A Physiology-Based Approach for Detecting Vibration Perception Threshold in the Plantar Foot

By

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Abstract

Stochastic-resonance-based vibration therapies have demonstrated the potential to improve balance in persons with somatosensory deficiencies to help prevent fall incidents. These vibrations must remain below vibration perception threshold (VPT) to be safe and effective. Several concerns exist regarding current approaches of detecting VPT, including inconsistent unit scales, limited knowledge of the physiological reliability of the methods, or potential effects they may have on standing balance. Recent assumptions that threshold detection tests have no impact on subsequent vibratory stimulations warrant further investigation. The purpose of this study was (a) to develop a new modified 4-2-1 VPT detection method (M421) based on existing approaches and underlying physiological principles, and (b) to identify potential effects the M421 may have on balance during or after threshold testing. To address the need for greater comparability between patient populations and across vibration systems, a common scale for expressing VPT was also established. Our results indicate that, among healthy adults, the M421 test does not significantly alter balance during or following threshold testing, and that a single trial conducted on both feet is comparable to separate tests of each foot. M421 demonstrates repeatable results and can be completed efficiently. Future studies will seek to further validate M421 through direct comparisons against existing methods to determine the optimal approach for detecting VPT prior to stochastic vibration interventions.

Acknowledgements

There are many individuals and groups of people to whom I am thankful for, too many to count yet alone write on one page. So, I will try to keep this brief.

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List of Abbreviations

ADL	Activities of Daily Living
APA	Anterior-Posterior Alpha Scaling Exponent
APL	Anterior-Posterior Path Length [m]
BLC	Trial Condition: Baseline, Eyes Closed
BLM	Trial Condition: Baseline on Vibratory Mat
BLO	Trial Condition: Baseline, Eyes Open
BSHB	Binary Search Halfway Between Method
CNS	Central Nervous System
COP	Center of Pressure
DFA	Detrended Fluctuation Analysis [α]
DML	Downward Method of Limits
EA	95% Fully Encompassing Ellipse Area [m^2]
EC	Eyes Closed Visual Condition
EO	Eyes Open Visual Condition
FAII	Fast-Adapting Type 2 Mechanoreceptors
H	Hypothesis (1-4)
HO	Healthy Older Participant Group
HY	Healthy Younger Participant Group
ICF	International Classification of Functioning
JND	Just Noticeable Differences
M421	Modified 4-2-1 VPT Detection Method
MLA	Mediolateral Alpha Scaling Exponent
MLW	Mediolateral Path Width [m]
MOL	Method of Levels
PNS	Peripheral Nervous System
PTC	Trial Condition: Post-Threshold, Eyes Closed
PTO	Trial Condition: Post-Threshold, Eyes Open
RT	Reaction Time
SA	Specific Aim (1-2)
SM	Staircase Method
SWMF	Semmes-Weinstein Monofilament Test
THR	Trial Condition: During M421 Threshold Testing
TOD	Total Distance of COP Path [m]
TUG	Timed-Up-and-Go Test
UML	Upward Method of Limits
VPT	Vibration Perception Threshold

Chapter 1: Clinical Significance

Setting the Stage

The research explained within is the first component of a broader research and development framework aimed at developing a novel balance rehabilitation tool to reduce fall incidents. To better understand the motivation behind this clinically driven engineering initiative, it is desirable to first call attention to the prevalence of falls, to detail the detrimental effects of falling, and to briefly review current fall prevention strategies.

Fall Statistics & Consequences

Disparity Between Incidence and Innovation

Simply stated, falls to the ground are an urgent health crisis in America and across the globe. A recent report from the U.S. Department of Housing and Urban Development revealed the magnitude of the current situation. Falls among the elderly, classified here as adults ages 65 and older, are expected to total nearly $60 billion in healthcare expenses in 2020 [1]. Through the aging of the Baby Boomer generation, and as global life expectancies lengthen, we are witnessing a dramatic increase in the number of elderly community-dwelling adults [2], [3]. This aging population is simultaneously experiencing a technological gap in medical advancements to prevent falling, or at least, a lack of adoption of existing solutions. Over one-third of elderly adults will fall at least once per year [1], [2], [4], but only 10-20% report using available mobility aids due to perceived social stigmas and inconvenience factors [5], [6]. Among all the incredible medical innovations of the 21st century, fall prevention has too often been overlooked, generating a growing population that could greatly benefit from so far non-existent technologies.

Aging has been associated with balance impairments and increased fall risk across a multitude of studies [4], [7]–[12]. Additional populations at increased risk of falling include persons with diabetes, Parkinson's Disease, HIV, Multiple Sclerosis, and stroke survivors, among others [2], [13]–[19]. That's not to mention falls among middle-aged adults (ages 40-64), a demographic whose fall incidence is grossly underestimated but who may benefit greatest from prolonged early-stage intervention strategies [20]. The previously mentioned fall statistics among the elderly do not fully encompass these other demographics, suggesting that the true incidence rate and economic cost of falls to the ground are both substantial. It is therefore in the best interest of healthcare systems, economic enterprises, and community members to develop new intervention strategies that prevent "first falls" from occurring, rather than waiting to address fall risk factors until after the first fall accident.

Falls Reduce Independence and Quality of Life

No matter the cause of a fall accident, all falls are dangerous and have the potential to be life-changing, traumatizing, or even fatal. Falls can have direct impacts on activities of daily living (ADL) through both physical and cognitive pathways. The World Health Organization's International Classification of Functioning (ICF) can be applied to explaining the multifactorial effects of fall incidents (**Figure 1**). In the acute phase following a non-fatal fall, physical injuries may persist which reduce motor performance, range of motion, or strength. Visible wounds may also occur. Examples include broken bones, bruised limbs, or skin lesions.

As a consequence of reduced physical abilities caused by the fall accident, individuals often are forced to or choose to limit components of their ADL. Common examples include reducing mobility around the house or more frequently requiring help with chores such as cleaning or cooking. Stairways can present unnerving challenges, often restricting an individual to a single level of their house. Severe injuries can require prolonged periods of sedentary daily living to allow for proper healing, but sedation without proper equipment adaptations can induce an even greater risk for a chain reaction of comorbidities in both the short and long terms (e.g. obesity, ulceration, cardiovascular problems).

One of the most life-changing effects of falling is not a physical pain, but rather the mental state of a fear of falling. Fear of falling significantly intensifies the two right-most branches of the ICF model. Combined with chronic injury, fear of falling may persuade an individual to leave their residence less often for non-essential reasons [1]. Fallers demonstrate reduced participation in community events such as social or religious gatherings, entertainment venues, and recreational activities. Complications due to falling are a leading factor in nursing home admission [21]. In whole, a single fall incident can negatively affect an individual's overall quality of life and reduce independent lifestyles.

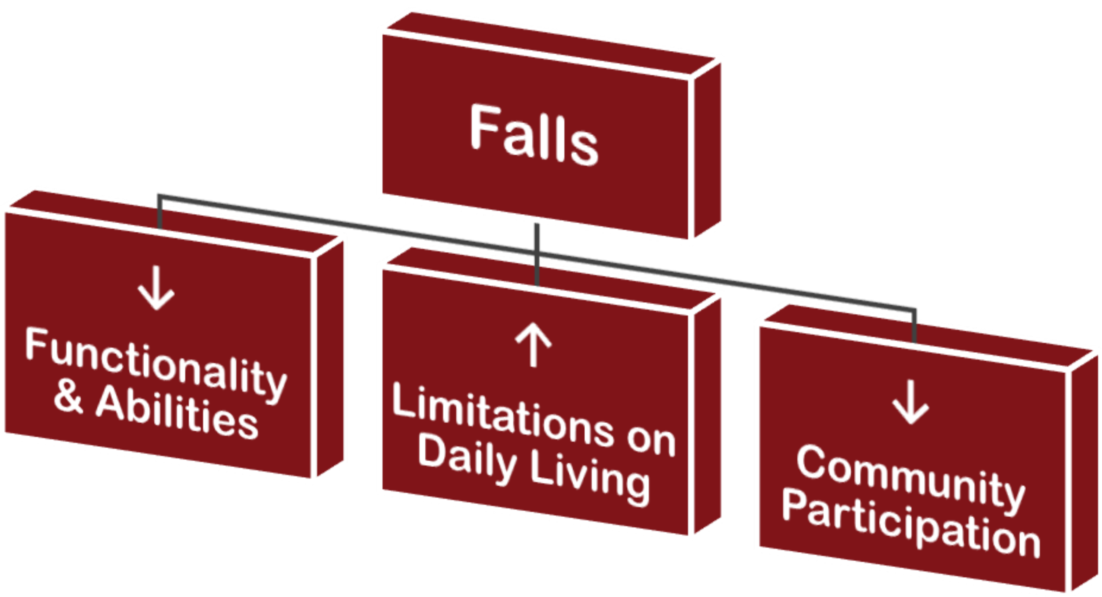

Figure 1. Effects of Falls on ADL through the ICF Model

Brief Overview of Existing Fall Prevention Modalities

There are a variety of existing techniques that aim to improve balance and reduce fall risk. Most approaches can be categorized as either clinical interventions, environmental adaptations, or mobility aids. From an engineering perspective, I argue that few, if any, of these current approaches are adequate applications of advanced 21st century biomedical technologies.

Clinical Interventions

A recent Cochrane systematic clinical review of over 150 independent research studies detailed a variety of effective clinical interventions for fall prevention [21], [22]. A variety of exercise and physical therapy programs demonstrated some of the greatest reduction in fall risk factors among the interventions analyzed. Fall prevention education was also a strong contributor to lower rates of falling when coupled with another intervention modality. At least one study has identified potential benefits of gradual withdrawal from psychotropic medications [21]. However, clinicians indicate a key complication in fall prevention: in order to be most effective at reducing fall risk, intervention programs must be personally tailored to suit the needs and abilities of each individual patient. As one might expect, identifying personalized strategies can be “complex, usually requiring a multidisciplinary team and a variety of assessments [21],” exhausting valuable time and resources from both patients and clinicians.

Environmental & Personal Safety Adaptations

Other common fall prevention modalities include simple home modifications [22]. Improving lighting in dimly lit spaces and removing trip hazards such as rugs are common recommendations from home safety experts and occupational therapists. Limiting stair use by moving most commonly used items to the same level of a house is also recommended. If stair use cannot be eliminated or reduced, railings or chair lifts may be encouraged. Bathroom modifications often include grab bars, non-slip shower mats, and installation of walk-in showers. Environmental modifications like these can be implemented by a trained safety expert upon referral from a physician. Although safety measures may be taken proactively (as they certainly should be), they are most often made in response to a person's first fall accident to prevent future falls.

Annual well-being check-ups are another important step that individuals should take for responsible fall prevention. Clear vison, hearing, and cognition are all necessary for safely carrying out ADL. Good cardiovascular health also contributes to safe mobility and balance [21]. Consulting physicians and complying with appropriate recommendations is one of the easiest ways an individual can improve their overall health and reduce fall risk.

Mobility Aids

Assistive devices such as canes, walkers, and wheelchairs are often used to address mobility restrictions caused by gait and balance impairments. Mobility aids allow for improved independence during ADL compared to without the device [5]. Although these assistive devices can be effective at reducing fall risk, they represent highly noticeable medical interventions. Many individuals who would benefit from such devices, and knowingly acknowledge the potential benefits, still choose to "chance it" without the recommended equipment due to strong social stigmas like weakness and aging that are frequently associated with mobility aids [6]. Fear of embarrassment coupled with the pre-existing fear of falling can dramatically deter daily lifestyles. There also exists a degree of inconvenience with existing devices; users report difficulties transporting their equipment and restricted use of their upper extremities instigated by the need to constantly hold on to the equipment [6].

From an Engineer's Perspective

While many current approaches are moderately effective at improving balance and reducing fall risk, over 1 in 3 elderly adults still fall annually [1], [2], [4]. Thirty-three percent failure rate is rarely acceptable in any engineering application. Based on biotechnological advancements, the fall prevention modalities described in the previous section lag in comparison to other modern medical practices. Consider for example, the extraordinary progressions over the last 100 years in healthcare fields such as cancer treatment, joint replacement, or organ transplantation. Fall prevention modalities, meanwhile, have remained largely unchanged – save for mostly stagnant evolution of recommended therapy exercises and iterative changes in design of mobility aids. Current interventions fail to adequately address all three branches of the ICF model. Millions of fall-risk individuals around the globe would benefit from revolutionary fall prevention devices that are personalized, discrete, hands-free, and affordable [3], [6].

