MEASUREMENT OF SYMPATHETIC NERVOUS SYSTEM ACTIVITY TO OBJECTIVELY ASSESS THE PERCEIVED CHALLENGE OF WALKING DURING COMPLEX WALKING TASKS AFTER STROKE

By

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To my family
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Abstract of Dissertation Presented to the Graduate School
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MEASUREMENT OF SYMPATHETIC NERVOUS SYSTEM ACTIVITY TO
OBJECTIVELY ASSESS THE PERCEIVED CHALLENGE OF WALKING DURING
COMPLEX WALKING TASKS AFTER STROKE

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Stroke-related impairments increase the perceived challenge of complex walking, as indicated by feelings of stress, anxiety, and fear of falling. A higher perceived challenge of walking has been associated with greater fall risk and avoidance of life-role activities. Perceived challenge is commonly measured by self-report which is susceptible to measurement bias and underreporting. Therefore, there is a need for an objective measure of perceived challenge to overcome limitations of self-report and to advance assessments of walking recovery. Increased sympathetic nervous system (SNS) activity is a physiological response (i.e., the fight or flight response) upregulated by feelings of stress, anxiety, and fear. Skin conductance is a well-accepted, non-invasive approach for robustly measuring SNS activity and could serve as an objective physiological probe of the perceived challenge of walking. Therefore, we tested the hypotheses that SNS activity would be significantly higher during lab-based complex walking compared to typical walking (Study 1); and during the walking phase of community-based complex tasks compared to rest (Study 2). Thirty one adults post-stroke performed various walking tasks including obstacles negotiation, dual-tasking,
and stairs in a cross-sectional study design. Skin conductance was recorded with a portable device and gait measures were assessed on an electronic walkway. Additionally, we also tested the hypothesis that SNS activity would be significantly reduced following a 12-week post-stroke gait intervention (Study 3). Nine adults post-stroke participated in an intervention to enhance gait coordination and function. Task-related and intervention-related differences in SNS activity were analyzed using repeated measures ANOVA. SNS activity was greatest for the most difficult walking tasks (e.g., obstacles negotiation, dual-tasking, and stairs) and lowest for easier tasks (e.g., typical walking, walking in dim lighting, walking on grass) (p<0.01). Consistent with this finding, participants exhibited cautious gait behaviors of decreased speed, shorter step length and wider step width during the difficult tasks (p<0.01). Following the intervention, SNS activity decreased especially for the most difficult tasks (obstacles negotiation and dual-tasking) (p=0.02). Collectively, these findings support that measurement of SNS activity is a robust approach for the assessment of post-stroke perceived challenge of walking, and intervention-induced reduction in SNS activity.
CHAPTER 1
INTRODUCTION

Stroke

The Incidence and Prevalence of Stroke in America

Stroke is a leading cause of long-term disability in the United States (American Stroke Association, 2017). Each year, approximately, 795,000 Americans experience a stroke, and of these, nearly 610,000 are first strokes, while 185,000 are reoccurring incidents (Centers for Disease Control and Prevention [CDC], 2017). The American Heart Association: 2017 Heart Disease and Stroke Statistics Report states that there are an estimated 7.2 million stroke survivors in the United States.\(^1\) While the risk of having a stroke increases with age, in 2009, it was reported that 34% of the stroke-related hospitalizations were in individuals less than 65 years of age.\(^2\) A combination of improved post-stroke life expectancy and increased incidence of ‘young strokes’ means that these individuals are likely to live longer with stroke-related disability which could markedly increase the social and financial burden frequently associated with stroke. It has been reported that stroke-related expenses cost the United States approximately $33 billion each year, in costs incurred from health care services, medications, and missed days of work (CDC, 2017).

Stroke Impact on Mobility Function

Stroke-related mobility impairments are a leading cause of long-term disabilities and pose an important clinical problem.\(^3\) Stroke impairments significantly decrease functional independence, severely restrict participation in meaningful activities pertaining to work and hobbies, and limit the fulfillment of important life-roles.\(^4\)
Collectively, poor mobility function after stroke has been associated with an overall decline in the quality of life, hospitalizations due to falls, and even early mortality.\textsuperscript{5,6}

Stroke-related mobility impairments are frequently characterized by poor postural control, impaired visuomotor coordination, decreased strength, impaired neuromuscular activation, abnormal muscle tone, decreased walking speed, asymmetrical step lengths, and increased gait variability.\textsuperscript{5,7,8,9} Collectively, these impairments increase the challenge experienced during walking after stroke, which may lead to higher levels of mobility-related anxiety, decreased balance confidence, increased fear of falling, and a greater risk for falls.\textsuperscript{5} Importantly, stroke impairments can lead to ‘cautious gait’ behaviors commonly characterized by decreased gait speed, shorter step lengths, and increased base of support.\textsuperscript{10} These behaviors are often counterproductive and can further increase the risk for falls. For instance, walking slowly with a shorter step length might interfere with the ability to quickly respond to unexpected changes in the walking surface or a sudden obstacle in the walking path, which could lead to loss of balance, and even a fall.

Poor mobility function and fear of falling may also lead to the avoidance of walking-related activities that are particularly challenging.\textsuperscript{11} Some factors that contribute to a greater perceived challenge during walking include the physical (i.e., strength, postural control) and cognitive (i.e., attention, planning) demands of the task, impaired motor and biomechanical control, higher levels of state/trait anxiety, and a prior poor task-related experience. For example, adults post-stroke may avoid stairs or uneven surfaces due to the greater challenge experienced during the performance of these tasks. Stroke-related impairments including decreased strength, impaired coordination,
poor postural control, impaired paretic muscle activation, could collectively increase the locomotor challenge. Likewise, individuals post-stroke might have poor balance and falls self-efficacy which could lead to higher levels of anxiety (i.e., state and/or trait anxiety) and fear of falling that further contributes to the task-related challenge. Similarly, a prior episode of loss of balance or fall on stairs/uneven surface could significantly add to the greater perceived challenge of walking. This is consistent with Shumway-Cook and colleagues\textsuperscript{12}, who reported that older adults with poor mobility function are more likely to avoid stairs and/or uneven surfaces, compared to their peers who are physically able. Negotiation of stairs requires adequate lower extremity strength and range of motion, and greater attention, visuomotor coordination, and postural control.\textsuperscript{13-16} Likewise, walking on uneven surfaces poses a challenge to attention, motor planning, visuomotor coordination, and the ability to quickly modulate gait patterns to adapt to the walking surface.

\textbf{Community Ambulation}

Community ambulation or ‘locomotion in environments outside the home’ is a very important part of everyday life.\textsuperscript{11} Preservation of community ambulation is essential for independent living and fulfilling significant life-roles pertaining to work and leisure.\textsuperscript{11,17,18} Likewise, a decreased ability to participate in community ambulation has been linked to an overall decline in the health status and quality of life, institutionalization, and early mortality.\textsuperscript{6,19,20}

\textbf{What is Community Ambulation?}

Community ambulation frequently involves the performance of activities of everyday life in complex environments involving stairs, slopes, and uneven surfaces such as those encountered in shopping malls, grocery stores, banks, restaurants, and
many more. Walking in a community environment is commonly integrated with functional task/s including walking in the mall while carrying a shopping bag, walking in a grocery store while pushing a shopping cart and trying to locate items from the shopping list, walking while having a conversation with a friend, or even walking while reading directions to a new restaurant.

The performance of community ambulation tasks can be especially challenging in noisy or distracting environments, and when factors such as time constraints, compliant or slippery walking surfaces, and fluctuations in weather and visibility also have to be considered. Some examples of these tasks include maneuvering around people in a busy and distracting shopping mall, crossing at an intersection before the ‘walk’ sign changes, walking on icy or slippery sidewalks, and walking in poor lighting conditions. Performance of walking-related tasks under these challenging conditions significantly increases the demands on the central and peripheral resources for attention, planning, decision making, visuomotor coordination, postural control and/or strength. For example, while crossing at a busy intersection an individual has to attend to their surroundings to avoid colliding with fellow pedestrians or any oncoming traffic. Similarly, individuals have to pay greater attention to their foot placements to avoid stumbling while walking on unpaved or slippery surfaces.

**Stroke Impact on Community Ambulation**

Restricted community ambulation is a severely disabling consequence of stroke-related impairments. The ability to walk outside one’s home is critical for independent living and is essential for the performance of everyday life activities, such as going to the place of work or shopping for groceries at the store. Approximately, 74.6% adults post-stroke report that being able to walk outside the home and in the
community is very important to them. However, only 50% of these individuals are able to successfully meet the demands of community ambulation tasks and engage in community walking activities. Of the stroke survivors who do engage in community walking activities, approximately 72% report that these activities are extremely challenging, and only 30% are satisfied with their post-stroke walking experience in the community environment.

**Domains of Community Ambulation**

Lerner-Frankiel and colleagues, Cohen and colleagues, and Shumway-Cook and colleagues were among the first to identify and describe domain-specific requirements for community mobility in older adults. Lerner-Frankiel and colleagues, and Cohen and colleagues, identified the mobility requirements for community ambulation pertaining to the domains of distance, time (i.e., temporal), and terrain (i.e., walking surface). Shumway-Cook and colleagues further expanded these domains and proposed a ‘person-environment-interaction’ framework with eight domains that capture an individuals’ interaction with the environment during the performance of community ambulation tasks. These domains include time constraints, distance, ambient conditions, terrain characteristics, external physical load, attentional demands, postural transitions and traffic density. More recently, Balasubramanian and colleagues have further developed this framework and proposed nine domains to capture walking adaptability in complex walking environments post-stroke. These domains include obstacle negotiation, temporal demands, cognitive dual-tasking, terrain demands, ambient demands, postural transitions, motor dual-tasking, physical load, and maneuvering in traffic.
Most researchers largely agree on the domain-specific requirements for community ambulation. For example, Shumway-Cook and colleagues\textsuperscript{12}, have proposed the ability to walk approximately 805 m (i.e., 1/2 mile) and climb stairs without assistance as an important criteria for successfully meeting the requirements of the distance and the terrain domains of community ambulation. Likewise, Lerner-Frankiel and colleagues\textsuperscript{18}, have suggested the ability to continuously walk a distance greater than 332 m, negotiate a 7 to 8 inch curb, and climb 3 steps and a ramp without holding on to handrails as the criteria for successfully negotiating the distance and the terrain domains. Cohen and colleagues\textsuperscript{17} reported that an ability to walk at least 360 m, and negotiate stairs and curbs as important criteria for the domains of distance and terrain. For the temporal domain requirements, both Cohen and colleagues\textsuperscript{17}, and Lerner-Frankiel and colleagues\textsuperscript{18}, have respectively reported the required walking speed of 73 m/min and 79 m/min to safely complete crossing the street at the stoplight. Interestingly, Shumway-Cook and colleagues\textsuperscript{12} reported that in their study, only 25% of the older adults with a disability could cross the street in the time allotted by the stoplight, whereas 100% of the adults without a disability were able to complete the same task within the allotted time. Perry and colleagues\textsuperscript{9} have reported that highest level of community ambulators post-stroke walk at the speed of 48 m/min, which is far less compared to the walking speed of healthy older adults who walk approximately at the speed of 80 m/min. This suggest that while the walking speed of individuals post-stroke might be sufficient to perform typical activities, their walking speed is not adequate for safely crossing the street within the time allotted at the stoplight.
The Perceived Challenge during Community Ambulation Varies by the Domain Complexity

The perceived challenge experienced during community ambulation varies by the domain-specific requirements, where certain domains are reported to be more complex and challenging than the others. Moreover, while individuals may be able to avoid certain domains, such as ambient conditions pertaining to bad weather or poor lighting, some domains such as terrain cannot be avoided completely. For instance stairs negotiation, which belongs to the terrain domain is commonly encountered in the community. Negotiation of stairs is also frequently cited as one of the most difficult tasks by community dwelling older adults. This is consistent with the demands of stair negotiation which places significantly higher demands on the cardiovascular and musculoskeletal systems, and requires integration of inputs from the somatosensory, visual and vestibular systems. Tinneti and colleagues conducted a survey of 272 reported falls and found that 75% of the falls on stairs in older adults occurred during stairs descent. In a review paper, Startzell and colleagues primarily attributed the higher incidence of falls on stairs to a significant decline in visual inputs including a decrease in depth perception and object recognition especially in poor lighting, a reduced ability to process visual information gathered from the surroundings and a limited span of visual attention across the field of vision. Other factors associated with falls on stairs include poor postural control, decreased sensory and proprioceptive feedback, and insufficient clearance of the swinging foot and the stair edge. Furthermore, adults with poor mobility function are also likely to alter their stair negotiation strategies which could further increase the risk for falls. For instance, these individuals might choose to descend down the stairs backwards. While this
strategy could decrease the demands on the musculoskeletal system, it also occludes the effective use of vision which is critical for safety on stairs.

Negotiation of obstacles is another feature that is commonly encountered in the community environment. While individuals may choose to go around taller or wider obstacles, objects such as small sticks or branches encountered on uneven paths could increase the risk of tripping and falling. Said and colleagues\textsuperscript{30} quantified the post-stroke deficits in obstacle negotiation by comparing the performance of individuals receiving inpatient stroke rehabilitation with age-matched healthy older adults. All participants were asked to step over three obstacle heights (1 cm, 4 cm, and 8 cm) and three obstacle widths (1 cm, 4 cm, and 8 cm), to simulate the obstacles frequently encountered in the community (e.g., uneven paths, electric cords, small sticks and branches) on two separate occasions. The taller obstacles were included to assess the ability to lift the leading and trailing limb for sufficient clearance, while the wider obstacles assessed the ability to take longer step lengths during obstacle negotiations. The obstacles were placed on a walkway and the participants walked a total distance of 80 m. While the participants were not allowed to use assistive devices during the testing sessions, they were allowed to visually and manually inspect the obstacles before engaging in the testing sessions. The testing was conducted in a well-lit environment with minimum distractions, and the obstacles were clearly visible to the participants. The attempt to cross the obstacle was considered unsuccessful if the obstacle was contacted by either the leading limb or the trailing limb and if assistance had to be given. For both occasions of testing, the authors recorded (on video) the choice of leading limb and the presence of any deficits pertaining to vision and post-stroke neglect. They reported
significantly higher number of falls related to obstacle negotiation in the stroke group (i.e., 54%), particularly while stepping over obstacles that were 8 cm in height (i.e., tall obstacle) or width (wide obstacle). About 33% of the participants post-stroke were reported to shuffle and take smaller steps before stepping over the obstacles. While the healthy older adults often chose to lead with the left leg, the participants post-stroke did not show a preference for the leading limb (i.e., paretic or non-paretic). Furthermore, the participants post-stroke showed greater inconsistencies with the choice of the leading limb during the two sessions.

The choice of leading limb is important for the successful negotiation of obstacles. The gait cycle encounters two single-limb support phases during obstacle negotiation. The first single-limb support phase occurs as the leading limb crosses over the obstacle, and this phase is considered to be the most destabilizing phase of obstacle negotiation. The second single-limb support phase occurs as the trailing limb clears the obstacles and is considered to be a comparatively more stable phase. Individuals post-stroke may choose to lead with the paretic limb and modify the limb trajectory and placement using visual feedback. This would also allow the individuals to use the non-paretic stance limb for greater stability. However, leading with the paretic limb requires adequate range of motion and strength to achieve foot clearance. Likewise, choosing to leading with the non-paretic limb increases the stability demands on the paretic stance limb. Furthermore, stroke-related somatosensory deficits and lack of visual guidance may increase the difficulty associated with achieving clearance of the paretic trailing limb.
The ability to meet the demands of the frequently encountered domains during community ambulation can differentiate the physically able individuals from those with a disability. Shumway-Cook and colleagues\textsuperscript{12}, used psychometric measures (e.g., health status questionnaire), performance measures (e.g., the Berg Balance Scale, the Tinetti Mobility Index, and the Short Physical Performance Battery), community activity/ trip logs and observational analysis (e.g., video recordings) to identify the domains that separated physically able older adults from those with a disability. Importantly, they reported that the physically able older adults could successfully maintain an optimal walking speed while crossing the street at a stoplight (i.e., temporal domain), carry items such as packages while walking (i.e. physical load domain), successfully negotiate stairs, curbs, slopes, and uneven surfaces (i.e., terrain domain) and maintain dynamic postural control, for example, while changing the direction of walking; bending below knee height to pick an object; or reach beyond the arm length (i.e., postural transition domain).

Shumway-Cook and colleagues\textsuperscript{12} also reported that 64% of the older adults with a physical disability used an assistive device, such as a walker or a cane during community ambulation. The use of assistive devices during community ambulation could add to the locomotor challenge of complex walking tasks.\textsuperscript{31} For instance, the use of assistive devices often involves lifting and advancing the device in synchrony with the walking pattern, which increases the demand on the attentional resources as well as requires strength and coordination. The use of assistive devices could also interfere with the normal pattern of walking and slow down individuals during tasks that have a time constraint such as crossing the street at the stoplight (i.e., temporal domain).
Furthermore, the individuals have to ensure that their device does not get caught with environmental objects, which could increase the risk of tripping and falling. Likewise, the use of devices such as the standard walker has been reported to delay reaction time, which could lead to adverse outcomes in the event of a sudden destabilizing perturbation.\textsuperscript{32} For example, the use of a walker could prevent the individual from using their arms or stepping to recover balance. Finally, the use of an assistive device is functionally restrictive as it limits the ability to dual-task by carrying items such as grocery bags during community ambulation.

