Exploring the Inter-relationship Between Cognitive and Motor Function in People with Lower Limb Amputations

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Abstract

The main objective of the present dissertation was to expand our understanding of the inter-relationship between cognition and mobility in people with lower limb amputations (PLLA). Study 1 systematically reviewed the literature to assess the effects of dual-task testing on the balance and gait of PLLA. A total of twenty-two studies were included. Overall, PLLA demonstrated a disproportionately greater dual-task effect than controls, characterized by increased sway velocity and reduced pace and rhythm, and increased asymmetry when balance or walking was paired with a secondary task. Additionally, the dual-task effect was not influenced by differences in etiology, level of amputation, or experience with a prosthesis. Study 2 examined the association between balance confidence, a proposed cognitive distractor, and basic walking abilities in community-dwelling people with unilateral transtibial level amputations. Forty-four people participated in Study 2, completing a questionnaire on balance confidence and an assessment of functional mobility. This study concluded that decreased balance confidence was independently associated with a longer time to complete the functional mobility test in both the single-task and dual-task conditions. Study 3 evaluated the association of cognitive function on tests of physical function in PLLA at discharge from inpatient prosthetic rehabilitation. Tests included examinations of global cognitive status, processing speed, executive function, and balance confidence. Physical function was assessed through gait velocity, dynamic balance, and functional mobility. Data from twenty-two participants demonstrated that better global cognitive status and executive function were independently associated with faster gait velocity and greater functional mobility for both conditions of single-task and dual-task, yet this was not observed for dynamic balance. Moreover, no association was observed between processing speed and balance confidence and any of the tests evaluated. PLLA are optimal candidates for dual-task balance and gait research as they are often being cognitively and physically challenged during ambulation with a prosthesis. The present findings are novel and provide evidence on the interplay between cognition and mobility in PLLA. Further research studies examining cognitive-motor capacity and its relationship to important markers of rehabilitation progress and future success are warranted in this group of people.

Keywords: *Amputation, postural balance, gait, multitasking behavior, performance anxiety, cognition.*

Summary for Lay Audience

Over half of people with lower limb loss fall each year. Falls have dire physical and emotional consequences, including fractures and a concern for falling that lessens quality of life. People with lower limb loss often express that they have to think about every step they take with a prosthesis. One way to test both thinking and physical abilities is by asking people to do two things at once, or dual-task. In real-life, we tend to dual-task often such as when walking and talking. However, many questions remain unanswered as to how thinking abilities and physical abilities interact with each other in people with lower limb loss. The present research project is made up of three studies. The first was a scientific review of existing research on how dual-task testing affects balance and walking in people with lower limb loss. A total of 22 studies were included for review. Dual-tasking in people with lower limb loss resulted in imbalance, and slower walking speeds, fewer steps, and increased walking unevenness when compared to healthy adults. The second study evaluated the relationship between having confidence in performing activities without losing balance and basic walking abilities. Study 2 concluded that having a low balance confidence was related to taking a longer time (worse function) to complete an L-shaped walking test in both simple walking and dual-task walking conditions. The last study examined the relationship between different tests of thinking abilities on the performance of a selection of tests for physical abilities (i.e., balance and gait) in individuals new at using a prosthesis. Study 3 found that better overall thinking abilities were related to faster walking speeds and taking less time to complete an L-shaped walking test in both single-task and dual-task conditions. The three research

studies provide new information in people with lower limb loss related to the inter-relationship between how they think and how they move within their surroundings. Future studies should seek to answer if the results of dual-task tests assist with predicting long-term outcomes such as social participation, quality of life, and falls.

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List of Abbreviations

3MS: Modified Mini-Mental Status Exam

3R60: Otto Bock 3R60 Prosthetic Knee Joint

ABC: Activities-specific Balance Confidence Scale

ANOVA: Analysis of variance

AP: Anterior-posterior plane

CI: Confidence interval

C-Leg: Otto Bock C-Leg Prosthetic Knee Joint

CN: Controls

CoP: Center-of-pressure

CoV: Coefficient of variation

D&B: Downs and Black Scale

DM: Diabetes mellitus

DT: Dual-task

DTC: Dual-task cost

EC: Eyes closed

EO: Eyes open

F8W: Figure-of-8 Walk Test

FAS: Verbal Fluency F-A-S Test

HS: Hard surface

IQR: Interquartile range

LSE: Local stability exponent

L Test: L Test of Functional Mobility

KD/TF: Unilateral knee-disarticulation or transfemoral amputation

MFCL: Medicare Functional Classification Level

ML: medial-lateral plane

MPK: Microprocessor prosthesis

MoCA: Montreal Cognitive Assessment

PLLA: People with lower limb amputations

PVD: Peripheral vascular disease

RMS: Root mean square

RSD: Residual standard deviation

Sen: Sample entropy

SNS: Mauch Swing and Stance Control Prosthetic Knee Joint

SS: Soft surface

ST: Single-task

TF: Unilateral transfemoral amputation

TMT-A: Trail Making Test A

TMT-B: Trail Making Test B

TT: Unilateral transtibial amputation

YA: Younger adults

XcoM: extrapolated center of mass

Chapter 1: LITERATURE REVIEW

1.1 Introduction

Each year approximately 7,405 Canadians undergo a lower limb amputation.[1] People with lower limb amputations (PLLA) face many challenges, such as decreased physical function, community engagement, and psychological health.[2–6] The average age of PLLA is 65 years old, and most amputations (80%) result from diabetes or peripheral vascular disease which are associated with decreased sensation, gait problems, and cognitive impairment.[7] Importantly, nearly half of PLLA discharged from inpatient rehabilitation have a fall in the first 6-months of living in the community.[8] Fall occurrences do not improve,[9] as 52% sustain a fall on an annual basis, even years after their amputation and intensive rehabilitation[10,11]. The consequences of falling are dire, including not only physical injury (e.g., fractures, soft tissue damage, etc.),[11] but also a concern for falling that results in a lack of prosthesis use and social withdrawal.[12] As walking with the prosthesis is the most common falls-related activity,[13] and is considered the utmost important factor to quality of life,[2] rehabilitation assessments in clinical practice for PLLA often rely on evaluations of physical function[14].

Cognition, or how we think, is an umbrella term used to encompass many different brain functions such as memory and attention, so called executive functions, which enable the processing of and response to incoming sensory information.[15] In PLLA, about 52.6-56.3% demonstrate cognitive impairment.[16,17] Additionally, in those who had an amputation due to diabetes or peripheral vascular disease, known collectively as dysvascular disease, executive dysfunction has been associated with walking and functional mobility problems.[18] This is unsurprising knowing the long-term consequences that micro- and macro-vascular diabetic damage[19] has on brain structure[20] and function.[21] Thus, the examination of cognitive capacity is also warranted as an avenue to explore to help explain the high rate of falls this population experiences.

Walking with a prosthesis is cognitively taxing with 41% of PLLA reporting having to think on every step they take,[10] and individuals also describing a cognitive burden with the planning associated with trying to keep safe while ambulating[22]. Walking is a complex motor task involving the integration of information from multiple systems to maintain balance, with cognition playing a key role.[23] The capacity sharing model states that cognitive resources used for information processing are limited, with each task demanding a certain amount of resources.[24,25] More complex tasks demand higher resources, such as activities involving divided attention in which simultaneous tasks are completed.[24,25]

Most activities we engage in demand the completion of two tasks at once, a motor task and a cognitive task, or dual-tasking.[26] Under dual-task gait testing, PLLA demonstrate decreased gait quality and increased instability.[27,28] Literature has not explored how robust dual-task testing during balance or gait tasks is as a clinical tool even though PLLA report that falls are often preceded by moments of distraction that lead to the disruption of walking with a prosthesis.[29] A synthesis of the current literature on the effect of dual-task testing on the balance and gait of PLLA is warranted as an important step toward understanding the value of this type of protocol for the assessment of cognitive-motor capacity. Moreover, psychological consequences of falls are common,[12] yet these factors have not been explored as to their relationship to the cognitive load associated with walking in this population. Nor has it been fully elucidated the variation in the magnitude of cognitive demands required amongst available tests of physical function, including those that are more challenging and demand more cognitive resources or that involve dual-task testing. Due to the expected increase in diabetes prevalence, the number of PLLA is likely to grow rapidly in the coming decades.[30] A better understanding of the intersection between cognition and mobility in PLLA is important in order to inform on the assessments and remediation options available to healthcare professionals working in this field.

Three research projects compose the present dissertation. The first research project was to systematically review the literature on the effect of dual-task testing on the balance and gait of PLLA. The second research project was to investigate the association between a concern for falls and walking in PLLA. The third and final research project was to explore the association between cognitive testing and physical function tests of varying complexity in this group of people.

1.2 Defining a Lower Limb Amputation

An amputation is a surgical procedure with the goal to bring upon increased physical function and quality of life through the removal of sections of a limb that is usually followed by a period of rehabilitation.[31] An amputation is considered a last resort procedure after other efforts for tissue and limb salvage have failed (e.g., wound care, stenting, etc.).[31] Some amputations are a result of either trauma or congenital factors which are more often seen in younger individuals, while most have an amputation due to dysvascular disease which is observed more in older individuals[1,32]. In general, younger adults with trauma or congenital-related limb loss have better mobility and a lower mortality rate than older adults who had an amputation due to dysvascular disease.[2–4] The most common types, or also called levels, of major lower limb amputations include hip disarticulation, transfemoral (through the femur), knee disarticulation, transtibial (through the tibia) and ankle disarticulation.[1,32] While other minor amputations exist (e.g., of the toes or through parts of the foot),[1,32] these are not considered major and thus are not subject of the present dissertation.

1.3 Epidemiology of Lower Limb Amputations

A total of 44, 430 lower limb amputations have been recorded within a six year period from 2006-2012 in Canada.[1] Estimates for the Canadian prevalence of people with lower limb amputations currently do not exist.[33] The most complete and analogous datasets related to limb loss originate from the United States, where 1.6 million people were estimated to be living with limb loss in 2005.[34] Moreover, the majority (65%) of these individuals had received a major lower limb amputation.[34] Projections of limb loss in the United States estimate a two-time increase in prevalence to 3.5 million people by the year 2050; an astonishing forecast mainly driven by an aging population and the high rate of dysvascular disease.[34] In Canada, older adults represent the fastest growing segment of the overall population (2018: 17.2%; 2068: 21.4-29.5%).[35] In conjunction with the aging of the population, the number of people diagnosed with diabetes is on the rise[36] and there has been an increase in the total number of lower limb amputations reported,[1] with older adults being disproportionally affected[37,38]. Therefore, the prevalence of PLLA is likely to grow and this has important implications to the Canadian healthcare system.

In PLLA, the burden of comorbidities is high, as much as 60% report having three or more health diagnoses,[39] and which are believed to affect the recovery and outcomes following an amputation[6,40]. The mortality rate is astonishingly high in this population, with an observed death for 9-22% at 30-days,[32,41] 44% at 1-year[41] and 77% at 5-years[41] in individuals after a major lower limb amputation.[41] Research also depicts that mortality rates are significantly worse in those who received an above-knee amputation compared to a below-knee amputation.[42] Nonetheless, and likely through the betterment of medical interventions, PLLA are expected to live for many years after their amputation and to require services that ensure an adequate quality of life.[34]

For lower limb amputations, the majority (60.7-63.7%) take place at or above the ankle joint and are thus considered major amputations.[34,43] More specifically, and within a period from 2006 to 2012, 31.5% of amputations were at the transtibial or ankle level, 25.6% were at the hip/pelvis, transfemoral or were knee disarticulations, and 42.9% involved the foot or toes.[1] Overall, there is a 1.42 times higher incidence rate of transtibial relative to transfemoral level amputations reported in the literature.[1]

Causes of an amputation vary widely, yet can generally be categorized as trauma (e.g., workplace, recreational or motor vehicle accidents, or military incidents) or non-trauma related, such as those resulting from dysvascular disease, cancer, infection or congenital issues. The most recent Canadian incidence data spanning over a 6-year period found that the majority (91.0%) of amputations were of diabetic, vascular or infection etiology, while trauma only accounted for 6.0% of these surgeries.[1] In samples of people with a history of diabetes who received an amputation, the majority (76%) were observed to have both peripheral artery disease and diabetes.[43] Although prevalence data is not currently available in Canada, estimates from the United States report that more than half (56%) of PLLA had an amputation secondary to dysvascular disease, 45% were related to trauma and <2% were from cancer.[34] Importantly, most of the increase in amputations projected for the coming years is expected to derive from a higher prevalence of dysvascular disease in the general population.[34,43]

1.4 Outcomes Associated with Lower Limb Amputations

1.4.1 The Economic Effect of Lower Limb Amputations

Lower limb amputations have a financial impact on the healthcare system, and on individuals and their families.[22,44–46] Research on PLLA due to trauma indicates that nearly all (97.4%) had a paying job immediately prior to their amputation, but one-year post-amputation this was 58.0%.[47] For those who did return to work, a 30% reduction in the physical demands of their job was noted, which alludes to a substantial role change within their workplace.[47] Subsequent research has also established that even years after an amputation, some (31.0%) are unable to return to work.[48]

1.4.2 Psychosocial Outcomes of Lower Limb Amputations

A lower limb amputation is a life-changing event that affects mental well-being. PLLA often experience body image disturbances,[22,49] suicidal ideation,[50] depression,[6,51,52] and anxiety[6,51]. This group of people also report low social functioning relative to the general population.[3,22,47,53] Quality of life improves after a lower limb amputation; however, most of the changes are observed within the first 6-months after the surgery,[2] and quality of life remains significantly lower than normative values even years after the amputation.[2,3,54]

1.4.3 Physical Outcomes of Lower Limb Amputations

After a lower limb amputation, many PLLA develop issues secondary to long-term prosthesis wear, an altered gait pattern, a problematic prosthetic fit (e.g., pain, wounds, osteopenia, osteoporosis, etc.) or a compromised intact limb (e.g., stress-related osteoarthritis of the joints).[3,4,55–57] Other common issues in PLLA include increased body weight, joint and low back pain, deconditioning, cardiovascular disease and renal disease.[3,4,47,55] Relative to the general population, PLLA have lower self-reported general health, physical functioning, and increased pain.[47,54] Moreover, the ability for symmetrical gait, balance maintenance, independent ambulation, the performance of recreational or routine activities, and driving are also reported to be negatively affected after a lower limb amputation.[3,22,53,57–60] Unsurprisingly, research that followed people undergoing a lower limb amputation has noted that many experience either a complete loss in the ability to walk (34.8%) or are unable to ambulate the same distance (45.7%) at 6-months post-amputation as they did prior to their surgery.[2] In fact, and on average, longitudinal research shows that although walking slowly improves after an amputation, walking abilities do not reach pre-morbid levels.[61] Some, as high as 46% are non-ambulatory 17-months post-amputation.[62]

1.5 Falls in PLLA

People with lower limb amputations are often middle-aged to older adults (mean range: 55.0-74.1 years),[1,39–41] have greater comorbidity burden and polypharmacy,[6,39,53,63] exhibit gait and balance impairments,[3,53,57,60] and cognitive dysfunction;[16,17,64] all of which are known factors for the risk of falls[65]. Expectedly, the prevalence of falls is high in PLLA,[9] and ranges between 42.5-57.7% annually.[8,10,11,13] To put these numbers into perspective, falls in older adults are considered a global public health concern[66] and their rate of falls among those community-dwelling ranges between 28.7-34.0%.[67,68] Falls in PLLA are arguably more aligned with what is observed in institutionalized older adults or individuals with dementia.[69–71] Specific risk factors for falls among PLLA include dysvascular etiology, level of amputation (higher level has an increased risk), issues with the residual stump, pain and a lack of feeling of vibrations.[9] Falls can result in serious and immediate physical consequences, such as fractures, dislocations, sprains/strains, and traumatic brain injury.[11,29] Other consequences from falls include immobility, low confidence, fear of falling, social isolation, and a reduced quality of life.[10,12,29,72] A vicious cycle can develop from a fall that elicits fear of falling which then leads to activity restriction, deconditioning and loss of muscle mass, which in-turn increases the risk for falls in the future.[73] Moreover, most falls occur while ambulating,[13] and PLLA report that independent ambulation is the most important factor to their life satisfaction[2]. Due to the negative effect of falls and the relationship between ambulation and numerous factors relevant to PLLA, healthcare professionals working with this population are often recommended to rely on clinical tests of physical function to examine abilities and falls risk, track progress and prognosticate future success.[14,74]

1.6 Rehabilitation and Mobility in PLLA

1.6.1 Stages of Rehabilitation in PLLA

Although the recovery from an amputation is different for every person based on a unique combination of factors (e.g., medical history, etiology, amputation level, healing progress) it is suggested that five stages exist: 1) preoperative, 2) acute postoperative (5-14 days post-amputation), 3) immediate post-acute (4-8 weeks post-amputation), 4) intermediate (4-6 months post-amputation), and 5) stable (12-18 months post-amputation).[31] For some, an artificial limb (i.e., a prosthetic device) used on the residual limb may be introduced as a way to enable walking.[75] Earlier stages of recovery from a lower limb amputation are characterized by substantial fluctuations in the size and shape of the residual limb which affects the introduction of a prosthetic device.[76] Initial prosthetic fitting takes place during the immediate post-acute stage, while the first long-term prosthesis is worn at the intermediate stage which is accompanied by a relatively stable residual limb size and more aggressive efforts for recovery of ambulation with the device.[31] Depending on the individual, it is in the stable stage where they may be introduced to more complex prosthesis designs (e.g., a microprocessor prosthesis) that may better fit with their ambitions and mobility goals.[31]

1.6.1.1 Acute Postoperative Stage

Interventions targeting rapid wound healing and pain management are an important aspect of care in the acute stage of recovery after a lower limb amputation.[31,75] During this time, swelling is common and changes the shape of the residual limb.[76] Pain is also prevalent after an amputation and may be experienced as residual limb pain and/or phantom limb pain.[77] Those who have an amputation due to dysvascular disease are at an increased risk for skin breakdown and infection due to poor circulation that slows down healing.[78] The ability to move is limited in the acute stage as individuals have not been fit for their lower limb prosthesis; thus, remain reliant on different methods for mobility, such as the use of a wheelchair or on placing all of their body weight onto their non-amputated side and using a mobility aid such as crutches or a walker. A this time in rehabilitation, PLLA are encouraged to move their limbs and train for strength to minimize the development of contractures, deconditioning, or the loss of muscle mass.[79] Falls at this stage of recovery are observed,[80] more of which are classified as injurious when compared to falls in other stages of recovery after a lower limb amputation (e.g., during inpatient rehabilitation or in community-dwelling PLLA)[9].

1.6.1.2 Immediate Post-acute Stage

Prosthetic rehabilitation usually takes place 6-8 weeks after an amputation and lasts around 3-6 weeks.[31,75] The prosthetic stage of rehabilitation in PLLA is dependent on the health status of an individual, their expectations and support for day-to-day activities, and their ability to learn the use of a lower limb prosthesis for walking.[81] In some cases, inpatient prosthetic rehabilitation may be available which involves intensive programming from different healthcare providers with the overarching goal of maximal independence and successful community reintegration.[81,82] The size and shape of the residual limb is of clinical relevance as different prosthetic devices will distribute weight differently and result in altered pressure points during gait.[83] The success of the prosthesis fit is related to progression within rehabilitation, weight-bearing abilities, the efficiency of gait, and the ability to use the prosthesis for longer portions of time.[83–85] However, not all PLLA are able to use a lower limb prosthesis, with factors such as increased age, dysvascular etiology and a more proximal level amputation being associated with complications with the prescription of prosthetic devices.[86,87] At a minimum, prosthetic rehabilitation tends to be specific to PLLA who are able to physically don and doff a prosthetic device and are able to learn how to safely use a prosthesis for navigating their environment.[81,82] During prosthetic rehabilitation, a drastic improvement and significant change in mobility, ambulation and gait parameters is observed.[2,53]

1.6.1.3 Intermediate and Stable Stages

Community reintegration is marked by a discharge from prosthetic rehabilitation and the resumption of taking part in recreational and work-related activities without substantial support from rehabilitation clinicians.[81,82] However, not all PLLA are discharged to where they had resided prior to their amputation.[88,89] At this stage, a relationship exists between the use of a prosthesis for walking and a higher overall quality of life.[2,54,90] Significant and clinically meaningful changes to physical function, physical activity and mobility are observed at this stage also.[53,91–94] However, physical function and mobility are believed to plateau around 6-months post-discharge from inpatient prosthetic rehabilitation (i.e., around 12-months from the date of amputation).[2,61] Impaired mobility and a reliance on the use of a mobility aid for walking are common even years after an amputation, completion of prosthetic rehabilitation, and successful community reintegration.[3,53,60,95]

1.6.2 Mobility and Gait Overview

Clinicians working with PLLA are encouraged to use assessments of physical function to evaluate abilities, identify impairments, and prognosticate outcomes.[14] Tests used by clinicians may be objective or subjective. Objective tests involve the performance of a task (e.g., walking the length of a hallway), while subjective testing inquire on peoples' perception of their abilities to complete a task, such as those not readily available to be performed in a clinic (e.g., walking on different terrain). Although each type of test used to evaluate physical function has its advantages, growing evidence supports the need to assess both objective and subjective measures of physical function due to the lack of congruency of findings between the two in PLLA.[91]

There are many ways in which physical function can be measured.[96] More broadly, physical function may be assessed as the ability to transition from one location to another (i.e., mobility); as an inquiry on specific aspects of walking like being able to maintain balance while moving (i.e., dynamic balance); or as the ability to successfully complete daily tasks (i.e., functional mobility).[96] Due to the fact that most falls in PLLA take place while walking,[13] gait assessments, or the manner and style of walking, are of utmost importance to clinicians.

1.6.2.1 The Gait Cycle and Gait Domains

The gait cycle is generally defined as the time interval for two successive foot contacts onto the ground to occur by the same limb.[97] A total of eight phases exist for the gait cycle and include: 1) initial contact, 2) loading response, 3) mid-stance, 4) terminal stance, 5) pre-swing, 6) initial swing, 7) mid-swing, and 8) terminal swing.[97] (Figure 1.1)

The initial five events occur when the foot is on the ground and entail the acceptance of weight until a single limb is fully supporting all bodyweight.[97] The other three events of the gait cycle entail the progression of gait forwards from toe off to the next initial foot contact.[97] As the gait cycle is comprised of the time from initial contact of one foot to the next initial contact onto the ground by the same foot, one gait cycle is therefore one stride or two steps.[97]

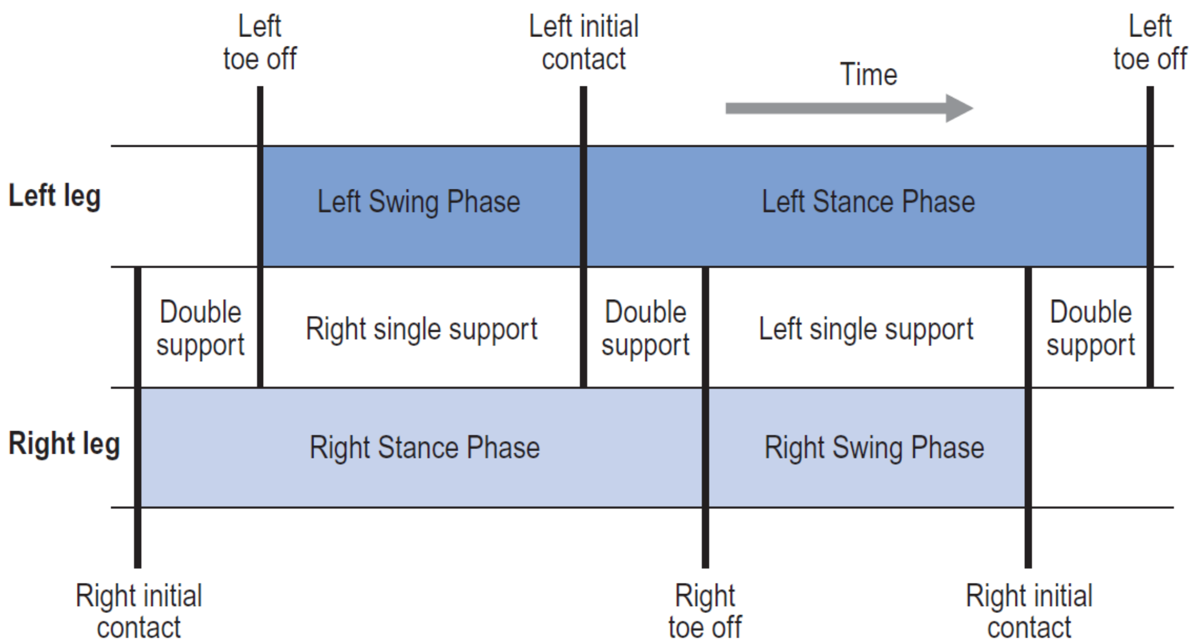

Figure 1.1: The Normal Gait Cycle (Adapted from Whittle M. 2007)

Gait can be characterized using a multitude of spatial (distance) or temporal (timing) parameters.[98] Five domains of spatiotemporal gait parameters exist, including: 1) pace, 2) rhythm, 3) variability, 4) asymmetry, and 5) postural control.[99] Pace encompasses the velocity of gait and the stride/step length, while the rhythm domain refers to the number of steps taken per minute (i.e., cadence).[99] The consistency of gait parameters is termed variability and is usually measured as the coefficient of variation,[100] while the domain of asymmetry examines the equality of left and right body hemispheres.[99] Lastly, postural control refers to the integrity of the base of support while walking.[99] A relationship exists between different gait domains and changes in age and cognitive function.[101] For example, stride time variability is considered a measure of motor task automaticity that relies on higher-order cortical control,[102] so increased gait variability is believed to be indicative gait instability due to its association with falls risk in older adults.[103,104] The relationship between gait and falls in PLLA has been studied to some degree;[105,106] however, this research has been limited and is not considered to be robust.

1.6.2.2 Gait in PLLA

In PLLA, gait is negatively affected by the loss of lower limb motor-sensory information, asymmetric weight-bearing and changes to force absorption and generation.[107–110] Compensatory mechanisms are observed and which are scaled according to the level of amputation with more proximal amputations altering gait the most.[97] For example, those with unilateral transfemoral level amputations often rely on a fully-extended knee, trunk flexion and the musculature around the hip for the absorption of forces related to ambulation due to a lack of an anatomical knee joint.[97] Moreover, and as result of a missing ankle joint, PLLA at the unilateral transtibial level lack the ability to dorsiflex and plantarflex which affects the timing and length of steps.[97] Compared to controls, those with unilateral transtibial amputations have slower gait velocities, shorter strides and an observed asymmetry in the timing between limbs in the stance phase of the gait cycle.[111,112] A larger difference in spatiotemporal gait parameters is observed between PLLA at the unilateral transfemoral level and controls, whereby those with transfemoral amputations have slower gait velocities and cadence, and higher step time asymmetry and variability values.[112,113] Within groups of PLLA, those with unilateral transtibial level amputations show faster gait velocities, longer steps, narrower step-to-step distances, and less asymmetry in the stance phase of the gait cycle than those with unilateral transfemoral amputations.[112,114]

1.7 Cognitive Impairment in PLLA

1.7.1 Cognition

Gait is a cognitively demanding motor task,[15,23] with 40.9% of PLLA reporting the need to concentrate on every step they take while walking using their prosthesis[10]. PLLA are constantly being cognitively and physically challenged during ambulation in order to accommodate to their environments, such as when completing transfers, making turns, walking on uneven surfaces, or when negotiating obstacles, weather effects, or maneuvering their own mobility aid.[15,23] The cognitive demands associated with safely using a prosthesis for walking is often described as a significant cognitive burden in PLLA of dysvascular etiology.[22] Broadly, cognition is considered an umbrella term used to encompass many different processes involved in the gathering, assimilation, manipulation, and use of information.[115] Three cognitive domains are of particular importance to understanding the relationship between cognition and mobility, specifically: 1) executive function, 2) attention, and 3) working memory.[115]

1.7.1.1 Executive Function

Executive function entails the higher order cognitive processes related to the completion of complex, goal-oriented behaviour.[116] Executive functions are involved in the control and direction of planning, volition, reasoning, vigilance, information inhibition, and the regulation of attention and working memory.[15,116] Executive function involves a network of cognitive processes and it spans over the dorso-lateral prefrontal cortex and anterior cingulate cortex areas of the brain, with connections from these sites to frontal, temporal, and parietal regions.[117,118] Impairments of executive function affect the ability to self-regulate and correct behaviour while also negatively affecting the reasoning and planning needed to successfully engage in novel tasks.[116]

1.7.1.2 Attention

Attention allows for the processing of relevant information while simultaneously suppressing irrelevant stimuli.[119] Attention can be controlled by top-down factors, such as previous experiences and current goals, or by a sensory stimulus that automatically orients attention (i.e., bottom-up factors).[120] Four different domains of attention exist: 1) orienting, 2) alerting, 3) divided, and 4) sustained.[116,119] Orienting attention involves the selection of specific information and concurrent suppression of distractors.[116,119] Alerting attention is the process of automatically disengaging from one stimulus to rapidly engage in another.[15,119] Divided attention enables for the completion of multiple tasks at once, while the ability to maintain focus over time is termed sustained attention.[15,119] Individuals with impaired attention struggle to assimilate and act upon novel information.[116]

1.7.1.3 Working Memory

Working memory is a term used to describe the various processes related to the short-term preservation and manipulation of information.[121] Working memory is most apparent whenever making sense of a continuous and unfolding series of events or stimuli as it enables for individuals to retain temporarily what has taken place in order to relate to future events.[116] Impairments of working memory result in an inability to retain information in the mind for manipulation, such as having difficulty mentally reorganizing a to-do list of items.[116] Working memory is a critical component of reasoning, allowing people to see connections that would otherwise may be perceived as unrelated.[116]

1.7.2 Epidemiology of Cognitive Impairment in PLLA

Impairment of cognitive functions is prevalent in people with lower limb amputations.[16,17,122] In a sample of PLLA mainly composed of those who had an amputation due to dysvascular complications, 52.6-56.3% demonstrated impaired cognition at admission or discharge from prosthetic rehabilitation.[16,17] Although lower at 23.5%, prevalence of cognitive impairment remains high in community-dwelling PLLA who were on average 4.6-5.0 years removed from their amputation surgery.[122] Similar self-reported cognitive concerns have been observed in community-dwelling PLLA of dysvascular compared to traumatic etiology; both groups which had a higher prevalence of subjective cognitive complaints than what is seen in the general population.[64] The discrepancy between the reported cognitive impairment in PLLA at earlier compared to later stages of rehabilitation may be explained by a number of factors, such as different cognitive testing, methodology, and sample heterogeneity.[122] Moreover, PLLA who have cognitive impairment in preoperative, preprosthetic, or prosthetic stages of rehabilitation have an observed higher risk of mortality and demonstrate lower rehabilitation gains than the cognitively healthy.