One promising avenue for such technology is stochastic resonance [2], [23], [24], which will be explained in Chapter 2. The work presented within this thesis is a foundational component of a relatively new engineering initiative to develop a vibrotactile device for balance rehabilitation based on physiological and stochastic resonance principles. Long term implications of this research may lead to a revolutionary home-based fall prevention tool that is non-invasive, affordable, and perhaps most importantly, discrete – and thus, free from social stigmas. Such a device would empower aging adults to take control of their own health and enable them to maintain independent, active lifestyles long into their Golden Years without a fear of falling.

Chapter 2: Background

Any technology designed to augment or replace a biological system will only be effective if it is properly accepted by the biological system. Thus, as with any biomedical engineering application, it is first critical to describe the physiological processes responsible for perceiving the environment and maintaining balance. I will then elaborate on the fundamentals of stochastic resonance, present an overview of known factors that affect vibration perception threshold (VPT), and thoroughly compare leading methods of detecting sensory thresholds such as plantar foot VPT.

Overview of Relevant Physiology

Perceiving and Responding to Sensory Stimuli

The body constantly gathers and responds to information about the world via communication between the central nervous system (brain and spinal cord) and the peripheral nervous system. Information is transmitted as electrical impulses through millions of neurons in the body. There are two primary categories of neurons. Afferent neurons carry pertinent sensory information about the internal and external environments towards the brain. Messages regarding vibratory stimuli at the feet ascend through the dorsal columns of the spinal cord to reach the parietal lobe of the brain, the main sensory processing region. The parietal lobe communicates with the premotor cortex to plan an appropriate motor response, which is then initiated by the primary motor cortex. Efferent neurons code the motor performance plan for the body to execute. Motor signals descend through the ventral and lateral corticospinal tracts of the spinal cord, and in the case of vibration at the feet, instruct the lower extremities how to maintain postural control. The core elements of the nervous system for processing vibratory stimuli at the feet are highlighted in **Figure 2**: (**2a**) simplified map of the central (CNS) and peripheral (PNS) nervous systems, (**2b**) midsagittal cross section of the brain, and (**2c**) horizontal cross section of the spinal cord.

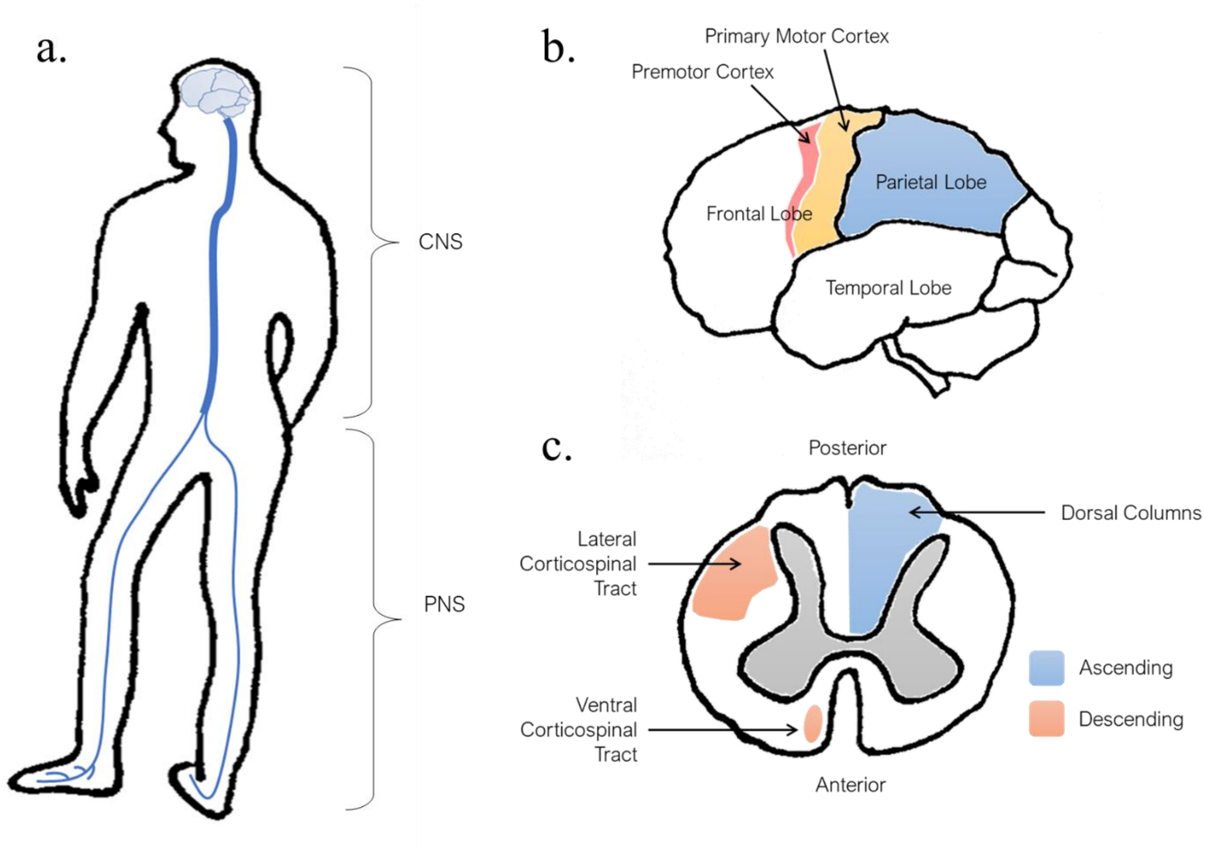

Figure 2. Neurophysiological Components of Perceiving Vibratory Stimuli

Sensory Systems Help Maintain Upright Balance

Postural control for maintaining upright balance involves a highly complex interaction between afferent (sensory) and efferent (motor) neurons. While this relationship is largely beyond the scope of this thesis, it warrants some mention. In short, continuous feedback from three sensory systems is used to orient postural awareness: these are the vestibular, somatosensory (touch and proprioception), and visual systems [8], [23], [25]. Diseases and disabilities can have various effects impairing one of more of these systems, introducing a state of sensory mismatch. Without medical intervention, sensory mismatch can cause dangerous falls to the ground. The body's natural response to combat sensory mismatch is to adapt through a process called sensory reweighting; inaccurate or unavailable sensory signals are ignored as much as possible and greater reliance is placed upon healthy systems to maintain balance [26]. For example, persons who experience peripheral neuropathy of the feet – a leading risk factor for falling – may subconsciously rely more heavily on visual and vestibular feedback due to the somatosensory impairments in their feet [25]. Other compensatory responses may include increased reliance on hip afferents [27]. Fall prevention approaches in this instance would likely include modalities of rehabilitating somatosensory processes in the feet to reduce sensory mismatch. Several such interventions have been reported, including vibration of the feet – a technique that has demonstrated increasingly high promise in both research and clinical settings for balance improvement [28].

Four Classes of Mechanoreceptors

There are four sub-classes of somatosensory afferent neurons that are responsible for perceiving vibration, touch, and pressure at the surface of the skin. These neurons are called cutaneous mechanoreceptors. In the late 1970's, Johansson & Vallbo were the first to offer the notion of four different classes of mechanoreceptors [29], [30]. Their work was largely guided by the preceding work of Verrillo's group throughout the 1960's on sensory thresholds [31]–[33]. The four classes of mechanoreceptors respond differently under varying pressure, temperature, and vibration frequency. Their physical properties (**Figure 3**) were explored throughout the 1980's and 1990's [34]–[37]. Cutaneous mechanoreceptors are distributed according to their properties at various depths within the skin (**Figure 4**, adapted from Viseux 2019 [28]) and in varying proportions around the body. In 2002, Kennedy and Inglis reported insight specific to the plantar foot by revealing a distribution map of the four classes of mechanoreceptors along the foot sole [38]. Over one hundred distinct afferent regions have been identified in the foot [38], [39].

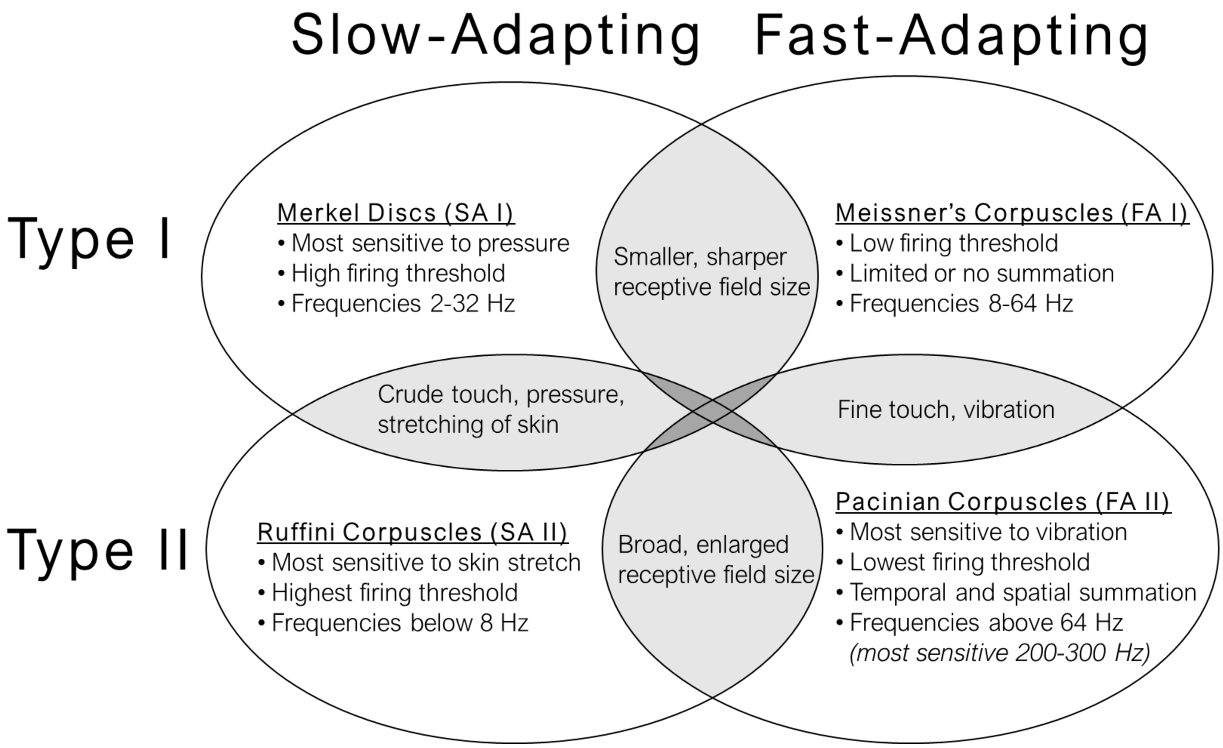

Figure 3. Properties of Cutaneous Mechanoreceptors

Sources: [28], [37]–[41]

