

Advancing Clinical Gait Assessment Methods with Low-Cost Triaxial Accelerometers:
Applications for Individuals with Neurodegenerative Diseases

by

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A thesis
presented to the University of Waterloo
in fulfillment of the
thesis requirement for the degree of

Doctor of Philosophy
in
Kinesiology

Waterloo, Ontario, Canada, 2024

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EXAMINING COMMITTEE MEMBERSHIP

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AUTHOR'S DECLARATION

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

STATEMENT OF CONTRIBUTIONS

Ben Cornish was the sole author for Chapters 1-3 and 5-9, which were written under the supervision of Dr. Bill McIlroy. This thesis consists of four main studies, all of which have aims for publication in future work. A statement of contributions for writing and roles in data collection are as follows:

Research presented in Chapter 4:

Dr. Bill McIlroy and Dr. Karen Van Ooteghem were primary investigators on the Ontario Neurodegenerative Disease Research Initiative's (ONDRI) Aim 4 on wearable sensors, which supported this work. This work was funded by the Ontario Brain Institute. Dr. Manuel Montaro-Odasso, Dr. Frederico Pieruccini-Faria, Matthew Wong, and Kyle Weber were co-authors on the publication that is presented in Chapter 4. Ben Cornish, Matthew Wong, and Kyle Weber led sensor deployment and data collection setup throughout the wearable sensor data collections within this specific aim of the ONDRI project. Erin Turner and Youness Demnati led data collections at Sunnybrook Health Sciences Centre. Ben Cornish and Matthew Wong were responsible for algorithm development and Ben Cornish led all data analysis with support from Andrew Chaston for gold-standard step detection. Ben Cornish wrote draft of the manuscript, which all authors provide intellectual input on, and Dr. Karen Van Ooteghem, Dr. Bill McIlroy, and Kyle Weber provided editorial feedback.

Citations:

Cornish, BF., Van Ooteghem K., Wong, M., Weber, KS., Pieruccini-Faria F., Montero-Odasso, M., McIlroy, WE. (2024). Evaluation of a finite state machine algorithm to measure stepping with ankle accelerometry: performance across a range of gait speeds, tasks, and individual walking ability. *Medical Engineering and Physics*. <https://doi.org/10.1016/j.medengphy.2024.104251>.

Research presented in Chapter 3, 5-7:

Dr. Bill McIlroy and Dr. Manuel Montero-Odasso were primary co-investigators of the Gait and Balance data platform within the ONDRI Foundational Longitudinal Research Study. This study was funded by the Ontario Brain Institute. Ben Cornish, Dr. Frederico Pieruccini-Faria, Julia Fraser, Anton Trinh, and Alanna Black were all part of the sensor setup and data collection protocol design. Data were collected at all the research centres and completed by trained site coordinators. Ben Cornish and Dr. Frederico Pieruccini-Faria were data platform coordinators and led data analysis and curation for ONDRI data releases. For the data used in these chapters, Ben Cornish led all data analysis.

As lead author for these research studies, Ben Cornish was responsible for contributing and conceptualizing study design, data analysis and drafting the manuscripts within this thesis. Dr Bill McIlroy and committee members have provided guidance all steps of research.

ABSTRACT

Clinical gait assessment provides objective measurement of a person's locomotor and dynamic balance control. Applications of wearable sensors for gait assessment have gained popularity over the past decade as a feasible tool to objectively measure gait in clinical settings. Commonly, clinical assessments and research studies limit a focus to steady-state walking relying on static thresholds to remove intra-bout phases, such as gait initiation and termination. Despite this historical focus on steady-state gait, the use of wearable technology affords the ability to provide insight into the variability of walking that occurs not only within (intra-stride) and between strides (stride-to-stride) but also variability of phases within a walking bout (intra-bout), measures that potentially have clinical importance. To achieve necessary details of intra-stride, stride-stride and intra-bout characteristics there continues to be a need to advance algorithm development to accurately detect gait characteristics specifically when applying across range of ages, task conditions, and gait control ability. The purpose of this thesis was to advance the analytical approaches of gait assessments performed in clinical environments with cost-effective wearable sensors in two meaningful ways: (1) advancing stride segmentation methods beyond standard stride or stance-swing segmentation using ankle-worn accelerometry and describe these metrics across tasks of varying difficulty, (2) identifying groups of strides that are representative of intra-bout phases and how these metrics change with task and understand their relation to gait-specific clinical metrics of mobility in older adults and neurodegenerative disease.

Using accelerometry data collected as part of the Ontario Neurodegenerative Disease Research Initiative (ONDRI) allowed for the development of a Finite State Machine (FSM) algorithm to segment gait cycles into unique intra-stride phases. The FSM algorithm was tested for stride detection accuracy, across cognitively intact young adults and people living with neurodegenerative disease (NDD) or cerebrovascular disease (CbVD), and during walking with varying speeds and secondary cognitive tasks. Temporal and accelerometry-based kinematic outcomes from the algorithm were evaluated across dual-

task walking conditions to identify compensatory gait strategies to secondary cognitive demands. These same FSM outcomes were used to quantify intra-bout phases using stride clustering approaches and examine how intra-bout phases and accelerometry-based kinematics might contribute to stride-to-stride variability within the dual task paradigm. In addition, the relationship between conventionally reported metrics, stride clustering outcomes, and gait-specific clinical markers was assessed to understand the interaction between mobility outcomes. In general, FSM stride detection performed well across tasks of varying difficulty and speed in young healthy adults during long treadmill walking and in people with NDD or CbVD during short overground walking tasks. Algorithm performance was also considered in the context of defining long periods of walking for implications in free-living environment; where depending on the parameters used to define a walking bout, the algorithm performance influenced the identification of the start and stop of walking. This approach to segment walking into stride-to-stride and intra-stride phases proves to be an accurate method using minimal data inputs with clinically feasible tools. Temporal and accelerometry-based kinematics (e.g., cycle time, accelerometer magnitudes) derived from the FSM methods were different between clinical walking tasks, such that cycle time gradually increased during dual task walking and across task difficulties and accelerometry kinematics decreased during dual task walking. Of particular interest was the significant differences between preferred walking tasks; the first preferred trial was typically different from the subsequent trials with the same conditions for conventionally reported and accelerometry based gait outcomes. In addition, when these outcomes were used to characterize intra-bout phases there were significant differences between preferred and dual task conditions across all cluster-based outcomes (e.g., initiation length). These outcomes suggest that the FSM can detect previously reported and novel kinematic outcomes to describe compensatory strategies selected by NDD and CbVD persons in response to secondary dual task walking. Clinically, these FSM or cluster-based outcomes can distinguish between groups that are stratified by commonly reported gait-specific markers of mobility, such as walking speed, dual task cost magnitude, or the Unified Parkinson's Disease Rating Scale gait score.

This work advances the detection of stepping with an adaptable algorithm that requires minimal data input, performs well across young and older adults including those with NDD, and can characterize compensatory strategies under dual task conditions. In addition to algorithm advancements, the present thesis expands stride clustering methodology to identify and characterize intra-bout phases across different dual-task conditions and understand how these representations of stride variability are related to clinical gait outcomes. Results from this study highlight the need to examine the contribution of intra-bout phases to gait variability and emphasizes the opportunity to expand our analytical approaches to gait assessment in and outside the clinic for optimal rehabilitative and therapeutic interventions.

ACKNOWLEDGEMENTS

I am sincerely thankful for the guidance and kindness extended to me throughout this thesis. I would like to acknowledge Dr. Bill McIlroy and Dr. Karen Van Ooteghem, who I have worked closely with for the past years. They provided invaluable guidance and support throughout my journey and have truly cheered me on throughout my thesis. The two combined have helped me grow professionally and personally throughout this degree and I cannot express the amount of gratitude I have for this experience.

I am very fortunate to have worked for Dr. McIlroy both prior to my PhD and throughout this degree, his dedication to producing good science, attention to detail, and exceptional insight and mentorship have shaped the way I think and personally impacted me as a person. I am grateful for the opportunity to have worked under his guidance and learned from his expertise.

I would like to extend many thanks to my examining committee. To Dr. Kaylena Ehgoetz Martens for the thoughtful and enthusiastic conversations early in the thesis projects, your kind words and encouragement fostered motivation throughout. To Dr. Andrew Laing for volunteering to fill in as a committee member for the final defense and provide valuable feedback and meaningful comments in the final moments. To the examining committee, Drs. Julie Nantel and James Tung, for their tough but supportive feedback in the final review of this research.

I have been apart of the Kinesiology department at UW for some time and have had many positive experiences and met wonderful people along the way. I'd like to acknowledge all the course instructors, who had either taught me throughout my undergraduate degree and those who I taught beside throughout graduate studies, it has been a pleasure to work alongside you. To all the support staff, Lowell Williamson, Jeff Rice, Alicia Nadon, and retirees Denise Hay, Marg Burnett, and Craig McDonald, you are such a great team and make the department function.

To all the friends and lab mates that I have met along the way. I will be sure to reach out and thank you all in person, your support and friendship has met the world to me. It has been great to create these wonderful relationships over the years.

DEDICATION

This thesis is dedicated to my parents, their unwavering support and strong work ethic has provided direction for me in my life. I am very fortunate to have such great role models. To my wife Valerie, for her endless encouragement and support, your personal accomplishments have helped guide me along the way, I am forever grateful for you and our life together.

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Chapter 1

GENERAL OVERVIEW

1.1 Introduction

Clinical gait assessment provides insight into the risk of adverse events (e.g., falling) and overall health (Franklin et al., 2015; Middleton et al., 2016; Studenski, 2011). Gait assessment has commonly relied on gait speed as a key indicator for gait performance and is sensitive to change. Clinicians and researchers rely on this metric of performance as a key clinical indicator, likely due to its ease of collection. Despite its wide accepted use, it remains that gait speed alone is not specific for understanding the root cause or mechanism of change (Wren et al., 2020). There is evidence from current research, that further quantification of gait characteristics (e.g., spatiotemporal, kinematic, kinetic, or electromyography assessments of gait) provides a more refined and accurate assessment of gait for multiple benefits (e.g., tracking progression of impairment, rehabilitation interventions) (Zhou et al., 2022). In addition, outcomes from gait assessment are typically single summary metrics (e.g., mean gait speed, mean cycle time) from steady state walking that assume no fluctuations associated with gait initiation, walking speed acceleration, or termination (Lord et al., 2011). There are two concerns with this focus on steady state walking. First, is whether the bout of walking is truly steady state where mean values would properly reflect control. Second, excluding a focus on fluctuations in walking is a lost opportunity for understanding control of mobility given that walking outside of the confines of a clinical environment involves these intra-bout phases that are not steady-state (e.g., gait initiation, termination, turning). The identification and assessment of walking that includes these phases may improve our understanding of walking and gait variability as it naturally occurs, by identifying, describing, and detecting distinct outcomes from these periods.

Wearable sensors (e.g., accelerometers or inertial measurement units (IMUs)) have become a clinically useful tool for gait assessment due to their portable nature, affordability, and kinematic tracking

of limb movement. These tools are well suited to overcome expensive equipment that is burdened by space limitations and allow for an expanded assessment of human movement. Combined with proper analytics, these tools can capture biomechanically important events from impact (e.g., heel strike) or large momentum changes (e.g. toe-off) to identify key events within the gait cycle (Motti Ader et al., 2021). Beyond gait event identification, gait stability and regularity can be assessed using methods that infer stability of the whole body from accelerometry waveform and patterns (Riva et al., 2013). Ankle worn sensors prove to be a highly accurate wear location for gait event detection (Storm et al., 2016). In the past, gait assessment has expanded beyond steady-state walking to better identify gait acceleration using stride velocity and other temporal parameters. This work identifies an association between longer acceleration duration and more steps in the gait initiation phase and fall history (Lindemann et al., 2008). Such work advances gait assessment by identifying the unique intra-bout phases but relies on proper pose estimation and layered analytical assumptions (e.g. assuming zero limb movement phases in the gait cycle (Sabatini et al., 2005)) to interpret velocity and position-based measures. In other work, the identification of walking phases has relied on clustering like strides (i.e., stride clustering methods) improves association of gait and postural control outcomes in people living with PD and identifies unique gait assessment approaches to identify impairment modalities related to human walking and balance control (Nguyen et al., 2019).

Importantly, much of the current gait assessment research using wearable sensors has aimed to reduce sensor burden and replicate gait analysis (e.g., assumed steady state walking). Moreover, much of the development in this area supports healthy young adults and may not consider the gait changes in pathological cohorts. Purposeful sensor wear for optimal and accurate assessment of walking is needed in combination with tailored algorithm design for specific outcomes to advance this area of research. Less work has examined gait control leveraging the acceleration kinematics during walking and identify steady state, or acceleration phases, of walking quantitatively. This thesis advances analytics to improve and expand gait assessment via two main approaches: (1) to improve intra-stride gait cycle identification and

description using acceleration kinematics from lower limb accelerometers and (2) identify different intra-bout phases of walking using gait specific outcomes from clinical walking tasks in a cohort of older adults including those with neurodegenerative disease.

1.2 Relevance & Significance

As the age of the Canadian population increases the number of seniors will have an impact on health care systems (*Surveillance Report on Falls among Older Adults in Canada*, 2022). Falls account for 85% of the number of injury related hospitalizations and 95% of all hip fractures for seniors in Canada totaling two billion in direct healthcare costs. Evaluating a person's gait performance can inform aspects of health, for example, gait speed measures are related to mortality and adverse health outcomes (Studenski, 2011) and may be a valuable tool for screening cognitive impairment (Montero-Odasso, Verghese, et al., 2012). In early mobility decline, compensation techniques can mask disability and lead to unreported mobility decline (Mänty et al., 2007). Quantitative assessment of short walking bouts in clinic can help overcome the pitfalls of self-report and provide a quantitative approach to assess risk of falling and health. However, the assessment of clinical walking does not always reflect naturally occurring walking (Hillel et al., 2019). Current approaches limit assessment to the middle of a walking bout, assuming steady-state walking, and ignore the intra-bout phase (e.g., acceleration phases), which have been linked to mobility risk (Lindemann et al., 2008) and distinct mobility scales of gait and postural control (Nguyen et al., 2019). There is need for clinical gait assessments that include the ability to evaluate these distinct phases of walking within bouts of walking.

Falls and related injuries are a common and serious health related event in older adults 65+ years, with 20-30% of seniors experiencing at least one fall per year (*Surveillance Report on Falls among Older Adults in Canada*, 2022). This frequency of falling is expected to rise alongside the increase diagnoses of MCI and dementia, as these populations are more susceptible to falling (Shaw, 2007). In neurodegenerative disease populations, 60% of fall incidence occur during walking, expanding the need to further evaluate mobility and dynamic stability across straight ahead and transitional walking

(Deprey, 2009). Gait assessment is recommended within the “core-battery” and “minimum-battery” of tests to probe both mobility and cognition recommended by the Canadian Consortium of Neurodegeneration in Aging (Montero-Odasso et al., 2019). Methodological approaches are important to standardize but previous research might suggest that more flexible approaches and fulsome analysis highlight mobility sensitivities excluded from the current standardized protocol (Nguyen et al., 2019; Shaw, 2007). To optimize the utility of clinical visits, high-quality quantitative outcome measures with accessible tools (e.g., portable tools or wearable sensors) are key. It is important to continue advancing the methods in which we approach gait analysis to identify accessible and identifiable markers for individuals, cohorts, or longitudinal tracking of mobility to maintain the longevity of independent mobility and walking for improved and fulfilling quality of life.

1.3 Overview of Thesis Objectives

The overarching objective for this thesis is to advance the approaches of clinical gait assessment with valid and clinically feasible tools, with a specific focus on the use of lower limb accelerometry. This work will seek to achieve several key outcomes, it will aim to:

- (1) To improve intra-stride gait cycle identification and description using acceleration kinematics from lower limb accelerometers by:
 - a. Advancing segmentation techniques to further divide the gait cycle into unique intra-stride phases linked to biomechanically important events.
 - b. Evaluate the utility of acceleration kinematics recorded by triaxial accelerometers to characterize gait performance across different clinical tasks.
- (2) Identify different intra-bout phases of walking across task difficulty and understand the relationship using gait specific outcomes from clinical walking tasks in a cohort of older adults including those with neurogenerative disease by:
 - a. Examining stride-to-stride and intra-bout phase relationships across different walking tasks and continue to advance approaches to describe gait variability.

- b. Assessing the relationship between stride-to-stride, intra-stride and intra-bout variability during single- and dual-task walking with clinical measures of gait and mobility.

To work towards the overarching objectives, this thesis will conduct an analysis of data collected as part of the gait and balance platform (Montero-Odasso et al., 2017) of the Ontario Neurodegenerative Disease Research Initiative foundational longitudinal study (Farhan et al., 2017) over four separate studies.

Chapter 2

BACKGROUND LITERATURE RELEVANT TO THE THESIS

Walking is considered an important determinant of overall health and independence (Garcia-Pinillos et al., 2016). For example, walking speed is an indicator for mortality and is referred to as the ‘sixth vital sign’ (Fritz & Lusardi, 2009) or ‘the grim reaper walk’ (Franklin et al., 2015). Quantifying a person’s gait has been linked to other key health related outcomes like risk of falling (Modarresi et al., 2019), mobility decline (Mehdizadeh et al., 2021), and musculoskeletal impairments (Kubota et al., 2007).

Clinical assessments largely rely on visual gait observation completed by a trained clinician to quantify performance. This method is limited in its effectiveness due to low inter-rater reliability (Brunnekreef et al., 2005) and ceiling effects when using an interval scale (e.g., UPDRS gait analysis) (Eisinger et al., 2017; Kohat et al., 2021) and are less sensitive to change due to their subjective nature. Simple tools to measure gait speed (e.g., stopwatch) are often used to quantify gait performance and gait speed is suggested as a key indicator for clinical assessment by the CCNA (Cullen et al., 2018) and other groups (Mehmet et al., 2020), providing recommendations on the assessment setup (e.g., acceleration periods, distance, tools). Including high resolution instrumentation can provide a better understanding of the mechanism that causes changes by providing objective assessment (e.g., whole body optical motion capture, force plates, and electromyography) however, these tools are not considered clinically feasible because they are expensive, time-consuming, and require expert personnel. Wearable sensors, such as inertial measurement units and accelerometers, are a feasible option for quantifying gait performance in clinical environments because they are affordable, portable, and provide high fidelity kinematic tracking.

2.1 Current status of quantitative clinical gait assessments

Clinical gait assessments are used to evaluate quality of walking patterns (i.e., gait) and provide insight to adverse events and overall health (Adam et al., 2023; Duan-Porter et al., 2019; Shinkai et al., 2000; Studenski, 2011). As an example, outcomes such as walking speed and stride-to-stride variability have

been linked to predicting fall risk and other adverse events. It is suggested that gait assessments should occur in controlled settings with adequate lighting, absence of noise and distractions, and patients should wear comfortable and non-restrictive clothing (Kressig et al., 2006). In addition to controlled settings, gait measurement aims to assess steady state walking and several walkway parameters are suggested to identify steady state. ***Steady state walking*** is a period of walking that is absent of non-steady intra-bout phases (e.g., acceleration and deceleration) and should be a minimum of 4 meters (Mehmet et al., 2020). To isolate steady walking from other intra-bout phases, static distances at the beginning and ending of the walkway are used to define acceleration (i.e., gait initiation) and deceleration (i.e., gait termination) phases. Current recommendations suggest for static definitions to range from 1 meter (Beauchet et al., 2017; Cullen et al., 2018), 2 meters (Kressig et al., 2006), or 2.5 meters (Mehmet et al., 2020) and should account for 2 to 3 gait cycles in older adults (Kressig et al., 2006). When this period is properly isolated from a walking bout, gait assessment evaluates a person's locomotor control and outcomes can reflect the intrinsic integrity of the musculoskeletal, affective, and the neural control system.

In clinical assessments, gait speed remains the most commonly reported outcome measure. It is clinically feasible, sensitive to change, and requires minimal equipment or analytic resources (Wren et al., 2020). When reporting outcomes from clinical gait analysis average speeds over a set distance and number of strides are used to describe performance that are assumably uninfluenced by intra-bout phases (Macfarlane & Looney, 2008; Wang et al., 2012). Gait speed can be influenced by many factors, such as: starting procedure, distance, flooring textures, and timing methods (Stuck et al., 2020) and it is therefore important to consider the setup prior to interpreting gait speed performance, specifically when comparing across different studies. The influence of clinical walkway properties (i.e., length, including turns, starting conditions) have all significantly impacted gait speed outcomes with differences larger than minimally clinical importance (Barnett et al., 2016; Krumpal et al., 2021; Lindholm et al., 2018; Pasma et al., 2014; Stuck et al., 2020). Of consideration is the differences between disease cohorts and gait assessment tasks, where performance metrics might be different between disease cohort (e.g., Chronic Obstructive

Pulmonary Disease (COPD) vs. Mild Cognitive Impairment (MCI)) that is dependent on the evaluation of the task (e.g., long distance versus short distance walking) (Pasma et al., 2014). Those with lower cognitive performance were linked to slower 4-m walking speed while those with COPD was linked to slower six-minute walk performance and these differences may be related to specific general impairment (i.e., cognitive decline and balance control vs. respiratory health and endurance). Beyond straight walking, other mobility assessments (e.g., timed up and go (TUG), six-minute walk (6MW), etc.) may provide insight to stability and aspects of mobility. However, these tests still rely on speed outcomes and are susceptible to similar influences discussed with straight ahead clinical walking tasks or ceiling effects (Rolenz & Reneker, 2016). One example regarding setup occurs during circuit type gait assessments, when distances between turns are shorter the test reports increases in stride length, step width, and temporal variability measures during the straight portion of the assessment (Barnett et al., 2016). Although gait speed is the most reported outcome for most gait and mobility tests, evidence suggests speed is influenced by many extrinsic factors and speed alone is not specific for identifying underlying mechanisms that explain change to gait. The details of individual steps are needed for better understanding gait control. Equipping gait assessment with a clinically feasible tools allows for objective measure of gait quality and improves clinical evaluation and risk of adverse events (e.g., falls) (Jepsen et al., 2022).

Providing a fulsome assessment of walking may provide insight into different aspects of gait control (e.g., balance control, speed acceleration, interaction with cognitive tasks) that are related to mobility and provide targets for therapeutic interventions. Current assessment may include strides apart of acceleration and this may affect outcomes such as gait variability (Lindemann et al., 2008) and ignoring acceleration periods does not reflect how walking occurs naturally (Van Ancum et al., 2019). Therefore, providing an assessment of transitional phases may provide insight into transitional states of gait as they relate to speed and gait control and will quantify characteristics of these phases as well (Wade et al., 2022; Zukowski et al., 2024). This is important because more transitional movement occupies shorter

walking bouts and tend to record more fall incidence compared to steady walking (Deprey, 2009; Meurisse et al., 2019). Current methodological tools (i.e. stopwatches, pressure sensor mats) are limited in their approach or by space (only capture a few steps at a time) but inertial measurement units provide high accuracy for gait event detection to replicate conventional outcomes and provide a solution to quantifying intra-bout phases of walking and therefore, are favourable for advancing gait assessment in clinical environments.

2.2 Current applications of wearable sensors for clinical gait assessment

Foundational research using wearable sensors (e.g., inertial measurement units (IMUs), accelerometers) in gait analysis has improved the accessibility of quantitative gait assessment in the clinic. Much research aims to detect gait events for spatiotemporal gait assessment to describe stability and control. Spatiotemporal measures of gait (from high quality tools) have accurate and reliable applications for detecting impairments that occur due to age or disease (Hollman et al., 2007, 2011; Kobsar et al., 2014; Lord et al., 2011), track severity of ailments or risk (Bloem et al., 2016; Mc Ardle et al., 2019; Wittwer et al., 2008b), and effectiveness of interventions (Patterson et al., 2015). Many algorithms leverage the key events surrounding impact and large momentum changes between stance and swing based on these biomechanically important events. Clinical and other biophysical interpretations of the gait cycle rely on this parameterization.

Sensor wear locations influence the accuracy of gait event detection and algorithms do not seamlessly transfer across wear locations. Sensors worn on the upper (Zijlstra, 2004) and lower trunk (Zijlstra & Hof, 2003) identify gait events based off the impact at heel strike and integrate acceleration to estimate walking speed and step length (McCamley et al., 2012). Algorithms designed for low back sensor wear translate well for chest- and waist-worn sensors for young adults but cause accuracy issues for describing temporal and spatial outcomes in older adults (Del Din, Hickey, et al., 2016). When sensors cannot detect gait events, analytic approaches have been used to characterize movement throughout the whole walking bout (Ma et al., 2016; Mayagoitia et al., 2002; Patterson et al., 2015; Spulber et al., 2012)

using frequency domain measures, accelerometer derivatives (Brodie et al., 2014), and autocorrelation methods (Riva et al., 2013). As an example, the log ratio of mediolateral/vertical jerk (a measure to reflect the steadiness of walking) from head and pelvis acceleration was able to classify age cohorts with 89% accuracy. In addition, to assess gait stability and fall risk a subspace clustering method that examined the interaction of variables showed that higher velocity and higher harmonics were related to higher stability (Brodie et al., 2014). Although methods exist to move beyond gait segmentation, identifying individual phases is an important feature in gait analysis and remains crucial for assessing gait in aging and pathological groups.

Ankle-worn sensors have shown improved gait event detection during clinical and free-living walking (Storm et al., 2016; Trojaniello, Cereatti, Pelosin, et al., 2014a). Bilaterally worn sensors on the lower limbs also provide accurate assessment for slower and asymmetric walking (Patterson et al., 2008). Identifying these biomechanically important features improves understanding of energetics within the gait cycle during aging (Begg & Sparrow, 2006) and allows for multi-modal (e.g., kinematics and electromyography) assessments anchored in time and phase for neurological cohorts. Further segmentation, beyond stance-swing phases, can be beneficial to understanding gait control. As an example, when increasing gait speed by 0.1 m/s there is a corresponding reduction in stance phase by 0.1% and increase in swing phase by 0.3% during normal walking (Hebenstreit et al., 2015). In this example, stance phase was redistributed between mid- and terminal stance to allow for increased terminal stance time and more push-off generation. Currently, characterizing these sub-phases with IMUs is not common, as typical segmentation relies on quick acceleration changes during impact or momentum shifts during toe-off, however moving beyond this may improve gait assessment in the clinic.

Single sensor models have been used to identify gait events to calculate spatiotemporal gait outcomes (e.g., swing, stance phases); however, leveraging multiple sensors can improve the assessment of gait due to the abundance of kinematic detail. As an example, multiple sensors on the shoe allow for distinction between terminal stance, mid stance, and heel-off sub-phases of the gait cycle beyond simple

stance-swing segmentation (Mariani et al., 2013). Identifying and segmenting the sub-phases of a gait cycle provides detailed description of gait and may advance gait assessment in pathological cohorts (e.g., interpreting loading characteristics and drop foot during swing). There are benefits to segment gait beyond stance-swing phases and to adopt the Los Amigos nomenclature for the phases of a gait cycle using inertial measurement units (Figure 2-1) (Gronley, 1984).

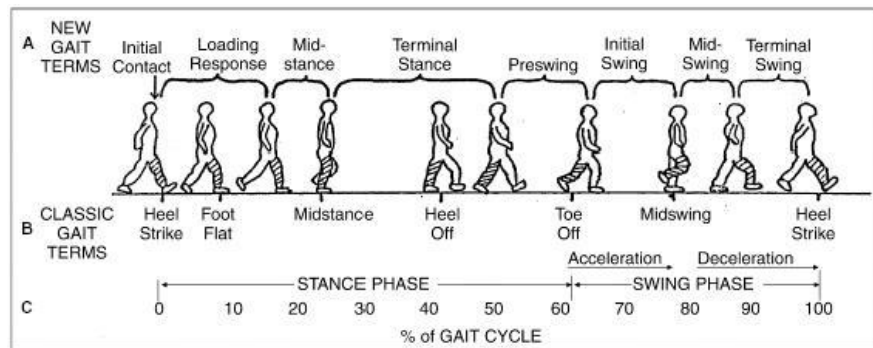


Figure 2-1. The phases of the gait cycle and segmentation terminology. In this depiction the leg with the stripes/shading is the leg that aligns with the labelled gait cycle phases [Image source: (Li et al., 2016)].

The location of ankle-worn accelerometers provides kinematic measurement of the lower limb through stance and swing phases that allow for analytics to assess limb movement throughout the whole gait cycle, compared to a pressure sensor mat which only allows stance phase assessment. Williamsen et al (1990) implemented a finite state machine (FSM) that leverages accelerometer inflection points to identify discrete moments akin to gait cycle sub-phases (e.g., push-off, swing-phase, heel strike, stance phase). This approach was successful at identifying the gait cycle with several rehabilitation applications, such as peroneal nerve stimulation to avoid foot-drop (Willemsen et al., 1990) and real-time prosthetics control machines during level ground walking (Shultz et al., 2014). Furthermore, these analyses of lower limb inertial data allow for discrete description of gait by outlining the sub-phases of the gait cycle that may be important indicators of impairments (e.g., terminal swing, loading phase, flat foot duration, heel-off). These methods can be expanded to identify different walking modes, including backward walking, stair climbing, and level ground walking in free-living environments (Kronenwett et al., 2017). Finite

state machines have the potential to expand their application to clinical assessment of the gait cycle sub-phases.

The gait cycle has a finite number of discrete sub-phases within its entirety and each phase follows its predecessor in a linear fashion. Finite state machines (FSM) are computational models that describe a process in a similar fashion, where the machine can be one of a finite number of different states and provide knowledge for advancing to the next state (Sweeney et al., 2000). Williamsen et al., (1990) designed a five state FSM model to detect gait cycle properties that included push-off, early swing, late swing, heel strike, and stance phase. Cycle identification relies on identifying push-off phases within this model, while other models rely on detecting stance phase to initiate the cycle time (Kronenwett et al., 2017; Seel, et al., 2014). Results from this Williamsen et al (1990) model design was promising, but errors occur for people with severe hemiparesis. Kotiadis et al., (2010) combined the vertical, anterior posterior accelerations, and the sagittal plane angular velocity to implement a three phase FSM model from shank worn IMUs for functional electrical stimulation (FES), four different algorithms were designed using a combination of these sensors and compared these algorithms to heel switch devices. Gyroscope and accelerometer data has been combined to design a FSM for step detection in healthy and stroke populations (Seel, et al., 2014). To improve step detection of walking speeds, this model adapted the acceptable amplitude and time ranges for flat-foot detection (i.e., the rest band widths), to reflect the changes of these parameters that are influenced by the walking speeds (Seel, et al., 2014). Building on these finite state models, individualized genetic fuzzy state models have been designed to characterize walking specific to someone's own gait pattern providing the possibility to extend the applications of classic FSMs (Alvarez-Alvarez et al., 2012). Identifying discrete sub-phases of gait has important applications in FES studies to overcome drop foot control problems (Kotiadis et al., 2010; Williamsen et al., 1990) and potentially many problems that are linked to a discrete timepoint in the gait cycle. Finite state machines provide many opportunities to advance segmentation methods in an iterative fashion and application to interpret clinical walking patterns has yet to be explored. Providing segmentation to gait

analysis beyond stance-swing timepoints could allow for an improved investigation to the control of walking particularly during transitional phases or in distinct loading and unloading phases on intra limb transitions.

Inertial measurement (and accelerometers) have been validated as gait assessment tools for typical and overground or treadmill walking (Khandelwal & Wickström, 2017; Pacini Panebianco et al., 2018; Trojaniello, Cereatti, & Della Croce, 2014). It is important to recognize that pathological cohorts with complex mobility impairments (e.g., people with neurodegenerative disease) and difficult walking conditions are two factors that influence kinematic characteristics. The same kinematic features that algorithms rely on to properly segment the gait cycle and describe gait outcomes related to stability or disease. These gait impairments need to be considered when introducing new analytic approaches.

2.3 The effect of aging and disease on clinical gait outcomes

Controlling for extrinsic factors that influence gait outcomes allows for gait assessment to reveal and assess intrinsic factors that affect gait control and assess risk. Gait assessment for older adults are important for identifying gait impairments, as they relate to balance control and risk of falling (Modarresi et al., 2019). Importantly, 20% of people aged 88 years or older do not present gait abnormalities (Bloem et al., 1992). The spatial and temporal parameters calculated during walking are indicators for control of the centre of mass and a person's ability to corral the centre of mass with preplanned foot placements or unexpected perturbations (Chong et al., 2009). Preplanned foot placement is typically planned four steps in the future during flat ground terrain compared to two step planning in more complex environments (Matthis et al., 2018), thus changes to dynamic stability likely reflect both feed-forward and feed-back control of the centre of mass during walking. Much research has characterized normative values for healthy human walking (Hollman et al., 2011; Lord et al., 2013) and identified statistical commonalities between performance variables to categorize into domains (e.g. pace, rhythm, variability, asymmetry, and postural control). These domains are a representation of gait control specific to steady state walking, however when additional elements of walking are included (e.g., turning) these domains begin to reflect

the demands of the task (Shah, McNamers, Mancini, Carlson-Kuhta, Nutt, et al., 2020). A person's strength, speed, and integrity of neural system are reflected in the stability of these outcomes (Snijders et al., 2007, Hausdorff & Alexander, 2005). Compensations and adaptations to impaired neuromuscular control can be demonstrated with reducing walking speed by taking shorter step lengths or lowering cadence with wider steps to increase size of base of support (Freire Junior et al., 2016). This often coincides with increase temporal and spatial variability revealing lower stability and regularity (Hausdorff, 2007). Understanding how changes to spatiotemporal measures of gait due to effect of task, balance, or environment and expanding on elements of walking (e.g., states of acceleration, dual task walking) to encompass walking in daily life is likely to improve intervention and care amongst at risk populations.

Aging is commonly associated with declining mobility and gait dysfunction revealed by increased spatiotemporal variability and declining balance control during walking. Walking requires optimal integration of the sensorimotor, cognitive, and musculoskeletal systems to create an adaptable and flexible motor program for successful and stable gait. Changes in strength, cognitive processes, or neuromuscular integrity are all processes that are associated with aging and contribute to gait impairments. Slower walking is a global measure and non-specific marker of impairment because it is reflected in cognitive (Dumurgier et al., 2016) and musculoskeletal (Demura et al., 2014) ailments and other comorbidities (Middleton et al., 2016). Gait speed in older adults aged 70-74 and ≥ 85 years old free of comorbidities reported normative gait speed of 1.17 m/s and 1.01 m/s respectively (Hollman et al., 2011) and younger age ranges reportedly walk faster (males >64 years: 1.41 m/s, females >64 years: 1.30 m/s) (Bohannon et al., 1996) older adults with average 69.5 years (1.26 m/s) (Lord et al., 2013)). Clinically important thresholds for gait speed fall between 0.8-1.0 m/s and walking speeds lower or within that range may have increased risk of falling and limited community ambulation (Middleton et al., 2016; Schmid et al., 2007). Although static thresholds for fall risk (based on gait speed) exist, Adam and colleagues (2023) report that a change in gait speed (over time) may be more indicative of risk. From a group of community

ambulatory older adults, 30% of older adults in this cohort reportedly walk faster than 1.0 m/s at baseline and still reported a fall over a 12-month period. However, those that decreased gait speed over time (change that was >0.1 m/s) had a 1.13 hazard ratio for falls and 1.44 hazard ratio for multiple falls irrespective of cognitive status. Gait speed changes reported here are consistent with minimal clinically important differences (MCID) of 0.1-0.2m/s (Bohannon & Glenney, 2014). Such changes in gait speed can serve as a risk indicator and change in health status but specific spatiotemporal measures provide more insight into mechanism of change (Wren et al., 2020).

Spatiotemporal measures provide more specificity for understanding the compensatory and adaptive strategies related to changes in gait speed (Fien et al., 2019). Previous research established changes to gait performance due to age such as lower gait speed, shortened step length, increased gait variability, increased step width, and reduced ground reaction forces (GRFs) (Freire Junior et al., 2016; Hollman et al., 2007; Modarresi et al., 2019; Winter, 1991). Variability in older adults is biologically meaningful beyond just noise in the locomotor system (Hausdorff, 2007) and reports of variability affected by changing gait speed are conflicting, whereas gait variability has been reportedly increased (Almarwani et al., 2016; Beauchet et al., 2009) or stayed the same with decreasing walking speed (Frenkel-Toledo et al., 2005). Between age groups, older adults show increased variability in all gait parameters during slow walking and in fast walking they are only more variable in step width (Almarwani et al., 2016). When older adults with no mobility impairments decrease their walking speed intentionally their measured step length, stride time, and swing time percentage variability measures are lower than age matched people with mobility impairments walking at preferred speeds (James et al., 2020). Brach et al. (2005) found no difference in gait speed, step length, stance time, or step time variability between those with and without fall history but did find that extreme values of step width variability (the lower or higher values) was better related to fall reporting. In community-ambulatory older adults, stance time variability is associated with incident of mobility decline after adjustments for gait speed are included (Brach et al., 2007). Identifiable differences may be due to age-related changes such as muscle strength and the

development of joint torques, myoelectric latencies, joint range of motion, and proprioception changes (Hausdorff & Alexander, 2005). Evidence suggests that decreases in leg strength and range of motion in older adults can contribute to increased variability during walking (Bogen et al., 2019; Kang & Dingwell, 2008) and in older adults increased report of physical activity (time spent walking) was associated with lower gait variability (Gamwell et al., 2022). These changes to gait variability in those with history of adverse events and age are present. Examining variability in those with diagnosed neurodegenerative disease provides insight into change to variability related to CNS integrity.

Gait assessments have been used to assess disease severity or prognosis by tracking change in gait parameters over time in those with the presence of cognitive impairment or other neurodegenerative disease (Cicarelli et al., 2022; Pieruccini-Faria et al., 2021). Slow gait has been reported as an early indicator of mild cognitive impairment, up to one decade prior to disease onset (Buracchio et al., 2010). The motor-cognitive risk (MCR) syndrome, a predementia syndrome, is defined by slowing of gait with subjective cognitive complaints in people free of dementia diagnosis and remain independent in activities of daily living (Mahlknecht et al., 2015; Verghese et al., 2013). In this syndrome slow gait was defined as one standard deviation below matched persons gait speed means, these values range from 0.81 m/s in men aged 70-74 years old to 0.58 m/s in women >85 years old. The difficulty is that complex heterogeneity within traditionally classified homogeneous cohorts is likely and limits the effectiveness of classifying status with minimal characterization. As such, slow gait is common among those with neurodegenerative disease though gait speed alone does not always differ between age matched cognitively intact controls (CNC) and those living with MCI under normal conditions (MacAulay et al., 2017). Gait speed is related to stride time variability during faster and slower walking speeds in older adults and people with Parkinson's Disease during treadmill walking tasks (Frenkel-Toledo et al., 2005). Knowing that changes to these variables occur over time warrants investigation to whether changes are detectable in a single session. This would allow for early detection of impairment and action. Although single-task walking might allow for early detection, the addition of secondary tasks might exacerbate symptoms related to gait

control, particularly for impairments affecting the central nervous system. In dual-tasking conditions, cognitive and motor performance compete for resources in the brain and performance in either one or both are reduced as a result.

2.4 The effect of secondary cognitive tasks on clinical gait outcomes

Including a secondary task to walking, such as an arithmetic or verbal fluency task, adds an additional challenge to the central nervous system. The secondary cognitive task utilizes cortical resources, (e.g., supplementary motor area (SMA)) that are recruited for both motor and cognitive tasks (Fritz et al., 2019). Dual task walking increases the demand on cortical regions which burdens the attentional and executive resources during walking (Young & Stanton, 2002), resulting in a slowing effect and increases in stride variability (Montero-Odasso, Muir, et al., 2012). Dual task walking is typically characterized by slowing gait speed and the percentage of slowing is referred to as Dual-task Cost (DTC) (Montero-Odasso, Verghese, et al., 2012). The relationship between motor and cognitive process is beyond dual task walking. Executive function and attentional indices are predictors of future fall risk in unadjusted and adjusted models (adjusted for age, gender, fall history, education, etc.) in community ambulatory older adults (Mirelman et al., 2012).

Several theories exist to explain the cognitive-motor interaction that occurs when there is need for integration of cortical areas and processes for complex movements such as walking. The motor cognitive interaction theories explain possible strategies the central nervous system adopts to manage these competing demands: (1) central bottleneck theory (motor and cognitive processing ‘bottleneck’ causing one process to be performed at a time (Ruthruff et al., 2009)), (2) 4-D multiple resource model (mental overload and multitasking (Wickens, 2008)), and (3) attentional resource theory (limited attentional resources that compete between cognitive and motor demands) (Young & Stanton, 2002)). Common across these theories is the need for the CNS to manage multiple demands by switching between tasks rapidly or reducing the allocated resources to each task simultaneously. During walking, each method compromises gait quality by causing slower walking speeds, shorter stride lengths, and increased stride

time variability (Goh et al., 2021; Hausdorff et al., 2008; Ma et al., 2022; Montero-Odasso, Verghese, et al., 2012). Differences in gait speed due to dual tasking does not only cause a decrease in average gait velocity but includes increased stride velocity variability (Figure 2-2). In this example, older adults walked slower and had higher stride velocity variability during both walking tasks compared to younger adults (Priest et al., 2008). Dual tasking in older and younger adults causes compensations to the motor task. Additional differences exist for those living with neurodegeneration and reduced cognitive resources.

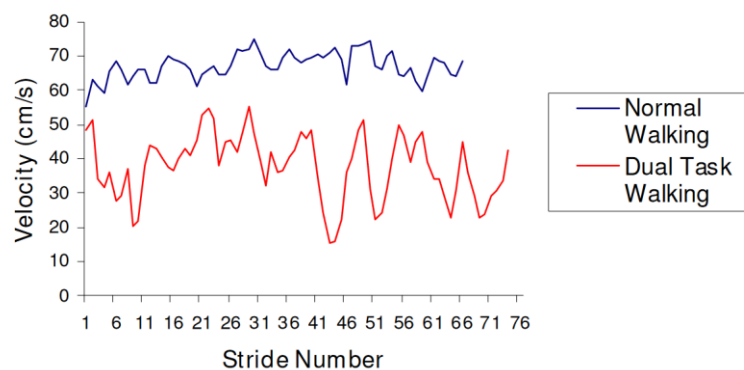


Figure 2-2. Example of stride velocity of an 87 year old participant. Mean velocity of the normal task is 0.67 m/s (5.9%CV) and dual task was 0.37 m/s (25.3%CV) [Image from (Priest et al., 2008)]

Gait slowing that occurs due to secondary tasks is common but substantial slowing (>20%) may be considered a marker of mild cognitive impairment (MCI) (Montero-Odasso, Muir, et al., 2012). Lower cognitive performance in older adults, compared to middle and younger aged adults, was negatively associated with gait speed and positively associated with stride velocity variability (Hollman et al., 2007). In those with MCI, slower walking speeds during dual tasking are predicted by executive function (e.g., working memory, attentional resources) over age, sex, education, or health status (MacAulay et al., 2017). Moderate to severe cognitive impairment are associated with lower mobility scores from several screening tools (Buchman et al., 2011). Mobility tools are clinically feasible but gait assessments provide accurate and replicable outcomes to support understanding mobility change in complex groups (Hill et al., 2021).

Cognitive and motor disease (e.g., neurodegenerative diseases) can be evaluated with gait assessment (e.g., decreased speed, increased gait variability) (Verghese et al., 2008). Gait speed differences exist broadly but interactions between stride time and stride time variability are important, as an example, those with MCI have larger stride time means and variability compared to cognitively intact across dual task difficulties (Belghali et al., 2017). Across the Alzheimer's disease progression (Control, Subjective CI, Mild CI, AD), stride to stride variability is significantly associated with Montreal Cognitive Assessment (MoCA) scores. In this population, double support time variability and stride time variability have been reported as the best predictor of disease diagnoses (Pieruccini-Faria et al., 2021). Dual task interference decreases regularity (increased stride to stride variability) and stability of walking in cognitively impaired persons. Changes to variability reflect increasing task difficulties too (Ramírez & Gutiérrez, 2021). In general, more difficult tasks increase the burden for older adults (Beauchet et al., 2005; Goh et al., 2021). To further disentangle the source of variability, research that aims to understand variability sources may provide insight into gait control and the effects of secondary tasks on these control features.

2.5 Effects of age, disease, and task on the phases of a single walking bout

A single walking bout requires three distinct phases, (1) gait initiation (the start of walking including the acceleration to preferred walking speed), (2) online control of stable and rhythmic walking, and (3) gait termination (slowing down and stopping walking). Static thresholds to define these phases are commonly used. Mehmet and colleagues (2019) reviewed fifty gait assessment papers (summarized in Table 2-1) that assessed gait over short distances (<15 meters) and concluded that 2.5 meters is needed for acceleration and deceleration at the beginning and end of the walking. Although this recommendation applies to many persons it may not account for all older adults with and without impairment and relying on some current guidelines for gait acceleration distances may cause non-steady state walking to be reflected in gait markers (Macfarlane & Looney, 2008). Further, these current approaches for gait assessment may not appropriately evaluate performance for all populations, particularly for those living with

neurodegenerative disease (NDD) (Shaw, 2007). As an example, without properly assessing gait initiation, gait impairments are lumped into description of gait control during steady state only and discount the impairment during initiation and termination phases.

