limitations and future directions.

Appendix A is a reliability analysis titled “Reliability of lower extremity muscle activation patterns of healthy young adults during dual-belt treadmill gait using Principal Component Analysis.” This analysis was completed on a sample of healthy young adults to provide reliability metrics pertaining to PCA methods and outcomes utilized in the current thesis.

Appendix B provides all ensemble averaged waveforms for each outcome variable studied in each objective and is sectioned by chapter.

Appendix C provides each high-low plot for the PCA analysis across the thesis to provide assistance with interpretations of PCA patterns. Appendix C is sectioned by chapter.

Appendix D provides description and a flowchart of the study samples in Chapters 4-8.

CHAPTER 2: LITERATURE REVIEW

2.1 OA BURDEN AND ECONOMICS

OA is a highly prevalent musculoskeletal disease that affects approximately one in eight adults worldwide [1]. This largescale impact creates a global challenge for health systems, as tremendous economic and societal burdens are associated with OA [92]. Years living with disability is used to contextualize the burden of disease, and OA accounts for 2.4% of all years lived with disability, ranked 10th as a global contributor [93]. Historical data between 1990 and 2013 demonstrated that OA is the third most rapidly rising condition associated with disability [93]. The trend of increasing OA prevalence is expected to continue as a result of population growth, increased life expectancy, increased obesity prevalence and a lack of treatments able to preclude disease progression [94].

The economic impact of OA is significant compared to other musculoskeletal diseases due to prevalence and high use of associated resources [95]. In Canada, health systems have difficulty managing OA, evidenced by physician consultation and surgical intervention wait times [96]. Nonetheless, the OA population in Canada is predicted to rise from 3.6 million in 2010 to 6.0 million in 2031, a 64% increase [97]. To a large extent, primary care physicians will be impacted by this increased workload, but an increase in total joint replacement surgeries is also anticipated [9]. Studies have predicted that this increased prevalence and health system capacity may cause a 160% increase in direct health costs associated with OA, increasing from 2.9 to 7.6 billion between 2010 and 2031 [97].

OA is associated with higher health care costs, and negatively impacts health related quality of life [98]. Studies have reported, patients with early stages of OA consume health care resources twofold compared to a general population [5], independent of patient characteristics and comorbidities [98]. Estimates reveal that almost 30% of the employed labor force has difficulty working because of OA [2], and pain and disability caused by OA are associated with an early exit from work [7]. Men and women diagnosed with OA in their knee have approximately 2x increased risk of sick leave and 40-50% increased risk of disability pension utilization compared to those without knee OA [6]. This same study reported that when comparing patients with OA to subjects drawn from a general population, 10.5% of the former reported reduction of work hours and 13.7% reported having retired early owing to illness compared to 1.7% and 3.4% of controls without OA [6]. Often, pain and disability are the drivers for job loss related to OA, with direct associations found between clinically confirmed OA and early exit from paid employment [7]. Reducing OA related pain and disability has the potential to improve health status, reduce indirect costs, and increase health-adjusted life expectancy for the population as a whole [99]. However, to accomplish this, we need a clearer understanding of OA, how the symptoms manifest and clear management strategies.

2.2 A SYNOPSIS OF OSTEOARTHRITIS

OA is a heterogenous disorder [100] that presents similar biological, morphological and clinical outcomes [29, 101-103]. The disease has been characterized by the degenerative state of the articular cartilage, however, this approach lacks emphasis on the involvement

of the entire synovial joint including the periarticular muscle, ligaments, synovial membrane, subchondral bone and joint capsule [101]. Over the past few decades, the 'wear and tear' ideology has evolved to include biochemical and inflammatory mediators that have a role in OA genesis [104]. This conceptual shift has not rejected the mechanical contributions as causative factors, but instead considers how mechanical forces interact with biochemical mechanisms at a pathophysiological level throughout OA development [105].

A standardized definition of OA was established [17] by Osteoarthritis Research Society International stating:

"Osteoarthritis is a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness."

The etiology of OA has been understood as a relationship between excessive mechanical stress (i.e. single or repetitive events of joint surface loading higher than physiological loads) and a destabilized biochemical balance of degradation and synthesis in the subchondral bone, extracellular matrix and articular cartilage [106, 107]. This dynamic

equilibrium of joint tissue metabolism is altered, shifting to favor catabolic pathways over repair mechanisms [108, 109]. Ultimately, the disease manifests with morphological, biochemical, molecular and biomechanical changes leading to a damage and loss of articular cartilage; sclerosis and remodeling of subchondral bone, osteophyte formation, synovial inflammation; and alterations to other joint tissues [110]. Certain risk factors increase an individual's susceptibility to OA, including age, sex, obesity, genetics, ethnicity, prior joint injury and physical activity level [100]. Furthermore, localized mechanical factors [111], such as abnormal joint geometry [112], knee malalignment [113], ligament laxity [114] and muscle weakness [69] also increase the risk of lower extremity OA. In knee OA, mechanical factors have been linked to an increased likelihood of OA initiation and disease progression [115, 116]. While this understanding of abnormal joint structures and functions as a biological system provides an outline of OA as a disease, the illness associated with OA is often difficult to define [17].

Illness often refers to the human response to disease [17, 117], and encompasses the variety of physical and emotional symptoms associated with OA. Joint instability, pain, tenderness, stiffness, intermittent effusion, crepitus, inflammation, depression, mobility concerns, and physical limitations can present themselves in various combinations in those with knee OA [16, 100]. These symptoms substantially impact quality of life and complicate the management strategy for health care providers. Current treatment modalities focus on reducing the impact of symptoms and improving joint function, but this strategy does very little to improve joint structure or intervene in disease progression [118]. Clinical practice guidelines recommend facilitating self-management through

education, weight management and increased physical activity [10]. In reality the management story is quite different, where studies report that drug and surgical interventions are overprescribed and weight loss and exercise messaging are not emphasized [11, 12]. This approach has contributed negatively to the current state of our total joint arthroplasty crisis [96], without providing much benefit to those with OA. Research has demonstrated knee OA limits mobility, and understanding the relationship between structural impairments, physical function and activity participation is important.

2.3 THE ICF AND PHYSICAL ACTIVITY IN KNEE OA

The International Classification of Functioning, Disability and Health (ICF) is a contextual health framework directed at facilitating standard definition, measurement and policy formation in health and disability [119]. The ICF model (Figure 2-1) is used in health-related fields designed for universal implementation and clear dissemination across health systems [119]. The ICF Comprehensive Core Set for OA lists *walking* and *maintenance of gait patterns* as key factors [120]. In fact, nine of the ICF's Comprehensive Core Set for OA factors focus on an individual's ability to remain mobile [120]. A main objective of the ICF is to provide an accurate description of an individual's health status with regards to function and restrictions to function [121]. In the context of knee OA, the theoretical framework provides an understanding that impairments to knee structures can cause limitations to activities such as walking, but a reciprocal relationship also exists where limitations to walking may cause further impairments to joint structures and functioning [58]. Targeting this relationship may provide important information regarding OA pathomechanics.

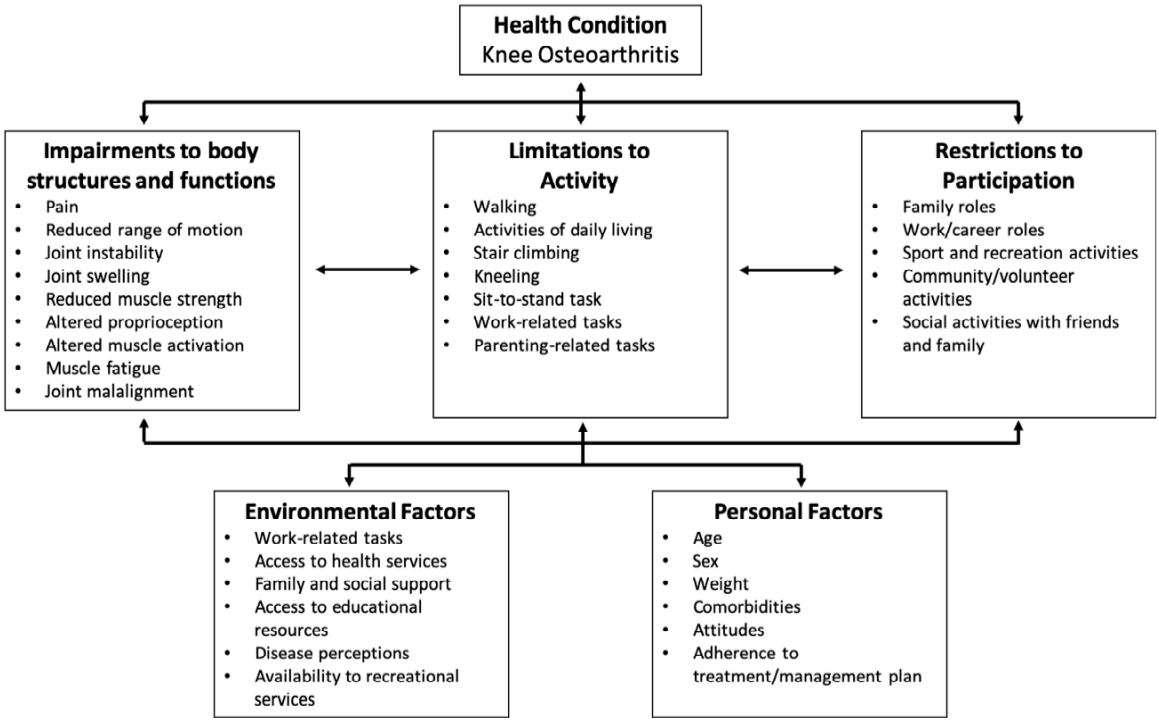

Figure 2-1: ICF framework considering the impact of knee OA. Modified from Ackerman et al. [122].

Physical activity is essential in preventing chronic diseases such as knee OA and paramount to health and well-being [13, 14], as advocated by provincial and federal Health and Wellness departments. Current physical activity guidelines recommend 150 minutes of moderate-to-vigorous intensity aerobic physical activity per week in bouts of at least 10 minutes to achieve health benefits [123]. But, these guidelines are not OA specific and evidenced-based work is needed to understand physically activity/walking dosage in this population [124]. Research has shown that engaging in physical activity is known to be protective against further functional limitations in those with OA [116, 125], yet a systematic review demonstrated that only a small-to-moderate portion of individuals with lower extremity OA met physical activity guidelines [126]. This may be because physical activity is not prescribed [127], individuals may feel that physical activity is

harmful rather than beneficial [128], or that individuals who do partake experience OA symptoms and/or walking difficulties and do not trust their knees to support them during these tasks [13, 129]. There are many different barriers to physical activity that those with knee OA experience [130] and in order to address these barriers, researchers seek to understand the relationship between joint impairments and activity limitations through biomechanical gait analysis.

2.4 KNEE OA GAIT MECHANICS

The initiation and progression of knee OA results from a complex and abnormal relationship between mechanical, structural and biological pathways [131]. When these pathways are disrupted, knee joint functioning is compromised [132]. Gait analyses provide an objective understanding of knee joint function and are well established for studying knee OA populations [31, 57, 61-63, 73, 91, 133-135] and the relationships between impaired body structure and function and limitations in activity are described in the ICF [58]. Gait analyses studies spatiotemporal characteristics, joint ROM (kinematics), joint moments (kinetics), and muscle activation levels and patterns (EMG). The following sections will review joint ROM, moments and muscle activation in series, highlighting key findings and considerations for understanding knee OA joint function.

2.4.1 KINEMATICS

Kinematics is a branch of mechanics concerned with motion without direct reference to the forces causing motion. For decades, movement profiles have been measured by non-invasive motion capture technology and used to evaluate the functional performance of

the knee [136]. The study of kinematics has helped to quantify knee angles during OA gait, with a particular focus on sagittal (forward/backward) and frontal (medial/lateral) planes [30, 31, 36, 62, 73, 115, 137-139].

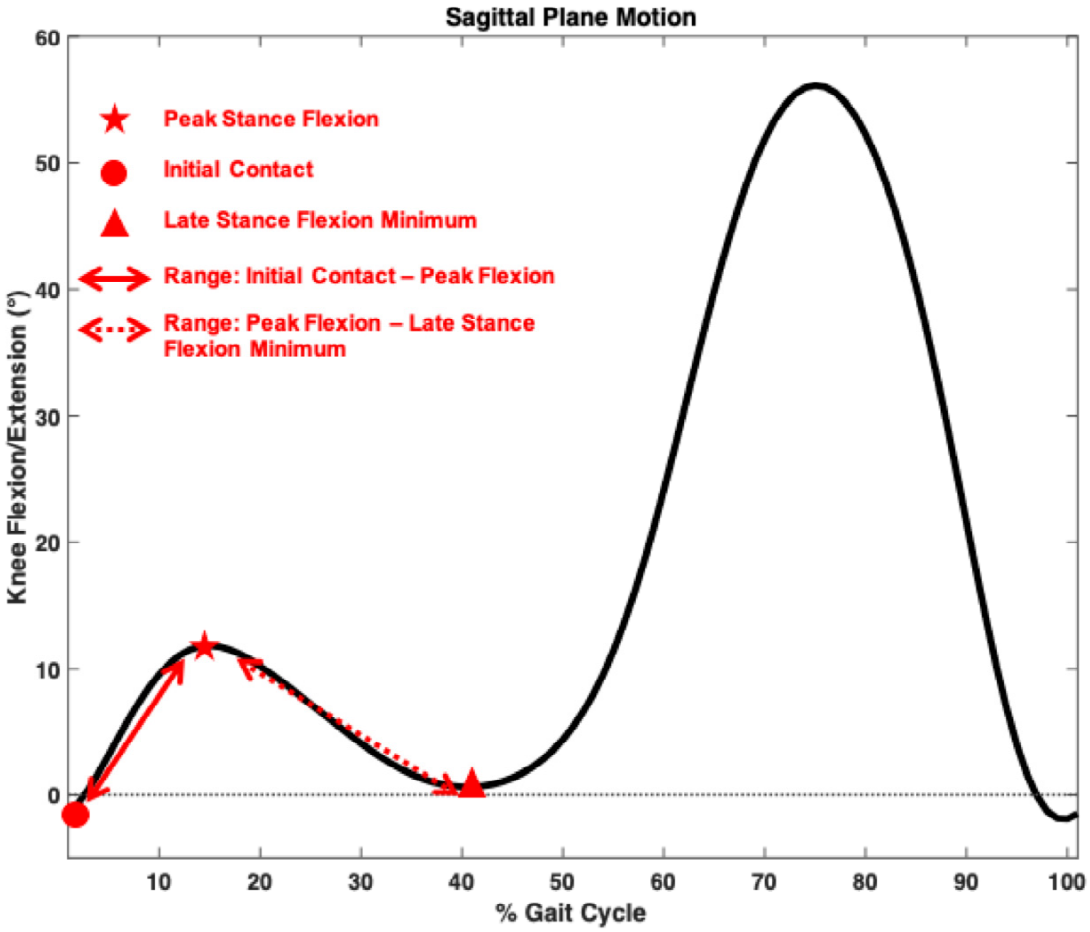

Figure 2-2: Ensembled averaged sagittal plane knee motion profile, outlining the kinematic variables discussed in 2.4.1. The gait cycle (0-100%) is represented on the x-axis and degrees of flexion/extension (+/-) is represented on the y-axis. Stance phase is from 0-60% and the swing phase is from 61-100% of the gait cycle. Key discrete and range metrics are described in the legend.

In knee OA literature, sagittal plane joint angles are altered, particularly when in a weight-bearing position during the first 60% of the gait cycle. Figure 2-2 illustrates a typical sagittal plane knee movement pattern and highlights key discrete metrics obtained for analysis across many studies [31-33, 35, 73, 90, 140]. Studies have found more knee

flexion at initial contact in those with knee OA compared to an asymptomatic group [32, 62, 129, 137, 141, 142]. More initial contact knee flexion is found in those with severe radiographic severity (KL III, KL IV), while those with less evidence of structural changes (KL I, KL II) had similar knee angles to an asymptomatic group [137, 141]. It is plausible that greater hamstring activation at initial contact [143] or passive tissue stiffness by way of flexion contracture [144] could explain this finding. Regardless, this finding of more flexion at initial contact has been positively associated with greater loss of medial tibial cartilage thickness in a group with knee OA [145]. The thickest regions of medial compartment cartilage has been associated with the initial contact knee flexion angle [146], therefore, if those with knee OA walk with higher knee flexion angles, the load bearing region of articular cartilage shifts [147] to areas not accustomed for that magnitude or pattern of loading [148, 149]. These findings suggest a link between OA joint structures, structural progression and sagittal plane joint motion.

The peak stance phase knee flexion angle is commonly measured in OA gait studies, with larger variability [150]. The peak knee flexion angle was found to be similar in those with increasing radiographic severity [143] selected based on similar walking speed. Conversely, progressively decreasing peak knee flexion angles were reported with knee OA groups with increasing clinical severity (asymptomatic, moderate, severe) and progressively slower self-selected walking speed [115]. Walking speed has an impact on the peak knee flexion angle, with higher velocities demonstrating higher peak flexion angles, likely driving the null finding in study assessing OA structural severity [143]. While limited evidence directly investigates the impacts of peak knee flexion angles on

cartilage integrity, Creaby et al. reported a positive correlation between the peak knee flexion angle and peak knee flexion moment [151], which has implications for knee joint loading [152, 153]. Limitations arise with utilizing single discrete points in gait waveforms, for instance absolute values can be influenced by standing calibration position, and whether or not angles are corrected. Furthermore, large variability and reduced reliability make comparisons between groups difficult [154, 155]. Ranges of motion have been utilized to reduce variability have been found to demonstrate higher reliability [155].

Less ROM from initial contact to peak stance knee flexion (ICPF) or from peak stance knee flexion to late stance flexion minimum (PFLM) is found in knee OA compared to an asymptomatic group [31-33, 35, 73, 90, 140]. Less ROM during stance has been associated with radiographic severity [43] and with greater loss of medial tibial cartilage thickness [145], suggesting it is linked to structural OA severity. Maly et al. hypothesize that smaller flexion-extension ROM causes structural joint damage, and consequently knee pain, by facilitating contact on areas of cartilage not accustomed to stance phase impacts [156]. Less stance phase knee ROM has also been interpreted as a compensatory strategy by the OA knee to increase knee joint stability [32, 73, 90], supported by findings that those who self-report knee instability impacting activity [139] and those with mechanical instability (anterior cruciate ligament deficient) [157] demonstrate less knee flexion range compared to asymptomatic groups. Together, these findings suggest that those with knee OA walk with altered sagittal plane knee angles, generally walking

with increased knee flexion at initial contact, decreased peak knee flexion angle and less ROM throughout the stance phase (ICPF, PFLM).

The majority of knee joint motion during walking occurs about a medial-lateral axis in the sagittal plane, however medial compartment OA is radiographically characterized by a progressively narrowing medial joint space [158], creating a potential for laxity [159, 160] which could alter movements in the frontal plane. Studies demonstrate a higher knee adduction angles at initial contact [161, 162] and during the stance phase [138, 162-164] in those with knee OA. In addition, individuals with more severe radiographic severity walk with increased adduction angles at initial contact and during stance compared to those with less structural severity (KL I, KLII) and an asymptomatic group [137]. Fukaya et al. 2019 reported that the maximum knee adduction angle during early stance is moderately, positively correlated with the knee adduction moment (KAM) [165] and suggests increasing knee adduction angles increase the KAM and the mechanical load on the medial compartment. Suggesting a relationship between frontal plane joint motion and moments and structural OA progression.

In those with medial compartment knee OA, the total frontal plane stance phase range is larger compared to the less symptomatic knee [162] and to an asymptomatic group [164]. This increased ROM has been associated with worse knee confidence [52], and when combined with strength deficits predicted impaired functional ability [166]. In clinical settings, orthopaedic health care specialist assess varus thrust, defined as an abrupt increase in frontal plane motion towards adduction in early stance [167]. Varus thrust is

often assessed visually and has been associated with pain [45, 168], stiffness [168], lower quadricep strength [169], radiographic knee OA progression [167], and higher peak knee adduction moments (pKAM). Cooperatively, these studies suggest altered frontal plane motion towards increased adduction in those with knee OA and these motions have associations with radiographic integrity and symptomatic status of the knee joint.

Limitations arise when estimating bone movements from skin mounted markers for three-dimensional motions. The accuracy of marker placement, virtual point digitization and soft tissue artifact influence the accuracy of the resulting joint angles [170, 171], specifically, for angles that occur in the frontal and transverse planes. These angles are more susceptible to kinematic crosstalk where motion is less pronounced. In the frontal plane, motion errors of ~4˚ have been recorded during stance [172] and is often larger than the total ROM [137], and the statistical difference between the groups [138, 164]. Furthermore, frontal plane outcome variables have demonstrated low reliability (Interclass Correlation Coefficient (ICC) = 0.60) in a population with knee OA [173]. Careful consideration must be made when interpreting frontal and transverse plane significant findings in biomechanical studies.

The study of knee joint kinematics provides a description of motion in those with knee OA with altered sagittal and frontal plane knee angles found in this population. Together, the evidence points to the common conclusion that individuals with OA walk with altered kinematics in the direction of less ROM in the sagittal plane and greater deviations from a normal profile in the frontal plane. These alterations become more marked as disease

severity increases. Despite these general conclusions, joint motions only provide the outcome of the underlying joint pathomechanics. To elucidate factors relating to joint loading, a kinetic analysis is needed to understand the moments created about the knee during gait. These data have been a significant focus in OA gait pathomechanics given purported role of loading and disease initialization and progression.

2.4.2 KINETICS

Joint moments are quantified using inverse dynamics, calculated using ground reaction forces (GRF) and moments, joint motions and inertial properties [174]. The moments are expressed in the joint coordinate system [175], either as internal or external moments, to understand the forces causing movement and resulting loads. Most often, the frontal and sagittal plane moments are discussed in knee OA. A longstanding theory in OA research is excessive or altered mechanical loading of knee joint tissues play a significant role in the pathogenesis of OA [102]. In knee OA, most commonly the medial tibiofemoral compartment demonstrates accelerated deterioration compared to the lateral, thought to stem from a loading asymmetry during weight bearing activities [176]. Frontal and sagittal plane moments have been termed surrogate measures of medial compartment contact forces [177, 178], most effectively in combination [179], and have received the majority of attention in OA literature.

The most widely studied biomechanical outcome in knee OA gait analyses is the net external KAM. This moment describes the load distribution between the medial and lateral tibial plateaus during stance [20, 176] where a greater KAM is interpreted to mean

greater medial compartment compressive loads. These indirect interpretations have been supported by *in vivo* data from instrumented knee implants [177, 178, 180] and joint contact force modeling [163]. Studies often report a larger pKAM in those with knee OA compared to asymptomatic groups [31, 35, 36, 138, 181-186] and contralateral limb [34, 187]. The pKAM has demonstrated a consistent relationship with the integrity of the joint structures [34, 36, 132, 183, 188]. A higher pKAM was positively correlated ($r = 0.51$) with higher thickness ratios in a healthy group, while a negative correlation ($r = 0.82$) was reported in those with knee OA, suggesting that the KAM may have opposing impacts on joint cartilage depending on joint health [132]. Bone marrow lesions are correlated with a higher pKAM [188] and structural disease progression [189], supporting the impact of the pKAM on joint integrity. In addition, a higher pKAM is found in those with more severe structural changes (KL III, KL IV) compared to less severe (KL I, KL II) [34, 36] and greater baseline KAM magnitude was a significant factor in a model able to identify those with knee OA who progressed to a TKA compared to those without, with a 74% classification rate [59]. Longitudinal studies have demonstrated the strong between relationship structural changes at the pKAM, with higher baseline pKAM predicting radiographic severity [190], worsening bone marrow lesions [191] and cartilage deterioration [153, 192]. Furthermore, radiographic severity has been moderately and significantly correlated with a higher overall magnitude of the KAM in a knee OA population, clinically defined as mild-to-moderate OA severity [43]. Together, these findings suggest that in individuals with OA, a higher pKAM interacts negatively with joint structure and can also impact disease progression and structural integrity. However, knee joint loading is not only influenced by the KAM. Walter et al.

demonstrated that the decreases in the KAM, produced by modified gait patterns, did not correspond to reductions in medial contact force during walking [193]. Furthermore, Manal et al. demonstrated that a regression model fit with both the pKAM and the PFM is a significant predictor of loading ($p=0.009$, $R^2=0.851$), improving on models including each factor alone [179]. To appreciate the impact of OA on the knee joint mechanical environment and its implications for joint function, both sagittal and frontal plane moments should be considered.

The sagittal plane moment, to a lesser extent than the KAM, has been studied during gait in those with knee OA [36, 57, 59, 133, 138, 151, 176, 184] however, the results are less consistent. Conflicting findings have reported higher peak flexion moments with more cartilage loss after a 5-year follow-up [153] and no relationship between the peak flexion moment and structural changes after 2-years [191] in individuals with tibiofemoral OA. When comparing individuals with knee OA and asymptomatic groups with similar structural severity (KL II), a lower peak flexion moment is found in those with OA [71]. This finding, along with the unclear evidence [153, 191, 194] relating the peak flexion moment with structural changes, suggests that OA symptoms or clinical OA severity may influence the peak flexion moment.

Sagittal plane moment dynamics (SPROM), the range from peak flexion moment to peak extension moment, have also been studied. Generally, in people with knee OA compared to an asymptomatic group [31, 43], the SPROM is less. A smaller sagittal plane moment range, along with elevated KAM, were features found in those who progressed to a TKA

(74% classification rate). This reduced SPROM has been described in the literature as a "stiffer knee" [59, 71] and interpreted to increase knee stability [59] and reduce sensations of knee pain at the joint [195]. Thus, the sagittal plane moment is a metric, in combination with the KAM, that can be useful to further understand OA pathomechanics during gait generally, and more specifically understand the implications of altered joint integrity and stability on walking.

Knee moments are often derived from inverse dynamics, which use marker trajectories, GRFs and anthropometrics inputs to estimate the force and torque joint reactions to various tasks (i.e. walking, stair climbing, etc.) [174]. Errors can stem from many different sources, and a prone to similar errors described for kinematics (marker placement, skin movement artifact, kinematic crosstalk) [170, 171]. Joint centre location inaccuracies, GRF and centre of pressure measurement accuracy and segmental parameter calculations can all impact joint moment calculation [196]. Caution should be taken in interpreting moment results, keeping in mind standard error of measurement values reported for health for young, healthy controls and treadmill walking (0.02-0.11Nm/kg) [155] and those with knee OA during over ground walking (0.03-0.14Nm/kg) [173].

Gait kinematics provide information regarding motion, without direct reference to the forces causing motion: whereas kinetics provide information regarding the forces, without information on how force is produced. This can limit our understanding of concepts such as loading, or "stiff knee" gait patterns. Over the past decade, researchers

have begun to understand the involvement of neuromuscular adaptations in knee OA. Together with joint motions and moments, muscle activation patterns provide researchers with a comprehensive understanding knee joint's mechanical environment during gait in those with knee OA.

2.4.3 MUSCLE ACTIVATION

The neuromuscular system plays an essential role in knee joint function. The muscles surrounding the knee joint control, maintain and terminate motions, influence load distributions and consist of three major muscle groups; the quadriceps, hamstrings and gastrocnemius. Muscle function deficits have been reported with knee OA [197], including reduced muscle strength [46, 198], muscle imbalance [46] and altered proprioception [199]. However, coordinated muscle activity is still necessary for efficient movements and are required to complete activities of daily living. Researchers have studied knee joint muscle activation magnitudes and patterns using surface EMG and gait analysis in an attempt to understand the relationship between how muscle activation patterns impact joint structures and vice versa [61, 63, 133, 143, 200-203]. Three common themes have been identified in OA literature; elevated, constant, and medial-to-lateral differential activation.

Elevated muscle activation suggests that those with knee OA require more knee activation to complete similar tasks, and this finding is most commonly reported in the vastus lateralis (VL), medialis (VM) and lateral hamstring (LH) [31, 61, 91, 133, 143, 202]. Researchers have attempted to identify possible mechanisms for higher muscle

activation. Structural OA severity has demonstrated conflicting results, with higher quadriceps and LH activation reported in those with severe structural severity (KL IV) compared to moderate (KL II, KL III), recruited based on similar walking speed [143]. Another study reported that those with moderate structural severity (KL II, KL III) demonstrated higher mean quadriceps and peak hamstring activation compared to those with more structural changes (KL IV) at a controlled walking speed [91]. Arguing that more structural changes to the passive osteoligamentous subsystems (i.e. osteophyte) would increase passive stability, thus reducing the requirement of neuromuscular subsystem. Astephen et al. 2011, using a 10cm analog radiographic severity scale, found that no features from quadriceps, hamstring or gastrocnemius demonstrated statistically significant correlations with this radiographic severity scale [43]. In a later study, Astephen et al. found increased LH activation in those with knee OA, compared to an asymptomatic group, both with radiographic KL II scores, suggesting that muscle activation patterns are linked to the symptomatic state of the knee joint [71]. In groups classified based on OA function [61], higher LH muscle activation in those with severe OA compared to moderate OA, and higher quadriceps and LH activation in those with moderate OA compared to an asymptomatic group [202] have been found. Knee joint effusion has also been shown to influence muscle activation amplitude, with higher quadriceps activation in those with knee effusion compared to those without [30]. The feature of elevated or higher muscle activation magnitudes is common in those with knee OA, linked with OA symptoms, clinical OA severity and structural changes and provide more active stiffness to the knee joint.

More constant activation across the gait cycle, suggests that the muscles surrounding the knee joint become less dynamic in response to increased demands required to maintain knee joint function. This pattern of activation has been reported in all muscles in those with knee OA compared to asymptomatic groups, either through prolonged quadricep or hamstring or through earlier and constant gastrocnemius activation [31, 32, 61, 143, 202]. Structural severity has been studied to understand its relationship with more constant activation. Constant quadriceps and gastrocnemius activation was reported in those with severe structural severity (KL IV), while more constant LH activation progressively increased with KL grade in those with knee OA [143]. However, more constant quadriceps activation, measure by higher quadriceps RMS, was reported between knee OA and asymptomatic groups with both with KL II grades, suggesting that more constant activation may be related to clinical severity and/or OA symptoms. Groups assessed to be clinically severe, demonstrated more constant LH [202] and gastrocnemius activation [133] compared to those with moderate disease severity. OA symptoms may also be a mechanism for more constant muscle activation patterns, as more constant lateral gastrocnemius (LG) was found to positively correlate with increasing pain severity [43] and the presence of knee effusion resulted in more constant medial hamstring (MH) and LH activation [30].

Medial-to-lateral differential activation has been found in those with medial compartment dominant knee OA, thought to be a method to assist unloading of the medial compartment and suggests a specific response linked to altered joint structures. Most commonly, a higher lateral-to-medial hamstring ratio is reported in those with knee OA

compared to asymptomatic groups [61, 62, 204, 205]. This greater lateral activation has been linked with structural severity, where higher medial compartment structural severity resulted in higher lateral-to-medial activation [202]. Hubley-Kozey linked higher co-activation to clinical severity, where those on the waiting list for a total knee arthroplasty (TKA) demonstrated higher MH and VM activation compared to asymptomatic and moderate OA groups, in which LH and VL increased with clinical severity [206].

These three neuromuscular themes reviewed all have implications for structural and clinical OA progression. Higher and more constant LH and more constant gastrocnemius activity at baseline walking was found in a group with knee OA and progressing medial joint space narrowing scores [207]. A higher medial-to-lateral co-activation ratio was positively correlated with medial cartilage loss after 2-years [63] and higher hamstring and more constant quadricep and hamstring activation at baseline was found in a group that progressed to a TKA [208]. These findings suggest that neuromuscular patterns interact with knee OA structural and clinical severity.

Elevated, constant and differential medial-to-lateral activation patterns in the knee joint all contribute to an overall increase in activation across the gait cycle. While, the exact mechanism is unknown, structural/clinical severity and OA symptoms likely play a role. In knee OA, the osteoligamentous and neuromuscular subsystems are altered, and an environment is created that may require increased contributions from the neuromuscular system. Patterns of elevated, more constant and differential medial-to-lateral activation

suggest that the OA knee requires more active stiffness, generally or specifically (medial compartment) [64, 200].

The OA knee demonstrates altered biomechanics, in the direction of less sagittal plane ROM during stance, less sagittal plane moment dynamics and increased KAM and higher and more prolonged activation of the knee musculature during stance. These findings have been linked to structural changes, clinical severity and OA symptoms, yet, these findings in combination are commonly interpreted as mechanisms to reduced knee joint loading and/or enhance knee joint stability. Studies have related many of the reviewed features of OA gait to counterbalancing sensations of instability, without objectively measuring the stability of the knee joint. In order to elucidate if knee joint stability is related to these gait alterations, it's important to understand how stability is impacted in the OA knee.

2.5 KNEE STABILITY

The knee is a complex hinge-joint that facilitates dynamic motion and endures large loads during activities of daily living [209]; the tibiofemoral articulation bearing most of the weight [210]. The collateral and cruciate ligaments prevent excessive movements of the tibia with respect to the femur and assist to prevent excessive motion [211]. The neuromuscular system is considered the "secondary" stabilizer of the knee joint, primarily functioning to produce and control knee motion [212]. The knee is susceptible to injury due to its position between the bodies longest lever arms and its role in mitigating loads [212]. Individuals with knee OA undergo degenerative changes,

accompanied by pain [55], physical limitations [51], joint inflammation [30, 213] and instability [79]. Symptoms can result in a lack of confidence in their joint's ability to support them during walking [25].

Definitions of joint instability in clinical settings often describe the severity of a symptom within the context of injury or disease, placing related joint issues within the state of the disease or injury [214, 215]. Clinical definitions aim to contextualize the functional state of the joint and the magnitude of deformation, putting instability as a continuous variable (i.e. the knee can be more or less stable). Other definitions of instability state that an unstable knee loses "single leg stance because the joint subluxes due to pathological laxity" [214]. While it is intuitive to link instability and laxity, several studies have found that valgus-varus laxity is not linked to perceived stability in both weight bearing [135] and non-weight bearing conditions [26, 216, 217]. Studies investigate anterior cruciate ligament deficient knees report that knee laxity resulting from ligamentous injury can be mutually exclusive from joint instability [218].

Joint instability, and the preservation of stability, should be considered a synergistic function in which ligaments, bones, joint capsule, muscles, tendons and the neural control centre function in harmony [64]. A standard clinical definition is lacking and essential to increase the inter-disciplinary understanding of knee joint stability. Stability, in research, is often understood as how a system behaves following a perturbation and if the state of that system remains within specific boundaries of control [74, 219-221]. However, objective measures for joint instability are still in development and patient perspectives,

or self-reported measure of instability have been used to being to understand this symptom [74].

2.5.1 SELF-REPORTED KNEE INSTABILITY

Researchers have relied on self-reported knee instability to understand its impact on function and self-reported instability is defined as a sudden loss of postural support during weight bearing as a result of buckling, shifting or giving way of the knee joint [25]. Approximately 60-80% of those with knee OA self-report instability [25, 74, 79] and 30-60% report that instability impacts their activity [26, 27, 54]. In those with knee OA and self-reported instability, slower walking speed, varus malalignment, lower muscle strength and lower KOOS scores [27, 76, 77, 89] have been reported compared to defined stable and asymptomatic groups. Self-reported instability is associated with worse future functional outcomes, lower performance-based functional scores [51], future pain exacerbations [222], an increased risk [223] and fear of falling [50] and activity limitations independent of knee pain and muscle strength [79]. The KOS-ADLS is often used to quantify self-reported instability and dichotomize those with knee OA into stable and unstable groups.

2.5.2 THE KNEE OUTCOME SURVEY - ACTIVITIES OF DAILY LIVING SCALE

The KOS-ADLS utilizes a 6-point Likert scale from 0-5, with 0 indicating “unable to perform” and 5 indicating “no difficulty”, to capture how knee symptoms impact activity. The KOS-ADLS has demonstrated validity and test-retest reliability (ICC = 0.72) in those

with degenerative OA [25, 224] and demonstrated construct validity to other knee-specific scales [225].

Table 2-1: The Knee Outcome Survey – Activities of Daily Living Scale Instability Question used to understand instability in those with OA and knee injury.

To what degree does giving way, buckling or shifting of your knee affect your daily activity level?	
5	I do not have this symptom
4	I have this symptom, but it does not affect my daily activity level
3	This symptom affects my activity slightly
2	This symptom affects my activity moderately
1	This symptom affects my activity severely
0	This symptom prevents me from performing my daily activities

Table 2-1 illustrates KOS-I aimed to quantify knee instability sensations and its impact on activity. This question has been utilized to understand knee OA and instability and its relationship to function [25, 26, 217] and to dichotomize those with knee OA into stable and unstable groups [27, 28, 77, 78, 90, 139, 226].

2.5.3 SELF-REPORTED INSTABILITY AND GAIT MECHANICS

Episodes of self-reported knee instability are most often felt during walking [54] and the presence of these sensation have been associated with walking difficulties [27]. With mobility a key factor in independence, investigating biomechanical or neuromuscular gait features that explain why individuals feel unstable or if individuals alter gait mechanics to improve instability sensations will help understand the mechanisms in which joint function is maintained.

Those with knee OA and self-reported instability experience biomechanical alterations that either arise to counteract instability sensations or create an environment where instability sensations are more likely. During over ground walking, greater ICPF range [27, 77], more knee flexion range during stance [226] and lower knee joint stiffness [77] have been found in those with self-reported instability impacting activity compared to groups dichotomized as OA stable. Studies have also reported larger average knee flexion moments during single limb stance [226] and greater contributions of the knee extensor moment to the total support moment [27] in an unstable group, however another study found no differences in the peak knee flexion moment, peak knee extension moment or the SPROM [77] in an unstable group compared to a stable group. Increased sagittal plane knee motion variability, medial tibia anterior-posterior translation [78] and longer medial joint contact excursions [227] has been reported those dichotomized as stable and unstable and an ASYM group. The frontal plane ROM has been studied, where those unstable groups reported more frontal plane range compared to an asymptomatic group [139] and Lewek found individuals with knee OA walked with greater frontal plane ROM and self-reported instability more often compared to asymptomatic controls [73]. Studies have investigated frontal plane motion during gait finding no relationship to instability, knee confidence, muscle strength, knee joint laxity and/or joint alignment [135, 159]. Together, the evidence suggests merit in investigating sagittal plane motion and moment alterations that may be linked with self-reported instability, however, studies lack one of the main contributors to stability and mobility; the muscles that surround the knee joint.

2.5.4 PANJABI'S THEORETICAL MODEL OF STABILITY

Joint stability can be understood in terms of the complex relationship between the passive osteoligamentous, active muscular, and neural control subsystems, originally proposed by Panjabi for the stability of the spine [66]. Panjabi discussed that for basic performance and function, the spine must allow for inter-segmental movements, load carrying, and spinal cord and nerve root protection, all of which require mechanical stability. Applying this framework to the knee joint (Figure 2-3), mechanical stability is required during biomechanical knee joint function (i.e. movements between the patella, tibia and femur; load carrying capacity of the knee; protection of internal structures). Panjabi's framework outlines that sufficient stability is required to match the varying demands from changing loads and body positions during static and dynamic activities in order to maintain normal joint function.

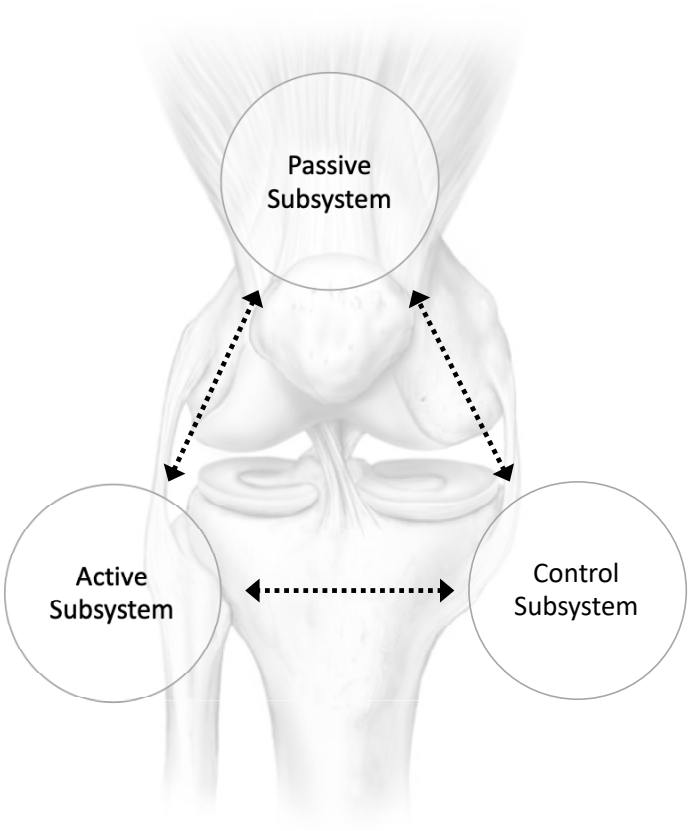

Figure 2-3: Panjabi's theoretical framework for understanding the knee joint adopted for the structures around the knee. Adopted from Panjabi [66].

The knee joint's passive osteoligamentous subsystem is comprised of the ligaments, capsule, articular cartilage, menisci and bone. The passive osteoligamentous subsystem is thought to guide the joint through normal ROM [64, 66], providing stability via physical restraint [228], sensory capabilities [229, 230] and/or articular congruency [231]. The active muscular subsystem consists of the muscles and tendons that surround the knee joint and is the principal means by which the joint generates forces and is protected [232], responding to required stability demands [66]. This subsystem is responsible for generating motion, carrying load, and protecting the joint from excessive force and motion [66]. Lastly, the neural control subsystem is comprised of various neural pathway and transducers within the structures surrounding the knee, the spinal cord and the brain

[64, 66]. The control subsystem is tasked with continuously monitoring the stability requirements, while simultaneously responding and adjusting the forces of the muscle acting about the knee [66]. Panjabi describes a reciprocal relationship between subsystems, therefore dysfunctions in each subsystem would require adaptations in others to maintain joint stability and function.

Degenerative changes occur across the subsystems in those with knee OA. These changes impact the knee joints ability to maintain stability and/or function. Panjabi's theoretical framework for joint stability is an excellent model to understand joint instability in a population with OA who self-report stable and unstable knees, as well as explore the mechanisms that may be impacting this self-reported symptom. Panjabi's framework and definitions stability provide support for studying challenged walking environments; to investigate if challenging subsystems by theoretically increasing the stability demands (i.e. gait perturbation), will generate an increased output in other subsystems in order to maintain the function of the knee during walking.

2.6 GAIT PERTURBATIONS

Gait analyses have traditionally utilized controlled walking environments to understand the pathomechanics of OA [27, 31, 36, 57, 59, 61, 62, 91, 106, 115, 138, 143, 161, 184, 186]. Interpretations of specific biomechanical and neuromuscular knee OA gait features have included maintaining or counterbalancing sensations of knee stability, but often measures of instability are not captured. External perturbations may be a method to alter the system and measure the response, to see if alterations occur in order to maintain joint

function. These types of analyses are of particular interest in OA sub-populations who have reduced knee confidence and/or report sensations of knee buckling, shifting or giving way. Gait perturbations have been implemented in the frontal and sagittal plane and have been studied in healthy and pathological gait [80-87].

Frontal plane perturbations are most common in the literature, examining the efficacy of evaluating fall recovery and/or cause and compensatory actions in gait in elderly and/or those who are unstable. Excellent between-session reliability has been reported for spatiotemporal variables during a challenged walking paradigm (ICC = 0.83 - 0.95) [81]. Stokes et al. reported that after continuous medio-lateral translations participants took wider, shorter and more variable steps compared to their normal walking profile [82], this was accompanied by increased overall muscle activation, and higher antagonist coactivations in the tibialis anterior, medial gastrocnemius (MG), soleus and peroneus longus [82]. Afschrift et al. reported similar findings of an increased step width, decreased step length, with increased soleus, gastrocnemius, tibialis anterior and gluteus medius activity in response to medio-lateral translations [87]. Van den Noort attempted to utilize the responses of the knee joint to lateral translations during walking to quantify knee joint instability [84]. This study measured three-dimensional joint motions as healthy young adults walked on a dual-belt instrumented treadmill and experienced lateral translations of varying intensities applied during stance. The study found increased knee flexion over the gait cycle that also increased with translation magnitude and knee abduction increases were found with increasing translation magnitude over the whole gait cycle in the first and second stride after the translation [84]. Similar spatiotemporal

changes in step length and width were reported [82, 84, 87]. These studies suggest efficacy in gait changes in response to frontal plane translations. OA commonly alters the medio-lateral loading environment of the tibiofemoral articulation, which has been understood to impact joint stability in this direction. Using frontal plane walkway translations may provide an understanding of the mechanics and strategies employed to maintain knee joint function during walking in those with OA, and those with OA who report knee instability.

Minimal work has been done to study the biomechanical and neuromuscular responses to frontal plane translations in a population with knee OA. It is evident that those with knee OA live with altered joint function, thought to be a byproduct of maintaining stability, managing OA symptoms and navigating the environment safely. Gait perturbations provide an opportunity to challenge the knee joint. How individuals respond may provide information on OA pathomechanics required in walking environments with unexpected elements.

2.6.1 GAIT PERTURBATIONS AND KNEE OSTEOARTHRITIS

A challenged walking paradigm utilized in the context of knee OA could provide information on how individuals with compromised joint structures maintain joint function in response to an environment where stability is dynamically challenged. Altered passive osteoligamentous and neuromuscular subsystem, within the context of Panjabi's framework, would suggest that the neuromuscular subsystems may increase demands, supported by increased activation amplitudes and altered temporal features (i.e.

prolonged/constant activation) found in those with knee OA [61, 63, 133, 143, 200-203]. Limited evidence is available to determine, when stability is challenged through dynamic translations, if those with altered neuromuscular environments or those who self-report instability symptoms demonstrate an altered neuromuscular and/or biomechanical response.

Gait perturbations are utilized to challenge individuals during a dynamics task, to see how they respond, and if responses differ between control and study groups. Two studies have implemented this methodology within a knee OA population [88, 89]. Both studies utilized a 13m walkway with a custom-built moveable perturbation platform that translated the symptomatic limb (direct perturbation) 5.8cm (0.4m/s) laterally at initial contact, while kinematics and surface EMG was captures. Kumar et al. compared an asymptomatic group to a group with medial compartment knee OA (60% KOS-I $\leq$ 4) [88]. While, Schmitt and Rudolph recruited individuals with medial compartment knee OA and dichotomized individuals into a self-reported stable (KOS-I = 5) and unstable (KOS-I $\leq$ 3) groups using the KOS-I (Table 2-1). Despite the study groups, both studies found similar results. Kumar et al. reported less sagittal plane knee ROM early and mid-stance phases of gait and increased medial and lateral quadriceps, hamstring and gastrocnemii activation in response to the direct perturbation, however, both asymptomatic and OA groups demonstrated these patterns [88]. Schmitt and Rudolph reported no differences in sagittal or frontal plane ROM between the stable and unstable groups, and higher medial quadricep-hamstring co-activation before and after direct perturbations [89]. These studies suggest, a stabilizing response is present in all samples,

similar to what has been discussed in OA literature as a stabilization strategy with increased active stiffness and decreased knee joint stance phase ROM.

These results, however, must be interpreted in light of limitations. Most importantly in the challenged walking methodology. Both studies discussed the participants ability to view or experience translations prior to testing, removing the unexpected nature of perturbations. Furthermore, a lack of perturbation variability further reduces the unexpected nature of the study. Participant could only experience a translation on their symptomatic limb, in the same direction and magnitude. Increasing the variability of perturbations, with different magnitudes, directions, legs and types, may reduce the ability of a participant to predict a walkway translation and improving the unexpected nature of challenged walking protocols. Preparatory neuromuscular responses were reported in both studies and could limit the magnitude of the perturbation response and impact the results of these studies. Both studies investigate the response of a lateral translation as a challenge in individuals with medial compartment knee OA, however, did not discuss their rationality. A lateral translation could theoretically destabilize the medial compartment of the knee joint, using an unnatural movement direction creating a compressive force on the lateral compartment and theoretically cause medial compartment "lift off." Medial translations may cause compressive forces on medial compartment of the knee, and lateral compartment "lift off", a more natural, but challenging movement for those with medial compartment knee OA [62]. Medial translations also may also push the body's base of support towards the midline, causing a

brief dissociation between the centre of pressure and centre of mass, increasing the challenge on our ability to maintain balance.

In summary, walkway surface translations provide a method of challenging dynamic stability and monitoring how the OA joint responds. Previous work has demonstrated increased active stiffness, though to be a stabilizing response at the knee joint, but no differences between those with OA and asymptomatic knees, and OA dichotomized into stable and unstable groups. This could be a result of preparedness, as previous methods were limited in their ability to create an unexpected environment. Work is needed to fully understand both direct and indirect gait perturbations and knee OA, thus motivating the objectives of this thesis.

CHAPTER 3: METHODOLOGY

The methodology was developed to address outlined Objectives 1-3 within Chapter 1 of this thesis. Recruitment, instrument selection, analysis procedures and statistical analyses were selected to effectively test thesis objectives. Protocols were approved by Nova Scotia Health Authority Research Ethics Board (Romeo #: 1020825, 101746 and 1025007). A general methodology is outlined below for the cross-sectional studies and the analyses of this thesis.

3.1 PARTICIPANT RECRUITMENT

3.1.1 ASYMPTOMATIC SAMPLE

The ASYM group was recruited as a sample of convenience from the local community using email, poster advertisement and social and conventional media. Interested individuals were contacted by Joint Action Research (JAR) Laboratory research staff and letters were sent outlining the study details. Interest was confirmed and participants were contacted via telephone. A custom script was used to determine participant eligibility. If the participant self-reported no cardiovascular, neurological and respiratory impairments, history of lower extremity injury within the last year and the ability to walk without a cane and/or walking aid and was greater than 50 years of age, an appointment was made, and study details were described. Participants email was obtained, and informed consent and details of visit documentation were provided.

3.1.2 KNEE OSTEOARTHRITIS SAMPLE

Individuals with MOA were recruited and identified by direct referral from local orthopaedic surgeons (Drs. William Stanish and Nathan Urquhart), diagnosed with OA using the American College of Rheumatology (ACR) guidelines [233]. The surgeons approached eligible patients with a standardized research introduction along with a letter explaining why they have been recruited. Patients were then asked to consent to transfer contact information to researchers. Patients were contacted by researchers via telephone using a standardized script to determine study eligibility, as described in 3.1.1. The script also captured the functional capabilities of walking a city block, climbing stairs reciprocally, jogging five meters [61], and their ability to walk continuously for 30 minutes. These functional criteria, alongside ineligibility for a TKA were used to help define the knee OA population as moderate disease severity. Once participant eligibility was confirmed, an appointment was set, and study details such as expectations, directions, study attire were discussed. The participant's email was obtained, and a detail of the visit form and informed consent documentation were sent for review.

3.2 PARTICIPANT PREPARATION

The JAR Laboratory within the School of Physiotherapy, Dalhousie University was utilized for all testing procedures. All participants were given a brief orientation to the laboratory, including an introduction to equipment used and a description of procedures and facilities. The informed consent documentation was then reviewed, with the opportunity for participants to ask questions, and informed consent was obtained. Study objectives and specific methods were reviewed prior testing.

Two questionnaires were completed before testing procedures began. The KOS-ADLS was used to determine knee symptoms and functional limitations during daily activities in individuals, and has demonstrated high test-retest reliability [224] and construct and content validity [225]. The KOOS measures patients' perspectives about their knee and associated symptoms in five subscales (Pain, Symptoms, Activities of Daily Living, Sport and Recreation and Quality of Life) within the past week. The KOOS has demonstrated validity [234] and moderate to excellent test-retest reliability (ICC = 0.60 - 0.95) across all five subscales with standard error of measurement and minimal detectable change (MDC) reported as 2.1 - 3.1 and 13.4 - 21.2 units, respectively, for patients with knee OA [225].

Participants were instructed to change into tight fitting shorts, t-shirt and remove footwear. Standard anthropometrics, including height, weight, and waist, hip, thigh and shank circumferences were measured and recorded using a physician beam scale with height rod and tape measure. Participants were then prepared for surface EMG consistent with guidelines and standard procedures [235]. Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) sensor locations were identified and marked by measuring distances between anatomical landmarks (Table 3-1). Afterwards, skin was lightly shaved and cleaned with 70% alcohol wipes to improve electrode to skin contact. Silver/Silver Chloride (Ag/AgCl) surface electrodes (10 millimetre (mm) diameter, 30mm inter-electrode distance, Red Dot, 3M Health Care, USA) were placed in bilateral configuration over the VM, VL, MH, LH, MG and LG [236]. A ground electrode was

placed on each anterior tibial shaft. Muscle palpation was used to determine electrode site location.

Table 3-1: The SENIAM recommendations for sensor locations of muscles of the quadriceps, hamstrings and gastrocnemii.

Muscle	Location
Vastus Medialis	80% on the line from the anterior superior iliac spine and the joint space in front of the anterior border of the medial ligament
Vastus Lateralis	2/3 on the line from the anterior superior iliac spine to the lateral side of the patella
Medial Hamstring	50% on the line between the ischial tuberosity and the medial epicondyle of the tibia
Lateral Hamstring	50% on the line between the ischial tuberosity and the lateral epicondyle of the tibia
Medial Gastrocnemius	35% on the line between the medial knee joint line to the tubercle of the calcaneus
Lateral Gastrocnemius	30% on the line between the lateral knee joint line to the tubercle of the calcaneus

Participants walked back-and-forth across the GAITRite™ pressure sensitive walkway (CIR Systems Inc., USA), until five walking trials were randomly recorded. The five walking trials were averaged to attain over ground walking speed and used to establish a self-selected walking speed for the instrumented treadmill. The GAITRite™ has reported validity and excellent reliability for measuring gait speed (ICC = 0.91 - 0.99) in older adults [237, 238]. Following GAITRite™ walking trials, the final EMG set up was completed, where lead lines were connected to the electrodes and a series of isometric contractions were completed for signal validation and gain adjustment.

Passive retro-reflective surface markers were affixed to participants, using standard laboratory procedures, to assess position and orientation of body segments [236, 239].

First, 4-marker clusters were fixed on rigid bodies and placed over the thorax and pelvis and bilaterally on the thigh, shank and foot. Individual markers were placed bilaterally on the spinous process of the 7th cervical vertebrae, the lateral aspects of the shoulders below the acromion process, greater trochanter, lateral and medial epicondyles of the femur and tibia, lateral and medial malleoli, atop the head of the 1st, 2nd and 5th metatarsal and posterior heels. A 3-marker cluster was affixed to the treadmill to track medial-lateral motion during walking surface translations. Lastly, participants were required to wear an upper body harness system attached to the ceiling to allow for unimpeded lower extremity movement and ensure participant safety.

3.3 GAIT ANALYSIS

Motion of the passive, retro-reflective markers were sampled at 100 Hertz (Hz) using eight Qualisys® OQUS 500 (Qualisys®, Sweden) motion analysis cameras. Three-dimensional GRFs were sampled at 2000Hz from bilateral treadmill force plates. Raw surface EMG was pre-amplified (500x), further amplified using two AMT-8™ Bortec Systems (Bortec Inc., Canada; bandpass filter 10-1000Hz, Common Mode Rejection Ratio (CMRR): 115 decibels (dB) at 60 Hz, input impedance =~10GΩ) and sampled at 2000Hz, in synchrony with motion and GRF data. All analog signals were acquired, analog-to-digital (A/D) converted (16bit, +/- 5V), and synchronized using Qualisys® Track Manager V2.10 software.

A standing calibration trial, with all markers visible, was collected following marker placement; used to compute reference value for kinematic analysis during walking.

Participants stood on the treadmill with feet approximately shoulder width apart, feet facing forward and knees as straight as possible. After the standing calibration, passive markers on the greater trochanters, femoral medial epicondyles, tibial medial and lateral epicondyles, medial malleoli and 1st and 5th metatarsals were removed. Virtual point trials were collected to complete joint axis definition, particularly to identify anatomical landmarks on the left and right anterior superior iliac spine and the sternal notch using a pre-calibrated wand.

Participants walked barefoot, at the self-selected walking speed determined by the GAITRite™ on a R-Mill dual-belt instrumented treadmill (Motekforce Link, the Netherlands). Participants were instructed to remain in the middle of the treadmill during walking and to walk with one foot on each treadmill belt. Participants walked for six-minutes to acclimatize to the level of exercise, marker set and surface electrodes, as well as the conditions of treadmill walking as recommended in both heathy [240] and knee OA populations [236]. At the 6th minute of walking, a 20-second baseline recording was collected.

3.3.1 PERTURBATION PROTOCOL

After the acclimatization period and as participants continued walking, participants were informed that the perturbation protocol would begin and were instructed to continue walking with one foot on each treadmill belt to the best of their ability. Participants did not experience or witness treadmill translations prior to this testing. Participants were instructed to avoid using the handrails unless necessary. Investigators would avoid

interaction with participants unless necessary. The treadmill surface was programmed to translate in medial and lateral directions, on left and right legs, at magnitudes of 1cm and 3cm at a rate of 0.1m/s. The translations occurred during the single support, mid-stance phase of the gait cycle (i.e. contralateral GRF < 50N) and recorded data included at least 3 strides before and after the translation. Eight translations occurred in order (Table 3-2) and were repeated three times for a total of 24 translations. Walking translations were unexpected to the participant, as participants were blinded to occurrence, direction and magnitude, as well as which leg was on the treadmill surface when translated. A researcher was located at the back of the treadmill as a safety precaution and to detect if participants crossed onto opposite plates or utilized hand supports in response to walking translations. After participants completed all translation trials, a 10-second post-baseline trial was recorded. Treadmill speed was briefly reduced, and the walking/perturbation protocol was ended. If the participant was able to complete the entire protocol, 24 perturbation walking trials were collected.

Table 3-2: Studies perturbation paradigm which includes eight, unexpected perturbations repeated three times in series.

Series	Leg	Direction	Magnitude (cm)
1	Left	Lateral	1
2	Right	Medial	3
3	Right	Lateral	1
4	Left	Medial	3
5	Right	Lateral	3
6	Left	Lateral	3
7	Left	Medial	1
8	Right	Medial	1

Passive retro-reflective markers were removed, and a resting muscle bias trial was collected with participants supine.

3.4 MUSCLE STRENGTH TESTING AND EMG NORMALIZATION

Following walking and perturbation experiments, maximum voluntary isometric contraction (MVIC) exercises were performed according to standardized laboratory procedures [72, 236] for the purpose of assessing strength and EMG amplitude normalization. The Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc., USA) was used for testing. The exercises were: 1) seated unilateral knee flexion (knee at 45˚ flexion), 2) seated unilateral knee extension (knee at 45˚ flexion), 3) standing unilateral heel raise [236]. Knee joint axis and dynamometer axis were aligned. Each maximal effort contraction was held for 3-seconds and repeated twice. As per recommendations, a practice trial was performed, standard verbal encouragement was provided, and adequate rest periods (40 seconds) were given between trials [47]. Torque data were gravity corrected and recorded with EMG data for knee flexion and knee extension exercises.

3.5 DATA PROCESSING

3.5.1 KINEMATICS

Three-dimensional motion capture using a Cartesian coordinate system is considered standard in reporting joint angle data [241]. The treadmill tracking coordinate system was used to maintain alignment of the global and treadmill force plate coordinate systems

during the treadmill translations. Kinematic data was transformed into the treadmill coordinate system (Equation 1). The average position of Treadmill Marker 1 was calculated for all trials previous to perturbations (Trials 1-12). The origin of the treadmill coordinate system in the treadmill pose [T] was corrected based on the difference between the original 12 trials and each perturbation trial. [T] was re-established, and marker locations beginning in the global coordinate system (P_{Global}) are transformed and represent the P_{Local} of each marker in the coordinate system of the treadmill.

(Equation 1) $$P_{Local} = inv\ [T]^* P_{Global}$$

All kinematic data was low pass filtered (Butterworth 4th order, Fc: 6Hz recursive) and processed using pre-programed software (JAR v4) written in MatLab 2015b (The Mathworks Inc., USA) utilized in the JAR lab previously [187, 239, 242, 243]. Local and technical anatomical bone embedded coordinate systems for the lower extremities were derived from skin markers, virtual points and rigid clusters. Accepted Cardan/Euler rotations were used to calculate joint angles [175] in a flexion/extension, adduction/abduction, internal/external rotation sequence. The primary flexion-extension axis of the knee was defined by a vector embedded between the medial and lateral femoral epicondyles. Orthonormal thigh coordinate systems were defined with the medial-lateral (ML) axis fixed, and anterior-posterior (AP) and distal-proximal (DP) axes a result of cross products. The orthonormal shank coordinate systems were defined with DP axis fixed, and AP and ML axes the results of cross products. Positive motion was described as flexion, adduction and internal rotation about the knee, and described as the

distal segment moving about a fixed proximal segment [175]. Excellent day-to day reliability has been reported in sagittal and frontal plane knee motion outcomes (ICC = 0.85 - 0.94) and high reliability has been reported in single point, sagittal and frontal plane knee motion outcomes (ICC = 0.73 – 0.77) using the methods described [155]. In an knee OA population, both over ground (ICC= 0.74 - 0.90) and treadmill (ICC = 0.65 - 0.93) walking have demonstrated good-to-excellent reliability [173, 244].

3.5.2 KINETICS

Each force plate embedded in the walking surface contains six sensors that output three-dimensional GRF and moments, after a calibration matrix was applied. The treadmill force plate coordinate system was aligned with the global coordinate system of the motion capture system using methods described in 3.5.1 (Equation 1). Raw GRF and moment data were lowpass filtered (Butterworth 4^{th} order, Fc: 30Hz recursive) and processed on pre-programmed laboratory software (JAR v4) written in MatLab 2015b (The Mathworks Inc., USA). GRFs, in conjunction with linear and angular segment accelerations, participant anthropometrics and inertial properties were used to calculate external joint moments using inverse dynamics [174].

Free body diagrams were established for the foot, shank and thigh to calculate forces and moments. A summation of the external forces and moments acting on each segments centre of gravity was used to calculate linear and angular momentum [174]. For example, to calculate net knee joint moments, ankle joint centre (defined as mid-way between the medial and lateral malleoli) and ankle joint reaction forces and moments (applied with

Newton's Third Law of Motion), knee joint centre (defined as mid-way between the medial and lateral femoral epicondyles), segment anthropometrics, velocities and accelerations were utilized [174]. Three dimensional joint forces and moments were calculated in the laboratory reference frame and projected into the joint coordinate system. For the knee, the flexion-extension axis was embedded in the femur, the internal-external rotation axis was embedded in the tibia, and the abduction-adduction axis was considered a floating axis orthogonal to flexion-extension and internal-external rotation. The direction conventions are equivalent to kinematic assessment. Moments were lowpass filtered (Butterworth 4^{th} order, Fc: 10Hz recursive) and normalized to body mass (Nm/kg). Excellent day-to day reliability has been reported in sagittal and frontal plane knee moment outcomes (ICC= 0.84 - 0.95) using methods described above [155] in healthy young adults. In a knee OA population, during over ground walking, sagittal and frontal plane knee moment outcomes displayed high-to-excellent day-to day reliability (ICC = 0.78 - 0.93) [173] and in treadmill walking environments knee OA populations have displayed good-to-excellent reliability (ICC = 0.57 - 0.89) [244].

3.5.3 ELECTROMYOGRAPHY

Surface EMG was processed on pre-programmed laboratory software (JAR v4) written in MatLab 2015b. All signals were visually checked for artifacts, saturation or ambient 60Hz noise during collection and processing procedures. Additionally, each EMG signal was verified in the power spectrum using a Fast Fourier Transform. Raw signals were corrected for participant bias, gain corrected, converted to micro-volts, bandpass filtered (Butterworth 4^{th} order, Fc: 10-500Hz), full-wave rectified [61] and low-pass filtered

(Butterworth 4th order, Fc: 6Hz recursive), depicted in Figure 3-1. A 100ms moving-average window algorithm (99ms overlap) identified maximal amplitude for each muscle across MVIC exercises and EMG waveforms were amplitude normalized to this value. High-to-excellent reliability for medial and lateral quadricep, hamstring and gastrocnemius muscle activation magnitudes and patterns using non-negative matrix factorization (ICC = 0.71 - 0.99) and mean and peak activation (ICC = 0.74 - 0.97) have been found in young healthy adults [155] using the method described above. High-to-excellent reliability using PCA outcomes (ICC = 0.73 - 0.97) in a population with knee OA has also been found [245].

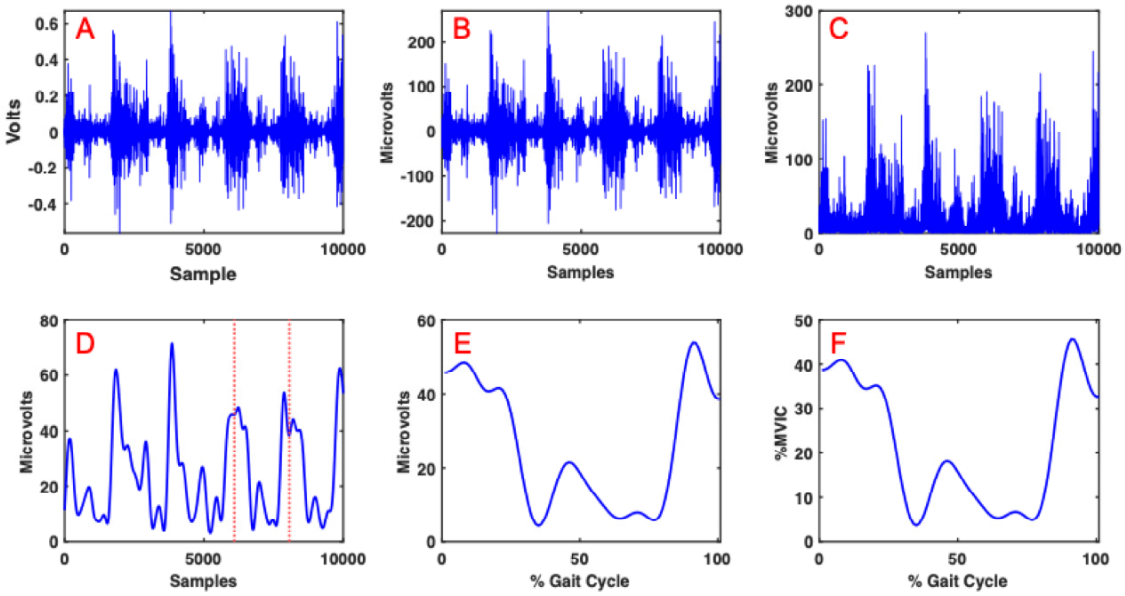

Figure 3-1: A medial hamstring representative waveform to depict the EMG processing steps. A) Raw waveform B) Corrected for participant bias, gain corrected, converted to microvolts and band-pass filtered C) Full-wave rectified D) Low-pass filtered (i.e. linear enveloped) E) Time Normalized F) Amplitude Normalized to MVIC.

3.5.4 GAIT WAVEFORM ANALYSIS

Joint motion and EMG waveforms were time normalized to represent 100% of the gait cycle, while joint moment waveforms were time normalized to represent 100% of the stance phase using a cubic spline interpolation. A gait cycle, depicted in Figure 3-2, was defined as the point of initial contact representing 0% following by the following initial contact of the ipsilateral leg (100%). Heel strike and toe off events were determined by the events in which the GRF passed above or below a 30N threshold and if those events have an association with a kinematic detection of heel strike or toe off [246]. This method defines a kinematic heel strike as the largest distance between a passive marker on the sacrum and the passive marker on the heel whereas toe off was determined by the minimum distance between a passive marker on the sacrum and a passive marker on the second metatarsal [246].

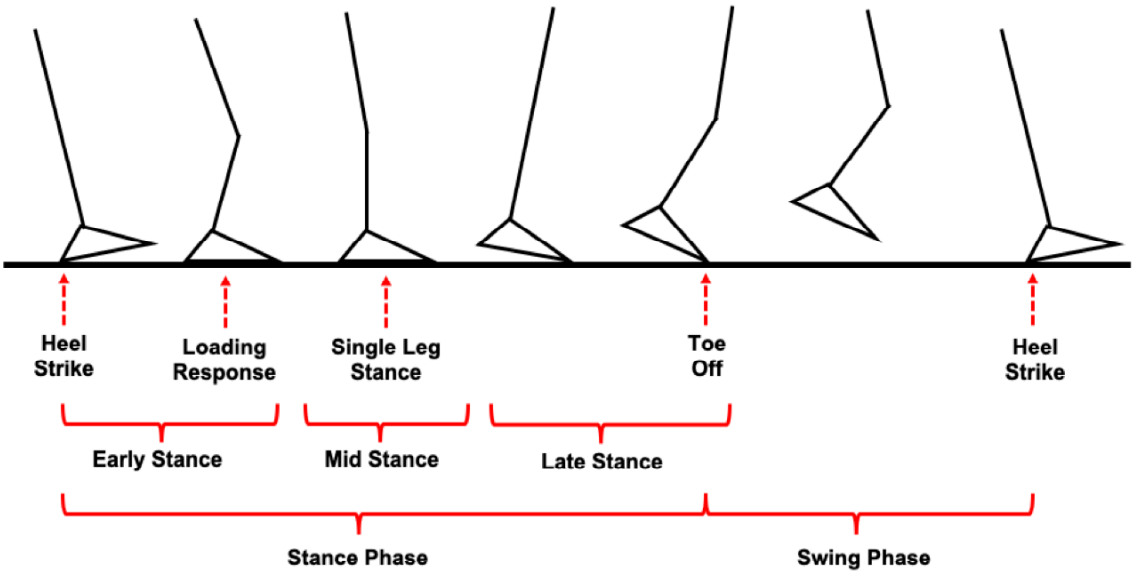

Figure 3-2: The gait cycle and defined gait events adopted from Simoneau [247].

3.5.5 ISOMETRIC MUSCLE STRENGTH

A Humac Norm Isokinetic Dynamometer was used to acquire muscle strength during MVIC exercises. Muscle strength was processed on pre-programmed laboratory software (JAR v4) written in MatLab 2015b. A 500ms moving average window algorithm was used to determine maximal amplitude of torque across a 3s contraction during MVIC exercises. Excellent day-to-day reliability has been published for knee extension (ICC = 0.93) and knee flexion (ICC = 0.95) using this method in a population of young, healthy individuals [155].

3.6 DATA ANALYSIS

Specific data and statistical analysis for each Objective is provided in Chapters 4-8. An overview of the general data analysis is provided. The most symptomatic leg was analyzed in individuals with MOA (i.e. the knee diagnosed with OA that deemed the individual eligible for the study), while a random leg was selected from the ASYM group. For Objective 1, strides from the 20s baseline walking trial were ensembled averaged and used for analysis. For Objective 2a and 3a, walking strides from direct gait perturbations were selected, where the symptomatic limb was translated and subsequent strides on the symptomatic limb were analyzed. For Objective 2b and 3b, walking strides from indirect gait perturbations were selected, where the asymptomatic limb was translated and the landing stride on the symptomatic limb was analyzed. For Objective 2 and 3, three strides before the translation occurred were averaged to represent a baseline (T0) and the first stride (T1) after the translation was obtained to represent the individuals biomechanical and EMG responses to the perturbation. For all objectives, metrics from

knee motion (Figure 3-3) included; 1) knee flexion ICPF range, 2) the range from PFLM, 3) the frontal plane knee range from initial contact to peak knee adduction angle (ICKAA) motion during stance, which have been tested previously in the context of OA and knee instability.

