ASSESSING SENSORY COMPLICATIONS OF TYPE 2 DIABETES THROUGH CONCURRENT BALANCE TESTING

by

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Dedicated to my loving wife Johanna and our dog Ivy

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PREFACE

Throughout my academic and professional career, I have developed a strong foundation in both the science of human movement and the clinical management of disease. My education in biomechanics and sensorimotor control, combined with hands-on clinical experiences, has allowed me to appreciate not only how research is conducted but also how scientific discoveries can directly improve patient care. These complementary experiences ultimately led me to pursue research at the intersection of human balance and Type 2 Diabetes (T2D).

My interest in human movement began during my undergraduate studies, where I became fascinated by the physiological and biomechanical processes that govern how the body functions. Coursework in anatomy, physiology, biomechanics, and exercise science provided the scientific foundation for this interest. Toward the end of my undergraduate education, I completed an internship at an outpatient vascular clinic, where I worked closely with patients affected by vascular disease. During this experience, I recognized the profound impact that T2D has on vascular health and mobility. I witnessed firsthand how complications associated with diabetes can threaten an individual's ability to walk and, in turn, dramatically diminish independence, quality of life, and overall health. This experience reinforced the importance of early identification and intervention for diabetes-related complications.

Following my undergraduate studies, I began my master's degree under the mentorship of Dr. Joshua Haworth. Through his guidance, I developed a deeper understanding of biomechanics and postural control while gaining valuable experience in scientific

research. During this time, I learned how quantitative measures of human movement can be used to investigate clinically relevant questions and improve our understanding of balance and mobility.

During my master's program, I also completed an internship with a primary care physician whose practice focused extensively on the management of patients with diabetes. This experience provided me with an in-depth understanding of the clinical approaches used to screen for, diagnose, and manage T2D and its associated complications. While working in this setting, I recognized that patients often undergo multiple specialized examinations to identify individual sensory complications, highlighting an opportunity to develop more accessible and efficient screening approaches.

The combination of these research and clinical experiences inspired the work presented in this dissertation. By integrating principles of biomechanics with clinically relevant questions in diabetes care, this research seeks to evaluate balance as a practical and functional means of screening for sensory complications associated with T2D. It is my hope that this work contributes to the development of accessible screening tools that facilitate earlier detection, improve clinical decision-making, and ultimately enhance the quality of life of individuals living with diabetes.

ABSTRACT

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Type 2 diabetes (T2D) is associated with microvascular complications that impair multiple sensory systems critical for maintaining balance, including proprioceptive, visual, and vestibular function. These impairments, commonly manifested as diabetic peripheral neuropathy (DPN), diabetic retinopathy (DR), and diabetic vestibulopathy (DV), contribute to increased postural instability and elevated fall risk. Current clinical approaches assess these complications independently using specialized diagnostic tools, limiting the feasibility of early, comprehensive screening. Therefore, there is a need for accessible, functional assessments capable of identifying sensorimotor impairments associated with T2D.

The purpose of this dissertation was to evaluate the utility of balance-based assessments, specifically the Modified Clinical Test of Sensory Interaction in Balance (mCTSIB), as a

screening tool for detecting T2D-related sensory complications. This work was conducted through a series of manuscripts that progressively examined the relationship between balance performance and sensory dysfunction.

The first study established the theoretical and physiological basis linking T2D related microvascular complications to impairments in sensorimotor control of balance. The second study investigated the relationship between mCTSIB performance and self-reported sensory complications using multivariate linear regression, demonstrating that increased postural sway was associated with the presence of T2D related impairments. The third study expanded upon these findings using logistic regression analyses to evaluate the ability of mCTSIB performance to discriminate between individuals with and without specific sensory complications. Measures of diagnostic accuracy, including odds ratios, sensitivity, specificity, and receiver operating characteristic curve analyses.

Collectively, the findings of this dissertation support the use of mCTSIB-derived measures of postural sway as a clinically feasible, non-invasive screening tool for identifying sensory complications in individuals with T2D. This work highlights the potential for functional balance assessments to provide an integrated evaluation of sensorimotor deficits, offering a practical approach for early detection and improved clinical management of T2D related impairments.

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LIST OF ABBREVIATIONS

T2D: Type 2 Diabetes

DPN: Diabetic Peripheral Neuropathy

DR: Diabetic Retinopathy

DV: Diabetic Vestibulopathy

oVEMP: Ocular Vestibular Evoked Myogenic Potential

cVEMP: Cervical Vestibular Evoked Myogenic Potential

VNG: Videonystagmography

DVA: Dynamic Visual Acuity

mCTSIB: Modified Clinical Test of Sensory Interaction in Balance

COP: Center of Pressure

CAN: Cardiac Autonomic Neuropathy

AR: Aldose Reductase

AGE: Advanced Glycation End Products

CNS: Central Nervous System

BG: Blood Glucose

NPDR: Non-Proliferative Diabetic Retinopathy

PDR: Proliferative Diabetic Retinopathy

DME: Diabetic Macular Edema

BRB: Blood-Retinal Barrier

VEGF: Vascular Endothelial Growth Factor

BtrackS: Balance Tracking System

Dxt: Time Since Diagnosis of T2D

ANOVA: Analysis of Variance

OR: Odds Ratio

CI: Confidence Interval

ROC: Receiver Operating Characteristics

AUC: Area Under the ROC Curve

CHAPTER ONE

INTRODUCTION

1.1 Introduction

Type 2 diabetes (T2D) is a prevalent and progressive metabolic disorder associated with a wide range of microvascular complications that impact multiple physiological systems. Among these, sensory complications such as diabetic peripheral neuropathy (DPN), diabetic retinopathy (DR), and diabetic vestibulopathy (DV), have profound effects on functional mobility and postural stability (1–4). Individuals with T2D are at an increased risk of falls, reduced mobility, and diminished quality of life, with balance impairments serving as a key contributor to these outcomes (5–8).

Postural control is a complex process that relies on the integration of visual, proprioceptive, and vestibular inputs to maintain stability (8,9). In individuals with T2D, each of these sensory systems may be independently or concurrently impaired. DPN disrupts somatosensory feedback from the lower extremities, reducing proprioceptive acuity (1,10,11). DR compromises visual input necessary for environmental orientation and motion detection (2,3,12,13). DV, though less frequently assessed in clinical settings, affects balance control and kinesthetic sense (6,14–16).

Current clinical practice recommends that patients with T2D undergo comprehensive foot and eye exams at least once every year, but less than 50% of people with T2D adhere to these guidelines (3,17–19). No current guidance exists for vestibulopathy testing for people with T2D, even though between 40-60% of the T2D population is known to be affected by vestibulopathy (6,20,21). Testing for DPN usually includes a nerve

conduction study, which assesses the nerves' response to electrical stimuli (22). DR is assessed through a retinal exam or imaging, where a trained professional visually confirms the presence and severity of lesions and edema in the retina (23–25). Testing for DV can be much more complicated since the vestibular organ has several structures that may be affected. Each structure requires a separate tool for assessing its function: ocular vestibular evoked myogenic potential (oVEMP) is needed to assess the saccular, cervical vestibular evoked myogenic potential (cVEMP) is needed to assess the utricle, and videonystagmography (VNG) or dynamic visual acuity (DVA) is needed to assess the semicircular canals and vestibular nerve (14,26,27). The multiplicity of tests needed to screen T2D patients for DPN, DR, and DV creates significant monetary and time burdens, making testing inconvenient or even inaccessible for many people.

Balance assessments provide a functional quantitative measure of the sensorimotor systems' abilities. The ability to maintain upright posture reflects the peripheral and central nervous system's capacity to collect and integrate sensory inputs then generate appropriate motor responses (8,9). The Modified Clinical Test of Sensory Interaction in Balance (mCTSIB) is a widely used protocol that systematically alters sensory conditions to assess reliance on visual, proprioceptive, and vestibular inputs (28–30). By manipulating surface stability and visual availability, the mCTSIB isolates the contribution of each sensory system to postural control.

Quantitative measures of postural sway, such as center of pressure (COP) path length, provide objective indicators of balance performance. Increased sway has been consistently associated with impaired sensory function and increased fall risk (31,32).

Advancements in portable force plate technology have enhanced the feasibility of using balance assessments as clinical screening tools, allowing for rapid, low-cost, and non-invasive evaluation of postural control (33,34).

Although the relationship between T2D and balance impairment is well established, several important gaps remain. First, there is a lack of research examining the concurrent contribution of multiple sensory impairments to balance dysfunction. Most studies evaluate DPN, DR, or DV in isolation, failing to capture the integrated nature of sensorimotor control. Second, there is limited evidence supporting the use of functional balance assessments as screening tools for specific sensory complications. While increased postural sway is associated with T2D (32), it remains unclear whether these measures can reliably distinguish between individuals with and without specific sensory impairments. Third, DV remains underrecognized and underdiagnosed, despite emerging evidence suggesting a high prevalence in individuals with T2D (6). The absence of routine vestibular screening contributes to an incomplete understanding of balance dysfunction in this population.

1.2 Purpose of Dissertation

The overall purpose of this dissertation is to evaluate the use of balance assessments as functional screening tools for identifying sensory complications associated with T2D. Specifically, this dissertation investigates whether performance on the mCTSIB can (1) characterize sensorimotor impairments in individuals with T2D and (2) Assess screening capabilities of the mCTSIB for T2D sensory complications.

1.3 Organization of dissertation

This dissertation is organized into a series of manuscripts that collectively address the purpose of this work. The first manuscript (Chapter 2) establishes the scientific foundation by describing the development of T2D and its associated microvascular sensory complications. This detailed overview provides an explanation of the pathophysiological mechanisms underlying DPN, DR, and DV, as well as how these conditions interact to impair the sensorimotor control of balance. Additionally, this chapter reviews current treatment approaches for each complication. The second manuscript (Chapter 3) presents an original study examining the relationship between overall mCTSIB performance and the presence of self-reported T2D sensory complications. Potential confounding variables were first assessed, followed by multivariate linear regression analyses to determine whether mCTSIB balance scores were associated with sensory complications. The purpose of this study was to explore the degree to which self-reported complications affect overall balance performance. The third manuscript (Chapter 4) expands on this work using a larger dataset and a test of the reversed directional relationship. Logistic regression analyses examined the relationships between specific mCTSIB conditions and corresponding self-reported complications (i.e., proprioceptive condition with DPN, visual condition with DR, and vestibular condition with DV). This analysis allowed for the estimation of odds ratios, area under the curve (AUC), sensitivity, and specificity for using mCTSIB sensory condition scores to predict T2D sensory complications. The purpose of this study was to determine whether the mCTSIB could function as a condition specific screening tool for T2D sensory

complications. The final chapter (Chapter 5) summarizes the findings of this dissertation and outlines future directions for this line of research.

