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Postural balance and acceleration threshold detection for anterior horizontal translation in diabetic and non-diabetic elderly

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POSTURAL BALANCE AND ACCELERATION THRESHOLD DETECTION FOR ANTERIOR HORIZONTAL TRANSLATION IN DIABETIC AND NON–DIABETIC ELDERLY

by

Venkatesh Balasubramanian, BE

A Dissertation Presented in Partial Fulfillment
Of the Requirements for the Degree
Doctor of Philosophy

COLLEGE OF ENGINEERING AND SCIENCE
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Date

We hereby recommend that the dissertation prepared under our supervision by VENKATESH BALASUBRAMANIAN entitled POSTURAL BALANCE AND ACCELERATION THRESHOLD DETECTION FOR ANTERIOR HORIZONTAL TRANSLATION IN DIABETIC AND NON–DIABETIC ELDERLY be accepted in partial fulfillment of the requirements for the Degree of Ph. D. in Biomedical Engineering

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ABSTRACT

Slips and falls, and even the fear of falling, can represent a major medical and functional deterrent to living independently, especially among the elderly population. Various groups of elders are at known risk for falling including, but not limited to, those with vestibular dysfunction, those with low visual acuity including visual neuropathies, and those with peripheral neuropathies. The first two groups are fairly well studied, but the relationship between the level of peripheral neuropathy and extent of falling has received relatively less attention.

In this study, using sliding linear investigative platform for analyzing lower limb stability (SLIP–FALLS), the psychophysical thresholds and strategies used for, detecting ultra–low–vibration horizontal translations in the elderly population (age range of 50 and 75 years) with adult–onset diabetes or peripheral neuropathy were determined. Acceleration thresholds for anterior horizontal movements of 1, 4, and 16 mm were determined. These detection thresholds were compared with healthy young adults (age < 35 years) and age–matched elders without neuropathy. The extent of peripheral neuropathy was quantified by standard clinical nerve conduction tests of the sensory and motor nerves of the lower extremity by the Neurological Service of the Overton Brooks VAMC.

Psychophysically, the acceleration thresholds have a negative power law relationship with the perturbation distance and are significantly higher for the elderly population when compared to young adults. A predictive Balasubramanian–Robinson model for determining acceleration thresholds for perturbation has been presented. Among the elderly, neurologically intact individuals were found to have a lower threshold for detection than those with neurological impairments. Conversely, the conduction velocities of the sensory and motor nerves were lower in case of the elderly with adult–onset diabetes or peripheral neuropathy. It was also found that cognitive and tactile sensory responses alone cannot be used to differentiate between the two groups of elderly. The diabetic elderly had a significantly higher lateral sway and increased reaction time for foot touch, platform perturbation, and auditory stimuli. These factors probably contribute to the increased risk of falling in the diabetic elderly.

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DEDICATION

Guru Brahma| Guru Vishnu|

Guru Devo Maheshwara|

Guru Sakshat Para Brahma Tasmai Sri Gurubyo Namaha||

(A teacher is the creator, protector and destroyer.

Salutations to the teachers who are my creators!)

This dissertation is dedicated to my gurus.

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NOMENCLATURE

2AFC	Two alternative forced choice
ANOVA	Analysis of variance
AP	Anterior–posterior
BRM	Balasubramanian–Robinson model
COM	Center of mass
COP	Center of pressure
EMG	Electromyograph
GS	Gastrocnemis soleus muscle
HP	Horse power
IRB	Institutional review board
ML	Medial–lateral
MMSE	Mini–mental status examination
NI	Neurologically intact
PEST	Parameter estimation by sequential testing
PMAC	Programmable multi–axis controller
PN	Peripheral neuropathy
Psi	Pounds per square Inch
RMS	Root mean square
ROC	Receiver operating characteristic
SLIP–FALLS	Sliding linear investigative platform for analyzing lower limb stability
TA	Tibialis anterior muscle
VAMC	Veterans Administration Medical Center
VI	Virtual instrument
WAIS	Wechsler adult intelligence scale

ACKNOWLEDGEMENTS

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CHAPTER 1

INTRODUCTION

1.1 Diabetes

Diabetes Mellitus is a metabolic disorder in which the body does not produce or properly use insulin. Insulin is a protein hormone that is needed to convert glucose into energy needed for daily activities. Diabetes has generally been attributed to genetic or environmental factors such as obesity and lack of exercise. There are two major types of diabetes: Type 1 is an autoimmune disease in which the body does not produce any insulin, most often occurring in children and young adults. This led to the colloquial naming of the diabetes as "juvenile diabetes." People with Type 1 diabetes must take multiple insulin injections daily to stay alive. Type 1 diabetes accounts for about 5 to10 percent of diabetes. Type 2 diabetes is a metabolic disorder resulting from the body's inability to make enough, or properly use, insulin. It is the most common form of the disease. Type 2 diabetes accounts for 90 to 95 percent of diabetes. The incidence of Type 2 diabetes is nearing epidemic proportions due to an increased number of older Americans and a greater prevalence of obesity and sedentary lifestyles [ADA].

Nearly 16 million Americans (5.9 percent) have diabetes with another 5.5 million having undiagnosed adult–onset diabetes. About 800,000 new cases will be diagnosed this year based upon data from the Centers for Disease Control and Prevention. Diabetes is the seventh leading cause of death (sixth–leading of death by disease) in the United States. Based on death certificate data, diabetes contributed to 198,140 deaths in 1996 [ADA]. Diabetes is a chronic disease that currently has no cure. In fact, diabetes is the most frequent cause of non–traumatic lower limb amputations. The risk of a leg amputation is 15 to 40 times greater for a person with diabetes. Each year, more than 56,000 amputations are performed among people with diabetes [ADA].

About 16 percent of VA clients have diabetic–related illness [VA press release October 2000]. In a recent study, the VA has identified "Agent Orange," a defoliating chemical used extensively in Vietnam as a cause for diabetes, making any Vietnam Veteran exposed to this chemical to be now considered at risk of getting Type 2 diabetes [VA press release – November 9, 2000].

One of the more prevalent side effects of diabetes is peripheral neuropathy. Sixty to 70 percent of people with diabetes have mild to severe forms of peripheral nerve damage. Peripheral neuropathy is the damage or impairment of sensory or motor axons (nerve cells) in the peripheral nervous system. This results in slowing of the conduction speed of the signals in the nerves. Well known clinical neurophysiological tests can be used to quantify the extent of any peripheral neuropathy. Long–term diabetes can result in a variety of subtle cerebral disorders. Individuals with diabetes have repeatedly been

reported to have lower reaction times, cognition, vascular dementia and a higher incidence of fall than their age–matched cohorts [Gispen, et al., 2000, Stewart, et al., 1998, Lord, et al., 1991]. Higher order neuropsychological dysfunctions are also observed in the diabetic population [Ryan, et al., 1988 and Strachan, et al., 1997].

1.2 Balance and Fall–Initiation Testing

Falls are incurred by one third of the elderly population and are a common source of morbidity and mortality. The risk of falls increases with age beyond the age of 60. The number of hip fractures that occur annually in the US from falls is close to 300,000 and represents a cost of $10 billion over the lifetime of the patients [Oddsson et al., 1998]. We balance ourselves in a potentially unstable equilibrium by using our skeletal muscles to counteract gravity. The ability to maintain postural control is critical to avoid fall and successfully perform activities of daily life. Most falls in older people result from an accidental slip or trip frequently associated with an unsteady gait [Alexander 1994].

Some falls may result from internal physiological disturbances (e.g., transient ischemia of the cerebellum or brainstem). However, it appears that many falls in the elderly occur due to the inability of posture control mechanisms to correct for unexpected displacements of the body [Lord, et al., 1991]. Hence a test that characterizes the relative stability of the response to transient perturbations will be a better predictor of falls than spontaneous sway measures.

Balance and fall–initiation testing can range from the simple modified Romberg test, where a person is asked to stand and walk by putting a heel in

front of a toe (similar to that performed by police to identify cases of intoxication), to completely instrumented tests. Earliest documented graphical recordings of human sway were obtained by Hinsdale in 1887 with an "ataxiagraph," a device developed by Vierord. Innovative mechanical devices have been used in combination with clever experimental protocols to study human balance control.

Instrumented tests are performed by perturbing the feet or ankles with respect to the rest of the body by translating or rotating the surface on which a person is standing; or vice versa, by perturbing the torso (i.e., with a push) with respect to a stable base of support at the feet. Both types of tests typically use a large displacement or rotation with a high velocity or acceleration for the perturbation. Thresholds for the detection of discrete translation movements have been shown to be similar, albeit slightly higher, to thresholds for the detection of sustained oscillatory motion [Winter, 1990].

Besides the work from Robinsons' group, there are very few who have studied the detection thresholds or reaction times to small displacements, standing or otherwise. For the US Air Force, Benson, et al. (1986) determined the acceleration detection threshold of a seated subject along the three body axes. However the study was performed on a rail bearing, which by itself could be providing a high vibration that could cue the subject of the perturbation.

Biometrics has standardized the description of posture. The Center of Pressure (COP) is the point location of the vertical ground reaction force vector at the ground [Winter, 1990]. It represents a weighted average of all the pressures over the surface of the area in contact with the ground and is generally

determined by an instrumented force plate of platform. The location of COP is related to the Center of Mass (COM) of the body, directly in the quiet standing case. If one foot is on the ground and the body is balanced, the net COP lies within that foot's footprint. If both feet are in contact with the ground, the net COP lies somewhere between the two feet, depending on the relative weight supported by each foot. Thus, when both feet are in contact with the surface, each foot affects the COP. When one force platform is used, only the composite COP is available. Two force platforms are required to quantify the COP changes under each footprint. In quiet standing, the location of the COP under each foot reflects the neural control of the ankle muscles but cannot be derived from it. Increasing plantarflexor activity (or decreasing dorsiflexor activity) moves the COP anteriorly, while increasing activity of ankle invertors moves the COP laterally. COP and COP changes are expressed in length units (mm). The rate of change of COP is usually referred to as sway and has velocity units [Winter, 1990].

There are four different common stance positions of the feet for which COP can be analyzed during a forward or backward perturbation. They are 1) side–by–side, 2) step, 3) tandem (heel–to–toe), and 4) one–legged. Goldie, et al. (1989), in a large–scale reliability study of these different stances concluded that the COP is a reliable discriminating measure only in the side–by–side stance.

Horak and Nashner (1986) proposed that two different strategies are commonly used to respond to a perturbation depending on the type and

magnitude of perturbation. They are 1) an ankle strategy, 2) a hip strategy, or 3) a combined strategy. The ankle strategy is seen in quiet stance and during small perturbations and assumes that the rest of the body acts biomechanically like an inverted pendulum. This strategy predicts that the ankle plantarflexors/ dorsiflexors alone can act to control the inverted pendulum and hence maintain balance. With a stronger perturbation, or when the ankle muscles cannot act, a hip strategy would involve the movement of COM posteriorly by flexing the hip, or by extending the hip to move COM anteriorly. A combined hip and ankle strategy could also be used instead of a pure ankle or hip strategy. The most common position of the feet is a side–by–side position, and the most commonly discussed postural control model in the anterior–posterior direction uses an ankle strategy [Winter, 1990].

The easiest way to identify the movement strategy is by monitoring the level of muscle activity through the recording of surface electromyograph (EMG) potentials. EMG activities of the gastrocnemis soleus (GS) and tibialis anterior (TA) muscle groups demonstrate their involvement in ankle control strategy [Nashner, 1985, Horak and Nashner, 1986]. Hamstrings and quadriceps muscle groups interact during a hip strategy, but they are also activated during an ankle strategy (if for nothing else than to keep the body rigid).

1.3 Psychophysical Testing of Threshold

Psychophysics is the field of physiological psychology that quantifies a subjective response to a quantifiable stimulus property [Levitt, 1971]. Detection thresholds, discrimination thresholds, and just–noticeable–difference thresholds,

stimulus scaling, and magnitude estimation are typical psychophysical variables. Many psychophysical theories describe the ability of the observer to detect or discriminate a signal in a background of noise [Taylor, et al., 1983].

Psychophysical responses are greatly influenced by the instructions given to a subject. Subjects only rewarded for detection (and not punished for misses) quickly realize they should always indicate that they detected the event and never indicate non–detect. Subjects asked to be always certain (i.e., conservative) will signal few if any detectable events. A more liberal instruction (i.e., signal if you even think that an event occurred), without any fear of punishments, will produce the opposite effect. Considerations of this type have given rise to the receiver–operating characteristic (ROC) curve in engineering and statistics. In psychophysics, it is referred to as psychometric curve. As indicated, the determination of an absolute detection threshold is difficult when the subject is presented with a "Yes / No" (Present / Absent) question because one is never certain of the liberal/conservative judgment criteria adopted by the subject.

A way around this dilemma is to use a two alternate forced choice (2AFC) paradigm in which the subject is FORCED to pick one alternative from two available choices presented sequentially. Most sensory modalities have a power law (log–log) relationship between the stimulus magnitude and the response magnitude [Taylor, et al., 1983].

In dealing with determinations of threshold, a first stimulus that is too large can bias the results. Thus the choice of the first stimulus magnitude and how

later stimuli are modified are important considerations. Ideally one would like to have a strategy where all perturbations are near threshold or at least rapidly converge towards a threshold value.

To address these issues, a special psychophysical testing technique, called the parameter estimation by sequential testing (PEST) method, was introduced by Taylor and Creelman (1967) and later modified by Findlay (1978). PEST is one of a class of adaptive psychophysical methods in which the task difficulty is changed dynamically to arrive at a desired level of performance. This technique reduces the number of measurements needed to converge to the "threshold" of an experiment.

Adaptive psychometric procedures estimate points on the psychophysical function by making use of the subject's previous responses to select new stimuli for testing. Adaptive testing procedures offer many advantages over conventional procedures, including higher efficiency, greater flexibility, and less reliance on restrictive assumptions. Although higher efficiency (and hence greater precision for a fixed number of observations) is often thought of as the major advantage of adaptive procedures, the latter advantages may well be of greater practical importance. Special problems also occur with small samples. Many of the theorems showing maximum efficiency or maximum rates of convergence are only asymptotically true, and testing procedures based on these results may be inferior in experiments of limited size [Madigan, et al., 1987, Taylor, et al., 1983, Levitt 1971].

PEST by itself is not a psychophysical procedure. It is a set of rules for changing the difficulty level of an embedded psychophysical procedure, coupled with rules for determining the difficulty level corresponding to a desired level of performance. It can essentially be viewed as an adaptive digital algorithm, where the selection of the next test stimulus level depends on the response (Correct/ Incorrect) given to the previous two or three stimuli. Threshold in PEST is assumed to have reached wherever the value of the stimulus increment falls below a certain percentage of the absolute stimulus level. The increments by which the stimulus is either increased or decreased are referred to as steps. They are categorized into two mutually exclusive groups, termed the UP group and the DOWN group, respectively.

The rule for controlling the stimulus level is analogous to the simple up–down rule, except that the stimulus level is changed only after a sequence of observations belonging to either the UP or DOWN groups is obtained. The stimulus level is not changed until such a sequence is obtained. Levitt (1971) presented the probability of positive response at convergence for the different sequence of Up–Down criteria used. For example, according to Entry 4 in Table 1 (staircase 71), the stimulus level would be increased after a negative response and decreased after two consecutive trials yielding correct responses. As the test progresses, one or other of these sequences must be obtained.

The optimum strategy for increasing or decreasing step size depends on the type and the extent of the changes that are likely to occur during a test, and the maximum number of trials that are desired in a given test sequence. These

factors are usually difficult to identify *a priori*. Since all subject responses are forced (i.e., via the 2AFC paradigm), some false–positive detection and some misses are statistically possible. However as the intensity of the stimulus increases, a decrease in these false positives and misses and an increase in true detection will occur. The importance of this study lies in determining the true thresholds, not the supra–threshold limits presented when all responses are correct. For this reason, the PEST target probability is set at a level of change rather than a percentage of "correct" responses.

Table 1. Response groupings for transformed up–down strategies and probability of positive response at convergence (adapted from Levitt, 1971)

Entry	UP Group Increase Level After	DOWN Group Decrease Level After	Probability of Positive Response At Convergence
1	− − − −	− − − + or − − + or − + or +	0.159
2	− −	− + or +	0.293
3	−	+	0.5
4	+ − or −	+ +	0.707
5	+ + − or + − or −	+ + +	0.795
6	+ + + − or + + − or + − or −	+ + + +	0.841

The rule for controlling the stimulus level is analogous to the simple up–down rule, except that the stimulus level is changed only after a sequence of observations belonging to either the UP or DOWN groups is obtained. The stimulus level is not changed until such a sequence is obtained. For example, according to entry 4 in Table 1 (staircase 71), the stimulus level would be increased after either a negative response on the next trial. The stimulus level is decreased after two consecutive trials yielding positive responses. Note that, as the test progresses, one or other of these sequences must be obtained.

Psychophysical studies of the perception of whole–body motion stimuli are a means of investigating the characteristics of the vestibular sensory system. However, care should be taken to exclude visual and auditory cues to minimize differential movement of body segments and to distribute applied forces over the

surface of the body. If these steps are taken, the detection of dynamic motion stimuli of liminal intensity is primarily determined by the integrity of the subject's vestibular apparatus.

1.4 Cognitive Evaluation

Examination of mental state is essential in evaluating the ability of subjects to follow instructions. The mental state of a person can affect the ability of a person to listen to instructions, remember them for a short duration, and react in a manner that they have been instructed. Some elderly subjects, particularly those with delirium or dementia syndromes, cooperate well only for short periods [Roth, 1967].

There are many batteries of test that can be performed to evaluate the cognitive status of a person. A standard Withers and Hinton's test comprises of 33 questions and requires about 30 minutes to administer and score. Other elaborate tests like the Wechsler Adult Intelligence Scale (WAIS) take an even longer time to administer. Folstein, et al. (1975) proposed a cognitive mental status examination, Mini–mental state examination (MMSE), that was thorough in cognitive aspects of mental functions. This test however excludes questions concerning mood, abnormal mental experiences, and the form of thinking. It requires about 5 to 10 minutes to administer.

1.5 Nerve Conduction Studies

Nerve signals are transmitted by action potentials, which are propagating rapid change in the membrane potential. Each action potential begins with a

sudden change from the normal resting, internally negative potential to a positive membrane potential, and then ends with an almost equally rapid change back to the negative potential. To conduct a nerve signal, the action potential moves along the nerve fiber until it comes to the fiber's end.

In myelinated axons, the action potentials can occur only at the nodes of Ranvier [Bear, et al., 1996]. The action potentials are conducted from node to node by a process called salutatory conduction. That is, electrical current flows through the surrounding extracellular fluids outside the myelin sheath, as well as through the axoplasm from node–to–node exciting successive nodes one after another. Thus, the nerve impulse jumps down the fiber.

Salutatory conduction is of value for two reasons. First, by causing the depolarization process to jump long intervals along the axis of the nerve fiber, this mechanism increases the velocity of nerve transmission in myelinated fibers as much as 5 to 50 – fold. Second, salutatory conduction conserves energy for the axon because only the nodes depoloarize, allowing perhaps a hundred times smaller loss of ions than would otherwise be necessary and therefore requiring little metabolism for reestablishing the sodium and potassium concentration differences across the membrane after a series of nerve impulses [Bear, et al., 1996].

Any factor that causes sodium ions to begin to diffuse inward through the membrane in sufficient numbers will set off the automatic regenerative opening of the sodium channels. This can result from simple mechanical disturbance of the membrane, chemical effects on the membrane, or passage of electricity through

the membrane. All these are used at different points in the body to elicit nerve or muscle action potentials: Mechanical pressure to excite sensory nerve endings in the skin, chemical neuro–transmitters to transmit signals from one neuron to the next in the brain, and the electrical current to transmit signals between muscle cells in the heart and intestine.

The usual means for exciting a nerve or muscle in the experimental laboratory is to apply electricity at the nerve or muscle surface through small electrodes, one of which is negatively charged and the other positively charged. When this is done, one finds that the excitable membrane becomes stimulated at the negative electrode.

The velocity of conduction in nerve fibers varies from as little as 0.25 m/s in very small unmyelinated fibers to as high as 100 m/s in very large myelinated fibers. The velocity increases approximately with the fiber diameter in myelinated nerve fibers and approximately with the square root of fiber diameter in unmyelinated fibers.

The energy used during propagation of a nerve impulse is derived from the potential energy stored in the form of concentration differences across the ions in the membranes. A high concentration of potassium inside the fiber and low concentration of sodium outside the fiber constitute a type of energy storage. Likewise, a high concentration of sodium on the outside of the membrane and a low concentration on the inside represent another storage of energy.

Conduction velocity in a peripheral nerve is measured by stimulating the nerve at two points at a known distance apart along its course. Subtraction of

the shorter latency from the longer latency gives the conduction time along the segment of nerve between the stimulating electrodes. Knowing the separation distance, the conduction velocity of the nerve can be determined. This velocity has clinical importance because the conduction velocity in a regenerating nerve fiber slows following nerve injury. Although field potentials from nerves are of much smaller amplitude than extracellular potentials from surrounding excitable muscle fibers, such potentials can be recorded with either concentric needle electrodes or surface electrodes. Nerve field potentials can be evoked by applying stimuli to "mixed" nerves that contain both motor and sensory components (such as the ulnar nerve of the arm), in which case the resultant field potentials are derived from both types of active fibers.

Nerve field potentials can also be elicited from a purely sensory nerve or from sensory components of a mixed nerve, in which the simulation is applied in a manner that does not excite the motor components of the nerve [Bear, et al., 1996].

1.6 SLIP–FALLS System

A precisely controlled test fixture that can move rapidly over long distances without detectable vibratory cues is a requirement to quantitatively test the kinesthetic and proprioceptive senses involved in balance. The sliding linear investigative platform for analyzing lower limb stability (SLIP–FALLS) is a system that helps separate the cues arising from somatosensory modalities from those of the visual and vestibular senses [Purucker, et al., 1996]. This system was first

built at the joint Rehabilitation Neuroscience Lab of the University of Pittsburgh and the Pittsburgh Highland Drive VAMC.

The system involves a core structure, its controller, a master computer, and other peripheral instrumentation. The core structure involves a force plate with four load cells mounted on a rail floating on air bearing. This force plate is referred to as the platform. A cover plate (183 cm length X 122 cm width x 0.64 cm thick aluminum plate) is used to protect the air bearings from dust particles and other impurities. The aluminum plate is supported by 1.91 cm thick cabinet grade wood around the periphery of the device and extending outward to beams spanning between the steel Unistrut P1000/P1001 posts and frame approximately 30 cm above ground level. The Unistrut assembly also supports a double beam, overhead rail–mounted harness [Robinson, et al., 1998], which was not used in this study (see Figure 1).

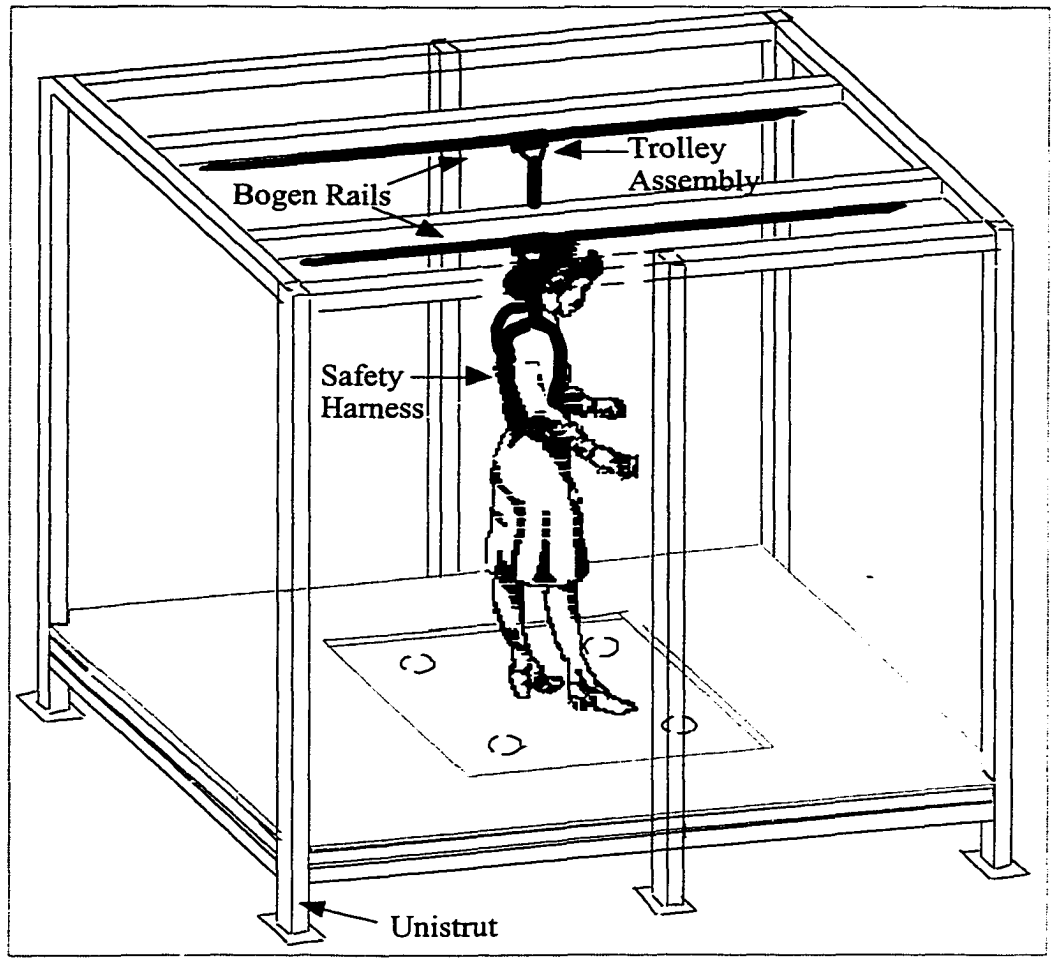


Figure 1. A descriptive sketch of the SLIP–FALLS system (adapted from Robinson, et al., 1998).

A commercial multi–axis motion controller (DMM–2004, Dover Instrument Corporation) was custom configured to control the sliding platform which was also manufactured by Dover. This controller's principal component is a commercially available single–board programmable multiple–axis controller (PMAC™, Delta Tau Systems), which determines nearly all aspects of SLIP performance. PMAC controls motor #1 (the linear motor) and uses output #2 to assist in the sinusoidal commutation of motor #1 [Purucker, et al., 1996]. A master computer interfaces to PMAC via a serial link. A data acquisition board

(National Instruments, Austin, TX) is also used for collecting the inputs (data) from the other peripheral instruments. LabVIEW™ (National Instruments, Austin, TX) software was used for the entire instrumentation.