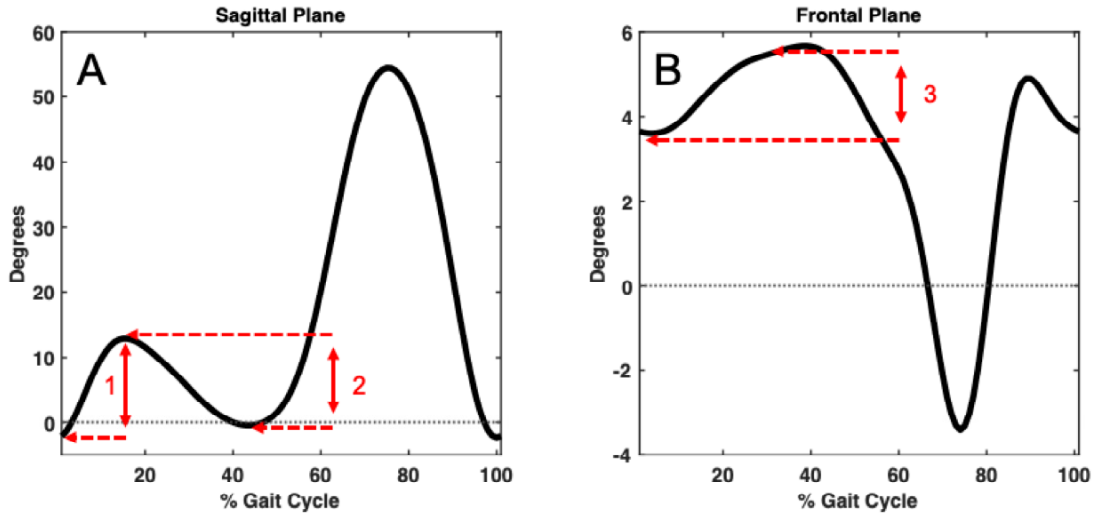

Figure 3-3: A) Sagittal and B) frontal plane ensemble averaged motion waveforms to demonstrate kinematic outcome variables; 1) knee flexion range from initial contact to peak flexion during stance, 2) the range from peak stance knee flexion to peak knee extension in late stance, 3) the total frontal plane knee range from initial contact to peak knee adduction angle.

Metrics from knee moments (Figure 3-4) included; 1) the SPROM and 2) the external pKAM.

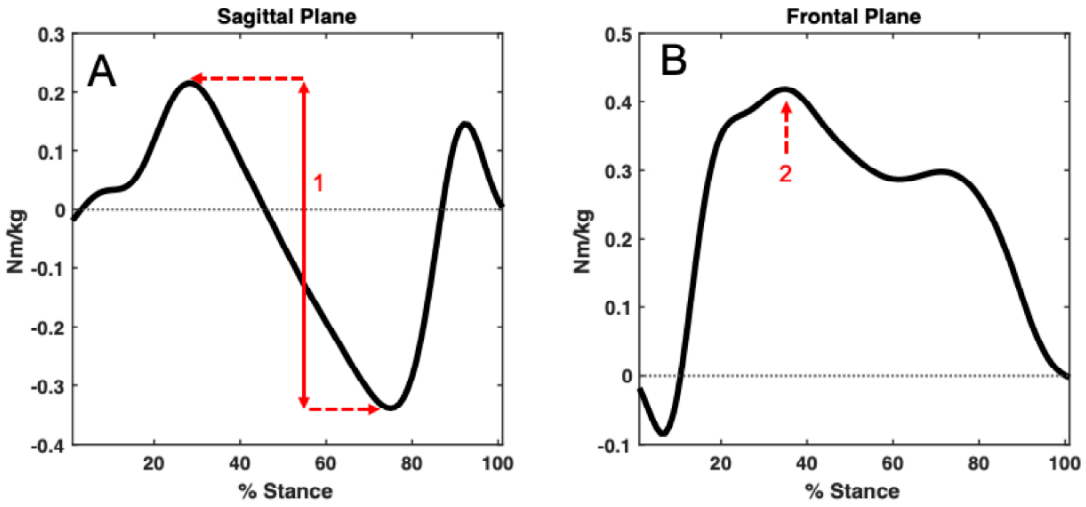

Figure 3-4: A) Sagittal and B) frontal plane ensemble average moment waveforms to demonstrate kinetic outcome variables; 1) the range between the peak knee flexion and peak knee extension external moment and 2) the external peak knee adduction moment.

PCA was implemented to capture unbiased waveform characteristics from the data itself. For all objectives, ensemble averaged time and amplitude normalized EMG waveforms were calculated for each participant, muscle and time. PCA was performed using MatLab 2015b and methods described in the literature [31, 61]. A separate PCA was performed for each chapter. Within each chapter, three separate PCAs were performed, one for each muscle group. Time normalized waveforms (n=101) from participants, muscles, and, if applicable before and after translations, formed three individual matrices (X). An eigenvector decomposition of the cross-product matrix ($[S]=[X^T]*[X]$) was completed, using standard notation U'SU=L, and yielded predominant orthonormal components or principal patterns (PP). Three PPs (PP1, PP2, PP3) explaining the greatest variation and explaining at least 90% of dataset variance were retained. Principal Pattern Scores (*PP-scores*) were computed in each analysis for each individual ensemble averaged EMG waveforms (*PP-score*=[X]*[U]). EMG waveforms can be accurately reconstructed by linear combinations of PPs multiplied by corresponding *PP-scores*. Individual *PP-scores*

for each group, time and muscle were scored against a common PP, allowing for statistical hypothesis testing.

3.7 STATISTICAL ANALYSIS

For Chapters 4, 7 and 8, participants with MOA were dichotomized using the KOS-ADLS instability question into participants reporting they do not have the symptom (KOS-I = 5), grouped as OA Stable (OAS) and individuals who reported that the symptom of instability impacted their activity (KOS-I ≤ 3), grouped as OA Unstable (OAU). Participants who reported the symptom, but no activity limitations were excluded from analysis (KOS-I = 4) [89]. ASYM participants were excluded from statistical analysis if they self-reported the symptom of instability (KOS-I < 5). For Objective 2 (Chapter 5 and 6), all MOA and ASYM participants were included in analysis.

All statistical procedures were performed in Minitab™ Ver.18 (Minitab Inc., USA). All continuous variables were tested for normality and equal variance using the Kolmogorov-Smirnov and Levene's tests (alpha = 0.05). If assumptions were not met, data were transformed using the Johnston Transformation in Minitab™ Ver.18. The Johnson Transformation optimally selects either a variable bounded, variable lognormal or variable unbounded distribution to transform data to follow a normal distribution [248]. One-way analysis of variance models (ANOVA) (Chapter 4, 7 and 8) and Student's t-tests (Chapter 5 and 6) were used to test for group differences in participant demographics, walking speed, muscle strength and KOOS subset scores. For Chapter 4, a one-way ANOVA determined between-group differences for biomechanical outcomes

variables and a two-way ANOVA was used to determine between and within group (muscle) main effects and interactions for quadricep, hamstring and gastrocnemius PP-scores. For Chapters 5-8, a two-factor Analysis of Covariance (ANCOVA), adjusting of walking speed, was used to determine between and within group (time) main effects and interactions. A three-factor, mixed model ANCOVA, with walking speed as a covariate, was used to determine between and within group (muscle, time) main effects and interactions for quadricep, hamstring and gastrocnemius PP-scores. Walking speed was included as a covariate for perturbation response analysis as it is currently unknown if walking speed influences the response to perturbations. If the assumptions of the ANCOVA were not met [249] or walking speed was not a significant contributor to the model, an ANOVA was used. Bonferonni post hoc adjustments were used for all significant effects and significance levels were adjusted to alpha = 0.05 depending on number of comparisons.

3.7.1 SAMPLE SIZE

A statistical analysis of the required sample size was completed for the perturbation study. From pilot work (NSHA-RS/2015-137), individuals with knee OA, using a difference of 5 degrees of knee motion and variability taken from knee OA populations studied previously, it was estimated that a sample size of between 14 and 24 individuals depending on whether paired (perturbation effect) or unpaired (group effect) for conducting this study. Given the developmental approach to the primary research question and the two other gait perturbation studies have used group sizes of 10 and 23 participants to detect significant differences in mechanics and muscle activation

amplitudes, an n of 24 individuals in each group was selected to make recruitment feasible over a short duration. Sample size for chapters 7 and 8 were impacted by the COViD-19 health crisis. With this understanding, chapters 7 and 8 are preliminary analyses.

CHAPTER 4: ALTERED MUSCLE ACTIVATION MAGNITUDES AND PATTERNS DURING GAIT IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS SELF-REPORTING KNEE INSTABILITY AFFECTING ACTIVITY

4.1 INTRODUCTION

Knee OA is a highly prevalent [1] and debilitating disorder [250], that is the strongest determinant of walking difficulty in older adults when compared to other chronic diseases [13]. During walking, those with knee OA are trying to safely navigate their environment by striking a balance between knee joint stability and mobility. This is often characterized by some combination of less sagittal plane knee ROM, reduced sagittal plane moment dynamics and elevated or prolonged patterns of knee muscle activation or co-activation as people attempt to maintain mobility in the presence of progressive alterations to joint structure, characteristic of OA [43, 60, 61, 73, 90]. These alterations have often been interpreted as a knee stabilizing strategy [43, 60, 61, 73, 90].

Self-reported instability is defined as the sensation of buckling, shifting or giving way of the knee joint. The symptom is reported in approximately 60-80% of individuals with knee OA [25, 74, 79] and 30-60% reporting instability impacts activities [27, 54, 251]. The KOS-ADLS [224] contains a question addressing how patients perceive symptoms of buckling, shifting or giving way of the knee and how it impacts activity. It is measured on a 6-point Likert scale from 0 (instability prevents all activity) to 5 (no symptom of instability). Those who self-report knee instability have been shown to demonstrate an increased risk [223] and fear [50] of falling, ultimately impacting knee joint confidence [52] and limiting activity because of knee instability concerns [50]. Limiting physical

activity may contribute to the lower KOOS scores found in those self-reported instability [216], linked to reduced future functional outcomes [51]. Improving knee instability has been deemed an important independent variable in the treatment and management of knee OA [252], particularly in individuals whose functional activity levels are limited by episodes of knee instability [25].

The symptom of knee instability in knee OA is most commonly felt during walking compared to other weight bearing tasks [54, 76] and those with instability that impacts physical activity are at greater odds of reporting walking difficulties [27]. To date, limited research has examined self-reported knee instability and its impacts on gait biomechanics [27, 77, 78, 139, 227]. Two studies reported greater knee flexion ROM in a knee OA group reporting the symptom of instability impacting function compared to a group of with knee OA either reporting no symptom of instability or reporting the instability with no impact on activity [27, 77]. When looking at knee joint moments, no differences have been reported in peak knee flexion moment, peak knee extension moment, or the SPROM [77], however those with self-reported instability impacting function demonstrated a lower overall total support moment [27]. Lower knee joint stiffness, defined as the change in sagittal plane knee joint moment divided by the change in sagittal plane knee joint angle, was also reported the unstable group [77]. Together, evidence supports that gait biomechanics are altered in individuals with knee OA reporting instability that impacts function, however, the current studies are few and have not explored the link between joint and muscle function by assessing both joint-level biomechanics and muscle activation magnitudes and patterns.

The knee joint musculature has been shown to provide active stiffness in those with knee OA during movement. Those with knee OA walk with elevated [61, 133] and prolonged [31, 32] quadricep activity, higher LH activity [31, 204], earlier and more constant LG activation [43] and greater lateral-to-medial co-contraction indices [73], where structural severity, effusion, self-reported pain and knee joint laxity have been associated with these neuromuscular alterations [30, 43, 71-73]. Higher co-activity, specifically increased lateral-to-medial activation is found in those with knee OA thought to counter elevated KAMs [62] and/or provide active knee stiffness during walking to match stability demands [253]. However, these studies did not assess the symptom of instability or the degree to which instability affects function and it is unknown whether these muscle activation magnitudes and patterns are influenced by self-reported knee instability. Knee OA pathology is characterized by alterations to the passive osteoligamentous and neuromuscular systems. This creates an environment for altered muscular responses during weight-bearing activities where sensations of giving way, shifting or buckling are more or less likely as individuals responds to the demands of walking. Understanding if muscle activation patterns, and joint biomechanics are in fact different during walking in individuals with knee OA who report these sensations, will provide important information on how joint function is maintained in this group.

The purpose of this study was to determine if quadricep, hamstring and gastrocnemius muscle activation magnitudes and patterns, and knee joint motions and moments differ during treadmill walking among individuals with moderate medial compartment knee OA

who self-report instability that impacts activity and individuals with MOA and an ASYM group who do not report the symptom. We hypothesized that those with knee instability impacting activity will walk with elevated and more prolonged quadricep, hamstring and gastrocnemius activation, reduced sagittal plane knee motion and reduced sagittal plane moment dynamics compared to the groups of individuals with knee OA and ASYM groups with no instability symptoms.

4.2 METHODOLOGY

4.2.1 PARTICIPANT RECRUITMENT

Participants with unilateral symptomatic, medial compartment knee OA were recruited from local clinics following a consultation with an orthopaedic surgeon, diagnosed using the ACR guidelines [233]. Standard anterior-posterior radiographs were obtained and scored using the Kellgren-Lawrence (KL) ordinal radiographic scale [68]. Individuals with OA were classified with moderate disease severity if they were not a candidate for a TKA and self-reported the ability to walk more than a city block, climb stairs reciprocally and jog 5m [61]. An age-matched ASYM group, considered a sample of convenience, was recruited using local advertisements. These individuals reported no pain in their lower extremities and had no history of lower extremity injury or disease. Participants, in all groups, were excluded if they had cardiovascular or neurological disorders that would impair walking ability, were unable to walk independently and reported lower extremity fractures or injuries other than a sprain or strain. The protocol was approved by the local institutional ethics review board.

4.2.2 DATA COLLECTION

All participants completed the KOS-ADLS [224] and KOOS [234] surveys prior to gait analysis. Height, mass and segment circumferences were measured. To obtain self-selected walking speed, participants walked back-and-forth across the GaitRITE™ (CIR Systems Inc., USA) pressure sensitive walkway and five trials were randomly recorded and averaged [31]. Knee effusion was assessed by an experienced physiotherapist using the bulge test [30]. Surface EMG procedures were completed using standardized guidelines [235]. Skin was lightly shaved and wiped with 70% alcohol pads. Surface electrodes (Ag/AgCl, 10mm diameter, 30mm inter-electrode distance, Red Dot, 3M Health Care, USA) were placed in a bipolar configuration over the VM, VL, MH, LH, MG and LG on both legs. A reference electrode was placed on a bony part of the tibial shaft. EMG was recorded using two AMT-8 8-channel measurement system (CMRR: 115dB at 60Hz, input impedance: ~10 GΩ, band-pass: 10-1000Hz, Bortec Inc., Canada).

Passive, retro-reflective individual markers and rigid marker clusters were fastened to participants with previously defined anatomical landmarks [239] using Velcro straps and adhesive tape. Virtual point trials were collected to identify the sternal notch and the right and left anterior superior iliac spines. Marker trajectories were tracked with eight Qualisys® OQUS 500 (Qualisys®, Sweden) motion analysis cameras at 100Hz.

Participants walked barefoot, at self-selected speeds recorded by the GaitRITE™, for six minutes on a dual-belt instrumented treadmill (R-MILL, Motekforce Link, The Netherlands). GRFs and EMG were sampled at 2000Hz (A/D 16bit, +/ 5V). Qualisys

Track Manager 2.10 (Qualisys®, Sweden) was used to synchronize GRF, EMG and marker trajectories. A 20s trial was recorded after the six-minute acclimatization period [236].

A resting muscle activation bias trial was collected following walking with participants supine. Participants performed a series of MVICs on a Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc., USA). One practice contraction was completed followed by two, 3s MVIC trials separated by 40s of rest. Standard verbal encouragement was given. Knee flexors and extensors were tested at 45˚ of knee flexion [236], with the dynamometer axis and knee joint axis aligned. Standing unilateral plantarflexion was completed [61].

4.2.3 DATA PROCESSING

Custom data processing scripts were written in MatLab™ 2015b (The Mathworks Inc., USA). Marker trajectories were filtered using a recursive, 6Hz - low pass, 4^{th} order, Butterworth filter and GRF and moments were smoother using a recursive, 30Hz - low pass, 4^{th} order, Butterworth filter. Bone embedded pelvis, thigh, shank and foot coordinate systems were derived from physical markers and virtual points. Knee joint angles were calculated using 6-degree of freedom Cardan/Euler rotations, described as the distal segment moving about a fixed proximal segment as previous [31]. Using inverse dynamics [174], net external knee joint moments were calculated and projected in joint coordinate system [175]. Moments were amplitude normalized to body mass (Nm/kg) and filtered using a recursive, 10Hz - low pass, 4^{th} order, Butterworth filter

[239]. Joint moments were time normalized to the stance phase, beginning at heel strike and ending at toe off. Raw EMG signals were filtered with a 10-500Hz - band pass, 4th order, Butterworth filter, corrected for resting muscle bias, full-wave rectified and linear enveloped using a recursive, 6Hz - low pass, 4th order, Butterworth filter. EMG waveforms were amplitude normalized to the highest 100ms window (99ms overlap moving average) from MVIC trials [61]. Joint angle and EMG waveforms were time normalized to the gait cycle, beginning and ending at heel strike. Strength was calculated using a 500ms moving average window finding maximal torque generated during two, 3s steady state MVIC trials. Maximal torque was amplitude normalized to body mass (Nm/kg).

4.2.4 DATA ANALYSIS

Sagittal plane ICPF and PLFM ranges and frontal plane ICKAA range were calculated from knee joint angle waveforms. The SPROM and pKAM were calculated from sagittal and frontal plane knee joint moment waveforms [236]. PCA was used extract mutually uncorrelated EMG PPs that collectively described over 90% of variability within the data set [61]. *PP-scores* were calculated, providing a weighting coefficient where higher scores indicate how similar an individual waveform matched a PPs. These methods have previously been published in detail and have been used to understand amplitude and temporal muscle activation patterns in knee OA gait [61]. EMG and biomechanical methods and outcome variables within over ground and treadmill walking environments have demonstrate good-to-excellent reliability in both ASYM [155] and knee OA populations [173, 244, 245].

4.2.5 STATISTICAL ANALYSIS

Given the purpose was to investigate knee instability impacting activity, participants with MOA were dichotomized using KOS-I into participants reporting no instability (KOS-I = 5), grouped as OAS and individuals reporting that the symptom of instability impacted their activity slightly, moderately or severely (KOS-I ≤ 3), grouped as OAU. Participants who reported the symptom, but no limitations were excluded from analysis (KOS-I = 4) [89]. ASYM participants were excluded from statistical analysis if they self-reported the symptom of instability (KOS-I < 5).

Equal variance and normality of response variables were determined from Levene's and Kolmogorov-Smirnov tests. Data with unequal variance or non-normal distributions were transformed using Johnson Transformation. A two-factor, repeated-measures ANOVA determined between and within group and muscle main effects and interactions for quadricep, hamstring and gastrocnemius *PP-scores*. One-way ANOVA models were used to determine between group differences for subject demographics, KOOS Scores, walking speed, strength and discrete biomechanical gait outcomes. Bonferonni post hoc adjustments were used for significant effects and the significance levels were adjusted to alpha = 0.05 depending on number of comparisons. All statistical procedures were completed using Minitab™ Ver. 18 (Minitab Inc., USA).

4.3 RESULTS

Seventy-nine individuals with MOA were recruited; 53 participants (67%) reported the symptom of instability, with 42 (53%) of those reporting that the symptom impacted activity. Forty-six ASYM individuals were recruited; only 2 participants (4%) reported the symptom of instability. In both groups, individuals reporting instability symptoms with no impact on activity (KOS-I = 4), were removed from analysis (MOA [n =11], ASYM [n = 2]).

Table 4-1: Mean and standard deviation (SD) subject demographics, walking speed, self-report scores, knee joint strength and radiographic scores. Differing letters denote significant difference.

	Asymptomatic	**OA Stable**	**OA Unstable**
N	44	26	42
Sex (M:F)	21:23 (52% Female)	16:10 (38% Female)	22:20 (48% Female)
Age (years)	61 (7)	64 (5)	60 (7)
Height (m)	1.68 (0.08)	1.70 (0.09)	1.69 (0.09)
Mass (kg)	70.3 (13.0) [a]	81.3 (13.7) [b]	86.5 (17.8) [b]
BMI (kg/m^2)	24.9 (3.4) [a]	28.0 (4.1) [b]	30.1 (4.4) [b]
Walking Speed (m/s)	1.16 (0.12) [a]	1.10 (0.13) [ab]	1.03 (0.13) [b]
KOS-I	44 [5]	26 [5]	17 [3] – 20 [2] – 5[1]
Brush Test [+:-] (% Positive)	4:40 (9% Positive)	13:13 (50% Positive)	19:23 (45% Positive)
NRS - Pain	--	--	--
Pre-Walking [n/10]	0 (0)	1 (1)	2 (2)
Post-Walking [n/10]	0 (0)	1 (1)	3 (3)
KOOS	--	--	--
Symptoms (n/100)	98.1 (3.9) [a]	68.5 (14.1) [b]	53.8 (11.7) [c]
Pain (n/100)	98.9 (2.9) [a]	69.6 (16.0) [b]	59.9 (18.2) [c]

Activities of Daily Living (n/100)	99.6 (1.2) [a]	80.0 (14.5) [b]	63.2 (19.2) [c]
Quality of Life (n/100)	97.6 (5.3) [a]	54.8 (15.4) [b]	37.8 (14.8) [c]
Radiographic Scores	**--**	**--**	**--**
KL0	--	0	2
KLI	--	9	15
KLII	--	10	17
KLIII	--	1	4
KLIV	--	0	0
Not Rated **	--	6	4
Knee Extension 45˚ (Nm/kg)	1.82 (0.41) [a]	1.50 (0.34) [b]	1.37 (0.54) [b]
Knee Flexion 45˚ (Nm/kg)	1.09 (0.27) [a]	0.92 (0.31) [ab]	0.80 (0.33) [b]

** Access to radiographs was unavailable due to ongoing COViD-19 health crisis.

Table 4-1 outlines group demographics, anthropometrics, walking speed, KOOS scores and muscle strength. Median KL-II grades were reported in both MOA groups. ASYM individuals reported lower mass, lower body mass index (BMI), and higher knee extension strength compared to both MOA groups ($p<0.001$). OAU demonstrated a slower walking speed and lower knee flexion strength compared to the ASYM group only ($p<0.001$). KOOS subset scores were different between all groups, with OAU self-reporting the lowest scores ($p<0.001$). Given the study objectives, only group main effects and group-by-muscle interactions are reported.

Table 4-2: Significant mean (SD) PP-scores. Group main effects were represented with muscle site collapsed. Differing letters denote significant differences.

Group Main Effects	**Asymptomatic**		**OA Stable**		**OA Unstable**	
Quad PP1	145.1 (90.0) [a]		143.1 (77.9) [a]		175.3 (89.1) [b]	
Quad PP2	-10.6 (22.7) [a]		0.0 (29.6) [b]		8.2 (30.5) [c]	
Group/Muscle Interactions	**Medial**	**Lateral**	**Medial**	**Lateral**	**Medial**	**Lateral**
Ham PP1	119.3 (63.1) [bc]	110.4 (60.0) [c]	114.4 (65.3) [bc]	174.6 (134.1) [ab]	146.3 (89.3) [abc]	197.4 (170.0) [a]
Ham PP2	-24.9 (37.6) [a]	-23.2 (40.7) [a]	-25.0 (33.7) [a]	8.5 (71.7) [b]	-22.6 (35.4) [a]	8.2 (68.2) [b]
Gast PP1	241.3 (88.4) [a]	169.7 (65.8) [c]	215.7 (81.1) [bc]	187.2 (56.0) [ab]	234.4 (100.2) [ab]	219.3 (84.5) [ab]
Gast PP3	-6.5 (50.5) [a]	21.7 (28.5) [b]	-5.8 (40.9) [a]	13.3 (33.6) [ab]	-2.6 (49.2) [a]	-2.5 (49.2) [a]

Table 4-2 displays the mean *PP-scores* for significant group main effects and group-by-muscle interactions. Quadricep EMG, PPs and PP interpretations are found in Figure 4-1. No group-by-muscle interactions were found. Group main effects were found in *PP1-* ($p=0.045$) and *PP2-scores* ($p=0.001$). *PP1-scores* were higher in the OAU group compared to ASYM and OAS groups. Higher quadricep *PP1-scores* reflects higher overall activation amplitude. OAU *PP2-scores* were higher than OAS and ASYM, and OAS *PP2-scores* were higher than ASYM. Higher *PP2-scores* captured prolonged activation during stance.

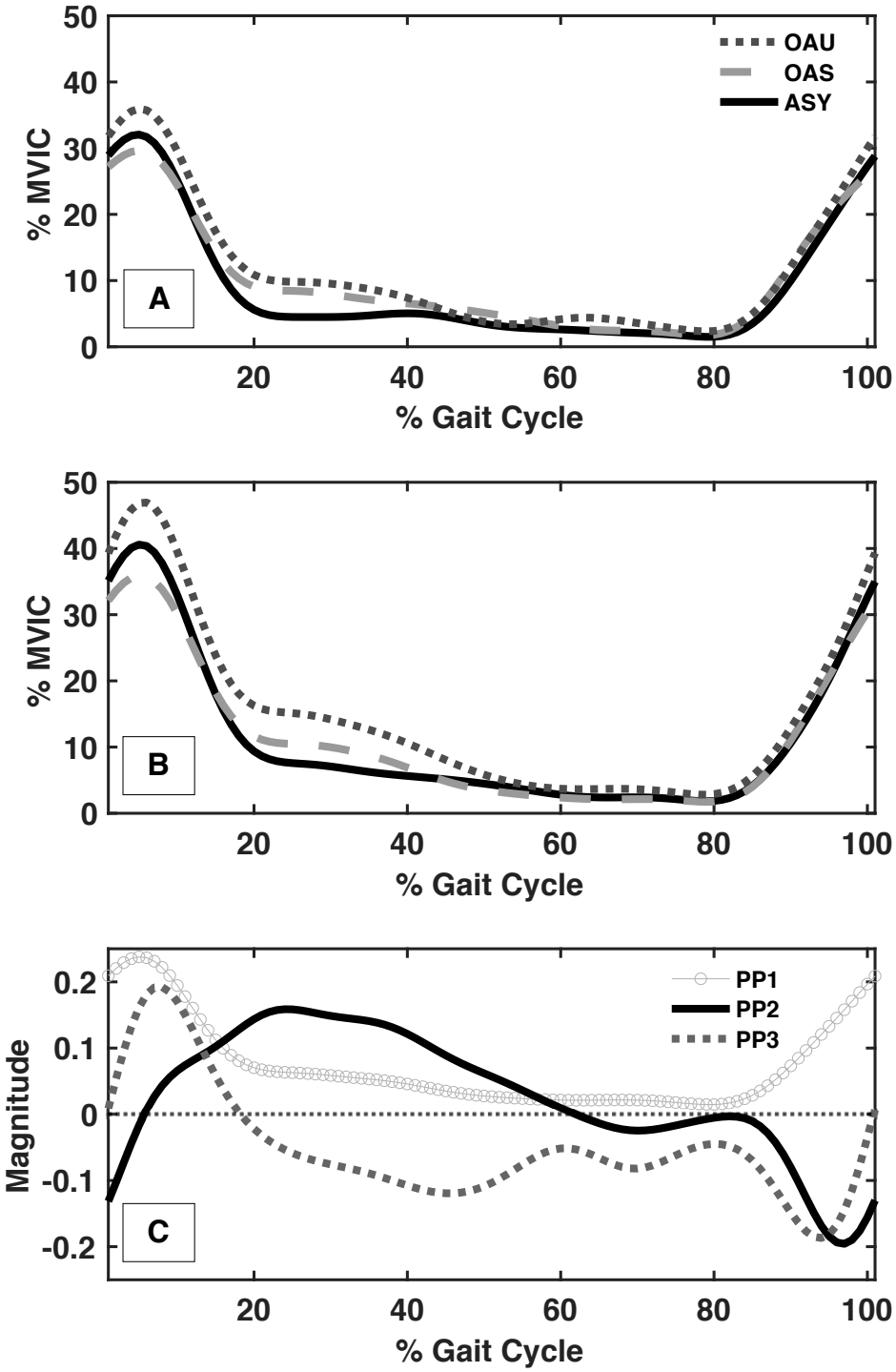

Figure 4-1: Ensemble averaged (A) VM and (B) VL amplitude normalized to % MVIC. (C) Three PPs captured 96% of the waveform variability. PP1 captured overall magnitude and shape explaining 92% of waveform variability. PP2 captured prolonged activation during stance explaining 2% of waveform variability. High PP3-scores captured a greater difference between early-to-mid stance and swing phases, explaining 2% of waveform variability.

Hamstring EMG, PPs and PP interpretations are found in Figure 4-2. Group-by-muscle interactions were reported for *PP1-* (p=0.004) and *PP2-scores* (p=0.025). LH *PP1-scores* were higher in OAU and OAS groups compared to the ASYM group, and MH *PP1-scores* across all groups were not statistically different. Higher hamstring *PP1-scores* reflects overall activation amplitudes are increased. Similarly, LH *PP2-scores* were higher in OAU and OAS groups compared to the ASYM group, and MH *PP2-scores* were not statistically different across all groups. Higher *PP2-scores* reflect prolonged activation during stance.

Gastrocnemius EMG, PPs and PP interpretations are found in Figure 4-3. Group-by-muscle interactions were reported for *PP1-* (p=0.003) and *PP3-scores* (p=0.005). MG *PP1-scores* were higher than LG in the ASYM group, while in OAU and OAS groups MG and LG *PP1-scores* were not different (p>0.05). OAU LG *PP1-scores* were higher than the ASYM group only. Higher *PP1-scor*es suggest overall activation amplitudes are increased. LG *PP3-scores* were higher than MG in the ASYM group, while the OAU and OAS group MG and LG *PP3-scores* were not different (p>0.05). LG *PP3-score*s were lower in the OAU group compared to the ASYM group only. All MG *PP3-scores* were not different (p>0.05). Higher *PP3-scores* indicate gastrocnemius activation was more delayed.

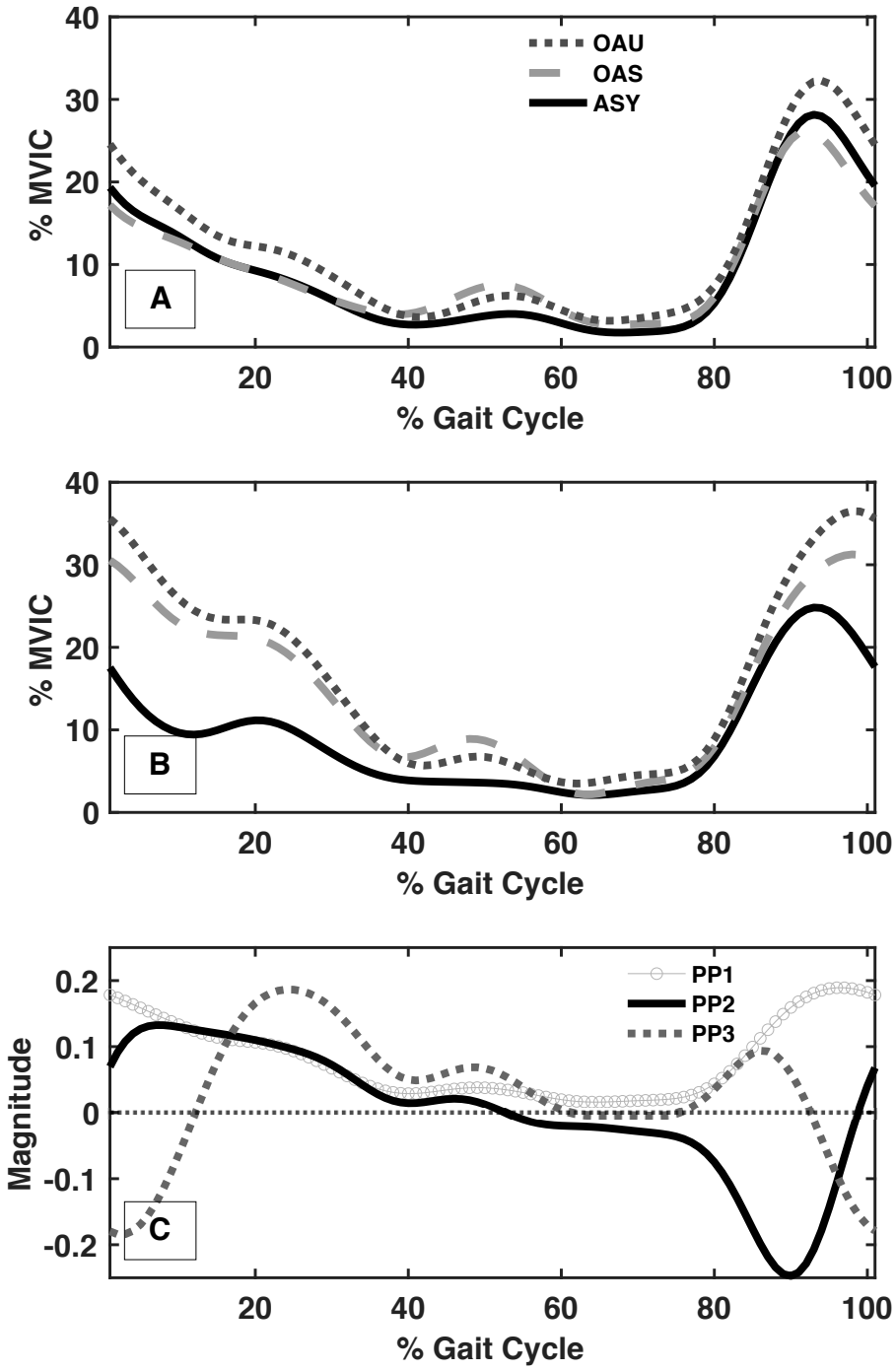

Figure 4-2: Ensemble averaged (A) MH and (B) LH amplitude normalized to % MVIC. (C) Three PPs captured 96% of waveform variability. PP1 captured overall magnitude and shape, explaining 86% of waveform variability. PP2 captures prolonged elevated activation during early stance where higher scores indicate more prolonged activation and explained 7% of waveform variability. PP3 captured a difference between early and late stance activation, where higher scores indicate a greater late stance activity, explaining 3% of waveform variability.

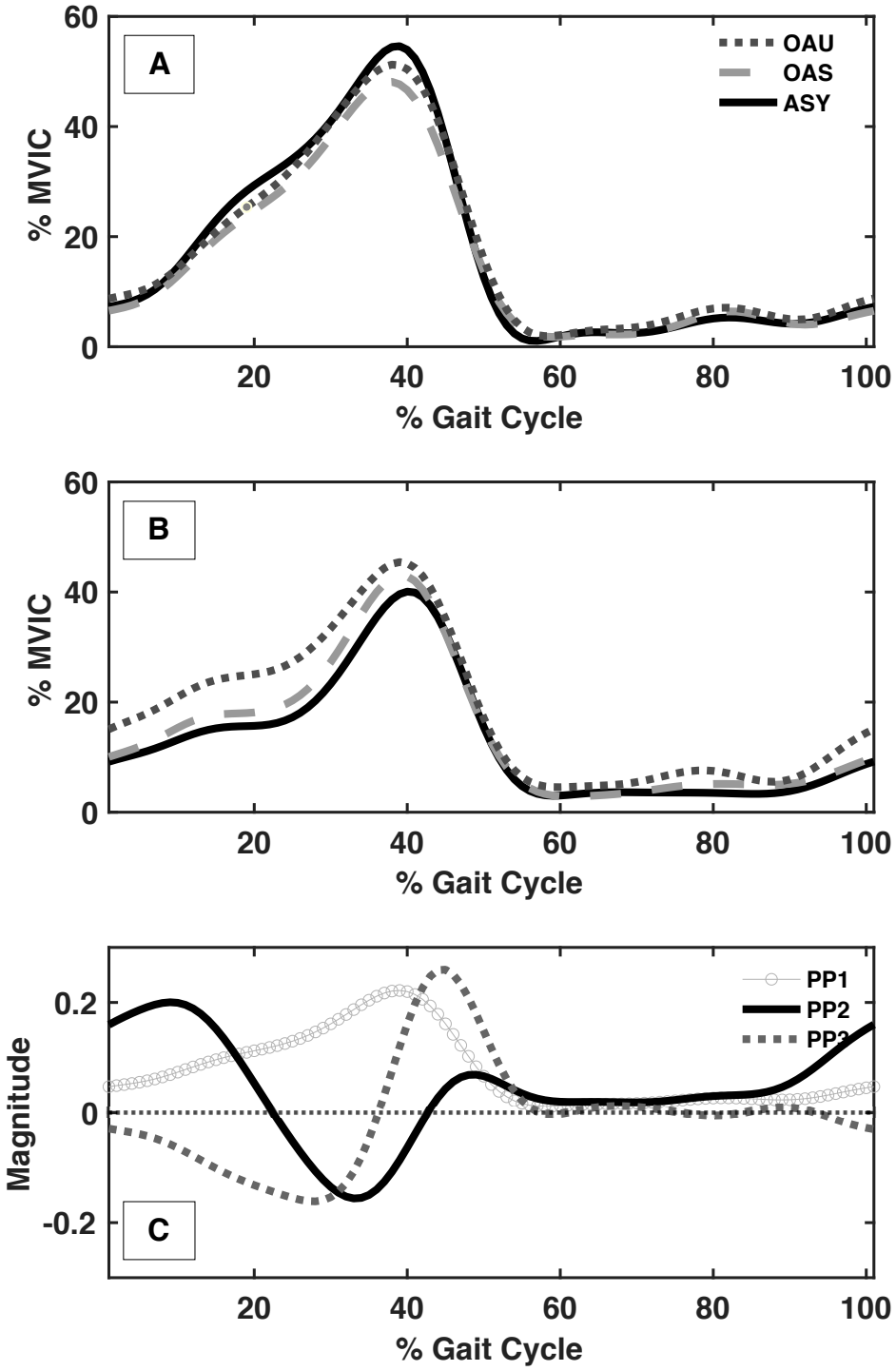

Figure 4-3: Ensemble averaged (A) MG and (B) LG amplitude normalized to % MVIC. (C) Three PPs captured 97% of waveform variability. PP1 captured overall magnitude and shape, explaining 90% of waveform variability. PP2 captured a difference operator between early and late stance phase and explained 4% of waveform variability, where higher scores signify a lower difference. PP3 captured a phase shift in activation where higher scores indicate a delayed activity and explained 3% of waveform variability.

Table 4-3 outlines the motion and moment outcome variables. Sagittal plane knee motion differences were found for both the range from ICPF and PFLM ($p<0.001$), where the OAU and OAS groups walk with reduced ROM compared to the ASYM group. Also, significant differences were reported in the SPROM ($p<0.001$), where OAU and OAS groups walked with less SPROM difference compared to the ASYM group. No group differences were reported in the pKAM ($p=0.110$).

Table 4-3: Mean and SD motion and moment outcomes. Differing letters denote significant differences.

	Asymptomatic	**OA Stable**	**OA Unstable**
ICPF (˚)	15 (4) [a]	11 (4) [b]	12 (4) [b]
PFLM (˚)	13 (6) [a]	10 (4) [b]	9 (4) [b]
SPROM (Nm/kg)	0.82 (0.28) [a]	0.67 (0.18) [b]	0.56 (0.22) [b]

4.4 DISCUSSION

This study aimed to determine if individuals with moderate, medial compartment knee OA self-reporting knee instability impacting activities demonstrated altered quadricep, hamstring and gastrocnemius muscle activation magnitudes and patterns and knee joint motions and moments compared to those with knee OA and ASYM groups with no symptom of instability. Based on previous literature, the study hypothesized that OAU group would walk with elevated and more prolonged quadricep, hamstring and gastrocnemius activation, reduced sagittal plane knee motion and reduced sagittal plane knee moment dynamics compared to the OAS and ASYM groups. Results partially support study hypotheses.

The current study identified group differences between ASYM and both MOA groups (Table 4-1) that are consistent with OA literature [47, 60, 61, 90, 133]. The MOA groups had a higher mass and BMI [60, 61, 133], lower scores for all KOOS subscales [60] and lower knee extension strength compared to the ASYM group [47, 90]. The MOA groups walked with more prolonged activation in VL, VM [31, 32] and LH [61, 62], higher LH activation amplitudes compared to the ASYM group [61, 143]. Gastrocnemius amplitude and temporal patterns were consistent with previous findings, where MOA groups recruited MG and LG to percentages of maximal voluntary activation that were not significantly different from each other, with no significant phase shift between medial and lateral muscle sites [61, 143]. Less sagittal plane range for ICPF and PFLM variables [73, 90], a less dynamic SPROM [43, 59], and no statistical difference in pKAMs were found in MOA groups compared to the ASYM group [62]. These findings support ASYM and MOA groups recruited are samples representative of a wider MOA population and strengthen MOA (OAS/OAU) group differences found in this investigation.

While similarities exist between OAS and OAU groups (Table 4-1) that have been attributed to altered knee joint function (KL grade, walking speed, muscle strength, effusion), these data suggest a differing presentation in those with knee OA who report instability affecting activity based on self-reported function [27, 77, 78, 89]. Alterations in muscle activation magnitude and patterns were found to accompany self-reported sensation of instability impacting activity. The quadriceps (VM/VL) were working at a higher percentage of maximal effort activation in the OAU group compared to OAS and

ASYM groups (Table 4-2). Since no statistical differences in activation amplitudes were found between OAS and ASYM groups, higher VM/VL activation in the OAU group suggests increased active stiffness contributions from the quadriceps specific to the OAU group. Schmitt and Rudolph reported higher agonist/antagonist co-contraction indices (VM-MH/VM-MG) in an unstable group compared to a stable group, and given that MH and MG activation were not statistically different in the current study, elevated unstable group co-activation reported by Schmitt and Rudolph could be driven by elevated VM activity [89]. Higher quadriceps activation has been reported in those with knee OA and effusion compared to those with knee OA and no effusion [30]. Using brush test methods, distributions of effusion detected (Table 4-1) between OAU and OAS groups were not different, suggesting effusion does not explain higher quadriceps activation in this study. The quadriceps complex is thought to reduce the impact on the joint at initial contact [254]. Higher quadriceps activation in the unstable group, particularly in early stance, may be a strategy to unload painful joint tissues [255]. Since episodes of instability most often occur during walking [54] and individuals with knee OA, on average, take 3500-5000 steps in a day [256], this strategy is generally effective, however, OA strength deficits [47], altered proprioception [199] and fatigue [257] may interfere with the ability to maintain this strategy, creating an environment where sensations of knee buckling, shifting or giving way are more likely. More prolonged quadriceps activation (*PP2-scores*) was also found in the OAU group compared to the OAS group. More prolonged OAU quadriceps activation suggests that these individuals are prolonging active stiffness during single leg support. More prolonged quadriceps activation was a feature found at baseline walking in those with moderate OA who progressed to a TKA compared to those

that did not [208]. Even though similar demographics, structural severity, strength, walking speed and self-report function were found [208]. Hatfield et al. 2020 did not collect self-reported instability sensations in this analysis, however patterns of more prolonged OAU quadriceps activation suggests conservative intervention should intervene, as this walking patterns suggest surgical intervention is more likely [208].

Both OAS and OAU groups walked with elevated and prolonged LH activation (*PP1- and PP2-scores*) compared to the ASYM group. Within OA literature, elevated and prolonged LH muscle activation in knee OA groups are related to increasing KAM [62], increasing radiographic severity [143], and interpreted as a method of counterbalancing knee joint instability and/or unloading the medial compartment [43, 61]. Elevated and prolonged LH increased has been found with increasing structural impairment [143] and increased lateral muscle activation has been found with increasing pKAMs, consistent with a strategy to prevent lateral knee joint opening [176] and to maintain frontal plane stability [62]. Both MOA groups had median KL-II grades, and no statistical differences in LH activation magnitude or pattern and pKAM, suggesting that these gait features commonly found in MOA groups are not explained by the dichotomy of self-reported instability.

Gastrocnemius amplitudes and patterns found between the MOA groups were not statistically different, however, the OAU group recruited LG to a higher percentage of maximal effort (*PP1-scores*) and peak activation was shifted earlier in the gait cycle (*PP3-scores*) compared to the ASYM group only. This combination of higher and earlier

activation suggests that LG is activating to unload painful joint tissues and/or provide active stiffness during single-leg stance, where the knee joint is in the most demanding position during walking. More constant LG activation during walking has been associated with higher self-reported knee pain interpreted as an attempt to unload a painful joint tissues [43], although self-reported instability demands were not captured. KOOS Pain subscales were lowest in the OAU group compared to OAS and ASYM groups, suggesting more self-report more pain in the OAU group during daily activities. More constant LG activation are also interpreted as providing active stiffness during single-leg stance, suggesting this finding in the OAU group could also be explained by more self-reported knee pain [43].

The OAS and OAU groups demonstrated comparable ICPF and PFLM motion outcomes and SPROM moment outcomes, however motion and moments ranges were reduced compared to the ASYM group. The results of this study partially contradict previous studies comparing OA stable and unstable groups [27, 77]. Previous studies found higher ICPF range in an unstable group compared to stable [27, 77], but no difference in SPROM [77]; finding reduced stiffness in those self-reporting knee instability impacting activity [27, 77]. Both studies did not capture muscle activation patterns, and the findings of this study suggest no biomechanical changes, but increased quadriceps activation unique to the OAU group providing increased active stiffness.

In combination, the OAU group recruited both VM and VL to higher percentages of maximal voluntary activation but walked with no significant differences in discrete

sagittal and frontal plane biomechanical outcome variables compared to the OAS group. These findings suggest that altered neuromuscular patterns maintain biomechanical function, despite accounts of instability and worse recounts of KOOS subscales. Literature suggests that altered muscle activation magnitudes and patterns may be associated with OA symptoms, some of which are theoretically linked to instability sensations (i.e. laxity, pain, muscle weakness, effusion, proprioception). Similar distributions in effusion and muscle strength between OAU and OAS groups, suggest that significant muscle activation findings do not explain these results. However, KOOS Pain was worse in the OAU group, and a measure of laxity was not captured. As discussed, more constant LG activation and higher lateral-to-medial activation has been found in those with OA and pain and laxity, in similar directions found in the current analysis. Future work could attempt to isolate OA symptoms or correct for influences of symptoms on muscle activation patterns and magnitudes to develop a more concrete link to self-reported instability. However, this study provides preliminary evidence of altered quadriceps activation and increased active stiffness in the OAU group; muscle activation patterns linked to clinical and structural progression OA [207, 208].

The KOS-I has been used to dichotomize OAU and OAS groups, however how this dichotomy is created varies in the literature [27, 28, 89]. This study used the presence instability and how it “slightly, moderately or severely impacts activity” to define an unstable group and those with no instability symptoms to define a stable and ASYM groups. The distinction being the symptoms impact on activity, as this is often a criterion in clinical care. Previous studies have included those who self-reported instability but no

impact on day-to-day activities within a stable group [27, 77]. This dichotomy may be misguided. The question remains; if instability symptoms do not impact activity, are they sensitive to gait alterations and/or merit a health care visit? Other methods have been used to dichotomize instability, where individuals who perceived at least one instability episode within a defined period of time (i.e. 6 weeks, 3 months) were grouped as unstable [74, 79]. This dichotomy does not provide information regarding how the symptom impacts daily function. Historically, findings suggest that altered gait mechanics have associations with knee OA symptoms [133, 187, 202], and if the objective is to investigate if the presence of instability alters gait mechanics, it is essential to understand if sensations of buckling, shifting or giving way impact activity participation.

4.5 CONCLUSION

The findings partially support the hypothesis. Higher and more prolonged quadricep activation was found in the OAU group compared to OAS and ASYM groups and higher and earlier LG activation was found in OAU group compared to the ASYM group only. These findings suggest that during walking self-reported instability impacting activity influences more active stiffness at the knee joint while motion and moment profiles are maintained but could be explained by lower KOOS score subscales and OA symptoms not captured. These findings provide preliminary evidence that the presence of self-reported knee joint instability is linked to increased muscle activation patterns and magnitudes to maintain knee joint function during walking.

CHAPTER 5: WALKING CHALLENGES IN MODERATE KNEE OSTEOARTHRITIS: A BIOMECHANICAL AND NEUROMUSCULAR RESPONSE TO MEDIAL WALKWAY SURFACE TRANSLATIONS

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This manuscript has been modified from its original format to conform to the structure of this thesis

5.1 INTRODUCTION

Sixty to 80% of individuals with knee OA report joint instability, defined by a sensation of buckling, shifting, or giving way of the knee [54, 76]. These sensations have been associated with reduced knee joint function confidence [52] and higher rates of falling [54], which may ultimately limit physical function.

Most often, sensations of instability are felt during walking compared to other dynamic tasks [54]. Previous studies have investigated if gait alterations occur in individuals who self-reported instability compared to those who do not [27, 78, 226]. Individuals with OA who self-reported knee instability walked with greater sagittal plane stance phase range of [27], larger external knee flexion moments [226], and an overall increased sagittal plane motion variability compared to stable groups [78]. Unfortunately, dichotomy exists in explaining these findings. First, strategies may be used to counteract instability, altering the mechanical environment to ensure continued walking [73]. Divergent, alterations found may create an environment where instability is more likely, and

therefore people report this sensation [27]. Regardless, improving knee stability is considered a fundamental component of knee OA management [252]. Currently, predictable gait environments used to investigate knee OA pathomechanics and muscle activation magnitudes and patterns have limited our understanding of instability in the context walking.

Stability is often defined as the way a system behaves following a perturbation, and if the state of that system remains within specific boundaries of control [258]. The interrelationship between osteoligamentous, muscular and neural subsystems is fundamental to joint function, as muscle forces create moments that govern motions to preserve joint stability [66]. Research is limited in knee OA gait to understand biomechanical and muscular responses that occur as a result of walking perturbations [88, 89].

OA gait studies focusing on perturbations during gait have targeted medial and lateral walkway surface translations of different magnitudes, comparing different populations of individuals with knee OA and asymptomatic individuals as well as with varying levels of preparedness from experiencing or visualizing the perturbations prior to testing to completely random and unexpected movements [88, 89, 259, 260]. Commonly, knee muscle activation is elevated, either specifically (i.e. increased medial co-contraction) [89] or generally (elevated gastrocnemius, hamstrings and quadriceps) [88, 260] in response to a perturbation, with knee biomechanical differences, such as knee motion and moments, less consistent [88, 89, 259]. Elevated muscle activation in individuals with

knee OA has been found in addition to altered knee biomechanics, specifically a less dynamic sagittal plane moment in those with OA [31]. This biomechanical feature has been interpreted as a knee stiffening strategy [59] thought to aid in stabilizing the knee joint. With multiple studies reporting elevated muscle activation and increased co-activity as a result of perturbations [88, 89, 260], it is possible that reduced ROM and less dynamic moments could be present as well. To date, understanding whether individuals with knee OA respond differently when compared to an asymptomatic group to unexpected walking surface translations in the medial/lateral direction is lacking.

In the perturbation protocols utilized previously [88, 89], participants were able to either observe [88] or experience the perturbation [89] before testing and the surface translation was in one direction (lateral) at the same magnitude (5.8cm). This methodology does not address the unexpected nature of instability reported by individuals with knee OA. Furthermore, studies [89, 259, 260] often lack a control group and thus it is unknown whether, like Kumar et al. found, how individuals with knee OA respond to unexpected walking surface translations compared to those without [88]. An unclear understanding remains of how individuals with MOA respond to unexpected frontal plane walking challenges. With every step, individuals with medial compartment knee OA are responding to adduction moments that alter medial compartment load [177] and may even induce lateral compartment lift-off [163] with instability often reported during walking. A response to unexpected medial translations may involve mechanical and neuromuscular factors that have implications for understanding how stability may be maintained in this group.

The purpose of this study was to determine how individuals with moderate medial compartment knee OA respond, biomechanically and through altered muscle activation magnitudes and patterns, to unexpected medial walkway surface translations during gait compared to an ASYM control group. As a response to walkway surface translations, compared to the ASYM group, it is hypothesized that individuals with MOA will walk with less sagittal plane knee motion, reduced sagittal plane external knee moment dynamics and elevated and prolonged gastrocnemius, hamstring and quadriceps activation.

5.2 METHODS

5.2.1 PARTICIPANT RECRUITMENT

Individuals with MOA were recruited from local orthopaedic clinics, diagnosed using ACR guidelines [233]. Individuals were classified as MOA using self-reported functional capabilities [61]. Individuals were excluded if they were candidates for TKA. An age-matched, ASYM group was recruited locally, through advertisements and considered a sample of convenience. Participants were included if they were over the age of 50 years, reported no cardiovascular/respiratory disease or neurological disorders and no factures/injury other than a sprain or strain within the last year. The protocol was approved by local ethics review committee (Romeo#:1020825).

5.2.2 DATA COLLECTION

Participants completed the KOS-ADLS and KOOS prior to perturbation testing. Participants changed into fitted shorts, T-shirt and removed footwear. Height, weight, and mid-thigh and mid-shank circumferences were measured. Participants then walked back-and-forth across the GAITRite™ (CIR Systems Inc., USA) pressure sensitive walkway using previously reported methods [236] to acquire self-selected gait speed.
Passive, retro-reflective skin surface markers were affixed to each participant. Rigid clusters (foot, shank, thigh, pelvis, thorax) and individual markers fixed to the lateral aspect of the shoulders below the acromion, spinous process of the 7th cervical vertebra, greater trochanters, lateral/medial femoral and tibial epicondyles, lateral/medial malleoli, head of the 1st and 5th metatarsal, atop the 2nd metatarsal, and posterior heel were placed bilaterally [236]. Virtual points were collected to define sternal notch, and the left and right anterior superior iliac spines. Retro-reflective marker motions were sampled at 100Hz using eight Qualisys® OQUS 500 (Qualisys®, Sweden) motion analysis cameras. GRFs and moments were sampled at 2000Hz from the R-Mill (Motekforce Link, Netherlands) dual-belt instrumented treadmill.

Surface EMG was completed using standard procedures [235]. Skin was shaved and cleaned with alcohol wipes (70% alcohol) and 10mm diameter electrodes (Ag/AgCl, 30mm inter-electrode distance, Red Dot, 3M Health Care, USA) were affixed bilaterally, in a bipolar configuration, over VM, VL, rectus femoris, MH, LH, MG and LG. A reference electrode was affixed to the tibia. Surface EMG was recorded using two AMT-8™ 8-channel EMG systems (input impedance: ~10 GΩ, CMRR: 115dB at 60Hz, band-

pass (10-1000 Hz)) (Bortec Inc., Canada) sampled with GRF at 2000Hz (A/D 16bit, +/ 5V) and synchronized with marker trajectories using Qualisys Track Manager V2.10 (Qualisys®, Sweden).

Participants were harnessed to the ceiling using an upper body system, while walking barefoot on the treadmill, at the speed determined by the GAITRite™. After a 6-minute acclimatization period [236], participants were informed the perturbation protocol would begin. The participants had not witnessed treadmill translation capabilities prior to testing and no practice trials were permitted. The perturbation protocol contained three blocks of eight unexpected, random 1cm and 3cm medial and lateral treadmill surface translations initiated during mid-stance on each leg. This block of eight perturbations was repeated three times. If participants, used handrails or stepped onto the other treadmill belt, the trial was excluded from analysis. Participants were blinded to perturbation occurrence, direction, and magnitude.

After gait testing, a supine resting muscle bias was recorded. A Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc., USA) was used to elicit MVIC. Gravity corrected knee flexor and extensor torque and muscle activation were tested at 45˚of knee flexion [236]. Standing unilateral plantarflexion was also completed [61]. Following one practice contraction, two, 3-second MVIC trials were completed, separated by 40-seconds of rest. Standard verbal encouragement was given.

5.2.3 DATA PROCESSING

Custom programs were written in MatLab™ 2015b (Mathworks Inc., USA). All kinematic data were low-pass filtered (Butterworth 4th order, 6Hz - recursive) and three-dimensional GRFs and moments were low-pass filtered (Butterworth 4th order, 30Hz - recursive) prior to processing. Joint angles were calculated using Cardan/Euler rotations and described as the distal segment moving about a fixed proximal segment [236]. External joint moments were calculated using inverse dynamics [174] and projected onto the joint coordinate system [175]. Moments were low-pass filtered (Butterworth 4th order, 10Hz - recursive) and normalized to body mass (Nm/kg). Raw EMG signals were band-pass filtered (Butterworth 4th order, 10-500Hz - recursive), corrected for resting bias, full-wave rectified, and low-pass filtered (Butterworth 4th order, 6Hz - recursive). EMG gait waveforms were amplitude normalized using the highest 100ms moving average window (99ms overlap) from MVIC trials [61]. Angle and EMG waveforms were time normalized to the gait cycle. Moments were time normalized to stance phase.

5.2.4 DATA ANALYSIS

The most symptomatic leg was chosen for the MOA group, while a random leg was determined for the ASYM group. Three strides preceding each perturbation were ensemble averaged to represent T0. The first stride after the perturbation was obtained to represent the T1. The ICPF and PFLM ranges were calculated from joint motions and the difference from peak knee moment flexion to extension and pKAM were calculated from joint moments, as previously reported [236]. These motion and moment planes have also

been investigated in the context of knee stability [27, 78]. These discrete gait metrics were calculated for statistical analysis.

PCA was used to capture mutually uncorrelated amplitude and temporal EMG waveform features (PPs) that together described at least 90% of data set variability [61]. To analyze the data using PCA, original waveform data were organized into matrix [X] for each muscle group containing T0 and T1 waveforms from participants. A cross-product matrix was computed [S]= [X]'*[X]. An eigenvector decomposition of [S] was completed to yield the eigenvectors (PPs) and eigenvalues [236]. PPs that hierarchically explained the waveform variance (PP1, PP2, etc.) were retained. *PP-scores* were computed for each participant to provide a weighting coefficient relating the PP to each measured waveform. The use of this multivariate statistical technique has been used to understand muscle activation magnitudes and patterns in knee OA gait [61].

5.2.5 STATISTICAL ANALYSIS

Student's t-test was used to determine between groups differences for subject demographics, KOOS scores, strength and walking speed. Assumptions of equal variance and normality were examined using Kolmogorov-Smirnov and Levene's test for continuous variables. If assumptions were violated, data were transformed using a Johnson Transformation. A two-factor, mixed model ANCOVA, adjusting for the effects of walking speed, was used for biomechanical variables to determine between and within group (time) main effects and interactions. For muscle data, a three-factor, mixed model ANCOVA, adjusting for walking speed, was used to determine between and within group

(muscle, time) main effects and interactions. Bonferonni post hoc testing was completed for all significant effects. P-values were adjusted to alpha = 0.05 depending on the number of comparisons. Statistical testing was completed using Minitab™ Ver.17 (Minitab Inc., USA).

5.3 RESULTS

Table 5-1 provides group demographics, anthropometrics, walking speed and self-report survey scores. MOA group KL grade was reported. No significant differences were found in age ($p=0.946$) and height ($p=0.864$) between groups. The MOA group was heavier ($p<0.001$) with a larger BMI ($p<0.001$) and walked with slower speed ($p=0.004$) compared to the ASYM group. The KOS instability question suggests 60% of MOA participants reported this sensation, with 40% reporting it impacted their activity. The MOA group demonstrated worse KOOS ($p<0.001$) scores compared to the ASYM group. No significant between group strength differences were found for knee extensors ($p=0.195$) and flexors ($p=0.067$).

Only medial perturbations were analyzed. On average, the translation occurred at 40% (+/-6%) of stance (i.e. 24% (+/-4%) of the gait cycle). The average translation distance was 31.8mm (+/-0.007mm) at a mean rate of 0.11m/s (+/-0.0029m/s). For all medial 3cm translations experienced, the ASYM group completed 47/60 and the MOA group completed 49/60 without stepping onto the other treadmill belt or using handrails (Table 5-1).

Table 5-1: Means and SD for subject group demographics, gait characteristics, self-report survey outcomes, radiographic grade distribution (MOA only), and strength measures. *indicate significant between-group differences ($p<0.05$).

Variable	**Asymptomatic**	**Moderate OA**
N	20	20
Sex (M:F)	11:9 (55% Female)	10:10 (50% Female)
Age (years)	62 (7)	62 (7)
Height (m)	1.69 (0.08)	1.69 (0.09)
Mass (kg)	67.4 (11.7) *	85.3 (13.9) *
BMI (kg/m²)	23.7 (3.2) *	30.3 (4.5) *
Walking speed (m/s)	1.17 (0.12) *	1.05 (0.14) *
KOS-I	[20] 5	[8]5 - [4]4 - [1]3 - [6]2 - [1]1
Successful Perturbations (n/60)	47	49
KOOS	**--**	**--**
Symptoms (n/100)	97.9 (4.7) *	62.3 (13.9) *
Pain (n/100)	98.6 (3.7) *	64.6 (16.1) *
Activities of Daily Living (n/100)	99.5 (1.6) *	67.2 (22.3) *
Quality of Life (n/100)	97.5 (6.4) *	46.9 (17.7) *
Radiographic Grade (n)	**--**	**--**
KL I	--	6
KL II	--	12
KL III	--	2
KL IV	--	0
Strength	--	--
Knee Extension - 45˚ (Nm)	116.8 (31.8)	129.0 (53.4)
Knee Flexion - 45˚ (Nm)	72.3 (16.9)	75.6 (38.1)

Given the study objective, only outcomes based on perturbation responses are reported (time or time interactions). In both groups, no significant differences in knee biomechanics were found in response to the medial 3cm translation. This included; i) knee ROM between ICPF (p=0.895), ii) ROM between PFLM (p=0.854), iii) sagittal plane moment range, (p=0.325) and iv) pKAM (p=0.338). Sagittal plane motion, moments and frontal plane moments in response to the perturbations are shown on Figure 5-1.

Table 5-2: P-values for biomechanics and EMG ANCOVA models. ***** indicates significant outcomes (p<0.05) that were post-hoc tested. Time main effects and interactions are bolded.

Biomechanics							
Variable	*Group*		*Time*		*Group*Time*		
ICPF	0.064		0.895		0.759		
PFLM	0.010*		0.854		0.647		
SPROM	0.014*		0.325		0.622		
pKAM	0.007*		0.338		0.734		
EMG							
Variable	*Group*	*Time*	*Muscle*	*Group* Time*	*Group* Muscle*	*Muscle* Time*	*Group* Time* Muscle*
Quad PP1	0.168	0.061	<0.001*	0.690	0.965	0.910	0.974
Quad PP2	<0.001*	**<0.001***	<0.001*	0.704	0.825	0.919	0.979
Quad PP3	0.546	**0.003***	0.187	0.309	0.956	0.618	0.884
Ham PP1	0.922	**0.001***	0.275	0.531	<0.001*	0.570	0.634
Ham PP2	0.132	**<0.001***	0.041	0.374	0.183	0.977	0.268
Ham PP3	0.914	0.509	0.626	0.645	0.067	0.416	0.951
Gast PP1	0.580	**0.005***	0.002*	0.942	0.118	0.336	0.741
Gast PP2	0.711	0.691	<0.001*	0.229	0.082	**0.016***	0.328
Gast PP3	0.479	**<0.001***	0.727	0.226	0.243	**0.014***	0.939

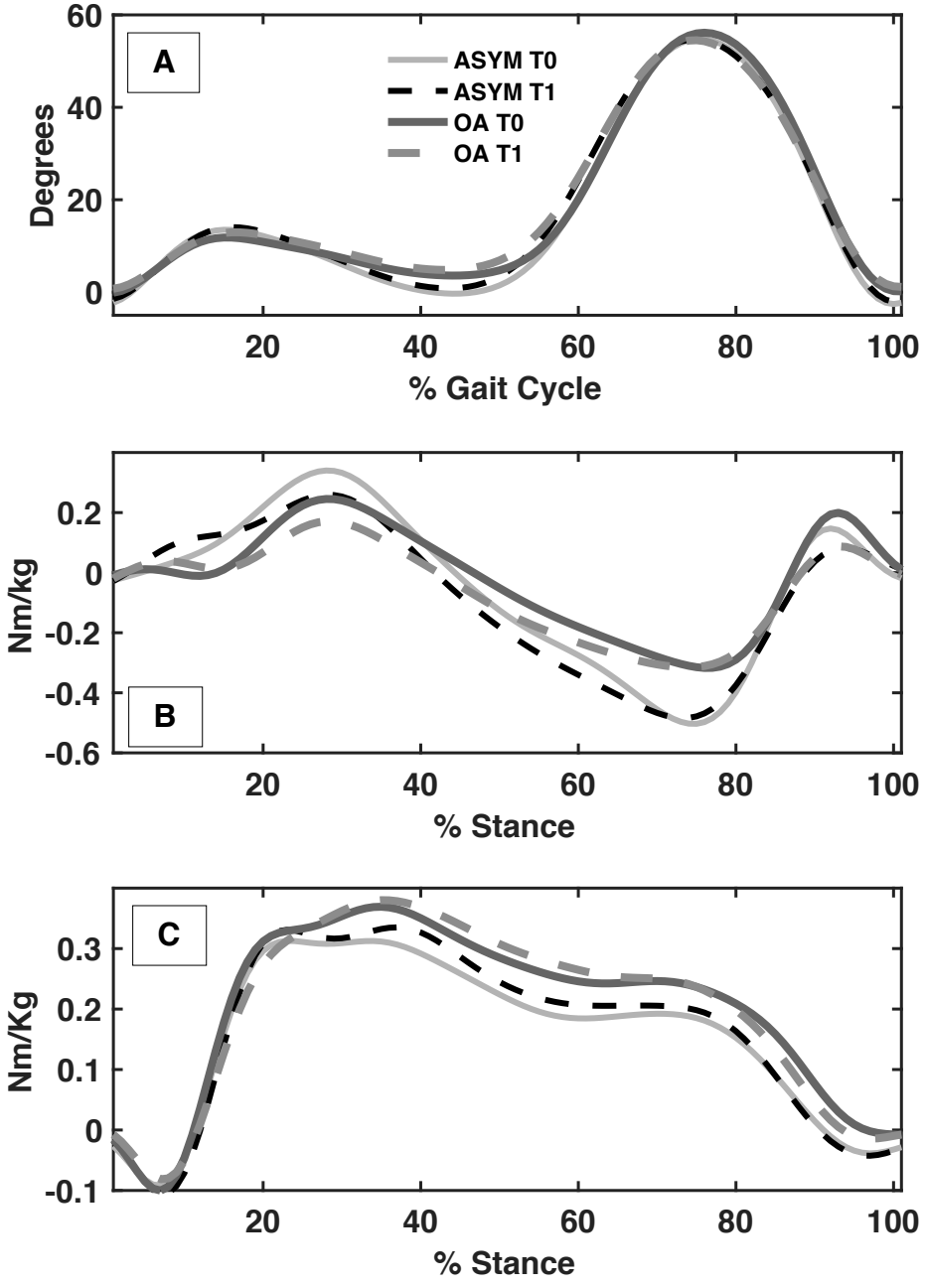

Figure 5-1: (A) Ensemble averaged knee sagittal plane motion time normalized to the gait cycle (B) Ensemble averaged net external sagittal plane knee moment time normalized to stance phase and amplitude normalized to body mass. Positive values indicate a net external flexion moment and negative values indicated external extension moments. (C) Ensemble averaged net external frontal plane knee moment time normalized to stance phase and amplitude normalized to body mass. Positive values indicate a net external adduction moment.

Gastrocnemius EMG, PPs and PP interpretations are found in Figure 5-2. Time effects were evident in gastrocnemius *PP1*-scores (p=0.005). *PP1-scores* were higher at T1 compared to T0. A time-by-muscle interaction was found for *PP3-scores* (p=0.014) where MG *PP3-scores* were higher at T1 compared to T0, while the LG *PP3-scores* were not significantly different at T0 and T1. MG and LG *PP3-scores* were not significantly different between T0 and T1. Higher *PP1-scores* suggest overall gastrocnemius activation amplitudes were increased at T1, whereas PP3 results suggest MG activation increased earlier (i.e. greater early stance activation) with respect later stance in response to the translation.

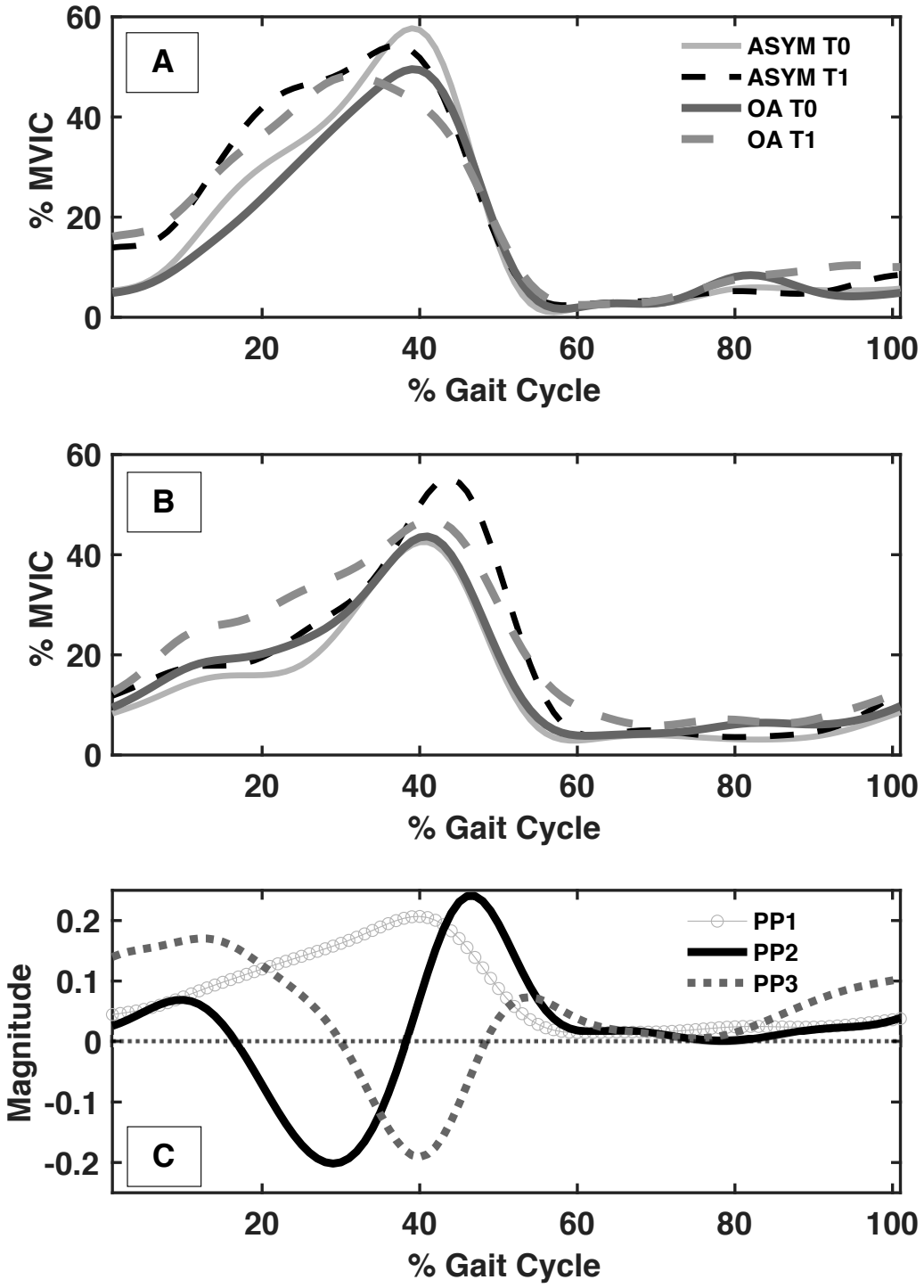

Figure 5-2: Ensemble averaged (A) MG and (B) LG amplitude normalized to % MVIC. (C) Three PPs captured 96% of waveform variability. PP1 captured overall magnitude and shape, explaining 86% of waveform variability. PP2 captures a phase shift in activation where higher scores indicate a delayed activity and explained 6% of waveform variability. PP3 captured a difference operator between early and late stance phase and explained 4% of waveform variability, where higher scores indicate a lower difference.