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CHAPTER TWO

CROSS-CUTTING EFFECT OF TYPE 2 DIABETES ON THE SENSORIMOTOR CONTROL OF BALANCE

2.1 – INTRODUCTION

Type 2 diabetes (T2D) is a systemic disease that can have a far-reaching effect on daily life. The microvascular complications associated with T2D directly interfere with the sensory components of balance, increasing the risk for falls and injury. Exercise is very important for the management of T2D and can even help improve the symptoms of these microvascular complications, but precautions should be taken for those with complications to ensure their safety. This work will review the current literature to compile what is known about 1. the pathomechanics of T2D and the sensory complications caused by it, 2.how the sensorimotor control of balance is affected, 3. proper exercise prescription and treatment options available for those with these sensory complications of T2D.

2.1.1 Sensorimotor Control of Balance

In a physical fitness-related setting, the ability to maintain, gain, or regain balance is crucial to completing tasks safely, and effectively. This can also be defined as postural control (1). Within postural, there are three different types of sensory integration, including proprioception, vision, and vestibular (2). These sensory systems work together to provide postural feedback in-order for the body to constantly reorganize and maintain balance (3). Each of these sensory components act as a fail safe for one another, but with the loss of each system an individual's stability suffers. While balance loss is primarily

seen as a physical impairment, it has also been shown to significantly affect psychological factors as well, such as increased fear of falling, denying independence as well as confidence in one's ability to perform certain tasks (4).

2.1.2 Proprioception

Proprioception is important in serving as an afferent-efferent neurological pathway to maintain body stability and orientation (5). Within the muscles, tendons, and skin are receptors such as muscle spindles and cutaneous receptors that when stretched or forced upon are stimulated, providing positional information of the affected area (6,7). The nervous system is responsible for relaying this information to the brain, any damage to these components may cause these signals to be altered and lead to injury through insufficient positional adjustments. During exercise the systems responsible for proprioception experience an increased demand as well as fatigue requiring accurate signaling to perform safely. Without proprioceptive neuromuscular function, the body struggles to "feel" destructive postural habits, as well as positional awareness of the affected limb (6,8). This may lead to unsteady balance or overexertion of the muscle/limb, which may have significant consequences during exercise. Research within proprioception still needs more development in regard to mending proprioceptive deficits to improve function and overall balance (5).

2.1.3 Vision

The visual component of balance relays information about the ever-changing surrounding environment checking for accuracy of the movement and possible readjustments that need to be made (9). Studies have shown that when visual information is available the

visual sense dominates the control of balance specifically during movement planning (10,11). When visual information is not available other systems compensate for this loss of information causing decreased stability (12). Impairments to the visual system have a detrimental effect on postural stability, impacting the sensorimotor and vestibular-ocular reflex (13). When the vestibular-ocular reflex is damaged maintaining eye positioning during movement becomes disturbed, resulting in disorientation (14). As vision deteriorates a person's field of vision may become blurred, distorted, or absent affecting their ability to see their surroundings and adapt to them.

2.1.4 Vestibular

The vestibular system works differently compared to the two prior senses, as its response is unaffected by the knowledge of the source and acts automatically through reflex (15). The vestibular system responds to acceleration of the head in space and therefore automatically signals self-motion. The three main structures related to balance are the semicircular canals, utricle, and saccule. All three of these are filled with fluid and contain small hairs that bend when the fluid shifts due to linear or rotational accelerations. These structures then send the information, via the vestibular nerve, to the brain (13). When any of these components become damaged, vestibulopathy is likely to appear resulting in damage to the vestibular-ocular reflex as well and instability (16).

2.2 Balance and Exercise

Exercise relies heavily on the ability to maintain postural control, with the central nervous system playing a crucial role of integrating the sensory information for proprioceptive, visual, and vestibular senses (17). Through the utilization of these

systems during exercise postural stability can also be enhanced through strengthening, adaptations, and compensations of these senses (18). Exercises such as Tai Chi, resistance/power training, three dimensional training, general physical activity, or computer based balance training have all been shown to improve postural stability (19). These improvements have been shown as a promising way of recovering lost sensation, reduced risk of falling, and increased physical function (19).

2.3 Balance and Diabetes

The sensorimotor component consists of the proprioception, vision, and vestibular senses (2,20). When any of the three sensory components become impaired, the persons balance capabilities are reduced, leading to an increase in falls risk. While age is known as a large contributing factor to balance loss, studies have shown that persons with T2D have increased balance impairment independent of age (21). The sensory complications of T2D (figure 1.) have the potential to affect all three of the sensorimotor components of balance. Neuropathy impacts proprioception (22), retinopathy impacts vision (23), and vestibulopathy impacts the vestibular system (24), making diabetics highly susceptible to balance impairments and falls (25,26). This, alongside diabetics impaired ability to heal, makes minor injuries from falls much more dangerous for those with T2D (27).

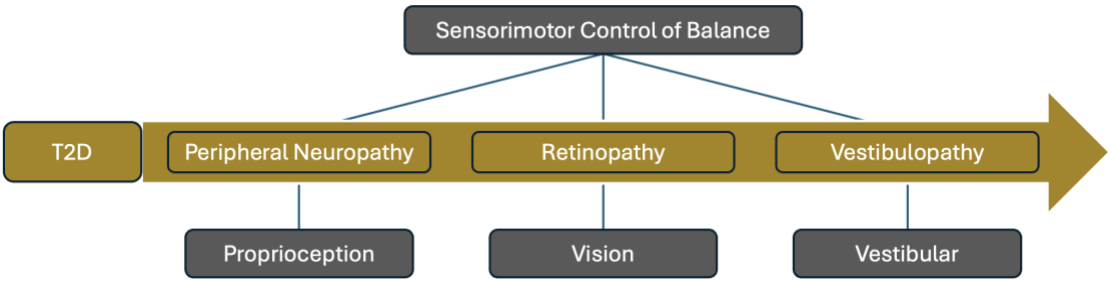

Figure 1. Diabetes sensory complications crosscut the sensorimotor control of balance by impacting proprioception, vision, and vestibular functions, the main sensory contributors to postural control and stability.

2.3.1 Diabetic Peripheral Neuropathy

Diabetic peripheral neuropathy (DPN) is one of the hallmark complications of T2D. Progression of DPN is often slow, with symptoms starting in the distal extremities first, where damage to the nerves of the feet and or hands cause increased sensitivity to pain, temperature, and eventually numbness (28). When left unmanaged or treated it can progress to more medial nerves, including those of the heart, resulting in cardiac autonomic neuropathy (CAN), which caused alterations to heart rate, blood pressure, and cardiac output (29). Screening for DPN is usually done using the monofilament test, sensory function tests, or symptomology of the peripheral extremities and Achilles tendon reflex (30). Further testing may be done to confirm diagnosis using a nerve conduction test to assesses electrical abnormalities in the nerve or a corneal confocal microscope to image the morphology of the nerve, though is not commonly used (31).

2.3.1.1 Pathology of DPN

DPN is a slow progressive disease that is thought to be caused by the microvascular occlusion and hyperglycemia found in T2D (32). While the exact mechanism causing DPN is not yet well understood, there are several theories that provide some insight into the onset and progression of DPN. Aldose reductase (AR) is a regulatory enzyme found in the polyol pathway that is upregulated in ischemic hyperglycemic conditions (33). This pathway is responsible for converting glucose into fructose and produces advanced glycation end products (AGE) and sorbitol which are known to cause oxidative stress (34–36). This oxidative stress in turn causes structural changes in the

peripheral nerve and to the dorsal root ganglion (33). It has been proposed that these structural changes are due to glycation, where AGE and sorbitol molecules are deposited into these nervous structures. AGE molecules induce oxidative stress and inflammation, which can directly harm nerve cells. Sorbitol, meanwhile, accumulates due to impaired glucose metabolism, leading to osmotic stress within Schwann cells. These factors contribute to toxicity, triggering apoptosis Schwann cells, demyelination, distal fiber degeneration, and impaired nerve regeneration (33,35). The result of these changes can be seen in the nerves reduced conductive ability, resulting in altered or absence of signaling, where the affected limb may go completely numb.

2.3.1.2 Relation to Balance

The presence and severity of DPN have been shown to increase postural instability (37). Measures of balance in patients with DPN are limited to postural sway during quiet standing, resulting in increased postural sway (38). Postural movements during both quiet standing and walking have demonstrated greater variability in patients with DPN, which suggests an increased difficulty in regulating movement, destabilizing the body even more in itself (39). DPN most commonly leads to a decay in the lower extremities and nervous system, not allowing the important sensory systems to function properly (40). This creates a dearth of proprioceptive information coming from the lower extremities, resulting in postural instability during static on non-static situations (41). In the late stages with the development of CAN, patients may develop orthostatic hypotension, where sudden changes in body positioning lead to a drop in blood pressure and result severe instability (29).

2.3.1.3 Treatment for DPN

The treatment for DPN primarily focuses around reducing pain, where a wide variety of drugs may be prescribed. The anticonvulsant drug pregabalin is recommended by the American Academy of Neurology as first-line therapy, which inhibits neurotransmitters in the CNS helping to block pain (32). Antidepressants, analgesic, and opioids may also be used when necessary to help reduce pain (32). However, a downside of these pharmacological options is further reduction of proprioception, which exacerbates problem with sensorimotor control. Additional treatment options include blood glucose, blood pressure, lipid and weight loss medications to help manage the symptoms and progression of the overarching disease, T2D.

2.3.1.4 Exercise Prescription

Recent studies suggested that aerobic physical activity, alone or in combination with resistance exercise, may be an effective therapeutic modality for T2D through revascularization and increased blood supply (42–44). It was found that a prescribed aerobic exercise regimen of mild intensity can positively influence both motor and sensory neuromuscular parameters (45). Diabetes patients are encouraged to do 30 minutes to an hour of aerobic activity most days of the week, as well as resistance training performed twice a week (46). More specific exercise programs such as sensory motor training or Tai Chi have been shown to improve neuromuscular structures and improve the symptoms of DPN (47). Specifically Tai Chi has been found to increase vascular function and improve blood flow to the peripheral limbs (48). There is also a risk with of those with DPN being unable to feel possible foot injuries and should take

special care if one is present by only performing non weight bearing exercises such as swimming or biking (49).