SLIP–FALLS also uses a white noise generator, wireless door bell and its receiver (Radioshack), a sound mixer, wireless speakers (Recotron) and headphones (Radioshack), four tri–surface EMG electrodes (Neurocom®), accelerometers, and a single axis force sensor.

The SLIP–FALLS system was moved from the Highland Drive VAMC, Pittsburgh, PA, to the Overton Brooks VAMC, Shreveport, LA, in January 1999. The assembly and integration of the system and update was performed at this new lab as described in the methods section.

CHAPTER 2

HYPOTHESIS

The objective of this study is to understand the effect of peripheral neuropathy and/or adult–onset diabetes on threshold level of acceleration needed to detect a short horizontal anterior movement and the strategies used to identify the movement. By the design of the study, the relationships in the realms of psychophysics, posture, and other clinical metrics are tested. The following hypotheses are postulated and are divided into three groups (psychophysical, postural, and clinical).

2.1 Psychophysical

1. The peak acceleration threshold will have a negative power law relationship with the perturbation distance. That is, a smaller perturbation distance will require a larger acceleration to be detected.
2. The peak acceleration threshold and its relationship with perturbation distance will differ among young adults, neurologically intact adults, and adults with peripheral neuropathy and/or diabetes.

2.2 Postural

3. At peri–threshold stimulus levels, a forward movement of the platform (or perturbation) cannot be detected when a person is leaning forward of their quiet standing location of COP.
4. There will be an increased lateral quiet standing sway in the population with higher acceleration detection threshold.

2.3 Clinical

5. Nerve conduction velocity findings (motor and sensory) will negatively correlate with detection threshold in the adult population.
6. A significant difference in tactile sensory perception at the feet will be observed between those with and without lower limb peripheral neuropathy.
7. There will not be a statistically significant difference between groups in the anthropometrics, sensorimotor function, or cognition.

CHAPTER 3

MATERIALS AND METHODS

3.1 SLIP–FALLS System

The SLIP–FALLS system originally constructed in the Rehabilitation Neuroscience Laboratory, Highland Drive VAMC, Pittsburgh, PA, was moved to Rehabilitation Neuroscience Laboratory, Overton Brooks VAMC, Shreveport, Louisiana. A general descriptive diagram of the SLIP–FALLS system is provided in Figure 2 (adapted from Robinson, et al., 1998). All the wiring and connections were tagged to easily identify them. The superstructure was reassembled with the help of VA maintenance staff. Connections to different A/D ports were then made. A list of modifications was made (described later in this chapter). A battery of tests was performed to evaluate and recalibrate the system. After practice trials with laboratory associates, testing was performed on subjects.

3.2 Additions to SLIP–FALLS

SLIP–FALLS was modified and recalibrated after relocation to perform this study. The following modifications were performed: 1) the air compressor and air dryer were upgraded; 2) the master computer was upgraded; 3) the platform and its load cells were recalibrated; 4) software was modified; and 5) new peripheral

devices were installed. Figure 2 describes a diagrammatic description of the modified system.

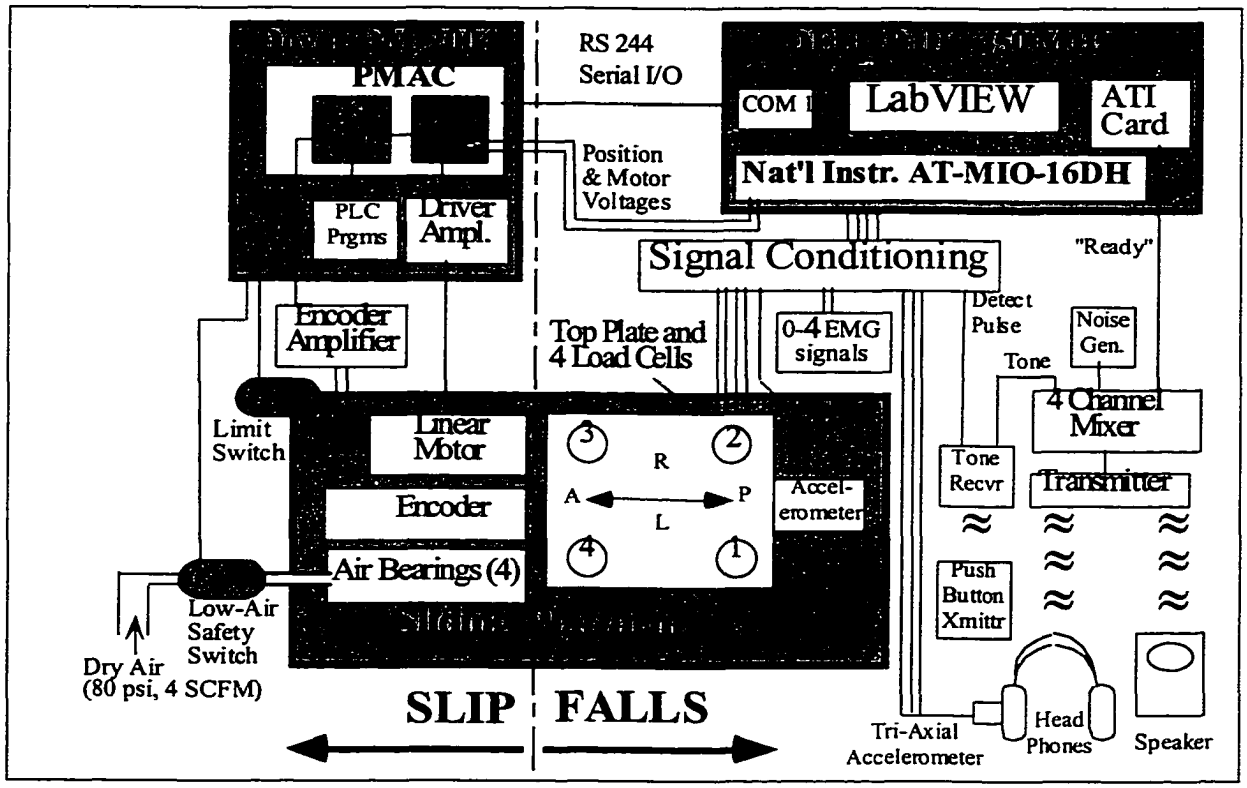


Figure 2. Diagrammatic description of the SLIP–FALLS system (adapted from Robinson, et al., 1998)

3.2.1 Air Compressor

An essential component for running the SLIP–FALLS system is a constant supply of compressed, ultra–dry air at a pressure greater than 70 pounds per square Inch (psi) and a flow rate of greater than 3.8 scfm. Since the air bearings are hermitically sealed, they would be irreversibly affected by the presence of moisture or oil in the compressed air supply. Thus, a single–stroke, oil–free air compressor with a large reservoir tank (30 gal) provides a buffered compressed

air source. Atmospheric moisture is absorbed in a pneumatic desiccant air dryer. The two chambers in the dryer are alternatively used for a span of 30 seconds. This continual switching regenerates the desiccant but also adds pulsations to the air output of the dryer. To eliminate this pulsed flow problem, a secondary storage tank is used. The compressor motor is loud and would cause vibration on the lab surface that would affect the working of SLIP–FALLS. Hence the compressor is located in an environmentally conditioned room 30 feet from the room where SLIP–FALLS is located.

Crossover plumbing in the compressor room allows supply from the primary compressor or its backup. Copper pipe (5/8") transmits compressed air to the lab. The desiccant dryer is located in the lab. Quarter inch, non–moisture–absorbing tubing transmits the dried compressed air between the dryer and the secondary reservoir tank, and from the tank 25 feet to the bearing inlets. Shut off valves and pressure gauges are mounted at the compressor reservoir tank, at the inlet to the dryer, at the output of the secondary reservoir tank and at the inlet to the bearing. Additionally, a flow meter is mounted next to the pressure gauge at the inlet to the bearings to monitor that the required 3.8 scfm of airflow is available. Bleed–off water drains are located on the compressors, at their outlet, at the inlet tube in the lab, and on the small storage reservoir.

The air compressor operates at its rated level of 120 psi. To avoid a large pressure loss on the supply line and, hence, insufficient pressure and flow at the air bearings, a newer and more powerful compressor motor (10 HP) with a larger reservoir tank having a capacity of 30 Gallons and a displacement of 21.2 scfm

(Sears, IL) was installed. A newer desiccant dryer with higher throughput of up to 9 scfm was installed. The engineering services at Overton Brooks VAMC provided materials and manpower to execute this setup.

3.2.2 Master Computer

A new computer, DELL Dimension (PIII, 450 MHz), which was faster than the one used in Pittsburgh was purchased. The interrupts and direct memory access registers of this computer were modified to enable its interface with the SLIP–FALLS and the National Instruments data acquisition card. A 32–bit ATI™ sound card replaced the 16–bit SoundBlaster™ sound card. The audio output from the sound card goes directly to the sound mixer.

3.2.3 Recalibrating the Platform

The four vertical load cells (rated at 90 kg, Eaton Lebow part #3173–200) that are installed under the top plate of the SLIP–FALLS device form the central part of the platform. Each of these load cells are placed 27.28 cm diagonally from the center of the top plate. This arrangement makes for a rectangle 69.85 cm width x 83.82 cm length. The top plate is fastened to the load cells which are mounted on the tie plate connecting the air bearings.

The top and bottom of top plate were trued on a milling machine to remove the unevenness on its surfaces. This machining of the top plate resulted in a slight weight loss, so the testing and calibration routines were modified to accommodate this altered weight. The load cell amplifiers gains and offsets were

also readjusted. PMAC was reprogrammed to change the tuning parameters of the platform.

The platform load cells must be periodically recalibrated. These are connected to the top plate carefully by adjusting the retaining nut in a stepped fashion. A 5/8" threaded stud screws into each of the load cells to fasten it to the top plate. Each stud is fastened to the top plate by means of a lock nut and aluminum washer on either side of the plate. In addition to aluminum washers, a synthetic washer is used on the topside to provide some relief once in alignment. The lock nut on the topside was used as a rating nut. A commercially available synthetic fluid (Lock Tight®) was used to secure the lock nut that is on the bottom side of the top plate. Figure 3 provides a schematic of the fastening mechanism.

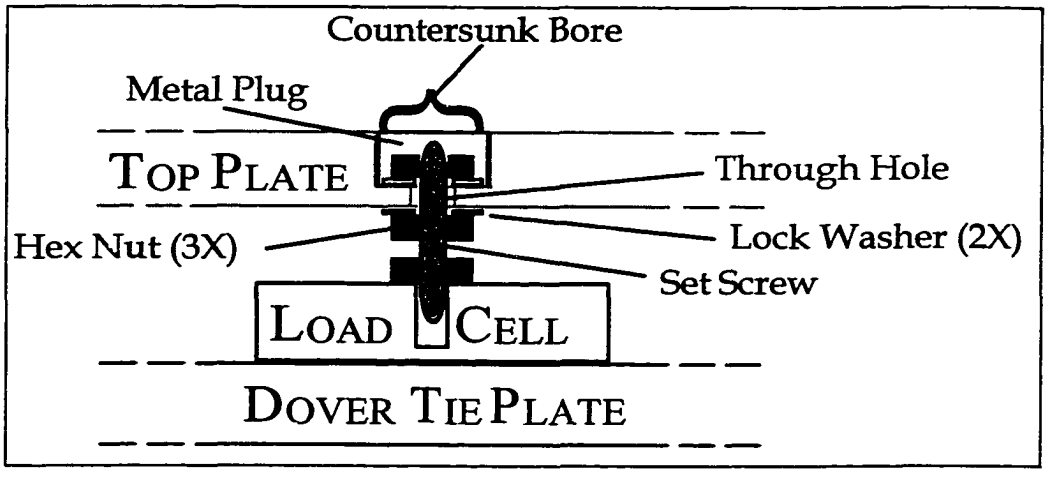


Figure 3. Descriptive sketch of the top plate fastening with Load Cell (adapted from Purucker, et al., 1996).

To calibrate, each load cell is separately loaded with calibrated weights (Figure 4), and the span and offset of its amplifier adjusted. Then the top plate is placed evenly on all the four load cells by adjusting the tops of all bottom nuts to

the same height. A spirit level is used to identify any tilt in the horizontal plane. Once the top plate is positioned evenly, each top nut is tightened incrementally, and in sequence, using a torque wrench. Tightening occurs in a retracing diagonal sequence (i.e., in the sequence 1, 3, 4, and 2, with the next increment at 2, 4, 3, and 1). Initially, the tightening increments are at 5 psi and are performed continuously with small intervals in between increments. Above 50 psi, the stress relaxation (readjustment of the crystalline structure) in material is a considerable factor. Hence the increments are reduced to 2 psi and a relaxation time of 24 to 36 hours is needed. The final two incremental adjustments are performed with a relaxation interval of 48 hours each so that each stud is under a final torque of 60 psi.

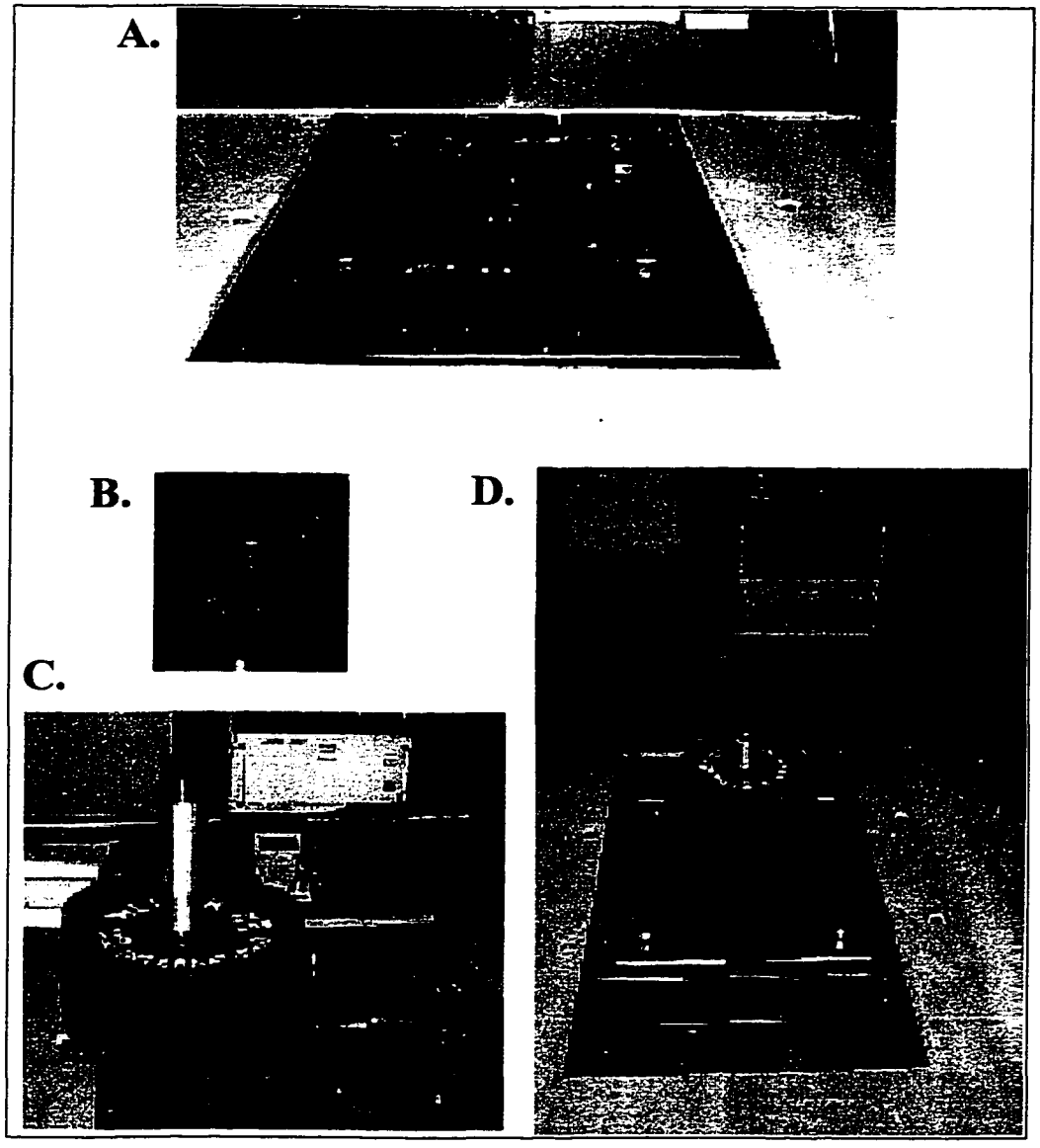


Figure 4. Load cell calibration. A. Four Eaton Lebow load cells on tie plate. Wires from each lead go to individual strain gage signal conditioners. Note the 17 mm plywood decking surrounding the opening, and the 13 mm aluminum cover on the rear half. B. An individual load cell with stud, bottom washer, and rating nut below the bottom washer. C. Calibration of an individual load cell by progressively stacking 10 kg masses onto a center sleeve threaded that has been threaded onto the load cell stud. Voltmeter used to adjust the span and offset of the load cell amplifiers. D. Calibration of the assembled force plate, which has been locked onto the four load cells, again by progressively stacking 10 kg masses onto a center sleeve threaded onto the top plate. Note the DMM–2004 controller (white color) in the relay rack in the back, and the Daytronics load cell strain gage amplifiers located just above it. The two air bearing races, two air bearings, the linear motor and the optical encoder are all visible at the front opening in the plywood decking. The decking is secured to a Unistrut sub–frame.

A periodic unexplained drift with a period of an hour or so was observed in the load cell readouts. The cause was determined to be the differential cyclic heating and cooling due to the air coming from an overhead air vent. This outlet in the lab was the first from the building's principal air conditioner. Thus, the draft flow was high, and the temperature extremes went from very cold or very hot. This problem was overcome by installing shields in and near the vent.

The calibrated load cell voltages are digitally low pass filtered at 20 Hz then used as inputs to a LabVIEW™ VI computer program (COPcalcD.VI), which is a center–of–pressure (COP) calibration algorithm [Robinson, et al., 1998]. From this algorithm, resolutions of 0.784 N total weight and 0.4 mm CoP distances can be obtained [Robinson, et al., 1998]. The voltage–to–distance conversions were calibrated to be 0.2095 mV/mm for anterior–posterior (AP) displacements and 0.1746 mV/mm for medial–lateral (ML) displacements.

3.3 Software Modifications

LabVIEW™ is a program development application that uses G, a graphical programming language, to create programs in block diagram form. LabVIEW™ programs are called virtual instruments (VI) because their execution, operation, and appearance simulate actual laboratory instruments [National Instruments, 1994]. The VI user interface is termed the front panel with various controllers, indicators, graphs, etc., accessible via knobs, buttons, and other simulated instrument controls. The VI receives its operating instructions from block diagrams, which are constructed in G. VI's are hierarchical and modular; the same VI can be used as the top–level program or as a subprogram (sub VI)

within other programs. Commands to control the SLIP–FALLS motion events were determined for PMAC and executed from LabVIEW™ VI's through an RS–242 serial interface with communication speeds of up to 38000 bits per second. To decrease the delay between a VI commanded action and the actual movement, the full PMAC command was often sent in 2 parts, with the first being an initialization character string, and the second an execute character string. Whenever possible, the execute string is minimized to two ASCII characters "/r" = (return).

Data acquisition, display, and analysis are performed primarily in LabVIEW™. An initialization VI starts PMAC, sets the platform zero position, and defines the analog input gains. It then moves the platform to a zero (home) position. Calibration VI's obtain initial values of the SLIP inputs before subject use and stores these reference voltages, enabling near real–time acquisition and analysis of the actual input signals in other VI's. Other VI's send platform control commands, provide for data acquisition, and store the raw values in a spreadsheet file for further analysis. Most data collection is performed using digital memory buffering to allow for concurrent use of dynamic links such as the use of wave format files for auditory commands and cues during data collection. An exhaustive library of programs to control and perform tests on SLIP–FALLS was written in the Rehabilitation Neuroscience Laboratory over the years. Of these, the psychophysical testing on young adults ("bravo" group) was of particular importance. Wald's (1947) method of sequential testing was designed specifically for minimizing the expected number of trials required for determining,

with specified error probabilities, whether or not a given hypothesis is true. For the case of binary data, the technique can be used to determine if the probability of a positive response lies within prescribed bounds. Faulkner, et al., 1998, had modified the PEST criterion by changing the Wald coefficient.

Wald coefficient (W) was computed according to the equation:

$$W = N_c - P_t * N_t$$

Where, N_c is the number of correct responses, P_t is the desired probability of correct detection at threshold, and N_t is the number of stimuli presented at a given stimulus level.

The available libraries of routines were modified for use in this study. The Veterans' group is the third in the series of protocols being performed in this lab. It was christened the "Delta" group. In order to compensate for potential fatigue factors in the elderly population, the adaptive PEST methodology was modified to 1) replace the Wald coefficient calculation with the staircase–71 (for first 10 moves with 70.9% accuracy), and staircase–79 (with 79.4% accuracy) determinations for deciding when to change the stimulus level, and to 2) limit the maximum number of runs to 30 per trial. When a threshold is not reached within 30 trials, a threshold level was chosen by determining when a stimulus level was detected at least 79% of the time.

3.4 Installing Peripheral Devices

The setup of peripheral devices has been discussed in detail in the previous publications from the lab [Purucker, et al., 1996, Robinson, et al., 1998,

Faulkner, et al., 1998.]. Brief summaries of adjustments made at Overton Brooks VAMC are given below.

During platform movement, sounds of up to 70 decibels (as measured by a portable sound level meter, Realistic / Radio Shack™, Catalog No. 33–2050) are produced. It is imperative to mask this potential movement cue while still allowing the subject to clearly hear the commands and the auditory cues needed for the psychophysical testing [Horak, et al., 1989]. Hence, a wide spectrum (white) noise is delivered to subject's earphones via a sound mixer, where it is patched with the auditory commands and cues. The white noise was produced by an AM radio from which the antenna was removed.

A wireless door chime (Radio Shack™, catalog number 63–874) provides a lightweight (30 oz) hand–held wireless detection switch that transmits to a receiver, which in turn produces an auditory tone to signal detection. The two receiver gate states are 0 V during the open switch position or 4 V, which occurs 47 milliseconds after the wireless doorbell switch is pushed. The change in state at the receiver takes approximately 3 milliseconds. Change in voltage of 0.5 V is counted as a switch closure. The tone generator gate signal is sent to one of the analog data collection inputs. The tone oscillator output is routed through the sound mixer to the wireless headphones to provide feedback to the subject that they appropriately pressed the signal detection switch one or two times. This mixed signal is presented to the subject at a measured level of 78 decibels.

A single wireless sound system transmitter (Recoton® with an adjustable carrier frequency between 912.5 and 914.5 MHz) transmits the mixer output to

the subject via a set of wireless headphones (Recoton® W500) and to a wireless speaker (Recoton® W440) to provide the investigators with confirmation. The wireless speaker output is also directed towards the platform to additionally mask any movement sounds and to provide cues to the subject if the headphones fail during a test.

Other transducers gather position and acceleration data. Platform displacement is read by a PMAC subroutine from the optical position encoder in either counts (20000 counts/mm) or millimeters and outputted from the DMM 2004 as an analog value with a choice of scale output. Digitally integrating the displacement data over time derives platform velocity. A double differentiated position signal yields platform acceleration. Platform acceleration is also determined directly from an accelerometer (Endevco 7290A–30) attached to the top plate. For accelerations less than 40 mm/s^2, the doubly integrated platform position signal is more accurate of the two due to ambient noise inherent in the Endevo 7290A–30.

Muscle EMG potentials are captured by four tri–surface electrode sets, amplified by Neurocom® EMG amplifiers that doubly–differentially–amplify the signal to reduce cross talk. A LabView™ VI filters the EMG at 20–400 Hz and calculates the RMS values over 25 ms windows as recommended by De Luca (1997). One electrode set is placed over the muscle belly of tibialis anterior muscle (see Figure 5). Another is placed just distal to the transition between the gastrocnemious muscle and achilles tendon in order to receive signals from the soleus muscle as well. The other leg has similarly placed electrodes.

A triaxial head accelerometer (TAA–31013–20) has an RMS noise of approximately 25 mm/s^2. Single axis force sensor (Sensotec model 31), with resolution of 0.012 N, serves as a tactile probe or as a signal switch during reaction time tests. This force sensor is used to measure applied force during reaction time tests for tactile sensation at the feet and as a signaling device for detection of auditory stimulus produced by the wireless doorbell tone. The single axis force sensor is calibrated to a zero state prior to each reaction time test series. A change of approximately 10 times the sensor's resolution (0.1 N) or greater is the trigger for a detection event. A change of more than 0.01 N is considered as the start time marker in the tactile reaction time tests, or the end time marker in the auditory reaction time tests.

3.5 Subject Recruitment

The protocol for testing and the informed consent document were reviewed and approved by institutional review board (IRB) of the Overton Brooks VAMC and Louisiana State University Health Science Center, Shreveport (see appendix A). An IRB–approved flyer was posted on the premises of the Overton Brooks VAMC to request volunteers in the 50 to 80 year old age group (see appendix B). Subjects were also recruited by word–of–mouth from throughout the Shreveport/Bossier and Ruston city area. The Social Service Department at Overton Brooks VAMC helped identify and recruit veterans, although volunteer subjects needed not to be veterans.

All participating subjects were compensated at $25 per four–hour session they attended. Subjects were initially screened by phone to ensure that they met

the age criteria and did not have any exclusionary criteria. They were also informed about the nature of the study and what would be expected of them during the course of the study.

3.6 Pre–Testing Protocol

For the purpose of uniformity, a standard protocol has been developed over a period of time for the Rehabilitation Neuroscience Laboratory. This protocol has been modified for the testing of the Delta group of subjects.

The lab and the various testing equipment are checked and setup before the arrival of the subject. The wireless headphones are charged for at least 12 hours before an experiment. The platform (force plate where the subject steps on) is disinfected using ethanol before and after any testing. A heating blanket is laid over the top plate to make sure the platform is warm when the subject steps on it. This would eliminate any decreased tactile sensation in the feet due to the cold surface. The heating blanket is placed over the platform between tests to ensure that the platform remains at approximately the same temperature throughout the testing. The protocol forms and IRB consent forms for the subject are previously filled out and placed in readiness. A five digit, unique alphanumeric code is assigned for each subject. The code has the subject's gender, age, group, and order in that group. For instance, a 64–year old male subject being tested second in the delta group would have a unique code as "M64DB."