Figure 5-3 illustrates the hamstring EMG, PPs and PP interpretations. Time main effects were found for hamstring *PP1-scores* ($p=0.001$) and *PP2-scores* ($p<0.001$). LH and MH *PP1-scores* and *PP2-scores* were greater at T1 compared to T0. Higher hamstring *PP1-scores* at T1 suggest higher activation amplitudes over the gait cycle, where higher hamstring *PP2-scores* suggests this activation is prolonged during early stance in response to the translation.

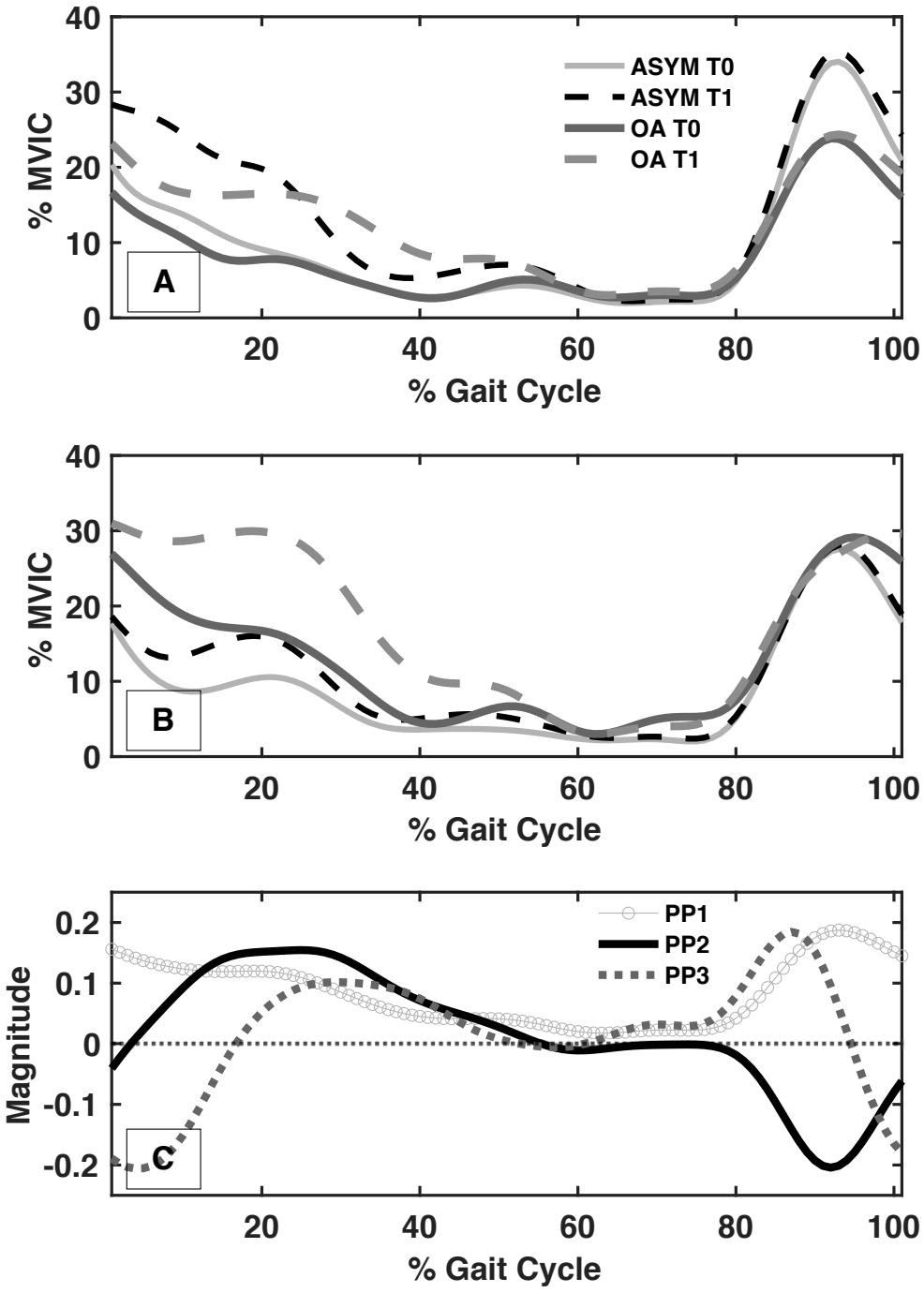

Figure 5-3: Ensemble averaged (A) MH and (B) LH amplitude normalized to % MVIC. (C) Three PPs captured 93% of waveform variability. PP1 captured overall magnitude and shape, explaining 80% of waveform variability. PP2 captures prolonged elevated activation during early stance where higher scores indicate more prolonged activation and explained 9% of waveform variability. PP3 captured a difference between early and late stance activation, where higher scores indicate a greater late stance activity, explaining 4% of waveform variability.

Figure 5-4 illustrates PPs, and PP interpretations and EMG of VL and VM. No significant time effect or time interactions were found for *PP1-scores*. Time main effect was found for quadriceps *PP2-scores* ($p<0.001$) and *PP3-scores* ($p=0.003$). At T1, individuals demonstrate higher *PP2-scores* and lower *PP3-scores*, suggesting the quadriceps activation is less dynamic in response to the translation with greater activation during mid stance (*PP2-scores*) less differential activation between early/mid stance and swing phases (*PP3-scores*).

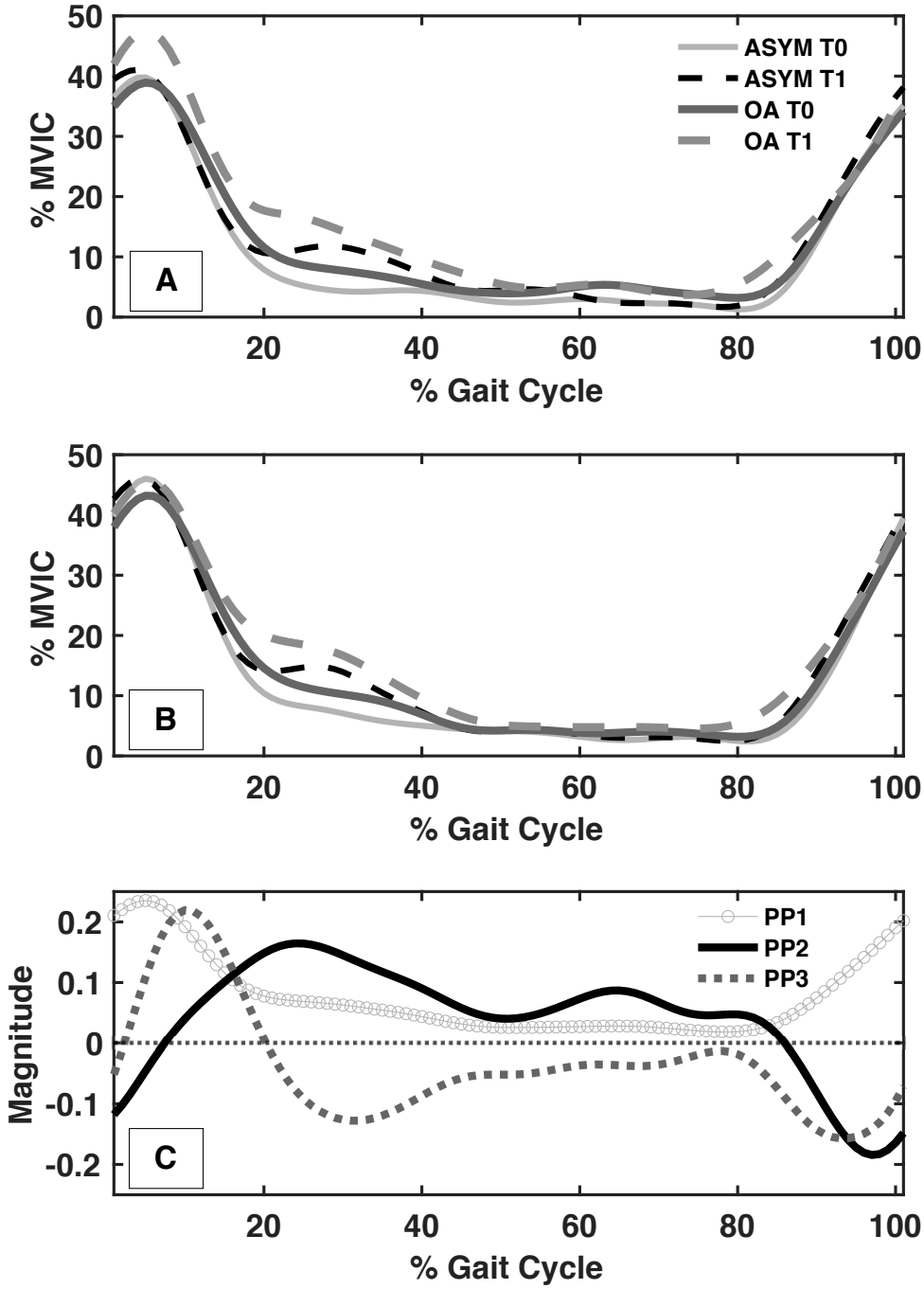

Figure 5-4: Ensemble averaged (A) VM and (B) VL amplitude normalized to % MVIC. (C) Three PPs captured 97% of the waveform variability. PP1 captured overall magnitude and shape explaining 92% of waveform variability. PP2 captured prolonged activation during stance explaining 3% of waveform variability. High PP3-scores captured a greater difference between early-to-mid stance and swing phases, explaining 2% of waveform variability.

5.4 DISCUSSION

Study results do not fully support the hypothesis of reduced sagittal plane motion and moment ranges and elevated and prolonged muscle action across all muscles sites in the MOA group compared to the ASYM group after medial 3cm walkway translations. This study demonstrated no statistically significant biomechanical alterations in both groups between T0 and T1. Altered muscle activations were evident, with elevated activation in hamstrings and gastrocnemius (*PP1-Scores*) and temporal alterations in all muscles (*PP2 and PP3-Scores*) at T1 compared to T0.

Detailed in Table 5-1, the MOA group was heavier, walked slower and self-reported worse KOOS outcomes compared to the ASYM group. The MOA group also demonstrated a median KL-II grade. Kumar et al. reported similar descriptive characteristics of their OA group, reporting more pain, knee related symptoms, and functional restrictions compared to controls, as well as similar radiographic severity (median KL-II grade) [88]. Both Kumar et al. and the present study reported neuromuscular findings that were not statistically different, however, the results contrasted in terms of changes in knee biomechanics as a result of challenged walking. Kumar et al. reported less knee flexion range during the loading responses after a perturbation compared to baseline in both the OA and control groups. The current results suggest no changes in either sagittal plane knee motion metrics, as well as no alterations in the sagittal and frontal plane knee moments. This could be explained by contrasting methods as Kumar et al. used larger (58mm) and faster (0.4m/s) perturbations [88]. A perturbation larger in magnitude, and quicker in speed may provide a larger challenge to

the groups, which could result in contrasting biomechanical alterations with the current work. Despite the smaller perturbations resulting in a lack of biomechanical change, significant changes in knee muscle activation were present.

It was hypothesized that muscle activation alterations would be present in the MOA group compared to the ASYM participants in response to perturbations, as elevated and altered muscle activation has been discussed previously to assist with providing stability during walking in the OA population [61, 88]. The results of this study did not fully support this hypothesis as muscle alterations were present, however, they were not different between the MOA and ASYM groups. Kumar et al. reported a general increase in MVIC normalized, mean loading response muscle activation in medial and lateral quadriceps, hamstring and gastrocnemius. Our response was in a similar direction, with elevated *PP1-scores* found in the hamstring and gastrocnemius, elevated *PP2-scores* found in the quadriceps and hamstrings and altered *PP3-scores* were found in the quadriceps and hamstrings. Elevated *PP1-scores* have been interpreted as increase overall activation, while elevated *PP2-scores* have been interpreted as prolonged activation during stance. Schmitt and Rudolph also demonstrated neuromuscular alterations in response of a perturbation, demonstrating elevated medial co-contraction in combination with no biomechanical alterations [89], supporting the results of our study. This, however, must be taken in light of different muscular normalization strategies and studying a population of OA individuals classified as stable and unstable based on the presence of self-reported instability. The neuromuscular responses demonstrated by both the MOA and ASYM in response to a perturbation are in the direction of the patterns

reported in OA gait literature. Rutherford et al. 2013 reported that quadriceps and hamstrings develop a pattern of elevated and more prolonged activation as the OA disease becomes more radiographically severe [143], suggesting that a response to a perturbation may be related to how individuals with OA walk day-to-day. With the majority of individuals with OA self-reporting sensations of instability [79], it may be that as individuals with OA consistently respond to gait challenges from sensations of buckling, shifting or giving way, that a habitual pattern of elevated and prolonged activation develops to counteract sensations of instability.

Knee instability is self-reported in 60-80% of individuals with OA [79], however it remains unclear how this symptom impacts gait mechanics in moderate and severe OA subpopulations. Given the implications of stability for rehabilitation [252]; understanding how individuals in an early disease state respond to challenges is important. KOS scores specific to instability have not been reported for a MOA group specifically, however the current findings establish that approximately 40% report these symptoms impacting their activity in some manner, slightly less than the general findings of those with OA [79]. During gait however, translating these subjective reports to biomechanical and muscle activation outcomes is less clear, while joint function is altered in the MOA state, these alterations may not have significant impacts on maintaining joint function during gait challenges.

The results from this study need to be interpreted considering certain limitations. The treadmill was translated at its maximum rate and is limited to a distance of 5cm from

midline. Magnitudes of 1 and 3cm were chosen for this study to ensure random perturbations (direction, leg) could be employed. Given the rate and magnitude and perturbations initiated during mid-stance (~40% of stance), there may have been some instances where the treadmill was still moving when the contralateral foot contacted the treadmill. While all perturbations were delivered in single-leg stance, the stimulus for response was standardized, yet we could not control for the response. Secondly, fitness level was not controlled, which may influence one's ability to respond to a perturbation. Less fit individuals may demonstrate altered neuromuscular and/or biomechanical response to perturbations compared to with a higher fitness level. KOOS scores suggest that function was limited in the MOA group, however the perturbation responses were generally the same between groups. Further work to understand how fitness level impacts perturbation responses is warranted. Lastly, not all individuals were able to successfully complete all 3cm perturbations (Table 5-1). The block of perturbations took approximately 24-minutes to complete after a 6-minute warm-up. Each participant completed at least one perturbation successfully. It was not possible to extend testing time on an individual basis to ensure all perturbations were completed. This also impacts the random nature of perturbations.

5.5 CONCLUSION

Both ASYM and MOA groups responded to unexpected medial walkway surface translations, with no biomechanical alterations, and features of elevated and prolonged muscle activation, indicative of a stabilizing strategy. The findings do not suggest OA specific neuromuscular response, but future studies could focus on groups of individuals

who report that instability impacts their functional abilities. Perturbation protocols that challenge stability may have utility in understanding mechanisms of knee OA gait pathomechanics.

5.6 SUPPLEMENTARY DATA

Table 5-3: Mean and SD for significant group main effects. Differing letters denote post hoc significant differences.

Group Main Effects	Asymptomatic	Moderate OA
ICPF (˚)	16 (4) [a]	12 (5) [b]
PFLM (˚)	14 (6) [a]	9 (4) [b]
SPROM (Nm/kg)	0.84 (0.30) [a]	0.59 (0.22) [b]
pKAM (Nm/kg)	0.37 (0.10) [a]	0.41 (0.13) [b]
Quad PP2	-10.48 (24.12) [a]	9.39 (34.1) [b]

Table 5-4: Mean and SD for significant time main effects. Differing letters denote post hoc significant differences.

Time Main Effects	Baseline (T0)	Response (T1)
Quad PP2	-7.47 (31.32) [a]	6.37 (29.38) [b]
Quad PP3	6.52 (26.95) [a]	-4.97 (27.34) [b]
Ham PP1	124.44 (66.28) [a]	160.7 (89.9) [b]
Ham PP2	-25.34 (42.67) [a]	6.63 (61.58) [b]
Gast PP1	212.66 (76.91) [a]	249.38 (86.76) [b]
Gast PP3	-16.76 (39.37) [a]	16.80 (57.10) [b]

Table 5-5: Mean and SD for significant interactions. Differing letters denote post hoc significant differences.

Group-by-Muscle Interaction	Asymptomatic		Moderate OA	
	MH	***LH***	***MH***	***LH***
Ham PP1	153.8 (65.8) [ab]	122.6 (55.2) [a]	119.4 (85.0) [a]	174.5 (99.1) [b]

CHAPTER 6: LANDING ON THE SYMPTOMATIC KNEE AFTER WALKWAY SURFACE TRANSLATIONS OF THE UNAFFECTED LEG: DOES THE NEUROMUSCULAR RESPONSE IN THOSE WITH MODERATE KNEE OSTEOARTHRITIS COMPARE TO AN ASYMPTOMATIC COHORT?

6.1 INTRODUCTION

Knee OA is a chronic joint disease where alterations in joint structures [101] are accompanied by combinations of physical and emotional symptoms [44], encumbering one's ability to participate in activities and reducing quality of life [261]. Knee joint instability, defined as sensations of buckling, shifting or giving was, is a common symptom reported in approximately 60-80% of those with knee OA [54, 74], and 30-60% report that instability impacts their ability to participate in activities [25, 27].

The sensation of buckling, shifting or giving way of the knee joint is a symptom associated with reduced knee joint confidence [52] and an increased fear of falling [50]. These psychosocial outcomes cause individuals with knee OA and instability to limit their activity because of knee instability concerns [50]. Reduced confidence and increased walking difficulties associated with knee OA and instability [27, 52] influences activity limitations, independent of muscle weakness and knee pain [79], causing poor joint and overall health outcomes [13, 14].

To begin to understand the role instability plays in altered knee OA walking patterns, it is important to see how individuals respond to challenged walking environments. This concept is substantiated by a definition of stability, stating that stability is the way a system behaves following a perturbation, and if the state of that system remains within

specific boundaries of control [258]. In essence, this response could be a result of a direct perturbation, for instance an external walkway surface translation while the symptomatic limb is on the walking surface, as tested previously [88, 89, 251]. These studies used differing magnitudes, directions, and levels of preparedness, yet all three studies reported elevated or prolonged muscle activation or co-activation in response to a perturbation and all study groups responded in the same direction [88, 89, 251]. Kumar et al. reported decreased stance phase ROM in both groups [88], while Schmitt et al. and Chapter 5 findings found no alterations to biomechanics in both groups [89, 251]. These findings suggest either; (1) a stabilizing strategy of increased active stiffness of knee musculature is found to maintain function after a direct perturbation, however this response does not seem to differ between those with a knee OA and instability that impacts function, knee OA and/or asymptomatic groups and (2) medial/lateral movements to the surface when the symptomatic knee is on the ground may not be an adequate challenge to elicit an altered response.

Alternatively, external translations could occur to the walking surface under the contralateral foot (asymptomatic limb); an indirect perturbation where individuals need to respond by stepping onto their symptomatic leg. The response step to a direct perturbation is completed by the contralateral knee [88, 89, 251], where an indirect perturbation, the potentially more challenging response step is completed by the symptomatic knee. To date, literature on an indirect perturbation environment was not found, despite the large percentage of people with knee OA reporting poor confidence in their OA knee [52]. The previous literature shows that groups of healthy participants and

individuals with knee OA respond to direct perturbations in ways that were not statistically different when investigating knee biomechanics and muscle activation outcomes [88, 89, 251], however, these results occur after the contralateral leg has initially responded to the perturbation. The presence of OA symptoms results in reduced confidence [52], movement avoidance and generalized deconditioning [262], thus how individuals with OA are able to respond to gait perturbations and landing on their symptomatic limb is a novel approach and may provide information on how they might maintain function.

The study's purpose was to determine if altered knee joint angles and muscle activation magnitudes and patterns are found in those with MOA compared to an ASYM group after an indirect perturbation. It was hypothesized that individuals with knee OA will respond with less sagittal and frontal plane ROM, and elevated and prolonged quadriceps, hamstrings and gastrocnemius muscle activation patterns on the symptomatic limb compared to a random leg of the ASYM group.

6.2 METHODOLOGY

6.2.1 PARTICIPANT RECRUITMENT

Using local orthopedic clinics, individuals with moderate unilateral, medial compartment knee OA were recruited. Participants were diagnosed using ACR guidelines [233], were not candidates for a TKA and self-reported functional criteria for moderate disease severity previously published [61]. Standard anterior-posterior radiographs were obtained and scored by a single, experienced orthopaedic surgeon using the KL ordinal

scale [68]. An age-matched, ASYM group, reporting no history of musculoskeletal injury or disease, was recruited using local advertising. The study excluded participants under the age of 50, reporting cardiovascular and/or respiratory disease, neurological disorders, fracture and/or injuries other than sprain or strain within one year and the inability to walk continuously for 30 minutes. The protocol was approved by the local ethics review board (Romeo: 1020825 and 1025007).

6.2.2 DATA COLLECTION

Participants gave informed consent and completed KOS-ADLS [224] and KOOS [234] prior to testing. Height, weight, and limb segment circumference was recorded and self-selected walking speed was determined as an average of 5 random trials as participants walked back-and-forth across GaitRITE™ pressure sensitive walkway (CIR Systems Inc., USA) [236]. Consistent with guidelines [235] and standard SENIAM procedures, participants were prepared for surface EMG. Skin was shaved and wiped with 70% alcohol. Bilaterally, over the VM, VL, MH, LH, MG and LG, Ag/AgCl surface electrodes (10mm diameter, 30mm inter-electrode distance, Red Dot, 3M Health Care, USA) were placed in a bipolar configuration in line with muscle fiber orientation. A reference electrode was placed on the tibial shaft and muscle palpation and isometric muscle testing verified placement position, signal validation and gain adjustments. EMG signals were pre-amplified (500x) the further amplified using two AMT-8 8-channel measurement systems (CMRR: 115dB at 60Hz, Input Impedance: ~10GΩ, band-pass: 10-1000Hz, Bortec Inc., Canada).

For motion capture, individual markers were placed on anatomical landmarks and rigid, 4-marker clusters were placed on the foot, shank, thigh, pelvis, and thorax using adhesive tape and Velcro straps [239]. A 3-marker clusters was affixed to the treadmill surface to capture medial-lateral treadmill movement during walking surface translations. Virtual point trials defined the sternal notch and left and right anterior superior iliac spines. Eight OQUS 500 (Qualisys®, Sweden) motion analysis cameras tracked marker motion at 100Hz.

Participants walked barefoot, at a self-selected speed calculated by the GaitRITE™ on a dual-belt instrumented treadmill (R-MILL, Motekforce Link, The Netherlands) while attached to a ceiling bracket with an upper body harness. GRF and EMG were sampled at 2000Hz (A/D 16bit, +/ 5V) and synchronized with marker trajectories using Qualisys Track Manager 2.10 (Qualisys®, Sweden). After a 6-minutes of walking [236], participants were advised that a series of perturbations would occur. A standardized perturbation protocol was followed [251], where participants experienced 8 unexpected walkway surface translations of different magnitudes (1cm/3cm), directions (medial/lateral) on each leg (left/right) in 3 repeated blocks. The walkway surface translations occurred randomly, triggered when the contralateral foot toed-off (GRF > 50N), and with the treadmill translating at a rate of 0.1m/s. If individuals used handrails or stepped onto the opposite treadmill belt, the trial was excluded from analysis. Participants were blinded to perturbation occurrence, magnitude and direction.

A supine resting muscle bias was collected after treadmill testing and a Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc., USA) was used to complete MVIC knee extensor and flexor exercises for EMG normalization and strength assessments. Participants were given one practice contraction before completing two, 3s gravity corrected MVICs at 45˚ of knee flexion aligning the knee joint and dynamometer axis. Trials were separated by 40-seconds of rest. Standing unilateral planter flexion exercises were completed for gastrocnemius normalization [61]. Standard verbal encouragement was provided for each exercise.

6.2.3 DATA PROCESSING

Custom MatLab™ 2015b processing scripts were used (The MathWorks Inc., USA). Marker trajectories were filtered (recursive, 6Hz, lowpass, 4^{th} order Butterworth) and pelvis, thigh, shank and foot bone embedded coordinate systems were calculated. Knee joint angles were calculated using Cardan/Euler rotations in a flexion/extension, adduction/abduction, internal/external rotation sequence [175]. Flexion, adduction and internal rotation are described as positive motion, with the distal segment moving about a fixed proximal segment [236]. Raw EMG was filtered (10-500Hz, bandpass, 4^{th} order Butterworth), corrected for resting bias, full-wave rectified, linear enveloped (recursive, 6Hz, lowpass, 4^{th} order Butterworth) and amplitude normalized to the highest moving average window (99ms overlap) of MVIC trials [61]. Motion and EMG were time normalized to the gait cycle, beginning and ending with heel-strike. Maximal knee flexion and extension torque was determined as the highest moving average window (500ms overlapping) during MVIC trials and amplitude normalized to body mass.

6.2.4 DATA ANALYSIS

The perturbations selected for analysis were indirect medial 3cm perturbations where the contralateral limb was translated, and the symptomatic leg was the landing leg. All participants experienced this perturbation three times. Three strides preceding the walkway translation were ensemble averaged to represent T0 and the first stride after the walkway surface translation was represented as T1 [251]. Discrete metrics from sagittal plane (ICPF, PFLM) and frontal plane (ICKAA) were calculated and used for statistical testing. PCA, a technique that captures unbiased amplitude and temporal waveform features [263] was applied to EMG waveforms. Three separate PCA models were calculated for the quadriceps, hamstring and gastrocnemius using ensemble averaged, time normalized medial and lateral muscle with T0 and T1 waveforms forming individual matrices (X). A cross product matrix was calculated ($[S]=[X^T]*[X]$) followed by an eigenvector decomposition of S creating a transform matrix (T) containing eigenvectors of the PPs and with a trace of associated variances. Three PPs, explaining at least 90% of variability were selected and *PP-scores* were calculated. *PP-scores* provide a weighting coefficient for how each individual waveform resembles the PP. PCA methods have been published previously in greater detail [61], demonstrate reliability in a knee OA population [173] and are commonly used to understand direction and patterns of muscle that occur in the dataset [264].

6.2.5 STATISTICAL ANALYSIS

All statistical procedures were completed in Minitab™ Ver. 18 (Minitab Inc., USA). Kolmogorov-Smirnov and Levene's test established normality and equal variance. Non-normal and/or data with unequal variance was corrected using a Johnson Transformation. Student's t-tests were used to determine demographic, KOOS subset, walking speed and strength group differences. A two-factor, mixed model ANCOVA, adjusting for walking speed, was used to determine between and within group (time) main effects and interactions. A three-factor, mixed model ANCOVA, with walking speed as a covariate, was used to determine between and within group (muscle, time) main effects and interactions. Bonferroni post-hoc testing was used on significant effects, adjusting significance (alpha = 0.05) for multiple pair-wise comparisons.

6.3 RESULTS

Thirty-four individuals with MOA and 46 ASYM individuals were recruited for the study. Two participants from each group (n=4) did not successfully complete the required walkway translation, either crossing onto the other plate or using handrails on each attempt and therefore were excluded from analysis. Thirty-two individuals with MOA and 44 ASYM individuals completed the protocol, with at least one successful perturbation response.

Table 6-1: Mean and SD participant demographics, walking speed, self-report scores, knee joint strength and radiographic scores. Differing letters denote significant difference.

	Asymptomatic	**Moderate OA**
N	44	32
Sex (M:F)	22:22 (50% Female)	16:16 (50% Female)
Age (years)	61 (7)	61 (6)
Height (m)	1.68 (0.08)	1.68 (0.10)
Mass (kg)	70.7 (13.1) [a]	86.1 (13.7) [b]
BMI (kg/m^2)	25.0 (3.3) [a]	30.4 (4.4) [b]
Walking Speed (m/s)	1.16 (0.12) [a]	1.06 (0.13) [b]
KOS-I	5 [42] - 4 [2]	5[12] - 4[6] - 3[5] - 2[8] - 1[1]
KOOS	**--**	**--**
Symptoms (n/100)	97.7 (4.3) [a]	60.5 (14.3) [b]
Pain (n/100)	98.5 (3.5) [a]	63.6 (16.0) [b]
Activities of Daily Living (n/100)	99.5 (1.2) [a]	69.0 (19.8) [b]
Quality of Life (n/100)	97.2 (5.8) [a]	46.3 (18.2) [b]
Radiographic Scores	**--**	**--**
KLI	--	7
KLII	--	13
KLIII	--	2
KLIV	--	0
Not Rated	--	10 **
Knee Extension – 45˚ (Nm/kg)	1.87 (0.54)	1.81 (0.59)
Knee Flexion – 45˚ (Nm/kg)	1.12 (0.26)	0.98 (0.33)

** Access to radiographs was unavailable due to ongoing COViD-19 health crisis.

Group means for descriptive data and MOA KL-grades are found in Table 6-1. The MOA and ASYM age, height, knee extension and flexion strength were not significantly different ($p>0.05$). The MOA group had a larger mass and BMI ($p<0.001$), slower walking speed ($p=0.001$) and worse scores for all KOOS subsets ($p<0.001$). The median radiographic grade for the MOA group was KL II. Based on the KOS-I, 63% of those with MOA report sensations of knee instability and 44% reported instability impacts activities. Only 5% of the ASYM group reported sensations of knee instability.

Table 6-2: Mean and SD for significant group main effects. Differing letters denote post hoc significant differences.

Group Main Effects	Asymptomatic	Moderate OA
ICPF	14 (4) [a]	12 (5) [b]
PFLM	12 (6) [a]	10 (4) [b]
ICKAA	2 (2) [a]	3 (2) [b]
Quad PP1	146.7 (93.0) [a]	199.5 (99.1) [b]
Quad PP2	-8.5 (33.8) [a]	5.7 (32.1) [b]

Mean and SD for significant group main effects (Table 6-2), time main effects (Table 6-3) and interactions (Table 6-4) are display in respective tables. Group main effects were demonstrated between the ASYM and MOA group, where the MOA group walked with less ICPF ($p=0.008$), PFLM ($p=0.002$), and ICKAA ($p=0.004$) ROM (Table 6-2). No significant time main effects or interactions were found for any joint motion outcome variables.

Table 6-3: Mean and SD for significant time main effects. Differing letters denote post hoc significant differences.

Time Main Effects	Baseline (T0)	Response (T1)
Quad PP1	151.9 (85.6) [a]	185.9 (105.1) [b]
Quad PP2	-11.8 (27.2) [a]	6.8 (37.6) [b]
Ham PP1	120.2 (80.0) [a]	162.2 (96.6) [b]
Ham PP2	-21.4 (43.8) [a]	5.0 (47.2) [b]
Gast PP1	193.3 (80.4) [a]	222.3 (89.7) [b]
Gast PP2	-21.3 (47.1) [a]	22.8 (55.3) [b]
Gast PP3	16.1 (38.9) [a]	-9.8 (48.6) [b]

Quadricep ensemble average waveforms, PPs, and PP-interpretations are found in Figure 6-1. Significant group main effects for quadriceps *PP1-* and *PP2-scores* (Table 6-2) were found, where higher scores were reported in the MOA group compared to the ASYM group. A time main effect (Table 6-3) was found for *PP1-* and *PP2-scores*, where higher scores were found at T1 compared to T0.

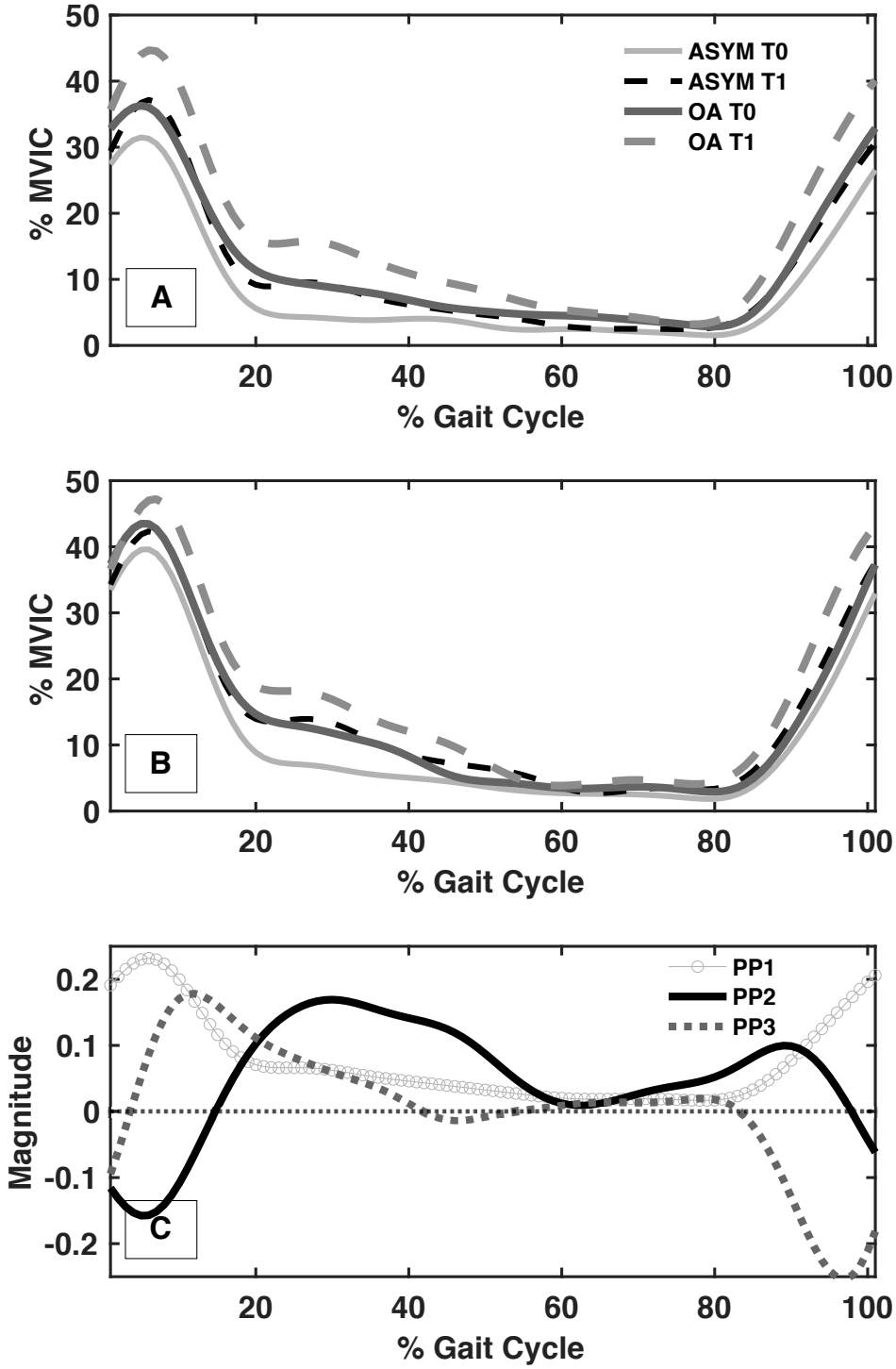

Figure 6-1: Ensemble averaged (A) VM and (B) VL amplitude normalized to % MVIC. (C) Three PPs captured 95% of the waveform variability. PP1 captured overall magnitude and shape explaining 90% of waveform variability. PP2 captured prolonged activation during stance explaining 3% of waveform variability. High PP3-scores captured a greater difference between early-to-mid stance and swing phases, explaining 2% of waveform variability.

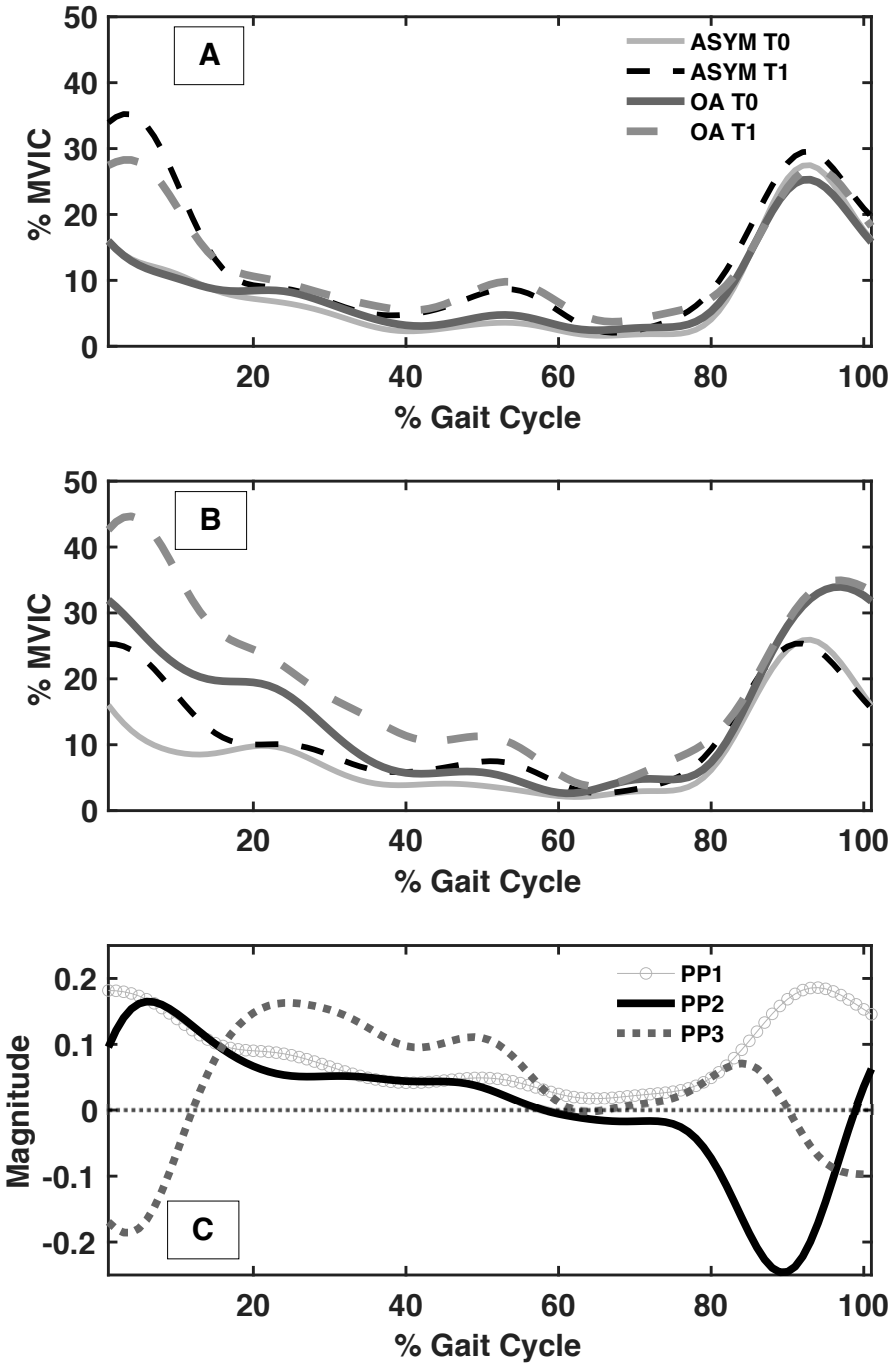

Figure 6-2: Ensemble averaged (A) MH and (B) LH amplitude normalized to % MVIC. (C) Three PPs captured 93% of waveform variability. PP1 captured overall magnitude and shape, explaining 82% of waveform variability. PP2 captures prolonged elevated activation during early stance where higher scores indicate more prolonged activation and explained 7% of waveform variability. PP3 captured a difference between early and late stance activation, where higher scores indicate a greater late stance activity, explaining 4% of waveform variability.

Hamstring ensemble average waveforms, PPs, and PP-interpretations are found in Figure 6-2. Group-by-muscle interactions (Table 6-4) were found ($p<0.05$) for *PP1-* and *PP2-scores* of the hamstrings, with MOA LH demonstrating higher *PP1-* and *PP2-scores* compared to MOA MH and ASYM LH and MH.

Table 6-4: Mean and SD for significant interactions. Differing letters denote post hoc significant differences.

Group-by-Muscle Interaction	**Asymptomatic**		**Moderate OA**	
	MH	***LH***	***MH***	***LH***
Ham PP1	132.4 (74.5) [a]	119.9 (67.5) [a]	124.8 (70.4) [a]	199.4 (128.3) [b]
Ham PP2	-11.3 (36.0) [a]	-16.2 (41.1) [a]	-15.2 (36.1) [a]	14.1 (66.8) [b]
	MG	***LG***	***MG***	***LG***
Gast PP1	235.1 (83.4) [a]	162.7 (72.0) [b]	230.3 (93.5) [a]	209.7 (79.3) [a]
Gast PP3	-11.1 (55.0) [a]	14.1 (30.1) [b]	5.3 (48.7) [ab]	5.4 (45.7) [ab]

Time main effects (Table 6-3) were found with higher hamstring *PP1-* and *PP2-scores* at T1 compared to T0 ($p<0.05$).

Quadricep ensemble average waveforms, PPs, and PP-interpretations are found in Figure 6-3. Significant group-by-muscle interaction ($p<0.05$) were found for gastrocnemius *PP1-* and *PP3-Scores*. ASYM LG *PP1-Scores* were lower than ASYM MG, while OA LG and MG scores were not statistically different. OA LG, MG and ASYM MG *PP1-Scores* were not statistically different, however; ASYM LG *PP3-Scores* were higher than MG, while no significant differences were reported between OA LG and MG. Time main effects were found with higher gastrocnemius *PP1-* and *PP2-scores* and lower *PP3-scores* at T1 compared to T0.

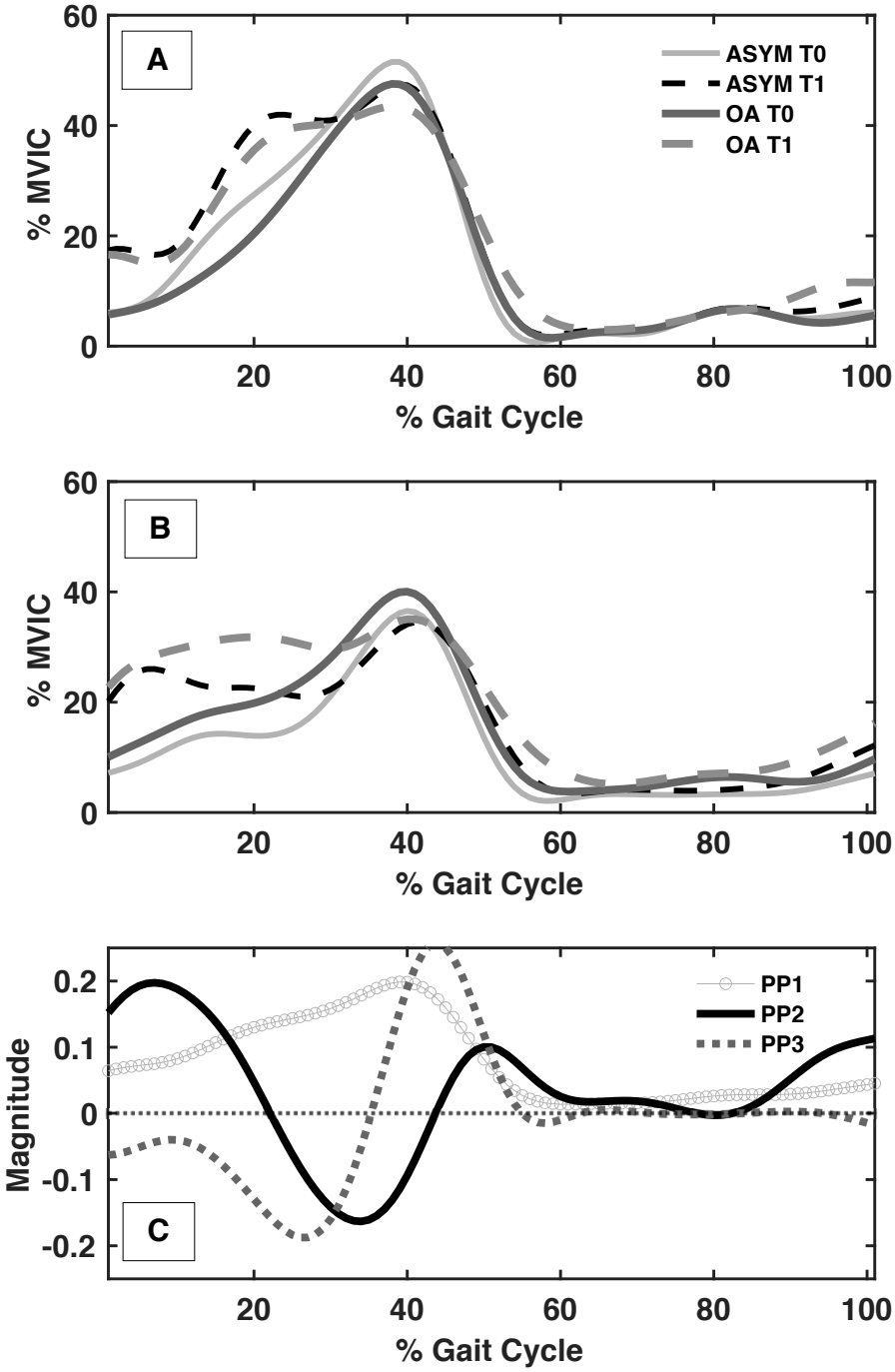

Figure 6-3: Ensemble averaged (A) MG and (B) LG amplitude normalized to %MVIC. (C) Three PPs captured 97% of waveform variability. PP1 captured overall magnitude and shape, explaining 85% of waveform variability. PP2 captured a difference operator between early and late stance phase and explained 5% of waveform variability, where higher scores indicate a lower difference. PP3 captured a phase shift in activation where higher scores indicate a delayed peak activity and explained 4% of waveform variability.

6.4 DISCUSSION

The purpose of this study was to determine if altered sagittal and frontal plane joint angles and muscle activation magnitudes and patterns are found between MOA and ASYM groups while landing on the symptomatic knee in response to indirect medial 3cm walkway surface translation. This was the first study to examine indirect perturbations in those with knee OA and in contrast to our hypothesis both groups responded with no changes in knee joint angles but with elevated and more constant quadriceps, hamstring and gastrocnemius activation, and earlier gastrocnemius activation. Collectively these muscle activation responses are consistent with providing active stiffness to the knee joint to maintain movement patterns.

The groups were well matched with respect to sex and age although the MOA group was heavier, walked slower and reported lower scores on all KOOS subsets compared to the ASYM cohort [140]. 63% of the MOA sample self-reported sensations of knee instability were present, and 44% reported that this symptom impacted their activities, similar to distributions in OA literature [27]. Group main effects found the MOA group walked with less sagittal plane ROM during stance (ICPF/PFLM), more frontal plane ROM, recruited VL, VM, LH and LG to higher percentages of maximal effort activation and VL, VM, LH activation was prolonged in baseline walking. Lower ranges of ICPF and PFLM motion, and increased muscle activation magnitudes and patterns at the knee have been interpreted as a knee stiffening/stabilizing strategy to counteract instability [43, 60, 61, 73, 90], but have also been found in those experiencing various OA symptoms [30, 43, 71-73]. These elevated and prolonged muscle activation patterns during baseline

walking activation would suggest that in order to respond, using evidence from direct perturbations [88, 89, 251], patterns of activation must be elevated even further to maintain knee joint function.

Landing on the symptomatic leg, directly after a medial 3cm surface translation to the contralateral leg, resulted in no group-by-time interactions. However, time main effects demonstrated both OA and ASYM groups responded with no statistical sagittal and frontal plane joint angles differences and higher (*PP1-Scores*) and more constant (*PP2-Scores*) quadriceps, hamstring and gastrocnemius activation and earlier peak gastrocnemius (*PP3-Scores*) activation. No group-by-time interactions were found, but using MDC's in Appendix A, there may be evidence of higher LH response in the MOA group. A mean change of 48.8 and 34.5 units was found in the MOA group *PP1-* and *PP2-scores*, respectively, compared to 27.3 and 19.3 units in the ASYM group. Appendix A, MDC's for LH *PP1-* and *PP2-scores* were 38.4 and 22.6. This suggests 1) the MOA group demonstrated a meaningful activation change, while the ASYM group remained the same and 2) there may be sample power issues in detecting group-by-time interactions. If in fact the MOA group is responding to indirect challenges with elevated and prolonged LH activation, this increased active stiffness in the landing leg may be an attempt to unload painful tissues, maintain excessive joint motion and/or maintain joint stability.

Based on the statistical findings, both groups responded in a similar direction, more specifically, the perturbation response of elevated and prolonged activation is consistent

with literature investigating knee OA and walking cross-sectionally [30, 43, 61, 71-73]. This suggests that individuals with early knee OA may be responding to internal perturbations (i.e. passive or neuromuscular alterations, instability, pain, laxity, etc.) that are adapted into walking patterns, found in moderate and severe OA, as they progress through the disease [43, 61, 143, 200, 202, 206]. Both ASYM and MOA groups however, we able to maintain balance and continue walking, demonstrating an adequate level of functional performance both the MOA and ASYM groups. Both groups had the capacity to increase muscle activation magnitudes and patterns to higher percentages of maximal effort activation, however with higher baseline muscle activation in the MOA group, it remains to be determined the impact this may have on the joint. Studies have suggested the role of activation and co-activation on joint loading and joint structural changes [63, 207, 265, 266], and it may be that a relationship exist, similar to those discussed between pKAM and cartilage thickness [132], where higher muscle activation or co-activation in the OA groups has detrimental effects on joint structures [63, 207, 265, 266].

The novel aspect of this study was an indirect perturbation methodology. Direct perturbations challenge the symptomatic limb and monitor the subsequent strides of the symptomatic limb (Objective 2a) [88, 89, 251]. Studies utilizing direct perturbations have not fully discussed the potential mechanism of this type of perturbation. In Chapter 5, it is suggested that medial translation to the symptomatic limb mimic OA movement patterns, where the knee joint moves towards adduction. This movement may compress the medial compartment and induce “lift-off” of the lateral compartment, but data is unavailable to support this theory. However, it remains unclear whether the challenge in direct

perturbations is the translation of the symptomatic joint when it's on the ground or completed by the asymptomatic leg in being landing leg after the translation occurs. Regardless, medial 3cm walkway surface translations, either to the symptomatic (direct) or asymptomatic limb (indirect), cause a brief unalignment of the body's centre of mass and centre of pressure, in which the initial attempt to regain control and maintain walking is the landing leg and subsequent strides attempt to continue walking and maintain joint function [84].

The study results need to be interpreted considering limitations. First, a lack of power to detect group-by-time interactions despite larger sample sizes may be present. Appendix A provides MDC values for PCA outcomes, suggesting some outcome variables exceeded MDC in response to perturbations. Second, knee joint moments were collected with methods published previously, however, due to the magnitude and rate of translation there were instances where the treadmill was still translating when the study limb contacted the ground. Joint moments would have provided a more comprehensive understanding of how joint loads were controlled, or if groups differed. Joint moments may provide evidence to discern loading characteristics between indirect and direct perturbations and discern a potential mechanism for increase muscle activation magnitudes and patterns found.

6.5 CONCLUSION

In comparison to pre-perturbation walking, both MOA and ASYM groups responded to medial 3cm indirect perturbations with elevated and prolonged quadriceps, hamstring,

and gastrocnemius muscle activation with the landing leg. No significant changes to knee biomechanics were found. Overall, the MOA group worked at a higher percentage of their maximum voluntary activation than the ASYM group and hence a potential difference in their capacity to respond.

CHAPTER 7: PEOPLE WITH KNEE OSTEOARTHRITIS AND SELF-REPORTED INSTABILITY HAVE SIMILAR BIOMECHANICAL AND NEUROMUSCULAR RESPONSES TO MEDIAL WALKWAY TRANSLATIONS COMPARED TO OSTEOARTHRITIS AND ASYMPTOMATIC GROUP REPORTING NO INSTABILITY

7.1 INTRODUCTION

Knee OA is highly debilitating [1] and can disrupt how individuals' participate in activities of daily living [267]. Many individuals with knee OA report a lack of confidence in their knee [52], predictive of functional decline [53]. Poor knee confidence is associated self-reported knee instability, where 30-60% of individuals with knee OA self-report that this symptom impacts daily activities [25-27]. Sensations of instability are most often felt during walking [54] and have been associated with walking difficulties and gait alterations, independent of varus alignment, knee extensor strength and knee joint laxity [27, 77].

Self-reported knee instability has been defined as the sensation of buckling, shifting or giving way of the knee joint [25]. The KOS-ADLS contains a question addressing how this symptom impacts activities [224]. This question is measured on a 6-point Likert scale from 5 (no instability) to 0 (instability prevents all activity) and has been used to understand instability in knee OA [26-28, 89]. This thesis, and previous studies have tried to understand gait mechanics and neuromuscular patterns in individuals with knee OA reporting instability [27, 77, 78, 226]. The analysis in Chapter 4, found OAU medial and lateral quadriceps muscle sites were recruited to higher percentage of maximum and prolonged into the stance phase compared to the OAS and ASYM participants. This

suggests, that the OAU during baseline walking are require higher baseline muscle activation to maintain joint function. The question remains, do those with OA and self-reported instability impacting activity have the capacity to increase muscle activation patterns during challenged walking to maintain function, or is a different strategy used based the increased OA symptoms reporting previously in this group (i.e. instability, pain, laxity, muscle weakness, etc.) [73, 76, 79, 216].

Research understanding biomechanical and neuromuscular responses that result from walking perturbations in those with knee OA and asymptomatic groups is limited (Chapter 5 and 6) [88]. These studies have targeted walkway surface translations of different magnitudes, directions and legs, with various degrees of preparedness. However, all studies have reported elevated quadricep, hamstring and gastrocnemius muscle activation in response to the translation, with no statistical differences between how the OA and asymptomatic groups responded (Chapter 5 and 6) [88]. A prevalence of individuals who may or may not report problems with instability likely exist in these OA samples. In fact, these studies report between 40-44% of these samples report sensations of knee instability impacting activity (Chapter 5 and 6) [88]. Stable and unstable groups may have different strategies to maintain joint function, therefore, to understand how these subgroups respond to perturbations, a dichotomized approach should be implemented.

One study has a challenged walking paradigm and dichotomized OA groups into stable and unstable cohorts using the KOS-I [89]. Schmitt and Rudolph found no differences in

sagittal or frontal plane stance phase ROM between unstable and stable groups, but with elevated stance phase medial quadriceps-hamstring and quadriceps-gastrocnemius co-activation in response to the lateral translation [89]. This study also reported higher medial quadriceps-hamstring activation in preparation for lateral translation, which may be influenced by methodology [89]. This paper provides preliminary evidence of a different strategy between stable and unstable groups within a challenged walking paradigm and concluded that the unstable groups use an ineffective stabilization strategy [89], but study limitations provide a few gaps that the current analyses will attempt to address. The moveable platform utilized in this study only translated in one direction (lateral), and participants were able to perform several practices trials, removing the unexpected nature of these challenges. Furthermore, this study lacked a control group, and we are unable to discern how these responses differ from asymptomatic knees. Finally, technological advancements over the past decade have introduced dual-belt treadmills with instrumented forces plates to understand the pathomechanics used to maintain joint function in a challenged walking paradigm.

The purpose of this preliminary analysis was to determine if differences between MOA participants dichotomized using self-reported presence of instability impacting activity and those with MOA and ASYM groups with no instability are present in sagittal and frontal plane knee joint motions and moments, and quadricep, hamstring, and gastrocnemius muscle activation patterns in response to direct medial 3cm midstance walking surface perturbations. It was hypothesized that individuals with knee OA and instability will demonstrate elevated and prolonged muscle activation and reduced

sagittal plane motion and moment ranges compared to knee OA and ASYM groups with no instability.

7.2 METHODOLOGY

7.2.1 PARTICIPANT RECRUITMENT

Individuals with unilateral, symptomatic medial compartment knee OA were recruited, referred from local orthopedic clinics and diagnosed using the ACR guidelines [233]. Those with clinically moderate disease severity were recruited, defined as individuals who are not candidates for TKA and self-reported their ability to jog five meters, walk a city block and climb stairs in a reciprocal fashion [61]. Standard anterior-posterior radiographs were obtained and scored using the KL ordinal radiographic scale [68]. An ASYM group was recruited through local advertisements as a sample of convenience. These participants reported no lower extremity pain or history of injury or disease. Participants from all groups were excluded if they were under the age of 50, reported cardiovascular/respiratory disease, neurological disorders, fractures/injury other than sprain or strain within the last year, or the inability to walk from 30 minutes continuously. The local ethics review board approved the research protocol (Romeo #: 1020825 and 1025007).

7.2.2 DATA COLLECTION

All individuals completed the KOOS and KOS-ALDS self-report surveys prior to walking. Individuals changed into fitted shorts, t-shirt and removed shoes and anthropometrics were measured. Self-selected walking speed was capture using a

GaitRITE™ (CIR Systems Inc., USA) pressure sensitive walkway using standard procedures [236]. Surface EMG standardized guidelines were followed [235]. Skin was shaved and wiped with 70% alcohol pads. Surface electrodes (Ag/AgCl, 10mm diameter, 20mm inter-electrode distance, Red Dot, 3M Health Care, USA) were positioned bilaterally, over the MG, LG, MH, LH, VM and VL in a bipolar configuration. Locations were verified using palpation and isometric muscle contractions. A reference electrode was placed on the tibial shaft.

Passive, retro-reflective rigid marker clusters and individual markers were attached using Velcro straps and adhesive tape using previously defined anatomical landmarks [239]. The sternal notch and right and left anterior superior iliac spines were defined using collected virtual point trials. Three markers were affixed to the walking surface to track treadmill movement.

A ceiling bracket and an upper body harness was used for safety measures as individuals walked barefoot, at the average self-selected walking speed calculated from the GaitRITE™, on a dual-belt instrumented treadmill (R-MILL Motekforce Link, The Netherlands). After a 6-minute acclimatization period [236], participants were informed the perturbation protocol would begin. A standardized perturbation protocol was followed outlined previously [251]. In short, participants experienced 3 blocks of eight unexpected, 1cm and 3cm, medial and lateral walking surface translations on each leg. The surface translations occurred at random periods during walking but were systematically initiated during mid-stance of the gait cycle. If individuals used handrails

or stepped onto the opposite treadmill belt, the trial was excluded from analysis. All individuals were blinded to occurrence, direction and magnitude of the walking translation.

After walking, a supine resting muscle bias was collected. Individuals performed a series of MVICs on a Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc., USA). One practice contraction was completed followed by two, 3s gravity corrected MVIC trials separated by 40s rest periods. Knee flexors and extensors were tested a 45˚ of knee flexion [155], with the knee and dynamometer axis aligned. Standing unilateral plantar flexion was completed [61]. Standard verbal encouragement was provided.

During the walking trials, marker trajectories were recorded at 100Hz with eight Qualisys® OQUS 500 (Qualisys®, Sweden) motion analysis cameras. Two AMT-8 8-channel EMG measurement systems (CMRR: 115dB at 60Hz, Input Impedance: ~10GΩ, band-pass: 10-1000Hz, Bortec Inc., Canada) were used. GRFs and EMG were sampled at 2000Hz (A/D 16bit, +/ 5V). All data were synchronized and recorded via Qualisys Track Manager 2.10 (Qualisys®, Sweden).

7.2.3 DATA PROCESSING

Custom processing scripts were written in MatLab™ 2015b (The MathWorks Inc., USA). Marker motions were filtered using a recursive, 6Hz low-pass, 4^{th} order Butterworth filter and GRF and moments were filtered using a recursive, 30Hz low-pass, 4^{th} order Butterworth filter. Pelvis, thigh, shank and foot bone embedded coordinate systems were

derived from virtual points and markers. Knee joint angles were calculated using Cardan/Euler rotations, represented as the distal segment moving about the fixed proximal segment [236]. Net external joint moments were calculated using inverse dynamics [174] and projected into the joint coordinate system [175]. Moments were filtered using a recursive, 10Hz low-pass, 4^{th} order Butterworth filter. Raw EMG was filtered using a 10-500Hz band-pass, 4^{th} order Butterworth filter, resting bias corrected, full-wave rectified and linear enveloped using a recursive, 6Hz low-pass, 4^{th} order Butterworth filter. EMG waveforms were amplitude normalized to the highest 100ms overlapping moving average window from MVIC trials [61]. Motion and EMG waveforms were time normalized to the gait cycle, beginning and ending at heel-strike. Moments were time normalized to stance, beginning at heel-strike and ending at toe-off. A 500ms overlapping moving average window determined maximal knee flexion and extension torque generated during MVIC trials. Maximal torque was amplitude normalized to body mass.

7.2.4 DATA ANALYSIS

The symptomatic limb was chosen for the MOA participants and a limb was randomly selected for the ASYM participants. Only medial 3cm walkway translations were analyzed. Three strides preceding each walkway translation was ensembled averaged to represent T0 and the first stride after the walkway translation represented T1 [251]. Knee joint ranges of motion in the sagittal plane (ICPF, PFLM) and in the frontal plane (ICKAA) were calculated from joint motion waveforms and SPROM and pKAM were calculated from sagittal and frontal plane joint moment waveforms [236], used as discrete

metrics for statistical analysis. PCA was used to extract three mutually uncorrelated PPs from quadriceps, hamstring and gastrocnemius waveforms that explain at least 90% of variability [61]. *PP-scores* were calculated, providing a weighting coefficient for how each individual waveform resembles the PP. These methods have been published in detail and are used to understand muscle activation amplitude and temporal patterns during gait [61].

7.2.5 STATISTICAL ANALYSIS

Given the studies purpose to investigate the response to walking surface translation in those with knee instability impacting activity, participants with MOA were dichotomized using the KOS-I. Individuals who reported no symptom of instability (KOS-I = 5) were grouped as OAS. Individuals reporting that symptoms of instability impact their activity (KOS-I $\leq$ 3) were grouped as OAU. Participants who reported the presence of knee instability with no limitations to activity (KOS-I = 4) were excluded from analysis [89]. Any ASYM participants that reported the symptom of instability (KOS-I < 5) were excluded from analysis.

Normality and equal variance of response variables were determined using Kolmogorov-Smirnov and Levene's tests, respectively. Non-normal distributions and/or unequal variances were corrected using a Johnson Transformation. One-way ANOVA models were used to determine between group differences for participant demographics, KOOS subscale scores, walking speed, and strength outcomes. For joint motion and moment outcome variables, a two-factor mixed model ANCOVA, adjusting of the effects of walking speed determined between and within group (time) main effects and interactions.

For EMG *PP-scores*, a three-factor, mixed model ANCOVA, adjusting for walking speed, was used to determine between and within group (time, muscle) main effects and interactions. Bonferroni post hoc adjustments were used for all significant effects with significance adjusted to alpha = 0.05 depending on number of multiple comparisons. Statistical procedures were completed with Minitab™ Ver. 18 (Minitab Inc., USA).

7.3 RESULTS

Thirty-four individuals with MOA and 46 ASYM individuals were recruited. Participants reporting the symptoms of instability did not impact activity (KOS-I = 4) were removed from analysis (MOA [n=6], ASYM [n=2]). Two individuals from the MOA cohort and 3 individuals from the ASYM cohort either crossed or used handrails on all three direct medial 3cm perturbations to the study limb and were removed from analysis. Twenty-six individuals with MOA completed the perturbation protocol; 14 (54%) of those reporting that the symptom of instability impacted their activity.

Table 7-1 outlines group demographics, anthropometrics, walking speed, KOOS scores, strength outcomes and MOA group KL-grades. Both MOA groups were had higher mass and BMI compared to the ASYM group ($p<0.001$), and the OAS group was older compared than OAU group only ($p=0.044$). The OAU group walked slower compared both OAS and ASYM groups ($p=0.002$). No differences were found in knee extension strength ($p>0.05$), however the ASYM group had higher knee flexion strength compared to the OAU group only ($p=0.018$). The ASYM group reported higher KOOS scores compared to both MOA groups ($p<0.001$), while the OAU group reported worse KOOS

scores on all subsets ($p<0.001$) compared to OAS group except Quality of Life ($p>0.05$).

A median KL of II was reported in both MOA groups.

Table 7-1: Mean (SD) subject demographics, walking speed, self-report scores, knee joint strength and radiographic scores. Differing letters denote significant difference.

	Asymptomatic	**OA Stable**	**OA Unstable**
N	41	12	14
Sex (M:F)	20:21 (51% Female)	7:5 (41% Female)	6:8 (57% Female)
Age (years)	60 (7) [ab]	65 (5) [a]	58 (7) [b]
Height (m)	1.68 (0.08)	1.70 (0.12)	1.67 (0.08)
Mass (kg)	70.9 (13.0) [a]	84.3 (12.7) [b]	84.9 (15.6) [b]
BMI (kg/m^2)	25.0 (3.4) [a]	29.2 (4.0) [b]	30.2 (4.1) [b]
Walking Speed (m/s)	1.16 (0.12) [a]	1.14 (0.11) [a]	1.02 (0.14) [b]
KOS-I	41 [5]	5 [12]	3 [6] – 2[7] – 1[1]
KOOS	--	--	--
Symptoms (n/100)	97.6 (4.4) [a]	66.7 (16.8) [b]	52.8 (10.4) [c]
Pain (n/100)	98.4 (3.6) [a]	68.5 (16.3) [b]	57.7 (17.6) [c]
Activities of Daily Living (n/100)	99.5 (1.3) [a]	78.9 (15.1) [b]	57.9 (21.4) [c]
Quality of Life (n/100)	97.1 (5.9) [a]	53.7 (19.5) [b]	42.0 (17.6) [b]
Radiographic Scores	--	--	--
KLI	--	3	4
KLII	--	5	5
KLIII	--	0	1
KLIV	--	0	0
Not Rated **	--	4	4
Knee Extension – 45˚ (Nm/kg)	1.85 (0.49)	1.66 (0.34)	1.68 (0.77)
Knee Flexion – 45˚ (Nm/kg)	1.08 (0.27) [a]	0.89 (0.21) [ab]	0.85 (0.37) [b]

** Access to radiographs was unavailable due to ongoing COViD-19 health crisis.

Means and SD for all significant group main effects are found in Table 7-2, significant time main effects are found in Table 7-3, and interactions are found in Table 7-4. For all biomechanical outcome variables, no time main effects or time interactions were significant in response to direct perturbations ($p>0.05$). Group main effects were found, with the less ICPF ($p=0.018$) and PFLM ($p=0.011$) range in the OAS compared to the ASYM group only.

Table 7-2: Mean and SD for significant group main effects. Differing letters denote post hoc significant differences for each outcome.

Group Main Effects	Asymptomatic	OA Stable	OA Unstable
ICPF (˚)	15 (4) [a]	12 (5) [b]	13 (5) [ab]
PFLM (˚)	13 (6) [a]	9 (4) [b]	11 (4) [ab]
Quad PP1	147.6 (88.7) [a]	159.3 (91.0) [a]	202.8 (96.0) [b]
Quad PP2	-6.5 (28.8) [a]	8.9 (33.2) [b]	4.8 (37.2) [ab]
Quad PP3	-2.4 (27.5) [a]	- 4.3 (31.8) [a]	13.1 (28.6) [b]
Ham PP2	-25.4 (41.5) [a]	3.8 (63.2) [b]	-1.5 (69.0) [b]

Group VM and VL ensemble averaged waveforms for T0 and T1, PPs and PP interpretations are represented in Figure 7-1. There was a significant group main effect for all quadriceps *PP-scores* ($p<0.05$) where the OAU group *PP1-* ($p=0.001$) and *PP3-scores* ($p<0.001$) were higher than OAS and ASYM groups and the OAS group quadricep *PP2-scores* was higher than the ASYM group only ($p=0.003$). Time main effects were found in quadriceps *PP-Scores*, with higher *PP2-* ($p<0.001$) and *PP3-scores* ($p=0.038$) at T1 compared to T0.

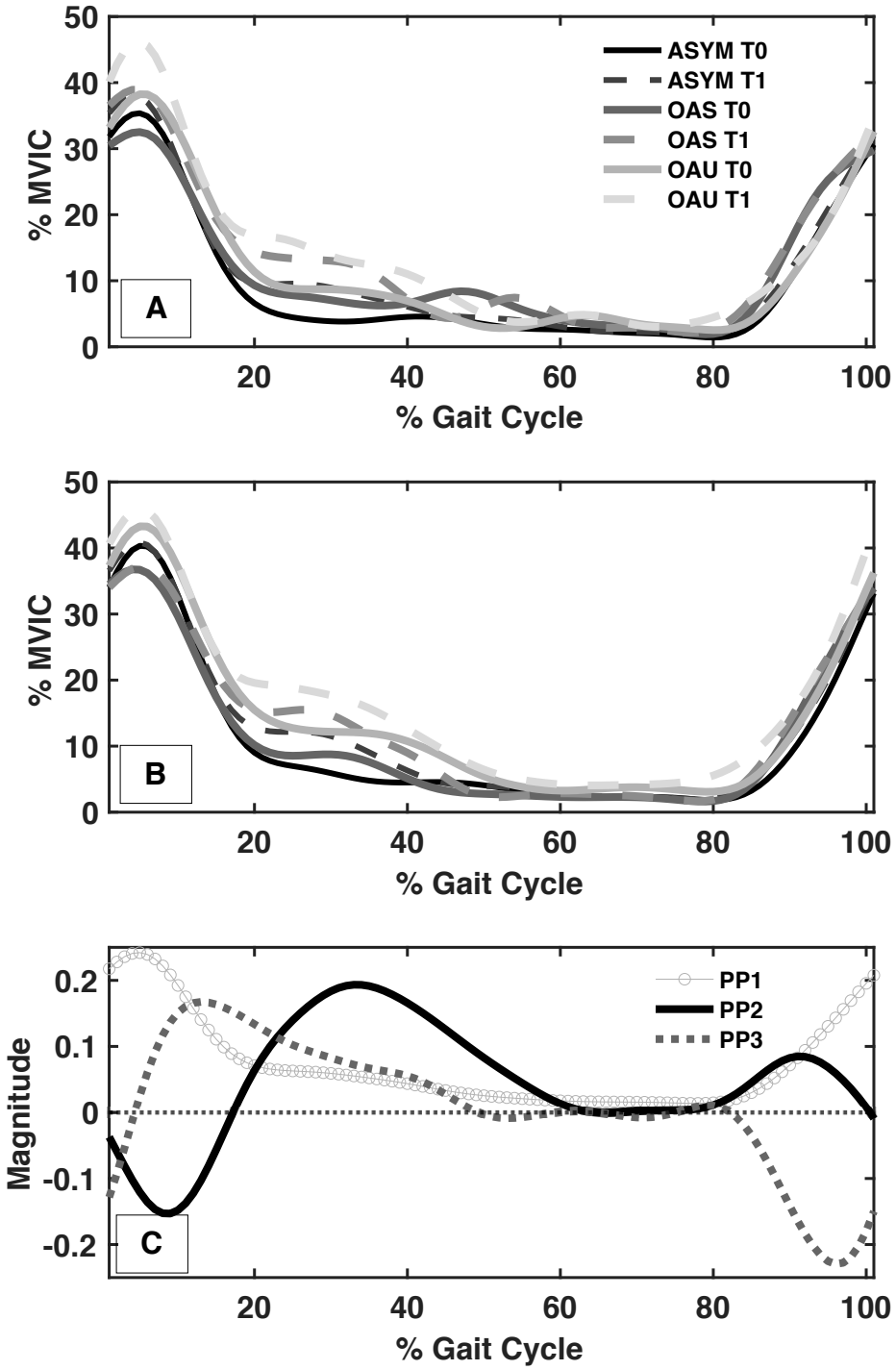

Figure 7-1: Ensemble averaged (A) VM and (B) VL amplitude normalized to % MVIC. (C) Three PPs captured 96% of the waveform variability. PP1 (91%) captured overall magnitude and shape. PP2 (3%) captured prolonged activation during stance where higher scores indicate more prolonged activation. High PP3-scores captured a greater difference between early-to-mid stance and swing phases, explaining 2% of waveform variability.