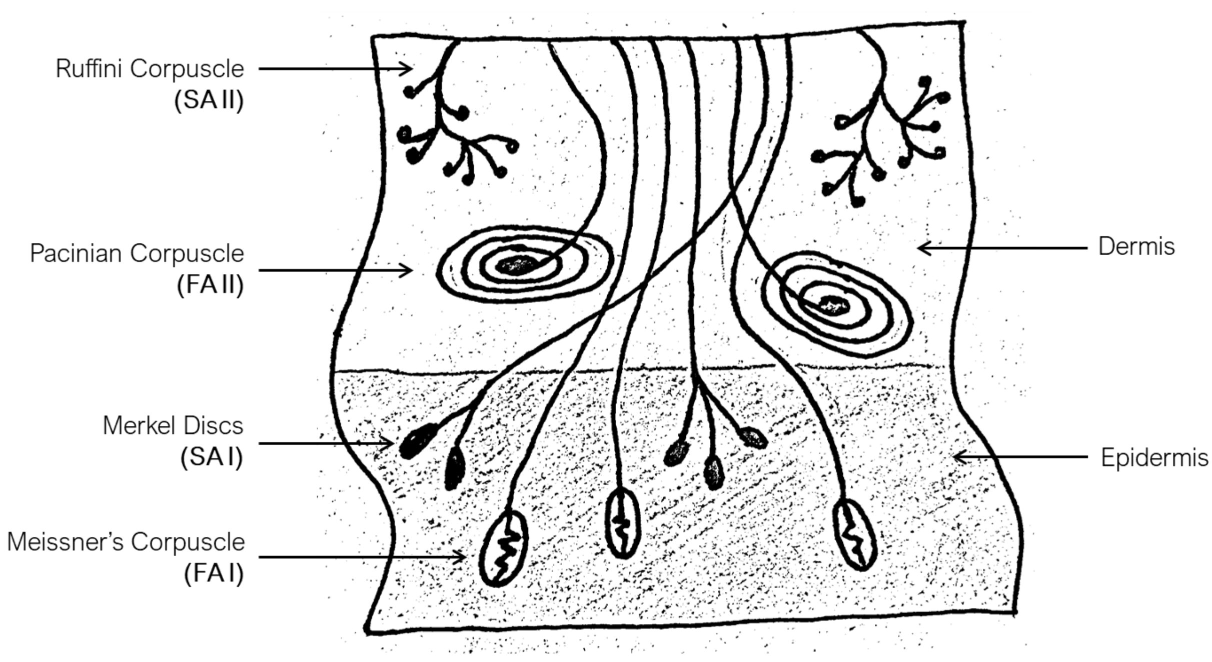

Figure 4. Four Mechanoreceptors of Touch in the Skin

Measurement of spatial and temporal changes in the center of pressure for maintaining healthy balance is a critical role of cutaneous mechanoreceptors in the foot soles [25], [28]. Studies have even suggested that these somatosensory messengers are so vital that they cannot be fully substituted by visual inputs [42]. As previously mentioned, multiple studies have indicated that certain vibratory stimuli at the plantar foot can augment weakened somatosensory pathways to improve or restore impaired postural control in fall-risk populations [9], [10], [12], [16], [28], [43]–[45]. Based on physiological and biomechanical evidence, vibration treatments should seek to specifically target fast-adapting type II (FAII) mechanoreceptors, which express heightened sensitivity to vibrations between 200-300 Hz. Further, treatments should be personalized to account for variability in somatosensory abilities between subjects, which can be caused by a variety of factors that will be discussed later in this chapter.

Enhancing Physiological Systems via Stochastic Resonance

The Basics of Stochastic Resonance

Most biological processes, such as human postural control, express some level of unsteady state (nonlinear) complexity to maintain health. One leading theory suggests that a certain dynamic balance between predictable and random behaviors allows a system to sustain rigid normal functioning while possessing the flexibility to adapt to abnormal circumstances [46], [47]. As a result of this relationship, nonlinear systems can be influenced by noise within a signal. Although noisy signals have traditionally been viewed as undesirable, more recent understandings of noise in nonlinear biological systems have discovered beneficial effects [2], [48], [49]. In fact, noise has even been labeled an “essential ingredient” to the health of biological systems [50].

When the presence of noise in a system improves output performance compared to in the absence of noise, it is known as stochastic resonance. Stochastic resonance only exists in the presence of a threshold. Weak signals below the threshold level (subthreshold) do not invoke output responses. Responses are only triggered by stronger events when magnitude is equal to or greater than threshold (suprathreshold).

Consider, for example, a weak sinusoidal signal oscillating below some constant response threshold (**Figure 5**). The system is only conditioned to trigger an output response when the signal magnitude reaches or surpasses the threshold magnitude. In the case of the subthreshold sinusoidal signal, no output response is triggered. This is comparable to damaged mechanoreceptors, which often lack the ability to initiate suprathreshold responses, impeding sensorimotor feedback loops. Now consider also a superficial random noise pattern that is lower in magnitude than both the signal and threshold. When combined with the signal, the noise provides a sense of "helpful randomness [49]" that permits the system to achieve suprathreshold magnitude at several instances (red asterisks). It is only in the presence of the artificial noise that the weak system achieves the desired output response. Stochastic resonance is the primary mechanism by which subthreshold noisy vibrations at the feet can improve impaired balance in fall-risk populations.

Stochastic Resonance Applications for Balance Rehabilitation

Stochastic resonance may occur naturally, but it is most often studied within engineering applications whereby subthreshold external noise is intentionally introduced to a weak system to understand potential benefits on the system. In fall-risk populations with impaired postural control systems, numerous studies have demonstrated that stochastic-resonance-based vibration stimuli at the plantar foot have potential benefits for improving balance [8], [9], [12], [43]–[45], [51]–[53].

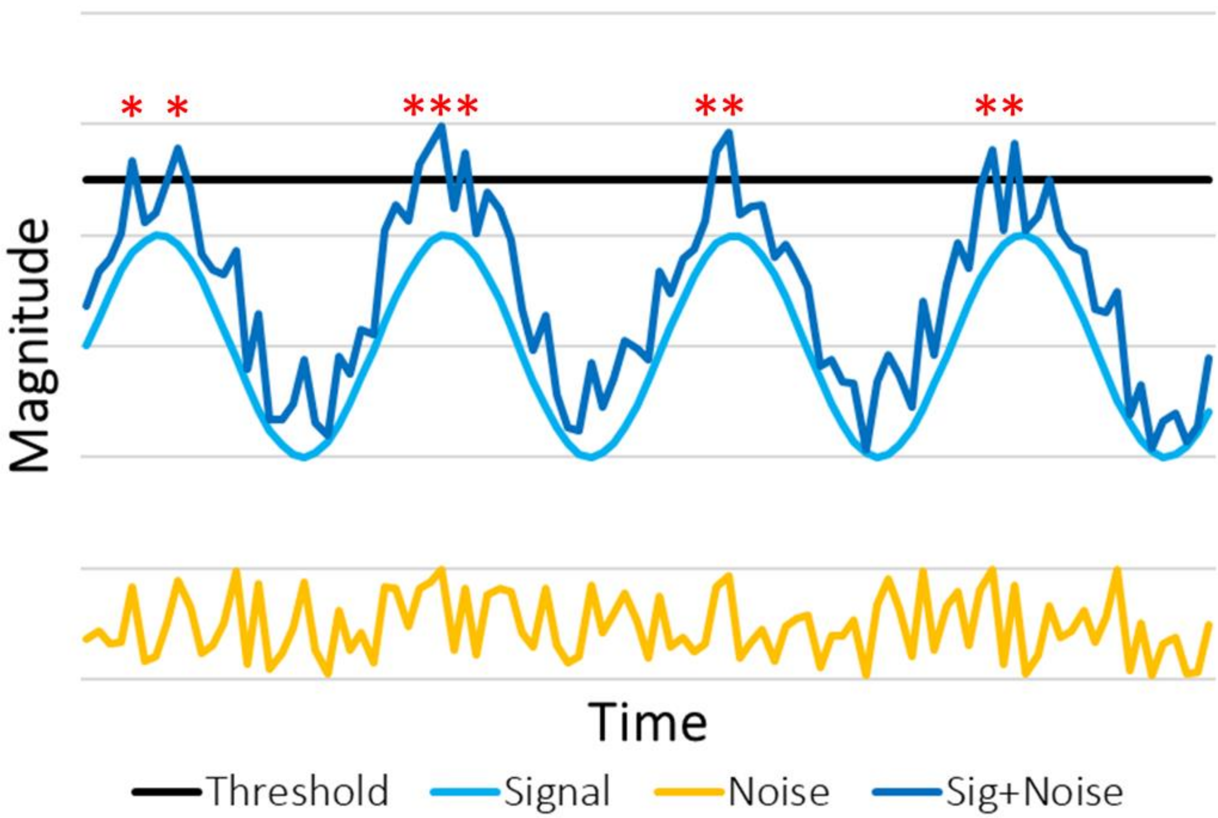

Figure 5. Principles of Stochastic Resonance

While the exact neurophysiological mechanism of how subthreshold vibrations augment weakened sensorimotor pathways remains unknown, the leading theory requires a basic understanding of neuron action potentials (**Figure 6**). Somatosensory deficient afferent neurons, which may be impaired by a variety of pathologies previously mentioned, are believed to exist in a state of hyperpolarization away from firing threshold. Noise stimuli are thought to partially depolarize unhealthy neurons back towards healthy polarization levels, closer to firing threshold. As it is returned to normal resting potential, the unhealthy afferent acquires enhanced (healthy/normal) sensitivity to external stimuli such as shifts in center of pressure at the feet, enabling sensorimotor pathways to resume necessary communication for maintaining balance [42], [45], [54].

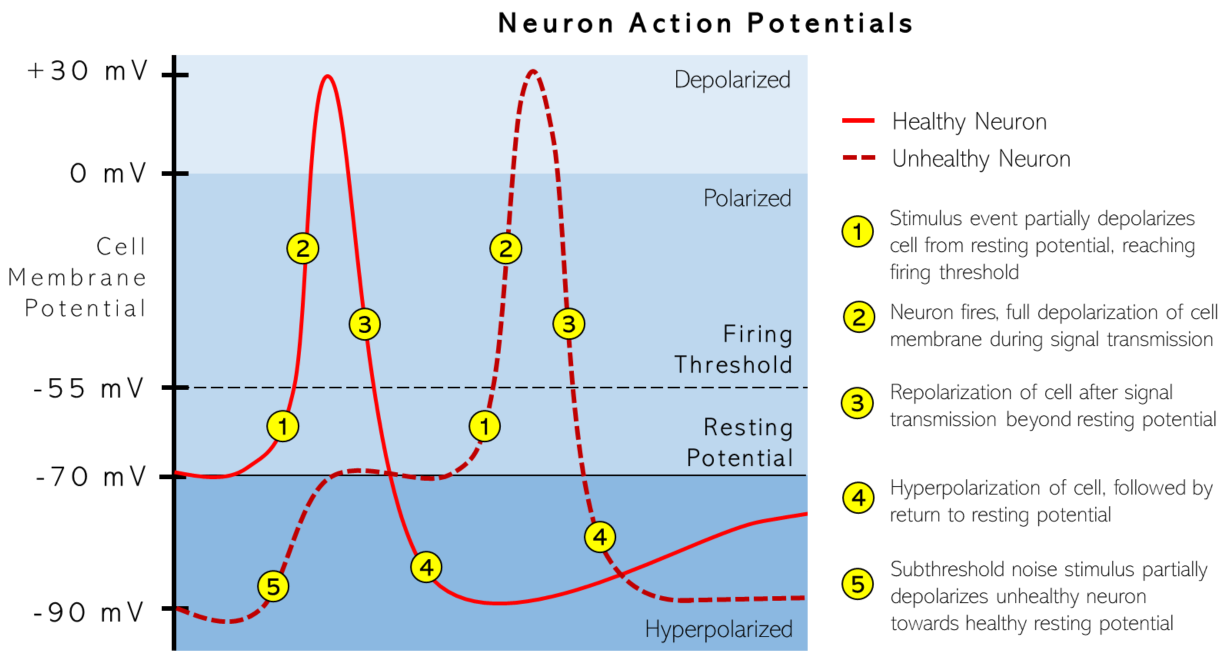

Figure 6. Healthy and Unhealthy Neuron Action Potential Behavior

Notably, a single set of noise characteristics (i.e. frequency content, magnitude) cannot be expected to be equally effective across multiple systems. McDonnell and Ward argue that artificial noise introduced to unhealthy biological systems must be perceived as physiologically “relevant” by the system in order to facilitate maximum system performance improvements [24]. Studies also suggest that noise magnitude should be optimized for each system in a way that increases sensitivity to relevant external stimuli without hypersensitizing the system to uncritical changes [2], [48], [49], [55]. For example, in **Figure 5**, the optimal noise condition would yield one output response (red asterisk) for each peak of the sinusoidal signal. The noise that is shown, however, produces unnecessary information (more than one red asterisk per peak) about the relatively predictable sinusoidal signal, potentially overloading the system.