2.3.2 Diabetic Retinopathy

Diabetic Retinopathy (DR) is a prevalent complication of T2D that results in the loss of vision. DR is a progressive disease that stems from the microvascular damage and vascular occlusion in the retinas and is considered to have two clinical stages. The first stage, non-proliferative diabetic retinopathy (NPDR), occurs when vascular permeability, microaneurysms, and capillary occlusion are observable in the retinal vasculature (23,50). The second stage, proliferative diabetic retinopathy (PDR), is more advanced stage that occurs with neovascularization, vitreous hemorrhage, or tractional retinal detachment (23,50). During either of these stages diabetic macular edema (DME) may present and is “the most common cause of vision loss in patients with DR” (50). DR is diagnosed by a retinal eye exam, where an ophthalmologist will visually inspect the retina for lesions, vascular abnormalities, and edema in the retina (51).

2.3.2.1 Pathology of DR

Hyperglycemia is responsible for the initial onset of NPDR, where elevated blood glucose levels cause retinal blood vessel dilation, pericyte apoptosis (cells providing structural support for capillaries), and endothelial cell apoptosis (52). With the loss of these pericyte cells, vascular permeability increases, microaneurysms formation, and breakdown of the blood-retinal barrier (BRB) in the capillaries of the retina occur. The onset of the second stage, PDR, is seen once progression of pericyte and endothelial cell death leads to retinal ischemia (from capillary occlusion) and upregulation of vascular

endothelial growth factor (VEGF) (53). VEGF is a strong angiogenic factor that causes increased vascular permeability and neovascularization (clinical feature of PDR) (54). During these events, the increased permeability and breakdown of the BRB in the retinal capillaries cause fluid to accumulate in the macula (center of the retina), causing it to swell and thicken and eventually lead to DME and vision loss (50).

2.3.2.2 Relation to Balance

Retinopathy is well understood as contributing to gait instability and falls (13,55). DR causes significant losses to a person's visual sense, causing individuals (especially in the later stages) to not be able to accurately perceive and adjust to their environment (23). These losses can either be due to a person's inability to receive the information (retinal damage) or accurately relay the information (ocular nerve damage) (56). With damage to the retina and the loss of visual information, greater reliance is put upon the other systems causing reduced postural stability. Loss of the peripheral visual field is another consequence of DR, that appears to cause a large effect on instability, specifically in side-to-side and forwards-backwards movements (57). With damage to the ocular nerve the vestibular-ocular reflex becomes impaired reducing eye tracking ability and ocular focusing, putting greater stress on the proprioception sense (14).

2.3.2.3 Treatment of DR

There are several forms of treatment available for those with DR. The most promising are the anti-VEGF medications that have been found to reduce and even reverse DR (58,59). This medication is injected monthly or bimonthly to help reduce VEGF levels in patients with DR. Intravitreal corticosteroids is a potent anti-

inflammatory drug that is used to treat the early stages of DR (NPDR) and DME when patients do not respond to the anti-VEGF (50). Alongside medications laser treatment is another option for treating DR. Laser photocoagulation has been found to reduce DME, prevent vision loss, and regress neovascularization, even though it is still unclear the exact mechanism behind this (50,60).

2.3.2.4 Exercise Prescription

Exercise prescription for visually impaired patients can be difficult to provide due to situations where complications can outweigh expected benefit, especially in subjects with diabetes. Although exercise is beneficial in diabetes, previous studies have shown contradictory and inconclusive results on how it affects DR (61). Some studies have found that physical activity has been shown to slow the progression (62). Aerobic exercise has been shown to do this through reduced inflammation and oxidative stress in the eye (63). Careful monitoring of the intensity of the exercise is very important for those with DR. More vigorous forms of exercise, such as sprinting or heavy resistance training, may induce greater hemodynamic pressure and cause more ocular hemorrhaging, and thus should be avoided (64).

2.3.3 Diabetic Vestibulopathy

Diabetic vestibulopathy (DV) is a prevalent complication of T2D that is not as well known (25). Studies have found that those with T2D are significantly more likely to have DV compared to those without T2D (65). The vestibular system is a small complex of organs located in the inner ear that are responsible for relaying information about head orientation, accelerations, neural reflexes (66). When any of these organs or the vestibular

nerve become damaged these senses and reflexes become impaired. There are several symptoms associated with DV, such as vertigo, nausea, intolerance to head movement, and postural instability (67). Testing for DV can be difficult due to the number of organs involved, with each requiring a different method to assess. The vestibulo-ocular reflex and the semicircular canals are assessed using a caloric test or video head impulse test, the vestibulo-spinal reflex and saccule can be assessed using a cVEMP, and the utricle is assessed using an ocular VEMP (24).

2.3.3.1 Pathology of DV

The exact pathology of T2D causing DV is not yet well understood, but evidence from animal studies provide some insight into the possible mechanisms behind it. It is theorized that DV can develop through hyperglycemias cascading effect on either the organs of the vestibular system or the vestibulocochlear nerve. The oxidative stress caused by chronic hyperglycemia was found to increase the extracellular matrix, lysosomes, and lipid droplets in the connective tissue of the saccule and utricle damaging the membrane and leading to impaired diffusion capabilities and ischemia (13,68). This then leads to type 1 hair cell (cells involved in large head acceleration) degeneration in the saccule and utricle. With the vestibulocochlear nerve, elevated AGEs from chronic hyperglycemia induce demyelination and lysosomal digestion of the nerve, resulting in myelin sheath thinning and reduced axonal fiber diameters (13). Both of these pathways lead to dysfunction of the vestibular sense shown by “longer latency and reduced amplitude of vestibular evoked potentials” (13).

2.3.3.2 Relation to Balance

Postural control relies on many sensory cues from the vestibular system, specifically with accelerations and head positioning. This information is something that the other senses are not able to easily compensate for, causing heavy reliance on the proprioceptive and visual information available (69). DV can either be unilateral or bilateral, without the presence of other sensory impairments, these two types of DV have similar effects on a person's postural stability, but once another sensory impairment is present, bilateral DV becomes significantly more impactful (70). DV has also been shown to have a multi-sense effect, with impairment of the vestibulo-ocular reflex also impacting a person's ability to control eye movements and tracking (71,72).

2.3.3.3 Treatment of DV

Currently there are no effective pharmacological or surgical treatment options available for those suffering with DV. The only form of treatment that has shown some DV related improvements is vestibular rehabilitation therapy (73). This exercise-based treatment program focuses on retraining aspects of a person’s motor control to compensate for the lack of vestibular input. Vestibular rehabilitation therapy has been shown to help alleviate symptoms such as dizziness and postural instability using specific balance exercises daily (73).

2.3.3.4 Exercise Prescription

As with the other sensory complications physical activity can act as a preventative measure to DV but with its onset and its symptomatology, continuing exercise may become difficult and more dangerous (74). Vestibular rehabilitation exercises have been

developed and can be utilized to train and compensate the vestibular sense with those experiencing DV safely (75). Balance retaining and goal-directed eye-head exercises have been found to significantly improve postural stability in those with DV (76,77). Head movements exercises such as head turns, head-trunk turns, and head walking turns have all been shown to help recalibrate the vestibulo-ocular reflex (78,79). Active body movements such as walking with sharp turns and sit-to-stand has been shown to help with vestibulospinal regulation (75,78,79).

2.4 Conclusion

This work summarized the pathomechanics of T2D and its sensory complications, their impact on the sensorimotor control of balance and exercise, and treatment options based on the current literature. DPN, DR, and DV directly impair proprioception, vision and the vestibular sense leading to a significantly higher risk of falls and loss of stability. While exercise is a key component to the management of T2D, special considerations must be taken to ensure patient safety when exercising with these complications. Improper exercise programming may lead to worsening of the conditions or injury, as such routine screening practices are needed for these complications to ensure proper treatment and exercise programing is prescribed. Development of better screening methods to improve adherence and detection of T2D complications will ensure that individuals with T2D are able to receive the care and treatments they need.

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CHAPTER THREE

STANDING BALANCE IMPAIRMENT IN PERSONS WITH TYPE 2 DIABETES IS PREDICTED BY PERIPHERLAL NEUROPATHY AND VESTIBULOPATHY

3.1 Introduction

Type 2 diabetes (T2D) is a highly prevalent disease affecting 1 in 10 Americans and is the most common form of diabetes (1). In a very simplistic way T2D has been predominantly considered a lifestyle disease (2), where the consequences of reduced physical activity and poor diet accumulates overtime, altering the body's ability to produce and utilize insulin. While T2D itself may not be considered fatal, when left uncontrolled it can cause irreversible harm to several important bodily systems and result in life altering complications if not diagnosed and treated early.

Diabetic peripheral neuropathy (DPN), diabetic retinopathy (DR), and diabetic vestibulopathy (DV) are highly prevalent complications of T2D (3–5) and can alter a person's ability to function in day-to-day life activities. Those that develop DPN may experience numbness or pain in their extremities, while DR can impair their vision, and DV will impact the kinesthetic sense. Complications such as these are progressive in nature and are reversible if caught early enough (6). Therefore, it is recommended that persons with T2D have comprehensive foot and eye exam every year to screen for DPN and DR (7). However, despite these recommendations, less than 50% receive proper screening for DPN or DR (8), and currently there are no guidelines for screening DV, which may be due to expense and accessibility (8). In order to assess DR and DV a patient must see a specialist (6), highlighting the need to develop an affordable and

accessible screening tool to help improve early detection and treatment of these complications.

Balance assessments can be used to assess different sensory components of a person's balance and may be a solution for an affordable and assessable screening tool. For instance, the Romberg test is a simple balance assessment used to screen for vestibulopathy, yet it has not been fully integrated into a modern clinical setting (9). Currently, research on balance assessments have shown that those that sway more during a static standing balance test are "more unstable" and have an increased risk of fall events (10). Both sex and age have a significant effect on a person's sway (10–13), with males swaying more than females and older individuals swaying more than younger individuals, and socioeconomic factors, e.g. low education and income, have shown to be related to increase falls risk (14,15). However, despite the research on balance assessments, the impact of chronic diseases such as T2D is more limited in scope and understanding.