The ON switches on the Daytronic signal conditioners (load cells), Gould signal conditioners (accelerometers), master computer, Neurocom® EMG box,

headphone transmitter, and mixers are checked. The air compressor is turned on. The moisture in the line and primary reservoir tank are blown out at a low pressure of 20 and 40 psi respectively. All the check valves are opened and the line checked for leaks. Operating pressure and flow at platform is checked (> 70 psi and 3.6 scfm). All the electrical connections are manually checked.

NIDAQ data acquisition software (National Instruments, TX) is run to check if the individual sensors were working properly. Channels 0 to 3 receive the output from load cell strain gauge conditioners 1 to 4 respectively. Channel 5 receives the acceleration signal of the platform. Channel 4 receives the platform position signal at selectable resolution from the DMM 2004 controller, which also outputs a signal proportional to motor voltage on channel 6. The motor voltage is proportional to the horizontal sheer force. Channel 7 receives input from the single axis force sensor DC output. Channels 8 to 11 receive EMG signals amplified and conditioned by the Neurocom® front end. Channels 12, 14, and 15 acquire zero–nulled voltages representing the acceleration in the X–, Y–, and Z–axes of the triaxial head accelerometer. Channel 13 receives the 0 v or 4 v output of the doorbell receiver gate signal.

The white noise generator, wireless headphones and speakers are then turned on. A VI, "Get_sound.VI," is then run to transmit a test signal (voice command in "wav" format) that is overlaid with the white noise with the mixed signal heard on the headphones/speakers, and the volumes are adjusted and mixed accordingly. The doorbell transmitter is pressed to check if the doorbell

feedback is audible in the mixed auditory input. A VI, "5_Randoms.VI," is then run to ascertain the order of the displacement (1, 4, and 16 mm) sequence.

Next, the VI's that are used during experimentation are opened. These VI's are, "VDA_Initialize_and_Home.VI, 5Jog.VI, FC_Learning.VI, EMG_CoP_Calibrate.VI, Forced_Choice_VDA.VI, VDA_Latencies.VI, and Reaction_VDA.VI." To ensure that the entire testing is performed in the shortest duration, a time log of the start and end of each activity during the test are maintained. This time log helps ascertain when unnecessary down times occur during testing and helps rectify that for future testing. By doing this, length of testing is minimized while providing maximum comfort to the subject.

3.7 Testing Protocol

Once the subjects arrive, they are introduced again to the nature and scope of the study. The subjects are then shown what a typical displacement is like (using the VI, "5jog.VI"). After these explanations, they are read the IRB approved, informed consent form that explains the scope and nature of the study and their rights (see appendix A). Any questions they might have are answered.

The testing is performed in three different parts. The first part is the clinical and cognitive evaluation; the next part, the threshold and reaction determination; and the last part, the nerve conduction study. The actual testing of the subjects is not necessarily in that order. Some subjects have their nerve conduction study performed on a different date than the other two due to the scheduling constraints of the Neurology Service at Overton Brooks, VAMC. However, all testing on a given subject is performed within a window of fourteen days time.

From the time log of the first three subjects, it was apparent that the optimum schedule of test sequencing that maximized subject comfort and minimized test time was to interlace the clinical and cognition evaluation with threshold testing. Thus an evaluation questionnaire was followed by threshold testing for a given displacement criterion.

3.7.1 Part I – Clinical and Cognitive Evaluation.

A detailed screening of the patient's medical history (cardiac, neurological, and orthopaedic) is performed using a pertinent standardized questionnaire developed by us and approved by the IRB (see appendix C). Individuals with one or more of the exclusion criteria are excused from participating further in the study. Vestibular stability, vision, myotactic reflex activation, joint acuity, and tactile threshold using calibrated Semms–Weinstein Monofilaments applied to the foot sole are tested. General anthropometrical measures were taken and recorded.

A short, standardized Mini–Mental status examination (MMSE) questionnaire evaluating the cognitive mental state of the subjects is administered. It concentrates only on the cognitive aspects of mental functioning and excludes questions concerning mood, abnormal mental experiences, and the form of thinking. The MMSE has two sections – the first requires vocal responses only and covers orientation, memory, and attention (see appendix D). The maximum score possible in this section is 21. The second part tests the subjects ability to name, follow verbal and written commands, write a sentence spontaneously, and copy a complex polygon similar to a Bender–Gestalt figure.

The maximum score possible in this section is 9. Thus, the maximum total score is 30. The test is not timed. However, it takes about 10 minutes to administer.

3.7.2 Part II – Threshold Detection on SLIP–FALLS System

After the initial screening, subjects changed into shorts and took off their shoes and socks. To keep their feet warm between testing, subjects wore a pair of disposable operating theater slip–on boots. The two alternative forced choice (2AFC) protocol was then explained to the subject. Since the actual instructions given have an effect on the subject performance, a standardized instruction script was used, and any questions that the subject may have are addressed.

> "With this doorbell transmitter, you will be able to tell me when you feel the platform move. For this test, you will be asked to step on the platform, place the headphones over your ears, and cover your eyes with the blindfold. From your headphones you will be hearing a constant 'masking white noise,' and four verbal cues: 'Ready,' 'One,' 'Two,' and 'Decide.' If you think that the platform moved between the words 'One' and 'Two,' press the button once; if between the words 'Two' and 'Decide,' press the button two times. All decisions should be made as quickly as possible after the word 'Decide.' Go ahead and try the button with your left hand to make sure you are comfortable with it. It may take several pushes to get the second doorbell chime."

Tri–electrode EMG electrodes are placed on the medial segment of the gastrocnemious soleus (backside of calf) and tibialis anterior (front of calf) muscle groups bilaterally with the help of a double–sided tape. To test the

integrity of the EMG recordings, subjects practice toe and heel stands for at least 20 seconds without holding any object for support. Once they are comfortable with this technique, they step barefooted on the platform of SLIP–FALLS and position their feet in a designated area.

The electrodes and load cells are then calibrated using the routine, "EMG_COP_Calibrate.VI." During the execution of this routine, the subject is asked to stand on the platform with eyes open and feet side–by–side. A sequence of toe stands, heel stands, and quiet standing for 20 seconds each is recorded. Subjects are then asked to slowly step down from the platform and take a seat without entangling themselves on the EMG leads.

The subject receives a second explanation of the 2AFC protocol. They are then asked to step on the platform to receive a practice run ("FC_Learning.VI") for the movement criteria to be tested based on the predetermined sequence for the subject. The practice trials are at a constant acceleration of 50 mm/s^2 for all displacement criteria and are not adaptive. For safety, a human spotter is used at all times to control aberrant postural changes. A slight perturbation is defined as a linear perturbation of less than 0.3 m/s^2 acceleration, 0.1 m/s peak velocity, and 70 mm displacement length. Typically there are 10 practice trials in which the subject has 4 or 5 trials with eyes open and the remaining with eyes closed. During these trials they are given a feedback via the headphones as to the interval in which movement occurred. After the completion of the practice trials, the subjects step down from the

platform and relax by sitting on a chair. The subject also gets to warm their feet with the heating blanket if they feel their feet are getting cold.

The routine "Forced_Choice_VDA.VI" is then run to determine the subjects acceleration threshold. This routine uses an adaptive psychophysical methodology (PEST) performed on a 2AFC protocol to determine the threshold. Subjects step on the platform and wear a blindfold (to cut off any visual cues). The EMG leads are taped to the platform so that they don't touch the legs (and hence provide an unwanted additional cue that a movement occurred). The head accelerometer is placed via Velcro fixture on the left headphone earpiece. The accelerometers X–axis is set horizontal with the help of a fixed spirit level while the head was held in a zero degree tilt position. Thus, the three orthogonal acceleration values that are collected are related to the head with "X" perpendicular to the frontal plane, "Y" perpendicular to the saggital plane, and "Z" perpendicular to the longitudinal plane (see Figure 5).

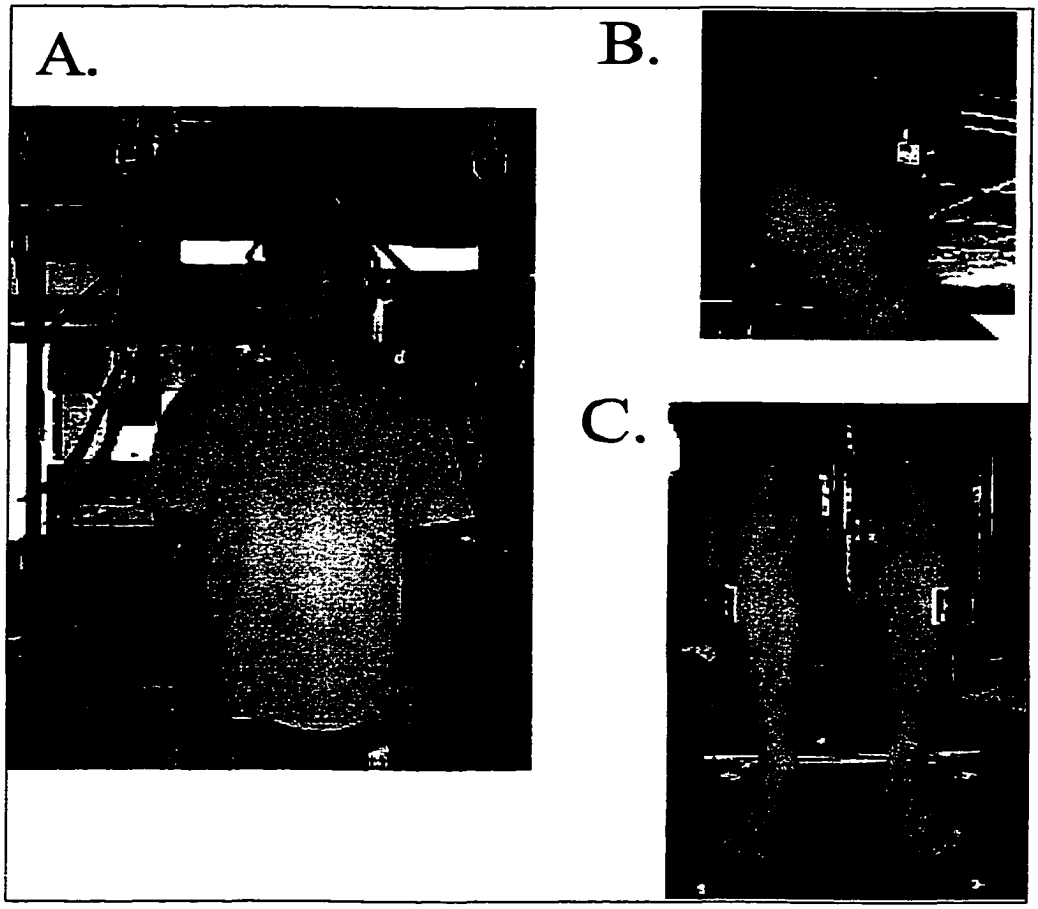


Figure 5. Psychophysical testing on SLIP–FALLS. A. Young adult subject being tested. Note headphones, blindfold and button transmitter (in left hand). Spotter's arm is shown coming in from left side to the mid–back region of the subject (but not touching it). B. Earphones with tri–axial accelerometer and small spirit levels attached along two axes. C. Foot placement on platform and location of TA EMG electrodes. Note that the sliding portion of SLIP is now completely surrounded by the 13 mm aluminum cover.

The test routine first collects data for 20 seconds of quiet standing. During this interval the patient is asked to stand still (via the headphones using a standard instruction), with eyes blindfolded and there are no perturbations involved. Signals are sampled at 1000 Hz. The initial acceleration value is set to be about 150% of the expected threshold. Further acceleration values are then determined using the modified PEST criteria for the given displacement. The test

runs for a maximum of 30 trials. The routine is stopped if threshold is achieved before the maximum, or if the subject wishes to stop for any reason. The subject then steps down and takes a seat to relax.

After a threshold is identified, its validity is checked by a second sequence of fixed stimuli tests called peri–threshold tials. Five trials at threshold and five trials at 125% of threshold are performed. In these trials, the perturbation occurs any time after the cue "READY." The subject has to buzz the doorbell transmitter as soon as they feel the perturbation. To make sure the patient was not buzzing at random, two control trials (no movement of platform) are also provided.

The subject is asked on what grounds they judged that a perturbation occurred. Their responses are recorded. The heating blanket is replaced on top of the platform to warm it again. After a few minutes, the subject undergoes the practice and threshold detection routine for the next movement distance. This process is repeated until all of movement distances are tested.

Finally, the reaction times to various stimuli are tested: 1) to platform perturbation under supra–threshold acceleration, 2) to foot touch, and 3) to auditory input. Supra–threshold acceleration was a large displacement of 20 mm at a constant acceleration of 100 mm/s^2. Reaction time was measured as the latency to respond (buzz) after being perturbed. The latency to respond to a touch by the single axis force sensor to the sole of the foot (greater toe), and the latency to respond to an auditory stimulus in the form of doorbell were recorded.

3.7.3 Part III – Nerve Conduction Study

Using a Nicolet Viking IV (Nicolet Biomedical Inc), nerve conduction studies of the lower extremity are performed at the Neurology Service of the Overton Brooks VAMC by a technician under the supervision of neurologist. Motor (peroneal and tibial nerve) and sensory nerves (sural nerve) are tested bilaterally. F– and M– latency tests that test the entire lower motor loop (sensory nerve –> vertebrae –> motor nerve) were initially performed to ascertain any problems in the Sherrington's final common pathway. However, the first two subjects expressed severe discomfort in undergoing that part of study. Hence the F– and M– latency tests were not performed in subsequent subjects.

The institutional standards for normal nerve conduction values are provided in the Tables 2 and 3 that follow.

Table 2. Overton Brooks VAMC institutional standards for motor nerve conduction study

Nerve	Recording Site	Minimum Velocity (m/s)	Max Distal Latency (ms)	Amplitude (mV)	Max F–Wave Latency (ms)
Median	Thenar (7 cm)	>=49	<=4.4	>=4.0	<=31
Ulnar	Hypothenar (7 cm)	>=49	<=3.3	>=6.0	<=32
Peroneal	EDB (9 cm)	>=44	<=6.5	>=2.0	<=56
Tibial	Abd Hall (9 cm)	>=41	<=5.8	>=4.0	<=56
Tibial	ADQ (10 cm)	>=41	<=6.3	>=3.0	N/A

Table 3. Overton Brooks VAMC institutional standards for sensory nerve conduction study

Nerve	Max Peak Latency (ms)	Amplitude (mV)
Median	<=3.5 (13 cm)	>=20
Ulnar	<=3.1 (11 cm)	>=17
Radial	<=2.9 (10 cm)	>=15
Sup. Peroneal	<=4.4 (14 cm)	>=6
Sural	<=4.4 (14 cm)	>=6

3.8 Analyses

3.8.1 Sway Analyses

Sway analyses were performed on the COP data. COP was computed from the four load cells of the platform [Robinson, et al., 1998]. COP was filtered using a third order Butterworth low–pass filter with a cutoff frequency of 5 Hz [Winter, 1990]. The routine used for computing the COP is presented in appendix E.

During quiet standing, the RMS and range of sway in AP and ML directions were computed. Quiet standing data was collected before threshold determination tests for each displacement. The average of the three values was taken as the quiet standing sway of the person.

The COP location and velocity during perturbation was determined. Perturbation was divided into three parts: 1) Initiation of platform move, 2) Mid point of move where the velocity is at its peak and a deceleration is initiated, and 3) The termination of move when the perturbation is terminated. Figures 6 and 7 explain the location of these three points.

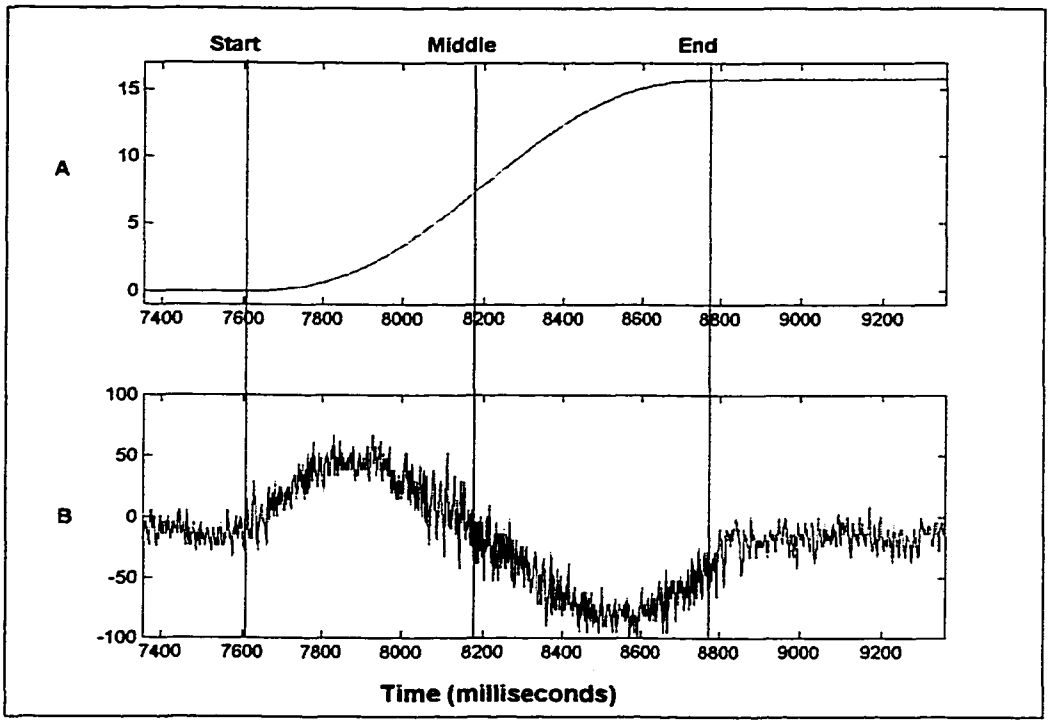


Figure 6. Acceleration profile during 16 mm perturbation in the subject F58DL. A. platform displacement, and B. acceleration of platform.

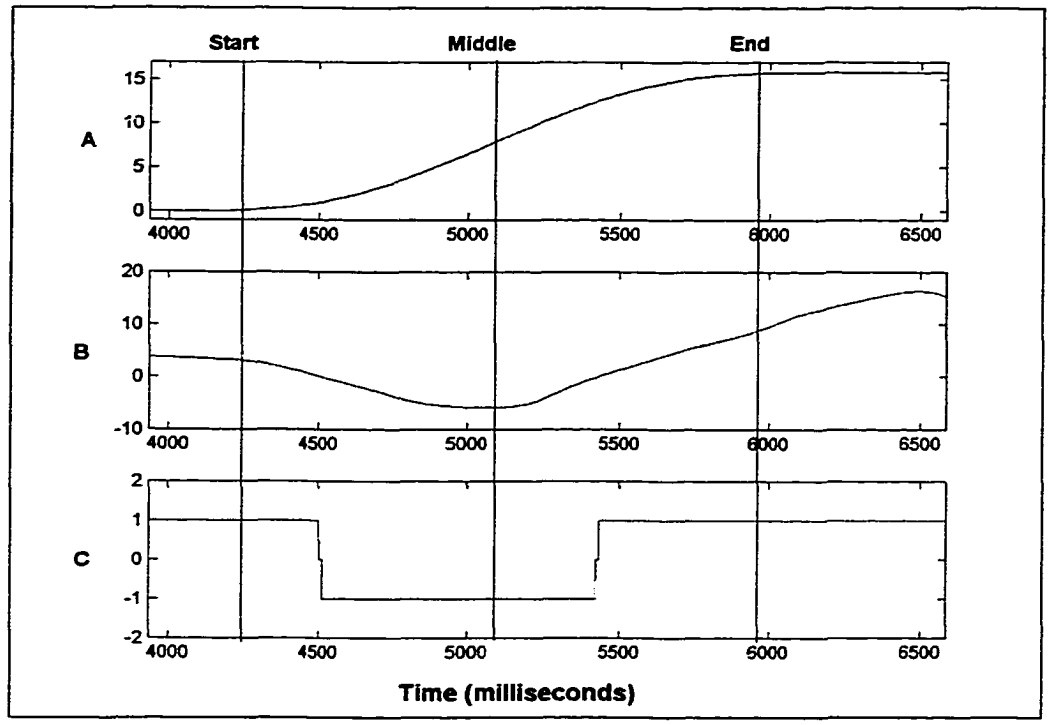


Figure 7. COP location during 16 mm perturbation in the subject M58DH. A. platform displacement, B. COP trace, and C. COP excursion with "-1" being back, and "+1" being forward of the mean COP.

3.8.2 Statistical Analyses

All statistical analyses were performed using statistical programs SAS and Systat™. Repeated measures ANOVA, regular ANOVA, paired t–tests and other appropriate statistical tests were performed as indicated in the results section.

CHAPTER 4

RESULTS

4.1 Overview

A total of 15 subjects were recruited and tested. The mean age of the subjects was 59.2 years, and their range was between 50 and 74 years. The gender ratio was four females to eleven males.

There were six subjects with diabetes whose mean age was 56.2 years, and their range was between 50 to 62 years. All these subjects had Type 2 diabetes. There was an additional subject (aged 74) who did not have any diabetes but had acute peripheral neuropathy. In all, there were seven subjects with either peripheral neuropathy and/or adult–onset diabetes with a mean age of 58.7 years and range between 50 and 74 years. The gender mix in this group was two females and five males.

There were seven age–matched, non–diabetic, neurologically intact subjects. Their mean age was 59.6 years, and they ranged between 52 years and 64 years. The gender mix in this group was again two females and five males. An additional subject aged 60 years with no known incidence of diabetes or neurological dysfunction participated in the study. However, this subject opted

not to participate in the nerve conduction study; hence, the neurological intactness of the subject could not be verified.

The data for young adults (< 35 years of age) that is cited in future sections was collected in the Pittsburgh lab as Bravo group [Faulkner, et al., 1998]. In this group a total of 11 subjects were tested. They had a median age of 24.8 years with a range between 19 and 32 years. All the subjects in this group were males.

4.2 Psychophysical Evaluation

4.2.1 Acceleration Threshold

Peak acceleration detection thresholds were identified during the testing for each displacement distance, which were 1, 4 and 16 mm. Acceleration threshold values for individual subjects are presented in Table 4 and the average peak acceleration threshold is given in Table 5. Figures 8 and 9 allow a comparison of the peak thresholds between the different groups tested. Figure 10 shows the threshold difference between the three groups by displacement.

Table 4. Acceleration threshold (mm/s^2) for individual subjects

Group	Subject ID	1 mm Perturbation	4 mm Perturbation	16 mm Perturbation
Diabetic/PN	F60DA	85.75	44.36	16.03
	M74DD	175	100	40
	M54DK	200	100	87.96
	F58DL	61.96	34.75	58.17
	M50DM	94.58	77.02	24.57
	M62DO	94.58	75.26	43.12
	M53DP	200	100	87.96
Non–Diabetic	M63DB	103.37	29.01	16.03
	M64DC	46.36	25.91	5.76
	M53DE	75.14	41.85	40.11
	F64DF	141.03	45.35	14.53
	M58DH	98.97	45.35	22.05
	F52DJ	61.12	46.98	6.51
	M63DN	164.86	89.4	15.54
Young Adults	M19BH	126.5	29.86	18.03
	M20BI	64.5	24	10.37
	M22BB	48.75	27.5	10.68
	M23BE	40	27.5	20
	M23BL	33	48.5	16.8
	M23BP	33	30	11.9
	M24BJ	55.1	33.2	11.9
	M27BN	124.4	11.33	24.33
	M29BS	40	17.44	9.48
	M31BR	89	16.34	6.69
	M32BQ	54	8.125	6.39

Table 5. Average peak acceleration threshold (mm/s^2) in the different groups

Perturbation	Diabetic/PN (mm/s^2)	Non–Diabetic (mm/s^2)	Young Adults (mm/s^2)
1 mm	130.3	98.7	64.4
4 mm	75.9	46.3	24.9
16 mm	51.1	17.2	13.3

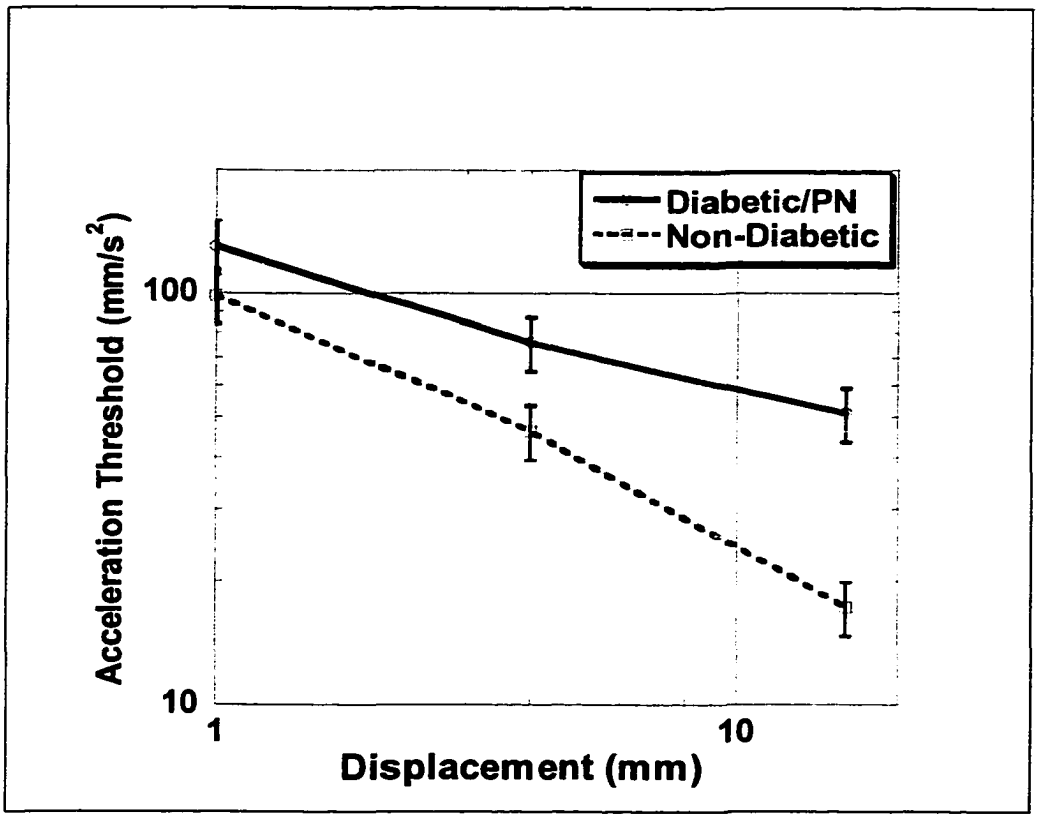


Figure 8. Threshold comparison between neurological diabetic/PN and non–diabetic elders

Figure 8 is a comparison plot between the peak acceleration threshold at 1, 4, and 16 mm displacement for the two elderly groups. The three groups are non–diabetic elderly and those with adult–onset diabetes and/or peripheral neuropathy. There were 7 subjects in each group. It is apparent from the graph that the stimulus–response curves of both populations obey a negative power law, and that a clear distinction exists between the two groups, especially in the offset values. Using a two–sample t–test, it was found that the non–diabetic elderly have a significantly ($p < 0.001$) lower acceleration threshold when compared to the population with adult–onset diabetes and/or peripheral neuropathy. This implies that the subjects with adult–onset diabetes and/or

peripheral neuropathy could be at a higher risk for falling as compared to their age–matched non–diabetic cohorts.