Specific cognitive domains affected in PLLA include executive function, attention, memory and visuospatial perception.[17] Advanced age and a higher comorbidity burden were factors related to worse cognitive performance in PLLA around the time of prosthetic rehabilitation, while other important characteristics such as etiology, level of amputation, length of stay after amputation surgery, and anxiety status were not.[17] In community-dwelling PLLA, those with impaired cognition tended to be older, use a mobility aid for walking, reported more comorbidity, and were more likely to be depressed.[122] Due to the wide range of cognitive domains affected in PLLA, it is speculated that those with cognitive impairments may struggle to effectively learn the skills needed to safely use a lower limb prosthesis for walking.[17] The specific prosthetic skills which are most difficult to acquire in PLLA with cognitive impairments during prosthetic rehabilitation has not been evaluated. What is known is that meaningful improvements to physical function as it relates to prosthetic rehabilitation and community reintegration are still observed in PLLA who demonstrate cognitive impairment, although the magnitude of these gains is smaller than in the cognitively healthy.[16,18,94]

1.7.3 Mechanisms for Cognitive Impairment in PLLA

Multiple reasons exist as to why PLLA may be more prone to developing cognitive impairments.[123] In general, increased age is a common factor for issues related to executive function, attention, and memory.[124–126] Advanced age may result in microlesions to widespread regions of the brain which are observed as sub-clinical cerebral infarcts, cerebral bleeds and white matter hyperintensities during neuroimaging.[127–130] White matter degeneration is associated with decreased prefrontal cortex function, a site critical for higher order cognitive processes such as executive function.[129,131] Moreover, research in healthy, community-dwelling older adults has found the presence of cerebral infarcts and/or bleeds is related to worse gait and balance performance.[127]

Incidence data shows that more than half of amputations take place in those who are 50 years and older, and most are attributed to dysvascular disease.[1,32] Over time, the dysregulation of blood glucose that is common in diabetes results in micro- and macro-level damage to the vascular system.[19] This damage entails the degradation of the endothelial cells that make up the inner lining of blood vessels, including those found within the brain, through increased oxidative stress.[132] Unsurprisingly, people with vascular-related issues often demonstrate structural brain abnormalities that negatively affect cognitive function.[20,21,133] As a result of the widespread damage to bodily tissues seen in people with diabetes, retinopathy, neuropathy, nephropathy, cardiovascular disease, and many other comorbidities are common.[19,134–136] Thus, people with diabetes also experience somatosensory, muscular, visual, vestibular, and neurobehavioral dysfunction.[20,21,133,137] It is through these cumulative pathological mechanisms related to accelerated aging and dysvascular disease that may explain why PLLA are more likely to demonstrate cognitive impairments, which to date are believed to partially explain the commonly observed issues with physical function and falls in this group of people.

1.8 Inter-relationship Between Cognition and Mobility in PLLA

1.8.1 The Capacity Sharing Model and Dual-task Testing

The capacity sharing model explains that every activity we engage in requires a certain amount of cognitive resources for processing and are scaled according to the complexity of the task.[24,25] Cognitive resources are finite, thus when people are asked to complete an activity above and beyond their cognitive capacity, interference or decreased performance is observed.[24,25] A similar effect may also occur if multiple tasks concurrently performed, known as dual-task testing, exert a cognitive load that is unable to be matched.[26] In this case, the performance of one or both tasks may be worse during dual-task testing than if each task was completed in isolation.[26] The difference in performance between single-task and dual-task trials is termed the dual-task cost.[26] Importantly, dual-task performance is part of most of our everyday activities, such as when we walk and talk.[15,23]

The dual-task paradigm is based on the assumption that for interference to occur, the tasks being performed need to be competing for the same cognitive resources.[24,25] Indeed, research has shown that worse performance on executive function, but not memory, is independently associated with higher stride length variability (i.e., a more inconsistent gait pattern) during dual-task gait testing in community-dwelling older adults.[138] In people with unilateral transfemoral or transtibial level amputations, worse executive function is independently associated with lower gains in functional mobility and gait velocity for both single-task and dual-task testing 4-months after discharge from inpatient prosthetic rehabilitation.[94] Overall, a close relationship is recognized to exist between cognition, gait and falls which has been exemplified by an array of dual-task and neuroimaging research in older adults and people with neurodegenerative diseases (e.g., Alzheimer's dementia, Parkinson's disease, etc.),[139,140] but this sort of research in PLLA remains limited. Assessments of capacity for the interplay between cognition and motor performance may allow for a better understanding of the ability of an individual to efficiently share cognitive resources during instances in which they are cognitively challenged and in which falls often occur.[139,140]

1.8.2 Dual-task Testing in PLLA (Rationale for Study #1)

People with lower limb amputations are optimal candidates for dual-task balance and gait research due to the following unique characteristics: a high prevalence of falls observed mainly while ambulating;[8,10,11,13] the increased cognitive requirement and motor learning associated with the use of a prosthesis for walking;[10,22] and the common presence of cognitive impairments and dysvascular disease[16,17,122]. Dual-task gait testing in PLLA results in decreased mobility performance[28] and worse gait parameters, such as a slower gait velocity, lower cadence, an increased stride time, and higher asymmetry values.[27]

Only one review in this topic had been published and it concluded that a disproportionate effect of dual-task testing on the performance of balance, but not gait, outcomes was observed in PLLA relative to controls.[141] Yet, this review was based upon twelve manuscripts, four specific to gait,[141] that were mainly published prior to later pivotal work used to standardize the assessment of dual-task paradigms[26]. Such a low number of studies gathered did not allow Morgan et al.[141] to determine what specific characteristics were important to the dual-task effect in PLLA. Prior to embarking in inquiries on the usefulness of dual-task testing for clinical use in PLLA, research needs to be updated to consolidate the full scope of published dual-task research[27,28,94,142–145] to see if and how dual-task testing uniquely affects the balance and gait of people in this population relative to others in order to better understand of the challenges associated with walking with a prosthesis.

1.8.3 Concern for Falls, Balance Confidence and Mobility in PLLA (Rationale for Study #2)

Among PLLA, an increased concern for falls is common,[146,147] and is associated with decreases in prosthesis use, socialization, and quality of life.[12,29,148] A concern for falls is an umbrella term for the various psychological consequences of falling, including: 1) fear of falling, 2) falls-related self-efficacy, 3) mobility-related self-efficacy, 4) consequences of falling, and 5) perceptions on falls.[149] Each of these five subdomains evaluate a related, yet distinct aspect of a concern for falls.[149]

Most research on concern for falls has been published on self-efficacy, or the belief that one is able to accomplish a specific task[73,150,151]. For PLLA, self-efficacy has mainly been examined through balance confidence, the belief that one is able to achieve a specific task without losing balance or becoming unsteady.[152] Balance confidence is persistently low in PLLA, even years after community reintegration, and is significantly worse in those not reporting walking automaticity[146,147]. In community-dwelling older adults without lower limb amputations, anxiety related to falls (i.e., low balance confidence) has been reported to increase the attentional demands of walking and results in worse gait performance.[153] Therefore, research suggests that a relationship exists between balance confidence and walking, whereby balance confidence may act as a distractor which exerts a cognitive load onto the already cognitively demanding motor task that is walking with a prosthesis.

Three studies have investigated the association between balance confidence and the mobility of community-dwelling PLLA.[148,154,155] However, this previous literature has lacked the use of a homogenous sample, more complex tests of mobility specifically designed for use in this group of people, or did not include conditions of dual-task testing which add a cognitive challenge that can be used to examine cognitive-motor capacity. Determining the extent to which balance confidence affects mobility is needed to improve our understanding of rehabilitation and falls-prevention in PLLA, a population at a high risk for falls.

1.8.4 The Relationship Between Cognitive and Physical Function Performance (Rationale for Study #3)

Intensive rehabilitation is required for many PLLA to restore physical function and to provide training for the use of a prosthetic device to ambulate.[31,75] As the majority of falls occur while walking[13] and the ability to walk independently is the most important factor to life satisfaction following a lower limb amputation,[2] clinicians working with PLLA are encouraged to use assessments of physical function during the rehabilitation process.[14] Tests of physical function allow for the recording of progress, to determine areas for targeted intervention, and can also be used to predict future success (e.g., upon community reintegration).

Many clinical tests of physical function exist;[14] however, little is known about the variation in the magnitude of cognitive demands amongst available tests of physical function in those inexperienced at walking with a prosthesis. For older adults, different secondary tasks within a dual-task protocol require different levels of cognitive resources and are therefore not interchangeable.[156] It is important for clinicians working with PLLA to understand the relative cognitive demands associated with the clinical tests that they commonly use as a mismatch in test selection may lead to the assessor being unable to appropriately challenge cognitive-motor capacity or detect deficits.

Chapter 2

Study 1 – The Effect of Dual-Task Testing on the Balance and Gait of People with Lower Limb Amputations: A Systematic Review

A version of this chapter has been published in PMR: The journal of injury, function, and rehabilitation.[157] [**Omana H**, Payne M, Viana R, Montero-Odasso M, Hunter SW. The effect of dual-task testing on the balance and gait of people with lower limb amputations: A systematic review. PM&R. 2021. Doi: 10.1002/pmrj.12702]. See Appendix A to view the copyright license agreement associated with use of the accepted version of this manuscript for the present dissertation.

2.1 Introduction

A lower limb amputation is a life-altering event with considerable repercussions to physical and psychological well-being.[2,3,22,50] Many PLLA require intensive rehabilitation when learning to use a prosthesis for walking. The majority of amputations result from diabetes or peripheral vascular disease, known as dysvascular disease, and decreased limb sensation, gait problems, and cognitive impairment are prevalent in these individuals.[,7,16,32,34] Unsurprisingly, falls are also common in PLLA[9,10] and can have serious consequences that impact numerous aspects of life.[12] As most falls occur while walking,[13] the assessment of gait in PLLA is considered essential for tracking rehabilitation progress and successful community reintegration.[14,74]

Gait is a complex motor task demanding of cognitive resources even when regulating routine walking.[15,23] Independent living requires increased cognitive and motor function as it involves navigating surroundings and completing transfers, turns, outdoor walking, and the negotiation of obstacles and gait aids.[15,23,158] Real-life ambulation relies on executive function, higher-order cognitive processes critical for the reasoning, planning, monitoring and adjusting inherent in mobility.[15] According to the capacity sharing model, resources for cognitive processing are limited and each task requires a certain amount of resources.[24,25] More complex activities or the simultaneous completion of tasks increases cognitive load.[24,25] Therefore, if the demands for the performance of multiple tasks at the same time surpasses an individual's cognitive capacity, cognitive-motor interference is observed alongside the performance deterioration of one or both tasks.[24,25] In PLLA, using a prosthesis is already cognitively demanding with many stating a cognitive burden to keeping safe,[22] and having to concentrate on every step when walking.[10] Moreover, cognitive impairment, including issues related to attention, memory, and executive function, have been reported in as high as 52.6-56.3% of PLLA,[16,17] and observed to be associated with mobility problems in those with vascular-related amputations.[18] The capacity for the allocation of cognitive resources is believed to be limited in PLLA in part due to the cognitive requirements associated with the use of a prosthesis, balance and gait impairments, as well as the commonly observed presence of executive dysfunction. Thus, the examination of cognitive-motor capacity is an important avenue to explore as it may help explain the high rate of falls this population experiences.

Dual-task testing, completing two tasks at once, and which is a component of most everyday activities,[23] is considered a measure of cognitive-motor capacity.[26,159] The relative change in the performance between single-task and dual-task conditions is known as the dual-task cost.[26] In PLLA, dual-task testing leads to worse mobility,[28] deteriorated gait parameters and increased instability.[27] Only one review on this topic has been published, reporting that the magnitude of the effect of dual-task on the balance, but not gait, was greater in PLLA relative to healthy adults.[141] However, conclusions drawn were limited due to the small number and methodology reported by the studies gathered, which did not enable the authors to determine what characteristics were important to the dual-task effect. In recent years a surge in dual-task related research in PLLA,[27,28,94,142–145] and related populations,[160] has been observed. Therefore, an updated systematic review on this topic is warranted.

The main study objectives were: to systematically review the literature on the effects of dual-task testing on the balance and gait of PLLA, and to determine if dual-task effects were dependent on level of amputation, etiology, type of prosthesis used, prosthesis experience, or secondary task used. It was hypothesized that dual-task testing would result in a disproportionally larger deterioration of balance and gait performance (i.e., a differential effect) in PLLA relative to controls (CN). A lesser dual-task effect would be observed in people with transtibial compared to transfemoral amputations, and in those with non-vascular compared to vascular amputations.

2.2 Methods

2.2.1 Search Strategy

Six electronic databases were searched: MEDLINE, EMBASE, CINAHL, PsycINFO, Web of Science and Scopus (inception-December 01, 2020). Each database was searched in duplicate without filtering and using a standardized search strategy developed in consultation with a research librarian. (Appendix B) The systematic review adheres to PRISMA guidelines[161] and was registered in PROSPERO (#42020178005).

2.2.2 Inclusion and Exclusion Criteria

The following inclusion criteria needed to be met: participants were adults 18 years or older with a transtibial, transfemoral, knee-disarticulation, or bilateral level lower limb amputation, and dual-task balance or gait was assessed using a secondary cognitive or motor task. Studies were excluded if not published in English, or if manuscripts were grey literature (i.e., not peer-reviewed). Also excluded were studies with participants with concurrent diagnoses not related to limb loss that may have affected mobility, or if no comparisons of performance were reported.

2.2.3 Study Selection

After the removal of duplicates, all titles and abstracts were assessed independently by two authors and a match was needed before entering full-text review. During full-text review, the same two authors assessed each manuscript using the inclusion/exclusion criteria. A third author was contacted for resolution if a consensus was not reached. All manuscripts were searched for additional articles not captured by the electronic search strategy.

2.2.4 Data extraction and Methodological Quality of Reporting

Data extraction was completed in duplicate by two authors using a standardized extraction sheet. The following information was extracted: sample size, inclusion/exclusion criteria, participant age, level and etiology of amputation, time since amputation, cognitive function testing, balance/gait task used, secondary task used, single-task and dual-task performance, statistical analysis, and results reported.

Many parameters are currently used to depict the performance of balance and gait. As a result, the present systematic review relied on different schemas to categorize the outcome measures reported by each study. Parameters related to static balance were grouped into three center-of-pressure (CoP) domains: distance– total CoP displacement; area– radius for CoP trajectory; and velocity– resultant of CoP distance over time.[162,163] Similarly, the Lord et al.[99] model was used to categorize spatial-temporal gait parameters into: pace– gait velocity and stride/step length; rhythm– cadence and stride/step time; variability– measures for the consistency of gait; asymmetry– measures for the equality between body hemispheres, and postural control– measures of postural stability and base of support integrity during gait. The Al-Yahya et al.[164] classification schema was used to categorize secondary tasks into: reaction time tasks, discrimination and decision-making tasks, mental tracking tasks, working memory tasks, verbal fluency tasks, and “other”.

The methodological quality of reporting was assessed using The Downs and Black scale.[165] This scale consists of 27 questions examining general reporting, internal validity bias, internal validity confounding and external validity. Total scores range from 0-32 with a higher value being indicative of better quality of reporting. The Downs and Black scale is a valid and reliable tool for use in observational studies.[165,166] Each article was assessed in duplicate by two authors working independently from one another. A meeting was held for the review of items for each study and a scoring consensus was required. If agreement was unable to be reached, a third author was contacted for resolution.

2.2.5 Data Analysis

A meta-analysis was planned *a priori*, whereby the pooled estimate dual-task effect difference was to be calculated and compared between PLLA and CN or between PLLA subgroups for each balance and gait domain. However, little to no overlap was observed regarding participant characteristics, tasks instructions, dual-task protocols, summary outcome measures, or balance/gait assessments used among the final pool of studies. The calculation of a single-point estimate was therefore deemed inappropriate due to substantial heterogeneity and a qualitative synthesis was performed instead.

2.3 Results

A total of 3,950 articles were screened, and 35 underwent full-text review (Figure 2.1). Twenty-two studies met inclusion criteria: four assessed dual-task balance,[142,167–169] and eighteen dual-task gait.[27,28,94,113,143,145,170–181] (Table 2.1) The main, non-mutually exclusive, reasons for exclusion were: not making performance comparisons or assessments of dual-task (n=9); not a research study or written in English (n=3); did not recruit adults or PLLA (n=2). (Appendix C)

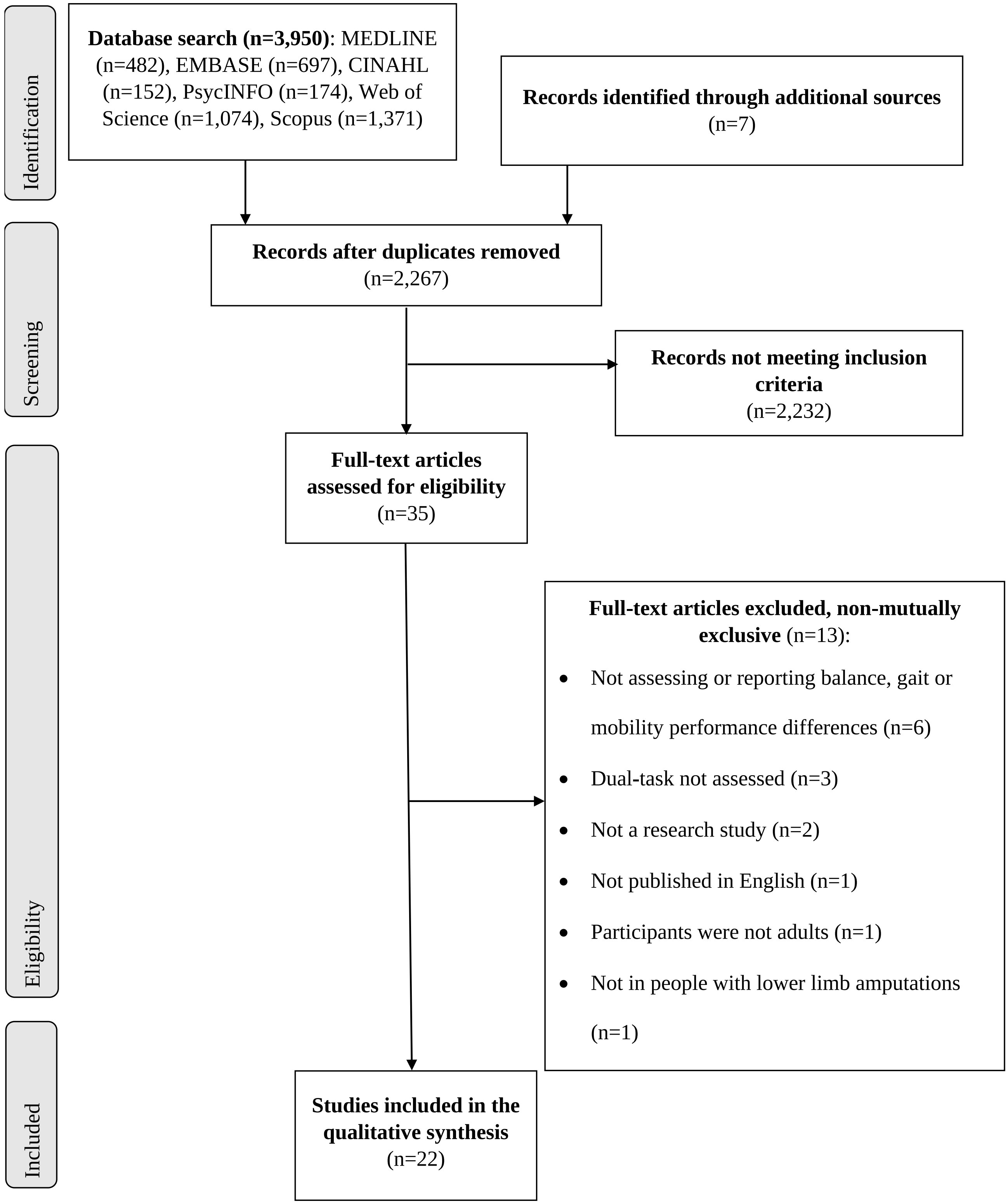

Figure 2.1: Flow diagram of literature search as per PRISMA guidelines.

Table 2.1: Participant characteristics and methodology details for articles included in the systematic review.

Lead author (Country)	**Sample size** (n, % male)	**PLLA Eligibility criteria**	**Age Mean ± SD (range)**	**Level of amputation Frequency (%)**	**Etiology of amputation**	**Years since amputation Mean ± SD (range)**	**Cognitive assessment Mean ± SD (range)**
Dual-task static and dynamic (feet-in-place) balance							
Geurts et al. 1991[167] (The Netherlands)	CN: 8 (62.5) PLLA: 8 (62.5)	**Inclusion:** Recent amputation, first prosthesis. **Exclusion:** Serious cognitive impairment.	CN: 65.6 ± 16.5 (NR) PLLA: 67.7 ± 18.1 (25-84)	KD/TF: 4 (50) TT: 4 (50)	PVD/DM: 4 (50) Infection: 2 (25) PVD: 1 (12.5) Trauma: 1 (12.5)	NR	NR
Geurts et al. 1994[168] (USA)	CN: 12 (75) YA: 8 (50)† PLLA: 12 (75)	**Inclusion:** Recent amputation, first prosthesis. **Exclusion:** Serious cognitive or	CN: 58.9 ± 18.3 (NR) YA: 24.9 ± 2.4 (NR) PLLA: 59.4 ± 18.3 (23-78)	KD/TF: 8 (66.7) TT: 4 (33.3)	PVD: 7 (58.3) Trauma: 3 (25) PVD/DM: 2 (16.7)	NR	NR

		sensory impairment.					
Vrieling et al. 2008[169] (The Netherlands)	CN: 9 (88.9) PLLA: 8 (75)	**Inclusion:** >18 years, >1-year post-amputation, daily prosthesis use, able to stand without aids and using their prosthesis for at least 30 minutes. **Exclusion:** Any medical issue affecting mobility, otitis media, visual impairment, or antipsychotic, antidepressant or tranquilizer drug use.	CN: 44.8 ± 9.9 (NR) PLLA: 51.8 ± 12.7 (NR)	TF: 3 (37.5) TT: 5 (62.5)	Trauma: 5 (62.5) Tumour: 2 (25) PVD: 1 (12.5)	21.5 ± 16.3 (NR)	NR
Howard et al. 2017a[142] (USA)	CN: 15 (47) PLLA: 13 (70)	**Inclusion:** 18-80 years, >1-year post-amputation, comfortable socket fit, no health problem	CN: 49 ± 16 (NR) PLLA: 46 ± 11 (NR)	TT: 13 (100)	Trauma: 6 (46.1) PVD: 5 (38.5) Infection: 2 (15.4)	8 ± 7 (1-22)	3MS CN: 95 ± 4 (88-100) PLLA: 95 ± 5 (88-100)

		affecting daily activities, able to stand without a mobility aid. **Exclusion:** NR					TMT-A (s) CN: 44 ± 13 (18-66) PLLA: 48 ± 10 (26-62) TMT-B (s) CN: 48 ± 12 (26-70) PLLA: 48 ± 13 (17-68) FAS (words) CN: 39.1 ± 13 (19-72) PLLA: 35.6 ± 8 (1-49)
Dual-task Walking							
Heller et al. 2000[170]	PLLA: 10 (70)	**Inclusion:** ≥5-year post-	PLLA: 38 ± NR (NR)	TF: 10 (100)	Trauma: 8 (80)	≥5	NR

(UK)		amputation, no stump issues, "general fitness" and high activity level. **Exclusion:** NR			Cancer: 2 (20)	(NR)	
Williams et al. 2006[171] (USA)	PLLA: 8 (87.5)	**Inclusion:** Individuals experienced at using a non-microprocessor prosthesis (8 hours/day for >3 years), able to ambulate 3 flights of stairs, able to walk 30 meters on an incline, did not use a mobility aid. **Exclusion:** Any neurologic or musculoskeletal issue affecting ambulation or a psychiatric disorder	PLLA: 48.5 ± 10.2 (29-61)	TF: 8 (100)	Non-dysvascular: 8 (100)	NR	NR

		affecting participation.						
Hafner et al. 2007[172] (USA)	PLLA: 17 (76.5)	**Inclusion:** >18 years, MFC level 2 or 3, >2-year post-amputation, use of mechanical knee prosthesis. **Exclusion:** Residual limb skin issues, any health issue that may limit study participation.	PLLA: 49.1 ± 16.4 (21-77)	TF: 17 (100)	Trauma: 10 (58.8) Cancer: 3 (17.6) Infection: 2 (11.8) Polio: 1 (5.9) PVD: 1 (5.9)	17.65 ± 18.39 (NR)	NR	
Hof et al. 2007[173] (The Netherlands)	CN: 6 (66.7) PLLA: 6 (66.7)	**Inclusion:** NR **Exclusion:** NR	CN: 43.3 ± 14.2 (21-55) PLLA: 40.5 ± 6.02 (32-50)	TF: 6 (100)	NR	24.50 ± 11.59 (6-40)	NR	
Seymour et al. 2007[174] (USA)	PLLA: 13 (84.6)	**Inclusion:** Individuals new at using a C-Leg, MFC level 4, no health issue limiting functional mobility. **Exclusion:** NR	PLLA: 46 ± 13 (30-75)	KD/TF: 13 (100)	"Non-vascular": 13 (100)	NR	NR	