Within the past couple years, new evidence has shown balance assessments to be a quick and easy way to assess many sensory aspects of postural sway for patients with T2D during a visit with their primary care physician (16). Specifically, the Modified Clinical Test of Sensory Integration in Balance (mCTSIB) can assess the three different sensory components of balance (proprioception, visual, and vestibular) (11,17), all of which can be directly affected by sensory complications of T2D. DPN affects the proprioceptive sense in the feet, DR affects the visual sense of the eyes, and DV affects the vestibular sense of the inner ear. Due to this relationship, it may be feasible to screen for these three complications using this form of balance assessment. Therefore, the goal of this study

was to assess the predictability of balance scores using T2D sensory complications and identify possible confounding variables as the initial steps in determining the feasibility of using balance testing as a screener for the sensory complications of T2D.

3.2 Materials and Methods

3.2.1 Participants

Participants were recruited from a local physician's office in metro Detroit Michigan. Participants were included in the study if they had physician diagnosed T2D, were 18 years or older, and were able to walk and stand unassisted. Participants were excluded from the study if they had any neurological disorders unrelated to T2D, had a lower limb replacement, or if they sustained a lower limb injury in the past 6 months. While limb amputation was not an explicit exclusion criterion, no participants in this study had an amputation or prosthetic. To reduce the risk of hypoglycemic episodes during testing, participants in this study were required to have a blood glucose level above 80 mg/dL. Informed consent was obtained after providing both written and oral explanations of the study procedures. The procedures of this study (FY2022-75) were approved by the Oakland University Institutional Review Board on 10/24/2021.

3.2.2 Testing Procedures

All testing on participants with T2D was conducted at the general physician's office during the participant's scheduled appointment. Fasting blood glucose, hemoglobin A1c, height, and weight were measured by physician's office staff during their appointment and then self-reported to the researcher. After consent was obtained participants completed a demographics questionnaire, which asked about their sex, age, ethnicity,

education, marital status, employment status, annual household income, and their number of dependents. Next, participants were asked questions related to their health history (e.g., years since T2D diagnosis, or multiple sensory complications). Presence of sensory complication was determined by self-report, participants were asked through separate lines of questioning whether a physician had ever diagnosed them with DPN, DR, or DV. During this time participants' blood glucose, A1c, height, and weight were recorded. Participant characteristics for the T2D group can be found in Table 1.

Balance testing was then performed using the modified Clinical Test of Sensory Integration in Balance (mCTSIB) on a BtrackS Balance Plate (Balance Tracking Systems Inc., CA, USA) connected to a 10" Windows 10 tablet (Fusion5, FWIN232 Plus S1) running BtrackS Assess Balance Advanced Software (v5.5.6).

The mCTSIB protocol evaluates the relative contributions of three sensory balance systems of postural sway control (11) with a high test-retest reliability (18). The mCTSIB consists of four different trials on a stationary force plate, each lasting 20 seconds. For each trial, the participant was instructed to stand as still as they can. The first trial (standard condition) had the participant stand still with eyes open. The second trial (proprioception condition) has the participants stand still with eyes closed. For the third trial (vision condition), and fourth trial (vestibular condition) the participant stands on a foam pad on top of the force plate with eyes open and then closed, respectively. Each condition was scored based on the amount of the participants' center of pressure (COP) path length (cm), where more COP path length resulted in higher scores. Higher scores indicate more postural sway and impaired postural stability, while lower scores indicate

less postural sway and healthier postural stability. COP path lengths and scores were calculated by the BtrackS Assess software (v5.5.6). Reference values for mCTSIB scores are available in the literature (12).

3.2.3 Measures

Categorical covariates included sensory complication (DPN, DR, DV, multiple complications), sex (male or female), ethnicity (white, African American, Hispanic, Asian, did not respond), education (high school or GED, associates or bachelor's degree, graduate or higher), marital status (single, married, widowed, divorced or separated) , employment status (full time, part time, retired, homemaker, unable to work), annual household income (<25k, $25k-$50k, $50k-$100k, $100k-$200k, >$200k), and the number of dependents (none, 1-2, 3-4, >4).

Continuous variables included age (years), height (cm), weight (kg), time since diagnosis of T2D (Dxt, years), A1C (%), blood glucose (BG, mg/dL), standard mCTSIB condition (cm), proprioception mCTSIB condition (cm), Visual mCTSIB condition (cm), Vestibular mCTSIB condition (cm), Total mCTSIB score (cm).

3.2.3 Statistical Analysis

Mean and standard deviation values were calculated for all continuous variables and percent and frequency were computed for all categorical variables (Table 1). Sample size was projected using G*Power, with a linear multiple regression, fixed model, with R^2 increases used to confirm the sample size calculation. The study was designed to detect a moderate effect size of about 0.30. The level of significance and power were set at 0.05 and 0.80, respectively. It was assumed that the most parsimonious final model will have

four tested predictors and seven total number of predictors. With these assumptions, the minimum sample size was 42. The realized sample was 52 participants.

A Shapiro-Wilk test was performed to assess the normality of total mCTSIB scores. A box plot was created to show the distribution of the mCTSIB total scores by T2D sensory complication. In a bivariate analysis, linear regression beta coefficients and 95% confidence intervals were calculated for each of the predictors in relation to total mCTSIB scores. Following, a multivariable linear regression analyses was conducted using total mCTSIB scores as the outcome and sensory complication categories (none, DPN, DV, multiple complications) as the predictors. Covariates in the multivariable linear regression model were selected based on known factors to affect postural sway and mCTSIB scores (11). A Wald's test was used on variables found to be significant in the bivariate analysis, with significance set at $p < 0.05$, to determine if they were to be included in the final multivariable linear regression model. The final model included the sensory complications, age, and sex. Equal variance of the multivariable linear regression model was assessed using a residual vs. predicted plot. Normality assumption (of residuals) of the multivariable linear regression was assessed using a two-way scatter plot between the residuals and predicted values form the model and a stem and leaf plot the residuals. Collinearity was assessed using VIF and was found to 1.11, indicating no relationship between predictor variables in the model. Leverage and influence were used to check for outliers, but no outliers were found. No effect modification was examined. All data was calculated using Stata statistical software version 18.0. Statistical significance was set a p-value of $p < 0.05$.

3.3 Results

3.3.1 Descriptive Characteristics and T2D Sensory Complications

Shapiro-Wilk test of the total mCTSIB confirmed the normal distribution of the outcome ($p>0.05$). There were an equal number of male (50%) and female (50%) participants in this study. The average age of participants was 60.53 (± 12.06) years of age, with the oldest participant being 86 years of age and the youngest being 38 years of age. Most participants reported to be white (75%), to have an associate or bachelor's degree (38.5%), working full time (44.2%), have an annual household income between $50,000 to $100,000 (34.6), and not have any dependents (55.8%).

A majority of participants did not report any sensory complications (69.2%), while DPN was the most frequent sensory complication to be reported (19%) (Table 1.). There were no reports of participants having DR alone, but there were 2 cases where a participant reported having DR in combination with DPN or DV making up the multiple complication category. Those that reported having DPN or DV were found to have the largest average total mCTSIB scores (275.94 cm ± 71.88), while participants that did not report any sensory complications had the lowest average mCTSIB scores (187.75 cm ± 55.78) (Figure 1.).

Table 1. Descriptive Characteristics

Frequency and percentage of categorical variables followed by mean ± standard deviation of continuous variables of study participants for descriptive characteristics.

	Total
	(n = 52)

		n (%)
T2D Sensory Complication		
	DPN	10 (19)
	DR	0 (0)
	DV	6 (11.5)
	Multiple Complications	2 (3.8)
Sex		
	Male	26 (50)
	Female	26 (50)
Ethnicity		
	White	39 (75.0)
	African American	5 (9.6)
	Hispanic	1 (1.9)
	Asian	6 (11.5)
	Did not respond	1 (1.9)
Education		
	High School or GED	17 (32.7)
	Associates or Bachelor's	20 (38.5)
	Graduate or Higher	15 (28.8)
Marital Status		
	Single	8 (15.4)
	Married	35 (67.3)
	Widowed	4 (7.7)
	Divorced or Separated	5 (9.6)
Employment		
	Full Time	23 (44.2)
	Part Time	7 (13.5)

Retired	18 (34.6)
Homemaker	3 (5.8)
Unable to work	1 (1.9)
Annual Income	
<$25k	4 (7.7)
$25k-$50k	5 (9.6)
$50k-$100k	18 (34.6)
$100k-$200k	13 (25.0)
>$200k	4 (7.7)
Did not answer	8 (15.4)
Number of Dependents	
None	29 (55.8)
1-2	17 (32.7)
3-4	4 (7.7)
>4	2 (3.8)
	Mean ± SD
Age (years)	60.53 ± 12.06
Height (cm)	169.69 ± 9.62
Weight (kg)	95.36 ± 23.24
Time Since Diagnosis (years)	14.63 ± 9.21
A1C (%)	7.23 ± 1.29
BG (mg/dL)	149.75 ± 71.16
mCTSIB Standard (cm)	21.38 ± 9.76
mCTSIB Proprioception (cm)	38.15 ± 19.06
mCTSIB Vision (cm)	44.38 ± 14.09
mCTSIB Vestibular (cm)	110.94 ± 43.19
mCTSIB Total (cm)	214.89 ± 73.1

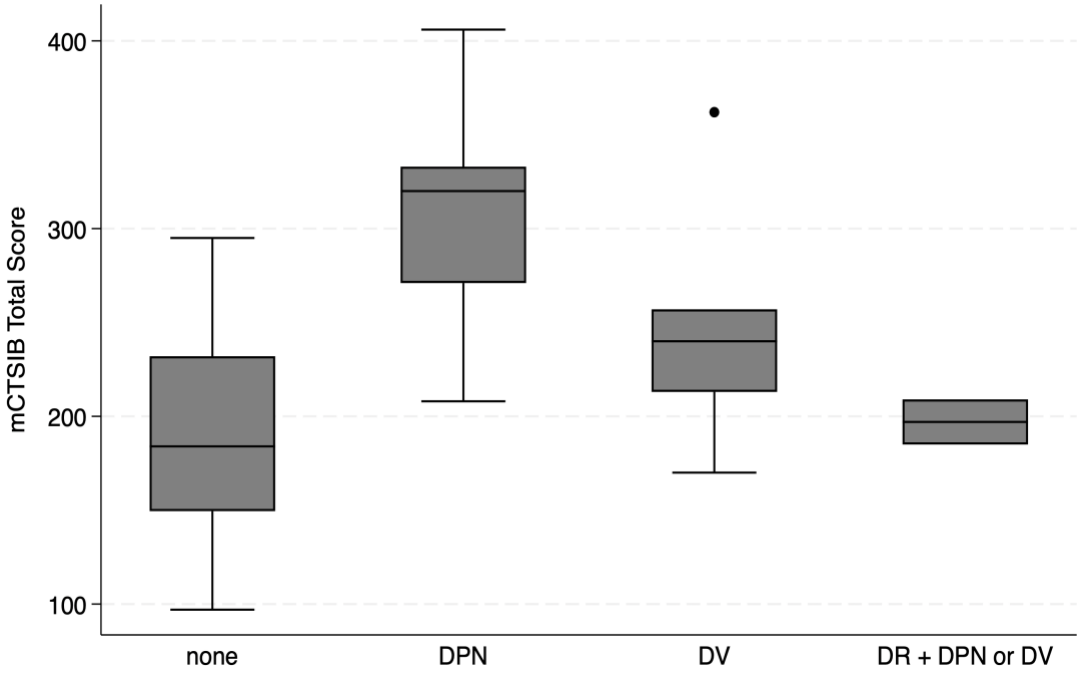

Figure 1. Box plot of mCTSIB total scores for each of the T2D sensory condition groups.