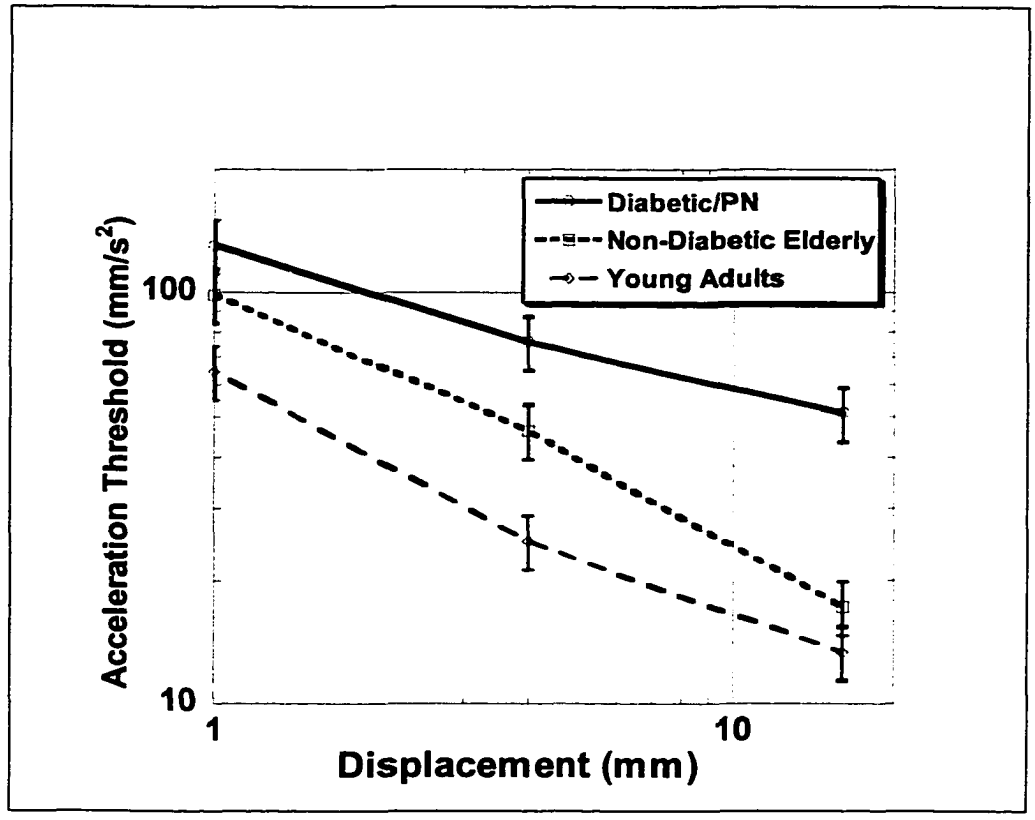


Figure 9. Peak acceleration threshold (mm/s^2) comparison between young adults, diabetic/PN elderly and non–diabetic elderly

Figure 9 compares the peak acceleration threshold at 1, 4, and 16 mm displacement for young adults and the two elderly groups. There were 11 subjects in the young adult population and 7 each in either elderly group. Note that elderly subjects (irrespective of the presence of diabetes or peripheral neuropathy) have a higher detection threshold when compared to young adults. It is also apparent from the graph that the stimulus–response profiles of all three groups obey a negative power law, but with a clear distinction between them.

Analysis of variance among the three groups showed that the young adults have a significantly lower ($p < 0.0001$) acceleration threshold when compared to both sets of elderly population. The non–diabetic elderly population had a significantly lower ($p < 0.001$) acceleration threshold when compared to the diabetic/PN elderly population.

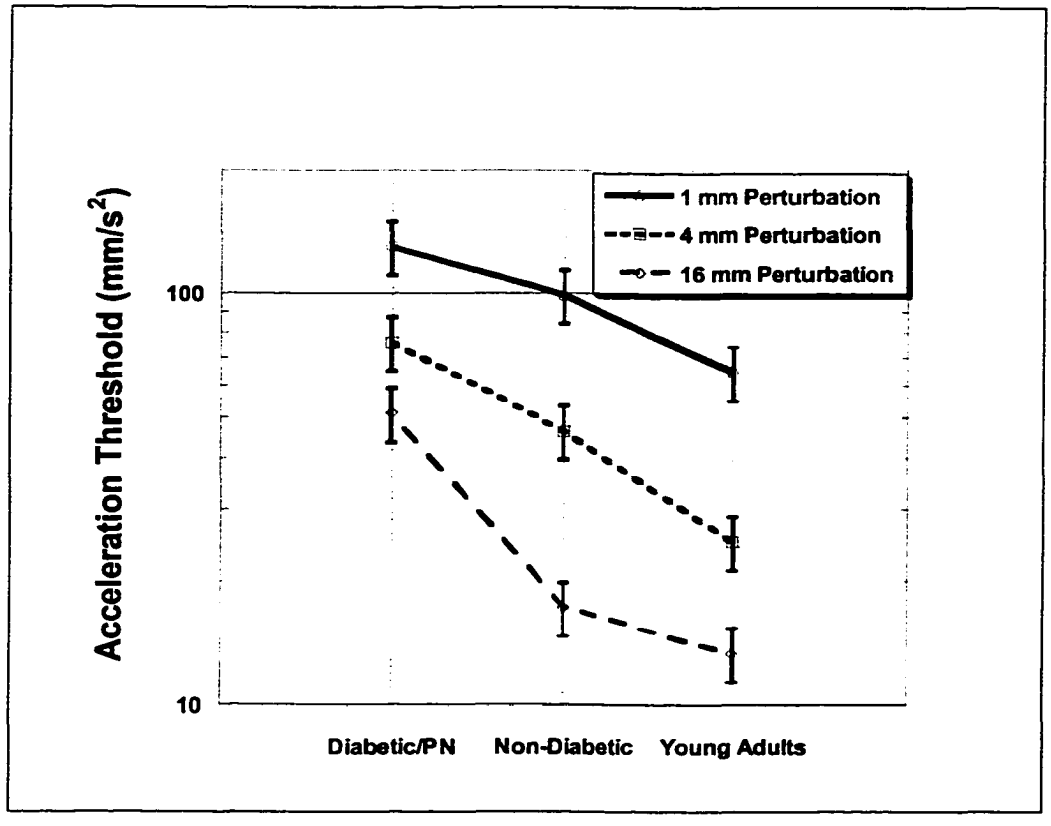


Figure 10. Categorical comparison of peak acceleration threshold (mm/s^2) between the diabetic/PN, non–diabetic and the young adults for 1, 4, and 16 mm perturbations

Figure 10 shows that the thresholds for different perturbation distances were significantly different ($p < 0.0001$) in each of the three groups. This implies that the subjects were able to clearly distinguish between a 1, 4, or 16 mm

perturbation. It is interesting to note that non–diabetic elderly have similar acceleration thresholds as young adults for large displacements. Results from an ANOVA are presented in Table 6, where it is apparent that there is a highly significant difference in the thresholds for by groups or displacements. These statistics are so strong that no significant interactions are seen between the groups and displacements.

Table 6. ANOVA table for identifying the threshold difference (‡ Indicates significance)

Source	Sum–of–Squares	DOF	Mean–Square	F–Ratio	P
Group	37377.928	2	18688.964	21.66	< 0.0001‡
Displacement	61612.578	2	30806.289	35.71	< 0.0001‡
Group X Disp.	3510.690	4	877.673	1.02	0.4046

From the Figures 8 and 9 it is apparent that the line connecting the threshold values for each displacement could be construed as linear. This implies that there exists a negative power law relationship between the displacement and the peak threshold at that displacement, as both the axes are on the log scale. There is also a significant difference in the detection threshold between the three groups. This verifies hypothesis #1 and #2 as true.

The power law relationship of threshold and displacement can be expressed mathematically as:

$$\text{Threshold} = A * (\text{Displacement})^{B}$$

Where A is the intercept, and B is the slope of the regression line.

The above equation can be rewritten as,

$$\text{Log (Threshold)} = \text{log (A)} + B * \text{Log (Displacement)}$$

Regression equations obtained from performing regression analyses on the mean threshold values (Table 10) for the three population groups are:

For diabetic/ peripheral neuropathic population:

$$\text{Log (Threshold)} = 4.86 - 0.34 * \text{Log (Displacement)} \quad (4.1)$$

For non–diabetic elderly population:

$$\text{Log (Threshold)} = 4.63 - 0.63 * \text{Log (Displacement)} \quad (4.2)$$

For young adult population:

$$\text{Log (Threshold)} = 4.04 - 0.54 * \text{Log (Displacement)} \quad (4.3)$$

The regression equation fits the points with an r^2 value of 99% for all the three displacements (1, 4, and 16 mm). With such a good fit, the threshold values for other displacements can be predicted within that range with a high degree of confidence. The regression equations under repeated measures ANOVA were found to be similar to the above equations. However, as expected the r^2 values for the regression equation of the threshold values based on all of the repeated measures data was lower than the values obtained for the mean threshold values.

4.2.2 Detection Percentage

The percentage of detects during each perturbation sequence was identified and presented in Tables 7, 8 and 9 for the diabetic, non–diabetic, and young adults respectively. Note that that these data were collected across a complete 2AFC PEST test run, and hence contain stimuli that are sub–threshold, peri–threshold, and supra–threshold. Since the pest methodology is an adaptive, iterative method, many, if not most, stimuli will be below threshold. At or above

threshold, at least 79% detection is theoretically expected by the definition of the staircase 79 formulations. Subjects either asymptotically approached threshold or oscillated around it.

Table 7. Percentage detection in the diabetic/PN population

Subject	1 mm Perturbation		4 mm Perturbation		16 mm Perturbation	
	# Trials	% Detect	# Trials	% Detect	# Trials	% Detect
F60DA	30	43.33	28	32.14	22	22.73
M74DD	30	33.33	30	36.67	30	30.00
M54DK	30	26.67	30	16.67	30	36.67
F58DL	30	33.33	30	36.67	30	26.67
M50DM	30	30.00	29	31.03	30	30.00
M62DO	30	23.33	30	36.67	30	36.67
M53DP	30	16.67	30	30.00	30	30.00

Table 8. Percentage detection in non–diabetic elderly population

Subject	1 mm Perturbation		4 mm Perturbation		16 mm Perturbation	
	# Trials	% Detect	# Trials	% Detect	# Trials	% Detect
M63DB	30	36.67	30	30.00	29	13.79
M64DC	30	40.00	30	36.67	17	23.53
M53DE	21	42.86	22	31.82	30	23.33
F64DF	30	40.00	23	43.48	19	15.79
M58DH	30	43.33	27	29.63	19	31.58
F52DJ	30	36.67	30	43.33	30	30.00
M63DN	30	36.67	30	33.33	26	15.38

Table 9. Percentage detection in the young adult population

Subject	1 mm Perturbation		4 mm Perturbation		16 mm Perturbation	
	# Trials	% Detect	# Trials	% Detect	# Trials	% Detect
M19BH	30	43.33	28	28.57	30	16.67
M20BI	30	43.33	22	18.18	30	13.33
M22BB	30	26.67	30	30.00	27	18.52
M23BE	30	43.33	30	40.00	30	23.33
M23BL	30	33.33	30	26.67	30	13.33
M23BP	28	32.14	30	23.33	30	30.00
M24BJ	22	45.45	30	43.33	30	26.67
M27BN	30	43.33	30	30.00	30	30.00
M29BS	30	43.33	30	36.67	26	26.92
M31BR	30	26.67	30	36.67	21	33.33
M32BQ	30	43.33	30	16.67	30	10.00

Repeated measures ANOVA was performed to determine the relationship between detect percentage and displacements. The least square means of percentage detect is presented in Table 10, and the ANOVA results are presented in Table 11.

Table 10. Least square means from repeated measures ANOVA for percentage detects in the three displacements for the three groups

Group	1 mm Perturbation	4 mm Perturbation	16 mm Perturbation
Diabetic/PN	29.523	30.693	30.391
Non-Diabetic	39.457	35.466	21.914
Young Adults	38.567	30.008	22.009

Table 11. Repeated measures ANOVA table for within subject effects on percentage detects for the three displacements in the three groups (‡ Indicates significance)

Source	Sum–of–Squares	DOF	Mean–Square	F–Ratio	P
Displacement	1514.706	2	757.352	15.87	$< 0.0001^{‡}$
Disp. X Group	877.443	4	219.361	4.60	$0.0035^{‡}$
Error (Disp.)	2100.318	22	47.735		

From the Table 11 it is clear that there is a significantly higher ($p < 0.0001$) percentage of detects for a smaller perturbation than for the larger perturbation. There is significant difference ($p < 0.0035$) between the percentages of detects in the different groups for the different displacements. The diabetic/PN in general had a lower percentage of detects when compared to the other two groups.

4.3 Postural Evaluation

Figure 7 shows the platform position (start, middle, end) and the COP excursion as backwards (-1) or forward (+1) during perturbation for a typical PEST trial. Tables 12 to14 tabulates the excursion of AP COP in threshold trials when the subjects detected the perturbation during the three displacements. Repeated measures ANOVA were performed to determine the statistical significance of the COP location during perturbation and their results are presented in Tables 15 and 16.

Table 12. Number of detects when COP position and velocity during the start, middle, and end of perturbation during the threshold trials (B: COP leaning backward, F: COP forward) in diabetic/PN elderly

Subject	Location	1 mm Perturbation		4 mm Perturbation		16 mm Perturbation	
		Back	Forward	Back	Forward	Back	Forward
F60DA	Start	5	8	5	4	2	3
	Center	5	8	7	2	5	0
	End	5	8	7	2	3	2
M74DD	Start	6	4	5	6	9	0
	Center	6	4	5	6	9	0
	End	6	4	8	3	8	1
M54DK	Start	7	1	4	1	8	3
	Center	7	1	5	0	11	0
	End	7	1	5	0	10	1
F58DL	Start	2	8	10	1	8	0
	Center	2	8	11	0	7	1
	End	3	7	11	0	5	3
M50DM	Start	6	3	2	7	2	7
	Center	6	3	4	5	6	3
	End	5	4	9	0	1	8
M62DO	Start	0	7	7	5	2	9
	Center	0	7	7	5	4	7
	End	0	7	8	4	0	11
M53DP	Start	1	4	5	4	5	4
	Center	2	3	8	1	8	1
	End	2	3	4	5	4	5

Table 13. Number of detects when COP position and velocity during the start, middle, and end of perturbation during the threshold trials (B: COP leaning backward, F: COP forward) in non–diabetic elderly

Subject	Location	1 mm Perturbation		4 mm Perturbation		16 mm Perturbation	
		Back	Forward	Back	Forward	Back	Forward
M63DB	Start	7	4	2	7	3	1
	Center	7	4	3	6	4	0
	End	7	4	4	5	4	0
M64DC	Start	1	11	4	7	0	4
	Center	2	10	6	5	0	4
	End	2	10	6	5	0	4
M53DE	Start	8	1	2	5	0	7
	Center	8	1	4	3	3	4
	End	8	1	4	3	0	7
F64DF	Start	12	0	10	0	3	0
	Center	12	0	10	0	3	0
	End	12	0	10	0	3	0
M58DH	Start	13	0	2	6	6	0
	Center	13	0	3	5	6	0
	End	12	1	4	4	2	4
F52DJ	Start	5	6	7	6	8	1
	Center	5	6	10	3	9	0
	End	6	5	12	1	8	1
M63DN	Start	11	0	6	4	2	2
	Center	11	0	7	3	3	1
	End	11	0	8	2	1	3

Table 14. Number of detects when COP position and velocity during the start, middle, and end of perturbation during the threshold trials (B: COP leaning backward, F: COP forward) in young adults

Subject	Location	1 mm Perturbation		4 mm Perturbation		16 mm Perturbation	
		Back	Forward	Back	Forward	Back	Forward
M19BH	Start	7	6	2	6	1	4
	Center	7	6	1	7	2	3
	End	7	6	3	5	3	2
M20BI	Start	12	1	4	0	0	4
	Center	12	1	4	0	1	3
	End	12	1	4	0	1	3
M22BB	Start	2	6	1	8	5	0
	Center	4	4	1	8	4	1
	End	4	4	1	8	5	0
M23BE	Start	7	6	5	7	4	3
	Center	7	6	4	8	4	3
	End	7	6	4	8	4	3
M23BL	Start	5	5	3	5	4	0
	Center	6	4	3	5	4	0
	End	7	3	5	3	3	1
M23BP	Start	7	2	6	1	7	2
	Center	7	2	7	0	5	4
	End	7	2	7	0	4	5
M24BJ	Start	2	8	11	2	4	4
	Center	2	8	11	2	7	1
	End	2	8	11	2	5	3
M27BN	Start	1	12	4	5	0	9
	Center	2	11	5	4	2	7
	End	2	11	4	5	0	9
M29BS	Start	3	10	9	2	5	2
	Center	3	10	9	2	5	2
	End	3	10	9	2	4	3
M31BR	Start	1	7	1	10	2	5
	Center	1	7	1	10	1	6
	End	1	7	1	10	0	7
M32BQ	Start	7	6	1	4	2	1
	Center	8	5	1	4	3	0
	End	8	5	2	3	3	0

Table 15. Least square means from repeated measures ANOVA for percentage detects when COP was back of quiet standing mean in the three displacements for the three groups

Location	Group	1 mm Perturbation	4 mm Perturbation	16 mm Perturbation
Start	Diabetic/PN	41.804	58.290	58.384
	Non–Diabetic	72.330	46.571	59.127
	Young Adults	42.719	49.178	51.963
Middle	Diabetic/PN	44.661	73.556	82.774
	Non–Diabetic	73.521	61.349	73.980
	Young Adults	47.299	49.594	59.376
End	Diabetic/PN	44.503	80.231	51.121
	Non–Diabetic	73.723	68.349	49.603
	Young Adults	48.208	54.946	52.838

Table 16. Repeated measures ANOVA table for within subject effects on percentage detects for the three displacements in the three groups (no significance was found)

Location	Source	Sum–of–Squares	DOF	Mean–Square	F–Ratio	P
Start	Displacement	358.826	2	179.413	0.20	0.816
	Disp. X Group	3693.760	4	923.440	1.05	0.390
	Error (Disp.)	38530.009	44	875.682		
Middle	Displacement	3476.088	2	1738.044	2.36	0.106
	Disp. X Group	3820.270	4	955.068	1.30	0.286
	Error (Disp.)	32387.969	44	736.090		
End	Displacement	3573.787	2	1786.894	2.42	0.101
	Disp. X Group	4690.132	4	1172.533	1.59	0.195
	Error (Disp.)	32516.227	44	739.005		

A simple t–test can be performed using the mean values and errors in Table 15 to compute the probability of location of COP being back of the mean quiet standing COP excursion at the start, middle, and end of perturbation. The t–test yielded a significant probability ($p < 0.01$) of detecting a move when the subject is back of mean quiet standing COP at the middle of perturbation. There was a trend for a higher detection for detecting during the end of the perturbation. However, this trend was not significant. Hence, a subject has a better probability of detecting a perturbation when he or she is slightly back of the quiet standing

mean COP location for an anterior perturbation. This verifies hypothesis #3 as true.

4.4 Clinical Evaluation

Nerve conduction velocity was used to identify peripheral neuropathy. Results from the nerve conduction study were compared with the institutional standard values to ascertain neuropathy in the subjects. Most subjects underwent nerve conduction study on the peroneal and tibial nerves (motor), and sural nerve (sensory) bilaterally. Two subjects preferred to have only a limited nerve conduction study and hence were studied on their preferred leg. All the subjects with adult–onset diabetes were found to have some extent of peripheral neuropathy. Nerve conduction velocity in the elderly subjects is presented in Table 17.

Table 17. Nerve conduction velocity in elderly subjects

Group	Subject ID	Tibial (m/s)	Peroneal (m/s)	Sural (m/s)
Diabetic/PN	F60DA	40.5	46.5	None Found
	M74DD	None Found	None Found	None Found
	M54DK	39	38.5	37.5
	F58DL	39	44.5	41
	M50DM	43	49.5	41.5
	M62DO	29	18	None Found
	M53DP	43	45.5	20
Non–Diabetic	M63DB	38	50	44
	M64DC	51	44	60
	M53DE	46.5	45.5	52
	F64DF	36.5	49.5	44
	M58DH	36	41	41
	F52DJ	47	49	Not Tested
	M63DN	33	34.5	44

Figures 11 to 13 compare the mean nerve conduction velocities between the two elderly groups. In the sample population studied, a paired sample t–test showed no significant difference in the conduction velocity between the two extremities (right and left) in either group. From a two–sample t–test it was determined that the mean conduction velocity of the sensory nerve was significantly different ($p < 0.05$) between the non–diabetic elderly and the elderly with adult–onset diabetes and/or peripheral neuropathy. The conduction velocity of the motor nerve was siightly higher in the non–diabetic population. However, there were no significant differences in the conduction velocities. It is interesting to note that most diabetic population had normal nerve conduction in their motor nerve.

Thus, neurologically intact adults had higher sensory nerve conduction velocities and lower detection thresholds at all perturbation levels than the population with peripheral neuropathy. This verifies hypothesis #5 as true.

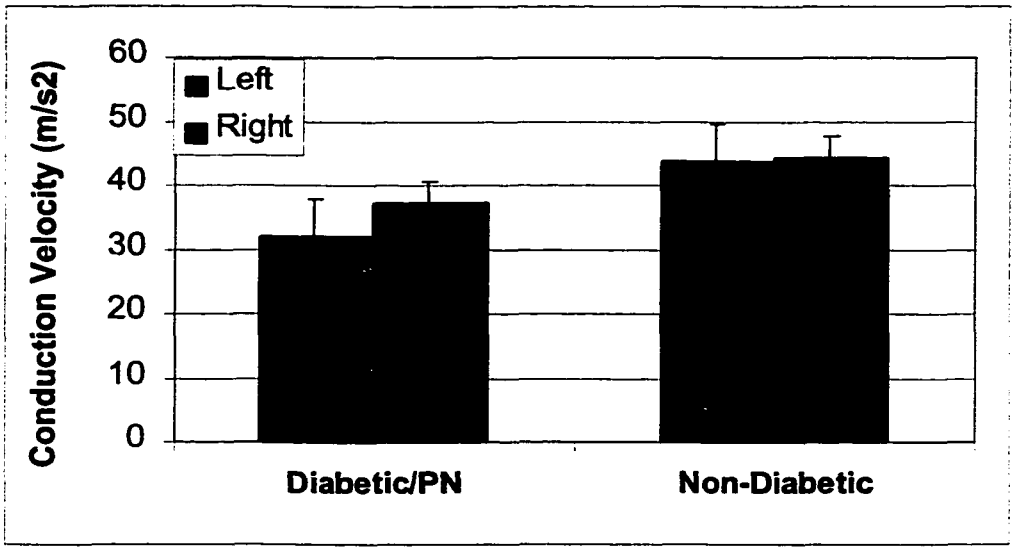


Figure 11. Mean motor nerve conduction velocity (m/s) in the peroneal nerve (ankle – fibular head)

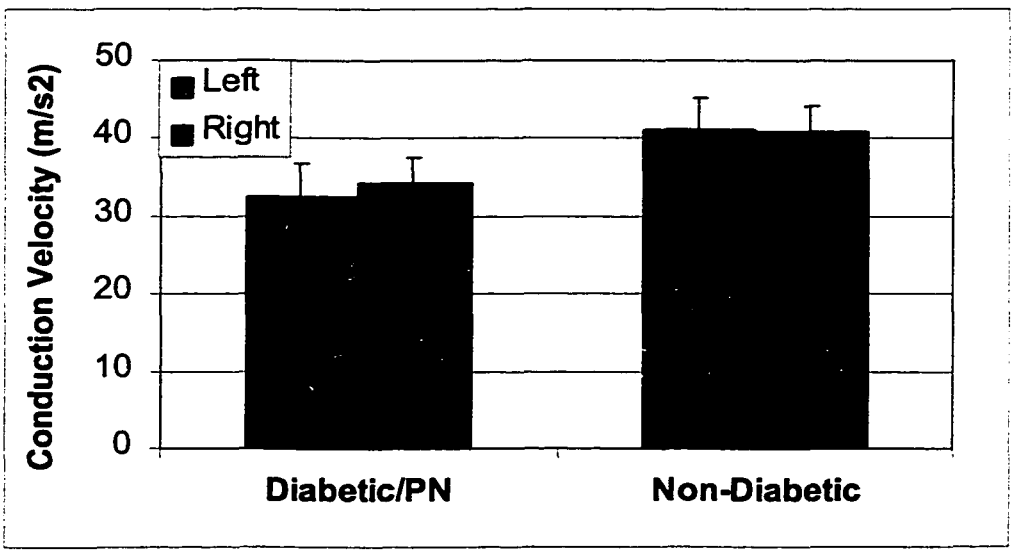


Figure 12. Mean motor nerve conduction velocity (m/s) in the tibial nerve (ankle–pop. fossa)

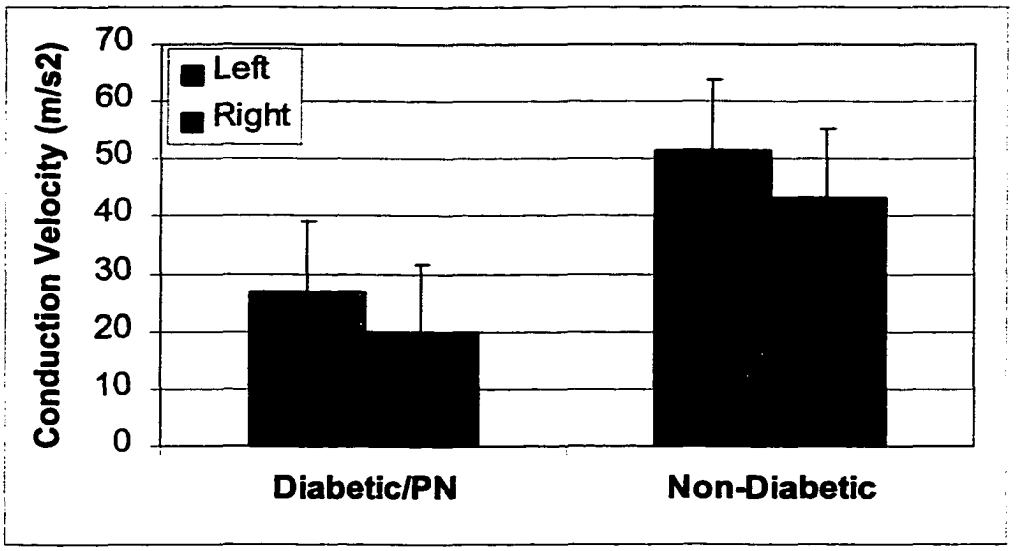


Figure 13. Mean sensory nerve conduction velocity (m/s) in the sural nerve (ankle – lower leg)

4.5 Tactile Sensory Response

Tactile sensory perception threshold at the base of the metatarsal and digit IV that was sensed by the subject when a monofilament was pressed against the foot sole were checked. The threshold values based on the load to first bending moment or buckling the calibrated Semms–Weinstein monofilament for the elderly subjects is presented in Table 18. Table 19 lists the tactile sensory perception threshold for touch as measured via Semms–Weinstein monofilaments based on the calibrated load to buckle of the fiber. Figure 14, shows the distribution of the values in Table 19. Table 20 lists the corresponding calibrated diameter. Figure 15, shows the distribution of the values in Table 20.