Table 2-1: Summary of walkway parameters from Mehmet et al., (2019)

Walkway Parameter		Reported device/parameter value (n studies reporting that value)	Recommendations (where applicable)
Equipment		Stopwatch or other timing device (47) GAITRite (2) Unspecified (1)	Stopwatch
Distances	Total distance (m)	2.4 (3), 3 (8), 4 (14) 4.5 (2), 4.6 (3), 4.8 (3) 5 (4), 6 (8), over 6 10 (2), 11 (3), 15	9 meters total length 4 meters timed distance
	Acceleration Phase (m)	None/Standing start (8) 1 (1) 2 (2) 2.5 (1) 3 (2) Not reported (36)	2.5 meters
	Deceleration Phase (m)	None/Finish standing (4) 1 (1) 2 (2) 3 (1) Not reported (42)	2.5 meters
Walking Aids Permitted		Unspecified (38) Permitted (10) Not permitted (1) Not required (1)	Permitted
Number of trials		Twice, one distance (19) Twice, two distances (1) Single (2) Unspecified (28)	2
Gait speed reported		Maximum gait speed (9) Average (8) Unspecified (33)	Fastest

Expanding the analysis of walking to appropriately evaluate and quantify gait initiation periods may extend the important assessment of walking for a wider range of cohorts. Lindemann et al. (2008) quantified the distances needed to achieve steady state velocity using wearable sensors. This study examined a complex cohort (27% Stroke, 4% PD, and 7% rheumatoid arthritis as well as 49% aid users

and 58% with previous fall history) and found, on average, 1.43 meters is sufficient to achieve steady velocity but for 11% of the cohort larger acceleration periods (≥ 2.5 meters) were needed. Walking speed did not affect the acceleration distances, the slowest walkers (≤ 0.54 m/s) reached steady state velocity within 1.02 m and faster walkers (≥ 0.85 m/s) in 1.63 m (Lindemann et al., 2008). Under normal walking conditions similar distances for young adults (1.72 m) and older adults (2.17 m) were reported by (Macfarlane & Looney, 2008). During fast walking these authors reported decreases in acceleration distance for young adults (1.22 m) and increases for older adults (3.23 m). It is important to know the characteristics of these intra-bout phases because much of walking in daily life occurs in short walking bouts and may be influenced by these distances (Orendurff, 2008). Research focussed on these distinct phases is well established in isolation and less research exists to examine how intra-bout phases distribute within a walking bout and contribute to stride-to-stride variability (Lindemann et al., 2008; Muir et al., 2014; Park et al., 2009).

Gait initiation is considered the transient phase between standing and walking (Miller & Verstraete, 1999). In young adults, there are few differences between the first step and steady state walking for several biomechanical outcomes (e.g., spatiotemporal, COP movements, joint angles, and EMG). For these young adults there is a steady increase of walking speed, stride time, and stride length into the second step (Park et al., 2009). When comparing steady-state and gait initiation muscle activity, activation is lower during single-task compared to dual-task activation (Waldon et al., 2023). Across age groups differences in initiation phase depends on gait speed. For younger and older adults (young: 20-25, old: 65-79) gait velocity did not increase after the third step but in the oldest group (80-91 years old) gait speed continues to increase (Muir et al., 2014). Between the young and older cohorts, although both increased speeds, the younger group walked faster than the older group throughout the gait initiation phase. Significant differences in the first step across measures of step variability, step length, and step width also existed between the age cohorts (Muir et al., 2014). Across all groups, step lengths increased throughout initiation steps and the first step was typically wider than subsequent steps. Younger adults

had less variability in the first step width compared to older adults and less step length variability for the second to fourth steps. These unique differences in step length and width, as well as the variability associated with each, might provide unique insight into the AP and ML control of COM during walking, particularly during impaired walking behaviours (Muir et al., 2014). Moreover, identifying these changes may allow for classification of gait acceleration within or between groups and within a single walking bout.

Gait initiation is also impacted by pathology and cognitive dual tasking. During gait initiation, stride lengths are lower and variability is higher in older adults that have a history of falling (Mbourou et al., 2003) and those living with Alzheimer's Disease (Wittwer et al., 2008b) or Parkinson's Disease (Roemmich et al., 2012). Gait initiation in those with a history of falling (e.g., stability concerns) have longer initial double support times compared to non-fallers and young adults (Mbourou et al., 2003). In addition, older adults who exhibit fear of falling have shorter first steps and greater postural sway during the initiation steps (Ellmers et al., 2020). Gait initiation time is also longer in people who are at risk for single and multiple fall events. Increases in gait initiation time are sometimes driven by longer first lateral movement of the center of mass during single task walking and longer swing time during dual tasking (Callisaya et al., 2017). Links to fall risk during gait initiation are also reflected in pathological groups. People with Alzheimer's disease exhibit increased variability of the second stride time and first double support time compared to cognitively intact controls during gait initiation (Wittwer et al., 2008b). During gait initiation, people with Parkinson's disease exhibit shorter steps with increased variability in spatial and temporal outcomes compared to older adults without PD (Roemmich et al., 2012). Although these differences are present in steady walking too, differences in gait initiation steps may be linked to the original position of the COM during stance, more lateral and posterior COM position was directly related to the initial step characteristics in PD with freezing of gait (Bayot et al., 2021), or control of COM in the antero-posterior direction during initial unloading (movement from double support to single support stance) (Palmisano et al., 2022). Shorter steps allow for more controlled COM movement during gait

initiation, this is also seen in people with Parkinson's Disease when evaluating COM-COP relationship after the first step (Hass et al., 2005). The addition of cognitive tasks adds additional strain to gait initiation. In an assessment of anticipatory postural adjustments (APAs) under single- and dual-tasks, the dual-task effect causes significant longer gait initiation in older adults who have fallen compared to non-fallers but no difference under single-task conditions (Uemura et al., 2012). Further, people with MCI have a increase in step length and width variability during gait initiation compared to cognitively intact controls and the difference between groups increases under dual task conditions (Boripuntakul et al., 2014). These increases in width or changes in variability are explained as compensations to support increasing gait speed with adequate stability. Understanding that pathology, history of falls, and dual tasking influences the beginning of a walking bout, there is need to quantify and assess these phases, in addition to steady walking, to capture all aspects of gait and mobility during walking.

The end of gait initiation coincides with the beginning of steady state walking, typically defined using stride-to-stride velocities within an acceptable variability band. While velocity seems to be a standard approach to define steady walking it is not clear if other biomechanical parameters may serve to define steady state walking. For example, in early work centre of gravity (COG) velocity was not different at the end of the first step when compared to the second step (Breniere & Do, 1986), claiming that steady state velocity is achieved after a single step. From an energetics perspective, on the basis of work done by Winter et al., (1976), steady state walking involves minimal fluctuations in net mechanical work and defining steady state with these parameters found gait initiation to end after three steps (Miller & Verstraete, 1996, 1999). Gait initiation distance (or step number) of this length are similar when defined using kinematic assessment of joint angular velocity (Mann et al., 1979). This may not be of concern for young healthy adults under easy task conditions, but little research examines these differences in difficult dual task walking or in NDD cohorts. Recommendations for quantifying steady state walking defined with several variables, like "centre of mass speed after second toe-off" (Halliday et al., 1998) or whole body momentum (Miller & Verstraete, 1999) and with different rules and parameters, like "when

step velocity does not fluctuate outside of a ± 3 SD range” (Lindemann et al., 2008). It is clear that static definitions vary (Table 2-2) and overlook potential mobility decline indicators when definitions presume that all walking after the criteria is met belongs to steady walking.

Table 2-2: Summary of different biomechanical parameters and the definition of steady state walking.

Paper	Parameter	Definition	Distance/Step Number
<u>Lindemann et al., (2008)</u>	Stride velocity	Stride velocity SD of six strides falls below the median SD of stride velocity over 20 strides/walking bout.	Varies with age, 2.47 meters for 89% of population
<u>Miller & Verstraete, (1996)</u>	Total body energy	When the total body energy was within a 95% confidence interval of total body energy during steady state walking.	3 strides
<u>Mann et al., (1979)</u>	Walking speed and joint angles	Speed comparison to normal walking	~3 steps
<u>Breniere & Do, (1986)</u>	Peak centre of gravity velocity	Comparison of peak centre of gravity during normal walking and reported values	1 step
<u>Macfarlane & Looney, (2008)</u>	Step length CV	When step length CV of three consecutive steps was <0.07	Young adults: <i>Preferred</i> =1.72 m; <i>Fast</i> =1.22 m Older adults: <i>Preferred</i> =2.17 m <i>Fast</i> =3.23 m

One method to quantify steady state walking examines the ‘likeness’ between strides to create clusters that represent similar intra-bout phases. Using static thresholds to group strides (e.g., standard deviation) similar strides were binned into unique stride clusters (e.g., constant, non-constant, turning) together to identify the different phases of walking (Nguyen et al., 2019). Assessing spatiotemporal outcomes from stride clusters presents unique outcomes to visual gait and postural control assessment (e.g., UPDRS gait and postural stability scores). This study restricted their assessment to a specific window length, such that non-constant strides (representing gait initiation) needed to fall within 25% of total walkway length and when constant stride bins were achieved, they remained in a constant bin until the last 25% of the walking bout. Putting restrictions on steady state definition may mis-represent how

stride clusters distribute across the walking bout when variability increases (e.g., fallers, those living with mobility impairment). In cases with large variability, fluctuations above and below static thresholds might occur during normal or complex walking tasks. There exists a unique opportunity to advance the assessment of gait using bilateral ankle-worn accelerometers by quantifying different phases of walking beyond steady state control. Improved methods would quantify the gradual variations in stride-to-stride gait speeds or temporal characteristics and identify these fluctuations as steady or unsteady gait rhythms. Although other tools might improve these descriptions of gait speed control, like radar (Morita et al., 2020), analytic approaches from wearable sensor data allow for spatiotemporal and biomechanical description of gait patterns.

2.5 Summary

Gait analysis is an effective tool to identify fall risk and track mobility impairments. Gait assessments are positioned to provide valuable information about a person's mobility, fall risk, and inform disease severities, such as neurodegenerative diseases. Many studies emphasize the utility of gait speed to summarize performance, but evidence suggests that more specificity can be revealed with spatiotemporal, kinematic, and kinetic analytic approaches. To further entangle the problem, commonly reported gait parameters are often reported as summary measures during small portions of the test. Part of the control of walking emphasizes the importance of speed control, which is compromised under dual task walking (cognitive demands) and in pathological cohorts. There is room for improvement to the method in which gait performance is described to better identify moment-to-moment changes. Wearable sensors that allow for the kinematic description of limb movement can be more descriptive with fit-for-purpose sensors and purposeful analytic approaches. Moreover, a more complete assessment of all the strides within all intra-bout phases can help assess the composition and uniqueness of the phases of walking. Advancements in these approaches to gait assessment may help identify changes to gait control across tasks and provide novel insight into markers of mobility.

2.6 Thesis Objectives

Clinical gait assessment commonly reports average gait speed for a single bout. Wearable technology provides an opportunity to overcome accessibility barriers (including cost) but also provide a unique ability to permit measurement unconstrained by ‘space’ allowing capture across a wider range of walking behaviour (i.e., free-living, or different phases within a single bout) in an economical manner.

Advancements in the use of wearable technology can allow for precise capture of human kinematics in a variety of settings and task conditions. Advancements would expand and refine standardized analytical approaches and identify important kinematic outcomes that are validated across different clinical cohorts. This thesis aims to advance methodological and analytic approaches for clinical gait assessment in preferred and dual task walking conditions using body worn triaxial accelerometers. Important to this thesis is the development of methods across neurodegenerative disease cohorts to capture variability. This thesis aims to expand stride detection using ankle worn accelerometry and parse individual strides into intra-stride phases (study 1) using a finite state machine algorithm. In addition to expanding detection methods, both conventional temporal and unique accelerometry derived gait outcomes will be identified and examined across a range of walking conditions with secondary cognitive tasks (study 2) to advance the methodological approach to gait assessment, this thesis will uniquely focus on outcomes related to identifying discrete phases of a walking bout (i.e., intra-bout phases) and the regularity of strides across task difficulty for understanding control of walking in those with neurodegenerative diseases (study 3). Finally, this work will explore these novel gait metrics cross-sectionally in individuals with NDD to understand how they relate to or dissociate from commonly used gait-specific clinical markers and commonly reported clinical evaluations. The primary research questions for each of the four studies comprising this thesis are described below:

1. Is a finite state machine algorithm, that relies on unilateral acceleration, an acceptable approach to detect strides during clinical walking tasks and does task difficulty (e.g., secondary cognitive

tasks) or walking speed affect the ability for an FSM algorithm to detect strides in short walking bouts?

2. Does the finite state machine identify the strides and intra-stride phases (e.g., swing phase) to appropriately describe temporal characteristics of walking when compared to a pressure sensor mat (i.e., GAITRite®)? Secondly, do conventionally reported temporal outcomes and accelerometry-derived outcomes change under difficult dual task walking conditions?
3. Can discrete phases of a walking bout (e.g. initiation phase) be identified using stride clustering approaches in short clinical gait tasks? Are descriptors of stride clustering outcomes different under difficult dual task walking conditions?
4. Are there relationships between conventionally reported outcomes, intra-bout phases, and gait-specific clinical descriptors of mobility (e.g., UPDRS gait score)? Are there differences between gait-specific outcomes when groups are stratified by clinically important thresholds (e.g., gait speed threshold, dual-task cost)?

Chapter 3

GENERAL THESIS METHODS

This thesis utilizes data collected and analyzed as part of the Ontario Neurodegenerative Disease Research Initiative (ONDRI) (Farhan et al., 2017). This multidisciplinary province-wide research study approached examining NDD from several different data platforms collected annually over four years (Figure 3-1, 3-2). To note, studies 2, 3, and 4 use data collected from the same sensor models and protocol for all cohorts and sites; while, Study 1 was part of an initial feasibility study in continuous monitoring that includes clinical walking tasks that uses different wearable sensors. Study 1 methods are described in section 4.2 Materials and Methods.

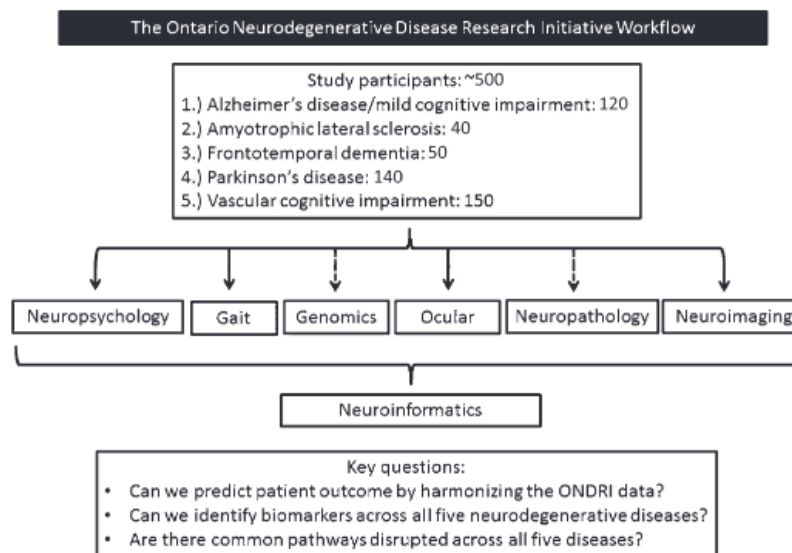


Figure 3-1. ONDRI participant and platforms workflow, from Montero-Odasso et al., (2017)



Figure 3-2. Timeline of visits within the ONDRI Longitudinal Study

3.1 Study Design

Studies 2, 3 and 4 are cross-sectional analyses of baseline data from a longitudinal observational cohort study called the Ontario Neurodegenerative Disease Research Initiative (ONDRI) (Farhan et al., 2017). These studies examine timeseries accelerometry data collected as part of the Gait and Balance data platform collected within ONDRI (Montero-Odasso et al., 2017).

3.2 Participants

In the ONDRI study, 520 participants were enrolled from five different NDD cohorts (Alzheimer's Disease & Mild Cognitive Impairment (ADMCI) (n=126), Amyloid Lateral Sclerosis (ALS) (n=40), Frontotemporal Dementia (FTD) (n=53), Parkinson's Disease (PD) (n=140), and Cerebrovascular disease (CbVD) (+/- cognitive impairment) (n=161)) between July 2014 and March 2017. Data collection took place in 13 different hospital sites across Ontario. General inclusion and exclusion criteria are outlined in Farhan et al., (2017) for the ONDRI wide enrollment. Further description of recruitment, enrollment, and withdrawal was published elsewhere by colleagues (Sunderland et al., 2023). Specific to the gait and balance data collection participants needed to be able to stand or walk independently, with or without a gait aid (Montero-Odasso et al., 2017).

3.3 Ethical Considerations

The ONDRI study protocol was approved by all participating institutions' Human Research Ethics Committees (Farhan et al., 2017). All participants provided written informed consent and for instances when the person living with disease was unable, their "substitute decision-maker" provided consent on their behalf.

3.4 Data Collection

Data collection for the gait and balance platform (GABL) within ONDRI was approximately one hour long and was part of a seven-hour clinical visit at the participant's respective research site. Within the

GABL platform, data collection was managed with a paper collection recording form (CRF). The CRF was used to gather anthropometric and mobility questionnaire data. A LabVIEW program was developed to manage collection of balance and accelerometer data. Site specific tablets (Samsung, Suwon-si, South Korea) were used to run the custom LabVIEW software with the collection program and used to organize data offload and save data locally before transfer and upload to a secure and central data server (www.braincode.ca).

3.4.1 Gait and Balance Platform Overview

Anthropometrics

Upon arrival participants provided their age and biological sex and basic anthropometric data, height (cm), weight (kg), leg length (cm), and calf circumference (cm) were recorded. Leg length was measured from the anterior superior iliac spine (ASIS) to the medial malleolus (Kirtley, 2006) and maximal calf circumference was recorded with the patient supine with knees raised at right angles to the thigh (Rolland et al., 2003).

Instrumentation

Triaxial accelerometers

Participants were instrumented with three X-16 triaxial accelerometers (Gulf Coast Data Concepts, Mississippi, USA) (Figure 3-3). Data was logged onto the sensor onboard storage. Sensors were worn bilaterally on the distal shank slightly above each of the lateral malleoli and one sensor on the right hip (Figure 3-4). The ankle accelerometers were fixed using a strap and the hip accelerometer was stuck to a safety belt with a hook and loop patch. Triaxial accelerometers were sampled at the hardware specified sample frequency and data logged to onboard storage, these specific accelerometers output a variable sample rate that is approximately 100 Hz.

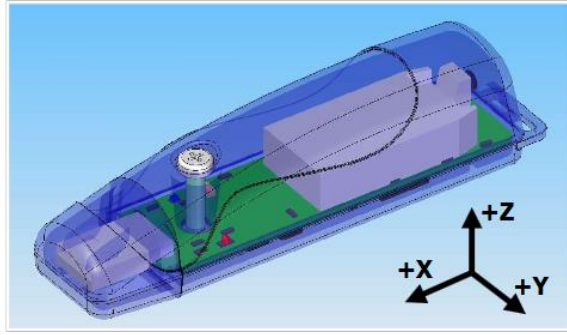


Figure 3-3. X-16 Triaxial Accelerometer (Gulf Coast Data Concepts, LLC, Waveland MS, USA) [Image from X-16 Accelerometer Manual]

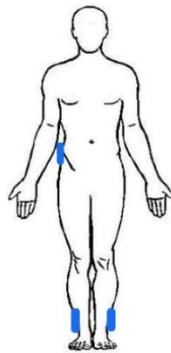


Figure 3-4. Placement of accelerometers on body. Blue tabs represent placement of the accelerometers located proximal to the left and right ankle and one secured to a safety belt worn by the participant.

Prior to the participant arrival, accelerometers were turned on and set at rest for ~20 seconds. After a rest period research coordinators slid the accelerometers on a flat surface six to 12 inches back and forth, approximately five to ten times. This movement allowed the accelerometers to be synchronized during preprocessing steps using a cross-correlation method. When data collection was finished, accelerometers were plugged into the Samsung tablet (via USB port) where data was merged into a single file and offloaded to the tablet.

Pressure Sensor Mats

At three research sites, Sunnybrook Health Sciences Center (SBH) and the London Health Science Centre (LHS) a GAITRite® (CIR Systems Inc., Franklin, NJ, USA) pressure sensor mat was used in addition to accelerometers for the gait assessment. GAITRite mats were setup in accordance with proper use described by the company using the GAITRite software and manuals. Pressure sensor mats have been the main collection tool for many gait analysis studies for many different neurodegenerative diseases and the reference system for IMU validation (Trojaniello, Cereatti, Pelosin, et al., 2014a).

Stopwatch/Manual Timer

Within the data collection program, a manual stopwatch was used for timing the walking trials. Time was output into an index file and was available for calculating walking speed (velocity = distance walking (m)/time (s)). This manual gait speed calculation was used in place of GAITRite or accelerometer data when it was invalid/corrupt (i.e., error coded, missing, etc.). Some examples of invalid or corrupt data are accelerometer synchronization error or GAITRite processing error.

Gait Protocol

Gait assessments occurred over a 6-meter walkway, each walkway included a 1-meter buffer at the beginning and end of the walkway to account for gait acceleration and deceleration (total walkway was 8 meters). Tape was used to mark the walkway at 0-, 1-, 7-, and 8-meter distances to mark the start, start timing, stop timing, and end of the walkway respectively (Figure 3-5). When pressure sensor mats were used, the mat was placed in the middle of the 1- and 7-meter markers. Manual stopwatch time was collected when the person crossed the 1-meter line and finished when the person crossed the 7-meter line.

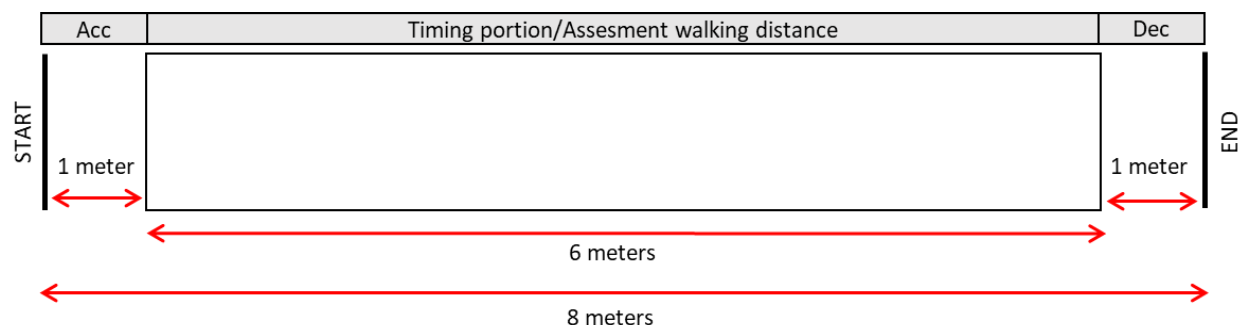


Figure 3-5. Figure outlining the Gait assessment protocol and collection distances. *Acc-* refers to the acceleration period/distance; *Dec-* is the deceleration period.

Gait assessments used five different walking conditions to evaluate gait performance. Participants completed three preferred walking trials, three different dual task walking trials (with varying difficulty), and a fast pace walking trial during the ONDRI Foundation Study. The order of trials was not randomized and the fast walking trials were not used Study 2, 3, or 4 of this thesis. Dual task walking trials increased in difficulty, starting with counting backwards by ones (DT-S1), followed by a verbal fluency task (naming animals; DT-An) and counting serial 7s (backwards by 7; DT-S7) to attempt to put these tasks in order of difficulty. These tasks are used and recommended by the Canadian Consortium on Neurodegeneration in Aging (Cullen et al., 2018). All trials are completed at a self-selected pace for each trial. If intentional slow or fast walking is included the difficulty increases in both cognitive and motor tasks (Patel et al., 2014). During dual task walking, participants were instructed to complete both tasks simultaneously not prioritizing one task over the other to best represent what happens in natural life (Verghese et al., 2007). To describe each condition, site coordinators followed a script during evaluation (Table 3-1). Participants were allowed to repeat trials if a technical issue occurred (e.g., an accelerometer were to fall off). If participants were unable to create verbal responses the coordinators were instructed to prompt the participant to continue with the task but not provide any response for the participant. If the tasks were too difficult, participants had right to refusal and data was not collected. After the gait trials,

participants were finished with the gait and balance platform collection, accelerometers were removed and ready for data offload.

Table 3-1: Walking task instruction scripts for ONDRI Gait task description.

Walking Condition	Task Instruction
Preferred walking	In this task, we are interested in measuring your normal walking pattern. When I say, “go”, please walk to the [INDICATE MARKER].
Dual task walking (same instructions with different tasks)	This time, I am going to ask you to walk to the [TESTER WILL INDICATE MARKER], but I am going to make it a bit more difficult by asking you to count backwards from 100 by 1’s, out loud as you’re walking. Try to maintain your normal, comfortable walking pace while you are doing the calculations. When I say, “go”, please walk to the [TESTER WILL INDICATE MARKER]. Remember that it is important that you do not stop your walking or counting”.
Fast pace	Finally, I am going to ask you to walk to the [TESTER WILL INDICATE MARKER] at a pace that is a little faster than your usual pace. Please go at a pace you feel comfortable at. No running please. “When I say, “go”, please walk to the [TESTER WILL INDICATE MARKER].

Data Analysis

Accelerometer Pre-processing & Analysis

Using a custom LabVIEW program, all accelerometer data underwent a common preprocessing pipeline.

Data were imported into LabVIEW and visually checked for data content (i.e., the accelerometers returned collected data versus zero), data were linearly interpolated to a 40 Hz sample rate. Data were synchronized by manually windowing/selecting the section of acceleration data (typically at the beginning of the time series data) and applying a cross-correlation function to output a time delay for each axis.

Timeseries data was referenced to the right ankle data and offsets were added to each of the accelerometers to temporally align accelerometer timeseries data. If the synchronizing method was unsuccessful data was discarded. To locate the walking tasks an interactive graph of all the accelerometer data with an event marker was used to section the beginning and the ending of all the walking trials and a file was saved that includes all the walks. A similar program with event markers was then used to identify the individual walking bouts within the whole gait assessment. Event markers plotted with the vertical

accelerometer (aligned with the longitudinal axis of the lower limb) and a sliding window was adjusted to identify the beginning and ending of each walking trial.

GAITRite Processing and Outcomes

As part of the ONDRI data collection, GAITRite data was processed following instructions outlined by software instructions. GAITRite outcomes were accessible in output files as summary measures or as step-to-step spatiotemporal measures.

Outlier Detection & Data Confirmation

As part of ONDRI project all data underwent multivariate outlier detection processes to identify outliers. Outliers were examined and a determination was made whether they were problematic for data quality (i.e., not representing their true outcomes) prior to data release. Detailed explanation of this is described in a previous publication (Sunderland et al., 2019).

Chapter 4

EVALUATION OF A FINITE STATE MACHINE ALGORITHM TO MEASURE STEPPING USING ANKLE WORN ACCELEROMETERS: PERFORMANCE ACROSS A RANGE OF GAIT SPEEDS, TASKS, AND INDIVIDUAL WALKING ABILITY.

This chapter has been **accepted** to the journal Medical Engineering and Physics.

Citation:

Cornish, BF., Van Ooteghem K., Wong, M., Weber, KS., Pieruccini-Faria F., Montero-Odasso, M., McIlroy, WE. (2024). Evaluation of a finite state machine algorithm to measure stepping with ankle accelerometry: performance across a range of gait speeds, tasks, and individual walking ability. *Medical Engineering and Physics*. Advance online publication. <https://doi.org/10.1016/j.medengphy.2024.104251>.

Highlights (3-5 bullet points):

- Wearable sensors increasingly used to assess gait in clinic and community settings.
- Detection algorithms need high accuracy across range of abilities and conditions.
- Finite state machines have advantages over threshold-based step detection methods.
- FSM method reports high stride detection accuracy for speed and dual task conditions.
- Potential advantages for expanding to free-living are favourable for FSM methods.

Abstract:

Wearable sensors, including accelerometers, are a widely accepted tool to assess gait in clinical and free-living environments. Methods to identify phases and subphases of the gait cycle are necessary for comprehensive assessment of pathological gait. The current study evaluated the accuracy of a finite state machine (FSM) algorithm to detect strides by identifying gait cycle subphases from ankle-worn accelerometry. Algorithm performance was challenged across a range of speeds (0.4-2.6 m/s), task conditions (e.g., single- and dual-task walking), and individual characteristics. Specifically, the study included a range of treadmill speeds in young adults and overground walking conditions in older adults with neurological disease. Manually counted and algorithm-derived stride detection from acceleration data were evaluated using error analysis and Bland-Altman plots for visualization. Overall, the algorithm successfully detected strides (>96% accuracy) across gait speed ranges and tasks, for young and older adults. The accuracy of an FSM algorithm combined with ankle-worn accelerometers, provides an analytical approach with affordable and portable tools that permits comprehensive assessment of gait unbounded by setting and proves to perform well in walking tasks characterized by variable walking. These algorithm capabilities and advancements are critical for identifying phase dependent gait impairments in clinical and free-living assessment.

Keywords (maximum 6):

Gait, Accelerometer, Wearable sensors, Finite state machine, Gait analysis, Signal processing

Abbreviations

Abbreviated word	Abbreviated Term
Activity of Daily Living	ADL
Wearable Technologies	Wearables
Neurodegenerative disease	NDD
Ontario Neurodegenerative Disease Research Initiative	ONDRI
Alzheimer's disease/mild cognitive impairment	ADMCi
Parkinson's disease	PD
Frontotemporal lobar degeneration	FTD
Cerebrovascular disease	CVD
Amyotrophic lateral sclerosis	ALS
Preferred treadmill speed	100PREF
60% Preferred treadmill speed	60PREF
80% Preferred treadmill speed	80PREF
120% Preferred treadmill speed	120PREF
140% Preferred treadmill speed	140PREF
Preferred overground walking average	PAVG
Dual-task Serial 1s	DT-1s
Dual-task Animal Fluency	DT-An
Dual-task Serial 7s	DT-7s
Fast overground walking	FAST
European Data Format	EDF
Analysis of Variance	ANOVA
Mean error	<i>me</i>
Limits of Agreement	LOA
Maximum resting period (2 and 6 seconds)	MRP2, MRP6
Dual-task walking	DTW

4.1 Introduction

Walking is critical for maintaining independence and quality of life, yet it is vulnerable to impairment as people age or experience declines in health. Questionnaires that probe independence, disability, or activities of daily living (ADLs) broadly address walking (Andersen et al., 2004) but these tools are subjective and results provide limited understanding of an individual's walking ability (Grau-Pellicer et al., 2019). Wearable sensors allow for detailed and objective gait assessment, including spatiotemporal characteristics of walking, that provide insight into gait quality (e.g., stride variability) and subsequent impairments. Importantly, such outcomes have been linked to overall health (Middleton et al., 2016), physical and cognitive impairment (Montero-Odasso, Muir, et al., 2012), and risk for negative health outcomes such as falls or hospitalization (Montero-Odasso et al., 2005). To maximize the utility of wearables for gait assessment, there is need for an approach that can easily capture and evaluate gait cycle characteristics despite task, age, or impairment. This study describes the development and evaluation of an algorithm intended for extracting detailed information about the phases (e.g., swing/stance) and sub-phases (e.g., midstance, terminal stance, pre-swing) of the gait cycle based on inputs from a single accelerometer mounted on the lower limb.

Decisions surrounding methods for using wearables to assess walking require careful consideration, including wear location, sensor configurations, and analytics which consider the context of assessment and the desired outputs (Del Din, Hickey, et al., 2016; Hickey et al., 2017). Further, to maximize utility, efforts should be made to establish methods that extend beyond the clinic to free-living environments with ease. Detecting walking with wearables has been validated at many wear locations but accuracy and precision have been shown to vary (Del Din, Hickey, et al., 2016; Dijkstra et al., 2008; Fortune, Lugade, Morrow, et al., 2014; Hickey et al., 2017; Orendurff, 2008). For example, a wrist-worn device can measure free-living walking however step detection accuracy can be low, particularly during slower walking with limited arm swing (Rhudy & Mahoney, 2018; Tudor-Locke et al., 2015) and data

captured from this location provides limited insight into step-to-step details. Lower limb inertial sensors at the ankle, shank, and foot provide the highest accuracy for gait detection given the proximity to heel impact and the amplitude of end-point motion during the swing phase, clearly revealing locomotor rhythm with and without gait impairments (Pacini Panebianco et al., 2018). Specifically, inertial measurement units (IMUs) worn on the shank proximal to the ankle have been shown to improve footfall detection compared to other wear locations (Storm et al., 2016). Further, when worn bilaterally, ankle- or shank-mounted devices can accurately characterize interlimb coordination (e.g., stride variability, symmetry) (Trojaniello, Cereatti, Pelosin, et al., 2014b) and with appropriate analytics, provide the opportunity to further characterize details of phases (e.g., stance/swing) and subphases (e.g., terminal stance, pre-swing, etc.) of the gait cycle. As a result, ankle-worn triaxial accelerometers can be considered optimal for gait assessment in a variety of settings. To expand the analytic approaches for the diverse needs and setups required for extended gait monitoring, algorithm development should accommodate single or bilateral wear. Algorithms of this nature may use heuristic approaches that leverage signal properties from known limb dynamics at that wear location for informative gait assessment. This is opposed to peak-detection and threshold-based algorithms that may not extend beyond steady state walking and decrease in accuracy during aging or impaired gait and free-living walking. Gait detection algorithms typically aim to identify distinct phases of the gait cycle (i.e., swing, stance) by leveraging key events (e.g., heel strike, toe off), using multiple sensors (Trojaniello, Cereatti, Pelosin, et al., 2014b), or frequency based approaches, such as continuous and stationary wavelets (Barralon et al., 2006; Khandelwal & Wickström, 2017). However, none of these approaches have assessed the potential to identify *sub-phases* of the gait cycle (e.g., terminal stance/swing, midstance, loading phase, etc.) which can be of significant interest for pathological gait and risk assessment (e.g., risk of falling). Segmenting the gait cycle into sub-phases provides opportunities to expand characterization of gait and evaluate differences between neurologic diseases (Zheng et al., 2009) or identify early changes to gait speed in aging populations (Sloot et al., 2021). The cyclical nature of the gait cycle provides a framework for a finite state machine (FSM) model to segment the gait cycle into discrete subphases for clinical application

and gait assessment (Willemsen et al., 1990). Finite state machine (FSM) algorithms also have the potential to advance free-living data collections by improving characterization of walking indoors, where GPS has lower accuracy (Kronenwett et al., 2017). Improved stride detection and partitioning of gait cycles into subphases may increase the potential to identify gait initiation and termination, placing less reliance on temporal thresholds to define gait bouts or walking patterns (Barry et al., 2015). An FSM approach, relying on a single ankle worn sensor, has potential to translate well into clinical settings by maximizing information gathered about gait with modest cost and low computational load (i.e., single device).

To examine the utility of the FSM approach, the algorithm was evaluated for its ability to identify stride from a variety of gait tasks and across individuals with varying degrees of gait instability to test the algorithm's accuracy to detect individual strides under a variety of circumstances (i.e., across participants and gait speeds, in treadmill and overground walking, and across task challenges (single versus dual tasking)). It was hypothesized the FSM algorithm would have a high degree of accuracy in all conditions.

4.2 Material and Methods

4.2.1 Participants & Study Design

Data from baseline visits for two studies collecting sensor based data were included in the evaluation of the FSM algorithm: 1) healthy young adults (n=20) who performed treadmill walking and 2) individuals living with neurodegenerative disease (NDD) or cerebrovascular disease (CVD) (n=35) who underwent clinical gait assessment as part of their involvement in the Ontario Neurodegenerative Disease Research Initiative (ONDRI) (ondri.ca) (Godkin et al., 2021). These studies were performed in line with the principles of the Declaration of Helsinki.

The study of young adults was designed to acquire control data for sensor testing and algorithm development. Individuals were eligible to participate if they were free of neurological or musculoskeletal disorders and had no contraindications to sensor wear. This study was approved by the University of

Waterloo Office of Research Ethics (ORE#: 31943) and all participants provided written consent prior to participation. The study of individuals with a clinical diagnosis of NDD or CVD was designed to assess the feasibility of continuous sensor wear in these complex disease cohorts (Godkin et al., 2021).

Participants were grouped based on one of the five following diagnoses, as confirmed by a neurologist: Alzheimer's disease/mild cognitive impairment (ADMCI; n=8), Parkinson's disease (PD; n=11), frontotemporal lobar degeneration (FTD; n=3), cerebrovascular disease (CVD; n=10), and amyotrophic lateral sclerosis (ALS; n=3). Detailed inclusion and exclusion criteria are provided by Godkin and colleagues (Godkin et al., 2021). In brief, participants were included if they self-reported proficiency in English language communication, enrolled with a study partner known for a minimum two years, and had no contraindications to sensor wear. This study was approved by the Sunnybrook Health Sciences Centre Research Ethics Board (March 14, 2019, No.: 1832) and all participants provided written consent prior to participation.

4.2.2 Data Collection

At baseline, demographic and medical history data were obtained alongside clinic-based gait assessments. Groups were instrumented with GENEActiv triaxial accelerometers (ActivInsights, Cambridgeshire, UK) bilaterally on the wrists with watchstraps and on the shank proximal to the lateral malleolus ankle with custom-made straps (Fabrifoam, PA). Acceleration was sampled at 75 Hz with a range of $\pm 8g$ and all data were stored using onboard storage before transfer to a secure server.

Young adults completed five treadmill walking trials at different speeds, scaled to the participant's self-selected, preferred walking speed. Preferred treadmill walking speed (100PREF) was completed for five minutes, the remaining trial speeds were scaled to 60% (60PREF) and 80% (80PREF) of 100PREF for two minutes and 120% (120PREF) and 140% (140PREF) for five minutes.

People living with NDD/CVD completed overground clinical gait assessments comprised of five different tasks for a total of seven trials: self-selected preferred speed (PAVG) (three trials), dual-task

walking (counting backwards by 1 (DT-1s), verbal fluency/animal naming (DT-An), counting backwards by 7 (DT-7s)), and fast walking (FAST) (Cullen et al., 2018). A six-meter walkway was set up to include an additional one meter at the beginning and end to capture acceleration phases of walking, for a total of eight meters. During dual-task trials, participants started the secondary cognitive task prior to the start of walking. Fast walking instructions were to walk as quickly and safely as possible without running. Gait speed was calculated as an average speed for the middle 6-meters using a stopwatch. Clinical gait and mobility outcomes included a situational gait aid use questionnaire (Thomson et al., 2023), modified Rankin Scale (Bruno et al., 2011), and a 10-point Likert scale to assess fear of falling (Montero-Odasso et al., 2017).

4.2.3 Data Analysis

A custom data processing pipeline (Python v3.8) was used to convert the raw GENEActiv data (binary format) into European Data Format (EDF) and synchronize the inertial data with respect to time (Beyer et al., 2024). Acceleration was down sampled to 40 Hz and low pass filtered with a single pass, second order, Butterworth filter with a cut-off frequency of 12 Hz. The input for the FSM algorithm was vertical axis acceleration (i.e., aligned with longitudinal axis of the lower limb) for unilateral stride detection (Willemssen et al., 1990). Acceleration data from each ankle was input separately into the FSM for step detection, the algorithm combined left and right strides to output the total stride count for each trial.

4.2.3.1 Gold standard step detection

The gold standard number of strides was computed by manually counting the steps that occurred for the right and left limb during all treadmill and overground walking. Accelerometer data was visualized using EDFBrowser (www.teuniz.net/edfbrowser/). Criteria for annotating a step was based on figures and descriptions of the gait phases described in previously published FSM studies (Willemssen et al., 1990). Prior to annotating, two experienced analysts examined sample datasets to confirm the gait cycle identification in both treadmill and single- and dual-task overground walking trials. Afterwards one of

these gait analysts counted strides during treadmill and overground walking trials for all participants with support from the second analyst to resolve any irregular/uncertain steps. The algorithm-detected strides were then plotted against accelerometer data and visualized for confirmation and comparison.

4.2.3.2 Finite state machine (FSM) algorithm for step detection

The stride detection algorithm was an adapted version of a real-time detection algorithm (Willemsen et al., 1990) (Figure 1). The implementation is an FSM with four transitional states based on sub-phases. The benefit of the algorithm lies in its ability to segment different states of the gait cycle and extract useful metrics from the individual phases. Another unique benefit of algorithm implementation is the ability to analyze single sensor wear locations, which expands the utility across different data collections, however outputs can be synchronized to describe bilateral stepping patterns. Among each state, unique requirements are met to determine the presence of the state. Strides are considered valid if all states are passed and at any point, if a state requirement is unmet, a potential step is labelled as ‘rejected’ (see State A). Algorithm output describes the timing of each successful and failed state during processing. Figure 4-1 outlines the possible paths of each state:

- A. *Push-off/ pre-swing detection*: The first state in the FSM model identifies potential positive slopes using a sliding window and correlates a template of push-off model, calculated from previously collected acceleration in older adults (template signal), with the vertical acceleration data from the trial. Correlations greater than 0.85 achieve the requirements for state A. If the detected push-off does not exceed the threshold the FSM model returns to the original state and labels the current push-off as ‘rejected’. A final check is then done to verify that this push-off does not overlap with any previously identified strides. If all criteria are met, the FSM proceeds to swing-phase detection.*Swing phase peak detection*: This version of the FSM algorithm combines the both decreasing and increasing slope detection states from the original algorithm into a minima peak detection within 0.5 seconds after the indexed push-off phase. If a minima peak value is found, the FSM proceeds to the foot-contact phase.

- B. *Foot-contact/heel strike detection*: The start of the foot-down phase can be identified through the sharp changes in acceleration from the heel strike. The derivative of the accelerometer signal was calculated with three consecutive points beginning at the index where the swing phase was detected (State B) for a duration of 0.5 seconds. If the derivative signal crossed a static threshold ($-5g/s$) within the foot contact window length, this state is considered successful.
- C. *Stance phase/time delay*: For algorithm implementation, search windows were established to limit stride detection within physiological constraints (e.g., two strides with the same foot cannot occur within 0.4s) (Trojaniello, Cereatti, Pelosin, et al., 2014b). The FSM applies a time constraint beginning at the end of the previously detected state, whereas the original algorithm was tied to push-off detection. In this implementation of the algorithm, vertical acceleration may have difficulty detecting the transition from contact to flat foot therefore a delay of 0.1 seconds was added to represent that transition time, required to mark the step as complete.

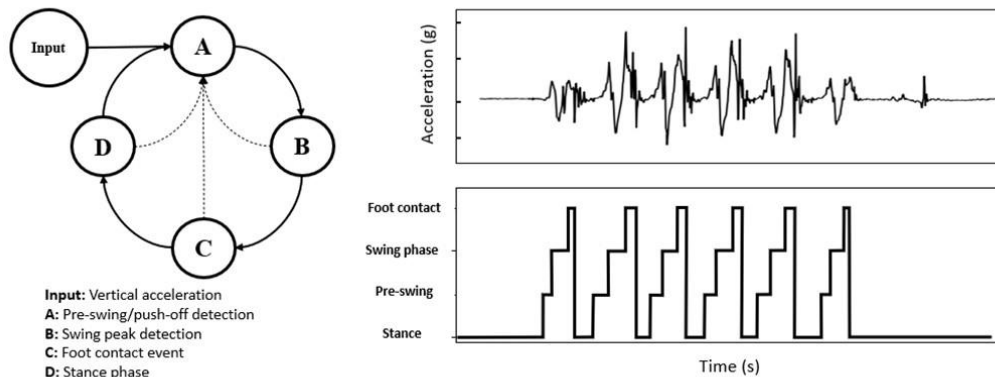


Figure 4-1. Description of the states that are included within the state space controller algorithm, adapted from Willemsen et al. (1990) The flow diagram (left) is displayed to show each state and the expected transitions between states when satisfied (black line) and the transition if the requirements of the state are unmet (dashed line), while accelerometer tracing of an overground clinical walking task is shown on the right with the successful state step plot below.

4.2.4 Statistical Analysis

For statistical analysis, both counted and algorithm detected strides were totaled by task and participants. Statistical tests were conducted using pingouin statistical package (Python v3.8) (Vallat, 2018) and all data were tested for normality and rank transformed if significant. Stride totals were compared between algorithm and counting for treadmill and overground walking conditions. Statistical analyses of algorithm performance were conducted using the absolute error calculated between the two detection methods and accuracy, sensitivity, specificity, and predictive values were calculated. The design of this algorithm allows for rejection of a step when a state requirement is not met. In this study, true negatives were counted as any instance in which the algorithm rejected a state detection properly which was confirmed by the expert analyst. Bland-Altman plots were used to visualize the agreement for overground walking tasks (Giavarina, 2015). Instances in which the algorithm failed (error states) were totalled and summarized within tasks.