Table 7-3: Means and standard deviations for significant time main effects. Differing letters denote post hoc significant differences for each outcome.

Time Main Effects	Baseline (T0)	Response (T1)
Quad PP2	-9.0 (29.9) [a]	6.2 (33.1) [b]
Quad PP3	-2.8 (31.8) [a]	3.8 (26.3) [b]
Ham PP1	120.0 (83.4) [a]	149.9 (101.2) [b]
Ham PP2	-29.9 (44.8) [a]	-0.2 (59.1) [b]
Gast PP1	192.6 (77.8) [a]	222.2 (85.8) [b]
Gast PP2	10.5 (43.4) [a]	-3.7 (64.1) [b]
Gast PP3	-13.4 (35.2) [a]	18.3 (51.5) [b]

Group MH and LH ensemble averaged waveforms for T0 and T1, as well as PP patterns and interpretations are represented in Figure 7-2. A significant group-by-muscle interaction was found for hamstring *PP1-scores* where the OAU and OAS group demonstrated higher LH *PP1-scores* compared to ASYM group ($p=0.005$), while MH of all groups was activated to levels that were not statistically different ($p>0.05$).

Table 7-4: Means and standard deviations for significant interactions. Differing letters denote post hoc significant differences for each outcome.

Group-by-Muscle Interaction	Asymptomatic		OA Stable		OA Unstable	
	MH	***LH***	***MH***	***LH***	***MH***	***LH***
Ham PP1	124.6 (62.8) [bc]	107.9 (54.8) [c]	111.0 (51.7) [bc]	205.7 (176.5) [ab]	137.1 (97.9) [abc]	202.1 (122.5) [a]

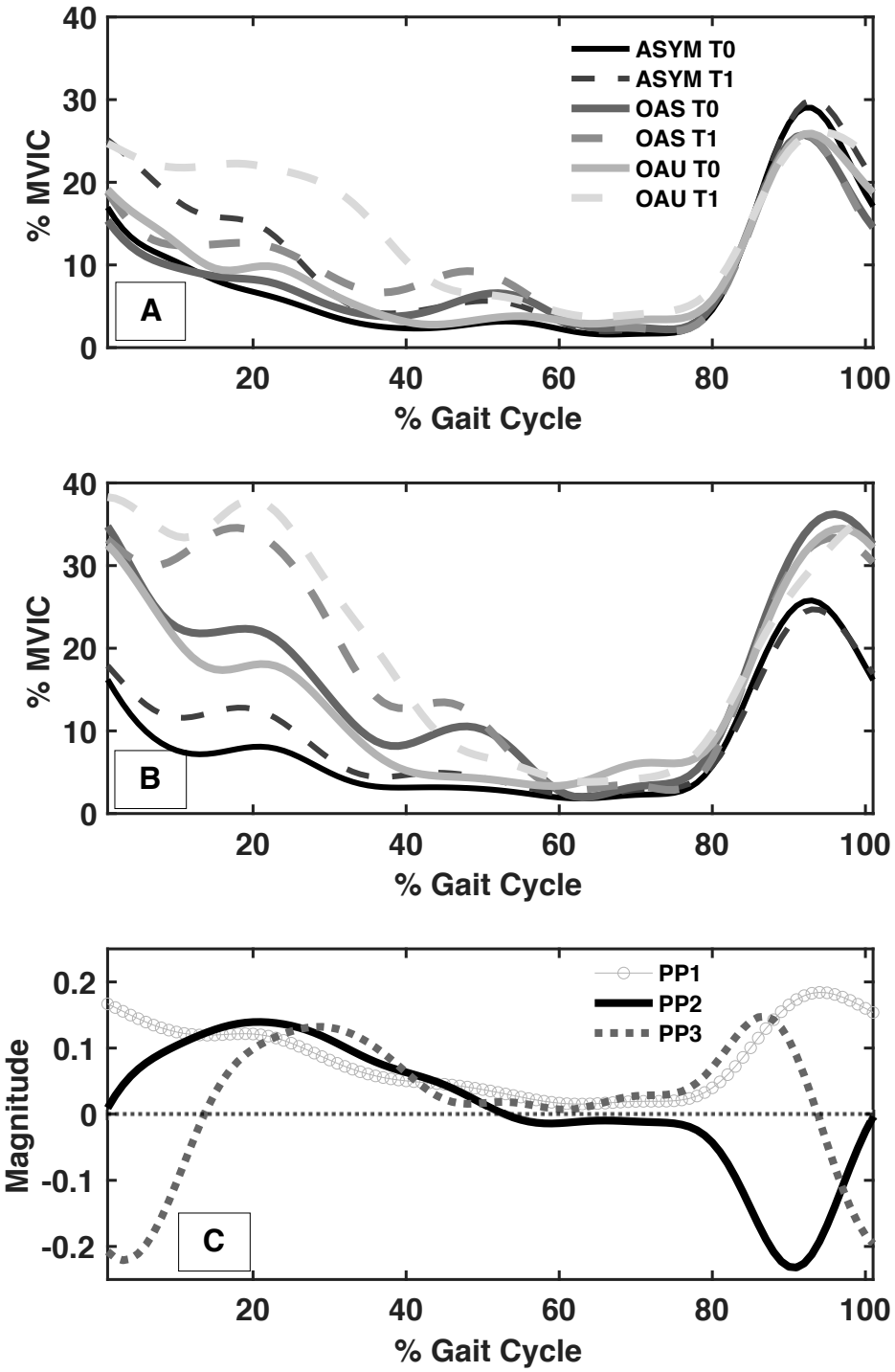

Figure 7-2: Ensemble averaged (A) MH and (B) LH amplitude normalized to % MVIC. (C) Three PPs captured 95% of waveform variability. PP1 (81%) captured overall magnitude and shape. PP2 (10%) captures prolonged elevated activation during early stance where higher scores indicate more prolonged activation. PP3 (4%) captured a difference between early and late stance activation, where higher scores indicate a greater late stance activity.

A hamstring *PP2-score* group main effect was significant, with OAU and OAS groups demonstrating higher scores compared to the ASYM group ($p=0.003$). No other group main effects or interactions were significant for the hamstrings ($p>0.05$). Significant time main effects were also found for hamstring *PP1-* ($p=0.004$) and *PP2-scores* ($p<0.001$) with higher scores at T1 compared to T0.

Group MG and LG ensemble averaged waveforms for T0 and T1, as well as PP patterns and interpretations are represented in Figure 7-3. No group main effects or interactions were reported gastrocnemius *PP1-*, *PP2-* and *PP3-score* ($p>0.05$). Significant time main effects were found in the gastrocnemius *PP-Scores* with higher *PP1-* ($p=0.008$) and *PP3-scores* ($p<0.001$) and lower *PP2-scores* ($p=0.014$) at T1 compared to T0.

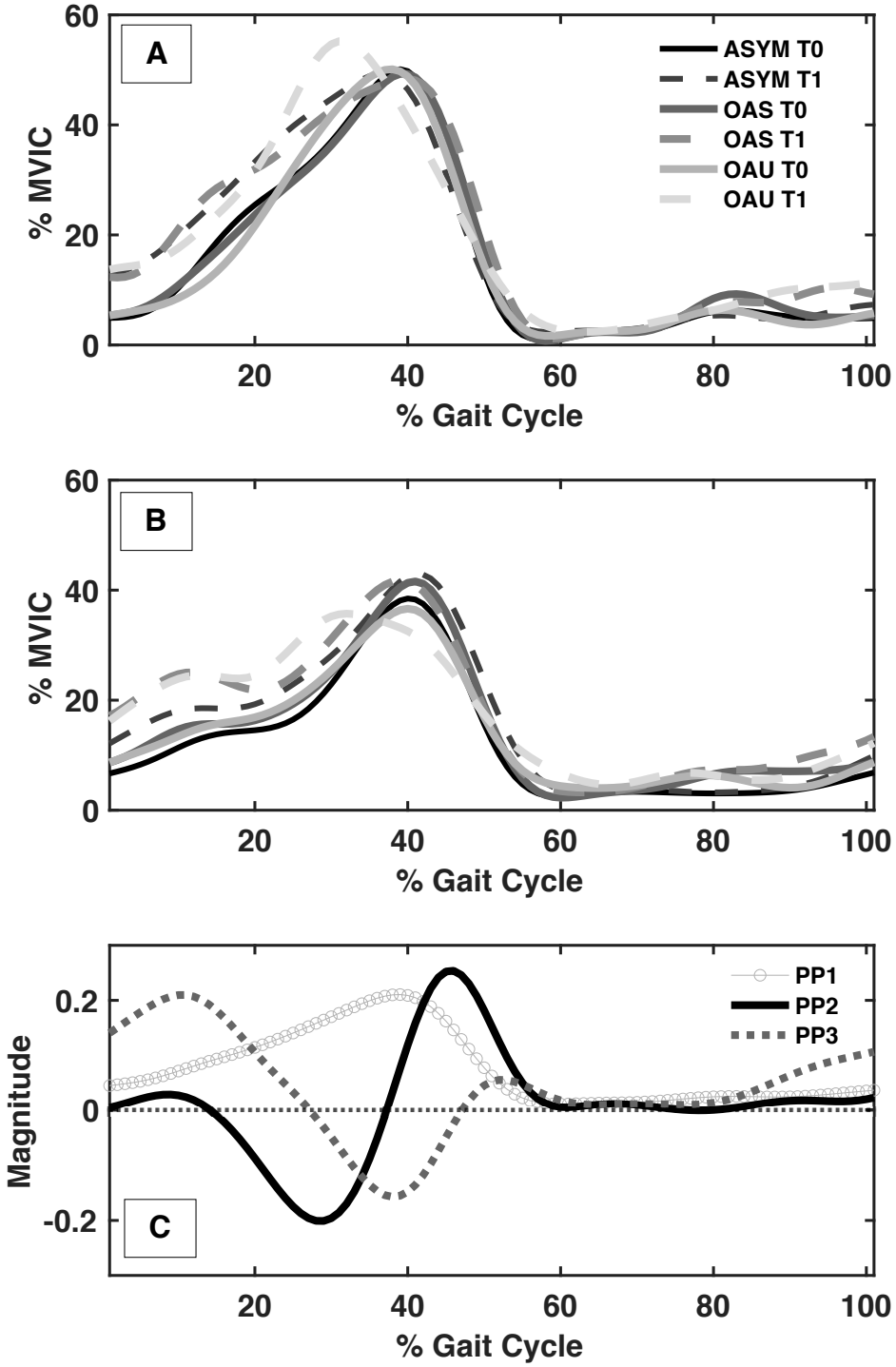

Figure 7-3: Ensemble averaged (A) MG and (B) LG amplitude normalized to %MVIC. (C) Three PPs captured 95% of waveform variability. PP1 (86%) captured overall magnitude and shape. PP2 (5%) captured a phase shift in activation where higher scores indicate a delayed. PP3 (4%) captured a difference operator between early and late stance phase where higher scores indicate a lower difference.

7.4 DISCUSSION

The purpose of this preliminary analysis was to investigate different biomechanical and neuromuscular responses to direct, medial 3cm midstance walking surface translations between OAU, OAS and ASYM groups. Study hypothesis were partially supported, with higher hamstring and gastrocnemius activation, more constant activation of all muscles, and earlier gastrocnemius peak activation in response to the direct perturbations, however all three groups had no statistical differences in perturbation responses.

Detailed in Table 7-1, both OAU and OAS groups demonstrated higher mass and BMI [60, 61, 133], and lower KOOS subscales [60] compared to the ASYM group, similar to previous chapters and consistent with literature. Commonly, walking speed is reduced in those with MOA compared to ASYM groups [61, 88, 268]. However, in this study, only the OAU group demonstrated walking speed differences compared to the ASYM group. This finding is consistent with the larger sample in Chapter 4, where the OAU group walked slower than the ASYM group only. This suggests that either KOS-I dichotomy or lower KOOS scores reported in the OAU group help explain slower walking speed [27, 89]. Slower walking speeds have been found to increase local dynamic stability [269], suggesting the OAU group self-selects slower walking speed to improve sensation of instability. However, reduced walking speed has also been found in those with knee pain and clinical OA severity [43, 133, 270], and may be a more generalized response to OA symptoms associated with knee OA.

Group main effects were found, where both MOA groups recruited LH to higher percentages of maximal effort activation (*PP1-scores*) compared to the ASYM group, while MH activation was not statistically different between all three groups. Demonstrating higher lateral-to-medial activation is consistent with findings in those with moderate severity disease [204, 206]. Higher LH activation has been found to increase with structural severity in a sample selected with no statistical differences in walking speeds [143]. Both OAS and OAU groups demonstrate median KL-II grades, and null LH *PP1-score* findings between MOA samples in this study is consistent (Chapter 4) [143]. The OAU group recruited VM and VL to higher percentages of maximum effort activation (*PP1-scores*) compared to OAS and ASYM groups. In combination with increased LH activation, the OAU group demonstrates the highest agonist/antagonist active stiffness in all three samples. Increased agonist/antagonist co-activation, specifically, higher medial quadricep-gastrocnemius co-activation, was found in an OA group with greater knee instability and higher medial laxity [73]. This increased active stiffness in the OAU group may be an attempt to control excessive motion to maintain joint function, however these patterns of higher activation bodes poorly for radiographic and clinical OA severity [207, 208, 265]. Furthermore, the OAU group is working at a higher percentage of maximal effort activation with every step, and the question remains if these individuals have the capacity to further increase muscle activation magnitudes and patterns to maintain joint function.

The group muscle activation differences found demonstrates differing levels of active stiffness at the knee joint during pre-perturbed walking, related to joint structures and/or

OA symptoms, including self-reported knee instability [30, 43, 143, 187]. Despite baseline walking group differences, the response to a direct gait perturbations was not statistically different across all groups in order to maintain joint function during challenged treadmill walking [88]. All groups responded to direct perturbations with elevated and more constant knee joint muscle activation, providing the knee with increased active stiffness [43, 47, 60, 61]. However, using a reliability analysis in Appendix A and associated MDCs, a difference in LH magnitude and pattern may be present, and not significant due to the power of this preliminary analysis. The mean change between T0 and T1 in LH PP1-scores in each group was 12.8, 27.7, and 60.1 units in the ASYM, OAS and OAU group while MDC was found to be a change of 38.4 units, suggesting the OAU group meaningfully changed LH activation in order to maintain function, while OAS and ASYM groups did not. Similarly, the mean change between T0 and T1 in LH PP2-scores in each group was 17, 34.8 and 68.8 units in the ASYM, OAS and OAU group while MDC was found to be a change of 22.6 units. This suggests a stepwise increase LH PP2-scores, interpreted as prolonged activation, where OAU and OAS groups demonstrate a meaningful change in response to the direct perturbation, and the OAU group recruit LH activation significantly higher than the OAS group. This potential differences in muscle activation in the OAU suggesting two things; 1) preliminary analyses are under powered and likely higher sample sizes are required to detected group-by-time interactions and 2) the OAU group responds to direct gait perturbations with a higher neuromuscular response compared to OAS group and ASYM groups to maintain joint function in a challenged walking environment.

There results of this study need to be interpreted considering certain limitations. Firstly, self-reported measure of instability and its impact on activity were used to dichotomize the MOA group. However, this dichotomy does not isolate self-reported instability as the only OA symptom. In this analysis, higher KOOS pain scores were reported in OAU group, and no measures of effusion, laxity, proprioception, etc. were captured. Some studies have controlled for specific variables, and gait alterations were found in unstable groups independent of other OA symptoms [77]. However, these altered magnitudes and patterns of muscle activation have also been discussed in those with OA symptoms [30, 43, 71-73]. This preliminary analysis should be interpreted with this understanding. Secondly, walking speed was controlled for. To the knowledge of the author, no studies have discussed the influence of walking speed on the perturbation response. Slower walking speed is a characteristic of knee OA and a dichotomy exists in the literature regarding how to handle this variable [271]. Therefore, main effects and interactions should be interpreted with the knowledge that walking speed was used as a covariate.

7.5 CONCLUSION

All groups responded to unexpected, direct perturbations with higher hamstring and gastrocnemius muscle activation, more constant activation in all muscles, earlier peak gastrocnemius activation and no biomechanical alterations. A pattern of active joint stiffening post-perturbation was found but did not influence sagittal plane motion or moments. Group main effects suggest varying levels of active stiffness in baseline walking, specifically, higher quadriceps activation in the OAU group and higher LH

activation in the OAU/OAS group. These individuals may demonstrate less capacity to respond, but direct perturbations did not trigger a loss of stability.

CHAPTER 8: IS THE NEUROMUSCULAR RESPONSE IN THOSE WITH MODERATE KNEE OSTEOARTHRITIS INFLUENCED BY THE PRESENCE OF SELF-REPORTED KNEE INSTABILITY WHEN LANDING WITH THE SYMPTOMATIC KNEE AFTER A WALKWAY SURFACE TRANSLATION?

8.1 INTRODUCTION

Episodes of buckling, shifting or giving way of the knee joint, defined as self-reported knee joint instability [73], are found in 60-80% of those with knee OA [74] and 30-60% report knee instability that hinders their ability to complete activities of daily living [54]. This symptom is associated with reduced knee joint confidence [52] and an increased risk [223] and fear of falling [50]. Episodes of knee buckling have been shown to influence future knee pain exacerbation [222] and thus improving knee instability has been determined a fundamental component of knee OA management [252].

The symptom of knee instability is most often felt during walking compared to other weight bearing tasks [54, 76] and results in walking difficulties [27]. Stability has been defined as the way a system behaves following a perturbation, and if the state of that system remains within specific boundaries of control [258]. Furthermore, using Panjabi's theoretical stability framework, for a joint to maintain function an interrelationship between the passive osteoligamentous, active muscular and neural control subsystems occurs [66]. In those with knee OA, mechanical stability is required during biomechanical joint function (i.e. joint motions, loading, and protecting internal structures). The passive osteoligamentous and neuromuscular subsystem in those with knee OA is altered, and therefore increased contributions from the active muscular and

control subsystems, found in OA literature [43, 60, 61, 73, 90], are required to maintain joint function.

Challenged walking paradigms are thought to provide an external stimulus to challenge the system dynamically and researchers monitor the response to see how function is maintained. Direct and indirect gait perturbations have been used throughout this thesis [Objective 2a, 2b, 3a] and in OA literature [88, 89], as OA commonly alters mediolateral loading environments understood to impact the frontal plane stability environments [73]. Studies have compared those with OA to asymptomatic control groups [Objective 2a and 2b] [88] and those with stable and unstable OA groups [Objective 3a] [89]. Most studies have investigated direct challenges [Objective 2a, 3a] [88], where the symptomatic (ipsilateral) limb is translated while on the ground and the response is the subsequent stride of the symptomatic (ipsilateral limb). Commonly, general MOA groups, MOA groups dichotomized by self-reported instability, and asymptomatic groups responded with either no changes in frontal or sagittal plane motion or moments [Objective 2a, 3a] or reduced sagittal plane mechanics [88], with elevated specific (i.e. increased medial co-contraction) or general (elevated quadriceps, hamstring, gastrocnemius) muscle activation [88, 89]. This finding was similar when investigating the response to indirect challenges [Objective 2b], where the asymptomatic (contralateral) limb is translated while on the ground and the response is the subsequent stride of the symptomatic (ipsilateral limb). In indirect challenges, when comparing MOA and ASYM groups, a response of higher and prolonged quadriceps, hamstring and gastrocnemius with no changes to biomechanics was found statistically [Objective 2b].

Indirect challenges utilized in Chapter 6, while responses were not statistically significant from baseline, suggest that the MOA group may be responding by recruiting LH to higher percentage of maximal effort activation and patterns of more prolonged activation using MDCs captured in Appendix A. These potential findings provide evidence of increased response in the symptomatic landing leg, compared to a random leg of the ASYM group. These symptomatic landing responses could be rationalized by a few explanations; (1) a strategy to counterbalance instability sensations, as 44% reported the sensation impacted activity; (2) reduce excessive loading of painful joint tissues, highlighted by a finding worse KOOS pain; and/or (3) influence from OA symptoms not described in this analysis (effusion, laxity, proprioception, etc.). Schmitt and Rudolph found that those in an unstable group after experiencing direct lateral translation, experienced more sensations of knee instability compared to the stable group, finding that the unstable group is self-reported more difficulties maintaining balance during perturbation testing [89]. It may be those self-reporting knee instability respond different compared to stable groups, and a preliminary analysis dichotomizing instability using indirect gait perturbation may support an increased neuromuscular response.

The purpose of this preliminary analysis is to determine if differences between OAU, OAS and ASYM groups are present in sagittal and frontal plane knee joint motions and quadricep, hamstring, and gastrocnemius muscle activation patterns in response to indirect medial 3cm midstance walking surface perturbations. It was hypothesized that the OAU will respond with greater reduction in sagittal and frontal plane ROM, and

elevated and prolonged quadriceps, hamstrings and gastrocnemius muscle activation patterns compared to OAS and ASYM groups.

8.2 METHODS

8.2.1 PARTICIPANT RECRUITMENT

Individuals with unilateral medial compartment knee OA were recruited by direct referral from local orthopaedic clinics. An orthopaedic surgeon diagnosed participants using the ACR guidelines [233] and ensured participants were not candidates for a TKA. Standard anterior-posterior radiographs were acquired and scored using the KL ordinal scale [68] by an experienced rater. MOA participants were defined as moderate disease severity using a telephone screening tool, where participants reported their ability to walk a city block, climb stairs reciprocally and jog 5m [61]. Additionally, participants reported the ability to walk for 30 minutes continuously as required by perturbation study methodology. An ASYM cohort was considered a sample of convenience and recruited using local advertisements. Participants in each group were included if: age > 50; no history of cardiovascular and/or respiratory disease; no history neurological disorders; no history of fractures and/or injuries other than a sprain/strain within the year. Protocol was approved by the local ethics review board (Romeo: 1020825 and 1025007).

8.2.2 DATA COLLECTION

Participants reviewed study protocol and completed informed consent. The KOS-ADLS [224] and KOOS [234] was then completed prior to gait testing. Participants changed into fitted shorts, a t-shirt and removed footwear before height, weight and limb segment

circumferences were measured. Self-selected walking speed was obtained using standard laboratory procedures [239] and the GaitRITE™ pressure sensitive walkway (CIR Systems Inc., USA). Surface EMG was completed using SENIAM standard procedures and consistent with guidelines [235]. On each leg, the muscle bellies of VM, VL, MH, LH, MG and LG electrode locations were marked with ink, shaved and wiped with 70% alcohol. A reference electrode was placed bilaterally on a bony aspect of the tibial shaft. Surface electrodes (Ag/AgCl, 10mm diameter, 30mm interelectrode distance, Red Dot 3M Health Care, USA) were placed in a bipolar configuration. Isometric muscle tests were used to validate signal, confirm placement and adjust gains. Surface EMG was collected using two AMNT-8 8-channel measurements systems (CMRR 115dB at 60Hz, Input Impedance ~10GΩ, bandpass 10-1000Hz, Bortec Inc., Canada). Individual markers and rigid, 4-marker clusters were placed on anatomical landmarks and body segments using adhesive tape and Velcro straps [239]. A 3-marker cluster, affixed to the treadmill surface, capture treadmill movement during walking surface translations. The sternal notch and left/right anterior superior iliac spines were defined with virtual point trials. Marker trajectories were captured using Eight OQUS 500 (Qualisys®, Sweden) motion analysis cameras at a sampling rate of 100Hz.

Using the self-selected walking speed calculated by the GaitRITE™, participants walked barefoot on a dual-belt instrumented perturbation treadmill (R-MILL, Motekforce Link, The Netherlands). As a safety precaution, participants wore an upper body harness attached to a ceiling bracket. GRFs and EMG were sampled at 2000Hz (A/D 16bit, +/ 5V) and synchronized with marker trajectories using Qualisys Track Manager 2.10

(Qualisys®, Sweden). Participants acclimatized to the laboratory conditions and treadmill walking for 6-minutes [236] before being notified that a series of unexpected perturbations would occur. A standard perturbation protocol was followed and published in detailed [251]. In brief, participants experienced 3 repeated blocks of 8 different, unexpected walkway surface translations. The walkway surface translations were combinations of 1cm/3cm magnitudes, medial/lateral directions occurring on the left/right legs. Translations were triggered at contralateral toe-off (Vertical GRF < 50N), therefore occurring at midstance of the ipsilateral leg. Rate of translation was 0.1m/s. Trials were excluded if the participants used handrails or stepped onto the opposite treadmill belt. Perturbation occurrence, magnitude and direction were blinded to participants.

After treadmill walking, a resting muscle bias was collected with the participant lying supine. Knee flexor and extensor muscle strength and MVIC testing were completed using a Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc., USA). Knee extensor and flexor strength was tested at 45˚ of knee flexion, with the knee joint and dynamometer axes aligned, and segment weight and gravity were corrected. One practice contraction was given to ensure proper technique and two, 3s MVIC were completed with 40s of rest separating trails. Standing unilateral plantar flexion was the completed [61] and standard verbal encouragement was provided.

8.2.3 DATA PROCESSING

Custom processing scripts were developed using MatLab™ 2015b (The Mathworks Inc., USA). Raw marker motion was filtered using a recursive, 6Hz, lowpass, 4th order Butterworth filter. From filtered data the pelvis, thigh, shank and foot bone embedded coordinate systems were derived. Knee joint angles were calculated using accepted Cardan/Euler rotations in a sequence of flexion/extension, abduction/adduction, internal/external rotation [175]. Knee motion was described as the shank moving about a fixed thigh with flexion, abduction and internal rotation as positive motion [175].

EMG signals were visually inspected for artifacts and/or signal saturation and verified in the power spectrum using a Fast Fourier Transform. Raw signals were then filtered using a 10-500Hz, bandpass, 4th order, Butterworth filter and corrected for participant resting muscle bias, gain corrected, converted to micro-volts, full wave rectified and filtered using a recursive, 6Hz, lowpass, 4th order, Butterworth filter. Signals were then amplitude normalized to the highest 100ms from MVIC using a 99ms overlapping moving average window [61]. Motion and EMG waveforms were time normalized to the gait cycle, beginning with heel-strike and ending with subsequent ipsilateral heel-strike. Maximal knee extensor and flexor torque was determined using a 500ms overlapping moving average window and amplitude normalized to body mass.

8.2.4 DATA ANALYSIS

From the ASYM group a limb was selected randomly and the symptomatic limb used from in MOA participants. Indirect perturbations, where the walking surface was

translated 3cm medially, were chosen for analysis. This perturbation was experienced three times and successful responses were ensembled averaged (T1). Three strides prior to the perturbation were ensembled averaged and represent T0. The range from ICPF, PFLM, and ICKAA were extracted and used for statistical testing. PCA is a factorization method common to EMG [31, 61, 133] used to capture amplitude and temporal features [263]. Three (quadriceps, hamstrings, gastrocnemius) PCA models were used compiling the medial/lateral and T0/T1 waveforms forming matrix (X). A cross product matrix ($[S]=[X^T]*[X]$) was computed, followed by an eigenvector decomposition of S. This created a transform matrix (T) containing a matrix of patterns with the diagonal describing associated variance. Three PPs were retained which in summation explain at least 90% of the variance. *PP-Scores* were computed and represent how well an individual waveform is represented by a PP [61]. *PP-scores* are used for statistical testing. PCA is the ideal factorization method to understand direction and pattern of individual muscle activation that occur in a data set [264].

8.2.5 STATISTICAL ANALYSIS

Given the study purpose in understanding walking surface translations and self-reported instability impacting activities, participants with MOA were groups based on their response to the KOS-I. Self-reported instability was represented on a 6-point Likert from 0 (instability impacts all activity) to 5 (no sensations of instability) [224]. Participants reporting no instability symptoms (KOS-I = 5) were grouped as OAS and individuals who reported instability impacted their activity (KOS-I $\leq$ 3) were grouped as unstable

[89]. Participants reporting a knee instability with no impact on function (KOS-I = 4) and ASYM participants reporting instability (KOS-I < 5) were excluded from analysis.

Statistics were completed in Minitab™ Ver. 18 (Minitab Inc., USA). Equal variance and normality were tested using Levene's and Kolmogorov-Smirnov methods, and transformed using a Johnson Transformation if non-normal distributions and/or unequal variances were determined. One-way ANOVA models determined between group difference for participant demographics, walking speed, KOOS subset scores and muscle strength outcomes. For sagittal and frontal plane joint motion variables, a two-factor mixed model ANCOVA adjusting for walking speed, determined between and within group (time) main effects and interactions. For EMG *PP-scores* response variables, a three-factor mixed model ANCOVA adjusting for walking speed, determined between and within group (time, muscle) main effects and interactions. Post hoc adjustments were tested using Bonferroni methods on all significant effects, adjusted to alpha = 0.05 depending on the number of multiple comparisons.

8.3 RESULTS

Thirty-four individuals with MOA and 46 ASYM individuals were recruited to complete the perturbation protocol, of which, 32 MOA and 44 ASYM individuals completed at least one successful perturbation trial, without crossing onto the contralateral plate or using handrails. From the MOA cohort, 63% reported the sensation of instability and 44% reporting that instability sensations impacted activity. Those reporting instability

with no impact on activity (KOS-I = 4) were excluded (MOA = 6, ASYM = 2).

Table 8-1 details group demographics, anthropometrics, walking speed, KOOS subset scores, muscle strength, and MOA KL-grade scores. No group differences were reported for age, height and knee extension or flexion between groups ($p>0.05$). MOA groups demonstrated a median KL-II grade. Both MOA groups had higher mass and BMI and reported worse KOOS scores across all subsets compared to the ASYM group ($p<0.001$). The OAU group reported worse KOOS score for the Symptoms, Activities of Daily Living and Quality of Life subsets ($p<0.001$) than the OAS group.

Table 8-1: Mean (SD) subject demographics, walking speed, self-report scores, knee joint strength and radiographic scores. Differing letters denote significant difference.

	Asymptomatic	**OA Stable**	**OA Unstable**
N	42	12	14
Sex (M:F)	20:22 (52% Female)	7:5 (42% Female)	7:7 (50% Female)
Age (years)	61 (7)	65 (5)	58 (7)
Height (m)	1.68 (0.08)	1.70 (0.12)	1.68 (0.09)
Mass (kg)	70.5 (13.3) [a]	84 (12.7) [b]	85.7 (14.7) [b]
BMI (kg/m^2)	25.0 (3.4) [a]	29.2 (4.0) [b]	30.3 (3.9) [b]
Walking Speed (m/s)	1.16 (0.12) [a]	1.14 (0.11) [ab]	1.02 (0.14) [b]
KOS-I	5 [42]	5 [12]	3[5] - 2[8] - 1[1]
KOOS	--	--	--
Symptoms (n/100)	98.0 (4.0) [a]	66.7 (16.8) [b]	53.3 (10.4) [c]
Pain (n/100)	98.8 (3.0) [a]	68.5 (16.3) [b]	58.3 (18.0) [b]
Activities of Daily Living (n/100)	99.5 (1.2) [a]	78.9 (15.1) [b]	59.6 (23.0) [c]
Quality of Life (n/100)	97.5 (5.4) [a]	53.7 (19.5) [b]	41.1 (17.8) [c]
Radiographic Scores	--	--	--
KLI	--	3	4
KLII	--	5	5
KLIII	--	0	1
KLIV	--	0	0
Not Rated	--	4**	4**
Knee Extension - 45˚ (Nm/kg)	1.82 (0.48)	1.77 (0.30)	1.89 (0.77)
Knee Flexion – 45˚ (Nm/kg)	1.10 (0.25)	1.02 (0.31)	1.02 (0.36)

** Access to radiographs was unavailable due to ongoing COViD-19 health crisis.

Mean and SD for significant group main effects are found in Table 8-2, significant time main effects are found in Table 8-3, and significant interactions are found in Table 8-4. No biomechanical group-by-time interactions or time main effects were found ($p>0.05$). A group main effect was found where the OAS group walked with less PFLM range

compared to the ASYM group (p=0.017) only. No ICPF and ICKAA differences were found between groups.

Table 8-2: Means and standard deviations for significant group main effects. Differing letters denote post hoc significant differences for each outcome.

Group Main Effects	Asymptomatic	OA Stable	OA Unstable
PFLM (˚)	12 (6) [a]	9 (4) [b]	11 (5) [ab]
Quad PP1	147.7 (93.9) [a]	174.6 (99.8) [a]	222.0 (96.4) [b]
Quad PP2	-7.8 (34.0) [a]	8.1 (31.3) [b]	2.0 (36.0) [ab]
Ham PP3	-5.8 (26.1) [a]	11.8 (48.6) [b]	-2.6 (38.0) [ab]

Group VM and VL ensemble average waveforms for T0 and T1, as well as PP patterns and interpretations are represented in Figure 8-1. No group-by-time interactions were found in quadricep PP-scores (p>0.05). Group main effects found higher quadriceps *PP1-scores* in the OAU group compared to OAS and ASYM groups (p>0.001) and higher quadriceps *PP2-scores* in the OAS group compared to the ASYM group (p=0.002) only.

Table 8-3: Means and standard deviations for significant time main effects. Differing letters denote post hoc significant differences for each outcome.

Time Main Effects	Baseline (T0)	Response (T1)
Quad PP1	150.8 (85.3) [a]	184.7 (105.3) [b]
Quad PP2	-13.0 (26.9) [a]	7.0 (38.5) [b]
Ham PP1	121.8 (82.3) [a]	163.5 (99.5) [b]
Ham PP2	-25.0 (43.6) [a]	0.7 (45.5) [b]
Gast PP1	193.9 (81.8) [a]	222.6 (90.1) [b]
Gast PP2	-23.3 (48.1) [a]	21.8 (56.1) [b]
Gast PP3	15.2 (39.7) [a]	-9.0 (50.2) [b]

Time main effects were found where higher quadriceps *PP1-* ($p=0.007$) and *PP2-scores* ($p<0.001$) at T1 compared to T0. No group or time main effects were reported for *PP3-scores* ($p>0.05$).

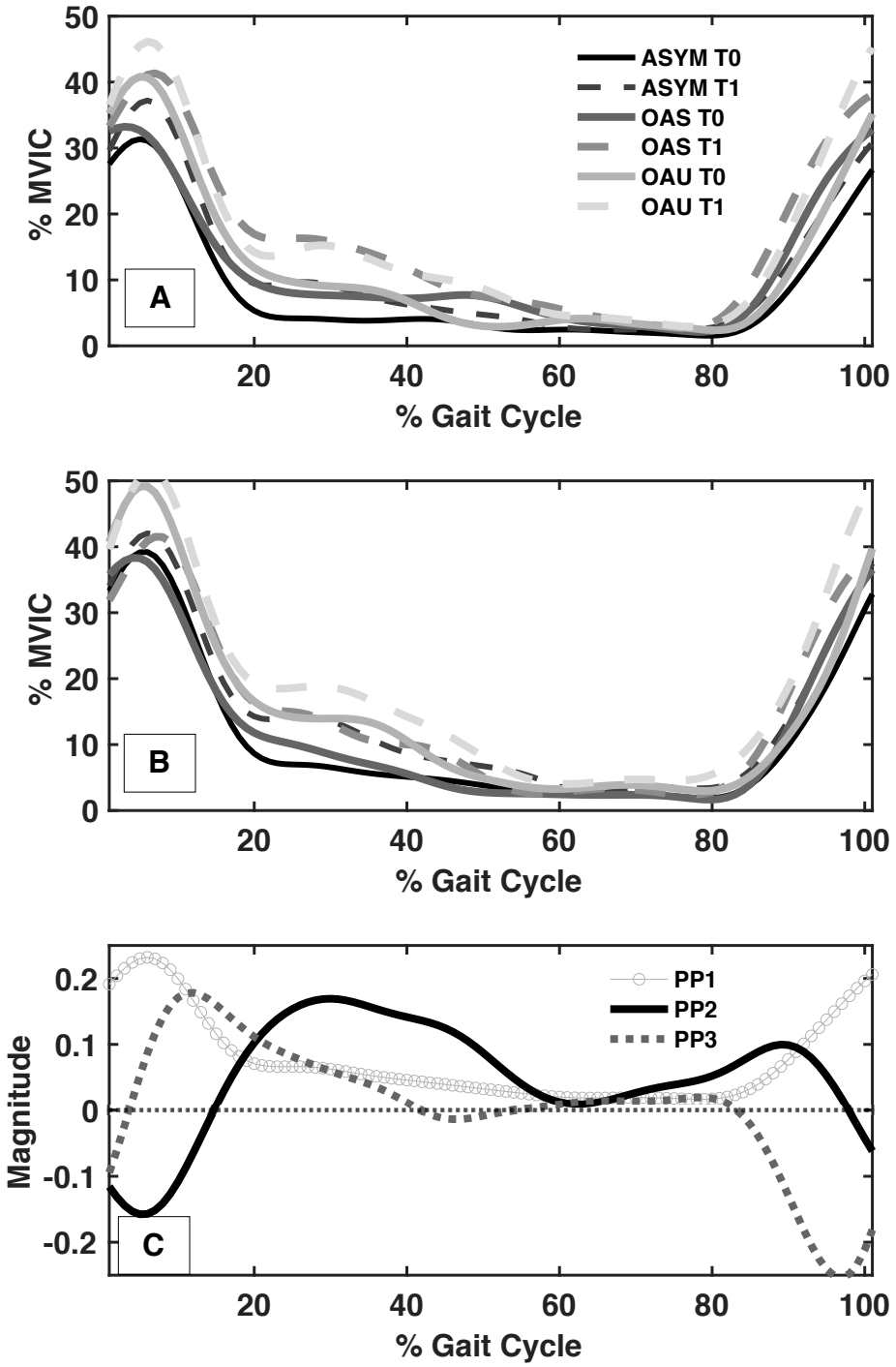

Figure 8-1: Ensemble averaged (A) VM and (B) VL amplitude normalized to % MVIC. (C) Three PPs captured 95% of the waveform variability. PP1 captured overall magnitude and shape explaining 90% of waveform variability. PP2 captured prolonged activation during stance explaining 3% of waveform variability. High PP3-scores captured a greater difference between early-to-mid stance and swing phases, explaining 2% of waveform variability.

Group MH and LH ensemble averaged waveforms for T0 and T1, as well as PP patterns and interpretations are represented in Figure 8-2. No group-by-time or group-by-time-by-muscle interactions were found for hamstring *PP-scores* ($p>0.05$). A group-by-muscle interaction was found for hamstring *PP1-scores* where both MOA groups had higher LH *PP1-scores* compared to the ASYM group ($p=0.001$), with MH *PP1-scores* that were not significant between groups ($p>0.05$).

Table 8-4: Means and standard deviations for significant interactions. Differing letters denote post hoc significant differences.

Group-by-Muscle Interactions	**Asymptomatic**		**OA Stable**		**OA Unstable**	
	MH	***LH***	***MH***	***LH***	***MH***	***LH***
Ham PP1	131.3 (72.9) ^{c}	118.3 (67.3) ^{c}	129.4 (55.7) ^{bc}	217.9 (168.3) ^{a}	131.8 (88.6) ^{abc}	206.8 (104.5) ^{ab}

A group main effect found in hamstring *PP3-scores*, where the OAS group had higher scores compared to the ASYM group ($p=0.009$) only. Time main effects were found for hamstring *PP1-* ($p<0.001$) and *PP2-scores* ($p<0.001$), with higher T1 scores compared to T0.

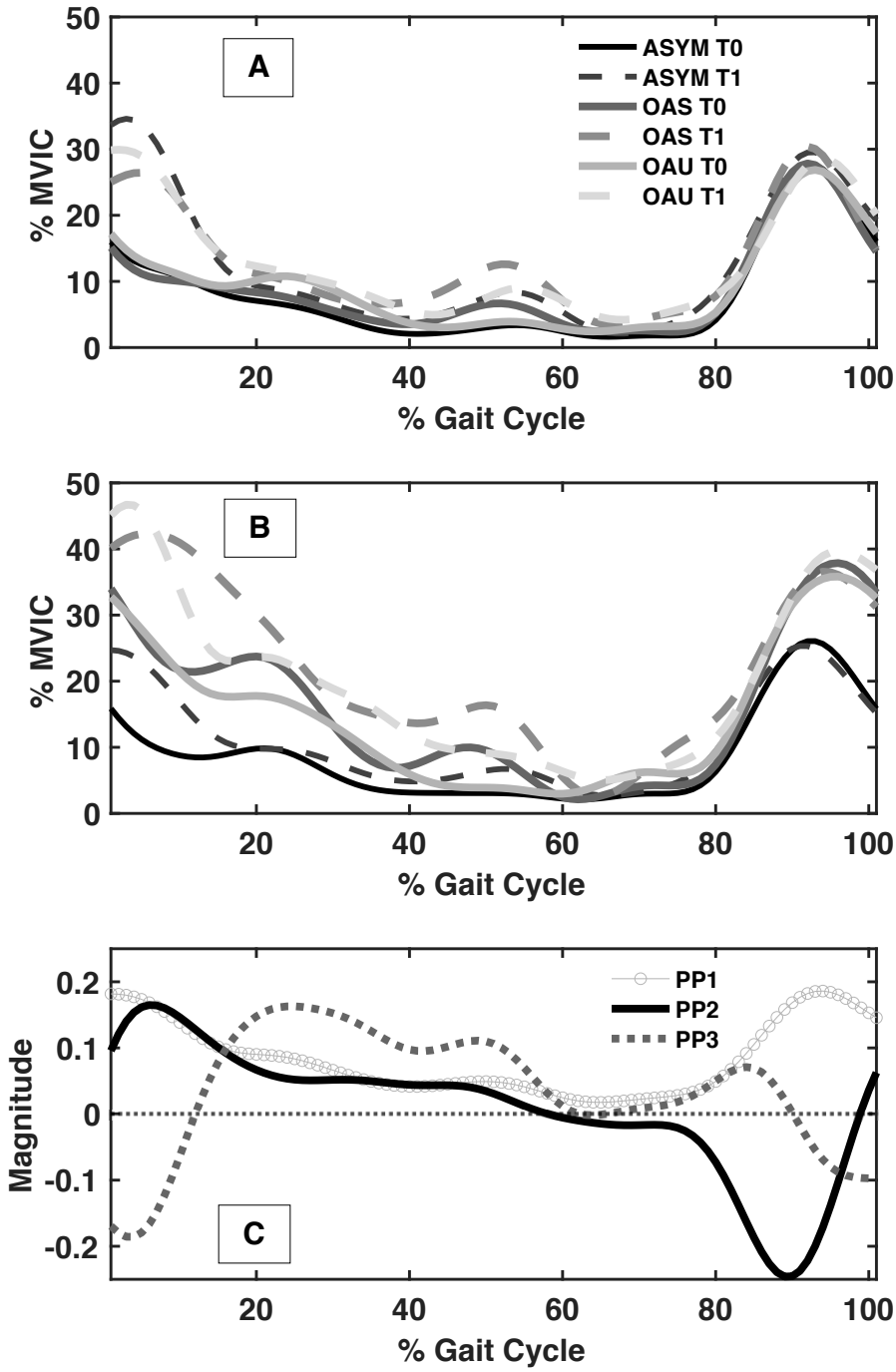

Figure 8-2: Ensemble averaged (A) MH and (B) LH amplitude normalized to % MVIC. (C) Three PPs captured 93% of waveform variability. PP1 captured overall magnitude and shape, explaining 82% of waveform variability. PP2 captures prolonged elevated activation during early stance where higher scores indicate more prolonged activation and explained 7% of waveform variability. PP3 captured a difference between early and late stance activation, where higher scores indicate a greater late stance activity, explaining 4% of waveform variability.

Group MG and LG ensemble averaged waveforms for T0 and T1, as well as PP patterns and interpretations are represented in Figure 8-3. No group interactions or main effects were reported for gastrocnemius *PP-scores* ($p>0.05$), however time main effects found higher *PP1-* ($p<0.001$) and *PP2-scores* ($p<0.001$) and lower *PP3-scores* ($p<0.001$) at T1 compared to T0.

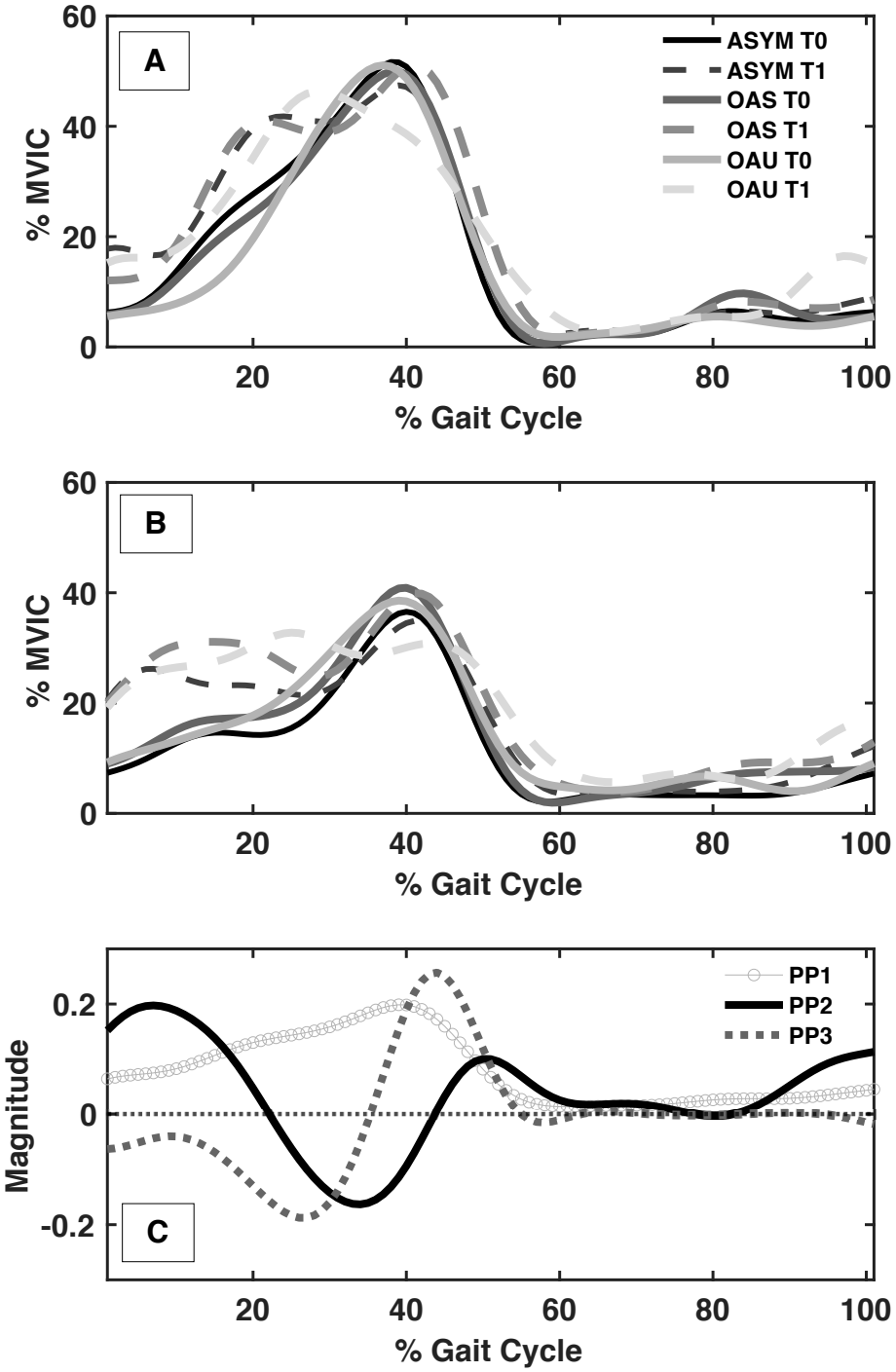

Figure 8-3: Ensemble averaged (A) MG and (B) LG amplitude normalized to %MVIC. (C) Three PPs captured 97% of waveform variability. PP1 captured overall magnitude and shape, explaining 85% of waveform variability. PP2 captured a difference operator between early and late stance phase and explained 5% of waveform variability, where higher scores indicate a lower difference. PP3 captured a phase shift in activation where higher scores indicate a delayed activity and explained 4% of waveform variability.

8.4 DISCUSSION

The purpose of this preliminary analysis was to determine if differences between OAU, OAS and ASYM groups were found in sagittal and frontal plane knee joint motions and quadricep, hamstring, and gastrocnemius muscle activation patterns in response to indirect gait perturbations. The results partially supported the hypothesis, as elevated and more constant quadricep, hamstring and gastrocnemius activation was demonstrated in all muscles at T1 compared to T0, but there were no statistical differences in the response detected among groups.

MOA groups were generally similar, however, worse KOOS symptoms, activity participation and quality of life scores were found in the OAU group. The OAU group also demonstrated a slower walking speed to the ASYM group only. Slower self-selected walking speeds are found in unstable groups compared to stable groups [27, 77, 89]; however, no statistical differences were found between these groups in this study. Regardless, MOA groups often demonstrate slower walking speeds to ASYM groups [27, 43, 77, 272]. While only the OAU group demonstrated statistically slower walking speed to ASYM groups in this analysis, worse self-reported symptoms in the OAU group (KOOS, KOS-I) support a relationship between worse OA symptoms and slower walking speeds [27, 43, 77, 272]. A slower walking speed is an indicator of reduced functional ability, physical inactivity and a risk of developing comorbidities in aging population [273].

Group main effects and group-by-muscle interactions demonstrates that differing levels of muscle activation magnitudes and patterns are required in pre-perturbation gait to maintain knee joint function. Similar structural severity (KL-II grade) was found between MOA groups, suggesting that clinical rather than radiographic severity is driving these findings [71, 187]. The OAU group, consistent with Chapters 4 and 7, are recruiting VM and VL to higher percentages of maximal effort activation compared to both OAS and ASYM groups. This finding is consistent with a study comparing groups with and without knee effusion, detected using the bulge test [30]. This analysis does not capture knee effusion between the subgroups; however, Chapter 4 demonstrated a similar finding, with even effusion distributions between OAU and OAS groups. In Figure 8-1, the OAU group recruited the quadriceps to the highest percentage of maximal effort and the largest difference between OAS and ASYM groups during loading response (0-15%). This increased agonist activation is not accompanied with findings increase antagonist (hamstring, gastrocnemius) activation in the OAU group compared to the OAS group. This creates an environment, where if gastrocnemius or hamstring activation is not sufficient to oppose quadriceps activation (i.e. muscle fatigue), sensations of shifting, buckling or giving way at the knee could occur. The link between hamstring coactivation and sensations of shifting or buckling has been investigated, concluding no association [274]. However, these findings were based on open kinetic chain quadricep exercises [274], when episodes of self-reported instability occur most often during walking [54]. Therefore, more work is needed to elucidate the role antagonist co-activation opposing elevated quadriceps muscle activation found in the OAU group and sensations of instability.

In response to indirect perturbations, no statistically significant group interactions were found, but significant time main effects showed that OAU, OAS and ASYM groups utilized higher and more constant quadriceps, hamstring and gastrocnemius muscle activation to maintain sagittal and frontal plane knee joint motions. Despite all groups having different muscle activation patterns and magnitudes during pre-perturbed gait, with highest active stiffness found in the OAU group, all groups had the capacity to recruit musculature to higher percentages of maximal effort activation in order to maintain treadmill walking and knee joint function. Walkway surface translations are thought to destabilize the overall system and challenge the knee joint, and consistently, despite translation direction, magnitude, level of preparedness or type (direct/indirect), the perturbation study results are similar (Chapters 5-7) [88, 89]. Higher and more prolonged muscle activation is recruited around the knee to maintain joint function in those with knee OA, a response to knee joint function during walking [61, 88, 275] by promoting stability. This finding strengthens the interpretations of previous OA studies that have reported elevated amplitudes and prolonged patterns are suggestive of a stabilizing strategy [43, 60, 61, 73, 90]. Commonly, unstable OA groups report more pain and greater symptoms based on the KOOS subscales (Chapter 4, 7) [27, 77, 89], however other OA symptoms not captured could also be responsible for the finding of increase activation [30, 43, 73]. However, this finding may support a relationship between higher magnitudes and patterns of activation in those with OA and instability and higher magnitudes and patterns activation found in response to challenged walking. It could be that to counteract internal perturbations or sensations of buckling, shifting or giving way

the knee joint is sensing, increased magnitudes and patterns of activation occur acutely, and overtime are adapted to guard the knee against these sensations. Regardless, these activation magnitudes and patterns in the OAU group bode poorly for knee joint structural and clinical OA progression [207, 208, 265].

Hamstring pattern response differences between the current study and Chapter 7 likely captures differing response strategies of direct and indirect challenges. Direct challenges resulted in higher patterns of MH and LH prolonged activation and may be more indicative of stabilizing, as the contralateral limb has responded to the initial impact. Indirect challenges demonstrate a burst of activation in MH and LH at initial contact and could be a strategy responding to initial impact (Figure 8-2). This thesis suggests different strategies are required to maintain joint function between responses to direct and indirect gait perturbations, and more work is needed to understand the mechanisms behind each perturbation response.

The preliminary analysis must be understood in the context of a few limitations. Small sample sizes in OAU and OAS group suggests the analysis does not have adequate power to detect group-by-time or group-by-time-muscle interactions. For example, a mean change of -23.9, -9.8 and -44 units were found between T0 and T1 of MG activation *PP3-scores* for ASYM, OAS and OAU groups respectively (Appendix A MDC = 34.7 units) and -19.0, -20.0 and -35.3 units were found between T0 and T1 of LG activation *PP3-scores* of the ASYM, OAS and OAU groups, respectively (Appendix A MDC = 34.4 units). Gastrocnemius *PP3-scores* are interpreted as phase-shifted activation, where

negative change would indicate earlier activation (Figure 8-3). These findings suggest unique patterns of activation in the OAU group, not detected statistically in Chapter 8, supporting the notion that the study is under powered.

8.5 CONCLUSION

Between groups, the perturbation response was not statistically different. In all groups the perturbation response included elevated and prolonged muscle activation patterns, no frontal or sagittal plane alterations in knee angle; suggestive of a stabilizing strategy, despite how groups self-reported knee instability. Group main effects illustrate that higher amplitudes (OAU) and more constant activation (OAS/OAU) potentially place the OAU joint at risk for increased joint loading and risk of muscle fatigue; an creating an environment that may be unstable at times. Perturbation protocols have demonstrated utility in challenging stability and support previous interpretations that increased activation and co-activation are strategies to stabilize the knee and maintain joint function.

CHAPTER 9: DISCUSSION

Our current understanding of self-reported instability and its impact on walking mechanics [27, 77, 78, 139] and gait perturbations [89] is limited given that few studies have addressed this topic. Some direction has been provided; however, a dearth of information is available that provides a comprehensive examination of the complex interactions of the biomechanical and neuromuscular systems. With every step, individuals with MOA are responding to altered structural and symptomatic environments with the biomechanical and neuromuscular adaptations found in knee OA thought to maintain joint function [30, 32, 43, 62, 115, 143]. Stabilizing or stiffening knee strategies are often discussed as combinations of reduced sagittal plane motion and moment ranges and elevated and more constant activation of the knee musculature [33, 43, 60-62, 64, 73, 90, 200, 276]. These interpretations have been formed in controlled walking environments providing foundational evidence to support the current thesis which was focussed on discerning the influence of OA and self-reported knee instability on walking tasks in both challenged and unchallenged environments that may have been encountered on day-to-day function.

As discussed in Chapter 2.5 (Knee Stability), our general understanding of stability is substantiated by a theoretical framework that the passive osteoligamentous, active muscular and neural control subsystems work cooperatively to maintain knee function [66] and from current definitions, stability involves the ability to maintain the joint within boundaries of control in response to perturbations [258]. Challenged walking paradigms [88, 89] provide a method to test how individuals with knee OA and/or knee OA and

instability respond to perturbations, specifically with a knee they don't have confidence will support them [52]. In turn, this may (1) provide researchers with an understanding of the strategy's individuals use to maintain knee joint function when challenged with external perturbations and (2) detail specific methods to understand the limitations in functional performance that those with knee OA may have, and how they impact day-to-day experiences.

The general thesis objective was to understand biomechanical and neuromuscular responses to treadmill walking and frontal plane walking surface translations in those with MOA, those with MOA with and without knee instability impacting activity and an ASYM group. The rationale for studying those with MOA was to determine alterations potentially influenced by self-reported instability before severe symptomatic changes have progressed individuals to require surgical intervention and identify OA features that can be managed through conservative means to slow disease progression. Determining and interpreting group differences between MOA and ASYM groups will provide context to findings in chapters where stability was dichotomized, and participants responded to direct and indirect perturbations. This also ensures the sample collected was comparable to OA populations discussed in literature over the past two decades.

9.1 LEVEL GROUND WALKING GROUP DIFFERENCES

9.1.1 ASYMPTOMATIC - MODERATE OA

For this thesis, individuals with knee OA were classified as moderate disease severity, where recruitment focused on individuals who were not candidates for a TKA determined

by an orthopaedic surgeon and reported the ability to walk a city block, jog 5-metres, and climb stairs reciprocally [61]. Other studies have defined moderate OA based on radiographic severity only (KL I-III), however in terms of group demographics, similar findings have been reported between those defined as structurally and/or functionally moderate disease severity and an asymptomatic groups [60, 115, 133, 143, 182, 202]. In summary, the results of Chapters 4-8 demonstrate that MOA groups have a higher mass and BMI, slower walking speeds, and worse KOOS subset scores compared to an ASYM cohort, consistent with previous literature [31, 61, 268]. Muscle strength differences were inconsistent throughout the thesis. In Chapter 4 lower knee extensor strength was found in both MOA (OAS and OAU) groups compared to the ASYM group [71, 143], where a 19% change between the ASYM and OAS group and a 28% change between the ASYM and OAU group was found. Only the OAU group had significantly lower knee flexor strength compared to the ASYM group (30% change). In Chapter 6, no significant strength differences were found between MOA and ASYM groups, with changes of 3% and 13% in the extensors and flexors respectively. To assist interpretation of this finding, an additional exclusion criteria was required along with the moderate disease severity classification [61] in Chapter 6. All participants self-reported the ability to walk continuously for 30 minutes, therefore a higher functioning MOA group may have been selected. Chapter 5-8 analyses were also smaller samplings of a larger dataset, and significant findings in the MOA group may be a result of sampling errors. Strength deficits have been found in OA populations [69, 277], however, disease severity may impact this result. A recent systematic review found more severe joint degeneration and higher pain were factors associated with muscle strength deficits [277]. Therefore, if the

MOA group sampled was more structurally and clinically severe, strength differences would be expected, as supported by the Chapter 4 OAU group (lowest KOOS symptom subscale).

The KOS-I was a primary focus of this thesis where 60-67% of individuals with MOA across all study samples self-reported the presence of knee instability, and 40-53% reported that this sensation slightly, moderately or severely impacted their day-to-day activity, similar to distributions in the literature [26-28, 54, 77, 78]. While, our sample was recruited to represent MOA, others have reported similar KOS-I distributions in those with KL ≥ II [27, 77, 78] and a general population of those with knee OA (i.e. no specific exclusion criteria reported) [25, 26].

9.1.1.1 BIOMECHANICS

A treadmill walking analysis was completed to investigate sagittal and frontal plane knee joint motion and moment outcomes and muscle activation magnitudes and patterns for the medial and lateral sites of quadricep, hamstring, and gastrocnemius muscles. Treadmill walking analyses in healthy young adults and knee OA groups have shown good-to-excellent reliability [155, 244]. In summary, those with MOA walked with less ICPF and PFLM, a less dynamic SPROM and no changes in the pKAM compared to the ASYM group. Sagittal plane motion findings are consistent with OA literature and have also been found in groups with OA related symptoms (i.e. pain, structural and clinical severity, effusion, laxity) [32, 33, 35, 73, 115, 145, 156]. The MOA group in this analysis had a moderate radiographic severity (median KL-II grade) and was included based on

clinically moderate OA severity [61]. However, the MOA group demonstrated larger distributions of effusion, and worse self-reported instability and pain, and reported more activity limitations compared to ASYM groups. Consistent with other studies [43, 59], the SPROM was reduced in the MOA group. This reduced range from peak flexion to peak extension has been attributed to a 'stiff knee' gait pattern, a strategy promote knee joint stability in those with knee OA [59]. In addition to a higher KAM magnitude at baseline walking, this biomechanical feature was predictive of those with moderate OA who progressed to a TKA at follow-up [59]. A null finding in the pKAM between MOA and ASYM groups is contrasted by some studies [35, 36, 181], but consistent with others [57, 62, 183] and this null finding is influenced by less radiographic changes (i.e. the median KL grade II) and moderate functional severity as a recruitment criteria [61] in the MOA groups [182, 278]. Biomechanical outcomes support altered knee function during walking in these samples of individuals with knee OA. Further analyses revealed accompanying alterations to the neuromuscular system.

9.1.1.2 ELECTROMYOGRAPHY

Factorization methods are becoming more common in investigating the contributions of muscle activation magnitudes and patterns during gait, as it derives temporal patterns not easily captured through discrete metrics [61, 264]. PCA was employed and, in summary, the MOA group walked with temporal LG and MG activation changes and elevated and prolonged LH and quadriceps (VM/VL) activation compared to ASYM groups. In moderate OA groups, the relationship between the LG and MG has been found to be altered compared to an asymptomatic group, where the timing and amplitude of peak

activation becomes similar in those with OA and while remaining different in asymptomatic groups [61, 279]. Fewer studies have focussed on gastrocnemius activation patterns, however, earlier peak activation in OA groups has been found [61, 279] and could be interpreted as a mechanism to increase stability during single leg stance. Elevated and/or prolonged LH activation is a common finding in OA literature [62, 91, 203, 204, 280], sensitive to structural severity [143, 207], progression to TKA [208], and related to the KAM [62]. Elevated LH activation patterns and magnitudes are thought to unload the medial compartment, counterbalancing high pKAMs [62], this feature is also found to increase with radiographic severity [143]. No significant differences in pKAM between OAS and OAU groups and comparable median KL-grades, suggest that these MOA group findings are not explained by an instability dichotomy. Finally, in those with OA, elevated and/or prolonged quadricep activation is often found [32, 88, 133, 143, 201], associated with structural [143] and clinical severity [133], OA symptoms [30] and progression to a TKA [208]. Recruiting quadriceps to higher percentages of activation may reduce impact loads at initial contact and through early stance, however quadriceps prolonged activation has been found at baseline walking in groups that progressed to a TKA at follow-up [208]. More prolonged quadriceps activation increases active stiffness and promote stability, but it also increases knee loading via co-activation that has been found to detrimental impacts on the clinical state of the joint [208]. Collectively, findings of increased levels of knee joint muscle activation in the MOA group support altered neuromuscular activation patterns maintain knee joint function during walking in those with knee OA, either through promoting compartmental stability (LH), or LG counterbalancing against impact or early stance loading (VL, LH, LG). Demographics,

biomechanics and altered muscle activations found in this thesis suggest that MOA and ASYM samples represent typical presentations provided in the literature. This increases confidence in reporting perturbation and dichotomized stability outcomes within the study groups.

9.1.2 SELF-REPORTED INSTABILITY

Self-reported knee instability is related to more painful and difficult walking [27], increased risk and fear of falling [50, 223] and these episodes of instability are most often reported during walking [54, 281]. Understanding walking mechanics associated with self-reported symptoms of instability may provide information on how joint function is maintained in a knee that individuals report poor confidence in. This thesis demonstrated that OAS and OAU groups are similar in some respects (age, mass, BMI, median KL Grade, muscle strength, effusion, walking velocity), however worse KOOS subset scores compared to OAS and ASYM groups were found and are consistent with previous literature [27, 77, 78, 89]. These findings support the use of an instability dichotomized approach, as the OAU groups reports not only that self-reported instability impacts activity, but that sensations of buckling, shifting or giving way of the knee is associated with worse KOOS pain, symptoms, physical function and quality of life [77]. While altered biomechanical and neuromuscular function may relate to lower KOOS outcomes, KOOS outcomes could also be the result of recurrent episodes of instability [222]. Therefore, understanding muscle activation magnitudes and patterns found in the OAU group can provide information on how joint function is maintained, and the potential mechanisms behind altered gait patterns.

9.1.2.1 BIOMECHANICS

Statistically significant biomechanical differences were not present in sagittal and frontal plane motion and moment outcomes between the OAU and OAS group. Specifically, no significant differences were reported in sagittal plane stance phase motion (ICPF, PLFM), as well as, in sagittal or frontal plane moments (SPROM, pKAM). This finding is conflicted in the literature dichotomizing stability, as unstable groups have been found with more ICPF range compared to stable groups [27, 77]. This finding could be influenced by two methodological characteristics.

First, studies have dichotomized stability using the KOS-I comparing those with instability impacting function (KOS-I ≤ 3) to those without instability or instability not impeding activity (KOS-I ≥ 4) [27, 77]. This definition of an unstable group corroborates the definition used in Chapter 4, 7 and 8, however, the stable group definition is identifying individuals who have experienced sensations of instability as a stable participant. These participants report instability, and therefore some specific gait features may be present in this group and influencing study findings [27, 77]. This thesis utilized a method consistent with Schmitt and Rudolph [89], where a stable group was defined as having no symptoms of instability (KOS-I = 5). This dichotomization method supports historical trajectories in OA research, where research has developed from looking at ends of the OA spectrum (severe OA vs asymptomatic individuals) to exploring the various OA subgroups and phenotypes.

Secondly, walking speed was considered a covariate in statistical analyses, as significant differences were reported in walking speed in these studies (OAU group walking slower), however, there is still debate on how walking speed should be handled in terms of the OA disease process [271]. A relationship between slower walking speed and more stable walking has been discussed [269, 282], therefore correcting for walking speed may remove important stabilizing gait alterations. These studies have found that unstable participants demonstrate decreased stiffness compared to stable groups, concluding that these patterns create an environment where instability is more likely [27, 77], but these studies have statistically controlled for walking speed. No significant biomechanical differences between OAS and OAU groups were found in Chapter 4, 7 and 8, however, muscle activation differences, particularly in the quadriceps were found. Findings suggest increased active stiffness at the knee during stance in the OAU group and support previous work [64]. The biomechanical differences previously reported [27, 77] could be a result of statistical manipulation. Faster walking speeds have been shown to increase the flexion angle [184], and walking speeds are reduced as a result of OA symptoms [43, 133, 270], including instability [27, 77], therefore using walking speed as a covariate could have inaccurate cause-and-effect conclusions [271]. More work is required to investigate the relationship walking speed and instability.

9.1.2.2 ELECTROMYOGRAPHY

Muscle activation group differences were found between the OAS and OAU group. The OAU group recruited quadriceps to higher percentage of maximal effort activation (*PP1-scores*) and demonstrated more prolonged activation (*PP2-scores*) compared to the OAS

group. Previous studies have reported elevated quadriceps activation amplitudes across radiographic knee OA severities (KL II, III, IV), with most pronounced amplitudes in those with KL IV [143]. Although several studies report a discordance between pain and structural symptoms [283, 284], this disagreement is less consistent in more severe OA [285]. Increased KOOS pain in the OAU group, similar to increased pain in those with severe OA [115] could also explain this feature of elevated quadriceps in the OAU group. The quadriceps role during the gait cycle is to reduce the impact of initial contact and to control knee flexion during the loading response, stabilizing the knee against external moments during and shortly after initial contact [254], therefore, this feature of activation in the OAU group could be a strategy to minimize stress on joint tissues, that if loaded excessively could result a variety of OA symptoms [255]. Also, increased quadricep magnitudes and patterns of activation increases active stiffness at the knee joint [64]. This strategy may help maintain joint function in those with MOA and OAU. The role of the quadriceps is to mediate impact loading during initial contact and throughout early stance [176], increasing active stiffness and mediating excessive loading on painful joint tissues. However, elevated and prolonged quadricep activation may also damage joint structures [63, 286], where more prolonged quadriceps activation at baseline was found in those who progress to TKA [208]. This thesis found that the OAU group walked with higher and prolonged quadriceps activation compared to the OAS group, a strategy to maintain joint function and potentially mediate sensations of buckling shifting or giving way. These altered quadricep patterns provide an environment with greater active stiffness, but effectiveness of this strategy might be lowered due to increased muscle fatigue potential because of sustained quadriceps activation [257, 287]. Altered muscle activation patterns

have also been associated with OA symptoms [30, 43, 71-73] (effusion, laxity, pain, muscle weakness, etc.) and could explain this finding as worse KOOS Pain and Symptoms scores were found in the OAU group.

No significant differences were reported in amplitude or temporal patterns of the hamstring muscles between the two groups, particularly LH activation. The OAU and OAS group pKAMs were not statistically different [62, 183] and comparable median KL-II grade [143], support the null finding between groups. No statistical differences in LH, suggests that individually, this feature may not relate to how an individual reports symptoms of knee instability. However, the relationship between quadriceps (agonist) and hamstring (antagonist) activation or co-activation may be related to sensation of instability [274]. No consistent relationship was reported between incident buckling or shifting and hamstring co-activation during open kinetic chain activities [274], however, since episodes of instability occurring during weight-bearing activity, more work is needed to assess if symptoms of instability and a lack of hamstring co-activation are associated. The OAU group shows an increase in amplitude and prolonged quadriceps activation. To maintain balance between joint stability and mobility, this increase theoretically should be counterbalanced by increased antagonist activation, but the question remains as to how much co-activation is sufficient. Antagonist hamstring activation is thought to prevent anterior tibial shear generated by the quadriceps [274] during activities. Given the OAU group walks with a higher percentage of maximal effort quadriceps activation, with no strength differences, it is plausible that more agonist activation is occurring at every step without concurrent increase in antagonist activation.

This may make the knee more susceptible to sensations of shifting during walking due to imbalance activation. However, more work is needed elucidate if antagonist activation from the hamstring and gastrocnemius are sufficient to counterbalance the high agonist activation in the OAU group.