Hafner et al. 2009[175] (USA)	PLLA (MFC-2): 8 (75) PLLA (MFC-3): 9 (77.8)	**Inclusion:** >18 years, MFC level 2 or 3, >2-year post-amputation, use of mechanical knee prosthesis. **Exclusion:** Residual limb skin issues, any health issue that may limit study participation.	PLLA (MFC-2): 57.1 ± 15.4 (33-77) PLLA (MFC-3): 41.9 ± 14.3 (21-67)	TF: 17 (100)	PLLA (MFC-2): Trauma: 5 (62.5) Infection: 1 (12.5) Polio: 1 (12.5) PVD: 1 (12.5) PLLA (MFC-3): Trauma: 5 (55.6) Cancer: 3 (33.3) Infection: 1 (11.1)	PLLA (MFC-2): 17.0 ± 22.7 (2-67) PLLA (MFC-3): 18.2 ± 15.0 (2-37)	NR
Lamoth et al. 2010[176] (The Netherlands)	CN: 8 (62.5) PLLA: 8 (62.5)	**Inclusion:** Able to walk independently using prosthesis and without a	CN: 45 ± 13.4 (24-70) PLLA: 43.8 ± 14.8 (19-69)	TF: 8 (100)	Trauma: 5 (62.5) Cancer: 2 (25)	15.8 ± 16.7 (0.25-43)	NR

		mobility aid for at least 20 minutes. **Exclusion:** NR			Vascular: 1 (12.5)		
Meier et al. 2012[177] (Norway)	PLLA: 12 (83.3)	**Inclusion:** 40-60 years, weighed <125 kilograms, >6 months of experience using a prosthesis, able to walk and navigate stairs without a mobility aid, no health issues affecting walking. **Exclusion:** A poor prosthesis fit.	PLLA: 46 ± 8.6 (NR)	TF: 12 (100)	Trauma: 7 (58.3) Congenital: 2 (16.7) Infection: 2 (16.7) PVD: 1 (8.3)	21 ± 15.6 (NR)	NR
Morgan et al. 2016[113] (USA)	CN: 14 (62.5) PLLA: 14 (64.3)	**Inclusion:** >18 years, >1-year post-amputation, >3 months of daily experience using a microprocessor	CN: 53.8 ± 13.4 (NR) PLLA: 53.8 ± 13.6 (36-77)	TF: 14 (100)	Trauma: 8 (57.1) Cancer: 3 (21.4) Infection: 2 (14.3)	21.6 ± 15.3 (4-57)	MoCA† CN: 28.3 ± 1.4 (NR) PLLA: 26.6 ± 1.3

		knee, able to walk without a mobility aid for 15 minutes, able to navigate ramps and stairs, no medical issue affecting mobility or cognition, no uncorrected visual or hearing impairment. **Exclusion:** NR			PVD: 1 (7.1)		(24-29)
Howard et al. 2017b[143] (USA)	CN: 13 (61.5) PLLA: 14 (78.6)	**Inclusion:** 18-80 years, >1-year post-amputation, comfortable socket fit, no health problem affecting daily activities, able to walk 10 meters at varying velocities. **Exclusion:** NR	CN: 46 ± 18 (NR) PLLA: 43 ± 12 (NR)	TT: 14 (100)	Trauma: 11 (78.6) Infection: 2 (14.3) PVD: 1 (7.1)	9 ± 7 (1-28)	3MS CN: 98 ± 1 (NR) PLLA: 96 ± 2 (NR) TMT-A (s) CN: 50 ± 6 (NR)

							PLLA: 48 ± 11 (NR) TMT-B (s) CN: 53 ± 8 (NR) PLLA: 46 ± 10 (NR)
Morgan et al. 2017[145] (USA)	CN: 14 (62.5) PLLA: 14 (64.3)	**Inclusion:** >18 years, >1-year post-amputation, >3 months of experience using a microprocessor controlled prosthesis that was comfortable, able to walk without a mobility aid for 15 minutes, able to navigate ramps and stairs, no medical issue	CN: 53.8 ± 13.4 (NR) PLLA: 53.8 ± 13.6 (NR)	TF: 14 (100)	Trauma: 8 (57.1) Cancer: 3 (21.4) Infection: 2 (14.3) PVD: 1 (7.1)	NR	MoCA† CN: 28.3 ± 1.4 (NR) PLLA: 26.6 ± 1.3 (NR)

		affecting mobility or cognition. **Exclusion:** NR					
Frengopoulos et al. 2018[28] (Canada)	PLLA: TT(vascular): 20 (90) TT(non-vascular): 24 (83.3) TT(non-established): 20 (60)	TT(vascular or non-vascular): **Inclusion:** >18 years, >6 months of daily experience using a prosthesis, medically stable, and functional use of the English language. **Exclusion:** Unilateral transfemoral or bilateral amputation. TT(non-established): **Inclusion:** >50 years, currently	TT(vascular): 60.36 ± 7.84 (NR) TT(non-vascular): 53.37 ± 14.95 (NR) TT(non-established): 61.07 ± 6.59 (NR)	TT(vascular): TT: 20 (100) TT(non-vascular): TT: 24 (100) TT(non-established): NR	TT(vascular): Vascular: 20 (100) TT(non-vascular): “Non-vascular causes”: 24 (100) TT(non-established): Vascular: 14 (70) Trauma, cancer or “other” causes: 6 (30)	NR	MoCA: TT(vascular): 26.05 ± 2.24 (NR) TT(non-vascular): 26.71 ± 2.40 (NR) TT(non-established): 26.80 ± 2.40 (NR)

		in rehabilitation for first major lower limb amputation, could walk 10 meters without being assisted by a person, and functional use of the English language. **Exclusion:** Any health issue affecting mobility, or severe depression.					
Hunter et al. 2018[27] (Canada)	PLLA: 24 (62.5)	**Inclusion:** >50 years, currently in rehabilitation for first major lower limb amputation, could walk 10 meters without being assisted by a person, and functional use of the English	62.72 ± 8.59 (NR)	TT: 24 (100)	DM: 16 (66.7) PVD: 4 (16.7) Cancer: 2 (8.3) “Other”: 2 (8.3)	NR	MoCA: 26.25 ± 2.80 (NR)

		language. **Exclusion:** Any health issue affecting mobility, or severe depression.					
Hunter et al. 2019[94] (Canada)	PLLA: 22 (59)	**Inclusion:** >50 years, currently in rehabilitation for first major lower limb amputation, could walk 10 meters without being assisted by a person, and functional use of the English language. **Exclusion:** Any health issue affecting mobility.	60.7 ± 6.5 (NR)	TT: 19 (86.4) TF: 3 (13.6)	DM: 15 (68.2) PVD: 2 (9.1) DM+PVD: 1 (4.6) Cancer: 1 (4.6) "Other": 3 (13.6)	NR	MoCA: 26.1 ± 2.5 (NR)
Pruziner et al. 2019[178] (USA)	CN: 12 (91.7) PLLA: 12 (91.7)	**Inclusion:** Able to walk on a treadmill for 15 minutes without the use	CN: 27.4 ± 3.9 (NR) PLLA: 33.7 ± 7.1 (NR)	TT: 12 (100)	NR	NR	NR

		of a mobility aid, <4/10 self-reported pain, no impairment affecting cognition, no drug or alcohol use during day of collection, and no vestibular, auditory or visual issue that may affect walking. **Exclusion:** NR					
Schack et al. 2019[179] (Norway)	PLLA: KD/TF: 22 (64) TT: 28 (57)	**Inclusion:** >18 years, >6 months of experience with a prosthesis, and be able to walk 500 meters without a mobility aid. **Exclusion:** Any comorbidity affecting the ability to	KD/TF: 52 ± 14 (NR) TT: 56 ± 12 (NR)	KD/TF: 22 (100) TT: 28 (100)	KD/TF: Trauma: 11 (50.0) Cancer: 5 (22.7) Congenital: 3 (13.6) Infection: 2 (9.1) “Other”: 1 (4.6)	KD/TF: 22 ± 18 (NR) TT: 16 ± 16 (NR)	NR

		complete protocol, or unable to speak Norwegian.			TT: Trauma: 16 (57.1) Vascular: 7 (25.0) Congenital: 3 (10.7) Cancer: 1 (3.6) “Other”: 1 (3.6)		
Möller et al. 2020[181] (Sweden)	CN: 16 (68.8) PLLA(non-MPK): 14 (85.7) PLLA(MPK): 15 (73.3)	**Inclusion:** >18 years, no additional physical limitations, be able to walk 500 meters with one walking aid if necessary, and speak Swedish or Norwegian. **Exclusion:**	CN: 47 (95%CI: 40-54) PLLA(non-MPK): 51 (95%CI: 42-60) PLLA(MPK): 51 (95%CI: 45-57)	PLLA(non-MPK): KD/TF: 14 (100) PLLA(MPK): KD/TF: 15 (100)	NR	PLLA(non-MPK): 19 95%CI: 11-27) PLLA(MPK): 18 (95%CI: 9-27)	NR

		Cognitive impairment or have a bone-anchored prosthesis.					
Schack et al. 2020[180] (Norway)	CN: 33 (57.6) PLLA: 39 (56.4)	**Inclusion:** >18 years, had an amputation due to non-vascular or non-diabetic reasons, >1-year of experience with a prosthesis, and be able to walk 500 meters without a mobility aid, and no known mental, neurological, or physical issue affecting the ability to complete collection. **Exclusion:** NR	CN: 53.6 ± 12.4 (NR) PLLA: 51.7 ± 12.3 (NR)	KD/TF 19 (48.7) TT: 20 (51.3)	Trauma: 24 (61.5) Cancer: 6 (15.4) Congenital: 6 (15.4) Infection: 1 (2.6) "Other": 2 (5.1)	22 ± 18 (NR)	MoCA: 27.1 ± 1.9 (NR) TMT-A: 34.0 ± 12.0 (NR) TMT-B: 81.0 ± 31.4 (NR)

Footnote: 3MS: Modified Mini-Mental Status Exam; CI: confidence interval; CN: controls; DM: diabetes mellitus; FAS: verbal fluency F-A-S test; KD/TF: unilateral knee-disarticulation or transfemoral amputation; MFC: Medicare Functional Classification; MoCA: Montreal Cognitive Assessment; MPK: microprocessor prosthesis; NR: not reported; PLLA: people with lower limb amputations; PVD: peripheral vascular disease; TF: unilateral transfemoral amputation; TMT-A: Trail Making Test A; TMT-B: Trail Making Test B; TT: unilateral transtibial amputation; YA: young adult. †, a second non-matched control group was recruited and composed of younger adults. †, a statistically significant difference was reported between groups.

2.3.1 Dual-task Testing on Balance Control

2.3.1.1 Study Participants

Overall 93 participants were recruited;[142,167–169] two studies described convenience samples from prosthetic clinics or workshops,[142,169] while the others did not report specifics.[167,168] All studies included both PLLA and CN.[168] Control groups were matched for age-and-sex[167,168] or age-and-education.[169] The average participant age ranged between 44.8-65.6 years for CN and 46.0-67.7 years for PLLA. Three studies recruited both people with knee-disarticulation/transfemoral or transtibial amputations,[167–169] while one recruited only people with transtibial amputations.[142] Participants had an amputation due to vascular issues,[167,168] or was a result of a tumour, trauma, or infection.[142,169] Although studies excluded participants with sensory impairments that affected mobility, none reported how sensory integrity was assessed.

2.3.1.2 Balance Control Domains

No study assessed all three balance domains of sway distance, area, and velocity. (Table 2.2) The most commonly reported balance domains were distance and velocity.[142,167,168]

2.3.1.3 Balance Methodology

All studies assessed balance control in standing with feet at approximately shoulder width apart,[142,167–169] and two included dynamic (feet-in-place) tests.[168,169] (Appendix D) Two studies standardized feet placement,[167,168] and two reported that participants self-selected their position[142,169]. To increase challenge, some studies included additional conditions of standing on foam[142] or with eyes closed.[142,169]

2.3.1.4 Dual-task Methodology

Most studies selected a discrimination and decision-making task for their secondary task, which included a modified Stroop test[167,169] or stating if a series of verbally presented additions (single-digit) were correct or incorrect[168]. (Appendix D) For Howard et al.[142] a mental tracking task of arithmetic subtractions and a verbal fluency task of listing words were reported. Moreover, each task was performed under different instructions: 1) not prioritizing any one task, and 2) prioritizing only the secondary task. Half of the studies,[168,169] did not report what instructions were given to participants related to which task, if any, to focus on (i.e., prioritization) during dual-task conditions.

2.3.1.5 Dual-task Testing on Sway Distance

PLLA had a higher anterior-posterior amplitude than CN in single-task.[142] Dual-task resulted in a higher total CoP path length, and anterior-posterior and medial-lateral amplitudes in PLLA, while CN were characterized only by an increase in anterior-posterior amplitude.[142] Geurts et al.[168] reported PLLA had increased anterior-posterior and medial-lateral amplitudes compared to CN. However, a differential effect of dual-task was not observed.[168]

2.3.1.6 Dual-task Testing on Sway Area

Between group differences were not observed in single-task for 95% sway area.[142] Although sway area was larger in the dual-task conditions for PLLA compared to CN, the statistical analysis employed by Howard et al.[142] did not allow for the interpretation of a differential effect.

2.3.1.7 Dual-task Testing on Sway Velocity

Across single-task and dual-task, studies reported PLLA had higher anterior-posterior and medial-lateral root-mean square velocities compared to CN.[167,168] PLLA demonstrated a larger effect of dual-task on balance performance as per absolute[168] and relative (i.e., differential or quotient dual-task cost)[167] changes in sway velocity.

2.3.1.8 Dual-task Testing on Dynamic Balance Control

Geurts et al.[168] had participants stand on force plates, and once cued, instructed to continuously shift their weight in the medial-lateral direction for 30 seconds, while Vrieling et al.[169] had participants stand as still as possible while being translated automatically in the anterior-posterior direction. (Table 2.3) Overall, PLLA had fewer successful shifts compared to CN,[168] and had higher center-of-pressure deviations in response to perturbations in both single-task and dual-task conditions.[169]

Table 2.2: Summary of the methodology and effect of dual-task testing on the static balance control of people with lower limb amputations.

Lead author	Balance task Secondary task (Category)	Balance domains			Results
		Distance	Area	Velocity	
Geurts et al. 1991[167(†)]	Balance task: Standing in a standardized position. Secondary task: Modified Stroop test (discrimination and decision-making task). Note: The DT protocol was completed			AP RMS velocity (mm/s): (ST) CN: 7.4 ± 2.7 PLLA (start): 18.8 ± 11.4 PLLA (end): 17.4 ± 9.8 (DT) CN: 7.8 ± 3.4 PLLA (start): 25.7 ± 13.5	ST: A statistically significant difference between PLLA(start and end) and CN for AP and ML RMS velocity (p<0.05). DT: A statistically significant difference between PLLA(start and end) and CN for AP and ML RMS velocity (p<0.05). DTC: A statistically significant difference

	twice, before and after prosthetic rehabilitation.			PLLA (end): 21.0 ±12.4 ML RMS velocity (mm/s): (ST) CN: 4.3 ± 2.0 PLLA (start): 10.7 ± 5.5 PLLA (end): 8.3 ± 5.2 (DT) CN: 3.9 ± 1.9 PLLA (start): 15.5 ± 5.4 PLLA (end): 11.0 ± 6.3 AP RMS velocity dual-task cost (differential: DT - ST):	between PLLA(start and end) and CN for ML RMS velocity dual-task cost differential and quotient ($p<0.05$) was observed. Similarly, a statistically significant difference between PLLA(start) and CN for AP RMS velocity dual-task cost differential and quotient ($p<0.05$) was also observed. Time: A statistically significant difference between PLLA(start) and PLLA(end) for: DT AP and ML RMS velocity ($p<0.05$), and DTC(differential) and ML RMS velocity ($p<0.05$). A differential effect of DT in PLLA compared to CN or YA was observed in sway velocity balance domains.

				CN: NR PLLA (start): NR PLLA (end): NR ML RMS velocity dual-task cost (differential: DT - ST): CN: NR PLLA (start): NR PLLA (end): NR AP RMS velocity dual-task cost (quotient: DT/ST): CN: NR PLLA (start): NR PLLA (end): NR ML RMS velocity	

				dual-task cost (quotient: DT/ST): CN: NR PLLA (start): NR PLLA (end): NR	
Geurts et al. 1994[168(†)]	Balance task: Standing in a standardized position. Secondary task: Arithmetic addition check task (mental tracking, discrimination and decision-making task). Note: The DT protocol was completed throughout prosthetic rehabilitation.	AP amplitude (mm): (ST) CN: 3.2 ± 0.7 PLLA: 4.2 ± 1.7 (DT) CN: 3.6 ± 1.3 PLLA: 5.3 ± 2.7 ML amplitude (mm): (ST) CN: 2.3 ± 0.7 PLLA: 4.0 ± 1.8		AP RMS velocity (mm/s): (ST) CN: 7.5 ± 2.6 PLLA: 18.0 ± 9.4 (DT) CN: 8.1 ± 2.9 PLLA: 22.9 ± 11.2 ML RMS velocity (mm/s): (ST) CN: 5.0 ± 2.2 PLLA: 11.9 ± 7.2	ANOVA#1: Group (PLLA/CN): A statistically significant main effect was observed for AP RMS velocity (p<0.005), ML RMS velocity (p<0.005), AP amplitude (p<0.05), and ML amplitude (p<0.005). Condition (ST/DT): A statistically significant simple main effect was observed for AP RMS velocity (p<0.01). Group x Condition: A statistically significant

		(DT) CN: 1.8 ± 0.5 PLLA: 4.2 ± 2.0 AP amplitude (mm): (ST) (week 0-8) YA: NR PLLA: NR (DT) (week 0-8) YA: NR PLLA: NR ML amplitude (mm): (ST)		(DT) CN: 5.0 ± 1.5 PLLA: 14.4 ± 7.9 AP RMS velocity (mm/s): (ST) (week 0-8) YA: NR PLLA: NR (DT) (week 0-8) YA: NR ML RMS velocity (mm/s): (ST) (week 0-8)	interaction was observed for AP RMS velocity ($p<0.05$), ML RMS velocity ($p<0.05$). ANOVA#2: Group (PLLA/YA): A statistically significant main effect was observed for AP RMS velocity ($p<0.01$), ML RMS velocity ($p<0.01$), AP amplitude ($p<0.05$), and ML amplitude ($p<0.005$). . Condition (ST/DT): No statistically significant main effects were observed ($p>0.05$). Time (week 0, 2, 4, 6, 8): No statistically significant main effects were observed ($p>0.05$).

		(week 0-8) YA: NR PLLA: NR (DT) (week 0-8) YA: NR PLLA: NR		YA: NR PLLA: NR (DT) (week 0-8) YA: NR	Interactions: A statistically significant interaction between group and test condition was observed for AP RMS velocity ($p<0.05$), ML RMS velocity ($p<0.05$). A differential effect of DT in PLLA compared to CN or YA was only observed in sway velocity balance domains.
Howard et al. 2017a[142]	Balance task: Standing with feet shoulder width apart. Secondary task: 1) An arithmetic subtraction task (mental tracking).	Path length (cm): (ST: HS/EO) CN: 26.0 ± 9.0 PLLA: 31.6 ± 12.9 (ST: SS/EC) CN: 90.4 ± 56.0 PLLA: 117.4 ± 61.9 (DT-none:	95% area (cm^2): (ST: HS/EO) CN: 1.67 ± 1.09 PLLA: 2.20 ± 0.90 (ST: SS/EC) CN: 9.37 ± 5.79 PLLA: 16.6 ± 12.6 (DT-none: HS/EO) CN: 4.80 ± 3.64		ANOVA#1 (ST): Group (PLLA/CN): A statistically significant main effect was observed for AP amplitude ($p=0.005$). Condition (HS/EO, SS/EC): a statistically significant main effect was observed for path length ($p<0.001$), 95% area ($p<0.001$), AP

	2) FAS test (verbal fluency). Note: Performed under two task prioritization conditions, no prioritization (none) and focus on the cognitive task (cog).	HS/EO) CN: 42.4 ± 13.3 PLLA: 60.1 ± 33.5 (DT-none: SS/EC) CN: 81.4 ± 37.7 PLLA: 138.4 ± 78.5 (DT-cog: HS/EO) CN: 35.4 ± 11.9 PLLA: 62.3 ± 58.6 (DT-cog: SS/EC) CN: 73.2 ± 30.6 PLLA: 113.2 ± 51.6 Path length DTC (%): (DT-none:	PLLA: 6.86 ± 5.87 (DT-none: SS/EC) CN: 8.54 ± 5.46 PLLA: 22.3 ± 14.4 (DT-cog: HS/EO) CN: 4.30 ± 5.89 PLLA: 12.6 ± 18.9 (DT-cog: SS/EC) CN: 7.35 ± 3.60 PLLA: 16.2 ± 9.0 95% area DTC (%): (DT-none: HS/EO) CN: -3.13 ± 3.79 PLLA: -4.67 ± 5.61 (DT-none: SS/EC) CN: 0.83 ± 5.08		amplitude (p<0.001), and ML amplitude (p<0.001). Group x Condition: A statistically significant interaction was observed for AP amplitude (p=0.004). ANOVA#2 (DT): Task (ST/DT): A statistically significant main effect was observed for path length (p=0.002), 95% area (p=0.001), AP amplitude (p=0.002), and ML amplitude (p=0.028) in PLLA. For CN, a statistically significant main effect was observed for AP amplitude (p=0.022). Condition (HS/EO, SS/EC): A statistically significant main effect was observed for path length, 95% area, AP amplitude, and ML amplitude in both PLLA and

		HS/EO) CN: -16.3 ± 15.7 PLLA: -28.5 ± 28.9 (DT-none: SS/EC) CN: 9.0 ± 35.3 PLLA: -20.9 ± 32.8 (DT-cog: HS/EO) CN: -9.3 ± 15.7 PLLA: -30.7 ± 50.7 (DT-cog: SS/EC) CN: 17.2 ± 37.4 PLLA: 4.3 ± 22.7 AP amplitude (cm): (ST: HS/EO)	PLLA: -5.72 ± 7.77 (DT-cog: HS/EO) CN: -2.63 ± 5.64 PLLA: -10.44 ± 18.4 (DT-cog: SS/EC) CN: 2.01 ± 5.01 PLLA: 0.38 ± 6.60		CN ($p<0.001$). Task x Condition: For CN, a statistically significant interaction was observed for path length ($p=0.016$), 95% area ($p=0.017$), AP amplitude ($p=0.009$), and ML amplitude ($p=0.001$). ANOVA#3 (Prioritization): Instruction (None/Cognitive task): A statistically significant main effect was observed for path length DTC ($p=0.03$) in PLLA. For CN, a statistically significant main effect was observed for path length DTC ($p=0.028$). Condition (HS/EO, SS/EC): A statistically significant main effect was observed for ML amplitude DTC in PLLA ($p=0.049$). For CN, a statistically significant main

		CN: 0.93 ± 0.4 PLLA: 1.1 ± 0.5 (ST: SS/EC) CN: 2.2 ± 0.73 PLLA: 3.7 ± 1.5 (DT-none: HS/EO) CN: 1.8 ± 0.9 PLLA: 2.9 ± 2.1 (DT-none: SS/EC) CN: 2.2 ± 1.0 PLLA: 4.7 ± 2.1 (DT-cog: HS/EO) CN: 1.8 ± 1.5 PLLA: 3.3 ± 3.3 (DT-cog: SS/EC) CN: 2.0 ± 0.74			effect was observed for path length, 95% area, AP amplitude, and ML amplitude (p=0.001–0.014). Instruction x Condition: For PLLA, a statistically significant interaction was observed for 95% area DTC (p=0.041). ANOVA#3 was analyzed as dual-task cost and not absolute change. Due to the statistical analysis applied a direct assessment of a differential effect of DT testing can not be made.

		PLLA: 4.0 ± 2.0 AP amplitude DTC (%): (DT-none: HS/EO) CN: -0.84 ± 0.7 PLLA: -1.8 ± 2.1 (DT-none: SS/EC) CN: 0.05 ± 0.9 PLLA: -0.94 ± 0.8 (DT-cog: HS/EO) CN: -0.86 ± 1.5 PLLA: -2.2 ± 3.2 (DT-cog: SS/EC) CN: 0.23 ± 0.8			

		PLLA: -0.30 ± 1.4 ML amplitude (cm): (ST: HS/EO) CN: 2.5 ± 1.0 PLLA: 2.4 ± 0.6 (ST: SS/EC) CN: 5.6 ± 1.5 PLLA: 6.0 ± 1.1 (DT-none: HS/EO) CN: 3.6 ± 1.8 PLLA: 3.7 ± 1.7 (DT-none: SS/EC) CN: 4.9 ± 1.4 PLLA: 6.5 ± 2.1 (DT-cog: HS/EO)			

		CN: 2.8 ± 1.3 PLLA: 3.8 ± 2.6 (DT-cog: SS/EC) CN: 4.8 ± 1.5 PLLA: 6.0 ± 6.0 ML amplitude DTC (%): (DT-none: HS/EO) CN: -1.1 ± 1.9 PLLA: -1.2 ± 1.6 (DT-none: SS/EC) CN: 0.73 ± 1.0 PLLA: -0.48 ± 1.5 (DT-cog: HS/EO) CN: -0.35 ± 1.1			

		PLLA: -1.4 ± 2.3 (DT-cog: SS/EC) CN: 0.85 ± 1.3 PLLA: -0.03 ± 1.1			

Footnote: ANOVA: analysis of variance; AP: anterior-posterior; CN: controls; CoP: center-of-pressure; DT: dual-task; DTC: dual-task cost; DT-cog: a dual-task condition in which the focus is cued to the secondary task; DT-none: a dual-task condition in which no instructions regarding the prioritization of tasks is given; EC: eyes closed; EO: eyes open; FAS: verbal fluency F-A-S test; HS: hard surface; ML: medial-lateral plane; NR: not reported; PLLA: people with lower limb amputations; RMS: root-mean square; SS: soft surface; ST: single-task; YA: young adult. †, Studies for which certain information related to balance control was unable to be extracted as they were only provided through graphs.

Table 2.3: Summary of the methodology and effect of dual-task testing on the dynamic (feet-in-place) balance control of people with lower limb amputations.

Lead author	**Balance task** **Secondary task** **(Category)**	**Balance parameters**	**Results**
Geurts et al. 1994[168(†)]	Balance task: Weight shifting in the ML direction. Secondary task: Arithmetic addition check task (mental tracking, discrimination and decision-making task). Note: The DT protocol was completed throughout prosthetic rehabilitation.	Number of weight shifts: (ST) CN: 12.2 ± 2.7 PLLA: 7.6 ± 4.2 (DT) CN: 11.2 ± 2.9 PLLA: 6.8 ± 5.2 Surplus CoP per weight shift (mm): (ST)	ANOVA#1: Group (PLLA/CN): A statistically significant main effect was observed for the number of weight shifts ($p<0.005$). Condition (ST/DT): A statistically significant main effect was observed for the number of weight shifts ($p<0.05$).

		CN: 43.8 ± 24.1 PLLA: 77.8 ± 26.6 (DT) CN: 34.7 ± 12.9 PLLA: 90.9 ± 68.6 Number of weight shifts: (ST) (week 2-8) YA: NR PLLA: NR (DT) (week 2-8) YA: NR PLLA: NR Surplus CoP per weight shift (mm):	Group x Condition: No statistically significant interaction was observed on any parameter ($p>0.05$). ANOVA#2: Group (PLLA/YA): A statistically significant main effect was observed for the number of weight shifts ($p<0.001$) and surplus CoP per weight shift ($p<0.05$). Condition (ST/DT): A statistically significant main effect was observed for the number of weight shifts ($p<0.001$). Time (week 0, 2, 4, 6, 8): A statistically significant main effect was observed for the

		(ST) (week 2-8) YA: NR PLLA: NR (DT) (week 2-8) YA: NR PLLA: NR	number of weight shifts (p<0.001). Group x Condition: No statistically significant interaction was observed on any parameter (p>0.05).
Vrieling et al. 2008[169]	Balance task: Stand as still as possible while force platform swayed in the AP direction. Secondary task: Auditory Stroop test. Note: Results displayed for affected and non-affected side for PLLA	Weight bearing index: (ST) CN: 1.15 ± 0.14 PLLA: 1.65 ± 0.42 (ST, EC) CN: 1.17 ± 0.15 PLLA: 1.67 ± 0.49 (DT) CN: 1.19 ± 0.18	ST: A statistically significant difference between CN and PLLA was observed for weight bearing index (p=0.025, EC: p=0.008), AP ground reaction (non-affected side: p<0.001, affected side: p=0.022, EC non-affected side: p=0.001), and AP center of pressure displacement (non-affected side: p=0.027, EC affected side: p=0.001).

		PLLA: 1.69 ± 0.49 AP ground reaction force (% body weight): (ST) CN: 23.1 ± 3.3 PLLA (non-affected side): 33.9 ± 4.5 PLLA (affected side): 30.9 ± 8.7 (ST, EC) CN: 23.7 ± 4.8 PLLA (non-affected side): 36.6 ± 7.8 PLLA (affected side): 33.0 ± 13.5 (DT) CN: 22.1 ± 5.1 PLLA (non-affected side): 32.1 ± 9.0 PLLA (affected side): 29.7 ± 15.3 AP center of pressure displacement	DT: A statistically significant difference between CN and PLLA was observed for weight bearing index (p=0.010), AP ground reaction force (non-affected side: p=0.013), and AP center of pressure displacement (non-affected side: p=0.043, affected side: p=0.003). Within group analysis determined that a statistically significant difference due to test condition was only found for AP center of pressure displacement between ST and ST(EC) in CN.