Table 18. Threshold of monofilament load to buckle (in grams) in the elderly population

Group	Subject ID	Left		Right	
		Meta–tarsal	Digit IV	Meta–tarsal	Digit IV
Diabetic/PN	F60DA	1.43	0.503	0.188	0.083
	M74DD	18.24	2.06	2.06	0.503
	M54DK	4.73	1.43	2.06	1.43
	F58DL	1.43	0.481	0.481	0.222
	M50DM	1.43	0.503	1.43	0.481
	M62DO	18.24	4.73	18.24	2.06
	M53DP	4.73	1.43	4.73	2.06
Non–Diabetic	M63DB	1.43	0.222	1.43	0.481
	M64DC	1.43	0.481	16.6	0.503
	M53DE	2.06	1.43	9.45	1.43
	F64DF	0.222	0.083	0.481	0.222
	M58DH	2.06	0.481	1.43	0.222
	F52DJ	0.481	0.188	0.481	0.481
	M63DN	0.503	0.481	2.06	1.43

Table 19. Semms–Weinstein monofilament threshold (load to buckle in grams)

Group	Left		Right	
	Meta– tarsal	Digit IV	Meta– tarsal	Digit IV
Diabetic/PN	7.176	1.591	4.170	0.977
Std. Dev	7.701	1.512	6.379	0.855
Non–diabetic	1.169	0.481	4.562	0.681
Std. Dev	0.768	0.449	6.164	0.525

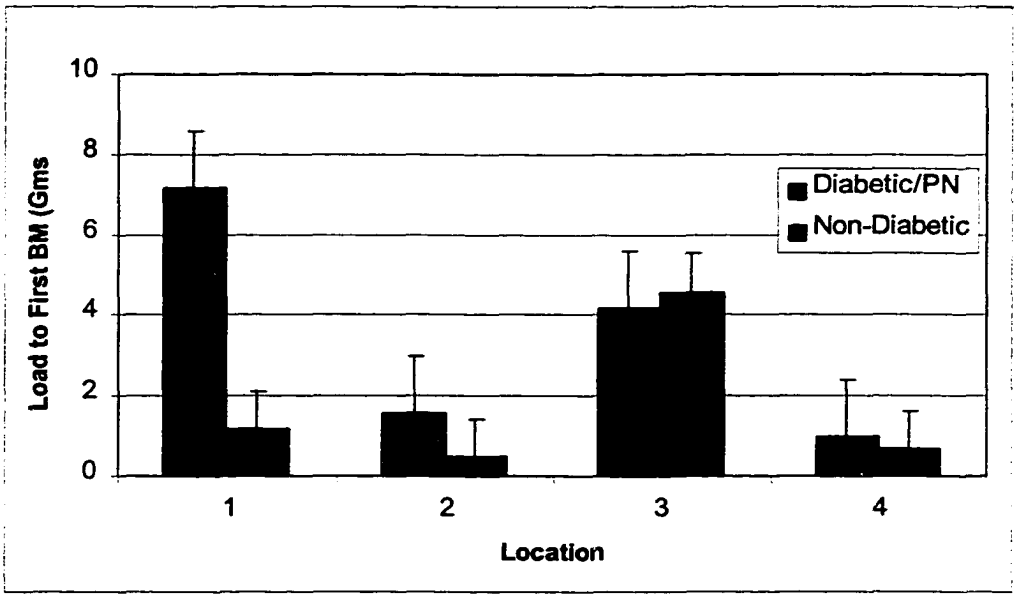


Figure 14. Semms–Weinstein monofilament threshold (load to buckle) in the elderly population, where location 1, is the left base metatarsal and 2, the digit IV on the left side. Locations 3 and 4 are corresponding values in the right leg

Table 20. Semms–Weinstein monofilament threshold (fiber diameter, $X10^{-3}$ inch)

Group	Left		Right	
	Meta–tarsal	Digit IV	Meta–tarsal	Digit IV
Diabetic/PN	14.286	10.143	11.571	8.714
Std. Dev	4.923	1.952	4.860	2.215
Non–diabetic	9.429	7.429	11.857	8.429
Std. Dev	1.512	1.618	4.375	1.272

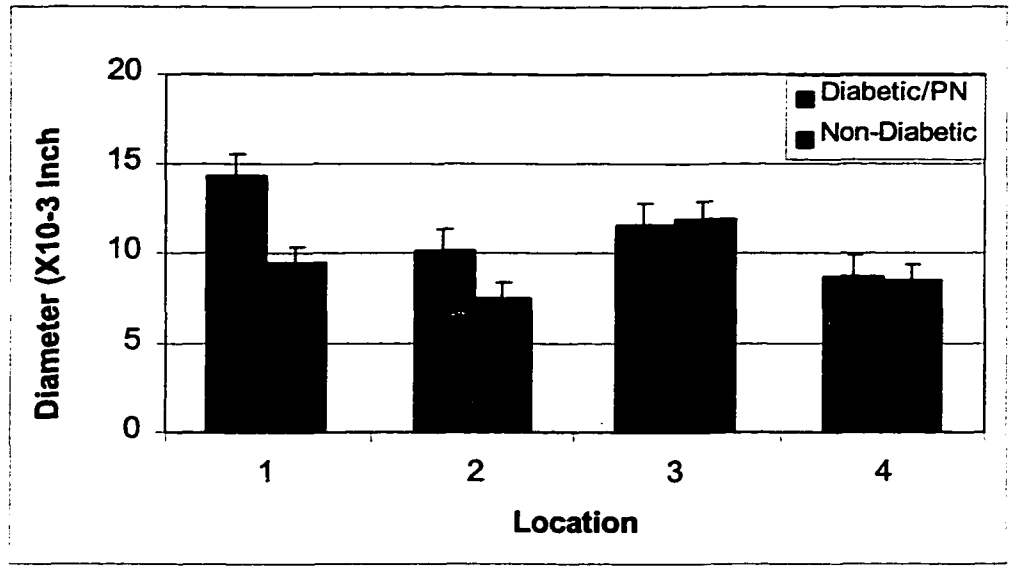


Figure 15. Semms–Weinstein monofilament threshold (diameter) in the elderly population, where location 1, is the left base metatarsal and 2, the digit IV on the left side. Locations 3 and 4 are corresponding values in the right leg

A repeated measure ANOVA was performed to determine the statistical significance in the monofilament threshold values. Results from the ANOVA test is presented in Table 21.

Table 21. Repeated measures ANOVA table for the threshold level of force required to buckle the monofilament (‡ Indicates significance)

Between	Source	Sum–of–Squares	DOF	Mean–Square	F–Ratio	P
Group	Hypothesis	43.124	1	43.124	1.280	0.280
	Error	404.141	12	33.678		
Legs	Hypothesis	0.001	1	0.001	0.000	0.993
	Error	111.048	12	9.254		
Location	Hypothesis	155.865	1	155.865	7.906	0.016‡
	Error	236.564	12	19.714		

In all cases (diabetic vs. non–diabetic and left vs. right), the threshold values of the base digit IV were significantly lower from the values for the base of the metatarsal. Note also that repeated measures ANOVA showed no

differences between the right and left leg but did show a significant difference ($p < 0.05$) across all subjects with the testing location on the foot. As expected, across all subjects the thresholds obtained from the base of digit IV were significantly lower than those obtained from the base of the metatarsal.

The subjects with adult–onset diabetes and/or neuropathy did not differ in tactile sensory perception when compared to the non–diabetic cohorts based on this test. This refutes hypothesis #6.

4.6 Cognitive Evaluation

The mean score on the cognitive evaluation test was 28.9. There was no difference in the cognition score of the diabetic and the non–diabetic. None of the subjects had any cognitive impairment (i.e., a score below 21). This implies that subjects clearly understood the communication or cues given to them. This also means that the subjects did not have a short–term memory loss, which could affect their ability to remember and respond to the stimuli at the appropriate interval in 2AFC.

Cognitive score for the elderly population from MMSE is presented in Table 22. The elderly group with adult–onset diabetes and/or peripheral neuropathy had a mean score of 29.4, which was not significantly different from that of the non–diabetic group who had a mean score of 28.4. The reason for the lower score in the non–diabetic group was due to one subject who had a low score of 24. Figure 16 shows the cognitive test evaluation distribution. The cognition test value alone cannot be used to discriminate between the two groups. This proves hypothesis #7.

Table 22. Cognitive score in elderly population from MMSE

Group	Subject ID	Score
Diabetic/PN	F60DA	29
	M74DD	29
	M54DK	29
	F58DL	30
	M50DM	30
	M62DO	30
	M53DP	29
Non–Diabetic	M63DB	30
	M64DC	24
	M53DE	29
	F64DF	29
	M58DH	30
	F52DJ	29
	M63DN	28

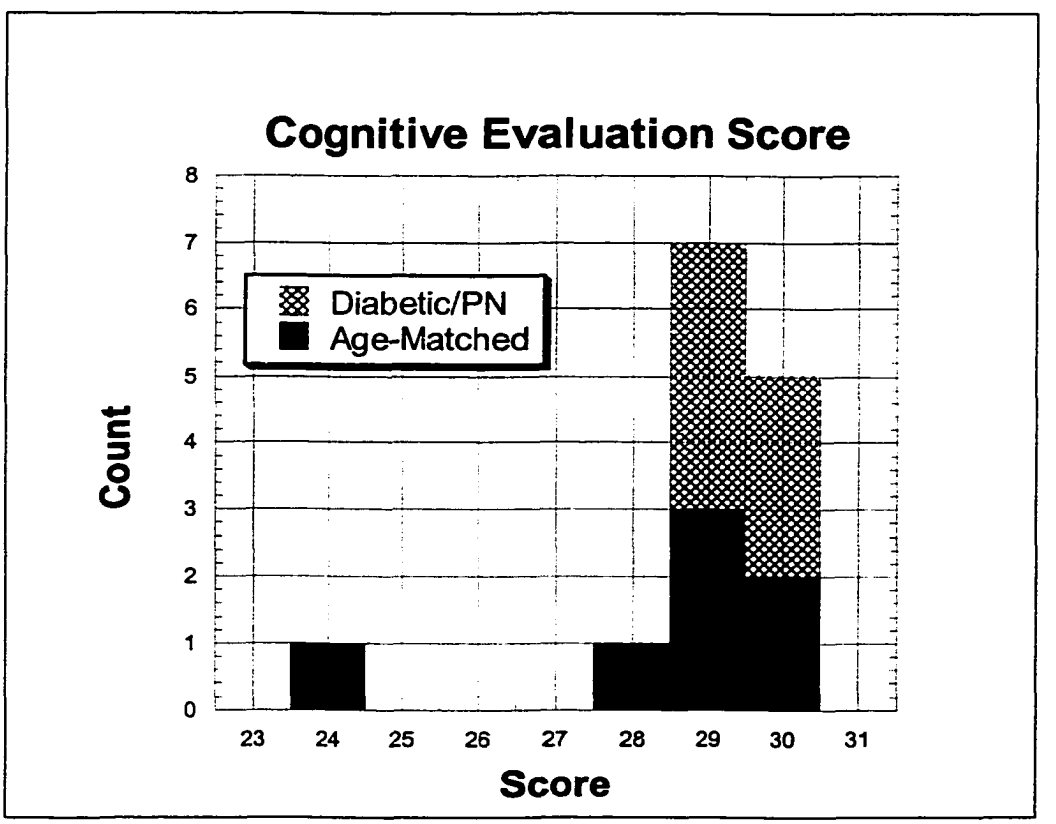


Figure 16. Cognitive evaluation results in the elderly population from the "Mini–Mental Status" questionnaire

4.7 Reaction Time to Stimuli

The response or reaction time to platform movement, touch, and auditory stimuli were identified. All these measures involve the function of cranial nerve VIII besides the sensorimotor system. A decline in the reaction time would indicate the existence of central neuropathy. Existence of peripheral neuropathy was verified by the nerve conduction study on the peroneal and tibial nerve bilaterally. The reaction time for supra–threshold perturbation, touch and auditory stimuli in the three groups of subjects is presented in Table 23. Figures 17 to 20 show the mean reaction time in each of the groups for supra–threshold perturbation, touch, and auditory stimuli.

Table 23. Reaction time to stimuli in the three groups of subjects

Group	Subject ID	Tone	Touch	Supra–Thresh
Diabetic/PN	F60DA	0.371	0.482	0.501
	M74DD	0.479	0.716	1.075
	M54DK	0.283	0.270	1.212
	F58DL	0.673	0.714	0.551
	M50DM	0.353	0.287	0.494
	M62DO	0.401	0.685	0.502
	M53DP	0.297	0.405	0.792
Non–Diabetic	M63DB	0.229	0.216	0.463
	M64DC	0.278	0.415	0.573
	M53DE	0.213	0.509	0.614
	F64DF	0.346	0.470	0.431
	M58DH	0.251	0.404	1.102
	F52DJ	0.295	0.280	0.183
	M63DN	0.335	0.306	1.506
Young Adults	M19BH	0.165	0.241	0.318
	M20BI	0.304	0.312	0.180
	M22BB	0.169	0.277	0.243
	M23BE	0.214	0.318	0.150
	M23BL	0.489	0.598	0.442
	M23BP	0.290	0.336	0.216
	M24BJ	0.238	0.285	0.104
	M27BN	0.282	0.256	0.091
	M29BS	0.307	0.263	0.176
	M31BR	0.243	0.226	0.278
	M32BQ	0.309	0.346	0.274

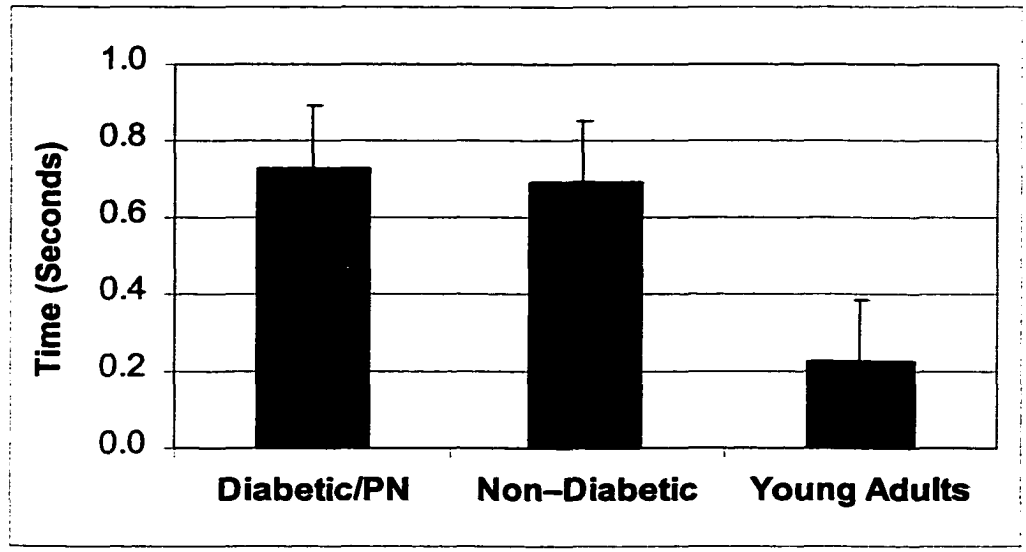


Figure 17. Reaction time to platform perturbation at supra–threshold (20 mm displacement at 100 mm/s^2) level

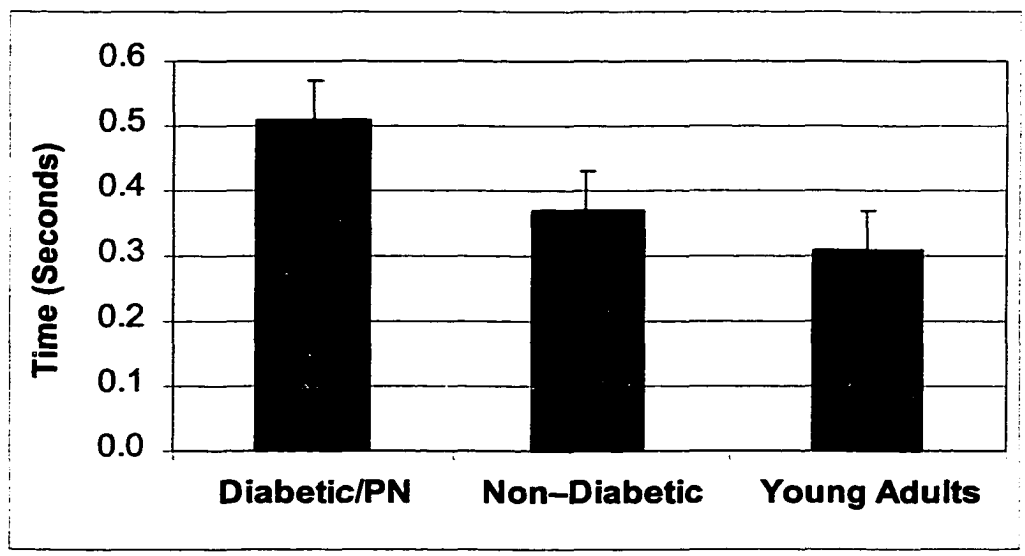


Figure 18. Reaction time to touch on foot sole in the three groups

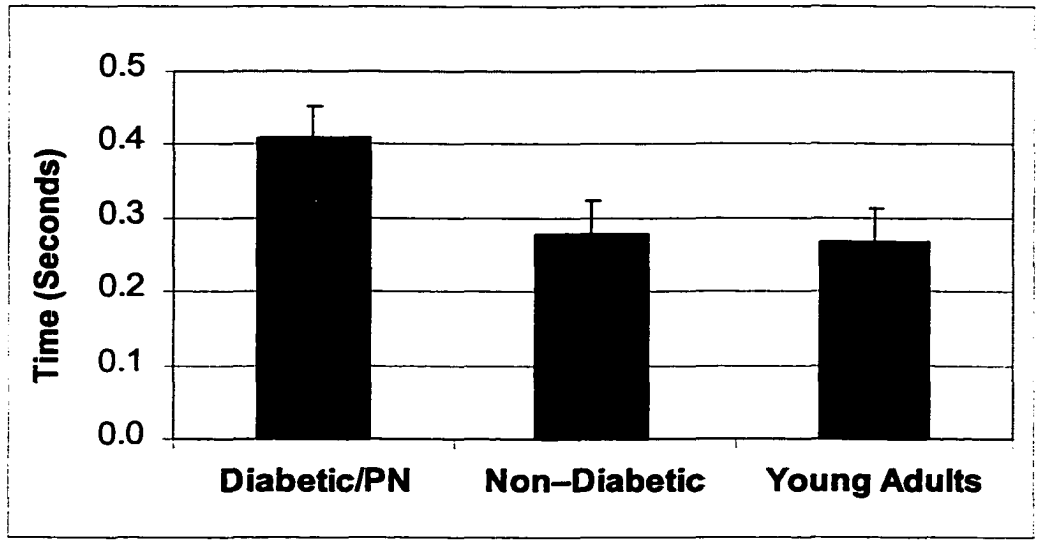


Figure 19. Reaction time to auditory stimuli in the three groups

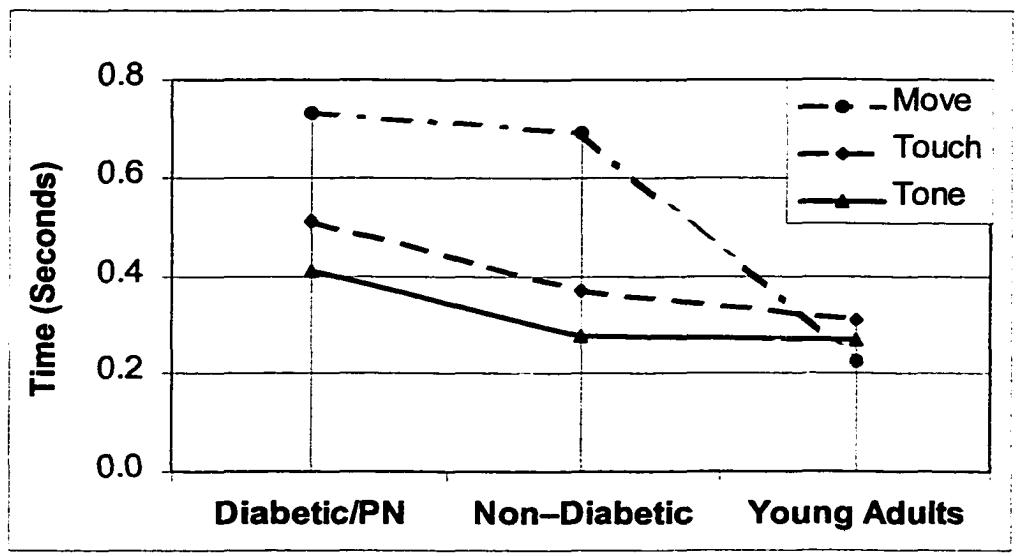


Figure 20. Reaction time by group for platform perturbation or movement at supra–threshold (20 mm displacement at 100 mm/s^2) level, touch and tone

A repeated measures ANOVA was performed to determine the statistical significance in the reaction time. During supra–threshold level perturbation, the reaction time for the elderly subjects was almost the same and was significantly

higher ($p < 0.05$) when compared to young adults. However, the reaction time for tone and touch was almost equal for the non-diabetic and young adult subjects and was significantly lower ($p < 0.05$) than the diabetic/PN subjects. This verifies hypothesis #5 as true.

4.8 Quiet Standing Sway

The RMS and range of quiet standing sway collected before the 1, 4, and 16 mm threshold tests in the elderly and young adults are presented in Tables 24 and 25 respectively. The mean RMS and range of sway is presented in Table 26. These values are comparable to what has been published in the literature [Prieto, et al. 1996, Sparto, et al., 1998]. Young adults and non–diabetic elderly had a similar sway pattern. A repeated measures ANOVA was performed to determine the statistical difference in the sway pattern between the groups and the results are presented in Table 27.