**Factors Impacting Safe and Successful Community Ambulation**

**Mobility-related anxiety and fear of falling during walking**

Individuals with poor mobility function often experience a greater challenge during walking in complex community environments. Persistence of a higher perceived challenge during walking could be a significant source of stress, mobility-related anxiety, and fear of falling during walking. For instance, Gage and colleagues\textsuperscript{33} have reported differences in how older and younger adults attend to the control of walking. During walking, younger adults pay greater attention to the relatively unstable single limb support phase of the gait cycle compared to the double limb support phase which is more stable since both the feet are in contact with the walking surface. This phase-dependent allocation of attention is not observed in older adults.\textsuperscript{34} Older adults are often anxious and fearful about losing their balance during walking and this anxiety and fear has been reported even in adults without a previous history of falls.\textsuperscript{35,36} It is therefore possible that allocating equal amount of attention to each phase of the gait cycle could be a strategy to counter the anxiety and fear associated with falls. Moreover, consistent with this observation, several authors have reported ‘cautious gait behaviors’ including
decrease in walking speed, shorter stride length, wider step width, and increase in double-limb support phase of the gait cycle in older adults.\textsuperscript{37,38} This change in walking pattern could be a strategy to minimize the task-related attentional demands as well as the fall risk, by decreasing the amount of time spent in single limb support.

Another interesting difference is how older adults with mobility-related anxiety and fear of falling negotiate the obstacles placed in their walking path. Compared to healthy young adults, anxious older adults have been reported to look at the obstacles in their walking path earlier and for a longer duration before actually stepping over them.\textsuperscript{39} Observing the obstacles for a longer duration could be an attempt to focus their attention on the objects they perceive as a threat to postural control.

Young and colleagues\textsuperscript{40} reported that anxious older adults who are at a higher risk for falls tend to look away prematurely from the stepping target or obstacle compared to their peers who are at a lower risk for falls. Shifting the visual gaze and attention prematurely during the swing phase of the gait cycle (i.e., during stepping over) can decrease foot clearance, stepping accuracy, and increase the risk for falls. This premature shifting of gaze, and inappropriate prioritization of the other obstacles in the walking path, has been attributed to an increase in mobility-related anxiety due to greater task complexity (i.e., presence of other obstacles) and a higher perceived threat to postural stability.

**Increased attention to internally-generated movement patterns**

Higher levels of mobility-related anxiety has been associated with increased attention to the monitoring and controlling of internally generated movements, such as foot placement on an uneven walking surface. The constant monitoring of movements could disrupt the walking pattern, which is largely automated with only occasional
demands on attention. McNevin and colleagues\textsuperscript{41} proposed the ‘constrained action hypothesis’, according to which paying greater attention or trying to consciously control movement patterns constrains the motor system by disrupting the automatic processes that normally control these movements.\textsuperscript{42} This increased attention to movement patterns interferes with the ability to attend to the immediate environment for potential threats and motor planning to successfully adapt the walking pattern and meet the task demands. Ellmers and colleagues\textsuperscript{43} reported that the constant monitoring or controlling of movements can interfere with effective gaze or visual search behavior during walking. An effective visual search is critical for scanning the environment for potential hazards as well as to modify and accomplish safe walking without tripping or falling. Furthermore, Wong and colleagues\textsuperscript{44}, reported increased monitoring of movement patterns in older adults who have a history of falls (i.e., elder fallers) compared to the non-fallers.

**Mobility-related self-efficacy and balance confidence**

Self-efficacy is a concept developed by the psychologist Albert Bandura\textsuperscript{45-48}, and is defined as ‘one’s belief in one’s ability to succeed in specific situations or accomplish a task.’ Self-efficacy is the perceived ability, which to a large extent, is not dependent on the actually ability to accomplish a task, and since its conception, has been widely applied to rehabilitation outcomes.\textsuperscript{49} Balance self-efficacy or balance confidence is a concept that is closely-related to self-efficacy, and refers to the perceived ability to perform a specific-activity, such as negotiate stairs or walk on uneven surfaces, without losing balance or becoming unsteady.\textsuperscript{50} Several authors have reported a strong association between self-efficacy and participation in life-roles after a stroke.\textsuperscript{51,52} Higher levels of mobility self-efficacy and balance confidence have been frequently associated
with greater engagement in challenging activities such as stairs negotiation.  

Likewise, lower levels of self-efficacy and poor balance confidence have been associated with avoidance of stairs negotiation, even though individuals might have sufficient musculoskeletal capacity to accomplish the task. Furthermore, both Manning and colleagues, and Rosengren and colleagues have reported that higher mobility self-efficacy during walking is associated with an increase in the walking speed and an improved control of walking. In contrast, low self-efficacy has been associated with cautious walking behaviors including slower walking speeds and shorter step lengths that are associated with higher levels of mobility-related anxiety, fear of falling, and an increased risk for falls.

The importance of self-efficacy during community ambulation has been highlighted in several studies. For instance, Lord and colleagues examined the factors that are important for community ambulation in 113 healthy, community dwelling older adults. Factors including balance confidence (measured by the Balance Evaluation Systems Test and the Activities-specific Balance Confidence Scale), cognitive functions (verbal fluency measured by the Controlled Oral Word Association Test), executive functions (attention measured by the Test of Everyday Attention and the Trail Making Test), anxiety and depression (measured by the Hospital Anxiety and Depression Test), and fatigue (measured by the Multidimensional Fatigue Inventory) were examined in this study. Additionally, gait variables including, gait speed, stride length, and double support time were also examined. The authors conducted a factor analysis which examined the contribution of four factors to community ambulation. These factors were movement control, self-efficacy, executive function, and cognitive-motor interference.
during dual-task gait. The authors determined that movement control (measured by balance confidence, gait speed and stride length), self-efficacy (measured by fear of falling, anxiety, mental and general fatigue), and executive function (measured by attention) were significant contributors to successful community ambulation. The authors noted that cognitive-motor interference (measured by the double support time during dual-task walking with an auditory stimulus) did not contribute as significantly to the model, possibly because this variable was tested indoors over a relatively shorter walking distance (10m) compared to the other gait parameters which were measured while walking outdoors. The findings of this study suggest that factors beyond the control of movement, such as self-efficacy, contribute significantly to successful community ambulation. Self-efficacy levels should be taken into consideration during assessments of walking impairment and while designing interventions that target rehabilitation of walking.

Likewise, a study by Robinson and colleagues\textsuperscript{60} highlighted the importance of balance and falls self-efficacy in increasing engagement in community-walking activities. In this study, the authors examined the association between the subjective and objective measures of participation in community ambulation in 50 adults post-stroke. Additionally, they also examined the association between personal factors and participation in community ambulation. Subjective measures of participation included self-reported perceived degree of difficulty in walking (measured by the MOSES questionnaire) and satisfaction with community ambulation (measured by items modified from the MOSES questionnaire). Objective measures included self-reported frequency of community trips and walking-related activities (recorded using a Trip
Activity Log), and the number of steps walked per day. Several personal factors including balance self-efficacy (measured by the Activities-specific Balance Confidence Scale) and fall self-efficacy (measured by the Swedish version of the Falls Efficacy Scale) and the importance of walking were also measured. The authors reported an overall weak association between the subjective and objective measures of participation, which is consistent with previous reports of a lack of association between the subjective self-reported and objective physiological measures. Moreover, Robinson and colleagues reported a lack of association between the number of steps taken per day, and the perceived satisfaction and difficulty experienced during community ambulation. Consistent with the findings of Lord and colleagues, self-efficacy related to balance and falls was found to be significantly associated with the measures of participation in community ambulation. Furthermore, the authors reported that individuals with higher levels of balance and fall self-efficacy reported greater satisfaction with community walking, reported a greater frequency of walking-related activities and had a lower perceived difficulty of walking. These suggest that rehabilitation interventions to increase engagement in community ambulation should focus on increasing balance and fall self-efficacy as these factors can influence the perceived challenge of walking and participation in walking related activities.

A significant association has been observed between balance self-efficacy and community reintegration. Pang and Eng examined the determinants of balance and mobility performance, and accidental falls in 39 community dwelling chronic stroke survivors with low hip bone mineral density which increased their susceptibility to fractures. They measured balance, mobility, strength of the lower limb, spasticity, falls-
related self-efficacy and recorded the history of falls experienced in the past 12 months to identify the ‘fallers’. Balance and mobility were assessed by the Berg Balance Scale, Timed-Up and Go Test, Timed stair climbing, and the 6 Minute Walk Test. Falls-related self-efficacy was assessed by the Activities-specific Balance Confidence Scale. Lower limb strength was assessed using a dynamometer and spasticity was assessed using the Modified Ashworth Scale. Seventeen of the participants were identified as fallers based on the history of falls. Examination of the characteristic differences between the fallers and non-fallers revealed that the fallers had a relatively lower falls-related self-efficacy score (p=0.08) The authors conducted regression analyses and found that falls-related self-efficacy was independently associated with performance on the balance and mobility tests. They reported that performance on balance and mobility tests was not a significant predictor of falls. However, falls-related self-efficacy was found to be a significant predictor of falls, where individuals with a score of ≤ 80/100 on the Activities-specific Balance and Confidence scale were at a higher risk for falls. These findings suggest that clinicians should consider self-efficacy levels related to falls and balance confidence in addition to the balance and mobility tests during the assessments of fall risk.

Balance self-efficacy is an important determinant of achieving independent community ambulation after stroke. Durcan and colleagues examined the association of multiple factors including age, medications, use of assistive devices, gait speed and balance self-efficacy with independent community ambulation in 40 community dwelling older adults post-stroke. They administered several assessments including the level of independence during community ambulation ranging from 1 (unable to walk outside) to
4 (independent community walkers) measured by the Community Ambulation Questionnaire; gait speed (10 Meter Walk Test); dynamic balance during walking (Timed-Up and Go); perceived balance confidence (Activities-specific Balance Confidence Scale); anxiety and depression (Hospital Anxiety and Depression Scale); and executive function (Trail-Making Test-Part B). They found that individuals with higher scores for gait speed and balance self-efficacy/confidence were more likely to be independent community ambulators (i.e., Level 4 on the Community Ambulation Questionnaire). On further examination using multivariate logistic regression, the authors found that balance self-efficacy/confidence was the only variable that was independently associated with higher levels of community ambulation (i.e., independent community ambulators). This finding is consistent with the reports of Pang and colleagues who reported that balance self-efficacy is an independent predictor of community reintegration in older adults after a stroke. The observation that neither gait speed nor dynamic balance could independently predict independence in community ambulation further suggests that community ambulation cannot be determined by the underlying physical abilities alone. In fact, this observation is in agreement with the reports of Lord and colleagues and Schmid and colleagues. Lord and colleagues reported that in spite of being able to walk independently and scoring highly on the measures of mobility function, approximately one-third of the adults post-stroke do not regain the ability to independently engage in community ambulation. Schmid and colleagues reported that balance self-efficacy, and not gait speed or walking capacity, was independently associated with activity and participation after a stroke. As discussed earlier in the chapter, community ambulation often requires walking in an unpredictable
environment while simultaneously attending to wide range of task demands. Therefore, in agreement with previous findings community ambulation cannot be determined in isolation by physical attributes such as strength and the gait speed.\textsuperscript{52,59,64}

**Subjective Assessments of Self-efficacy, Fear of Falling, and Fear Avoidance**

This section provides a brief overview of the psychometric measures commonly used to assess self-efficacy in the context of falls and balance confidence, the perceived ability to control/manage falls, and activity restrictions due to fear of falling and fear avoidance. Falls self-efficacy is assessed with the Falls Efficacy Scale. Balance confidence is assessed with the Activities-specific Balance and Confidence Scale. The perceived ability to control or manage falls is assessed by Perceived Control over Falling, and the Perceived Ability to Manage Falls and Falling questionnaires. Finally, lower self-efficacy and poor balance confidence can lead to the avoidance of some domains of community ambulation that are perceived as more challenging than the others. Activity restriction due to fear of falling and fear-avoidance are assessed by the Survey Of Activities And Fear Of Falling In The Elderly (SAFE) and the Environmental Assessment Of Mobility Questionnaire (EAMQ)

**Falls Efficacy Scale**

Tinetti and colleagues\textsuperscript{65} developed the Falls Efficacy Scale (FES) to assess the fear of falling in older adults. FES measures the fall-related self-efficacy or self-confidence in the ability to perform everyday life activities without falling. The FES has 10 questions that assess fall-related self-efficacy during the performance of everyday activities such as walking around the house, answering the door or telephone, or reaching into cabinets or closets, and has been reported to be a good measure of fall-related self-efficacy in frail older adults.\textsuperscript{66} Higher functioning older adults have been
shown to demonstrate a ceiling effect since the activities on the scale are comparatively less challenging for them.67 The FES is scored using an ordinal scale ranging from 1 (very confident) to 10 (not confident at all), and the cumulative scores range from 0 to 100. The FES score ≥70 indicates a fear of falling. FES is a versatile scale which has been widely modified to quantify the fear of falling in community dwelling older adults (using the modified version of FES)68 and in clinical populations, for example, post-stroke (using the Swedish version of the FES (i.e., FES[S])).69 The FES[S], in particular, is more suitable for assessing fall-related self-efficacy in individuals post-stroke with moderate to low mobility function. The FES[S] is a 13-item activity questionnaire that consists of 10 activities from the FES developed by Tinneti and colleagues65, and 3 additional activities, including, getting in and out of bed, grooming, and toileting. The additional items were included in the FES[S] since these activities are often challenging post-stroke. Similar to the FES, FES[S] is scored based on 10 point visual analog scale (0 = not confident at all, 5 = fairly confident, 10 = completely confident). Hellstrom and Lindmark69 reported a high test-retest reliability of the FES[S] administered on two separate occasions (intraclass correlation coefficient (ICC) = 0.97) in 30 individuals post-stroke. The ICC for personal ADL scores (items 1-6) was 0.93 and for the instrumental ADL scores (items 8-13) was 0.97. Overall, ICC for individual items on the scale ranged from 0.76 to 0.97.

**Activities-specific Balance Confidence Scale**

Powell and Meyers50 developed the Activities-specific Balance Confidence Scale (ABC Scale) to assess balance confidence in higher functioning older adults. Similar to the FES, this 16-item questionnaire assesses an individual’s confidence in their ability to perform everyday activities without losing balance or becoming unsteady. The ABC
Scale includes walking-related tasks performed in a community environment, for example, walking in a crowded mall, riding an escalator, walking across the parking lot, and performing postural transitions at various levels (i.e., above, at, and below the eye level). To avoid any inconsistency in the interpretation of the questions, the ABC Scale was developed to be more context-specific compared to the FES Scale. For example, the ABC Scale assesses balance confidence during reaching above eye level while rising to toes. In contrast, the FES assesses confidence during reaching into the cabinets/closets, where the task is more susceptible to subjective interpretation. For each task, the individuals are asked to assign a percentage of confidence ranging between 0% (no confidence) to 100% (complete confidence). The ABC Scale score of ≤67% is indicative of low perceived balance confidence and a risk for falling.  

**Perceived Control over Falling and Perceived Ability to Manage Falls and Falling**

Lawrence and colleagues developed the Perceived Control Over Falling Scale which has 4 items that assess an individual’s ability to control the environment, their mobility, and the ability to prevent a fall. The 5-point response format ranges from strongly disagree to strongly agree. Additionally, Lawrence and colleagues also developed the Perceived Ability to Manage Falls and Falling, which is a 5-item scale that assesses an individual’s beliefs regarding managing a fall including being able to get up after a fall or being able to protect themselves if they do fall. The authors reported that individuals with a higher perceived ability to manage falls also demonstrated a lower fear of falling.

**Survey of Activities and Fear of Falling in the Elderly**

Lachman and colleagues developed the Survey of Activities and Fear of Falling in the Elderly (SAFE) to assess activity levels, the fear of falling, and associated
consequences such as activity restriction in older adults. The survey examines activities of daily living (e.g., go to the store), instrumental activities of daily living (e.g., prepare a simple meal, take a tub bath), mobility tasks (e.g., go to a crowded place, walk several blocks), and social activities (e.g., visit a friend or relative). For each task, the participant is asked six questions addressing activity level, fear of falling, and activity restriction by comparing to the frequency of doing that task 5 years ago. Activity level is scored as 0 (for no and non-response) and 1 (yes); the scoring of Fear of Falling is such that 0 = no fear at all and 3 = very worried; and Activity restriction is scored based on the number of activities that are reported as doing less compared to 5 years ago (ranging between 0 to 11). SAFE has been reported to differentiate the levels of fear, and also between individuals who do / do not restrict their activity level due to a fear of falling.

Environmental Assessment of Mobility Questionnaire

Shumway-Cook and colleagues\textsuperscript{72} developed the Environmental Aspects of Mobility Questionnaire (EAMQ) which is a self-report measure that assesses the effect of the physical environment on community mobility. The questionnaire includes 24 features of the physical environment which are grouped into eight dimensions, including distance, time constraints, ambient conditions, terrains, physical load, postural transition, attention, and density/crowded places. Individuals report the frequency of encounter and avoidance behavior using a five point ordinal scale with responses including never, rarely, sometimes, often, and always. The responses never and rarely are combined and coded as not encountered or avoided, and the remaining (i.e., sometimes, often, and always) responses are combined and coded as encountered or avoided. The overall percentage of features encountered and avoided for each physical dimension is assessed. For example while assessing encounters Shumway-Cook and
colleagues\textsuperscript{72} reported that more than 70\% of physically able older adults encountered one flight of stairs in their trip to the community compared to 35\% of the disabled older adults. Similarly, while assessing avoidance they reported that 58\% of the physically able older adults and 100\% of the older adults with physical disability avoided carrying a physical load.

**Limitations of Subjective Self-report Assessments**

The perceived challenge of walking in healthy individuals and clinical populations is often measured indirectly, by subjective assessments of balance and falls self-efficacy, as discussed in the previous section. Even the commonly used assessments of perceived exertion, such as the Borg Rating of Perceived Exertion Scale, are based on self-report. Subjective self-report measures are widely used in research and are valuable because they are standardized, inexpensive, easy to administer, and often time-efficient.\textsuperscript{65,73} However, the self-report approach is also extremely susceptible to subjective measurement bias which limits the scope of interpretation and quantification of the responses.\textsuperscript{74,75} Some factors that commonly induce subjective measurement bias are discussed in this section.