A repeated measures one-way analysis of variance (ANOVA) compared walking speeds and the rank transformed absolute error from task conditions (within group factor) in both overground walking and treadmill walking. Paired t-tests were conducted post hoc to examine main effects. Significance was set to $p < 0.05$, and where appropriate, Bonferroni corrections were applied.

To determine the effect of the algorithm's accuracy on outcomes for particular use cases, the effect of missed steps in clinical and continuous walking applications were examined. It was reasoned that a difference of a single step between methods during short distance, overground walking, was meaningful since a single missed stride in clinical gait analysis has significant effects on the mean and variability of spatiotemporal measures. This was also tested during continuous walking, where missed strides can cause algorithms to identify pauses during walking. Further, two maximum resting periods (MRPs) (6 and 2 seconds) were tested to understand their impact on algorithm performance with respect to identifying continuous walking.

4.3 Results

4.3.1 Participants & Data summary

All 20 participants from the young cohort completed treadmill trials at all walk speeds totalling 100 trials. For the 35 participants in the NDD/CVD cohort, all preferred and fast trials were completed, while four dual-task walking (DTW) trials were missing. One participant did not complete DTW (three trials) due to cognitive impairment and a second participant opted out of completing DT-7s. As a result, there were a total of 241 overground walking trials available for analysis from participants with NDD/CVD. The average age of the young and NDD/CVD cohorts was 21.9 (SD=3) and 66.7 (9) years old, respectively. Details of participant demographics, clinical characteristics, mobility aid use, balance confidence, and fear of falling are listed in Table 4-1.

Table 4-1: Participant demographic and clinical details

	Young (n=21)	ADMCI (n=8)	PD (n=11)	FTD (n=3)	CVD (n=10)	ALS (n=3)
Demographics						
Sex (% female)	14 (67)	2 (25)	5 (45)	1 (33)	3 (30)	2 (33)
Age (SD)	21.9 (3)	72.7 (6.7)	65.6 (6.1)	63.6 (15.9)	68.6 (7.1)	56.3 (14)
% right-handed	18 (86)	8 (100)	11 (100)	1 (33)	10 (100)	2 (66.7)
Height (cm)	171.6 (8)	172.7 (8.7)	170.5 (10.2)	161.6 (14.6) ^a	166.5 (8.9)	172.7 (13.6)
Weight (kg)	70 (13)	83.4 (9.0)	76.1 (19.4)	77.5 (7.4) ^a	79.2 (14.8)	75.8 (15.4)
Clinical Gait & Mobility Outcomes						
Gait aid use						
<i>Inside room</i>	-	-	-	Walker (1)	-	Cane (1)
<i>Short halls</i>	-	-	-	Walker (1)	-	-
<i>Long halls</i>	-	-	-	Walker (1)	-	Cane (1), Walker (1), Wheelchair (1)
<i>Outside</i>	-	-	Walking poles (1)	Walker (2)	Cane (2)	Cane (1), Walker (1), Wheelchair (1)
Fear of Falling*	0.8 (1.2)	0.88 (1.3)	3.1 (5.2)	2 (2.6)	1.7 (2.9)	4.0 (4.0)
Balance Confidence [†]	7.9 (1.7)	7.25 (2.5)	7.5 (3.6)	4.7 (4.1)	7.3 (2.3)	5.0 (4.6)
Clinical Assessments						
MoCA	-	24.5 (1.7) ^b	25.4 (6.9)	22.5 (0.7) ^a	25.4 (3.9)	23.7 (1.5)
MRS	-	1.88 (1.0)	1.6 (1.4)	3.5 (0.7) ^a	1.1 (1.1)	3 (0) ^a

MoCA: Montreal Cognitive Assessment; MRS: Modified Rankin Scale., ADMCI: Alzheimer's disease and mild cognitive impairment; PD: Parkinson's disease; FTD: Frontotemporal dementia; CVD: Cerebrovascular disease; ALS: Amyotrophic lateral sclerosis

*Fear of falling: greater score indicates increased fear of falling

[†]Balance Confidence: greater score indicated more confidence in balance ability

Missing data: ^a one participant, ^b two participants

4.3.2 Treadmill walking

4.3.2.1 Treadmill gait speed

On average, preferred treadmill walking speed was 1.10 m/s. The mean incremental difference between the scaling intervals (60, 80, 100, 120 and 140% of preferred) was 0.22 m/s, with a main effect of walking speed ($F(4,76)=369.3$, $p<.01$) (Table 4-2). Significant differences between all treadmill speeds were revealed with post-hoc comparison ($p<0.05$). Gait speeds across all trials and participants ranged from 0.4 m/s to 2.19 m/s.

Table 4-2: Walking speeds for all treadmill tasks

Treadmill Walk Task	Step Counts (mean (SD))	Speed (SD) (m/s)
60PREF	212.5 (54.1)	0.65 (0.15)*
80PREF	208.6 (32.0)	0.86 (0.19)*,†
100PREF	423.7 (59.6)	1.08 (0.25)*,‡
120PREF	465.1 (56.0)	1.30 (0.30)*
140PREF	496.9 (57.8)	1.50 (0.34)‡

60PREF: 60% the preferred self-selected walking speed, 80PREF: 80% preferred walking, 100PREF: Self-selected preferred treadmill walking speed; 120PREF: 120% preferred walking speed, 140PREF: 140% preferred walking speed. *, †, ‡ indicates significant difference

4.3.2.2 Step detection outcomes between walking speeds

Strides from both left and right sensors, resulted in a total of 34,993 strides detected across all participants and trials (Table 4-2). The FSM algorithm detected 34,773 total strides, resulting in a grand average of 99.8% accuracy, 98.9% sensitivity, and 82.4% specificity (Table 4-3). There were no significant differences in absolute error between treadmill walking speeds ($F(4,76) = 2.04$, $p=0.09$) (Figure 4-2). Error, medians, and interquartile ranges (Q1-Q3) were: 60PREF: 2 (1-6.25), 80PREF: 1 (1-2), 100PREF: 1 (0-1.25), 120PREF: 1 (0-3), 140PREF: 1 (1-2.25) (Table 4-4). Stride detection accuracy across participants and between treadmill gait speeds ranged from 97.7% (60PREF) to 99.5% (100PREF) (Table 4-3).

Table 4-3: Mean total error and limits of agreement, calculated using confidence intervals (CI), with step detection percent accuracy.

Cohort	Task	Mean Error	Limit of Agreement (95% CI)	Validation Outcomes				
				Accuracy (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)
NDD/CVD (Overground walking)	Total	0.71	0.23 – 1.13	95.91	99.86	70.04	95.61	98.75
	PAVG	0.27	0.08 – 0.45	98.05	99.76	83.25	98.10	97.55
	<i>PREF1</i>	0.31	0.09 – 0.54	97.94	99.82	80.95	97.93	98.08
	<i>PREF2</i>	0.31	0.03 – 0.60	97.53	99.63	81.43	97.63	96.61
	<i>PREF3</i>	0.17	0.00 – 0.34	98.69	99.82	87.93	98.75	98.08
	DT-1s	0.44	0.12 – 0.76	97.47	100.00	77.61	97.23	100.00
	DT-An	0.82	0.32 – 1.32	95.71	100.00	72.55	95.16	100.00
	DT-7s	0.94	0.34 – 1.54	94.75	99.81	70.64	94.18	98.72
	FAST	1.77	0.73 – 2.81	88.30	100.00	34.74	87.53	100.00
Young adults (Treadmill walking)	Total	2.62	0.31 – 4.05	99.12	99.82	93.05	99.20	98.34
	60PREF	4.65	0.96 – 8.34	97.73	99.70	90.38	97.47	98.80
	80PREF	1.45	0.34 – 2.56	98.83	99.68	93.85	98.96	98.01
	PREF	1.40	-0.01 – 2.81	99.49	99.88	96.69	99.53	99.22
	120PREF	2.05	0.41 – 3.69	99.42	99.91	93.84	99.46	98.94
	140PREF	1.35	-0.17 – 2.87	99.38	99.82	83.64	99.54	92.98

95% CI: 95% Confidence interval; PPV: Positive predictive value; NPV: Negative predictive value; NDD/CVD: Neurodegenerative disease/Cerebrovascular disease; PAVG: Average over the preferred walking trials (PREF1, PREF2, PREF3); DT-1s: Dual task serial 1s; DT-An: Dual task naming animals; DT-S7: Dual task serial 7s; 60PREF: 60% the preferred self-selected walking speed, 80PREF: 80% preferred walking, 100PREF: Self-selected preferred treadmill walking speed; 120PREF: 120% preferred walking speed, 140PREF: 140% preferred walking speed.

Mean error was calculated the difference between the gold standard (visual) minus the output from the finite state machine.

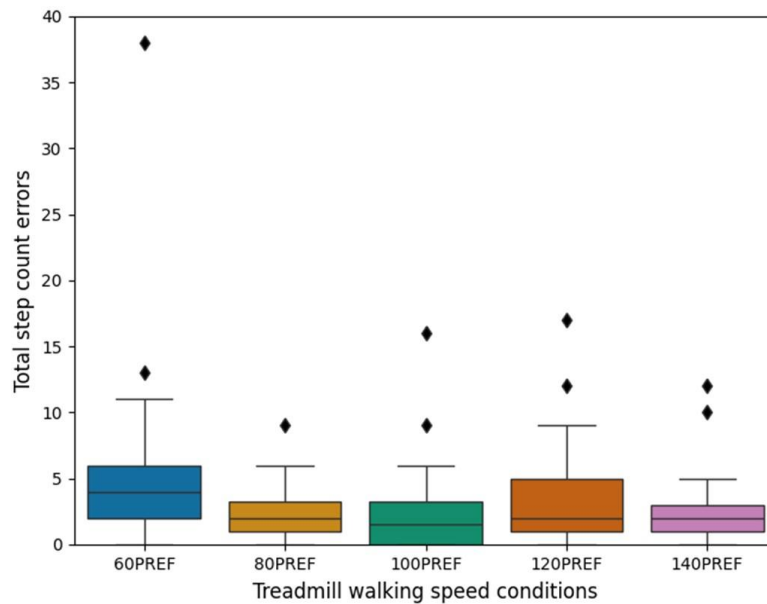


Figure 4-2. Absolute step count errors for the young adult treadmill walking conditions. Boxplots represent first to third quartile ranges (Q1-Q3) with range, outliers labelled with diamond (♦). Treadmill speeds represent a percentage of self-selected preferred treadmill walking speed (60PREF is 60% of self selected preferred, 80PREF: 80% of self-selected walking speed; 100PREF: self-selected walking speed; 120PREF: 120% of self-selected walking speed; 140PREF: 140% of selected walking speed).

4.3.2.3 Magnitude of errors/bias

Error occurrence was low ($n=337/34993$, 0.01%) and of these errors 82.7% were false negatives (Table 4-4). Most false negatives occurred while detecting mid-swing (state B) and heel contact peaks (state C) in both 60PREF and 80PREF treadmill speeds (Table 4-4). In total, stride count differences were minimal (me (95% confidence interval (CI)) = 2.76 (1.61-3.90)).

Table 4-4: Absolute errors by tasks for treadmill walking (young adults) and overground walking (NDD & CVD)

Cohort	Task	Absolute error (SD)	Error interquartile ranges					FSM State Fails								
			min	25%	50%	75%	max	False negatives					True negatives			
								A	B	C	D	Missed	A	B	C	D
NDD/CVD (Overground walking)	PAVG	0.32 (0.53)	0	0	0	0.5	2.67	1	8	8	7	8	6	52	14	95
	PREF1	0.31 (0.68)	0	0	0	0	3	1	3	4	1	3	1	12	6	34
	PREF2	0.43 (0.81)	0	0	0	0.5	3	0	3	2	5	3	2	22	5	30
	PREF3	0.23 (0.49)	0	0	0	0	2	0	2	2	1	2	3	18	3	31
	DT-1s	0.44 (0.96)	0	0	0	1	5	2	6	3	1	5	3	16	2	33
	DT-An	0.82 (1.48)	0	0	0	1	6	0	6	5	4	12	1	19	6	49
	DT-7s	0.94 (1.74)	0	0	0	1	8	1	12	8	1	12	4	22	4	48
	FAST	1.77 (3.14)	0	0	0	2	15	0	0	4	13	45	0	10	4	19
Young adults (Treadmill walking)	60PREF	4.75 (8.35)	0	1	2	6.25	38	1	35	42	8	1	8	108	14	854
	80PREF	1.85 (2.23)	0	1	1	2	9	4	12	8	5	0	8	38	8	588
	PREF	1.80 (3.00)	0	0	1	1.25	11	0	6	8	2	1	6	24	8	1101
	120PREF	2.55 (3.76)	0	0	1	3	15	0	4	4	1	2	11	23	10	701
	140PREF	2.15 (3.01)	0	1	1	2.25	12	2	4	5	2	0	12	34	5	173

NDD/CVD: Neurodegenerative disease/Cerebrovascular disease; PAVG: Average over the preferred walking trials (PREF1, PREF2, PREF3); DT-1s: Dual task serial 1s; DT-An: Dual task naming animals; DT-S7: Dual task serial 7s; 60PREF: 60% the preferred self-selected walking speed, 80PREF: 80% preferred walking, 100PREF: Self-selected preferred treadmill walking speed; 120PREF: 120% preferred walking speed, 140PREF: 140% preferred walking speed.

FSM State fails correspond to the finite state machine transitional points where A: the pre-swing state, B: peak swing phase detection, C: Foot-contact/heel strike detection, D: Stance phase/midstance/time delay, Missed: represents any steps that were not detected

4.3.3 Overground walking – NDD and CVD cohorts

4.3.3.1 Effect of task and cohort on gait speed

When comparing gait speed across task conditions, there was a main effect of task ($F(4,124)=107.12$, $p<0.001$). Post-hoc analysis confirmed FAST walking (1.78 m/s) was significantly greater than DT-1s (1.11m/s), DT-An (1.03 m/s), DT-7s (0.96m/s), and PAVG (1.15 m/s) ($p<0.05$). PAVG walking speeds were not significantly different than DT-1s ($p>0.05$) and both PAVG and DT-1s were greater than DT-An ($p<0.05$) and DT-7s ($p<0.05$). DT-An was not different from DT-7s walking speeds ($p>0.05$) (Table 4-5).

Table 4-5: Overground walking speeds across conditions and cohorts.

Task	Gait speed (m/s)					
	Overall Average	ADMCI (n=8)	PD (n=11)	FTD (n=3)	CVD (n=10)	ALS (n=3)
PAVG	1.15 (0.29)	1.22 (0.15)	1.18 (0.31)	0.80 (0.25)	1.24 (0.31)	0.93 (0.18)
<i>PREF1</i>	1.13 (0.31)	1.17 (0.18)	1.18 (0.33)	0.81 (0.30)	1.22 (0.33)	0.89 (0.29)
<i>PREF2</i>	1.15 (0.29)	1.23 (0.15)	1.18 (0.29)	0.79 (0.34)	1.22 (0.32)	0.98 (0.15)
<i>PREF3</i>	1.17 (0.3)	1.25 (0.15)	1.19 (0.31)	0.79 (0.41)	1.27 (0.29)	0.92 (0.15)
DT-1s	1.11 (0.32) ^{*,†}	1.19 (0.21)	1.12 (0.35)	0.66 (0.66) ^a	1.19 (0.3)	0.90 (0.16)
DT-An	1.03 (0.32) [†]	1.05 (0.22)	1.04 (0.32)	0.63 (0.66) ^a	1.13 (0.35)	0.88 (0.13)
DT-7s	0.96 (0.35)	1.00 (0.29)	0.94 (0.35)	0.67 (0.68) ^a	1.04 (0.36)	0.6 (0.29) ^a
FAST	1.78 (0.52) [*]	1.94 (0.37)	1.77 (0.68)	1.36 (0.50)	2.01 (0.24) ^a	1.47 (0.39)

ADMCI: Alzheimer's disease and mild cognitive impairment, PD: Parkinson's disease, FTD: frontotemporal lobar degeneration, CVD: Cerebrovascular disease, ALS: Amyotrophic lateral sclerosis, PAVG: Preferred trial average, PREF: Preferred trial, DT-1s: Dual task serial 1s, DT-An: Verbal fluency (animal naming) task, DT-7s: Dual task serial 7s; ^{*}, [†] indicate significantly different gait speeds; Missing data: ^a one participant

4.3.3.2 Step counting error between tasks

Strides detected from both left and right sensors, resulted in a total of 3853 strides counted across all participants and trials. On average there were 15.9 strides in each walking bout, with ranges: PAVG: 11-32, DT-S1s: 11-30, DT-An: 10-33, DT-S7s: 11-30, FAST: 8-23. The FSM algorithm detected 3684 total strides, resulting in a grand average of 95.91% accuracy, 95.61% sensitivity, and 98.75% specificity (Table 4-3). For overground walking detection errors, there was a main effect of task ($F(6,192)=3.53$, $p=0.002$) however no statistically significant differences were detected during post-hoc testing (Figure 4-

3). Stride detection accuracy decreased during FAST gait (88% accuracy) compared to other walking tasks, 100% stride detection did occur for trials across the range of gait speeds and walking tasks for 161 of 241 trials (7/35 participants had 100% detection in all trials) (Figure 4-4). Specifically, algorithm performance was poorer (<70% accuracy) on seven FAST gait trials and achieved 100% stride detection on 11 FAST trials. Mean absolute error ranged from 0.57-2.02 missed strides while error medians ranged from 0 to 2 based on walking condition (Table 4-2).

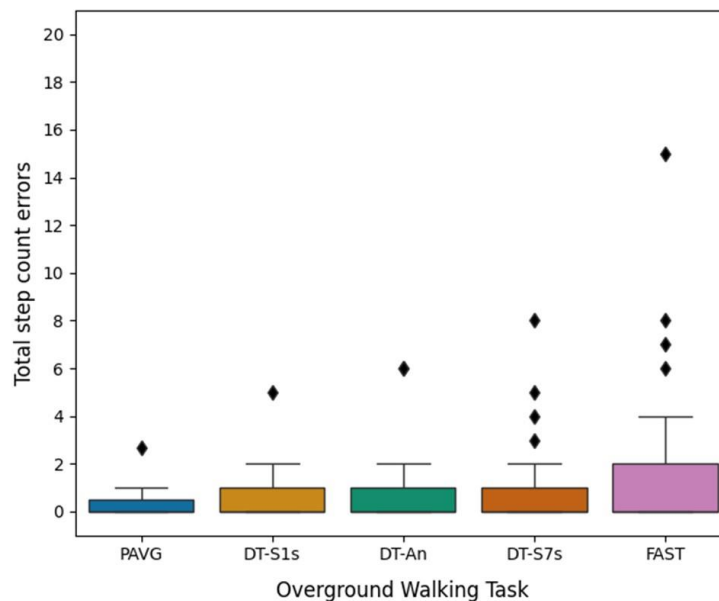


Figure 4-3. Absolute step count errors for the overground walk trials completed by people living with NDD. Boxplots represent first to third quartile ranges (Q1-Q3) with range, outliers labelled with diamond (♦). Walking tasks are preferred walking (PAVG), dual task counting backwards by 1s (DT-S1s), dual task naming animals (DT-An), dual task counting backwards by 7s (DT-S7s), and fast walking (FAST).

4.3.3.3 Magnitude of errors/bias

For overground walking, stride detection error was low ($n=174/3853$, 4.7%) and of these errors 97.1% were false negatives (Table 4-3). Difference in stride detection was positive across disease cohorts and gait tasks (me (CI) = 0.71 (0.23-1.13)). Like treadmill walking, false negatives more often occurred due to missing swing peaks or missing detection of heel contact (Table 4-4). Although not significantly different, FAST walking (me (CI) = 1.77 (0.73-2.81)) showed more error compared to the other task conditions.

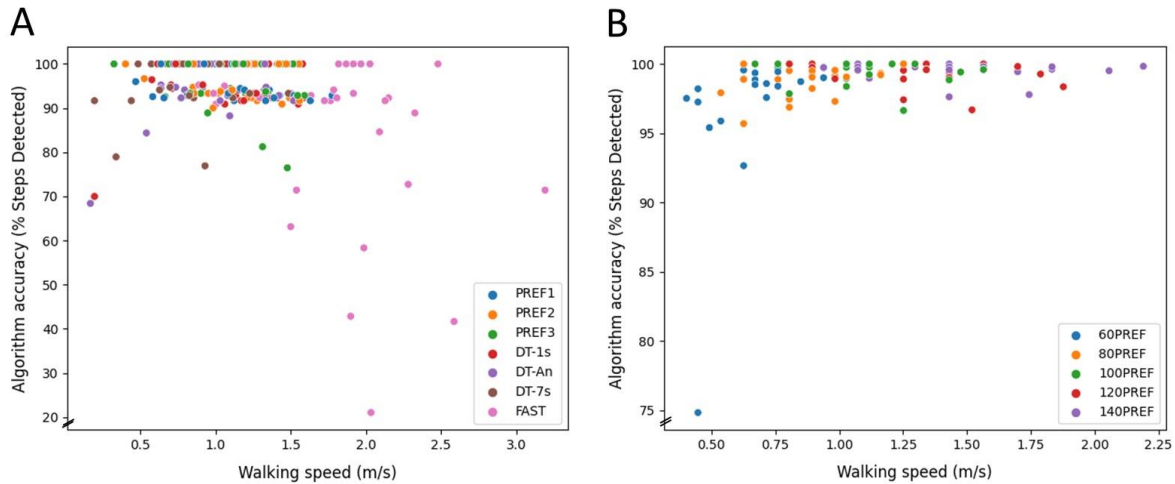


Figure 4-4. Step count error and clinical accuracy outcomes for overground walking across all walking tasks. Bland-Altman plots show the individual overground walking trial error compared to the number of counted steps for (A) preferred walking, (B) dual-task walking, and (C) fast walking. Each plotted point represents a single trial, each histogram represents the frequency in which that difference occurs. D shows the percent of total trials that have less than two steps difference between counted and algorithm detected step counts.

4.3.4 Impact of accuracy and relevance for clinical application of algorithm

A detection error greater than one stride occurred in at least one trial for all overground walking tasks for NDD/CVD cohorts. In total, 32/241 trials had more than one missed stride (11/35 FAST (31.4%), 12/101 DTW (11.9%), and 9/105 PREF (8.6%)). Missed strides were not accounted for by differences in cohorts as all had similar proportion of trials with greater than one missed stride in DTW and/or FAST walking (Figure 4-6). During treadmill walking, missed strides caused bout definition errors for both the MRP2 and MRP6 thresholds. On average the number of distinct bouts identified was less with MRP6 (average ranges: 1.1-1.36 bouts identified) compared to MRP2 (average ranges: 2.35-6.5 bouts identified) and slower walking increased the number of walking bouts when using MRP2 thresholds.

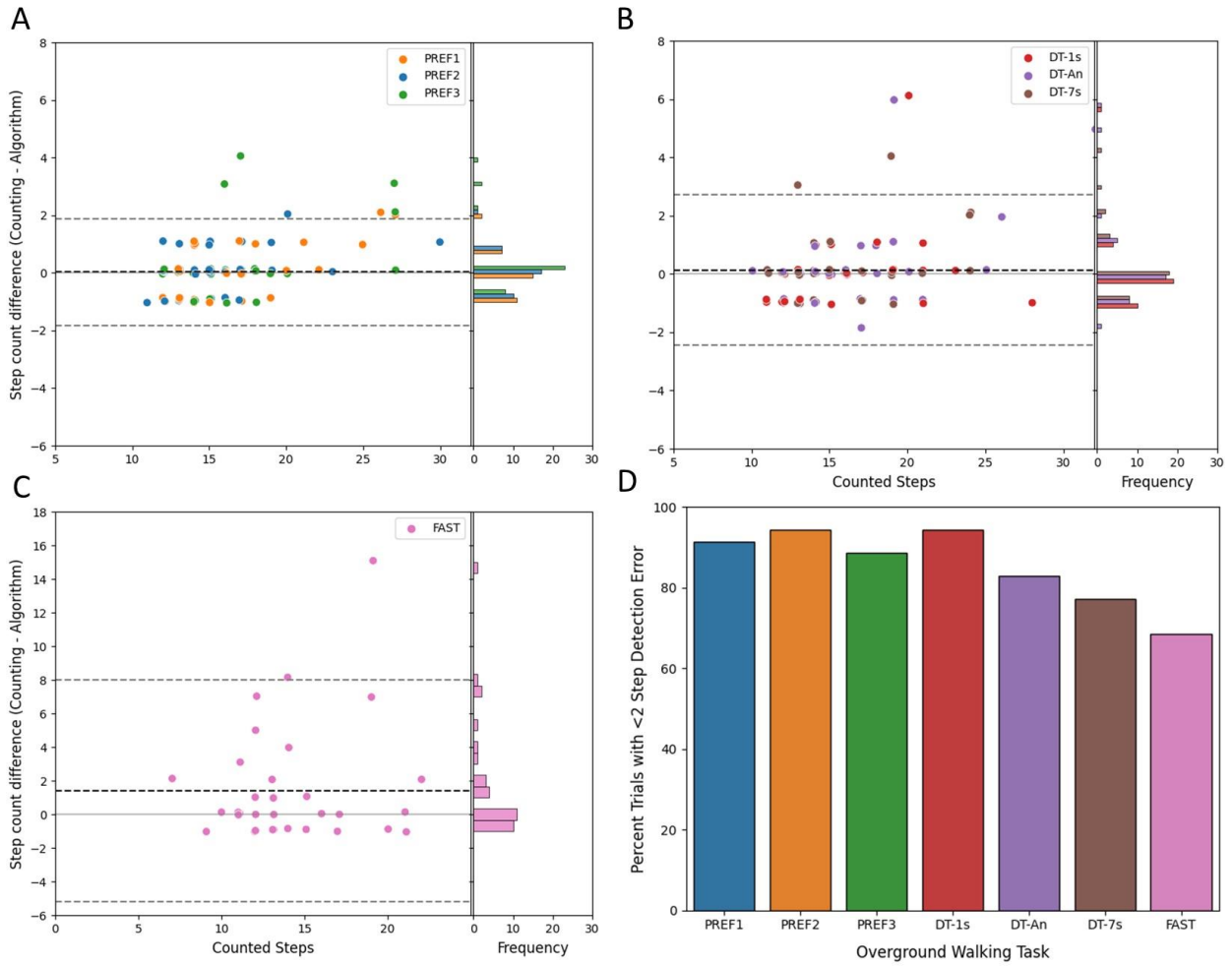


Figure 4-5. Scatter plots comparing the algorithm accuracy of individual trials to the walking speed for each trial during (A-C) overground walking and (D) treadmill walking.

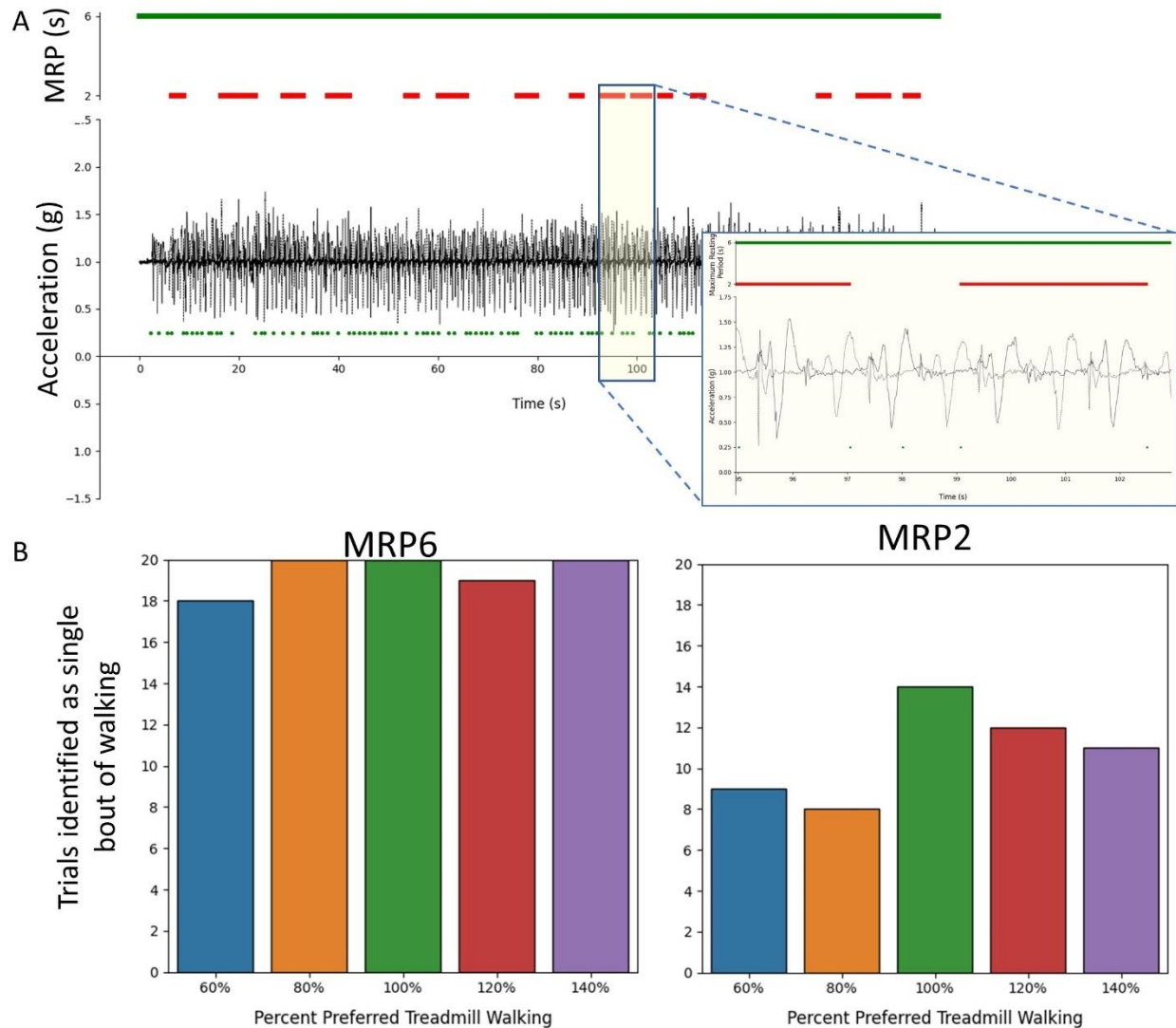


Figure 4-6. Timeseries and bar plots demonstrating the effect of algorithm performance and maximum resting periods for detecting continuous walking. (A) Example of the effect of maximum resting period (MRP) times on single bout detection during treadmill walking. Raw accelerometry (bilateral ankles) during 60PREF treadmill trial shown in black. Each successfully detected step (green dot) represents the beginning of the push-off phase for a detected step. The identified walking bouts for different MRP (MRP6 seconds (green), MRP2 seconds (red)) thresholds are plotted using horizontal bars. The continuous green bar illustrates the single walking bout detected using MRP6 while breaks in the red bars indicated “resting periods” detected as a product of MRP2 thresholding. B indicates the total number of trials identified as a single walking bout (correct identification) using respective MRP thresholds (MRP: maximum resting period).

4.4 Discussion

The objective of this study was to detect strides by identifying subphases of the gait cycle using an FSM algorithm with uniaxial acceleration data obtained from a lower limb worn device (shank just proximal to the ankle). The algorithm demonstrated excellent performance across a range of speeds and

clinical gait tasks that represent naturally occurring gait, in young adults and persons living with neurodegenerative or cerebrovascular disease. High detection accuracy was maintained for slower gait speeds and during cognitively demanding tasks; conditions that have been shown to increase stride variability (Montero-Odasso, Muir, et al., 2012). Importantly, the algorithm performed well throughout the entire gait bout including during non-steady state walking phases (e.g., gait acceleration and termination) that may be important for understanding gait control. The success of this low-burden approach has important implications for advancing gait assessment, both in clinic and at home, where the goals are to monitor and characterize underlying gait impairments, track efficacy of interventions, and provide personalized care.

Accurate stride detection during slow walking is specifically important for extending analytical approaches to positively impact the assessment of mobility, fall risk, and independence in older adults and those living with mobility impairments (Grau-Pellicer et al., 2019; Weber et al., 2023). Conversely, accurate stride detection during faster-paced walking is important outside of the clinic because it may reflect brisk walking that is commonly used as daily exercise (Callisaya et al., 2017; Dai et al., 2015) and for evaluating exercise capacity (Canning et al., 1997). In the present study, algorithm performance was tested across a wide range of walking speeds during treadmill and overground walking. Algorithm performance was high for both conditions (99% and 96% accuracy respectively) across these speeds; however, in both instances, there were modest decreases in detection accuracy associated with the extremes of walking speeds. The slowest treadmill speed (97.9%) and fast overground walking (88.6%) had the lowest percent accuracies (Figure 4-5). Error analysis showed that during slow walking, greater detection errors occurred due to missing peak detection during swing phase (state B) or heel strike detection (state C) for both treadmill and overground walking. While fast overground walking had larger errors in stance phase detection (state D) and few errors occurred during the fastest treadmill walking (Table 4-4). Although these error outcomes can aid in further detection, one limitation with this model is the sequential nature of these states such that if the model rejects a stride in state A, it is unknown if the

consecutive states would meet their requirements. The walking speed ranges in this study were 0.4 to 2.19 m/s and 0.16 to 2.6 m/s for treadmill and overground walking, respectively, showing robust range to test the algorithm. The average gait speed of overground walking (1.78 m/s) was slightly higher than the 140PREF treadmill speed (1.50 m/s) which could contribute to these differences seen at the high end of walking speeds. Another potential source for the modest decrease in accuracy is an interaction between stride length, swing phase impulse, and cadence during treadmill and overground walking speeds that caused errors for the extremes of walking speed. Previous work has reported higher cadence for treadmill walking compared to speed-matched overground walking, and faster walking speeds for overground walking compared to fast treadmill walking for some post-stroke cohorts (Callisaya et al., 2017). Gait speed alone may not singularly influence detection accuracy and how speed is achieved plays an important role for algorithm performance.

Observed differences between treadmill and overground walking could help identify areas for improvement to the FSM algorithm, as stride length and cadence directly affect limb acceleration and stance time, respectively. Changing kinematics (increased step length or cadence) and/or kinetics (rate of push-off force development), both which alter acceleration waveforms during stepping, are methods to change walking speed. Across many peak detection and heuristic algorithms, including the FSM algorithm, duration thresholds are applied to timing of specific gait phases between steps and are used to avoid incorrect step identification (Barralon et al., 2006; Canning et al., 1997). These thresholds are likely not singularly affected by gait speed but affected by the interaction between speed and cadence, resulting in increased detection error. Although these high speeds and cadences are unlikely to be sustained in free-living environments outside of exercise, it is notable that the FSM algorithm performed reasonably well during range of FAST overground walking speeds (speed range: 0.8-2.6 m/s) with increased limb acceleration and shorter stride times. Expanding push-off templates within the FSM model to include and represent faster or slower walking may improve stride detection in these extreme paces and improve the

ability to analyze and assess a wider range of activities, including fast walking during exercises done at home.

Novel to this study was inclusion of different dual task walking conditions among people with NDD/CVD to expand the evaluation of the FSM algorithm. Dual task walking has been shown to negatively impact bilateral coordination for people with PD (Plotnik et al., 2013) as well as decrease gait velocity and increase stride time variability in people with mild cognitive impairment (Montero-Odasso, Muir, et al., 2012). As suggested, slow overground walking changes both kinematic and kinetic measures of gait in healthy adults (Plotnik et al., 2013) which may affect the performance of heuristic step detection algorithms. Detecting stepping in DTW was nearly as successful as preferred pace walking (>94%), elevating the success of the algorithm during highly variable and slow walking conditions. Although there is no assessment of cognitive ability within this study, dual task walking did produce slower walking speeds across all task conditions compared to preferred pace. Testing the algorithm under tasks of varying difficulty may also indicate potential success in free-living walking which is more similar to dual task walking with slower speeds and increased spatiotemporal variability compared to preferred walking in a controlled setting (Hillel et al., 2019). The ankle location in combination with an algorithm that examines gait cycle patterns may have benefits over traditional peak detection methods when examining extreme walking conditions. One instance that illustrates the robustness of the algorithm is shown during walking with a mobility aid. While not a focus of the current work, it was observed that three participants required gait aids (cane, walker, and handrail) to complete overground walking and results showed very good stride detection during these instances. Highlighting these individuals recognizes the impact that gait aid use can have on step detection with wearable sensors that are located for convenience (e.g., wrist) versus purpose (Park et al., 2017). When an object is being held in hand the upper limb and trunk motion are profoundly impacted, limiting the ability of trunk- or arm-worn sensors to detect features of walking.

Evidence from continuous monitoring studies shows that daily walking tends to occur in bouts of less than 10 seconds in both healthy and impaired populations (Del Din, Godfrey, et al., 2016). The FSM

algorithm was robust under short bout conditions (stride counts in overground walking ranged from 8 to 33 strides over 8 metres) in participants living with NDD/CVD, including during periods of acceleration and deceleration. An opportunity to advance analytics in unsupervised walking detection may be linked to the distinct spatiotemporal and kinetic properties of the acceleration phases of gait (Del Din, Godfrey, et al., 2016; J. Park et al., 2017). Algorithms designed for unsupervised gait detection can be improved by detecting instances of gait initiation and termination features to avoid static thresholds like maximum resting periods or exclusion of these phases. These advancements could positively impact gait analysis by allowing for proper assessment of gait initiation and termination, as well as improved bout detection and activity classification during free-living assessments (Barry et al., 2015; Orendurff, 2008). This study did not specifically outline acceleration phases; however it does provide a foundation for improving characterization of these steps. When examining the impact of algorithm performance and application, clinical walking detection was excellent and continuous walking was influenced by the maximum resting period duration. Relatively few overground walking bouts had more than one missed stride across all gait tasks and NDD/CVD cohorts, with one third of these trials occurring during fast walking. During continuous walking, unidentified steps combined with a shorter MRP2 identified more pauses across the whole walking bout than a longer MRP duration (Figure 4-6). Examination of these algorithm specific errors was unique to this study, revealing that algorithm performance can affect gait specific outcomes. Many overground walking trials were considered acceptable within the conservative threshold however, concern exists for those trials with a missed step likely occurring during the acceleration periods of walking. Along with the influence of speed, error detection may be driven by gait initiation and termination phases as they are likely different than steady state walking and may not meet the state requirements with the FSM model (e.g., low push-off amplitude). Identifying the interaction between step detection and interruptions to continuous walking was important in this study because of the extension of wearable sensors to free-living monitoring. Uniquely the interaction between bout identification and algorithm performance is seldomly assessed but important to macro-assessment of walking in continuous monitoring studies. Although a secondary assessment of algorithm performance these applications are

important for future use of step detection algorithms, specifically when translating between clinical and free-living environments for people with mobility impairments. As algorithms are extended from clinical assessment to free-living scenarios, their validity may be further influenced by disease in combination with change in environment (Del Din, Godfrey, et al., 2016). In similar research, waist or lower back sensors with peak detection methods have been used to detect stepping across range of gait speeds (Fortune, Lugade, Morrow, et al., 2014) and provide analysis of macro- (behavioural patterns) during continuous, free-living protocols (Hickey et al., 2017) but approaches are influenced by wear locations (Del Din, Hickey, et al., 2016; Fortune, Lugade, & Kaufman, 2014). This study demonstrates that ankle worn sensors, with heuristic analytic approaches, can capture behavioural patterns from uniaxial acceleration using either unilateral or bilateral sensors. Further work that examines multi-dimensional acceleration may provide more precise indicators of stride characteristics (Rhudy & Mahoney, 2018), including direction of stepping, better refined gait cycle sub-phases, and indoor walking localization (Kronenwett et al., 2017). Previously, multi-sensor wear was required to identify turning during walking in daily life activities (Shah, McNamara, Mancini, Carlson-Kuhta, Spain, et al., 2020) but based on the current success, a more advanced FSM shows promise for improving the evaluation of walking with minimal sensor wear. Importantly, this study confirms that the single ankle-worn sensor can accurately detect strides to describe gait volumes/bouts and extract spatiotemporal characteristics.

4.5 Conclusion

This study evaluates performance of an adapted stride detection algorithm utilizing a single, ankle-worn accelerometer. Results of our novel application of an FSM algorithm reveal a robust approach for stride detection from identifying cycle sub-phases across a range of walking speeds, tasks, and individual abilities. The key features of an FSM algorithm are its modular components anchored in biomechanically important phases of the gait cycle and the potential adaptability for changing environments or populations of interest. Finite state models provide insight and context to indoor walking (Kronenwett et al., 2017) with low computational load, but are seldomly reported as preferred methods for free-living or clinical

gait description. This study demonstrates utility of the algorithm to assess both steady state and acceleration phases of gait, laying an important foundation for future application of these models to assess gait quality in both clinic and free-living walking. The FSM algorithm is viewed as a strong candidate for free-living gait detection because it requires minimal inputs (e.g., acceleration) and places minimal burden on the patient (e.g., single ankle-worn sensor) permitting extended wear durations. These benefits serve to optimize the viability and utility of gait assessment for clinical application including health or disease monitoring, health-care decision making, and measurement of treatment efficacy.

Acknowledgements & Declarations

Submission declaration and verification

This work has not been published previously and is not under consideration for publication elsewhere.

This publication is approved by all authors and explicitly by the responsible authorities where this work was carried out.

Consent for publication

Informed consent was collected at study enrollment and included consent for the publication.

Availability of data and materials

Data are available to researchers for purposes of reproducing the results or replicating the procedures.

Available data files will be released through Brain-CODE (www.braincode.ca), accessible through a data access request. Please see the Ontario Brain Institute website for information on when the data will be released and how to access the data (<https://braininstitute.ca/>). Source code for the adapted state space controller step detection algorithm can be found at <https://github.com/nimbal/acstatespace>.

Competing Interests

None declared.

Funding

This research was conducted with the support of the Ontario Brain Institute, an independent non-profit corporation, funded partially by the Ontario government. The opinions, results, and conclusions are those of the authors and no endorsement by the Ontario Brain Institute is intended or should be inferred. This research was also supported by the Natural Sciences and Engineering Research Council of Canada (NSERC).

Author contributions

BFC, WEM, KVO, MMO, KSW were involved in study concept and design.

KSW was involved in data collection.

BFC, MW, FPF conducted data analysis and algorithm design.

BFC drafted manuscript, figures, and tables.

All authors reviewed and edited manuscript.

Acknowledgments

This research was conducted with the support of the Natural Sciences and Engineering Research Council of Canada (NSERC grant 1145753) and the Ontario Brain Institute. The Ontario Brain Institute is an independent non-profit corporation, funded partially by the Ontario government. The opinions, results, and conclusions are those of the authors and no endorsement by the Ontario Brain Institute is intended or should be inferred.

The authors thank ReMiNDD participants and study partners, as well as ONDRI investigators and the ONDRI project management team for their input and administrative support of this project. Special acknowledgments are extended to Erin Turner and Youness Demnati for data collection, interviews, sensor management, and more during the collection of data for ReMiNDD.

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BFC, MW, FPF conducted data analysis and algorithm design.

BFC drafted manuscript, figures, and tables.

All authors reviewed and edited manuscript.

Acknowledgments

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Chapter 5

THE EFFECT OF TASK DIFFICULTY ON CONVENTIONAL SPATIOTEMPORAL AND ACCELEROMETRY-BASED KINEMATICS DURING CLINICAL WALKING TASKS IN PEOPLE LIVING WITH NEURODEGENERATIVE DISEASE

5.1 Introduction

Walking is important for quality of life and assessing risk of falling (Alosco et al., 2014; Bechtold et al., 2021). Subjective evaluations are limited in their ability to detect change and compensation can mask self-reporting of mobility change (Mänty et al., 2007). Quantitative gait assessments are a useful tool for objectively evaluating a person's dynamic balance control. This is specifically relevant to those with neurodegenerative disease because they are at an increased risk of falling and fall related injury (Delbaere et al., 2012; Shaw, 2002). Therefore, it is important to assess gait in these cohorts and expand analytical tools to appropriately capture gait impairment.

Wearable technologies ('wearables') allow for an economical way to objectively assess gait in clinical and at-home environments (Jarchi et al., 2018; Kourtis et al., 2019). These low-cost tools allow for gait assessment to expand beyond steady-state walking and examine stride-to-stride outcomes across all intra-bout phases. Wearable sensors have been validated for gait assessments across pathological cohorts (Trojaniello, Cereatti, Pelosin, et al., 2014b) and task challenges (Soulard et al., 2021). Commonly, the combination of accelerometers and gyroscopes affords accurate step detection and spatial gait characteristics (Rebula et al., 2013) from sensors worn on the lower back (Godfrey et al., 2015), trunk (Zijlstra, 2004), or lower limb (Trojaniello, Cereatti, Pelosin, et al., 2014a). A single sensor wear location (e.g., at the low back) is driven by minimal sensor wear, however ankle worn sensors have demonstrated better accuracy of gait event detection (Storm et al., 2016). Stride detection algorithms are most accurate using wavelet approaches (Khandelwal & Wickström, 2017) but this limits the description of gait at the stride-to-stride level, ignoring intra-stride phases. Finite state machines (FSM) provide an approach to expand walking description with context based on acceleration characteristics and identify intra-stride phases as an option for further stride segmentation (Kronenwett et al., 2017).