Table 24. Quiet standing sway in the elderly subjects

Group	Subject ID	Direction	RMS Sway (mm)			Sway Range (mm)		
			1mm	4mm	16mm	1mm	4mm	16mm
Diabetic/PN	F60DA	AP	5.33	7.08	9.30	23.49	31.56	37.44
		ML	1.28	2.20	1.25	6.01	10.00	7.30
	M74DD	AP	10.72	7.60	6.22	51.20	36.48	27.87
		ML	3.47	3.25	1.85	18.54	23.98	12.46
	M54DK	AP	4.79	4.29	3.89	25.21	20.75	22.83
		ML	1.42	1.94	2.02	6.47	8.16	10.58
	F58DL	AP	4.39	3.50	4.02	25.59	19.26	20.32
		ML	3.00	2.05	3.72	14.50	9.67	18.22
	M50DM	AP	3.86	4.79	4.56	22.45	28.51	20.68
		ML	1.59	0.93	1.19	7.62	5.39	5.17
	M62DO	AP	9.01	11.82	12.51	40.73	55.42	55.14
		ML	4.56	4.39	11.21	17.35	18.28	39.49
	M53DP	AP	3.84	5.79	6.05	22.94	29.93	32.39
		ML	3.91	3.63	2.88	16.01	13.57	19.46
Non–Diabetic	M63DB	AP	4.17	2.69	3.38	22.39	17.43	17.45
		ML	1.93	1.32	2.15	8.31	7.17	10.85
	M64DC	AP	1.62	2.72	2.32	7.65	10.82	14.23
		ML	0.59	0.78	0.66	2.92	4.02	3.16
	M53DE	AP	6.01	3.72	6.32	29.97	15.11	29.39
		ML	3.55	1.60	1.92	27.26	13.14	8.71
	F64DF	AP	2.55	2.89	4.14	10.98	11.67	17.33
		ML	2.01	0.64	1.13	8.87	3.65	5.73
	M58DH	AP	3.85	7.53	3.77	17.13	39.04	16.97
		ML	0.82	1.98	1.21	3.62	16.50	4.97
	F52DJ	AP	4.69	4.25	3.35	20.01	15.90	16.19
		ML	1.03	1.05	1.79	5.36	4.83	9.39
	M63DN	AP	8.10	6.21	6.31	36.89	30.61	30.64
		ML	1.74	1.51	1.53	9.73	8.43	7.05

Table 25. Quiet standing sway in the young adult population

Subject ID	Direction	RMS Sway (mm)			Sway Range (mm)		
		1mm	4mm	16mm	1mm	4mm	16mm
M19BH	AP	7.81	3.80	4.87	29.89	18.04	25.96
	ML	0.86	1.22	1.47	4.43	6.02	6.28
M20BI	AP	2.78	4.87	3.36	16.69	18.98	17.95
	ML	0.98	0.47	0.68	4.52	2.53	4.00
M22BB	AP	4.22	2.97	4.09	22.57	14.54	20.17
	ML	1.12	1.08	1.59	6.50	5.02	10.68
M23BE	AP	2.57	13.07	19.31	12.40	39.02	74.80
	ML	0.50	3.47	3.52	2.47	19.71	16.64
M23BL	AP	3.62	11.56	3.49	25.68	43.02	17.25
	ML	1.30	2.92	1.33	7.22	15.11	6.49
M23BP	AP	6.93	6.05	4.98	29.08	23.06	29.66
	ML	1.21	1.25	1.54	5.52	5.64	7.84
M24BJ	AP	3.68	3.57	2.72	20.35	18.09	14.15
	ML	1.91	0.40	0.64	15.13	2.62	3.25
M27BN	AP	3.85	5.76	3.70	16.36	32.54	22.57
	ML	1.07	1.87	2.86	5.95	14.12	26.47
M29BS	AP	11.91	2.66	1.96	54.82	10.48	10.88
	ML	3.15	0.89	2.10	21.42	6.01	14.50
M31BR	AP	3.34	6.98	4.13	16.31	39.82	23.87
	ML	0.66	2.99	1.39	3.49	23.48	8.54
M32BQ	AP	2.09	2.25	2.70	9.38	9.35	15.12
	ML	0.64	0.84	0.35	3.50	4.16	2.03

Table 26. Eyes–closed quiet standing sway († indicates significant group difference, ‡ indicates a trend)

Group	RMS (mm)		RANGE (mm)	
	AP	ML†	AP‡	ML‡
Diabetic/PN	6.4	2.9	30.9	13.7
Non–Diabetic	4.3	1.5	20.4	8.3
Young Adults	5.2	1.5	24.0	8.8

Table 27. ANOVA table for quiet standing sway in elderly. "Tot" is the vector sum of the AP and ML values († indicates significance and ‡ indicates a trend)

Source	Sum–of–Squares	DOF	Mean–Square	F–Ratio	P
AP RMS	14.630	2	7.315	1.381	0.272
Error	116.548	22	5.298		
ML RMS	10.957	2	5.479	4.673	0.02†
Error	25.791	22	1.172		
Tot RMS	22.791	2	44.396	1.893	0.174
Error	132.224	22	6.010		
AP Range	409.124	2	204.562	2.787	0.083‡
Error	1614.703	22	73.396		
ML Range	133.185	2	66.593	2.642	0.094‡
Error	554.494	22	25.204		
Tot Range	533.355	2	266.678	3.038	0.068‡
Error	1931.267	22	87.785		

Quiet standing RMS sways in the medial–lateral direction alone was significantly different between the three groups. The diabetic population had a significantly higher ($p < 0.05$) medial–lateral RMS sways when compared to the non–diabetic and young adults. There was also a trend of higher range of sway observed in the diabetic/PN population. This verifies hypotheses #4.

CHAPTER 5

DISCUSSION

5.1 Overview

Visual, vestibular, somatic (touch and proprioceptive), and kinesthetic sensory inputs are constantly being provided to the postural and balance control systems that detect potential fall conditions. Activating or modulating the output drive to selected limb and trunk muscles to provide appropriate compensation achieves the ultimate control. The fidelity of these inputs, the robustness of the outputs, the appropriateness of the compensation, and the speed of signaling along a pathways [trigger –> input –> compensation –> output –> (re)action] are essential if these systems are to help us remain upright during quiet standing or to detect and prevent an incipient slip or fall during movement by initiating fall–preventing maneuvers like stepping.

In this study the acceleration threshold while standing was identified for the diabetic and non–diabetic population. Acceleration was used as the primary measure for sensitivity to motion since both vestibular, somatosensory, and neuromuscular systems are able to sense acceleration effects during standing, walking, falls, and near–fall perturbations. Benson, et al. (1986) points out that most of the previous attempts to understand displacement, velocity, and

acceleration thresholds in the past are suspect owing to the insufficient description of the experimentation including how the measurements were made, the nature and criteria governing subject's responses, and the means of expressing these responses as threshold values.

There is a general bias of the conventional testing devices towards large displacements. Commercially available perturbation platforms have a problem of unintentional vibration or jerk due to the worm–gear drive mechanism (Neurocom®). The air bearings used by SLIP–FALLS gives it a smooth ride and avoids the vibration or jerk that could cue the subjects of the perturbation [Robinson, et al., 1998].

Transient perturbations can lead to anticipatory adaptations that would not occur in actual falls. For example, higher apprehension may cause subjects to stiffen up through co–contraction of antagonist muscle groups, and repetitive testing required for accurate estimation of transient response can lead to adaptive changes in postural synergies and/or initial posture like bending of knee observed in this study.

A horizontal acceleration of the platform on which the subject stands creates a relative acceleration between the feet and the upper body. However, because the balance test is performed during two–footed stance, the simulation of the kinematics of gait perturbations is not ideal. Although large perturbations during gait may produce complex bilateral responses, smaller gait perturbations have been found to produce balancing responses similar in organization to the responses to perturbations applied during stance [Maki, et al., 1987]. Therefore,

the balance test results may be indicative of the responses to small gait perturbations. More complex responses are required once base of support saturation occurs in stance.

The movements and forces sensed by the muscle, tendon, joint, and plantar mechanoreceptors are also directly linked to the sway motion, with the exception of the anterior–posterior shearing forces on the feet. These forces transmit the platform acceleration to the body and hence do not reflect the influence of sway alone; however, little is known about the role that sensory feedback of shear force might play in postural control [Maki, et al., 1987].

5.2 Threshold

Threshold values in diabetic/PN and non–diabetic elderly, and young adults were significantly different from each other ($p < 0.0001$). Elderly in general, had a higher acceleration detection threshold when compared to the young adults (see Figures 8 to 10, Chapter 4). Diabetic/PN elderly had a significantly higher threshold than their neurologically intact, non–diabetic cohorts. Increased threshold *per se* is, at this time, not a predictor of the risk of a slip or fall. The elevated threshold in the elderly and the diabetic/PN might well prove to be a quantitative measure for their higher incidence of falls.

The percentage of detects within a subject significantly differed ($p<0.0001$) for the different perturbations conditions. The percentage of detects was maximum for the 1 mm perturbation and least for the 16 mm perturbation. This implies that the muscle spindles, which are sensitive to rapid stretch, could detect the small perturbations at higher acceleration with a high fidelity. The vestibular

system might play the main role in detecting a longer perturbation at a lower acceleration. The decreased percentage of detects during a long perturbation alludes to the point that the vestibular inputs play a reduced or no role.

The peak acceleration detection threshold for a seated posture in young adults as detected by Benson, et al., (1986) was 62.5 mm/s^2 in the X (AP) direction. The stimulus in that study was applied for a fixed duration of three seconds. Hence not knowing the displacement, it would be futile to make a one to one comparison. Also during a seated posture, more surface area of the skin is in contact with a relatively stationary surface. This increases the tactile activation of the skin, and hence, might explain the lower threshold than in standing.

Care should be taken in understanding that the above–mentioned study was performed to identify the detection threshold for linear acceleration to investigate changes in threshold following space flight and not for fall prediction. Hence the data on the linear acceleration threshold presented in this dissertation might be a more reliable indicator of balance control.

During the threshold detection, PEST trials and the PEST determined peri–threshold trials, subjects were informed that the perturbation would be forward. Subjects were also given 10 practice trials before the threshold detection trials. As the subjects had a prior knowledge of the kind of perturbation, they did not have any confusion about the direction of perturbation.

However, during the fixed–level supra–threshold detection runs, the perturbation was alternated between the forward and backward direction.

Subjects could clearly identify the perturbation but were not certain about the direction of perturbation. Few reported perceiving the alternating direction of perturbation. This lack of sensing the direction of perturbation suggests that the physiological mechanism to detect the direction of acceleration could be different from the mechanism to detect acceleration. It can also be hypothesized that direction perception has a higher threshold than magnitude perception. This issue should be further investigated to identify the difference in the threshold for perceiving an acceleration perturbation and detecting its direction. It would be of interest that during the threshold level runs for seated subjects, many subjects were confused with the direction of perturbation and reported a bi–directional perturbation [Benson, et al., 1986].

The vestibular otoliths could be the principal sense organ responsible for detecting the linear acceleration of the head in an absolute reference frame. Horizontal perturbation creates incongruence between the otoliths and the other sensory modalities. Other researchers have questioned the otoliths' contribution to relatively rapid balancing responses because of their slow dynamic response and their inability to distinguish between gravitational and inertial stimuli [Nashner, et al., 1990]. From preliminary analyses of head acceleration data collected by SLIP–FALLS, contribution of head acceleration in detecting threshold level perturbations could not be verified (unpublished research).

Women in the young adult group (tested in Highland VAMC, Pittsburgh) were unable to complete the study. This led us to speculate that there was a sex difference in the ability to undergo standing, eyes–closed, balance test.

However, all the elderly women who participated in the study completed it with ease. On a general observation, elderly women were comfortable throughout and after the test. The difference in daily activity between the participating young and elderly women was not recorded; so no distinction can be made in anthropological terms between the two groups of women. However, it can be safely concluded that there are no obvious sex–based inabilities to participate in a visually impaired balance test.

During the five fixed–level threshold or the peri–threshold trials at the difficulty level resulting from the PEST tests, the mean detection was 70%. While performing the five fixed–level threshold trials at 125%, the threshold level and the mean detection were at 80%. This probability of detection is in agreement with the finding of Taylor, et al. (1983). They performed tests with PEST runs targeted at a probability of 0.80 (staircase 79) and immediately followed it by fixed–level trials at the difficulty level resulting from the PEST run. They found that the fixed–level runs yielded a probability of about 0.75.

PEST permits the subject to keep track of what he is trying to detect; whereas, in the fixed–level method, performance is disrupted by memory failure [Taylor, et al., 1983]. This implies that the probability of detection is much higher if a subject detects a preceding move. This trend was observed in this study. However, owing to the limited number of trials at fixed–level threshold, this trend could be verified only anecdotally.

No group or leg difference for threshold detection by Semms–Weinstein monofilament was found. Birke, et al. (1986) had determined that the threshold

for plantar sensory detection in ulcerated foot was 10 grams. Diabetic and non–diabetic elderly had a lower threshold for detection than this value. This is in agreement with the general consensus that contribution of somatosensory receptors to the perception of threshold level whole–body linear acceleration cannot be absolutely excluded.

It was also observed that the location of testing had a significant difference in threshold. Metatarsal skin (i.e., the sole) had a significantly higher ($p < 0.05$) threshold than on digit IV. This increased threshold between the locations of test is in agreement with the common understanding that the two–point discrimination test has a higher resolution at the distal periphery [Bear, et al., 1996].

5.2.1 Balasubramanian–Robinson Model (BRM)

From the log–log plot in Figure 9 (Chapter 4), the line connecting between the thresholds values for each displacement appears straight. This implies that there is a negative power law relationship between the perturbation distance and the detection threshold. Power law implies that the values of threshold and displacement have relationship like

$$\text{Threshold} = A * (\text{Displacement})^{B}$$

Where A is the intercept, and B is the slope of the regression line.

The above equation can be rewritten as,

$$\text{Log (Threshold)} = \text{Log (A)} + B * \text{Log (Displacement)}$$

These equations were presented in previous chapter as equations 4.1, 4.2 and 4.3. Rewriting those relationships in the traditional power law form, and

slightly adjusting the exponents the following models for peak acceleration threshold (Ta) can be constructed:

$$Ta = 149 * (Disp)^{-1/3}, \text{ For Diabetic/PN} \quad (5.1)$$

$$Ta = 91 * (Disp)^{-2/3}, \text{ For age–matched neurologically intact} \quad (5.2)$$

$$Ta = 55 * (Disp)^{-1/2}, \text{ for young adults} \quad (5.3)$$

Using the above relationships, the threshold values can be estimated for perturbations lengths that were not tested. Table 28 lists the expected threshold values for perturbations ranging from 0.125 to 27 mm, while Figure 21 shows a plot of these expected values.

Table 28. Expected threshold values based on the BRM model

Condition	Model	Displacement (mm)						
		0.125	0.25	1	4	8	16	27
Diabetic/NP	$Ta = 149 * (Disp)^{-1/3}$	298	238	149	93	75	58	50
Non–Diabetic	$Ta = 91 * (Disp)^{-2/3}$	364	234	91	35	23	14	11
Young–Adults	$Ta = 55 * (Disp)^{-1/2}$	156	110	55	28	19	13	10

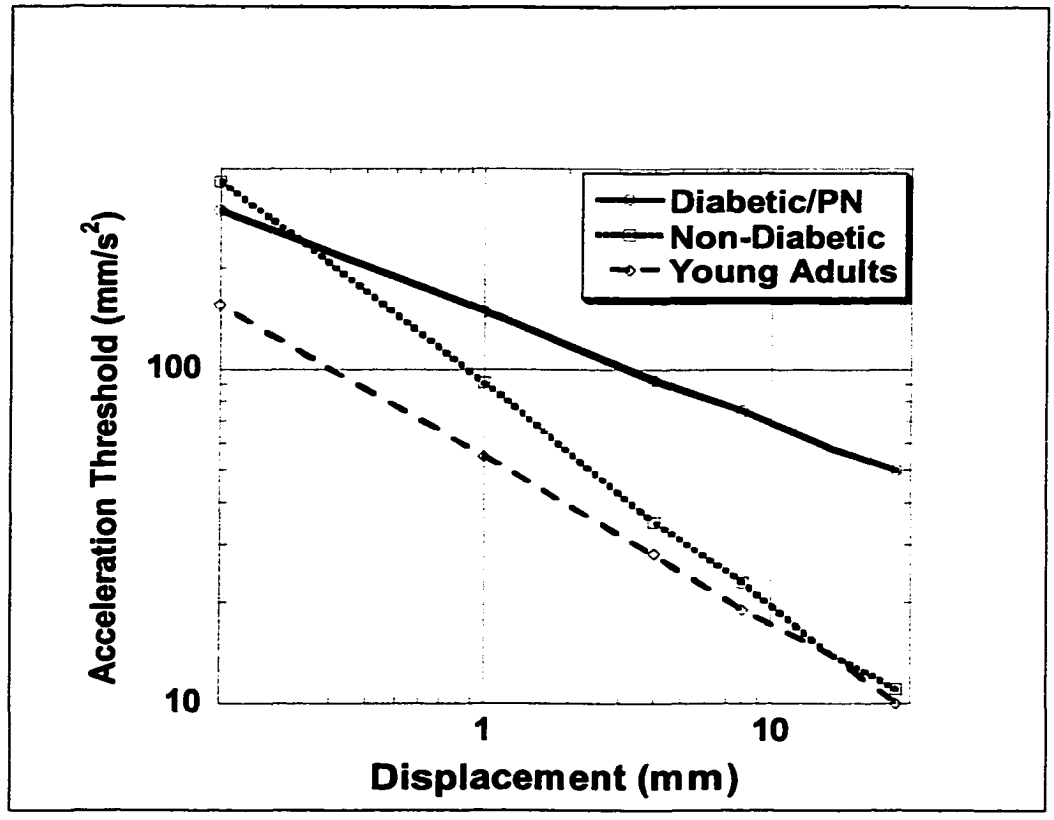


Figure 21. Expected acceleration threshold based on the BRM model

On observation, it is apparent that the diabetic/PN group has an extremely high threshold when compared to the neurologically intact or the young adults. This puts them at a disadvantage over the other group. This could also be a reason for the higher incidence of falls observed among the diabetic population during icy days.

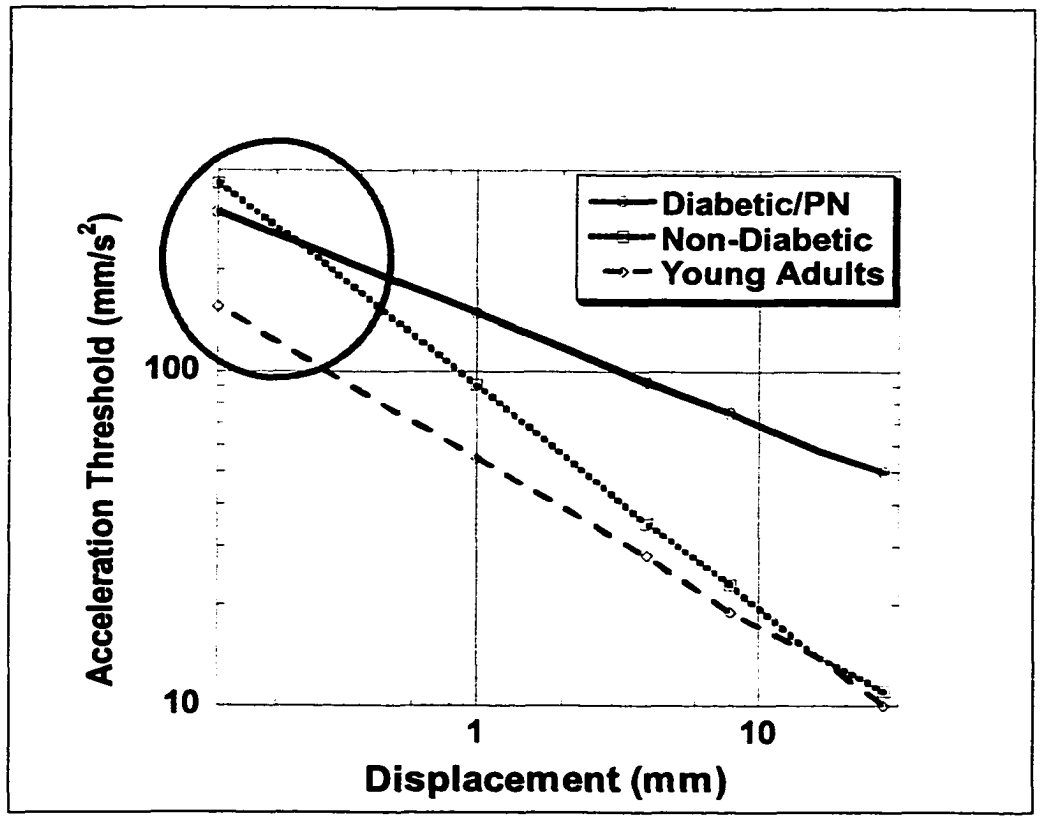


Figure 22. Expected threshold for small perturbations based on the BRM model.

The ellipse in Figure 22 shows the extreme condition of the model when the perturbation is very small. This condition is similar to what would be experienced when a person steps on a ball or is given a small swift push. The acceleration threshold for the elderly is much higher than the acceleration threshold for the young adult population. One could note that the acceleration threshold difference between the diabetic and non–diabetic population for a very small perturbation is insignificant. In fact, it appears that the diabetic population has a lower threshold than the non–diabetic population. This is suggestive of a higher risk for falling in the elderly at these acceleration levels that is not particularly limited to just the diabetic population.

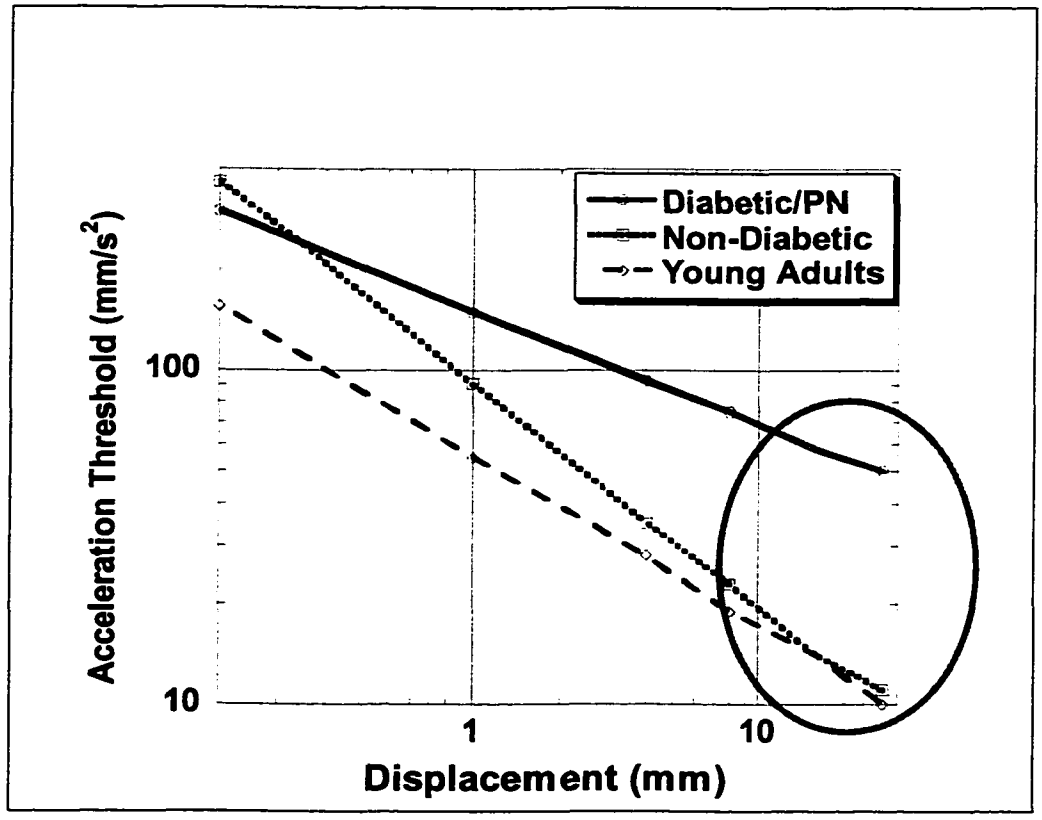


Figure 23. Expected threshold for large perturbations based on the BRM model.

The ellipse in Figure 23 shows the extreme condition of the model when the perturbation is long. This condition is similar to what would be experienced when a person steps on a patch of black ice or banana peel. One is expected to glide for a large distance (> 10 mm) under these circumstances. The acceleration threshold for the diabetic/PN elderly is much higher than the acceleration threshold for the non–diabetic and young adults. One could note that the acceleration threshold for the non–diabetic elderly and young adult populations are almost equal. These large displacement perturbations are the ones that are encountered in activities of daily life. It can be concluded from the model that the diabetic elderly are at a higher risk for falling when compared to

non–diabetic elderly and young adults owing to their high acceleration detection threshold, which is almost four times higher.

This model is based on a regression from the tested range of 1 to 16 mm. The actual threshold for perturbations outside of this range is from extrapolation. Caution should be exercised while using this model for longer or shorter perturbation conditions, which were not in the tested range.

To find the relationship between the threshold levels for each group the equations can be rewritten as:

$$(149/T_D)^3 = (91/T_{NI})^{1.5} = (55/T_{ya})^2$$

Hence,

$$T_D = 10 * (T_{ya})^{2/3} \quad (5.4)$$

$$T_{NI} = 0.5 * (T_{ya})^{4/3} \quad (5.5)$$

Where T_D is the threshold in diabetic/PN, T_{NI} is the threshold in non–diabetic, and T_{ya} is the threshold in young adult subjects.

Using the above relationship, the threshold values can be estimated for perturbations that were not tested. Table 29 shows the expected threshold values based on the above equations. Figure 24 graphs the expected values from Table 29.

Table 29. Expected acceleration threshold values based on the BRM model

Condition	Model	Acceleration Threshold (mm/s^2)						
Diabetic/PN	$T_a = 10 * (T_{ya})^{2/3}$	270	243	201	170	135	97	46
Non–Diabetic	$T_a = 0{,}5 * (T_{ya})^{4/3}$	363	295	201	144	92	47	11
Young–Adults	T_{ya}	140	120	90	70	50	30	10

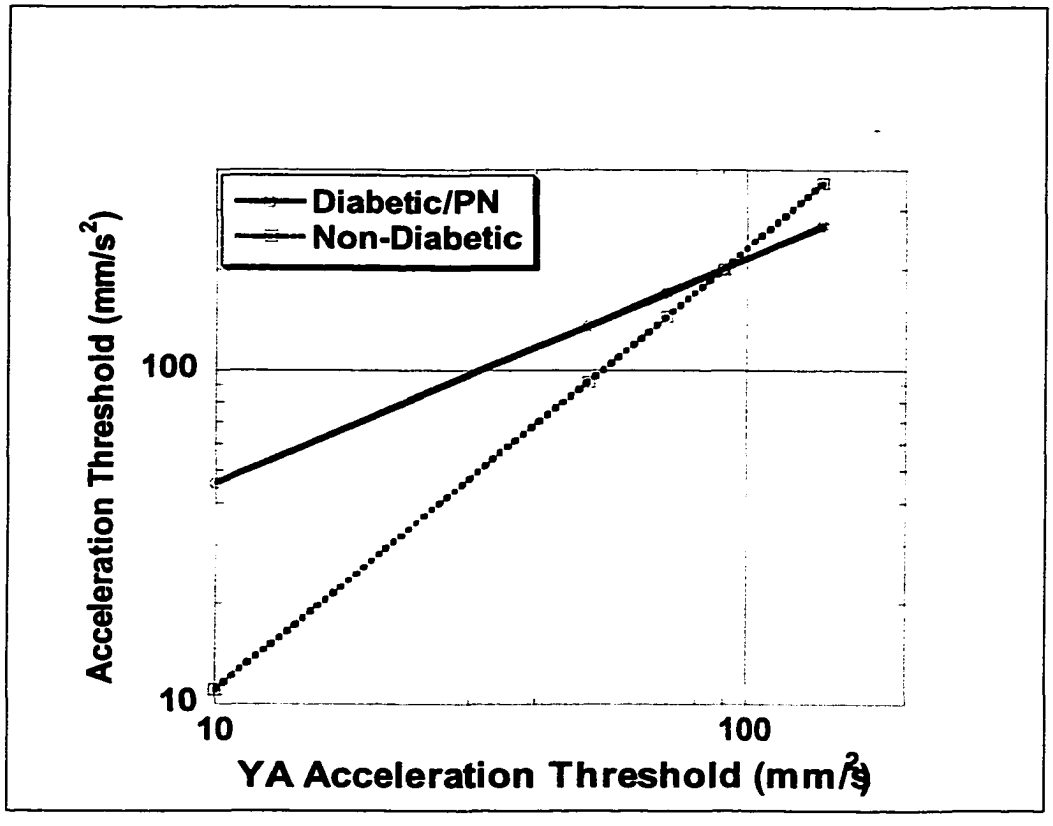


Figure 24. Expected threshold based on the BRM model.