**Demand Characteristics**

This is a common form of response bias where participants alter their responses or behaviors to comply with the investigators and the ongoing experiment. For instance, a participant may alter their responses based on their interpretation of the purpose of the experiment, or adopt certain behaviors that they believe would benefit the experimental paradigm. A response bias occurs because participants alter their responses to please the investigator.\textsuperscript{76,77}
Introspective Ability

A participant may inadvertently provide an inaccurate response because they might lack introspective ability to correctly interpret the question and provide an accurate response.

Social Desirability Bias

A participant may deny their undesirable traits, and adopt traits that they perceive as being socially desirable. For instance, a participant may over-report positive behavior or under-report negative behavior. 77,78

Response Shift

A participant’s self-evaluation may change as a result of several factors including a change in the participant’s internal standards of measurement (i.e., scale recalibration), a change in the participant’s values/beliefs, or a redefinition of the target construct (i.e., reconceptualization). 79

Acquiescence Bias

A participant may demonstrate a tendency to agree with all the items on a self-report questionnaire. Agreeing with every item on a questionnaire could lead to contradictory responses, which are difficult to interpret. 77

Response Style Effects

A participant’s personality traits may systematically influence their responses to the items on a questionnaire. 77,80 For instance, the participant may have a tendency to select the extreme scores of a rating scale (e.g., choosing only 1s or 10s on a 10-point scale) regardless of the specific item content. Conversely, the participant might consciously refrain from choosing extreme responses and demonstrate a tendency to
choose scores that fall in the middle of the scoring scale (i.e., 5s or 6s on a 10-point scale). This form of a response could lead to a central tendency bias.

**Ordinal Measures**

The items on self-report questionnaires are often scored on an ordinal scale. While ordinal data provides information about the order of ranking, it does not inform about the distance between the ranks. Consequently, ordinal data is not particularly useful for capturing the magnitude of responses. For example, the Likert scale which is commonly used for scoring questionnaires assumes that the distance between each successive item category is the same.

**Dichotomous Responses**

Self-report questionnaires often follow a dichotomous response design (i.e., yes/no response format). While this form of response provides a broader sense of impairments, they do not necessarily capture the actual level of impairment. For instance, items for assessing activity restriction might limit the response choices regarding the performance of a specific activity to rarely and often, or less than 5 times/week and more than 5 times/week. Based on this format of scoring, individuals who might perform the activity once/week would receive the same score as an individual who performs the same activity 4 times/week.

**Individual Differences**

Individual factors such language proficiency, cultural norms, and the level of literacy may impact a participant’s ability to understand and accurately interpret the assessment items on a self-report questionnaire.

For these reasons, the development of an objective measure of the perceived challenge of walking could supplement the self-report assessment or even serve as an
alternative. The measurement of the sympathetic nervous system activity is one such novel approach that could greatly enhance the assessment of a higher perceived challenge of walking frequently associated with increased task-related physical and/or cognitive demands, mobility-related anxiety, poor balance and falls self-efficacy. The following section of this dissertation discusses prior work\textsuperscript{81,82} that supports the measurement of the sympathetic nervous system activity to assess the perceived challenge during walking in healthy individuals and community dwelling older adults. Next, we propose to further advance the measurement of the sympathetic nervous system activity by testing the feasibility of this approach to assess the perceived challenge during walking in the post-stroke neurologic population.

**The Sympathetic Nervous System**

**Autonomic Responses**

The autonomic nervous system plays an important autoregulatory role in the maintenance of homeostatic functions including body temperature, heart rate, blood pressure, and gut motility. It is also responsible for the upregulation of these homeostatic functions to successfully meet the behavioral demands.\textsuperscript{83} The sympathetic nervous system (SNS) is one of the two main divisions of the autonomic nervous system. The other division is the parasympathetic nervous system. SNS has an ‘excitatory’ effect which balances the parasympathetic ‘inhibitory’ functions of ‘rest and digest’. The SNS has an important role in priming the body for action and the execution of movements, as discussed in the following section.

**The Sympathetic ‘Flight or Flight’ Response**

The sympatho-adrenal ‘fight or flight’ response is a primitive physiological response that is triggered by stress inducing and/or fear evoking situation that are
perceived as threatening or challenging. SNS activity can be increased by tasks demands that are both physically and/or cognitively challenging. Highly stressful or challenging situations can lead to the upregulation of neuroendocrine systems causing an increase in the levels of stress hormones including epinephrine and norepinephrine, cortisol, growth hormone, and prolactin. SNS activation is associated with increased heart rate, respiratory rate, blood pressure, sweating, and gastrointestinal and bladder activity, and diversion of blood flow away from the gut and towards the muscles. These regulatory changes ensure that the individual is able to respond quickly and meet the task demands, for example, a need for greater walking speed, strength and agility.

In particular, from an evolutionary perspective, the SNS activation of sweating has a protective role. Adelman and colleagues studied the role of the SNS activation of the sweat glands present on the paws of various animals in stress inducing situations. They reported that the activation of these sweat glands (and sweating on the paws) in animals is a stress response to increase mechanical friction and prevent the animal from slipping while running, climbing, and fleeing away from a stressful situation. However, while moderate levels of SNS activation is helpful in directing attention to the threat, and preparation for task-appropriate response, higher levels of activation can also lead to disorganized and detrimental behaviors.

Emotional Sweating

Neurophysiological Control of Emotional Sweating

Sweating is controlled by the cholinergic sympathetic activation of the sweat glands. In particular, palmar and plantar sweating serves as an important index of emotional behavior. ‘Emotional sweating’ in humans is characterized by the sympathetic activation of the palmar and plantar sweat glands in response to situations causing pain,
anxiety, fear, and increase in physical and/or cognitive demands. The pathways triggering emotional sweating are relatively different from those modulating sweating to maintain thermoregulation. Emotional sweating is triggered by the activation of the parts of the limbic system including the insula, amygdala, hippocampus, and cingulate gyrus. The signals then travel through the brainstem and activate the preganglionic sympathetic neurons. This response to threat and/or fear is very similar to the increased sweat gland activity on the paws of animals in stressful situations reported by Adelman and colleagues. Unlike emotional sweating, thermoregulation is primarily controlled by the hypothalamus through the sympathetic distribution of the autonomic pathways. An increase in the core or skin temperature activates the thermoreceptor afferent fibers and the brain centers responsible for thermoregulation. Thermoregulatory signals originating from the posterior hypothalamus travel via the pontine tegmentum and the medullary raphe regions to the intermediolateral column of the spinal cord.

The post-ganglionic pathways of thermoregulatory and emotional sweating are similar. In the spinal cord, the neurons emerge from the ventral horn and synapse in the sympathetic ganglia. The postganglionic non-myelinated C-fibers pass through the gray ramus communicans, combine with the peripheral nerves, and travel to the sweat glands where the nerve fibers 'entwine around' the periglandular tissue of the sweat gland. Sweat gland activity is then triggered by the postganglionic sudomotor nerves. Each sweat gland is innervated by multiple sudomotor fibers and each sudomotor fiber innervates a skin area of about 1.28 cm². The average firing rate of these fibers is 0.62Hz and the collective firing of multiple fibers at the same time generates an impulse, which can be recorded as an electrodemal response.
Measurement of sweat gland activity to assess the magnitude of SNS activation has an important advantage. Physiological variables such as heart rate, blood pressure, and respiration are controlled by both the sympathetic and parasympathetic branches of the autonomic nervous system. As a result, these variables reflect contributions from both the systems of control. Measurement of sweat gland activity affords the ability to investigate the sympathetic contribution to the autonomic nervous system and could serve as a valuable physiological probe for monitoring the magnitude of SNS activity.83

**Eccrine Sweat Gland Activity is a Measure of Emotional Sweating**

There are three types of sweat glands in humans, eccrine, apocrine, and apoeccrine glands.88 Of these, the eccrine sweat glands are highly sensitive to psychological stimuli such as anxiety, worry, or fear, and are of particular interest. These sweat glands are coiled, tubular structures extending from the epidermis to lower dermis and secrete water, electrolytes, and mucin. Furthermore, these glands have smaller secretory coils than the other types of sweat glands (e.g., apocrine glands) and the excretory tube of the glands expel sweat directly to the surface of the skin. Eccrine sweat glands are very highly concentrated on the palms, soles, forehead, forearms, trunk and lower limbs as opposed to the apocrine glands which predominantly populate the axillary and perianal regions.89

**Emotional Sweating is Largely Independent of Ambient Temperature**

Kerassidis90 demonstrated that palmar sweating can serve as an objective measure of the emotional state of an individual and can occur independently of the ambient temperature. Palmar and plantar sweating in response to emotional or psychological stimuli has also been reported in the works in Quinton91 and Sato87,92. Kerassidis90 assessed SNS activation by measuring the secretion of sweat from the
forehead, chest, left palm and sole of healthy individuals. Sweating was measured as the participants performed various physical and cognitive tasks including pedaling on a stationary bicycle, mental arithmetic, and relaxing quietly in an armchair. The room temperature during these tasks was set at 55°C (for 9 participants) and 60°C (for 8 participants). Kerassidis observed that the amount of plantar and palmar sweat secretion was significantly less (i.e., almost negligible) compared to the forehead and the chest as the participants relaxed in a high temperature environment. Importantly, a subset of participants with hyperhidrosis (i.e., excessive sweating) also showed a similar finding. Interestingly, the amount of plantar and palmar sweating increased significantly as the same subset of hyperhidrotic participants performed mental arithmetic, when the ambient temperature was decreased to 24°C. This suggests that sweating in the palms and soles is independent of the environmental temperature when an individual is in a relaxed state. This is consistent with prior reports\textsuperscript{93} that sweating in response to high ambient temperature is controlled by the hypothalamus, whereas emotional sweating is mediated, in part, by the premotor cortex.\textsuperscript{94} Furthermore, the region-specific differences in sweating also suggest that sweat glands on the palms and soles could be activated by neural mechanisms that are different from those for the forehead and the chest regions. Finally, the authors reported a moderate increase in palmar sweating in the participants who performed the cycling task, the mental arithmetic task, and then relaxed in a high temperature environment for 3-4 minutes. These findings suggest that palmar sweating is only moderately influenced by the ambient temperature when the individual is exposed to greater physical or cognitive effort.
Emotional Sweating in New Born Infants

The phenomenon of emotional sweating has been demonstrated even in new born infants. Newborn infants are limited in their ability to express emotionally distressing experiences such as pain or discomfort. Therefore, Harpin and Rutter\textsuperscript{95} proposed the measurement of palmar sweat gland activity in infants to provide an objective, quantifiable measure of physiological arousal, and monitor the emotional state of newborn infants, even when the responses are not overtly expressed (e.g., infants in intensive care units might not cry due to sedation but may still experience pain). They measured palmar water loss by measuring the rate of evaporation of water from the skin of 124 infants. Additionally, they also measured the palmar water loss in 22 infants, in response to heel prick, a procedure used for routine blood sampling. The change in palmar water loss from a resting state of sleep or being quiet, to crying in response to the heel prick, and then calming down again was recorded. They reported that mature infants (i.e., gestational age of at least 37 weeks), in particular, showed a wide range of palmar water loss, which was the lowest during sleep and highest during crying. This is in contrast to sweating in infants to maintain thermoregulation. Sweating in response to higher ambient temperatures has been reported in infants aged 2 weeks, independent of the gestational age. The loss of palmar water in response to emotional arousal was more prominent as the infants grew older. This is consistent with the reports that infants of a gestational age of 43 weeks, show emotional sweating comparable to that in anxious adults.

**Historical Overview of Electrodermal Recordings**

While the term electrodermal activity was introduced by Johnson and Lubin in 1966, the earliest recordings of biosignals from the skin can be traced to the
experiments by the German researcher, DuBois-Reymond in 1849. In these early experiments, DuBois-Reymond observed that the skin was electrically active, and reported a flow of current between the voluntarily contracting limb and the relaxed limb when the research participants immersed their hands and feet into a zinc sulfate solution. DuBois-Reymond’s experiments were followed by those conducted by Hermann and Luchsinger who demonstrate a connection between sweat gland activity and the flow of electric current in the skin. They used a cat model to demonstrate that electrical stimulation of the sciatic nerve led to the secretion of sweat and conduction of electric current in the footpad of the animal, even after the administration of curare, which is a muscle relaxant that blocks the transmission of the nerve impulses at the myoneural junction. Furthermore, in subsequent experiments on humans, Hermann and colleagues also observed regional differences in the sweat gland activity. They noted that the secretion of sweat was stronger in the palms and fingers, and that these regions had a greater skin conductivity compared to the wrist and the elbow.

As reviewed by Neumann and Blanton, the works of Vigouroux, Fere, Tarchanoff helped to establish an association between cognitive stimulus and skin conductivity. Vigouroux, and Fere reported changes in skin resistance in patients suffering from Histrionic personality disorder. Broadly, they found that emotional stimulation affected skin resistance, where higher emotional stimulation improved skin conductivity and decreased the resistance of the skin. Similar findings were observed by Tarchanoff who reported higher skin potentials following sensory stimulation, imagination, mental arithmetic, expectation / anticipation and voluntary muscle
contractions. Finally, Gildemeister and Rein further advanced the field of electrodermal research by demonstrating that injuring the skin (i.e., the second recording site) below the first recording site, disrupted skin conductivity and localized the generation of skin potentials to the uninjured site of recording.

**Measurement of Electrodermal Activity**

Skin conductance is a form of exosomatic recording of electrodermal activity that refers to how well the skin conducts electricity between two electrodes following the application of an external direct current of constant voltage. Skin conductance is measured in microsiemens (µS) and is a widely accepted approach for indirectly measuring attention, emotional arousal, and task-related cognitive and/or physical demands. Perhaps the most widely known application of skin conductance is for the assessment of physiological stress response during a polygraph, also known as the lie-detector test.

Skin conductance level (SCL) and skin conductance response (SCR) are the two commonly analyzed components of skin conductance. SCL and SCR are differentiated based on the ‘time scale and the relationship to the evoking stimuli’. SCL is an indicator of the tonic changes in the cumulative skin conductivity over a longer span of time and represents a more general level of arousal. SCR is an indicator of the phasic changes in the skin conductivity and reflect a higher-frequency variability of the skin conductance signal superimposed over the slower changes in tonic skin conductivity as shown in Figure 1-1. SCR is thought to represent the underlying activity of the sudomotor nerves of the sympathetic plexus that innervate the eccrine sweat glands that are highly sensitive to emotional stimuli.
While both SCL and SCR have been used extensively to assess SNS activation during cognitive tasks\textsuperscript{90} or dual-task / and complex walking\textsuperscript{82}, the usefulness of these measures in assessing the physical and/or cognitive challenges associated with mobility have not been compared during complex walking tasks. This is a gap in literature that should be addressed and future studies are needed to determine whether the measurement properties of SCL or SCR are better suited for assessment of the SNS activation during complex walking.

**Clinical Validation of Skin Conductance Measurements**

**Skin conductance is a valid measure of anxiety**

Najafpour\textsuperscript{109} tested the validity of measuring skin conductance to assess anxiety in 151 children, aged 5-7 years, during invasive dental procedures. They measured the levels of anxiety at the beginning and the end of the treatment sessions by measuring skin conductance, and subjective questionnaires such as the Modified Child Dental Anxiety Scale (MCDAS) and the Clinical Anxiety Rating Scale (CARS). They compared the findings, and reported a moderate association between skin conductance and the subjective measurements of anxiety (MCDAS $R^2=0.62$, $p=0.02$; CARS $R^2=0.44$, $p=0.032$). The authors concluded that measurement of skin conductance is a reliable and valid approach for identifying clinically anxious children and assessing anxiety-related to dental procedures. These findings are consistent with the reports of Caprara and colleagues\textsuperscript{110}, who also reported a significant correlation between skin conductance and anxiety caused by fear of injection (measured by Clark’s Dental Concerns Assessment Questionnaire) in adults.
Skin conductance can assess fear of falling due to postural instability

Adkin and colleagues\textsuperscript{111} examined the influence of fear of falling or postural instability on the displacement of the center of mass and center of pressure, neuromuscular adjustments to control posture, and voluntary movements to recover balance. Importantly, they measured skin conductance to assess the physiological response to the fear of falling caused by postural instability. Skin conductance was measured from the palms of healthy young adults during a seated resting task and during lab-based tasks that required the participants to rise to toes on platforms of heights ranging from 0.4 m to 1.6 m. The percent change in skin conductance level from the resting baseline to the active toe rise tasks was calculated. In addition to the change in surface height, the participants were instructed to either stand at the edge or away from the edge of the platform. Their ability to take a step to recover balance was either restricted (i.e., Low / High Edge) or they could take a step to recover balance (i.e., Low / High Away). The participants were asked to rise to toes on being given a verbal cue and were asked to maintain the position for 3 seconds. For each task level, the perceived confidence (ranging from 0% confidence to 100% confidence), perceived stability (ranging from 0% to 100%), and anxiety (measured by the modified version of The Sport Anxiety Scale, adapted from Smith\textsuperscript{112}) were assessed using self-report measures. The authors reported a significant increase in the skin conductance level (change of 63.5%) when the participants were asked to rise to toes during the High Edge task compared to the Low Away task. Furthermore, this finding was in agreement with the self-reported measures, where the participants reported significantly lower levels of perceived confidence (change of 46.0%), lesser perceived stability (change of 44.0%),
and higher levels of anxiety (change of 77.3%) during the High Edge task compared to the Low Away task.