Identifying segmentation of intra-stride phases provides further insight into phase specific kinematic changes that have been shown to reveal walking differences in people with neurologic disorders (Ohta et al., 2023; Soo, 2020). Combinations of pressure insoles and inertial units have been used to identify foot

off during gait initiation (Novak et al., 2013) and identification of intra-stride phases (e.g., flat foot, heel off) (Mariani et al., 2013). Identifying specific gait cycle subphases can help explain strategies for changes to spatiotemporal outcomes during speed increases of treadmill walking (Hebenstreit et al., 2015) or focus on the push-off force development during gait initiation between single- and dual-tasking walking for stroke survivors (Melzer et al., 2010). Kinematic changes described with accelerometry are not often reported but peak total acceleration from foot mounted accelerometers can identify both temporal and amplitude differences between normal and stiff ankle walking conditions (Patterson & Caulfield, 2013). During stiff ankle walking, peak total acceleration during initial swing and time between acceleration peaks (proxy of swing phase) are reduced (Patterson & Caulfield, 2013). Peak acceleration recorded from tibia mounted accelerometers is also related to gait speed and significant differences in peak acceleration identify change in gait speed of 0.25 m/s (Rios et al., 2010). There is evidence that ankle-worn accelerometers can identify gait changes in response to walking velocity and joint level manipulations, but no research has examined these differences during dual task walking paradigms in clinical cohorts.

Dual task walking is a commonly employed paradigm to evaluate motor-cognitive interaction during walking (Hausdorff & Alexander, 2005; Montero-Odasso, Muir, et al., 2012). Walking with a secondary cognitive task interrupts cortical control of gait and dynamic balance as the central nervous system balances the two competing demands. The dual-task walking paradigm widely reports slower walking speeds but speed may not be sensitive enough for fall prediction (Menant et al., 2014). Although spatiotemporal data may provide sensitivity to identify differences, a more recent study showed no spatiotemporal differences between cognitively intact older adults classified as fallers and non-fallers over single- or dual-task walking (Freire Júnior et al., 2017). However, dual task paradigm still appears to interrupt locomotor control during walking. Speed differences and stride-to-stride variability are present in those with mild cognitive impairment when compared to cognitively intact older adults across dual task difficulties (Montero-Odasso, Muir, et al., 2012). In older adults, differences in spatiotemporal measures

and kinematic properties of the lower limb are different between difficult dual tasks; such that, there is an increase in the variability of hip and knee angular velocities (Piche et al., 2022). Even younger healthy controls exhibit decreases in inter-joint segmental control and deviations in the stance and swing phases during dual-task walking (Wang et al., 2021). Differences in joint angles during dual-task walking are also present in people with Parkinson's disease who experience freezing of gait (Pinto et al., 2020) but little research has explored changes to accelerometry kinematics during dual-task walking in a range of neurodegenerative disease cohorts.

Study 1 of this thesis confirmed the ability of a finite state machine to detect stepping using uniaxial acceleration collected from wearable sensors worn at the ankle in clinical walking tasks with varying difficulty in a cohort of people living with neurodegenerative disease or cerebrovascular disease. The focus of study 2 is to compare FSM gait outcomes against pressure sensor outputs and to describe walking performance using temporal and acceleration kinematics from wearable devices recorded by an ankle worn triaxial accelerometer (e.g. timing of gait sub-phase and acceleration metrics) during short clinical walking tasks ranging in difficulty and in people living with neurodegenerative disease (e.g., ADMCI, PD, CbVD (+/- CI), and FTD). There are three main objectives of this study:

- 1) Examine the association of conventional temporal measures (e.g., swing time, cycle time) between FSM output parameters and outputs from a pressure sensor mat.

H1: It is hypothesized temporal measures will be strongly associated between accelerometer- and pressure sensor- data.

- 2) Explore the relationship between stride velocity (measured by the pressure sensor mat) with accelerometry kinematics (e.g., push-off slope, peak swing phase acceleration).

H2: It is hypothesized that accelerometry kinematics will have a moderate to strong relationship with stride and gait velocity and that the peak-swing acceleration magnitude

will have the highest association with velocity outcomes compared to other accelerometry measures.

3) Assess the effect of secondary cognitive tasks on the conventional (e.g., velocity and temporal parameters) and accelerometer-based (e.g., outcomes from FSM algorithm) outcomes to describe gait performance.

H3a: It is hypothesized that the secondary cognitive task will cause gait velocity to decrease and cycle time to increase in response to increases in task difficulty.

H3b: It is hypothesized that accelerometer-based outcomes from the FSM will change in response to the addition of difficult secondary cognitive tasks, it is expected that the value with the highest association with gait velocity will be most sensitive to change with the addition of cognitive tasks.

5.2 Methods

5.2.1 Study Design

This study is a cross-sectional analysis of baseline data collected part of the Gait and Balance platform in the ONDRI Longitudinal Study. For validation of gait outcomes, data collected from three specific sites, London Health Science Centre (LHS), Parkwood Health Institute (PKH), and Sunnybrook Health Science Centre (SBH) were used because of the availability of GAITRite® pressure sensor mats (CIR Systems Inc., Franklin, NJ). To assess the effect of dual task walking, all sites were included in the study.

5.2.2 Participants

A total of 520 participants were enrolled in the longitudinal ONDRI study and included in the gait and balance data collection. For this study, participants with a diagnosis of Alzheimer's Disease and Mild Cognitive Impairment (ADMCI; n=126), Frontotemporal Lobar Degeneration (FTD; n=50), Parkinson's Disease (PD; n=140), and Cerebrovascular Disease with and without cognitive impairment (CbVD;

n=160) were included. The ALS cohort was excluded from this study because enrollment numbers and accelerometer data availability (<57%) was low for baseline visits. This study was performed in line with the principles of the Declaration of Helsinki.

A sub-group of the total cohort was used for algorithm comparison with pressure sensor outcomes, 199 total participants enrolled at LHS (n=44), SBH (n=41), and PKH (n=114) for baseline data collections. These participants included: ADMCI (n=43), FTD (n=31), PD (n=47), and CbVD (n=54).

5.2.4 Data collection and analysis

Data was collected at the different collection sites apart of the ONDRI study outlined in [Chapter 3](#).

GAITRite® data was processed on site as described in [Chapter 3](#) of this thesis by trained research staff and GAITRite® outcome files were saved for further processing and stride alignment. Accelerometer data processing underwent the same data processing as described in [Chapter 4](#). The Finite State Machine algorithm was adapted to meet the collection parameters and a temporally scaled push-off detection window was created (due to different sample frequencies between studies). Further processing was done using python programming language (Python v3.9) as described below.

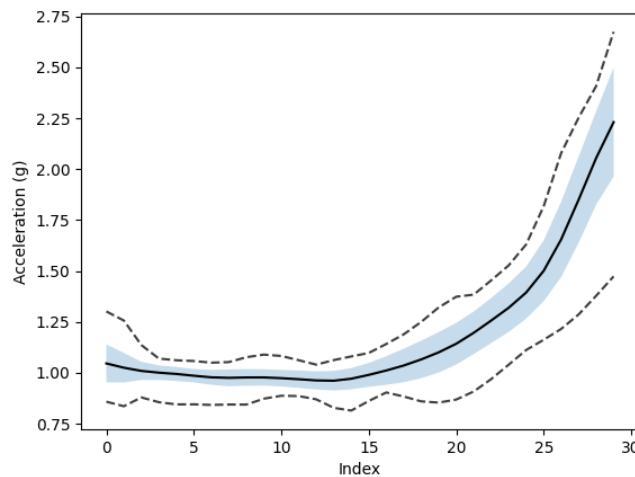


Figure 5-1. Template push-off slope used to detect the potential push off locations in acceleration data.

In addition to minor adjustments to the collection parameters within the algorithm two additional states were added to the FSM: State E: *Flat foot detection*, State F: *Heel off/heel rise* detection (note original states: State A: *Push-off/ pre-swing detection*, State B: *Swing phase peak detection*, State C: *Foot-contact/heel strike detection*, State D: *Stance phase/midstance/time delay*).

- D. *Flat foot detection*: The start of the flat foot phase begins at the identified heel strike (State C). The flat foot search window includes the heel strike index and the next 0.5 seconds of accelerometer data. A rolling standard deviation, window length of three data points, is created from the search window. Standard deviations values are then Z-scored (Scipy, Python, v3.9) and first three consecutive z-scores under the mean (less than zero) are identified, with the first of these three indices labelled as the flat foot point.
- E. *Heel off/heel rise*: Detecting the heel rise uses a similar approach to detecting the flat foot instances. Heel rise detection occurs after the detection of States A-D in the original and begins at every identified end-push off peak (the peak at the end of State A). The heel rise search window includes the end-push off peak and the previous 0.5 seconds of accelerometer data. A rolling window (three datapoints) calculates the standard deviation of the acceleration data. The standard deviation data is z-scored and the algorithm searches for the first value that crosses from negative to positive z-scores (crosses zero), this first value that cross the threshold is identified as the heel-off moment in the stance phase.

Timeseries accelerometer data recorded during walking was segmented into their respective sub-phases (A: Pre-swing/push-off phase, B: Swing phase/peak acceleration, C: Initial contact, D: Stance phase, E: Flat foot, F: Heel off/rise) using the FSM algorithm. All clinical gait trials were visually inspected for accuracy and inaccuracies were manually corrected. Instances where state or cycle definition were questionable the trial was removed from analysis. The temporal description of the

individual sub-phases was output from this analysis as a description of the intra-stride phases and the full gait cycle was reconstructed from these intra-stride phases.

Temporal variables

Mean stride time was calculated as the average between left and right strides. Stride time was defined as the time between the end of push-off phases between consecutive strides. Temporal variability was represented with the standard deviation (SD) of all strides. The standard deviation is the preferred measure of variability when increases in SD are not proportional to the within subject mean values (Moe-Nilssen et al., 2010) however coefficient of variation should be used if the SD is proportional to the within subject mean (Thingstad et al., 2015). Swing time was calculated as an approximate swing period based on inflection points within the accelerometer data. Swing time was defined as the time between the end of State A (end-push off peak) and State C (heel strike), which encompasses a negative and positive slope surrounding the mid-swing peak (State B).

Accelerometry-derived outcomes

The sum vector magnitude (SVM) of the triaxial accelerometer was calculated to represent the kinematic movement of the lower limb during walking. The SVM is needed to overcome the logistical assumptions of sensor placement and inaccurate orientation estimations with accelerometer data. There were three different accelerometer magnitudes output for analysis:

- *Push-off slope*: The push-off slope was calculated as the slope between the detect heel off point (State F) and the end of the push-off phase (end of State A). This slope was calculated as a linear slope between these two points to approximate the steepness or rate of change of heel-rise during push-off.
- *End push-off peak*: The end of the push-off (end of State A) accelerometer magnitude was extracted to represent the acceleration of the limb at toe-off or immediately prior to toe-off.

- *Mid-swing peak*: The detection of State B, mid-swing peak, was extracted as a representation of the movement of the limb through swing phase.

These outcomes were selected to investigate the relationship between sum vector magnitude acceleration with gait velocity as they were considered biomechanically important features that may be linked to control of gait velocity. Gait speed from accelerometers attached to the ankle (with the combination of gyroscopes) is commonly reported but requires gyroscope data for orientation estimates and relies on zero-velocity updates to avoid integration drift. Variability of stride velocity and stride time will be an important relationship to examine as these measures can influence spatiotemporal and variability outcomes in gait performance.

Matching Accelerometer and GAITRite Strides

The accelerometers used in this protocol collected stride data prior to stepping onto the GAITRite® mat, unfortunately there was no synchronization between GAITRite and accelerometer data. An initial analysis step was to identify the strides within the accelerometer data that aligned with the strides that fell onto the GAITRite mat. For each participant, the number of strides reported by the GAITRite software was used to create a window length for stride alignment. A sliding window, with a length that matched the GAITRite stride number, was used to calculate mean stride time across the strides output from the accelerometer. The window of strides that was used to represent the aligned accelerometer strides was the window that had the minimum mean stride time differences between accelerometer and GAITRite for that participant and trial.

5.3.5 Statistical Analysis

Statistical analysis was completed using Pingouin statistical package (Vallat, 2018) and statsmodels (v0.14.3) (Seabold & Perktold, 2010) in python programming language. Data were inspected for normality using Q-Q plots and statistically tested using the Kolmogorov-Smirnov test because the sample size is greater than 30. If normality was violated data was treated in two ways. For correlational analysis

non-parametric testing (spearman correlation) was used and to compare means, data was rank transformed and parametric statistical tests were used.

Correlational analysis was used to examine the association of temporal stride characteristics between FSM analytics and GAITRite® outcomes. Correlations were conducted on walking tasks separately to examine the effects of task difficulty on the association between measurements. Error analysis was used to explore the differences between the FSM and GAITRite temporal characteristics, such that positive errors showed FSM underestimating the temporal outcomes and negative values show overestimations of temporal outcomes. Bland-Altman plots were used to visualize and examine this error for accuracy (Giavarina, 2015). Analysis of variance (ANOVA) was used to compare error magnitude across the different task difficulties. Pairwise comparisons were used to understand task differences and a Bonferroni-Holm correction was used for multiple comparisons. Significance was set to $p < 0.05$.

To examine the relationships between gait velocity and accelerometry-derived outcomes correlational and regression analysis was used. Linear mixed model regression was used to examine the relationship between gait velocity and accelerometer outcomes. Linear mixed models predicted gait velocity outcomes from regression models using all accelerometer peaks and error between the predicted and GAITRite reported velocities. Beyond mean level outcomes, stride level velocities were compared with stride level accelerometry-outcomes. Partial correlations, with task used as a repeated measure, were used to examine the associations between stride level velocities.

To evaluate the effect of walking task (e.g., single- and dual-task walking) on velocity, temporal, and accelerometry-derived outcomes, a repeated measures analysis of variance (ANOVA) with within-subjects factor (tasks) was used to compare gait velocity and temporal outcomes measures across task difficulty. To examine whether differences between accelerometry-derived outcomes while considering velocity and subject as covariates, a linear mixed model was used to predict accelerometry-derived outcomes with these two variables as covariates. Predicted outcomes were compared using a repeated measures analysis of variance. Pairwise comparisons were used to examine the differences between tasks

when main effects were statistically significant. Statistical significance level was 0.05 for all statistical tests, where necessary Bonferroni-Holm corrections were used for multiple comparisons.

5.4 Results

5.4.2 Participants & Data Availability

Participants & Data for Validation purposes

Of the total 199 participants, 171 completed some or all of the gait and balance collection. After data processing, cleaning, and outlier detection (Sunderland et al., 2019) there were 136 participants with both acceleration and GAITRite data available for at least one dual task and one preferred walking trial. Some reasons for removal result from ONDRI outlier analysis and 8 participants had errors during FSM processing resulting in discard. Data that was discarded typically had acceleration profiles during walking that did not represent cyclical nature of the gait cycle (e.g., large deviations in magnitude or timing of the cycle that did not represent walking). From the 136 participants there were a total of 800 trials with valid accelerometer and GAITRite data across the three preferred walking trials (P1, P2, P3), walking while counting backwards ones (DT-S1s), walking while listing animal names (DT-An), and walking while counting backwards by sevens (DT-S7s). The number of tasks in each condition are as follows: P1:136, P2:136, P3:135, DT-S1:134, DT-An:131, DT-S7:128.

Table 5-1: Participant demographic details (GAITRite & Accelerometers).

	NDD and CbVD <i>Mean (SD)^c</i>	ADMCi	FTD	PD	CbVD
n	136	32	18	40	46
Sex (% female)	29.4%	34.3%	33.3%	27.5%	26.1%
Age (SD)	69.7 (7.1)	71.8 (8.2)	68.2 (7.1)	69.8 (6.2)	68.7 (6.8)
Height (cm)	172.9 (10.3)	173.6 (10.2)	169.3 (12.3)	175.6 (9.6)	171.5 (9.8)
Weight (kg)	82.5 (14.9) ^b	84.2 (15.3)	79.9 (17.5) ^a	80.7 (14.9) ^a	84 (13.7)
Gait aid use	18/136				
Fear of Falling*	1.9 (2.7)	1.3 (2.5)	3.4 (3.7)	2.2 (2.7)	1.4 (1.8)
ABC Scale[†] (/100)	87.8 (15.8)	93.7 (10.1)	75 (22.2)	82.7 (18.3)	93.3 (7.4)
MoCA (/30)	24.1 (3.3)	22.3 (2.7)	21 (3.3)	25.5 (2.4)	25.6 (3.1)

MoCA: Montreal Cognitive Assessment; ABC: Activities of Balance Confidence; ADMCI: Alzheimer's disease and mild cognitive impairment; PD: Parkinson's disease; FTD: Frontotemporal dementia; CVD: Cerebrovascular disease; ALS: Amyotrophic lateral sclerosis.

*Fear of falling: greater score indicates increased fear of falling; scored on 11 point Likert scale; FoF scores have 12 missing datapoints: ADMCI (3), PD (4), CbVD (5).

[†] Activities of Balance Confidence: greater score indicated more confidence in balance ability

Missing data: ^a one participant, ^b two participants

^c mean and standard deviation are shown where applicable

Participants & Accelerometer data for testing between tasks

There were 49 participants who were not part of the study after initial enrollment across all data collection sites, leaving 471/520 active participants available for gait and balance collection. For all data collection sites, 401 participants of the 520 participants (ADMCi: 99, FTD: 34, PD: 129, CVD/VCI: 139) had valid and useable accelerometer data (e.g., bilateral sensor data, successful sensor synchronization, confirmed walking identification). From these participants, there were a total of 2349 trials that were successfully processed with the FSM model: P1: 400, P2: 394, P3: 386, DT-S1: 398, DT-An: 391, DT-S7: 380. Important for regression models and gait velocity outcomes was to include a reference gait velocity metric and thus 2332 trials were matched with a summary gait velocity metric as part of the ONDRI data release and included within this study. Task breakdown for these trials is as follows: P1: 391; P2: 392; P3: 386; DT-S1: 397; DT-An: 397; DT-S7: 374.

Table 5-2: Participant demographic details (all accelerometers).

	NDD and CbVD <i>Mean (SD)^c</i>	ADMCi	FTD	PD	CbVD
n	401	99	34	129	139
Sex (% female)	30.2%	37.4%	35.3%	23.3%	30.2%
Age (SD)	69.1 (7.4)	71.1 (8.1)	68.2 (7.0)	67.9 (6.4)	69 (7.6)
Height (cm)	171.6 (9.7) ^a	170.8 (10.5)	169.2 (10.8)	173.5 (9.1) ^a	171.0 (9.2)
Weight (kg)	81.6 (16.2) ^c	77.9 (15.5)	81.0 (18.3) ^a	82.3 (17.2) ^a	83.9 (15.0) ^a
Gait aid use	54/401	17/99	9/34	9/129	19/139
Fear of Falling*	1.9 (2.6)	1.5 (2.5)	2.5 (3.2)	2.0 (2.4)	1.8 (2.6)
ABC Scale[†]	87.1 (15.6)	90.2 (14.2)	75.1 (25.4)	85.7 (15.2)	89.2 (12.1)
MoCA	24.5 (3.3)	22.7 (2.9)	21.2 (3.6)	25.9 (2.6)	25.3 (3.0)

MoCA: Montreal Cognitive Assessment; ABC: Activities of Balance Confidence; ADMCI: Alzheimer's disease and mild cognitive impairment; PD: Parkinson's disease; FTD: Frontotemporal dementia; CVD: Cerebrovascular disease; ALS: Amyotrophic lateral sclerosis.

*Fear of falling: greater score indicates increased fear of falling; scored on 11 point Likert scale; FoF scores have 44 missing datapoints: ADMCI (9), PD (20), CbVD (15).

[†] Activities of Balance Confidence: greater score indicated more confidence in balance ability

Missing data: ^a one participant, ^b two participants, ^c three participants

^c mean and standard deviation are shown where applicable

5.4.2 Temporal gait outcomes quantified using GAITRite and Finite State Machine methods

Conventional temporal outcomes (e.g., stride time, swing time, and temporal variability) were output for both the GAITRite® pressure sensor mat and the Finite State Machine analysis. FSM temporal outcomes were restricted to those steps that occurred within the GAITRite sensor field, mean level outcomes are described in Table 5-3 for all walking conditions.

Table 5-3: Temporal and error analysis outcomes between FSM and GAITRite outcomes.

Task	GAITRite					Finite State machine				# of matche d steps	Mean Error	
	Velocit y (m/s)	Cycle time		Swing time		Cycle time		Swing time			Cycle time (SD)	Swing Time (SD)
		mean	SD	mean	SD	mean	SD	mean	SD			
P	1.04	1.17	0.03	0.41	0.02	1.19	0.04	0.47	0.07	7.03 (1.94)	-0.012 (0.06)	-0.064 (0.044)
P2	1.08	1.15	0.02	0.40	0.02	1.16	0.04	0.47	0.07	6.79 (1.90)	-0.007 (0.027)	-0.063 (0.042)
P3	1.09	1.14	0.03	0.40	0.02	1.15	0.04	0.46	0.07	6.77 (1.95)	-0.007 (0.029)	-0.06 (0.043)
DT-S1	0.99	1.24	0.04	0.49	0.02	1.25	0.06	0.49	0.08	6.99 (2.11)	-0.009 (0.10)	-0.060 (0.044)
DT-An	0.91	1.31	0.07	0.43	0.04	1.31	0.08	0.50	0.09	7.49 (2.53)	-0.009 (0.11)	-0.053 (0.064)
DT-S7	0.88	1.37	0.09	0.46	0.04	1.38	0.10	0.51	0.09	7.66 (2.66)	-0.007 (0.057)	-0.056 (0.073)

5.4.2 Association between temporal outcomes between Finite State Machine and GAITRite

A series of spearman correlations were run for each walking task to assess temporal outcomes (mean cycle and swing time) and the associated variability (standard deviation) between the two measurement methods. The correlation analysis revealed significant positive associations ($p < 0.001$) for mean cycle time between the two methods for all tasks (Figure 5-1). The highest correlation was during DT-An ($\rho(134)=0.98$, $CI95\%=(0.97-0.98)$, $p < 0.001$) and the lowest correlation was during the first preferred walking task (P1: $\rho(136)=0.91$, $CI95\%=(0.87-0.93)$, $p < 0.001$). There was a positive moderate-strong relationship between mean swing time when comparing the two methods, with the strongest correlation occurring during DT-S1 ($\rho(134)=0.73$, $CI95\%=(0.64-0.8)$, $p < 0.001$) and the lowest during the third preferred trial (P3: $\rho(135)=0.52$, $CI95\%=(0.39-0.63)$, $p < 0.001$). These strong correlation values for the temporal measures of gait suggest the finite state machine can segment the stride consistently and characterize mean temporal gait measures similarly to the reference system (GAITRite). Spearman correlation analysis were also completed for the variability measures of both cycle time and swing time to compare variability outcomes between the FSM model and the reference system (GAITRite). Cycle time standard deviations relationships were positive and ranged from statistically significant moderate during DT-An ($\rho(128)=0.74$, $CI95\%=(0.65-0.81)$, $p < 0.001$) to lower moderate relationships in P3 ($\rho(135)=0.49$, $CI95\%=(0.35-0.61)$, $p < 0.001$). Relationships for swing time standard deviations were also positive and ranged from moderate during DT-An ($\rho(131)=0.58$, $CI95\%=(0.45-0.68)$, $p < 0.001$) to weak in P2 ($\rho(136)=0.23$, $CI95\%=(0.07-0.39)$, $p=0.006$). All significant relationships between variability measures reported power > 0.78 . Correlation analysis of the temporal variability outcomes between methods had generally less strength compared to mean level outcomes for both cycle time and swing time variability but relationships remained positive with no clear factor or difference in relationship due to task difficulty or under preferred conditions.

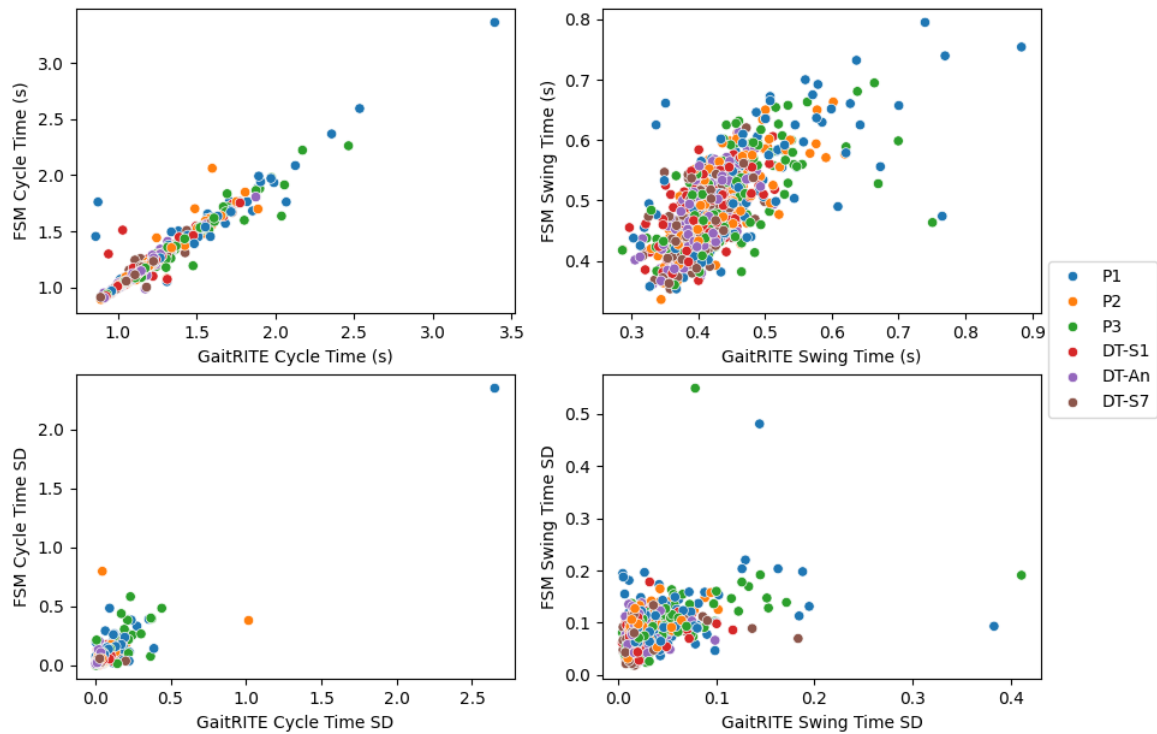


Figure 5-2. Scatterplots for temporal outcomes from the Finite State Machine (*vertical axis*) compared to the reference GAITRite® system (*horizontal axis*). Cycle time and cycle time variability (*sd*) are plotted on the top and bottom left respectively and swing time and swing time variability are plotted on the top and bottom right, respectively. Each plotted point represents a single trial and participant.

5.4.3 Reported differences in mean temporal values between FSM and GAITRite methods

For mean cycle time measures, grand average differences between the GAITRite and FSM time outputs was -0.005 seconds across all tasks, with all but P1 reporting less than 10 ms in temporal difference.

Grand average differences between GAITRite and FSM swing time was -0.059 s across all tasks.

Differences between mean level temporal outcomes were minimal across measures and tasks (<0.01 seconds). Overall, differences between methods show the finite state machine has a slight bias to over

estimate the temporal measures of gait across all tasks when compared to the pressure sensor mat. Visual representation of accuracy is seen in Bland-Altman plots (Figure 5-2).

The effect of task on error magnitude was examined using a repeated measures ANOVA. Differences between methods were not normally distributed ($p < 0.05$), data were rank transformed and ranked data were input to the repeated measure ANOVA model and paired-sample t-tests were used to examine main effects. A main effect was found across tasks for mean cycle time ($F(5,620) = 2.52$, $p_{gg} = 0.03$, $np^2 = 0.02$). Post-hoc analysis revealed no significant differences between error magnitudes across the different walking tasks ($p > 0.05$) (Figure 5-2). There were no statistical main effects of task when testing swing time error ($F(5,620) = 1.60$, $p_{gg} = 0.175$, $np^2 = 0.012$).

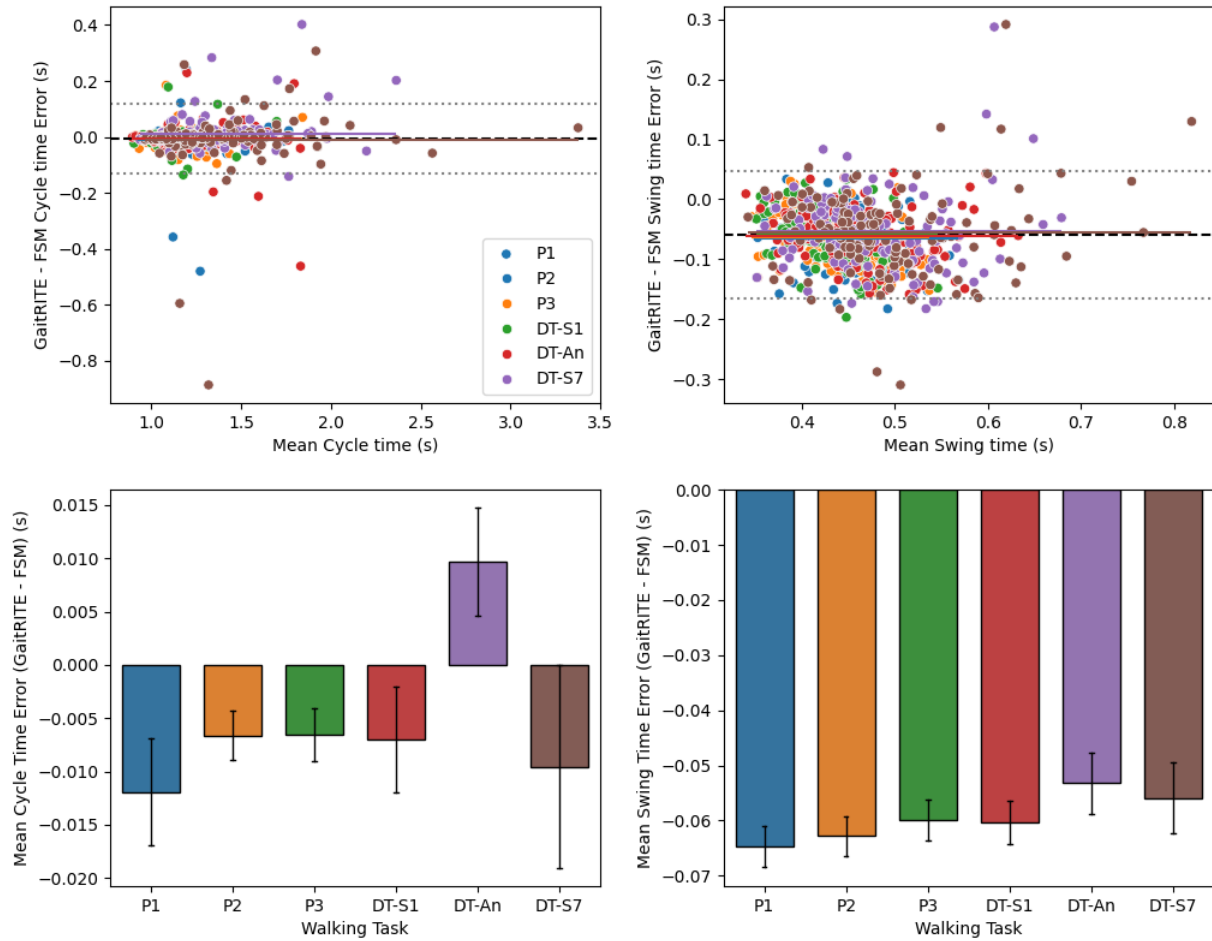


Figure 5-3. Bland-Altman plots (top) compare the difference between the GAITRite and FSM cycle times (y-axis) against the mean of GAITRite and FSM cycle times as a reference value (x-axis). Bland-Altman plots show individual task means as well as overall all mean error (black dashed) and confidence intervals (grey dotted). Bar graphs (bottom row) shows the average error between GAITRite and FSM temporal cycle times (bottom-left) and swing times (bottom-right) across all walking tasks with standard deviation error bars.

5.4.5 Associations between gait velocity and mean spatial outcomes from the FSM model

Spearman correlation analysis was used to determine the association between the kinematic accelerometer outcomes from the finite state machine with gait velocity reported from the GAITRite software. At the mean level, the mid-swing peak acceleration (the transition between swing down and swing up states) had the strongest associations (across tasks) when compared to mean stride velocity, followed by the acceleration slope during the push-off phase and the peak acceleration at the end of push-off. Mid swing peak acceleration: Within the mid-swing peak associations all task correlations were

statistically significant ($p < 0.05$) with strong to moderate positive associations. Between tasks the DT-An reported the strongest association ($\rho(131) = 0.742$, $CI_{95\%} = (0.65-0.81)$, $p < 0.001$) while all three preferred trials had lower association strengths in comparison (preferred rho values were 0.67, 0.60, 0.56 for P1, P2, P3 respectively). For this acceleration peak, larger acceleration magnitudes at this instant in the gait cycle are associated with the higher gait velocity during these different walking conditions. Interestingly, the three preferred trials showed modestly lower correlation strengths compared to dual task walking. End push-off peak acceleration: Across all walking tasks, the peak acceleration along vertical axis at the beginning of swing phase (transition between State A and State B) had statistically significant moderate positive associations with mean gait velocity. Across tasks the third preferred trial reported the highest strength correlation ($\rho(135) = 0.627$, $CI_{95\%} = (0.51-0.72)$, $p < 0.001$) and the lowest strength correlations was reported during the DT-S7 task ($\rho(128) = 0.471$, $CI_{95\%} = (0.32-0.60)$, $p < 0.001$). The peak acceleration of the limb at the beginning of swing phase (terminal stance) had a positive association, therefore the larger peak acceleration values were associated with higher gait velocity during these walking conditions. No clear association difference existed between the preferred and dual task conditions for gait velocity and this peak during walking. Push-off acceleration slope: For all walking tasks, the mean push-off slopes of the acceleration during the push-off state had statistically significant moderate to strong positive associations with mean gait velocity. Between tasks, the association was strongest during DT-S1 ($\rho(134) = 0.676$, $CI_{95\%} = (0.57-0.76)$, $p < 0.001$) and the lowest correlation values occurred during the preferred trials (rho was 0.556, 0.494, 0.443 for P1, P2, P3 respectively). The positive association between the acceleration slope during push-off compared to gait velocity shows that larger magnitude push-off slopes (steeper slope) are associated with higher reported gait velocities during walking. Similar to the peak mid swing acceleration value, the dual task conditions had stronger associations with the gait velocity compared to the moderately associated preferred walking trials.

Table 5-4: Gait velocity and accelerometry-derived kinematic mean outcomes across all tasks.

Task	n	Gait Velocity (m/s (SD))	Finite State Machine Outcomes (mean (SD))		
			Push-off Slope (<i>State A Slope, g/s</i>)	Mid-Swing Peak (<i>State B-C Transition, g</i>)	Peak at Push-off (<i>State A-B Transition, g</i>)
P	136	1.04 (0.23)	1.944 (0.622)	0.417 (0.093)	0.063 (0.022)
P2	136	1.08 (0.23)	2.021 (0.601)	0.427 (0.088)	0.065 (0.023)
P3	135	1.09 (0.23)	2.033 (0.601)	0.435 (0.091)	0.067 (0.024)
DT-S1	134	0.99 (0.25)	1.835 (0.714)	0.408 (0.098)	0.062 (0.023)
DT-An	131	0.91 (0.26)	1.702 (0.711)	0.377 (0.100)	0.060 (0.022)
DT-S7	128	0.88 (0.28)	1.557 (0.731)	0.387 (0.096)	0.058 (0.022)

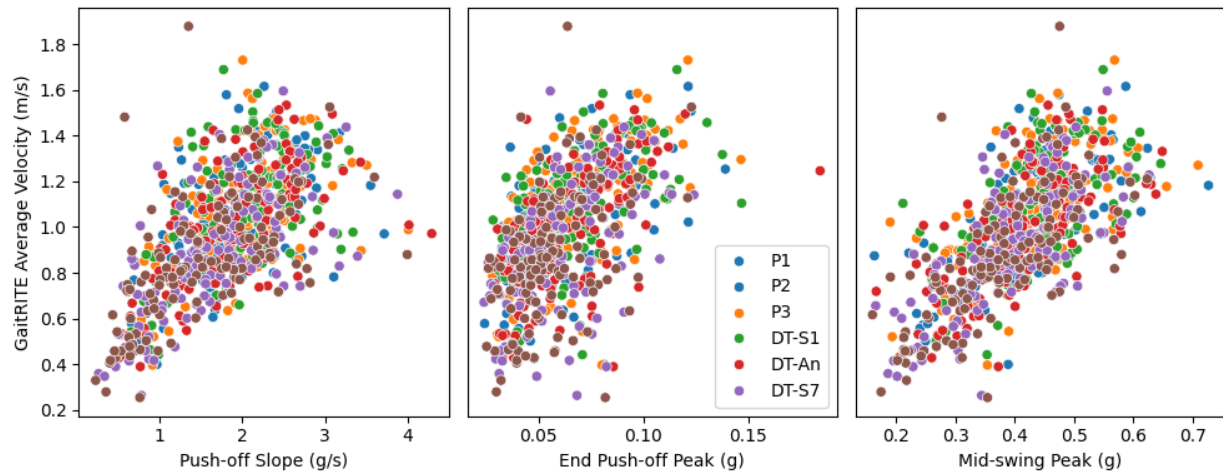


Figure 5-4. Scatterplots showing the relationships between comparing GAITRite average velocity with each accelerometer-derived outcome.

Partial spearman correlations were used to assess the stride-to-stride relationship between acceleration kinematics with stride velocity outcomes from the GAITRite mat while including individual subjects as a covariate. Partial correlation outcomes are listed in Table 5-5. When controlling for subject, all tasks and all accelerometer kinematic outcomes were significantly related to their matched stride velocities ($p < 0.05$). Partial correlations were weak to moderately positive with rho values ranging from 0.35-0.68. Positive correlations suggest that larger accelerometer kinematic values correspond with faster stride velocity outcome measures. Partial correlations for peak acceleration at start of swing phase had generally lower partial correlation strength compared to the push-off slope and the mid swing peak acceleration when compared with stride velocities.

Table 5-5: Partial correlation results for stride-to-stride accelerometry kinematics and stride velocity outcome from GAITRite mat across all walking tasks.

Task	n	Push-off Slope (<i>State A Slope</i>) rho (CI)	Mid-Swing Peak (<i>State B-C Transition</i>) rho (CI)	Peak at Push-off (<i>State A-B Transition</i>) rho (CI)
P	807	0.535 (0.48-0.58)	0.622 (0.58-0.66)	0.429 (0.37-0.48)
P2	784	0.509 (0.46-0.56)	0.594 (0.55-0.64)	0.477 (0.42-0.53)
P3	774	0.478 (0.42-0.53)	0.566 (0.52-0.61)	0.500 (0.45-0.55)
DT-S1	787	0.602 (0.56-0.65)	0.653 (0.61-0.69)	0.437 (0.38-0.49)
DT-An	819	0.553 (0.50-0.60)	0.621 (0.58-0.66)	0.399 (0.34-0.46)
DT-S7	821	0.676 (0.64-0.71)	0.683 (0.64-0.72)	0.346 (0.29-0.41)

5.4.6 Predicating gait velocity from FSM Acceleration Kinematic outcomes and associated error

To determine if gait velocity could be predicted from the accelerometer kinematics at specific finite state periods, a linear mixed model was used to predict gait velocity from accelerometer kinematic outcomes across subjects. The model included 800 inputs from 136 groups (individual subjects) and was statistically significant ($F(5,795)=404.32$, $p<0.0001$). The model reported marginal $r^2=0.543$ and conditional $r^2=0.860$. Predicted gait velocity outcomes from the regression model had an overall gait velocity 0.9962 m/s were slightly higher than the overall GAITRite mat stride velocity average of 0.9959 m/s. Individual task averages and error are shown in Table 5-6.

Table 5-6: Predicted gait velocity outcomes from regression model.

Task	n	GAITRite gait velocity (m/s $\pm$ SD)	Predicted gait velocity (m/s $\pm$ SD)	Error (m/s $\pm$ SD)
P	136	1.04 (0.23)	1.01 (0.18)	0.016 (0.17)
P2	136	1.08 (0.23)	1.04 (0.17)	0.033 (0.17)
P3	135	1.09 (0.23)	1.05 (0.17)	0.036 (0.17)
DT-S1	134	0.98 (0.25)	0.99 (0.20)	-0.006 (0.16)
DT-An	131	0.91 (0.26)	0.94 (0.20)	-0.041 (0.18)
DT-S7	128	0.88 (0.28)	0.91 (0.21)	-0.041 (0.19)

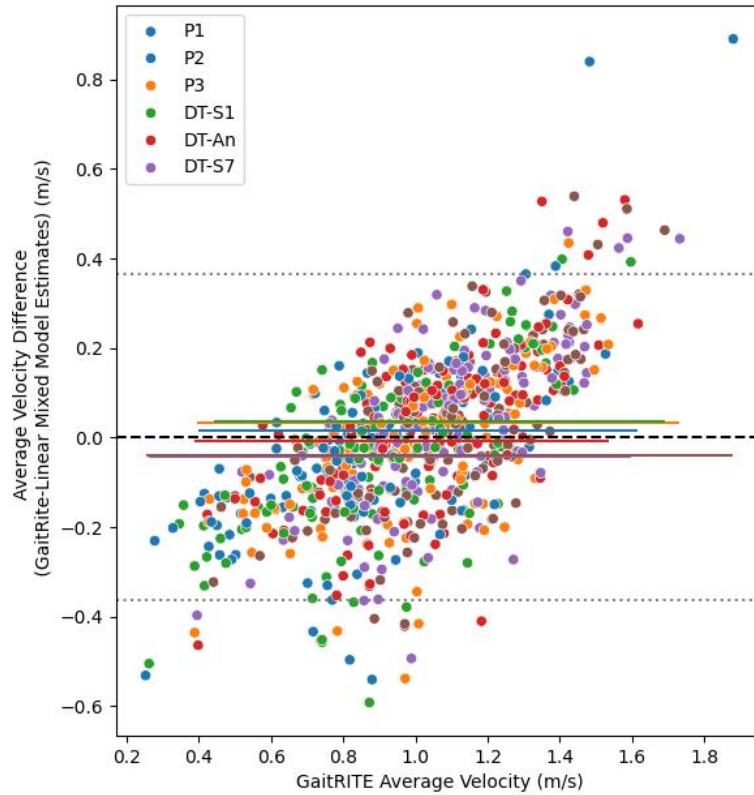


Figure 5-5. Bland-Altman plot showing the difference between the GAITRite and Predicted mean gait velocity outcomes compared to the GAITRite velocity reference value.

5.4.4 The effect of task difficulty on velocity and temporal gait outcomes

Repeated measures ANOVAs were used to compare gait outcome measures (FSM derived temporal and spatial outcomes) across walking tasks (single and dual task walking). Due to the significant associations between temporal, spatial, and accelerometry kinematic outcome measures, data was modelled using a linear mixed model regression with reported gait speed as a covariate. All predicted mean outcomes were not normally distributed ($p < 0.05$), therefore a rank transform was used to normalize the data prior to using a parametric one-way repeated measures ANOVA.

Gait velocity

Gait velocity was compared across all tasks and a main effect of task was determined ($F(5,1770)=250.31$, $p_{gg}<0.001$, $\eta^2=0.414$). Post-hoc analysis revealed that in general all the preferred walking tasks were faster than the dual task walking conditions ($p<0.05$). Furthermore, as secondary cognitive tasks became more difficult (DT-S1 < DT-An < DT-S7) the walking speed decreased significantly (DT-S1: mean (SD) = 0.822 (0.26) m/s; DT-An: 0.756 (0.25) m/s; DT-S7: 0.712 (0.25) m/s, $p<0.001$). Interestingly, P1 (mean (SD) = 0.904 (0.26) m/s) was significantly slower than both P2 (mean (SD) = 0.927 (0.25) m/s, $t(354)=-3.746$, $p<0.001$, $d=-0.096$) and P3 (mean (SD) = 0.941 (0.27) m/s, $t(354)=-4.525$, $p<0.001$, $d=-0.123$) preferred trials and no difference existed between the P2 and P3 trials ($p=0.296$). These gait velocity outcomes indicate that as participants become acclimated to the clinical gait task (at baseline) they walk faster as they completed preferred walking trials (three total) as the second and third trials were faster than the first trial. These outcomes also indicate that dual tasks influenced walking speed, such that when participants completed dual task walking, they walked slower compared to preferred walking trials. The effect of dual tasking also corresponded with task difficulty, as the secondary task become more difficult (DT-S1 < DT-An < DT-S7) the walking velocity decreased.