3.3.2 Bivariate and Multivariable Linear Regression analysis

Crude analysis of sensory complications showed that DPN and DV had a significant effect on total mCTSIB scores as well as education, employment, annual income, and age (Table 2.). Each year increase in age and retirement status were associated with increased total mCTSIB scores, while higher education and annual income were inversely related to total mCTSIB scores.

Although education, employment, and annual income were statistically significant in the bivariate analysis, they were not significant in the final model using the Wald's test ($p > 0.05$) and were removed from the final model. Sex was included in the model even though it was not statistically significant in the final model because previous literature has demonstrated that that mCTSIB balance scores differ by sex (11). The final model explained 45% of the variability observed in the balance scores (adjusted $R^2 = 0.45$).

The age and sex adjusted multivariable linear regression analysis showed that T2D sensory complications were positively associated ($p < 0.01$) with mCTSIB scores, as shown in Table 3. The total mCTSIB score, was 108.89 cm ($p < 0.01$) higher comparing those DPN to those without a T2D sensory complication. Although DV was positively associated with elevated mCTSIB total scores, the magnitude of the beta coefficient 58.34 cm ($p = 0.04$), was about half of that of DPN.

Table 2. Bivariate Analysis

Crude analyses of the descriptive characteristics in relation to total mCTSIB scores.

Bivariate Analysis	**Total (n = 52)** **Total mCTSIB Scores** **β (95%CI)**	**p**
Categorical Variables		
T2D Sensory Complication		
None	ref	ref
DPN	**121.03 (77.71-164.35)**	**<0.01**
DV	**60.65 (5.17-116.13)**	**0.03**
Multiple complications	9.25 (-75.20-93.70)	0.83
Ethnicity		
White	ref	ref
African American	-10.45(-87.32-66.42)	0.77
Hispanic	-23.20 (-171.61-125.21)	0.75
Asian	58.3 (-5.88-122.48)	0.07
Did not respond	62.8 (-85.61-211.21)	0.40
Education		
High School or GED	ref	ref

	Associates or Bachelor's	**-60.37 (-107.24- -1.45)**	**0.01**
	Graduate or Higher	**-50.72 (-99.98- -1.45)**	**0.04**
Marital Status			
	Single	ref	ref
	Married	-11.37 (-65.69-42.94)	0.68
	Widowed	76.75 (-8.12-161.62)	0.75
	Divorced or separated	58.60 (-20.41-137.61)	0.14
Employment			
	Full Time	ref	ref
	Part Time	-8.55 (-64.33-49.23)	0.79
	Retired	**46.86 (5.47-88.25)**	**0.03**
	Homemaker	-35.03 (-115.77-45.71)	0.39
	Unable to work	**208.30 (73.94-342.67)**	**<0.01**
Annual Income			
	<$25k	ref	ref
	$25k-$50k	-19.05 (-133.38-75.28)	0.69
	$50k-$100k	-49.47 (-27.20-28.25)	0.21
	$100k-$200k	**-90.71 (-171.11- -10.31)**	**0.03**
	>$200k	-91.00 (-190.43-8.43)	0.07
	Did not answer	24.25 (-110.36-61.86)	0.57
Number of Dependents			
	None	ref	ref
	1-2	-25.00 (-69.16-19.15)	0.26
	3-4	-76.66 (-153.76-0.43)	0.05
	>4	-37.91 (-143.59-67.76)	0.47
Continuous Variables			
Age (years)		**2.50 (0.93-4.07)**	**<0.01**

Height (cm)	1.86 (-0.24-3.95)	0.08
Weight (kg)	0.61 (-0.26-1.49)	0.17
Time Since Diagnosis (years)	-0.58 (-2.83-1.67)	0.61
A1C (%)	7.29 (-8.69-23.27)	0.36
BG (mmHg/dL)	0.19 (-0.09-0.48)	0.18

Table 3. Multivariable Model

Adjusted analyses of T2D sensory complications in relation to total mCTSIB scores.

Multivariable Model	**Total (n = 52)** **Total mCTSIB Scores** **β (95%CI)**	**p**
Adjusted model with Sex and Age		
T2D Sensory Complication		
None	ref	ref
DPN	**108.89 (66.02 -151.75)**	**<0.01**
DV	**58.34 (4.09-112.59)**	**0.04**
Multiple complications	-16.83 (-99.76-66.09)	0.685
Sex	-24.37 (-55.47-6.73)	0.12
Age	**1.63 (0.25-3.01)**	**0.02**

3.4 Discussion

This study sought to examine the association and predictability between the sensory complications of T2D and balance. The final multivariable linear regression model demonstrates significant relationships between T2D sensory complications and balance scores when adjusted for sex and age. Our findings align with other previous studies showing that T2D sensory complications have a significant effect on balance (3,19,20). A previous study by Agrawal (3), found these three sensory complications of T2D to have a direct effect on self-reported fall risk. The findings from this study further the understanding in this area with the utilization of quantifiable balance scores instead of self-reported falls risk.

The impact that DPN and DV have on balance may be explained through the interaction that each of these complications have with the sensory components of balance. According to Peterka (17), the three main sensory components of balance are proprioception, visual feedback, and vestibular sense. The sensory complications of T2D directly impair each of these systems, such as DPN distorting the tactile feedback from the feet limiting the proprioceptive sense (21), vestibulopathy causing damage to the nerve and complexes within the vestibular organ, resulting in reduced and distorted vestibular feedback (22). It is important to note that the presence of multiple sensory complications was not significantly ($p > 0.05$) related to mCTSIB scores. This lack of relationship appears confusing given that both DPN and DV were significant. Though only two participants in the multiple complications category limits the interpretation of multiple complications on balance performance.

While it is clear that T2D sensory complications have a direct effect on a persons' balance, it is still unclear how drastic of an effect that each of these complications has. Bonnet et al. (19) argued that DPN has the largest effect on balance, while others such as Agrawal (3) say that DV is the largest contributor. Our findings suggest that DPN caused the largest increase in COP path length but also show a large significant impact by DV, suggesting that DV warrants much more consideration in the context of balance control in persons with T2D.

Although an important consideration, several difficulties surround the diagnosis and study of DV, in persons with T2D. First, there are no current clinical guidelines for diabetic screening of DV, meaning that individuals with diabetes are rarely tested for DV, compared to DPN which is assessed at least annually (7). Moreover, even though DV was assessed in this study, all information on diagnosis of T2D sensory complications was self-reported and DV was additionally assessed by the symptoms the participant may have been experiencing (ex. vertigo, chronic dizziness, etc.), since many participants where not familiar with DV by name. These challenges highlight the difficulty in properly characterizing individuals with DV and may have limited the true number of participants that may have had DV in this study. While it may still be unclear how much each of these T2D sensory complications affect balance, our model provides preliminary evidence of the role of sensory complications as predictors of balance scores.

A strength of this study was that balance was using a quantifiable analysis, compared to similar studies that utilized surveys or proxies. Another strength was that that diagnosis of T2D sensory complications were collected and analyzed together on the same population,

although no participants were found to only have DR limiting the ability to assess the effects of DR alone. Additionally, the prevalence of the T2D sensory complications was below the expected prevalence of each, especially for DR and DV, which may limit the ability to generalize findings for individuals with DR and DV. This may be due to the limitations of self-reporting sensory complications by the participant. Due to the difficulty in collecting accurate diagnoses of DV, future research that screens for T2D sensory complications using objective diagnostic measures is needed to further examine the quantifiable effects of each T2D sensory condition.

3.5 Conclusion

This study was the first of its kind to use a quantifiable balance assessment to examine the relationship between T2D sensory complications and balance. It was found that self-reported diagnosis of DPN and DV may be used to predict balance scores when adjusted for sex and age. While more objective diagnostic measures of sensory complications are needed to confirm, this work provides the first pieces of evidence that balance assessments may be used as a screening tool for the sensory complications of T2D.

3.6 References

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CHAPTER FOUR

MULTISENSORY CONTRIBUTIONS TO POSTURAL CONTROL IN TYPE 2 DIABETES: LINKING PROPRIOCEPTIVE AND VISUAL DEFICITS TO MICROVASCULAR COMPLICATIONS

4.1 INTRODUCTION

Type 2 diabetes (T2D) is a prevalent global health condition, affecting approximately 589 million adults aged 20–79 as of 2024. Projections estimate this number will rise to 853 million by 2050, underscoring its rapidly growing burden (1). Among its most common and debilitating long-term consequences are microvascular complications that affect sensory function. Diabetic peripheral neuropathy (DPN), diabetic retinopathy (DR), and diabetic vestibulopathy (DV) are three such complications, impairing proprioceptive, visual, and vestibular systems respectively (2–5). These sensory systems are essential to postural stability, and their dysfunction significantly elevates fall risk in individuals with T2D (6–8).

Peterka's sensorimotor control model provides a foundational framework for understanding balance regulation through multisensory integration. The model describes a dynamic reweighting of sensory inputs, wherein proprioceptive information is prioritized under stable conditions, followed by visual and then vestibular input. When proprioceptive feedback is diminished, as in cases of DPN, the central nervous system compensates by increasing reliance on visual and vestibular cues (8). However, when multiple sensory systems are concurrently impaired, as is often observed in T2D, these compensatory mechanisms become insufficient, leading to impaired postural stability (6,9). DPN, resulting from degradation of peripheral nerves, has been linked to greater

medial-lateral sway and higher fall incidence during daily activities (10,11). DR further compromises visual acuity and spatial orientation, limiting visual compensation for balance deficits, while DV, though frequently underrecognized, impairs the brain's ability to interpret head and body motion in space, further destabilizing postural stability (6,10,12). Epidemiological data underscore the prevalence of these microvascular complications in T2D, with approximately 26–28% of adults affected by DPN (13,14), 27–34% by DR (4,15), and DV is reported in 50–80% of individuals depending on assessment methods and populations studied (16,17).