**Skin conductance can assess anxiety during dual-task walking**

Hadjistavropoulos and colleagues\(^8\) examined the effect of anxiety on gait and dual-tasking performance in 107 community dwelling older adults. Older adults participating in the study were asked to perform walking tasks including walking on a flat surface (i.e., walking on the floor) and walking on an elevated platform. Dual task performance was assessed by asking the participants to carry a wooden tray while performing each walking task. Titling of the tray during dual tasking was assessed by using an inclinometer attached to the tray. Task-related anxiety was assessed by recording skin conductance from the ring and index fingers of the non-dominant hand. The authors also measured subjective outcomes including the Medical Risk Factor Questionnaire to assess medical factors such as orthopedic impairments or visual impairments that are associated with falling; Survey of Activities and Fear of Falling in the Elderly to assess fear of falling, activity restrictions and activity levels in older adults; Activities-specific Balance Confidence Scale to assess balance confidence; and the trait anxiety component of the State-Trait Anxiety Inventory to assess trait anxiety. The physiological and subjective measures were assessed to confirm that the task manipulations were indeed successful in impacting the anxiety levels. Importantly, the authors reported a progressive increase in skin conductance as the task difficulty increased. Skin conductance was significantly higher during dual-task walking on an elevated platform with a tray compared to walking on the floor with or without a tray. This finding is consistent with previous reports of an increase in the level of anxiety and fear of falling in response to a postural threat during performance of tasks on an
Skin conductance recordings were comparable during the walking tasks performed on the floor (i.e., with and without the tray), and while walking on the floor and an elevated platform.

**Skin conductance can assess the challenge experienced during complex walking**

Clark and colleagues were among the first to assess SNS activation by skin conductance during the performance of various complex walking tasks in older adults with mild to moderate mobility impairments. The participants were instructed to walk at their preferred speed during the typical walking ‘control task’, and the complex walking tasks including dual-tasking with a verbal fluency task, walking in dim lighting, walking with a tray, negotiating obstacles, and walking while wearing a weighted vest. Sympathetic activation was measured by recording skin conductance bilaterally from the palmar aspect of the index and ring fingers of the participants during the preparation and performance phase of each walking task. The authors reported that SNS activity measured by skin conductance was increased in older adults when they performed obstacle crossing and dual-task walking (with a verbal fluency task) compared to typical walking. Importantly, SNS activation measured by skin conductance was significantly higher during the preparation phase of the complex walking tasks compared to the control task. This increase in sympathetic activation is consistent with prior reports of increase in SNS activity in anticipation of the task to be performed. Interestingly, the authors also reported a continued increase in skin conductivity during the performance phase of the complex walking tasks. This is an interesting observation that could predict complex walking outcomes in individuals with mobility impairments and should be investigated further by longitudinal study designs. It is possible that the continued increase in SNS activity is an effort to mobilize the central resources to
increase the metabolic output (e.g., diverting blood flow to the muscles from the gut, increasing heart and respiratory rate) and achieve a state of preparedness to meet the task demands for greater attention, visuomotor coordination, postural control, and even strength.

Collectively, these studies support the feasibility and validity of measuring SNS activity using skin conductance to assess the physiological stress response during static and dynamic activities. The physiological response may be triggered by multiple factors such as task-related anxiety, low balance confidence, low self-efficacy, and fear of falling. While the exact cause of heightened sympathetic activation cannot be isolated, measurement of SNS activity could serve as a broader measure for capturing impairment across the mobility spectrum of everyday life. Additionally, the measure could be particularly useful in assessment of perceived challenge in individuals with mild to moderate cognitive impairments who may not be able to overtly express the magnitude of task-related difficulty.

At present, it is not known if SNS response to the challenge of complex walking tasks in neurologically impaired populations, such as post-stroke, would be similar to this prior work\textsuperscript{10,27,82}. This gap in our knowledge should be addressed. It is reasonable to expect that the SNS in adults post-stroke would respond similarly to the prior observations noted in infants, children, healthy young adults, and older adults. Therefore, the purpose of this dissertation was to advance this line of investigation by testing the feasibility and validity of measuring SNS activity by skin conductance to assess the perceived challenge during complex walking tasks in adults with chronic post-stroke hemiparesis. The feasibility and validity of this approach was tested over the
course of three experimental studies. The first study investigated the hypothesis that SNS activity measured by skin conductance would be significantly higher during lab-based complex walking tasks compared to typical walking. The second study investigated the hypothesis that SNS activity measured by skin conductance would be significantly higher during community-based ‘real world’ complex walking tasks that are perceived to be more challenging. Our third study investigated the hypothesis that SNS activity measured by skin conductance would be significantly reduced following a 12-week post-stroke gait rehabilitation intervention, suggesting a beneficial reduction in the physiological stress response during complex walking tasks.

The findings of this dissertation will also help in establishing the value of measuring skin conductance to assess the physiological stress response associated with a higher perceived challenge during walking, even in a population that is exposed to significant amounts of mobility-related stress, anxiety, and fear of falling. For instance, individuals post-stroke often have poor mobility function and might be in a constant state of anxiety (i.e., chronic anxiety) and worry about loss of balance control and greater susceptibility to falls. It would be beneficial to investigate if the robustness and the physiological range of responses are dampened to some extent in this population due to the chronic state of stress and anxiety. In a review paper, Hoehn-Saric and McLeod\textsuperscript{84} discussed that patients with chronic anxiety show increased muscle tension but not hyperactivated autonomic response at rest as assessed by measurements of heart interbeat interval, blood pressure, skin conductance, and respiration. Counter to expectations, chronically anxious individuals have been reported to demonstrate weaker physiological response to stimulus in a laboratory environment,
which often are not as stress-inducing as the situations experienced in real life. The constant state of stress, anxiety, and worry might lead to physiological adaptations that can diminish the range of autonomic responsiveness to lab-based triggers in these individuals compared to the non-anxious individuals. Therefore, the assessment of the physiological response to comparably challenging walking tasks in a lab-based and a real world environment affords the ability to investigate the robustness of measuring skin conductance to assess SNS response even in populations who might be in a generalized state of anxiety.
Figure 1-1. Decomposition of skin conductance signals. SCL is shown in dark grey and SCR is shown by the blue spikes superimposed over the SCL.
CHAPTER 2
SYMPATHETIC NERVOUS SYSTEM ACTIVITY IS INCREASED DURING LAB-BASED COMPLEX WALKING POST-STROKE

Background

Stroke-related motor impairments restrict mobility including reduced, community ambulation, independence, and participation in life-role activities. An important factor that helps to explain mobility restrictions after stroke is the perceived challenge of walking, as measured by self-reported higher levels of state anxiety, fear of falling, low mobility self-efficacy, and poor balance confidence. The perceived challenge of walking may be particularly increased during complex tasks such as walking over irregular terrain (e.g., stairs, curbs, ramps and uneven surfaces), walking in distracting environments where attention is divided (e.g., a shopping mall), and walking under differing ambient conditions such as in poor lighting. Impaired performance on complex walking tasks and/or avoidance of environments requiring complex walking contributes significantly to mobility disability and restricted community ambulation. Likewise, several studies have suggested that higher levels of balance confidence and falls self-efficacy are strongly associated with the individuals' perceived physical function, recovery of mobility, decrease in avoidance of environmental barriers, increased participation in walking related activities and greater satisfaction with community walking.

The use of self-report to assess the perceived challenge of walking is a valuable approach, but this form of assessment can be susceptible to subjective measurement bias and error. This may include overestimation or underestimation of one's own capabilities; misinterpretation of assessment wording; feelings of guilt, embarrassment or denial pertaining to one's own capabilities; and providing responses that the
individual thinks will be desirable to the researcher. To avoid these biases, a physiologically-based measure of the perceived challenge of walking would be valuable to objectively gauge this important aspect of mobility function and recovery.

One promising approach to gauge the perceived challenge of walking involves measurement of the sympathetic nervous system (SNS). Increased SNS activity is an autonomic stress response that contributes to the mobilization of physiological resources for behavioral performance. The SNS is responsive to physical exertion and cognitive load including both current and anticipated demands. SNS activity can be readily and non-invasively measured by recording skin conductance from the palmar surface of the hands. Several studies have shown that skin conductance is responsive to the increased challenge experienced during complex walking tasks in individuals without neurological deficits. Clark and colleagues reported that SNS activity measured by skin conductance was increased in older adults when they performed obstacle crossing and dual-task walking (with a verbal fluency task) compared to typical walking. Adkin and colleagues reported an increase in both skin conductance and self-reported state anxiety (measured by a modified version of The Sport Anxiety Scale) when healthy young adults were asked to rise to their toes while standing at the edge of an elevated platform. Similarly, Hadjistavropoulos and colleagues reported increased skin conductance and self-reported state anxiety when older adults performed dual-task walking (while holding a tray) on an elevated platform, relative to typical walking. Collectively, these findings suggest that complex walking tasks elicit a physiological stress response from the SNS that can be quantified by skin conductance assessment. However, the validity of this approach for people with post-
stroke neurological impairments has not been investigated. Therefore, the purpose of this study was to test the hypothesis that SNS activity measured by skin conductance during walking would be increased during lab-based tasks of complex walking relative to typical walking in adults post-stroke. Additionally, spatiotemporal measures of gait were assessed to explore the associations between SNS activity and gait function.

**Methods**

**Participants**

Inclusion criteria for participating in this study was age >21 years; at least 6 months post-stroke; medically stable; able to follow 2-stage commands; hemiparetic gait pattern; Fugl-Meyer Motor Assessment (FMA) lower extremity score<30; and Mini-Mental State Exam Score (MMSE) ≥21.

Participants were excluded if they had any condition that would interfere with the ability to safely and appropriately participate in the protocol, such as uncontrolled hypertension, lower extremity pain, severe obesity (body mass index > 40), poor cardiopulmonary and/or renal function, severe perceptual or cognitive deficits or active drug/alcohol abuse; significant balance disturbances; lower motor neuron damage or radiculopathy, myocardial infarction or heart surgery in the prior year, bone fracture or joint replacement in the prior six months, or diagnosis of a terminal illness.

Inclusion criteria for the young adults were age 18-30 years and self-reported absence of any medical conditions that affected walking ability. Participants provided written informed consent at the time of enrollment and the study procedures were approved by the local Institutional Review Board.
Walking Assessments

Participants were instructed to walk 3 laps at preferred speed around a designated path while performing four separate walking tasks: 1) typical walking ("typical" task), 2) walking in dim lighting ("dim" task), 3) dual-task walking with a verbal fluency task ("verbal" task), and 4) walking over obstacles ("obstacles" task). For typical, the walking path was unobstructed and well-lit. For dim, the lights in the room were turned off, but some exterior light was allowed to come in through an open door. For verbal, the participants were asked to say as many words as possible that began with a randomly assigned letter while walking. A new letter was assigned at the beginning of each lap. For obstacles, the participants were asked to step over six small objects (shoes) evenly spaced within each lap. Task order was randomized for each participant. Each walking task was separated by at least two minutes of rest, and was preceded by a quiet standing period of at least 30 seconds to provide reference baseline data for skin conductance measurements.

Spatiotemporal gait data were acquired during the walking tasks from an instrumented walkway (GaitRite®, CIR Systems Inc., Sparta, NJ).

Sympathetic Nervous System Activity Measured by Skin Conductance during Walking

SNS activity was measured by skin conductance using a commercially available portable data acquisition unit (Flexcomp Infiniti, Thought Technologies Ltd., QC, Canada). Adhesive electrodes (10mm Ag/AgCl recording surface) with conductive paste (0.5% saline in a neutral base) were placed on the palmar surface of the proximal phalanges of the index and ring fingers, bilaterally. Skin conductance signals were sampled at 32 Hz, acquired separately from each hand for each participant, and saved
directly to an onboard flash memory card. These data were later downloaded to a computer for offline analysis.

**Data Analysis**

Data analysis was conducted with Matlab version R2015a (The Mathworks, Natick MA) using Ledalab v3.4.7 and custom analysis programs. The raw skin conductance data were down-sampled to 8 Hz and visually examined for the presence of motion artifact, as indicated by high frequency fluctuations in the signal amplitude. Relatively few artifacts were identified, and the ones that were found were removed and replaced by linear interpolation. Continuous decomposition analysis\(^{118}\) was performed in Ledalab v3.4.7 to separate the tonic component (skin conductance level, or SCL) and the phasic component (skin conductance response, or SCR) of the signal. A minimum amplitude criterion of 0.04 µS was applied when identifying SCRs.

For each walking task, two values were extracted from the tonic skin conductance level (SCL) data. The first value was the minimum SCL during the baseline period of quiet standing that preceded each walking task. The minimum SCL was selected in order to capture the most relaxed state of the SNS. The second value was the mean SCL during the duration of the walking task. The primary outcome variable for SCL is the percent change in SCL (denoted by \(\Delta\text{SCL}\)) between the resting and walking phases of each task using the following formula:

\[
\Delta\text{SCL} = \left[ \frac{\text{Walking Average} - \text{Resting Minimum}}{\text{Resting Minimum}} \right] \times 100
\]

A similar approach was used for analysis of SCR. The rate of SCRs was calculated during the duration of the resting phase that preceded the walking task, as well as during the duration of the walking task. The rate of SCRs refers to the number of SCRs detected, divided by the duration of the recording period. The primary outcome
for SCR is the change in the rate of SCR (denoted by ΔSCR) from the resting to the walking phase of each task using the following formula:

\[ \Delta \text{SCR} = (\text{Rate of SCR during walking} - \text{Rate of SCR during rest}) \]

**Statistical Analysis**

Statistical analysis was conducted using JMP software (JMP® 11. Cary, NC: SAS Institute Inc.). Task-dependent differences in SNS activity were assessed with separate two-way repeated measures ANOVA models (Task × recording site) for each skin conductance variable (ΔSCL and ΔSCR) and for each baseline sample (stroke and healthy young groups). An exploratory analysis of the link between SNS activity and gait performance was performed. First, each participant’s ΔSCL value from typical walking was subtracted from the ΔSCL value from each complex walking task. The resultant change value was then used to evenly divide participants into “Low” and “High” SCL subgroups. Subgroups were defined separately for each complex walking task. An analogous procedure was used to define “Low” and “High” SCR subgroups. Task-related change in gait parameters were calculated in a similar manner as for the SNS variables, including change in gait speed, step width, step length, and step length variability. Differences in these gait performance outcomes between subgroups were assessed with t-tests. The significance threshold for all analyses was set at \( p<0.05 \).

**Results**

Thirty one adults with chronic post-stroke hemiparesis participated in the cross-sectional walking assessments. Demographic and clinical information for all stroke participants are shown in Table 2-1. A group of eight healthy young adults (age = 22.4 ± 3.7 years) was also tested on each walking assessment to provide reference data on task-related changes in SNS activity for a healthy unimpaired nervous system.
SNS Activity Measured by Skin Conductance

Within the stroke group, there was a significant main effect of Task on ΔSCL ($p<0.0001$, Figure 2-1.). Post hoc analysis revealed that ΔSCL was significantly greater for obstacles (12.4%) compared to verbal (9.0%, $p=0.04$), dim (5.4%, $p=0.0005$), and typical (4.3%, $p<0.0001$). ΔSCL for verbal was significantly greater than typical ($p=0.02$). The main effect of recording site was not significant ($p=0.82$).

Within the young group, there was a significant main effect of Task on ΔSCL ($p=0.009$, Figure 2-1.). Post hoc analysis revealed that ΔSCL was significantly greater for obstacles (21.0%) compared to verbal (13.1%, $p=0.03$), dim (3.8%, $p=0.01$), and typical (3.4%, $p=0.04$). ΔSCL for verbal was significantly greater than dim ($p=0.04$). A trend towards greater ΔSCL was observed for verbal compared to typical ($p=0.07$). The main effect of recording site was not significant ($p=0.97$).

Within the stroke group, there was a significant main effect of Task on ΔSCR ($p=0.002$, Figure 2-1.). Post hoc analysis revealed that ΔSCR was significantly greater for obstacles (0.13 responses/sec, $p=0.007$) and verbal (0.13 responses/sec, $p=0.003$) compared to typical (0.04 responses/sec). ΔSCR for verbal was significantly greater than dim (0.06 responses/sec, $p=0.02$). A trend towards greater ΔSCR was observed for obstacles compared to dim ($p=0.09$). The main effect of recording site was not significant ($p=0.79$). Within the young group, the main effect of Task on ΔSCR was not significant ($p=0.66$, Figure 2-1.).

Linear regression was used to further explore the consistency of skin conductance measurements from each recording site. When ΔSCL was pooled across all walking tasks within each group, there was a strong association between the paretic and non-paretic sides for the stroke group ($r = 0.73$, $p<0.0001$) and between the left and
right sides for the young group \((r = 0.96, p<0.0001)\). Similarly, when \(\triangle SCR\) was pooled across tasks, there was a strong association between sides for the stroke group \((r = 0.50, p<0.0001)\) and for the young group \((r = 0.70, p<0.0001)\).

**Task-Related Differences in Spatiotemporal Measurements of Gait**

Gait data for the stroke participants are shown in Table 2-2. There was a significant main effect of Task on gait speed \((p<0.001)\), step length \((p<0.0001)\), step length variability \((p<0.0001)\), and step width \((p<0.008)\). Post hoc analyses were conducted for each gait variable. Gait speed was significantly slower for *obstacles* compared to *verbal, dim and typical* \((p<0.001)\). Gait speed was significantly slower for *verbal* compared to *dim* \((p=0.0003)\) and *typical* \((p=0.0001)\). Step length was significantly shorter for *obstacles* compared to *verbal, dim and typical* \((p<0.001)\). Step length for *verbal* was significantly shorter than *dim* \((p<0.0002)\) and *typical* \((p<0.0001)\). Step length variability was significantly greater for *obstacles* compared to *verbal, dim and typical* \((p<0.01)\). Step width was significantly greater for *verbal* \((p=0.02)\) and *dim* \((p=0.016)\) compared to *typical*.