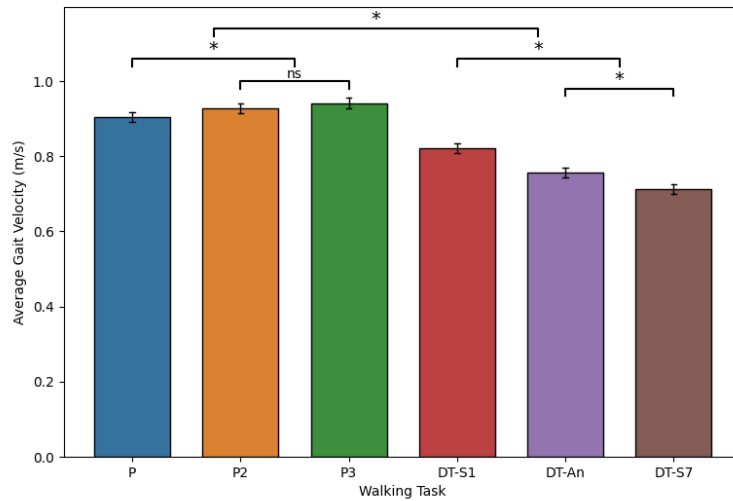


Figure 5-6. Bar plot comparing the differences in gait velocity across difference tasks. * indicates statistical difference ($p < 0.05$) between clinical gait tasks.

Cycle time and cycle time variability:

A repeated measures ANOVA was conducted to compare across walking tasks to determine the effect of dual task walking on cycle time and cycle time variability output by the finite state machine. The ANOVA output showed a main effect of walking task for cycle time ($F(5,1770)=40.033$, $p_{gg} < 0.001$, $np^2=0.472$). Adjusted and ranked cycle times were different between all tasks ($p < 0.01$) except for between DT-S7 compared to DT-An and P1 compared to P3. The significant differences show that cycle time is different between preferred walking tasks and influenced by secondary cognitive tasks during dual task walking. Cycle times are longer in the first preferred walking but not different between the second and third preferred walking task supporting similar familiarization periods previously reported velocity differences. Dual task walking largely had an overall effect on cycle time averages compared to preferred walking and when tasks increased in difficulty cycle times were longer. The variability of cycle time was compared across task difficulty using a repeated measures ANOVA and revealed a significant main effect of task ($F(5,1770)=12.929$, $p_{gg} < 0.001$, $np^2=0.035$). Pairwise comparisons revealed differences between trials when variability was adjusted for gait velocity. Between the preferred tasks, P2 was different from P1 ($t(354)=-4.79$, $p < 0.001$, $d=-0.316$) and P3 ($t(354)=3.12$, $p=0.001$, $d=0.193$). All comparisons between

dual task walking conditions were different ($p<0.05$) with increasing variability as secondary tasks became more difficult. Significant differences between dual task and preferred trials existed with three exceptions, DT-S7 was not different from P2 and DT-An was not different from P or P3. The effect of cognitive secondary tasks on cycle time variability is evident for the most difficult task, which causes a statistically significant increase in cycle time variability compared to single task and less complex dual task walking conditions.

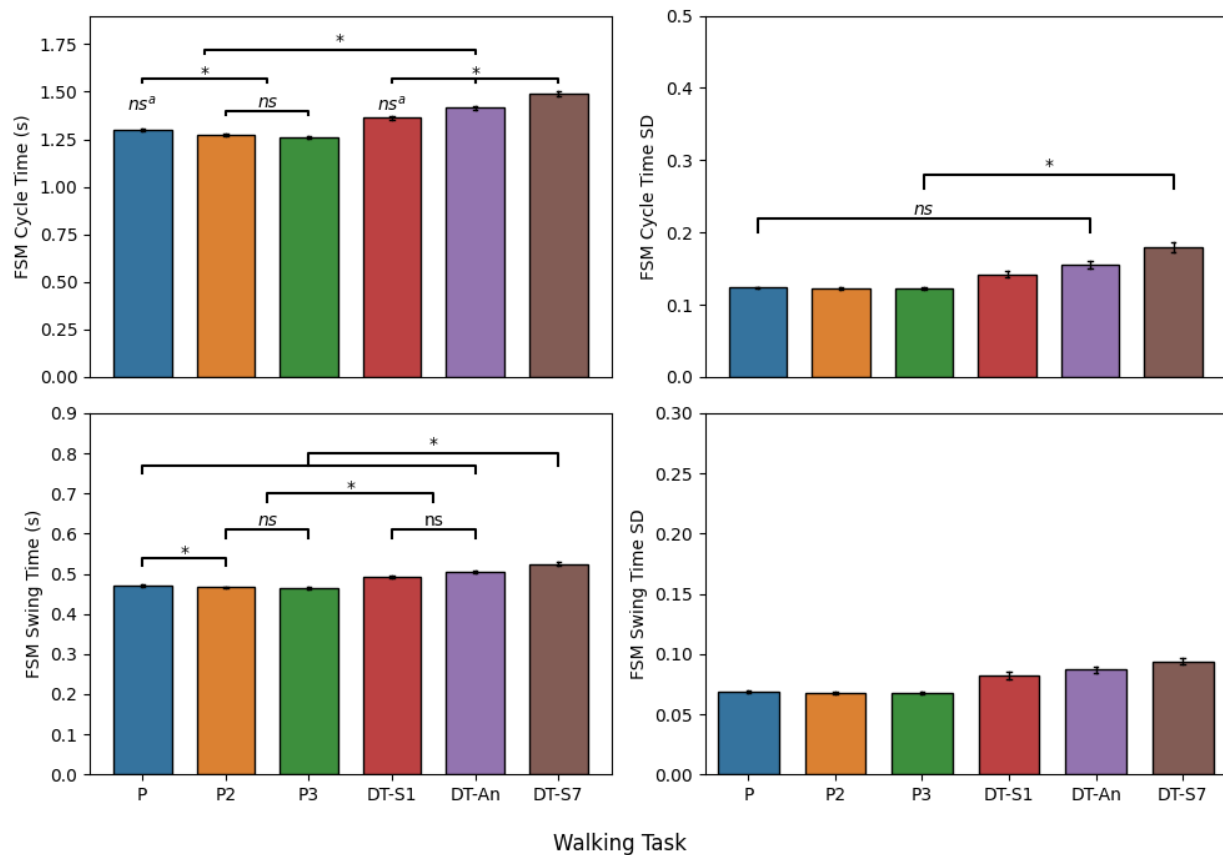


Figure 5-7. Bar plot comparing the differences in finite state machine calculated cycle time and cycle time variability (top) and swing time and swing time variability (bottom) across different tasks. * indicates statistical difference ($p<0.05$) between clinical gait tasks.

Swing time and swing time variability:

Repeated measures ANOVA revealed a significant main effect of task for mean swing times ($F(5, 1770)=21.366$, $p_{gg}<0.001$, $np^2=0.057$) and swing time variability ($F(5, 1770)=13.905$, $p_{gg}<0.001$,

$np^2=0.038$). Post-hoc pairwise comparisons showed mean swing time values were significantly longer during the P1 (mean (SD)=0.471 (0.05) s) when compared with P2 (mean (SD)=0.466 (0.05) s, $t(354)=4.349$, $p<0.001$, $d=0.249$) but not with P3 ($p>0.05$). There were no differences between P1, DT-S1 (mean (SD)=0.492 (0.065) s, $p>0.05$), or DT-An (mean (SD)=0.504 (0.07) s, $p>0.05$) but all three trials were significantly shorter than DT-S7 (mean (SD)=0.522 (0.087) s, $p<0.001$). The remaining preferred trials (P2 and P3) were different from all dual task conditions ($p<0.05$). There were some statistical differences between P1 and the other preferred trials that may be attributed to a learning effect during the first, albeit the magnitude of difference was minimal (<0.01 s). Although there was no difference between DT-S1 and DT-An, swing time generally increased with difficult secondary tasks. Swing time variability outcomes were significantly different between P1 and P2 ($t(354)=3.058$, $p=0.02$, $d=0.20$) and P3 was not significantly different from other the preferred trials ($p>0.05$). Dual task serial 7s swing time variability was different than DT-S1 (mean (SD)=0.082 (0.063), $t(354)=-4.376$, $p<0.001$, $d=-0.35$) and all the preferred trials ($p<0.001$). The results from these statistical tests revealed that swing time variability generally increased with dual task walking conditions. Swing time variability increased with more difficult cognitive tasks compared to less difficult cognitive tasks.

5.4.5 The effect of task difficulty on accelerometry gait outcomes

State A Slope (Push-off Acceleration Slope): Push-off acceleration slope was compared across walking tasks using repeated measures ANOVA design with gait velocity as a covariate. Rank transformed data was input into the ANOVA model and there was a significant main effect of task ($F(5,1770)=43.704$, $p<0.001$, $np^2=0.11$). Pairwise comparisons were used to determine the differences between tasks. The first preferred trial (P1: mean(SD)=0.419 (0.177) g/s) was significantly lower than P2(mean(SD)=0.485 (0.183) g/s, $t(354)=-6.42$, $p<0.001$, $d=-0.45$) and P3 (mean(SD)=0.5 (0.19) g/s, $t(354)=-6.24$, $p<0.001$, $d=-0.50$). The first preferred trial was not different from DT-S1 or DT-An ($p>0.05$) but was significantly larger than DT-S7 (mean(SD) = 0.301 (0.21) g/s, $t(354)=-6.293$, $p<0.001$, $d=-0.586$). Contrary to P1, P2 and P3 were significantly larger than all the dual task conditions ($p<0.001$). Between dual task walking

conditions, there was no statistical difference between DT-An and DT-S1 ($p>0.05$) and DT-S7 was significantly lower than both DT-S1 (mean(SD)=0.411 (0.19) g/s, $t(354)=7.662$, $p<0.001$, $np^2=0.557$) and DT-An (mean(SD)=0.389 (0.20) g/s, $t(354)=6.390$, $p<0.001$, $d=0.411$). Statistical results reveal the influence of task difficulty on the slope of State A within the finite state machine and the ability to identify gait changes from dual task walking using accelerometry kinematics. In this instance, there was difference in the preferred walking tasks, such that P1 was significantly lower than both P2 and P3. Further, during dual task walking, there is a statistical difference which shows more difficult dual task walking causes a decrease in the slope of acceleration generated during this phase.

End State A Magnitude (End push off peak): A main effect of task was found as a result of a repeated measures ANOVA for the end push off peak while controlling for gait velocity ($F(5,1770)=16.494$, $p_{gg}<0.001$, $np^2=0.044$). Statistically, all preferred trials were different from each other, P1 (mean(SD)=0.033 (0.008) g) was significantly lower than both P2 (mean(SD)=0.036 (0.01) g), $t(354)=-4.669$, $p<0.001$, $d=-0.315$) and P3 (mean(SD)=0.038 (0.009) g), $t(354)=-6.719$, $p<0.001$, $d=-0.512$) and P2 was significantly lower than P3 ($t(354)=-3.308$, $p<0.001$, $d=-0.008$). The first preferred trial was not different from any of the dual task trials but P2 was significantly higher than both DT-An and DT-S7 ($p<0.01$) and P3 was significantly higher than all three dual task trials ($p<0.001$). Differences between dual task conditions were not significant ($p>0.05$). Results show the influence of dual task compared to preferred walking, where preferred walking had larger peak acceleration magnitudes compared to dual task walking in most cases, particularly between the second and third trials and when walking with the more difficult cognitive tasks.

Mid-swing peak acceleration: A main effect of task was found as a result from the repeated measures ANOVA for mid-swing peak acceleration magnitude ($F(5,1770)=28.376$, $p<0.001$, $d=0.074$). Similar to previous outcomes, P1 (mean(SD)=0.237 (0.02) g) had statistically lower peak acceleration magnitude compared to the P2 (mean(SD)=0.244 (0.03) g, $t(354)=-3.974$, $p<0.001$, $d=-0.251$) and P3 (mean(SD)=0.246 (0.02), $t(354)=-4.279$, $p<0.001$, $d=-0.379$). The second and third preferred trials were

not different from each other ($p>0.05$), but these trials were statistically different from all dual task trials ($p<0.01$). The first preferred trial was not different from DT-S1 (mean(SD)=0.237 (0.02) g) or DT-An (mean(SD)=0.233 (0.02) g) ($p>0.05$) but was significantly higher than DT-S7 (mean(SD)=0.224 (0.03) g, $t(354)=-5.33$, $p<0.001$, $d=-0.487$). Dual task counting backwards by ones was not statistically different from DT-An ($p>0.05$) but was statistically larger than DT-S7 ($t(354)=5.722$, $p<0.001$, $d=0.447$) and there was a statistical difference between DT-An and DT-S7 ($t(354)=4.520$, $p<0.001$, $d=0.290$). Overall, there was an effect of the task on peak mid-swing acceleration magnitudes. Results showed preferred walking trials tended to have a greater push-off magnitude compared to the dual task walking and walking with more difficult secondary tasks tended to have lower peak push-offs compared to other tasks.

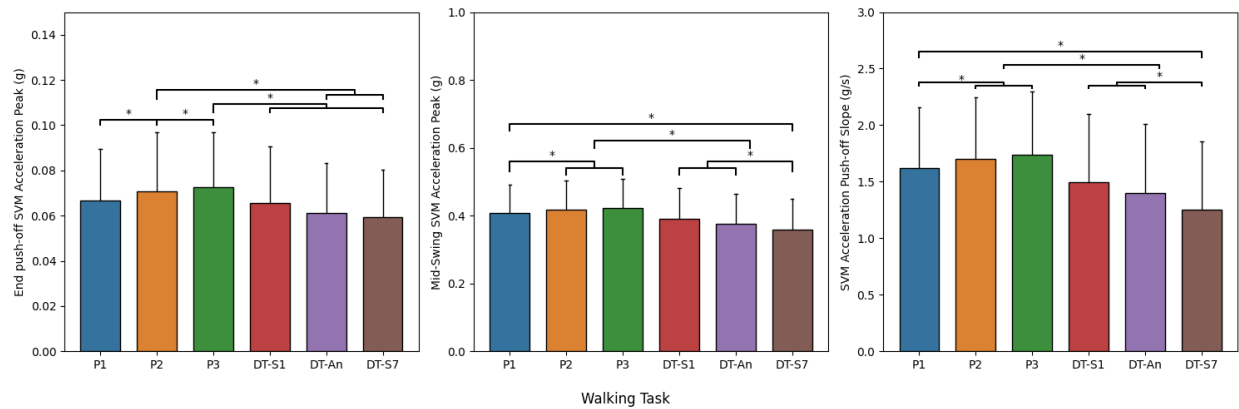


Figure 5-8. Bar plot comparing the differences in accelerometry derived outcomes across difference tasks. * indicates statistical difference ($p<0.05$) between clinical gait tasks.

5.5 Discussion

The main objective of this study was to determine if FSM algorithm was accurate for describing conventional gait performance metrics and to determine whether dual task walking caused significant changes to these gait metrics. The study results supported the first hypothesis and shows that temporal and accelerometry-based outcomes from the FSM are associated with conventionally reported gait metrics (e.g., mean stride time) when compared with GAITRite reporting. The FSM algorithm proves to be a reliable approach for segmenting strides while identifying unique accelerometry based kinematic features

that have relationships with gait velocity during overground walking. With respect to the second hypothesis, mean accelerometry outcomes (e.g., acceleration slope during push-off, mid-swing peak acceleration) had moderate-to-strong relationships with mean stride velocities from the matched GAITRite strides. Regression model predicted gait velocity with a mean error less than 0.05 m/s (predicted average speed: 99.62 cm/s; GAITRite average speed: 99.59 cm/s) but had increased error at the slower and faster velocities. These exceptions suggest that kinematic differences exist for walking speeds at the extremes compared to mean levels across all tasks and participants. These differences in kinematic magnitudes may be a results of gait impairments (e.g., symmetry) in the face of difficult dual tasks (Gillain et al., 2019). Regarding objective three, study results supported the hypothesis that conventionally reported gait outcomes change during dual task walking compared to single-task walking. Furthermore, study results show that accelerometry kinematics (e.g., push-off slope, mid-swing peak) are different during dual-task walking compared to single-task walking. The FSM temporal gait outcomes were different across dual task walking with a gradient response to increasing task difficulty. Increases in task difficulty were compensated with decreased gait velocity, increased cycle time, and increases in cycle time variability from FSM segmentation. Accelerometry-based kinematics also changed in response to the addition of dual task walking with lower accelerometer magnitudes and suggest novel insight into measuring lower limb kinematics with clinically practical tools during dual-task walking. This study builds on previous research utilizing finite state machine algorithms to describe temporal gait using single sensor worn unilaterally to describe cycle time and intra-stride segments (e.g., swing time) changes in the face of dual task walking. This further advances the utility of these algorithms to identify key kinematic features of limb trajectory control (changes in acceleration of the lower limb) with novel segmentation methods and identify key biomechanical events that also change in these conditions.

Finite state machine for gait segmentation and reporting conventional gait outcomes

Accurate calculation of conventionally reported gait outcomes are key to advancing analytical approaches for clinical gait assessment. This study expanded on algorithm framework in study 1, an

adapted version of a finite state machine for stride detection was tested across gait tasks of varying difficulty in NDD or CbVD cohorts. Cycle times between methods were strongly correlated ($\rho > 0.9$ for all tasks) and swing time outcomes were moderately associated across all tasks (lowest correlation $\rho = 0.52$). During preferred walking, FSM mean cycle times were between 1.19-1.38 seconds (min-max range: 0.91-1.81 sec), which are similar to other studies (mean range: 1.05-1.35 sec) that validated algorithm development in people with gait impairment during comfortable walking trials (Trojaniello, Cereatti, Pelosin, et al., 2014a). When strides were temporally matched, mean error was -0.005 s (absolute error = 0.008 s), reported error had similar magnitudes compared to a previous study (cycle time mean absolute error range = 0.01-0.013 sec) (Trojaniello, Cereatti, Pelosin, et al., 2014a). Temporal gait outcomes are influenced by severity of gait impairment and are closely related to gait velocity. The current study did not include healthy older adults and reported mean gait velocities ranges of 1.04-1.09 (range: 0.44-1.66) m/s during preferred walking compared to mean velocity ranges of 0.61-1.17m/s during comfortable walking in healthy older adults (Trojaniello, Cereatti, Pelosin, et al., 2014a). Differences between swing time were larger than cycle time error and reported a consistent bias in over-estimating the swing time length of 0.053 to 0.064 seconds compared to the reference. This larger difference is likely due to the definition of swing time within the FSM model, which is defined by intra-stride phases from inflection points within the vertical acceleration signal not discrete gait event detection. This study did a robust evaluation of the differences in temporal outcomes from the FSM model during complex dual task walking, confirming the FSM segments the gait cycle accurately across different clinical tasks. Further work is needed to define the toe-off and heel-strike moments with reference to a gold standard event detection or expand the detection into different axis of the triaxial accelerometer. Accelerometry magnitudes have little previous research but were selected from biomechanically important events for speed control during the gait cycle. The little description of these values presents a barrier for interpretation of these magnitudes and how they might change within or between walking tasks. When comparing between people with PD and healthy cohorts, ground reaction force peaks were larger and stride time and single support times (i.e., swing time) were shorter in PD cohorts; however, when

controlling for gait speed differences in single support, double support times remain different but stride time was similar between groups (Patoz et al., 2023). Consequently, to properly interpret and assess specific gait outcomes there is need to consider them in the context of velocity or a proxy of velocity. Few studies examine the relationship between specific acceleration kinematics from outcomes and their relationship to mean or stride-to-stride velocity outcomes. The FSM model identifies accelerometry inflection points (peaks, or changes in acceleration) that are characteristic to strides to understand the association between accelerometry and gait velocity characteristics. Mean accelerometry outcomes had positive correlations with gait velocity, specifically, swing phase peaks reported the highest ($\rho=0.74$). As seen in previous research, swing phase kinematics are segmented for the calculation of gait speed (Gradl et al., 2018; Laudanski et al., 2011; Seel, et al., 2014) or isolated for stride length and speed calculations (Trojaniello, Cereatti, Pelosin, et al., 2014a). The association between stride-to-stride outcomes had a weaker relationship (range 0.34-0.68) compared to mean level associations. The lower stride-to-stride correlations could be due to several reasons, such as: gait impairments which can impose higher or lower acceleration kinematics during walking, minimal previous research of stride-to-stride variability of these accelerometry-based outcomes, and the utility of a sum vector magnitude which encompasses all directional movement, including movement not associated with forward progression. Associations between mean level gait velocity and simple accelerometry outputs indicates the possibility for accelerometry outcomes to account for the variability in spatiotemporal gait analysis.

Estimating gait speed from accelerometry derived outcomes

Clinical gait speed is an important marker and continues to be the most reported outcome for clinical gait assessments. Current approaches to calculate stride velocity rely on zero-velocity update algorithms to estimate stride lengths and output velocities (Rebula et al., 2013; Trojaniello, Cereatti, Pelosin, et al., 2014a). Other methods in free-living environments rely on subject-specific velocity models (Baroudi et al., 2020). The potential to model gait velocity from acceleration alone is not commonly reported but may have advantages during complex multi-directional movements such as free-living

mobility or complex sport movements (Baroudi et al., 2020; Gradl et al., 2018) and computational benefits (e.g., complexity, drift/pose estimation, speed) during longer data collections. In the current study accelerometry outputs were used as inputs to predict gait velocity. Average velocity estimations had an average difference of 0.03 m/s compared to GAITRite velocity. Although minimum difference in average velocity, Bland-Altman plot analysis reveals a positive association between errors and referenced gait velocity (Figure 5-4), such that lower walking speeds are over predicted by the regression model and higher walking speeds are under predicted by regression model. This suggests that accelerometry alone may not perform well for gait speed estimation across all velocities. Few studies have used strictly accelerometer kinematics to estimate walking speed. One study reported $6.9 \pm 5.5\%$ mean relative error (~ 0.2 m/s mean absolute error) when compared with optical motion capture during straight ahead walking and higher error rate of $16.5 \pm 5.5\%$ when comparing with complex movements between light gate-based reference data (Gradl et al., 2018). This parametric matching algorithm used foot worn sensors and noted that multidirectional sport movements with higher velocity or walking with shuffling may cause increases in velocity error estimations. Although this study used ankle-worn sensors, which have been reported to have better accuracy compared to foot worn IMUs (Laudanski et al., 2011), errors may still be driven by gait impairments and input variables relationship with gait velocities. Estimating gait speed from simply accelerometer outcomes would benefit the study of walking in free-living environment by providing accurate free-living velocity outcomes from minimal acceleration inputs. Studies that have advanced in this area utilize subject-driven models relying on stride frequency from thigh worn accelerometers in free-living environments and have reported mean level differences between -0.058 and 0.116 m/s and most subjects with 97% of individual stride velocity errors between ± 0.2 m/s of actual walking speed estimation (Baroudi et al., 2020). Although finite state machine algorithms have been used to identify strides and walking modalities in free-living environments, this study shows that further stride segmentation is useful to evaluate gait parameters such as temporal features of gait and this unique segmentation method may support subject-specific models for potential use in estimating gait velocity from multidirectional acceleration magnitudes.

The effect of dual task walking on gait outcomes in people with neurodegenerative disease

Under dual task walking conditions, changes to gait represent a compensatory strategy to maintain stability to prevent falling under these competing demands. In this current study, secondary tasks of varying difficulty produced lower gait velocity outcomes and increased cycle time under difficult secondary tasks. Cycle time variability only increased during the most difficult secondary tasks (e.g., serial 7s) compared to all other conditions (slope and magnitude). Accelerometry based kinematics were also statistically lower during dual task walking conditions. In previous research, decreasing velocity and increases in cycle time and cycle time variability have been reported between single-task walking, DT-An, and DT-S7s across people with and without MCI (Beauchet et al., 2005; Montero-Odasso, Verghese, et al., 2012). Cycle time and cycle time variability are affected more during dual-task walking with cognitive impairment compared to those with intact cognition (Montero-Odasso, Verghese, et al., 2012). Increases in gait variability are present during dual tasks for the whole cohort in this study, all of who have been diagnosed with NDD or CbVD by a neurologist. This study did not aim to compare between cognitive status but includes approximately 126 people with cognitive impairment (~26%) based on MoCA scores <22.1 (Dong et al., 2010; Hoops et al., 2009; Nasreddine et al., 2005). Cycle time variability in the current cohort was only different during DT-S7s, while previous research has shown differences across DT-An and DT-S7 walking tasks. This sample includes a larger percentage of people with normal cognition which may impact the differences between tasks. Although there were no significant differences, there were still increases in cycle time variability across all dual task conditions. Heterogeneity of gait outcomes in this cohort is not strictly related to cognition but could include disease-specific physical or behavioural differences between cohorts (Fritz et al., 2016; Mc Ardle et al., 2019), between the affected cognitive domains of these cohort and their relationship with gait outcomes (Morris et al., 2016; Tian et al., 2017), or the severity of disease in people (Gillain et al., 2016). Cognitive differences alone may not explain the heterogeneity in these complex samples but aspects of balance control, affective characteristics, and mental-wellbeing (Hausdorff et al., 2008). Uniquely there was little

change to our proxy of swing time and swing time variability. Swing time was increased for the most difficult cognitive task conditions but no differences were seen in swing time variability. Previous research reports swing time decreases to increase the foot-to-ground contact time (i.e. a more stable position for the COM) (Plotnik et al., 2011). Interestingly, since swing time does not increase it appears that within this specific model of gait segmentation identifying these negative and positive slopes (State B) outlines accelerometer inflections that are not linked entirely to gait events. Although identifying gait events is useful, there is still value in recognizing when these specific time periods change and understanding whether that highlights a unique compensatory mechanism during dual task walking.

Across dual-task walking there were significant decreases in the sum vector magnitude acceleration slopes and peaks during clinical walking tasks when controlling for gait speed. Previous research shows similar decreases in sum vector magnitude acceleration when comparing between stiff and unrestricted ankle motion during walking with sensors located on the dorsum of the foot (Patterson & Caulfield, 2013). Characterizing the limb movement with SVM acceleration and using the FSM segmentation method may provide insight into the unique characteristics of limb movement. The mechanism of change in accelerometry kinematics is clear with range limiting orthotic devices. Under dual-tasking conditions, novel outcomes that are identified by lower limb acceleration inflections under dual task conditions, possibly provides compensatory accelerometry kinematics that is otherwise unexplained by changes in gait speed. Further, although utilizing the SVM provides a summation of lower limb movement (summary of all concurrent degrees of freedom) it cannot describe the kinematics proximal to the ankle that produce end-point movement control. Assessment of lower limb kinematics using optical motion capture identifies the exact gait phase in which joint angles differ with dual task walking. People living with PD with freezing of gait assessed in their 'off' state decrease joint angles for their hip, knee, and ankle during dual task walking at the peak flexion during swing and peak extension before heel strike (Pinto et al., 2020). Conversely, these results are not seen in patients that are in the 'on' state of anti-parkinsonian medication phases (Ribeiro et al., 2019) and without medication there may be increases in compensatory movement

to maintain stability and reduce risk of falling. Beyond spatial kinematics, hip and knee angular velocities described with inertial measurement units decrease for dual task walking compared to single task walking (Piche et al., 2022). In this study, identification of discrete accelerometer moments and comparison between tasks show differences in accelerometer magnitude worn at the ankle, however these differences are likely to reflect changes at all levels proximal to the sensor location (i.e. intersegmental dynamics) which can be affected by dual tasking (Wang et al., 2021). Changes to accelerometer peaks provides insight into movement of the whole limb during walking and this study shows that clinical assessment can be instrumented with affordable accelerometers and detect changes beyond gait velocity with specific analytic approaches. Movement of lower limb and its relation to COM movement via spatiotemporal characteristics provide cause to further investigate whether accelerometry kinematics at the lower limb are linked to walking phases or mobility outcomes in people living with NDD. There is motivation to understand how these novel outcome measures may relate to distinct walking goals such as gait initiation and termination and if differences within these phases are detectable with these metrics.

Gait protocols and the learning effect in clinical environments for people with NDD

Careful selection of gait outcomes is necessary to inform clinical decision making and evaluating mobility needs. Current guidelines suggest that there is necessary walkway and environmental considerations (Kressig et al., 2006) that need to be controlled to avoid extrinsic influence over gait outcomes and that select trials, including dual task, should be used for a full clinical assessment in neurologic populations (Cullen et al., 2018). This study used specific instructions to avoid task prioritization that affects walking speeds during single- and dual-tasking (Goh et al., 2021; Kelly et al., 2010) and included tasks of varying difficulty to detect change during walking (Bishnoi & Hernandez, 2021; Montero-Odasso et al., 2017). Findings from this study report significant differences between P1 and P2 or P3 across velocity, temporal, and accelerometry-based outcomes. Clinical tests to assess stability may require the need for improved methodological approaches and single tests of preferred walking may not represent the capacity of someone's ability to walk. In two currently used guidelines

there is no mention of need for multiple preferred walking tasks (Beauchet et al., 2017; Cullen et al., 2018), however for people with neurodegenerative disease, novel environments and new space may pose additional distractions or influences over gait outcomes. This may compound the findings of stability and gait control when using a single walking task to evaluate but also adds additional effect of any dual task outcomes that reference these single trials.

This study aimed to identify the utility of temporal and accelerometry based outcomes from the FSM to characterize walking in clinical gait tasks. There are several key limitations to this study that future research should assess for FSM outcomes. This study assessed dual-task walking conditions in a large cohort of NDD and CbVD older adults with multi co-morbidities. Differences between cohorts, across different cognitive abilities, and the addition of an aging population serves as a limitation to conclusive outcomes for specific groups. Although these individual groups were not assessed, task difficulty had a widespread effect on kinematic, velocity, and spatiotemporal outcomes across all people included. Future research should address the heterogeneity issue within this project by comparing between cognitive ability and between or within disease cohorts to address the complexity of these diseases. A novel element to this study is the use of triaxial accelerometers, the benefit of these simple tools is their ability to track lower limb kinematics in clinic but also in extended continuous monitoring studies but excluding additional sensors (e.g., gyroscopes) limits some advancement in this study. The inclusion of angular velocity would provide the ability to quantify sensor orientation for several key validation purposes: apply ZUPT algorithm approaches and estimate better stride to stride velocity outcomes and allow for assessment acceleration characteristics with anatomical alignment (i.e., pose estimation). Therefore, although methods in this study advance analytical approaches there is need to further validate outcomes for clinical interpretation. Another limitation to the validation between methods occurred during data collection. Data collection occurred without synchronization between devices, therefore statistical approaches were used to align the strides between the two devices. The statistical method to synchronize strides was estimated on the lowest difference between the reported mean cycle

times from a window length equal to GAITRite stride count. Improving data collection methods to synchronize these outputs or using a separate reference system (additional wearable) may be useful in obtaining accurate stride matching. Although high association was found across all tasks, calculated mean error was affected by walking task, where DT-An and DT-S7 had less error magnitude compared to some of the preferred walking tasks which may be influenced by this synchronization method. Future research that considers these approaches will continue to advance assessment of gait for clinical assessment of neurologic disorders and continue to advance continuous monitoring studies using wearable accelerometers.

5.6 Conclusion

This study examines the changes to gait performance using cost-effective accelerometers when individuals with NDD or CbVD are challenged with secondary cognitive tasks of varying difficulty during short clinical walking bouts using an FSM model to segment accelerometry. The finite state machine algorithm segments the gait cycle by identifying distinct intra-stride phases based on accelerometry inflection points. However, since this method does not replicate gait event detection there is caution needed in interpreting the exact stance and swing time phases one might traditionally report. Outcomes from this method reveal a decrease in gait velocity, increases in cycle time, and decreases in accelerometry-derived magnitudes as a compensatory response to a cognitive task. This suggests that with minimal sensor and kinematic data, there are opportunities to reveal compensatory strategies to gait during dual task walking in people living with NDD or CbVD who may have a range and variety of gait impairments. Changes to gait outcomes due to cognitive tasks have been previously reported from various sensor wear locations, including the lower limb, and have been identified as potential markers for cognitive impairment. This study uniquely identifies the temporal outcomes previously reported with the advantage of further segmenting a gait cycle into intra-stride phases that are linked to limb trajectory control and biomechanically significant events. An unexpected finding in this study were statistically significant differences between single task preferred walking trails. These differences suggest there is

need to consider habituation or familiarization effects with clinical walking tasks for neurologic cohorts. Further investigation is needed to fully understand the impact of these assumptions and selection of reference trials. This study examined the utility of the FSM to identify compensatory gait characteristics in response to a secondary cognitive task in a cohort of people with various impairments living with NDD or CbVD. It was reported that the FSM algorithm accurately identified conventionally reported gait outcomes and identified key accelerometer kinematic features that both changed during dual task walking. Interestingly, this study elevates a significant matter in the differences in single-task preferred walking, where there is need to reflect on the importance of protocol for clinical gait tasks and selection of preferred gait, particularly if disease biomarkers are to be identified or referenced from a single preferred walking task.

Chapter 6

APPLYING STRIDE CLUSTERING TECHNIQUES TO IDENTIFY AND ASSESS THE PHASES OF A WALKING BOUT DURING CLINICAL GAIT ASSESSMENTS IN PEOPLE LIVING WITH NEURODEGENERATIVE DISEASE

6.1 Introduction

Quantitative gait assessments provide insight into the impact of brain health and disease on gait stability and fall risk (Wren et al., 2020). Traditionally, these assessments isolate the middle of walking, labelled as steady state walking, to assess gait performance without the influence of acceleration and deceleration phases (Beauchet et al., 2017; Cullen et al., 2018; Kressig et al., 2006). In daily life, walking requires gait initiation or termination for each bout and half of daily life walking is comprised of short walking bouts which are composed largely of these transitional periods (Orendurff, 2008). Stable steady walking over short distances reflects naturally occurring stride-to-stride variability of human walking. However, separating steady state from acceleration phases is largely assumed and may not capture the fluctuations between distinct phases in the middle of walking, particularly when attention shifting is needed during dual task walking. Those living with neurodegenerative disease may approach gait with differing strategies than their cognitively normal comparisons (Shaw, 2007). Therefore, alternative approaches for characterizing gait performance may be necessary to reveal unique gait control changes and tackle the heterogeneity of gait control for those living with neurodegenerative diseases.

Conventional approaches used to assess gait in clinical settings often report performance as velocity or summarize spatiotemporal measures as mean values during the presumed steady state gait. Speed is the most common reported measure for gait analysis, it is the simplest to measure and typically interpretable for patients and clinicians. Gait speeds, along with other spatiotemporal measures, are reported as averages over the middle of the walking path to remove the influence of acceleration and deceleration periods of walking. Gait speed is reportedly sensitive to change but not specific as it does not always distinguish between groups or tasks (Goh et al., 2021). Predefined acceleration buffers are used to account for speeding up and are appropriate for methodological tools that are restricted by space, such as pressure sensor mats or optical motion capture. Unique from steady walking, these acceleration periods are likely to reflect difficulties related to stability control, providing good reason to include these phases as part of gait assessment. Further, these distances are unrelated to walking speed (Lindemann et al.,

2008), indicating that acceleration periods likely reveal a different aspect of stability control beyond speed and simply extending these buffers for slower or faster walkers or different distances may be inappropriate to account for the gait acceleration phases. Further, longer versus shorter walking tasks affect performance measures such as gait velocity and spatiotemporal measures during walking (Krumpal et al., 2021) and neurologic disorders can cause changes to the initiation period (Wittwer et al., 2008a).

Recognizing steady state walking periods is common practice in clinical assessment attempts to remove the acceleration phases of walking from the assessment (Kressig et al., 2006; Mehmet et al., 2020). Several researchers have quantitatively defined steady state walking using clinically feasible approaches. Gait initiation periods are reported to be up to 2.5 meters and 4-5 steps to obtain desired walking pace in a cohort of frail older adults and is based in stride-to-stride velocity (Lindemann et al., 2008). In neurologic diseases gait initiation length also has increased stride to stride variability (Wittwer et al., 2008b), which was also reported in people that have longer initiation periods (Lindemann et al., 2008). Stability control and task causes variation in the necessary gait initiation or termination phases of walking (Boripuntakul et al., 2014) and defining the correct steady state walking period depends on the measure used. Laboratory grade instrumentation (e.g., whole body motion capture) can assess steady energetics (Miller & Verstraete, 1996, 1999), but these tools are not clinically feasible. Nguyen and colleagues, (2019) examined stride clustering methods with both stride velocity and cycle time measures. From this, non-steady periods of walking (i.e., non-constant strides) were more associated with UPDRS postural control scales while steady walking (e.g., constant strides) were more associated with UPDRS gait scores (Nguyen et al., 2019). The current steady state walking definitions provide insight into gait initiation behaviour, but current definitions may not reveal all intra-bout phases of walking, particularly during difficult tasks or for people with low stability.

Concerns with the current methodology for defining steady state walking exist. First, when steady state is established, current methods do not permit fluctuations in and out of steady state. In the

conventional definition, a walking bout would include acceleration, steady state, and termination in that order; however, with complex tasks (e.g., dual task walking) or gait impairment, intra-bout phases may not be as distinct. Second, there are few examples of defining steady state beyond velocity. Other spatiotemporal or kinematic measures may be more appropriate. For example, gait velocity has little predictive value towards fall risk unlike stride-to-stride variability, therefore, defining the period using a different gait metric might provide valuable information for risk assessment or in a different setting. In instances when gait events are undetectable, gait stability and regularity can be inferred from the accelerometer waveform patterns. These waveform patterns reveal unique stability related outcomes from kinematic components of an accelerometer signal (Kobayashi et al., 2014; Kobsar et al., 2014; Riva et al., 2013). Lower limb accelerometry kinematics may also be linked to initiation phases of walking from a waveform-based approach. Analytic approaches to identify the transitions from gait initiation to steady state largely rely on an appropriate method for assessment in clinic but there are valuable applications for these methodological approaches in free living gait analysis.

6.2 Study Objective & Hypotheses

Given the importance of gait initiation during walking there is need to better quantify these intra-bout phases for clinical and free-living assessments. This study aims to characterize intra-bout phases during clinical walking tasks that vary in difficulty (e.g., preferred walking, three dual-task walking conditions) in a cohort of people living with neurodegenerative disease (e.g., ADMCI, PD, CVD, and FTD). The two primary objectives of the current study are:

- (1) To evaluate the use of temporal and accelerometry kinematics with stride clustering methods to identify intra-bout phases of walking (e.g., gait initiation, steady state walking) during short clinical walking bouts and determine differences during dual-task walking.

H1: It is hypothesized that when gait cycles are compared using stride-clustering methods, acceleration kinematics data will identify distinct acceleration, deceleration, and steady state

phases of walking during preferred walking conditions and the duration of these phases will be different between stride clustering approaches.

H2: It is hypothesized that accelerometry clustering methods, will reveal longer acceleration phases and more distinct phases and strides (i.e., not standard accelerate-steady-decelerate pattern) with increasing task difficulty and among individuals with NDD.

(2) To evaluate whether the stride-to-stride relationships between accelerometry waveforms are different during single- and dual-task walking trials and whether these inter-stride relationships can identify intra-bout phases during short clinical walking tasks of varying difficulty in a cohort of people with NDD.

H3: It is hypothesized that average stride-to-stride relationships between accelerometry waveforms will be different between single- and dual-task walking.

H4: It is hypothesized that relationships between accelerometry waveforms will identify intra-bout phases (e.g., initiation phases and fluctuations during dual task walking) and be different between single- and dual-task walking conditions.

6.3 Methods

6.3.1 Study Design

This study is a cross-sectional analysis of data collected as part of the Gait and Balance platform in the ONDRI Longitudinal Study using data collected from the baseline visit. This study utilizes triaxial accelerometer data in combination with the FSM stride segmentation techniques from all research sites within the ONDRI dataset.

6.3.2 Participants

Description of participant enrollment and data availability can be found in Study 2 section [5.3.2 Participants](#). In brief, there were 497 participants included in this study from four different neurodegenerative disease cohorts: Alzheimer's Disease and Mild Cognitive Impairment (ADMCI;

n=126), Frontotemporal Lobar Degeneration (FTD; n=50), Parkinson's Disease (PD; n=140), and Cerebrovascular Disease with and without cognitive impairment (CbVD; n=160).

6.3.3.Data collection and analysis

Data was collected at the different sites following the description provided in [Chapter 3](#). Accelerometer data (X-16 triaxial accelerometers, Gulf Coast Data Concepts, Waveland, MS) was processed and segmented into strides using the Finite State Machine algorithm described in [Chapter 4](#) and gait metrics were described in [Chapter 5](#). Outcome measures from the Finite State Machine were used for stride clustering and inter-stride correlation analysis. All data processing was done using python programming language (Python v3.9).

6.3.3.1 Stride clustering

Gait variables

Temporal and accelerometry derived gait variables from the FSM algorithm were used for stride clustering applications. Temporal variables used for stride clustering were the cycle time (summation of all the FSM states to calculate the whole gait cycle) and swing time (time period between the end of State A and the instance of State C). Acceleration derived outcomes were extracted from a specific instance, or the summary of a state from the FSM algorithm. Accelerometry outcomes used for stride clustering were the push-off slope (slope of acceleration in State A), the peak acceleration at the end of push-off (peak acceleration at the end of State A), and the mid-swing peak acceleration (peak acceleration at State B). Gait variables are described and explained in Study 5 section [5.3.4 Data Analysis](#).

Stride Clustering Approach

Stride clustering classified strides as constant or non-constant strides. Constant stride clusters represent steady straight ahead walking and non-constant stride clusters were defined as parts of transitions, gait initiation, or gait termination. To classify constant and non-constant strides, individual stride metrics were compared to static thresholds (Nguyen et al., 2019). Static thresholds provided a variability band for

clustering. Strides that were within the band of variability were considered constant strides and when the stride metrics were outside of the band of variability it was considered a non-constant stride (Figure 6-1). There was an additional requirement of a minimum two consecutive strides within the same cluster to classify a transition between constant and non-constant strides.

Novel to this study was the comparison between dual-task and single-task walking, such that several different threshold approaches were examined that included threshold calculated from dual-task or single-task walking. Some cases calculated stride clusters during dual-task walking from thresholds calculated from a preferred walking task. Under these circumstances the calculated variability band was added and subtracted with the mean of the dual-task being clustered.. Additionally, if single-task trials were used as reference, the randomly selected single-task trial was consistently used as reference for all the walks for that participant. Several static thresholds were used to identify constant and non-constant strides. The different static thresholds used to identify constant and non-constant strides are described here:

Whole bout two standard deviation (SD): The walk standard deviation threshold is calculated as a two standard deviation window from all the strides within the current trial. All SD thresholds are calculated as the standard deviation within the same trial.

One standard deviation of the whole preferred trial (PREF): The PREF method will calculate the standard deviation of a randomly selected single-task walking trial (P2 or P3), P1 was not considered within random selection to avoid familiarization/habituation period effects that were demonstrated in Study 2. The standard deviation is added and subtracted from the mean of the trial being analyzed to create a variability threshold band anchored about the trials mean.

One and two standard deviations from an assumed steady state single-task trial (PREF STEADY 1SD/PREF STEADY 2SD): The PREF STEADY 1SD threshold is the standard deviation calculated from an assumed steady state window. From current clinical gait assessment

guidelines, a 1-meter or two step duration was used as an acceleration buffer (Montero-Odasso et al., 2017). For this analysis, two steps were cropped from the beginning and ending of the walking to isolate steady-state. A standard deviation was calculated from the middle portion of the walk, minus the cropped steps at the beginning and end. The standard deviation is multiplied by two for the PREF STEADY 2SD threshold. Thresholds are added and subtracted to the mean of the trial being analyzed prior to creating stride clusters.

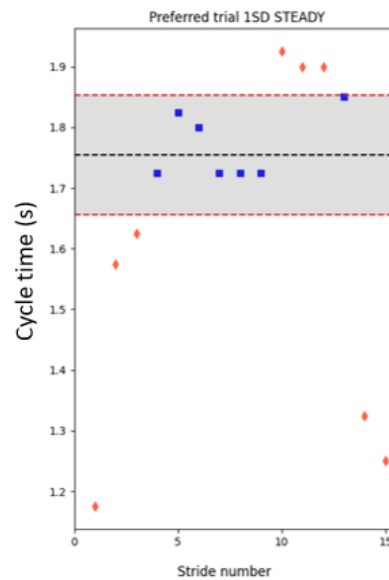


Figure 6-1. Stride metrics are compared to static threshold (red dotted lines) where constant strides (blue squares) fall within the acceptable variability band (grey shaded area) and non-constant stride fall outside the acceptable range (red diamonds).

Stride clustering outcomes

Stride clusters were characterized with three distinct outcomes that aimed to identify different characteristics of intra-bout phases during walking. Different clusters or distribution of strides were characterized to describe gait initiation or unique measures of variability between intra-bout phases (Figure 6-2).

Length of gait initiation was defined as the number of strides in the first cluster that fell outside of the clustering thresholds. If the first cluster only contained constant strides, then it was assumed

steady walking occurred within the first step and gait initiation was zero strides. The number of strides within this cluster was used to characterize the length of gait initiation.