These concepts provide additional justification for noisy vibrations to be personalized to each patient for balance rehabilitation purposes. In order to do so, however, a stochastic-resonance-based therapeutic tool must accurately and reliably detect vibration perception threshold (VPT) on a subject-by-subject basis to determine appropriate vibration treatment characteristics. The primary goal of this thesis was to develop and validate a universal method for detecting VPT for use in future fall-prevention applications.

Factors Influencing Vibration Perception Threshold

For vibrational stochastic resonance applications to be most effective, the external vibration system must first be able to detect the threshold of the internal biological system. While this may seem straightforward to the unassuming observer, several variables quickly add complexity to the challenge. VPT's are influenced by a variety of physiological factors and stimulus characteristics (**Figure 7**). Even within the same participant, it is not unreasonable for VPT to fluctuate daily or even hourly based on gradual changes in the internal and external environments. A robust VPT detection method should ideally be universal enough to accommodate the wide threshold variability attributed to these factors. Implications of incorrectly detecting VPT include, but are not limited to, increasing fall risk through inappropriate vibration treatment. It should be noted that lower VPT is representative of higher sensitivity, and typically, better health.

Human Factors

It is well-documented that VPT increases with age [8], [33]–[36], [40], [56]–[58]. The relationship between age and VPT at the feet is approximately linear until ages 65-72, where a sharp increase in threshold is observed [33], [57], [58]. VPT also increases with plantar foot skin stiffness (hardness), including in the presence of calluses [39], [41]. In age-matched comparisons, males are generally more sensitive than females [59]. Skin temperature also effects VPT. Although the relationship between temperature and threshold magnitude is dependent upon stimulus frequency, the trend follows a U-shaped pattern across nearly all frequencies [37], [60], [61]. **Figure 7** displays the relationship between VPT and temperature for a stimulus frequency of 250 Hz, which corresponds to the peak sensitivity of FAII mechanoreceptors. Within the same participant, VPT is expected to be higher at the foot when standing compared to sitting [41], and is lower in the peripheral digits compared to proximal regions [62].

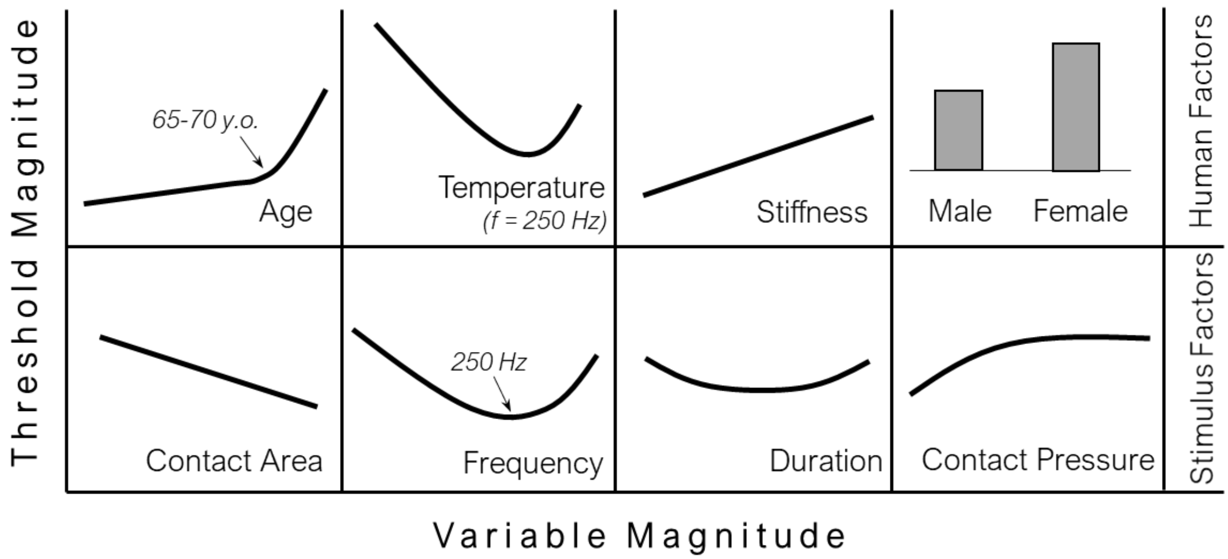

Figure 7. Influence of Physiological & Stimulus Factors on VPT

**Diagrams indicate generalized trends only. Individual graphs are not to scale.*
Sources: [8], [30]–[36], [38]–[40], [55]–[62]

Stimulus Factors

In addition to being influenced by biological variables, VPT is dependent upon several stimulus parameters. Larger contact areas are associated with lower VPT's, especially for stimuli targeting FAII receptors which are capable of spatial summation [34]–[37]. As previously alluded to, stimulus frequency is highly associated with variation in VPT. Thresholds are most sensitive to frequencies between 200-300 Hz, typically expressing peak sensitivity (i.e. lowest VPT) near vibrations at 250 Hz [31]–[33], [37], [40], [59], [61]. Stimulus duration also impacts VPT. Thresholds are lower for stimuli greater than one second than those less than one second, once again particularly notable in FAII receptors which are capable of temporal summation [34]–[37]. VPT does, however, gradually increase during prolonged application of pressure [63], but it is difficult to know just how long it takes for this effect to set in. Based on our preliminary observations, one might expect that VPT would begin to increase after just 30-60 seconds of applied pressure. Separately, increased contact pressure raises VPT [63].

Implications of Incorrectly Detecting VPT

Although there are many variables that continuously influence VPT, it is not necessary to measure every variable each time threshold is calculated. Rather, VPT detection systems should simply operate regardless of these factors to detect a patient's threshold at the precise moment in time immediately prior to stochastic-resonance-based vibration therapy. In other words, VPT drift over the course of time is not a concern so long as the system's vibratory range is wide enough to encompass all reasonable VPT magnitudes.

Incorrect VPT detection can lead to significant consequences. Because cutaneous mechanoreceptors at the feet contribute to postural awareness and stable balance [25], [27], introducing inappropriate stimuli can lead to false representations of center of pressure – which may induce falling. If the detected VPT is higher than the actual physiological threshold, vibration treatment will consist primarily of suprathreshold stimuli. This error can induce whole-body motor responses (tilt or sway) away from the relatively strong vibration [27], [64], which in the case of balance rehabilitation, may lead to an undesirable increased risk of falling. If VPT is recorded lower than actual threshold, vibration treatment will remain too far subthreshold and afferent mechanoreceptors will not reach firing threshold. The benefits of stochastic resonance would be absent, but a patient may falsely believe they have been "treated." This false sense of confidence could yet again lead to increased risk of falling.

Existing Methods for VPT Detection

There are several existing sensory threshold methods that have been applied to VPT detection for measuring somatosensory abilities at the plantar foot. Preferable approaches are robust, relatively quick to perform, and inclusive of large subject-to-subject variation in VPT. **Figure 8** displays a representative comparison for the six methods that will be explained. These six approaches can be categorized as either reaction time inclusive (displayed as circles) or reaction time exclusive (squares). Data shown for the 4-2-1 method is directly from Dyck's introduction of the method in 1993 [65]. Other methods shown are subjective representations of what a VPT test might look like for the same participant based on those experimental 4-2-1 responses. Shown in parentheses are VPT's calculated according to the rules of each method, which will be explained next.

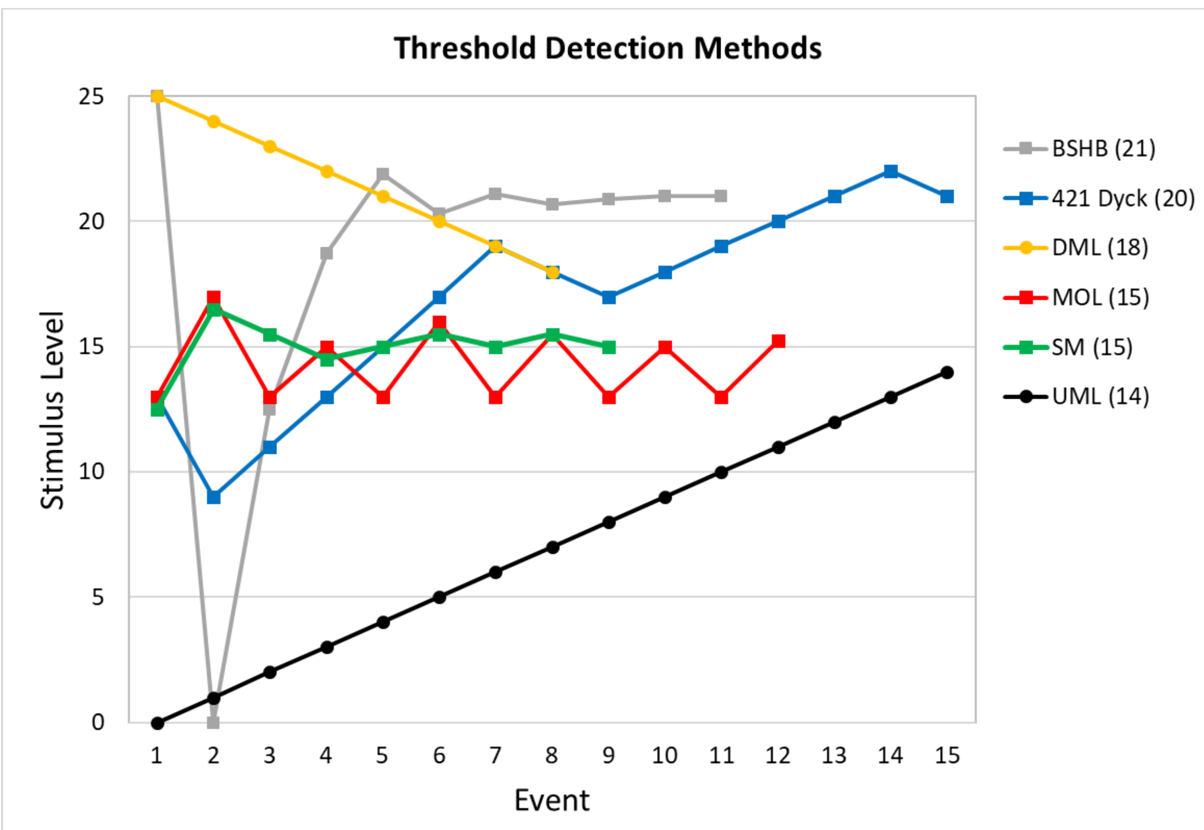

Figure 8. Comparison of Existing VPT Detection Methods

Sources: [41], [65]–[68]

Reaction Time Inclusive VPT Methods

Reaction time (RT) inclusive methods include two comparable but opposite approaches: (1) Upward Method of Limits (UML), and (2) Downward Method of Limits (DML). These methods apply a continuously increasing (UML) or decreasing (DML) stimulus to the foot sole. Subjects are prompted to indicate “the moment” when they either begin feeling (UML) or cease feeling (DML) the applied stimulus, respectively. Indication is typically given via spoken word, a push button, or similar. The methods are considered inclusive of RT because there is an inherent delay, namely the participant’s unique reaction time, between “the moment” of true threshold and the instant of indication. During this brief delay, the stimulus magnitude continues to rise or fall. In this way, RT inclusive methods are influenced by the rate of stimulus change (slope in **Figure 8**), an issue that was seemingly uncontrolled for in early applications of stochastic-resonance-based vibrations for balance interventions [9], [16], [44], [45]. RT inclusive methods are therefore subject to identifying VPT values slightly higher (DML) or lower (UML) than true threshold. While attempts have been made to adjust for error caused by reaction time [15], methods of limits are typically viewed as inferior to RT exclusive methods.

Another concern of RT inclusive VPT detection methods observed by our team through preliminary studies is the issue of relativity. Vibration begins at zero/minimum power in the UML, while vibration begins at maximum power in the DML. Through our experience, these two methods often produce drastically different VPT values. We believe subjects are more likely to notice low-level vibrations in the UML since the relative comparison is no/minimum vibration. In the DML approach, subjects are more likely to indicate threshold at a higher magnitude because they are perceiving each stimulus relative to maximum vibration power. A simple comparison can be drawn to weather temperatures. In the spring, a 50°F day feels warm and pleasant compared to winter's freeze. In autumn though, a 50°F day seems crisply cool compared to the summer heat. These temperature relativities are comparable to the inconsistencies observed in the UML and DML, respectively.