		(m): (ST) CN: 1.91 ± 0.62 PLLA (non-affected side): 3.38 ± 1.69 PLLA (affected side): 1.36 ± 0.41 (ST, EC) CN: 2.82 ± 0.87 PLLA (non-affected side): 4.28 ± 2.18 PLLA (affected side): 1.39 ± 0.41 (DT) CN: 2.14 ± 0.61 PLLA (non-affected side): 3.47 ± 1.67 PLLA (affected side): 1.30 ± 0.30	

Footnote: ANOVA: analysis of variance; AP: anterior-posterior plane; CN: controls; CoP: center-of-pressure; DT: dual-task;

EC: eyes closed; ML: medial-lateral plane; NR: not reported; PLLA: people with lower limb amputations; ST: single-task;

YA: young adult. †, Studies for which certain information related to balance control was unable to be extracted as they were only provided through graphs.

2.3.1.9 Dual-task Balance Testing on Secondary Task Performance

No significant differences in secondary task performance were observed between PLLA and CN in two studies,[167,168] while Howard et al.[142] reported that dual-task resulted in better secondary task performance in PLLA. Performance-resource operating characteristic graphs indicated that PLLA and CN maintained a posture-second strategy during dual-tasking. When dual-task was performed on foam, the CN group adopted a posture-first strategy, while when instructed to prioritize the cognitive task, only PLLA adopted a posture-first strategy.

2.3.2 Dual-task Testing on Gait

2.3.2.1 Study Participants

Eight studies compared PLLA and CN,[113,143,145,173,176,178,180,181] four were within PLLA,[27,28,94,179] and seven assessed microprocessor versus non-microprocessor prostheses.[170–172,174,175,177,181] One study on the use of microprocessor prostheses made comparisons to both CN and PLLA using a non-microprocessor prosthesis.[181] Overall, studies described recruiting convenience samples from a health center, prosthetic clinics, workshops, or social groups;[113,143,145,170,171,174,179–181] from inpatient or outpatient clinics;[27,28,94] or recruitment specifics were not reported.[172,173,175–178] The average participant age ranged from 33.7-62.7 years for PLLA and from 27.4-53.8 years for CN. For manuscripts comparing PLLA to CN: four had age-and-sex matched CN,[113,145,176,181] two were only sex-matched,[173,178] and one was age-and-education matched.[143] Most studies recruited only people with knee-disarticulation/transfemoral amputations[113,145,170–

[177,181] and few included those with both knee-disarticulation/transfemoral or transtibial amputations.[94,179,180] The majority of samples were composed of people who had an amputation due to trauma or other non-vascular reasons.[113,143,145,170–172,174–177,180] All studies excluded participants who had any health issues unrelated to lower limb amputations that may have affected mobility; however, only two specified that this was assessed by a healthcare professional,[172,175] and none provided details as to how motor and/or sensory impairment was determined.

Five studies examined if cognitive function differed between PLLA and CN,[113,143,145,180] or within PLLA groups.[28] The Montreal Cognitive Assessment (MoCA) was the most commonly used test.[27,28,94,113,145,180] Compared to CN, PLLA had significantly lower MoCA scores,[113,145] yet others reported no such differences.[143,180] It is important to note that the two studies that stated a lower cognitive function for PLLA used the same sample of participants who self-reported a higher number of falls per year and had a lower balance confidence relative to age-and-sex matched CN. No differences in MoCA scores were observed between people with transtibial level amputations according to etiology or prosthesis experience.[28]

2.3.2.2 Gait Domains

The most commonly reported gait domain was pace,[27,94,113,143,145,171–173,175,176,178] followed by rhythm,[27,113,143,173,176,178,181] and postural control.[27,113,145,170,173,176,178] (Table 2.4, Table 2.5, Table 2.6)

Table 2.4: Summary of the methodology and effect of dual-task testing on the gait of people with lower limb amputations relative to controls.

Lead author	Walking task Secondary task (Category)	Gait domains: Pace	Rhythm	Variability	Asymmetry	Postural control	Results
Hof et al. 2007[173]	<u>Walking task:</u> Treadmill walking at three different speeds (slow, usual, fast). <u>Secondary task:</u> Stroop test (discrimination and decision-making task).		Stride time (s) (ST-slow) CN (left): 1.51 ± 0.17 PLLA (affected): 1.51 ± 0.13 (ST-usual) CN (left): 1.31 ± 0.11 PLLA (affected): 1.35 ± 0.13			Stride width (cm) (ST-slow) CN (left): 8.2 ± 3.5 PLLA (affected): 12.3 ± 3.0 (ST-usual) CN (left): 8.6 ± 3.3 PLLA (affected):	ST: A statistically significant difference between groups on stance time (affected side: p<0.05, non-affected side: p<0.001), stride width (p<0.05), and mean minimum lateral distance between CoP and XcoM (affected side: p<0.001). DT: A statistically significant difference between groups on

	Note: Results displayed for affected and non-affected side for PLLA.		(ST-fast) CN (left): 1.19 ± 0.08 PLLA (affected): 1.29 ± 0.10 (DT) CN (left): 1.34 ± 0.09 PLLA (affected): 1.35 ± 0.13 Stance time (% of stride) (ST-slow) CN (left): 63.1 ± 1.6 CN (right): 65.3 ± 0.9 PLLA (affected): 59.4 ± 1.1			12.9 ± 4.0 (ST-fast) CN (left): 8.8 ± 2.5 PLLA (affected): 14.7 ± 4.8 (DT) CN (left): 8.8 ± 2.4 PLLA (affected): 14.4 ± 4.6 Mean minimum lateral distance between CoP and XcoM (cm) (ST-slow) CN (left): 1.40 ± 0.72	stance time (affected and non-affected sides: p<0.001), stride width (p<0.05), and mean minimum lateral distance between CoP and XcoM (affected side: p<0.001). No statistically significant difference between normal speed and the DT condition within each group was observed (p>0.05). Due to the statistical analysis applied a direct assessment of the differential effect of DT testing can not be made.

			PLLA (non-affected): 67.4 ± 1.7 (ST-usual) CN (left): 64.1 ± 0.9 CN (right): 64.4 ± 0.9 PLLA (affected): 60.4 ± 3.0 PLLA (non-affected): 68.0 ± 1.6 (ST-fast) CN (left): 64.1 ± 0.6 CN (right): 64.3 ± 0.9 PLLA (affected): 58.5 ± 2.9 PLLA (non-affected):			CN (right): 1.35 ± 0.74 PLLA (affected): 2.42 ± 0.36 PLLA (non-affected): 1.62 ± 0.42 (ST-usual) CN (left): 1.61 ± 0.71 CN (right): 1.67 ± 0.70 PLLA (affected): 2.74 ± 0.54 PLLA (non-affected): 1.90 ± 0.62 (ST-fast) CN (left): 1.81 ± 0.61 CN (right): 1.86 ± 0.57	

			67.5 ± 1.5 (DT) CN (left): 64.3 ± 0.7 CN (right): 64.8 ± 1.2 PLLA (affected): 60.3 ± 3.0 PLLA (non-affected): 67.8 ± 2.1 Double contact (% of stride) (ST-slow) CN (left): 14.3 ± 1.1 CN (right): 14.2 ± 1.0 PLLA (affected): 13.6 ± 1.1			PLLA (affected): 3.25 ± 0.88 PLLA (non-affected): 2.20 ± 0.92 (DT) CN (left): 1.65 ± 0.60 CN (right): 1.66 ± 0.57 PLLA (affected): 2.99 ± 0.46 PLLA (non-affected): 2.11 ± 0.69 SD minimum lateral distance between CoP and XcoM (cm)	

			PLLA (non-affected): 14.1 ± 2.1 (ST-usual) CN (left): 13.9 ± 0.9 CN (right): 14.8 ± 0.8 PLLA (affected): 14.4 ± 2.3 PLLA (non-affected): 14.2 ± 1.5 (ST-fast) CN (left): 13.6 ± 0.7 CN (right): 14.9 ± 0.5 PLLA (affected): 13.4 ± 2.6 PLLA (non-affected):			(ST-slow) CN (left): 0.325 CN (right): 0.319 PLLA (affected): 0.403 PLLA (non-affected): 0.289 (ST-usual) CN (left): 0.378 CN (right): 0.362 PLLA (affected): 0.384 PLLA (non-affected): 0.278 (ST-fast)	

			12.8 ± 1.3 (DT) CN (left): 14.1 ± 0.9 CN (right): 15.1 ± 0.7 PLLA (affected): 14.7 ± 2.7 PLLA (non-affected): 13.6 ± 1.7			CN (left): 0.403 CN (right): 0.363 PLLA (affected): 0.477 PLLA (non-affected): 0.320 (DT) CN (left): 0.338 CN (right): 0.302 PLLA (affected): 0.400 PLLA (non-affected): 0.301	
Lamoth et al.	<u>Walking task:</u> Indoor and	Velocity (m/s)	Stride time (s)	Stride time variability		AP RMS amplitude	Group (PLLA/CN): A statistically significant

2010[176(†)]	outdoor walking in loops. Secondary task: Arithmetic subtraction task (mental tracking).	(ST) CN: 1.41 ± 0.15 PLLA: 1.27 ± 0.22 (DT) CN: 1.33 ± 0.19 PLLA: 1.18 ± 0.18 (outdoors on even surfaces) CN: 1.49 ± 0.15 PLLA: 1.23 ± 0.19 (outdoors on uneven surfaces) CN: 1.49	(ST) CN: 1.08 ± 0.50 PLLA: 1.15 ± 0.11 (DT) CN: 1.11 ± 0.64 PLLA: 1.18 ± 0.13 (outdoors on even surfaces) CN: 1.06 ± 0.44 PLLA: 1.16 ± 0.11 (outdoors on uneven surfaces) CN: 1.07 ± 0.48 PLLA: 1.14 ± 0.12	(%) (ST) CN: 2.2 ± 1.4 PLLA: 3.3 ± 2.1 (DT) CN: 3.0 ± 1.8 PLLA: 3.3 ± 1.2 (outdoors on even surfaces) CN: 2.9 ± 1.9 PLLA: 3.7 ± 1.9 (outdoors on uneven surfaces) CN: 3.6 ± 2.6		(across test conditions) CN: NR PLLA: NR ML RMS amplitude (across test conditions) CN: NR PLLA: NR AP LSE (across test conditions) CN: NR PLLA: NR ML LSE	main effect was observed for velocity (p=0.04), ML RMS amplitude (p=0.02), AP LSE (p=0.03), ML LSE (p=0.04), and ML SEn (p=0.03). Condition (ST/DT/outdoor on even grounds/outdoor on uneven grounds): A statistically significant main effect was observed for velocity (p<0.01), stride time (p<0.01), AP RMS amplitude (p=0.01), ML RMS amplitude (p<0.01), AP LSE (p<0.01), ML LSE (p=0.03), and ML SEn (p=0.02). Group x Condition: A statistically significant interaction was observed for ML LSE (p=0.04), AP SEn (p=0.02), and ML SEn

		± 0.15 PLLA: 1.27 ± 0.22		PLLA: 4.5 ± 2.2		(across test conditions) CN: NR PLLA: NR AP SEn (across test conditions) CN: NR PLLA: NR ML SEn (across test conditions) CN: NR PLLA: NR	(p=0.01). Evidence of a differential effect of DT in PLLA compared to CN not directly observed or described.
Morgan et al. 2016[113]	<u>Walking task:</u> Usual pace, straight path.	Velocity (m/s) (ST)	Cadence (steps/min) (ST)	Step time variability (CoV%) (ST)	Step time asymmetry (s) (ST)	Step width (m) (ST)	Group (PLLA/CN): A statistically significant main effect was observed for velocity (p=0.001), stride length

	<u>Secondary task:</u> Auditory Stroop test (discrimination and decision-making task).	CN: 1.387 ± 0.177 PLLA: 1.167 ± 0.166 (DT) CN: 1.413 ± 0.196 PLLA: 1.150 ± 0.165 Stride length (m) (ST) CN: 1.520 ± 0.138 PLLA: 1.355 ± 0.172 (DT) CN: 1.518 ± 0.145	CN: 109.3 ± 9.2 PLLA: 104.0 ± 7.0 (DT) CN: 111.5 ± 8.8 PLLA: 104.7 ± 7.8 Step time (s) (ST) CN: 0.553 ± 0.046 PLLA: 0.583 ± 0.041 (DT) CN: 0.542 ± 0.042 PLLA: 0.580 ± 0.046	CN: 2.6 ± 0.6 PLLA: 7.3 ± 3.3 (DT) CN: 2.5 ± 0.6 PLLA: 7.8 ± 4.5 Step time variability (SD, s) (ST) CN: 0.013 ± 0.003 PLLA: 0.018 ± 0.005 (DT) CN: 0.012 ± 0.003	CN: 0.010 ± 0.007 PLLA: 0.075 ± 0.042 (DT) CN: 0.011 ± 0.006 PLLA: 0.080 ± 0.058	CN: 0.121 ± 0.025 PLLA: 0.188 ± 0.041 (DT) CN: 0.130 ± 0.021 PLLA: 0.197 ± 0.045	($p=0.006$), step width ($p<0.001$), step time ($p=0.043$), step time asymmetry ($p<0.001$), step time variability ($p=0.004$), and step time variability (CoV%, $p<0.001$). Condition (ST/DT): A statistically significant main effect was observed for cadence ($p=0.036$), step width ($p<0.001$), and step time ($p=0.049$). Group x Condition: No statistically significant interaction was observed for any gait parameter ($p>0.11$). A differential effect of

		PLLA: 1.331 ± 0.177		PLLA: 0.017 ± 0.006			DT in PLLA compared to CN was not observed.
Howard et al. 2017b[143]	Walking task: Slow, usual, and fast pace straight path walking. Secondary task: 1) An arithmetic subtraction task (mental tracking). 2) Spelling task (mental tracking and working memory).	Velocity (cm/s) (ST-slow) CN: 94 ± 21 PLLA: 82 ± 16 (ST-normal) CN: 134 ± 21 PLLA: 111 ± 16 (ST-fast) CN: 161 ± 23 PLLA:	Cadence (stride/min) (ST-slow) CN: 46 ± 5 PLLA: 42 ± 5 (ST-normal) CN: 55 ± 4 PLLA: 49 ± 4 (ST-fast) CN: 61 ± 6 PLLA: 53 ± 5 (DT-arithmetic) CN: 51 ± 5				ST: A statistically significant difference between groups for velocity (normal and fast: p<0.01), and cadence (normal and fast: p<0.01) was observed. DT: A statistically significant difference between groups for velocity (arithmetic and spelling: p<0.01), stride length (arithmetic: p<0.01), and cadence (arithmetic and spelling: p<0.01) was observed.

		133 ± 21 (DT-arithmetic) CN: 112 ± 24 PLLA: 78 ± 20 (DT-spelling) CN: 113 ± 24 PLLA: 86 ± 22 Stride length (cm) (ST-slow) CN: 121 ± 16 PLLA: 116 ± 15 (ST-	PLLA: 41 ± 6 (DT-spelling) CN: 51 ± 6 PLLA: 43 ± 6 Cadence (RSD) (ST-across all ST) CN: 0.9 ± 0.3 PLLA: 1.0 ± 0.3 (DT-across arithmetic and spelling) CN: 1.0 ± 0.3 PLLA: 1.5 ± 0.6				ANOVA: Group (PLLA/CN): A statistically significant main effect was observed for RSD stride length (p=0.02), and RSD cadence (p=0.03). Condition (ST/DT): A statistically significant main effect was observed for RSD stride length (p=0.001), and RSD cadence (p=0.0008). Group x Condition: A statistically significant interaction was observed for RSD stride length (p=0.0006), and RSD cadence (p=0.009). A differential effect of DT in PLLA compared

		normal) CN: 145 ± 15 PLLA: 135 ± 15 (ST-fast) CN: 158 ± 15 PLLA: 149 ± 19 (DT-arithmetic) CN: 131 ± 17 PLLA: 112 ± 17 (DT-spelling) CN: 131 ± 17 PLLA: 118 ± 18					to CN was only observed for RSD stride length and RSD cadence.

		Stride length (RSD) (ST-across all ST) CN: 2.4 ± 0.7 PLLA: 2.5 ± 0.8 (DT-across arithmetic and spelling) CN: 2.5 ± 0.8 PLLA: 4.2 ± 1.6					
Morgan et al. 2017[145]	Walking task: Usual pace, straight path walking on foam.	Velocity (m/s) (ST) CN: 1.42 ± 0.17 PLLA:		Step time variability (SD, s) (ST) CN: 0.01 ± 0.003	Step time asymmetry (s) (ST) CN: 0.01 ± 0.01	Step width (m) (ST) CN: 0.111 ± 0.027 PLLA:	Group (PLLA/CN): A statistically significant main effect was observed for velocity (p<0.001), step width (p<0.001), step time asymmetry (p<0.001), and step time variability

	Secondary task: Auditory Stroop test (discrimination and decision-making task).	1.12 ± 0.19 (DT) CN: 1.45 ± 0.18 PLLA: 1.10 ± 0.17		PLLA: 0.02 ± 0.01 (DT) CN: 0.01 ± 0.003 PLLA: 0.02 ± 0.01	PLLA: 0.07 ± 0.05 (DT) CN: 0.01 ± 0.01 PLLA: 0.08 ± 0.06	0.191 ± 0.047 (DT) CN: 0.115 ± 0.020 PLLA: 0.203 ± 0.050	(p<0.001). Condition (ST/DT): A statistically significant main effect was observed for step width (p=0.003). Group x Condition: A statistically significant interaction was observed for step time asymmetry (p=0.03). Evidence of a differential effect of DT in PLLA observed for gait asymmetry.
Pruziner et al. 2019[178(†)]	Walking task: Usual pace, dual-belt treadmill. Secondary task: Object		Stride time (s) (across test conditions) CN: NR PLLA: NR	Stride time variability (CoV%) (across test conditions) CN: NR		Stride width (m) (across test conditions) CN: NR PLLA: NR	Group (PLLA/CN): No statistically significant main effect was observed for any gait parameter (p>0.097). Condition (ST/DT-

	detection (discrimination and decision-making task) at low and high level of difficulty.		Double limb support time (s) (across test conditions) CN: NR PLLA: NR	PLLA: NR Double limb support time variability (CoV%) (across test conditions) CN: NR PLLA: NR Stride width variability (CoV%) (across test conditions) CN: NR PLLA: NR			low/DT-high): A statistically significant main effect of test condition was observed for stride width (p=0.004), and stride width variability (p=0.015). Group x Condition: A statistically significant interaction was observed for stride time variability (p=0.041). A differential effect of DT in PLLA compared to CN was only observed for stride time variability between the least difficult DT task and ST trials.

Möller et al. 2020[181]	Walking task: Usual pace, straight path. Secondary task: Sorting keys (discrimination and decision-making task).		Cadence (steps/min) (ST) CN: 112.00 ± 10.58 PLLA (non-MPK): 95.00 ± 11.58 (DT) CN: 110.00 ± 7.22 PLLA (non-MPK): 97.00 ± 8.85				ST: A statistically significant difference between groups was observed for cadence ($p=0.001$). DT: A statistically significant difference between groups was observed for cadence ($p<0.001$). Due to the statistical analysis applied a direct assessment of the differential effect of DT testing can not be made.
Schack et al. 2020[180]	Walking task: Figure-of-8 Walk Test at a usual pace and also on an uneven surface.	**Other:** Time to complete (s) (ST) CN: 8.0 ± 1.9					ST(uneven): A statistically significant difference between groups was observed for time to complete ($p<0.01$), and number of steps ($p<0.001$).

	Secondary task: Carrying a tray with two cups filled with water (motor).	PLLA: 9.0 ± 2.0 (ST-uneven) CN: 8.6 ± 1.9 PLLA: 10.1 ± 2.4 (DT) CN: 9.4 ± 2.0 PLLA: 10.6 ± 2.2 Steps (n) (ST) CN: 12.6 ± 2.0 PLLA: 13.8 ± 2.5 (ST-uneven) CN: 13.1 ± 1.9 PLLA: 15.0 ± 3.0 (DT) CN: 14.3 ± 1.9	DT: A statistically significant difference between groups was observed for time to complete ($p<0.01$), and number of steps ($p<0.001$). Linear mixed model Group x Condition (PLLA/CN x ST/ST-uneven/DT-high): No statistically significant interaction was observed for any F8W performance parameter ($p>0.073$). Evidence of a differential effect of DT in PLLA not observed.

		PLLA: 15.8 ± 2.9	

Footnote: ANOVA: analysis of variance; AP: anterior-posterior plane; CoV: coefficient of variation; CN: controls; CoP: center-of-pressure; DT: dual-task; XcoM: extrapolated center of mass; F8W: Figure-of-8 Walk Test; LSE, local stability exponent; ML: medial-lateral plane; MPK: microprocessor prosthesis; NR: not reported; RMS, root mean square, RSD, residual standard deviation; SD: standard deviation; SEn, sample entropy; PLLA: people with lower limb amputations; ST: single-task. †, Studies for which certain information related to gait performance was unable to be extracted as they were only provided through graphs.

Table 2.5: Summary of the methodology and effect of dual-task testing on gait within samples of people with lower limb amputations.

Lead author	Walking task Secondary task (Category)	Gait domains					Results
		Pace	Rhythm	Variability	Asymmetry	Postural control	
Frengopoulos et al. 2018[28]	Walking task: Usual pace, L Test of Functional Mobility. Secondary task: An arithmetic subtraction task (mental tracking).	**Other:** Time to complete (s) (ST) TT(vascular): 31.31 ± 7.30 TT(non-vascular): 23.68 ± 3.56 TT(non-established): 55.50 ± 36.93 (DT) TT(vascular): 36.76 ± 10.53 TT(non-vascular): 28.69 ± 5.13					ST: A statistically significant difference in time to complete the L Test was observed between TT(vascular) and TT(non-established) (p<0.05), and between TT(non-vascular) and TT(non-established) (p<0.05). DT: A statistically significant difference in time to complete the L Test was observed between TT(vascular) and TT(non-established)

		TT(non-established): 65.98 ± 43.33 (Task cost) TT(vascular): -17.00 ± 15.70 TT(non-vascular): -21.50 ± 15.08 TT(non-established): -18.51 ± 15.33					(p<0.05), and between TT(non-vascular) and TT(non-established) (p<0.05). DTC: No statistically significant difference in time to complete the L Test was observed between groups (p>0.05). No evidence of a differential effect of DT testing was observed between novice versus experienced PLLA.
Hunter et al. 2018[27] (†)	<u>Walking task:</u> Usual pace, straight path. <u>Secondary task:</u> An arithmetic subtraction task (mental	Velocity (cm/s) (ST) PLLA: 58.15 ± 23.16 (DT) PLLA:	Cadence (steps/min) (ST) PLLA: 76.65 ± 15.84 (DT) PLLA:	Stride time variability (CoV%) (ST) PLLA: 8.69 ± 18.28 (DT)	Step length asymmetry (ST) PLLA: 1.15 ± 0.31 (DT) PLLA: NR	Stride width (cm) (ST) PLLA: 12.37 ± 2.36 (DT) PLLA:	DTC: A statistically significant difference between test conditions was observed for velocity (p=0.008), cadence (p=0.002), stride time (p=0.005), step length asymmetry (p=0.046), stance time asymmetry (p=0.011), and single support time asymmetry (p=0.006).

	tracking).	50.92 ± 21.16 (Task cost) PLLA: 8.43 ± 21.69 Stride length (cm) (ST) PLLA: 88.01 ± 22.70 (DT) PLLA: 87.04 ± 20.31 (Task cost) PLLA: -0.23 ± 8.93	67.85 ± 15.76 (Task cost) PLLA: 10.11 ± 15.87 Stride time (ms) (ST) PLLA: 1094.04 ± 458.28 (DT) PLLA: 1241.44 ± 513.73 (Task cost) PLLA: -15.62 ± 26.70	PLLA: 9.75 ± 9.23 (Task cost) PLLA: -79.00 ± 167.50 Stride length variability (CoV%) (ST) PLLA: 5.01 ± 2.32 (DT) PLLA: 5.54 ± 3.37 (Task cost) PLLA: -54.84 ± 213.30	Stance time asymmetry (ST) PLLA: 1.02 ± 0.10 (DT) PLLA: 0.95 ± 0.06 Single support time asymmetry (ST) PLLA: 1.07 ± 0.23 (DT) PLLA: 0.89 ± 0.13	12.85 ± 2.50 (Task cost) PLLA: -4.41 ± 11.86	

					Double support time asymmetry (ST) PLLA: 0.96 ± 0.19 (DT) PLLA: NR		
Hunter et al. 2019[94]	Walking task: 1) Usual pace, straight path. 2) Usual pace, L Test of Functional Mobility. Secondary task: An arithmetic subtraction task (mental	Velocity (cm/s) (ST-discharge) PLLA: 54.89 ± 26.53 (DT-discharge) PLLA: 44.97 ± 24.68 (ST-4					Condition (ST/DT): A statistically significant main effect was observed for time to complete (p<0.001) and velocity (p<0.002). Time (discharge/4 month follow-up): A statistically significant main effect was observed for time to complete (p=0.001) and velocity (p=0.009).

	tracking).	month follow-up) PLLA: 71.86 ± 25.81 (DT-4 month follow-up) PLLA: 62.28 ± 28.62					Condition x Time: No statistically significant interaction was observed for any outcome measure (p>0.121). No evidence of a differential effect of test condition between time points of recovery.
		Other: Time to complete (s) (ST-discharge) PLLA: 74.96 ± 50.68 (DT-discharge) PLLA: 93.90 ± 73.80 (ST-4 month follow-up) PLLA: 52.40 ± 38.53					

		(DT-4 month follow-up) PLLA: 60.54 ± 42.99	
Schack et al. 2019[179]	Walking task: Figure-of-8 Walk Test at a usual pace and also on an uneven surface. Secondary task: Carrying a tray with two cups filled with water (motor).	**Other:** Time to complete (s), median (25-75%) (ST) PLLA(KD/TF): 9.8 (8.0-10.9) PLLA(TT): 8.2 (7.7-10.0) (ST-uneven) PLLA(KD/TF): 11.2 (8.9-12.0) PLLA(TT): 9.7 (8.1-11.6) (DT) PLLA(KD/TF): 11.6 (10.5-15.9) PLLA(TT): 9.9 (8.4-11.1) Steps (n), median (25-75%) (ST)	Friedman's testing: A statistically significant difference for time to complete and steps between ST-uneven and DT compared to ST ($p<0.001$) was observed for both groups. A statistically significant difference for steps between ST-uneven and DT was only observed for PLLA(KD/TF) ($p<0.004$). A statistically significant difference for smoothness between all test conditions was observed for both groups ($p<0.003$). Mann–Whitney U

		PLLA(KD/TF): 14.1 (12.9-15.9) PLLA(TT): 13.8 (12.3-15.2) (ST-uneven) PLLA(KD/TF): 15.1 (14.0-17.3) PLLA(TT): 14.9 (13.6-17.0) (DT) PLLA(KD/TF): 16.9 (14.9-19.6) PLLA(TT): 15.2 (13.7-17.0) Smoothness (score), median (25-75%) (ST) PLLA(KD/TF): 1.9 (1.6-2.6) PLLA(TT): 3.0 (2.4-3.0) (ST-uneven) PLLA(KD/TF): 1.0 (1.0-1.3) PLLA(TT): 1.4 (1.0-2.8) (DT)	testing: ST: A statistically significant difference between groups was observed for smoothness (p<0.001). ST-uneven: No statistically significant difference between groups was observed (p>0.161). DT: A statistically significant difference between groups was observed for time to complete (p=0.003), and smoothness (p<0.001). Some evidence of a differential effect of DT for the F8W according to PLLA level of amputation.

		PLLA(KD/TF): 1.5 (1.0-2.0) PLLA(TT): 2.6 (2.0-2.8)	

Footnote: ANOVA: analysis of variance; CoV: coefficient of variation; DT: dual-task; DTC: dual-task cost; F8W: Figure-of-8 Walk Test; KD/TF: unilateral knee-disarticulation or transfemoral amputation; NR: not reported; PLLA: people with lower limb amputations; ST: single-task; TT: unilateral transtibial amputation;. †, Studies for which certain information related to gait performance was unable to be extracted as they were only provided through graphs.