Number of state transitions was calculated as the number of transitions between constant to non-constant that occurred during the walk. To calculate this outcome the number of transitions between clusters was counted. To avoid single stride clusters, a cluster transition was defined when minimum two consecutive strides were within the same state (two consecutive non-constant strides) before identifying a new cluster.

Percent non-constant was calculated as a percentage of strides classified as non-constant from the total number of strides within the walking bout. The total number of non-constant strides were counted across the whole walk and was compared to the total number of strides within the walk.

$$\% \text{ nonconstant} = \left(\frac{\# \text{ nonconstant stride}}{\text{total \# strides}} \right) * 100$$

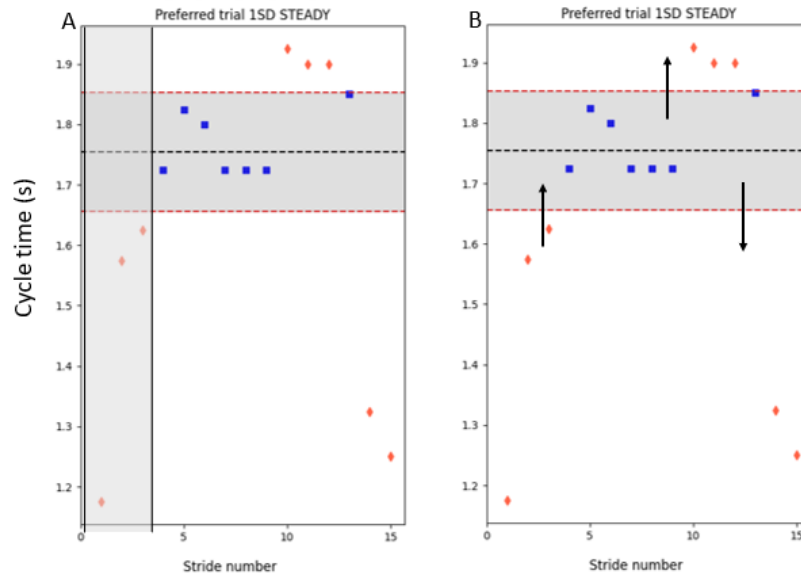


Figure 6-2. Intra-bout phases are derived from clustering strides against static thresholds. A: demonstrates the parameters that are calculated to represent an initiation cluster and B: represents the clusters that cross variability thresholds that are considered when calculating the number of state transitions.

Inter-stride correlation

Time series strides identified by the finite state machine were used to create an inter-stride correlation to quantify the relationship between stride-to-stride accelerometry kinematics during walking. To evaluate the inter-stride correlation within a walking bout, strides were resampled to match the length of the stride with the smallest duration. Evaluating the relationship of accelerometer waveform pattern this way has been done before using an inter-item correlation test to evaluate the internal consistency of APAs detected with a lower back worn IMU (Martinez-Mendez et al., 2011) and inter-item correlations of 0.5 were considered strong. Inter-stride correlations were calculated for each stride across all tasks and compared across task difficulties. Inter-stride correlations were used in two ways: (1) to evaluate the overall average of inter-stride accelerometry kinematics as a representation of stride-to-stride variability (Figure 6-3B) and (2) to apply stride clustering methods for each individual stride average (Figure 6-3A). To calculate the overall inter-stride average, a correlation matrix (to compare between each stride) was output for each walking task. The upper-right quadrant of the correlation matrix was averaged to represent the inter-stride correlation for that task. Inter-stride correlations were also used to create stride cluster outcomes. An average inter-stride correlation was calculated for each stride individually. From each correlation matrix, each column was averaged (dropping the diagonal) to represent a single stride's relationship with the other strides. To classify constant and non-constant strides, a static threshold was set at 0.5 (Martinez-Mendez et al., 2011). Stride correlations that were below 0.5 were considered non-constant because the correlation average indicates low relationship with other strides and constant strides were those with averages above 0.5. The same criteria were used to identify the initiation cluster, number of state transitions, and percent non-constant strides.

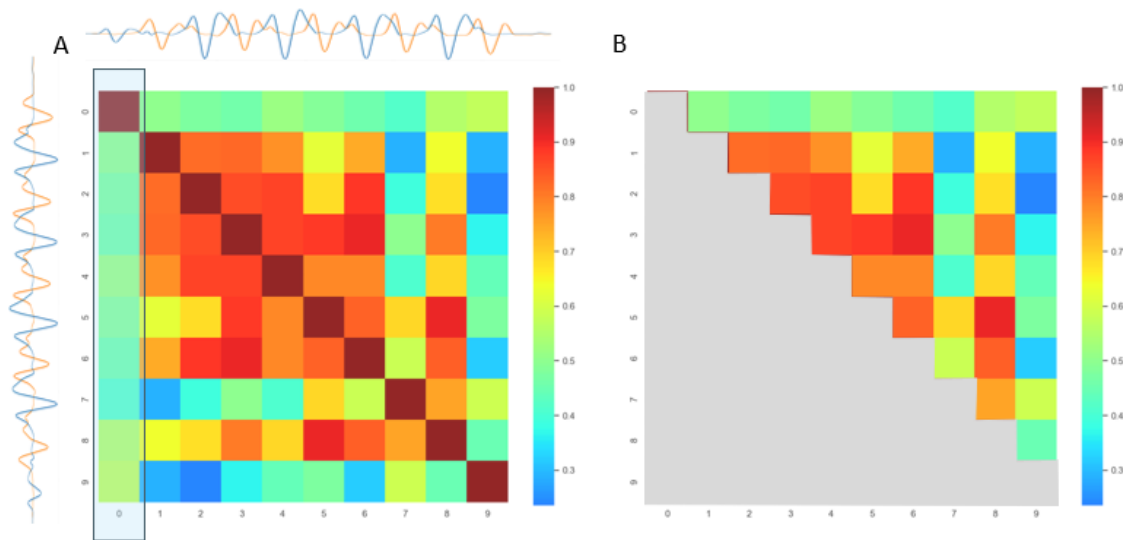


Figure 6-3. Representation of the correlation matrix calculated between individual stride waveforms to represent association between individual strides. A: A representation of calculating the individual inter-stride correlation values used to stride clustering. B: A representation of the upper quadrant of the correlation which was averaged to describe whole bout variability.

6.3.4 Statistical Analysis

Statistical analysis was conducted using the python programming language (Python v3.9) with the Pingouin (Vallat, 2018) and Statsmodels packages (Seabold & Perktold, 2010). Data was tested for normality using the Kolmogorov-Smirnov test. Data that violated normality was rank transformed and further was conducted using parametric statistical tests on the ranked data.

To examine the effects of stride clustering parameters (e.g., gait variables and threshold definition) to identify intra-bout phases, several combinations of cluster parameters were examined across the preferred walking trials. Cluster outcomes were compared using a series of one-way repeated measures ANOVAs to identify cluster outcomes that were different between preferred walking trials (within factors). Pairwise comparisons were used to determine which differences exist between preferred walking trials, and a Bonferroni-Holm correction accounted for multiple comparisons. These tests were exploratory in nature to examine the differences between clustering parameter between the preferred trials.

To examine the difference of cluster outcomes (initiation cluster length, number of state transitions, and percent non-constant) across single- and dual-task walking trials, one-way repeated measures ANOVAs compare across tasks for a subset of gait variables. Pairwise comparisons were used to identify specific task differences with a Bonferroni-Holm correction to account for multiple comparison.

To evaluate the effect of dual task walking on inter-stride correlation means, one-way repeated measures ANOVAs compared across walking task difficulty (within factor). Two different inter-stride means were compared. First, an inter-stride average that crops the first and last two strides was used to determine if differences exist without these initial strides. Second, comparisons between inter-strides averages that included all the strides was assessed to determine if outcomes are different from those that include the initiation strides. Stride cluster outcomes defined using inter-stride correlation methods were also compared across task difficulty using a one-way repeated measures ANOVA.

6.4 Results

6.4.1 Participants and Data availability

Description of participants and data used in this study is available in [Chapter 5](#). In brief, 401 of the 520 participants (ADMCI: 99, FTD: 34, PD: 129, CVD/VCI: 139) had valid and useable accelerometer data and had identifiable strides (either with FSM or manual collection). Of these participants, there were a total of 2349 trials that were successfully processed with the FSM model: P1: 400, P2: 394, P3: 386, DT-S1: 398, DT-An: 391, DT-S7: 380. See [Table 5-2](#) for participant demographic and mobility scales.

6.4.2 Understanding the effect of gait variables on stride clustering outcomes in preferred walking

Defining steady and non-steady strides is dependent on variability of strides used to derived reference thresholds and the variability of the strides being clustered. Descriptive statistics of all the cluster methods and gait variables were used to select the parameters that described the cluster outcomes. Mean values

and variability (*sd*) of the cluster methods were calculated for the preferred trials and contrasted to identify differences between preferred trials across the clustering parameters (e.g., threshold and gait variables). Of the total subjects, there were 1180 trials (P1: 400, P2: 394, P3: 386) used to compare between clusters and across the preferred trials. The mean and absolute range for gait clusters across all gait variables are: 1.68 (0-28) strides for length of initiation cluster, 1.2 (0-12) for number of cluster transitions, and 20.89 (0-100) percent non-constant strides. Description of mean and standard deviation of cluster outcomes across the difference gait variables are described in Table 6-1.

Table 6-1: Stride cluster outcomes from all cluster parameters during preferred walking trials.

		Mean (min – max)*				
		Cycle Time	Swing Start Acceleration	Mid-swing Acceleration	Push-off Slopes	Swing Time
Initiation Cluster (# strides)	Pref Whole 1SD	0.38 (0-5)	0.12 (0-13)	0.42 (0-3)	0.40 (0-5)	0.24 (0-10)
	Pref Steady 1SD	1.88 (0-11)	1.42 (0-19)	2.68 (0-19)	2.86 (0-18)	2.07 (0-19)
	Pref Steady 2SD	0.97 (0-9)	0.28 (0-13)	1.00 (0-13)	1.22 (0-9)	0.53 (0-14)
	SD	1.04 (0-6)	0.88 (0-9)	1.29 (0-13)	1.63 (0-11)	1.15 (0-14)
Number of Cluster Transitions	Pref Whole 1SD	0.47 (0-6)	0.11 (0-5)	0.42 (0-3)	0.40 (0-5)	0.23 (0-6)
	Pref Steady 1SD	2.34 (0-8)	1.16 (0-7)	1.47 (0-6)	1.62 (0-6)	1.26 (0-8)
	Pref Steady 2SD	1.01 (0-6)	0.22 (0-4)	0.78 (0-4)	0.87 (0-3)	0.48 (0-8)
	SD	1.58 (0-7)	0.97 (0-6)	1.08 (0-6)	1.27 (0-6)	0.95 (0-7)
Percent non-constant	Pref Whole 1SD	4.53 (0-100)	1.16 (0-100)	2.97 (0-33)	2.82 (0-42)	2.17 (0-100)
	Pref Steady 1SD	37.1 (0-100)	18.1 (0-100)	25.7 (0-100)	28.4 (0-100)	23.3 (0-100)
	Pref Steady 2SD	13.3 (0-100)	2.56 (0-100)	8.16 (0-86)	10.1 (0-56)	5.44 (0-100)
	SD	18.3 (0-100)	11.8 (0-73)	11.6 (0-100)	14.9 (0-75)	12.3 (0-100)

*averages and range (min-max) is average across all tasks, and range reflect

A series of one-way ANOVAs were used to contrast between the cluster parameters (e.g., the four cluster methods and the five different variables) across the preferred walking trials (e.g., P1, P2, P3) to examine the effects of cluster parameters on cluster outcomes. Tables 6-2, 6-3, and 6-4 summarize the p-values from these one-way ANOVA analyses and reveal some commonalities across cluster methods and gait variable used for clustering. In total, of 12 of 60 comparisons were significantly different. No single cluster threshold appeared to differentiate between the trials compared to other threshold methods. Of the

specific gait variables, the push-off slope and mid-swing peak showed the most differences for our spatial outcomes and cycle time showed more differences than swing time for temporal differences.

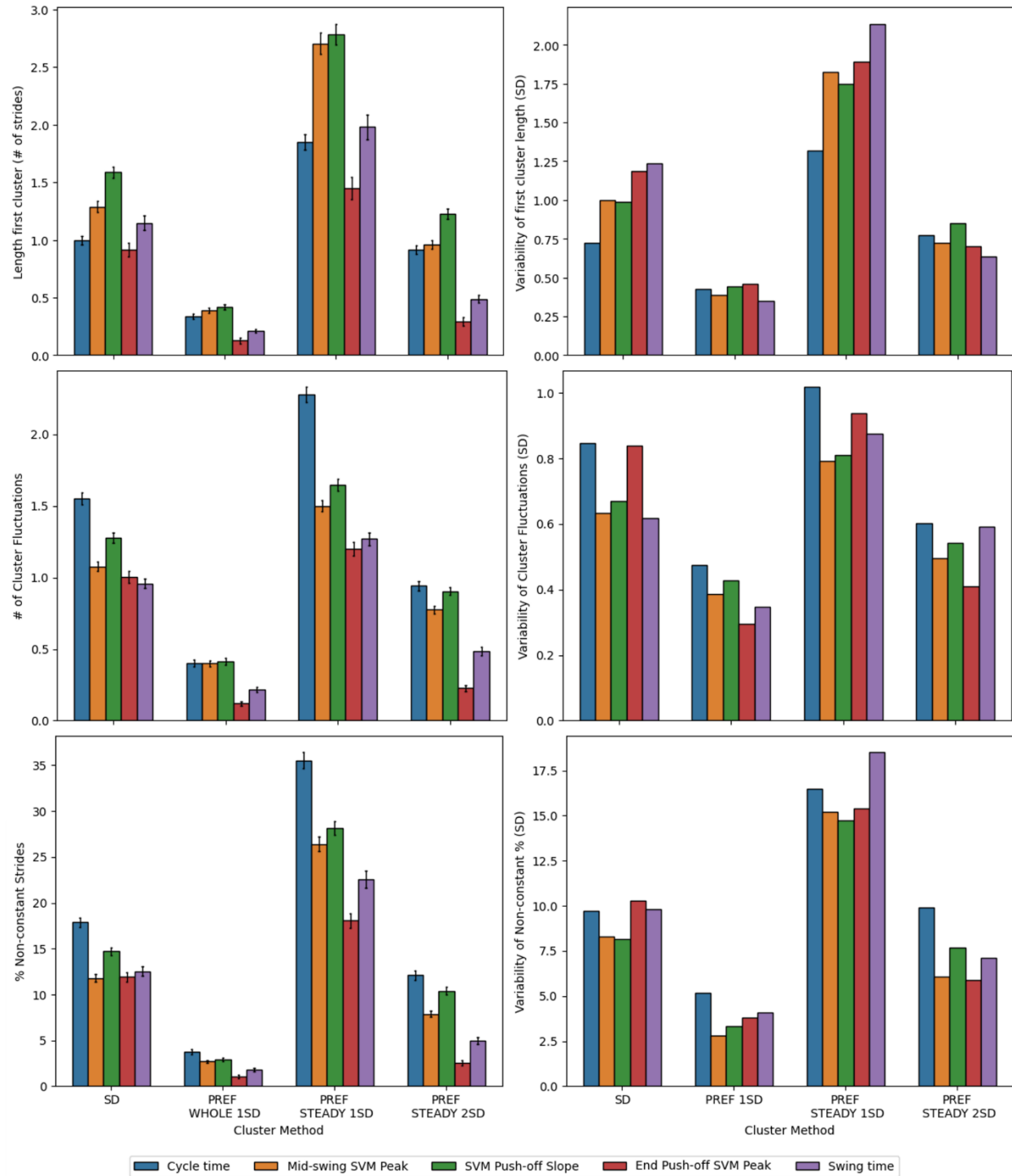


Figure 6-4. Preferred walking trial cluster outcomes across different clustering parameters (colours = gait variables; x-axis = cluster thresholds). *Left column:* mean and standard error, *right column:* standard deviation.

Pairwise comparisons were run to contrast the individual trial differences from the ANOVA main effect. Differences between trials were not consistent for all comparisons but there were more differences between P versus P2 and P3 compared to other combinations (7/12 comparisons indicated that P was different than both P2 and P3, one comparison between P and P2 and between P and P3 was significant, 2/12 comparisons indicated there were differences between all preferred trials). Less differences between trials may reveal the effects of selecting a narrow threshold band versus a wider threshold band of variability. The cluster method may effect cluster outcomes in opposite directions, such that strict narrower threshold (PREF STEADY 1SD) could cause many strides to fall outside of the threshold while wide bands (e.g., the SD of trial) may cause more strides to fall within, even if there is variability between strides. Using a preferred trial (within a person) to create cluster threshold provides more instances of statistical difference, which is largely differences between P and P2 and/or P3, (although differences between P2 and P3 exists there are relatively less).

Table 6-2: One-way repeated measures ANOVA comparing length of first cluster for single-task walking trials.

Length of the First Cluster		Variables				
		Cycle Time	Swing Start Acceleration	Mid-swing Acceleration	Push-off Slopes	Swing Time
Methods	Pref Whole 2SD	0.001 ^{*,†}	0.288	0.010 [†]	0.171	0.984
	Pref Steady 1SD	0.205	0.222	0.742	0.237	0.711
	Pref Steady 2SD	0.011 [*]	0.230	0.063	0.931	0.996
	SD	0.155	0.042	0.313	0.069	0.672

Red: No significant main effect of task from one-way ANOVA results

Green: Significant main effect of task from one-way ANOVA results

^{*,†,‡} Representing pairwise comparisons significant differences (^{*}P vs. P2, [†]P vs. P3, [‡] P2 vs. P3)

Table 6-3: One-way repeated measures ANOVA comparing number of state transitions for single-task walking trials.

Number of state transitions		Variables				
		Cycle Time	Swing Start Acceleration	Mid-swing Acceleration	Push-off Slopes	Swing Time
Methods	Pref Whole 2SD	<0.001 ^{*,†}	0.453	0.027 ^{*,†}	0.179	0.115
	Pref Steady 1SD	0.316	0.118	0.109	0.213	0.714
	Pref Steady 2SD	0.002 ^{*,†}	0.894	0.298	0.015 ^{*,†}	0.766
	SD	0.323	0.562	0.085	0.384	0.077

Red: No significant main effect of task from one-way ANOVA results

Green: Significant main effect of task from one-way ANOVA results

^{*,†,‡} Representing pairwise comparisons significant differences (^{*}P vs. P2, [†]P vs. P3, [‡] P2 vs. P3)

Table 6-4: One-way repeated measures ANOVA comparing percent non-constant for single-task walking trials.

Percent Non-constant Strides		Variables				
		Cycle Time	Swing Start Acceleration	Mid-swing Acceleration	Push-off Slopes	Swing Time
Methods	Pref Whole 2SD	<0.001 ^{♦,†}	0.508	0.021 ^{♦,†}	0.229	0.076
	Pref Steady 1SD	0.07	0.209	0.031 [†]	0.170	0.911
	Pref Steady 2SD	<0.001 ^{♦,†,‡}	0.907	0.531	0.060	0.939
	SD	0.16	0.614	0.209	0.163	0.226

Red: No significant main effect of task from one-way ANOVA results

Green: Significant main effect of task from one-way ANOVA results

^{♦,†,‡} Representing pairwise comparisons significant differences ([♦]P vs. P2, [†]P vs. P3, [‡] P2 vs. P3)

6.4.3 Differences in stride clustering due to task difficulty

To compare across walking tasks (i.e., preferred and dual task conditions), a single conservative cluster method (e.g., PREF STEADY 2SD) was used to cluster strides from three different gait variables (e.g., cycle time, mid-swing acceleration, push-off acceleration slope). Data was not normally distributed based on Kolmogorov-Smirnov test for normality ($p < 0.01$) and therefore data were rank transformed for parametric statistical testing. A series of one-way ANOVAs were run for each of the cluster outcomes to examine main effects of task.

Length of the First Cluster

Cycle time: One-way ANOVA results indicate a main effect of walking task when using cycle time to characterize the length of the first cluster ($F(5, 1810) = 4.625$, $p_{gg} < 0.001$, $\eta^2 = 0.012$). Comparisons between preferred tasks indicate significant differences between P1 and P2 ($t(362) = 2.983$, $p = 0.04$, $d = 0.183$) but no differences with P3 (Table 6-5). Dual task walking had longer initiation clusters compared to preferred trials for all conditions, specifically DT-An was different from P2 ($t(362) = 3.086$, $p = 0.03$, $d = 0.207$) and DT-S7 was different from P2 ($t(362) = 4.269$, $p < 0.001$, $d = 0.293$). Between dual task walking conditions, the more difficult the task resulted in longer initiation clusters on average, however none of the tasks were significantly different ($p > 0.05$). Characterizing the length of the first cluster comparing cycle time with a two standard deviation threshold from a preferred trial revealed an effect of

dual task walking on the length of this first cluster for some comparisons, where in general, there were more strides in the initiation cluster as tasks increased in difficulty.

Table 6-5: Pairwise comparisons of the length of initiation cluster defined by cycle time between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	1.08 (1.16)	0.87 (1.0)	0.95 (0.94)	1.22 (1.66)	1.49 (2.05)	1.74 (2.43)
P1	p-val Cohen (d)		0.039	1	1	1	0.634
P2			0.184	0.634	0.361	0.031	<0.001
P3			-	-	1	1	0.064
DT-S1			-	-	-	1	0.155
DT-An			-	0.207	-	-	1
DT-S7			-	0.293	-	-	-

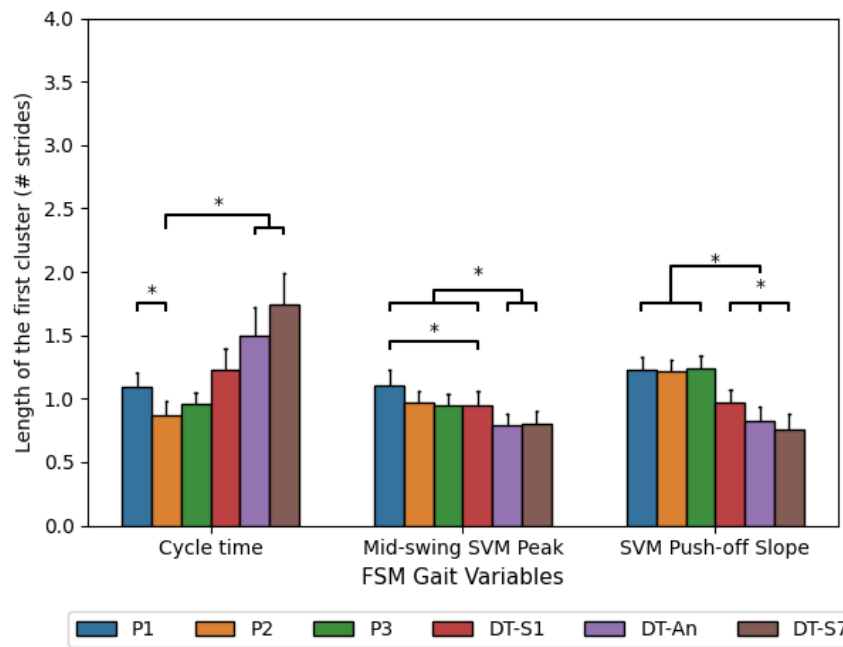


Figure 6-5. Bar plot comparing the length of the first cluster across different gait variables (x-axis) between preferred and dual task walking conditions (colours). *indicates significant difference between tasks

Mid-swing acceleration peak: One-way ANOVA results indicate a main effect of walking task when using the mid-swing peak to characterize the length of the first cluster ($F(5,1810)=1.0146$, $p_{gg}<0.001$,

$np^2=0.027$). Pairwise t-tests were used to examine the differences between preferred and dual task walking. No significant differences existed between the preferred walking trials ($p>0.05$). In general, there were longer preferred walking initiation clusters compared to dual task walking. All preferred walking trials, although small mean level differences, had significantly longer initiation clusters compared to DT-S7 and DT-An (Table 6-6). Between dual task conditions DT-S1 was significantly different from both DT-An ($t(362)=-3.459$, $p=0.007$, $d=-0.201$) and DT-S7 ($t(362)=3.063$, $p=0.021$, $d=0.182$). Differences reveal that the length of the first cluster is less during dual task walking compared to most of the single task walking trials when defined with the mid-swing peak.

Table 6-6: Pairwise comparisons of the length of initiation cluster defined by the mid-swing peak acceleration magnitude between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	1.10 (1.15)	0.96 (0.89)	0.94 (0.94)	0.94 (1.04)	0.79 (0.91)	0.79 (0.98)
P1	p-val Cohen (d)		0.204	0.139	0.039	<0.001	<0.001
P2		-		1	1	0.004	0.004
P3		-	-		1	0.008	0.021
DT-S1		-	-	-		0.006	0.021
DT-An		-0.356	-0.239	-0.214	-0.201		1
DT-S7		-0.338	-0.220	-0.195	0.182	-	

Push-off acceleration slope: One-way ANOVA results reveal a main effect of task when comparing the length of the first cluster when characterized with the push-off acceleration slope ($F(5,1810)=47.50$, $p_{gg}<0.001$, $np^2=0.116$). Paired t-tests were used to understand task differences within the ANOVA main effect. There were no significant differences between the preferred walking trials ($p>0.05$). All preferred walking trials were significantly different from all dual task walking conditions ($p<0.05$). Differences between dual task trials, such that DT-S1 was significantly different from DT-An ($t(362)=-2.958$, $p=0.016$, $d=-0.157$) and DT-S7 ($t(362)=5.474$, $p<0.001$, $d=0.291$), and DT-An was different from DT-S7 ($t(362)=2.688$, $p=0.03$, $d=0.134$). These differences reveal that, dual task walking typically showed lower initiation cluster lengths compared to preferred walking trials and as tasks became more difficult the length of the first cluster also decreases.

Table 6-7: Pairwise comparisons of the length of initiation cluster defined by push-off slope between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	1.22 (1.08)	1.22 (0.93)	1.24 (1.03)	0.96 (1.05)	0.82 (0.96)	0.75 (1.19)
P1	p-val		1	1	<0.001	<0.001	<0.001
P2		-		1	<0.001	<0.001	<0.001
P3		-	-		<0.001	<0.001	<0.001
DT-S1		-0.272	-0.325	-0.320		0.016	<0.001
DT-An	Cohen	-0.432	-0.490	-0.484	-0.157		0.030
DT-S7	(<i>d</i>)	-0.568	-0.630	-0.623	0.291	0.135	

Number of State Transitions

Cycle time: One-way ANOVA results indicated a main effect of walking task on the number of transitions between stride clusters ($F(5,1810)=27.75, p_{\text{gg}} < 0.001, \eta p^2 = 0.071$). Pairwise comparisons reveal differences between the preferred walking trials, where P1 had significantly more cluster transitions compared to P2 ($t(362)=3.47, p=0.003, d=0.238$) but no differences with P3 ($p > 0.05$). Among other dual task conditions, DT-An and DT-S7 both had significant differences to all preferred tasks ($p < 0.001$). When comparing between dual task conditions, DT-S1 had significantly less transitions than DT-An ($t(362)=2.94, p=0.017, d=0.183$) and DT-S7 ($t(362)=-3.91, p < 0.001, d=-0.225$), but there were no differences between DT-An and DT-S7 ($p > 0.05$). These results indicate that the dual task walking causes significantly more transitions between constant and non-constant stride clusters compared to single task walking conditions as well as some significant differences between the first preferred trial and other preferred trials. Further, task difficulty influences the number of transitions, such that the more difficult the cognitive tasks cause more transitions between clusters when characterizing these outcomes using cycle time.

Table 6-8: Pairwise comparisons of the number of state transitions defined by cycle time between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	1.17 (1.08)	0.92 (0.84)	0.96 (0.81)	1.46 (1.44)	1.74 (1.65)	1.86 (1.81)
P1	p-val Cohen (d)		0.003	0.121	0.121	<0.001	<0.001
P2			0.238	0.252	<0.001	<0.001	<0.001
P3			-	-	<0.001	<0.001	<0.001
DT-S1			0.360	0.267		0.017	<0.001
DT-An			0.324	0.549	0.183		0.40
DT-S7			0.364	0.585	-0.225	-	

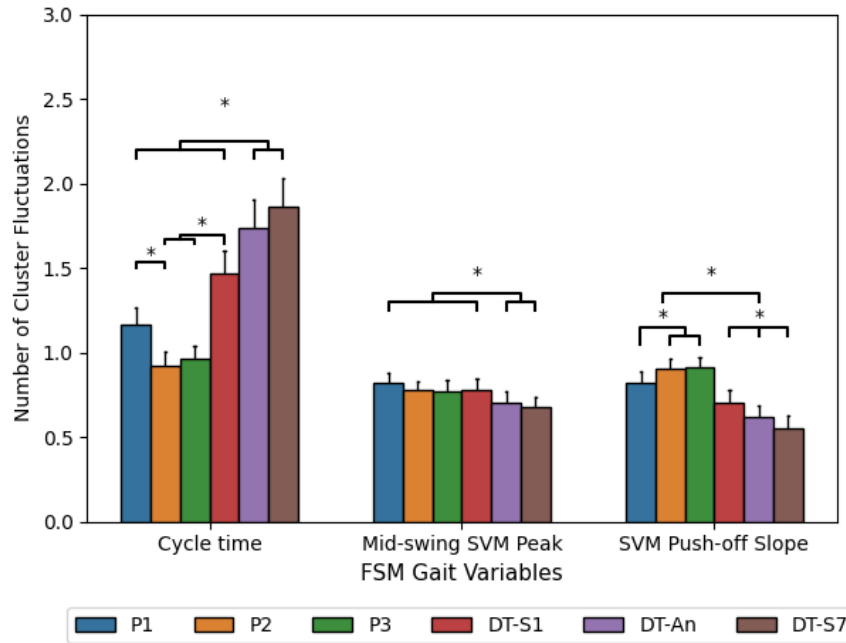


Figure 6-6: Bar plot comparing the number of cluster fluctuations with different gait variables (x-axis) between preferred and dual task walking (colours). *indicates significant difference between tasks.

Mid-swing acceleration: One-way ANOVA results revealed a main effect of task ($F(5,1810)=6.90$, $p_{gg}<0.001$, $np^2=0.019$) for the number of fluctuations between constant and non-constant strides when classified using the mid-swing acceleration peak. Pairwise comparisons revealed significant differences between specific walking tasks (Table 6-9). There was no significant difference between the preferred trials ($p>0.05$) nor was DT-S1 different from any preferred trials ($p>0.05$). There were significant differences between DT-S7 and DT-An compared with all preferred trials ($p<0.05$). Between dual task walking conditions, DT-S1 was significantly different from DT-An ($t(362)=-3.33$, $p=0.012$, $d=-0.195$) and

DT-S7 ($t(362)=0.304, p=0.025, d=0.176$) but there was no difference between DT-An and DT-S7 ($p>0.05$). As hypothesized the dual task conditions were statistically different from preferred walking however, direction of this differences was unexpected. Dual task conditions showed less cluster transitions compared to the preferred walking tasks for the more difficult cognitive walking tasks compared to preferred and simpler walking tasks when characterized with the mid-swing peak.

Table 6-9: Pairwise comparisons of the number of state transitions defined using the mid-swing peak acceleration magnitude between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	0.81 (0.60)	0.78 (0.59)	0.77 (0.64)	0.78 (0.67)	0.70 (0.70)	0.68 (0.65)
P1	p-val		1	1	1	<0.001	<0.001
P2		-		1	1	0.023	0.025
P3		-	-		1	0.025	0.042
DT-S1		-	-	-		0.012	0.025
DT-An		-0.282	-0.204	-0.194	-0.195		1
DT-S7	Cohen (d)	-0.264	-0.184	-0.174	0.176	-	

Push-off acceleration slope: One-way ANOVA results revealed a significant main effect due to walking task on the number of fluctuations between constant and non-constant clusters when classified using the push-off acceleration slope ($F(5,1810)=47.50, p_{gg}<0.001, np^2=0.116$). From the pairwise comparisons, there were significant differences with P1 compared to P2 ($t(362)=-2.83, p=0.025, d=-0.148$) and P3 ($t(362)=-2.71, p=0.025, d=-0.157$) but no differences between P2 and P3 ($p>0.05$). All preferred walking trials were significantly different than all dual task trials ($p<0.001$). differences between preferred trials reveal a difference with the first walking trial compared to the second and third, indicating the potential for some learning effects. Differences between dual task walking and the preferred walking trials show that dual tasking influences the number of transitions between states however unexpectedly there are less transitions during dual task walking compared to single task.

Table 6-10: Pairwise comparisons of the number of state transitions defined using the push-off slope between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	0.82 (0.63)	0.90 (0.62)	0.91 (0.64)	0.70 (0.70)	0.62 (0.66)	0.55 (0.71)
P1	p-val Cohen (d)		0.025	0.025	<0.001	<0.001	<0.001
P2		-0.148		0.836	<0.001	<0.001	<0.001
P3		-0.157	-		<0.001	<0.001	<0.001
DT-S1		-0.220	-0.365	-0.371		0.025	<0.001
DT-An		-0.374	-0.521	-0.526	-0.148		0.025
DT-S7		-0.494	-0.639	-0.642	0.269	0.124	

Percent Non-constant Strides

Cycle time: The one-way ANOVA revealed a main effect of task when the percent of non-constant stride clusters is classified using the cycle time ($F(5,1810)=26.43$, $p_{gg}<0.001$, $np^2=0.068$). Paired t-tests compared individual trials to determine which walking tasks were significantly different and revealed significant differences between all comparisons. The first preferred trial was significantly different from both P2 and P3. There was no significant difference between P1 and DT-S1 ($p>0.05$) and all other dual task conditions were significantly higher than preferred walking conditions ($p<0.05$). Between dual task conditions, DT-S1 was significantly different from DT-An ($t(362)=2.59$, $p=0.039$, $d=0.154$) and DT-S7 ($t(362)=-3.759$, $p=0.001$, $d=-0.226$). There was no significant difference between DT-An and DT-S7 ($p>0.05$). Significant differences between the preferred and dual task conditions reveals an effect of dual tasking that increases the percentage of strides (within the walking bout) to be clustered as non-constant compared to preferred single task walking. Differences between dual tasking conditions reveals an effect of task difficulty on the percentage of strides classified as non-constant while the differences between preferred, while significant, are small in comparison to the other differences within comparisons.

Table 6-11: Pairwise comparisons of the percent non-constant defined by cycle time between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	15.8 (16.1)	11.5 (13.0)	12.5 (13.1)	21.0 (23.8)	26.8 (29.0)	29.0 (30.4)
P1	p-val Cohen (d)		<0.001	0.026	0.258	<0.001	<0.001
P2		0.286		0.185	<0.001	<0.001	<0.001
P3		0.167	-		0.001	<0.001	<0.001
DT-S1		-	0.369	0.256		0.039	0.001
DT-An		0.252	0.525	0.414	0.154		0.258
DT-S7		0.325	0.594	0.486	-0.226	-	

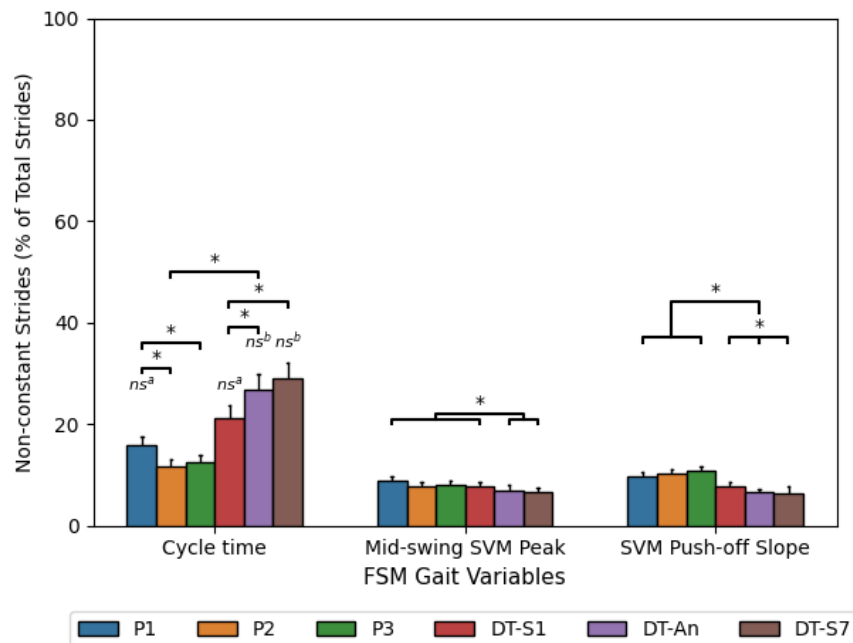


Figure 6-7. Bar plot comparing the percent non constant strides of different gait variables (x-axis) between preferred and dual-task walking (colours). *indicates significant different between tasks; ns^a represent no significant difference between P1 and DT-S1; ns^b represents no significant difference between DT-An and DT-S7

Mid-swing acceleration: One-way ANOVA results indicate that there is a main effect of task on the percent of non-constant strides when classified using the mid-swing acceleration peak ($F(5,1810)=10.64$, $p_{gg}<0.001$, $np^2=0.029$). Pairwise comparisons revealed significant differences between walking tasks. There were no differences between any of the preferred walking tasks ($p>0.05$). Preferred walking trials were also not significantly different from DT-S1s ($p>0.05$) but preferred did report significantly larger percentages compared to DT-An and DT-S7 ($p<0.05$). Between dual task conditions, DT-S1 had

significantly higher percent non-constant strides compared to both DT-An ($t(362)=-3.15$, $p=0.015$, $d=-0.182$) and DT-S7 ($t(362)=3.01$, $p=0.022$, $d=0.173$) and there was no significant difference between DT-An and DT-S7 ($p>0.05$). Differences between task suggests an influence of cognitive tasks on the percentage on constant and non-constant strides, unexpectedly the dual task conditions causes a slightly lower non-constant percentage compared to the preferred walking conditions. Furthermore, differences between dual task conditions suggest that task difficulty also affect the percent of strides that are classified as non-constant strides.

Table 6-12: Pairwise comparisons of the percent non-constant strides defined by mid-swing peak acceleration magnitude between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	8.75 (9.35)	7.75 (7.34)	7.99 (8.16)	7.70 (9.46)	6.91 (9.55)	6.51 (8.67)
P1	p-val Cohen (d)			1	1	0.091	<0.001
P2					1	<0.001	<0.001
P3						1	0.001
DT-S1						0.016	0.022
DT-An							1
DT-S7							
		-0.333	-0.259	-0.289	-0.183		
		-0.325	-0.251	-0.250	0.173	-	

Push-off accelerometer slope: One-way ANOVA results indicated there was a main effect of task on the percent of non-constant strides when classified using the push-off accelerometer peak ($F(5,1810)=57.06$, $p_{gg}<0.001$, $np^2=0.136$). Pairwise comparisons revealed significant differences between specific task conditions. In general, there were no significant differences between preferred walking trials ($p>0.05$) and all preferred walking trials had significantly larger percentages of non-constant strides compared to dual task walking conditions ($p<0.05$). All dual task comparisons were different as well, DT-S1 were significantly larger percent of non-constant strides compared to DT-An ($t(362)=-3.219$, $p=0.007$, $d=-0.165$) and DT-S7 ($t(362)=5.447$, $p<0.001$, $d=0.286$) and DT-An had significantly larger percentage of non-constant strides compared to DT-S7 ($t(362)=2.594$, $p<0.039$, $d=0.124$). Differences revealed in this statistical test suggest that dual task walking decreases the amount of strides that fall outside the preferred 2SD threshold (non-constant) compared to preferred single task walking when classified with the push-off

acceleration slope. Furthermore, differences between dual task conditions suggest that task difficulty also affect the percent of strides that are classified as non-constant strides.

Table 6-13: Pairwise comparisons of percent non-constant defined by push-off slope between preferred and dual task walking trials

Task		P1	P2	P3	DT-S1	DT-An	DT-S7
	mean (SD)	9.59 (9.1)	10.2 (8.55)	10.6 (9.33)	6.44 (8.07)	7.74 (9.18)	6.36 (12.0)
P1	p-val Cohen (d)		0.054	0.054	<0.001	<0.001	<0.001
P2		-		0.754	<0.001	<0.001	<0.001
P3		-	-		<0.001	<0.001	<0.001
DT-S1		-0.257	-0.378	-0.389		0.007	<0.001
DT-An		-0.428	-0.553	-0.563	-0.165		0.039
DT-S7		-0.548	-0.675	-0.684	0.286	0.124	

6.4.4 Limb kinematic features as an indicator of stride clustering

To examine the stride-to-stride relationships across walking tasks (i.e., preferred and dual task conditions) the grand mean of all unique stride-to-stride correlation values was calculated for both whole and assumed steady state strides. Stride cluster outcomes were also output to examine the differences across tasks in stride cluster outcomes using the stride correlation method. Correlation means and cluster outcomes were not normally distributed based on Kolmogorov-Smirnov test for normality ($p < 0.01$) and therefore data were rank transformed for parametric statistical testing. A series of one-way ANOVAs were run for each of the cluster outcomes to examine main effects of task.

Stride-to-stride correlation means

Whole walking bout: Repeated measures one-way ANOVA results indicated a main effect of walking task for mean stride to stride correlations ($F(5,1810)=32.89$, $p_{gg} < 0.001$, $np^2=0.083$). Paired t-tests were used to contrast the correlation means of individual walking tasks. Preferred walking tasks were not statistically different and had minimal differences in mean values, with P1 (mean (SD) = 0.717 (0.10)) reporting a slightly lower mean correlations compared to P2 (mean (SD) = 0.724 (0.10)) and P3 (mean (SD) = 0.723 (0.10)). Statistically significant differences existed between the majority of dual task and preferred single task walking comparisons ($p < 0.001$), the only exception was between DT-S1 (mean (SD) = 0.7 (0.11))

and P1. Each comparison between dual-task walking conditions were statistically significant, mean correlation values from DT-S1 were greater than both DT-An (mean (SD) = 0.680 (0.12), $t(362)=-2.97$, $p=0.016$, $d=0.142$) and DT-S7 (mean (SD) = 0.666 (0.13), $t(362)=6.45$, $p<0.001$, $d=0.317$) and DT-An was greater than DT-S7 ($t(362)=3.77$, $p=0.001$, $d=0.170$). Statistical differences between the mean stride to stride correlations across tasks indicated that walking with a secondary task decreased kinematic relationships between strides compared to preferred single task walking. Stride to stride relationships also got lower during more difficult dual task conditions (e.g., verbal fluency, counting by 7s) compared to the easier task condition (e.g., counting by 1s). ***Steady state walking:*** One-way repeated measures ANOVA compared the mean correlation values of the middle portion of strides during clinical gait tasks revealing a main effect of task ($F(5,1810)=27.23$, $p_{gg}<0.001$, $np^2=0.069$). Pairwise comparisons (paired t-tests) were used to compare the steady state correlation values across walking tasks. Preferred walking trials were not statistically different from each other and similar to the whole walking bout P1 (mean (SD) = 0.721(0.11)) had slightly larger mean compared to P2 (mean (SD) = 0.730(0.11)) and P3 (mean (SD) = 0.730(0.11)). Dual task conditions were mostly significantly different from preferred walking trials ($p<0.01$) apart from DT-S1(mean (SD) = 0.710(0.12)) and P1 ($p>0.05$). Comparing dual task walking conditions reveal differences between all dual task conditions; DT-S1 was significantly greater than DT-An (mean (SD) = 0.696(0.12), $t(362)=-2.77$, $p=0.03$, $d=0.130$) and DT-S7 (mean (SD) = 0.676(0.13), $t(362)=6.15$, $p<0.001$, $d=0.306$) and DT-An was greater than DT-S7 ($t(362)=3.88$, $p<0.01$, $d=0.178$). Statistical results reveal that stride-to-stride relationships are lower during dual tasks compared to the preferred walking trials. Differences across dual task conditions reveal that as dual task conditions increase in difficulty the stride-to-stride relationships also decreased with task difficulty. These differences also reveal that changes to stride-to-stride relationships are not solely driven by the first two or the last two strides and there are differences within the middle portion of walking across task difficulty.