**SNS Subgroup Differences in Spatiotemporal Measurements of Gait**

Figure 2-2. shows the change in spatiotemporal measures of gait for each complex walking task relative to typical walking. These gait values are averaged by task across subgroups of participants with “Low” or “High” SNS activity during complex walking, as described in the Statistics section. There were no statistically significant differences between groups. However, of a total of 24 comparisons (3 complex tasks x 4 gait variables x 2 SNS variables), 13 had a moderate to large effect sizes \((\geq 0.25)\) favoring the “Low” subgroups (gray highlighted values in Figure 2-2), as compared to just 3 comparisons that favored the “High” subgroup (boxed values in Figure 2-2).
These findings suggest that group differences might exist, but that the present study is underpowered for gait outcomes. We propose that individuals with lower SNS activity during complex walking (particularly lower SCL) have a gait pattern that is less disrupted by the added difficulty of complex walking tasks. For example, the “Low” SCL subgroups appeared to have less slowing of gait during complex walking tasks (relative to typical walking), with moderate to large effect sizes ranging from 0.28 – 0.67. Similarly, the “Low” SCL subgroup had less of an increase in the variability of step length for the dim and verbal tasks (relative to typical walking), with effect sizes of 0.72 and 0.55, respectively.

Discussion

This study demonstrated that SNS activity measured by skin conductance in adults post-stroke is acutely increased during complex walking tasks relative to typical walking. This finding is consistent with a heightened physiological stress response due to the perceived challenge of performing complex walking tasks. These results provide preliminary support for the feasibility of using skin conductance to gauge task-related differences in the perceived challenge of various walking tasks after stroke.

The primary finding was that adults post-stroke exhibited increased ∆SCL and ∆SCR during lab-based complex walking tasks compared to the ‘typical’ task (i.e., obstacles and verbal > typical). Skin conductance data acquired from the paretic and non-paretic hands were strongly correlated. The consistency of skin conductance across both peripheral measurement sites strongly supports that our findings are driven by central SNS activity. Furthermore, the ability to detect SNS activity remained robust even on the paretic side despite the potential for deterioration of measurement conditions after stroke, such as due to spastic clenched fist or altered skin health. In the
young group, ΔSCL increased significantly during complex walking compared to the 'typical' task (i.e., obstacles > typical). SNS activity for the stroke and young groups was not compared statistically in this study, because our primary objective was to assess task-dependent changes in SNS activity. The rationale for including a young control group was to provide additional context for interpreting the stroke group data by also observing how an unimpaired nervous system responds to the same walking tasks. It is notable that the stroke group exhibited a significant increase of both ΔSCL and ΔSCR for complex walking tasks, while in the young group only ΔSCL was significantly greater. The reason for this lack of increase in ΔSCR for the young group is unclear because both ΔSCL and ΔSCR are measures of SNS activity. It may be that skin conductance responses (i.e., SCR) are more indicative of specific anxiety provoking events. For example, a moment of unsteadiness might trigger an acute SNS response (i.e., SCR) and would be expected to occur more often for individuals with hemiparetic gait. The increase in SCL during complex walking tasks for both groups is likely because of the generally heightened SNS activity that accompanies increased attention to task demands and movement control.

The spatiotemporal gait assessments in the stroke group showed that individuals post-stroke significantly decreased their walking speed and step length during obstacles and verbal compared to typical. This finding is consistent with the assumption of an increased challenge level during complex walking tasks that involve greater demand for visuomotor, postural, and/or cognitive resources.

Our study did not reveal any statistically significant differences in gait performance between subgroups of participants with lower versus higher levels of SNS
activity during complex walking tasks. Nevertheless, a majority of the statistical comparisons did exhibit moderate to high effect sizes that favored better performance by the subgroups who had lower levels of SNS activity. Most notably, the reduction of gait speed between typical and complex walking conditions seemed to be less pronounced for the “Low” subgroups. This finding seems consistent with the premise that people who are less challenged by complex walking tasks will exhibit lower levels of SNS activity. Future research with larger sample sizes will be needed to further investigate this relationship.

In conclusion, SNS activity during lab-based complex walking was significantly higher compared to typical walking. Additionally, gait performance also deteriorated during complex walking compared to the typical walking task. The findings of this study suggest that the measurement of SNS activity by skin conductance during walking could be beneficial for identifying complex tasks that are particularly difficult and pose a greater risk for adverse outcomes. This information could be valuable for clinicians and assist in designing rehabilitation interventions to decrease the perceived challenge during walking tasks that are particularly difficult for mobility impaired populations.
Table 2-1. Stroke group clinical characteristics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>59.2±10.1</td>
</tr>
<tr>
<td>Stroke chronicity (in months)</td>
<td>15.26±7.93</td>
</tr>
<tr>
<td>Sex (Female/Male)</td>
<td>12F/19M</td>
</tr>
<tr>
<td>Paretic side (Right/Left)</td>
<td>14R/17L</td>
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<tr>
<td>ABC scale score (out of 100)</td>
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<tr>
<td>FMA (out of 34)</td>
<td>23.93±4.65</td>
</tr>
<tr>
<td>Gait parameters</td>
<td>Scores</td>
</tr>
<tr>
<td>-----------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Walking speed (cm/sec)</td>
<td></td>
</tr>
<tr>
<td>Typical</td>
<td>53.25(20.40)</td>
</tr>
<tr>
<td>Dim</td>
<td>52.40(18.9)</td>
</tr>
<tr>
<td>Verbal</td>
<td>47.30(18.05)</td>
</tr>
<tr>
<td>Obstacles</td>
<td>39.90(18.12)</td>
</tr>
<tr>
<td>Step width (cm)</td>
<td></td>
</tr>
<tr>
<td>Typical</td>
<td>19.38(4.71)</td>
</tr>
<tr>
<td>Dim</td>
<td>20.22(4.71)</td>
</tr>
<tr>
<td>Verbal</td>
<td>20.00(4.53)</td>
</tr>
<tr>
<td>Obstacles</td>
<td>19.62(4.68)</td>
</tr>
<tr>
<td>Step length (cm)</td>
<td>Paretic</td>
</tr>
<tr>
<td>Typical</td>
<td>43.29(10.44)</td>
</tr>
<tr>
<td>Dim</td>
<td>42.78(12.82)</td>
</tr>
<tr>
<td>Verbal</td>
<td>40.10(11.30)</td>
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<tr>
<td>Obstacles</td>
<td>38.22(19.40)</td>
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<tr>
<td>Step length variability</td>
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<tr>
<td>Typical</td>
<td>2.66(1.36)</td>
</tr>
<tr>
<td>Dim</td>
<td>3.63(5.80)</td>
</tr>
<tr>
<td>Verbal</td>
<td>2.96(2.94)</td>
</tr>
<tr>
<td>Obstacles</td>
<td>12.21(12.37)</td>
</tr>
</tbody>
</table>

Figure 2-1. Stroke group spatiotemporal gait measurements.
Figure 2-2. ∆SCL and ∆SCR for the stroke and young groups. A) ∆SCL in the stroke group, B) ∆SCL in the young group, C) ∆SCR in the stroke group, D) ∆SCR in the young group.
Figure 2-3. Change in spatiotemporal gait measurements during complex walking compared to typical walking by SNS activity subgroups. SCL (or SCR) subgroups were defined by dividing participants into “High” or “Low” SNS activity based on the difference in ∆SCL (or ∆SCR) for each complex task relative to typical walking. Gait variables were calculated as the difference between each complex walking task relative to typical walking. Values shown are subgroup mean ± standard deviation. Effect sizes highlighted in gray indicates that the “Low” subgroup exhibited the more similar gait characteristics when comparing typical versus complex walking. Effect sizes in boxes indicates that the “High” subgroup exhibited the more similar gait characteristics when comparing typical versus complex walking.

<table>
<thead>
<tr>
<th></th>
<th>SCL subgroups</th>
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<th>SCR subgroups</th>
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<tr>
<td></td>
<td>High</td>
<td>Low</td>
<td>Effect size</td>
<td>p</td>
</tr>
<tr>
<td><strong>Walking Speed (cm/sec)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dm</td>
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<td>-0.36±5.86</td>
<td>0.28</td>
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</tr>
<tr>
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</tr>
<tr>
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<td>0.20</td>
</tr>
<tr>
<td><strong>Step Width (cm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dm</td>
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<td>0.13±1.35</td>
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</tr>
<tr>
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<tr>
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<td>0.30±2.49</td>
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<tr>
<td><strong>Step Length (cm)</strong></td>
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<tr>
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<td>-6.12±3.59</td>
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CHAPTER 3
SYMPATHETIC NERVOUS SYSTEM ACTIVITY IS INCREASED DURING COMMUNITY-BASED COMPLEX WALKING TASKS POST-STROKE

Background

Individuals with stroke-related mobility impairments are less likely to engage in community ambulation, which can greatly limit independence and participation in life-roles. A contributing factor to this loss of mobility is self-reported higher levels of state anxiety\textsuperscript{119}, fear of falling\textsuperscript{69}, low mobility self-efficacy\textsuperscript{120}, and poor balance confidence\textsuperscript{73} during walking. All of these findings reflect an overarching increase in the challenge posed by locomotor control after stroke. A particular concern is the heightened challenge of complex walking tasks, which are more demanding of locomotor control resources.\textsuperscript{11,27,82} Complex walking tasks include, for example, negotiation of stairs, curbs, ramps, and uneven surfaces; walking in noisy or distracting environments; maneuvering to avoid oncoming traffic; and walking under ambient conditions such as poor lighting.\textsuperscript{11,27,82} Accumulating evidence has shown that mobility disability is characterized in part by impaired performance on complex walking tasks and/or avoidance of environments that contain complex walking tasks.\textsuperscript{11,72}

Self-report assessments are a common approach for gauging the perceived challenge of walking.\textsuperscript{73} However, self-report is susceptible to subjective measurement bias\textsuperscript{77,78} such as overestimation of one’s own capabilities; assessment wording that is confusing or misinterpreted; feelings of guilt, embarrassment or denial about one’s own disability; and attempting to please the researcher by giving desirable answers (i.e., demand characteristics).\textsuperscript{76} For these reasons, an objective physiologically-based measure of the perceived challenge of walking would be valuable for assessing this important construct of mobility function and recovery.
One promising approach for objective assessment of the perceived challenge of walking is to measure sympathetic nervous system (SNS) activation. SNS activation is a physiological response that is known to accompany conditions of heightened attention, state anxiety, cognitive loading and physical exertion.\textsuperscript{81,82} Skin conductance measured from the palmar surface of the fingers is a well-established and widely accepted technique for robustly measuring SNS activation.\textsuperscript{89} SNS activation leads to heightened activity in sudomotor nerves innervating eccrine sweat glands, which leads to decreased electrical resistance and increased conductivity of the skin. The palmar surface of the hand and fingers are densely populated with sweat glands and are particularly prone to “emotional sweating” in response to SNS activity.\textsuperscript{89,96} A number of recent studies have shown that skin conductance is responsive to the challenge posed by complex walking tasks in people without neurological injury. Clark and colleagues\textsuperscript{82} reported heightened skin conductance during complex walking tasks such as obstacle crossing and dual-tasking relative to typical steady state walking in elderly adults. Adkin and colleagues\textsuperscript{111} reported increased skin conductance and concomitant increase in self-reported state anxiety when healthy young adults were asked to rise to their toes while standing at the edge of an elevated platform. Similarly, Hadjistavropoulous and colleagues\textsuperscript{81} reported that skin conductance and self-reported state anxiety increased when older adults walked over an elevated platform while holding a tray, relative to typical walking. These findings provide evidence that skin conductance is responsive to the perceived challenge of walking tasks in healthy individuals. Whether this is also true for people with neurological injury is not currently known. For example, cerebral damage
after stroke could alter the behavior of the autonomic nervous system and affect the responsiveness of skin conductance to challenging walking tasks.121,122

Here we conduct a feasibility study to determine 1) whether adults post-stroke exhibit walking-related changes in SNS activity measured by skin conductance; and 2) whether SNS activity measured by skin conductance is responsive to the perceived challenge of “real world” walking tasks performed in a community setting. We hypothesized that SNS activation measured by skin conductance would be greater during the walking phase of complex tasks compared to the resting phase in people post-stroke. We further hypothesized that skin conductance would be increased more for walking tasks that are perceived to be more challenging.

Methods

Recruitment of Participants

Inclusion criteria for stroke participants was age 18-80 years, occurrence of a single unilateral stroke at least 6 months prior to study enrollment (with no other diagnosed neurological condition), hemiparesis resulting in gait deficits, the ability to ambulate without assistance from another person and the ability to follow a 3-step command. Participants were excluded if they had any condition that would excessively interfere with the individual’s ability to perform the protocol, such as pain when walking, poor cardiopulmonary function, and severe perceptual or cognitive deficits. A control group of young adults was recruited to serve as a reference for how the sympathetic nervous system responds to challenging walking tasks under conditions of ideal health. Inclusion criteria for young adults were age 18-30 years and absence of any medical conditions that affected walking ability. All study participants provided their written
informed consent at the time of enrollment and the study procedures were approved by the local Institutional Review Board.

**Protocol and Equipment**

All stroke participants completed a battery of standardized clinical assessments including the Activities-specific Balance and Confidence (ABC) Scale, the State-Trait Anxiety Inventory (STAI), the Short-Form Survey (SF-36), and the Dynamic Gait Index (DGI). Post-stroke self-selected walking speed was determined by the 10 Meter Walk Test (10 MWT).

The walking assessment involved a series of complex walking tasks conducted in a community setting (publicly accessible areas in and around a major hospital). The assessment was designed to simulate community ambulation by occurring in a “real world” setting (i.e., outside of the lab environment) and by including many of the previously reported domains that characterize community ambulation as described in Table 3-1. To reduce the potential effect of task order, the starting point of the assessment was randomized for each participant. Furthermore, each task was preceded by a seated rest period approximately two minutes in length in order to avoid excessive fatigue and to provide reference baseline data for interpreting task-dependent changes in skin conductance (see next paragraph). Just prior to and during each task, study personnel provided simple standardized directions of where to go (e.g., “turn left and descend the stairs”) and what to do (e.g., “enter the store and locate the paper towels”), but did not provide instructions for how to perform the tasks. Study personnel followed closely behind the participants during walking, but did not provide physical assistance. Study personnel also recorded the time at which each walking task was started and completed. Immediately after completion of each task, the participants were
asked to rate their balance confidence on a scale of 0-100%. In accordance with the approach used for the Activities Specific Balance Confidence Scale, participants were asked: “How confident were you that you would not lose your balance or become unsteady?”

To record skin conductance, adhesive electrodes (10mm Ag/AgCl recording surface) with conductive paste (0.5% saline in a neutral base) were placed on the palmar surface of the proximal phalanges of the index and ring fingers. Skin conductance signals were acquired separately from both hands for each participant. Throughout the entire walking assessment, skin conductance signals were acquired at 32 Hz using a commercially available portable data acquisition unit (Flexcomp Infiniti, Thought Technologies Ltd., QC, Canada). The beginning and end of each walking task was time-stamped with an event marking switch connected to the unit. All data were saved directly to an onboard flash memory card and later downloaded to a computer for offline analysis.

**Data Analysis**

Data analysis was conducted with Matlab version R2011b (The Mathworks, Natick MA) using Ledalab v3.4.7 and custom analysis programs. The raw skin conductance data were downsampled to 8 Hz and visually examined for the presence of signal artifact. Relatively few artifacts were identified, and the ones that were found were removed and replaced by linear interpolation. Continuous decomposition analysis\textsuperscript{118} was performed in Ledalab v3.4.7 to separate the phasic component (skin conductance response; SCR) and tonic component of the signal (skin conductance level; SCL). A minimum amplitude criterion of 0.05 µS was applied for identifying SCRs.
Figures 3-1. and 3-2. illustrate the decomposition of tonic and phasic components and the identification of SCRs, respectively.

For each walking task, two values were extracted from the phasic skin conductance response (SCR) data. The first value was the rate of SCRs occurring during the duration of the seated resting phase that preceded the walking task. The second value was the rate of SCRs occurring during the walking task. The rate of SCRs refers to the number of SCRs divided by the duration of the recording period for each task. The primary outcome for SCR is the change in the rate of SCR (denoted by \( \Delta \text{SCR} \)) from the resting to the walking phase of each task using the following formula:

\[
\Delta \text{SCR} = (\text{Rate of SCR during walking} - \text{Rate of SCR during rest})
\]

For each walking task, two values were extracted from the tonic skin conductance level (SCL) data. The first value was the minimum SCL that occurred during the seated resting phase that preceded the walking task. The second value was the median SCL occurring during the duration of the walking task. The primary outcome variable for SCL is the percent change in SCL (denoted by \( \Delta \text{SCL} \)) between the resting and walking phases of each task using the following formula:

\[
\Delta \text{SCL} = \left( \frac{\text{Walking Median} - \text{Resting Minimum}}{\text{Resting Minimum}} \right) \times 100
\]

**Statistical Analyses**

Statistical analyses of the skin conductance data were conducted using JMP software (JMP® 11. Cary, NC: SAS Institute Inc.). Within each group, paired t-tests were used to assess differences between the resting and walking phases of each task for SCR and SCL. The false discovery rate procedure was used to correct for multiple comparisons. Pearson product-moment correlation coefficient was conducted to
assess the strength of the association between the skin conductance measures (i.e., ΔSCR and ΔSCL) acquired from each hand.

Results

Participants

Eight individuals with chronic post-stroke hemiparesis and eight healthy controls participated in this study. The mean age of the stroke group was 63.1 ± 9.9 years (chronicity = 68.1 ± 54.6 months post-stroke) and that of the control group was 22.4 ± 3.7 years. For the stroke group, 10m walking speed was 0.6 ± 0.2 m/s and the scores on standardized clinical assessments were: Activities-specific Balance Confidence Scale (out of 100) = 75.3 ± 12.3; State-Trait Anxiety Inventory (out of 100) = 49.2 ± 13.5; Dynamic Gait Index (out of 24) = 16 ± 3.6; SF-36 Physical functioning (out of 100) = 64.8 ± 17.9; and SF-36 Role limitations due to physical health (out of 100) = 43.7 ± 47.7. The walking tasks were completed by the stroke and young group in 24 ± 5.76 and 13 ± 1.28 minutes, respectively.