Table 2.6: Summary of the methodology and effect of different prosthesis types on the dual-task gait performance of people with lower limb amputations.

Lead author	**Walking task** **Secondary task** **(Category)**	**Gait domains** **Pace**	**Rhythm**	**Postural control**	**Results**
Heller et al. 2000[170]	Walking task: Treadmill walking at constantly changing speeds. Secondary task: 1) Reading numbers (reaction time task). 2) Stroop test (discrimination and decision-			Mean sway velocity (mm/s) (DT-reaction time) PLLA(non-microprocessor): 205.8 ± 42.5 PLLA(intelligent): 181.0 ± 46.4 (DT-Stroop) PLLA(non-microprocessor): 219.3 ± 44.9 PLLA(intelligent): 189.4 ± 45.1	Condition: A statistically significant difference between test conditions was observed for mean sway velocity (p=0.0005). Prosthesis: A statistically significant difference between prosthesis types was observed for mean sway velocity (p=0.0.047). Due to the statistical analysis applied a direct assessment of the differential effect of DT testing can not be made.

	making task).			Mean sway velocity ratio (reaction time/Stroop) PLLA(non-microprocessor): 1.1 ± 0.0 PLLA(intelligent): 1.0 ± 0.1	
Williams et al. 2006[171]	<u>Walking task:</u> Usual pace, indoor loop. <u>Secondary task:</u> 1) An arithmetic subtraction task (mental tracking). 2) The Controlled Oral Word	Self-selected velocity (m/s) (DT-over tests 1-3) PLLA(non-microprocessor): 1.03 ± 0.06 PLLA(C-Leg): 1.06 ± 0.06			<u>Linear mixed model:</u> Prosthesis (non-microprocessor/C-Leg): No statistically significant difference between prosthesis type on velocity was observed (p>0.21). Due to the statistical analysis and reporting a direct assessment of the differential effect of DT testing can not be made.

	Association Test (verbal fluency). 3) The Category Test (verbal fluency and working memory).				
Hafner et al. 2007[172(†)]	<u>Walking task:</u> Usual pace, outdoor loop. <u>Secondary task:</u> Number recall (mental tracking task).	Velocity (m/s) (DT) PLLA(non-microprocessor test#1): NR PLLA(non-microprocessor test#2): NR PLLA(microprocessor test#1): NR PLLA(microprocessor test#2): NR			Prosthesis (non-microprocessor/microprocessor): No statistically significant difference between prosthesis type and session on velocity was observed (p>0.05). Due to the statistical analysis a direct assessment of the differential effect of DT testing can not be made.
Seymour et al. 2007[174]	<u>Walking task:</u> Usual pace, indoor obstacle course.	**Other:** Time to complete (s)			ST: A statistically significant difference between prosthesis type was observed for time to complete (p=0.004), steps (p=0.004) and step-offs (p=0.03)

	Secondary task: Carrying a weighted laundry basket (motor).	(ST) PLLA(non-microprocessor): 12.7 ± 2.4 PLLA(C-Leg): 11.5 ± 2.4 (DT) PLLA(non-microprocessor): 15.6 ± 3.7 PLLA(C-Leg): 11.5 ± 2.4 Steps (n) (ST) PLLA(non-microprocessor): 17.0 ± 3.1 PLLA(C-Leg): 15.6 ± 2.9 (DT) PLLA(non-microprocessor): 18.2 ± 4.6 PLLA(C-Leg): 15.6 ± 2.9 Step-offs (n) (ST)	DT: A statistically significant difference between prosthesis type was observed for time to complete (p=0.007). Due to the statistical analysis a direct assessment of the differential effect of DT testing can not be made.

		PLLA(non-microprocessor): 0.5 ± 0.4 PLLA(C-Leg): 0.2 ± 0.3 (DT) PLLA(non-microprocessor): 0.4 ± 0.5 PLLA(C-Leg): 0.3 ± 0.4 Stumbles (n) (ST) PLLA(non-microprocessor): 0 PLLA(C-Leg): 0 (DT) PLLA(non-microprocessor): 0 PLLA(C-Leg): 0			
Hafner et al. 2009[175]	Walking task: Usual pace, outdoor loop. Secondary task: Number	Velocity (m/s) (DT) PLLA(MFCL-2, non-microprocessor): 0.83 ± 0.17			Prosthesis: A statistically significant difference between prosthesis type on velocity was observed for MFCL-2 (p=0.02). Some evidence of a differential

	recall (mental tracking task).	PLLA(MFCL-2, microprocessor): 0.93 ± 0.18 PLLA(MFCL-3, non-microprocessor): 1.08 ± 0.20 PLLA(MFCL-3, microprocessor): 1.11 ± 0.22			effect of prosthesis type on DT performance for MFCL-2 compared to MFCL-3.
Meier et al. 2012[177(†)]	Walking task: Usual pace, indoor obstacle course. Secondary task: An arithmetic subtraction task (mental tracking).	**Other:** Time to complete (s) (ST across all stages of obstacle course) PLLA(3R60): NR PLLA(C-Leg): NR PLLA(SNS): NR (DT across all stages of obstacle course) PLLA(3R60): NR PLLA(C-Leg): NR PLLA(SNS): NR			Prosthesis (3R60/C-Leg/SNS): A statistically significant main effect was observed for time to complete the overall course ($p<0.001$), foam section ($p=0.01$), zig zag section ($p<0.05$), and rock section ($p<0.05$). Condition (ST/DT): A statistically significant main effect was observed for time to complete the overall course ($p=0.04$) and sand section ($p=0.001$). Prosthesis x Condition: No

					statistically significant interaction was observed for any section (p>0.05). No evidence of a differential effect of test condition according to prosthesis type on performance.
Möller et al. 2020[181]	Walking task: Usual pace, straight path. Secondary task: Sorting keys (discrimination and decision-making task).		Cadence (steps/min) (ST) PLLA (non-MPK): 95.00 ± 11.58 PLLA (MPK): 105.00 ± 8.46 (DT) PLLA (non-MPK): 97.00 ± 8.85 PLLA (MPK): 106.00 ± 7.61		ST: A statistically significant difference was observed for cadence (p=0.014) between groups. DT: A statistically significant difference was observed for cadence (p=0.008) between groups. Due to the statistical analysis applied a direct assessment of the differential effect of DT testing can not be made.

Footnote: 3R60: Otto Bock 3R60 prosthetic knee joint; ANOVA: analysis of variance; AP: anterior-posterior plane; C-Leg: Otto Bock C-Leg prosthetic knee joint (microprocessor); DT: dual-task; MFC: Medicare Functional Classification; MPK: microprocessor prosthesis; NR: not reported; PLLA: people with lower limb amputations; SNS: Mauch swing and stance control prosthetic knee joint; ST: single-task. †, Studies for which certain information related to gait performance was unable to be extracted as they were only provided through graphs.

2.3.2.3 Gait Methodology

Spatial-temporal gait parameters were recorded using motion capture,[113,145,170,178] an instrumented walkway or treadmill,[27,94,143,173] accelerometers,[176] a velocity meter,[171] or was not specified.[172,175,181] (Appendix D) Straight path walking was most common,[27,94,113,143,145,170,173,176,178,181] while others had participants walk indoor or outdoor loops,[171,172,175,176] obstacle courses,[174,177] the L Test of Functional Mobility (L Test),[28,94] or the Figure-of-8 Walk Test.[179,180] An assessment of steady state gait was mentioned in six studies,[27,94,113,143,145,181] with the majority also reporting that participants walked at a self-selected speed.[27,28,94,113,143,145,171,172,174–176,178–181]

2.3.2.4 Dual-task Methodology

The most common secondary task involved arithmetic subtractions or manipulations (mental tracking),[27,28,94,143,171,172,175–177] followed by the Stroop test or object detection (discrimination and decision-making),[113,145,170,173,178,181] and motor tasks.[174,179,180] (Appendix D) For arithmetic subtraction tasks, participants were required to subtract by threes,[27,28,94,171,177] or sevens.[143,177] For motor tasks, participants carried a tray with cups of water,[179,180] or a weighted basket.[174] Three studies included multiple secondary tasks[143,170,171] and one used different levels of task difficulty.[178] Importantly, close to half of studies did not report on secondary task specifics (e.g., subtraction number used)[113,145,170,171,173–177,181] or task prioritization instructions.[170–176,178,181]

2.3.2.5 Dual-task Testing on Pace

For studies comparing PLLA to CN, two reported dual-task was associated with a slower velocity[176] and a higher stride length (residual standard deviation).[143] Compared to CN and across test conditions, PLLA were observed to have lower velocities and shorter stride lengths.[113,145,176] A differential effect, whereby PLLA had significantly higher stride length (residual standard deviation) values than CN upon dual-task was reported.[143]

Three studies assessed dual-task performance with the use of a microprocessor prosthesis.[171,172,175] The use of a microprocessor prosthesis increased dual-task gait velocity in people with transfemoral level amputations classified as Medicare Functional Classification level #2 (MFCL-2), but not in those classified as MFCL-3.[175] Prospectively, Hunter et al.[94] reported that dual-task gait velocity, recorded over 6-meters using an instrumented walkway, improved four months after prosthetic rehabilitation discharge, yet the magnitude and direction of improvement was similar to single-task conditions.

2.3.2.6 Dual-task Testing on Rhythm

Upon dual-task, cadence was observed to decrease while stride time increased in people with transtibial amputations.[27] During both single-task and dual-task, PLLA had higher stance times,[173] higher step times,[113] a lower cadence[143,181] and a higher cadence (residual standard deviation)[143] compared to CN. A differential effect of dual-task in PLLA was observed for cadence (residual standard deviation) when compared to CN.[143] Other studies either found no statistically significant main effect of group,[176,178] group and test condition interactions,[113,176,178] or did not employ an appropriate statistical analysis to assess this.[27,173,181]

Regarding type of prosthesis used, Möller et al.[181] observed PLLA using a microprocessor prosthesis had a significantly higher cadence than those using a non-microprocessor prosthesis across test conditions (including dual-task).

2.3.2.7 Dual-task Testing on Variability

Within a sample of people with transtibial amputations, no statistically significant difference between single-task and dual-task conditions for stride length variability or stride time variability were observed.[27] For studies comparing PLLA to CN, only two[113,145] stated PLLA had higher stride time variability values across test conditions. The interaction between group and test condition was either not assessed[27] or not statistically significant.[113,145,176] In contrast, Pruziner et al.[178] observed that stride time variability was lower during the least difficult dual-task condition compared to single-task trials only in PLLA, but was found not to be different between the most difficult dual-task condition and single-task trials.

2.3.2.8 Dual-task Testing on Asymmetry

Upon dual-task, PLLA at the transtibial level had significantly shorter step lengths and spent less time on the amputated side as per stance time and single support gait phases.[27] Compared to CN, PLLA had higher step time asymmetry values across test conditions.[113,145] An interaction between group and test condition was reported in a study that had participants walking on foam.[145] According to Morgan et al.[145], dual-task resulted in increased asymmetry only for people with transfemoral amputations that used a microprocessor prosthesis; thus suggesting that under challenging situations a differential effect is observed on left-to-right temporal step times.

2.3.2.9 Dual-task Testing on Postural Control

Regardless of test condition, PLLA were observed to have a larger stride/step width, medial-lateral root-mean square amplitude, anterior-posterior and medial-lateral local stability component, and medial-lateral sample entropy compared to CN.[113,145,173,176,178] A group and test condition interaction effect was observed on medial-lateral local stability component, and anterior-posterior and medial-lateral sample entropy.[176] Although PLLA had an overall worse postural control, metrics for postural regulation and stability improved with increased difficulty, while for CN this was observed to be similar across test conditions. However, not all interactions were detailed, which limited the examination of a differential effect related to dual-task.

Regarding the type of prosthesis used, dual-task testing significantly increased whole body sway velocity (mm/s); yet lower values were observed when using a microprocessor knee compared to when using a non-microprocessor prosthesis.[170]

2.3.2.10 Dual-task Testing on Clinical Measures of Gait

People with transtibial amputations performed the Figure-of-8 Walk Test with greater “smoothness” (a rater-recorded fluency metric) for the single-task condition and faster with greater “smoothness” in dual-task compared to those with knee-disarticulation/transfemoral level amputations.[179] People more experienced at walking with a prosthesis were significantly faster at the L Test in relation to novice PLLA across test conditions;[28] yet no group differences were observed for dual-task cost. Compared to CN, PLLA had a significantly higher time to complete and number of steps for the Figure-of-8 Walk Test in a complex single-task (foam surface) and a dual-task condition, but not during usual walking on a firm surface.[180]

Compared to non-microprocessor prostheses, Seymour et al.[174] observed that using a C-Leg resulted in a significantly reduced number of steps, fewer path deviations, and a faster time to complete an obstacle course in the single-task trials but only a faster time for dual-task trials. Similar, but not as pronounced, performance improvements upon the use of a C-Leg were observed by Meier et al.[177] in what was arguably a more challenging obstacle course. Interestingly, one study prospectively evaluated L Test performance.[94] Results demonstrated that although L Test dual-task performance significantly improved between prosthetic rehabilitation discharge and a 4-month follow-up, the recovery effect was not different in relation to single-task performance. The lack of an attenuation in the cognitive demands of walking with a prosthesis may indicate that the learning associated with prosthesis walking does not entirely compensate for the many sensorimotor changes observed after an amputation.

2.3.2.11 Dual-task Gait Testing on Secondary Task Performance

For studies comparing PLLA to CN, two reported that no secondary task differences between groups existed.[176,178] Morgan et al.[113] stated that dual-task gait testing resulted in longer auditory Stroop test response times across groups. However, PLLA were observed to be slower than CN only when dual-task gait testing was performed over a foam surface,[145] as opposed to when walking on a firm, flat surface.[113]

Within PLLA, group differences were only observed for seated corrected response rates between the experienced and novice people with transtibial amputations but not in relation to cognitive task cost (i.e., involving walking).[28] In a group of PLLA, Williams et al.[171] observed that the performance of an arithmetic subtraction task, a semantic verbal fluency task or a phonemic verbal fluency task was similar when using a non-microprocessor or microprocessor prosthesis. Similarly, Hafner et al.[172] reported that number recall was not different according to prosthesis type used; even when compared between MFC-2 and MFC-3 PLLA.[175]

2.3.2.12 Methodological Quality of Reporting

The average Downs and Black score was 16.00 ± 2.45 (range: 11-20). (Appendix E) Methodological quality of reporting was similar between dual-task balance (14.25 ± 2.22) and gait (16.39 ± 2.38) studies. No scores were awarded on reporting item #8, external validity item #12, internal validity items #14-15 and 23-24, and power item #27.

2.4 Discussion

Standing sway distance and velocity, and dynamic (feet-in-place) balance control were observed to be worse in PLLA compared to CN regardless of test condition. However, evidence of a differential effect of dual-task in PLLA was only observed for sway velocity measures. In single-task and dual-task, PLLA performed worse on gait pace, rhythm, variability, asymmetry, and postural control. Dual-task testing resulted in a disproportionally slower pace, reduced rhythm, and an increased left-to-right step time asymmetry in PLLA. Moreover, the effect of dual-task on gait was not selectively different according to level of amputation, etiology, or experience with a prosthesis.

To date, one review has synthesized the effects of dual-task testing in this population[141]; concluding that a differential effect of dual-task in PLLA relative to CN was observed for balance control but not gait. Furthermore, using a microprocessor prosthesis resulted in better dual-task performance than when using a non-microprocessor prosthesis, but only in PLLA with limited mobility as depicted by a level-2 Medicare Functional Classification.[141] The present manuscript builds upon previous work published in 2017, through the addition of ten manuscripts for a total of 22 studies. Nine of which examined walking and provide at least some support for a disproportionately greater dual-task effect being observed in PLLA relative to age-and-sex matched adults. Results are unsurprising knowing the physical function and mobility challenges faced by PLLA,[2,3,61] and the long-term consequences that micro- and macro-vascular diabetic damage[19] has on brain structure[20] and neurobehavioral outcomes.[21,182] Results are also likely driven by the more complex scenarios observed in the new studies, such as different walking path configurations (indoor loops, Figure-of-8 Walk Test, L Test), surfaces (outdoors, foam), and speeds (slow, usual, fast). A larger array of secondary tasks has also been used (object detection, motor), alongside the examination of various difficulty levels for secondary tasks, the use of more than one type of task within a single study protocol, the assessment of task prioritization, dual-task cost, and dual-task performance over time.

Only one additional study that examined the effect of using a microprocessor prosthesis on the dual-task performance of PLLA has been published in the last four years. Our systematic review did not find any substantial evidence that the use of a microprocessor prosthesis improved dual-task gait performance relative to when individuals used a non-microprocessor prosthesis. Moreover, the magnitude of the dual-task effect was not different according to level of amputation, etiology or experience using a prosthesis. However, it is important to note that these studies generally examined performance differences on each test condition independently (i.e., no interaction terms) using clinical tests and not through spatial-temporal gait analysis which is considered more sensitive. Future research in this population is critical and should aim to establish with certainty what PLLA-specific characteristics, such as level of amputation, etiology, experience using a prosthesis, and walking automaticity, influence the interference effect that dual-task has on balance or gait. The following list outlines important considerations for future dual-task balance or gait research based on the trends that were observed:

(1) Cognitive function screening is important for the characterization of participant samples, yet only a minority of studies included standardized tests within their protocols even though cognitive impairment is prevalent in this population.[16,17]

(2) The majority of amputations occur as a result of dysvascular disease which can affect lower limb sensation;[7,16,19,32,34] however, assessments for sensory integrity or proprioception were never reported even though this can confound results.

(3) Preferably, the reporting of outcome measures should include both absolute and relative (i.e., dual-task cost) performance. Due to their influence on the effect of dual-task testing,[26,183] proper reporting should involve the reasoning behind the

selection of the secondary task and details related to the instructions for task prioritization provided to participants.

(4) The recording of secondary task performance is critical not only as a way to better understand task prioritization, but also to ensure secondary task performance is not being disregarded altogether during dual-task.

(5) The interpretation of a differential effect of dual-task testing in PLLA is challenging without a robust statistical analysis. For example, an interaction term may be used to establish if the effect of dual-task on gait is dependent on group status (i.e., PLLA versus CN). Alternatively, and if applied to dual-task cost, pairwise comparisons may be sufficient to assess if a greater magnitude of change in performance between single-task and dual-task conditions is observed in PLLA relative to CN.

(6) To avoid underpowered studies that minimize the ability to observe a true effect, *a priori* sample size calculations should be reported and be based on effect sizes from similar published research or be informed by a protocol pilot.

Although a demand exists for the assessment of balance and gait using instrumented technology, future research on dual-task testing using clinical tests is also important due to its clinical applicability. Currently, many clinical tests of mobility are available;[14,74] however, the L Test of Functional mobility remains the only test specifically designed for PLLA and for which a condition of dual-task has been shown to be valid and reliable.[28,94,144,184] Dual-task testing assesses cognitive-motor capacity, and offers healthcare professionals the ability to examine situations resembling real-life[26,159] which are often associated with experiences of falls.[29] In spite of this, the falls-related predictive validity for dual-task tests of balance or gait remains unexplored in this population.[9] Similarly, only one study in PLLA has been published on the effect to mobility of dual-task balance and gait training.[185] Results are encouraging, depicting dual-task training as a more effective intervention than usual care at improving dual-task gait in those with transfemoral amputations. Future research should prioritize prospective studies to understand the relationship between dual-task testing and falls across PLLA rehabilitation. Moreover, and as it relates to dual-task training, a focus should be placed on establishing specific protocols for clinical care, and research to assess for the longitudinal effects of this kind of intervention on a more generalizable sample of PLLA.

The effect of dual-task testing on the balance and gait of PLLA reported by the studies within the present systematic review are likely to be underestimates. Studies captured recruited mainly male, middle-aged adults, with predominantly transfemoral level amputations of non-vascular etiology. Therefore, our results are not generalizable to all PLLA, as on average individuals with lower limb amputations are closer to 65 years of age, and living with a transtibial level amputation stemming from dysvascular disease.[1–3,32,34] Participants represented a higher functioning group as most studies sought only experienced people at using a prosthesis and excluded anyone using a walking aid even though close to 80% of PLLA report using an assistive device for ambulation.[60] Six months of experience walking with a prosthesis, another common requirement, also places individuals between the intermediate and stable stages of recovery whereby the residual limb integrity and volume stabilizes.[31,76] However, physical function remains an issue years after a lower limb amputation.[3] In addition, earlier stages of prosthetic rehabilitation are characterized by rapid mobility changes[2,61] and age is known to be an important factor for the prediction of mobility after lower limb amputations[186]. In order for dual-task research to be generalizable to all individuals with lower limb amputations, future studies in this field should seek to recruit a wider range of participants from different age groups, levels of amputation, etiology, and experience walking with a prosthesis while minimizing within sample heterogeneity.

Regarding our systematic review methodology, one manuscript was excluded because it was not published in English.[187] As per the English-written abstract, and in a sample of people with transfemoral amputations (n=24), walking paired with a secondary cognitive or motor task resulted in worse spatial-temporal gait parameters when compared to usual walking. Since the study did not include a comparator group, and that it is unknown if other exclusion criteria would have been met upon full-text review, it is unlikely the inclusion of this study would have provided new information not already reported by other manuscripts. Importantly, the present systematic review searched across six major databases with no restrictions to ascertain all available information on this topic. The authors are confident that this represents the most comprehensive assessment to date of the effect of dual-task on the balance and gait of PLLA.

2.5 Conclusions

As initially hypothesized, some evidence of a differentially worse performance in PLLA was observed, characterized by increased sway velocity and reduced pace and rhythm, and increased asymmetry when balance or walking was paired with a secondary task. A lesser dual-task effect was not observed based on level of amputation or etiology; however, this was driven by a lack of studies specifically assessing for the association between PLLA-specific factors and dual-task performance. The inclusion of dual-task testing within mobility assessments may prove to be advantageous, reflective of real-life situations and a marker for the cognitive load associated with the use of prosthesis for walking. The recent surge in studies examining the cognitive-mobility link using dual-task paradigms may serve to provide a better understanding of the many challenges associated with walking with a prosthesis, including the high rate of falls experienced in this population.

Chapter 3

Study 2 – The Association Between Balance Confidence and Basic Walking Abilities in People with Unilateral Transtibial Lower Limb Amputations: A Cross-Sectional Study

A version of this chapter has been accepted for publication in Prosthetics and Orthotics International pending minor revisions. [**Omana H**, Frengopoulos C, Montero-Odasso M, Payne MW, Viana R, Hunter SW. The association between balance confidence and basic walking abilities in people with lower limb amputations: A cross-sectional study. Prosthetics and Orthotics International. Accepted with minor revisions June 26, 2022]. See Appendix F to view the confirmation of acceptance for this manuscript.

3.1 Introduction

Each year 7,405 Canadians have a lower limb amputation.[1] The average age for people undergoing a lower limb amputation is 65 years old,[1] and eighty percent of amputations result from diabetes or peripheral vascular disease which are associated with chronic vascular damage that can lead to somatosensory and motor dysfunction.[7,19] Importantly, over 50% of PLLA sustain a fall at least once annually,[10] and falls can have serious physical and psychological consequences, such as a concern for falling that impacts prosthesis adherence, social interaction and quality of life.[29,154]

A concern for falls is a multidimensional term used to encompass the negative psychological factors associated with falls.[149] Fear of falling, falls-related self-efficacy, mobility-related self-efficacy, consequences of falling and perceptions on falls, each provide unique avenues to understanding concern for falls.[149] Among subdomains of concern for falling, self-efficacy, the belief that one can achieve a specific task,[73] remains the most widely examined.[149] In PLLA, self-efficacy has been mainly studied through balance confidence, the belief one is able to achieve a specific task without losing balance or becoming unsteady.[152] Reduced balance confidence (i.e., an increased concern for falls) is associated with anxiety about falling, which in other populations has been shown to increase attentional needs and results in adverse gait.[153] This is important as most falls occur while walking,[13] and the ability to ambulate is the most important factor contributing to life satisfaction.[2] Therefore, examining if a concern for falls affects walking is needed to improve our understanding of PLLA rehabilitation.

The use of a prosthesis increases subjective reports of cognitive demands,[10] with an estimated 41% of PLLA reporting having to concentrate on every step they take[10]. In general, cognitive resources are finite;[26] however, PLLA are impacted by a high prevalence of cognitive impairment which limits the capacity for the allocation of cognitive resources[16,17]. Dual-task gait testing, walking while completing a second task, allows for the quantification of the inter-relationship between cognitive and motor function.[26] If cognitive demands surpass a person's cognitive capacity, then performance of one or both tasks is adversely affected.[26] The dual-task cost refers to the relative change in performance between single-task and dual-task.[26] Quantitative research supports an increase in cognitive demands for PLLA during dual-task walking, and which is accompanied by a reduction in gait pace, rhythm and increased asymmetry.[27] Additionally, balance confidence is also reported to be low in this population, yet significantly impaired in those reporting having to think about every step they take during walking (i.e., non-automatic gait).[146] This suggests that a relationship exists between balance confidence and walking, whereby low balance confidence may act as a distractor and exerting an additional load onto the already cognitively demanding task of walking with a prosthesis.

Four studies have assessed the effect that balance confidence has on the mobility of community-dwelling PLLA.[148,154,155,188] Miller et al.[154] and Wong et al.[155] concluded that low balance confidence was independently associated with decreased self-reported mobility. More recently, Mandel et al.[188] reported a moderate positive correlation between balance confidence and total number of steps, while Sions et al.[148] determined that low balance confidence was independently associated with an impaired Timed Up & Go and the Six Minute Walking Test performance. To date, the literature on this topic has relied on indirect assessments of mobility, such as using questionnaires, correlational analyses or the use of outcome measures not specific to this population. In contrast, the L Test is an objective mobility test that was designed to assess basic walking ability in PLLA.[189] The L Test evaluates level walking, sit-to-stand and stand-to-sit transfers, and turns to both directions that are considered the minimal needs for mobility in the home.[189] Yet, walking in the real world also requires the ability to perform simultaneous tasks while walking.[26] The L Test with a dual-task component becomes a complex clinical testing protocol that is arguably more relevant to everyday mobility and the challenges often experienced by PLLA.[29]

The main objective of the present manuscript was to examine the association between balance confidence and L Test performance in both single-task and dual-task conditions in PLLA. It was hypothesized that decreased balance confidence would be independently associated with a longer time to complete the L Test.

3.2 Methods

3.2.1 Participants

This was a secondary analysis of a cross-sectional study of community-dwelling individuals from the Amputee Rehabilitation Program at Parkwood Institute in London, Ontario (March 2016-January 2017). The inclusion criteria was: ≥18 years of age; English language proficiency; have a lower limb amputation; and >6 months of daily experience using a lower limb prosthesis for walking. For this study, only those with a unilateral, transtibial level amputation were included as these are the most common amputations and to minimize sample heterogeneity.[1,7] Individuals presenting with medical issues that significantly impacted walking were excluded. Participants provided written informed consent. The study was approved by the Health Sciences Research Ethics Board at the University of Western Ontario and by the Clinical Resources Impact Committee at the Lawson Research Institute.

3.2.2 Outcome Measures

Clinical and demographic characteristics collected were: age, sex, height and weight with their prosthesis, etiology and time since amputation, 12-month falls history, mobility aid used, number of prescription medications, comorbidities using a standardized checklist, and cognitive status as per the MoCA.[190] For the MoCA, scores range from 0-30, with higher scores indicating better cognitive function and those ≤25 determined to be reflective of cognitive impairment.[190] (Appendix G) A fall is defined as: “an unexpected event in which the participant comes to rest on the ground, floor, or lower level”.[191]

3.2.2.1 Balance Confidence

The Activities-specific Balance Confidence Scale (ABC) was used to assess balance confidence,[152] a form of falls-related self-efficacy and a subdomain of concern for falls.[149] (Appendix H) The long-form ABC was used, which is a 16-item questionnaire that asks individuals to rate their level of balance confidence, from 0% (no confidence) to 100% (completely confident), when completing an array of daily activities without losing balance or becoming unsteady. The mean across all items represents the total score. A lower ABC indicates an increased level of concern for falls. The ABC protocol used in the present study has been previously shown to be valid and reliable in this population.[184]

3.2.2.2 Basic Walking Abilities

The L Test of Functional Mobility, a modified Timed Up & Go, was used to assess basic walking abilities.[189] (Appendix I) From a seated position on an armless chair, participants were asked to stand, walk three meters, turn 90º, walk seven meters, turn 180º, and then backtrack the same path to the seated starting position. Single-task (ST) performance was the time to complete the course once at a self-selected walking speed, which was recorded to the nearest hundredth of a second using a stopwatch.