No significant amplitude or temporal gastrocnemius differences were found between the two groups. The OAU groups did however walk with altered LG activation compared to ASYM groups, suggesting the combination of OA and instability impacting function may result in earlier and higher LG activation. As discussed, LG and MG peak activation timing and amplitude was altered in those with moderate OA, where timing and amplitude in the MOA group were not statistically different compared to asymptomatic groups [61, 288]. Previous work found moderate OA present with reduced MG activation and earlier LG activation in over ground walking [61]. In the current work, no significant change in MG activation occurred, but LG activation increased.

More constant LG activation has been found in those with OA and more severe knee pain [43], however this specific study did not capture instability sensations. Regardless, this study identified more constant LG activation may be an attempt to unload painful joint tissues [43]. In OAU groups, LG activation was recruited higher, but also phase-shifted earlier. This higher and earlier LG activation provides the knee joint increased active stiffness, promoting joint stability at a potential event in the gait cycle where sensations of instability are more likely (i.e. single leg stance). However, the OAU groups in this

thesis were also found to have higher KOOS pain [43], shown to specifically alter the pattern of LG activation, and may explain OAU LG findings in Chapter 4.

Higher and more prolonged quadriceps activation in the OAU group may have implications for joint structures and function. These muscle activation differences are in the direction of those with more severe clinical and structural severity despite, MOA recruitment criteria and median KL-II grade. These muscle activation magnitudes and patterns may be influenced by OA symptoms, evidenced by worse KOOS Pain, KOOS symptoms and the presence of self-reported instability. More prolonged quadriceps activation has been reported in groups who progressed to a TKA 5-8 years later [208] and higher LH and more constant LH and LG activation as baseline has been reported in groups who had medial compartment JSN score progression at follow-up [207]. Differing baseline activation patterns between OAU and OAS groups may influence how they progress through the disease process, with the OAU group likely to require a surgical intervention sooner [208].

In combination, no significant changes in joint motion or moments are demonstrated between those OAU and OAS groups, suggesting that alterations in the neuromuscular system are maintaining joint biomechanics, despite accounts of instability. The OAU group demonstrated more activation, mainly in the quadriceps (compared to OAS/ASYM), but also in the gastrocnemius (compared to ASYM only), that increases active stiffness around the knee joint, thought to promote stability, but these muscle activation patterns and magnitudes have been found to be influenced by various OA

symptoms [30, 43, 71-73]. These findings suggest that OAU walking patterns are indicative of those more likely to progress radiographically and towards surgical intervention [207, 208]. These sensations and episodes of instability are also associated with future pain exacerbations [222] and supporting an instability treatment strategy, especially in those self-reporting instability symptoms, as an central component of OA management [252].

9.2 PERTURBATION RESPONSES

This thesis employed direct and indirect perturbations, monitoring the symptomatic limb in those with MOA and a random limb in the ASYM groups. The direct perturbation occurred when the foot of the symptomatic knee was on the ground in midstance and the walking surface translated 3cm in the medial direction. The indirect perturbation occurred when the foot of the asymptomatic knee was on the ground in midstance and the walking surface translated 3cm in the medial direction, forcing participants with OA to respond with their symptomatic leg. Both analyses recorded the following stride of the symptomatic limb as the response. Direct gait perturbations have been utilized in the OA literature [61, 88], while indirect gait perturbations during treadmill walking was a novel approach.

9.2.1 DIRECT PERTURBATIONS

It was hypothesized that elevated and prolonged muscle activation alterations would be present in the MOA and OAU groups compared to ASYM and OAS groups in response to direct gait perturbations in Chapter 5 and 7, as these features have been discussed

previously to promote stability during walking in OA populations [61, 88]. The study hypotheses were not fully supported, as muscle alterations in response to the direct perturbation were present, however, they were not statistically different between groups.

In response to the direct gait perturbation, no significant changes in knee joint motion, moments were found and statistically higher and prolonged muscle activation patterns were found across all groups. Elevated and prolonged activation has been interpreted as a stabilizing strategy, and the findings of Chapter 5 and 7 suggest that direct perturbations generate a stabilizing response of the surrounding knee musculature. Despite disease presence (MOA/ASYM) or the presence of self-reported instability (OAU/OAS/ASYM), responses of elevated hamstring and gastrocnemius and prolonged quadricep, hamstring and gastrocnemius activation patterns were not statistically different across groups in the first step following the perturbation. A similar response was reported by Kumar et al., who found an increase in MVIC normalized, mean loading response activation in the medial and lateral gastrocnemius, hamstring and quadriceps [88]. Schmitt and Rudolph also found neuromuscular alterations in response to a perturbation, where elevated medial co-contraction occurred in the stable and unstable groups [89]. Given the MOA severity in the current work, both groups had the capacity to generate increase muscle activation magnitudes and patterns to sufficient percentages of maximal effort activation to maintain joint function in response to the direct gait perturbations.

The muscle activation responses demonstrated by all groups in response to direct perturbations are in the direction of those OA group differences reported in this thesis,

OA gait literature [61, 63, 133, 143, 200-203] and in those that self-reporting instability in Chapter 4. Elevated and prolonged LH and prolonged quadriceps (VM/VL) are a common finding in the OA literature [61, 63, 133, 143, 200-203], thought to provide active stiffness by increased co-activity of agonist (VM/VL) and antagonist (LH) muscle sites. Time main effects were reported after direct perturbations, with higher and more prolonged hamstring (MH/LH) and more prolonged quadricep (VM/VL) activation after direct challenges, suggesting higher agonist/antagonist co-activity, but also increased medial/lateral co-activity found in all groups, a feature more commonly reported in a severe OA population [200, 206]. The strategy to maintain joint function in response to direct perturbations was not statistically different across all groups. Individuals are responding to challenges that acutely require higher active stiffness to maintain joint function. In the knee OA groups, given the alterations to the passive osteoligamentous and neuromuscular systems, if they continue to experience challenges to joint function (i.e. during everyday walking), over time, this may lead to the chronic muscle activation and biomechanical patterns that are consistently reported in the literature across in various OA severities [61, 63, 133, 143, 200-203].

9.2.2 INDIRECT PERTURBATIONS

Similar to direct gait perturbations, it was hypothesized that elevated and prolonged muscle activation alterations would be present in the MOA and OAU groups compared to ASYM and OAS groups in response to indirect gait perturbations utilized in Chapter 6 and 8. The study hypotheses were not fully supported. Muscle alterations in response to the indirect challenge were present, but they were not statistically different between

MOA and ASYM groups or between OAU, OAS and ASYM groups; a finding similar to direct perturbations.

Indirect gait perturbations were completed to determine how individuals with OA and those with and without instability land on the symptomatic limb after an unexpected medially directed walkway surface translation. Responses of elevated and prolonged quadricep, hamstring and gastrocnemius activation, earlier peak activation of the gastrocnemius muscles and no significant changes in joint motion were not statistically different between groups. Indirect perturbations demonstrated statistically higher activity in all muscle groups studied, while direct perturbations demonstrated quadricep muscle activation amplitudes that were not statistically different than pre-perturbed walking. Therefore, indirect challenges may result in a more comprehensive muscle response. Elevated quadricep activation could be a unique response in indirect perturbations to reduce higher impact force on the knee at initial contact and loading response. Evidence of a greater impact response was also noted in the hamstring muscles (comparing Figure 7.2 to Figure 8.2). No studies, to the current knowledge of the author, utilize indirect gait perturbation as a methodology.

In response to indirect perturbations, muscle activation alterations were not statistically different between groups. This finding suggests that healthy ASYM older adults, those with MOA and a subset with self-reported instability, despite differing symptoms and baseline walking patterns, have the capacity to increase muscle activation magnitudes and patterns across the gait cycle. Agonist/antagonist and medial/lateral co-activity increases

active stiffness to maintain joint function and potentially reduce impact forces on the joint during landing. Similar to the findings in direct gait perturbations, the resultant muscle activation responses were in the in the direction of findings reported in the literature between OA and asymptomatic individuals [61, 63, 133, 143, 200-203], suggesting that challenged walking, via direct or indirect perturbations, may simulate challenges experienced by those with OA day-to-day. Studies investigating structural and functional OA severity, found that those with severe OA walk with even further elevated and prolonged activation compared to those with moderate OA severity and therefore the question remains whether those with severe OA have the capacity to respond to challenges such as those performed in this thesis. Direct and indirect perturbations demonstrate that all participants, despite presence of MOA or instability sensations, had the capacity to respond to challenges. Despite altered passive osteoligamentous and neuromuscular alterations in the MOA groups, the level of functional performance in response to walking challenges was similar to the ASYM group.

9.3 CONCLUSION

In conclusion, individuals dichotomized with MOA and self-reports of instability impacting activity, walk with biomechanical outcomes that were not statistically different but recruited the VM and VL to higher percentages of maximal effort activation and more prolonged VM and VL activation compared to OAS and ASYM groups. Furthermore, LG is phase-shifted earlier in the stance phase in the OAU group compared to ASYM groups only. These findings suggest that altered muscle activation magnitudes and patterns promote active stiffness in the OAU group to maintain biomechanics and knee joint

function during walking, but this strategy may be unreliable, as sustained activity creates an environment more prone to fatigue, and therefore episodes of instability are more likely. These gait alterations may also put those with OAU at a higher risk of structural and clinical OA progression.

After direct and indirect perturbations, responses of higher and more prolonged muscle activation magnitudes and patterns and no statistical differences in biomechanical outcomes was found in all groups compared to non-perturbed walking. All group (MOA/ASYM, OAU/OAS/ASYM) responses were not statistically different. Indirect perturbations resulted in elevated quadriceps activity, while direct perturbations did not, which may demonstrate an activation strategy purposed to minimize impact load and stress as the symptomatic foot lands on the moving treadmill belt in response to the translation. This demonstrates that all groups, despite varying structural alterations, OA symptoms and baseline walking patterns, maintain sufficient capacity to increase muscle activation amplitude and temporal patterns to maintain knee joint function in this environment. Findings of an increased neuromuscular response after challenged walking supports the interpretation that increased active stiffness promotes joint knee stability. The responses to perturbations are in the direction of muscle activation magnitudes and patterns those with MOA and those with instability impacting activity utilized in non-perturbed walking environments, suggestive of a strategy that is responding to OA knee joint challenges (altered joint structures and elevated symptoms). However, MOA groups demonstrated sufficient capacity to increase muscle activation patterns to higher percentages of maximal effort activation, maintaining their joint function and

demonstrating functional performance in response to challenged walking similar to ASYM groups.

9.4 LIMITATIONS

This study investigated self-reported instability, direct gait perturbations and a novel investigation of indirect gait perturbations. However, limitations to the study need to be considered when interpreting the findings.

This study dichotomizes instability using the KOS-I, and self-reported instability literature has demonstrated a variety of approaches to this dichotomy. Studies have defined an OAU group as individuals who self-report instability impacting activity in some manner, but only few have defined a stable group as having no instability symptoms. This dichotomy has shown that those with OAU self-report worse pain, symptoms and function from the KOOS and these findings could explain differing gait mechanics. Isolating instability may require an objective measure of instability. It is currently not clear if a such a metric exists, although many outcomes have been used to define gait stability [74]. Our method of dichotomizing those without symptoms and with symptoms that impact activity was a method to mediate this limitation. As an option with a larger sample size, the KOS-I could be used in a regression analysis or visual analog scale of instability could be created that would allow a continuous measure of instability, similar to work understanding gait and OA pain severity [43]. This would follow the natural progression OA biomechanics have taken, where traditionally there was a dichotomous comparison of OA and ASYM, and more recently a greater understanding

of the OA group has been sought after narrowing in on OA features (i.e. pain, effusion, strength, alignment), clinical and structural severity. Expanding the instability literature, to include larger samples, refined evaluations, and a mix of subjective and objective measures of stability may fill gaps in the current literature to define the impact of this impairment on gait more clearly.

Direct and indirect perturbations were limited in translation magnitude and rate due to the mechanical properties of the R-MILL dual-belt instrumented treadmill. Treadmill translations were triggered using the GRF from the contralateral force plate, where once a GRF below 30N was registered, the treadmill would execute the translation. The mechanical characteristics of the perturbation are found in Chapter 5, where treadmill translations occurred at 40% (+/-6%) of the stance phase, at a magnitude of 31.8mm (+/-0.007mm) and mean rate of 0.11m/s (+/-0.0029m/s), on average. These settings were also used to address Objective 3. Differing walking speeds could influence the perturbation response. Stride and stance time is increased with increased walking speed [184], therefore, moving faster participants through translations quicker, with some entering double limb support before the translation was complete. To manage this potential influence, walking speed was used as a covariate in the perturbation response analyses.

Objective 3 formed a preliminary study, presented in Chapter 7 and 8. The inability to detect significant differences in interaction effects within three-factor ANCOVA's could have been a result of small sample size. In Chapter 7, a mean change of 68.8 units, 43.1 units and 17 units in the OAU, OAS and ASYM groups respectively, were found in LH

PP2-scores from T0 to T1. Appendix A outlined a reliability assessment, finding an MDC of 22.6 units for this hamstring pattern. Using the MDC value, a stepwise response could have been reported after direct perturbations in this case. In Chapter 8, a mean change of 44.4 and 35.3 units was found MG and LG *PP3-scores* for the OAU group, representing earlier peak activation. MDC's of 27.5 and 31.9 units was reported (Appendix A). The OAS and ASYM groups reported lower mean change values and suggest that a group-by-time interaction might have been undetected due to sample size. These preliminary analyses provide encouraging evidence that differences in responses to perturbation testing based on self-reported instability dichotomies may exist, however more participants across groups is required.

9.5 FUTURE DIRECTIONS

This thesis brought a novel and comprehensive approach to understanding direct and indirect gait perturbations and self-reported instability in those with MOA. However, the findings of this study lay groundwork for future research in the following areas:

1. Muscle activation pattern differences were reported in Chapter 4 between groups dichotomized by self-reported instability. However, the OAU group demonstrated other significant differences, specifically in the KOOS scores that may explain these findings and other OA symptoms associated with instability were not captured (laxity, alignment, proprioception, etc.). KOOS Pain scores demonstrated a stepwise decrease among ASYM, OAS and OAU groups, with the OAU group self-reporting the worse KOOS pain outcome. Pain and instability are

presumably linked; however, every episode of instability may not be the result of pain, just as every episode of pain may not be result of instability. It is important to understand this link between pain and instability, however, this thesis focussed on the self-reported symptom of instability (i.e. buckling, shifting or giving way) and its impact on gait mechanics and perturbation responses. Isolating the influence of self-reported instability could be achieved by either controlling for each factor in a cross-sectional study design, however, both self-reported instability and self-reported pain are subjective. Isolating symptoms and obtaining more objective measures of pain and instability during walking (alongside self-report measures) could help shed light on this relationship.

2. The study used medial 3cm indirect and direct gait perturbations to understand the biomechanical and neuromuscular responses in those with MOA, stability dichotomized MOA and ASYM groups, finding no differences. This suggests that all groups are demonstrating appropriate knee joint functioning to increase muscle activation magnitudes patterns to maintain knee joint biomechanics and continue treadmill walking in response to medial 3cm indirect and direct perturbations. The perturbations employed were in the medial-lateral direction. Other types of challenged walking (i.e. uphill, downhill, independent belt speed changes, slips/trips) have been used in other populations to challenge individuals walking [80, 81, 83, 85-87, 289-292]. A scenario may exist where unique responses are found between MOA and ASYM groups in particular challenged walking environments and further work to elucidate this challenged environment is needed

to better understand reports of instability during functional activities and how knee function is maintained.

3. A methodological decision was made to remove perturbation responses where participants crossed onto the other plate or utilized the handrails for support. The rationale for this decision was that if participants utilized the handrails, regaining/or maintaining balance would be improved by upper body contact points, potentially reducing the demand on the lower extremity. Foot crosses onto contralateral force plate were removed, as centre of pressure data would be invalid. Outlined in Chapter 5, out of all the medial 3cm direct perturbations experienced the ASYM group completed 47/60 and the MOA group completed 49/60 without stepping onto the other treadmill belt or using handrails (Table 5-1). The participants were informed to attempt to keep each foot on each plate in response to perturbation. Missteps may demonstrate information on the pathomechanics involved when a participant could not place their feet where they intend to, and the response of the active muscular and neural control subsystems to maintain balance. These data may provide information on muscle activation magnitudes and patterns and lower extremity joint motions involved when the signal sent from the control subsystem is not correctly executed or potentially altered mid-stride.

4. The results of this thesis set groundwork for the development of a stress-testing paradigm in joint function. Stress-testing paradigms are implemented in cardiac

and pulmonary care, for example, to objectively understand organ function. A challenged walking paradigm could be feasible as a stress test for the functional performance of the joint. All groups were able to perform and maintain balance during the challenged walking environment. Therefore, it could be concluded that despite self-reports of reduced physical function, instability, and increased pain, their perturbation responses were not significantly different to a comparison group of healthy older adults. These findings are encouraging and may support sufficient capacity and function to maintain walking ability in the MOA group. More work is needed to understand this paradigm, including; implementing other challenges (i.e. uphill/downhill, slips/trips, gait speed changes, etc.); testing severe OA participants scheduled for a knee replacement; and understanding the threshold between performing adequately versus sub-optimally. This thesis provided preliminary evidence of the utility of a challenged walking paradigm to support these further investigations.

APPENDIX A: RELIABILITY OF LOWER EXTREMITY MUSCLE ACTIVATION MAGNITUDES AND PATTERNS OF HEALTHY YOUNG ADULTS DURING DUAL-BELT TREADMILL GAIT USING PRINCIPAL COMPONENT ANALYSIS.

INTRODUCTION

Gait analyses are the current gold standard in assessing alterations in walking patterns associated with knee OA. These analyses quantify the coordinated kinematics, kinetics and muscle activation magnitudes and patterns that generate locomotion.

Reliability of gait outcomes have been reported in over ground walking for healthy individuals and individuals with knee OA [154, 173, 245, 293], as well as treadmill walking environments [155, 244]. Specifically, for over ground walking environments, ICCs for knee sagittal and frontal plane motion (ICC > 0.60), moment (ICC > 0.78) and EMG (ICC > 0.73) muscle outcomes have been found [173, 245]. While, good to excellent reliability outcomes have also been found in during treadmill walking, where motion (ICC > 0.65), moment (ICC > 0.57) and EMG (ICC > 0.71) outcomes are reported [155, 244]. These studies demonstrate high-to-excellent reliability of gait outcomes utilized in the gait analyses of this thesis, with exception to day-to-day reliability of muscle activation magnitudes and patterns measured via PCA in a treadmill walking environment, as this has yet to be determined.

The purpose was to quantify day-to-day reliability of quadriceps, hamstring and gastrocnemius activation patterns from treadmill walking in healthy young adults at self-

selected walking speed using PCA. We hypothesize that muscle activation magnitudes and patterns will demonstrate excellent repeatability (ICC > 0.80).

METHODS

Twenty healthy young adults (10 females, 10 males) were recruited using local advertisements and participated in two standardized data collections, one week apart. Participants were included if: (i) age between 18 and 35 years old (ii) no musculoskeletal disease or injury within the past year (iii) no cardiovascular or neurological disease (iv) no lower extremity surgery and (v) ability to walk independently on a treadmill. The study protocol was approved by the local ethics review board.

Each data collection followed a standard procedure [236], starting with participants changing into tight fitting shorts, a t-shirt and removing footwear. Height and mass were recorded. Participants walked back-and-forth across a GaitRITE™ (CIR Systems, USA) pressure sensitive walkway and five trails were randomly recorded to determine averaged walking speed. Participants were prepped for EMG consistent with standardized guidelines [235]. Surface electrodes (Ag/AgCl, 10mm diameter, 30 mm inter-electrode distance, Red Dot, 3M Health Care, USA) were placed in a bipolar configuration over the VM VL, MH, LH, MG and LG on each leg. Bilateral reference electrodes were placed on the tibial shaft. Electrode placement was verified using isometric muscle testing, which also assisted with signal validation and gain adjustments. Surface EMG were pre-amplified (500x) and further amplified using two AMT-8 measurement systems (CMRR:

115dB at 60Hz, Input Impedance: ~10GΩ, band-pass: 10-1000Hz, Bortec Inc., Canada). EMG signals were sampled at 2000Hz (A/D 16bit, +/ 5V).

Participants walked on a dual-belt instrumented treadmill (R-Mill, Motekforce Link, The Netherlands) for 6min. Walking speed was set to average speed calculated from the GaitRITE™ walkway at each data collection. After 6 min of walking, allowing for the participant to acclimatize to the treadmill environment [236], a 20s measurement was made. Following walking participant were instructed to lay supine and a resting muscle activity trial was recorded. Using a Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc.), MVICs were determined. Dynamometer gravity corrections were completed prior to each muscle test. Hamstrings and quadriceps were tested at 45˚ of knee flexion, with the dynamometer and knee joint axis aligned. Gastrocnemii were tested using a standing unilateral plantarflexion exercise [72]. Practice/warm-up contractions were followed by two, 3s MVICs with 40s of rest between trials. Standard verbal encouragement was provided.

Custom MatLab™ 2016b (The Mathworks Inc., USA) scripts were used to complete data processing. Raw EMG signals were filtered (bandpass, 10-500Hz, 4^{th} order, zero-phase Butterworth filter), resting bias corrected, converted to microvolts, full wave rectified, and linear enveloped (lowpass, 6Hz, 4^{th} order, zero-phase Butterworth filter) [61]. EMG profiles were amplitude normalized to the highest 100ms window from MVIC trials and time normalized to the gait cycle.

PCA has been used to understand amplitude and temporal features of muscle activation waveforms in knee OA gait EMG [61]. Three separate PCA models were completed for each muscle group (quadriceps, hamstring, gastrocnemius). An eigenvector decomposition of the cross-product matrix ($S=X^T*X$) was completed yielding PPs. Three PPs were retained (PP1, PP2, PP3) explaining at least 90% of the variance of the dataset. *PP-Scores* were computed and provide a weighting coefficient for how each pattern related to each waveform [294].

For each participant, the study limb was randomly selected and matched between days for further analysis. Test-retest reliability was assessed using $ICC_{2,k}$ with 95% CI, standard error of measurement and the MDC. ICC cut-points were as follows: Excellent (ICC ≥ 0.8), High (0.60 ≤ ICC ≤ 0.79), Fair (0.40 ≤ ICC ≤ 0.59) and Poor (ICC ≤ 0.39) [155]. Statistical analyses were completed using MatLab™ 2016b (The Mathworks Inc., USA).

RESULTS

Age, height, mass and BMI were 24 +/- 4 years, 1.73 +/- 0.08 m, 73.4 +/- 9.4kg, and 24.5 +/- 2.4 kg/m^2, respectively. The participants walking speed on each day was 1.25 +/- 0.11 m/s and 1.26 +/-0.10m/s respectively. The 95% CI, ICC, SEM and MDC have been published previously [155]. Each data collection mean +/- SD, mean difference, ICC (95%CI) SEM and MDC values for EMG outcomes are presented in Table A-1.

Table A-1: Mean and Standard Deviation (SD), Intraclass Correlation Coefficient (ICC), Upper (UB) and Lower (LB) Bound ICC 95% Confidence Intervals (CI), Standard Error of Measurement (SEM) and Minimal Detectable Change (MDC) values for EMG PP-Scores.

Variable	Day 1 Mean	Day 1 SD	Day 2 Mean	Day 2 SD	ICC	UB 95%CI	LB 95%CI	SEM	MDC
VM	--	--	--	--	--	--	--	--	--
PP1	67.0	32.7	65.8	34.4	0.90	0.96	0.74	10.6	29.2
PP2	4.5	10.1	1.3	9.3	0.93	0.98	0.68	2.6	7.1
PP3	0.3	9.7	0.1	7.1	0.88	0.95	0.70	2.8	7.9
VL	--	--	--	--	--	--	--	--	--
PP1	75.0	40.8	71.2	42.0	0.93	0.97	0.82	10.9	30.3
PP2	3.7	13.0	0.7	11.9	0.95	0.98	0.82	2.7	7.6
PP3	1.1	12.3	0.0	7.0	0.84	0.94	0.60	3.9	10.8
MH	--	--	--	--	--	--	--	--	--
PP1	77.7	63.6	69.5	53.5	0.95	0.98	0.88	13.0	36.0
PP2	5.0	13.8	5.3	17.7	0.78	0.91	0.44	7.3	20.3
PP3	-0.2	11.4	0.8	13.0	0.54	0.82	-0.20	8.2	22.8
LH	--	--	--	--	--	--	--	--	--
PP1	75.2	53.1	75.1	41.8	0.91	0.97	0.78	13.8	38.4
PP2	4.9	18.8	7.0	23.3	0.85	0.94	0.62	8.1	22.6
PP3	-0.9	15.3	1.0	18.9	0.77	0.91	0.42	8.2	22.6
MG	--	--	--	--	--	--	--	--	--
PP1	278.5	83.6	260.4	84.7	0.84	0.93	0.63	32.6	90.2
PP2	-20.7	56.5	-21.9	50.5	0.96	0.99	0.91	9.9	27.5
PP3	2.4	41.4	1.3	41.8	0.91	0.96	0.76	12.5	34.7
LG	--	--	--	--	--	--	--	--	--
PP1	212.8	100.2	212.7	94.4	0.90	0.96	0.76	29.9	82.8
PP2	9.8	55.1	8.8	62.6	0.96	0.98	0.90	11.5	31.9
PP3	1.3	20.8	2.3	27.4	0.73	0.90	0.31	12.4	34.4

Ensembled averaged waveforms, as well as PPs and PP interpretations, for quadricep (Figure A-1), hamstring (Figure A-2) and gastrocnemius (Figure A-3) are is presented.

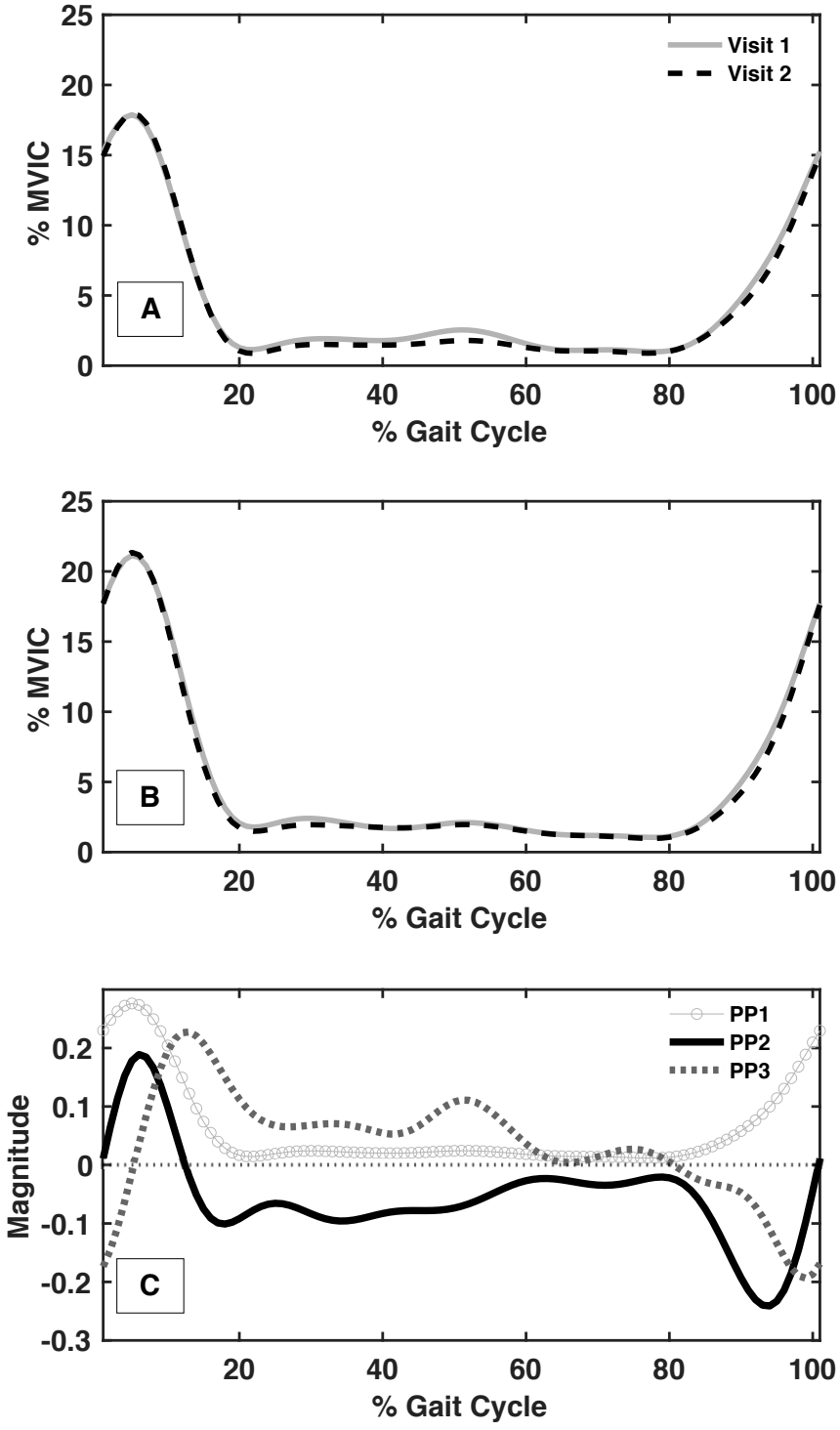

Figure A-1: Thee principal patters captured 99% of the waveform variability. PP1 (96%) captured the overall magnitude and shape, high PP2 (2%) captured a prolonged activation and high PP3 (1%) scores captured a greater difference between early-to-mid stance and swing phases.

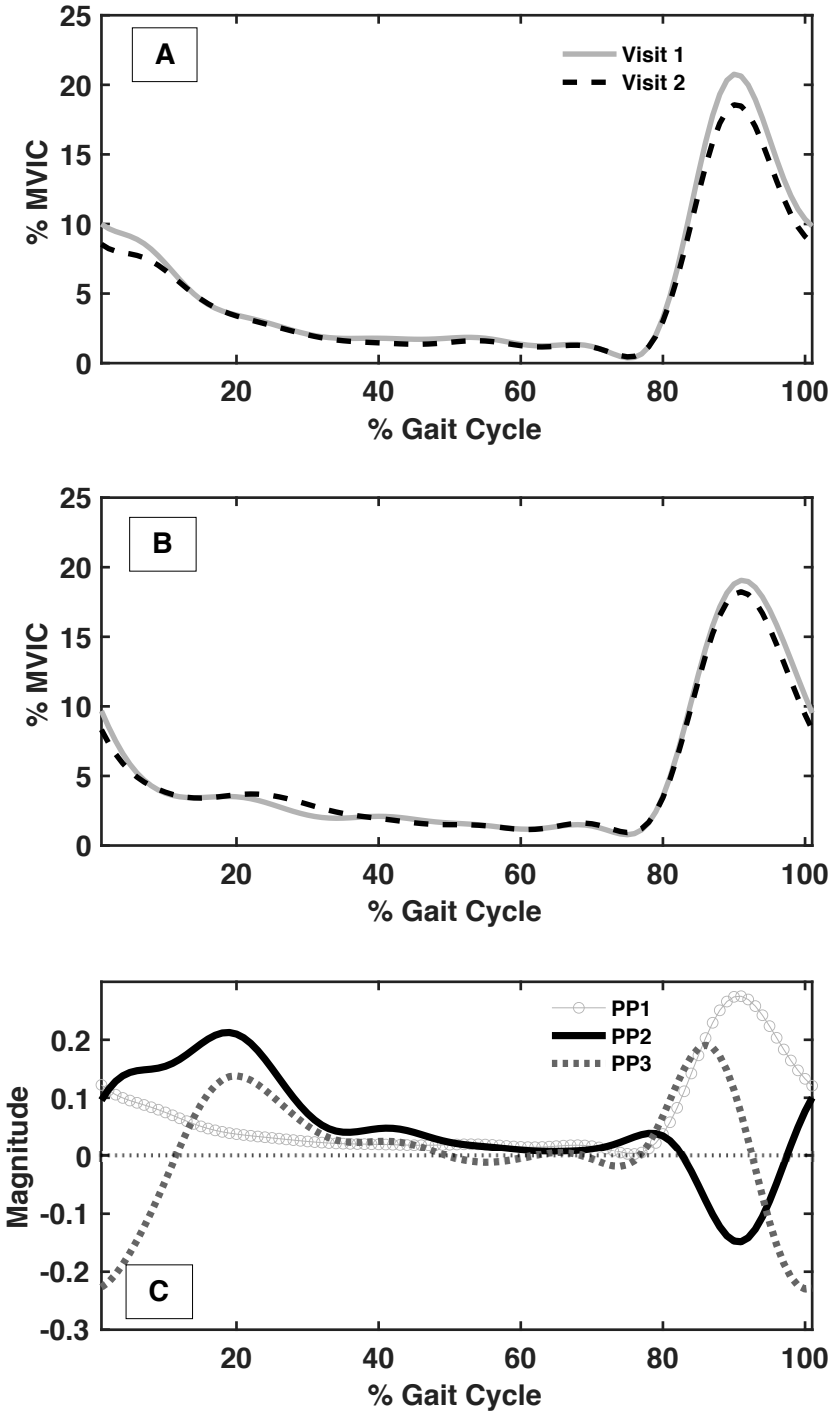

Figure A-2: Thee principal patters captured 98% of the waveform variability. PP1 (92%) captured the overall magnitude and shape, high PP2 (4%) captured a prolonged activation and a burst of activity during later swing and high PP3 (1%) scores captured a difference between early and late stance activation, where greater scores indicate greater late stance activity.

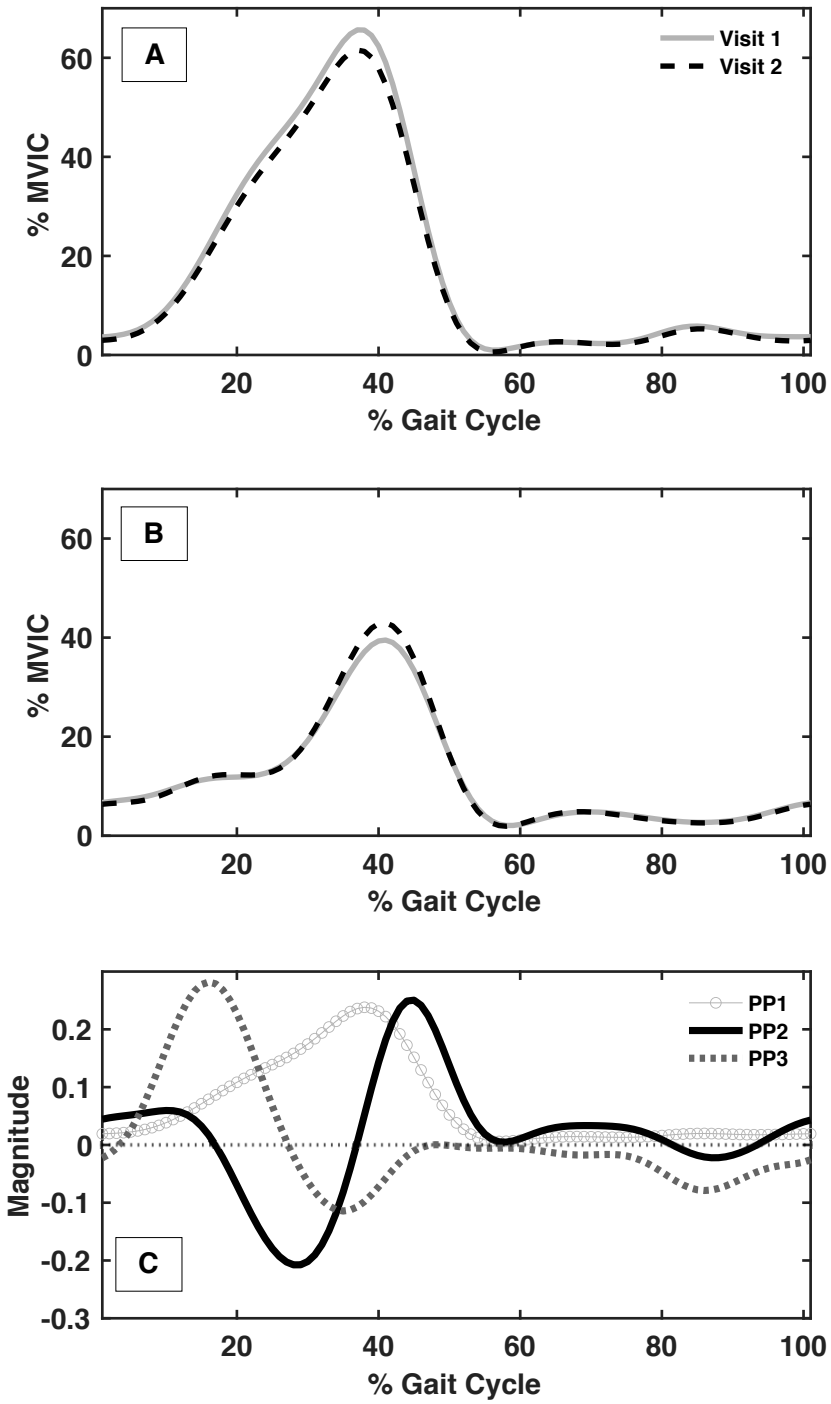

Figure A-3: Thee principal patters captured 99% of the waveform variability. PP1 (92%) captured the overall magnitude and shape, high PP2 (5%) captured a phase shift in activation where higher scores indicated delayed activity and high PP3 (2%) scores captured a difference between early and late stance activation, where greater scores indicate a lower difference.

DISCUSSION

There is strong evidence for gait outcome reliability during over ground and treadmill walking, however, in relation to the thesis objectives, the reliability of treadmill EMG outcomes assessed using PCA had not been explored. Therefore, the purpose was to quantify day-to-day reliability of EMG outcomes, assessed using PCA, during treadmill walking in healthy young adults. This study is an addition to recently published work, using the same methodology and cohort, completing a comprehensive understanding of the reliability of muscle activation magnitudes and patterns using non-negative matrix factorization and mean/peak muscle activation, as well as spatiotemporal and biomechanical outcome variables [155]. The data provided supports our hypothesis of high-to-excellent reliability of the lower extremity muscle activation magnitudes patterns identified using PCA.

Factorization methods are methods to identify data features that explain maximal amounts of variance in a dataset [263]. PCA and non-negative matrix factorization are often employed on EMG datasets to reduce the dimensionality of muscle activation envelopes [61, 288], however, no method is ideally suited in EMG analysis [295]. While non-negative matrix factorization selects features of muscle synergies and co-activations, PCA helps to explain the directions and patterns of activation within the dataset [264]. However, both methods have been shown to perform similarly when employed on an experimental dataset [296]. Rutherford et al. 2020 reported three F-Scores that explained variance in the dataset and provide a foundation to assist in the interpretation of the PCA results in this thesis [155]. F-Score ICCs were previously reported ranging from 0.60-

0.95 for the quadriceps (VM/VL), 0.88-0.97 for the hamstrings (MH/LH) and 0.84-0.95 for the gastrocnemius (LG/MG) [155]. Similar ranges were reported in this study, however, VM Factor 3 had lower reliability than VM PP3, while MH PP3 had a lower reliability than MH Factor 3, suggesting different features being identified in each method. However, the findings of this study are suggesting a high-to-excellent reliability of PCA identified EMG patterns in treadmill gait of young healthy adults.

CONCLUSION

High-to-excellent ICC values for EMG were found using treadmill walking with the exception of MH *PP3-Scores*, supporting the use of this methodology to assess lower extremity muscle function.

APPENDIX B: GAIT WAVEFORM VARIABILITY

This appendix provides all ensembled averaged waveforms used to glean sagittal and frontal plane outcome variables and muscle activation waveforms used in the PCA analysis. Each Chapter is titled with corresponding title in the thesis. The variability plots are labeled with the x-axis representing the stance phase or gait cycles and the y-axis representing degrees, Nm/kg or %MVIC in the waveforms. Baseline strides and response strides were identified in the title and are found throughout Chapters 5-8.

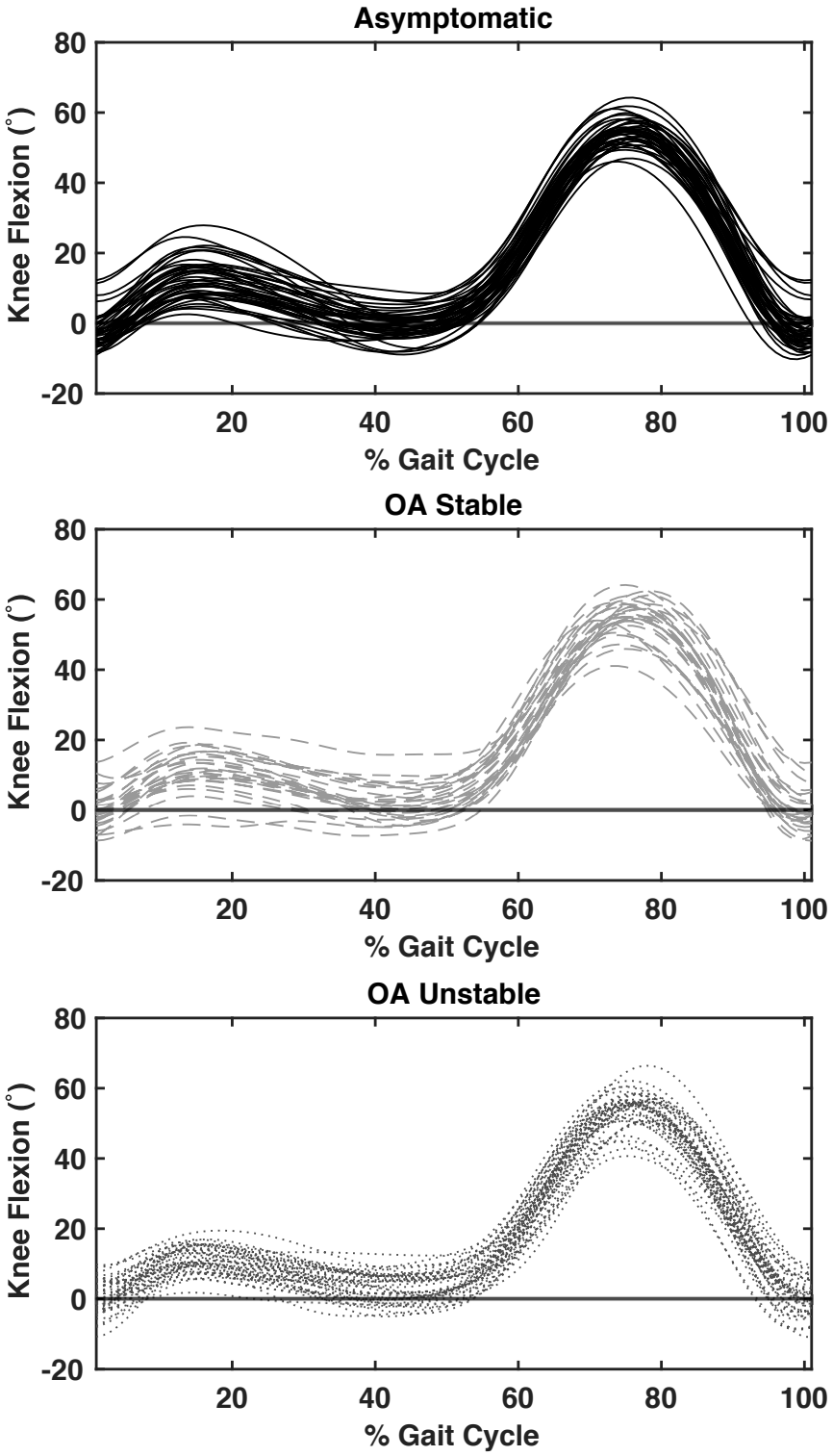

Figure B-1: Sagittal plane motion ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Knee flexion (degrees) is represented by positive values on the y-axis and percentage of the gait cycle is represented on the x-axis.

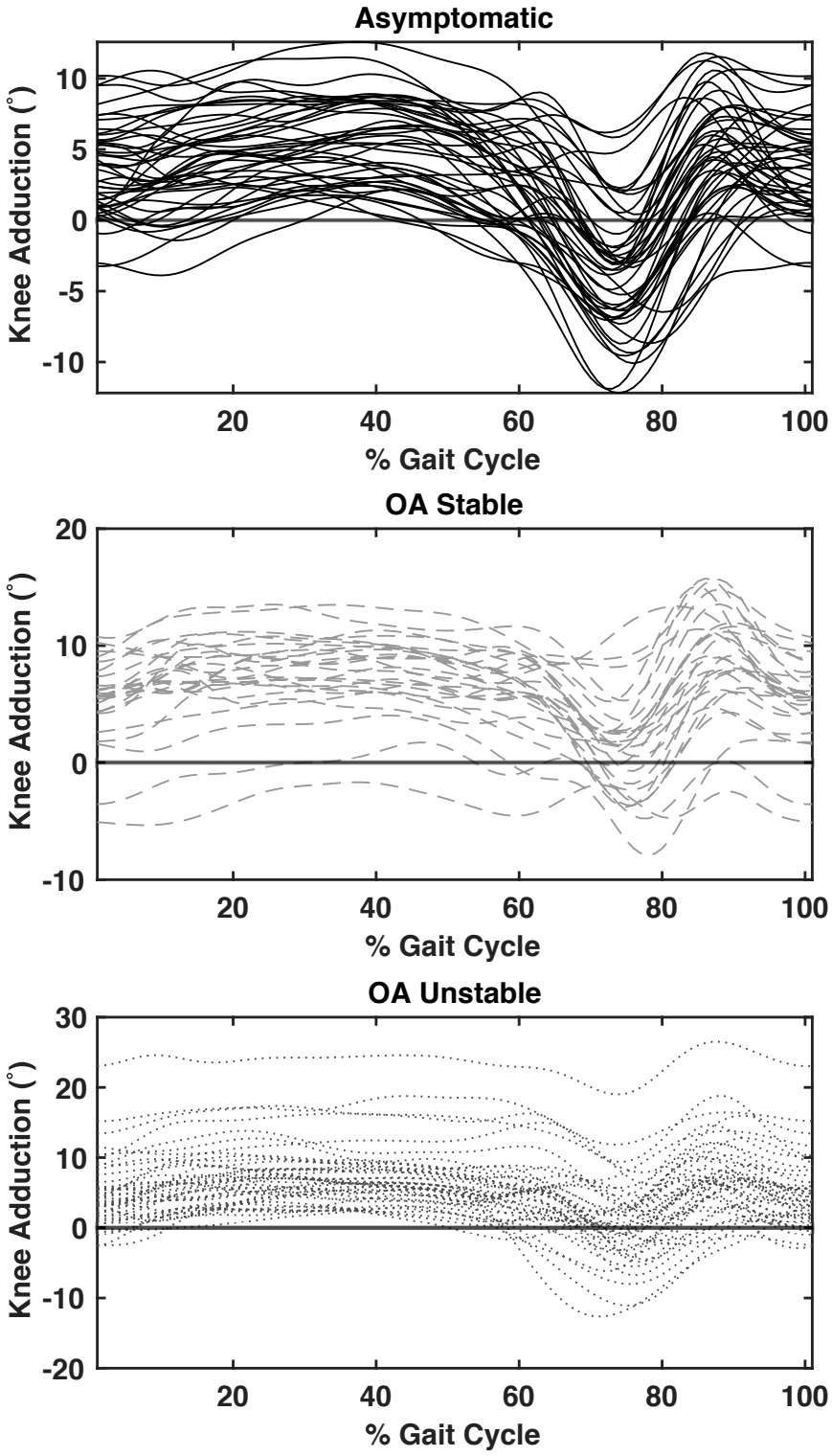

Figure B-2: Frontal plane motion ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Knee adduction (degrees) is represented by positive values on the y-axis and percentage of the gait cycle is represented on the x-axis.

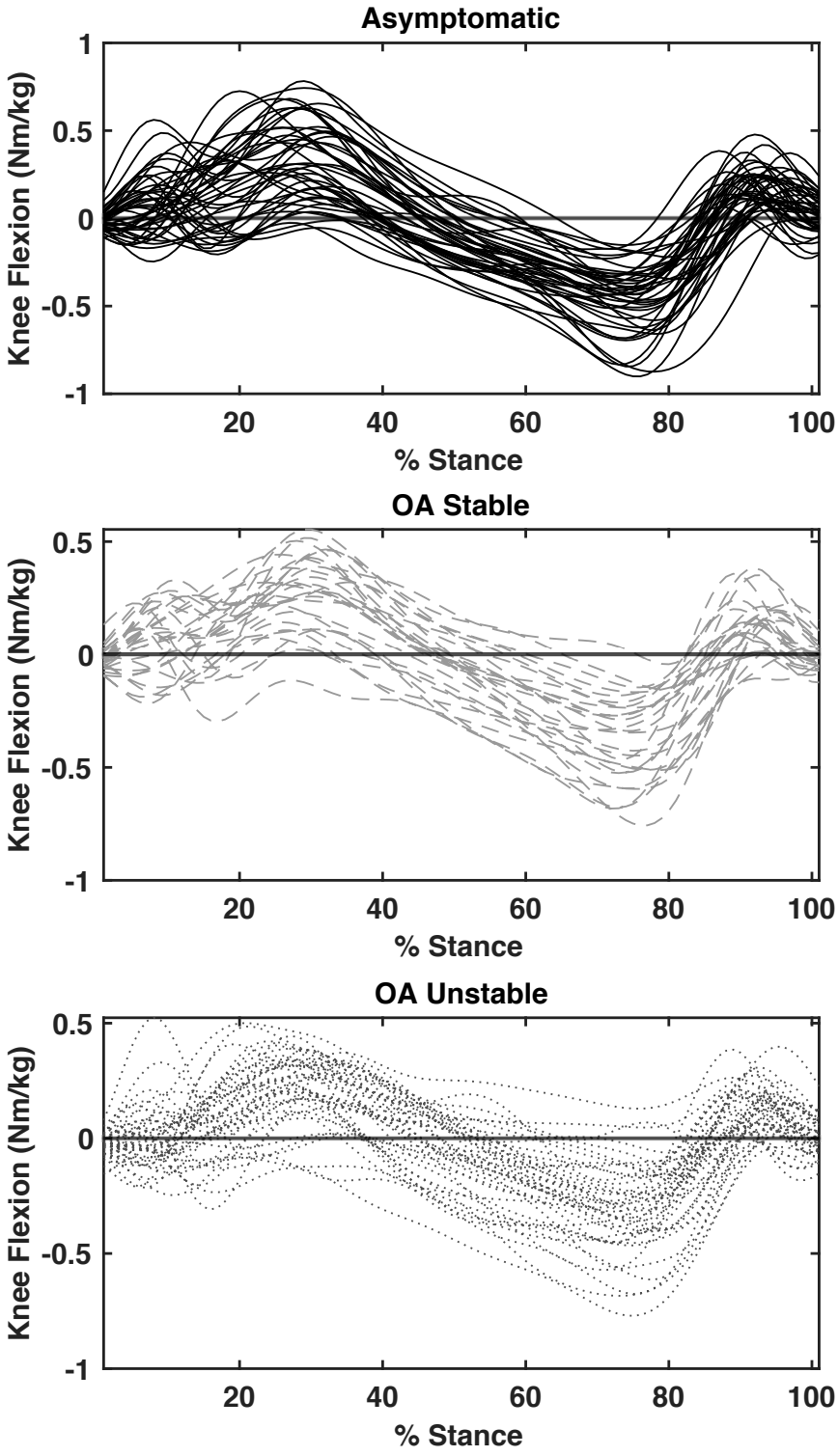

Figure B-3: Sagittal plane moment ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Knee flexion (Nm/kg) is represented by positive values on the y-axis and percentage of the stance phase is represented on the x-axis.

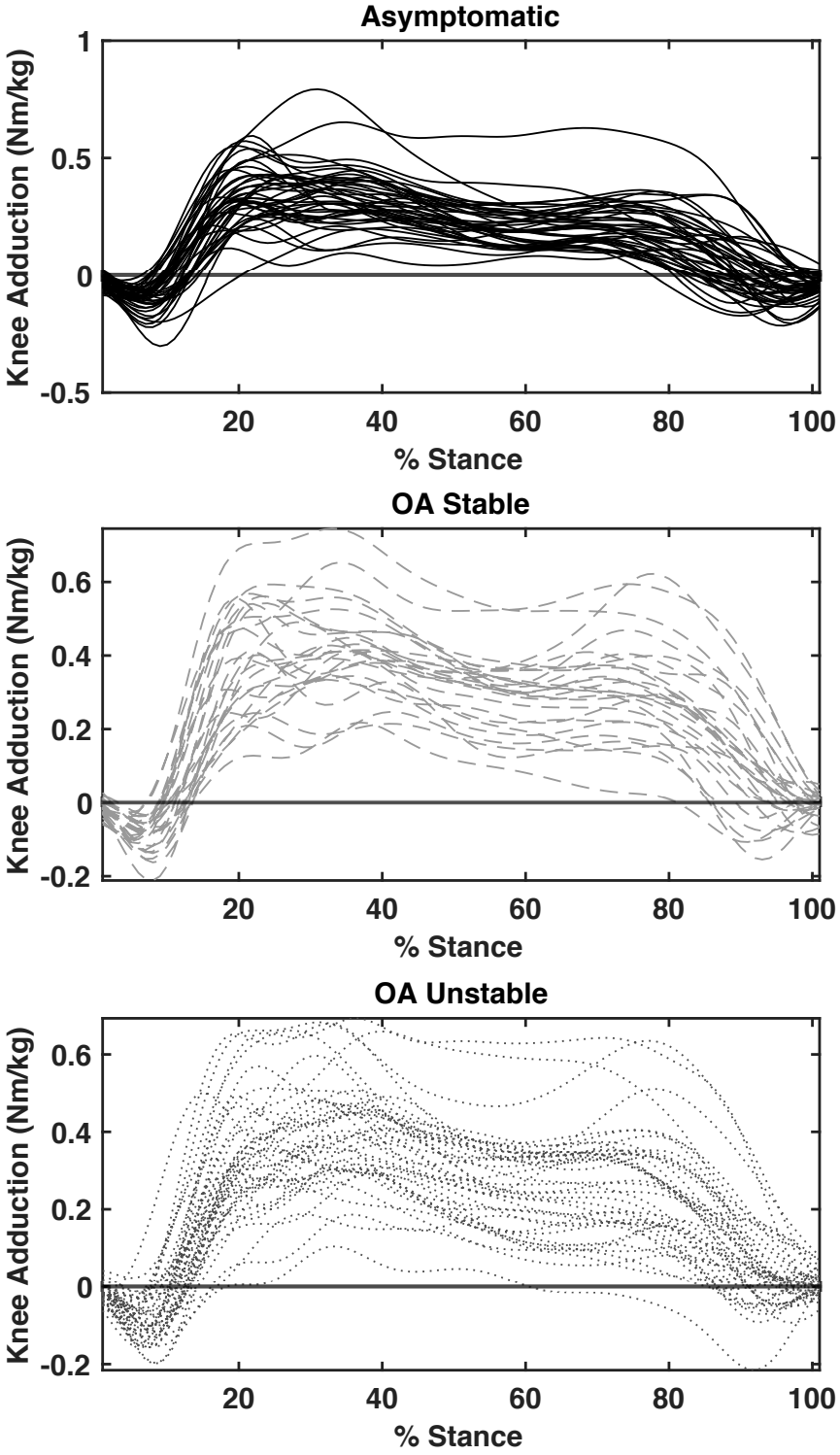

Figure B-4: Frontal plane moment ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Knee adduction (Nm/kg) is represented by positive values on the y-axis and percentage of the stance phase is represented on the x-axis.

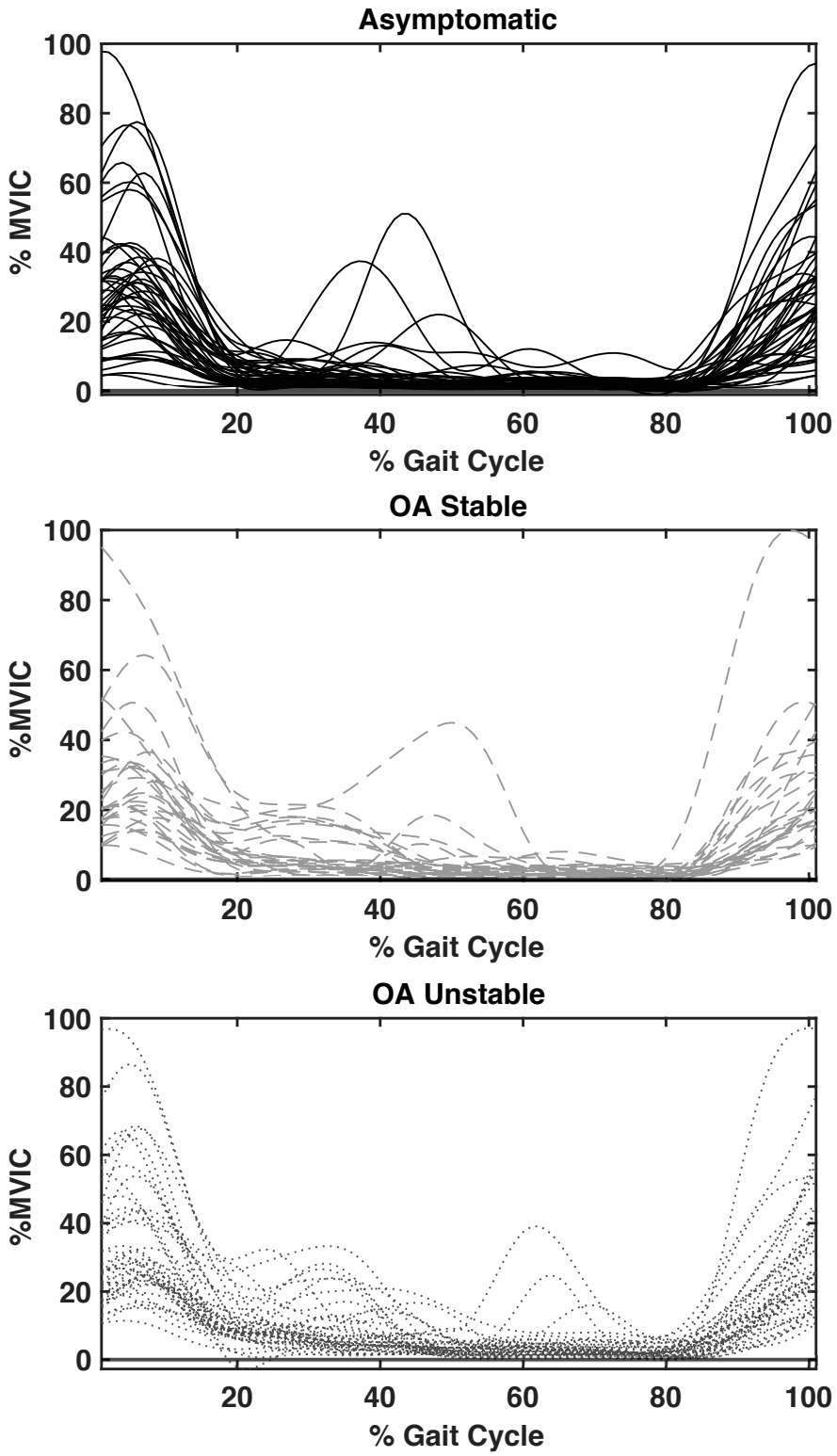

Figure B-5: Vastus medialis ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

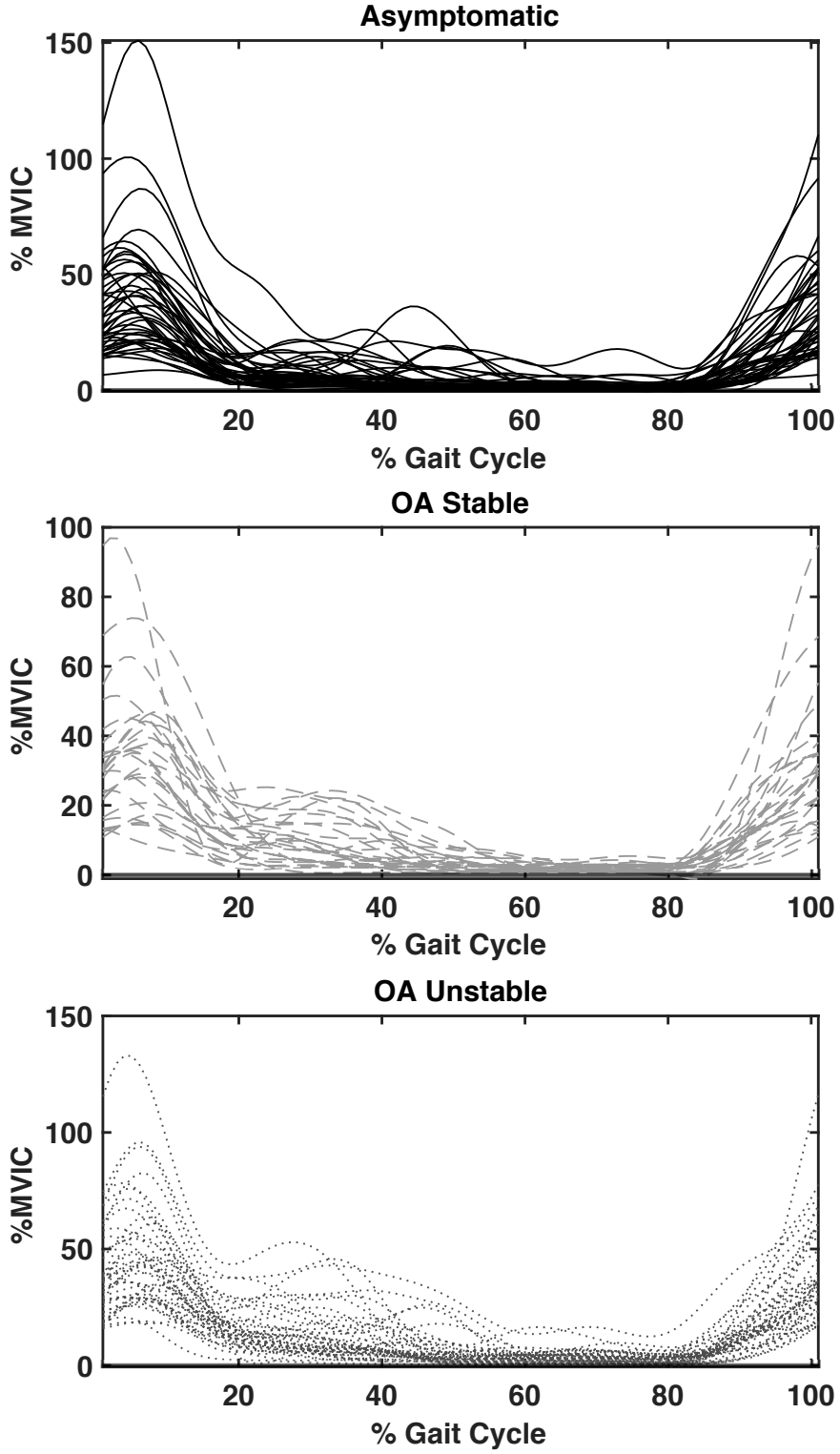

Figure B-6: Vastus lateralis ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

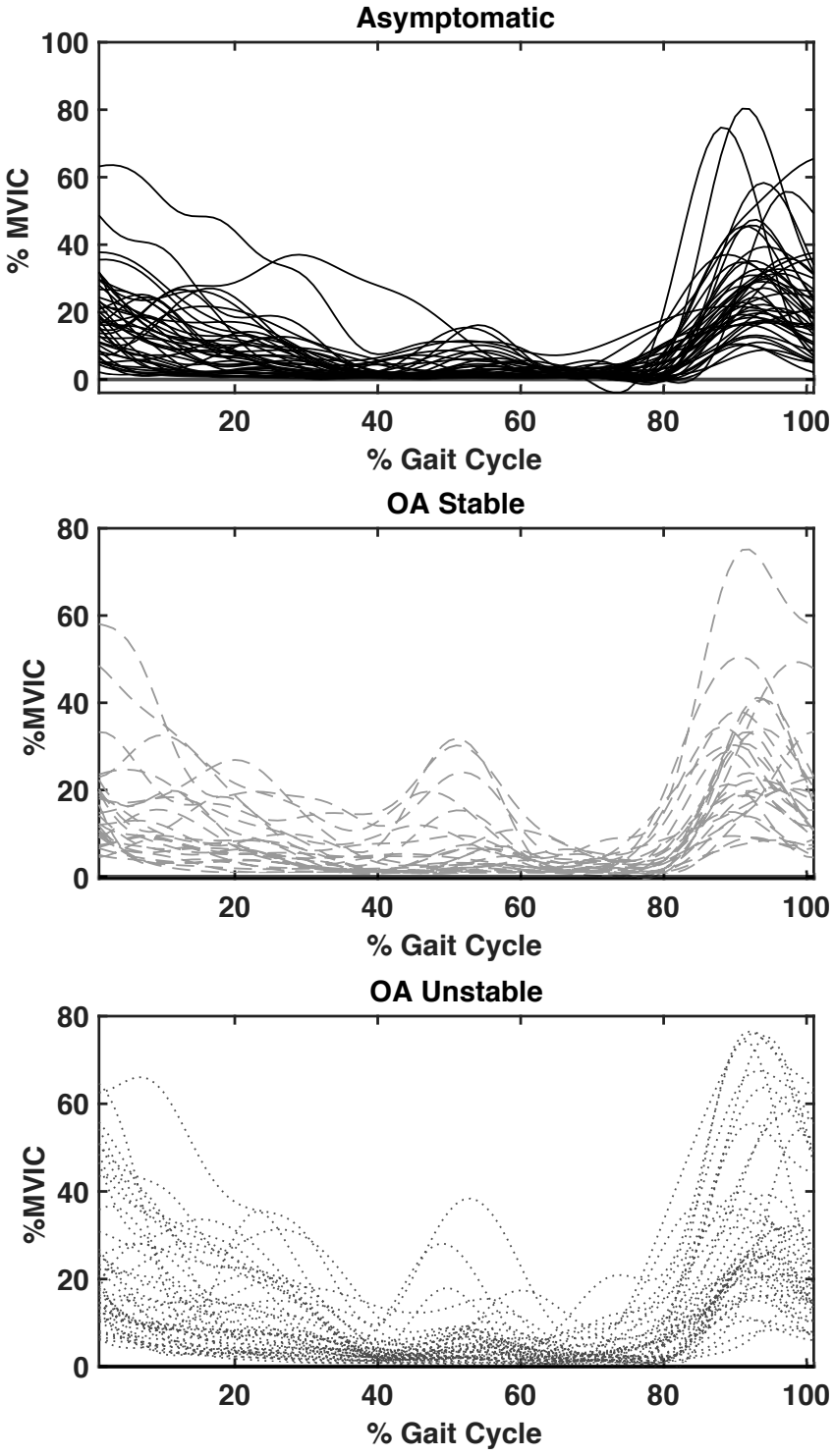

Figure B-7: Medial hamstring ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

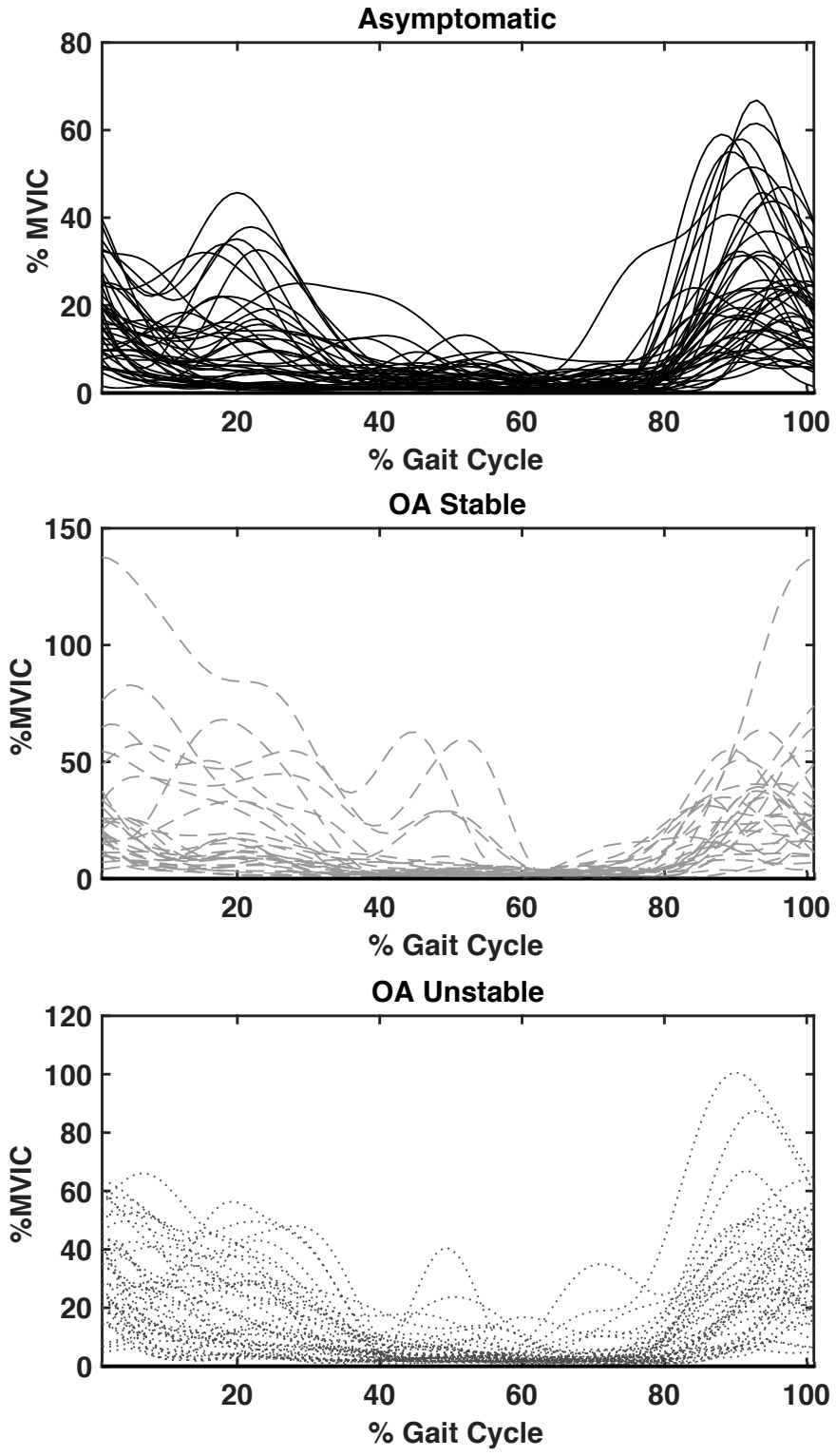

Figure B-8: Lateral hamstring ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