Reaction Time Exclusive VPT Methods

Several RT exclusive sensory threshold methods have been applied for plantar foot VPT detection. These include the Method of Levels (MOL), the Staircase Method (SM), the Binary Search Halfway Between (BSHB) method, and the original version of the 4-2-1 Stepping Algorithm as introduced by Dyck et. al. [65]. The sections that follow detail the necessary steps and calculations for each of these four approaches.

Method of Levels. The Method of Levels (MOL) was originally developed for thermal pain threshold applications [68], [69], and its starting point was very low (32°C). However, it is included here as it is a valid sensory threshold approach that could be selected for VPT detection. As shown in **Figure 8**, MOL has been slightly modified based on the previously described relativity factor by adjusting the initial value to a more reasonable vibration magnitude of 50%. In this way, we model the "best case scenario" for MOL in vibratory applications.

To conduct the MOL, vibration is initially set to 50% magnitude. The first stimulus event is administered by increasing vibration power by 4 levels. Immediately following completion of the stimulus event, vibration returns to its initial level of 50%; this is not technically considered an event, but instead allows a neutral wait period until the next stimulus is applied. The participant is instructed to respond following each stimulus event to state 'Yes' if a change in vibration magnitude was perceived or 'No' if the change was not noticeable. A simple hand-raise or button press may be substituted for verbal responses, as long as the response method maintains a binary ‘forced-choice’ characteristic. Notably, different applications of the MOL have chosen to either (a) prompt the participant for a response after each stimulus event, or (b) provide a single set of instructions at the beginning of the test and not notify the participant when each stimulus event occurs. Our team’s concerns regarding these inconsistent approaches will be reviewed later.

Following the initial stimulus event, the next vibration is decreased by 4 levels following a ‘Yes’ response or increased by 4 levels upon a ‘No’ response. The magnitude of stimulus change (step size) remains constant until the first ‘turnaround’ – where consecutive event responses switch from ‘Yes’ to ‘No’ or vice versa. At each turnaround, the step size is halved. The process continues until the step size reaches 0.25 levels (4 turnarounds). VPT is calculated as the average of the last recorded ‘Yes’ and ‘No’ stimulus levels.

Staircase Method. The Staircase Method (SM) is most similar to the MOL, except that it does not include the return periods to the initial vibration level. SM has also been modeled in a ‘best case scenario’ for vibration applications, starting from 50% vibration level (**Figure 8**). Step size for SM begins at 4 vibration levels, just like the MOL. However, following the first ‘Yes’ response, step size is decreased to 1 vibration level until the next ‘No’ response is recorded. Step size is then reduced to 0.25 levels for the remainder of the test and stimulus events continue until a total of four ‘No’ responses are recorded. VPT for the SM is calculated as the average vibration level during the phase of 0.25 step sizes [68].

Binary Search Halfway Between. The Binary Search Halfway Between (BSHB) method administers the first stimulus event at maximum vibration, followed by a second stimulus at zero/minimum vibration level (**Figure 8**). If a participant does not respond 'Yes' to the first event and 'No' to the second event, the test is immediately terminated and reattempted after a short rest period. The third stimulus level is administered halfway between the first and second's magnitudes (50% power). Following this pattern, each consecutive stimulus magnitude is halfway between the minimum perceived vibration level and the maximum unperceived vibration level. In other words, vibration is delivered halfway between the lowest 'Yes' response and the highest 'No' response. The test concludes after 11 stimulus events and is recommended to be repeated three times. VPT is calculated as the average vibration level during the 11^{th} event of all three trials [41].

4-2-1 Stepping Method. The 4-2-1 Stepping Method is a derivation of the MOL but is rooted in stronger physiological principles. Namely, stimulus intensity range is divided into 25 intervals referred to as "just noticeable differences" (JND's). As originally proposed by Dyck, JND's identify the minimal step size necessary to detect a difference between two consecutive stimuli that are both within the bounds of sensory threshold and pain tolerance [65], [66]. The width between JND's is not fixed, allowing for a more physiologically relevant scale for measuring stimulus intensity. However, because sensory ranges can drastically differ in patient populations compared to healthy groups, identifying true JND's for patient populations can be both difficult and time consuming [66].

VPT detection using the 4-2-1 stepping method begins by delivering an initial stimulus at Level 13 out of the 25 JND's (**Figure 8**). Subjects indicate if they perceive the stimulus by stating 'Yes' or 'No' following vibration termination. 'Yes' responses always decrease the next stimulus intensity, while ‘No’ responses increase the next intensity. The first step size is four JND’s. Like the MOL, step size changes at ‘turnarounds’ – where consecutive event responses switch from ‘Yes’ to ‘No’ or vice versa. In this method, step size remains at four JND’s until the first turnaround, reduces to two JND’s until the second turnaround, and then remains constant at a step size of one JND for the remainder of the test. Plantar foot VPT is calculated as the average stimulus intensity at each turnaround event within the final phase.

The original 4-2-1 stepping method includes 20 total stimulus events. However, five of these events are null stimuli. No vibration is administered during a null stimulus, but all other aspects of the test procedure remain the same. The five null events are randomly distributed amongst the 15 vibratory events. Subjects are not informed that null events will be included. If a participant indicates perception of a null stimuli, the test is terminated and repeated after a short break. Implementing random null stimuli helps to reduce participant and observer bias while protecting the calculated VPT from false perceptions by the participant [65]. The 4-2-1 method is the only VPT detection method that incorporates null events, further improving its physiological relevance compared to other RT exclusive approaches.

Concerns Regarding Previous Vibration Studies

Previous applications of stochastic-resonance-based vibrations on standing balance have opted for differing VPT detection methods. This inconsistency in threshold detection methods introduces a degree of complexity when attempting to compare stochastic vibration intervention studies. Several other differences in methods between studies further complicate comparisons and reviews for clinical recommendations. Vibration apparatus, threshold measurement units, and instructions provided to participants each have the potential to alter the outcomes of a vibratory balance intervention. Greater consistency in VPT detection methods is necessary before the effects of stochastic vibrations on balance can be better understood.

Inconsistencies in Delivering Vibration

A recent meta-analysis [53] of a small sub-sample of stochastic resonance interventions identified moderate effects for balance improvement but high (and undesirable) cross-study heterogeneity ($60\% < I^2 < 70\%$). Some studies have utilized linear actuators or mechanical indenters for administering vibration [15], [44], [58], [70]. In these instances, participants are most commonly positioned standing on a perforated platform while fine-tipped probes are oscillated beneath their feet. Many other applications have incorporated thin piezoelectric vibrators within silicone or foam insoles for treatment [8], [9], [11], [12], [51], [54], [71]. At least two studies have applied vibration via small coin motors positioned beneath the feet [72], [73].

For practical everyday use, a fall prevention device that incorporates linear actuators would likely be bulky, inconvenient, and not easily transportable. Further, if the standing platform were more than just a few inches off the ground, fall risk would actually increase when subjects stood atop it. Piezoelectric vibrators can be precision tuned which makes them a great candidate for personalized therapies. Their thin profile also allows for potential uses in rehabilitation devices such as shoe insoles or standing mats. However, piezoelectric vibrators can be very expensive, which could significantly hinder the affordability of an assistive tool that incorporates several of them. Coin motors provide an affordable alternative to piezoelectric components while exhibiting many of the same advantages.

Inconsistencies in VPT Measurement Scales

At least in part due to the different vibratory apparatuses selected for various studies, there is also a wide array of units that have been utilized to describe VPT magnitude. Actuator and filament studies tend to report VPT either in units of compressed distance, such as microns (μm) [15], [33], [37], [44], [58], or in units of applied force, such as millinewtons (mN) [39]. At least one study has reported VPT as voltage output by the vibratory device [71]. Another group measured vibration magnitude in gravitational acceleration units ($g = 9.81\ m/s^2$), but did not report VPT along the same scale [70].

A majority of studies over the past two decades, however, have continued to report VPT as a percentage of maximum vibration level for the specific apparatus utilized [9], [12], [15], [16], [44], [51], [54], [72]. While this approach may be simplest to report, it is least useful for advancing the field of knowledge. Without the use of a standardized unit scale for reporting thresholds, only studies that use the exact same vibration apparatus can be compared. It is nearly impossible to directly compare or compile data across dissimilar intervention methods. The broader field of stochastic-resonance-based vibration for fall prevention therefore consists of small pockets of information divided by vibration apparatus, threshold units, and often research groups. Unfortunately, these segmented research findings do not yet form a cohesive undisputable argument in favor of vibratory applications for balance rehabilitation, which likely explains the low adoption rate of these interventions by clinicians over the last twenty years.

Inconsistencies in Participant Instructions

There are two opposing frameworks for instructing subjects how to conduct RT exclusive VPT detection methods. The first approach provides a single set of instructions to the participant before testing begins. Subjects are informed of what to expect and instructed how to respond when they feel vibrations. Over the course of testing, no additional instructions are given. In other words, subjects are not aware of when each stimulus is administered, and they are not prompted to respond to each event. The second approach includes similar starting instructions, but subjects are then directly prompted to indicate whether they perceived a stimulus following each event. We believe the latter method is more likely to promote false positive perceptions because subjects are instantaneously notified when each stimulus occurs, which may lead them to believe that they "should have felt something" – as was the case in our preliminary investigations. This effect could be particularly exacerbated in methods that don't incorporate null stimuli and would likely yield VPT values lower than true sensory threshold.

A final key difference between existing studies is the use of auditory masking. Certain vibration apparatuses produce audible noises when vibration is administered. If a participant can't feel the stimulus at their feet but can hear the byproduct sound of the vibration, they may be inclined to indicate that they perceive the stimulus, which would lead to inaccurate VPT results. Different research groups have opted to prevent this effect by masking vibration sounds. At least a few studies have administered auditory white noise through a set of headphones that the participant wears during testing [8], [16], [70]. However, this approach may make it difficult to differentiate the biomechanical effects of vibratory stimuli from the effects of auditory stimuli, since noisy perturbations of both auditory and somatosensory systems have demonstrated the potential to alter postural sway [74]. Ideal scenarios would include either vibratory systems that do not produce audible sounds or masking via headphones without the use of auditory noisy stimuli.

Recommendations for VPT Detection

Returning the Focus to Detecting Threshold

It is apparent that too many biomedical researchers have been prematurely over-focused on the effects of subthreshold stochastic vibrations on balance as opposed to the way in which threshold is detected. For example, the UML remains the most popular method for detecting VPT due to its simplicity and rapid testing time. It is not uncommon for researchers to simply instruct participants to turn a dial to increase vibration magnitude until they find a threshold level that feels comfortable and reasonable. This popular derivation of the UML is highly concerning considering the importance of maintaining optimized subthreshold magnitude during treatment. Physiologists widely dispute the UML's ability to identify true sensory threshold due to the previously addressed issues regarding reaction time inclusivity and stimulus relativity. We further predict that it is highly unlikely that the UML is a robust and repeatable VPT detection method, especially when self-conducted by untrained research subjects. Consequently, the results of many stochastic vibration studies should be carefully considered before reaching clinical conclusions or recommendations.

Recommended Parameters

To determine the true clinical efficacy of vibratory fall prevention methods, there is a need for establishing study design parameters that are standardized and methodically based upon both physiological and stochastic resonance principles. Our group believes insufficient examination of VPT systems against these principles can at least partially explain currently inconsistent data regarding the use of stochastic-resonance-based vibrations for balance rehabilitation. After a thorough review of the literature, the following system parameters are recommended for developing robust VPT detection systems.

Preferred VPT Detection Method. RT exclusive methods are preferable to RT inclusive approaches. Dyck's 4-2-1 stepping method is advantageous for its inherent limitation of false positive responses by incorporating random null stimuli. However, modifications may be necessary for fall-risk populations since identifying the full range of 25 JND's can be time consuming.

Preferred Unit Scale. VPT measurement scales should be based on standardized physical units to improve comparability across studies [15]. We find the use of gravitational acceleration units (G's/g-forces) [70] to be preferable since it is easily translatable across a wide array of vibration apparatuses (i.e. mechanical indenters, piezoelectric vibrators, coin motors).