Phasic Skin Conductance Response (SCR)

When ΔSCR was pooled across all walking tasks and participants, there was a strong association between the paretic and non-paretic sides for the participants post-stroke (r = 0.47, p < 0.05) and between the left and right sides for the control participants (r = 0.93, p < 0.05). Therefore, ΔSCR values were averaged across both sides for each participant prior to subsequent analysis.

Within group paired t-tests were conducted to assess differences between resting SCR rate and walking SCR rate for each task. In the stroke group, walking SCR rate was significantly higher than resting SCR rate for all of the tasks. In the control group, walking SCR rate was greater than the resting SCR rate for only a subset of the
tasks. The range across tasks for $\Delta$SCR was 0.1 to 0.4 responses/second for the stroke group and 0.05 to 0.3 responses/second for the control group (see Figure 3-3.). The average $\Delta$SCR across all tasks was 0.2 ± 0.2 and 0.1 ± 0.2 responses/second for the stroke and control groups, respectively. Specific findings for each task (resting SCR rate versus walking SCR rate) are reported in Figure 3-4.

**Tonic Skin Conductance Level (SCL)**

When $\Delta$SCL was pooled for all walking tasks and participants, there was a strong association between the paretic and non-paretic sides for the participants post-stroke ($r = 0.82$, $p < 0.05$) and between the left and right sides for the control participants ($r = 0.92$, $p < 0.05$). Therefore, $\Delta$SCL values were averaged across both sides for each participant prior to subsequent analysis.

Within-group paired t-tests were conducted to assess differences between resting SCL and walking SCL for each task. In both the stroke and control groups, walking SCL was significantly higher than resting SCL for all tasks. The range across tasks for $\Delta$SCL was 9.0 to 33.2% for the stroke group and 10.1 to 28.2% for the control group. The average $\Delta$SCL across all tasks was 23.7 ± 18.6% and 17.4 ± 20.8% for the stroke and control groups, respectively (see Figure 3-3.). Specific findings for each task (resting SCL versus walking SCL) are reported in Figure 3-5.

**Self-Reported Outcome Measures**

The stroke group self-reported confidence (%) after completing each walking task were: Cafeteria (97 ± 5.1%), Dim Lighting (95 ± 12.2%), Ramp (93 ± 7%), Store (93 ± 7%), Elevator (93 ± 10.3%), Conversation (85 ± 7%), Outdoor Stairs (85 ± 11.6%), Grass (80 ± 13.2%), and Indoor Stairs (80 ± 18.3%).
Discussion

This study assessed the novel question of whether sympathetic activity measured by skin conductance is responsive to the challenge posed by complex walking tasks in adults post-stroke. Another novel aspect of the study is that we conducted our walking assessments in a true community setting that encompassed many domains of community ambulation (see Table 3-1.), which provided high ecological validity compared to traditional lab-based assessments. The primary findings of this study are that adults’ post-stroke exhibited walking-related changes in skin conductance and the magnitude of the changes were linked to the perceived challenge of the walking tasks. Furthermore, we observed a strong association between the skin conductance data recorded from the paretic and non-paretic sides, suggesting that our data was not excessively influenced by stroke-related changes in peripheral factors affecting skin conductivity such as a spastic clenched fist or degradation of skin quality. A qualitative comparison between the stroke and control data suggests that even after stroke, the SNS behaves similarly in its responsiveness to the challenge of complex walking tasks. Therefore, SNS activity measured by skin conductance may be valuable for objectively quantifying the challenge posed by walking tasks after stroke, particularly for repeated-measures study designs (such as in the present study or a rehabilitation trial) where each individual serves as his/her own reference.

When addressing the first hypothesis we found that the rate of SCRs and the change in SCL was increased significantly during active phase versus the resting phase of each walking task for the stroke group. Task-related increases of SCL and SCR in the stroke group were qualitatively similar to those observed in healthy young adults.
When addressing the second hypothesis we found that the participants post-stroke exhibited increased SCR during walking which was particularly pronounced during the task of descending stairs. This is consistent with the finding that the stairs tasks had among the lowest scores for balance confidence. Furthermore, the observed increase in SCR during the stair task is consistent with the known demands (i.e., to balance, coordination and strength) of stair descent relative to walking on a flat surface, as well as the potentially more severe consequences if a fall was to occur.\textsuperscript{13,14} And indeed, previous research reports that community dwelling older adults find negotiation of stairs to be a particularly difficult mobility task.\textsuperscript{13} The ability to successfully negotiate stairs is critical for independent living and is an important characteristic of physically able individuals.\textsuperscript{12} Conversely, low stairs confidence is associated with exhibition of hesitant or cautious behaviors that often reflect a fear of falling, increased risk for falls, and could lead to avoidance of negotiating stairs.\textsuperscript{14,67,72}

The magnitude of SNS activation during walking might be affected by the use of compensatory strategies in the post-stroke group. Compensatory strategies might decrease the challenge of walking by making the tasks easier, thereby reducing anxiety\textsuperscript{124} and consequent SNS activation. For example, compared to the young group the participants post-stroke walked much slower (i.e., took about twice as long to complete the community mobility assessment), used cautious biomechanical strategies (e.g., small steps with wide base of support), used handrails when descending stairs and a subset used assistive devices (cane or ankle/foot orthosis). We permitted these behaviors in the present study because we wanted the mobility assessment to feel as natural as possible to the participants. Future studies should further examine the use of
compensatory strategies and assistive devices on SNS activation during walking after stroke.

The development of an objective assessment of the perceived challenge of complex walking is prudent and could benefit many diverse populations in addition to people post-stroke, including older adults with a high risk for falls and persons with other forms of neurological injury or disease. Challenge-related outcomes including low balance confidence and falls self-efficacy have been consistently associated with poor physical functioning and mobility.\textsuperscript{60,69,120} Therefore, from a rehabilitation perspective, the perceived challenge of walking may negatively impact the rehabilitation outcomes for recovery of walking. A study of post-stroke mobility reported that self-efficacy independently predicted the level of satisfaction with reintegration into daily activities.\textsuperscript{52} Similarly, greater self-efficacy has been shown to be associated with lower restrictions in participation and greater fulfillment of life-roles in people post-stroke.\textsuperscript{51,60} Importantly, individuals who have greater self-efficacy and perceived walking-related tasks as less challenging perform a greater number of mobility activities during their trips to the community and consequently increase their satisfaction of being involved in ‘life situations’.\textsuperscript{60} Cumulatively, the literature supports that contemporary rehabilitation efforts should actively focus on reducing the perceived challenge associated with walking activities to facilitate greater engagement in the community after a stroke.

In conclusion, measurement of SNS activation using skin conductance holds potential as an objective quantitative outcome measure to gauge the challenge of complex walking in a community setting after stroke. The development of an objective measure could be valuable for assessments of walking impairment and recovery in
diverse populations including older adults at a risk for falls and individuals with neurological impairments. Additional research is warranted for further developing this promising approach of assessing walking-related challenge.
<table>
<thead>
<tr>
<th>#</th>
<th>Walking Task</th>
<th>Domain(s)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Ramp</td>
<td>Terrain</td>
<td>The participants walked along an outdoor ramp (mild decline then moderate incline) through a busy and noisy loading dock area.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maneuvering in traffic</td>
<td>The cafeteria is a busy and noisy space with many people walking about in irregular paths. Participants were instructed to enter the cafeteria, use overhead menu boards to determine the price of a hamburger and the price of a coffee, then exit the cafeteria.</td>
</tr>
<tr>
<td>B</td>
<td>Cafeteria</td>
<td>Cognitive dual-tasking</td>
<td>The convenience store is a relatively busy space with narrow aisles. It was common for participants to walk in close proximity to other shoppers and around racks/shelves, and to bend down to view shelves of different heights. The participants were instructed to locate soft drinks and paper towels.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maneuvering in traffic</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Convenience Store</td>
<td>Cognitive dual-tasking</td>
<td>The participants were instructed to walk down a hallway and follow signs to the elevator, then to push the buttons necessary to call the elevator and take it to the 2nd floor. They then exited the elevator and proceeded to walking a short distance down the hallway.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postural transitions</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Elevator</td>
<td>Cognitive dual-tasking</td>
<td>The participants were instructed to open the door to a stairwell, descend one flight of stairs, and open another door to exit the stairwell.</td>
</tr>
<tr>
<td>E</td>
<td>Indoor Stairs</td>
<td>Terrain</td>
<td>The participants walked briefly on an outdoor covered walkway then descended a flight of stairs.</td>
</tr>
<tr>
<td>F</td>
<td>Outdoor Stairs</td>
<td>Terrain</td>
<td>The participants walked for approximately 20 meters on grass.</td>
</tr>
<tr>
<td>G</td>
<td>Grass</td>
<td>Terrain</td>
<td>The participants walked on an outdoor sidewalk while engaged in casual conversation with a staff member. Standardized questions with relatively neutral content were used to guide the conversation, such as the location of the participant's home, how many years he/she has lived in the area, and his/her commute to the study site.</td>
</tr>
<tr>
<td>H</td>
<td>Conversation</td>
<td>Cognitive dual-tasking</td>
<td>The participants walked 3 laps on a designated path in a large darkened room. The lights were turned off, but some exterior light was allowed to come in through an open door.</td>
</tr>
<tr>
<td>I</td>
<td>Dim Lighting</td>
<td>Ambient conditions</td>
<td></td>
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</tbody>
</table>
Figure 3-1. Decomposition of skin conductance. Exemplar data showing the raw skin conductance signal (solid black line) decomposed into the tonic component (dashed gray line) and phasic component (solid gray line).
Figure 3-2. Skin conductance responses. Exemplar data showing phasic skin conductance signals and location of skin conductance responses. The dots at the top of the figure indicate the onset location of skin conductance responses (SCRs) from the left (black) and right (gray) phasic skin conductance signals. The rate of SCRs within a given period of time was calculated as the number of SCRs divided by the duration of time.
Figure 3-3. ∆SCR and ∆SCL for the stroke and control groups. A) ∆SCR from the resting to the walking period of each task, B) ∆SCL from the resting to the walking period of each task. The stroke group is shown in dark grey and the control group is shown in light gray. The error bars denote the standard error.
<table>
<thead>
<tr>
<th>Walking Task</th>
<th>Stroke Group</th>
<th>Control Group</th>
<th>p-value</th>
<th>Effect size</th>
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<table>
<thead>
<tr>
<th>Walking Task</th>
<th>Stroke Group</th>
<th>Control Group</th>
<th>p-value</th>
<th>Effect size</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Resting SCR</td>
<td>Walking SCR</td>
<td></td>
<td></td>
</tr>
<tr>
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<tr>
<td>Conversation</td>
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<td>0.30 (0.17)</td>
<td>0.15</td>
<td>0.55</td>
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<tr>
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<td>0.28 (0.11)</td>
<td>0.24</td>
<td>0.51</td>
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<tr>
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<tr>
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Figure 3-4. Stroke and control group ΔSCR at rest and during walking. Standard deviation reported in parenthesis. *p< 0.05
Figure 3-5. Stroke and control group ∆SCL at rest and during walking. Standard deviation reported in parenthesis. *p< 0.05

<table>
<thead>
<tr>
<th>Walking Task</th>
<th>Stroke Group</th>
<th>p-value</th>
<th>Effect size</th>
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<td>Grass</td>
<td>7.30 (2.73)</td>
<td>7.96 (2.87) *</td>
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CHAPTER 4
SYMPATHETIC NERVOUS SYSTEM ACTIVITY IS BENEFICALLY REDUCED FOLLOWING A 12-WEEK GAIT REHABILITATION INTERVENTION POST-STROKE

Background

The perceived challenge of walking is increased after stroke, as measured by self-reported higher levels of mobility-related anxiety, fear of falling, low mobility self-efficacy and poor balance confidence. Importantly, the perceived challenge of walking is especially increased during the performance of complex walking tasks, for example, walking over irregular surfaces (e.g., stairs, curbs, ramps), dual-task walking (e.g., walking while having a conversation) and walking under various ambient conditions (e.g., poor lighting). Furthermore, several studies have reported an association between higher perceived challenge of walking and avoidance of environments or activities that require complex walking. Continued avoidance of complex walking activities restricts community ambulation and contributes significantly to mobility disability after stroke. Likewise, several studies have suggested that higher levels of balance confidence and falls self-efficacy can strongly influence an individual’s perception of their physical abilities, improve recovery of mobility function, and decrease avoidance of environmental barriers, increased participation in complex walking activities and increase the overall satisfaction with community ambulation. For these reasons, reducing the perceived challenge of walking should be an important rehabilitation goal.

The perceived challenge of walking is commonly measured by self-report. While this is a valuable approach, this form of assessment can be susceptible to limitations including subjective measurement bias and error, especially due to underreporting. Some sources of measurement bias include overestimation or
underestimation of one’s own capabilities; misinterpretation of assessment wording; feelings of guilt, embarrassment or denial pertaining to one’s own capabilities; and providing responses that the individual thinks will be desirable to the researcher. Therefore, to overcome the limitations of self-report, a physiologically-based measure of the perceived challenge of walking would be valuable to objectively gauge this important aspect of mobility function and recovery.

The measurement of the sympathetic nervous system (SNS) activity is a promising approach to objectively assess the perceived challenge during complex walking. Increased SNS activity is an autonomic stress response that contributes to the mobilization of physiological resources for behavioral performance, also known as the ‘fight or flight’ response. The SNS is responsive to physical exertion and cognitive load and can be readily and non-invasively measured by recording skin conductance from the palmar surface of the hands. Several studies have shown that skin conductance is responsive to the increased challenge experienced during complex walking tasks in healthy young and older adults. Clark and colleagues\textsuperscript{82} reported that SNS activity measured by skin conductance was increased in older adults when they performed obstacle crossing and dual-task walking (with a verbal fluency task) compared to typical walking. Adkin and colleagues\textsuperscript{111} reported an increase in both skin conductance and self-reported state anxiety (measured by a modified version of The Sport Anxiety Scale\textsuperscript{112}) when healthy young adults were asked to rise to their toes while standing at the edge of an elevated platform. Similarly, Hadjistavropoulos and colleagues\textsuperscript{81} reported increased skin conductance and self-reported state anxiety when older adults
performed dual-tasking walking (while holding a tray) on an elevated platform, relative to typical walking.

Taken together, these findings suggest that physiological stress response (i.e., SNS response) to the perceived challenge of complex walking tasks can be quantified by measuring skin conductance. However, it is not known if SNS activity is reduced in response to rehabilitation interventions focusing on recovery of walking after stroke. A rehabilitation-induced decrease in SNS activity during complex walking would suggest a reduction in the physiological stress response and a decrease in the perceived challenge of walking. Therefore, the purpose of this study was to test the hypothesis that SNS activity measured by skin conductance during complex walking would be reduced in response to a 12-week post-stroke gait rehabilitation intervention.

Methods

Participants

Inclusion criteria for participating in this study was age >21 years; at least 6 months post-stroke; medically stable; able to follow 2-stage commands; hemiparetic gait pattern; Fugl-Meyer Motor Assessment (FMA) lower extremity score<30; and Mini-Mental State Exam Score (MMSE) ≥21.

Participants were excluded if they had any condition that would interfere with the ability to safely and appropriately participate in the protocol, such as uncontrolled hypertension, lower extremity pain, severe obesity (body mass index > 40), poor cardiopulmonary and/or renal function, severe perceptual or cognitive deficits or active drug/alcohol abuse; significant balance disturbances; lower motor neuron damage or radiculopathy, myocardial infarction or heart surgery in the prior year, bone fracture or joint replacement in the prior six months, or diagnosis of a terminal illness.
**Walking Assessments**

Participants were instructed to walk 3 laps at preferred speed around a designated path while performing four separate walking tasks: 1) typical walking ("typical" task), 2) walking in dim lighting ("dim" task), 3) dual-task walking with a verbal fluency task ("verbal" task), and 4) walking over obstacles ("obstacles" task). For typical, the walking path was unobstructed and well-lit. For dim, the lights in the room were turned off, but some exterior light was allowed to come in through an open door. For verbal, the participants were asked to say as many words as possible that began with a randomly assigned letter while walking. The letters for the verbal fluency task were randomly selected from this list: B, D, G, N, P, R, and T. A new letter was assigned at the beginning of each lap. The letters assigned during the assessment of dual-task walking at baseline and post-intervention were different. For obstacles, the participants were asked to step over six small objects (shoes) evenly spaced within each lap. Task order was randomized for each participant. Each walking task was separated by at least two minutes of rest, and was preceded by a quiet standing period of at least 30 seconds to provide reference baseline data for skin conductance measurements.

Post-stroke balance confidence was assessed by the Activities-specific Balance Confidence (ABC) Scale, and motor impairment was assessed by the Fugl-Meyer Motor Assessment (FMA) lower extremity score.

**Sympathetic Nervous System Activity Measured by Skin Conductance during Walking**

SNS activity was measured by skin conductance using a commercially available portable data acquisition unit (Flexcomp Infiniti, Thought Technologies Ltd., QC, Canada). Adhesive electrodes (10mm Ag/AgCl recording surface) with conductive paste
(0.5% saline in a neutral base) were placed on the palmar surface of the proximal phalanges of the index and ring fingers, bilaterally. Skin conductance signals were sampled at 32 Hz, acquired separately from each hand for each participant, and saved directly to an onboard flash memory card. These data were later downloaded to a computer for offline analysis.