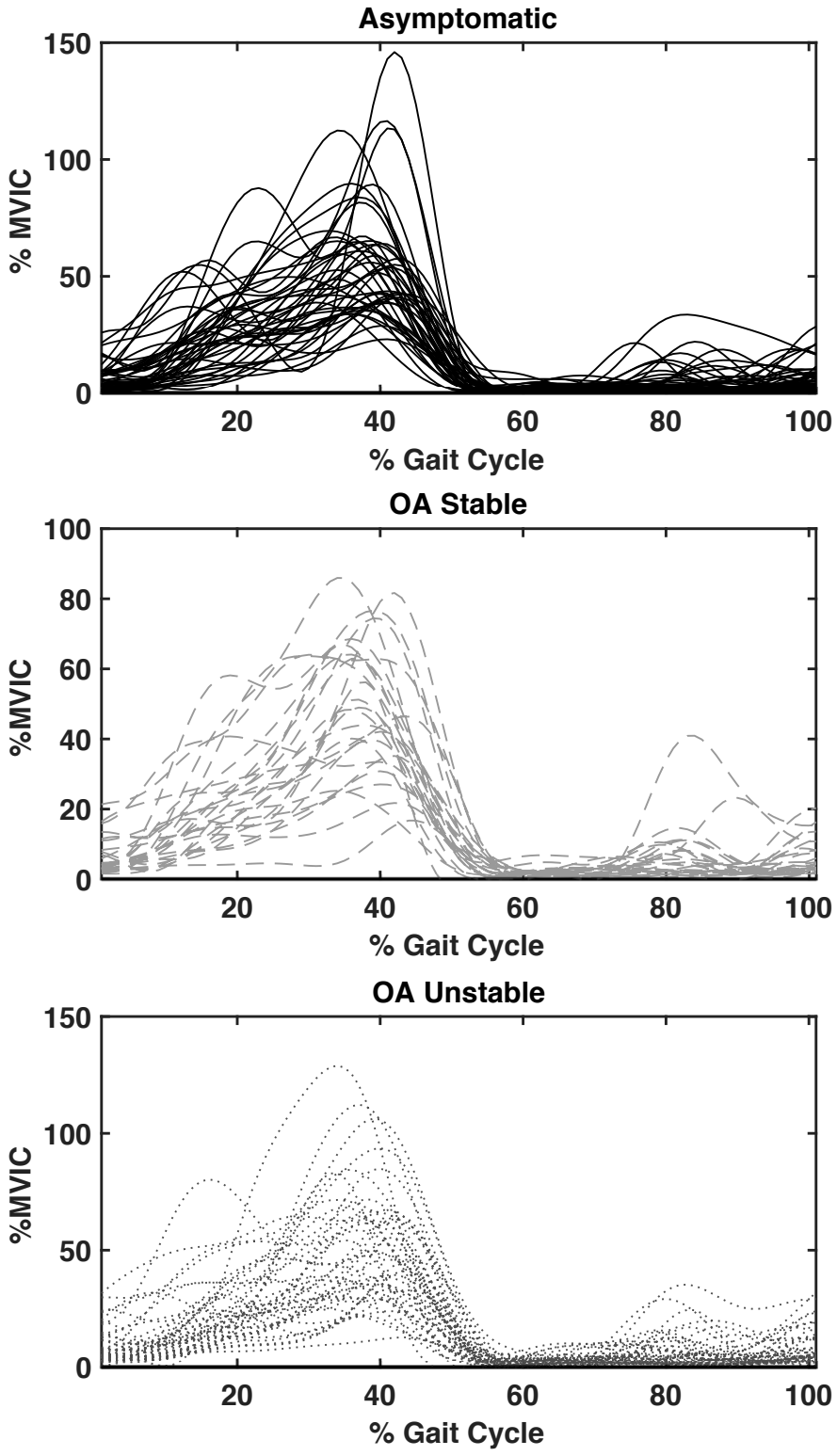

Figure B-9: Medial gastrocnemius ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

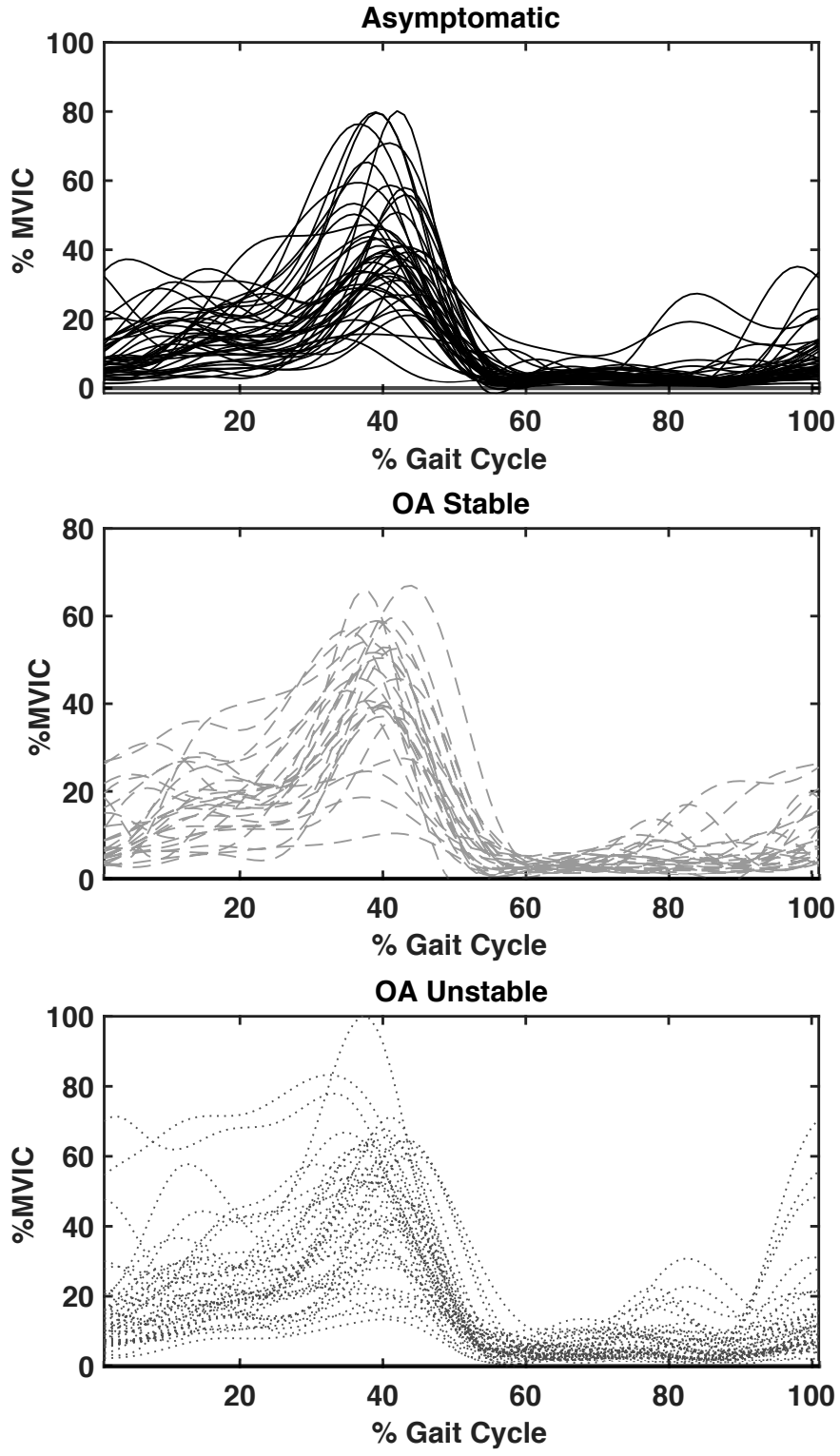

Figure B-10: Lateral gastrocnemius ensembled averaged waveforms for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

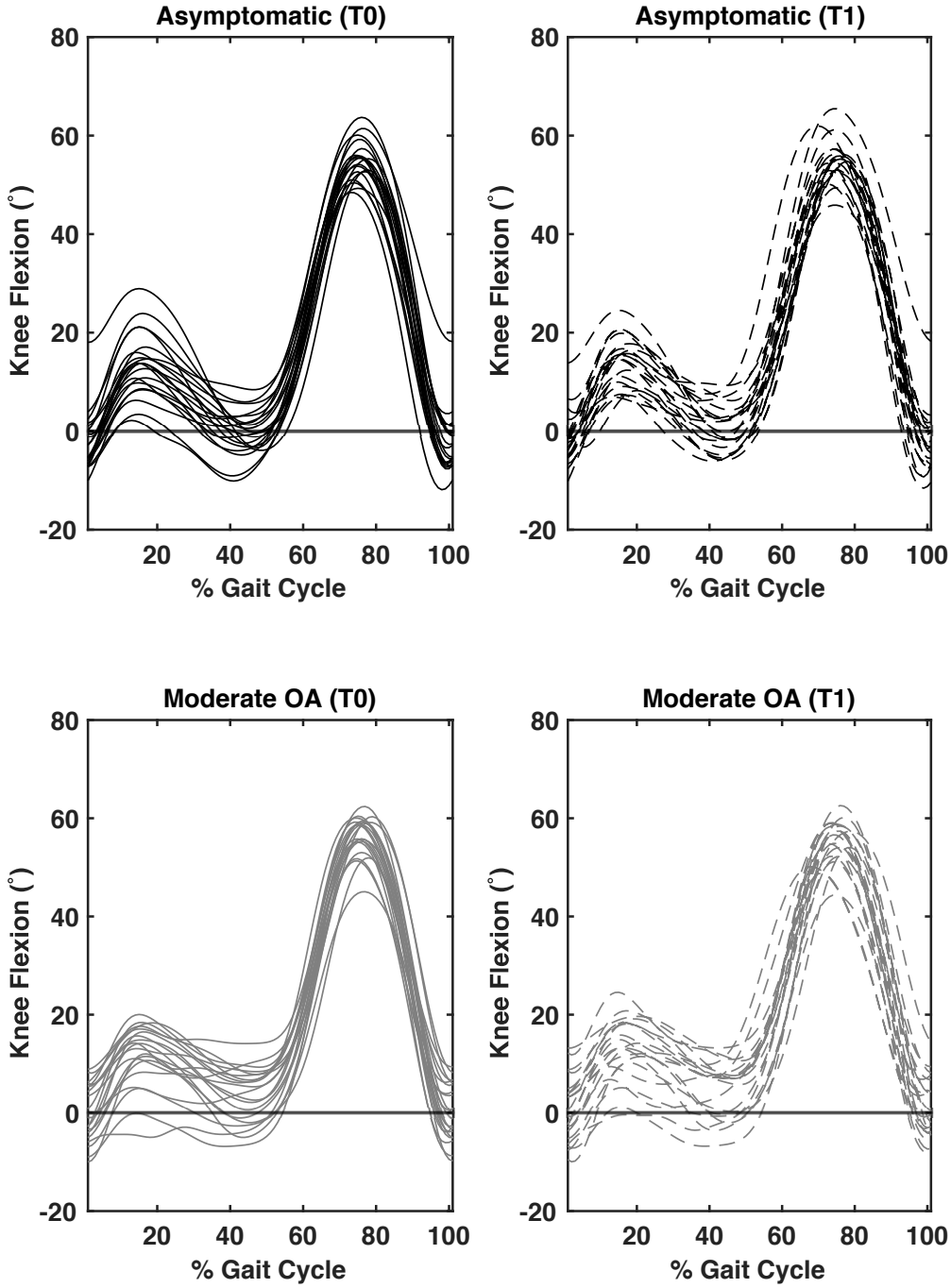

Figure B-11: Sagittal plane motion ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM and MOA groups. Knee flexion (degrees) is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

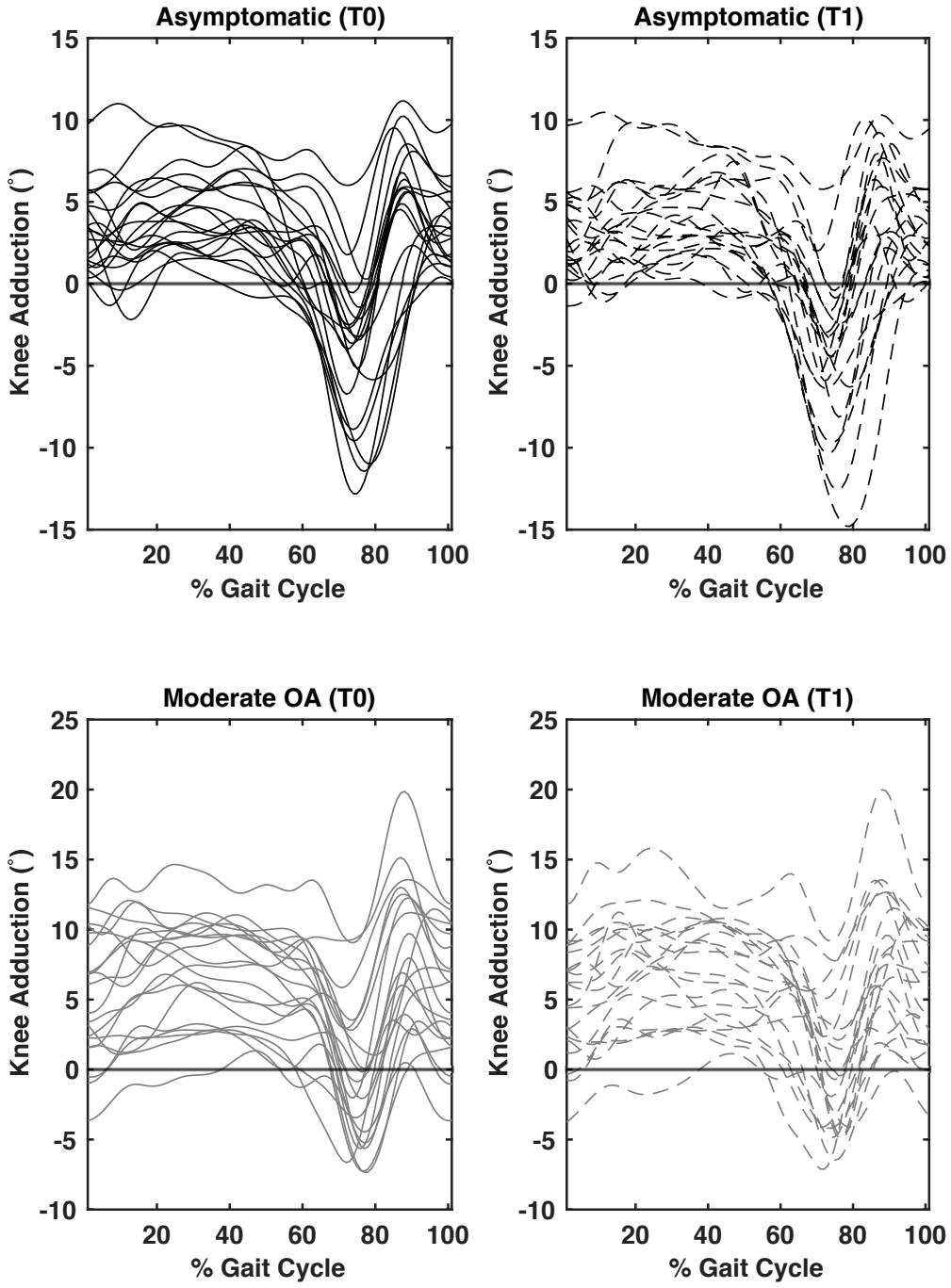

Figure B-12: Frontal plane motion ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM and MOA groups. Knee adduction (degrees) is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

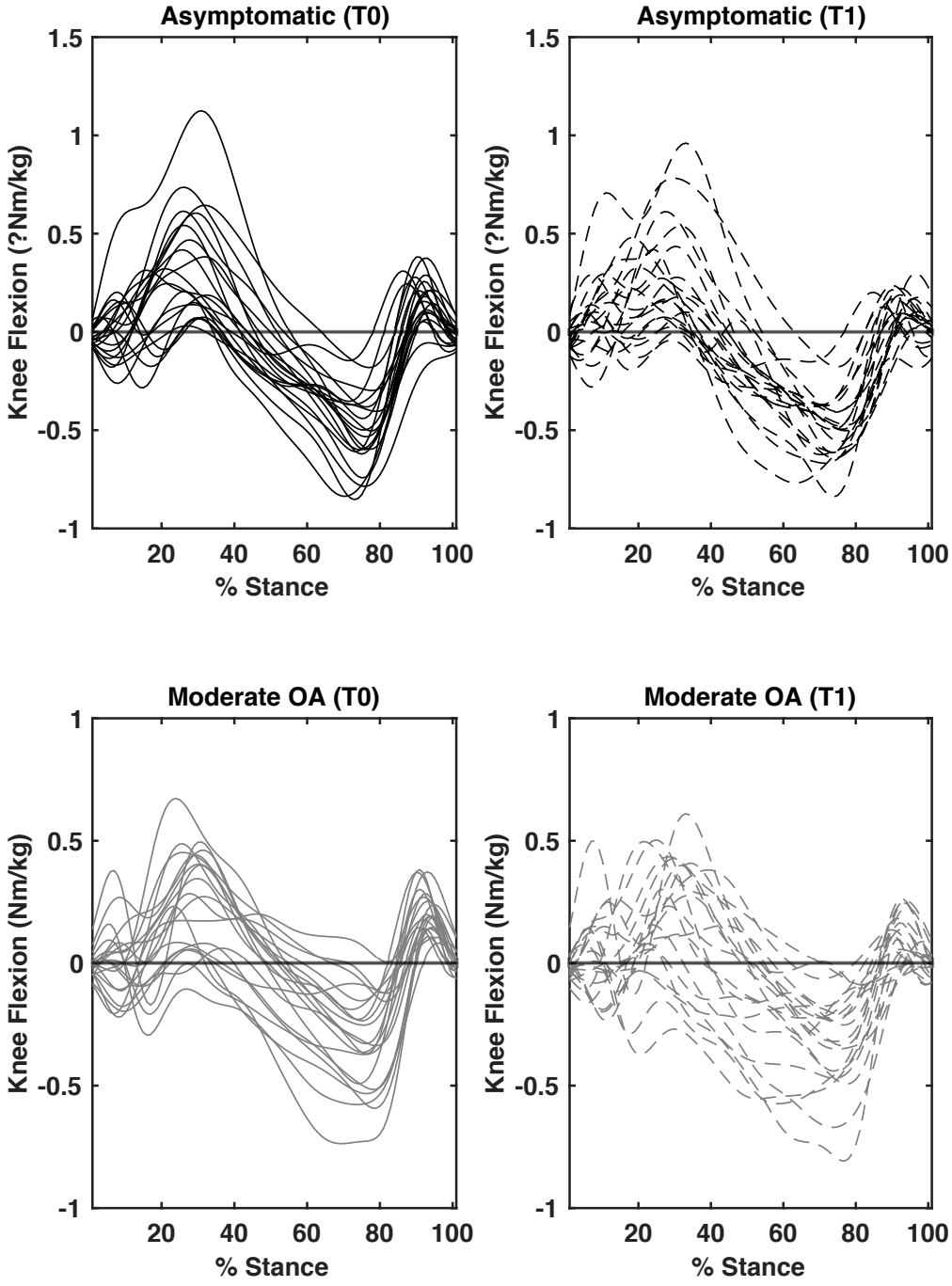

Figure B-13: Sagittal plane moment ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM and MOA groups. Knee flexion (Nm/kg) is represented on the y-axis and percentage of the stance is represented on the x-axis.

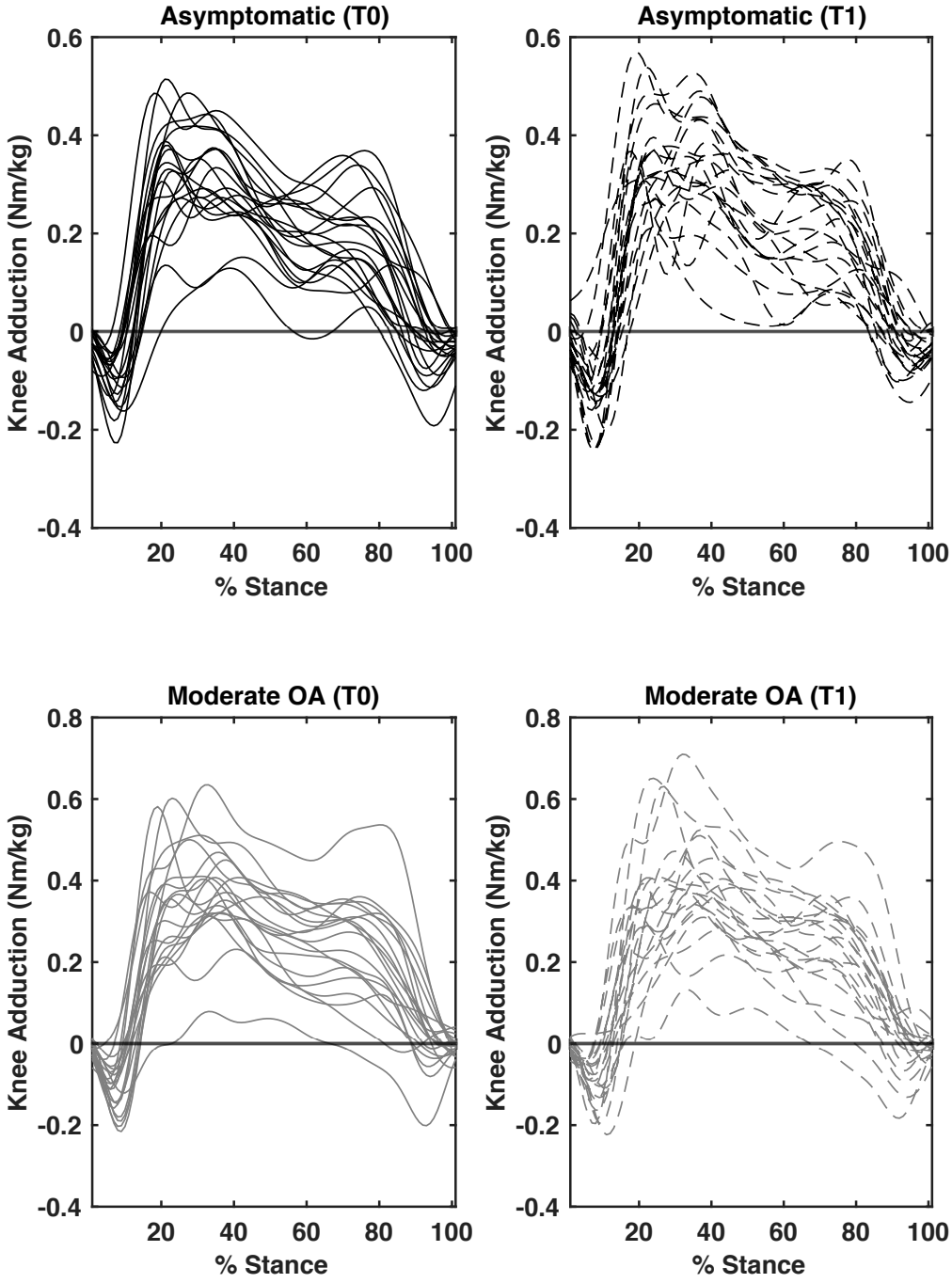

Figure B-14: Frontal plane moment ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM and MOA groups. Knee adduction (Nm/kg) is represented on the y-axis and percentage of the stance is represented on the x-axis.

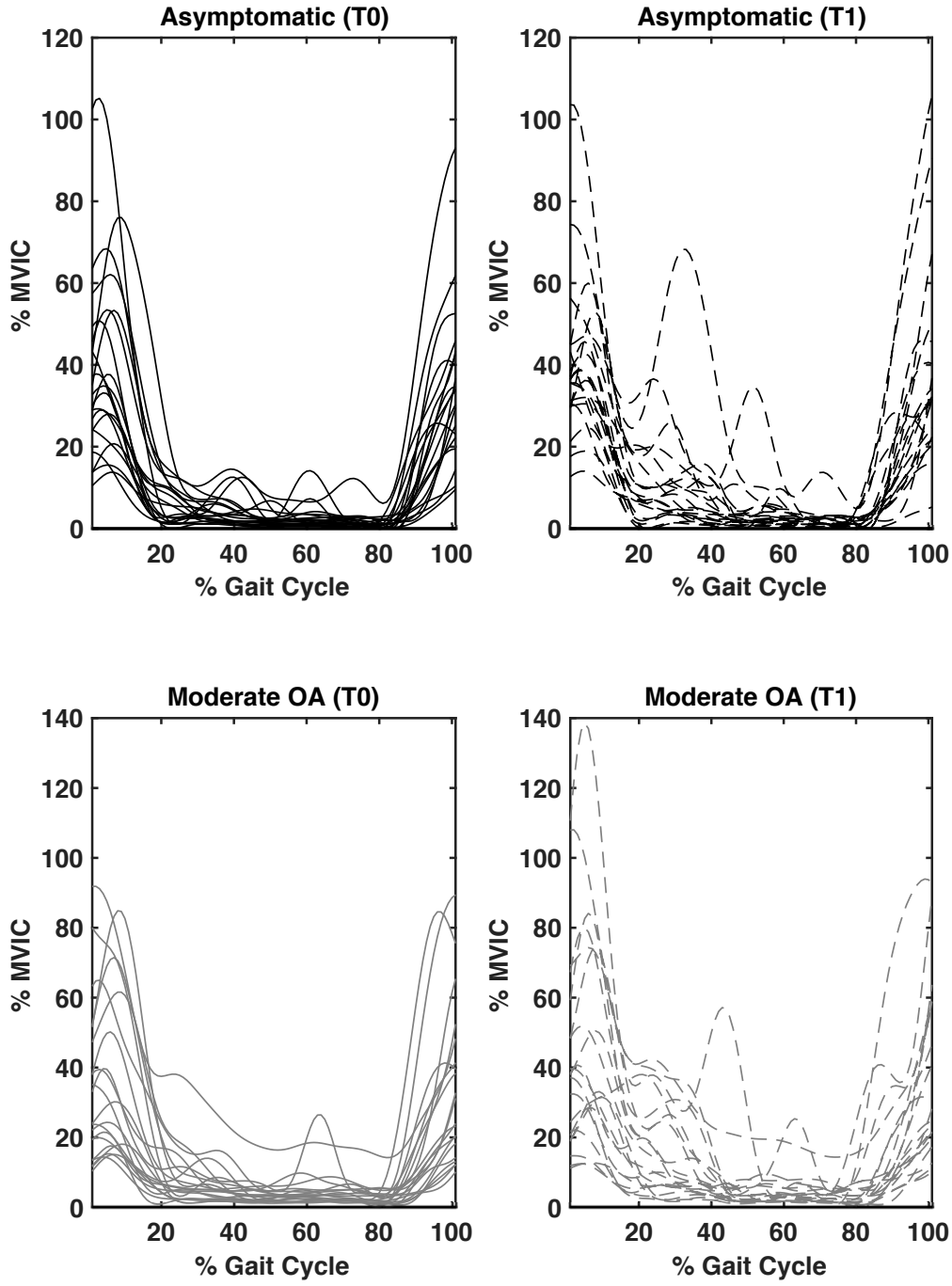

Figure B-15: Vastus medialis ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

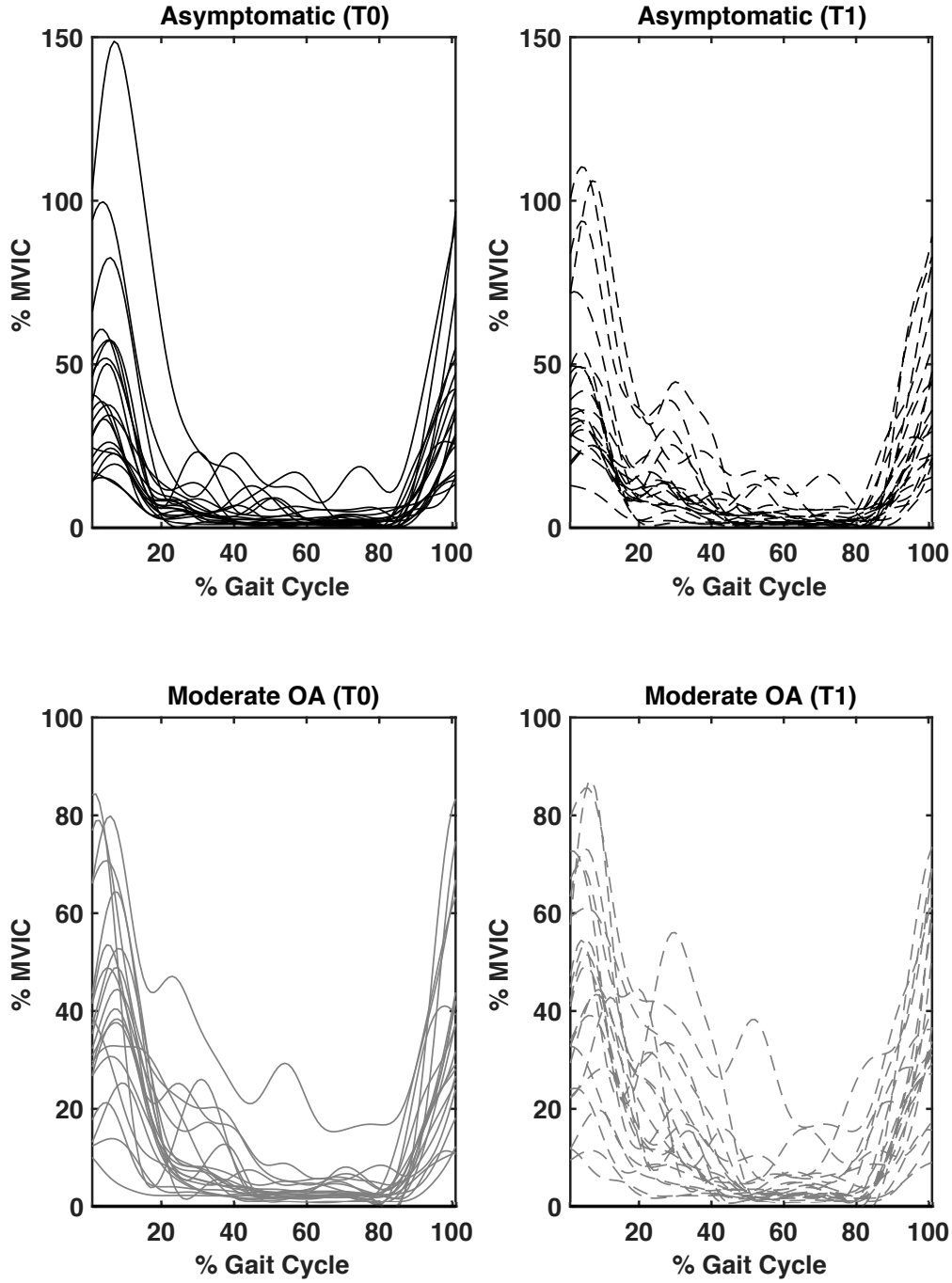

Figure B-16: Vastus lateralis ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

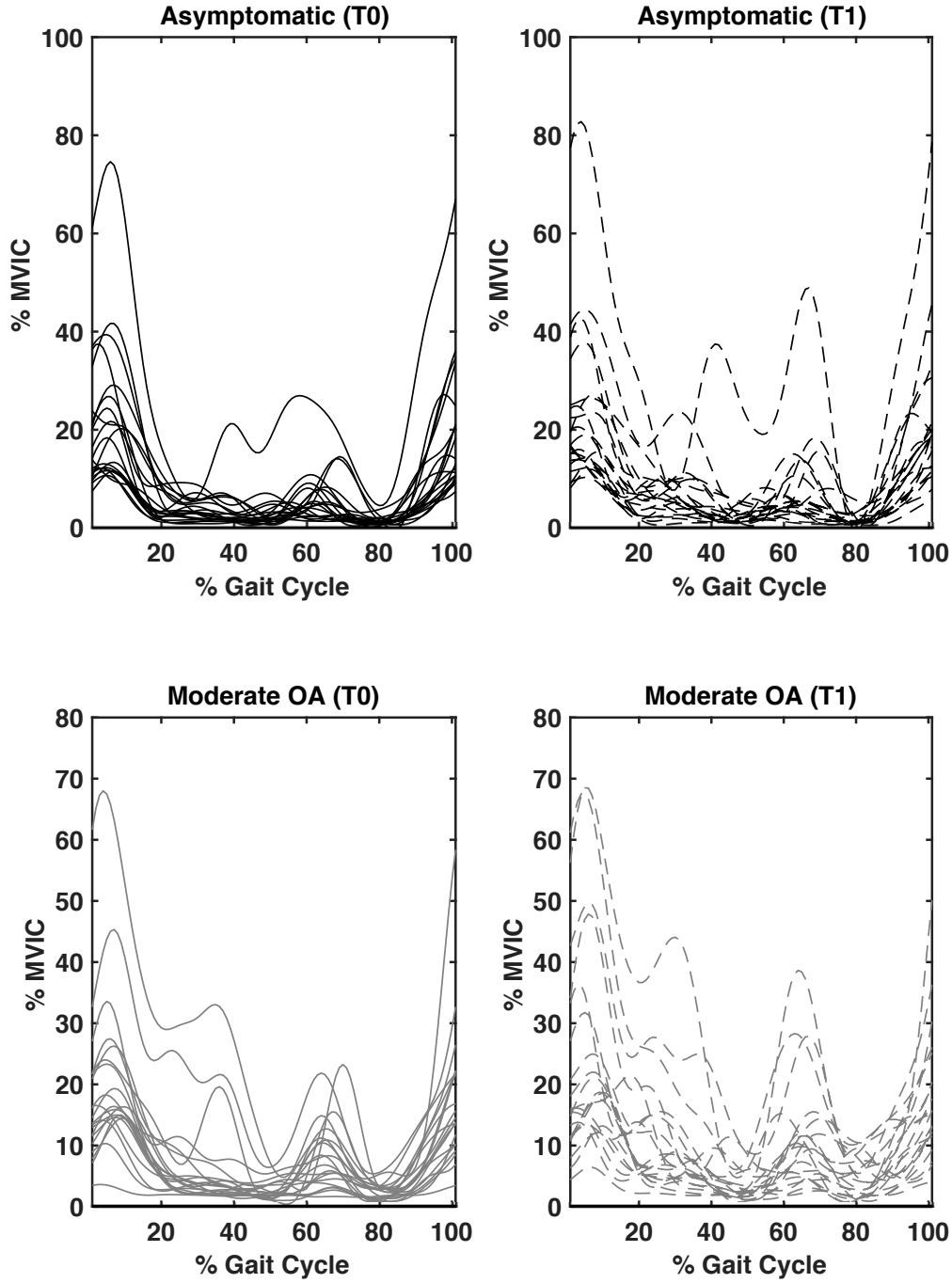

Figure B-17: Rectus femoris ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

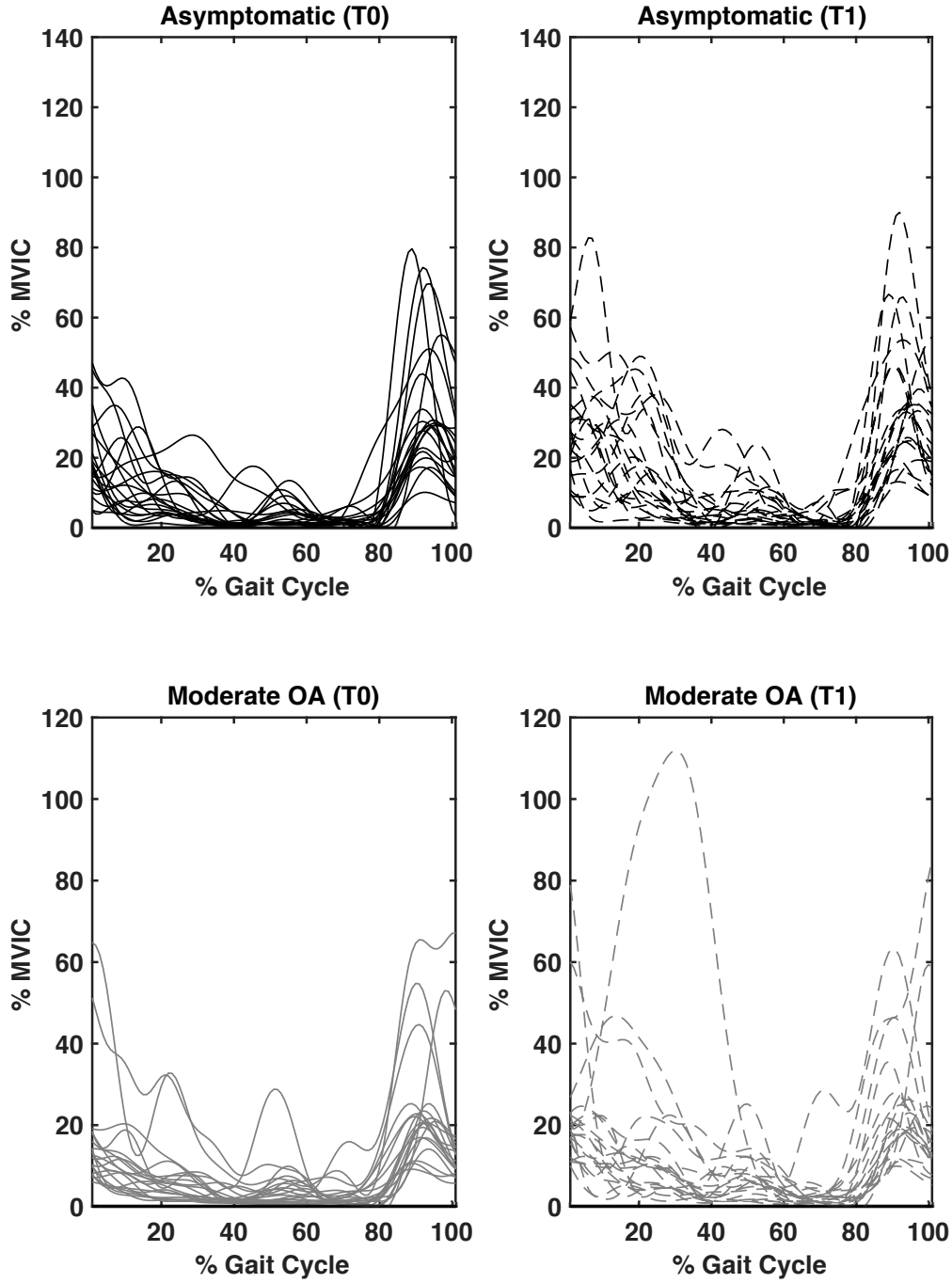

Figure B-18: Medial hamstring ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

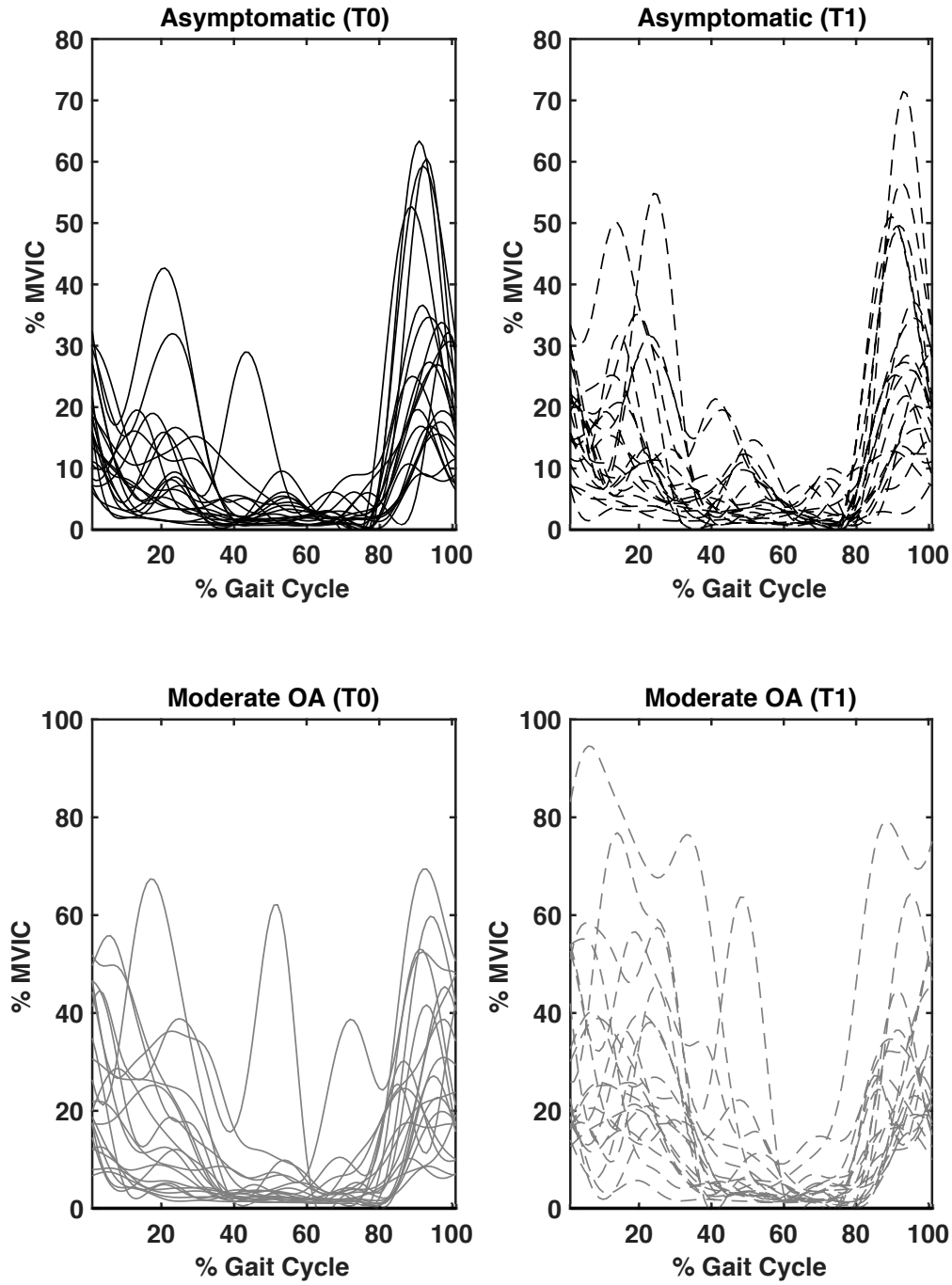

Figure B-19: Lateral hamstring ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

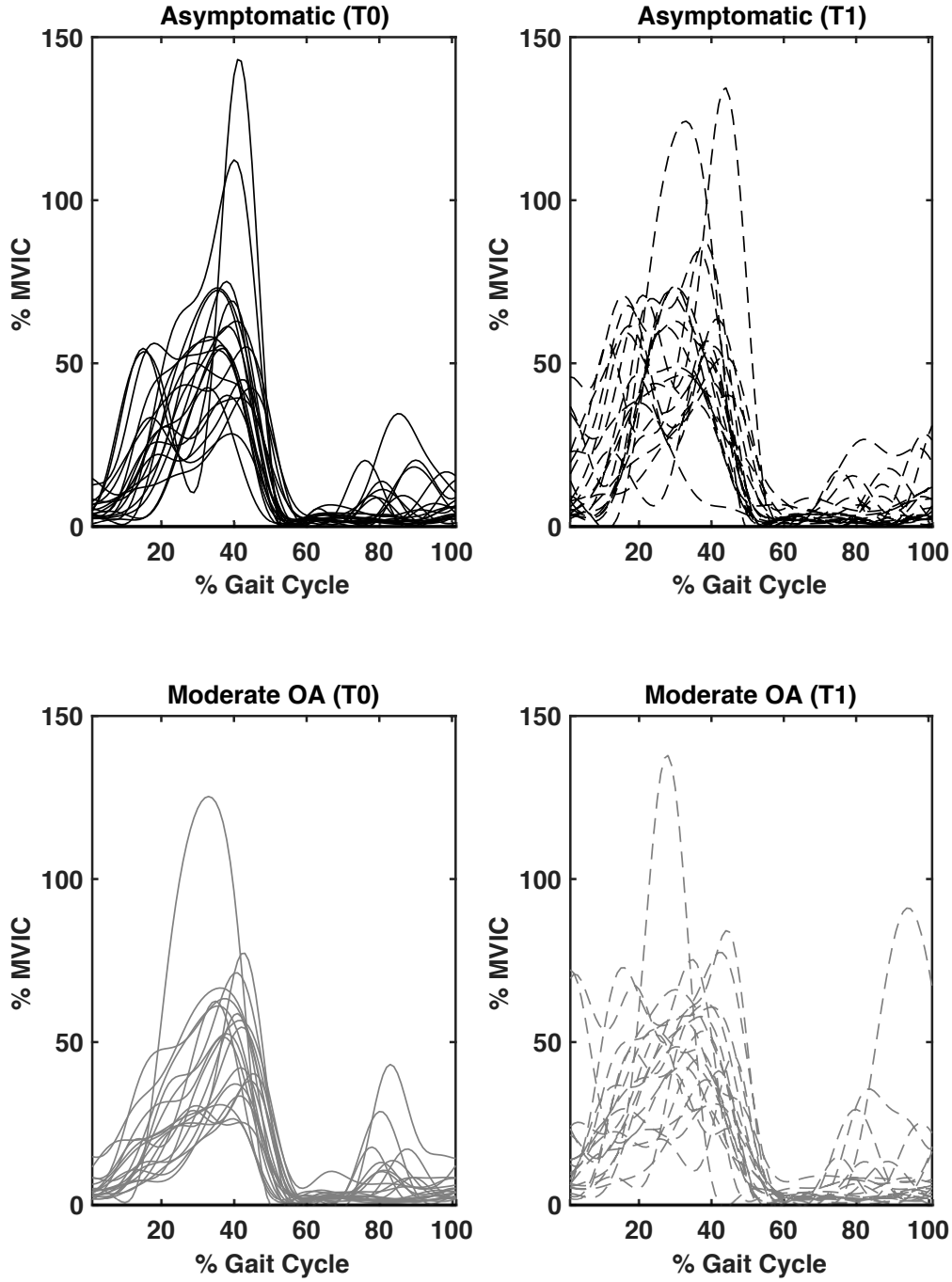

Figure B-20: Medial gastrocnemius ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

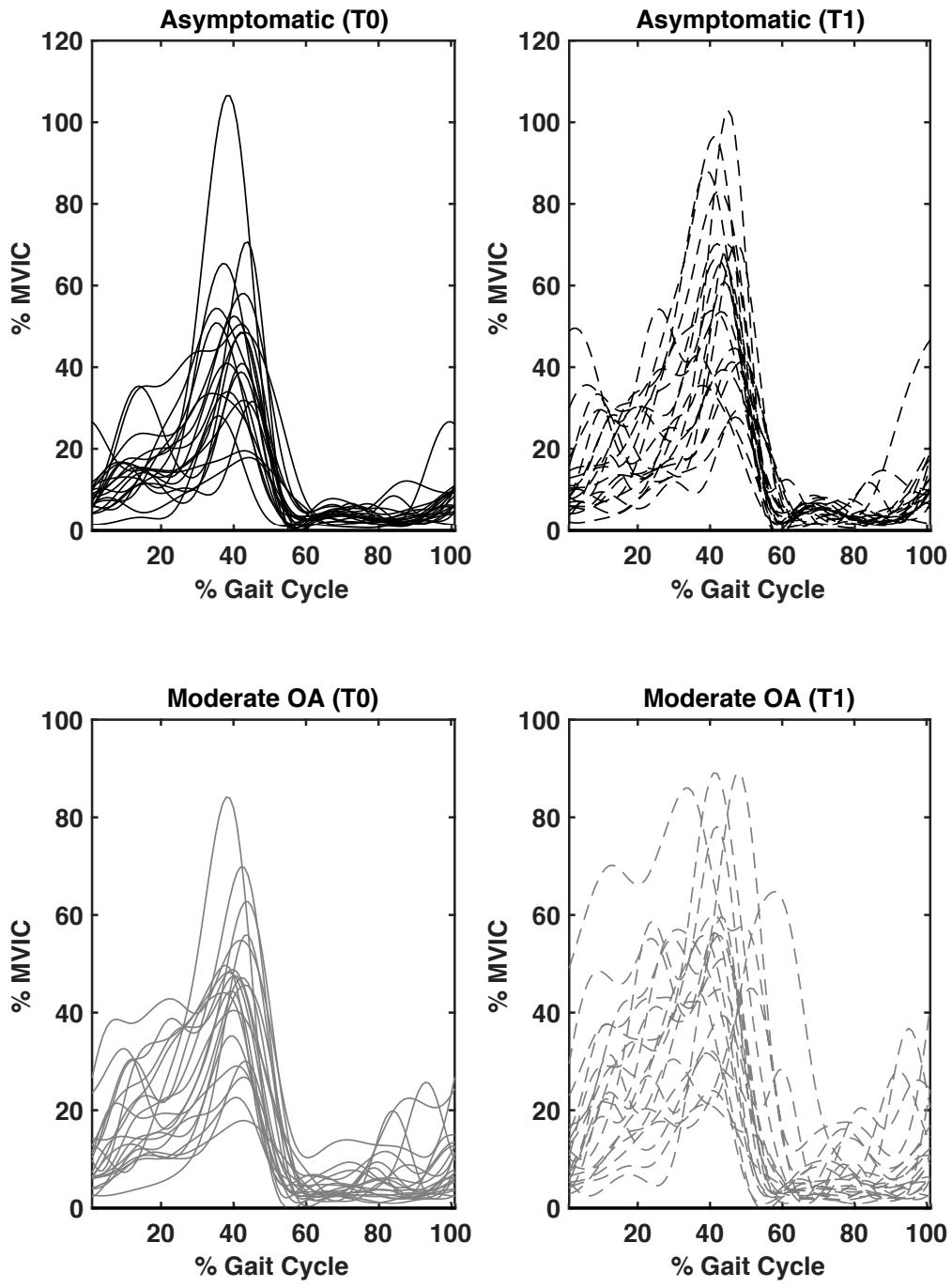

Figure B-21: Lateral gastrocnemius ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

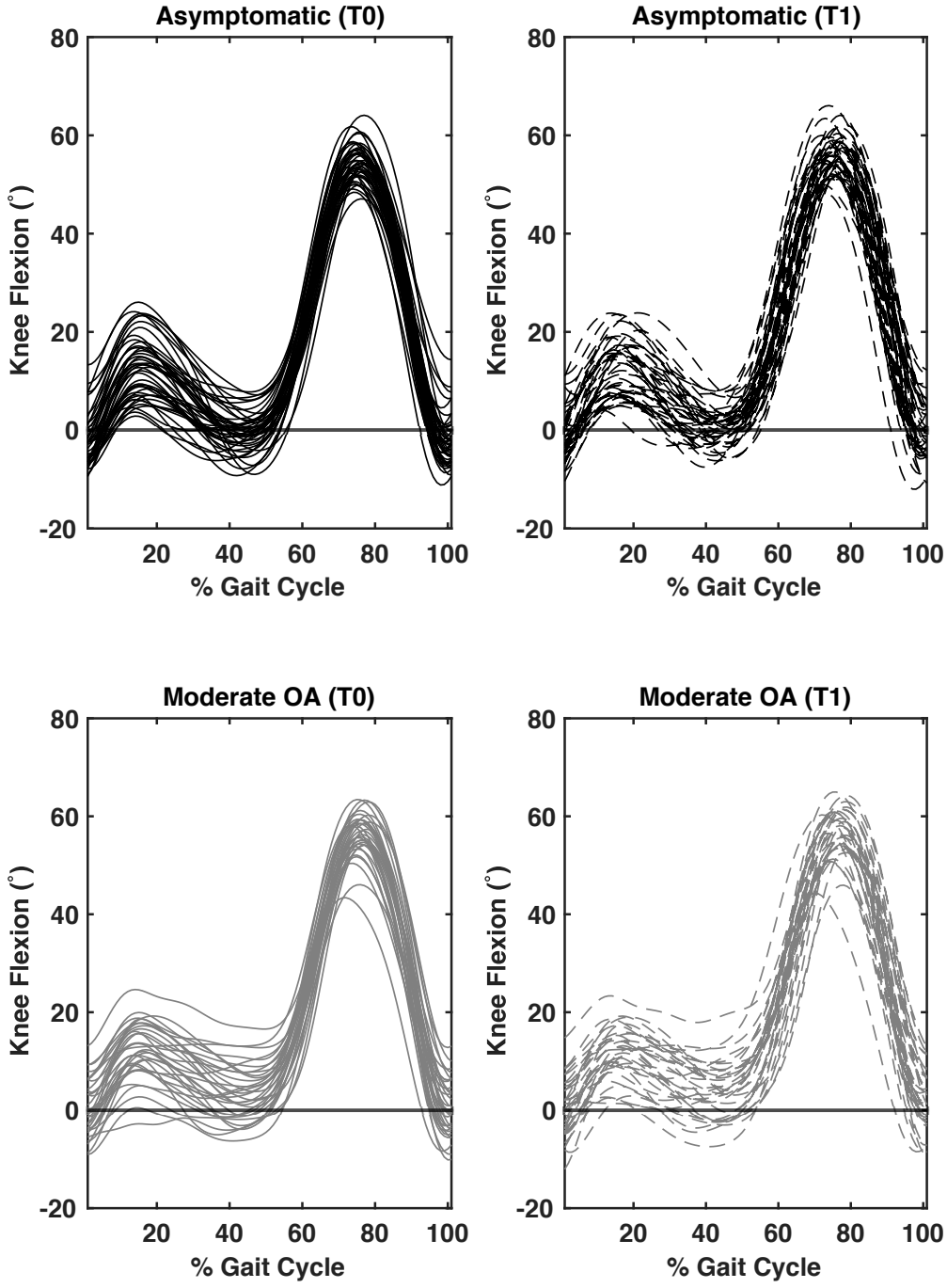

Figure B-22: Sagittal plane motion ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM and MOA groups. Knee flexion (degrees) is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

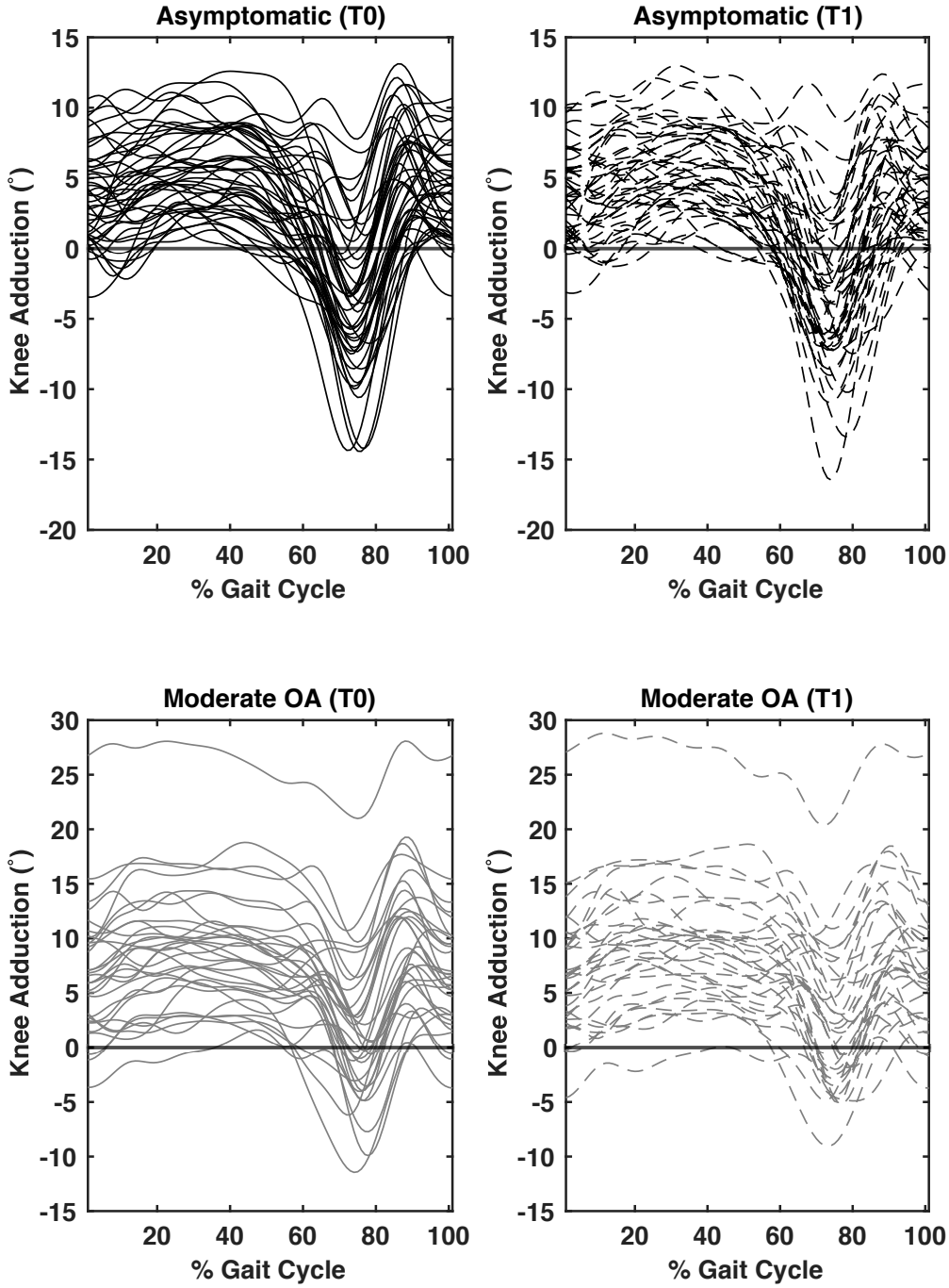

Figure B-23: Frontal plane motion ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM and MOA groups. Knee adduction (degrees) is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

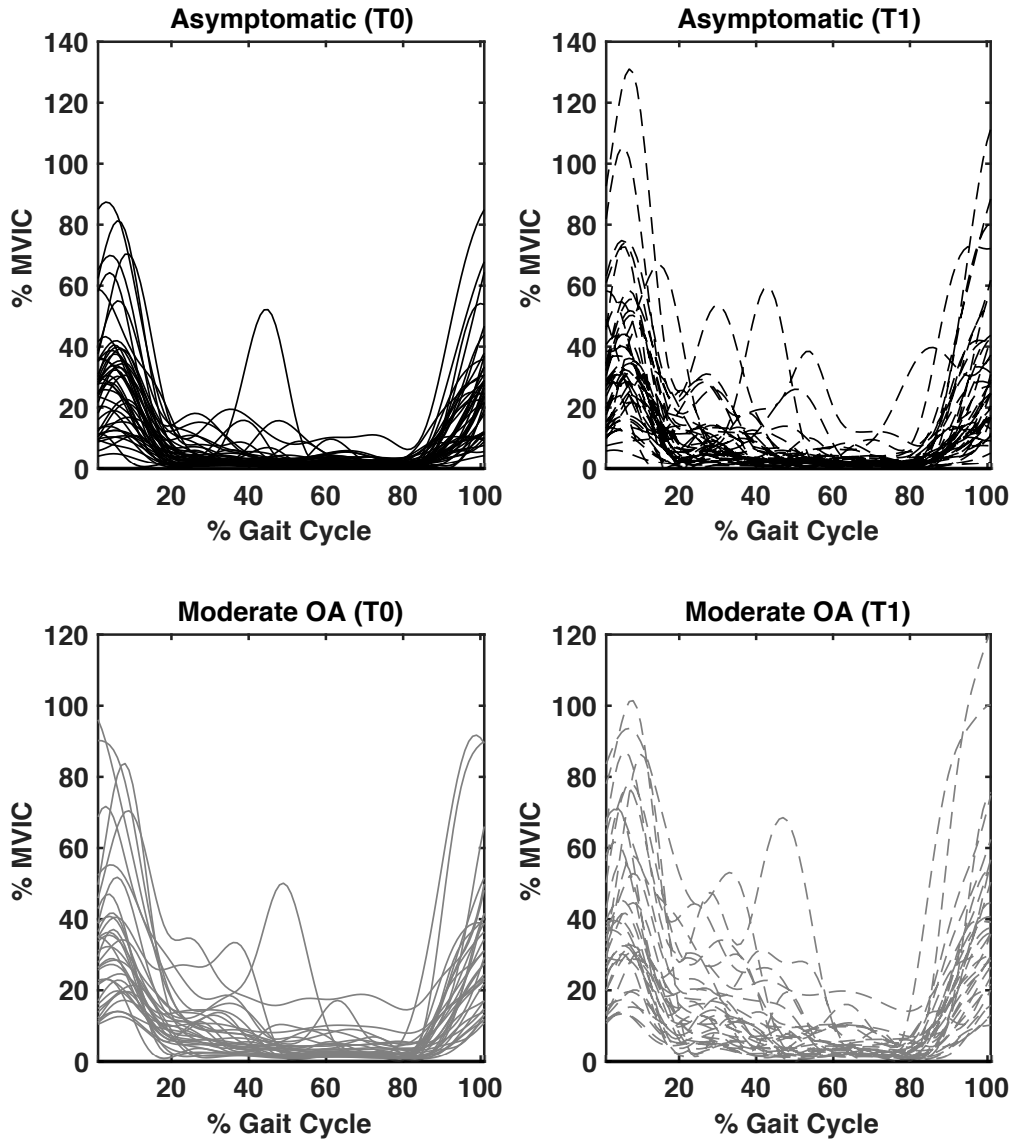

Figure B-24: Vastus medialis ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

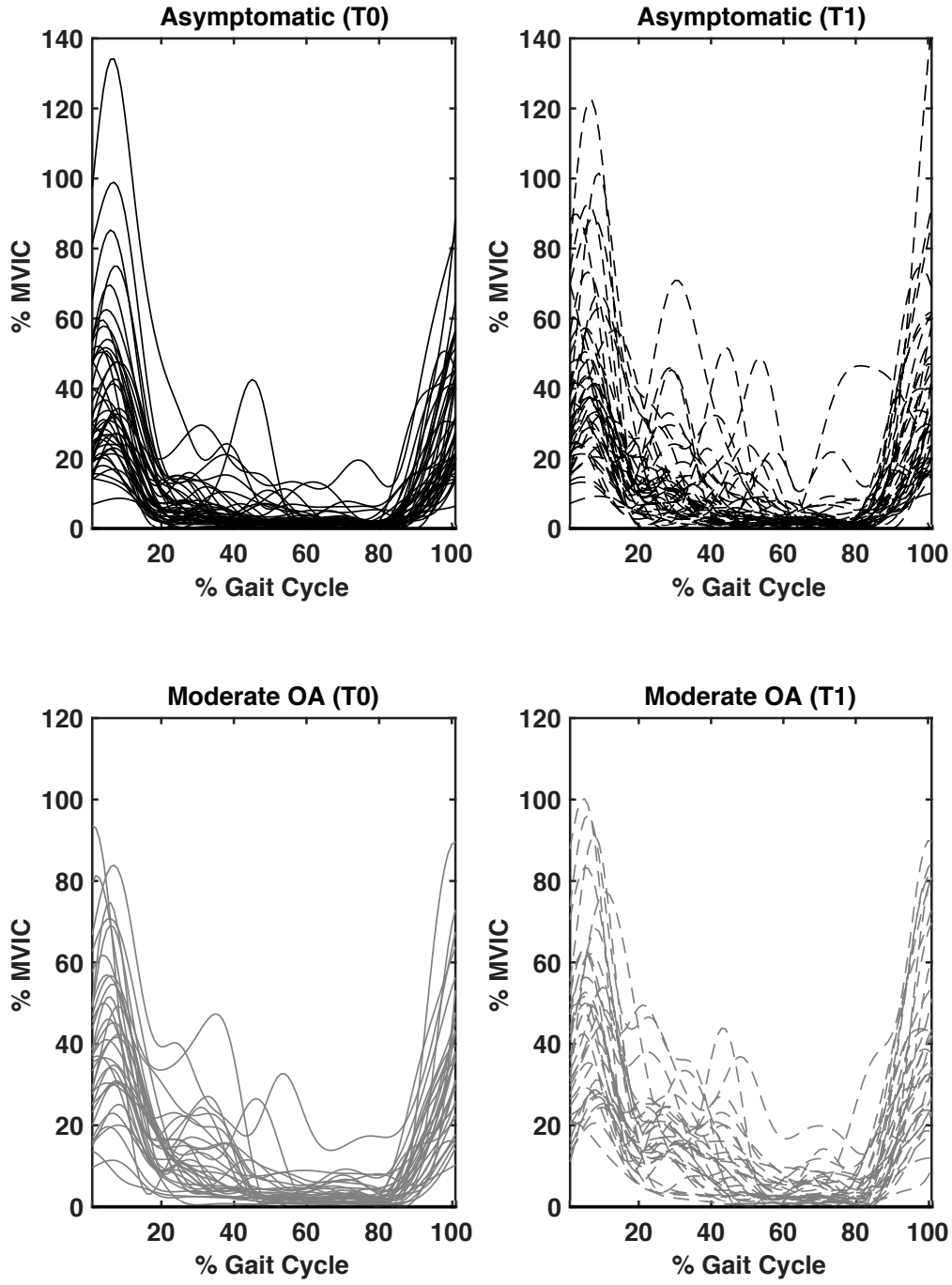

Figure B-25: Vastus lateralis ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

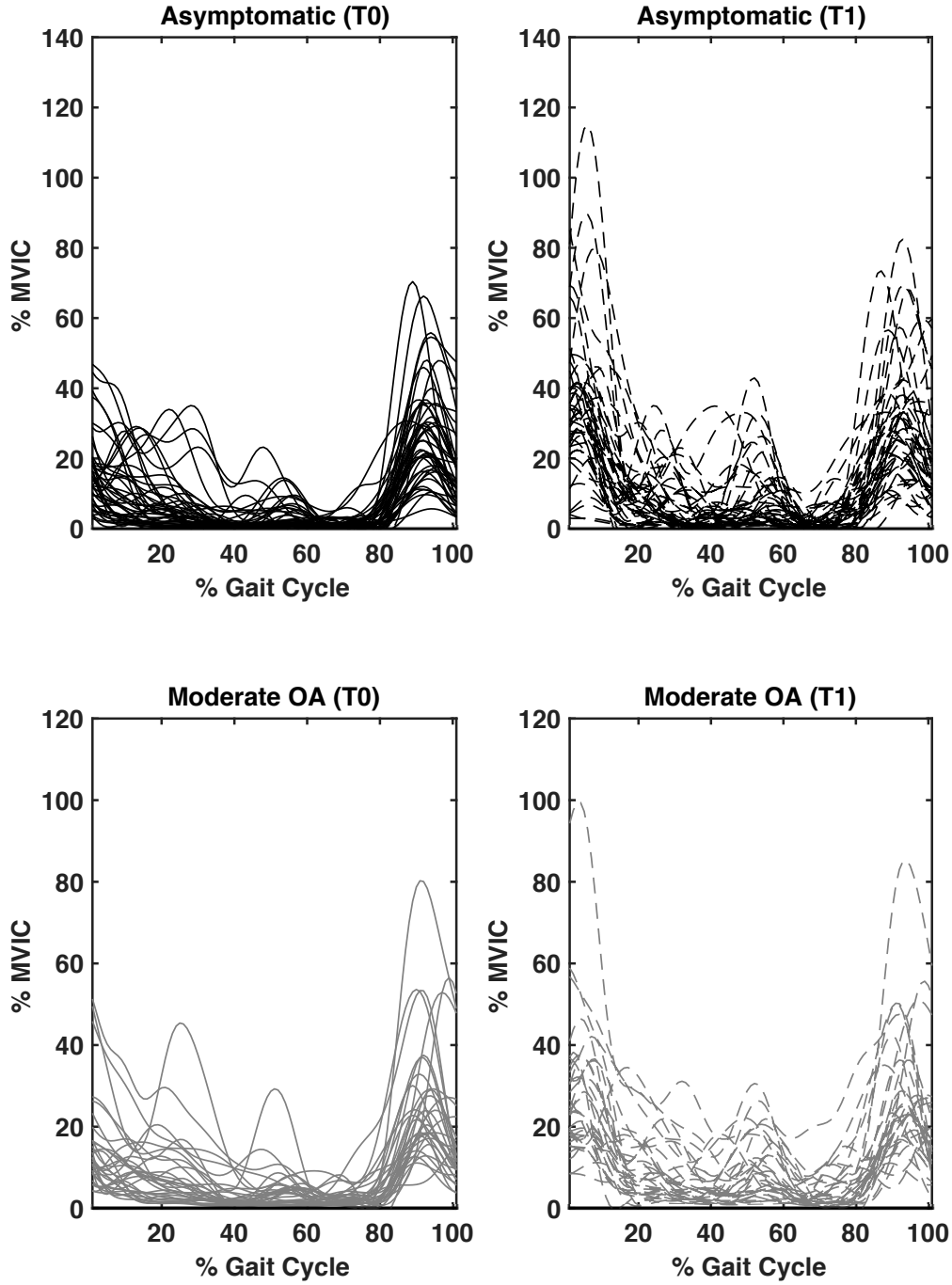

Figure B-26: Medial hamstring ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

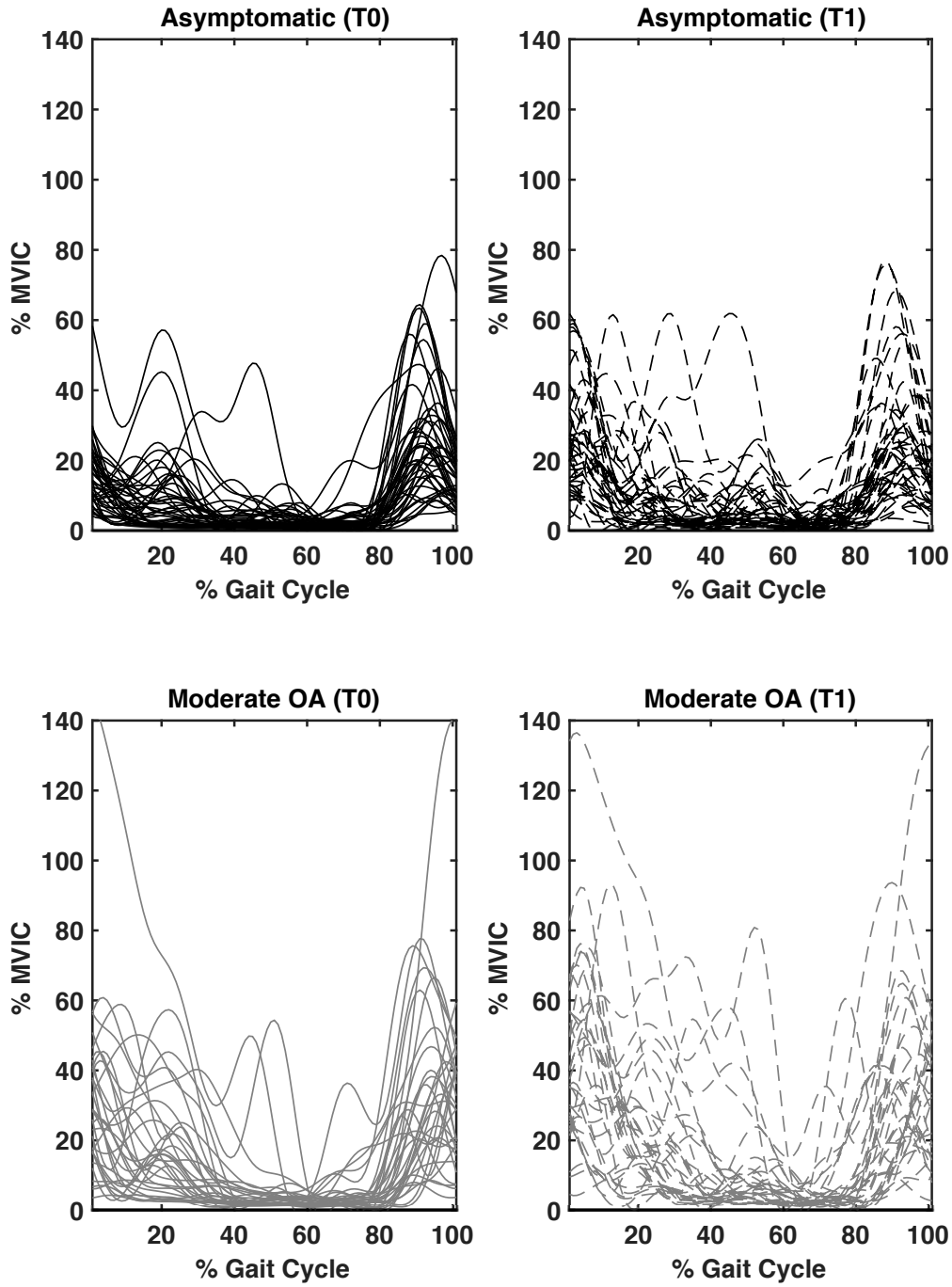

Figure B-27: Lateral hamstring ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