Balance assessments provide an effective means of evaluating the functional contributions of individual sensory systems to postural stability, particularly in populations with multisensory impairments such as those with T2D (18). The modified Clinical Test of Sensory Interaction and Balance (mCTSIB) is a validated tool designed to isolate proprioceptive, visual, and vestibular influences on balance by systematically manipulating visual input and surface stability (19–21). This approach enables quantification of sensory-specific postural stability by assessing the degree of sway under a proprioception, visual, and vestibular condition. Prior studies have demonstrated the mCTSIB's sensitivity in detecting distinct patterns of sensory impairment among individuals with T2D, including those with DPN, DR, and DV, supporting its value as an objective screening tool for sensory-related balance dysfunction in this population (6,18,22).

This study sought to demonstrate that objective measures of sensory-specific postural stability in individuals with T2D relate to self-reported microvascular complications

(DPN, DR, DV). We hypothesized that the proprioception, visual, and vestibular conditions of the mCTSIB will correspond with increased odds ratio for DPN, DR, and DV, respectively.

4.2 Research Design and Methods

4.2.1 Participants

Participants were recruited from a primary care physician's office in metropolitan Detroit, Michigan. Inclusion criteria required a physician-confirmed diagnosis of Type 2 diabetes, age 18 years or older, and the ability to walk and stand unassisted. Exclusion criteria included the presence of neurological disorders unrelated to Type 2 diabetes, lower limb amputation or replacement, or a lower limb injury sustained within the past six months. To minimize the risk of hypoglycemic events during testing, participants were required to present with a blood glucose level above 80 mg/dL.

All participants provided written informed consent after receiving both oral and written explanations of the study procedures, in accordance with the ethical guidelines approved by the Oakland University Institutional Review Board.

Table 1. Participants characteristics for each group. One-way ANOVA with post hoc Tukey test did not show any significant difference between groups on any of the characteristics.

	Mean ± Standard Deviation			
All (n = 90)	T2D only (n = 63)	DPN (n = 13)	DR (n = 5)	DV (n = 9)

Age (years)	60.46 ± 11.06	57.76 ±11.08	67.08 ± 11.43	65.25 ± 3.30	63.86 ± 5.11
Height (cm)	169.39 ± 9.57	169.43 ± 9.04	171.87 ± 11.32	167.64 ± 11.91	166.81 ± 11.98
Weight (kg)	92.46 ± 23.72	92.27 ± 21.92	98.47 ± 35.47	85.37 ± 22.22	88.69 ± 20.59
HbA1c (%)	7.15 ± 1.40	7.08 ± 1.42	7.15 ± 0.89	7.25 ± 0.89	7.67 ± 2.39

4.2.2 Testing Procedures

All testing for participants with T2D was conducted at the participating physician's office following their regularly scheduled appointments. Fasting blood glucose, hemoglobin A1c (%), height (cm), and weight (kg) were measured by clinical staff as part of routine care and subsequently reported to the research team. After providing informed consent, participants completed a brief health history form documenting sex, age, years since T2D diagnosis, and the self-reported presence of DPN, DR, DV, or multiple concurrent microvascular complications. Participant characteristics are summarized in Table 1.

Balance testing was performed using the mCTSIB protocol on a BTrackS Balance Plate (Balance Tracking Systems Inc., San Diego, CA, USA) connected to a 10-inch Windows 10 tablet (Fusion5 FWIN232 Plus S1) running BTrackS Assess Balance Advanced Software (version 5.5.6). The mCTSIB quantifies the relative contributions of proprioceptive, visual, and vestibular systems to postural stability and has demonstrated high test–retest reliability (19,21,23,24). The assessment consists of four 20-second stance trials on a stationary force plate: Standard condition, eyes open on firm surface;

Proprioceptive condition, eyes closed on firm surface; Visual condition, eyes open on foam surface; Vestibular condition, eyes closed on foam surface.

For each condition, participants were instructed to stand as still as possible with arms at their sides. Center-of-pressure (COP) path length (cm) was recorded for each trial, with greater COP path length indicating increased postural sway and reduced stability. Lower COP values reflected better postural stability. COP path lengths were automatically calculated by the BTrackS Assess software and used as the primary outcome measure of balance performance.

4.2.3 Statistical Analysis

Descriptive statistics were calculated for all demographic and clinical variables and are presented as mean ± standard deviation (SD).

Participants were split into four groups based on their self-report microvascular complications: those that only had T2D (n = 63), those that only had DPN (n = 13), those that only had DR (n = 5), and those that only had DV (n = 9). Group differences in participant characteristics (age, height, weight, and A1c) and balance performance scores across sensory conditions (proprioceptive, visual, vestibular) were examined using one-way analysis of variance (ANOVA) followed by post hoc Tukey tests to identify pairwise differences between groups. Although a two-way ANOVA design would be reasonable with the structure of the data, it was decided to focus the statistical power on the one-way analysis of group with-in each balance condition, based on evidence from the literature that performance is expected to differ between the conditions (18,23,25,26).

To examine associations between sensory-specific balance performance and the presence of diabetic microvascular complications, binary logistic regression analyses were conducted. Separate models were used to evaluate the relationship between each mCTSIB condition and its corresponding microvascular complication: proprioceptive score with DPN, visual score with DR, and vestibular score with DV. Odds ratios (OR) and 95% confidence intervals (CI) were calculated to estimate the likelihood of having each complication per unit increase in postural sway. All tests were two-tailed, statistical assumptions of normality and homogeneity of variance were verified prior to analysis.

Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the ability of mCTSIB balance measures to discriminate between participants with and without each T2D sensory complication (DPN, DR, and DV). The area under the ROC curve (AUC) was calculated to quantify overall discriminative performance. Optimal probability thresholds were selected based on a screening-oriented approach, which favors higher sensitivity over specificity. Corresponding sensitivity and specificity values were computed. All analyses were conducted in Microsoft Excel with a significance level set at $\alpha = 0.05$.

4.3 Results

4.3.1 Participant Characteristics

Descriptive characteristics are presented in Table 1. A one-way ANOVA was significant for age across groups but the follow up post-hoc Tukey tests were found to be nonsignificant. The additional one-way ANOVAs revealed no significant differences

among groups for height, weight, or A1c (all $p > 0.05$), indicating that participant characteristics were comparable across groups.

4.3.2 Balance Performance

Average postural sway scores for each sensory condition and group are shown in Table 2. Separate one-way ANOVAs were performed for each sensory condition. During the Proprioceptive condition (eyes closed, firm surface), participants with DPN exhibited significantly greater sway (52.67 ± 23.71 cm) compared with the T2D -only group (31.46 ± 14.09 cm; $p < 0.05$), indicating impaired proprioceptive balance control. During the visual condition (eyes open, foam surface), the DR group demonstrated significantly higher sway (61.75 ± 19.79 cm) than the T2D only group (40.78 ± 13.97 cm; $p < 0.05$), reflecting visual-system-related postural instability. During the vestibular condition (eyes closed, foam surface)**,** no significant differences in sway were observed among groups (all $p > 0.05$). These results indicate that proprioceptive and visual impairments are associated with greater COP path length, while balance performance in the vestibular condition did not differ significantly among groups.

Table 2. Average balance scores (± standard deviation) for each of the groups, * indicates significance compared to Type 2 diabetes Only Group of same condition.

	Proprioceptive Scores (cm)	Vision Scores (cm)	Vestibular Scores (cm)
T2D Only Group	31.46 ± 14.09	40.78 ± 13.97	99.59 ± 42.96
DPN Group	**52.67 ± 23.71***	54.50 ± 18.45	149.08 ± 50.78

DR Group	44.00 ± 17.45	**61.75 ± 19.79***	123.75 ± 38.79
DV Group	42.71 ± 16.46	47.29 ± 13.35	114.00 ± 29.77

4.3.3 Logistic Regression Analyses

Binary logistic regression analyses were conducted to examine the relationship between sensory-specific balance performance and the presence of corresponding microvascular complications (Table 3). Greater COP path length during the proprioceptive condition was associated with increased odds of having DPN (OR = 1.063, 95 % CI = 1.021–1.105, $p < 0.01$). Discriminative performance was good (AUC = 0.80) for DPN during the proprioceptive condition. A probability threshold of 0.14 corresponded to a sensitivity of 84% and specificity of 66%. Greater COP path length during the visual condition was associated with increased odds of having DR (OR = 1.078, 95 % CI = 1.078–1.149, $p = 0.02$). Discriminative performance was good (AUC = 0.84) for DR during the vision condition. A probability threshold of 0.09 corresponded to a sensitivity of 80% and specificity of 80%. COP path length during the vestibular condition was not significantly associated with DV (OR = 1.007, 95 % CI = 0.991–1.024, $p = 0.39$). However, ROC analysis demonstrated acceptable discrimination (AUC = 0.71). At a probability threshold of 0.11, corresponding to a sensitivity of 78% and specificity of 64%. Overall, increased postural sway in proprioceptive and visual conditions was predictive of corresponding microvascular complications, whereas vestibular performance did not show a significant association.

Table 3. Odds ratios and 95% confidence ratios based on balance scores for each corresponding sensory condition to complication (proprioceptive score relates to the odds of having DPN, vision score relates to the odds of having DR, and vestibular scores relate to the odds of having DV). * Indicates significance

	Odds Ratio (OR)	95% Confidence Interval (CI)	*p*-value
Proprioception ↔ DPN	**1.063***	1.021 - 1.105	< 0.01
Vision ↔ DR	**1.078***	1.078 - 1.149	0.02
Vestibular ↔ DV	1.007	0.991-1.024	0.39

4.4 Conclusion

This study examines the relationship between balance performance in individuals with T2D using mCTSIB with self-reported T2D microvascular complications (DPN, DR, and DV). The results show that increased proprioceptive and visual condition scores are related to increased odds of the corresponding T2D microvascular complication (DPN and DR, respectively). Proprioceptive and visional sway demonstrated good discrimination for DPN and DR, while vestibular sway demonstrated acceptable discrimination for DV, despite not reaching statistical significance. These findings provide evidence to the mCTSIB's ability to detect each complication separately and act as a screener for T2D sensory complications.