Preferred Vibration Apparatus. We propose the use of coin motors as the preferable vibratory apparatus for their relatively low cost, diverse programmability, low profile, and light weight. Coin motors should stimulate the plantar foot with subthreshold vibrations between 200-300Hz and should be positioned to target FAII mechanoreceptors. Overall vibration range of a system should accommodate large naturally occurring variability between sensory abilities that may be caused by the physiological or stimulus factors discussed earlier.

Preferred Testing Protocol. To reduce risk of false positive responses, we recommend eliminating all prompts between stimulus events and masking undesirable auditory sounds with non-noise-based blocking mechanisms, such as standard ear plugs or headphones required by personal safety regulations.

The primary motivations for this thesis were to (1) develop a robust vibration system inclusive of a modified 4-2-1 VPT detection method and based upon the above recommendations, (2) validate the system's reliability to detect VPT in healthy adults, and (3) determine if vibrations perceived during threshold detection influence standing balance. Chapter 3 will highlight these efforts.

Chapter 3: Development and Validation of a Modified 4-2-1 Method

A custom vibration system was developed based upon physiological principles and the aforementioned recommendations. The system, which consists of a vibrating rubber mat and associated software, utilizes a modified version of Dyck's original 4-2-1 stepping algorithm for detection of plantar foot vibration perception threshold (VPT). Two studies were conducted to validate the system for future use in stochastic-resonance-based balance interventions for fall-risk populations. **Specific Aim 1**: verify the reliability of the system to detect VPT. **Specific Aim 2**: investigate the measurable effects on postural sway during and following VPT detection. The sections that follow will introduce the custom vibration system and describe these two research studies. We believe that before conducting stochastic vibration interventions, it is not only critical to ensure that a system can accurately detect VPT, but also for investigators to understand possible changes in balance caused by threshold measurement. To the best of our knowledge, the studies herein represent one of the most complete examinations to date for understanding the effects of a VPT detection method on balance.

Custom Stochastic-Resonance-Based Vibration System

Stand-On Vibratory Mat

The full development of the custom stand-on vibratory mat will be detailed in an accompanying manuscript. Briefly, four sizes of eccentric rotating mass coin motors (Precision Microdrives, London, UK) are embedded within a low-profile silicone mat. The silicone has a Shore A50 hardness rating [75] and a tensile strength of 50 psi. The prototype mat (**Figure 9**) is similar to the system developed by Keshner et. al. [72]. Motors are positioned beneath the participant's feet to align with FAII mechanoreceptors (**Figure 10**) according to widely accepted physiology literature

[38], [39]. Vibrations between 20-400 Hz can be administered at varying amplitudes to accommodate a wide range of sensory thresholds.

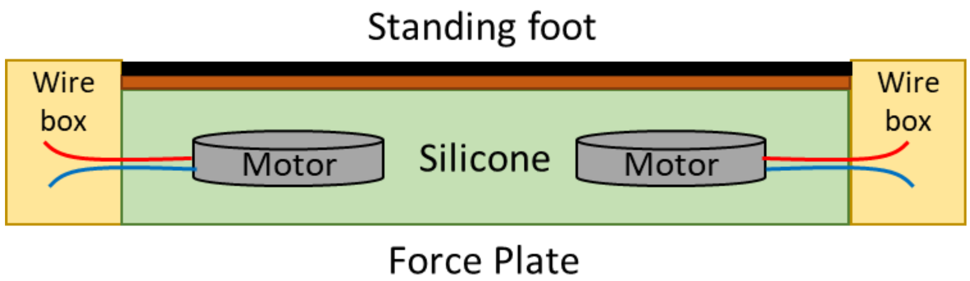

Figure 9. Elements of a Custom Vibratory Mat

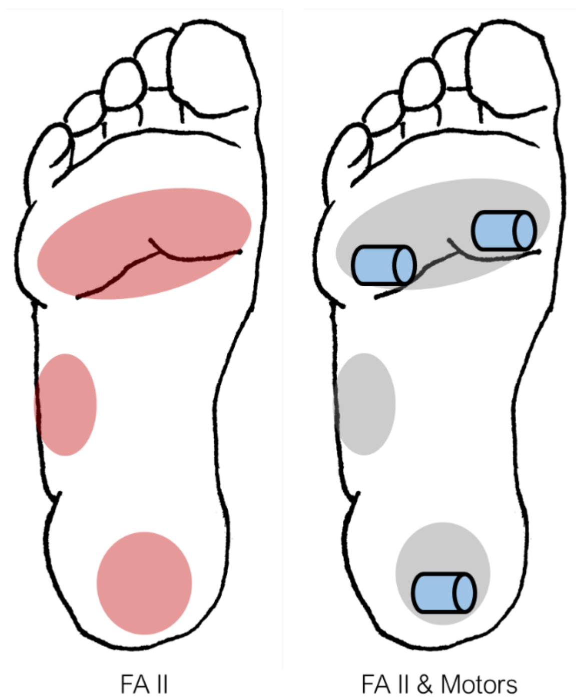

Figure 10. Foot Distribution of Receptors & Motor Placement

Modified 4-2-1 Algorithm

The vibratory mat was designed to be used for subthreshold stochastic resonance balance intervention studies. As such, it was necessary to select a VPT detection method and develop a robust system capable of performing sensory threshold testing. The 4-2-1 stepping algorithm was selected as the preferable VPT detection method. The 4-2-1 approach is exclusive of reaction time (RT), is the only method to block against false positives using random null stimuli, and when executed by a computer program, doesn't take much longer to complete than simpler methods [65]. However, as other groups have done before us [39], we did opt to carefully modify the original 4-2-1 algorithm as proposed by Dyck to improve efficiency and versatility. Modifications include the replacement of non-constant "just noticeable differences" (JND's) with equal step sizes, the elimination of verbal response prompting via instantaneous automated feedback, and the introduction of a pre-calibration period.

Replacing JND's with Constant Step Sizes. Perhaps the most distinguishing characteristic of Dyck's 4-2-1 stepping algorithm is the use of non-constant JND step sizes based on iterative sensory testing. While JND's may allow physiologists or clinicians to better relate VPT to somatosensory diagnoses, the tradeoff of this approach is that it can be highly time consuming to determine the 25 JND levels. Our vibratory system is designed to accommodate healthy younger adults, healthy older adults, and various patient populations. These different groups are expected to have widely different sensory abilities. Consequently, it would be a lengthy and labor-intensive process to identify a fully representative scale of JND's for each patient and calibrate the system accordingly before each use. One study suggested 4-2-1 could take up to six times longer in patient populations than the Upward Method of Limits (UML) [66], increasing the risk of fatiguing the patient before vibration intervention begins.

Instead of using Dyck's original scale of 25 uneven JND's, we chose to base the modified 4-2-1 (M421) system off 25 equal vibration magnitude intervals – similar to the Binary Search Halfway Between (BSHB) method. While it is important that a VPT detection method is reliable, it also must be relatively quick to administer in order to retain practicality for clinical applications – especially for fall-risk populations. As such, there exists a design tradeoff between physiological accuracy and testing efficiency in choosing any VPT detection method. We believe retaining the use of random null stimuli on a constant 25-step scale is a fair and reasonable middle ground. To retain the clinical relevance of VPT values as Dyck's original method intended, we express vibration amplitudes as gravitational acceleration units ($g = 9.81\ m/s^2$). The common scale also allows for easier comparisons between patient populations and vibration apparatuses.

Replacing Prompting with Instantaneous Feedback. The original 4-2-1 approach's main preventative measure against false positive perceptions of vibration is the incorporation of null stimuli. However, a heightened risk of recording false positives still exists when subjects are prompted to respond 'Yes' or 'No' following each stimulus event. False positive responses are subject to producing VPT values lower than true sensory threshold. To eliminate this effect, we replaced prompting with continuous and instantaneous feedback from the participant during threshold testing.

Subjects are given a handheld button that is connected to a digital encoder. At the beginning of the testing period, the participant is instructed to push the button anytime they perceive vibration and to continue depressing the trigger until the perception of vibration dissipates.

When vibration is not perceived, they are to release the button. The button provides a constant binary signal to the algorithm controller that is indicative of the participant's instantaneous perception of vibration.

While the push button approach is similar to some applications of RT inclusive methods, our system is strategically designed to block against reaction time effects. Each stimulus event consists of a 6 second vibration at constant magnitude. In order for the algorithm to initiate an upwards or downwards step change in vibration magnitude, the participant must indicate that they perceive the stimulus for at least two-thirds of the duration of the event (i.e. four or more seconds). It is not necessary that the four seconds of perception be consecutive, just as long as the total perception time within the stimulus time frame totals four or more seconds. New stimuli are automatically administered every six seconds by the system, maintaining a double-blinded experiment similar to previous studies [15], [72].

M421 testing includes 15 stimuli, in accordance with Dyck's original algorithm. Through preliminary testing, it was determined that including five random null stimuli was both time-consuming and unnecessarily repetitive. No false positives were reported during null stimuli. Consequently, the five random null events were replaced by a single null stimulus near the end of the test to maintain the important physiological check for false positives while reducing overall testing time.

Introduction of Pre-Calibration. Through our preliminary investigations, we identified the need to familiarize subjects with what the vibration feels like before beginning VPT testing. Several initial participants indicated they weren't sure if they felt vibration because they "didn't know how strong of a vibration they should be expecting." To overcome this concern, we implemented a 10-second pre-calibration period at the start of the M421 algorithm. The calibration consisted of a constant stimulus set at a vibration level approximately equal to 14 or 15 out of 25. Pre-calibration was succeeded by a five second rest period before testing began at the same initial stimulus level as the calibration. At least one other research group has utilized a calibration period prior to 4-2-1 VPT assessment [76], though their use of the Upwards Method of Limits for calibration is not preferable due to the concerns addressed in Chapter 2. M421 assessments last between 105-111 seconds each, depending on the result of the 15th stimulus. A 16th stimulus is administered when the 15th does not result in a turnaround, consistent with Dyck's method [65].

Specific Aim 1. Reliability of VPT Detection

Introduction

After developing the custom modified 4-2-1 VPT detection algorithm, it was necessary to test the reliability of the system before deploying it for threshold detection in stochastic resonance intervention studies. Specifically, **Specific Aim 1** (SA1) sought to determine if there were differences in detecting VPT in both feet simultaneously compared to single foot tests in the right or left foot. We have found limited investigations into this research question. Hijmans et. al. indicated no significant differences in VPT between feet among diabetic patients [71], so one might expect there to also be limited differences between feet in healthy subjects. However, additional support is necessary before claiming this argument to be true, particularly when considering that applying vibrations that are subthreshold to one foot but suprathreshold to the other foot could lead to destabilizing effects on balance. SA1 also aimed to test the overall reliability of the M421 method to detect VPT on healthy adult subjects.

Methods

Participants. Healthy adults ages 18-65 who self-reported no significant health history concerns were recruited from the local campus and town communities. Persons with preexisting musculoskeletal, neurologic, vestibular, or mobility deficiencies were excluded from the study. All participants provided written consent approved by the University of Kansas Institutional Review Board. Participating healthy individuals (n = 12, age: 37.8± 12.9, 4 males) were classified by age as either younger (18-34 yrs., n=6), middle aged (35-49 yrs., n=4), or older adults (50-65 yrs., n=2).

Protocol. Each participant completed two thirty-minute sessions spaced at least three hours apart. Within each session, three assessments were conducted with the M421 algorithm to detect VPT. Two assessments consisted of an isolated single foot stimulation on either the right or left foot. A third applied equal magnitude vibrations simultaneously to both feet. During each assessment, participants stood upon the vibration mat while remaining still and quiet. Headphones typical of standard personal protective equipment were worn by the participant for auditory masking. No noise was administered by the headphones. Participants held the button in their dominant hand and were provided instructions as described above.