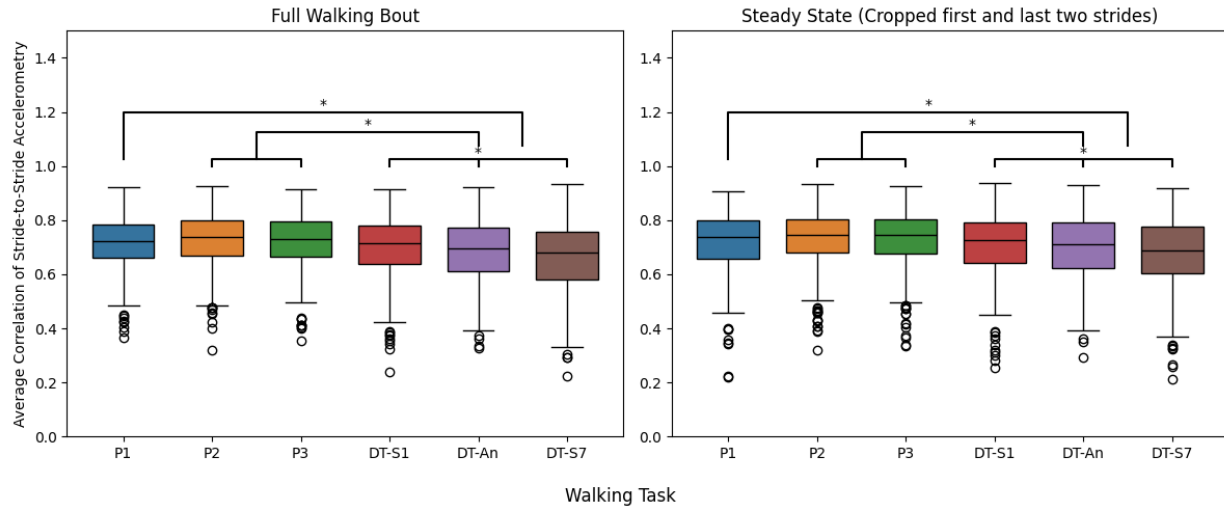


Figure 6-8. Boxplots showing the difference between tasks for inter-stride correlation value. *Left:* Boxplot comparing all the inter-stride correlations for the whole walking bout (inclusive of the assumed initiation and termination phases of walking). *Right:* Boxplots comparing the inter-stride correlations for the walking bout without the first and last two strides of the walking bout *indicates significant differences between tasks

6.4.5 Difference in stride clusters across task when using kinematic correlation values

Cluster outcomes were compared across tasks to examine how stride cluster outcomes differed when classified using stride-to-stride correlation values due to walking task. Cluster outcomes were not normally distributed based on Kolmogorov-Smirnov test for normality ($p < 0.01$) and therefore data were rank transformed for parametric statistical testing. A series of one-way ANOVAs were run for each of the cluster outcomes to examine main effects of task.

Length of first cluster

Repeated measures one-way ANOVA results revealed a main effect of task ($F(5,1810)=2.39$, $p_{gg}=0.03$, $np^2=0.006$). Pairwise comparisons only revealed one statistically significant difference between DT-S1 (mean (SD) =0.73(0.69) strides) and P1 (mean (SD) =0.91(0.84) strides, $t(362)=-3.24$, $p=0.01$, $d=0.212$). Mean and standard deviation values are reported in Table 6-14.

Number of cluster fluctuations

Repeated measures one-way ANOVA revealed a main effect of task ($F(5,1810)=2.33$, $p_{gg}=0.04$, $np^2=0.006$) but no pairwise comparisons were statistically significant during post-hoc testing ($p>0.05$). Mean and standard deviation values are reported in Table 6-14.

Percent non-constant strides

Repeated measures one-way ANOVA revealed a main effect of task ($F(5,1810)=2.95$, $p=0.01$, $np^2=0.008$) but no pairwise comparisons were statistically significant during post-hoc testing ($p>0.05$). Mean and standard deviation values are reported in Table 6-14.

Table 6-14: Inter-stride correlations for both cropped and full walking bout comparisons and stride clustering for all walking tasks using stride correlation clustering methods.

Tasks	Stride Correlations (<i>mean (sd)</i>)		Stride cluster outcomes (<i>mean (sd)</i>)		
	Whole bout	Steady state	Length initiation cluster (# of strides)	Number of cluster fluctuations	Percent non-constant strides (%)
P1	0.71 (0.10)	0.72 (0.11)	0.91 (0.84)	0.78 (0.46)	9.03 (14.01)
P2	0.72 (0.11)	0.73 (0.11)	0.83 (0.73)	0.74 (0.54)	8.45 (13.17)
P3	0.72 (0.11)	0.73 (0.12)	0.84 (0.82)	0.73 (0.58)	8.42 (12.80)
DT-S1	0.70 (0.11)	0.71 (0.12)	0.74 (0.69)	0.74 (0.66)	9.07 (15.72)
DT-An	0.68 (0.12)	0.69 (0.13)	0.97 (1.40)	0.82 (0.85)	10.68 (17.65)
DT-S7	0.66 (0.13)	0.67 (0.14)	0.98 (1.16)	0.88 (0.87)	13.07 (20.80)

6.5 Discussion

The goal of this study was to examine the methodological approaches to identify and assess the intra-bout phases during short clinical walking tasks of varying difficulty. Although identifying gait initiation periods commonly relies on stride velocity, this work aimed to advance stride clustering approaches with alternative measures (Nguyen et al., 2019). With respect to objective 1, the results from this study supported the hypothesis that stride clustering parameters (gait variables and static thresholds) would cause different intra-phase descriptions across preferred walking trials. Additionally, results also supported the hypothesis that dual task walking conditions would cause changes to the intra-bout phases when compared between tasks and with single-task conditions. This study examined changes to intra-bout

phases across single- and dual-task walking. Characterizing changes to these phases allows for identification of gait variability at the intra-bout phase level compared to stride-to-stride variability. Several clustering parameters were applied to single-task walking and compared across single-task trials. Differences between single-task trials for some parameter combinations were reported but no consistent differences were identified with parameter clusters. Dual-task walking had significant effects on length of initiation cluster, number of transitions, and percent-non-constant for all the gait variables carried forward (e.g., cycle time, mid-swing acceleration peak, and acceleration push-off slope). Interestingly, the direction of change during dual-tasking depended on the gait variable used (e.g., temporal or accelerometry-derived) which may aid in revealing specific locomotor control strategies or a link to accelerometry kinematics and temporal outcomes during walking. With respect to objective 2, the results of this study support the hypothesis that inter-stride correlations can reveal differences across task difficulty, but these results did not confirm differences in intra-bout phases using stride similarity parameters. Inter-stride correlations were statistically lower during dual-task walking compared to single-task walking suggesting that limb trajectory control may reveal differences in walking conditions. This study expanded stride clustering methodology used in previous research by testing stride clustering approaches with an expanded set of gait variables, across different tasks and in shorter walking bouts. Further, this study used a broader and larger cohort of participants with neurological disorders (e.g., NDD or CbVD). Stride clustering outcomes provide an alternative method to describe stride-to-stride variability during shorter clinical walking tasks. Examining the acceleration profile of the limb during walking also revealed that rhythmicity of spatiotemporal outcomes and regularity of limb trajectory may both be impacted by cognitive secondary tasks.

Identifying intra-bout phases using different stride clustering parameters

Stride clustering approaches aim to bin strides to represent intra-bout phases. This study examined stride clustering parameters between single task walking trials. Additionally, this study evaluated changes to intra-bout phases across single- and dual-task walking. Across all gait variables,

there were statistically different cluster outcomes during dual-task walking when compared to single-task trials. When clustering strides with cycle time, there were increases in the initiation cluster length between the two most difficult dual-task trials (DT-An and DT-S7) and there was a longer initiation period during P1 compared to P2 and P3. Gait initiation research reports increased stride-to-stride variability during gait initiation during dual-task walking compared to single-task walking in people with MCI (Wittwer et al., 2008a) and increases in length and step count in frail elderly adults (Lindemann et al., 2008), both are factors that can contribute to longer initiation clusters during dual-task walking. Increased gait initiation time may be due to difficulty maintaining stability or an adaptation to the initiation phase to maintain stability in the face of decreasing balance control. Using cycle time to cluster strides increased the number of state transitions during dual-task walking, revealing an increase in fluctuations of states as well strides that deviate from the mean for several consecutive strides during dual-task walking. This is a unique description of stride-to-stride variability (using intra-bout phases) to provide context for increases in stride variability. In addition, percent non-constant also increased during dual-task walking when characterized using cycle time. Increases in percent non-constant quantifies the total number of strides that deviate outside the static threshold (i.e., incorporates both the number of state transitions and length of initiation cluster). Different from previous research in stride variability, these measures of intra-bout phases identify strides that have large deviations from the mean and therefore, increases in these outcomes may identify highly variable gait but overlook minor changes to gait variability. Stride clustering using, accelerometry-derived gait variables caused a different effect on intra-bout phases during dual task walking. Stride cluster outcomes were different in the opposite direction (i.e., a decrease in the length of initiation clusters, number of state transitions, and percent non-constant strides) during dual task walking. One explanation for lower stride cluster outcomes during dual task walking may related to the variability of accelerometry kinematics. Variability of accelerometry kinematics are not well understood and the use of a sum vector magnitude might mask multi-directional movement variability. Exploration into multi-directional compensatory movements or extensions beyond these single moments of acceleration magnitudes or slopes might be needed to properly represent the

differences within and between strides during walking. Alternatively, these decreases represent actual change in accelerometry kinematics that are linked to dual task. Lower variability of accelerometry kinematics may be linked to tighter control of limb trajectory or simply decrease magnitude of joint kinematics as a compensatory action under cognitive load. In healthy adults and Parkinson's disease, lower knee and hip flexion has been seen in healthy (Lin & Lin, 2016) and Parkinson's disease (Pinto et al., 2020). Piche et al (2022) found there was no difference in joint angle comparisons but there were differences in angular velocity at the hip and knee in a similar comparison. Further, there is evidence to suggest that integration of somatosensory and peripheral information influence specific phases of the gait cycle in a different manner suggesting that phases of the gait cycle could influence variability and inter-joint coordination (Wang et al., 2021). Few studies comment on the variability of lower limb kinematics during walking in neurodegenerative disease with lower limb kinematics. However, increases in gait variability are consistently reported in neurologic and older adults during dual task walking across many gait outcomes (Goh et al., 2021; Hausdorff et al., 2008; Hollman et al., 2007; Montero-Odasso, Verghese, et al., 2012; Priest et al., 2008). There is need for further investigation of lower limb kinematics during dual task walking.

Stride-to-stride relationships to represent consistency across clinical walking tasks

Stride consistency within a walking bout was investigated by calculating inter-stride correlations across the whole walking bout. In this study, regularity of strides was assessed by examining the relationships between stride-to-stride accelerometry waveforms. Dual task walking caused lower stride correlation means compared to single task walking where nearly all dual task walking conditions had lower correlation averages when compared to single tasks. Lower correlation averages showed less consistency between strides. Similar findings in previous research have shown that lower limb regularity outcomes distinguish between single- and dual-task walking in people with Parkinson's disease (Ahmadi et al., 2021). Decrease in limb trajectory consistency may be due to changes in accelerometer magnitude caused by changing speed or a change in temporal proportion (stance-swing time) of the gait cycle.

Similar gait changes are seen in older adults during dual task walking (Plummer-D'Amato et al., 2010) and in free-living environments (Lunardini et al., 2021). Examining the relationship between stride kinematics includes both the temporal and spatial movement of the limb throughout the whole walking bout. The approach used in this study to evaluate regularity is different from previous methods in two ways. First, this research relies on a unique stride segmentation method to assess lower limb consistency of accelerometry kinematics rather than trunk-worn inertial measurement units (Riva et al., 2013), which has been documented previously (Ahmadi et al., 2021) and does not rely on segmentation. Analyzing 3D movement of the trunk and head to view similarities between strides has been used to assess stability and identify specific stability control problems such as parkinsonian gait (Brodie et al., 2014). Further, this work examines the relationship between strides of both limbs compared to acceleration from a single limb which may expand its utility to identify bilateral coordination or asymmetry related outcomes. Stride level correlations were used to identify stride clusters but no differences between tasks were reported. Stride level correlations to define clusters may be similar across tasks because of the definitions used to classify non-constant strides (0.5 correlation) such that this value may not properly evaluate stride consistency. These threshold levels were referenced from previous research from a different task (i.e., APAs). Further research should investigate the relationship between these stride correlations to understand how thresholds may be used to define cluster outcomes. This current work expands beyond simply trunk and head worn outcomes and builds on current research assessing gait from lower limb accelerometry kinematic outcomes. Significant differences exist between dual task walking trials, such that more difficult secondary tasks had lower correlation means compared to the easier counterparts. Differences between dual task trials are important to recognize changes due to cognitive-motor interference of the secondary cognitive task during walking (Beauchet et al., 2005; Goh et al., 2021). These novel insights advance understanding of provide insight into the effect of difficult secondary tasks on limb lower trajectory and may probe stride-to-stride variability in novel ways.

Providing insight into gait variability beyond stride-to-stride outcomes

The results from this study show that there are differences in stride cluster outcomes when comparing dual task and single task walking in clinical gait assessments. Identifying different clusters of strides may provide insight into the characteristics of intra-bout phases and how they might contribute to stride variability. This work advances stride clustering outcomes from previous work in methodological approaches and has analytical and clinical implications. Although this study used stride clustering methods, there was no restriction on gait initiation periods allowing prolonged initiation clusters which differed from previous research which assumed gait acceleration occurred in the first 25% of strides (Nguyen et al., 2019). Further, this study permitted fluctuation between constant and non-constant states in the middle of walking which may relate better with stride fluctuations. Under the dual task paradigm and attentional resource theory, identifying these fluctuations may relate to strategies associated with cognitive performance (e.g., attention switching between walking and cognitive responses). These methodological approaches may have the ability to improve interpretation of gait during both free-living and clinical assessments by better identifying steady state walking during short and long walking periods. Task differences in clinical walking reinforces the need for careful interpretation of changes during dual task walking and how it might relate to gait or cognitive impairment. Identifying unique clusters of strides and the effect of dual task walking on intra-bout phases may be linked to specific mobility outcomes, such as increased initiation periods during walking and the risk of falling in frail older adults (Lindemann et al., 2008). A second clinical implication relates intra-bout phases to stride-to-stride variability. During short clinical gait assessments, longer gait initiation periods or fluctuations outside of steady rhythm (or to a new steady rhythm) may influence gait variability measures. These contextual influences would systematically alter stride variability. Stride variability requires a larger number of steps to properly characterize locomotor control, although numerous studies indicate that variability is properly assessed during short walking bouts this limitation still exists. Identifying clusters of strides outside the variability band (percent non-constant) or the frequency in which these transitions occur (number of state transitions)

may provide insight into variability during short clinical walks without the need for increased number of strides to interpret locomotor control. More work is needed to ensure that these measures correspond with gait initiation but also provide an appropriate representation of gait variability. Outside of the clinical environment, the identification of stride clusters and intra-bout phases may improve assessment of stride-to-stride outcomes in free-living environments by providing context of stride-to-stride outcomes in complex highly variable free-living walking.

While this study examines the phases of a walking bout using stride clustering methodology and provides an examination of the effects of dual task walking on these outcomes, there are several items that may limit the interpretation of these findings. Although this study provides novel insight into these core ideas, the definition of intra-bout phases using stride clustering outcomes were not compared to classically defined gait initiation (e.g., stride and gait velocity) definitions. Traditionally gait initiation periods are defined using speed thresholds (Halliday et al., 1998; Lindemann et al., 2008; Muir et al., 2014) and require the calculation of stride velocities. Little research investigates the relationship of spatiotemporal outcomes to define steady walking. Nguyen et al., (2019) used temporal and stride velocity metrics to identify intra-bout phases (constant and non-constant strides) but did not compare between the two methods. However, they did confirm differing relationships between UPDRS subsection scores and stride clusters. Future research should continue to build on the understanding of intra-bout phases in relation to disease specific mobility outcomes for advancement in rehabilitative and therapeutic interventions. The present study had novel contributions to characterizing intra-bout phases using stride clustering methods, there is need for further research to understand the influence of intra-bout phases on stride-to-stride variability and other clinical measures of gait and mobility. A second limitation in this study is that the approaches used did not consider left and right limbs individually. The FSM algorithm segments strides from individual limbs and combines the individual limbs together to characterize constant and non-constant clusters. In future studies, the impact of asymmetric gait should be considered when creating clusters. Gait asymmetry also affects inter-stride correlations, however, accelerometry

signals between left and right limb are correlated without considering asymmetry. This study builds upon past research to describe stride-to-stride variability within gait assessments. Stride clustering outcomes and kinematic assessment of variability aim to understand contributors to variability and locomotor control.

6.6 Conclusion

This study aimed to identify intra-bout phases of walking tasks conducted within a clinical gait assessment. Temporal and accelerometry derived outcomes were used to bin like strides into distinct clusters that might contribute to gait variability. Further, to expand the assessment of variability, inter-stride correlations were assessed to examine variability from a kinematic perspective beyond summary spatiotemporal outcomes. In general, both temporal and accelerometry derived outcomes identified differences in stride clusters when comparing across task difficulty. Interestingly the direction of change that dual task caused on stride cluster outcomes was different for temporal outcomes versus accelerometry outcomes, reflecting tighter control of accelerometry outcomes compared to cycle time or a strong relationship with gait velocity. Inter-stride correlations were also significantly different between tasks, where lower average correlations were reported during dual task compared to single task walking. This suggests that variability is not singularly affecting the rhythmicity of walking but also the regularity of lower limb kinematics. Although further work is needed, identifying these unique clusters and inter-stride correlations are novel ways to investigate gait variability and further understand the changes to locomotor control during dual tasking. Identifying intra-bout phases of walking may help understand the contribution of strides to gait variability and overall dynamic stability. Importantly, this study examined gait in a clinical setting with low-cost sensors in a method to advance analytical approaches that may benefit understanding of gait in free-living environments.

Chapter 7

EVALUATING THE ASSOCIATION BETWEEN THE ACCELEROMETRY, STRIDE CLUSTERING, AND INTER-STRIDE CORRELATION OUTCOMES WITH CLINICAL MARKERS OF MOBILITY AND GAIT

7.1 Introduction

In Canada, cases of dementia are expected to rise to over a million by 2038, with Alzheimer's Disease and Vascular Dementia being the leading cause for dementia cases (Dudgeon, 2010). The number and severity of falls for cognitively impaired people is a growing problem. There is evidence of a strong relationship between dementia and mobility. The effectiveness of gait assessments to inform mobility risk in these disease cohorts continues to emerge as a priority marker of dynamic stability and may provide an assessment disease severity and prognosis. Currently, clinical scales (e.g., UPDRS, Timed-up-and-go (TUG), etc.) and gait speed are relied upon by clinicians, but these outcomes may not appropriately evaluate mobility in all people. Improving the assessment of mobility and gait to outline markers of stability and independence is important for optimal therapeutic or rehabilitative interventions.

Gait assessments are an important context in which mobility, fall risk, and independence can be evaluated. Walking is a complex movement pattern that relies on intact cortical and sub cortical areas (i.e., motor and cognitive) for success (IJmker & Lamoth, 2012; Montero-Odasso, Verghese, et al., 2012; Wilson et al., 2019). Evidence supports that visuospatial (e.g., frontal–hippocampal circuits) and executive control (e.g., prefrontal–striatal circuits) are key processes involved in gait performance. Burden within these networks are cause for gait dysfunction (e.g., slow walking speeds, increased variability) (Beauchet et al., 2014; De Melo Coelho et al., 2012; Montero-Odasso, Verghese, et al., 2012). Even in healthy aging brains white-matter hyperintensities can affect the activation of neighbouring regions which may be linked to gait impairment (Nordahl et al., 2006). These overlapping areas of motor and cognitive cortical areas are where motor-cognitive interaction occur (Morris et al., 2016; Tian et al., 2017).

Gait and cognitive impairment assessed concurrently has introduced unique relationships within neurologic disorders such as motor cognitive risk syndrome (Verghese et al., 2013), motor phenotypes (Campbell et al., 2020; Mc Ardle et al., 2020), and motor-cognitive profiles of specific neurodegenerative diseases (Gillain et al., 2016; Kikkert et al., 2016). Alzheimer's Disease and Parkinson's disease with

cognitive impairment are clinically characterized by impairment in several cognitive domains including memory (episodic, working, and semantic), visuo-spatial and language abilities, and executive attention control (Aarsland et al., 2021) and are burdened during dual tasking in the clinic. Gait assessment, along with several mobility-based tasks, has the potential to be a valuable part of initial screening in functional mobility assessments (Thomson et al., 2023). Gait and mobility assessments may also have a role to track aspects of disease over time (Cezar et al., 2021; Collyer et al., 2022), however relationships between gait outcomes and clinical scales are not commonly compared.

Functional mobility scales provide clinicians with useable and clinic friendly assessment tools. These scales can be specific for modalities of mobility (e.g., posture, gait, and balance). Some examples for the aging population include assessments of balance and fall risk (e.g., Berg Balance Scale (Berg et al., 1992)), identifying motor phenotypes (e.g., Postural Gait Instability Score of the MDS-UPDRS (PIGD score) (Prime et al., 2020; Stebbins et al., 2013)), evaluate psychometric properties of balance confidence and fear of falling (e.g., Fear of falling questionnaire, Falls efficacy scale (FES) (Yardley et al., 2005), Activities specific Balance Confidence (ABC) (Powell & Myers, 1995)), and functional disability and independence (e.g., Instrumented Basic Activities of Daily Living (BADL) (Giebel et al., 2014)). Reportedly, many of these scales have inadequate performance and have not undergone sufficient testing for widespread adoption (Bloem et al., 2016). Quantitative gait assessment provides an objective measure to identify cognitive decline. Slower walking speeds are associated with cognitive impairment and dementia (Grande et al., 2019). Assessments can estimate the transition from cognitively impaired to different dementia types, specifically wider steps and larger cycle time variability during dual task walking (De Cock et al., 2019). Both single and dual task walking conditions can distinguish between dementia and mild cognitive impairment (Bovonsunthonchai et al., 2022). In a systematic review of people living with dementia, gait outcomes were characterized by increased double support time variability, use of mobility aids, and higher UPDRS scores for those at risk of falling. Gait assessment outcomes have the precision to overcome the ceiling effects of subjective reporting. Specifically, gait

assessment was associated with recurrent falls while none of the mobility scales reported such a relation (Modarresi et al., 2019). Clinical scales of disease or balance control often incorporate gait assessments, however these scales are subjective and quantitative gait assessment is likely to improve the specificity of diagnosis and assessments of disease (Mirelman et al., 2019). There is need to continue to examine the relationship between gait outcomes and clinical scales.

7.2 Study Objectives & Hypotheses:

Gait assessments are important for assessing mobility and overall health. Intra-bout phases may be valuable in describing aspects of mobility. Primarily, this study aims to assess the associations between conventional gait-specific measures (e.g., conventionally reported outcomes from gait and clinical scales of mobility) with quantitative gait outcomes (e.g., accelerometry kinematics, stride clustering, inter-stride correlations) for people with neurodegenerative disease. A second aim of this study is to evaluate the differences in gait performance between groups stratified by clinically important gait related thresholds. This work strives to understand the benefit of stride cluster outcomes beyond conventional clinical gait outcomes, using these two specific aims:

1. To assess the association between conventional spatiotemporal outcomes, clinical gait outcomes, stride clustering, and stride correlation outcomes during preferred and dual task (DT-S7) walking.

H1: It is hypothesized that conventional spatiotemporal gait outcomes will have a moderate-strong association with clinically reported gait outcomes.

H2: It is hypothesized that clustering outcomes and stride correlation outcomes will have a moderate-strong association with spatiotemporal gait outcomes and clinical measures of mobility.

2. To evaluate the differences in conventional spatiotemporal gait outcomes, stride clustering outcomes, and stride correlation outcomes during single- and dual-task (serial 7s) walking when people are stratified and defined by clinically important thresholds of gait and mobility function.

H1: It is hypothesized that conventional spatiotemporal outcomes, stride clustering, and correlation outcomes will identify differences between clinically stratified groups, such that groups with lower mobility performance will have slower velocities, lower performance on cluster outcomes, and lower stride correlation means.

7.3 Methods

7.3.1 Study Design

This study is a cross-sectional analysis of gait and mobility-specific clinical data collected as part of the ONDRI Foundational Study. Data included in this study are conventional spatiotemporal gait outcomes, novel gait assessment outcomes (e.g., stride clustering, accelerometry-based kinematics, and stride correlation outcomes) and gait-specific and mobility-specific clinical markers (e.g., gait sub-section of the UPDRS).

7.3.2 Participants

Description of participant enrollment and data availability can be found in [Chapter 5.3.2](#). In brief, there were 497 participants included in this study from four different neurodegenerative disease cohorts: Alzheimer's Disease and Mild Cognitive Impairment (ADMCI; n=126), Frontotemporal Lobar Degeneration (FTD; n=50), Parkinson's Disease (PD; n=140), and Cerebrovascular Disease with and without cognitive impairment (CbVD; n=160).

7.3.3 Data Collection

Data was collected at the different collection sites following the description provided in [Chapter 3](#). Accelerometer data (X-16 triaxial accelerometers, Gulf Coast Data Concepts, Waveland, MS) were processed and segmented into strides using the Finite State Machine algorithm described in [Chapter 4](#) & [Chapter 5](#). Stride clustering outcomes and inter-stride correlation outcomes were previously described in [Chapter 6](#). All data processing was done using python programming language (Python v3.9).

Mobility and gait-specific clinical measures were collected at clinical sites by site coordinators. Specifically used in this study were the following clinical scales and markers:

Fear of falling: Fear of falling was assessed with an 11-point Likert scale and participants were asked to rank their fear of falling on a Likert scale from 0 (no fear) – 10 (very afraid) by answering this question:

“Using a scale from 0 – 10 where 0 is “not afraid” and 10 is “extremely afraid”, how afraid of falling are you?”

0 1 2 3 4 5 6 7 8 9 10

Activities-specific Balance Confidence Questionnaire: The ABC is a validated tool to assess activity difficulty in daily lives of person greater than 65 years old (Powell & Myers, 1995). This tool has been extensively used to describe the psychometric assessment of balance confidence and mobility or fall risk in many cohorts like stroke (Botner et al., 2005), mild cognitive impairment (Rolenz & Reneker, 2016), and Parkinson’s Disease (Mak & Pang, 2009). The full 16-item scale was used in this study to evaluate person’s confidence when completing activities commonly completed in daily life. Responses range from 0 (no confidence) to 100 (completely confident) (Table 7-1).

Table 7-1: Activities of Balance Confidence

“How confident are you that you will not lose your balance or become unsteady when you...”											
0% (no confidence) to 100% (completely confident)											
1. Walk around the house?	0	10	20	30	40	50	60	70	80	90	100
2. Walk up and down stairs inside your home?	0	10	20	30	40	50	60	70	80	90	100
3. Bend over and pick up a slipper from the front of a closet floor?	0	10	20	30	40	50	60	70	80	90	100
4. Reach for a small can off a shelf at eye level?	0	10	20	30	40	50	60	70	80	90	100
5. Stand on your tip-toes and reach for something above your head?	0	10	20	30	40	50	60	70	80	90	100
6. Stand on a chair and reach for something?	0	10	20	30	40	50	60	70	80	90	100
7. Sweep the floor?	0	10	20	30	40	50	60	70	80	90	100
8. Walk outside the house to a car parked in the driveway?	0	10	20	30	40	50	60	70	80	90	100
9. Get into or out of a car?	0	10	20	30	40	50	60	70	80	90	100
10. Walk across a parking lot to the mall?	0	10	20	30	40	50	60	70	80	90	100
11. Walk up or down a ramp?	0	10	20	30	40	50	60	70	80	90	100
12. Walk in a crowded mall where people rapidly walk towards you and pass you by?	0	10	20	30	40	50	60	70	80	90	100
13. When people bump into you as you walk through the mall?	0	10	20	30	40	50	60	70	80	90	100
14. Step on or off an escalator while holding onto a railing?	0	10	20	30	40	50	60	70	80	90	100
15. Step onto or off an escalator while holding onto parcels such that you cannot hold onto the railing?	0	10	20	30	40	50	60	70	80	90	100
16. Walk outside on icy sidewalks?	0	10	20	30	40	50	60	70	80	90	100

Movement Disorders Society-Unified Parkinson’s Disease Rating Scale (MDS-UPDRS): Scales and descriptions of the MDS-UPDRS tasks are available from the International Parkinson and Movement Disorders Society on the MDS webpage (www.movementdisorders.org) (Goetz et al., 2019). Each section is rated on a scale of ability: 0 - *Normal*, 1 - *Slight*, 2 - *Mild*, 3 - *Moderate*, and 4 - *Severe*. For data analysis in this study ‘Moderate’ and ‘Severe’ were grouped as a single group (Moderate-Severe). Specific sections of the UPDRS have previously been used to identify motor phenotypes postural instability & gait disturbance (PIGD) or tremor dominant (TD) in Parkinson’s Disease (Prime et al., 2020; Stebbins et al., 2013). Although this examines and identifies phenotypes, selecting the sub-sections of the UPDRS may provide insight into specific gait related impairment and represent distinct visual gait assessment strategies by trained neurologists. Previous research has identified the UPDRS gait and postural control scores as having unique relationships between stride cluster outcomes (Nguyen et al.,

2019), therefore, this study used these two specific sub-sections to represent visual assessment of balance control and gait:

- Part 3.10 Gait: Instructions to examiner: Testing gait is best performed by having the patient walking away from and towards the examiner so that both right and left sides of the body can be easily observed simultaneously. The patient should walk at least 10 meters (30 feet), then turn around and return to the examiner. This item measures multiple behaviors: stride amplitude, stride speed, height of foot lift, heel strike during walking, turning, and arm swing, but not freezing.
- Part 3.12 Postural stability: Instructions to examiner: The test examines the response to sudden body displacement produced by a quick, forceful pull on the shoulders while the patient is standing erect with eyes open and feet comfortably apart and parallel to each other.

Montreal Cognitive Assessment (MoCA): The Montreal Cognitive Assessment (MoCA) is a general cognitive screening tool (Nasreddine et al., 2005). This test has been used in many disease and aging populations, including PD (Hoops et al., 2009) and vascular disease (Dong et al., 2010). Total MoCA score can be interpreted as follows: normal cognition (26-30 points), MCI (18-25 points), moderate CI (10-17 points), severe CI (<10 points). As it relates to disease, cognitive intact persons score >26 (average 27.4), people with MCI score 22.1 on average, and those with Alzheimer's disease score 16.2 on average (Dong et al., 2010; Hoops et al., 2009; Nasreddine et al., 2005). For this study a threshold of 22.1 was used to stratify cognitive impairment and normal cognition.

Falls history (12-month Follow-up): A fall history questionnaire evaluated one year fall history recall. Fall history can be indicative of future fall events (Greany & Di Fabio, 2010) and severe falls that include hospitalization have stronger relations to future fall events (Grau-Pellicer et al., 2019). Persons will be labelled as 0 – no falls, or 1 – at least one fall within the last 12-months.

7.3.3 Data Analysis

All conventional gait outcomes, clinical datasets, and functional mobility questionnaires have been released as part of the ONDRI Foundational Study (www.ondri.ca) and have undergone data quality cleaning and outlier detection protocols (Sunderland et al., 2019).

Temporal gait variables, accelerometry based outcomes, and bout clustering outcomes were described in Chapters 5 & 6 of this thesis. Although several dual tasks were used in the full gait assessment protocol, only DT-S7s was used in this analysis of outcomes associations.

To compare between groups that are stratified by clinically important thresholds (preferred walking speed, dual task cost percentage, and the UPDRS-Gait scores) outcome measures were grouped by the respective thresholds. There were three different thresholds used to stratify groups:

- *Preferred Walking Speed*: A threshold for preferred walking speed of 0.8 m/s was chosen to reflect those that are at increased risk of reduced function (Middleton et al., 2016; Ostir et al., 2007; Perry et al., 1995). Those with less than 0.8 m/s preferred trial walking speed are classified as “Poor” walking and above were classified as “Normal”. The same randomized trial used in Study 3 was carried forward for each subject in this study.
- *Dual-task Cost (during DT-S7)*: Dual task cost expresses the change in velocity as a percentage of the preferred walking speed (Montero-Odasso, Verghese, et al., 2012). Cost percentages greater than 20% have been linked to increased risk of mild cognitive impairment, therefore participants with velocity costs greater than 20% were listed as at risk (“>20%”) and below was labelled as no risk (“<20%”).
- *Unified Parkinson’s Disease Rating Scale Sub-Section III*: The gait item of the UPDRS motor sub-scale (item 3.10) was used to stratify participants based on the criteria outlined within the UPDRS, there are five different categories people can be labelled: Normal,

Slight, Mild, Moderate, and Severe. For this study Moderate and Severe were binned together to create four different UPDRS categories.

7.3.4 Statistical Analysis

Statistical analysis were completed using the python programming language (Python v3.9) using the Pingouin (Vallat, 2018) and Statsmodels (Seabold & Perktold, 2010) packages. Data was checked for normality using the Kolomogorov-Smirnov test and Q-Q plots were output to display the skewness and kurtosis characteristics of the data.

To determine the association between clinical markers and gait outcomes spearman correlations were used when normality was violated. A focussed correlation method was taken to determine the association between conventional, clinical scales, and novel gait outcomes. To determine a baseline associative relationship of gait outcomes, the correlation between conventionally reported quantitative gait outcomes and gait-specific clinical markers (e.g., velocity, dual task cost (velocity), cycle time variability and clinical markers) were completed. To assess the relationship of single- and dual-task outcomes from the FSM algorithm, spearman correlations compared relationships of FSM outcomes with conventionally reported gait outcomes and UPDRS Part III, item 3.10 (gait)score. Stride cluster outcomes were compared to conventionally reported single and dual-task gait outcomes and select clinical scales. The length of initiation cluster was assessed with UPDRS Part III, item 3.12 (postural stability), the Activities Balance Confidence scale, and 12-month fall history to assess it relationship with potential clinical-markers of fall risk, while number of state transitions and percent nonconstant were compared to UPDRS gait scores and the MoCA score to assess variability and association of cognition with performance. Stride correlations were compared with variability measures and the UPDRS gait score, 12-month fall history, and total MoCA score. Spearman correlations were considered significant when $p < 0.01$ and all correlations that were between -0.25 and 0.25 were greyed out in results tables due to weak association.

To determine the differences between groups stratified by preferred gait speed (0.8 m/s threshold), independent samples t-tests will compare between groups for gait outcomes during dual task and preferred walking. Data were tested for normality using the Kolomogorov-Smirnov test and Levene's test was used to test for homogeneity of variance. For all tests between variables, Bonferroni-Holm correction was applied to account for multiple comparisons between the walking speed stratified groups. The same statistical steps were taken to compare between groups stratified by their dual task cost percentage (percentage of slowing).

To determine the differences between UPDRS gait score classifications, a one-way between subjects ANOVA was used to compare between the UPDRS scores for gait outcomes during dual task and preferred walking conditions. A Bonferroni-Holm correction was be applied to all main effects from the one-way repeated measures ANOVA and significance level of $p < 0.05$ will be used. When significant main effects are calculated, pairwise comparisons will be used to determine the significant differences between groups within gait variables with a Bonferroni-Holm correction applied to account for multiple comparisons.

7.4 Results

Spearman correlations were used to evaluate the association of conventional gait outcomes (gait speed, cycle time variability), stride clustering outcomes, and inter-stride correlations during single- and dual-task walking with gait specific clinical markers of mobility.

7.4.1 Participants & Data Availability

Participants included in this study are as outlined in Chapter 3 and Chapter 4 of this thesis. In total, 480 participants were included in the study and are described in Table 7-2. All participants did not complete all clinical scales, or questionnaires, Table 7-3 shows the demographic and clinical outcomes that have missing participants.

Table 7-2: Participant demographic information

NDD and CbVD <i>Mean (SD)^a</i>		ADMCi	FTD	PD	CbVD	
n	480	126	53	140	161	
Age (SD)	69.1 (7.4)	71.03 (8.16)	67.84 (7.06)	67.94 (6.35)	69.21 (7.41)	
Sex (% female)	32.9%	45.2%	35.8%	22.1%	31.7%	
Height (cm)	171.6 (9.7)	169.58 (10.72)	171.27 (11.91)	173.71 (9.07)	170.58 (9.28)	
Weight (kg)	81.6 (16.2)	77.06 (16.15)	81.8 (18.87)	82.2 (16.8)	83.08 (15.32)	
Fall history (12-mo)	150/480	43	24	38	45	
Number of Falls (min-max)	1-200	1-8	1-200	1-100	1-50	
Fear of Falling*	1.9 (2.6)	1.66 (2.64)	2.16 (3)	1.91 (2.31)	1.77 (2.49)	
MoCA	24.5 (3.3)	22.67 (3)	21.45 (3.93)	25.84 (2.57)	25.23 (3)	
ABC Scale [†]	87.1 (15.6)	89 (14.98)	70.4 (32.43)	85.36 (15.1)	88.44 (12.77)	
Unified Parkinson's Disease Rating Scale						
Gait	Normal	301	92	31	58	120
	Slight	126	18	7	68	33
	Mild	21	1	5	11	4
	Moderate-Severe	18	1	10	3	4
Postural Stability	Normal	335	92	30	98	115
	Slight	79	15	6	29	29
	Mild	19	1	1	9	8
	Moderate-Severe	31	4	15	4	8

MoCA: Montreal Cognitive Assessment; ABC: Activities of Balance Confidence; mo: month; ADCi: Alzheimer's disease and mild cognitive impairment; PD: Parkinson's disease; FTD: Frontotemporal dementia; CVD: Cerebrovascular disease; ALS: Amyotrophic lateral sclerosis.

*Fear of falling: greater score indicates increased fear of falling; scored on 10-point Likert scale

[†] Activities of Balance Confidence: greater score indicated more confidence in balance ability

^c mean and standard deviation provided where applicable

Table 7-3: Number of participants for each clinical measures that were missing from reported values above

	NDD and CbVD	ADMCi	FTD	PD	CbVD
n	480	126	53	140	161
Height	475	125	50	139	161
Weight	473	125	49	139	160
Fear of Falling*	426	115	49	119	143
ABC Scale[†]	474	126	49	140	161
UPDRS - Gait	466	112	53	140	161
UPDRS – Postural Control	464	112	52	140	160

ABC: Activities of Balance Confidence; ADCi: Alzheimer's disease and mild cognitive impairment; PD: Parkinson's disease; FTD: Frontotemporal dementia; CVD: Cerebrovascular disease; ALS: Amyotrophic lateral sclerosis.

Table 7-4: Summary of stride cluster outcomes for cycle time and mid-swing peak across all walking tasks

Cluster Metric	Gait Variable	Walking Task	NDD & CbVD	ADMCI	FTD	PD	CbVD
Length of Initiation Cluster (# strides)	Cycle Time	PREF	0.95 (0-9)	0.89 (0-4)	0.82 (0-3)	1.13 (0-9)	0.85 (0-5)
		DT-S7	1.74 (0-12)	1.75 (0-12)	2.35 (0-10)	1.43 (0-9)	1.88 (0-12)
	Mid-swing Peak	PREF	0.97 (0-4)	1.01 (0-4)	0.82 (0-2)	1.05 (0-3)	0.90 (0-4)
		DT-S7	0.79 (0-8)	0.62 (0-3)	0.74 (0-3)	0.89 (0-6)	0.83 (0-8)
Number of State Transitions	Cycle Time	PREF	0.95 (0-6)	0.90 (0-4)	0.94 (1-2)	1.12 (1-6)	0.82 (0-4)
		DT-S7	1.85 (0-12)	1.96 (1-12)	2.96 (1.5-8)	1.56 (1-6)	1.79 (0-10)
	Mid-swing Peak	PREF	0.76 (0-2)	0.76 (0-2)	0.79 (0-2)	0.82 (0-2)	0.69 (0-2)
		DT-S7	0.67 (0-4)	0.69 (0-4)	0.67 (0-2)	0.65 (0-2)	0.68 (0-4)
Percent Non-constant (%)	Cycle Time	PREF	12.3 (0-100)	12.2 (0-75)	8.91 (5.41-25)	15.0 (7.14-100)	10.6 (0-69.2)
		DT-S7	29.0 (0-100)	31.6 (5.62-100)	44.9 (17.0-100)	23.7 (6.66-100)	28.4 (0-100)
	Mid-swing Peak	PREF	7.90 (0-35.7)	8.15 (0-35.7)	6.85 (0-20)	8.65 (0-27.7)	7.30 (0-33.3)
		DT-S7	6.51 (0-75)	7.00 (0-75)	5.66 (0-21.4)	6.33 (0-60)	6.54 (0-61.5)

Table 7-5: Summary of inter-stride correlation averages to represent walking bout variability

Gait Variable	Walking Task	NDD & CbVD	ADMCI	FTD	PD	CbVD
Inter-stride Correlation	PREF	0.72 (0.31-0.92)	0.71 (0.64-0.91)	0.72 (0.67-0.87)	0.72 (0.67-0.90)	0.72 (0.66-0.92)
	DT-S7	0.66 (0.22-0.93)	0.64 (0.56-0.86)	0.59 (0.51-0.85)	0.68 (0.62-0.93)	0.67 (0.58-0.89)

Table 7-6: Summary of conventionally reported gait outcomes from gait assessment using dual task paradigm

Gait Variable	Walking Task	NDD & CbVD	ADMCI	FTD	PD	CbVD
Velocity (m/s)	PREF	0.94 (0.19-1.91)	0.94 (0.76-1.91)	0.79 (0.60-1.50)	0.97 (0.79-1.70)	0.95 (0.79-1.71)
	DT-S7	0.70 (0.21-1.67)	0.66 (0.29-1.67)	0.49 (0.23-0.93)	0.76 (0.23-1.60)	0.74 (0.24-1.67)
Cycle Time SD	PREF	0.07 (0.01-0.73)	0.07 (0.04-0.30)	0.08 (0.05-0.18)	0.07 (0.04-0.22)	0.07 (0.04-0.73)
	DT-S7	0.13 (0.01-1.97)	0.13 (0.06-0.61)	0.27 (0.09-1.97)	0.11 (0.06-0.74)	0.12 (0.06-1.11)
Velocity Dual Task Cost (%)	DT-S1	11.6 (-124-59.2)	14.5 (3.78-54.2)	18.7 (7.63-59.2)	6.43 (-2.1-49.7)	11.8 (3.16-45.8)
	DT-An	18.6 (-39.-75)	22.8 (9.23-75)	24.1 (10.1-58.9)	15.1 (5.48-59.3)	17.2 (8.47-52.6)
	DT-S7	24.5 (-34.-78.0)	28.7 (17.3-77.6)	31.9 (24.4-71.2)	20.3 (5.79-78.0)	23.3 (13.7-63.4)

7.4.2 Associations between conventionally reported gait outcomes

Conventional spatiotemporal gait outcomes were correlated to one another as well as clinical markers, cluster outcomes, and inter-stride correlations. Preferred gait velocity and preferred cycle time variability were not associated with any dual task cost outcomes or cycle time variability during preferred or dual task walking trials, drawing little relationships with any conventionally reported objective measures of walking (all $p < 0.250$). Preferred gait velocity had negative weak to moderate associations with the UPDRS Part III Gait score ($\rho = -0.324$, $p < 0.01$) and UPDRS Part III Postural Stability score ($\rho = -0.273$, $p < 0.01$) and positive weak to moderate relationship with Activities of Balance Confidence scale ($\rho = -0.329$, $p < 0.01$). Preferred cycle time variability had no moderate relationships with clinical measures of mobility and gait. Interestingly, dual task cost velocity outcomes had positive moderate-strong relationships (rho range = 0.6-0.683, $p < 0.01$) with other dual task cost velocity outcomes and had weak-moderate relationships with dual task cycle time variability (ρ range = 0.253-0.438, $p < 0.01$). Preferred gait velocity was the only outcome showing some association with clinical tools but interestingly showed no relationship with other gait outcomes measures, similarly, to preferred cycle time variability. The negative relationships with UPDRS scores (lower scores align with better gait and balance) and positive relationship with ABC scale explain that faster walking speeds are generally related to better clinical

scores. Dual task outcomes did not have associations with clinical mobility scales, but these outcomes did have relationships with other velocity dual task costs and cycle time variability during dual task walking, such that the larger the dual task cost the more variability existed.

Table 7-7: Correlations between conventionally reported gait outcomes.

Conventional Gait Measures		Velocity				Cycle Time Variability			
		PREF	DT-S1 DTC	DT-An DTC	DT-S7 DTC	PREF	DT-S1	DT-An	DT-S7
Velocity and Velocity Change	PREF	1*							
	DT-S1 DTC		1*	0.602*	0.6*		0.35*	0.253*	
	DT-An DTC		0.602*	1*	0.683*		0.264*	0.331*	0.287*
	DT-S7 DTC		0.6*	0.683*	1*		0.334*	0.378*	0.438*
Cycle time Variability	PREF					1*			
	DT-S1		0.35*	0.264*	0.334*		1*	0.456*	0.409*
	DT-An		0.253*	0.331*	0.378*		0.456*	1*	0.553*
	DT-S7			0.287*	0.438*		0.409*	0.553*	1*

*indicates statistically significant relationship; $p < 0.01$

Table 7-8: Correlations between conventionally report gait outcomes and clinical measures or modifiers of mobility.