**Gait Rehabilitation Intervention**

Nine individuals with post-stroke hemiparesis participated in a 12-week rehabilitation intervention focusing on enhancing coordination (60 sessions, by a licensed physical therapist, 3 hours per day, five times per week). Also included were therapeutic exercises to improve balance and strength. The training paradigm included progression from simple to complex movement tasks (i.e., moving from in synergy to out of synergy lower extremity movement patterns) to facilitate motor learning of appropriate coordination patterns. Positions of sidelying, prone, supine, and seated were used to mitigate the effects of gravity and abnormal muscle tone, in order to facilitate the practice of the high quality movement patterns. The standing position was used in order to practice coordination of movements in the upright position. The newly-acquired coordinated movements were then integrated into the practice of gait. Gait coordination training focused on ankle dorsiflexion, knee flexion and hip flexion during the swing phase; knee flexion at toe-off and knee extension before heel strike; knee and hip extension during the stance phase; and whole body balance control during weight shifting. The motor learning principles used in the gait training protocol included movement practice as close to normal as possible, high number of repetitions, attention to the motor task, and rapid progression of task difficulty while maintaining integrity of
the task movements. The intervention protocol used in this study has been successfully implemented in prior studies by Daly and colleagues\textsuperscript{127-129}.

**Data Analysis**

Data analysis was conducted with Matlab version R2015a (The Mathworks, Natick MA) using Ledalab v3.4.7 and custom analysis programs. The raw skin conductance data were down-sampled to 8 Hz and visually examined for the presence of motion artifact, as indicated by high frequency fluctuations in the signal amplitude. Relatively few artifacts were identified, and the ones that were found were removed and replaced by linear interpolation. Continuous decomposition analysis was performed in Ledalab v3.4.7 to separate the tonic component (skin conductance level, or SCL) and the phasic component (skin conductance response, or SCR) of the signal. A minimum amplitude criterion of 0.04 µS was applied when identifying SCRs.

For each walking task, two values were extracted from the tonic skin conductance level (SCL) data. The first value was the minimum SCL during the baseline period of quiet standing that preceded each walking task. The minimum SCL was selected in order to capture the most relaxed state of the SNS. The second value was the mean SCL during the duration of the walking task. The primary outcome variable for SCL is the percent change in SCL (denoted by ΔSCL) between the resting and walking phases of each task using the following formula:

\[
\Delta \text{SCL} = \left( \frac{\text{Walking Average} - \text{Resting Minimum}}{\text{Resting Minimum}} \right) \times 100
\]

A similar approach was used for analysis of SCR. The rate of SCRs was calculated during the duration of the resting phase that preceded the walking task, as well as during the duration of the walking task. The rate of SCRs refers to the number of SCRs detected, divided by the duration of the recording period. The primary outcome
for SCR is the change in the rate of SCR (denoted by ΔSCR) from the resting to the walking phase of each task using the following formula:

\[
ΔSCR = (\text{Rate of SCR during walking} - \text{Rate of SCR during rest})
\]

**Statistical Analysis**

Statistical analysis was conducted using JMP software (JMP® 11. Cary, NC: SAS Institute Inc.). A three-way repeated measures ANOVA (Time x Task x recording site) was used to compare intervention-induced changes in SNS activity for each variable (ΔSCL and ΔSCR). Post hoc analysis using Tukey’s HSD was used to further investigate significant main effects. The significance threshold for all analyses was set at \( p<0.05 \).

**Results**

Nine participants underwent the intervention protocol. Demographic and clinical information for all stroke participants are shown in Table 4-1. Linear regression was used to further explore the consistency of skin conductance measurements from each recording site. When ΔSCL was pooled across all walking tasks within each group, there was a strong association between the paretic and non-paretic sides for the stroke group (\( r = 0.73, \ p<0.0001 \)). Similarly, when ΔSCR was pooled across tasks, there was a strong association between sides for the stroke group (\( r = 0.50, \ p<0.0001 \)).

**Skin Conductance before and after Gait Rehabilitation**

For ΔSCL, there was a significant main effect of Time (\( p=0.02 \)), such that ΔSCL was significantly lower post-intervention compared to baseline during walking assessments (Figure 4-1). Post hoc analysis revealed that ΔSCL was significantly lower for obstacles at post-intervention compared to baseline (\( p=0.04 \)). ΔSCL did not change
significantly for verbal (p=0.35), dim (p=0.23) and typical (p=0.23). The main effect of recording site was not significant (p=0.21).

For ∆SCR, there was a significant main effect of Time (p=0.02) on ∆SCR, such that ∆SCR was significantly lower post-intervention compared to baseline for the walking assessments (Figure 4-1). Post hoc analysis revealed that ∆SCR was significantly lower for obstacles (p=0.008) and verbal (p=0.01) at post-intervention compared to baseline. ∆SCR was not significantly different for dim (p=0.59) and typical (p=0.29) at post-intervention compared to baseline. The main effect of recording site was not significant (p= 0.44).

Balance Confidence before and after Gait Rehabilitation

Balance confidence improved following the post-stroke gait rehabilitation intervention, as measured by changes in the ABC Scale (70.41% ± 11.01 at baseline versus 79.29% ± 9.91 at post-assessment, p=0.04).

Fugl-Meyer Motor Assessment before and after Gait Rehabilitation

The post-stroke FMA lower extremity score at baseline and following the gait rehabilitation intervention were similar (21.0 ± 4.74 at baseline versus 20.88 ± 5.94 at post-assessment).

Discussion

This study demonstrated that SNS activity measured by skin conductance in adults post-stroke is decreased significantly following a 12-week gait rehabilitation intervention. The decrease in SNS activity suggests a beneficial reduction in the perceived challenge of walking as indicated by the reduction in walking-related stress response.
Skin conductance data acquired from the paretic and non-paretic hands were strongly correlated. The consistency of skin conductance across both peripheral measurement sites strongly supports that the findings are driven by central SNS activity. Furthermore, the ability to detect SNS activity remained robust even on the paretic side despite the potential for deterioration of measurement conditions after stroke, such as due to spastic clenched fist or altered skin health.

Both, $\Delta SCL$ and $\Delta SCR$ decreased significantly in response to the gait rehabilitation intervention. The reduced SNS activity after the rehabilitation intervention was particularly notable for the complex walking tasks obstacles and verbal. It could be speculated that improvements in motor control, strength, and/or balance reduced the perceived challenge of walking, thereby reducing the physiological stress response of complex walking tasks. However, due to the lack of non-intervention control group we cannot be certain that the intervention is responsible for this finding. It may be that reduced SNS activity is due to increased familiarity with the research environment during repeated assessment, as opposed to actual reduction in the perceived challenge. The confounding effect of task familiarity is tempered somewhat by the fact that the assessment tasks were completely different from the intervention tasks.

The gait intervention protocol used in this study was not specifically designed to decrease the perceived challenge of walking by reducing mobility-related anxiety and/or increasing balance and falls self-efficacy during walking. Rather, we performed a secondary analysis on skin conductance data obtained from a sample of convenience enrolled in an existing clinical trial. Our goal was to examine if a gait intervention designed to enhance walking function would also decrease the perceived challenge of
walking frequently associated with higher mobility-related anxiety, fear of falling and poor balance confidence. Consequently, we cannot be certain about what aspects of the intervention contributed to the decrease in SNS activity measured by skin conductance. A future randomized controlled trial specifically designed to decrease the perceived challenge of walking may be needed to confirm and explain the finding of reduced SNS activity during walking after rehabilitation.

In conclusion, SNS activity during complex walking measured by skin conductance was significantly decreased following a 12-week gait rehabilitation intervention. The decrease in SNS activity was most pronounced for the dual-task walking and obstacle negotiation tasks. These findings suggest that the measurement of SNS activity could be valuable for quantifying the effectiveness of gait rehabilitation interventions in reducing the perceived challenge during complex walking tasks.
Table 4-1. Clinical characteristics of the study participants

<table>
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<th>Demographics</th>
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<tr>
<td>Age (in years)</td>
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<tr>
<td>Stroke chronicity (in months)</td>
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<tr>
<td>Sex (Female/Male)</td>
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<tr>
<td>Paretic side (Right/Left)</td>
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<td>ABC scale (out of 100)</td>
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<td></td>
<td>79.29(9.91)</td>
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<td>FMA (out of 34)</td>
<td>21.0(4.74)</td>
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<td>20.88(5.94)</td>
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</table>
Figure 4-1. A) $\Delta$SCL at baseline and post-intervention, B) $\Delta$SCR at baseline and post-intervention.
CHAPTER 5
GENERAL DISCUSSION

Measurement of the Perceived Challenge of Walking

Complex walking tasks, such as dual-task walking\textsuperscript{130,131} and obstacle negotiation\textsuperscript{30,132}, increase the locomotor challenge in adults with post-stroke hemiparesis. An increase in the challenge during walking can interfere with the fulfillment of life-related activities, and has been associated with a greater risk for falls, decreased participation in community walking activities, and increased fear-avoidance of activities that are perceived as more difficult.\textsuperscript{5,11} The perceived challenge of walking after stroke is commonly measured by self-report\textsuperscript{73}, which is frequently susceptible to subjective measurement bias due to the reasons discussed in the previous chapters. The measurement of SNS activity by skin conductance is a promising objective approach to overcome the limitations of self-report measures and has been used in prior studies\textsuperscript{10,81,82,114} to robustly assess the perceived challenge during walking tasks that challenge dynamic stability and postural control in healthy young and older adults. Importantly, increased SNS activity is a physiological stress response (i.e., the fight or flight response) to situations that are perceived as threatening and/or challenging. Consequently, greater SNS activity is associated with higher levels of mobility-related anxiety, fear of falling, and/or increased task-related physical (e.g., strength, agility) and cognitive demands (e.g., attention, motor planning). However, the feasibility of measuring SNS activity during walking has not been investigated in adults post-stroke. Furthermore, it is not known if SNS post-stroke responds similarly to the healthy nervous system to the challenge experienced during walking. Therefore, this dissertation addresses an important existing gap in the literature by testing the feasibility
of measuring SNS activity by skin conductance during various complex walking tasks in adults post-stroke.

**Summary of Dissertation Studies**

Study 1 investigated the hypothesis that SNS activity would be significantly higher during lab-based complex walking tasks compared to typical walking after stroke (see Chapter 2). Additionally, this study also examined the relationship between SNS activity and gait function in adults post-stroke. The primary finding of Study 1 was that the adults post-stroke exhibited increased SNS activity (measured by ∆SCL and ∆SCR) during lab-based dual-task walking and obstacles negotiation compared to the control walking task (i.e., typical walking). The increase in SNS activity is consistent with a greater perceived challenge of walking due to higher task-related physical and cognitive demands pertaining to the maintenance of dynamic stability and postural control, visuomotor coordination, and increased attention and motor planning. The increased difficulty of these tasks was confirmed by decreased gait speed and shorter step length compared to typical walking. Both these findings are consistent with prior work in young and older adults\(^{10,82}\) and supports the robustness of measuring SNS activity to assess the perceived challenge of walking, even in individuals with a neurologic injury, such as post-stroke. Importantly, we reported that the nervous system even when injured by a stroke responds similarly to a healthy uninjured nervous system (i.e., data obtained from healthy young adults) to the task-related challenges. This information is important because several studies have reported autonomic dysregulation after stroke\(^{121}\), which has been suggested to bias a significant increase in SNS response in these individuals. Likewise, injury to the cortical and subcortical brain regions could decrease the SNS response to tasks that are cognitively demanding and require greater attention, motor
planning, and decision making.\textsuperscript{133,134} Therefore an important motivation for conducting this study was to investigate how the SNS responds to task-related challenge after a stroke. Prior to conducting this study, we did not know if a skin conductance-based measurement of SNS activity would show ceiling or floor effects. For instance, a significantly higher SNS activity at resting baseline might lack the physiological flexibility to robustly respond to the task-related challenges, leading to little or no change in SNS response during activity. Similarly, as discussed in Chapter 1, individuals post-stroke might have chronic mobility related anxiety and fear of falling which could impact the recording of skin conductance signals. As discussed in the review by Hoehn-Saric and McLeod\textsuperscript{84}, chronically anxious individuals demonstrate weaker physiological responses to lab-based tasks, which are relatively less threatening than the tasks performed in an unpredictable real-world environment. Chronic anxiety and constant worry is thought to cause physiological adaptations that can diminish the autonomic responsiveness to lab-based stimuli.

Study 2 investigated the hypotheses, that SNS activity in adults post-stroke would be 1) higher during the active phase of community-based complex walking tasks compared to the resting phase; and 2) higher during the performance of complex walking tasks that are perceived as more challenging (see Chapter 3). The primary findings of Study 2 were that adults post-stroke exhibited increased SNS activity (measured by $\Delta$SCL and $\Delta$SCR) during the active phase versus the resting phase of the community-based walking tasks, and SNS activity was significantly higher during walking tasks of a greater difficulty level. Importantly, SNS activity was particularly higher during the task of descending stairs. In agreement, the stairs tasks also had
among the lowest scores for balance confidence, self-reported verbally by the participants. The increase in SNS activity during the stair task is consistent with the known demands (i.e., to balance, coordination and strength) of stair descent.\textsuperscript{13,14} This finding is also in agreement with prior work that suggests that negotiation of stairs is particularly difficult for the older adults living in the community.\textsuperscript{13-15}

Our findings from the lab-based and community-based studies are consistent in that SNS responses were consistently higher during tasks that are known to be more challenging (i.e., negotiating obstacles and stairs, and dual-task walking). This is in agreement with our hypotheses that SNS activity would be significantly higher during the tasks that are perceived as more challenging. Prior to conducting Study 2, we did not know if we would be able to record good quality signals and interpret skin conductance data acquired in a noisy and unpredictable community environment. Therefore, the findings of Study 2 lend further support to the robustness and feasibility of measuring SNS activity to assess the post-stroke perceived challenge of walking even in a ‘real world’ environment. Importantly, this information could contribute significantly to the development of wearable sensors designed to monitor post-stroke neurophysiological interactions with the environment in a real world setting. In particular, long-term monitoring of these interactions could improve the ability to identify complex walking tasks that are particularly challenging and could increase the risk for falls after stroke.

Study 3 investigated whether SNS activity is reduced in individuals post-stroke following a 12-week gait rehabilitation intervention, suggesting a beneficial reduction in the perceived challenge due to decreased stress response during complex walking
tasks. The primary finding of Study 3 was that SNS activity (measured by ΔSCL and ΔSCR) decreased significantly in response to the gait rehabilitation intervention. Importantly, reduced SNS activity after the rehabilitation intervention was particularly notable for the dual-task walking with the verbal fluency task and the obstacle negotiation task. Furthermore, the self-reported balance confidence scores of the participants, measured by the Activities-specific Balance and Confidence Scale were increased significantly following the gait rehabilitation intervention compared to the baseline assessments. The rehabilitation intervention was based on ‘The Gait Coordination Protocol’ designed by Daly and colleagues.\textsuperscript{127-129} The protocol is based on the principles of neural plasticity and associated motor learning principles including high repetitions of task-specific practice, emphasis on the production of desired movement patterns, increased attention to and the awareness of the sequence of movement patterns being performed, verbal and tactile feedback to enhance movement patterns as needed, and progression of the speed of movement. The gait rehabilitation intervention was delivered by a licensed physical therapist 5 times per week, and the duration of each session was 3 hours. Collectively, the adults post-stroke participated in 60 gait intervention sessions over a period of 12 weeks.

The emphasis on coordinated movement patterns, and improvements in balance and strength has been previously shown to successfully decrease mobility impairments, improve sensorimotor function, and enhance motor coordination leading to an increase in the participation in life-roles in adults post-stroke with moderate to severe gait deficits.\textsuperscript{127-129} One plausible explanation for the reduced SNS activity (in Study 3) is that possible intervention-induced improvements in motor control, balance, and/or strength.
made walking less challenging. The decreased challenge during walking could have reduced the overall physiological stress response to the task-demands of obstacle negotiation and dual-task walking. This is also in agreement with the increase in the self-reported balance confidence after the intervention. It is likely that the participants benefited from the motor control, balance and strength gains which made them more confident, and they perceived the walking tasks as relatively less challenging. It is also plausible that SNS activity was reduced due to repeated exposure to the assessment tasks at baseline and post-intervention, which could have decreased task-related anxiety or fear of falling. Furthermore, the lack of a non-intervention control group somewhat limits our ability to attribute the finding of reduced SNS activity solely to the intervention. Additionally, as discussed in Chapter 4, the gait intervention used in this study was not specifically designed to reduce SNS activity during walking. While our secondary analysis of the skin conductance data showed that SNS reduced following the intervention, we cannot be certain about what components of the intervention induced this reduction. Future studies designs should address these limitations and further investigate how the magnitude of SNS activity during complex walking is affected by the rehabilitation efforts for walking recovery after stroke.

**Cognitive Control of Walking**

In our studies we found that dual-task walking was particularly challenging based on the observed increase in skin conductance. This may be due to a high demand for cognitive resources to control walking after stroke. The control of walking in healthy adults is largely automated and coordinated by lower levels of the neural network including the spinal cord, brainstem, and cerebellum.\textsuperscript{135,136} Together, these regions coordinate the automatic control of walking, which is relatively effortless with occasional
demands on attention.\textsuperscript{135,137,138} In contrast to healthy adults, the automaticity of walking is markedly decreased in individuals with mobility impairments, including older adults and adults post-stroke.\textsuperscript{135,138} It is likely that these individuals compensate for the decreased automaticity by increasing their reliance on the cognitive control of walking. The cognitive control of walking involves increased engagement of the attentional resources (e.g., greater attention to postural control) and a need for greater motor planning during the walking tasks.