Motors within the mat are operated by a custom Arduino program (Adafruit LLC, New York, NY) which administers vibration stimuli centered around 250 Hz. Vibration perception responses are recorded at 100Hz and VPT is subsequently calculated via a custom MATLAB program (Mathworks, Natick, MA) according to the original calculation steps by Dyck [65] outlined in Chapter 2. The outcome for a representative assessment of VPT detection via the M421 method is shown in **Figure 11**. Each data point represents a six second stimulation event. Events shown in green represent “Yes” responses to vibration perception, indicated by the participant pushing the button for 4 or more seconds during the event. “No” responses are shown in red. Turnaround events that count towards VPT calculation are displayed as a black “X” mark with vibration level indicated; threshold is equal to the average of these five events.

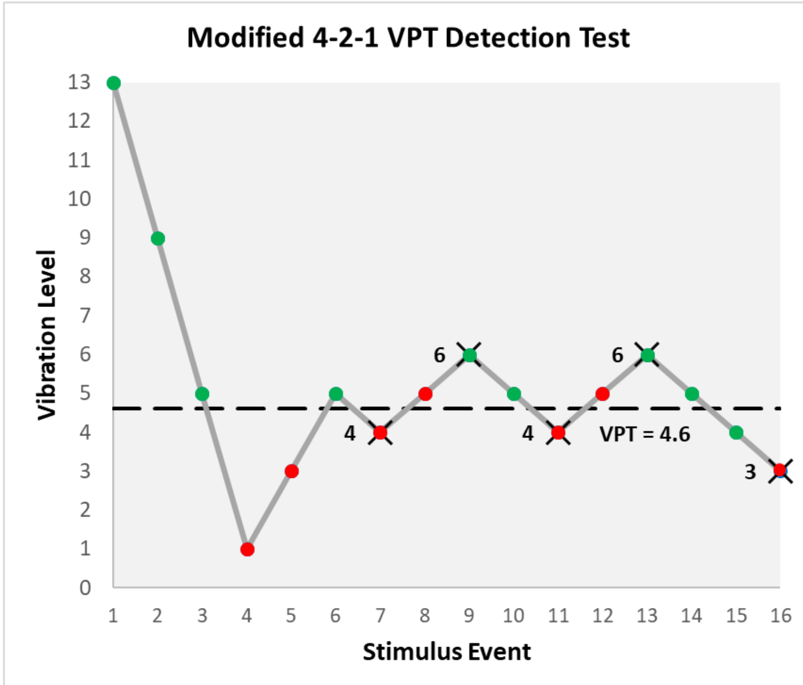

Figure 11. Representative VPT Trial Responses & Calculation

Data Analysis. VPT values expressed as motor power were converted to g-forces (G's) through custom equations derived from experimental force plate data. To obtain the conversion equations for each of the four motors, vertical ground reaction forces (N) during threshold trials were bandpass filtered between 20-400 Hz to remove any signals from participant sway or transient noise. Newton values were then converted to g-forces by dividing by the quantity [participant mass (kg) * 9.81 (m/s/s)]. Next, force data during each threshold test was temporally aligned with corresponding motor power levels and the average g-force was calculated for each available motor level across all trials. G-forces were thus obtained for any motor power level that was expressed thru the M421 algorithm during one or more VPT assessment trials. Best fit quadratic regression equations were calculated via Microsoft Excel for each motor size relating motor power level to expected g-force administered at the plantar foot. These became the conversion equations for expressing participant VPT values as expected g-forces. VPT values for the right, left, and both feet trials were compared via two-tailed Kruskal-Wallis one-way ANOVA in SAS v.9.4. (SAS, Cary, NC). VPT's were compared across age and gender by one-tailed unpaired student's t-tests. No critical value adjustments were made for SA1 statistical tests ($\alpha = 0.05$) because there were more than ten subjects in the sample (n=12).

Hypotheses

Among healthy adult subjects, **Hypothesis 1** (H1) predicted that there would be no significant differences in VPT when evaluated in a single foot vs. both feet. In the absence of any diagnosed preexisting conditions, there is no reason to believe that sensory thresholds would be drastically different between the right and left feet. Accordingly, assuming there are no differences between individual feet, we also expect that a single threshold test conducted with equal magnitude vibrations applied at both feet simultaneously would yield similar VPT levels to separate single foot tests. If our first hypothesis is supported, stochastic-resonance-based balance interventions can reduce overall treatment time period by performing a single test on both feet.

Hypothesis 2 (H2) expected that our custom vibratory system would be able to detect thresholds in all subjects studied and that individual thresholds could be compared utilizing gravitational acceleration units (G's / g-forces). Our system, which includes the custom vibration mat and the M421 VPT detection method, is designed to accommodate a wide range of sensory abilities. It is our proposition that the implementation of a universal scale such as g-forces will enable thresholds to be more easily compared within and across studies.

Results

G-Force Conversion Equations. Quadratic regression equations for relating vibration amplitude as motor power to estimated g-force are displayed in **Table 1** for each of the four motor sizes within the mat [Large (LA), Medium (MD), Small (SM), and Mini (MI)]. Equations were considered valid at and above each motor's minimum acceptable power as determined by frequency content, or the absolute minimum of the quadratic, whichever occurred at the higher vibration amplitude. The minimum acceptable power was then set as vibration level zero on the 25-step scale. **Figure 12** shows the full valid range of estimated g-forces for each motor size across the 25-step scale. The absolute maximum vibration amplitude for the custom system is $16.5x10^{-3}$ G's while the minimum acceptable vibration is $0.33x10^{-3}$ G's. It should be noted that the g-force estimation equations were derived from experimental data obtained in **Specific Aim 2**, however they are presented here since all VPT values from this point forward will be expressed as either G's or mG's ($Gx10^{-3}$). Each equation was derived from the available number of SA2 trials for each motor, as indicated in Table 1.

Table 1. G-force Regression Equations for the Custom Vibration System

Motor	Estimation Equation (Y: G-force, X: Motor Power)	Correlation Coeff. (R^2)	# of trials
Large (LA)	$Y = 0.0306 * x^2 – 0.0191 * x + 0.005$	0.7138	n = 11
Medium (MD)	$Y = 0.0106 * x^2 – 0.0049 * x + 0.0009$	0.9831	n = 1
Small (SM)	$Y = 0.0076 * x^2 – 0.0054 * x + 0.0015$	0.6187	n = 11
Mini (MI)	$Y = 0.0225 * x^2 – 0.0235 * x + 0.0067$	0.9864	n = 1

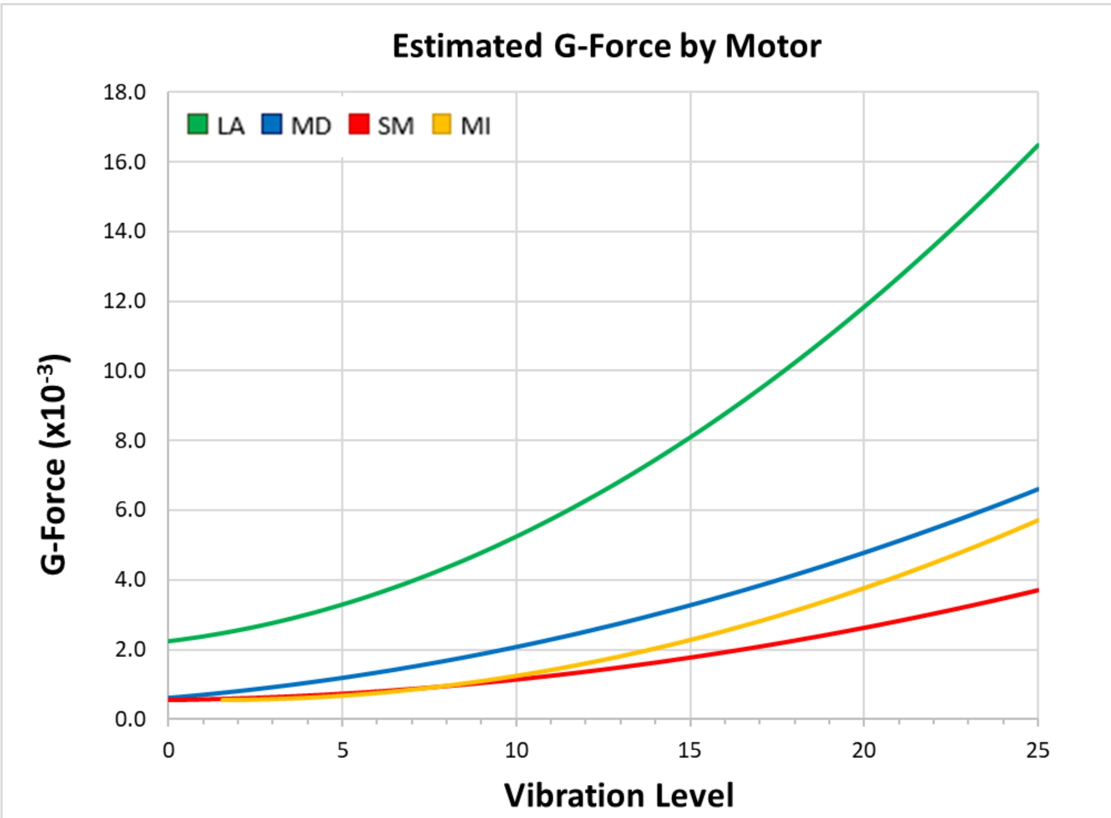

Figure 12. G-Force Output Ranges

VPT Values and Statistics. No significant differences were identified in average VPT values when threshold detection was performed on a single foot (right or left) or both feet (**Table 2**). Retrospective power analysis in SAS identified 99% statistical power to detect an effect size of two standard deviations or greater between foot conditions. Although the order of foot conditions was not randomized in SA1, post-hoc analysis revealed testing order did not influence VPT (p=0.335).

Table 2. VPT Comparison by Foot Condition

Trial Condition		**Average VPT** (G's x 10^{-3}) *n=2*		
		Right Foot	**Left Foot**	**Both Feet**
Participant	1	0.593	1.155	0.725
	2	0.783	1.926	1.028
	3	0.701	1.345	0.538
	4	1.503	1.667	0.764
	5	0.697	0.581	0.541
	6	0.799	0.765	0.647
	7	1.304	--	0.670
	8	1.142	1.177	0.712
	9	1.241	1.462	1.128
	10	5.879	5.112	4.960
	11	3.609	2.777	2.007
	12	1.201	0.800	0.773
AVG		1.621	1.706	1.208
STD		1.563	1.286	1.247
P-values		0.703 (Right Foot vs. Left Foot)		
			0.091 (Left Foot vs. Both Feet)	
		0.264 (Right Foot vs. Both Feet)		

Consistent with physiology literature on sensory thresholds, healthy younger ($\bar{x} = 0.728 \pm 0.166$ mG's, p=0.004) and healthy middle-aged ($\bar{x} = 0.789 \pm 0.247$ mG's, p=0.021) adults had significantly lower thresholds than healthy older adults ($\bar{x} = 3.48 \pm 2.09$ mG's). There were not strong significant differences between the two younger age groups (p=0.326) nor between gender groups (p=0.389), although on average males ($\bar{x} = 1.05 \pm 0.635$ mG's) had lower VPT's than females ($\bar{x} = 1.28 \pm 1.50$ mG's), consistent with physiology literature. The M421 VPT detection method was able to successfully detect VPT in all 12 participants. Threshold could not be calculated for Participant #7 during the isolated left foot condition due to too few turnarounds on the 4-2-1 calculation, but VPT was successfully detected for this participant during the right foot and both feet conditions.

Discussion

Support for H1. Results from SA1 provided support for H1. In a sample of 72 trials using the modified 4-2-1 VPT detection method, we found no significant differences between conducting the test on each foot separately compared to a single test on both feet. We had observed that many previous studies that applied stochastic resonance vibration for balance intervention had only performed VPT testing with stimulation applied to both feet simultaneously, either with RT inclusive or exclusive approaches. However, there was limited reported evidence that this approach was appropriate. In validating the M421 method, we also sought to confirm what had previously been seemingly assumed. Our findings provide much needed support for the single trial approach. This conclusion is particularly important when considering the implementation of the M421 method for VPT detection prior to stochastic-resonance-based balance interventions. By reducing the need for two separate threshold tests to one trial, preparation time for the vibratory treatment can be reduced. Quicker intervention time lowers the risk of patient fatigue, which can be a significant risk factor for falling.