Conventional Gait Measures		Clinical Measures or Modifiers of Mobility					
		UPDRS Gait Score	UPDRS Postural Stability Score	Activities of Balance Confidence	Fall History (12mo)	MoCA	Age
Velocity and Velocity Change	PREF	-0.324*	-0.273*	0.329*	-0.198	0.199*	-0.157*
	DT-S1 DTC	-0.08	0.015	0.014	0.032	-0.24*	0.116
	DT-An DTC	-0.042	0.037	0.031	0.034	-0.128*	0.102
	DT-S7 DTC	-0.042	-0.04	0.009	0.105	-0.129*	0.057
Cycle time Variability	PREF	0.177*	0.156*	-0.15*	0.188	-0.117	0.079
	DT-S1	0.049	0.052	-0.078	0.103	-0.229*	0.125
	DT-An	0.033	0.063	0.002	0.165	-0.133*	0.133*
	DT-S7	0.006	0.006	-0.062	0.185	-0.113	0.096

*indicates statistically significant relationship; $p < 0.01$

7.4.3 Associations between finite state outcomes and gait-specific clinical markers

Finite state machine outcomes (mid-swing peak and cycle time) were compared with clinically important markers of gait. Both the accelerometer based and temporal measures during preferred and dual tasks had weak to moderately-strong associations with conventionally reported gait outcomes from preferred walking and dual task walking (absolute ρ range = 0.254-0.705). Accelerometry based mid-swing peak values were positively associated with velocity ($\rho=0.36$, $p<0.01$) and negatively associated with cycle time ($\rho=-0.551$, $p<0.01$) in both preferred and dual task walking, showing that lower magnitude swing-peaks are associated with slower walking and longer cycle times. Some of the preferred and dual task cycle times and accelerometer-based outcomes reported statistical significance ($p<0.01$) with the UPDRS Part III Gait scores but all associations were weak ($\rho<0.199$).

Table 7-9: Correlations between cycle time and mid-swing peak amplitude with conventionally reported gait outcomes and UPDRS Gait score.

FSM Gait Outcomes		Conventional Gait Outcomes						
		Preferred Gait			Dual Task Serial 7s			Clinical
		Velocity	Cycle Time	Cycle Time SD	DT-S7 DTC	Cycle Time	Cycle Time SD	UPDRS Gait Score
PREF	Cycle Time	-0.418*	1*	0.381*		0.575*	0.281*	0.199*
	Mid-Swing Peak	0.36*	-0.551*			-0.385*		-0.161*
Dual Task Serial 7s	Cycle Time	-0.254*	0.575*		0.54*	1*	0.71*	0.031
	Mid-Swing Peak	0.336*	-0.429*		-0.439*	-0.705*	-0.527*	-0.177*

*indicates statistically significant relationship; $p<0.01$

7.4.4 Gait initiation stride clustering and specific clinically gait and balance markers

Initiation clusters (the length of the first cluster) were compared to clinically important markers of gait, clinical balance scales, and fall history. Initiation clusters defined using cycle time during dual task walking was weak-moderately related to dual task cycle time variability ($\rho=0.336$, $p<0.01$), no associations with clinical balance scales or fall history existed.

Table 7-10: Correlations between length of initiation cluster (with cycle time and mid-swing time) with conventional and balance specific clinical outcomes.

Length of Initiation Cluster		Conventional Gait Outcomes				Clinical		
		Velocity	Velocity DT-S7 DTC	PREF Cycle Time SD	DT-S7 Cycle Time SD	UPDRS Postural Stability	ABC Scale	Fall History (12 mo)
PREF	Cycle Time					-0.022	0.022	-0.004
	Mid-Swing Peak					-0.028	0.082	0
Dual Task Serial 7s	Cycle Time					-0.045	0.061	0.013
	Mid-Swing Peak					0.034	-0.018	-0.032

*indicates statistically significant relationship; $p < 0.01$

7.4.5 Number of state transitions and percent non-constant stride associations with clinically specific gait outcomes and MOCA scores

The number of state transitions were compared to important markers of gait and the Montreal Cognitive Assessment scores. During preferred walking when classifying the number of transitions using cycle time there was positive weak associations with preferred cycle time standard deviations ($\rho = 0.278$, $p < 0.01$). Dual task transition number determined using cycle time had positive weak to moderate associations with the dual task cost velocity ($\rho = 0.364$, $p < 0.01$) and the cycle time variability ($\rho = 0.513$, $p < 0.01$) during these walking tasks. None of the number of state transition outcomes were positively associated with the UPDRS Part III Gait outcome or the cognitive assessment.

Table 7-11: Correlations between number of state transitions (cycle time and mid-swing peak) with conventional and clinical measures of gait and cognitive outcomes.

Number State Transitions		Conventional Gait Outcomes				Clinical	
		Velocity	Velocity DT-S7 DTC	PREF Cycle Time SD	DT-S7 Cycle Time SD	UPDRS Gait	MoCA
PREF	Cycle Time			0.278*		0.032	0
	Mid-Swing Peak					0.032	-0.038
Dual Task Serial 7s	Cycle Time		0.364*		0.513*	0.002	-0.061
	Mid-Swing Peak					-0.004	0.023

*indicates statistically significant relationship; $p < 0.01$

Percent non-constant had similar relationships with the conventional gait outcomes, the clinical UPDRS Part III Gait outcome, and MoCA scores. Relationships for preferred cycle time percentages were related to preferred cycle time variability and dual task cycle time percentages were related to the velocity DTC and cycle time variability. No relationships were present with clinical UPDRS or MoCA scores.

Table 7-12: Correlations between percent non-constant (cycle time and mid-swing peak) with conventional gait outcomes and clinical measures of gait and cognition.

Percent Non-constant stride		Conventional Gait Outcomes				Clinical	
		Velocity	Velocity DT-S7 DTC	PREF Cycle Time SD	DT-S7 Cycle Time SD	UPDRS Gait	MoCA
PREF	Cycle Time			0.317*		-0.067	0.008
	Mid-Swing Peak					-0.084	0.018
Dual Task Serial 7s	Cycle Time		0.332*		0.558*	-0.069	-0.005
	Mid-Swing Peak					-0.065	0.095

*indicates statistically significant relationship; $p < 0.01$

7.4.6 Inter-stride correlation averages associations with clinically important markers

Stride correlation averages were compared with conventional gait outcomes, UPDRS Part III Gait, fall history, and MoCA scores. Preferred inter-stride correlations had moderate negative associations with preferred cycle time variability and dual task inter-stride averages had negative weak-moderate associations with DT-S7 velocity DTC and DT-S7 cycle time variability. No inter-stride averages were related to clinical scores.

Table 7-13: Correlations between inter-stride correlation averages with conventionally reported gait outcomes and clinical measures of gait, falls, and cognition.

		Conventional Gait Outcomes				Clinical		
		Velocity	Velocity DT-S7 DTC	PREF Cycle Time SD	DT-S7 Cycle Time SD	UPDRS Gait	Fall History (12mo)	MoCA
Stride Correlation Means	PREF			-0.528*		-0.005	-0.167	0.044
	DT-S7		-0.39*		-0.659*	0.011	-0.158	0.124

*indicates statistically significant relationship; $p < 0.01$

7.4.5 Differences in gait outcomes between clinically stratified groups

Clinically important gait speed threshold

When the entire cohort was stratified by clinically important gait speed threshold of 0.8 m/s, there were some differences between velocity, cluster, and inter-stride correlations during both preferred and dual task walking. Independent sample t-tests were used to compare gait outcomes between the poor (< 0.8 m/s) and normal (≥ 0.8 m/s) gait speed groups. Expectedly, during preferred walking the groups had different walking speed ($t(438.14) = 27.05$, $p < 0.05$, $d = 2.23$) but interestingly these groups also had significantly different DT-S7 gait speed as well ($t(406.1) = 14.57$, $p < 0.05$, $d = 1.25$). These groups also had differences between mid-swing percent non-constant ($t(310.78) = 2.92$, $p < 0.05$, $d = 0.29$) and cycle time variability ($t(183.26) = -4.107$, $p < 0.05$, $d = -0.50$) during preferred walking but no other differences existed between clinical gait speed groupings outcomes.

Table 7-14: Gait outcomes stratified by clinical gait speed and dual task cost thresholds

Walking Task	Gait Variable	Preferred clinical gait speed grouping (0.8 m/s)			Dual task cost velocity groups		
		Poor	Normal	<i>p</i>	<20% DTC	≥20% DTC	<i>p</i>
Preferred	Velocity (m/s)	0.65 (0.11)	1.06 (0.21)	<0.001	0.93 (0.28)	0.94 (0.26)	0.435
	Cycle Time Variability	0.08 (0.04)	0.06 (0.05)	<0.001	0.07 (0.06)	0.07 (0.04)	0.315
	Mid-swing Percent non-constant (%)	6.9 (6.8)	8.36 (8.04)	0.002	7.9 (7.8)	7.9 (7.6)	0.761
	Mid-swing Number State Transitions	0.8 (0.66)	0.74 (0.59)	0.937	0.76 (0.61)	0.76 (0.61)	0.836
	Inter-stride Correlation	0.73 (0.11)	0.71 (0.09)	0.448	0.72 (0.10)	0.72 (0.10)	0.474
DT-S7	Velocity (m/s)	0.51 (0.15)	0.79 (0.36)	<0.001	0.87 (0.26)	0.59 (0.2)	<0.001
	Cycle Time Variability	0.15 (5.17)	0.13 (0.16)	0.001	0.11 (0.19)	0.15 (0.13)	<0.001
	Mid-swing Percent non-constant (%)	5.2 (6.3)	7.09 (9.4)	0.014	7.5 (9.1)	5.7 (8.3)	0.040
	Mid-swing Number cluster fluctuations	0.66 (0.60)	0.68 (0.66)	0.741	0.72 (0.60)	0.64 (0.68)	0.388
	Inter-stride Correlation	0.66 (0.13)	0.67 (0.12)	0.757	0.70 (0.11)	0.70 (0.11)	<0.001

Dual task velocity threshold

Stratifying the group by a clinically important threshold from dual task cost performance (20%) reveals were compared using independent sample t-test. Gait speed during dual task serial 7s was expectedly different between groups ($t(310.99)=27.05$, $p<0.05$, $d=2.23$) but did not identify differences between the preferred walking speeds ($p>0.05$). During dual task walking there was also differences between the inter-stride correlation outcomes between dual task cost grouping, where those with low dual task cost had higher inter-stride correlations compared to those with high DTC (greater than 20%) ($t(368.62)=4.42$, $p<0.05$, $d=0.45$). When stratify by DTC cost velocity outcomes, no outcome measures were significantly different during the preferred walking trials.

Unified Parkinson's Disease Rating Scale Part III Gait Groups

One-way repeated measures ANOVAs were used to compare across the different groups stratified by their performance on the UPDRS Gait Part III score. During both preferred walking and dual-task walking ANOVA tests indicated significant differences between UPDRS groups for gait velocity (PREF: $F(3,440)=26.01, p<0.001, np^2=0.15$; DT-S7: $F(3,428)=10.02, p<0.001, np^2=0.06$) and inter-stride correlation outcomes (PREF: $F(3,379)=9.42, p<0.001, np^2=0.07$; DT-S7: $F(3,366)=4.15, p=0.006, np^2=0.01$), and only during preferred walking, was there significant differences of cycle time variability between UPDRS groups ($F(3,379)=12.75, p<0.001, np^2=0.09$).

Pairwise comparisons were used to compare between individual UPDRS gait categories when one-way repeated ANOVAs were significantly different. During preferred walking, walking velocity for the Normal group was different from Slight, Mild, and Moderate-Severe groups ($p<0.05$). There were also differences between Slight when compared to Mild ($t(14.041)=-9.31, p=0.002, d=-0.53$) and Moderate-Severe (Slight: $t(21.26)=-7.38, p<0.05, d=-1.23$) but no differences between Mild and Moderate-Severe. Cycle time variability during preferred walking was not different between Normal and Slight categories ($p>0.05$) but these two categories were different from Mild (Normal: $t(21.72)=2.91, p=0.008, d=0.72$; Slight: $t(27.21)=2.83, p=0.008, d=0.68$) and Moderate-Severe (Normal: $t(9.47)=4.56, p=0.001, d=1.79$; Slight: $t(10.4)=4.51, p=0.001, d=1.66$) with no differences between Mild and Moderate-Severe groups. Inter-stride correlations during preferred walking were also significantly different between Moderate-Severe compared to the Normal ($t(9.28)=-3.27, p=0.009, d=-1.61$) and Slight ($t(9.83)=-3.34, p=0.007, d=-1.52$) groups.

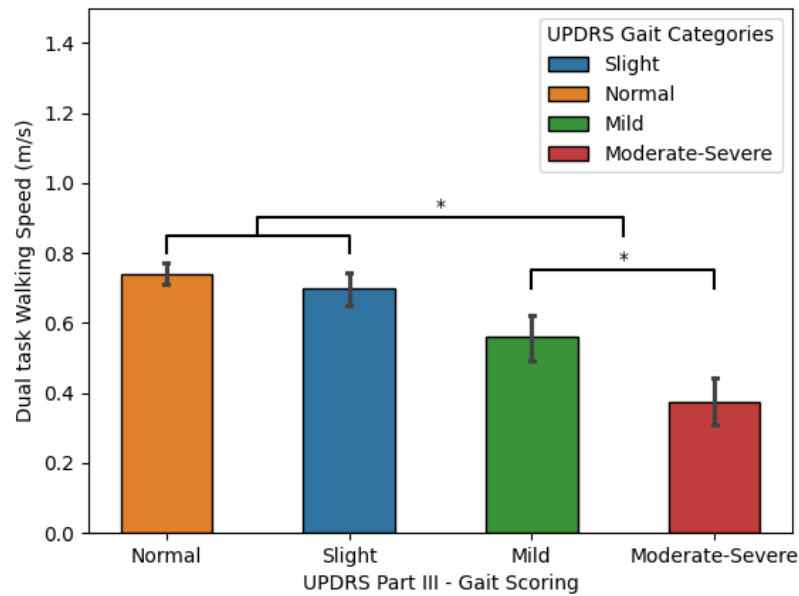


Figure 7-1. Comparing dual task walking speed (m/s) between UPDRS gait subsection groups. **indicates significant difference between groups*

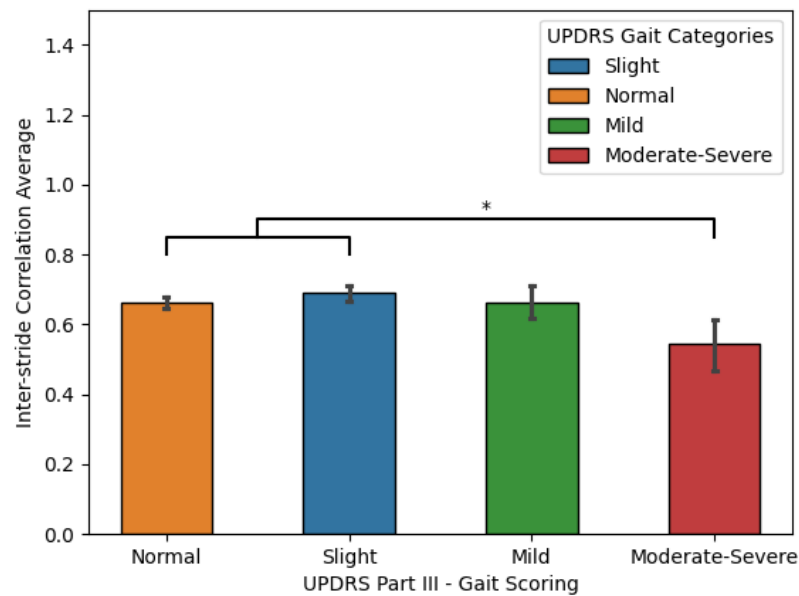


Figure 7-2. Comparing inter-stride correlation averages between UPDRS gait subsection groups during single-task walking. **indicates significant differences between groups*

Pairwise comparisons also compared between dual task walking outcomes when ANOVA analysis indicated differences. During dual task walking, gait velocity was not different between Normal and Slight groups ($p>0.05$) but these groups were different from Mild (Normal: $t(28.45)=-4.69$, $p<0.01$, $d=-0.71$; Slight: $t(42.84)=-3.20$, $p=0.002$, $d=-0.54$) and Moderate-Severe (Normal: $t(14.04)=-9.31$, $p<0.001$, $d=-1.42$; Slight: $t(21.26)=-7.38$, $p<0.001$, $d=-1.23$) groups. Differences between Mild and Moderate-Severe were also significant ($t(26.26)=3.67$, $p=0.001$, $d=1.24$). Dual task walking showed no significant differences in cycle time variability between these UPDRS groups but there were differences of inter-stride correlation between UPDRS groupings. Inter-stride correlations were significantly different between Moderate-Severe compared to the Normal ($t(28.45)=-4.69$, $p<0.01$, $d=-0.71$) and Slight ($t(28.45)=-4.69$, $p<0.01$, $d=-0.71$) groups.

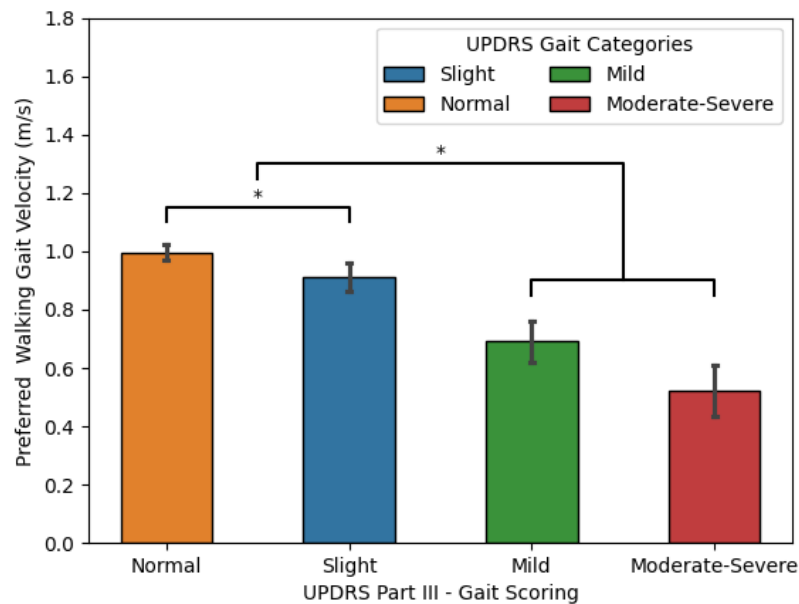


Figure 7-3. Comparing preferred/single-task walking speed between UPDRS gait subsection groups.
**indicates significant difference between groups*

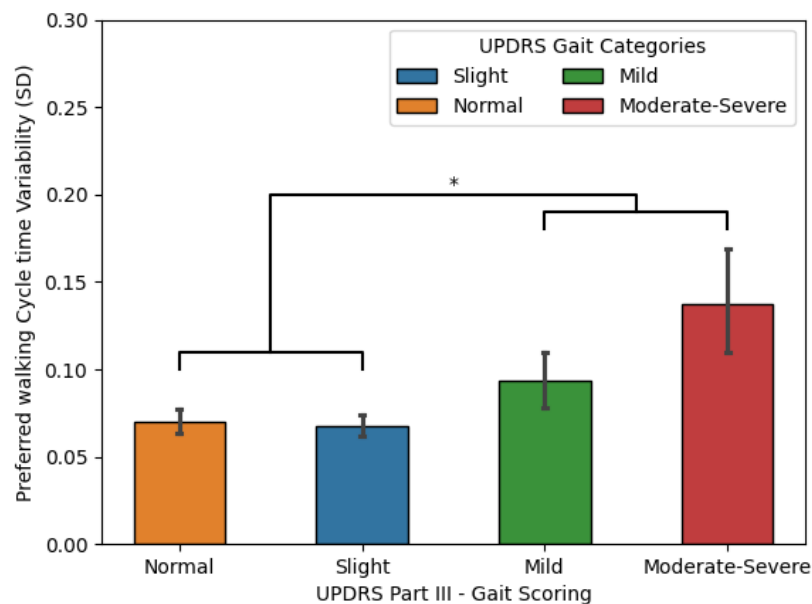


Figure 7-4. Comparing preferred/single-task cycle time variability between UPDRS gait subsection groups.
**indicates significant differences between groups*

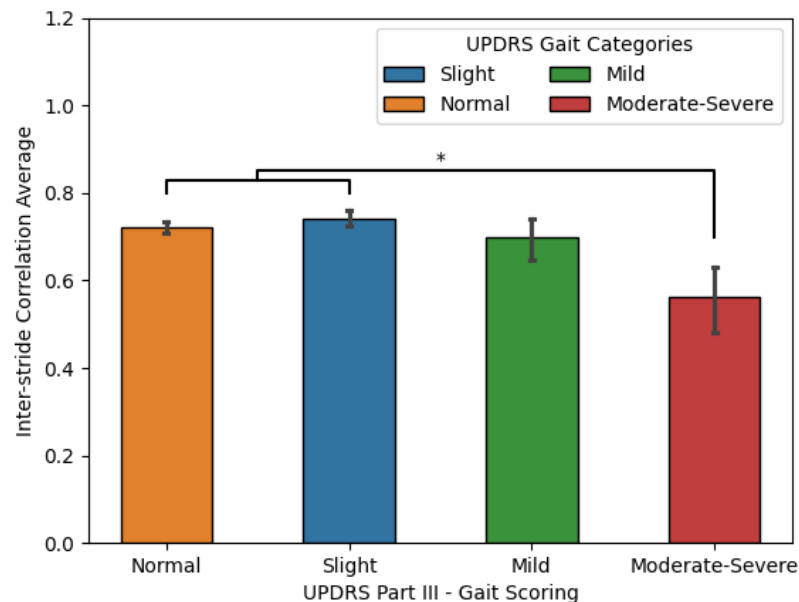


Figure 7-5. Comparing inter-stride correlation averages during single-task walking between UPDRS gait subsections groups. *indicates significant differences between groups

7.5 Discussion

The main purpose of this study was to investigate the association between gait-specific clinical markers of mobility and conventional gait metrics, stride clustering, and inter-stride correlations during single- and dual-task walking. With respect to objective 1, the current study did not generally support the hypothesis that moderate to strong associations would exist between the clinical markers and quantitative gait outcomes. An exception to this general finding was evidence of a modest relationship between preferred single-task gait velocity and a select few clinical outcomes (e.g., UPDRS gait and postural stability subsection scores, and ABC scale). There are several possible explanations for the absent/modest relationships observed in this study between clinical scales and quantitative gait metrics which are discussed in following paragraphs. It is proposed that the lack of association is more likely accounted by unique information expressed with the intra-stride and intra-bout measures as contrasted to the clinical measures of disease severity or gait (e.g., UPDRS subsections) and summary measures of walking such as

gait speed. With respect to objective 2, comparisons between clinically stratified groups generally supported the hypothesis that these clinical groups would have significantly different gait metrics. In general, measures that examined stride-to-stride variability were different between stratified groups across task difficulty, with one exception. When groups were stratified by dual task velocity performance (i.e. dual task cost >20%), there were no significant differences across any preferred walking gait metrics. This elevates the need for selecting purposeful gait tasks in clinical environments to reveal subtle differences between groups. Although results from this study may not fully support the hypothesis there is potential that these metrics are still valuable for assessing mobility.

The implications of variability on associations between clustering and conventional gait metrics

There are several possible explanations for generally low to modest relationships between clinical scales of mobility and stride clustering or inter-stride correlation outcomes. As mentioned, quantitative gait outcomes show a range of variability within this cohort. For example, gait initiation lengths ranged from 0-12 strides during single- and dual task walking conditions with ~15-24% of participants requiring more than 3 strides during this phase of walking and the number of state transitions range from 0-12 with ~16-30% of participants having more than 2 state transitions during both single and dual task walking conditions. These ranges provide insight into strides that fall outside a preferred variability threshold and are typically referred to as steady state walking in conventional gait assessments. However, in spite of this variability there was little association to clinical indices. One possible explanation for absent/modest associations is that the current cohort, while all were clinically diagnosed with a specific NDD or vascular disease, were characterized by relatively high function and/or mobility. For example, about 75% (301 out of 480) were clinically scored as 'normal' on the UPDRS gait item. An additional explanation for modest relationships may be the actual clinical measures and the association with control of gait. For example, the UPDRS Gait score is assessed under single task conditions. Single task walking may allow for more resources to help compensate for any mobility impairments and allow for faster walking speeds to link to better UPDRS scores. An alternative explanation is that quantitative gait assessment provides

more information and assesses mobility beyond ceiling effects of subjective gait evaluation (Hill et al., 2021). Better assessments of mobility may utilize the dual task paradigm to evaluate stability of walking under difficult conditions to represent the demanding tasks of walking in everyday environments (Hillel et al., 2019). In addition, the UPDRS gait item 3.10, is based on observation of the need for assistance, slowness or movement and 'awkwardness'. These categorical scales, including other examples such as the ABC or the Berg Balance Scale, have ceiling effects and are limited in their ability to provide distinction between people or assess fall risk (Balasubramanian, 2015) while quantitative gait assessment provides more information and assesses mobility beyond ceiling effects of subjective gait evaluation (Hill et al., 2021). Improvements in the assessment may require both items but requires quantitative information for effective assessment and prediction for adverse events (Jepsen et al., 2022). While such outcomes have served as a useful global index of capacity for mobility (i.e., testing different types of movement beyond straight ahead walking), they do not provide real insight into the control of walking. As a result, the hypothesizing moderate to strong associations between IMU based indices of gait control to clinical outcomes that reflect functional capacity or independence may have been unrealistic. Even so, the relative lack of association in this work may serve to reinforce the importance of continuing to develop and implement outcomes specifically linked to the control of walking to better understand disease related impact on gait and balance and to be able to better target mobility specific interventions.

Opportunity for quantitative gait outcomes to provide insight to mobility

Gait velocity during preferred walking is the only outcome that appears to have relationships, albeit weak-to-moderate interactions, with clinical scales of mobility. Gait velocity reportedly remains key for mobility assessments and predicting fall risk (Jepsen et al., 2022). However, the inclusion of multiple aspects of mobility better assess risk of falling compared to single assessment measurements (Jepsen et al., 2022). Gait velocity may better represent a global summary of walking performance and the overall integrity of neuromuscular and musculoskeletal systems, compared to specific risk. Outcomes from mobility scales are similar, such that the UPDRS generally classifies gait performance on crude

measurement of stride characteristics. Although, gait velocity may be predictive for mobility-related outcomes, there are aspects of gait (e.g., gait initiation) that are not described with the summary measures (Lindemann et al., 2008). Mobility tests are limited in their ability to assess risk. When persons are evaluated using single tests of mobility (e.g., functional reach, single-leg stance, Tinetti performance-oriented mobility assessment, Berg Balance Scale, ABC scale) there is not consistent diagnostic ability to assess fallers in older adults (Balasubramanian, 2015; Omaña et al., 2021). There is need to move beyond single measures of performance, such as gait speed, to properly assess the complexity of gait and gait related risks. In this report, gait velocity had little relationship to specific stride-to-stride, intra-stride, or intra-bout aspects of mobility but gait variability during both dual tasking and preferred walking showed some relationship to these outcomes. In previous research, initiation lengths (e.g., number of steps or distance in meters) are not different across older frail adults who are grouped by preferred walking speeds (Lindemann et al., 2008). Lindemann et al., (2008) reported that stride velocity variability increased when more strides were included in the variability calculation. Initiation cluster and stride variability reported a lower relationship during single- versus dual-task walking and increases under dual task conditions may align with increased cycle time variability measures. Furthermore, percent non-constant and number of state transitions are weak-to-moderately related to cycle time variability. These specific intra-bout descriptions quantify the number of strides that have large differences in stride-to-stride variability which may mask some of the relationship with conventionally reported cycle time variability. Assessment of these phases has been related to disease specific mobility scales in previous research. Gait parameters (both the mean and variability) calculated during constant, non-constant, or turning improve the classification for people with Parkinson's Disease impairments based on UPDRS gait and postural stability scores (Nguyen et al., 2019). The current study did not find relationships between mobility outcomes (i.e., UPDRS gait and postural stability) with the unique intra-bout characteristics of variability. This study reported description phases rather than the characterization of stride-to-stride characteristics of these distinct phases which might contribute to the relationship strength. There is concern in interpreting the meaning of stride-to-stride variability over a small number of strides because this value can

misrepresent gait variability. However, defining and describing these phases may benefit gait assessment by providing novel assessments of variability beyond mean stride-to-stride variability and gait velocity outcomes. Describing gait parameters provide benefits to the assessment of mobility in clinic beyond visual assessment and clinical scales and when combined with UPDRS disease severity scales, outcomes can improve the description of disease heterogeneity that currently exists (Hill et al., 2021).

Complex dual task conditions to provide insight into performance during clinical gait assessments

Unique to this work was the focus on different walking task condition including speed and dual task conditions. Associations between variables depended on task conditions. For example, walking speed and variability were only evident in dual task walking. Specifically, dual task velocity cost was moderate-to-strongly related to stride-to-stride and intra-bout variability measures during dual task walking. This suggests that the addition of a secondary cognitive task may influence both the velocity and cycle time variability. When older adults perform purposeful slowing in dual task walking both tasks increase stride to stride variability, but there is significantly more effect on these outcomes with attention demanding tasks (Dubost et al., 2006). Intra-bout relationships with cycle time variability under dual task conditions are linked by increases in variability under these conditions. Dual task conditions increase variability during steady walking as well as during gait initiation in healthy older adults and people with mild cognitive impairment (Wittwer et al., 2008b, 2013). The selection of walking tasks is important for revealing impairment to gait performance. In addition to univariate relationships, gait outcomes were compared between groups that were stratified by clinically important thresholds. Thresholds include both preferred walking (>0.8 m/s) and dual task walking ($>20\%$ DTC) performance. Mobility related thresholds are designed using specific gait measures that are clinically important, but might vary across populations or purposes (Middleton et al., 2016) (i.e., several velocity based measures might exist for different purposes). When groups were stratified by community ambulation thresholds during preferred walking speeds there were more significant differences within the preferred walking tasks (e.g., velocity, cycle time variability, mid-swing percent non-constant) compared to during dual task walking tasks (e.g.,

velocity). When stratified by dual task cost, differences during dual task walking (e.g. velocity, cycle time variability, inter-stride correlation) existed while no differences occurred with single-task trials. Uniquely, when stratified by cost or preferred walking speed, velocity was not unanimously different between groups. This suggests preferred walking speed and the effect of dual task on walking speed may have an aspect of independence from each other. Previous research has outlined the effects of dual task conditions and mild cognitive impairment (Montero-Odasso, Verghese, et al., 2012; Patel et al., 2014; Priest et al., 2008) but there is need to understand these relationships from a preferred walking perspective as well to avoid the confounds of performance anxiety and provide equitable assessment of gait. When groups were characterized by preferred walking, differences in cycle time variability were present in preferred walking but not dual task walking. Although cycle time variability is not different, variables such as percent non-constant and inter-stride correlation values do differentiate between groups (Goh et al., 2021). Suggesting elements or expressions of gait variability at the kinematic level or clusters of strides may be different between groups. Dual task changes at the kinematic or intra-bout phases have been identified during dual task walking before such as increased variability (which may increase initiation length) (Wittwer et al., 2008b), change to the lower limb trajectory (Ahmadi et al., 2021), or force development (Melzer et al., 2010) during phases of the gait cycle. Gait outcomes were also compared across groups stratified by their UPDRS Part III gait specific score (e.g., Normal, Slight, Mild, Moderate-Severe) and comparisons of velocity and cycle time variability distinguished between most group categories during both preferred and dual tasking while inter-stride correlation outcomes found differences only between the least impaired (Normal and Slight) when compared to the most impaired (Moderate-Severe) groups. These differences may provide added benefits to characterize cohorts using these mobility based scales (Hill et al., 2021; Schniepp et al., 2021). From these comparisons, cycle time was only different during preferred walking and not dual task walking. Stratifying by clinically important thresholds also provides insight into differences in gait-specific outcome measures, however further research is needed to best understand the role of dual task walking and how it relates to these group performances.

This study aimed to describe a relationship between clinical measures of mobility and key gait specific outcomes from quantitative gait assessments. During clinical assessments participants walked under preferred and dual task conditions of varying difficulty however, in this current study the only dual task serial 7s task was used. Serial 7s was chosen because it was the more difficult task and selected to appropriately challenge these cohorts during walking, particularly with the high-level functioning of the group. However, there are chances this task is too difficulty for some older populations (Piche et al., 2022) and may have caused burden for some of the cohort. However, in this study data cleaning included the removal of trials in which participants could not perform the dual task. It remains important that there should be several task difficulties included in clinical assessment to appropriately challenge people (Beauchet et al., 2017). Although we only examined the relationship between a single most difficult task, therefore more work can expand on other dual task modalities. This study was limited to a few clinical scales of mobility (e.g., ABC) and included disease severity scales (e.g., UPDRS subsections, MoCA). Inclusion of more clinically oriented assessments of mobility (i.e., TUG, sit to stand) may improve the specific assessment of mobility and identify specific relationships between intra-bout phases of walking. Although this is considered a limitation, the inclusion of disease specific scales may allow for the identification of specific disease phenotypes that are identified by certain impairments that summary gait metrics can not describe. Similar to the focus on specific subsections of the UPDRS to identify PIGD phenotypes of PD (Stebbins et al., 2013), specific decline in gait variability metrics (intra-stride and intra-bout) may provide distinction between aging or disease cohorts. Further research expanding these outcomes should understand how these cluster outcomes can be related to other forms of mobility assessments in clinical settings and across these different environments, cohorts, and task challenge.

7.6 Conclusion

This study provided an evaluation of the relationships between conventional gait, FSM outcomes, cluster and inter-stride correlation with clinical markers of gait and mobility. While there was a modest association between gait velocity and clinical outcomes there was little to no association between clinical

outcomes and stride/bout measures. It is proposed that the absence of association may be primarily associated with the limitations of conventional clinical measures of mobility to reflect insight into the control of walking, but rather reflecting outcomes linked to functional capacity and independence. Significant differences between groups stratified by clinically important threshold did identify differences between gait outcomes suggesting that there may be links between stride and bout characteristics and disorder gait. The study also reinforced the importance of extending walking conditions between preferred walking to include challenging conditions such as dual task walking to increase the potential to detect disordered control of walking. Dual task conditions revealed some insight into the relationship between conventional measures of gait variability with stride clustering theory and outcomes measures. Further investigation about how cluster outcomes may or may not contribute and influence variability is needed to advance this technique and these unique outcomes measures. This study expanded the use of stride clustering by identification of the cluster characteristics rather than computing mean values over these short periods with less strides. Identification of clusters explores the utility of novel measures to identify these differences between groups but has practical applications. Extending this work with a focus on individuals with more specific gait deficits (e.g., such as freezers in PD or poor stability control) may yield more insight into the potential utility of such stride and bout measures as diagnostics/or prognostic indicators directly associate with the control of walking. The work also continues to reinforce the importance of continuously advancing approaches to improve the measures used to assess gait in clinical settings including the measures but also the task conditions.

Chapter 8

GENERAL CONCLUSIONS

Gait assessments have an important role for older adults and those with neurodegenerative disease by identifying motor phenotypes and disease prognosis, aid in screening for cognitive impairment associated with disease, while also informing understanding of gait stability and fall risk. Importantly, there is need to advance the approaches used to assess gait with fidelity and the nuance required to properly reveal impairments in those living with disease. This includes a focus on cost-effective solutions, such as body worn accelerometry, that could be translated to clinical care and identifying novel assessments of walking as it naturally occurs. This thesis focussed on advancing and evaluating analytic approaches based on a single leg worn triaxial accelerometer. Importantly, this thesis extended the focus to a range of clinical gait assessment tasks of varying difficulty (e.g., single- and dual-task walking) and compared with clinical markers of functional mobility. Approaches applied in this work aimed to move beyond the more conventional focus on steady state preferred walking tasks for a healthy population and focussed on developing approaches using clinically feasible tools in people living with disease.

In study one, a gait segmentation approach was evaluated for its effectiveness to properly segment gait cycles from time series accelerometer data. Important to this work was to simultaneously overcome some major barriers to continuous monitoring studies, such as: battery life, data storage, cumbersome sensor wear protocols, all which are burdened using multiple sensors at different wear locations and sensing data types (e.g., magnetometer and gyroscope). This version of the FSM analytic approach overcomes these barriers by relying on uniaxial acceleration measured at a single wear location. The framework of these algorithms are beneficial to continuous monitoring because they are adaptable across different modes of walking (e.g., forward, backward) (Kronenwett et al., 2017). Study two and three aimed to compare novel gait metrics across difficult dual task walking conditions. Study two identified key temporal and accelerometry-based kinematic outcomes and examined changes to these

metrics across tasks. This study also explored the relationship between kinematic outcomes and gait velocity. Study three used a subset of these key temporal and accelerometry-based kinematic outcomes to identify intra-bout phases of walking and examined changes to these phases across single- and dual-task walking conditions. Study three also investigated stride-to-stride variability from lower limb kinematic features to evaluate the association of strides within a single bout and examine change of association across different dual task conditions. Cumulatively these studies advance gait assessment with a focus on methodological and analytic approaches. Advancements allow for conventionally reported gait parameters and intra-stride segmentation to be output from tools that could be practically incorporated into clinic (i.e., low-cost accelerometers). Segmentation beyond normal stride or stance-swing identification may be beneficial for clinical use and identify gait impairments specific to disease pathology, such as changes to foot kinematics in early or late swing or mid-stance vaulting compensations. In addition, identification of intra-bout phases provides methodological advancement in the interpretation of gait and gait variability during clinical tasks. These phases improve our understanding of gait variability in novel ways by quantifying initiation and steady periods of walking. It is proposed that these methodological considerations expand our understanding of locomotor control and identify discrete phases that are linked to clinically actionable interventions, such as controlling gait initiation.

Part of this thesis examined the univariate relationship between intra-stride and intra-bout phases during single- and dual-task walking with gait specific clinical markers of mobility (i.e., clinical scales). It was hypothesized that gait metrics and clinical outcomes would be related but these univariate relationships were not generally related. One possible reason may be the ceiling effect of clinical scales. These limitations of clinical scales reduce their ability to provide the subtle distinction between people that gait-specific metrics allow. Further, clinical scales rely on subjective assessment with categorical evaluations of gait performance. This partly explains the single relationship with gait velocity as it may be easy to claim better gait performance for fast walkers, which is not consistently true. These two limitations in combination, may explain why the relationship is absent between the continuous gait

outcomes compared to subjective evaluation of mobility. Lack of relationships may not singularly be due to the fidelity of clinical scales. One main limitation to this study was the lack of gold standard reporting of intra-bout phases, specifically gait initiation. In clinical settings the use of multiple sensors allows for a fulsome assessment of gait. For example, multiple lower limb sensors combined with trunk and arm sensors may provide disease specific outcomes (e.g., reduced arm swing) or a multifaceted approach to quantifying dynamic stability (e.g., proxy of COM movement with spatiotemporal measures). This study utilized acceleration alone but the inclusion of triaxial gyroscopes and additional sensors would allow for pose estimation and spatial estimates of human movement. This includes stride-to-stride velocities estimates to validate gait initiation in the traditional definition. Although these advancements are feasible in clinical settings with little additional cost to expand sensor numbers and include gyroscope measurement, this thesis focussed on the advancement of methodology with sensors that could seamlessly integrate into free-living environments. Without the collection of gyroscope data, battery life and on-board data storage allow for longer data collection periods (e.g., up to several weeks or months). Further, the ability to accurately capture and segment gait cycles into intra-stride phases with a single sensor on the ankle reduces subject burden without compromising outcomes during continuous monitoring studies. More research is needed to expand these methodological approaches in clinical environments with aims of developing and expanding these approaches into free-living, continuous monitoring studies and understand the associations between novel outcomes and individual gait and stability control.

Despite the lack of association in the last study, there is motivation to continue to explore the benefit of including these methodological approaches in clinical assessment of gait and mobility. The addition of further quantitative description of gait performance, by defining and characterizing intra-bout phases of walking, in combination with current markers of gait stability or fall risk may benefit classification of stability in several ways. Some examples might include the emergence of unique markers of impairment in clinical and free-living environments that are linked to intra-bout phases (i.e., domains of mobility), parse and identify distinct phenotypes within aging or disease spectrums or help better

predict the likelihood of adverse event occurrence. Beyond direct implications for risk or impairment identification, proper assessment (i.e., identifying and classifying both non-steady and steady state intra-bout phases) allows for expanded opportunities in clinical and free-living environments. In clinical environments, characterizing intra-bout phases can provide a comprehensive assessment of gait variability at the stride-to-stride and intra-bout phase level. Identification of these phases can also extend to complex walking tasks (e.g., 2- or 6-minute walking, continuous shot-circuit assessments) where discrete segmentation of turning and acceleration may be identified and analyzed, all while maintaining the conventionally used assessments. These advancements will continue to build a repository of mobility related outcomes to properly contextualize walking across settings where mobility is evaluated.

This thesis provides support for advancing gait assessment with attention to clinical assessments among older adults and those with neurodegenerative disease. Although much research has examined the nuances of gait and stride characteristics during walking, the use of these quantitative measures have not extended to routine clinical care for many reasons. As a result, the current work focussed on advancing the measurement using a low-cost sensor with low-burden that could be used during clinical assessments. Importantly, this work extends the focus of outcomes from sensors beyond the typical reliance on gait velocity and a single composite index of gait variability to provide novel insight to intra-stride or intra-bout phases of walking. It is proposed that such measures, in addition to conventional gait measures and expanded task conditions, may provide a more fulsome assessment gait and mobility for older adult and those with neurodegenerative diseases to improve prognostic, diagnostic and therapeutic decision making.

8.1 Future Directions

Across these four studies there were novel aims to advance gait assessment using wearable accelerometry. Methodological and analytic approaches were examined and presented as outcomes to describe gait variability and ultimately gait performance outcomes.

The first study implemented an accelerometer-based FSM model that requires unilateral and uniaxial acceleration to detect strides walking during overground and treadmill walking. Gait detection models using heuristic frameworks provide opportunity to expand the rules within the model to improve detection. Future models of the FSM detection method may expand to multi-axis movement that exist within the local frame of the ankle-worn accelerometers. Other work has expanded these models in similar fashion to detect localized indoor walking with multiple directions (Kronenwett et al., 2017) and similar approaches may be employed to help improve the specificity and sensitivity of an accelerometer based FSM model during clinical and free-living walking. A second method to improve detection methods may develop data driven models, that are impairment or person specific. This may provide a method to improve detection in the face of specific gait impairments since stride detection accuracy may be largely influenced by gait impairment or outdoor walking (Khandelwal & Wickström, 2017). The challenge will be to develop a protocol that will permit valid event and intra-stride detection in the face of person specific differences and may rely on complex models for development and widespread use (Caldas et al., 2017).

Study two and three of this thesis evaluated the accelerometer kinematics during clinical tasks of varying difficulty to determine if compensatory movements were detectable using novel kinematic outcomes and whether these outcomes could identify intra-bout phases of walking. There is need to continuously expand the description of accelerometry kinematics across these different clinical tasks to expand the understanding of compensatory movements and their variability. Identifying unique kinematic characteristics can expand the assessment of tasks and walking in clinical or varying environments. Future work that expands the understanding of accelerometry patterns may help identify deviations from healthy normal movement and assess differences across tasks or through time to reveal the onset and trajectory of gait quality in the aging or disease populations. Beyond stride-to-stride outcomes there is need to understand the unique phases within a walking bout and determine their contribution to gait variability. Although this study quantified an example of intra-bout phases there may be need to further

validate these approaches across different measures that were not presented in these studies. Future work should also begin to understand these clustering techniques in free-living environments to help provide context to walking in people's daily life. The advancements of this work will continue to build on the clinical evaluation of gait but extend to work outside of the clinic. In clinical environments, future work will build upon the description of gait variability measures to move beyond stride-to-stride but consider the intra-bout phases as part of gait variability. One of the potentially important advances forward would be to extend this model to include multiple low-cost IMUs to expand the assessment of gait in clinical environments, such as bilateral comparisons, intersegmental dynamics, and other movement outcomes like angular velocity or spatial estimates.

In the last study of this thesis a broad evaluation of the relationship between intra-stride and intra-bout phases with gait-specific measures of mobility was explored. Important to the objective was distinct links between outcome measures that may have unique relationships (e.g., dual task walking with measures of cognition). Future research needs to continue to build markers of mobility that are clinically relevant. This will require specific comparisons of the IMU based metrics among carefully described cohorts with disease-specific gait control impairments. Proposed case examples would include shuffling gait among those with Parkinson's disease, gait initiation/freezing and turning deficits in PD, and hemiparetic gait in stroke survivors. Focussed associations between disease to reveal known impairments that affect mobility in that disease maybe one method to expand the understanding and impact of mobility within and between disease cohorts. Providing an understanding of the unique relationships between and within these groups may allow for directed therapeutic or rehabilitative interventions. Further, quantifying performance with increased specificity can help evaluate the effectiveness of treatment or prognosis of impairment over time.

These future directions may help provide context to changes in variability outcomes and identify phenotypes of instability within aging or disease trajectories in clinical environments. Applications of this work extend beyond the clinic to free-living environments. Currently in free-living gait descriptions,

macro-gait outcomes (e.g., step count, bout number, etc.) are commonly reported as outcome measures for walking in everyday environments. Stride-to-stride outcomes are reported but lack context causing concern for interpretation and its potential to highlight key mobility outcomes. Improvements in this area can help expand gait assessment in daily life and can improve the assessment of mobility in aging and people with neurodegenerative disease.

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