Participants with self-reported DPN exhibited significantly higher COP path length during the proprioceptive condition compared to those with T2D alone, indicating proprioceptive impairment. Those with DR had significantly increased COP path length

during the visual condition, indicating impairment. The logistic regression findings revealed that increased postural sway in the proprioceptive and visual mCTSIB conditions was significantly associated with higher odds of DPN and DR, respectively. Specifically, each one-centimeter increase in COP path length corresponded to a 6.3% higher likelihood of having DPN and a 7.8% higher likelihood of DR. These results indicate that subtle decrements in postural stability are functionally meaningful and may reflect underlying sensory degradation within the corresponding physiological systems. The strong relationship between proprioceptive instability and DPN supports prior evidence that peripheral nerve dysfunction compromises afferent input from the lower limbs, leading to increased sway amplitude and impaired balance adaptation (10,11). Similarly, the association between visual sway and DR underscores the compensatory role of vision in maintaining postural stability and the consequences of diminished visual acuity on sensory reweighting (4,6,9).

Importantly, the present findings provide clinically interpretable sway thresholds that may be used to screen for these complications. Using the proprioceptive condition to predict DPN, yielded high sensitivity (84%) with acceptable specificity (66%), supporting its use as a screener. For using the vision condition to predict DR, it was found to have a high sensitivity of 80% and high specificity of 80%, representing a strong and balanced classification profile. These results demonstrate that both the proprioceptive and visual condition not only discriminates well between groups but also has the potential to provide a more convenient and accessible method for screening . However, these estimates should be interpreted cautiously given the modest number of DPN and DR cases in this study.

In contrast, sway in the vestibular condition was not significantly associated with DV. This may reflect the underdiagnosis of DV or limitations of self-reported vestibular symptoms rather than the absence of a true relationship. Previous studies have shown that vestibular impairments are prevalent in individuals with T2D (12,16). However, DV remains poorly recognized in clinical practice due to the absence of standardized vestibular assessment in diabetic care and the often-subtle nature of vestibular symptoms (27). Despite the lack of statistical significance, vestibular sway demonstrated acceptable discrimination (AUC = 0.71), with a sensitivity of 78% and specificity of 64% at the threshold of 0.11, suggesting potential utility as a screening measure. The higher average sway observed for all groups in the vestibular condition, likely reflects the increased task difficulty and altered sensory weighting inherent to this condition. Specifically, the removal of reliable visual and proprioceptive input forces reliance on vestibular information alone, whereas in other conditions the vestibular system remains intact and can compensate. As a result, all participants exhibit greater baseline sway, leading to higher absolute values and cutoff thresholds. This pattern is consistent with prior literature demonstrating increased postural instability when visual and somatosensory inputs are disrupted, with the foam eyes-closed condition producing the greatest sway due to reliance on vestibular control alone (23-26). Given the vestibular system's critical role in spatial orientation and postural stability, particularly under conditions where visual or proprioceptive cues are compromised, further research is needed to explore the relationship between DV and postural stability in T2D.

Given the collective findings of this study, the mCTSIB shows promise as a practical and clinically feasible screener for microvascular complications in individuals with T2D.

Because the test isolates proprioceptive, visual, and vestibular contributions to balance, it provides a functional snapshot of each sensory contribution to balance. The fact that proprioceptive and visual sway reliably predicted and discriminate DPN and DR in this study suggests that abnormal mCTSIB performance could serve as an early indicator of microvascular complications, prompting further diagnostic evaluation before the complications progress to more advanced stages. Although vestibular sway was not significantly associated with self-reported DV, the mCTSIB's vestibular condition may still offer value in identifying subtle deficits that patients do not recognize or report. This is particularly important given that DV is frequently underdiagnosed in diabetic care despite its known contribution to dizziness, imbalance, and fall risk. Incorporating the mCTSIB into routine diabetes management could provide clinicians with a quick, low-cost, and noninvasive tool to screen for emerging sensory dysfunction, triage patients for specialized testing (e.g., nerve conduction studies, retinal imaging, or vestibular evaluation), and guide individualized interventions aimed at reducing fall risk and improving overall functional outcomes.

Several limitations should be considered when interpreting these findings. First, the relatively small number of participants with specific microvascular complications, particularly DR and DV, may limit the stability and generalizability of the reported effect sizes, and sensitivity and specificity estimates. Small group sizes increase the likelihood that these estimates are sample-dependent and may vary in larger or more diverse populations. Additionally, the use of self-reported diagnoses may introduce misclassification bias, particularly for conditions such as DV, which is often underdiagnosed. Finally, the cross-sectional design precludes conclusions regarding

causality or the predictive utility of mCTSIB performance over time. Future studies with larger, clinically confirmed samples and longitudinal designs are needed to validate these findings and determine clinically applicable screening thresholds.

In conclusion, this study demonstrates that sensory-specific balance impairments measured through the mCTSIB are strongly related to key microvascular complications in individuals with T2D, particularly DPN and DR. Proprioceptive and visual sway not only differed significantly between groups but also meaningfully predicted the likelihood of these complications, underscoring the value of the mCTSIB as a potential indicator of microvascular complications. The identification of clinically interpretable sway thresholds further strengthens the translational relevance of these findings and highlights the potential for integrating balance assessment into routine clinical screening. Integrating objective balance assessment into routine diabetes care could enhance detection of emerging microvascular complications, support more targeted referrals for diagnostic testing, and ultimately contribute to reducing fall risk and improving functional outcomes for individuals living with T2D.

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CHAPTER 5

SUMMARY AND FUTURE DIRECTIONS

6.1 Summary of Findings

This dissertation aimed to evaluate the utility of balance-based assessments as functional screening tools for identifying sensory complications associated with Type 2 Diabetes (T2D). Specifically, (1) characterize sensorimotor impairments in individuals with T2D and (2) determine the sensitive, specificity, and score thresholds for the Modified Clinical Test of Sensory Interaction in Balance (mCTSIB) to act as a screener for detecting diabetic peripheral neuropathy (DPN), diabetic retinopathy (DR), and diabetic vestibulopathy (DV).

The first manuscript established the scientific and clinical foundation for this work by characterizing the pathophysiological mechanisms underlying T2D-related microvascular complications and their impact on sensorimotor control. This chapter highlighted how impairments in proprioceptive, visual, and vestibular systems disrupt the integration of sensory inputs required for maintaining postural stability. This chapter also looked at the potential treatment options available at the different stages of these complications, highlighting the importance of early detection and treatment.

The second manuscript examined the relationship between mCTSIB performance and self-reported T2D sensory complications. Results from multivariate linear regression analyses demonstrated that increased postural sway was significantly associated with the presence of sensory impairments (DPN and DV), even after accounting for potential confounding variables. These findings provided initial evidence that balance performance

reflects underlying sensory impairments and may serve as a functional indicator of impairment.

Building on this work, the third manuscript evaluated the ability of mCTSIB performance to discriminate between individuals with and without specific sensory complications using logistic regression modeling. By pairing individual mCTSIB conditions with their corresponding sensory systems, this study demonstrated that increased sway in the proprioceptive condition was associated with higher odds of DPN, and increased sway in the visual condition was associated with higher odd of DR. Furthermore, receiver operating characteristic curve analyses revealed that mCTSIB-derived metrics could achieve strong levels of diagnostic accuracy (AUC > 0.8) for DPN and DR, and moderate levels of diagnostic accuracy (AUC > 0.7) for DV with acceptable sensitivity and specificity values for identifying sensory impairments. These findings supported the potential use of mCTSIB as a screening tool rather than solely a descriptive measure of balance performance.

Collectively, the findings of this dissertation demonstrate that balance impairments in individuals with T2D are closely linked to underlying sensory complications and that the mCTSIB provides a practical and clinically feasible method for detecting these complications. By capturing the effects of multiple sensory systems on postural control, the mCTSIB offers a unique advantage over traditional screening approaches that assess each system in isolation.

6.2 Limitations

Several limitations should be considered when interpreting the findings of this dissertation. First, earlier manuscripts relied on self-reported diagnoses of sensory complications, which may be subject to recall bias or misclassification. Discrepancies between self-reported and clinically confirmed conditions may have influenced the results, especially for DV, which is not routinely assessed for those with T2D. Second, sample sizes for certain complications, particularly DR and DV, were relatively small in preliminary analyses. This may have limited statistical power and affected the stability of regression models and classification thresholds. Future studies with larger and more balanced samples are needed to confirm these findings. Finally, while the mCTSIB provides valuable information regarding postural control, it represents a relatively static assessment. Additional dynamic measures of balance may further enhance sensitivity to subtle impairments and should be explored in future research.

6.2 Future Directions

Building on the findings of this dissertation, several avenues for future research are warranted. A primary next step is the replication of logistic regression analyses using objective clinical diagnostics rather than self-reported T2D sensory complications. This approach will further validate and determine mCTSIB derived screening thresholds as well as strengthen the clinical applicability. Additionally, longitudinal studies are needed to determine whether mCTSIB performance can track the progression of sensory impairments, thereby establishing its utility not only as a screening tool but also as a method for ongoing monitoring. Expanding beyond static postural assessments to include dynamic balance measures, such as limits of stability or functional movement tasks, may

also improve sensitivity to subtle impairments and better reflect real-world balance demands. From a translational perspective, future research should evaluate the feasibility and cost-effectiveness of implementing mCTSIB based screening in clinical settings, including primary care and endocrinology practices, to reduce the burden associated with multiple specialized diagnostic tests. Furthermore, integrating balance assessments with other accessible tools, such as wearable sensors or patient-reported outcomes, may enhance screening accuracy and provide a more comprehensive evaluation of sensorimotor function. Finally, intervention-based studies are needed to determine whether identifying specific sensory deficits through balance screening can guide targeted rehabilitation strategies and ultimately improve postural control and reduce fall risk in individuals with T2D.

APPENDICES

A. Informed Consent Form

You are being asked to be in a research study that is being done by Trevor Lopatin, under the direction of Dr. Joshua Haworth from the Human Movement Science Department at Oakland University.

Your decision to participate in this study is voluntary.

You can choose to stop your participation at any time or skip any part of the study if you are not comfortable.

Your decision will not affect your present or future relationship with Oakland University, the researcher, the Human Movement Science Department, nor with your physician.

What is the purpose of this study?

The purpose of this research study is to examine the effects of type 2 diabetes and peripheral neuropathy on balance and mobility.

Who can participate in this study?

You are being asked to participate in the study because you fit the inclusion criteria of:

18+ years old, has type 2 diabetes, and is able to walk unassisted.