This is a complimentary relationship between the thresholds for the different age groups. This model describes that for low acceleration threshold values, the non–diabetic and young adults have a similar trend. However, at higher acceleration values, the non–diabetics behave like the diabetic group.

It can be concluded from the above model that aging in general affects the mechanisms of the body involved in detecting small displacements of the body. However, the body sensors that are used for detecting large displacements, which occur in the activities of daily life, are affected in the diabetic population. Further research to isolate the sensory cues utilized in identifying such perturbations are to be studied and appropriate relief could be provided to the diabetic to reduce their risk for falling.

5.3 Reaction Time

Reaction time for tone and touch was significantly higher ($p < 0.05$) in the diabetic/PN elderly. There was, however, no significant difference in the reaction time between the non–diabetic elderly and the young adults. This implies that diabetes affects the auditory and propriceptory pathways. This effect appears to be in excess of the normal aging process in elderly. An increased reaction time for foot touch sense affects the ability of the person to recognize small variations, and could directly result from the sensory peripheral neuropathy seen in the diabetic/PN population.

The reaction time for the tone was around 400 milliseconds for the diabetic elderly and 280 milliseconds for the young adults and non–diabetic elderly. Auditory stimuli evoke muscle discharge at a minimum latency of 100 milliseconds [Marsden, et al., 1978]. It would take a few more milliseconds after the muscle discharge to actually move the digits to express the reaction. An auditory command–triggered muscle movement in the form of supination of forearm takes in excess of 250 milliseconds [Evarts and Vaughn, 1978]. This

implies that the reaction times found in this study are acceptable. Hence, it can be inferred that aging *per se* does not seem to have an impact on the auditory reaction time. However, there is a significant increase in the auditory reaction time of the diabetic elderly population. It should be noted that all subjects were presumed to have a "normal" hearing ability; however, no tests were performed to evaluate their hearing acuity.

Biessels, et al., (1994) developed an animal model of diabetes and demonstrated impairments of spatial learning in association with distinct changes in hippocampal synaptic plasticity. They suggested that there are neurophysiological and structural changes in the brain of a diabetic subject. The decline in the reaction time for tone and touch in the diabetic population could be a result of these neurophysiological changes in the brain.

During supra threshold trials, when a constant stimulus is provided for the three groups, there is a significant drop in the reaction time for the young adults when compared to the elderly. This implies that aging in general affects the pathway that is being utilized in the identification of horizontal accelerations in the body. A probable pathway could be the proprioception (or other sensory input) –> spinal chord –> vestibulospinal tract –> motor cortex (Area 4/6 for motor planning) –> descending tract –> reaction (pressing of the door bell alarm) [Bear, et al., 1996, Diamond, et al., 1985].

Lord, et al. (1991), and Ring, et al. (1988) argues that the peripheral sensation is the most important sensory system in the maintenance of static postural stability. In this study, there was a significant decrease ($p < 0.05$) in the

sensory nerve conduction in the diabetic elderly population when compared to the non–diabetic elderly population. This implies that sensory nerve inputs would take a longer time to reach the spinal cord in the case of the diabetic elderly. It was also found that there was no significant difference in the nerve conduction in motor nerves (peroneal and tibial) between the two groups of elderly. There was also no significant difference in the nerve conduction between the left and right leg in the subjects tested.

The reaction time to supra–threshold was similar in the two groups of elderly. Therefore, it can be inferred that the mechanisms involved in detecting a supra–threshold perturbation is affected by some age–related problems in the pathway above the spinal cord involving the VIII cranial nerve. A corollary to it is that diabetes mellitus does not adversely damage the pathway involved detecting supra–threshold perturbation.

Thickening of capillary basement membranes, the hallmark of diabetic microangiopathy, has been demonstrated in the brain of diabetic humans and animals. Diabetes also has been implicated in the damage of clinically relevant end–organs in the CNS as a result of both acute and chronic metabolic and vascular disturbances [Stewart, et al., 1999].

It is of interest to note that the perceptual discrimination time is around 50 milliseconds, and a response selection time takes about 150 milliseconds [Gregory (ed.), 1987]. Hence, any reaction time that involves perception and discrimination should have a reaction time greater than 200 milliseconds. The young adults population had a reaction time of around 270 milliseconds for the

supra–threshold trials. This is over the minimum time and is in agreement with the expected values.

5.4 Posture

Individuals with diabetes have a higher sway during quiet standing than the non–diabetic elderly. Sway has been reported to increase with alterations to visual and peripheral sensation, and especially when both are altered concurrently (Lord, et al., 1991, Ring, et al., 1988). In this study, the sway was determined during quiet standing without any perturbations to the blindfolded subject.

Many studies have quantified the quiet standing metrics for elderly. Prieto, et al. (1996) measured significantly higher AP RMS and AP/ML range of sway in elderly. Baloh, et al. (1994) found significantly higher sway velocity in older subjects. Bergin, et al. (1995) found that sway and vibration perception were significantly increased in the patients with neuropathy.

The medial–lateral RMS sway was the only significantly different ($p<0.05$) sway between the diabetic/PN and non–diabetic elderly. It was also found that the increased sway in the diabetic elderly is associated with a higher detection threshold for horizontal perturbation. On performing a study of quiet standing sway on elderly who were prone to fall, Maki, et al., (1994) argues that the lateral spontaneous–sway amplitude could be the single best predictor of falling risk in elderly. Therefore, it can be concluded that the increased threshold and medial–lateral sway together increase the risk of fall in the diabetic elderly.

There were no differences between the quiet standing sway recorded before the 1 mm, 4 mm, and 16 mm threshold detection trials. This repeatability of quiet standing sway indicates that the subject was not fatigued during the testing protocol. This also verifies that the instrumentation of the SLIP–FALLS does not have a drift during a testing process.

The probability of detecting a threshold level perturbation appeared to be higher when the subjects had their knee bent at the start of a perturbation. By bending the knee, a person tends to sway at the ankle–knee–hip level and lower their center of gravity. This observation however, was not quantifiable in the current experimental setup. Further study should utilize optical motion analyses devices to monitor the movement at knee as a strategy for detecting acceleration perturbation.

Tse and Bailey (1991) also made a similar anecdotal observation of the bent knee strategy used by T'ai Chi (a martial art) practicing elderly population. The T'ai Chi practicing elderly also had a significantly better postural control than the non–practitioners.

The probability of detecting anterior horizontal acceleration perturbation in the present study was significantly higher ($p < 0.01$) when the COP was in back of the mean quiet standing COP during the middle of perturbation. There was a trend for higher detection probability for a backward position of COP at the end of perturbation.

The platform perturbation is obtained by a combination of two accelerations (Figure 6, Chapter 3). The first one is a positive acceleration, and

the second one is a deceleration bringing the platform to a stop. Since the perturbation was horizontal, the first positive acceleration tries to push the person in the forward direction, and the second sequence starting at about the mid–point of the perturbation tries to push the person back. At the mid point of perturbation, there is zero acceleration and maximum velocity and jerk.

Assume that a person is leaning back at the start of the perturbation. If the subject is leaning far backward, an anterior acceleration cues the subject to recognize a potential fall condition. The subject tries to recover by correcting the sway and tries to match the direction of the acceleration. As the subject moves forward, they are hit by the deceleration. This might cue the subject to identify positively that there was a perturbation. Hence at the mid–point, if the subject is backward, he or she is getting a secondary cue that increases the probability of detection. This observation cannot be firmly concluded from the current analyses. In the future, using a fuzzy logic controller, the COP location and velocity should be tracked at the start, middle, and end of perturbations. That can be used to identify with a higher confidence the COP based cues to detect anterior horizontal accelerations.

Maki, et al. (1987) proposed a negative feedback postural control system as a strategy to detect the horizontal accelerations. This system proposes a physical necessity of maintaining the inherently unstable skeletal linkage in an upright position, in opposition to destabilizing perturbations. This strategy should be further investigated to understand the COP–based cues for detection.

Remember that postural dyscontrol reflects subclinical pathologies affecting one or more components of the postural control system. Hence, postural control systems can be used as a clinical tool to not only help determine and educate a subject about potential fall, risk but also the onset subclinical pathologies thereby improving the quality of life of the elderly.

5.5 Other Measurements

No significant cognitive score difference between the diabetic elderly and the non–diabetic elderly was observed using the MMSE. However, many researchers have reported that elderly diabetics have shown cognitive performance deficits and increased risk of dementia in a wide range of neuropsychological tests including MMSE [Stewart, et al., 1999]. Knopman, et al. (2001) performed cognitive assessments on 10,963 individuals and found greater decline in the cognitive scores using WAIS on diabetic population. However, the decline identified by them was small and might not be clinically significant to the participants.

Cognitive decline appears to be a long–term effect of diabetes. Subjects in this study had diagnosed diabetes ranging from 2 to 8 years. This probably is a short duration for diagnosis of cognitive decline using a simple MMSE.

Somatic sensory threshold using the monofilament had no association with the cognitive level of the subjects. Lustman, et al. (1992) argued that exclusion of somatic symptoms from diagnostic criteria had little effect on the observed prevalence of major depression in diabetics.

There were no significant differences between the two groups of elders in the various anthropometrical measures except for height. The mean height of the neuropathic and diabetic population (1803.4mm) was significantly ($p < 0.03$) higher that the mean height of the control (1678.2mm). It should also be noted that the population was small, and there were two unusually tall (6'8" and 6'5") subjects in the neuropathic group.

The diabetics were heavier (86.7 $\pm$ 10.5 kg) compared to the non–diabetic (75 $\pm$ 14 kg) population. However, this difference was not significant. None of the participants was unusually obese or thin.

5.6 Conclusion

One should remember that there is a diminished vestibular and somatosensory function and slowing of sensorimotor reflexes accompanying the normal aging process. This by itself places the elderly at a higher risk for falling. In the case of those with diabetes, there is an accelerated decline in the above function, which places them at a higher risk. The ability to predict with confidence the risk of future falling in individuals is a necessity before balance tests find clinical application in screening and targeting of high–risk individuals for preventive intervention.

Using SLIP–FALLS system, it has been statistically verified that the elderly in general have a higher detection threshold for an anterior horizontal acceleration when compared to young adults. Thresholds are significantly higher in the diabetic population when compared to non–diabetic cohorts and young

adults. Hence, it can be concluded that the risk for falling is much higher in the elderly, and diabetics in particular, than the young adults.

It was observed that acceleration detection threshold was high for small perturbations. The acceleration detection threshold had a negative power law relationship with the perturbation distance. The BRM model describing the relationship between acceleration threshold and perturbation distance has been built, and it successfully predicts the acceleration threshold.

Different mechanisms of the body are involved in detecting small and large perturbations. Elderly in general seem to have a decreased fidelity in detecting small perturbations. In case of the diabetic, the sensory input to ascertain large perturbations appears to be affected. For a large perturbation based on the BRM model, non–diabetic and young adults have a much lower threshold compared to the diabetic. This implies that in situations as stepping on top of ice or walking on wet floor, the diabetic would be gliding and yet would not detect the motion. This could partially explain the increased risk of falling in the diabetic population.

Reaction times to touch, tone and supra–threshold perturbation are significantly different between the three groups. Diabetics have a significantly higher response time than the non–diabetic cohorts and young adults. This implies that after detecting a potential fall, the time to initiate fall–breaking maneuvers would be delayed in those with diabetes. This increases the risk of an actual fall and the associated problems with it in the diabetic population.

Peripheral neuropathy was observed in all the diabetic population. The sensory neuropathy was more progressively improved than in the motor nerves. This could be a possible reason for a higher detection threshold and the high incidence of falling in the diabetic population. Higher number of perturbations was detected when the person was backward during the middle or end of an anterior horizontal acceleration perturbation.

One should remember the assumption that group effects seen here represent a population, and that people with decreased function have the same underlying predisposing influences. However, there are different strategies and perceptional weightings used by different individuals. The statistical evidence for the group cannot test how a particular individual will weigh one major sensory input versus another.

5.7 Future Directions

To verify the anecdotal observation that bending the knee reduces the center of gravity and the sway moment arm, future tests should use goniometer or a marker–based motion analyses system. These systems can help identify the knee movement during perturbation and its relation to detection.

The actual threshold for detecting a movement and the direction of movement could be significantly different. Future tests should try to evaluate the threshold difference for detecting a perturbation and the direction of perturbation and its variation in aging.

The elderly in general had a higher threshold for a small perturbation. However, the diabetic population had a significantly higher threshold than the

non–diabetic and young adult population for large perturbations. This probably implies that there is subclinical pathology in the diabetic population, which affects their ability to detect large displacement perturbations. Since large displacement perturbations might be the primary reason for falls, further research is called for to isolate the sensory cues used in identifying large displacement perturbations.

The location of COP alone does not appear to be a good metric for detecting an anterior perturbation. Further studies should identify the effect of rate of change of COP or sway to investigate the postural control strategies. More powerful statistical tools like fuzzy logic controllers should be used to determine the COP based cues in detecting anterior horizontal acceleration.

To evaluate the muscle activity involved in using the hip–strategy, future studies should collect EMG signals from the hamstring and quadriceps group of muscles. It was also observed that time–series modeling in general is not a powerful tool to analyze the EMG activity (unpublished results). One should probably try using a simpler frequency and time domain characteristics to analyze the muscle activity based cue in detecting small perturbation.

While collecting quiet standing data, subjects were blindfolded. In future, eye–open quiet standing measures should be acquired. This would allow the researcher to better understand the effect of visual impairment in standing and compute standardized ratio like the Romberg coefficient.

In general, the diabetic population was seen to have some extent of neuropathy and a significantly higher detection threshold for anterior acceleration perturbation. It would be of interest to know if there are any differences between

the diabetic and non–diabetic peripheral neuropathy populations. This could be used as a substantial evidence to prove the existence of subclinical pathology in diabetes mellitus that affect the body mechanism to detect accelerations.

APPENDIX A

IRB CONSENT FORM

VA Department of Veterans Affairs

VA RESEARCH CONSENT FORM
PROTOCOL # H00-022

Subject Name: _____ **Date:** _____

Title of Study: Threshold Detection of Postural Control in Diabetic Neuropathy and Aging

Principal Investigator: C. J. Robinson, DSc, PE; A. M. Hollister, MD **VAMC:** Shreveport

We are asking you to volunteer to take part in a research study at the Shreveport Veterans Affairs Medical Center (VAMC) and Louisiana State University Medical Center (LSUMC). It is important that you read and understand the information on this form.

DEFINITION OF CONSENT FORM

This Consent Form gives detailed information about the research study which you will be able to discuss with your doctor. It is not meant to frighten or alarm you; it is an effort to make you better informed in order for you to make a decision as to whether or not you wish to participate. This process is known as "informed consent."

PURPOSE OF STUDY AND SELECTION OF SUBJECTS

Slips and falls, and even the fear of falling, can represent a major medical and functional barrier to living independently. A fall is normally prevented by the detection of abnormal motion and by strategies used to correct or compensate for imbalances. Therefore, to react to a potential slip or fall, one must be able to detect motion changes that may lead to slips or falls.

You are invited to participate in a research study related to standing balance and postural control. Researchers at the Overton Brooks VAMC and Louisiana State University Medical Center hope to learn how much the senses of the limbs (touch sense, joint angle sense, muscle tension sense) contribute to stability. Such knowledge may well lead to better evaluation and training methods in order to prevent slips and falls. You were selected as a possible participant in this study because you have had a life event (diabetes) that will help us separate potential differences from the average healthy adult; or because your senses are intact and your responses will be used as a reference. You should be 50 years old or older to participate in this study. Before proceeding further, we need your permission to ask you if you have had certain illnesses or neurological problems which might confound our study results, and hence, make you not a candidate for this particular research study. Your answers will remain confidential. May we ask you some questions about your medical history, and verify them from the information in your medical chart (if available within the VA)?

Yes or No: _____ Initials: _____

SUBJECT'S IDENTIFICATION (I.D. plate of give name - last, first, middle)	Subject's Initials: _____

VA Department of Veterans Affairs

VA RESEARCH CONSENT FORM
PROTOCOL # H00-022

Subject Name: _____ **Date:** _____

Title of Study: Threshold Detection of Postural Control in Diabetic Neuropathy and Aging

Principal Investigator: C. J. Robinson, DSc, PE; A. M. Hollister, MD **VAMC:** Shreveport

QUESTIONS

Persons with severe cardiac or cardiopulmonary involvement, chronic lower back spasms or pain, central neurological deficits, history of non-healing skin ulcers or peripheral vascular occlusive disease, current drug or alcohol dependence, or orthopaedic deformities (such as kyphosis, arthritic changes or amputation) must be excluded from this study. Those with a history of repeated falls must also be excluded. (Any information obtained during this study and identified with you as a subject will remain confidential and will be disclosed only with your permission.)

You do not have now, or have ever had, any of the problems just listed. Yes or No: _____ Initials: ____

If you answered "Yes," thank you for your time and effort in volunteering to participate, but we cannot use you in this particular study. Please fill out the personal information on the last page before you go.
If you answered "No," then you are a likely candidate for our study, which we will now explain to you.

PROCEDURES

If you are an older adult or a person with a peripheral nervous system change you may have had a change in how you sense changes in the standing environment. If you are in good health, have no physical or neurological problems, you will serve in a group that we call "control." A comparison of these groups will allow us to have a better understanding of how the nervous system assists in maintaining postural stability and dynamic balance.

If you decide to participate in this research study you will be asked to answer a brief medical history questionnaire to determine which population group you belong, and a questionnaire that measures your mental status. This may be done over the phone or in the laboratory. All subjects will be evaluated for sensory and motor function, lower limb strength and joint range-of-motion, and any possible lower limb asymmetries. We will also measure how fast the nerves of your lower limb transmit their signals by doing nerve-conduction tests on both legs. This test requires that a small shock be delivered to the surface of the skin at one location, and the resultant nerve activity be measured via small patch electrodes taped to another location. The test will be carried out by a colleague who is trained in this procedure.

The main test will have you standing with bare feet on a platform that will be stationary for approximately 30 seconds then moving forward during randomized time intervals. You will be informed when a possible move may occur and you will be asked to state whether the device is moving. In these tests the plat-form will move your whole body. You will be wearing a blindfold that will restrict your vision and headphone to reduce outside noise, so that you may only receive motion inputs from your sensory system or balance system. For all tests you will be wearing surface muscle activity sensors on your legs. If you go through all tests, we estimate that their completion will take less than four hours. We may stop testing if you become dizzy, or nauseous. You can stop the test at any time that you wish, without reprisal.

Subject's Initials _____

VA Department of Veterans Affairs

VA RESEARCH CONSENT FORM
PROTOCOL # H00-022

Subject Name: _____ **Date:** _____

Title of Study: Threshold Detection of Postural Control in Diabetic Neuropathy and Aging

Principal Investigator: C. J. Robinson, DSc, PE; A. M. Hollister, MD **VAMC:** Shreveport

DISCOMFORTS AND RISKS

All motions of the platform will be near your natural sway change of position. Because of this, you may not always be able to feel the device move. Also because the movements will be so slight, there is very little chance of your falling. During the times when the platform is moving and while your eyes are closed or blindfolded, and you are wearing the headphones to block out external noises, you may feel a slight loss of balance, dizziness or nausea. With your eyes closed or blindfolded and a slight change in the position of the platform, you may experience some fright as you begin to move. You will be spotted by an investigator standing behind you who will correct your position before a potential fall event can occur.

For all tests, all joint motions will be small and fairly slow. However there is a possibility that your ankle or knee joints could be injured in these tests, especially if the joints are already weakened. For this reason if you have a previous joint injury or have been diagnosed with a bone or articular cartilage disease, we ask you tell us now and not participate in this study.

Since we use properly isolated electrical amplifiers, there should be no risk of shock from our measurement of muscle activity. The muscle activity sensors will be held to your skin with a small piece of double-sided tape. The gel that helps conduct your muscle activity the sensors may have a salt base. You may experience some redness from the tape or conduction gel. This is common and the redness should disappear within a few hours.

BENEFITS

You may not personally be helped by taking part in this study, but your participation may lead to knowledge that will help others. We will review your own results with you before you leave, and significant overall findings developed as a result of this study will be provided to you at the conclusion of the study.

OTHER TREATMENT AVAILABLE

Participation in this project will not effect your usual clinical treatment here at the VA. You are aware that you are under no obligation to participate in this study and you may withdraw at any time without prejudice to your medical care or loss of benefits to which you are entitled. Should you choose not to participate, you will still receive the usual medical care and treatment to which you are entitled. You may withdraw participation from the project at any time without prejudice.

Subject's Initials _____

VA Department of Veterans Affairs

VA RESEARCH CONSENT FORM
PROTOCOL # H00-022

Subject Name: _____ **Date:** _____

Title of Study: Threshold Detection of Postural Control in Diabetic Neuropathy and Aging

Principal Investigator: C. J. Robinson, DSc, PE; A. M. Hollister, MD **VAMC:** Shreveport

RESEARCH RESULTS

Information and research results will be used to further the field of posture and balance control and to benefit the evaluation and therapy processes related to posture and balance. Therefore the research results will possibly be used for scholarly papers, presentations, and future grant applications.

Any information obtained during this study and identified with you as a subject will remain confidential and will be disclosed only with your permission.

If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. Your medical records will be maintained according to this medical center's requirements.

By signing this form you are giving permission for us to make records available to the Shreveport VAMC and LSU Medical Center's Institutional Board for Human Research to which information will be released, all of whom must maintain confidentiality.

SPECIAL INFORMATION

You will be paid $25.00 by check for each session in which you participate. A session may last up to 4 hours. Payment will be through the Overton Brooks VAMC in Shreveport, LA.

1. You are not required to take part in this study — your participation is entirely voluntary.
2. You can refuse to participate now or you can withdraw from the study at any time after giving your consent. This will not interfere with your regular medical treatment, if you are a patient.
3. Your decision whether or not to participate in this study will not involve any penalty or loss of rights nor will it prejudice your future relation with the VAMC or LSUMC. If you decide to participate, you are free to discontinue participation at any time without penalty or loss of benefits to which you are entitled.
4. There will be no costs to you for any of the treatment or testing done as part of this research study.
5. Eligibility for medical care is based upon the usual VA eligibility policy and is not guaranteed by participation in a research study.
6. In case of adverse (bad) effects or physical injury resulting from this study, eligible veterans are entitled to medical care and treatment. Compensation may or may not be payable in the event of physical injury arising from this study under applicable federal law. Further information about compensation and medical treatment may be obtained from the medical administration service at this VA medical center. Non-eligible veterans are entitled only to medical emergency care and treatment on a humanitarian basis.
7. If you have questions about your rights as a research participant, you may contact the Chairman of the Institutional Review Board at (318)-675-5409 or the Chief of Staff, Overton Brooks VA Medical Center at (318)-424-6089.
8. If you are a patient, a copy of this consent form will be placed in your medical record.

Subject's Initials _____

VA Department of Veterans Affairs

VA RESEARCH CONSENT FORM
PROTOCOL # H00-022

Subject Name: _____ **Date:** _____

Title of Study: Threshold Detection of Postural Control in Diabetic Neuropathy and Aging

Principal Investigator: C. J. Robinson, DSc, PE; A. M. Hollister, MD **VAMC:** Shreveport

AFFIRMATION FROM SUBJECT

RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above. Dr. Charles Robinson or his associate has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

In case there are medical problems or questions, I have been told I can call Dr. Charles Robinson at (318)-424-6080 or Dr. Anne Hollister (675-6181) during the day and Dr. Robinson at (318)-513-9122 after hours. If any medical problems occur in connection with this study the VA will provide emergency care.

I understand my rights as a research subject, and I voluntarily consent to participate in this study. I understand what the study is about and how and why it is being done.

I will receive a signed copy of this consent form.

You are making a decision whether or not to participate. Your signature indicates that you have read the information provided above. If you decide to participate you are free to discontinue at any time.

"I have been given the opportunity to ask questions and have them explained to me."

_____ _____
Subject's Signature Date

_____ _____
Signature of Witness Witness (print)

_____
Signature of Investigator

Institutional Review Board Approval Start Date 3/27/00 - End Date 03/26/01

Subject's Initials _____

VA FORM
JAN 1990 10-1086

APPENDIX B

FLYER

Subjects Needed

Investigators:
Charles Robinson, DSc, PE, Anne Hollister, MD, and Venkatesh Balasubramanian, BE,
Overton Brooks VA Medical Center, Shreveport, LA and
Louisiana Tech University, Ruston, LA.

Adults aged 50-80, with or without Diabetes, are being recruited for a study in Human Movement Detection

We are looking for individuals who are healthy or who have diabetes. All subjects must not have a history of acute heart or lung problems, back spasms, pain or other spinal problems, central neurological deficits, stroke or head trauma, or other problems that might preclude a person from standing blindfolded for 10 to 15 minute increments over a two-hour period. A neurological screening will be performed, and a psychological test also administered. Individual research results will be retained by the researchers and are not made part of the subject's clinical record.

Maximum time commitment: 4 hours (Usually 3-4 hours.)
Location: Overton Brooks VAMC, LA.
Compensation: $25 each session (up to 4 hours)

If you are interested in participating, or for further information,
Contact: Venkatesh Balasubramanian, B.E.,
Or Charles Robinson, DSc., PE
Phone: (318) 424-6080 or Email: vba001@coes.latech.edu

LSUHSC-S IRB Approved 03/27/2000

APPENDIX C

QUESTIONNAIRE

Initial Contact Questionnaire

Name: _____ Date of Contact(mm/dd/yy)_____

How did subject learn of study? Paper Announcement Internet Word of Mouth

Subject informed of: Age Criteria: _____ Exclusion Criteria: _____

Scope of Research: _____ Benefit of Research: _____

Time Required: _____ Financial Compensation: _____

Is subject interested in participating in study? Yes No

Has Subject been found to be Vestibularly Normal? Yes No Unknown

Is subject able to get to the Overton Brooks VAMC lab? Yes No

Subject Contact via: Phone : _____ Internet:_____

Address: _____

Subject Availability: Date (mm/dd/yy)_____ Time(hh:mm)_____

Alternate: Date (mm/dd/yy)_____ Time(hh:mm)_____

How has subject been given directions to lab? Phone Internet Mail Personally

Subject's Date of Birth (mm/yy): _____ Subject's Gender: Male Female

Subject Code: _____ _____ _____ _____ _____

Gender Age Age Alpha Alpha

The above information, and provided medical history is true to the best of my knowledge.