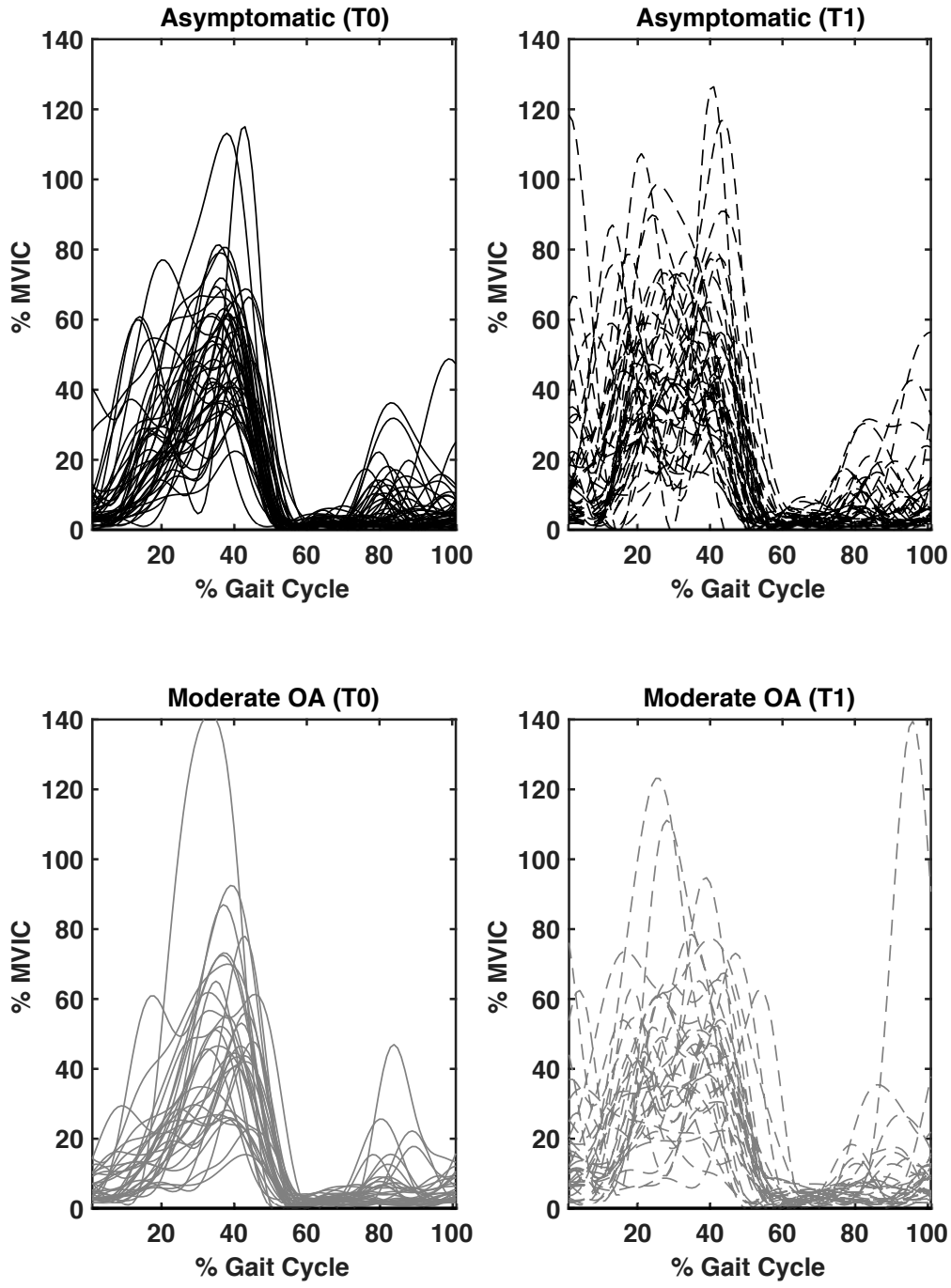

Figure B-28: Medial gastrocnemius ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

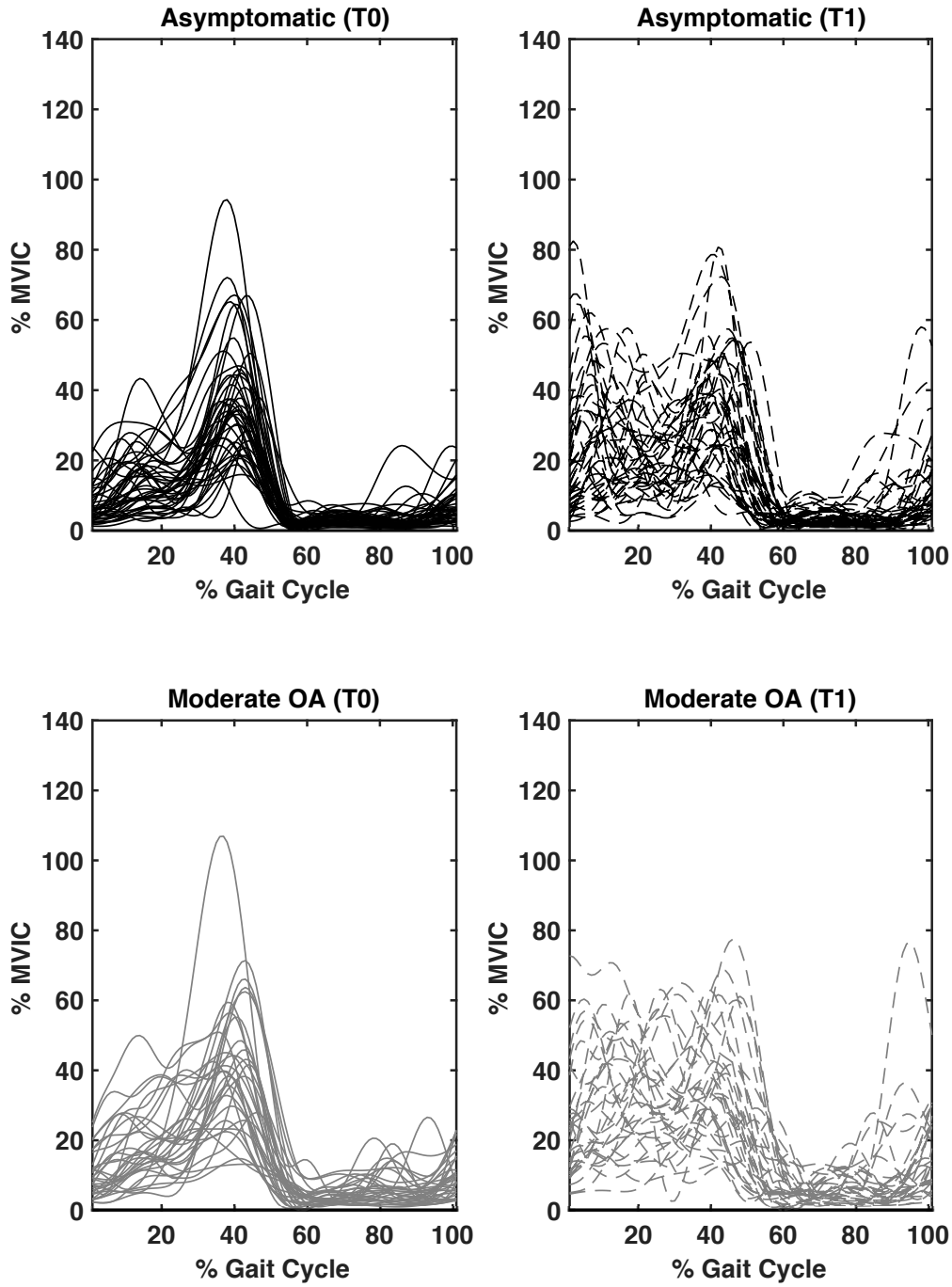

Figure B-29: Lateral gastrocnemius ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within MOA and ASYM groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

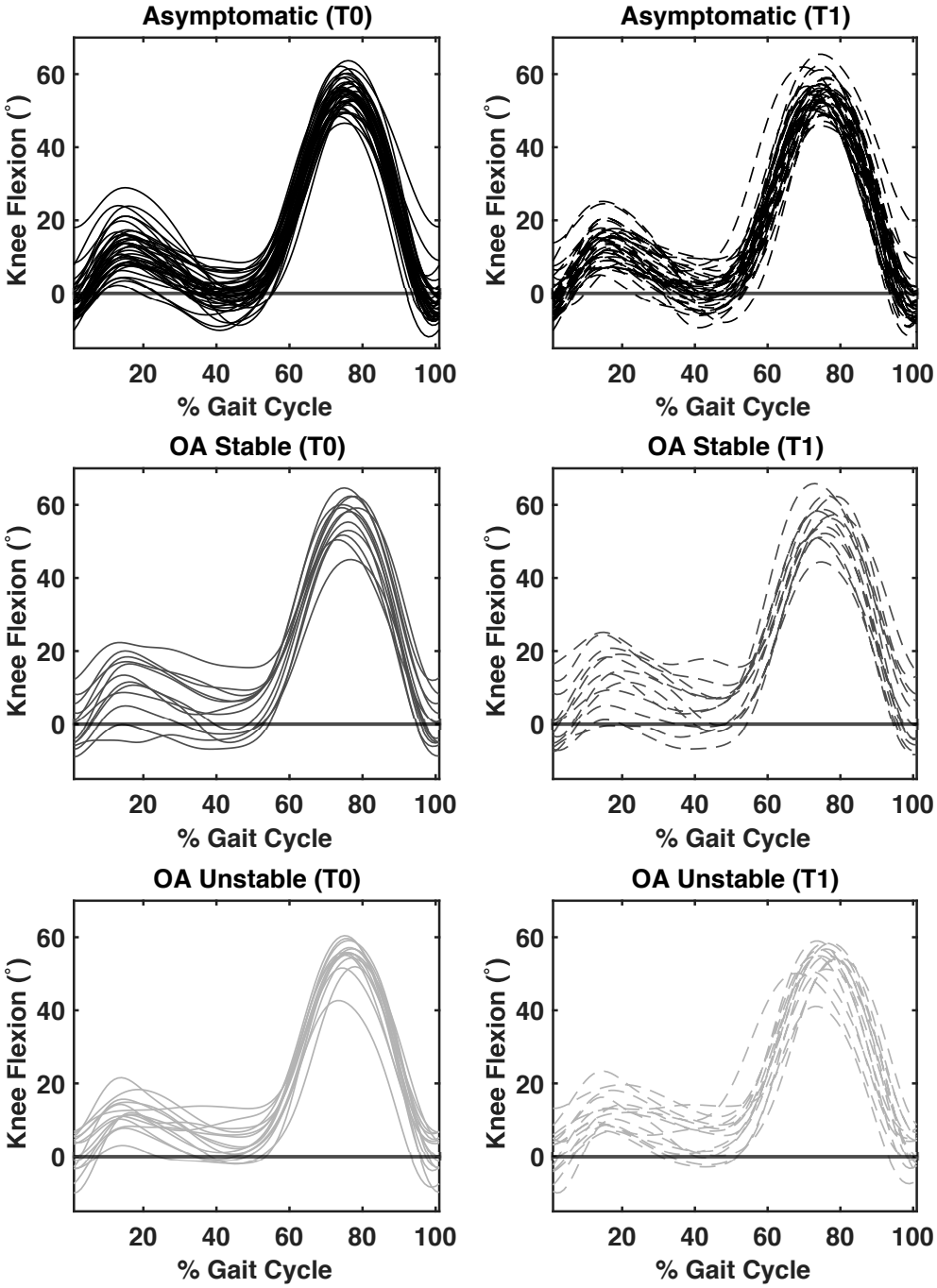

Figure B-30: Sagittal plane motion ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Knee flexion (degrees) is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

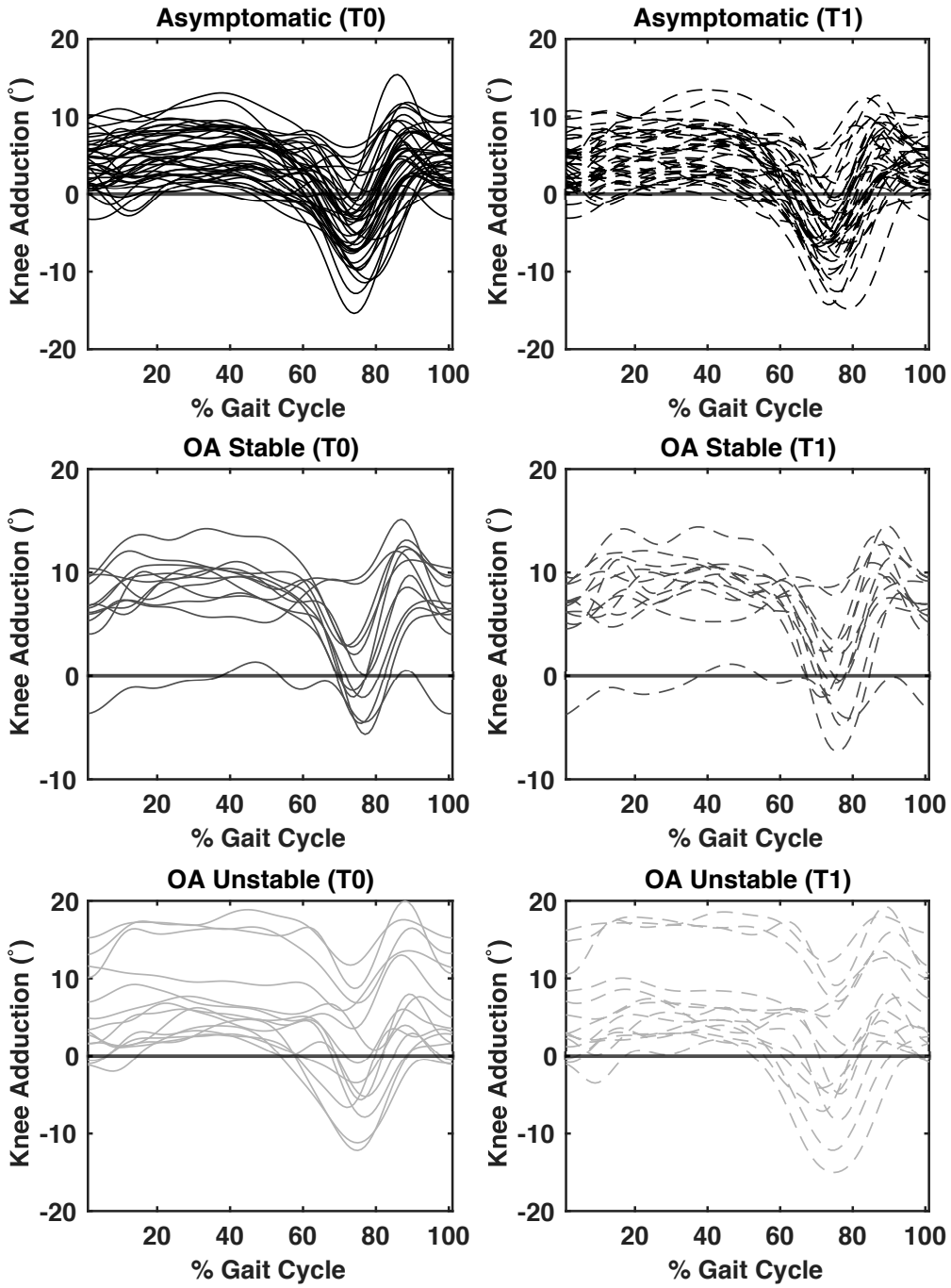

Figure B-31: Frontal plane motion ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Knee adduction (degrees) is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

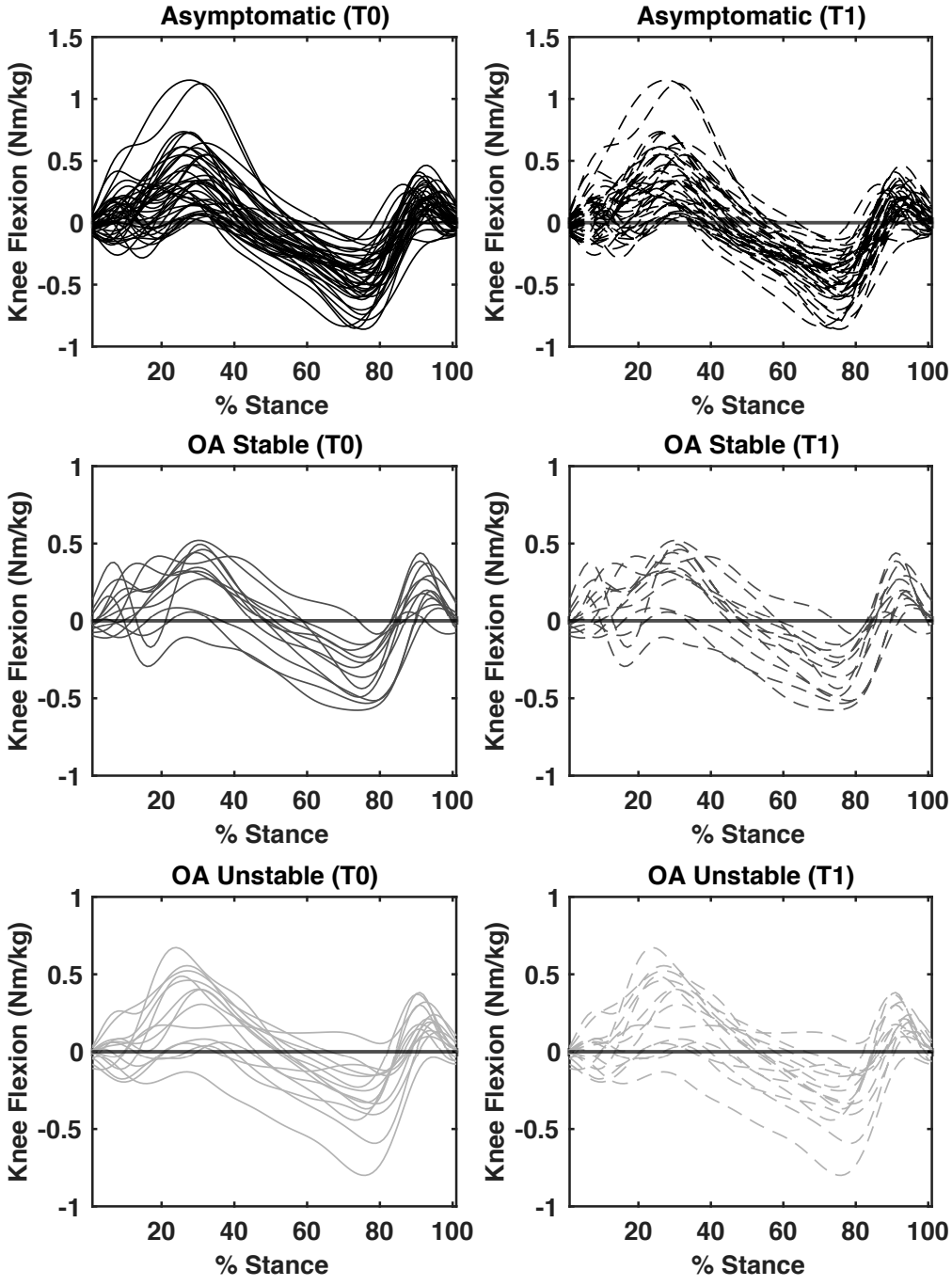

Figure B-32: Sagittal plane moment ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Knee flexion (Nm/kg) is represented on the y-axis and percentage of the stance is represented on the x-axis.

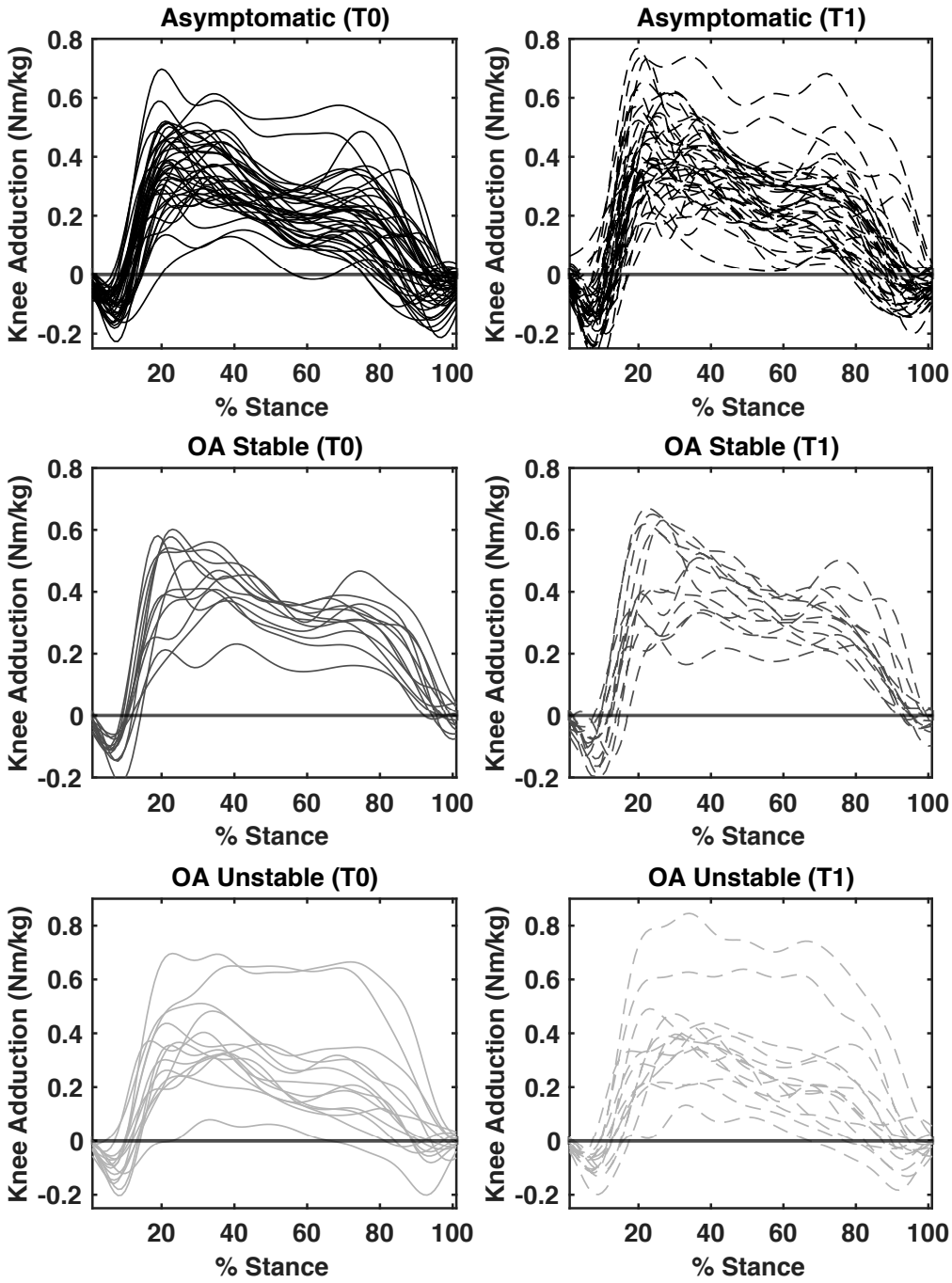

Figure B-33: Frontal plane moment ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Knee adduction (Nm/kg) is represented on the y-axis and percentage of stance is represented on the x-axis.

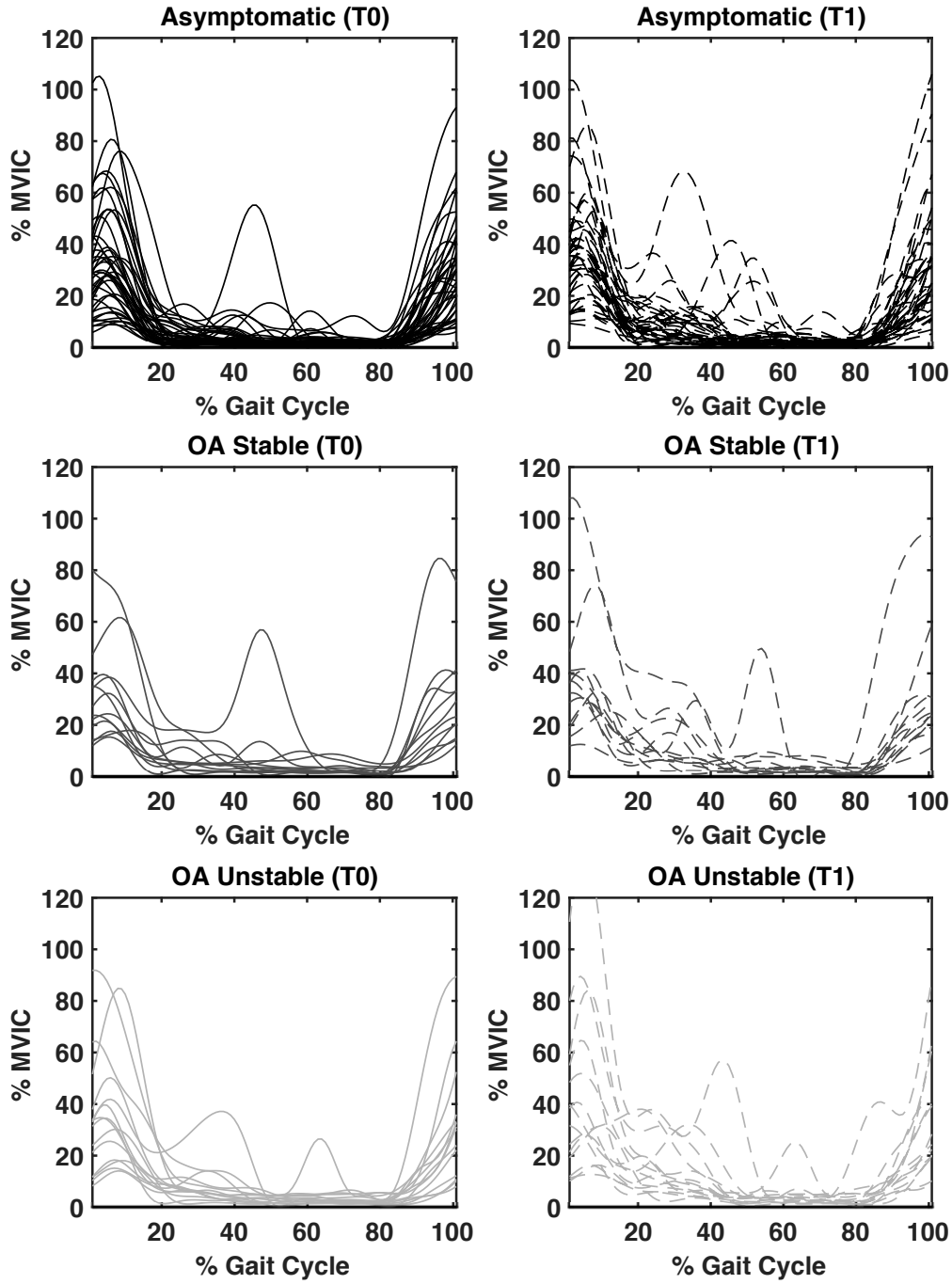

Figure B-34: Vastus medialis ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

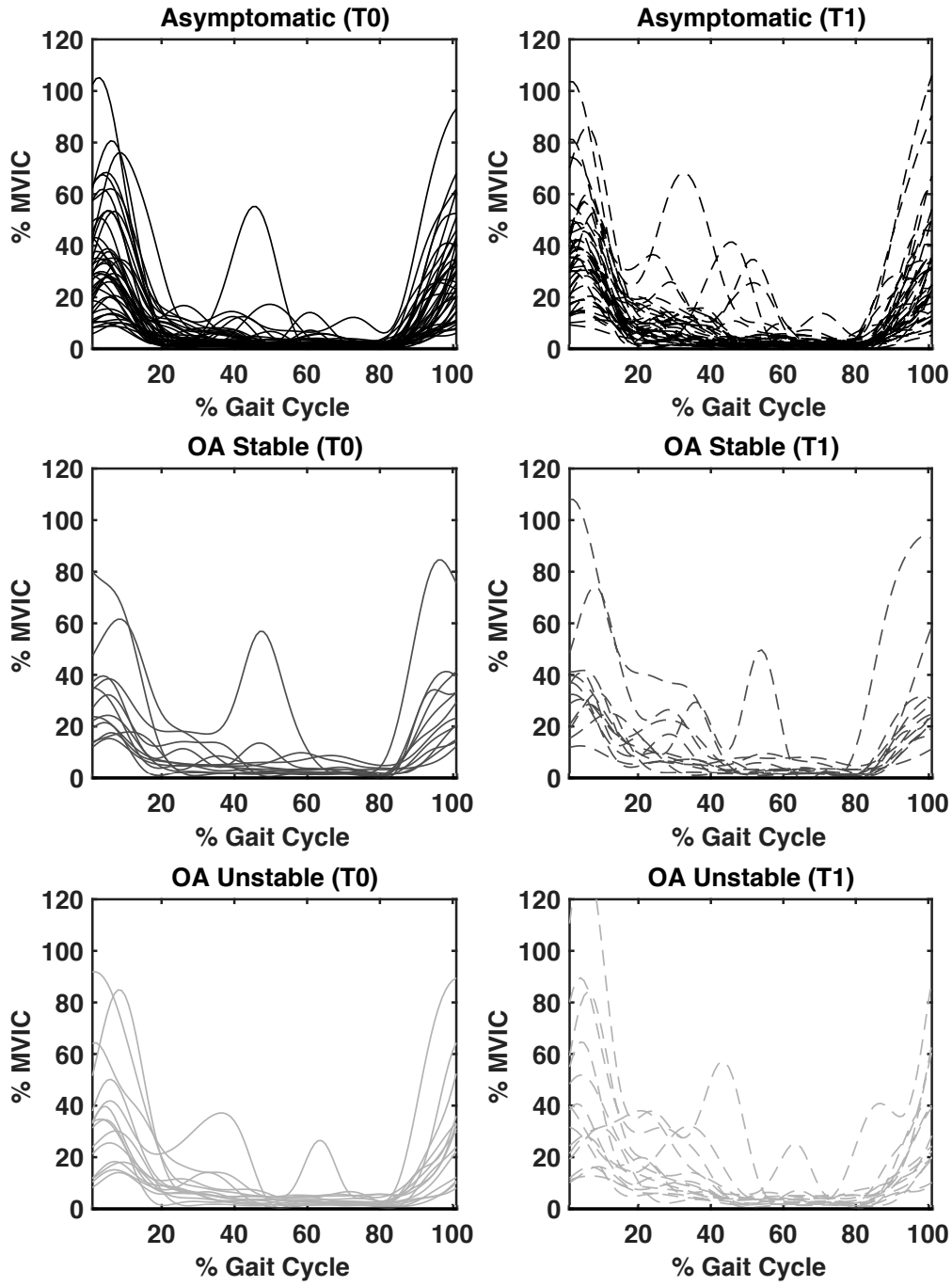

Figure B-35: Vastus lateralis ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

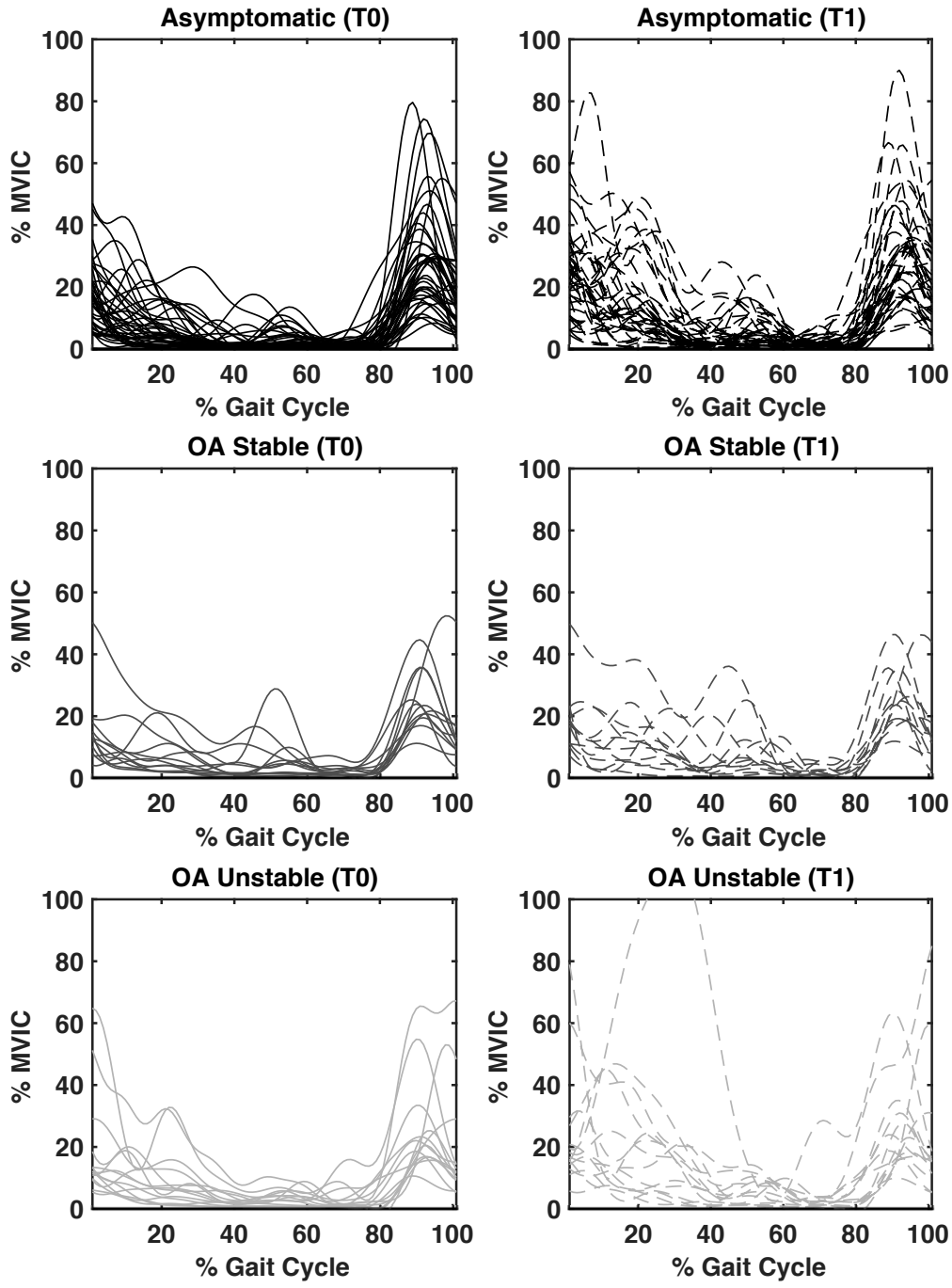

Figure B-36: Medial hamstring ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

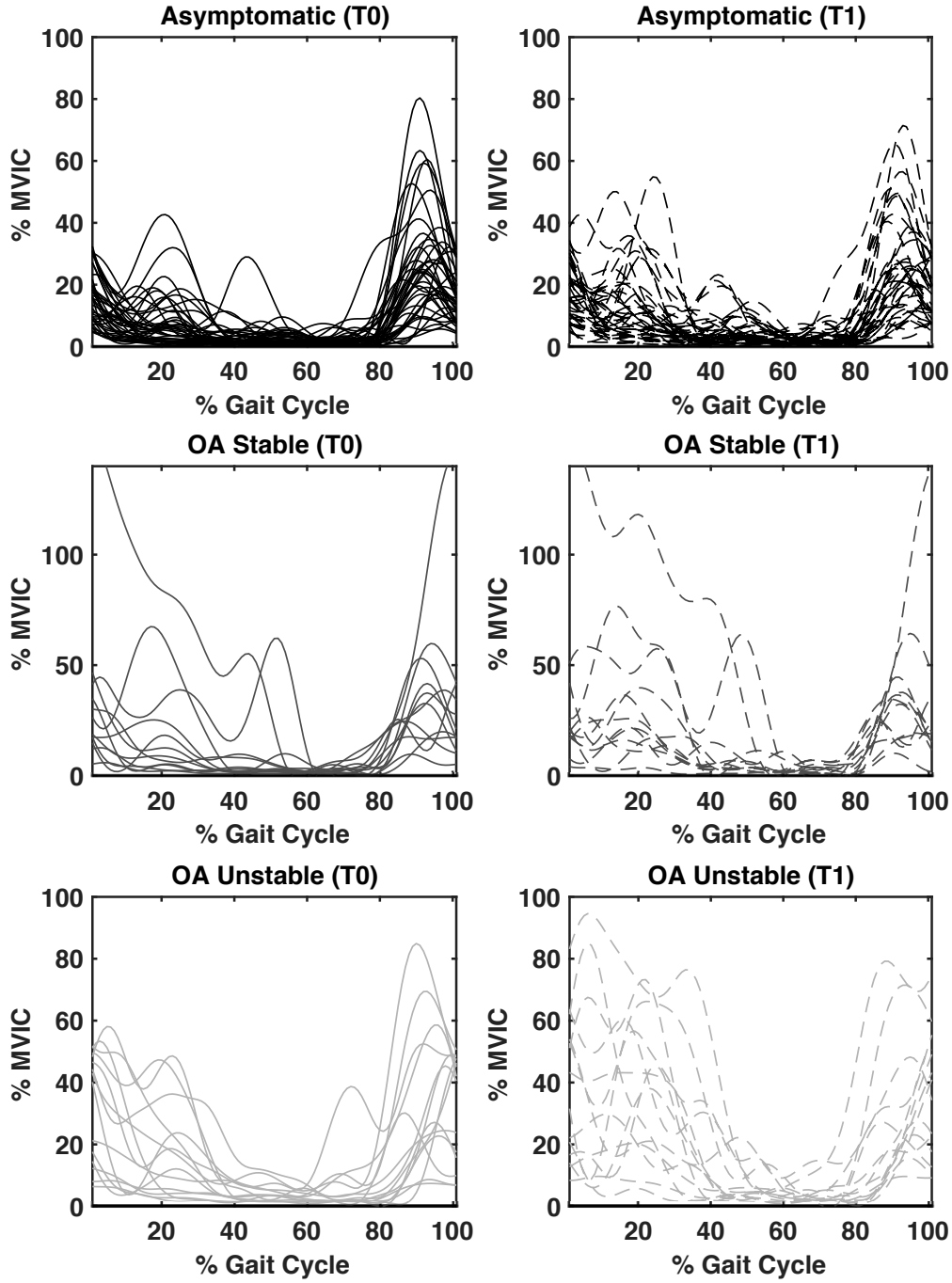

Figure B-37: Lateral hamstring ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

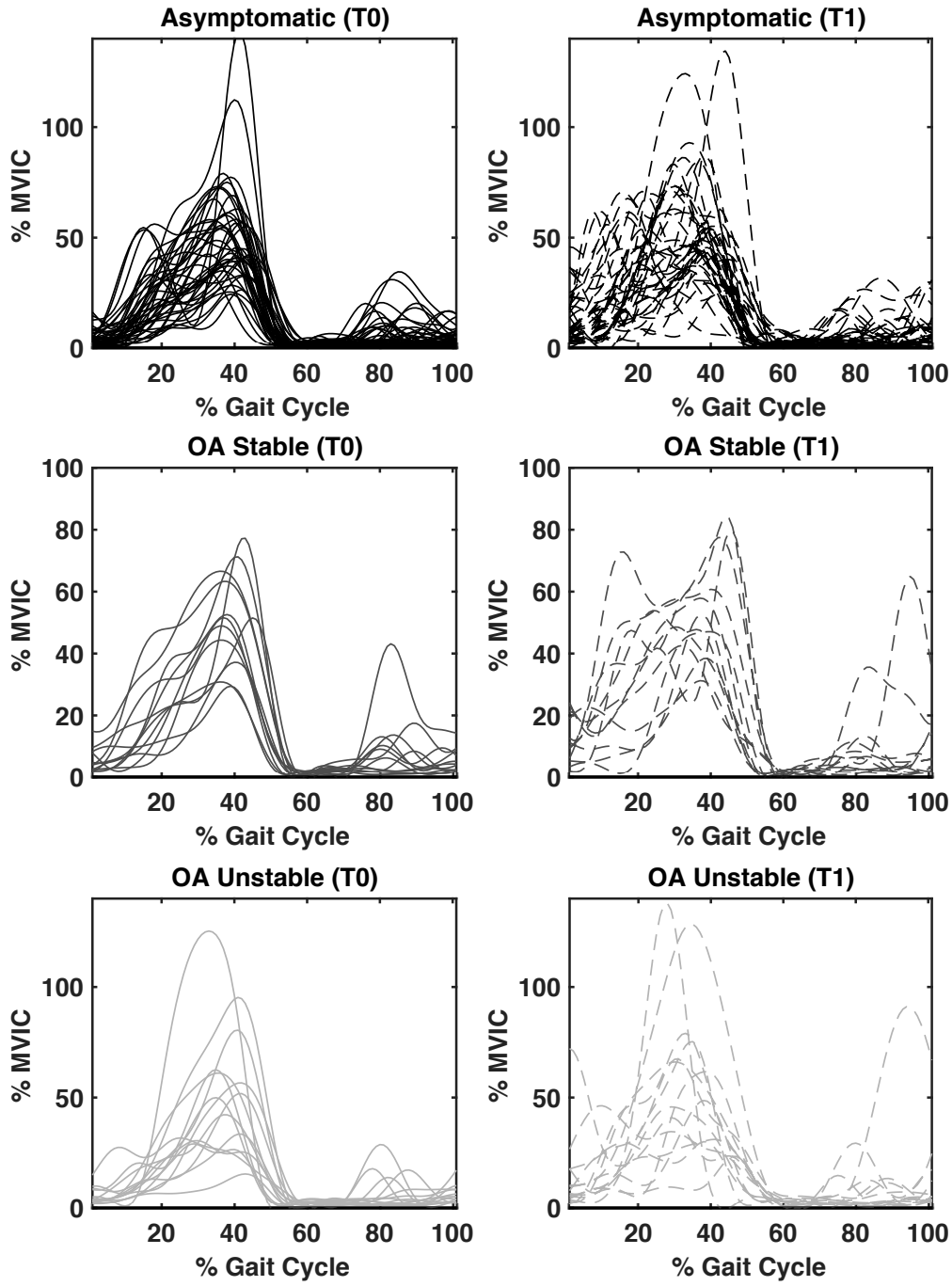

Figure B-38: Medial gastrocnemius ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

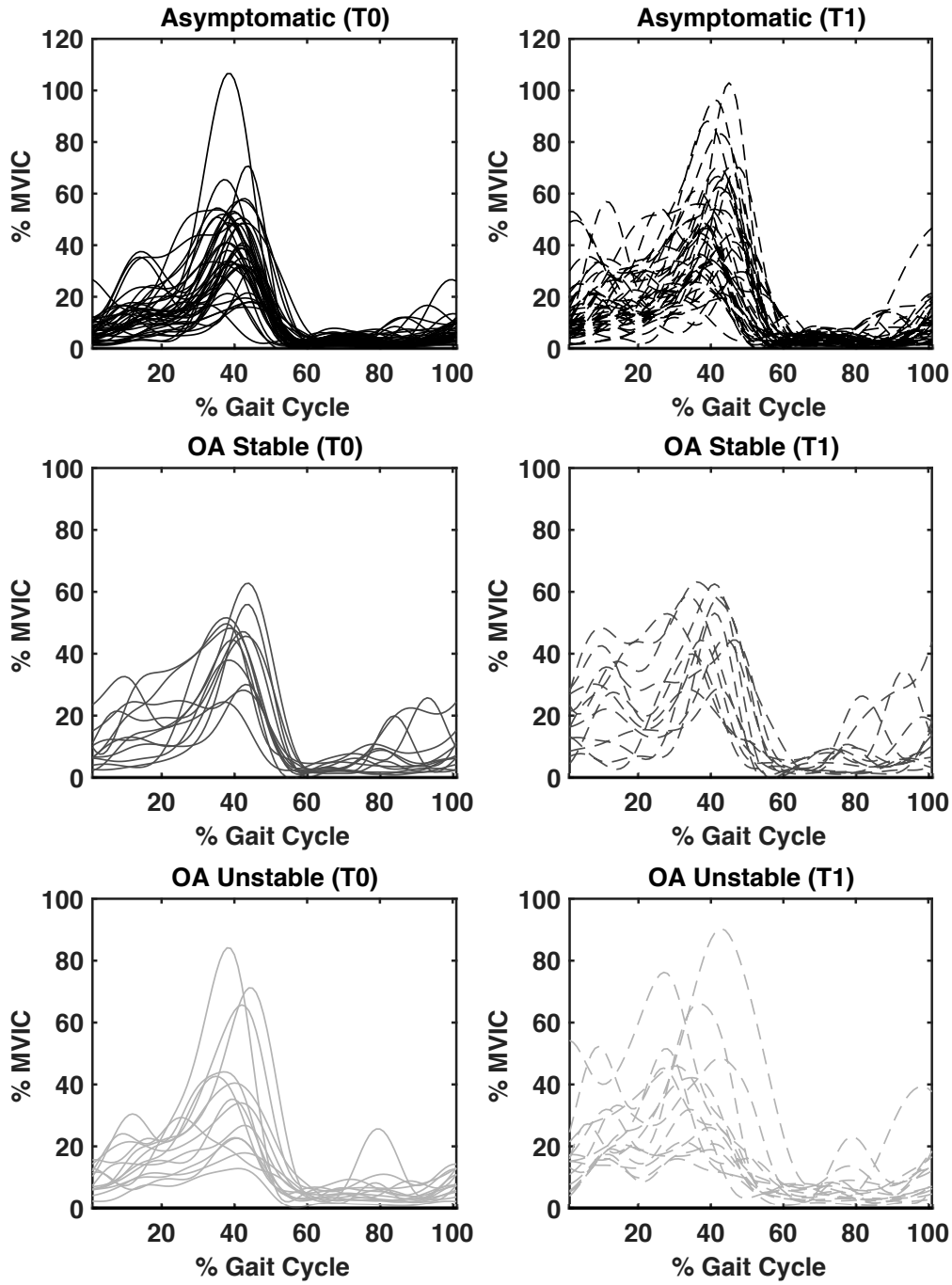

Figure B-39: Lateral gastrocnemius ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

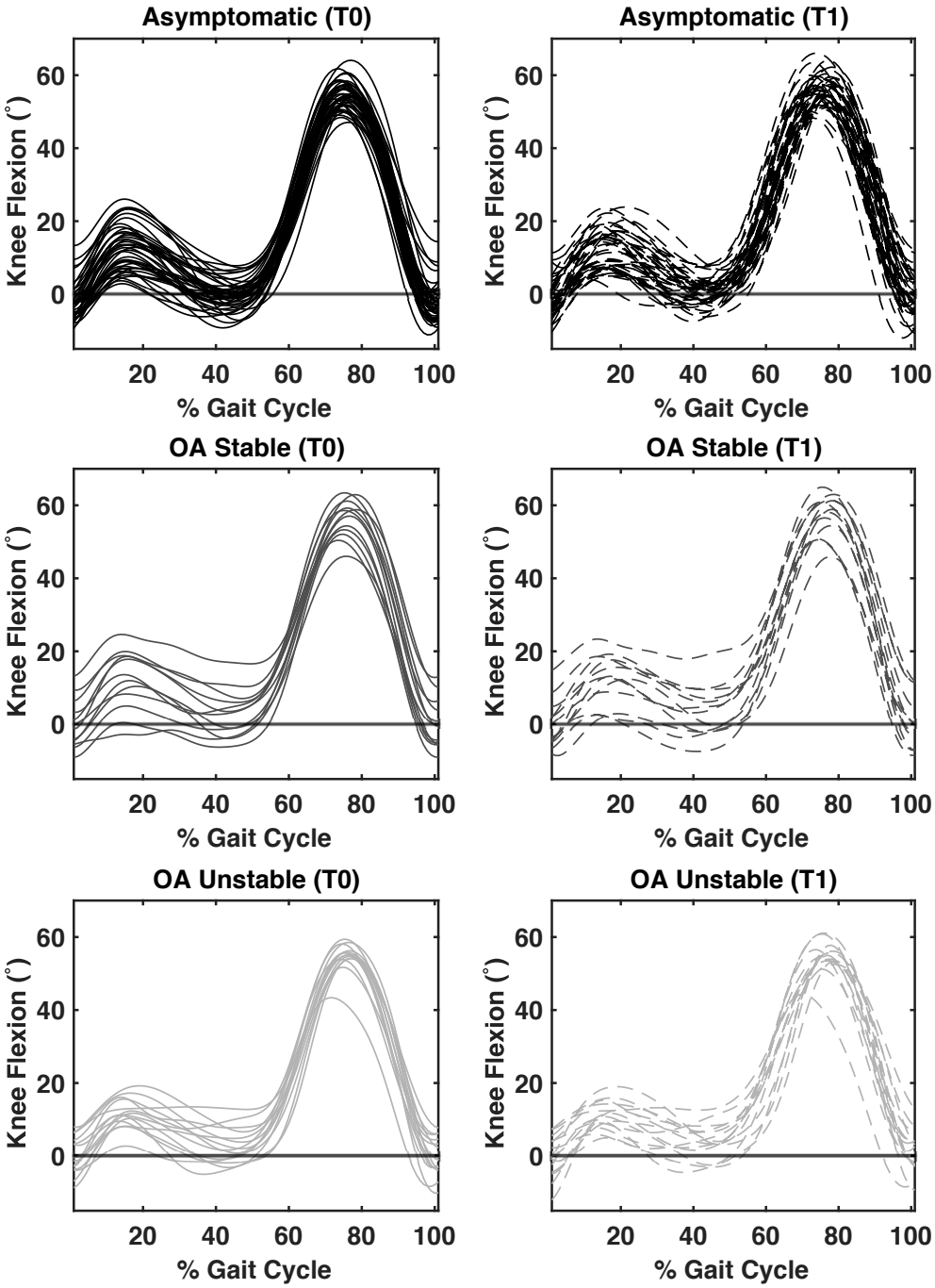

Figure B-40: Sagittal plane motion ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM, OAS and OAU groups. Knee flexion (degrees) is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

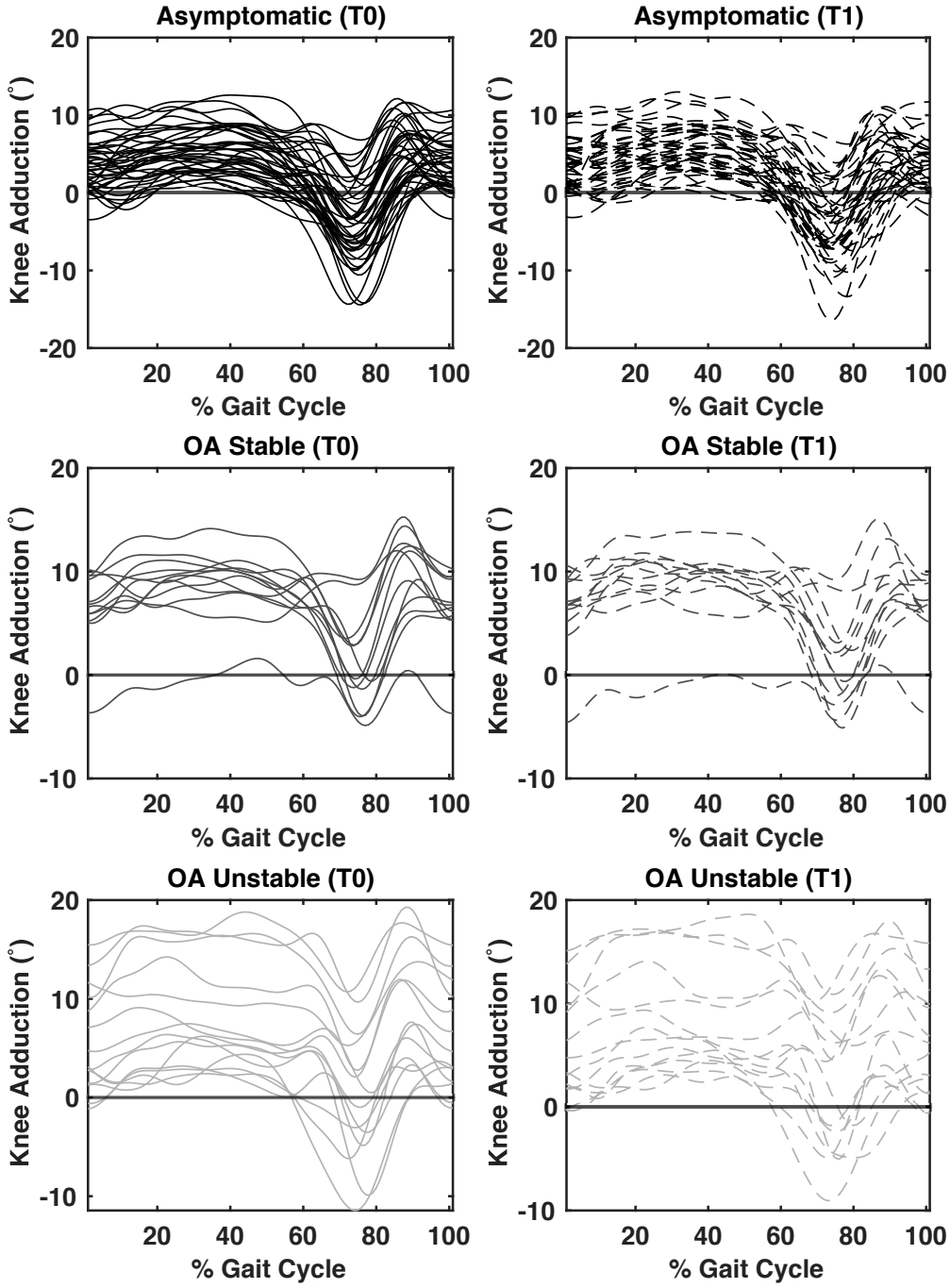

Figure B-41: Frontal plane motion ensembled averaged waveforms for before (T0) and after (T1) direct perturbations for each participant within ASYM, OAS and OAU groups. Knee adduction (degrees) is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

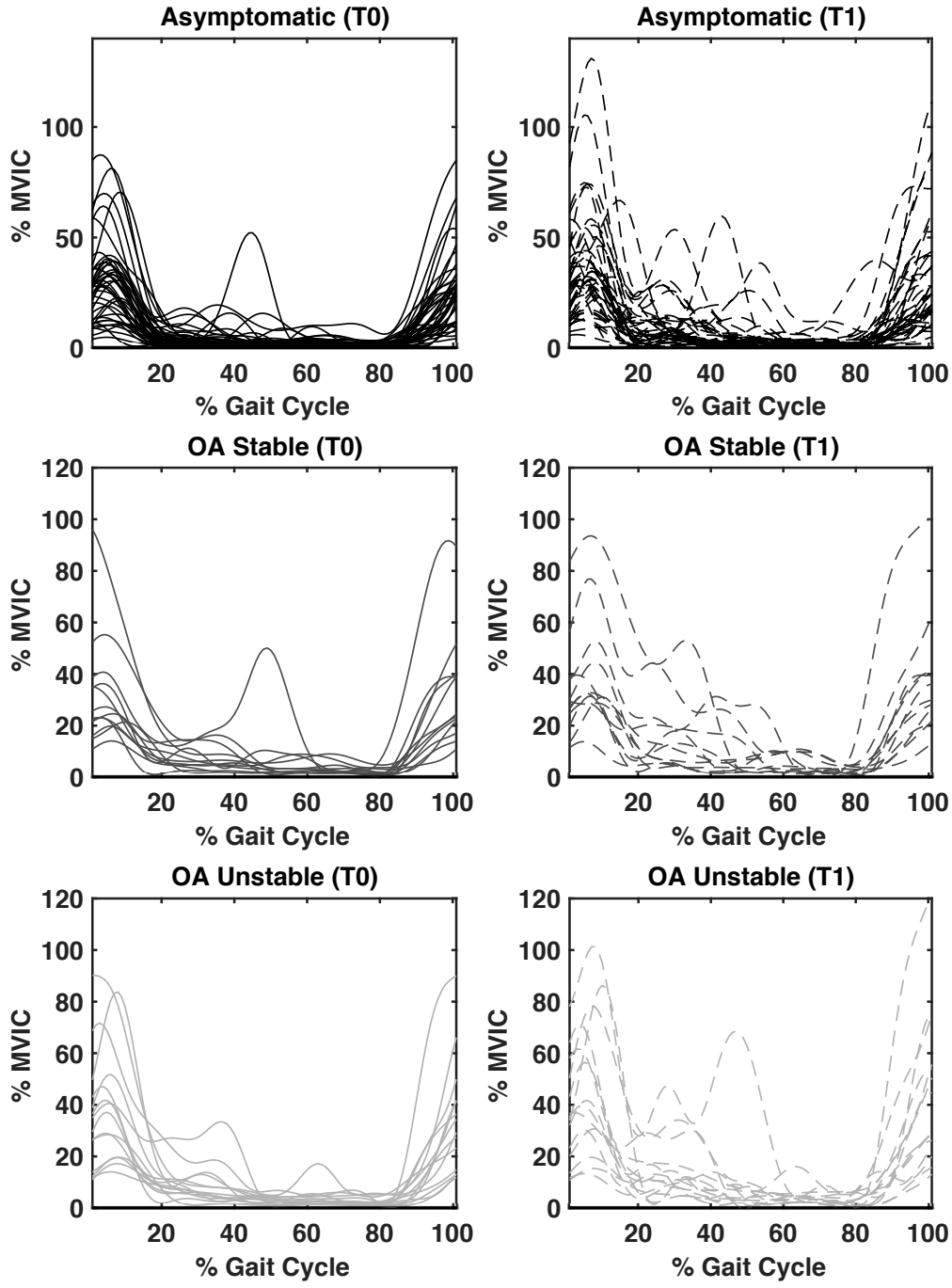

Figure B-42: Vastus medialis ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

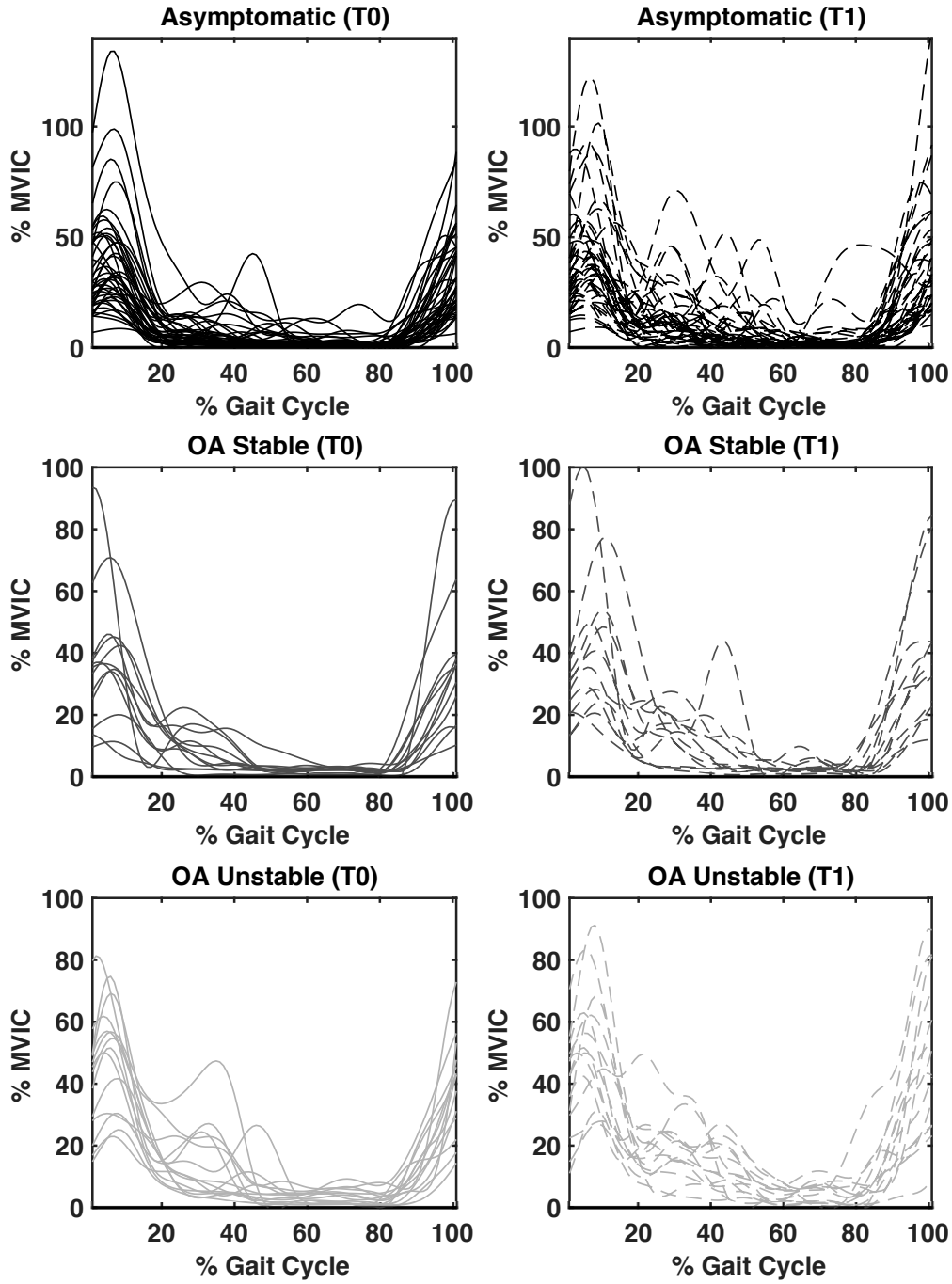

Figure B-43: Vastus lateralis ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

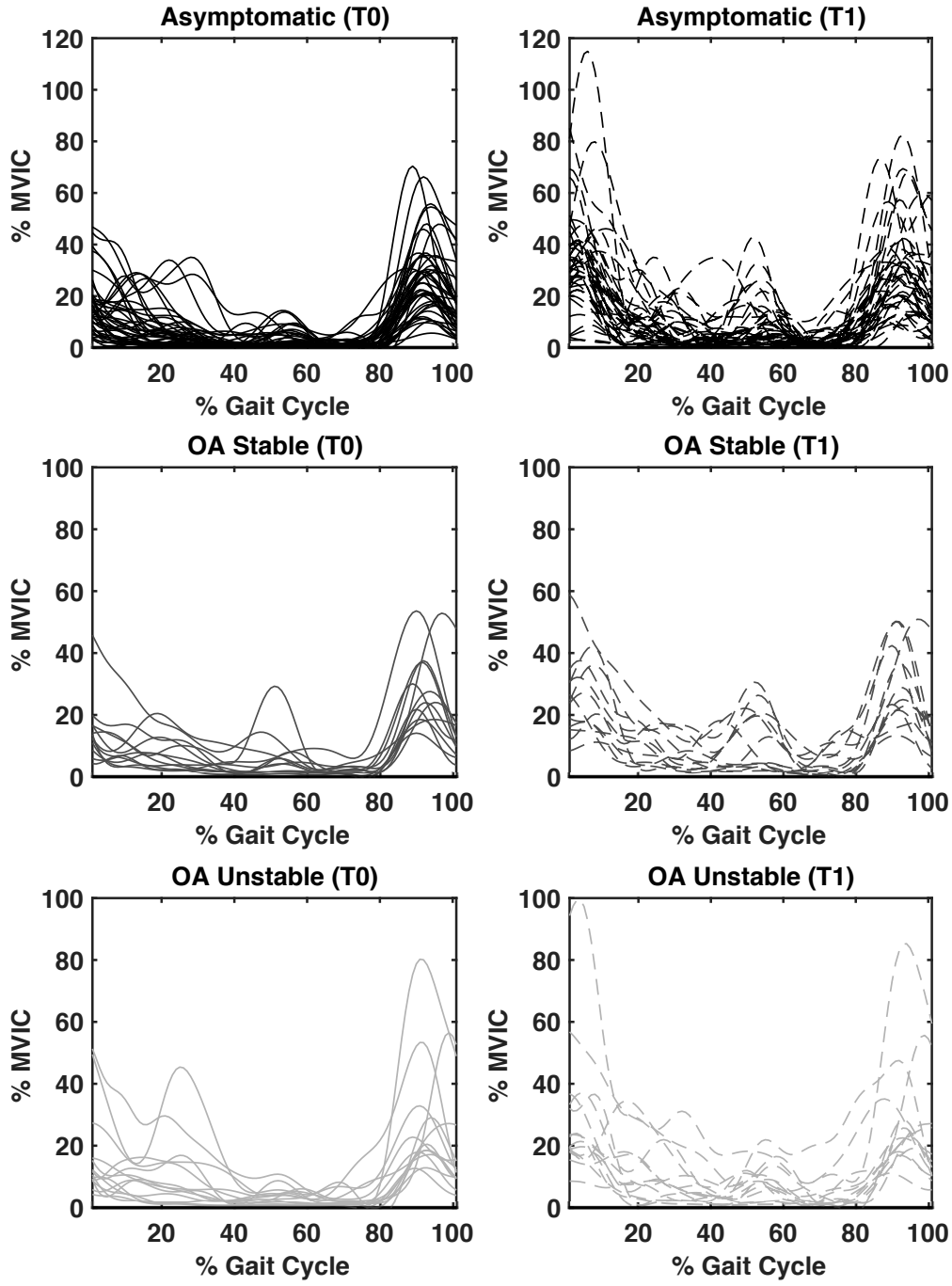

Figure B-44: Medial hamstring ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

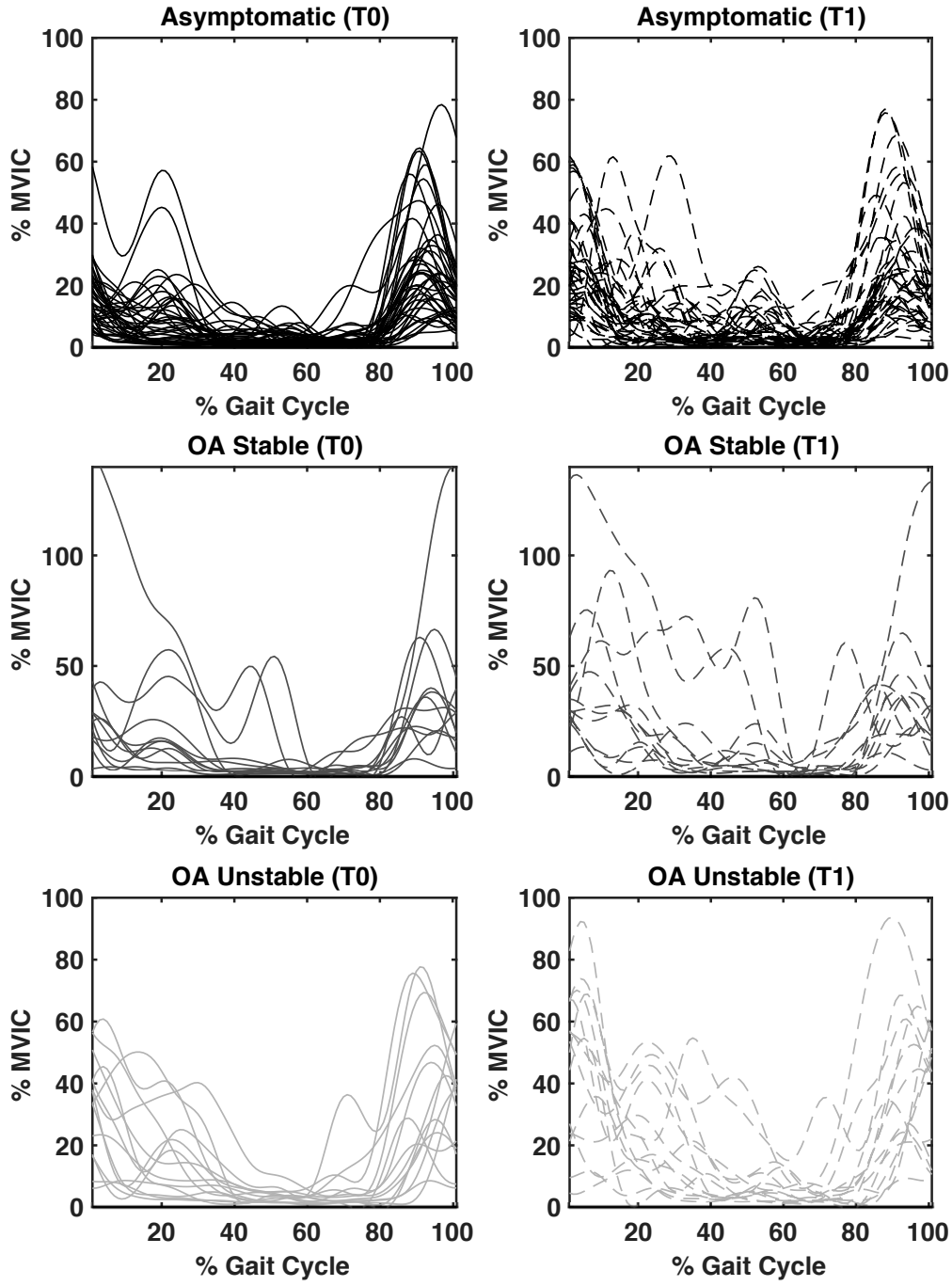

Figure B-45: Lateral hamstring ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

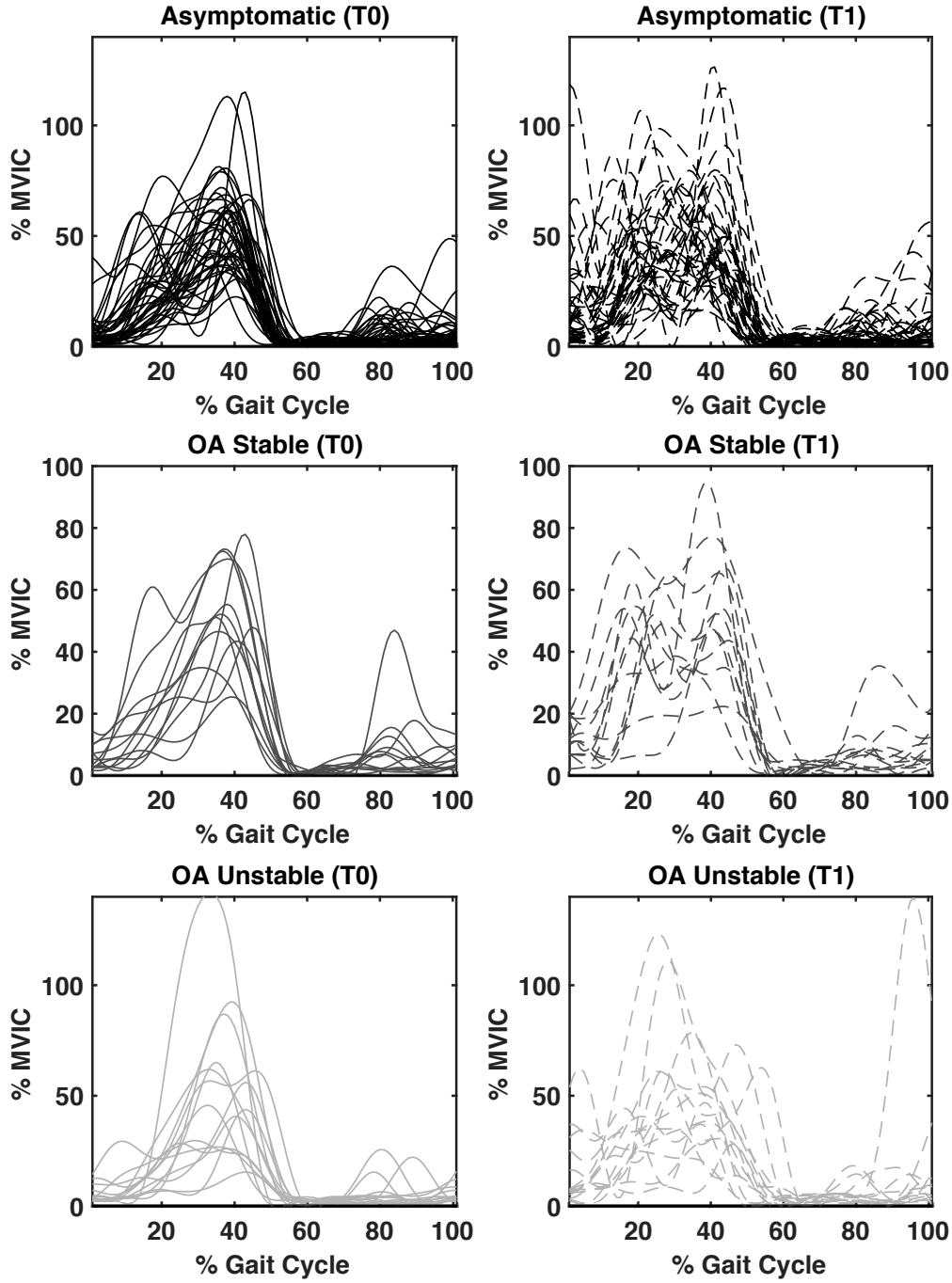

Figure B-46: Medial gastrocnemius ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represented on the x-axis.