Though you will not be able to participate if

You had a fall event or injury in the last 6 months,

Known balance impairment, unrelated to diabetes, e.g. Muscular Dystrophy, Cerebral Palsy, multiple sclerosis

Had a lower body joint replacement

If you have a blood glucose level below 80 mg/dL.

How long will I be in the study?

About 1 hour and 30 minutes at the end of your clinical visit: Balance and Mobility assessments (on site)

Where will this study take place?

This study will take place at the current clinic you are at now, after your doctors appointment.

What do I have to do? You will be asked to:

1. Agree to this consent form.

2. Measurements collected during your clinical visit will be recorded anonymously. These include your age, height, weight, shoe size, heart rate, blood pressure, blood glucose, A1C and neuropathy score.

3. There will also be a short (less than 2 minutes) demographics survey that you will be asked to take. Questions include your ethnicity, education, marital status, employment status, annual income, and number of dependents.

4. We will then ask you to stand on the BTrackS force plate with your shoes off, the procedures are the following (see page 2 for reference):

a. Test A - Limit of Stability: During this test, you will stand on the force plate with your hands on your hips, feet on a designated spot on the plate. You will be facing a monitor (for visual feedback) then asked to lean as far as possible on the plate to create the largest possible coverage without lifting your feet for either 20 or 60 seconds.

5. On your second assessment (still on the BTrackS), the procedures are the following (see page 2 for reference):

a. Test B - Balance test (CTSIB): During the second test, you will stand on the force plate with your hands on your hips, feet shoulder width apart. There are 4,20 second trials (with breaks between trials < 10s), trial A) Standing as still as possible with your eyes open B) Standing as still as possible with your eyes closed C) Standing as still as possible on a 2-inch-thick foam pad with your eyes open D) Standing as still as possible on a 2inch-thick foam pad with your eyes closed.

Are there any risks to me?

For balance testing (mCTSIB & LOS), the potential risks and discomforts that we know of are fall risks during the balance assessments.
To prevent this, there will be a four-point walker around the balance board. If you are aged 65 or older an additional person will be present to act as a spotter and assist in fall prevention.

Any Covid related risk are no greater due to participation in this research compared to the clinic visit. Anything that you may come in contact with will be sanitized before and after each use.

Your data is being recorded anonymously, and your participation will not be discussed with anyone.

When the results of this research are published or presented at conferences, no information will be included that personally identifies you.

Are there any benefits to me?

Although there may be no direct benefits to you, the results of this study may benefit type 2 diabetes in the future.

Will I receive anything for participating?

Who could see my information? Your anonymous research records may be shared and reviewed by the following groups:

• Representatives of the Oakland University Institutional Review Board and/or other regulatory compliance staff, whose job is to protect people who are in research studies.

• Regulatory authorities who oversee research (Office for Human Research Protections, or other federal, state, or international regulatory agencies).

Anonymous data may be used or distributed to another investigator for future research use without additional informed consent from you.

When the results of this research are published or discussed in conferences, no information will be included that personally identifies you.

What if I want to stop participating in this study?

If you want to stop participating in this study, you may stop the procedure and leave at any time.

Who do I contact if I have questions about this study?

Student Researcher: Trevor Lopatin, tlopatin@oakland.edu, 248-961-9726, OR

Faculty Advisor: Joshua Haworth PhD, jhaworth@oakland.edu, 248-364-8793

I consent, begin the study

I do not consent, I do not wish to participate

B. Demographics & Socioeconomic Questionnaire

Demographics Questionnaire

Participant Number (For researcher to enter before giving to participant)

Thank you for taking this questionnaire, all of your answer will be completely anonymous.

How would you describe yourself? Please select all that apply.

- White
- Black or African American
- Hispanic, Latino, or Spanish origin
- Asian
- American Indian or Alaska Native
- Native Hawaiian or Pacific Islander
- Other

What is the highest degree or level of school you have completed?

- Less than a high school diploma
- High school degree or equivalent (e.g. GED)
- Some college, no degree
- Associate degree (e.g. AA, AS)
- Bachelor's degree (e.g. BA, BS)
- Master's degree (e.g. MA, MS, MEd)
- Doctorate or professional degree (e.g. MD, DDS, PhD)

What is your marital status?

- Single (never married)
- Married, or in a domestic partnership
- Widowed
- Divorced
- Separated

What is your current employment status?

- Employed full time (40 or more hours per week)
- Employed part time (up to 39 hours per week)
- Unemployed and currently looking for work
- Unemployed not currently looking for work
- Student
- Retired
- Homemaker
- Self-employed
- Unable to work

What is the level of your annual household income?

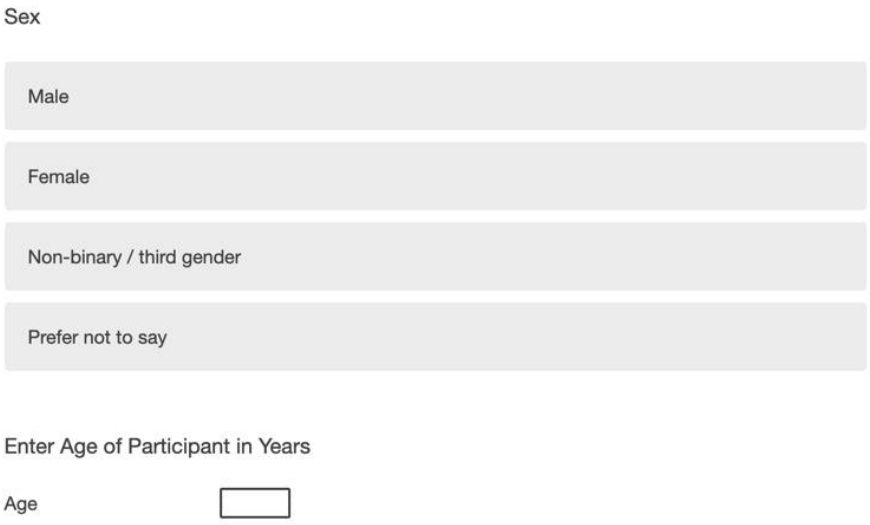
- Less than $25,000
- $25,000 - $50,000
- $50,000 - $100,000
- $100,000 - $200,000
- More than $200,000
- I prefer not to say

How many dependents do you have?

- None
- 1-2
- 3-4
- more than 4
- I prefer not to say

C. Health History & Data Collection Form

Qualtrics Data Collection



Enter Height of Participant

Feet

Inches

Enter Weight of Participant in Pounds (Lb)

Weight

Enter Shoe Size of Participants (US untis)

Gender (F or M)

Shoe Size Number

Width (S-standard or W-wide)

How many years ago were you diagnosed with Type 2 Diabetes in years

What was your most recent A1C in percent

Have you been diagnosed with any of the following complications related to Type 2 Diabetes? (please select all that apply)

- Peripheral Neuropathy
- Retinopathy
- Vestibular dysfunction

Have you ever been diagnosed with

- [ ] Heart Disease
- [ ] COPD or other lung disease
- [ ] PVD or PAD
- [ ] Cancer
- [ ] Renal disease
- [ ] Arthritis

- [ ] Q21

Clarifications for above or other

Q22

Pain Score between 1-100

Enter Heart Rate of Participant in BPM

HR

Enter Blood Pressure of Participant in mmHg

Systolic

Diastolic

Enter Blood Glucose of Participant in mg/dL

Blood Glucose

LoS First Trial

Front left

Front right

Back Left

Back right

Total

mCTSIB

Trail 1

Trail 2 (eyes closed)

Trail 3 (foam pad)

Trail 4 (foam pad, eyes closed)

Total

LoS Second Trial

Front left	
Front right	
Back Left	
Back right	
Total	

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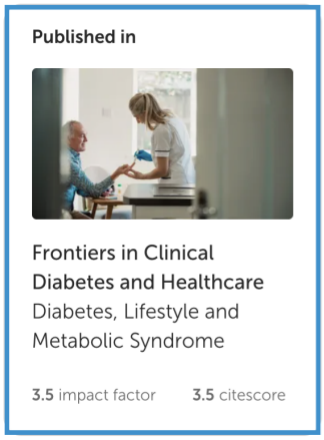

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Cross-cutting effect of type 2 diabetes on the sensorimotor control of balance

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Standing balance impairment in persons with type 2 diabetes is predicted by peripheral neuropathy and vestibulopathy

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E. IRB Approval Letter

OAKLAND UNIVERSITY
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Kate Wydeven <kwydeven@oakland.edu>

Re: Request for in person research procedures # 2022-75 PI Lopatin
1 message

Judette Haddad <haddad@oakland.edu> Tue, Oct 26, 2021 at 11:43 AM
To: Kate Wydeven <kwydeven@oakland.edu>

Dear Kate,

Thank you for the summary. Since the project involves no more than minimal risk (expedited review), I, as the IRB Manager, provide permission to start in-person research on behalf of the Vice President for Research with the following understanding:

- All researchers are fully vaccinated.
- All aspects of the patient/participant's experience will be guided by the COVID precautions of the clinic, which include the use of masks, handwashing, and hand/equipment sanitization between uses.
- A permission from the research site, Waterford Adult and Pediatric Medicine (St. Joe's medical group), has been provided in the IRB submission.

I have added my comment to the summary and attached it to this message.

Judette

On Mon, Oct 25, 2021 at 11:30 AM Kate Wydeven <kwydeven@oakland.edu> wrote:

> Hi Judette,
>
> Attached is a summary of IRB # 2022-75 *Postural Control in Type 2 Diabetes*
> PI Trevor Lopatin, FA Josh Haworth
>
> Most of the data collection is occurring as a part of a clinical visit. The PI is employed at this clinic. There is an additional 10 minutes of data collection beyond the normal clinical visit. Julie Kruse has reviewed and approved of these procedures.
> Let me know if these in person procedures are permitted.
>
> Thanks,
> Kate Wydeven
> *The IRB uses the online system, Cayuse.*
> *For information regarding Cayuse, please visit the **IRB webpage**.*
>
> Regulatory Compliance Specialist
> Research Office
> 524 Wilson Hall
> Oakland University
> Rochester MI 48309
> 248-370-4306
> kwydeven@oakland.edu
> Pronouns: she/her

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>'<>'<>'<>'<>'<>'<>'<>'<>'<>'<>'<
Judette Haddad, PhD

IRB Manager
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Rochester, MI 48309-4401
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IRB webpage
www.oakland.edu/research

Lopatin & Hayworth- 2022-75 In person research Summary - JH comment.docx
16K