Subject signature: _____ Date(mm/dd/yy): _____

Investigator signature: _____ Date(mm/dd/yy): _____

Initial Screen Questionnaire
Medical History

Subject Code: _____ _____ _____ _____ _____
Gender Age Age Alpha Alpha

Subject weight as measured by the weighing scale: _____

Does the subject have any history of (Check if Yes):

Cardiac Problems: Tachy/Bradycardia: _____ Cardiac Arrhythmias: _____

Heart / Lung Disease: _____ Shortness of Breath: _____

Other: _____

Neurologic Problems: Stroke/TIA: _____ Head Injury: _____

Peripheral Nerve Injury: _____ Spinal Injury: _____

Advanced Diabetes: _____ Vision Loss: _____

Hearing Loss / Ear Infections: _____ Loss of Balance: _____

Memory/Concentration Deficits: _____ Sensory Loss: _____

Muscle Tone Abnormalities: _____ Coordination Deficits: _____

Other: _____

Orthopaedic Problems: Arthritis / Joint Disease: _____ Osteoporosis: _____

Lower Back Pain/Spasms: _____ Spinal Stenosis: _____

Fractures: _____ – Specify: _____

Other: _____

Alcohol consumption (per week): NONE < 3 3–14 >14

Record Caffinated Items within last 12 hours: _____

Medication / Drug Use:

Pain Medication: _____ Depressants: _____ Anti–Depressants: _____

Psychoactive: _____ Other: _____

Initial Sensory–Motor Screen

Subject Code: _____ _____ _____ _____ _____ Date/Time: _____
Gender Age Age Alpha Alpha

Reflex Testing (+ = normal, – = abnormal, 0= absent):

Patellar Reflex: Right: _____ Left: _____

Achilles' Reflex: Right: _____ Left: _____

Vision Testing (+ = normal, – = abnormal, 0= absent):

Read Newsprint: _____ Read _____ point font @ 20 feet: _____

Uses Eyeglasses / Contacts: _____

Visual Fields: Right: _____ Left: _____ Up: _____ Down: _____

Sharpened Romberg Test Findings (+ = normal, – = abnormal, 0= absent):

Balance: _____ Recovery from Loss of Balance: _____

Time to Loss of Balance (seconds): _____

Precession Test: (Subject hops on one foot should remain facing forward)

Right Foot: _____

Left Foot: _____

Limb Angle Matching – Shoulder Abduction, Shoulder External Rotation and Elbow Flexion Angles – (+ = normal, – = abnormal, 0= absent):

Right: 90,90,90: _____ 90, 0, 135: _____ 45,0,45: _____

Left: 90,90,90: _____ 90, 0, 135: _____ 45,0,45: _____

Tactile / Somato–Sensory Tests with Stoelting Monofilaments to Foot Sole (mm diameter):

Right: Base MetaTarsal: _____ Base Digit IV: _____

Left: Base MetaTarsal: _____ Base Digit IV: _____

Initial Therapeutic Screen

Subject Code: _____ _____ _____ _____ _____ Date/Time: _____
Gender Age Age Alpha Alpha

Posture and Balance (+ = normal, – = abnormal, 0= absent):

Sit to Stand: _____ Standing eyes Closed: _____ Ambulation: _____

Motor: Range of Motion and Strength.

Joint:	**AROM**	**Right**	**Left:**	**Strength Right:**	**Left:**
Shoulder Flexion / Extension:		_____	_____	_____/_____	_____/_____
Elbow Flexion / Extension:		_____	_____	_____/_____	_____/_____
Hip Flexion / Extension :		_____	_____	_____/_____	_____/_____
Knee Flexion / Extension:		_____	_____	_____/_____	_____/_____
Ankle Flexion / Extension:		_____	_____	_____/_____	_____/_____
Ankle Inversion / Eversion:		_____	_____	_____/_____	_____/_____

Joint Stiffness / Tone (+ = normal, – = abnormal, 0= absent):

Shoulder: _____ Elbow: _____ Hip: _____ Knee: _____ Ankle: _____

Limb / Body Segment Length (mm):

Length of Foot: Right: _____ Left: _____

Floor to Lateral Malleolus: Right: _____ Left: _____

Floor to Lateral Epicondyle of the Femur: Right: _____ Left: _____

Floor to Greater Trochanter: Right: _____ Left: _____

Floor to Lateral Aspect of Humeral Head Right: _____ Left: _____

Floor to Top of Head (Total Height): Dorsal Aspect: _____

Lat. Aspect Humeral Head to Lat. Epicondyle of the Humerus: Right: _____ Left: _____

Lat. Aspect Humeral Head to Tip Digit III: Right: _____ Left: _____

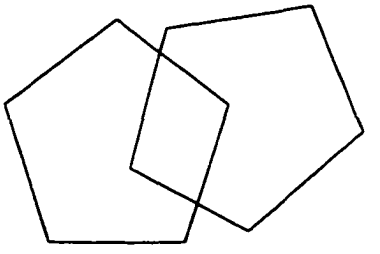
APPENDIX D

MMSE

Mini – Mental State Examination (MMSE)

Make the subject comfortable and establish rapport. Ask questions in the order listed.
Maximum possible score is 30.

Maximum	Score	
		ORIENTATION
5	_____	What is the (year) (season) (date) (day) (month)?
5	_____	Where are we (state) (county) (city) (hospital) (floor)?
		REGISTRATION
3	_____	Name 3 objects (e.g., "apple," "table," "penny"). Take 1 second to say each. Then ask the subject to repeat all 3. Give 1 point for each correct answer. Then repeat them until s/he learns all 3. Count trials and record. Trials: _____
		ATTENTION AND CALCULATION
5	_____	Serial 7's backwards. Stop after 5 answers. Alternatively, spell "WORLD" backwards. The score is the number of letters in correct order (D_L_R_O_W)
		RECALL
3	_____	Ask for the 3 objects named during registration above. Give 1 point for each correct answer. (Note: Recall cannot be tested if all 3 objects were not remembered during registration).
		LANGUAGE
2	_____	Name a "pencil" and "watch."
1	_____	Repeat the following: "No ifs, ands, or buts."
3	_____	Follow a 3–stage command: "Take a paper in your hand, fold it in half, and put it on the floor. "
1	_____	Read and obey the following: "CLOSE YOUR EYES."
1	_____	Write a sentence.
1	_____	Copy the following design:



Total Score: _____

APPENDIX E

PROGRAMS

Table 30. List of Matlab programs

Table 31. List of SAS programs

Matlab Programs

```
function y = firstderiv(x,order)
% function y = firstderiv(x,order)
% This function calculates the first derivative of x
% Venkatesh Balasubramanian

L=length(x);

if order == 1,
    for i=1:L-1,
    y(i)=(x(i+1)-x(i));
  end
else
  y(1)=2*(x(2)-x(1));
  y(2)=x(2)+x(3)-2*x(1);
  for i=3:L-2,
    y(i)=x(i+2)+x(i+1)-x(i-1)-x(i-2);
  end
end
```

```
function [y] = high_pass(data)
% This function performs a high pass filter using the chebyshev (cheby1) filter for
the EMG data.
% This is a 5th order filter with a ripple factor of 0.5.
% The high pass cutoff is at 10Hz.
% Input to this filter is the "data" that needs to be filtered
% Output is the high pass filtered data.
% Venkatesh Balasubramanian

% To detrend the EMG data
datad=detrend(data(:,[2 3 4 5]));
%datad=data(:,[2 3 4 5]);

% To perform the high pass filter
Wn=10/500;
[b,a]=cheby1(5,0.5,Wn,'high');
high=filter(b,a,datad);

% To organize the columns and send the output
hi_temp(:,1) = data(:,1);
hi_temp(:,[2 3 4 5]) = high;
y = hi_temp;
```

```
echo off
```

```
function [lat_lag] = lat_lag
% This function loads the latency files (*lat.raw).
% Detects the when platform moved by difference method.
% Determines the time when the first dectect pulse is sent.
% Computes the lag between platform movement and detect pulse.
% Saves the lag value in hard drive.
% Venkatesh Balasubramanian

% Initial variables
i1=1;
substr={'F64DF'};
trialstr={'as1fflat'};
titlestr={'Smooth 1mm forward free'};
    sstr=char(substr(1));
    astr=char(trialstr(i1));
    fstr=[sstr '1' astr];

% Get summary file info
  sumstr=['H:\F64df_raw\' fstr '.sum'];
    fid=fopen(sumstr);

    for j1=1:4,
    A=fgetl(fid);
        end %j1

    SUM1=fscanf(fid,'%f',[9,100]);
    SUM1=SUM1';
    fclose(fid);

  detect=SUM1(:,3);
  displa=SUM1(:,7);

  clear SUM1

% Trial Loop
    for i2=[1:12],
    if i2<10,
        rawstr=['H:\F64df_raw\' fstr ' ' num2str(i2) '.raw'],
      fid=fopen(rawstr);,
      if fid==-1, break, end;
           for j1=1:7,
               A=fgetl(fid);
               end %j1
```

```
        clear A
        RAW=fscanf(fid,'%f',[16,inf]);
      RAW=RAW';
      %RAW=RAW(1:10:length(RAW),:);
  fclose(fid);

  % Determine when the Platform moves
  [ind, mov] = max(diff(RAW(:,5)));

  % Find the first point of Detect pulse
        for i = 1:length(RAW),
            j = max(RAW(i,16));
            if j>3, break
            end
        end
        buzz = i;

  lat_lag(i2) = (buzz-mov); % Compute the lag in Latency
end

if i2>9,
    rawstr=['H:\F64df_raw\' fstr num2str(i2) '.raw'],
  fid=fopen(rawstr);,
  if fid==-1, break, end;
        for j1=1:7,
                A=fgetl(fid);
            end %j1

        clear A
        RAW=fscanf(fid,'%f',[16,inf]);
      RAW=RAW';
      fclose(fid);

  % Determine when the Platform moves
  [ind, mov] = max(diff(RAW(:,5)));

  % Find the first point of Detect pulse
        for i = 1:length(RAW),
            j = max(RAW(i,16));
            if j>3, break
            end
        end
        buzz = i;

        % Compute the lag in Latency
```

```
            lat_lag(i2) = (buzz-mov);
    end
  end %for

% To save the lag values.
save e:F64df1_lat.lag lat_lag -ascii -double -tabs
```

```
function [y] = notch(data)
% This function is to eliminate the 60Hz and its harmonic 120Hz noise for the
EMG data.
% This is performed using a 4th order Butterworth (butter) filter.
% The notch is from 59 to 61 (for 60Hz) and 119 to 121 (for 120Hz)
% Input to this filter is the "data" that needs to be filtered
% Output is the notch filtered data.
% Venkatesh Balasubramanian

% To detrend the EMG data
datad=detrend(data(:,[2 3 4 5]));
%datad=data(:,[2 3 4 5]);

% To perform the 60Hz notch filter
Wn = [59/500 61/500];
[b,a]=butter(4,Wn,'stop');
y60 = filter(b,a,datad);

% To perform the 120Hz notch filter
Wn1=[119/500 121/500];
[b1,a1]=butter(4,Wn1,'stop');
emg_filt=filter(b1,a1,y60);

% To organize the columns and send the output
temp(:,1) = data(:,1);
temp(:,[2 3 4 5]) = emg_filt;
y = temp;

echo off
```

```
function [RAW] = open_file(rawstr)
% This function opens the file and sends out the values as "RAW"
% Venkatesh Balasubramanian

fid=fopen(rawstr);,
if fid==-1, break, end;
    for j1=1:7,
```

```
    A=fgetl(fid);
end %j1
clear A
RAW=fscanf(fid,'%f',[16,inf]);
RAW=RAW';
fclose(fid);
```

```
function [peri_move] = peri_move_emg(data)
% This function determines the platform movement and extracts the emg and
platform position around the move.
% As a rule 4 seconds before the move and 6 seconds after the move. Sampling
frequency is 1000Hz.
% Detects the platform movement by difference method and idetifies the 10 sec
window.
% Performs the high pass and notch filter for the EMG.
% Sends out the filtered data on all the EMG channels and platform movement in
the selected window.
% Venkatesh Balasubramanian

% To isolate the platform movement

platform = data(:,5);

% To detect when platform moved.
[ind,move]= max(diff(platform));

% To identify the 10 sec window of EMG and platform movement.
data = data((move-4000)+1:move+6000, [5 9 10 11 12]);

% To detrend and high pass filter
data = high_pass(data);

% This performs the notch filter and sends the window out
data = notch(data);

% To define the time of event
time = (0:(1/1000):10);

% To organize the columns and send the output
out_temp(:,1) = ((1/1000):(1/1000):10)';
out_temp(:,[2 3 4 5 6]) = data;
peri_move = out_temp;

echo off
```

```
% This program determines the Position and Velocity of COP for threshold
% Computed at start, middle and end of platform movement
% COP is filtered with a low pass of 5 Hz using 3rd order Butterworth filter.
% Venkatesh Balasubramanian

% clear previous entries
clear
pack

% Initial variables
substr={'f60dan'};
trialstr={'3as1ff' '1as2ff' '2as3ff'};
dirstr={'H:\f60da_raw\'};
i1 = 1; i4 =0;
det11=0; det12=0; det21=0; det22=0; det31=0; det32=0;

% Condition loop
while i1 <= 3,     % Displacement criteria

  dstr=char(dirstr(1));
  sstr=char(substr(1));
    astr=char(trialstr(i1));
    fstr=[dstr sstr astr];
  sumstr=[fstr '.sum'];
  qsm = qsmean(fstr); % QS mean

% Get calibration values
  calstr=[fstr '1.cal'];
  fid=fopen(calstr);
  CAL=fscanf(fid,'%f',[16,inf]);
    CAL=CAL';
    fclose(fid);
  mcal=mean(CAL(.10*length(CAL):.90*length(CAL),:));
  fpcal=mcal(:,1:4)+.0821;

  clear CAL mcal

% Get info from summary file
    fid=fopen(sumstr);
    for j1=1:4,
    A=fgetl(fid);
        end %j1
    SUM1=fscanf(fid,'%f',[9,100]);
    SUM1=SUM1';
    fclose(fid);
```

```
filenm=SUM1(:,1);
buzz=SUM1(:,3);
vel=SUM1(:,5);
displ=SUM1(:,7);

clear SUM1

% Threshold Testing loop
for i3=[1:length(buzz)],
  %if (i1==2 & i3 == 4), i3=i3+1; end    % To skip the nonexistent data
  if i3<10,rawstr=[fstr ' ' num2str(i3) '.raw']; end
  if i3>9,rawstr=[fstr num2str(i3) '.raw']; end
     RAW=open_file(rawstr);

  FP1=RAW(:,1)-fpcal(1);
    FP2=RAW(:,2)-fpcal(2);
    FP3=RAW(:,3)-fpcal(3);
    FP4=RAW(:,4)-fpcal(4);
    APCOP=209.55*(FP3+FP4-FP1-FP2)./(FP3+FP4+FP1+FP2+.3284);
  [ind, move] = max(diff(RAW(:,5)));

    clear FP1 FP2 FP3 FP4 RAW

  APCOP1 = APCOP-qsm;

  Wn = [5/500];    % Filter the signal
     [B,A]=butter(3,Wn);
     COP1=filtfilt(B,A,APCOP1);
  %Cvel1=diff(COP1);

  if move >= 3000 & move <= 9000, % Limit error values
    start=round(move-((displ(i3)/vel(i3))*1000));
    stop=round(move+((displ(i3)/vel(i3))*1000));
    cposs = COP1(start); cposm = COP1(move); cpose = COP1(stop);
  else
    cposs = 0; cposm = 0; cpose = 0;
  end

  clear APCOP COP COPvel

  detect = 0;  % Initialize the detect to be false
     if (buzz(i3) == 1 & move < 6000),
    detect = 1; i4 = i4+1;
  elseif (buzz(i3) > 1 & move > 6000),
    detect = 1; i4 = i4+1;
```

```
    end

    if detect == 1,
      if (cposs < 0), det11=det11+1; end
      if (cposs > 0), det12=det12+1; end

      if (cposm < 0), det21=det21+1; end
      if (cposm > 0), det22=det22+1; end

      if (cpose < 0), det31=det31+1; end
      if (cpose > 0), det32=det32+1; end
       end
    val(i3,1)=cposs; val(i3,2)=cposm; val(i3,3)=cpose;

  end % Threshold loop

  if i1 == 1,
    det(1,1)=det11; det(1,2)=det12;
    det(2,1)=det21; det(2,2)=det22;
    det(3,1)=det31; det(3,2)=det32;
  elseif i1 == 2,
    det(4,1)=det11; det(4,2)=det12;
    det(5,1)=det21; det(5,2)=det22;
    det(6,1)=det31; det(6,2)=det32;
  elseif i1 == 3,
    det(7,1)=det11; det(7,2)=det12;
    det(8,1)=det21; det(8,2)=det22;
    det(9,1)=det31; det(9,2)=det32;
  end

    i4
  i1= i1+1;
    det11=0; det12=0; det21=0; det22=0; det31=0; det32=0;
  i4=0;

end % while loop

det(10,1)=(det(1,1)+det(4,1)+det(7,1));
det(10,2)=(det(1,2)+det(4,2)+det(7,2));
det(11,1)=(det(2,1)+det(5,1)+det(8,1));
det(11,2)=(det(2,2)+det(5,2)+det(8,2));
det(12,1)=(det(3,1)+det(6,1)+det(9,1));
det(12,2)=(det(3,2)+det(6,2)+det(9,2));

det
```

```
save d:\f60da\cpos\det_thresh_new.txt det –ascii –double –tabs
save d:\f60da\cpos\val_thresh_new.txt val –ascii –double –tabs
```

```
function[acopmean]=qsmean(fstr)

% This program determines the mean Quiet standing COP for threshold trials
% File name is used as input and the mean COP value is returned.
% Venkatesh Balasubramanian

% Get calibration values
  calstr=[fstr '1.cal'];
  fid=fopen(calstr);
  CAL=fscanf(fid,'%f',[16,inf]);
    CAL=CAL';
    fclose(fid);
  mcal=mean(CAL(.10*length(CAL):.90*length(CAL),:));
  fpcal=mcal(:,1:4)+.0821;
  clear CAL mcal

% Get static sway values
  stastr=[fstr '.sta'];
    fid=fopen(stastr);

    for j1=1:2,
    A=fgetl(fid);
        end %j1

    STA=fscanf(fid,'%f',[16,inf]);
    STA=STA';
    fclose(fid);

  FP1=STA(:,1)–fpcal(1);   % Obtain the COP values
  FP2=STA(:,2)–fpcal(2);
  FP3=STA(:,3)–fpcal(3);
  FP4=STA(:,4)–fpcal(4);
  APCOP=209.55*(FP3+FP4–FP1–FP2)./(FP3+FP4+FP1+FP2+.3284);
  MLCOP=174.63*(FP2+FP3–FP1–FP4)./(FP3+FP4+FP1+FP2+.3284);

  acopmean=mean(APCOP); % APCOP measures
    clear FP1 FP2 FP3 FP4 fpcal STA APCOP MLCOP
```

```
% This program determines the mean and RMS sway and its velocity during
quiet standing.
% Sway is computed from the COP caluclated from the Load cells
```

```
% COP low pass filtered at 5 Hz.
% Venkatesh Balasubramanian

% clear previous entries
clear
pack

% Initial variables
substr={'m53dpn'};
trialstr={'1as1ff' '1as2ff' '1as3ff'};
dirstr={'H:\M53dp_raw\'};
i1 = 1;

% Condition loop
while i1 <= 3,     % Displacement criteria

  dstr=char(dirstr(1));
  sstr=char(substr(1));
    astr=char(trialstr(i1));
    fstr=[dstr sstr astr];

% Get calibration values
  calstr=[fstr '1.cal'];
  fid=fopen(calstr);
  CAL=fscanf(fid,'%f',[16,inf]);
    CAL=CAL';
    fclose(fid);
  mcal=mean(CAL(.10*length(CAL):.90*length(CAL),:));
  fpcal=mcal(:,1:4)+.0821;
  clear CAL mcal

% Get static sway values
  stastr=[fstr '.sta'];
    fid=fopen(stastr);

    for j1=1:2,
    A=fgetl(fid);
        end %j1

    STA=fscanf(fid,'%f',[16,inf]);
    STA=STA';
    fclose(fid);

  FP1=STA(:,1)-fpcal(1);   % Obtain the COP values
  FP2=STA(:,2)-fpcal(2);
  FP3=STA(:,3)-fpcal(3);
```

```
  FP4=STA(:,4)-fpcal(4);
  APCOP=209.55*(FP3+FP4-FP1-FP2)./(FP3+FP4+FP1+FP2+.3284);
  MLCOP=174.63*(FP2+FP3-FP1-FP4)./(FP3+FP4+FP1+FP2+.3284);

  clear FP1 FP2 FP3 FP4 fpcal STA

    Wn = [0.5/500 5/500];  % Filter the signal
    [B,A]=butter(3,Wn);
    SAPCOP=filtfilt(B,A,APCOP);
    SMLCOP=filtfilt(B,A,MLCOP);

  clear APCOP MLCOP

  acopmean=mean(SAPCOP);    % APCOP measures
    qsway(1,i1)=rms(SAPCOP-acopmean);
    acopmax=max(SAPCOP);
    acopmin=min(SAPCOP);
  qsway(2,i1)=acopmax-acopmin;

    mcopmean=mean(SMLCOP); % MLCOP measures
    qsway(3,i1)=rms(SMLCOP-mcopmean);
    mcopmax=max(SMLCOP);
    mcopmin=min(SMLCOP);
  qsway(4,i1)=mcopmax-mcopmin;

  azerox=zero_cross(SAPCOP,0);    % Compute the zero crossings
  qsway(5,i1)=azerox;
  mzerox=zero_cross(SMLCOP,0);
  qsway(6,i1)=mzerox;

  i1= i1+1;
end

qsway

% Save String
save d:\m53dp\qssway.txt qsway -ascii -double -tabs
```

```
function [react_lag] = react_lag
% This function loads the Reaction files (*react*.raw).
% Detects the when platform moved by difference method.
% Determines the time when the first dectect pulse is sent.
% Computes the lag between platform movement and detect pulse.
% Saves the lag value in hard drive.
% Venkatesh Balasubramanian
```

```
% Initial variables
i1=1;
substr={'F64DFreact'};
sstr=char(substr(1));

% Get info from summary file
  sumstr=['H:\F64df_raw\' sstr '.sum'];
    fid=fopen(sumstr);

    for j1=1:4,
    A=fgetl(fid);
        end %j1

    SUM1=fscanf(fid,'%f',[9,100]);
    SUM1=SUM1';
    fclose(fid);

  detect=SUM1(:,3);
  displa=SUM1(:,7);

  clear SUM1
  %length(detect)
% Trial Loop
    for i2=[1:10],
    rawstr=['H:\F64df_raw\' sstr num2str(i2) '.raw'],
     fid=fopen(rawstr);,
     if fid==-1, break, end;
            for j1=1:7,
            A=fgetl(fid);
            end %j1

        clear A
        RAW=fscanf(fid,'%f',[16,inf]);
        RAW=RAW';
        %RAW=RAW(1:10:length(RAW),:);
    fclose(fid);

    % Determine when the Platform moves
    [ind, mov] = max(diff(RAW(:,5)));

    % Find the first point of Detect pulse
        for i = 1:length(RAW),
            j = max(RAW(i,16));
            if j>3, break
            end
```

```
        end
        buzz = i;
        react_lag(i2) = (buzz-mov);    % Compute the lag in Latency
  end %for

% To save the lag values.
save e:F64df_react.lag react_lag -ascii -double -tabs
```

```
function c=signchange(x,order)
% function c=signchange(x,order)
% length should be even;(ideal 2);
% Venkatesh Balasubramanian

L=length(x);
c=0;

if order == 1,
    if (x(1) < 0) & (x(2) >= 0 ),
     c=1;
  end
  if (x(1) >= 0) & (x(2) < 0 ),
    c=1;
  end
end

if order ==2 ,
  if (x(1) < 0) & (x(2) < 0 ) & (x(3) >= 0) & ( x(4) >= 0) ,
    c=1;
  end
  if (x(3) < 0) & (x(4) < 0 ) & (x(1) >= 0) & (x(2) >= 0) ,
    c=1;
  end
end

 if order ==3 ,
  if x(1) < 0 & x(2) < 0 & x(3) < 0 & x(4) >= 0 & x(5) >= 0 & x(6)>=0,
    c=1;
  end
  if x(4) < 0 & x(5) < 0 & x(6) < 0 & x(1)>= 0 & x(2)>= 0 & x(3)>= 0,
    c=1;
  end
end

if order ==4 ,
  if x(1:4) < 0 & x(5:8) >= 0,
```

```
    c=1;
  end
  if x(5:8) < 0 & x(1:4) >= 0,
    c=1;
  end
end
```

```
function [i, j] = touch(valu)
% This function loads identifies the value where the touch value reaches 3
% Returns the index of the matrix
% Venkatesh Balasubramanian

for i = 1:length(valu),
j = max(valu(i,2));
    if j>3, break
  end
end
```

```
function n=zero_cross(signal,local_base)
% function n=zero_cross(signal,local_base)
% This function calculates the number of times the local base–line is crossed.
% Venkatesh Balasubramanian

n=0;
c=0;
L=length(signal);
for i=8:L,
    c=signchange((signal(i–7:i)–local_base),4);
    if c==1,
    n=n+1;
    end
end
```

SAS Programs

ANOVA

```
data one;
infile'I:\Disser_Document\Statistic\Threshold.txt';
input group d thresh; proc print;
proc glm;
classes group d;
model thresh = group d d*group;
lsmeans group d group*d / PDIFF STDERR;
run;
proc sort;
by d; proc glm;
by d; class group;
model thresh = group;
lsmeans group / pdiff stderr;
run;
```

Repeated Measures ANOVA

```
data one;
infile'I:\Disser_Document\Statistic\detect.txt';
input group d1 d2 d3;
proc glm;
classes group;
model d1–d3 = group / nouni;
Repeated time;
lsmeans group ;
Title Repeated measures to find difference in detect % between displacements
run;
```

T–Test

```
data one;
infile'I:\Disser_Document\Statistic\height.txt';
input group value;
proc ttest;
classes group; var value;
Title Comparing Group Means – HEIGHT
run;
```

Paired Comparison

```
data one;
infile'I:\Disser_Document\Statistic\sural_lr.txt';
input group left right;
Diff = left – right;
proc means mean stderr t prt;
var Diff;
Title Paired Comparison T–Test
run;
```

Regression Model

```
data one;
infile'I:\Disser_Document\Statistic\thresh_reg_1.txt';
input thresh disp;
LT = log(thresh);
LX = log(disp);
proc reg;
model LT=LX;
run;
```

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