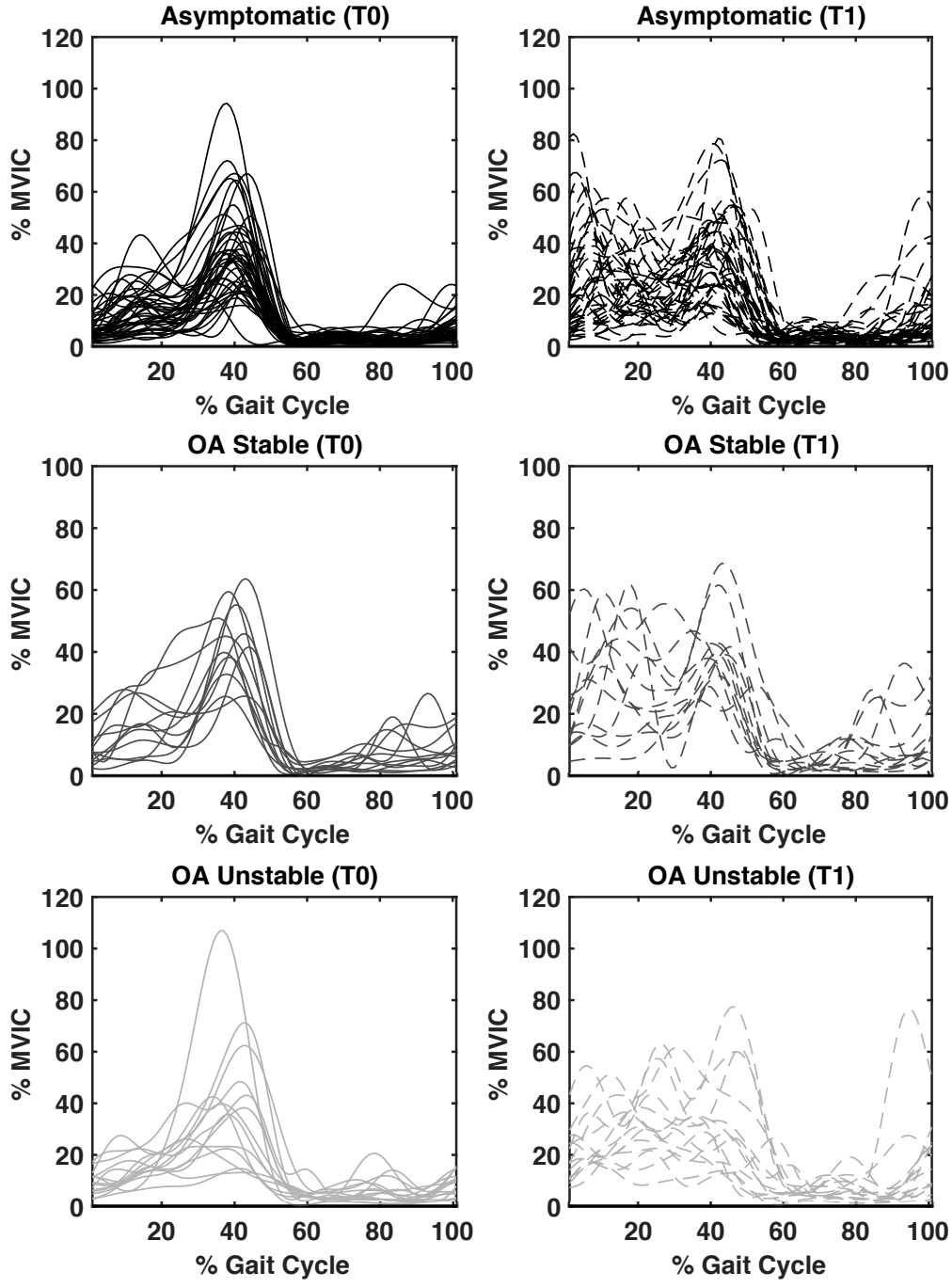

Figure B-47: Lateral gastrocnemius ensembled averaged waveforms for before (T0) and after (T1) indirect perturbations for each participant within ASYM, OAS and OAU groups. Percentage of MVIC is represented on the y-axis and percentage of the gait cycle is represent

APPENDIX C: HIGH-LOW PLOTS

This appendix provides high-low plots for the PCA used in Chapters 4-8. Each plot will have two ensembled averaged waveforms containing example subject waveforms that represent high and low (95%) principal component scores for the indicated measure and principal component. The quadriceps, hamstring and gastrocnemius high-low plots are presented for each chapter. In all figures, percentage of gait cycle is represented by the x-axis and percentage of MVIC is represented by the y-axis.

CHAPTER 4

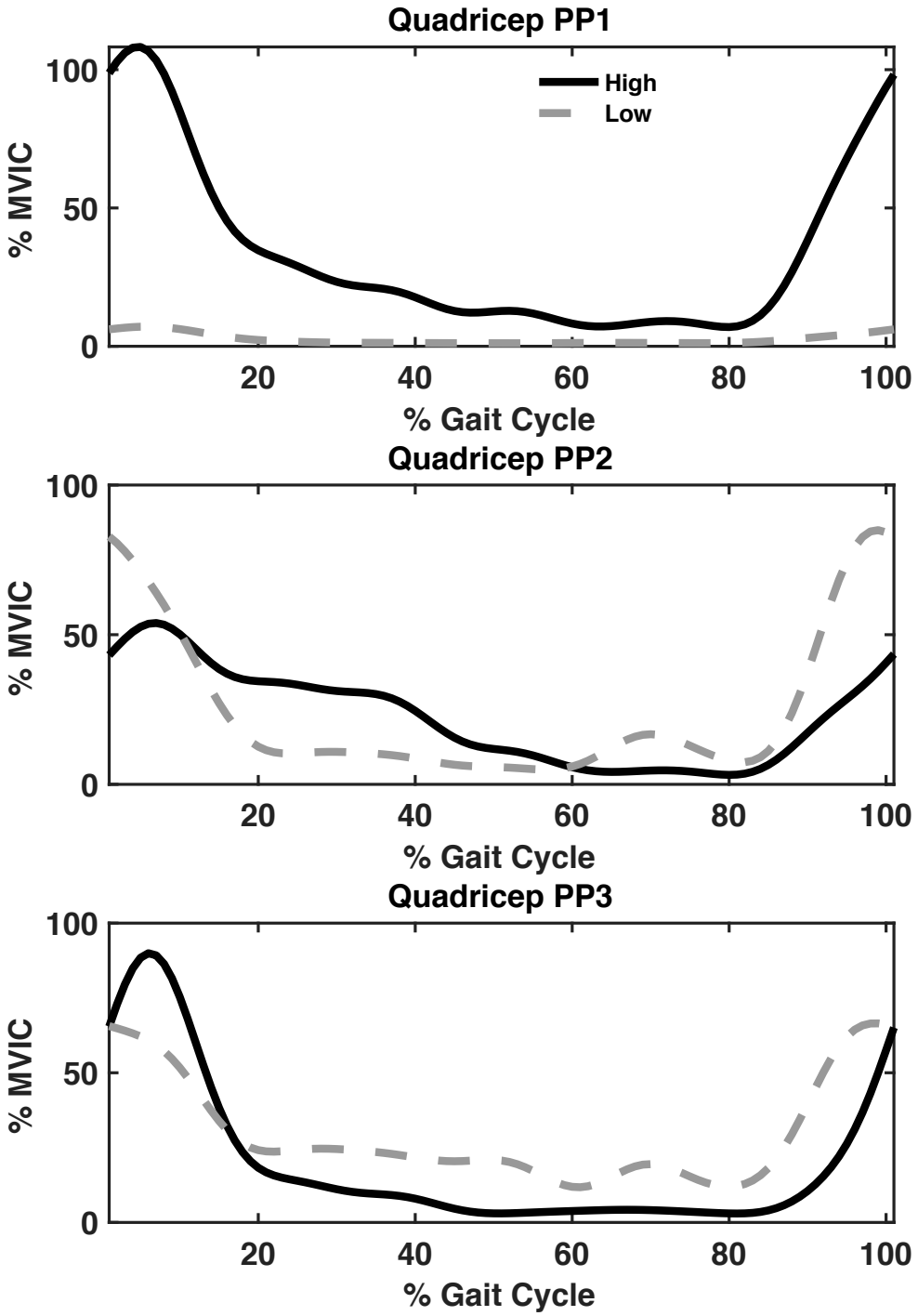

Figure C-1: High-low (95%) waveforms for quadriceps PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 4.

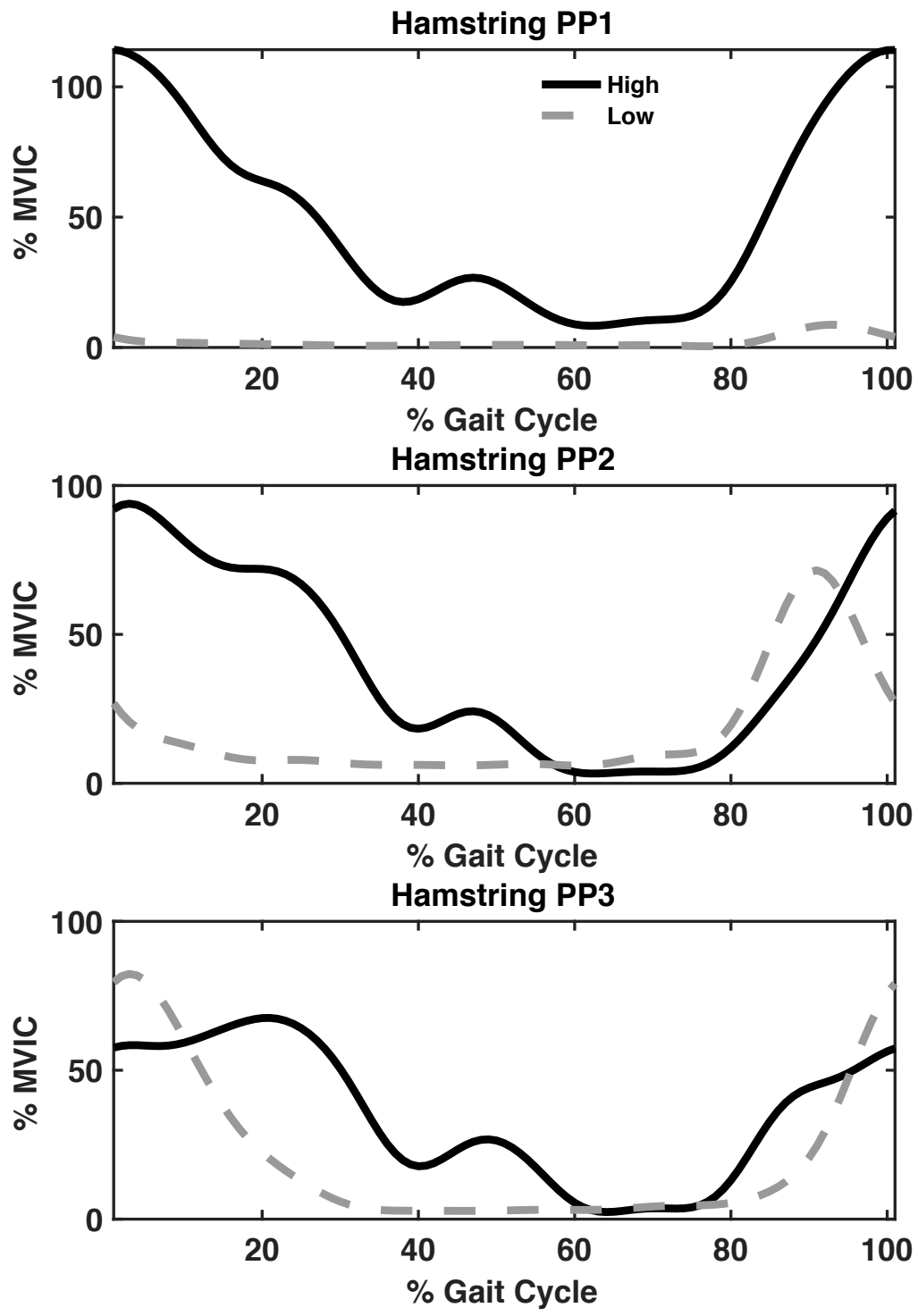

Figure C-2: High-low (95%) waveforms for hamstring PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 4.

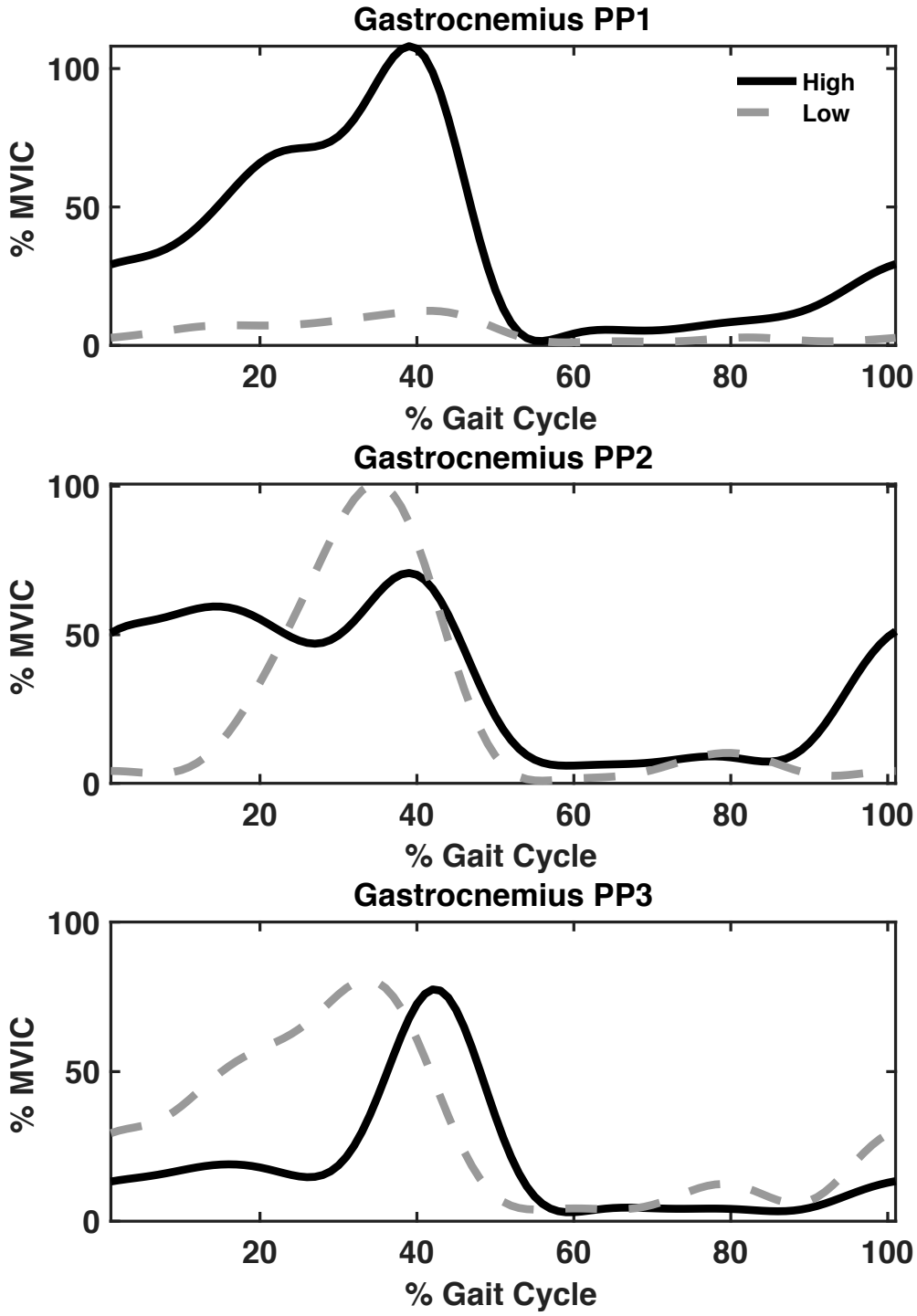

Figure C-3: High-low (95%) waveforms for gastrocnemius PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 4.

CHAPTER 5

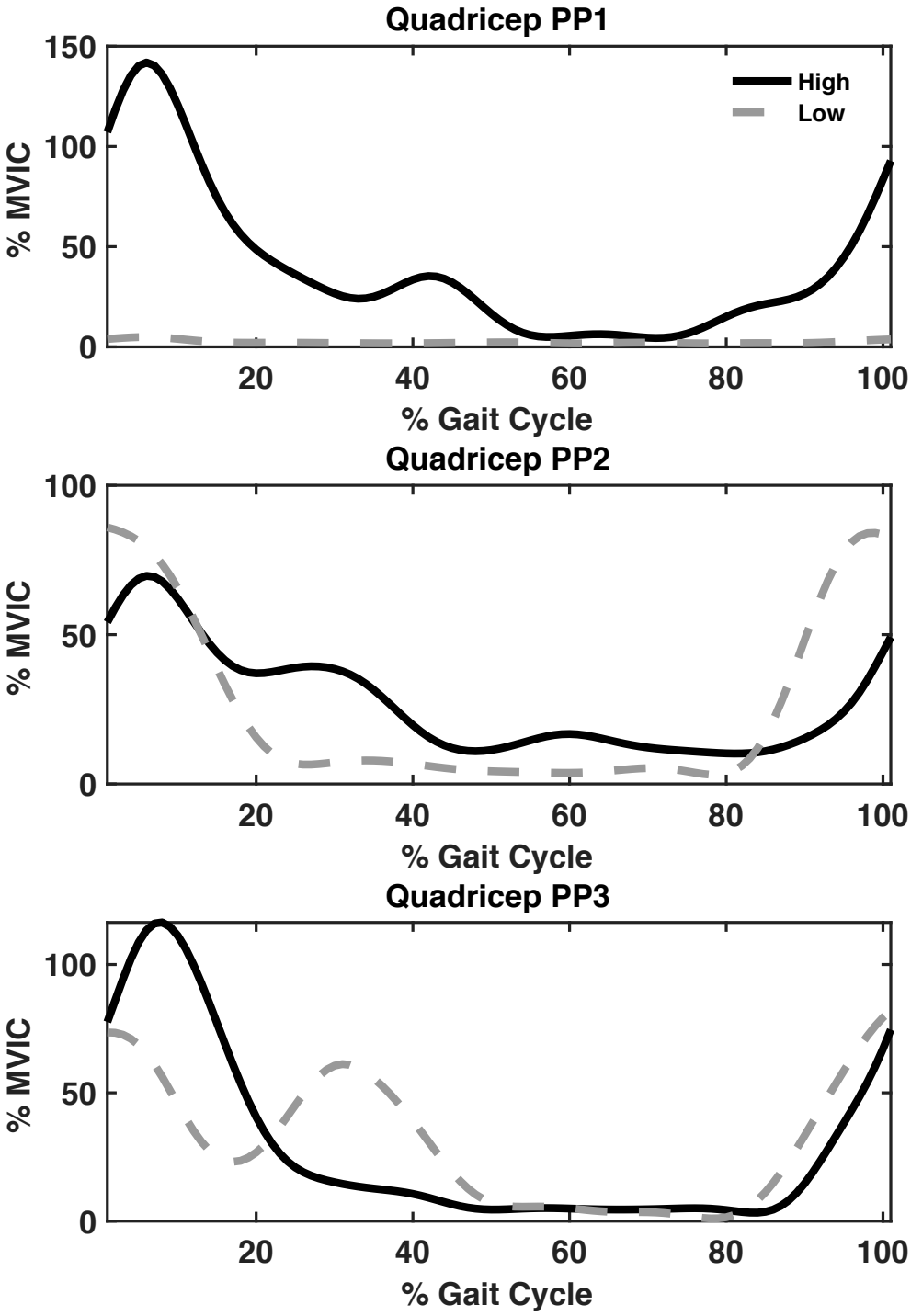

Figure C-4: High-low (95%) waveforms for quadriceps PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 5.

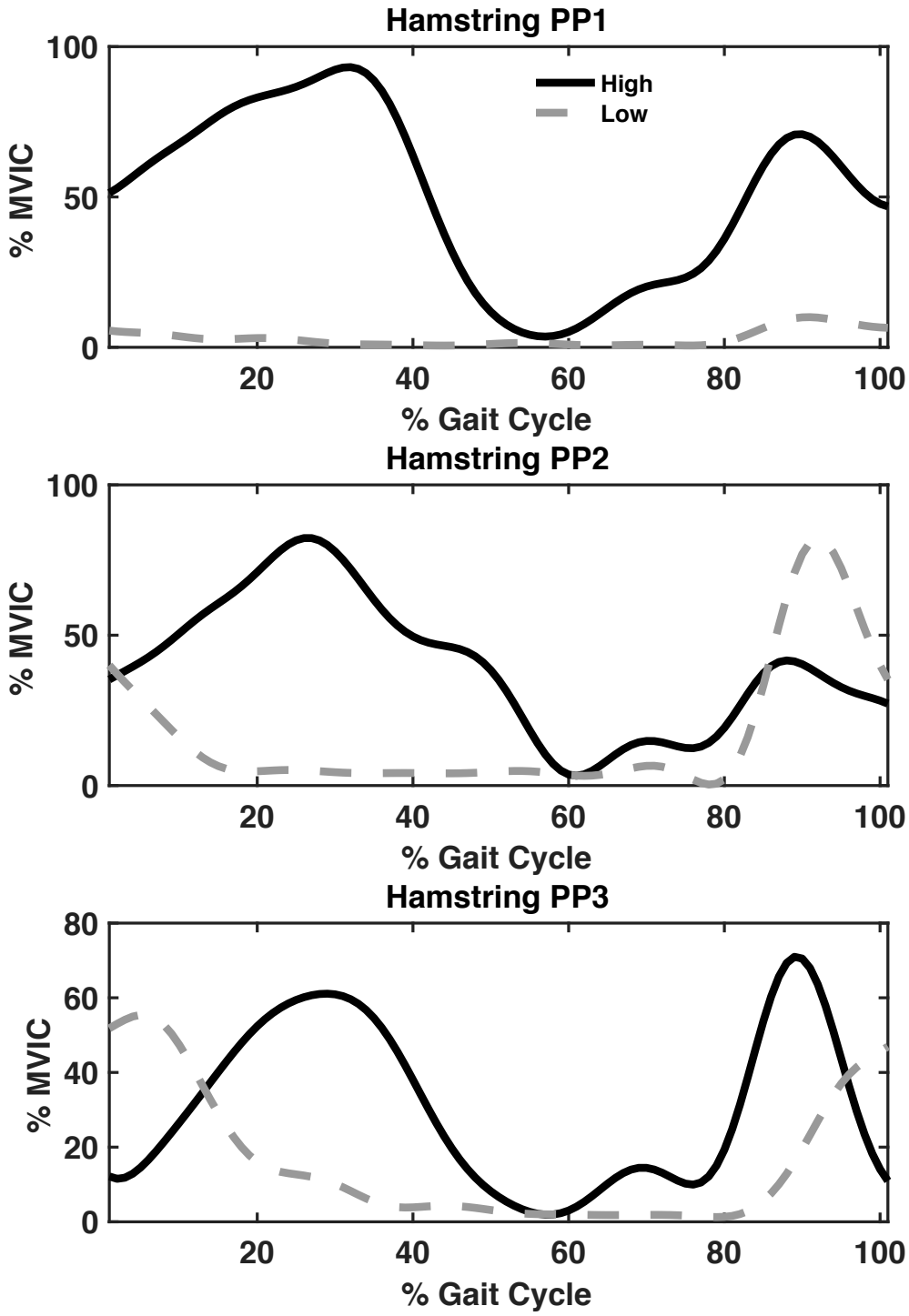

Figure C-5: High-low (95%) waveforms for hamstring PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 5.

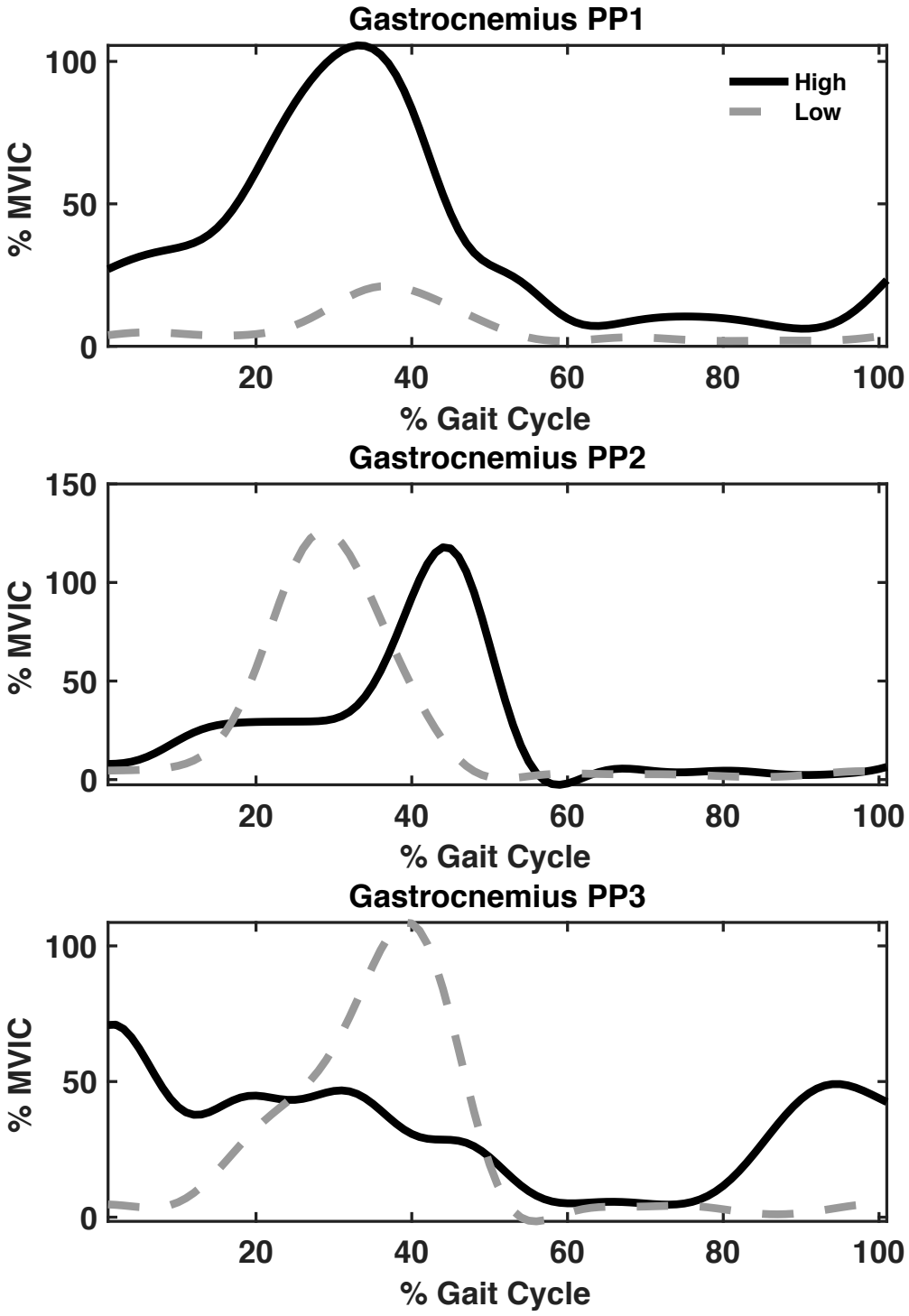

Figure C-6: High-low (95%) waveforms for gastrocnemius PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 5.

CHAPTER 6

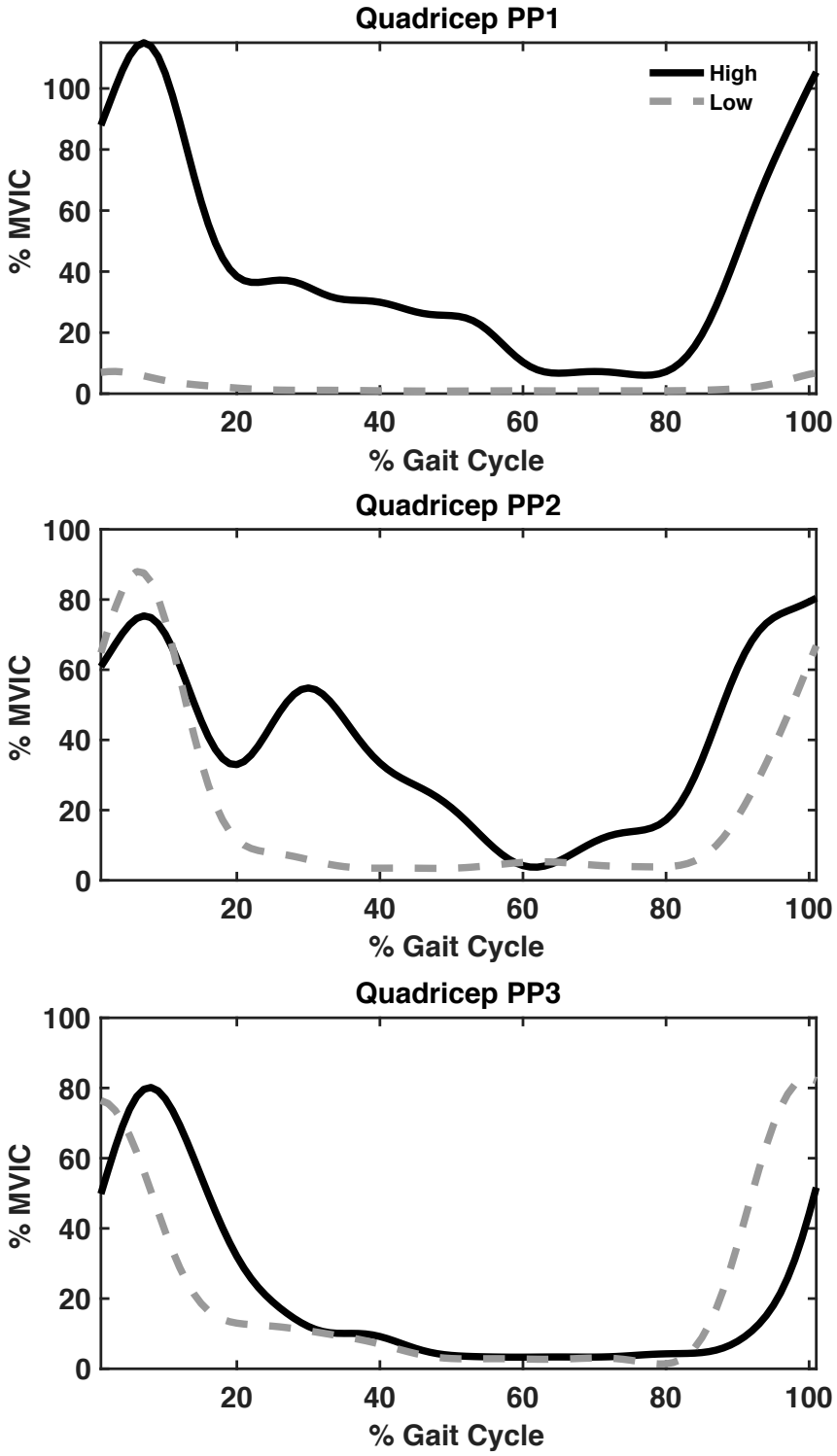

Figure C-7: High-low (95%) waveforms for quadricep PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 6.

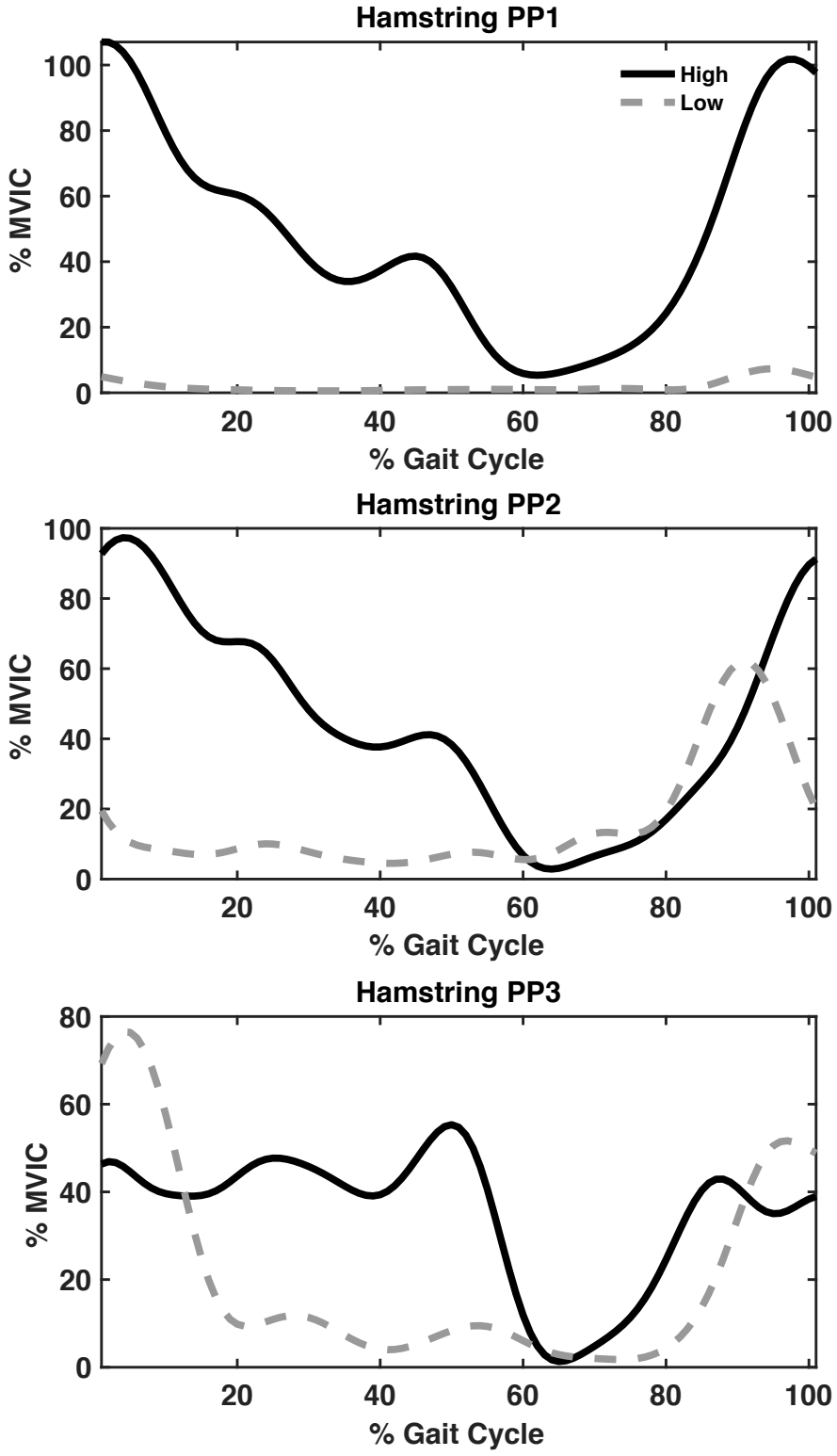

Figure C-8: High-low (95%) waveforms for hamstring PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 6.

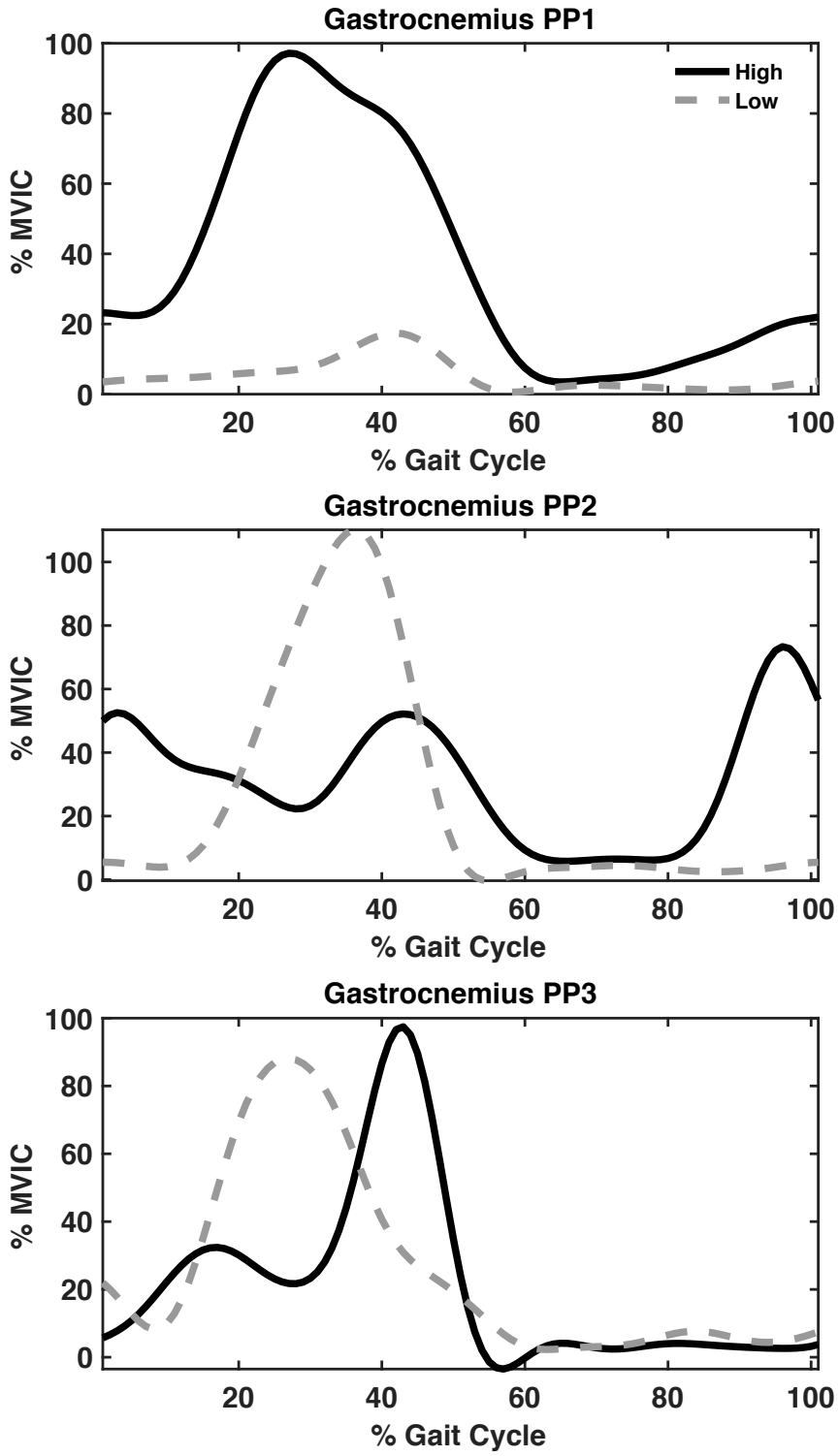

Figure C-9: High-low (95%) waveforms for gastrocnemius PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 6.

CHAPTER 7

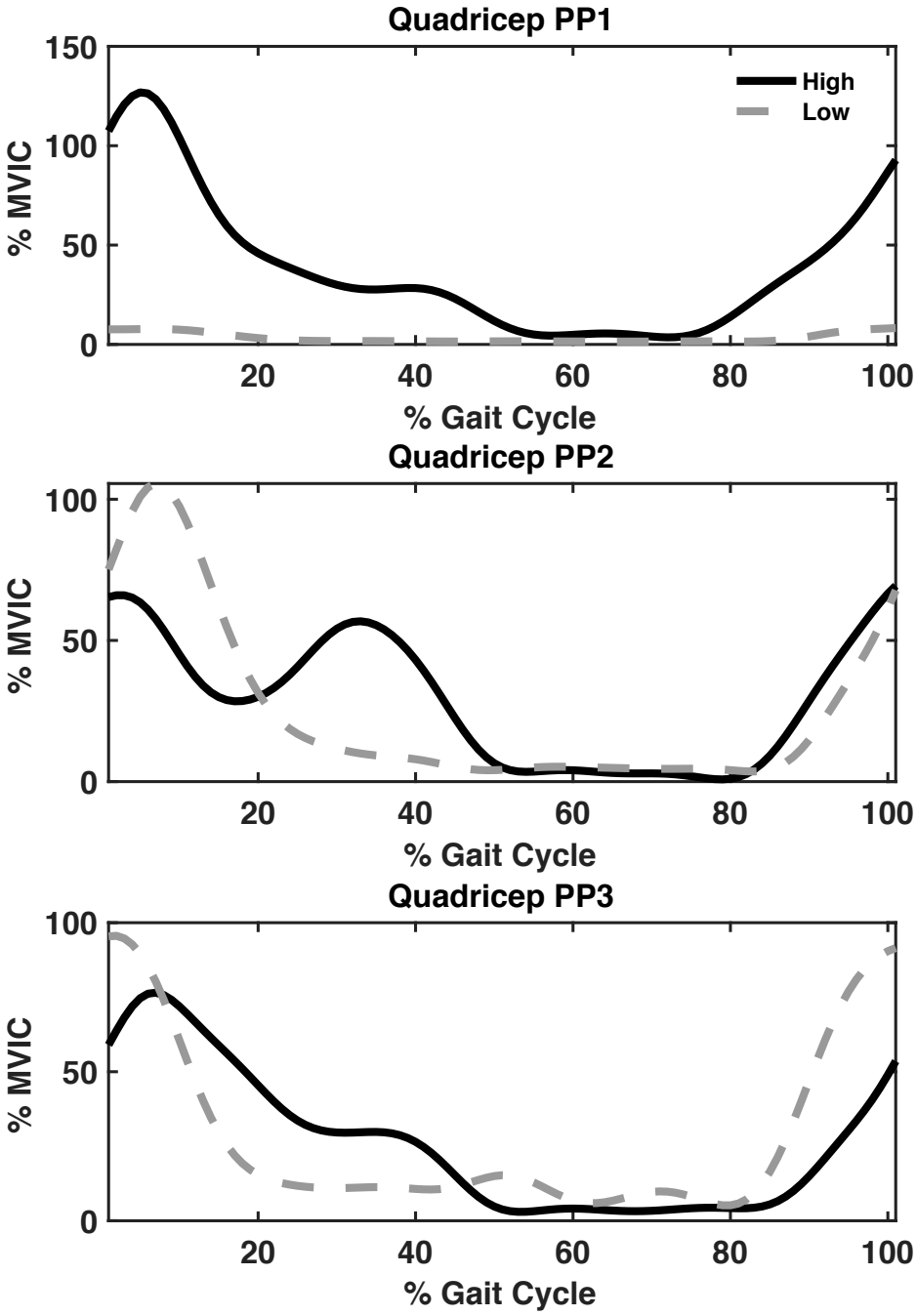

Figure C-10: High-low (95%) waveforms for quadriceps PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 7.

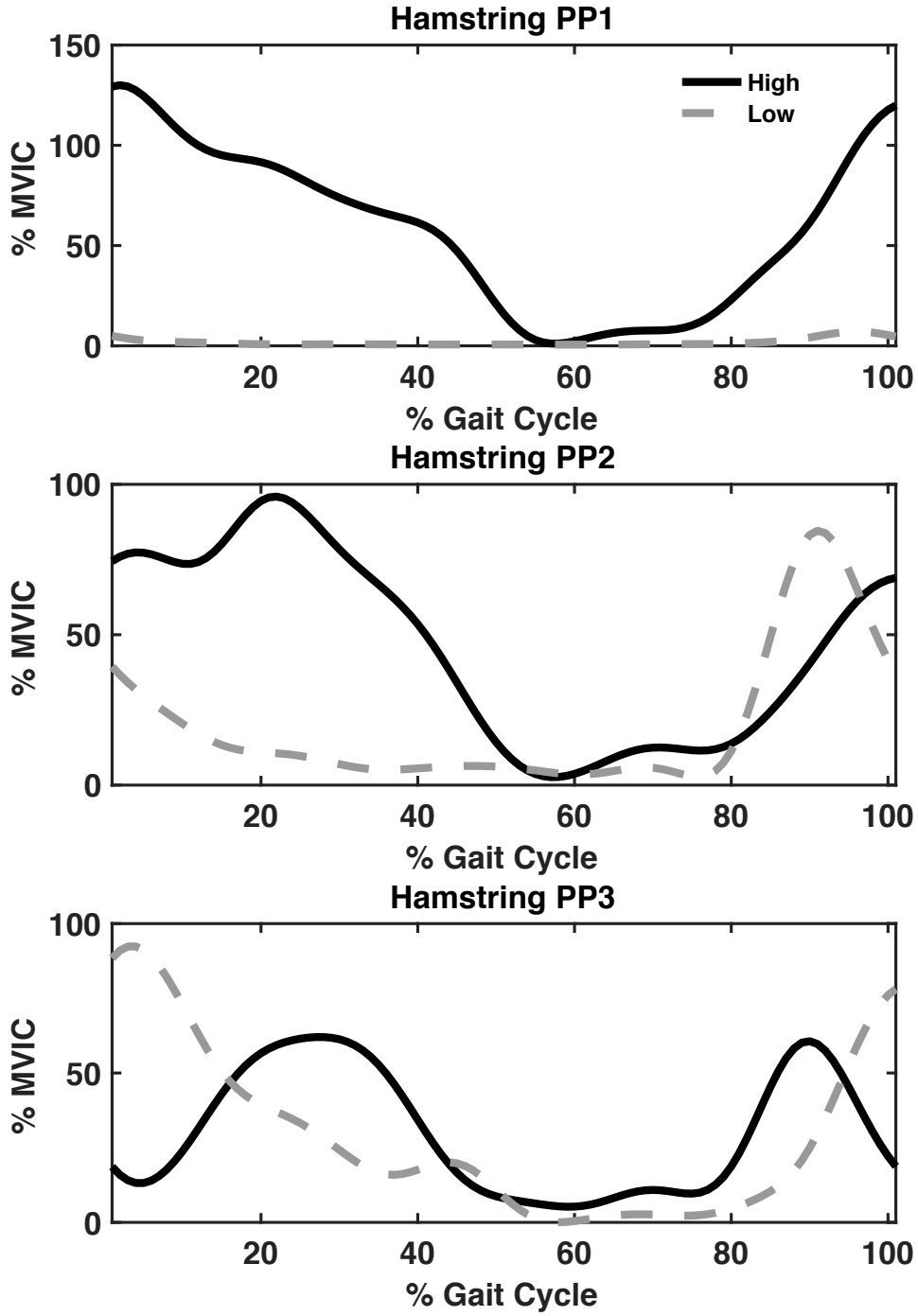

Figure C-11: High-low (95%) waveforms for hamstring PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 7.

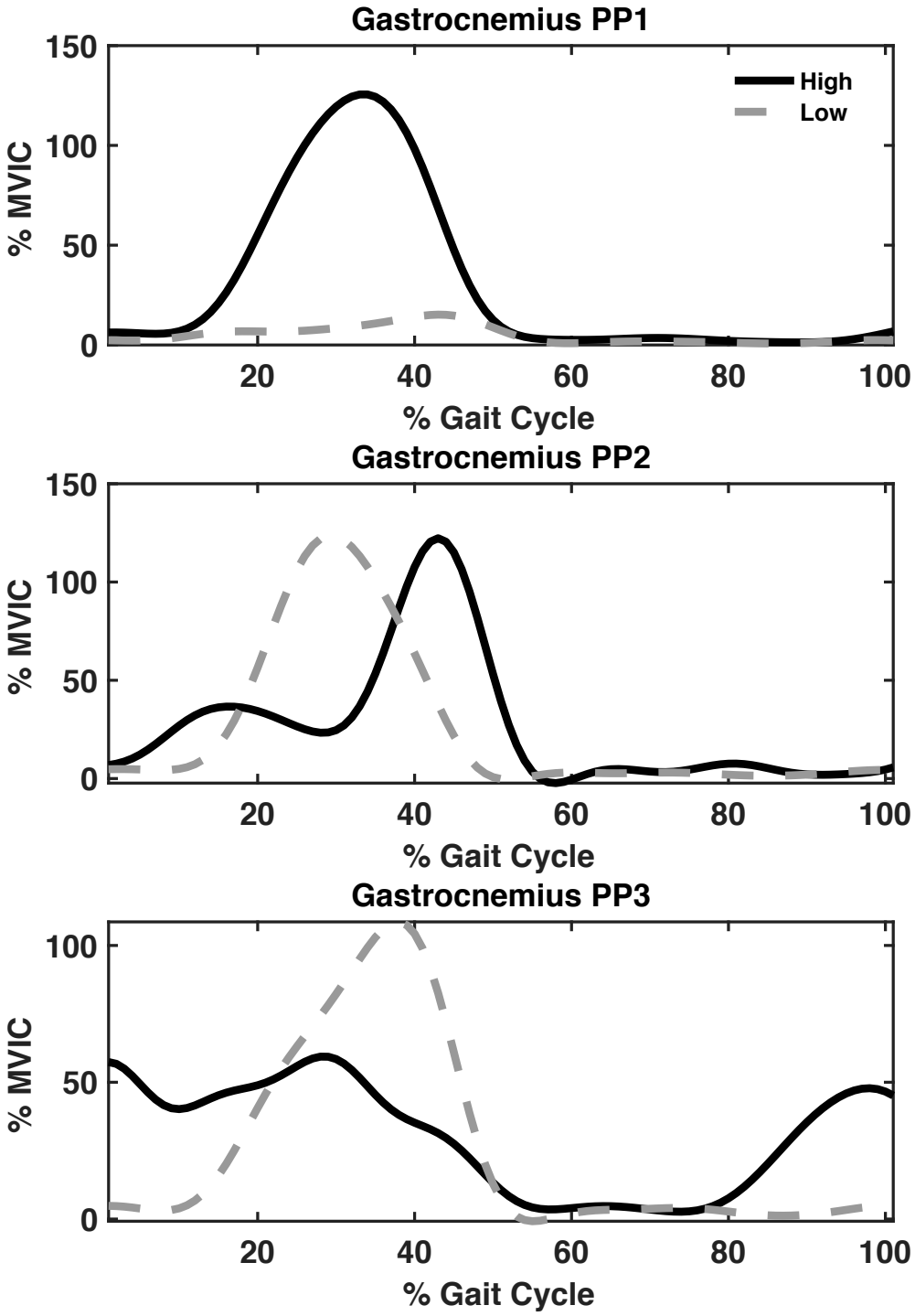

Figure C-12: High-low (95%) waveforms for gastrocnemius PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 7.

CHAPTER 8

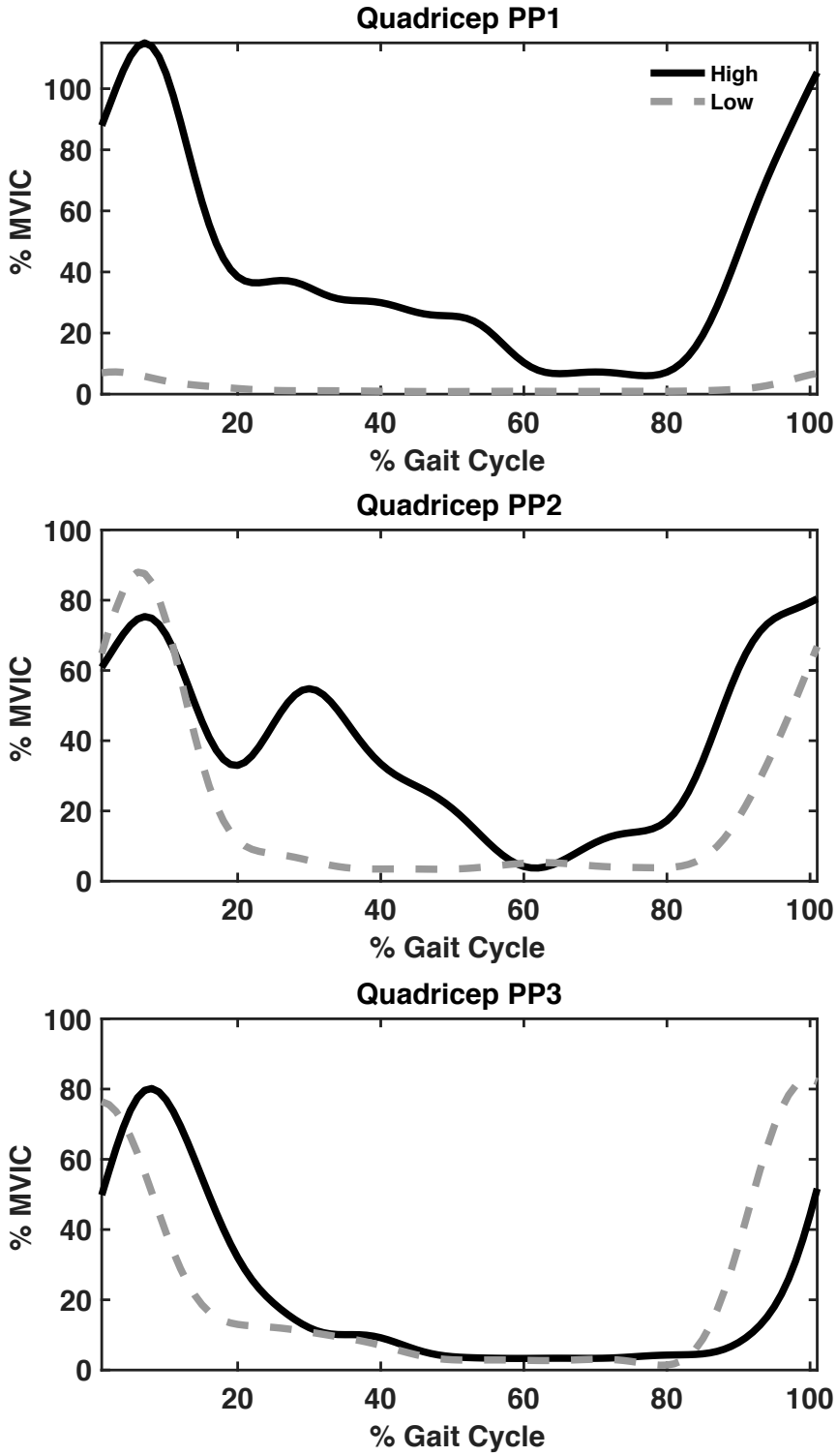

Figure C-13: High-low (95%) waveforms for quadriceps PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 8.

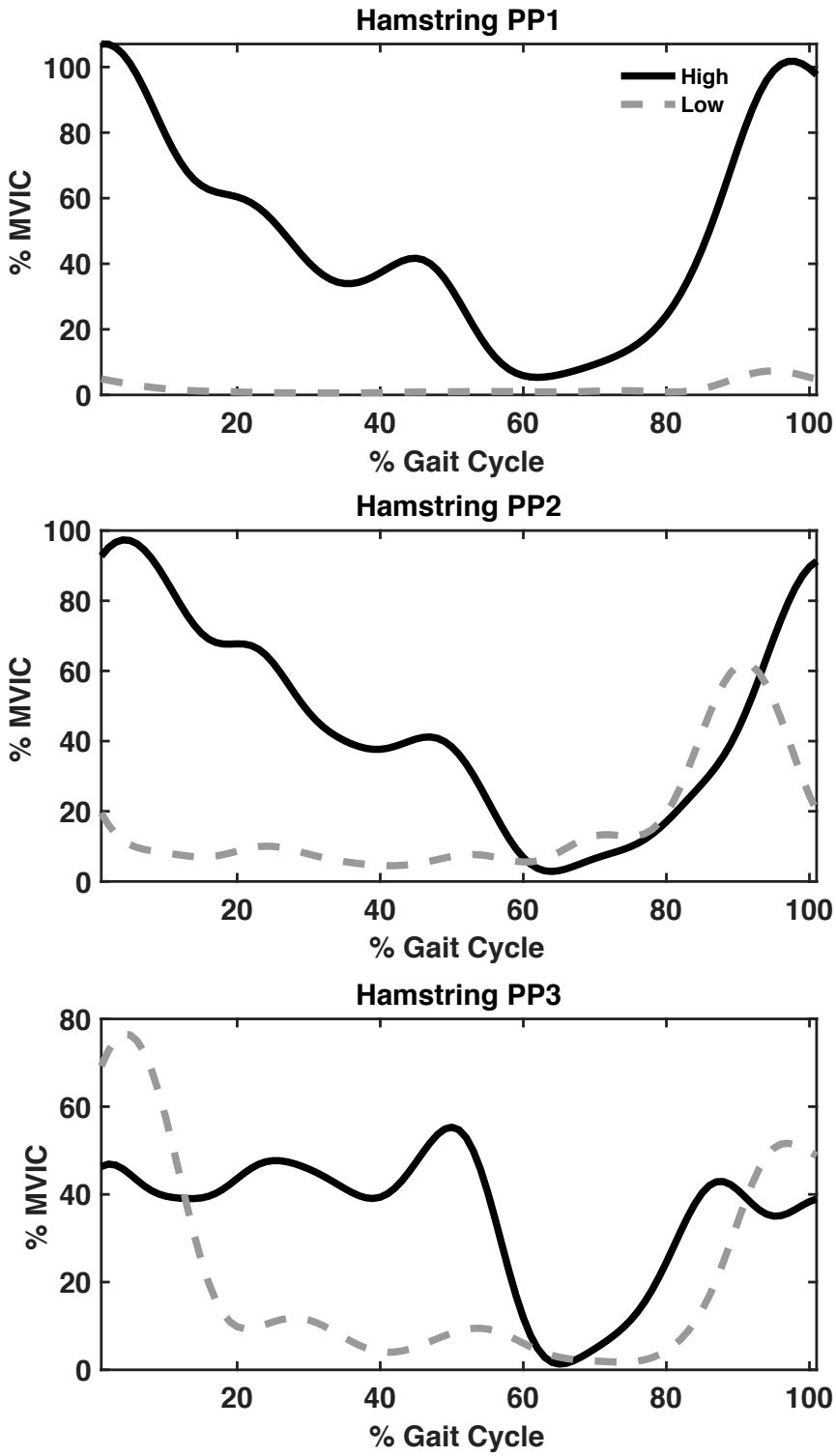

Figure C-14: High-low (95%) waveforms for hamstring PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 8.

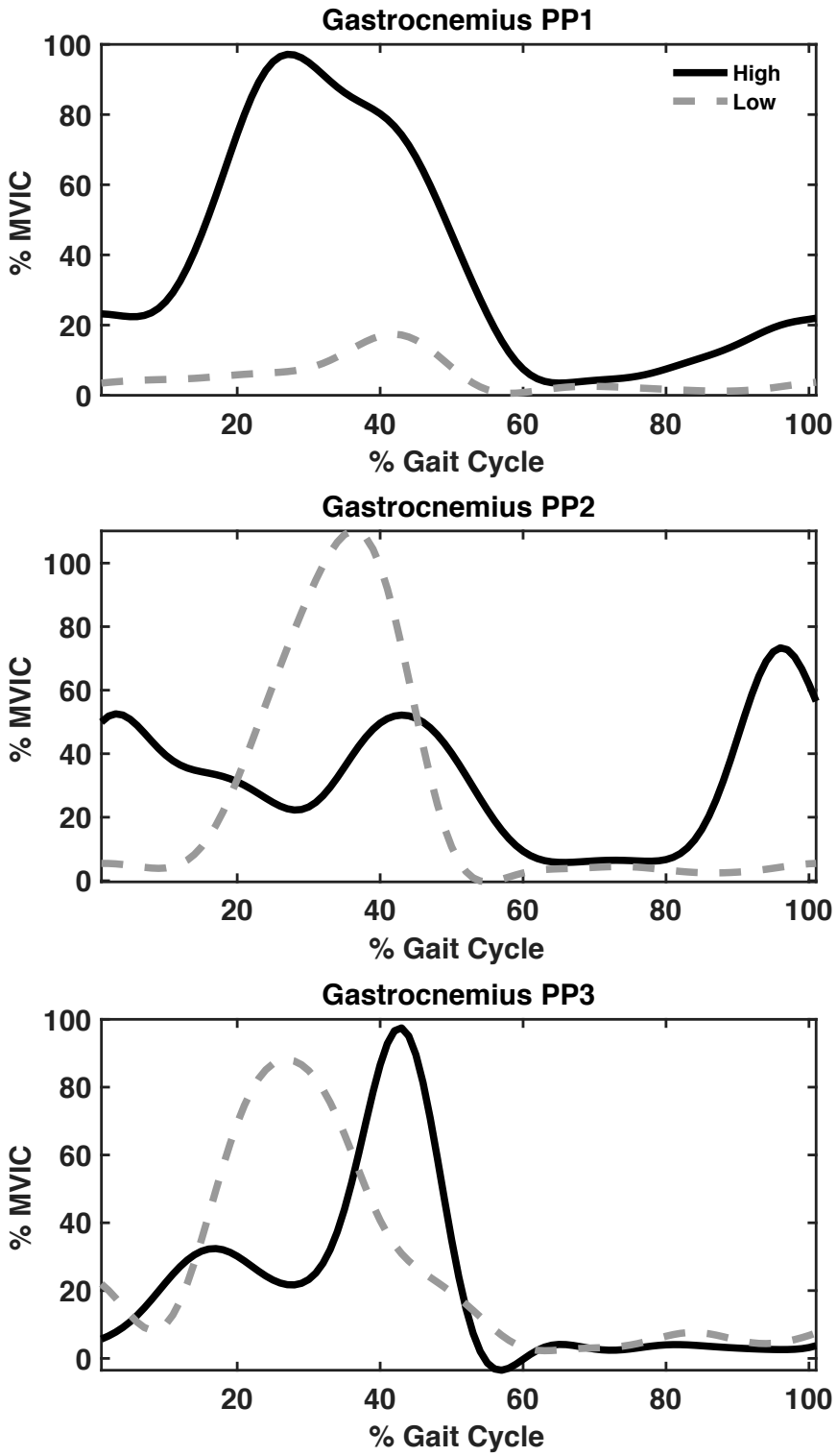

Figure C-15: High-low (95%) waveforms for hamstring PP1 (top), PP2 (middle) and PP3 (bottom) in Chapter 8.

APPENDIX D: STUDY SAMPLE FLOWCHART

This appendix provides a description and flowchart to understand the study and preliminary analysis samples recruited and in each chapter.

Chapter 4 was an analysis of stable treadmill walking and included participants from a variety of studies that completed identical methodologies. The treadmill walking dataset included 125 ASYM and MOA participants and were all used to generate PCA patterns. All ASYM and MOA participants completed the KOS-I and participants were dichotomized into ASYM, OAS and OAU groups. 2 of 46 ASYM participants and 11 of 79 MOA participants scored a KOS-I=4 and were excluded from analysis, justified within Chapter 4. The remaining sample included, 44 ASYM and 68 MOA participants: 26 OAS and 42 OAU participants.

Chapter 5 was an analysis of direct perturbations, completed prior to the collection of the full JAR perturbation dataset and compared MOA and ASYM participants. The ASYM and MOA groups each included 20 individuals and was published in Human Movements Sciences.

Chapter 6 was an analysis of indirect perturbations comparing MOA and ASYM participants. The total perturbation dataset included 80 ASYM and MOA participants. Four participants (2 MOA, 2 ASYM) were not able to complete a medial 3cm indirect perturbation on the study limb and were removed from analysis. The final sample included 76 participants; 44 ASYM participants and 32 MOA participants.

Chapter 7 was a preliminary analysis of direct perturbations comparing OAU, OAS and ASYM participants. The total perturbation dataset included 80 ASYM and MOA participants. Five participants (3 ASYM, 2 MOA) were not able to complete a medial 3cm direct perturbation on the study limb and were removed from analysis. Leaving a sample of 75 participants; 43 ASYM participants and 32 MOA participants. It is important to note that participants removed based on crosses from Chapter 6 were not the same as participants removed from Chapter 7. All ASYM and MOA participants completed the KOS-I and participants were dichotomized into groups. 2 of 43 ASYM participants and 6 of 32 MOA participants scored a KOS-I=4 and were excluded from analysis. The MOA group was then dichotomized into OAS and OAU groups using the KOS-I. The final sample included 41 ASYM participants, 12 OAS participants and 14 OAU participants.

Chapter 8 was a preliminary analysis of indirect perturbations comparing OAU, OAS and ASYM participants. The total perturbation dataset included 80 ASYM and MOA participants. Four participants (2 ASYM, 2 MOA) were not able to complete a medial 3cm indirect perturbation on the study limb and were removed from analysis. Leaving a sample of 76 participants; 44 ASYM participants and 32 MOA participants. It is important to note that participants removed based on crosses from Chapter 7 were not the same as participants removed from Chapter 8 but were the same participants from Chapter 6. All ASYM and MOA participants completed the KOS-I and participants were dichotomized into groups. 2 of 43 ASYM participants and 6 of 32 MOA participants

scored a KOS-I=4 and were excluded from analysis. The MOA group was then dichotomized into OAS and OAU groups using the KOS-I. The final sample included 42 ASYM participants, 12 OAS participants and 14 OAU participants.

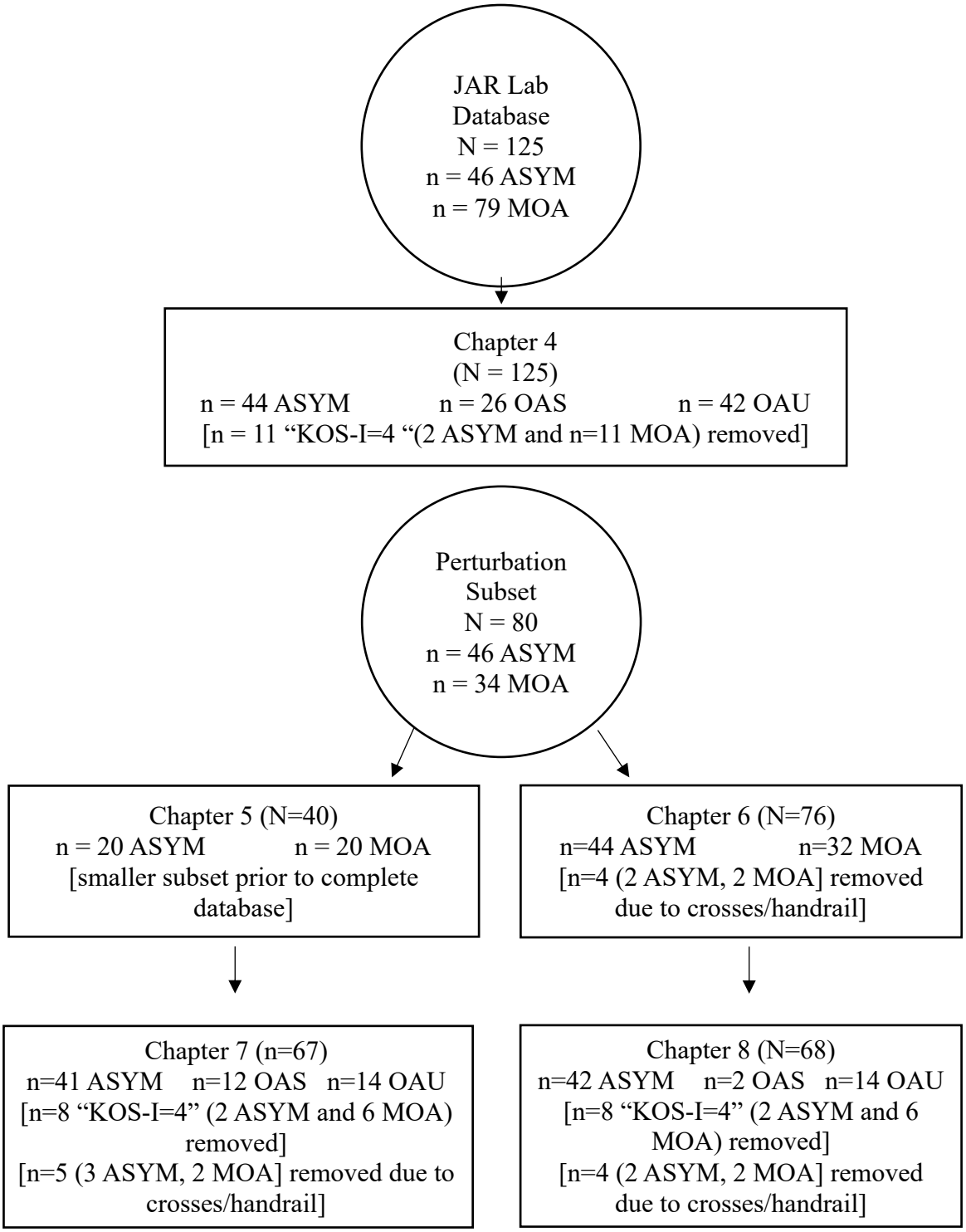

Figure D-1: Flowchart representing samples used in Chapters 4-8.

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