The increased reliance on the cognitive control of walking often leads to performance decrements (measured as decreased gait speed), especially during dual-tasking, which demands the allotment of cognitive resources, such as attention and planning, to two tasks being performed simultaneously, for example, dual-task walking with a cognitive task. The decrease in task performance is also known as the dual-task effect\textsuperscript{139}, where a greater dual-task effect indicates an increased reliance on the cognitive resources. The dual-task effect in individuals with mobility impairments have been reported widely in the literature. Lundin-Olsson and colleagues\textsuperscript{140} reported that individuals with severe mobility impairments, such as after stroke, ‘stop walking when talking’. Similarly, Plummer-D’Amto and colleagues\textsuperscript{139} have reported a decrease in gait speed when participants post-stroke were asked to produce spontaneous speech while walking. The decrements in motor/gait performance during dual-tasking with a cognitive task suggest an increased interference between the shared resources for motor actions and cognition (i.e., cognitive-motor interference). Dual-task walking with a verbal task is especially challenging for individuals with poor mobility function because of the increased demand on attention and programming during walking (motor task) and
speech production (cognitive task). Conversing during walking increases the demands on the resources that are simultaneously engaged in the processing of motor actions and speech, thereby, creating a greater competition for the already limited cognitive resources.\textsuperscript{141} Likewise, a similar competition could also occur during obstacle negotiation, due to an increased demand on visual attention and motor planning, a greater need for visuomotor coordination, and increased threat to postural control.\textsuperscript{132} Additionally, the task-related increase in physical exertion and cognitive loading could be a significant source of anxiety that further consumes attention\textsuperscript{142} and contributes to mobility-related fear of falling, as individuals become aware of the diminishing cognitive resources.

**The Inverted U Hypothesis**

Increased SNS activity and decrements in gait performance during dual-task walking and obstacle negotiation is in agreement with prior work that suggests an inverse relationship between the magnitude of SNS activation and task-performance. This is an important observation that should be investigated during the performance of various walking tasks in future studies. Yerkes and Dodson in 1908,\textsuperscript{143} examined the relationship between the strength of a non-injurious electrical shock and the learning of a discrimination task in mice. They reported that electrical shock of moderate strength was most beneficial in facilitating the learning of the task. In contrast, shocks that were weak or very strong were associated with slower learning, as demonstrated by the need for higher number of trials before the task could be learned. The findings of Yerkes and Dodson (i.e., the Yerkes and Dodson law) were further developed into the ‘Inverted U Hypothesis’ theory.\textsuperscript{143} According to this theory, optimal task-performance occurs at the intermediate level of physiological arousal (i.e. moderate SNS activation). In contrast,
very low or high SNS activation has been associated with poor task-performance. Furthermore, the curvilinear shape of the hypothesis can be influenced by several factors such as the level of skill (i.e., novice vs. expert), personality of the individual (extraversion vs. introversion), and complexity of the task to be performed (i.e., simple vs. complex). Of another interest is a study by Arent and Landers\textsuperscript{144} who reported that optimal performance on reaction and movement times during a pedaling task occurred at 60-70\% of the participants’ maximal physiological arousal (determined by heart rate reserve). Additionally, they also investigated the influence of cognitive (e.g., negative concerns regarding performance, decreased attention) and somatic (e.g., increased heart rate, feeling shaky) anxiety on task performance. Pre-performance anxiety, self-confidence, and concentration were measured by the Competitive State Anxiety Inventory-2 and the Sport Anxiety Scale\textsuperscript{112}. Using regression analysis, they reported that the variability in task performance was explained more by anxiety than by physiological arousal alone. Similar conclusions have also been drawn by VaezMousavi and Osanlu\textsuperscript{145} where they assessed the relationship between SNS activation (i.e., target readiness) and the performance on a quiet standing balance task assessed by the center of pressure displacements. They reported that the performance on the standing balance task declined significantly (measured as increased sway) with greater task-related activation of the SNS (measured by skin conductance). Importantly, there was a curvilinear relationship between task performance and SNS activation, where individuals with moderate levels of task-related SNS activations appeared to perform better on the standing balance task, compared to individuals with low or high task-related SNS activation.
Important Considerations for Recording Skin Conductance after Stroke

The findings of our study support the robustness of measuring SNS activity by skin conductance to assess the perceived challenge of walking in healthy young adults and adults post-stroke. In our study, both the groups demonstrated a similar response to the task-related challenge during complex walking. However, there are several possible confounders that should be considered during recording skin conductance signals in the stroke population. Some of these factors have been discussed in this section:

**Autonomic Dysregulation**

Autonomic dysregulation after stroke is reported to favor an increase in SNS response and a decrease in parasympathetic activity,\textsuperscript{146} and could be a confounding variable that impacts the skin conductance measurements. Stroke-related lesions have been reported to impact the autonomic regulation of sweating. For instance, Naver and colleagues\textsuperscript{147} reported asymmetrical sweating in 23\% of their stroke patients, and observed decreased sweating on the paretic side compared to the non-paretic side in individuals with hemispheric lesions. Likewise Korpelainen and colleagues\textsuperscript{122} reported increased sweating on the paretic side after brain stem lesions. Furthermore, complex regional pain syndrome (CRPS) is a neuropathic pain disorder of central and autonomic origin that is reported in a significant number of individuals with moderate to severe stroke impairments.\textsuperscript{148} CRPS heightens SNS response, and the symptoms commonly include pain, swelling, hyperalgesia, change in skin temperature, change in skin hydration, and trophic changes in the affected extremity. Consequently, these factors could affect the ability to accurately record skin conductance signals from the affected extremity.
Injury to the Cortical and Subcortical Regions

Post-stroke neurologic injury/lesions could influence the ability to measure skin conductance. As reviewed by Critchley, injury to the cortical and subcortical regions could impact the generation of skin conductance responses. In particular, injury to the prefrontal cortex, anterior cingulate, and right parietal lobe have been reported to decrease the magnitude of skin conductance responses. For instance, injury to the ventromedial prefrontal cortex has been reported to decrease anticipatory arousal and could affect the generation of skin conductance responses during tasks requiring decision making. Likewise, injury to the amygdala, has also been associated with a decrease in anticipatory skin conductance responses, as well as a decrease in responses to stimuli that are emotionally meaningful (e.g., learning of behavior that is rewarded or avoiding behavior that is punished).

Compensatory Strategies

Post-stroke adaptations to maximize task-efficiency and functional gains include the use of walking aids or handrails, orthoses, or seeking assistance from other individuals while navigating complex environments. Individuals post-stroke might also rely on compensations including slowing of walking speed during dual tasking or during walking on uneven surfaces. These strategies to decrease the task-related challenge and optimize functioning could potentially mask anxiety to some extent. Consequently, the investigators' decision to allow or restrict the use of these strategies could markedly impact the magnitude of skin conductance recordings. For instance, restricting the use of assistive devices or requiring that the participant complete the experimental tasks within a certain time frame could significantly increase the magnitude of SNS activity.
due to heightened levels of anxiety, fear of falling, and greater task-related physical and cognitive demands.

Collectively, these factors could impact the recording of skin conductance signals and introduce variability in the data. Therefore, these variables should be carefully considered during measuring and interpreting skin conductance data acquired from the stroke population.

**Future Directions**

Technological advancements in the past century have improved our ability to record biosignals from the skin with relative ease, and have broadened its application to several clinical and non-clinical populations. In particular, the recording of skin conductance has emerged as a widely-accepted and robust approach for non-invasively measuring SNS activity to assess the physiological stress response associated with task performance, as demonstrated by Hadjistavropoulos and colleagues, and Clark and colleagues. Traditionally, skin conductance has been recorded to measure the SNS response to the challenge of cognitive tasks (e.g., mental arithmetic) or physical exertion induced by pedaling tasks on stationary bicycles. More recently, a growing body of literature suggests that skin conductance can be used to successfully measure SNS response to the locomotor challenge experienced during ambulatory tasks performed in a lab-based or ‘real-world’ environment. Of particular interest is an Android-based gait-monitoring device developed by Sejdic and colleagues to record multisystem physiological signals during challenging walking conditions. They reported strong multisystem interactions between ambulation, and electrodermal (measured by skin conductance), respiratory (measured by respiratory rate) and cardiovascular (assessed by electrocardiogram readings) systems. Examination of the
physiological responses from multiple systems could be particularly useful in assessing the challenge experienced during walking tasks not only in the individuals with overt mobility impairments but also in subclinical populations where mobility impairments might not be as apparent (e.g., adults with mild stroke-related deficits or early stage Parkinson’s disease). The collective findings of these studies, as also discussed in previous chapters, warrants further investigation of the stress response during various ambulatory tasks by future studies.

**Wearable Sensors and Assessment of Electrodermal Responses**

The availability of wearable sensors has afforded us the ability to continuously monitor electrodermal responses outside the laboratory and clinical settings. Poh and colleagues\textsuperscript{114} are among the first to measure SNS activity using skin conductance in a real-world environment. They used a wearable electrodermal activity sensor (wristband) and measured skin conductance in adults aged 18-56 years. All participants were instructed to perform a physical task (i.e., pedaling as fast as possible on a stationary bicycle for 5 minutes), a seated cognitive task (i.e., mental arithmetic and Stroop word-color matching task) and an emotional task (i.e., watching a horror movie clip for 5 minutes). Skin conductance was measured at baseline (10 minutes), during the task, and during recovery period (10 minutes) for all three tasks. The authors reported that compared to the baseline and recovery phases, skin conductance was higher during the performance phase of all three tasks. Skin conductance level increased as the participants performed the pedaling task. Similarly, a steep rise in the skin conductance level was observed at the beginning of the mental arithmetic task, which remained elevated throughout the task. Furthermore, nearly 73\% of the participants showed a higher increase in skin conductance during the Stroop test. Both the skin conductance
level and the rate of skin conductance responses was higher as the participants watched the horror movie clip. Interestingly, anticipatory skin conductance responses were observed as the participants were informed about the movie genre. Additionally, a young adult was instructed to wear the wristband for one week (i.e., 24/7) to continuously monitor skin conductance in a real-world environment. This allowed the authors to monitor the patterns of skin conductance modulation over a relatively longer period of time as the young adult performed activities of everyday life, including attending classes, studying for exams, doing homework, watching television, and socializing with friends.

**Future Considerations**

The advancements in the field of electrodermal research have led several authors to associate skin conductance recordings to specific regions in brain.\(^83,94,96\) Briefly, their reports suggest that skin conductance recorded from different body regions (e.g., left wrist vs. right wrist, or left palm vs. left sole) are controlled by different areas in the brain, and that even the control of ipsilateral and contralateral skin conductance recordings differ. Namely, the responses influenced by thermoregulatory and emotional stimuli are thought to be controlled by the limbic-hypothalamic region (EDA1), and the responses influenced by specific motor actions are thought to be controlled by the premotor-basal ganglia region (EDA2). The EDA1 pathway is thought to activate electrodermal responses on the ipsilateral side of the body, while the EDA2 pathway is thought to activate the responses on the contralateral side. Additionally, electrodermal responses generated by a generalized state of arousal are thought to be modulated by the reticular formation.\(^94\)
As discussed in Chapter 1, while several studies have measured the components of skin conductance (i.e., SCR and SCL) to assess SNS activation during cognitive tasks, and relatively fewer studies for assessing SNS activity during dual-task walking/complex walking, it is currently not known which of these two components have measurement properties better suited for the assessment of the mobility-related challenges. This is an important gap in the literature that should be addressed. There exists a line of research that suggests that the two skin conductance components, SCR and SCL, are generated by different neural mechanisms and pathways. Nagai and colleagues used functional magnetic resonance imaging (fMRI) and reported that the neural activity within the striate and extrastriate cortices, anterior cingulate and insular cortices, thalamus, hypothalamus and lateral regions of prefrontal cortex reflected the change in the rate of SCR. While the neural activity in the ventromedial prefrontal cortex and the orbitofrontal cortex was associated with SCL. However, Nagai and colleagues measured skin conductance during visually-guided, biofeedback-based relaxation and arousal tasks. In this study, the participants were instructed to move the horizontal lines presented on a screen in the downwards direction by either mentally relaxing (relaxing task) or increasing mental alertness and attention (arousal task). Skin conductance was measured as the participants either tried to relax or increase their level of attention. It is not known if these regional differences in brain activation and their association with SCR and SCL would persist during the performance of dynamic tasks such as complex walking.

Taken together, these findings are of a great interest and could influence the recording and interpretation of the components of skin conductance. This is a relatively
unexplored area of electrodermal research that should be investigated by future studies to improve the understanding of this highly promising and feasible, non-invasive approach for assessing the physiological stress response to task-related challenges.

**Strengths and Limitations of the Dissertation**

**Overcome the Limitations of Self-report Measures**

We have used a unique measurement approach to develop a robust objective physiological index for assessing the perceived challenge of walking after stroke. This objective measure might overcome the limitations of measuring perceived challenge by subjective self-report. Our future studies will compare the two measurement approaches to determine if an objective physiological measure can supplement the self-report assessments of perceived challenge or even serve as an alternative.

**Ecological Validity**

An important strength of our study design is that it establishes the reliability and ecological validity of using a skin-conductance based measurement of SNS activity to assess the perceived challenge of walking in healthy young and post-stroke populations. We found that SNS responded robustly to our walking assessments conducted in a predictable lab-based, and an unpredictable ‘real-world’ community environment. Importantly, our study assessments included a wide variety of domain-specific complex walking tasks that are frequently encountered at home and in the community. Based on prior work, several studies have noted the need for mobility assessments that include a wider range of assessment tasks performed in various environments.\textsuperscript{11,12,27,72,82,135,151}
Feasibility Study

The purpose of this dissertation was to demonstrate the feasibility of measuring SNS activity to assess the perceived challenge of walking in individuals post-stroke. As such, when we conducted our pilot studies we did not know the sample size that would be needed to demonstrate the robustness of our measure. The participants recruited in our study were a sample of convenience, and the sample size was not determined by a power analysis. However, even though our sample sizes were relatively small for Study 2 and Study 3, we were able to enroll an adequate number of participants and had sufficient study power to establish the robustness of our measure to assess the perceived challenge of walking and intervention-induced reduction in SNS activity. The information gained from our pilot studies will help us design a larger randomized clinical trial in the future to further develop our measurement of SNS. Our future studies will further investigate the measurement properties of the skin conductance components (i.e., SCL and SCR) in assessing perceived challenge of walking, and also examine the relationship between our objective measurement and the commonly used self-report measures.

Intervention Design

As discussed in Chapters 4 and 5, the intervention used in Study 3 was not specifically designed to reduce the perceived challenge of walking. Rather, we performed a secondary analysis on skin conductance data obtained from a sample of convenience enrolled in an existing clinical trial to improve gait coordination and function after stroke. And even though we have demonstrated robust reductions in SNS activity especially for the most difficult walking tasks, we cannot be certain about what aspects of the intervention contributed to the decrease in SNS activity. In future, during
our intervention sessions, we will measure physiological variables such as heart rate, blood pressure, and the participant’s rating of perceived exertion to assist us in gauging the intensity of our intervention. These variables could also assist us in differentiating between generalized physiological arousal and physiological activation in response to task-related challenges. As discussed earlier in the dissertation, our intervention study did not include a control group that did not receive the intervention. This limits our ability to attribute the post-intervention reduction in SNS activity solely to the intervention. Additionally, we do not know if factors such exposure to the walking assessment tasks at baseline and post-intervention could have contributed to the reduced SNS activity. Our future studies will address this limitation by including skin conductance-based measurements of SNS activity at multiple time points during the course of the intervention study.
CHAPTER 6
CONCLUSIONS

The findings of this dissertation support the feasibility and validity of measuring SNS activity by skin conductance to assess the perceived challenge during complex walking in adults-post stroke. The measurement of SNS activity could greatly benefit assessments of mobility impairment and recovery in individuals with (and without) neurologic injury. For instance, measurement of the magnitude of SNS activity during walking tasks could help in identifying the individuals who are anxious and/or fearful, and therefore at a higher risk for falls during walking. Furthermore, the magnitude of SNS activity could also assist in identifying the complex walking activities that are particularly challenging after stroke. These are important aspects of mobility impairment and recovery that should be investigated by future studies. Additionally, the measurement of SNS activity to assess the perceived challenge during walking could inform about the effectiveness of rehabilitation interventions in decreasing the physiological stress response to walking-related tasks, which could greatly benefit the advancement of existing rehabilitation interventions. An intervention-induced reduction in the perceived challenge during walking could encourage greater participation in walking-related activities at home and in the community, and increase the engagement in important life-roles in individuals with impaired mobility.
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BIOGRAPHICAL SKETCH

Sudeshna Chatterjee is a licensed physical therapist with several years of experience in conducting gait research in neurologically impaired populations. She received a bachelor’s degree in physiotherapy from Maharashtra University of Health Sciences, India. She has a master’s degree in kinesiology (with minor in gerontology) from Iowa State University. Under the mentorship of Dr. Ann Smiley-Oyen, she examined trunk accelerations to gauge walking smoothness and the direction of gait instability in adults with mild to moderate Parkinson’s disease. She received a PhD in Rehabilitation Science from the University of Florida, where under the mentorship of Dr. David Clark, she worked on multiple federally-funded clinical trials of walking rehabilitation in adults post-stroke. During her doctoral training she has been exposed to a wide range of neurophysiological and biomechanical data acquisition and analysis techniques including measurement of muscle activation (electromyography), brain activation (functional near-infrared spectroscopy), sympathetic nervous system activity (skin conductance), motor evoked potentials, and biomechanical analysis of gait. She has also been involved in delivering therapeutic interventions to stroke participants enrolled in the walking rehabilitation studies, often serving as the lead therapist. During her time at the University of Florida, she served as a Teaching Assistant for the Department of Physical Therapy and assisted with multiple courses, including Biomechanics, Motor Control and Learning, and Neurological Rehabilitation. Sudeshna plans to continue her research on walking rehabilitation after stroke as a post-doctoral researcher at the NFSG VA Brain Rehabilitation and Research Center, and the University of Florida under the mentorship of Drs. David Clark and Dorian Rose.