After a seated five-minute break, a dual-task (DT) condition using a secondary cognitive task was completed. Participants walked while simultaneously subtracting 3's from a random number between 100-150 out loud. No instructions were given to prioritize any one task and all secondary task responses were recorded for number of responses and accuracy. If applicable, participants used their walking aid to complete the tests. One trial of each condition was performed by participants and recorded by the same assessor. The L test was first demonstrated and explained to the participant using a standardized set of instructions. The L Test protocol used in the present study has also been shown to be valid and reliable among PLLA.[144]

3.2.2.3 Single-task Cognitive Testing

While sitting, participants were asked to complete 10 arithmetic subtractions by 3's from 100 to obtain an independent assessment of the cognitive task. The time to complete the test was recorded to the nearest hundredth of a second using a stopwatch. Additionally, answers were recorded to determine the rate based on the number of responses and accuracy.

3.2.3 Data Analysis

For clinical and demographic information, the normality of continuous variables was assessed using Shapiro-Wilks tests and a visual inspection of histograms and Q-Q plots. Age and MoCA scores were summarized using means and standard deviations, while all other continuous variables did not meet normality and were reported as medians and interquartile ranges (25^{th}, 75^{th} percentiles).

Two new variables were calculated from single- and dual-task tests: walking task cost and cognitive task cost. Walking task cost was calculated as the relative difference between single-task and dual-task L Test conditions:

$$Walking\ Task\ Cost = \left[\frac{ST - DT}{ST}\right] x(100)$$

Similarly, cognitive task cost was depicted as the change in performance from the seated, single-task condition to the dual-task condition. First, the single-task correct response rate (CRR) was calculated to take into account accuracy and speed:

$$Correct\ response\ rate\ (CRR) = responses\ per\ second\ x\ percentage\ of\ correct\ responses$$

$$Cognitive\ Task\ Cost = \left[\frac{\text{CRR walking in DT} - \text{CRR seated}}{\text{CRR seated}}\right] x(100)$$

For walking and cognitive task cost, a negative value indicates poorer performance and a positive value indicates improved performance upon dual-task.

Four separate multivariable linear regression models were used to evaluate the independent association of balance confidence on: single-task L Test, dual-task L Test, walking task cost and cognitive task cost. Regression models were examined for the assumptions of autocorrelation and homoscedasticity using the Durbin-Watson statistic and residual scatterplots, respectively; multicollinearity using variance inflation factors analysis; and residual normality. As cognitive task cost did not meet normality assumptions, statistical analysis was carried out using square root transformed data. No outliers were detected and no data was missing for any participant.

Regressions were adjusted for the confounders of sex (binary: male, female), etiology (binary: vascular, non-vascular) and number of comorbidities (continuous) to yield the most parsimonious model. Confounders were selected according to clinical significance, previous research,[148,154,155] availability of variables and an observed ≥10% change in the unstandardized ABC beta values with the introduction of each. The first block of each regression assessed the univariate relationship between the ABC and the L Test, while the second also contained all confounders.

An *a priori* analysis using G*Power (version 3.1.9.6)[192] estimated that 97% power could be attained assuming $\alpha=0.05$, the use of four predictors (omnibus $R^2=0.55$)[154] and the availability of 44 participants. The software package SPSS version 25.0 (SPSS, Inc., Chicago, IL) was used for all statistical analyses with a 0.05 experiment-wise alpha.

3.3 Results

A total of 44 people participated. (Table 3.1) The mean age was 56.6 ± 12.6 years, 86.4% were male and close to half (45.5%) reported having an amputation due to diabetes and/or peripheral vascular disease. The average MoCA score was 26.41 ± 2.33 (min: 20, max: 30) and 31.8% of participants were observed to have impaired cognition. The median ABC score was 85.94% (min: 33.13%, max: 100.00%) and was higher than what is typically reported[146,193]. (Table 3.2) As expected, the median time to complete the L Test was longer for dual-task than single-task trials.

Multivariable linear regression modelling demonstrated an independent association of the ABC to single-task ($p<0.001$) and dual-task ($p=0.008$) L Test performance. (Table 3.3) A 1% ABC increase was related with a 0.24 (95% CI: 0.35, 0.14) and 0.23 (95% CI: 0.39, 0.06) second reduction on the single-task and dual-task L Test, respectively. Overall, 56% of the variance in single-task (ABC $\Delta R^2=0.22$) and 43% of the variance in dual-task (ABC $\Delta R^2=0.10$) L Test performance were explained by the full regression models. No associations between the ABC and walking task or cognitive task cost were observed for any of the models.

Table 3.1: Demographic and clinical characteristics of a sample of adult, prosthesis users with a transtibial level amputation. (n=44)

Variable	Mean ± SD, Median [IQR] or n (%)
Age (years)	56.6 ± 12.6
Sex, n (% male)	38 (86.4)
Body Mass Index (kg/m^2)	27.58 [25.25, 33.24]
Amputation Etiology, n (%)	
Trauma	17 (38.6)
DM	13 (29.6)
PVD	3 (6.8)
DM and PVD	4 (9.1)
Other (cancer, congenital, etc.)	7 (15.9)
Time Since Amputation (years)	4.2 [1.7, 21.7]
History of Falls in the Past 12 Months, n (% yes)	15 (34.1)
Walking Aid, n (% yes)	8 (18.2)
Montreal Cognitive Assessment Score	26.41 ± 2.33
Number of Medications	4.0 [1.0, 9.0]
Number of Comorbidities	2.0 [1.0, 3.0]
Summary of Comorbidities, n (% yes)	
DM	20 (45.5)
Hypertension	18 (40.9)
Osteoarthritis	11 (25.0)
Dyslipidemia	10 (22.7)
Other	26 (59.1)

Footnote: DM: diabetes mellitus; IQR: interquartile range; PVD: peripheral vascular disease.

Table 3.2: Performance on the Activities-specific Balance Confidence Scale, L Test of Functional Mobility, and walking task cost and cognitive task cost in a sample of adult, prosthesis users with a transtibial level amputation. (n=44)

Outcome	**Median [IQR]**
Activities-specific Balance Confidence Scale (%)	85.94 [76.33, 95.32]
L Test, single-task (s)	24.11 [22.06, 32.27]
L Test, dual-task (s)	29.99 [25.19, 36.35]
Gait task cost (%)*	-15.12 [-27.69, -7.28]
Cognitive task cost (%)*	-16.86 [-39.25, 14.62]

Footnote: IQR: interquartile range; L Test: L Test of Functional Mobility. *, negative values are indicative of impaired performance upon dual-task testing relative to single-task trials.

Table 3.3: Multivariable linear regression modeling for the association of the Activities-specific Balance Confidence Scale (independent variable) on the L Test of Functional Mobility performance (dependent variable) in people with a transtibial level amputation. (n=44)

Dependent variable	**Unadjusted unstandardized β (95%CI)**	**p-value**	**R^2**	**Adjusted unstandardized β (95% CI)***	**p-value**	**R^2**
L Test, single-task (s)	**-0.32 (-0.41, -0.22)**	**<0.001**	0.53	**-0.24 (-0.35, -0.14)**	**<0.001**	0.56
L Test, dual-task (s)	**-0.34 (-0.48, -0.20)**	**<0.001**	0.35	**-0.23 (-0.39, -0.06)**	**0.008**	0.43
Gait task cost (%)	-0.11 (-0.41, 0.20)	0.48	0.01	-0.19 (-0.53, 0.15)	0.27	0.13
Cognitive task cost (sqrt%)	0.04 (-0.03, 0.10)	0.25	0.01	0.07 (-0.004, 0.14)	0.06	0.04

Footnote: ABC: Activities-specific Balance Confidence Scale; CI: confidence interval; L Test: L Test of Functional Mobility. *, regression modeling adjusted for sex (binary: male, female), etiology (binary: non-vascular, vascular), and number for comorbidities (continuous). Statistical significance was $p < 0.05$.

3.4 Discussion

Decreased balance confidence was independently associated with longer times to complete the single-task and dual-task L Test in a sample of community-dwelling, transtibial PLLA. Regression modelling showed no association between balance confidence and the magnitude of change between conditions (i.e., dual-task cost). Our research expands on the literature to provide further support that balance confidence, a subdomain of concern for falls, influences basic walking abilities which were assessed in dual-task and gathered using a clinical test specifically designed for PLLA.

Previous research by Miller et al.[154] and Wong et al.[155] established that low balance confidence was associated with impaired self-reported mobility as per the Prosthetic Evaluation Questionnaire and Houghton Scale. However, making inferences on objective mobility from self-reported assessments, or vice versa, is not recommended in this population.[91] Our study findings are consistent with Sions et al. who also evaluated balance confidence using the ABC, but inquired on physical performance using different tests (i.e., Timed Up & Go and the Six Minute Walking Test).[148] Similar regression results were reported even though our study only included those with transtibial amputations, whereas Sions et al.[148] recruited people with transtibial and transfemoral amputations. Individuals with transfemoral amputations are observed to have impaired performance in measures of self-reported or objective mobility compared to those with transtibial amputations.[189,194] The absence of a knee joint increases balance instability and is a known risk factor for falls.[10] It is unknown if the results may have been biased towards PLLA with transfemoral amputations, as Sions et al.[148] did not examine if a difference in mobility tests was observed according to level of amputation, nor was it controlled for in the regression modelling. To put our results into perspective, the minimal detectable change for the L Test is 2.15-3.19 seconds (dual-task: 3.71-7.76 s),[144] while the minimal clinically important difference is 4.5 seconds;[195] thus indicating that at least a 18.75% change in the ABC would need to be observed. The present manuscript provides evidence for the effect of balance confidence on gait in a more homogeneous sample of PLLA than previous research. Moreover, our study protocol used single-task and dual-task L Test conditions that required a higher level of skill. Dual-task testing addresses that most everyday activities include the performance of multiple concurrent tasks and provides an additional challenge that is used to examine cognitive-motor capacity.[26] The protocol used is considered of higher ecological validity, reflecting real-life situations of dual-tasking, obstacle negotiation and changes in direction which are challenging for PLLA.

A concern for falls is usually assessed through self-efficacy,[149] which in our study was evaluated using the Activities-specific Balance Confidence Scale. An inter-relationship exists between self-efficacy and the completion of progressively more complex activities, known as mastery experiences.[73] The more experience a person has with being successful at completing tasks, the higher their self-efficacy will be.[73] Participants in our study had already developed a variable level of proficiency for complex walking situations, including dual-task, through their experiences in the community. However, it is important to note that only one concern for falls subdomain was assessed and that each subdomain examines a unique construct.[149] Nonetheless, low balance confidence is very common in PLLA, persisting years after community re-integration and is significantly impaired in those not reporting walking automaticity.[146,147] Balance confidence is also associated with and predicts future social participation.[148,154] Low balance confidence can result in PLLA limiting their engagement in activities they are physically capable of performing which subsequently increases the challenge of tasks and the risk for falls as a consequence of deconditioning.[73] Therefore, interventions specifically targeting balance confidence are warranted in an attempt to minimize the cognitive burden associated with walking using a prosthesis.

Even though mastery experiences are considered the most influential sources for developing self-efficacy, other strategies do exists.[73] Vicarious experiences can allow individuals to adjust expectations and model behaviour based on the observation of others, while verbal persuasion can facilitate the successful completion of difficult tasks previously believed to be outside of one's own capabilities.[73] Currently, interventions such as home-based exercises or a multifaceted falls-prevention approach have been shown to increase balance confidence in older adults.[196] However, most of these interventions have relied on the administration of physical activity, home safety assessments or falls risk education.[196] For PLLA, physical function and balance confidence are believed to be related yet distinct from one another.[91,92] Research has found that while physical function improves after discharge from prosthetic rehabilitation[91] there is an absence of change in balance confidence[92]. Indeed, and among community-dwelling older adults, it appears the most successful interventions target physical function alongside the additive use of therapeutic approaches that specifically address psychological aspects related to concern for falls (e.g., self-perceived physical capacity, anxiety, etc.), such as through cognitive behavioural therapy or motivational interviewing.[197] Unfortunately, this is an area with little direction for healthcare professionals working with PLLA.[198] The gaps in the literature include a lack of protocols with demonstrated efficacy for the enhancement of self-efficacy, as well as preventative strategies, that are specific to this population. Future research also needs to expand on the present protocol and evaluate how other relevant factors (e.g., falls history, cognitive status, etc.) influence the inter-relationship between balance confidence and gait at various timepoints of rehabilitation.

Our results should not be generalized to all PLLA as the sample was composed of only people with unilateral, transtibial amputations who were younger than the average[1,7] and were also considered higher functioning. Moreover, the range of time since amputation for the participants was wide (0.7-55.0 years) and mastery of walking with a prosthesis and a concern for falls may differ at other stages of rehabilitation. A concern for falls is multidimensional, yet only one subdomain was assessed. Future studies should expand on the present work, examining the relationship that exists between different aspects of concern for falls and gait across different aetiologies, age groups and levels of experience using a lower limb prosthesis. A strength of this study was the execution of a well-developed methodology and the recruitment of a homogenous sample that is reflective of the PLLA typically seen in an outpatient setting.[1,7]

3.5 Conclusions

Lower scores on the Activities-specific Balance Confidence Scale were independently associated with impaired single-task and dual-task L Test performance in community-dwelling, transtibial prosthesis users. There was no association found on relative measures of performance (i.e., dual-task cost). Due to its influence on basic walking ability, routine care for PLLA should also involve interventions specifically targeting balance confidence. Future research needs to examine how other factors, such as level of experience, may affect the inter-relationship between balance confidence and gait. This line of research is novel and offers the possibility for alternative avenues for focus in rehabilitation and falls-prevention in a population at a high risk for falls.

Chapter 4

Study 3 – Association Between Measures of Cognitive Function on Physical Function in Novice Users of a Lower Limb Prosthesis

4.1 Introduction

Undergoing a lower limb amputation is a life-changing event with serious implications for physical and psychological well-being.[3] For many PLLA, intensive rehabilitation is required to restore physical function and to provide training for the use of a prosthetic device to ambulate. Nonetheless, falls are prevalent[9] and can result in serious injury and immobility that negatively affects daily life[154]. The majority of falls occur while walking,[13] and the ability to walk and be independent is reported to be the most important factor to life satisfaction following a lower limb amputation[2]. As a result, physical function assessments are encouraged for use by healthcare professionals during the rehabilitation process.[14]

Walking with a prosthesis is a complex motor task that is cognitively demanding[10,15] and described by PLLA as a cognitive burden[22]. Gait is intimately related to higher-order cognitive processes, known as executive functions, that allow for the planning, monitoring and adjustments required for mobility.[15] A greater cognitive load is observed when engaging in more complex activities or when simultaneously performing multiple tasks (i.e., dual-task testing). Cognitive resources are finite in capacity and each task requires a certain amount of these resources for cognitive processing. Thus, worse performance can be expected if the demands for a task, or multiple tasks, exceeds an individual's cognitive capacity.[24] The ability to meet increased demands for cognitive resources is complicated in PLLA as 52-56% demonstrate cognitive impairment.[16,17] Therefore, physical function tests that challenge cognitive-motor capacity and approximate real-life instances in which falls often occur may result in a better evaluation of abilities, tracking of progress and prognostication of outcomes.

Physical function can be measured in many ways, such as the ability to transition from one location to another (i.e., mobility), being able to maintain balance while moving (i.e., dynamic balance), or as the ability to successfully complete daily tasks (i.e., functional mobility).[96] Clarity regarding variation in the magnitude of cognitive demands required by the various available tests of physical function is limited. In PLLA new at walking with a prosthesis, better scoring on cognitive testing is independently associated with better performance on functional mobility and walking endurance.[16,18] However, such results were based on one cognitive test and none of the physical function testing involved different levels of difficulty or conditions of dual-task.[16,18] When examining the gradation of task difficulty using dual-task gait testing in older adults and older adults with mild cognitive impairment, Hunter et al.[156] concluded that not all dual-task gait test protocols demand the same level of cognitive resources and are therefore non-interchangeable. An inappropriate physical function test selection may lead to being unable to properly challenge cognitive-motor capacity. This is an important avenue to explore as healthcare professionals should understand the relative cognitive demands associated with the clinical tests that they commonly use, as a more appropriate examination of cognitive-motor ability may elicit an earlier response to accommodate for any deficits detected.

The objective of the present manuscript was to evaluate the association of cognitive function on tests of physical function (gait, dynamic balance and functional mobility) in PLLA at discharge from inpatient prosthetic rehabilitation. It was hypothesized that worse cognitive function would be independently associated with lesser physical function, and that a stronger effect would also be observed in the more complex tests.

4.2 Methods

4.2.1 Study Design

This was a secondary analysis of a cross-sectional study of PLLA from inpatient prosthetic rehabilitation of the Amputee Rehabilitation Program at Parkwood Institute in London, Ontario, Canada (April 2016-September 2017). All participants provided informed consent. The initial study protocol was approved by the Health Sciences Research Ethics Board at the University of Western Ontario and by the Clinical Resources Impact Committee at the Lawson Research Institute.

4.2.2 Participants

Previous research has established that people with transtibial amputations, the most common amputation type,[1] demonstrate better physical function compared to those with transfemoral or bilateral amputations[189]. Therefore, only PLLA with unilateral transtibial amputations were considered. Acceptance criteria for inpatient prosthetic rehabilitation required individuals to be adults (≥18 years of age), medically stable and capable of taking part in an intensive program. For the present study, the following eligibility criteria were also applied: ≥50 years of age, English-language proficiency, have a unilateral transtibial amputation and be able to walk ≥10 meters without the help from others although walking aids were allowed. Those presenting with non-amputation medical problems affecting gait were excluded.

4.2.3 Data Collection

Clinical and demographic characteristics collected were: age, sex, height and weight, years of education, time since amputation and etiology, 12-month falls history as defined by Lamb et al.[199], prescription medications and comorbidities. Information was either self-reported using a standardized questionnaire or extracted from participant's medical charts. All outcomes were collected within 48 hours of discharge.

4.2.4 Outcome Measures

4.2.4.1 Spatiotemporal Gait

The instrumented GAITRite® walkway (CIR System Inc, Franklin, NJ, USA) was used to record gait velocity on a 6-meter straight path. Gait velocity was selected based on its sensitivity for change upon dual-task,[157] and for its relationship to cognitive function and falls risk[101]. To record only steady state ambulation, participants walked one meter before and after the walkway boundaries. Walking trials were completed at a usual, self-selected pace in single-task and dual-task conditions. For dual-task testing, walking while subtracting threes from a random number between 100-150 out loud was performed. All responses were recorded to assess for accuracy and no instructions on task prioritization were given. Two trials per condition were performed, which were averaged for results. The gait testing protocol used has been shown to be effective in increasing cognitive load and results in gait interference in PLLA.[27]

4.2.4.2 Dynamic Balance

The Four Square Step Test (FSST) is a measure of dynamic balance involving rapid steps forwards, sideways and backwards while avoiding stationary obstacles.[200] (Appendix J) The present study used a modified version of the FSST in which participants had to step over tape placed on the floor in a cross pattern, creating four quadrants, as opposed to the canes in the original FSST[200]. The use of tape instead of canes is believed to improve the floor effect observed with the original version.[14,201] Participants were encouraged to always be facing forwards during stepping, and to avoid touching the tape or starting a new stepping sequence without first having both feet contact the ground. Performance was recorded as the time to complete the test to the nearest hundredth of a second using a stopwatch. A lower time is indicative of better dynamic balance. A practice trial was followed by two collection trials, but only the fastest trial was used.[200] The FSST has been shown to be valid and reliable in PLLA.[201,202]

4.2.4.3 Functional Mobility

The L Test was developed to examine the minimal walking skills needed for independent living in PLLA.[189] (Appendix I) Participants start seated on an armless chair, and when prompted, stand, walk forward three meters, turn 90^{o}, walk seven meters, turn 180^{o}, and then follow the same L-shaped path back to their initial position. Performance is the time to complete the course once, with a longer time being indicative of worse functional mobility. The single-task L Test was completed first, and after a seated break, participants performed the dual-task condition which involved serial subtractions by threes from a random number between 100-150 counted out loud. All responses were recorded to assess for accuracy and no instructions on task prioritization were given. The single-task and dual-task L Test has been shown to be valid and reliable in PLLA.[144,189]

4.2.4.4 Cognitive Function

The MoCA evaluated global cognitive function.[190] (Appendix G) The MoCA contains seven domains for assessing visuospatial/executive function, naming, attention, language, abstraction, delayed word recall, and orientation to time and space. Scores range from 0-30 with higher scores indicating better cognition and those ≤25 indicating cognitive impairment.[190]

4.2.4.5 Processing Speed and Executive Function

The Trail Making Tests (TMT) was used to evaluate processing speed and executive function.[203] (Appendix K) The first part (TMT-A) requires participants to connect a series of numbers in ascending order. The second part (TMT-B) is more challenging, requiring memory and mental flexibility as participants alternate between numbers and letters in ascending order. Both parts are timed and completed as quickly as possible. A slower time is indicative of worse processing speed and executive function.

4.2.4.6 Balance Confidence

The ABC assessed balance confidence.[152] (Appendix H) Balance confidence is a form of fall-related self-efficacy that inquires about a person's belief of being able to complete tasks without losing balance or becoming unsteady.[73] Participants are asked to rate their level of confidence on 16 daily activities using a continuous response scale from 0% (no confidence) to 100% (completely confident). The mean across all items represents the total score and a higher score indicates greater balance confidence. The reliability and validity of the ABC has been established in PLLA.[184] In older adults, decreased balance confidence is associated with higher anxiety about falling, which increases the cognitive load of gait and results in adverse performance.[153] Reduced balance confidence may be a cognitive distractor for PLLA as lower values are independently associated with worse physical function.[154]

4.2.5 Data Analysis

For clinical and demographic information, the normality of continuous data was assessed using Shapiro-Wilks tests and a visual inspection of histograms, Q-Q plots and boxplots. Means and standard deviations, medians and interquartile ranges (25^{th}, 75^{th} percentiles), or frequencies and percentages were used to summarize results, as appropriate.

Separate multivariable linear regressions were used to evaluate the independent association of global cognitive function (MoCA), processing speed (TMT-A), executive function (TMT-B) and balance confidence (ABC) on: single-task and dual-task gait velocity, single-task and dual-task L Test, and the Four Square Step Test. Testing diagnostics were performed to ascertain that all linear regression assumptions were met. The first block of each regression examined univariate relationships, while the second block was adjusted for confounders [age (continuous) or sex (binary: male, female), etiology (binary: vascular, non-vascular) and number of comorbidities (continuous)]. The confounders were selected based on data availability, clinical significance, proven relationship to physical performance[16,148] and an observed change ≥10% in the unstandardized beta values of the exposure with the introduction of each.

An *a priori* analysis using G*Power (version 3.1.9.6)[192] estimated that 86% power could be attained assuming α=0.05, the use of four predictors and an omnibus R^2 of 0.45 based on previous literature[16,148]. The statistical package SPSS (version 25.0; SPSS, Inc., Chicago, IL) was used to run all analyses with a 0.05 experiment-wise alpha.

4.3 Results

Twenty-two people participated (age: 62.3 ± 8.9 years, 68.2% were male). The median time since amputation was 108.5 days (88.5, 159.3) and most (81.8%) had an amputation due to diabetes mellitus or peripheral vascular disease. (Table 4.1) The median MoCA score was 27 (24, 29) and 40.9% demonstrated cognitive impairment. (Table 4.2) Dual-task testing resulted in worse gait velocity and L Test performance. The median FSST was 26.64 seconds (20.76, 42.17).

Table 4.1: Sociodemographic and clinical characteristics of a sample of people with unilateral transtibial level amputations discharged from inpatient prosthetic rehabilitation. (n=22)

Variable	Mean ± SD, Median [25^{th}, 75^{th} percentiles] or n (%)
Age (years)	62.3 ± 8.9
Sex, n (% male)	15 (68.18)
Body Mass Index (kg/m^2)	28.43 ± 6.72
Years of Education (years)	12.77 ± 2.72
Etiology of Amputation, n (%)	
Diabetes Mellitus	15 (68.18)
Peripheral Vascular Disease	3 (13.64)
Other (cancer, congenital, etc.)	4 (18.18)
Time Since Amputation (days)	108.5 [88.5, 159.3]
12-Month Falls History, n (% yes)	18 (81.82)
Number of Prescription Medications	8.96 ± 4.53
Number of Comorbidities	4.0 [2.0, 5.0]
Summary of Comorbidities, n (% yes)	
Diabetes Mellitus	17 (77.3)
Hypertension	14 (63.6)
Dyslipidemia	9 (40.9)
Osteoarthritis	7 (31.8)
Other	17 (77.3)

Table 4.2: Values for cognitive function, balance confidence, dynamic balance, functional mobility and gait velocity in a sample of people with unilateral transtibial amputations. (n=22)

Outcome	**Mean ± SD or Median [25th, 75th percentiles]**
Montreal Cognitive Assessment Score	27 [24, 29]
Trail Making Test Part A	40.56 [27.83, 57.02]
Trail Making Test Part B	95.87 [78.70, 124.92]
Activities-specific Balance Confidence Scale (%)	75.94 [63.13, 81.25]
Four Square Step Test (s)	26.64 [20.76, 42.17]
L Test of Functional Mobility, single-task (s)	45.07 [33.02, 57.03]
L Test of Functional Mobility, dual-task (s)	56.62 [36.09, 72.43]
Gait velocity, single-task (cm/s)	57.75 [47.93, 75.90]
Gait velocity, dual-task (cm/s)	49.00 [41.65, 67.68]

Multivariable linear regression modelling demonstrated an independent association between the MoCA and single-task ($p=0.002$, $R^2=0.46$) and dual-task ($p=0.01$, $R^2=0.20$) gait velocity. (Table 4.3) A 1-point increase in the MoCA was associated with a 5.45 cm/s (95%CI: 2.35, 8.54) and 5.04 cm/s (95%CI: 1.33, 8.75) increase in gait velocity for the single-task and dual-task conditions, respectively. The MoCA was also independently associated with the L Test for single-task ($p=0.001$, $R^2=0.45$) and dual-task ($p=0.005$, $R^2=0.38$). For the L Test, a 1-point increase in the MoCA was associated with a 4.75 second (95%CI: 7.22, 2.28) reduction in the single-task and a 5.27 second (95%CI: 8.74, 1.80) reduction in the dual-task condition.

The TMT-B was independently associated only with the single-task ($p=0.03$, $R^2=0.20$) and dual-task ($p=0.02$, $R^2=0.30$) L Test. (Table 4.3) A 1-second TMT-B increase was associated with a 0.21 second (95%CI: 0.03, 0.39) increase in the single-task and a 0.29 second (95%CI: 0.06, 0.51) increase in the dual-task L Test. The TMT-A ($p>0.07$) or ABC ($p>0.15$) were not associated with any of the tests of physical function.

Table 4.3: Multivariable linear regression modeling for the association of the Montreal Cognitive Assessment, Trail Making Test and Activities-specific Balance Confidence Scale on the Four Square Step Test. (n=22)

Cognitive test	**Unadjusted unstandardized β (95% CI)**	**p-value**	**R^2**	**Adjusted unstandardized β (95% CI)***	**p-value**	**R^2**
Outcome: Four Square Step Test						
Montreal Cognitive Assessment Score	**-3.19 (-5.14, -1.25)**	**0.003**	0.34	-2.07 (-4.78, 0.64)	0.13	0.31
Trail Making Test Part A	**0.42 (0.17, 0.67)**	**0.002**	0.35	0.30 (-0.03, 0.62)	0.07	0.35
Trail Making Test Part B	**0.17 (0.06, 0.28)**	**0.003**	0.33	0.11 (-0.06, 0.28)	0.19	0.29
Activities-specific Balance Confidence Scale	-0.13 (-0.77, 0.51)	0.68	0.00	-0.05 (-0.80, 0.69)	0.89	0.00
Outcome: L Test of Functional Mobility (Single-task)						
Montreal Cognitive Assessment Score	**-3.79 (-5.55, -2.03)**	**<0.001**	0.48	**-4.75 (-7.22, -2.28)**	**0.001**	0.45
Trail Making Test Part A	0.22 (-0.09, 0.52)	0.155	0.05	0.13 (-0.30, 0.55)	0.54	0.00
Trail Making Test Part B	**0.17 (0.06, 0.28)**	**0.005**	0.30	**0.21 (0.03, 0.39)**	**0.03**	0.20
Activities-specific Balance Confidence Scale	-0.46 (-1.08, 0.16)	0.14	0.06	-0.24 (-0.91, 0.43)	0.46	0.10

Outcome: L Test of Functional Mobility (Dual-task)						
Montreal Cognitive Assessment Score	**-4.80 (-7.21, -2.40)**	**<0.001**	0.44	**-5.27 (-8.74, -1.80)**	**0.005**	0.38
Trail Making Test Part A	0.30 (-0.10, 0.70)	0.13	0.07	0.14 (-0.39, 0.68)	0.59	0.02
Trail Making Test Part B	**0.24 (0.10, 0.38)**	**0.002**	0.37	**0.29 (0.06, 0.51)**	**0.02**	0.30
Activities-specific Balance Confidence Scale	-0.48 (-1.31, 0.36)	0.25	0.02	-0.22 (-1.14, 0.71)	0.63	0.01
Outcome: Gait Velocity (Single-task)						
Montreal Cognitive Assessment Score	**4.79 (2.58, 7.00)**	**<0.001**	0.48	**5.45 (2.35, 8.54)**	**0.002**	0.46
Trail Making Test Part A	**-0.40 (-0.76, -0.04)**	**0.03**	0.18	-0.29 (-0.78, 0.20)	0.23	0.10
Trail Making Test Part B	**-0.21 (-0.35, -0.07)**	**0.005**	0.29	-0.20 (-0.44, 0.03)	0.08	0.18
Activities-specific Balance Confidence Scale	0.74 (-0.01, 1.49)	0.05	0.13	0.63 (-0.25, 1.50)	0.15	0.03
Outcome: Gait Velocity (Dual-task)						
Montreal Cognitive Assessment Score	**3.56 (0.95, 6.18)**	**0.01**	0.25	**5.04 (1.33, 8.75)**	**0.01**	0.20
Trail Making Test Part A	-0.17 (-0.56, 0.22)	0.38	0.00	-0.13 (-0.68, 0.43)	0.64	0.00
Trail Making Test Part B	-0.13 (-0.28, 0.03)	0.11	0.08	-0.21 (-0.46, 0.05)	0.10	0.00
Activities-specific Balance Confidence Scale	0.52 (-0.25, 1.30)	0.18	0.05	0.36 (-0.52, 1.23)	0.40	0.01

Footnote: CI: confidence interval. *, regression modeling adjusted for age (continuous), etiology (binary: non-vascular, vascular) and number for comorbidities (continuous) for the Montreal Cognitive Assessment and Trail Making Tests, while for the Activities-specific Balance Confidence Scale, sex (binary: male, female) was used instead of age. Statistical significance was $p < 0.05$.

4.4 Discussion

Better global cognitive and executive function were independently associated with faster gait velocity and greater functional mobility, yet this was not observed for dynamic balance. No association was observed between processing speed or balance confidence and any of the physical function tests evaluated. This is the first study to examine the association between different measures of cognition and an array of clinical tests of physical function, including the FSST and dual-task testing, in novice users of a lower limb prosthesis.

Previous research in novice ambulators with a prosthesis only included the use of the MoCA to measure its association to functional mobility and walking endurance as per the L Test and Two-minute Walk Test, respectively.[16,18] Although an independent association was found between better global cognitive status and greater functional mobility and walking endurance,[16,18] it is important to note that these studies did not include different tests of cognitive function, or other tests of physical function that ranged in difficulty or that included dual-task conditions.[16,18] Moreover, the testing for cognitive function was performed as part of admission to inpatient prosthetic rehabilitation, while physical function testing was completed at discharge.[16,18] As prosthetic rehabilitation involved upwards of four weeks of intensive programming for learning the use of a lower limb prosthesis, it is reasonable to expect that temporal misalignment for the collection of outcomes may have affected the association between the variables of interest.

In the present study, more measures of cognitive function were independently associated with L Test performance compared to gait velocity or the FSST. Relative to other assessments, such as walking a straight line, the L Test provides a greater challenge as it involves the ability to complete transfers and to turn towards the prosthetic and intact limbs.[189] A relationship exists between executive function and curved-path walking, suggesting ambulation in complex paths is more cognitively demanding.[158] Interestingly, global cognitive status was associated with straight path gait velocity, but none of the measurements of cognitive function were associated with the FSST. These results may be explained by the fact that we used an instrumented walkway, which is considered a more sensitive methodology for recording gait. Our protocol also relied on a modified FSST using tape to designate different quadrants as opposed to using canes,[200] which may have reduced the challenge for this test as participants did not have to think about lifting their feet enough to clear obstacles.

Careful selection is required as different measures of cognition were associated with different tests of physical function. As demonstrated through our work, reduced cognitive function should not deter the use of the FSST as an assessment of dynamic balance. On the other hand, low cognitive function was independently associated with worse L Test performance and slower gait velocity in both single-task and dual-task; thus, these tests may be preferred for clinicians trying to understand how reduced cognitive functions may be affecting functional mobility and gait. Of course, a caveat remains that cognitive impairment was present in 41% of our sample, which is lower than what is typically reported in this population (52-56%)[16,17] and indicates that our results are likely a conservative estimate of the strength of the association between cognitive and physical functions. Future research for the creation of a framework for the progressive increase in complexity within tests of physical function, including dual-task conditions, would be valuable to help minimize instances of under- or over-challenging individuals; thus, optimizing the falls risk-related information that can be gathered from testing.

Dual-task testing is reflective of instances of divided attention that are often linked to falls or near-falls in PLLA[29] The mental tracking task used, involved remembering and manipulating information before each response.[164] There is a growing body of research on dual-task gait testing in PLLA that has been published in recent years,[157] with a variety of secondary tasks being reported and which have been used to successfully examine cognitive-motor capacity, such as serial subtractions by sevens,[143] the Stroop test,[113] listing items and spelling[143] and motor tasks (e.g., carrying a tray with cups[179]). The addition of a secondary task serves to increase cognitive challenge, but if too difficult it can result in people stumbling or stopping walking altogether. Moreover, different secondary tasks may be necessary if vision, hearing or cognitive function are impaired, or if other barriers exist (e.g., language, education level). Among commonly used tests of physical function,[14] the L Test is the only one shown to be both valid and reliable in a condition of dual-task for PLLA[144,189]. Healthcare professionals working with PLLA who have reduced cognitive function may elect to assess dual-task performance using the L Test. Dual-task training could be a treatment in instances where dual-task performance is low. Only one study has examined the effect of dual-task training on mobility in people with unilateral transfemoral amputations.[185] Individuals who underwent dual-task training over a 4-week period were shown to have a greater magnitude of improvements in functional mobility and static and dynamic balance than those who received single-task training.[185] Research examining the longitudinal relationship between dual-task testing and important outcomes such as falls, or specific protocols for dual-task training in clinical practice, do not currently exist for PLLA.

There are several limitations that should be mentioned. The results of the present study are not generalizable to all PLLA as we included only those with unilateral transtibial amputations who were able to complete all the physical function testing and did not include participants with severe cognitive impairments. A strength to our study was the use of a comprehensive battery of cognitive tests and that we included the more well-known and established tests of physical function which varied in complexity[14].

4.5 Conclusions

The present study is the first to report that better global cognitive status and executive function were independently associated with improved performance on gait velocity and the L Test for both conditions of single-task and dual-task in people who recently learned to walk using a prosthesis. Importantly, no association was observed between cognitive function and the FSST, or between processing speed and balance confidence and any of the tests evaluated. Future research should seek to develop a framework that outlines a gradation of complexity among clinical tests of physical function to minimize instances of under- or over-challenging PLLA.

Chapter 5: SUMMARY OF FINDINGS

The main objective of the present dissertation was to expand our understanding of the inter-relationship between cognition and mobility in PLLA. Study 1 consolidated the full scope of published dual-task balance and gait research in those with lower limb amputations. For balance, standing sway distance and velocity were worse in PLLA, but a differential dual-task effect relative to controls was only observed for measures of sway velocity. PLLA were also observed to have a disproportionally slower pace, reduced rhythm, and an increased step time asymmetry during dual-task gait testing than controls. Our systematic review did not find substantial evidence that the use of microprocessor prosthetic devices improved dual-task balance or gait performance to a greater degree than in PLLA who used a non-microprocessor prosthesis. Nor was there evidence for the magnitude of the dual-task effect on balance or gait to be any different according to level of amputation, etiology, or experience using a prosthesis. Study 2 evaluated the association between balance confidence and basic walking abilities in community-dwelling people with unilateral transtibial level amputations. A lower balance confidence (i.e., an increased concern for instability or loss of balance) was independently associated with worse performance on functional mobility in both single-task and dual-task gait conditions. Due to the prevalence of low balance confidence among PLLA[146,147] and the influence that balance confidence has on functional mobility, it is suggested that interventions targeting balance confidence are warranted. Study 3 examined the association of different aspects of cognitive function on tests of physical function in PLLA discharged from inpatient prosthetic rehabilitation. Better global cognitive and executive function were independently associated with faster walking and greater functional mobility in both single-task and dual-task gait conditions. No association was found between cognitive function and dynamic balance, or between processing speed or balance confidence and any of the tests evaluated. Overall, careful selection is required as different measures of cognition were associated with different tests of physical function.

The findings of the three studies that compose this dissertation are novel and provide evidence on the interplay between cognition and mobility in PLLA, which is uniquely challenged in this group of people. Alternative avenues for focus in rehabilitation and falls-prevention are suggested for healthcare providers with the intent to minimize the cognitive burden associated with walking using a prosthesis. The understanding of the link between cognition and mobility was broadened using different research inquiries and the use of cognitive-motor capacity testing, which will be useful for future studies examining ways to attenuate the risk for falls in people with lower limb amputations.

Chapter 6: FUTURE DIRECTIONS

The high risk for falls observed in PLLA,[8,10,11,13] alongside the increased cognitive demands and learning required for using a lower limb prosthesis[10,22] and the common presence of cognitive impairments and dysvascular disease[16,17,122], all indicate that future research should be emphasized on the topic of understanding the inter-relationship between cognition and mobility. Even after intensive prosthetic rehabilitation, falls and their consequences are an ongoing concern for PLLA that requires better assessment and remediation options. This is important as the number of PLLA is expected to rise in the coming decades.[30] Dual-task balance and gait testing allow for the assessment of cognitive-motor capacity in situations that resemble real life[139,140] and are often associated with falls in PLLA[29]. Future research should also seek to expand on how clinical markers, including those designed to challenge the cognitive-motor capacity of PLLA, are associated with successful community reintegration, quality of life, and future falls.

Regarding the effect of dual-task balance and gait testing in PLLA, certain aspects remain unexplored. Future studies in this field should recruit PLLA of different age groups, levels of amputations, etiology, and experience walking with a prosthesis. It has yet to be demonstrated the influence that certain PLLA-specific characteristics have on the effect of dual-task balance and gait testing. A prospective study is also recommended to examine the association between dual-task gait testing and important outcomes (e.g., prosthesis use, socialization, independence, quality of life, and falls) across all stages of PLLA rehabilitation. This type of predictive validity study should adopt the use of a clinical test with a condition of dual-task in order to increase clinical applicability, as opposed to the use of a protocol reliant on instrumented technology not commonly used in clinics.

Another research path to explore is that of dual-task training. In PLLA at the unilateral transfemoral level who were experienced at walking with a prosthesis, dual-task balance and gait training for 4-weeks demonstrated benefits of a greater magnitude for functional mobility, static and dynamic balance, and gait velocity than in those who received only single-task training.[185] However, this research study is not generalizable to all PLLA and remains the only one in this topic. Moreover, we have yet to understand what the longitudinal effects of this kind of intervention are for PLLA particularly on patient relevant outcomes such as falls, quality of life and community reintegration. Many avenues for research in dual-task gait testing and training exist for this group of people; all of which will eventually allow clinicians to more accurately assess and intervene for impairments that often lead to falls.

Evidently, balance confidence, and by proxy a concern for falls, is an issue in PLLA that can negatively impact many areas of life.[12,29,148] Although Study 2 concludes that a low balance confidence was independently associated with worse functional mobility in community-dwelling PLLA at the unilateral transtibial level, this was all evaluated within the one domain of falls-related self-efficacy for a concern for falls. Each domain for a concern for falls examines a different construct.[149] Therefore, future research needs to build upon the present work to establish the relationship that each of the different domains of a concern for falls has to mobility in PLLA across different etiologies, levels of amputation, and cognitive function. It is suggested through Study 2 that interventions targeting balance confidence may be beneficial. A specific protocol for clinical use that can enhance self-efficacy does not currently exist in this population.[198] Future research ought to investigate which combination of physical and mental well-being therapeutic approaches is most optimal to decrease concern for falls in PLLA in an attempt to attenuate the cognitive demands associated with walking with a prosthesis.

The assessment of physical function in PLLA is important to delineate progress and to reveal any impairments. A plethora of different clinical tests of physical function are readily available to healthcare professionals working in this field.[14] Yet, even though it is clear that cognitive impairments are common in PLLA,[16,17,122] little is known about the level of cognitive resources required for the completion of any given test of physical function. Future research is needed for the development of a framework for the progressive increase in complexity within clinical tests of physical function, including dual-task conditions. All which should take into consideration that barriers may exist, such as impaired vision and hearing, language, or education level. The importance of this proposed research inquiry is for clinicians to be able to select tests of physical function that are neither too easy nor too challenging. Therefore, optimizing the information that can be gathered through tests of physical function that is used to formulate interventions and prognosticate future success.

A lower limb amputation is a life-changing event that has many negative consequences to the individual, their family, and the healthcare field.[2–6,22,44–46] The examination of cognitive-motor capacity is warranted and an avenue to explore to help explain the mobility issues[3,53,60,95] and high rate of falls this population experiences[8,10,11,13]. Various paths for future research are identified, emphasizing for researchers to further investigate how certain assessments, such as dual-task balance and gait tests, can help detect those most likely to struggle and intervene early. Moreover, also examining the role that falls-related psychological factors have on the ability for individuals to walk successfully using their lower limb prosthesis. Broadening our understanding of this interplay between cognition and mobility in PLLA may enable a more patient-centered falls prevention evaluation that will help meet the group's unique healthcare needs.

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Appendix B: Example of search strategy for Web of Science database for Study 1.

Topics ("All fields")[†]	Key terms and operators
Grouping #1: population and prosthetic equipment	amputation (OR amputees OR amput* OR "artificial limbs" OR prosthesis OR prosthetic OR prosthe* OR microprocessor OR "microprocessor knee" OR "microprocessor-controlled" OR "C-Leg" OR "bone-anchored" OR "bone anchored" OR osseointegration OR osseointegrat* OR osseo-integrat* OR lock* OR "manual-locking" OR "manual locking" OR adaptive OR artificial OR biomechatronic OR bionic OR intelligent OR powered OR "single-axis" OR "single axis" OR "multi-axial" OR "multiaxial" OR "weight-activated" OR "weight activated" OR polycentric OR hydraulic OR pneumatic OR "friction controlled" OR "friction-controlled")
"AND"	
Grouping #2: outcome of interest	balance (OR equilibrium OR posture OR postur* OR stabilometry OR "postural control" OR "postural stability" OR "postural balance" OR "postural sway" OR sway OR "center of pressure" OR "center of mass" OR gait OR walking OR ambulation OR kinetics OR kinematics OR mobility OR movement)
"AND"	
Grouping #3: intervention	"dual-task" (OR "dual task" OR "dual-tasking" OR "dual tasking" OR "multi-task" OR "multi task" OR "multi-tasking" OR "multi tasking" OR "secondary task" OR "motor task" OR "cognitive task" OR distract*)

Footnote: †, No filtering, restrictions or limitations were applied.

Appendix C: Reasons for article exclusion after full-text review for Study 1.

Article Reviewed	Exclusion criteria met	Reason(s) for exclusion
Crea S, Edin BB, Knaepen K, Meeusen R, Vitiello N. Time-discrete vibrotactile feedback contributes to improved gait symmetry in patients with lower limb amputations: Case series. Physical therapy. 2017 Feb 1;97(2):198-207.	1	Did not report balance, gait or mobility performance differences.
Demirdel S, Erbahçeci F. An Investigation of The Effects of Dual Task on Gait in People with Trasfemoral Amputation. Turkish Journal of Physiotherapy Rehabilitation-Fizyoterapi Rehabilitasyon. 2017 Dec 1;28(3):118-24.	1	Not published in English.
De Pauw K, Cherelle P, Tassignon B, Van Cutsem J, Roelands B, Marulanda FG, Lefeber D, Vanderborght B, Meeusen R. Cognitive performance and brain dynamics during walking with a novel bionic foot: A pilot study. PloS one. 2019;14(4).	1	Did not assess balance, gait or mobility performance differences.
Frengopoulos C, Burley J, Viana R, Payne MW, Hunter SW. Association between Montreal Cognitive Assessment scores and measures of functional mobility in lower extremity amputees after inpatient rehabilitation. Archives of physical medicine and rehabilitation. 2017 Mar 1;98(3):450-5.	1	Did not include a dual-task testing.
Huang S, Wensman JP, Ferris DP. Locomotor adaptation by transtibial amputees walking with an experimental powered prosthesis under continuous myoelectric control. IEEE Transactions on Neural Systems and Rehabilitation Engineering. 2015 Jun 4;24(5):573-81.	1	Did not include a dual-task testing.
Hunter SW, Frengopoulos C, Holmes J, Viana R, Payne MW. Determining reliability of a dual-task functional mobility protocol for individuals with lower extremity amputation. Archives of physical medicine and rehabilitation. 2018	1	Did not report balance, gait or mobility performance differences.

Apr 1;99(4):707-12.		
Knaepen K, Marusic U, Crea S, Guerrero CD, Vitiello N, Pattyn N, Mairesse O, Lefeber D, Meeusen R. Psychophysiological response to cognitive workload during symmetrical, asymmetrical and dual-task walking. Human movement science. 2015 Apr 1;40:248-63.	1	Did not recruit people with lower limb amputations.
Nakamura R, Moriai N, Sajiki N. Reaction times of normal subjects and amputees with below-knee and above-knee prostheses during stepping. Prosthetics and orthotics international. 1984 Jan 1;8(2):100-2.	1	Did not assess balance, gait or mobility performance differences.
Ořechovská K, Svoboda Z, Janura M, Kováčiková Z. Postural stability in transtibial amputees assessed by laboratory and clinical tests. Gait & Posture. 2015(42):S54-5.	1	Not a research study (conference abstract)
Peng F, Hu T, Zhang C. A Multi-Task Mode Control Method for Powered Knee-Ankle Prosthesis. In2019 International Conference on Advanced Mechatronic Systems (ICAMechS) 2019 Aug 26 (pp. 338-343). IEEE.	3	Not a research study (conference abstract), participants were not 18 years of age or older, and did not include a dual-task testing.
Petrini FM, Valle G, Bumbasirevic M, Barberi F, Bortolotti D, Cvancara P, Hiairrassary A, Mijovic P, Sverrisson AÖ, Pedrocchi A, Divoux JL. Enhancing functional abilities and cognitive integration of the lower limb prosthesis. Science translational medicine. 2019 Oct 2;11(512):eaav8939.	1	Did not assess balance, gait or mobility performance differences.
Ramstrand N, Rusaw DF, Möller SF. Transitioning to a microprocessor-controlled prosthetic knee: Executive functioning during single and dual-task gait. Prosthetics and orthotics international. 2020 Feb;44(1):27-35.	1	Did not assess balance, gait or mobility performance differences.
Shaw EP, Rietschel JC, Hendershot BD, Pruziner AL, Wolf EJ, Dearth CL, Miller MW, Hatfield BD, Gentili RJ. A comparison of mental workload in individuals with transtibial and transfemoral lower limb loss during dual-task walking under varying demand. Journal of the International Neuropsychological Society. 2019 Oct;25(9):985-97.	1	Did not assess balance, gait or mobility performance differences.

Appendix D: Detailed dual-task methodology for articles included in the systematic review for Study 1.

Lead author	**Balance or gait task**	**Secondary task (Category)**
Dual-task static balance		
Geurts et al. 1991[167]	Standing in standardized position (8.4 cm apart from med. heel and at 9º ext. rot from sagittal plane) for 30 seconds (ST: 15 seconds, DT: 15 seconds). The DT protocol was completed twice, before and after prosthetic rehabilitation.	Modified Stroop test (discrimination and decision-making task): Instructed to state the colour of written words. Always incongruent. Three PLLA were asked to do an arithmetic subtraction task instead (mental tracking): Subtracting three from a random number between 50-100. Instructed to maintain the same balance strategy during dual-task.
Geurts et al. 1994[168]	Standing in standardized position (8.4 cm apart from med. heel and at 9º ext. rot from sagittal plane). For static balance tests, subjects stood with their hands behind their back for 30 seconds. Note: The DT protocol was completed throughout prosthetic rehabilitation.	Arithmetic addition check task (mental tracking, discrimination and decision-making task): Participants were provided with a random addition and asked to state if the math was correct. No specifics reported regarding the instructions for the secondary cognitive task.
Howard et al. 2017a[142]	Standing with feet shoulder width apart, shoes on, and arms at their sides for 30 seconds. Feet	While standing participants completed either:

	placement was marked for within collection consistency.	1) An arithmetic subtraction task (mental tracking): Subtracting seven from three-digit number. No specifics on starting number selection. 2) FAS test (verbal fluency): List words starting with a specific letter. Letters J, K, Q, U, X, Y, and Z were excluded to decrease task difficulty. Dual-task conditions were performed under two task prioritization conditions: 1) No prioritization, and 2) focus on the cognitive task ("increase correct responses by 50%").
Dual-task dynamic (feet-in-place) balance		
Geurts et al. 1994[168]	For the weight shifting test condition, participants were asked to look at a screen showing their real-time CoP. The goal was to shift their weight towards a cued site on the screen in the ML direction for 30 seconds. Note: The DT protocol was completed throughout prosthetic rehabilitation.	Arithmetic addition check task (mental tracking, discrimination and decision-making task): Participants were provided with random addition and asked to state if the math was correct. No specifics reported on the instructions for the secondary cognitive task.
Vrieling et al.	Standing with feet at a self-selected position with	Auditory Stroop test (discrimination and decision-

2008[169]	arms on the sides. Force platform swayed in the AP direction for 60 seconds (1 Hz, 0.02 m amplitude). Participants were instructed to stand as still as possible.	making task): Instructed to state the pitch of the voice while ignoring the word ("high", "low"). No specifics on the congruent/incongruent ratio. No specifics reported on the instructions for the secondary cognitive task.
Dual-task gait: PLLA compared to CN		
Hof et al. 2007[173]	Treadmill walking at three different walking speeds (0.75, 1.00 and 1.25 m/s). Walking speed was adjusted according to leg length and each trial was two minutes per test condition.	Stroop test (discrimination and decision-making task): Instructed to state the colour of written words. The congruent/incongruent ratio was not reported. Instructions on task prioritization not reported.
Lamoth et al. 2010[176]	Walking conditions: ST – indoor walking, DT – indoor walking paired with a secondary task, outdoor walking on an even surface (pavement), and walking outside on an uneven surface ("roughly paved"). Each test condition consisted of 6 minutes of continuous walking without the use of a mobility aid.	Arithmetic subtraction task (mental tracking): No specifics on starting number selection or subtraction value. Instructions on task prioritization not reported.
Morgan et al. 2016[113]	Usual pace, straight path indoors (NR x 8.8 m).	Auditory Stroop test (discrimination and decision-making task): Instructed to state the pitch of the voice while ignoring the word ("high", "low"). No specifics on the congruent/incongruent ratio. Participants instructed to focus on the cognitive task.
Howard et al. 2017b[143]	Slow, usual, and fast pace straight path walking indoors (0.6 x 5.2 m).	1) An arithmetic subtraction task (mental tracking): Subtracting seven from a three-digit number. No specifics on starting number selection.

		2) Spelling task (mental tracking and working memory): Spelling backwards five letter words. No other specifics provided. No instructions on task prioritization were given.
Morgan et al. 2017[145]	Usual pace, straight path indoors walking on a low-density closed-cell foam surface (path: 0.6 x 8.8 m, foam: 3.8 cm thick with a 48-72 Kg/m^3 density).	Auditory Stroop test (discrimination and decision-making task): Instructed to state the pitch of the voice while ignoring the word ("high", "low"). No specifics on the congruent/incongruent ratio. Participants instructed to focus on the cognitive task.
Pruziner et al. 2019[178]	Usual pace walking on a dual-belt treadmill.	Object detection (discrimination and decision-making task): Participants were presented with shapes of different colours. 1) Low level: Detect and press a button when a square is seen regardless of colour. 2) High level: Detect and press a button when both the shape or colour of two stimuli were the same (e.g., red circle and red square). Instructions on task prioritization not reported.

Möller et al. 2020[181]	Usual pace, straight path walking indoors (NR x 14.0 m).	Sorting keys (discrimination and decision-making task): Participants provided with eight keys of three different colours and marked with three different numbers. Participants instructed to use one hand while walking and find the appropriate key. However, task details or task prioritization were not reported.
Schack et al. 2020[180]	Figure-of-8 Walk Test: 1) Usual pace. 2) Usual pace on an uneven surface (six foams 1.5 cm thick and additional foam slices around cones).	Carrying a tray with two cups filled with water (motor). Participants instructed to focus on not spilling any water.
Dual-task gait: Within samples of PLLA		
Frengopoulos et al. 2018[28]	The L Test of Functional Mobility at a usual pace.	An arithmetic subtraction task (mental tracking): Subtracting three from a three-digit number between 100 and 150. No instructions on task prioritization were given.
Hunter et al. 2018[27]	Usual pace, straight path indoors walking (0.64 x 6 m).	An arithmetic subtraction task (mental tracking): Subtracting three from a three-digit number between 100 and 150. No instructions on task prioritization were given.
Hunter et al. 2019[94]	1) Usual pace, straight path indoors walking (0.64 x 6 m).	An arithmetic subtraction task (mental tracking): Subtracting three from a three-digit number between 100 and 150. No instructions on task prioritization were

	2) The L Test of Functional Mobility at a usual pace.	given.
Schack et al. 2019[179]	Figure-of-8 Walk Test: 1) Usual pace. 2) Usual pace on an uneven surface (six foams 1.5 cm thick and additional foam slices around cones). An additional six slices of foam were placed underneath (1.5 cm).	Carrying a tray (44 x 33 cm) with two cups (1 kg) 30 cm apart and filled with water 1 cm from the top (motor). Participants instructed to focus on not spilling any water.
Dual-task gait: Microprocessor versus non-microprocessor prosthesis		
Heller et al. 2000[170]	Straight path walking on a treadmill with constantly changing speed (0-20 seconds: 0 to 4 km/h, 20-30 seconds: 4 to 2 km/h, 30-40 seconds: 2 to 4 km/h, and 40-60 seconds: 4 to 0 km/h).	1) Reading numbers (reaction time task): Reading out loud a number from one to ten presented on a screen. 2) Stroop test (discrimination and decision-making task): Instructed to state the colour of written words. The congruent/incongruent ratio was not reported. Instructions on task prioritization not reported.
Williams et al.	Usual pace, indoor walking on a loop (NR x 60 m).	1) An arithmetic subtraction task (mental tracking):

2006[171]		Subtracting three from 100 for one minute. No instructions on task prioritization were given. 2) The Controlled Oral Word Association Test (verbal fluency): List words starting with a specific letter for 1 minute (three letters in total). No other specifics given. 3) The Category Test (verbal fluency and working memory): List words belonging to a specific category for one minute (two categories in total). No other specifics given. Instructions on task prioritization not reported.
Hafner et al. 2007[172]	Usual pace, outdoor walking two sides of a city block.	Number recall (mental tracking task): Participant was provided with 20 groups of randomized numbers (in a series of two, three four and five numbers) and asked to recall out loud the series backwards onto a cellphone. Instructions on task prioritization not reported.
Seymour et al. 2007[174]	Usual walking on an indoor obstacle course (NR x 12.2 m). Participants started and ended the task sitting on a chair. Obstacles included: a crutch to step over, a trash can to walk around, and carpets to walk over.	Carrying a weighted (4.5 kg) laundry basket (motor): No dimensions of the basket were reported or instructions on task prioritization.
Hafner et al. 2009[175]	Usual pace, outdoor walking two sides of a city block.	Number recall (mental tracking task): No specifics provided. Instructions on task prioritization not

		reported.
Meier et al. 2012[177]	Usual walking on an indoor obstacle course (6 x 11 m) with seven sections: 1) foam (1 x 3 x 0.15 m), 2) zig zag chairs (0.5 m between), 3) simulated sand (1 x 3 m), 4) uneven rock (1 x 3 m), 5) downward ramp (1.4 x 1.5 m, 5 degree) 6) 90-degree turn, and 7) stairs (NR x NR, 0.12 m height). Total length was 23.2 m.	An arithmetic subtraction task (mental tracking): Subtracting three or seven from a three-digit number. No other specifics were reported. No instructions on task prioritization were given.
Möller et al. 2020[181]	Usual pace, straight path walking indoors (NR x 14.0 m).	Sorting keys (discrimination and decision-making task): Participants provided with eight keys of three different colours and marked with three different numbers. Participants instructed to use one hand while walking and find the appropriate key. However, task details or task prioritization were not reported.

Footnote: AP: anterior-posterior; CN: controls; CoP: center-of-pressure; DT: dual-task; Ext. rot: external rotation; FAS: verbal fluency F-A-S test; Med: medial; ML: medial-lateral plane; NR: not reported; PLLA: people with lower limb amputations; ST: single-task.

Appendix E: Summary of Downs & Black for the methodological quality of reporting of papers in the systematic review for Study 1.

Author	Item#																											Total Score
	Reporting										Ext. Val.			Int. Val (bias and confounding)													Power	
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	
Dual-task Balance																												
Geurts et al. 1991[167]	1	1	0	1	2	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	0	0	0	1	0	0	12
Geurts et al. 1994[168]	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	1	0	1	1	1	1	0	0	0	1	0	0	13
Vrieling et al. 2008[169]	1	1	1	1	2	1	1	0	0	1	0	0	0	0	0	1	0	1	1	1	1	0	0	0	1	0	0	15
Howard et al. 2017a[142]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	0	0	0	1	0	0	17
Dual-task Gait																												
Heller et al. 2000[170]	1	1	1	1	2	1	0	0	0	1	1	0	1	0	0	0	1	0	1	1	1	0	0	0	0	0	0	14
Williams et al. 2006[171]	1	1	1	1	2	1	1	0	1	1	1	0	1	0	0	1	1	1	1	1	1	0	0	0	0	1	0	19

Hafner et al. 2007[172]	1	1	1	1	2	1	1	0	1	0	1	0	1	0	0	1	1	1	1	1	1	0	0	0	1	0	0	18
Hof et al. 2007[173]	1	1	0	1	2	1	1	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	0	0	0	0	11
Seymour et al. 2007[174]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	0	0	0	1	0	0	17
Hafner et al. 2009[175]	1	1	1	1	2	1	1	0	1	1	1	0	1	0	0	1	1	1	1	1	1	0	0	0	1	1	0	20
Lamoth et al. 2010[176]	1	1	0	1	2	1	1	0	0	1	0	0	0	0	0	1	0	1	1	1	1	0	0	0	1	0	0	14
Meier et al. 2012[177]	1	1	1	1	2	1	1	0	0	1	0	0	0	0	0	1	1	1	1	1	1	0	0	0	0	0	0	15
Morgan et al. 2016[113]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	0	0	0	1	0	0	17
Howard et al. 2017b[143]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	0	0	0	1	0	0	17
Morgan et al. 2017[145]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	0	0	0	0	0	0	16
Frengopoulos et al. 2018[28]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	1	0	0	0	0	0	17
Hunter et al. 2018[27]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	1	0	0	1	0	0	18

Hunter et al. 2019[94]	1	1	1	1	2	1	1	0	1	1	1	0	1	0	0	1	1	1	1	1	1	1	0	0	1	0	0	20
Pruziner et al. 2019[178]	1	1	0	1	2	1	1	0	0	1	0	0	0	0	0	1	0	1	1	1	1	0	0	0	0	0	0	13
Schack et al. 2019[179]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	0	0	0	1	0	0	17
Möller et al. 2020[181]	1	1	1	1	2	1	1	0	0	1	1	0	1	0	0	1	0	1	1	1	1	0	0	0	1	0	0	17
Schack et al. 2020[180]	1	1	1	1	2	1	1	0	0	1	0	0	0	0	0	1	0	1	1	1	1	0	0	0	1	0	0	15
Average Score ± SD																												16.00 ± 2.45

Notes: Ext. Val. = external validity; Int. Val. = internal validity.

Appendix F: Email of Study 2 acceptance pending revisions.

Jun 03, 2022

RE: POI-D-22-00041, entitled "The association between balance confidence and basic walking abilities in people with unilateral transtibial lower limb amputations: A cross-sectional study"

Dear Mr. Omaña,

I am pleased to inform you that your paper has been found acceptable for publication pending appropriate revision to address our reviewers' comments. The reviewers' comments regarding the manuscript are included at the bottom of this letter.

In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s). Please include with your revised submission an itemized, point-by-point response to the reviewers which details the changes made. The revised manuscript should be submitted by Aug 26, 2022; if you anticipate that you will be unable to meet this deadline, please notify the Editorial Office.

OPEN ACCESS
If you would like your submission, if accepted, to be open access, please complete the following steps. Further information is available at http://links.lww.com/LWW-ES/A48.
1. A License to Publish (LTP) form must be completed for your submission to be made open access. Please download the form from http://links.lww.com/LWW-ES/A49, sign it, and submit the file as part of your revision (using the Attach Files submission step in Editorial Manager).
2. Upon acceptance of your submission, you will receive an Open Access Publication Charge letter from the Journal's Publisher, Wolters Kluwer, with instructions on how to submit any open access charges. The email will be from publicationservices@copyright.com with the subject line 'Please Submit Your Open Access Article Publication Charge(s)'. The cost for publishing an article as open access can be found at https://wkauthorservices.editage.com/open-access/hybrid.html.

To submit a revision, go to https://www.editorialmanager.com/poi/ and log in as an Author. Please go to the "Submissions Needing Revision" folder to view a copy of this letter, access the Reviewers' comments and download your submission files. To begin the revision process, click on 'Revise Submission'.

Your username is: homana@uwo.ca
https://www.editorialmanager.com/poi/l.asp?i=61329&l=JUR5R3CD

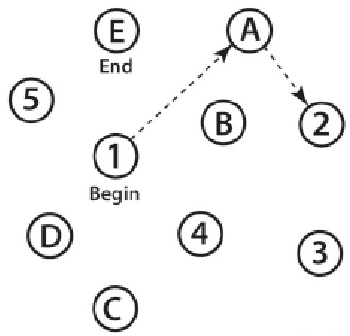
With Kind Regards,

Appendix G: Montreal Cognitive Assessment (MoCA).

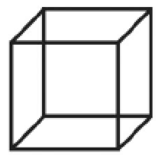
MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education :
Sex :
Date of birth :
DATE :

		POINTS
VISUOSPATIAL / EXECUTIVE		



[ ]



Copy cube

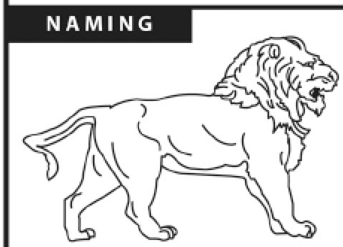
[ ]

Draw CLOCK (Ten past eleven)
(3 points)

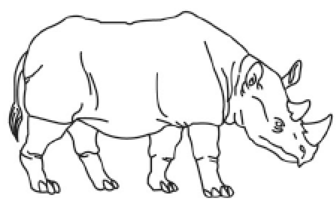
[ ] Contour [ ] Numbers [ ] Hands

___/5

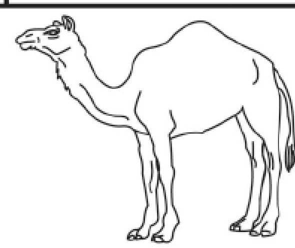
NAMING



[ ]



[ ]



[ ]

___/3

MEMORY

Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.).
Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2
___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B
___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**
___/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]
___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)
___/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler
___/2

DELAYED RECALL

Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional Category cue						
Multiple choice cue						

___/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City
___/6

www.mocatest.org
Normal ≥26 / 30
TOTAL ___/30
Add 1 point if ≤ 12 yr edu

Administered by: ____________________

Appendix H: The Activities-specific Balance Confidence (ABC) Scale.

The Activities-specific Balance Confidence (ABC) Scale*

Instructions to Participants:

For each of the following, please indicate your level of confidence in doing the activity without losing your balance or becoming unsteady from choosing one of the percentage points on the scale form 0% to 100%. If you do not currently do the activity in question, try and imagine how confident you would be if you had to do the activity. If you normally use a walking aid to do the activity or hold onto someone, rate your confidence as it you were using these supports. If you have any questions about answering any of these items, please ask the administrator.

The Activities-specific Balance Confidence (ABC) Scale*

For each of the following activities, please indicate your level of self-confidence by choosing a corresponding number from the following rating scale:

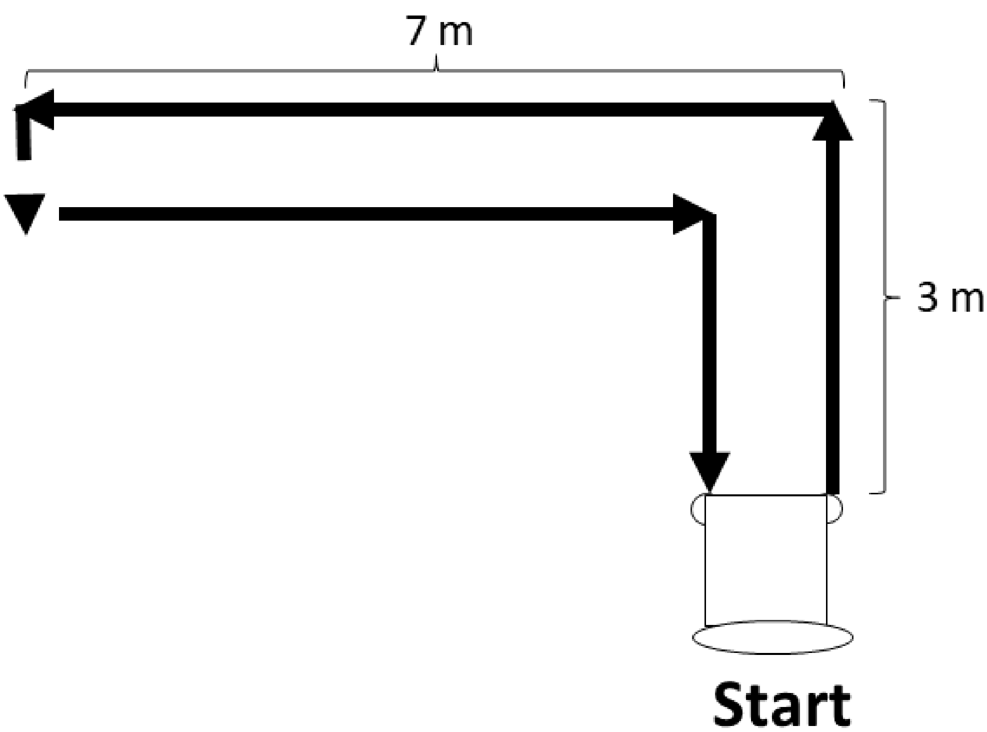
0% 10 20 30 40 50 60 70 80 90 100%
no confidence completely confident

"How confident are you that you will not lose your balance or become unsteady when you…

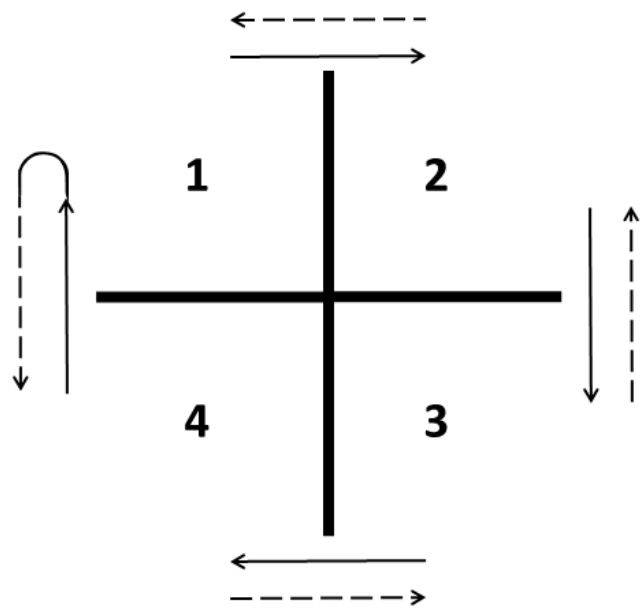
1. …walk around the house? ____%
2. …walk up or down stairs? ____%
3. …bend over and pick up a slipper from the front of a closet floor ____%
4. …reach for a small can off a shelf at eye level? ____%
5. …stand on your tiptoes and reach for something above your head? ____%
6. …stand on a chair and reach for something? ____%
7. …sweep the floor? ____%
8. …walk outside the house to a car parked in the driveway? ____%
9. …get into or out of a car? ____%
10. …walk across a parking lot to the mall? ____%
11. …walk up or down a ramp? ____%
12. …walk in a crowded mall where people rapidly walk past you? ____%
13. …are bumped into by people as you walk through the mall?____%
14. … step onto or off an escalator while you are holding onto a railing? ____%
15. … step onto or off an escalator while holding onto parcels such that you cannot hold onto the railing? ____%
16. …walk outside on icy sidewalks? ____%

*Powell, LE & Myers AM. The Activities-specific Balance Confidence (ABC) Scale. *J Gerontol Med Sci* 1995; 50(1): M28-34

Appendix I: Illustration of the L Test of Functional Mobility (L Test).



Appendix J: Illustration of the Four Square Step Test (FSST).



Footnote: For the Four Square Step Test, participants started in square #1 facing square #2. Upon being cued, participants stepped as fast as possible from Square #1 to #2, #3, #4, #1 and then back to #4, #3, #2, #1.

Appendix K: The Trail Making Tests Part A and Part B (TMT-A, TMT-B)

Trail – Making Tests

From the MOCA: Montreal Cognitive Assessment

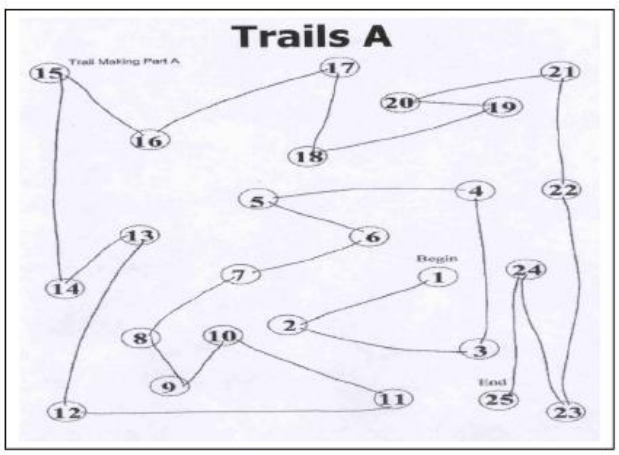
The Tests:

" The trail making tests A and B from the MOCA requires immediate recognition of the symbolic significance of number and letters, ability to scan the page continuously to identify the next number or letter in sequence, flexibility in integrating the numerical and alphabetical series, and completion of the these requirements under the pressure of time " (Reitan, 1992).

General Instructions

<u>Trail Making Part A:</u>

1. Provide the person with the sample trails A first. Once completed <u>correctly</u> then move on to the actual Trails A.
2. Instruct the individual to, "Please draw a line connecting the numbers 1, 2, 3, 4 etc. in order until you reach the end. Try to draw the lines as fast as you can."
3. If the person makes a mistake on the sample Trails A point it out to them and explain the error. i.e. "you skipped a circle; you started with the wrong number, etc." Repeat the sample Trails A with correction instructions until they have completed it correctly or it becomes evident that they are unable to do the task.
4. Once the sample trails A has been completed correctly give them the real Trails A. Repeat the instructions as given in step one.
5. Start timing the test as soon as the instruction is given to begin the test.



Trail Making Part B:

1. Provide the individual with the sample Trails B. Once they have completed it correctly then move on to the actual Trails B.
2. Instruct the individual that this second part of the test is slightly more difficult as it requires them to alternate between numbers and letters. Say "On this page are some numbers and letters. Begin at 1 and draw a line from 1 to A, A to 2, 2 to B, and so forth until you reach the end. Remember first you have a number, then a letter, then a number, and so on. Draw the lines as fast as you can."
3. If the person makes a mistake on the sample Trails B, point out the error and explain why it is incorrect. Repeat this procedure until the task is performed correctly or it becomes apparent they cannot complete the task.
4. After the person has completed the sample Trails B provide them with the actual Trails B. Repeat the instruction given in point 2. Timing begins as soon as the person is told to begin.
5. Be altert for mistakes. If the person makes a mistake point it out to them immediately, return the person to the last correct circle and continue the test from that point. Continue timing and record the number of errors made until task is completed

Scoring Trails A and B

1. Part A and B are scored separately. The score for each part is the number of seconds required to complete the task.
2. More than 1 error or scoring below the 10th percentile in the time (in seconds) taken raises concerns (50th percentile is given for comparison).
3. Generally time over 3 minutes or > 1 error is a failure.

Norms for Trails A and B by age (in seconds) and education

Age	Percentiles	Trails A* (education – no change)	Trails B ≤Grade 12	>Grade 12*
65-69	50 **10**	37 seconds **53**	86 **137**	68 **77**
70-74	50 **10**	38 **61**	101 **172**	84 **112**
75-79	50 **10**	46 **70**	120 **189**	81 **178**
80-84	50 **10**	52 **93**	140 **158**	128 **223**

Regional Geriatric Program of Eastern Ontario
Programme gériatrique régional de l'Est de l'Ontario
RGPs OF ONTARIO
GiiC geriatrics interprofessional interorganizational collaboration
CERAH Centre for Education & Research on Aging & Health

Curriculum Vitae

Name: Humberto Adolfo Omaña Moreno

POST-SECONDARY EDUCATION

Post-secondary Education and Degrees

Academic Institution	Degree	Subject	Thesis Title	Date Conferred
The University of Waterloo	BSc (Honours, co-op)	Kinesiology	--	2013
The University of Waterloo	MSc	Kinesiology (Stream: Neuroscience)	"The Influence of Dual-tasking on Cortical Responses Associated with Balance"	2017
The University of Western Ontario	PhD	Health & Rehabilitation (Stream: Physical Therapy)	"Exploring the Inter-Relationship Between Cognitive and Motor Function in People with Lower Limb Amputations"	*In progress*

Academic Employment

Position	Department	Institution	Date(s)
Graduate Research Assistant	School of Physical Therapy	The University of Western Ontario	Sep 2018 – Jul 2022
Graduate Teaching Assistant	School of Physical Therapy	The University of Western Ontario	Sep 2018 – Dec 2021
Graduate Teaching Assistant	Kinesiology	The University of Waterloo	2014 – 2016

Research Assistant	Kinesiology	The University of Waterloo	2013 – 2014
Research Assistant	Heart & Stroke Foundation Centre for Stroke Recovery	Sunnybrook Health Sciences Centre	2012 – 2013

DISTINCTIONS AND AWARDS

Distinction/Award	Awarding Organization	Date
"Top Doctoral Poster Presentation" (Category: Rethink)	2021 Health and Rehabilitation Sciences Graduate Research Conference	Feb 2021
Libin International Trainee Symposium Travel Award ($1,000)	The University of Calgary	Feb 2020
CIHR Doctoral Award Nomination	The School of Graduate and Postdoctoral Studies (SGPS), The University of Western Ontario	Nov 2019
Faculty of Health Sciences Graduate Conference Travel Award ($364)	The University of Western Ontario	Aug 2019
The Origins of Balance Deficits and Falls (OBDAF) Research Cluster's 2019 Wearable Sensors for Balance & Movement Summer Program Travel Award ($1,400)	Canadian MSK Rehab Research Network	Aug 2019
2019 RehabWeek Student Poster Competition, Second Place ($655) *Second author and mentor*	RehabWeek	Jun 2019
Institute Community Support (ICS) Travel Award ($500)	Canadian Institute of Health	May 2019

	Research	
ISPO Canada Student Poster Competition, "Best Abstract Award" ($1,000) *Second author and mentor*	International Society for Prosthetics and Orthotics Canadian National Society (ISPO)	Apr 2019
Graduate Studies Research Travel Award ($500)	The University of Waterloo	Sep 2015
Honorable Mention, Three Minute Thesis (3MT) Applied Health Sciences	The University of Waterloo	Feb 2015
Graduate Studies Research Travel Award ($500)	The University of Waterloo	Sep 2014
IEEE Canada Humanitarian Initiatives committee (HIC) Student Design Contest, Third Place ($300)	Institute of Electrical and Electronics Engineers (IEEE)	May 2011
Top 20 Outstanding Youth ($1,000)	Sears Canada	Jul 2008
Applied Health Sciences Entrance Scholarship ($500)	The University of Waterloo	Jul 2008

SCHOLARSHIPS AND RESEARCH FUNDING

Scholarship/Grant	Awarding Organization	Date
Mary Horney Fellowship in Rehabilitation ($30,000)	The Parkwood Institute Research-Student Endowment (PIR-SE), St. Joseph's Health Care Foundation	August 2022 – 2023
CIHR Planning and Dissemination Grant "Planning a National Limb Loss Registry" *Co-applicant*	Canadian Institutes of Health Research	Jul 2022 – 2023

Ontario Graduate Scholarship (OGS) ($15,000)	Government of Ontario	Sep 2021 – Aug 2022
Western Graduate Research Scholarship ($5,000)	The University of Western Ontario	Sep 2021 – Aug 2022
Ontario Graduate Scholarship (OGS) ($15,000)	Government of Ontario	Sep 2020 – Aug 2021
Joseph A. Scott Studentship in Mobility and Aging ($10,500)	The Parkwood Institute Research-Student Endowment (PIR-SE), St. Joseph's Health Care Foundation	Sep 2020 – Aug 2021
Western Graduate Research Scholarship ($5,000)	The University of Western Ontario	Sep 2020 – Aug 2021
Joseph A. Scott Studentship in Mobility and Aging ($10,500)	The Parkwood Institute Research-Student Endowment (PIR-SE), St. Joseph's Health Care Foundation	Sep 2019 – Aug 2020
Western Graduate Research Scholarship ($13,493)	The University of Western Ontario	Sep 2019 – Aug 2020
Western Graduate Research Scholarship ($13,493)	The University of Western Ontario	Sep 2018 – Aug 2019
Applied Health Sciences Graduate Experience Award ($2,516)	The University of Waterloo	Sep 2016 – Dec 2016
University of Waterloo Graduate Scholarship ($2,390)	The University of Waterloo	Sep 2015 – Dec 2015

Applied Health Sciences Graduate Experience Award ($4,674)	The University of Waterloo	Sep 2014 – Apr 2015

Articles in Peer-reviewed Journals

1. **<u>Omana H</u>**, Madou E, Divine A, Wittich W, Hill KD, Johnson AM, Holmes JD, Hunter SW. "The differential effect of first-time single-point cane use between healthy young and older adults". *The journal of Injury, Function, and Rehabilitation*. 2021 Dec;13(12):1399-409. Doi: 10.1002/pmrj.12559.
2. **<u>Omana H</u>**, Madou E, Montero-Odasso M, Payne M, Viana R, Hunter S. "The effect of dual-task testing on balance and gait performance in adults with type 1 or type 2 diabetes mellitus: A systematic review". *Current Diabetes Review*s. 2021 Jun 1;17(5):82-98. Doi: 10.2174/1573399816999201001203652.
3. **<u>Omaña H</u>**, Bezaire K, Brady K, Davies J, Louwagie N, Power S, Santin S, Hunter SW. "Functional Reach Test, Single-leg Stance Test, and Tinetti Performance-oriented Mobility Assessment for the prediction of falls in older adults: A systematic review". *Physical Therapy*. 2021 Oct;101(10):pzab173. Doi: 10.1093/ptj/pzab173.
4. Hunter SW, Divine A, **<u>Omana H</u>**, Madou E, Holmes J. "Development, reliability and validity of the Safe Use of Mobility Aids Checklist (SUMAC) for 4-wheeled walker use in people living with dementia". *BMC Geriatrics*. 2020 Dec;20(1):1-9. Doi: 10.21203/rs.2.22127/v1.
5. Cieslak G, **<u>Omana H</u>**, Madou E, Frengopoulos C, Viana R, Payne MW, Hunter SW. "Association between changes in subjective and objective measures of mobility in people with lower limb amputations after inpatient rehabilitation". *American Journal*

of Physical Medicine & Rehabilitation. 2020 Nov 1;99(11):1067-71. Doi: 10.1097/PHM.0000000000001490.

6. Hunter SW, Divine A, Madou E**, <u>Omana H</u>**, Hill KD, Johnson AM, Holmes JD, Wittich W. "Executive function as a mediating factor between visual acuity and postural stability in cognitively healthy adults and adults with Alzheimer's dementia". *Archives of Gerontology and Geriatrics*. 2020 Jul 1;89:104078.
7. Baker J, de Laat D, Kruger E, McRae S, Trung S, Zottola C, **<u>Omaña H</u>**, Hunter SW. "Reliable and valid measures for the clinical assessment of balance and gait in older adults with dementia: A systematic review". *European Journal of Physiotherapy*. 2020 Jul 2:1-2. Doi: 10.1080/21679169.2020.1788638.
8. Hunter SW, **<u>Omana H</u>**, Madou E, Wittich W, Hill KD, Johnson AM, Divine A, Holmes JD. "Effect of dual-tasking on walking and cognitive demands in adults with Alzheimer's dementia experienced in using a 4-wheeled walker". *Gait & Posture*. 2020 Mar 1;77:164-70. Doi: 10.1016/j.gaitpost.2020.01.024.
9. Fuller K, **<u>Omaña Moreno HA</u>**, Frengopoulos C, Payne MW, Viana R, Hunter SW. "Reliability, validity, and agreement of the short-form Activities-specific Balance Confidence Scale in people with lower extremity amputations". *Prosthetics and Orthotics International*. 2019 Dec;43(6):609-17. Doi: 10.1177/0309364619875623.
10. Hunter S, Divine A, **<u>Omana H</u>**, Wittich W, Hill K, Johnson A, Holmes J. (2018). "Effect of learning to use a mobility aid on gait and cognitive demands in people with mild to moderate Alzheimer's dementia: Part I -Cane.". *Journal of Alzheimer's Disease*. 2019 Jan 1;71(s1):S105-14. Doi: 10.3233/JAD-181169.

11. Hunter S, Divine A, **Omana H**, Wittich W, Hill K, Johnson A, Holmes J. (2018). "Effect of learning to use a mobility aid on gait and cognitive demands in people with mild to moderate Alzheimer's dementia: Part II – Wheeled walker". *Journal of Alzheimer's Disease*. 2019 Jan 1;71(s1):S115-24. Doi: 10.3233/JAD-181170.

Articles in Peer-reviewed Journals (ahead of print or accepted)

1. **Omana H**, Madou E, Hunter SW. (2022). "Beneficial effects on gait of 4-wheeled walker use in people with Alzheimer's dementia: A pilot study". *Journal of Alzheimer's Disease*. Accepted June 29, 2022. Reference #: JAD-220331R1.

2. **Omana H**, Frengopoulos C, Montero-Odasso M, Payne MW, Viana R, Hunter SW. "The association between balance confidence and basic walking abilities in people with lower limb amputations: A cross-sectional study". *Prosthetics and Orthotics International*. Accepted with minor revisions June 26, 2022. Reference #: POI-D-22-00041.

3. **Omana H**, Madou E, Divine A, Wittich W, Hill K, Johnson A, Holmes J, Hunter S. "The differential effect of first time 4-wheeled walker use on the gait of younger and older adults". *The journal of Injury, Function, and Rehabilitation*. 2021. Doi: 10.1002/pmrj.12700.

4. **Omana H**, Madou E, Montero-Odasso M, Payne MW, Viana R, Hunter SW. "The effect of dual-task testing on the balance and gait of people with lower limb amputations: A systematic review". *The journal of Injury, Function, and Rehabilitation*. Doi: 10.1002/pmrj.12702.

Submitted for Publication/under Review

1. Adebero T, **Omana H**, Somerville L, Lanting B, Hunter SW. "Impact of Prehabilitation on Functional Outcomes following Total Joint Arthroplasty for Osteoarthritis: A Systematic Review and Meta-analysis of Randomized Controlled Trials". *The journal of Injury, Function, and Rehabilitation*. Submitted July 18, 2022. Reference #: ARCHIVES-PMR-S-22-01055.