Support for H2. Our custom vibration system, which includes the vibration mat and the modified 4-2-1 algorithm, was able to detect plantar foot VPT for all 12 subjects. These results support H2. Vibration magnitude administered by the system was presented as g-forces. Two prior studies involving vibration at the fingertip have expressed threshold [77] or stimulus magnitude [70] in G's, but to the best of our knowledge, our study is the first to present plantar foot VPT values as G's. The use of g-forces is also commonplace in civil engineering analyses of whole body vibrations perceived within structures [78]. Denoting plantar foot VPT's as G's is expected to facilitate threshold comparisons across the various vibratory apparatuses used by complementary research groups. It is relatively straightforward to derive gravitational acceleration units from common apparatuses including actuators, piezoelectric vibrators, and coin motors. Adopting g-forces as a universal language for describing VPT's would also improve comparisons between target populations, potentially aiding physicians with diagnosis of peripheral neuropathies.

Limitations and Future Studies (Engineering Notes). G-force equations for the motors within our system were derived from dynamic loading conditions during M421 assessments, when participants stood atop the vibration mat. Ideally, static loading conditions with steady masses would be used for obtaining these relationships. Due to lab access restrictions, however, only dynamic trials were available at this point. Nevertheless, the g-force relationships herein represent our research group's first effort to standardize VPT values within our system – and perhaps eventually, across the field. Future studies will seek to fine-tune the current equations by conducting static loading trials.

Also notable is the directionality of the vibrations. Estimated G's represent vibration components in the vertical direction only. By the nature of the eccentric rotating mass coin motors, there also exists vibratory components in the horizontal plane. These vibration components, which are expected to be weaker than their vertical counterparts, represent shear in the anterior-posterior or mediolateral directions. Shear forces along the plantar foot are primarily perceived by slow-adapting type 2 mechanoreceptors. However, VPT detection systems are designed to target FAII mechanoreceptors, which primarily perceive direct vibrations at high frequencies. For these reasons, only vibration in the vertical direction was included in these initial g-force estimations. Future analyses with static loading could consider evaluating the magnitude and frequency of the horizontal vibration components to detect if there are relevant contributions that could be perceived by FAII receptors, and if significant, include them in final g-force estimation equations.

G-force analysis revealed significant overlap in output amplitude between the four motor sizes (**Figure 12**). For example, a VPT of 4 mG's could be administered by large, medium, or mini motors. From an engineering design perspective, this indicates that future derivations of the vibration system may not need to incorporate all four motor sizes. Devices specifically targeting fall-risk populations such as the elderly or persons with neuropathy likely only need to include large and medium motors, which would reduce fabrication costs and time.

Limitations and Future Studies (Clinical Notes). Although we did not find significant differences in VPT when assessed during separate single foot trials or on both feet simultaneously, there are situations where detecting VPT separately in each foot would still be recommended. For example, in patient populations where neuropathies or other pathologies may exist unilaterally, it is reasonable to assume significant sensory differences between the affected foot and the unaffected foot. Administering vibration based on the both feet condition alone could induce asymmetric effects on the right and left sides, potentially increasing fall risk. Irregular sensory abilities can also exist in persons without diagnosed conditions; Participant 7 provides an example. Although the participant reported no diagnosed somatosensory impairments, results suggest reduced sensory abilities in the left foot (VPT was unable to be detected in either assessment with isolated vibration at the left foot).

We conclude that the decision to conduct two single-foot VPT trials or one combined assessment on both feet should be made on a patient-specific basis by researchers, clinicians, and participants. While performing two separate trials would increase testing time, the consequences of inaccurately detecting VPT in either foot overshadow the drawbacks of lengthening test time. Short rest breaks are recommended between threshold assessments of each foot to limit fatigue.

It is important to note that several clinical screening tools exist for diagnosing somatosensory deficiencies like neuropathies. Two commonly used examples include the Michigan Neuropathy Screening Index [58], and the Semmes Weinstein Monofilament Test [8], [79], which was performed within Specific Aim 2. VPT testing should not replace these existing tools, but rather supplement existing diagnostics. The primary intended use of the M421 algorithm is for detecting VPT prior to vibration-based balance interventions, not for diagnosing sensory conditions.

Specific Aim 2. Effects of Modified 4-2-1 on Sway

Introduction

Accurate detection of VPT is critical for the safety and efficacy of stochastic-resonance-based vibration interventions for balance rehabilitation. Vibrations are typically administered at 90% of threshold to ensure subthreshold stimuli [9]. Subthreshold stimuli at the plantar foot are thought to augment impaired neural pathways, as described in Chapter 2, gradually improving balance. Suprathreshold stimuli, on the other hand, have shown to manipulate balance in more jolting patterns [25], [27]. In order to detect threshold, VPT methods strategically apply both suprathreshold and subthreshold stimuli until the vibration magnitude narrows in on true threshold. The presence of both subthreshold and suprathreshold vibrations poses the question that while VPT testing does identify sensory threshold, it may also influence postural sway. We know of very few, if any, studies that have investigated this research question to date. **Specific Aim 2** (SA2) aimed to examine the effects of the modified 4-2-1 VPT detection method on standing balance during and following threshold assessment.

Methods

Participants. Six healthy adults were recruited from the campus community under the same exclusion criteria and IRB approval as SA1. Participants were divided into two equal sized groups: healthy younger (HY: n=3, age: 23.3 ± 2.31, 0 males) and healthy older (HO: n=3, age: 56.3 ± 4.93, 1 male).

Protocol. Participants completed four testing sessions each spaced at least two days apart. At the beginning of the first session, two common clinical tests for neuropathy were performed: the Semmes-Weinstein monofilament (SWMF) test and the Timed-Up-and-Go (TUG) test. SWMF is a simple non-invasive test of sensory ability. A thin nylon monofilament (SW 5.07, 10 grams) is gently touched to each of the participant's bare feet at 10 locations (9 plantar foot, 1 dorsal). Persons who successfully perceive the monofilament at all 10 sites are considered healthy and free from foot neuropathies. TUG is a test of gait and balance abilities, which are directly affected by somatosensory deficiencies. From a seated position, participants are instructed to stand up, walk 10 feet forward at a self-identified comfortable walking pace, turn around, then walk back to the chair and sit down. Typically, completing the task in less than 15 seconds is considered free from concern of fall risk. While there are numerous clinical scales for assessing neuropathies that could have been selected, both SWMF [8], [79] and TUG [12] have been previously used for assessing health of participants in stochastic vibration studies.

A total of six trials (**Table 3**) were performed during each session for sway analyses. The first two trials (BLO, BLC) collected quiet standing balance directly atop the firm, flat surface of the force plates (Ground). One trial was completed with eyes open (EO), and the other with eyes closed (EC). Order was randomized between subjects. Participants stood atop the vibration mat for the third trial (BLM), but no vibration was administered. The purpose of this trial was to collect baseline balance on the rubber mat. Following BLM, participants received a sitting break for 3-4 minutes. Threshold assessment was performed during the fourth trial (THR) using the M421 VPT detection method with eyes open. The fifth and sixth trials (PTO, PTC) occurred immediately after THR, following a brief 15-20 second transition period where participants stepped forward from the mat to ground surface. PTO and PTC replicated the first two ground trials, with EO and EC conditions again performed in random order. All trials lasted 90 seconds, except THR trials which take 105-111 seconds.

Table 3. Sway Analysis Trial Conditions

#	Trial Condition	Surface Condition	Visual Condition	Abbreviation
1-2	Baseline	Ground	Eyes Open	BLO
	Baseline	Ground	Eyes Closed	BLC
3	Baseline	Mat	Eyes Open	BLM
4	Threshold	Mat	Eyes Open	THR
5-6	Post-Threshold	Ground	Eyes Closed	PTC
	Post-Threshold	Ground	Eyes Open	PTO

Equipment for SA2 was consistent with SA1. **Figure 13a** displays the vibration mat positioned behind two force plates (AMTI, Watertown, MA) used for balance analysis. The mat sits atop a third force plate. Ground trials were recorded at 100 Hz by a data acquisition board (CED, Cambridge, UK); trials atop the vibration mat were collected at 2500 Hz. Stance width and angle were held constant across all trials and participants [80]. The handheld button used for instantaneous feedback during the M421 assessment is shown in **Figure 13b**.

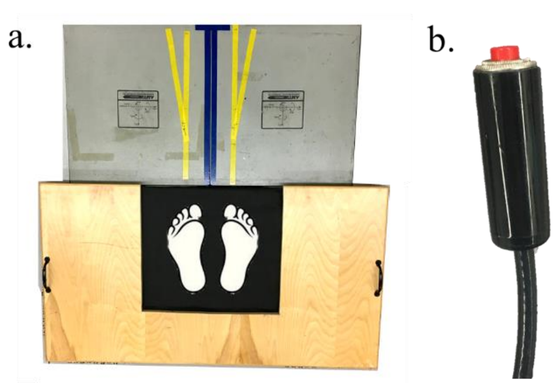

Figure 13. Components of Experimental Set Up

Data Analysis. Force plate output signals include applied forces and moments in the anterior-posterior, mediolateral, and vertical directions. Data sets were lowpass filtered at 20 Hz to ensure the only contributory components would be participant sway. Three linear measures of balance and two nonlinear measures were calculated from each trial. All five parameters have been commonly used in analyses of balance under the effects of plantar foot vibration [9], [12], [16], [44], [45], [73], [81]. Center of pressure (COP) trajectory ranges in the anterior-posterior (APL) and mediolateral (MLW) directions indicate the overall length and width, respectively, of the COP pathway during each standing trial. The ellipse area (EA) encompassing 95% of the COP trajectory was also calculated. The major axis of EA was not fixed in the anterior-posterior direction, contrary to previous applications [12], [81]. This change was made to allow for rotations of the ellipse axes to represent the COP pathway more accurately.

The fourth and fifth COP measures calculated were detrended fluctuation analysis (DFA) in the anterior-posterior (APA) and mediolateral (MLA) directions. DFA is a nonlinear variable that indicates temporal correlation of a signal while blocking against the effects of external noise [73], [82]. While linear measures describe magnitude of a signal, nonlinear parameters such as DFA can provide insight into the behavior of the COP in terms of variability. For this reason, nonlinear parameters have risen in popularity over the last two decades for describing characteristics of biological systems. The resultant scaling exponent of DFA, α, is a quantitative representation of signal complexity. Moderate α values are believed to be preferable for healthy movement compared to patterns of lower ($\alpha \cong 0.5$) or higher ($\alpha \cong 1.5$) complexity [46], [47]. Minimum and maximum time windows for DFA analysis in this study were set to 0.5 and 15 seconds, respectively [83]; an analysis frequency of 50 Hz was used based on previous balance studies [84], [85].

COP measures were statistically compared across two primary research questions for SA2. The first question sought to identify what effects on balance occur during VPT detection. Balance during threshold assessment (THR) was compared to baseline balance on the vibration mat (BLM) to investigate this question (**Table 3**). The second question of SA2 pertained to possible retained effects of VPT detection, or in other words, how balance after the VPT assessment compares to balance before. Comparisons of baseline (BLO, BLC) and post-threshold (PTO, PTC) balance were performed within visual conditions (**Table 3**). Two-way repeated measures ANOVA was performed to check for significant effects between these three trial comparisons across the four sessions. The expected magnitude differences between HO and HY groups were controlled for in the statistical model. Within participant comparisons were also evaluated via one-sample paired student t-tests of the average difference between trials (i.e. $\bar{x}_{BLO} - \bar{x}_{PTO}$). Critical value was set to $\alpha = 0.10$ for all SA2 statistical tests due to the small sample size (n=6).

Hypotheses

As previously mentioned, very little attention has been given to the effects of threshold assessment in prior balance literature. Many studies have analyzed the effects of subthreshold stochastic vibrations on balance during and following stimulation. However, few if any have studied postural sway during VPT detection that must be performed before the stochastic vibrations are administered. Based on this lack of prior knowledge, our null hypotheses anticipated that the modified 4-2-1 VPT detection method would have no effects on standing balance. Specifically, **Hypothesis 3** (H3) predicted that there would be no significant changes in balance during the threshold assessment (BLO-THR) or following VPT testing with either visual condition (BLO-PTO, BLC-PTC). **Hypothesis 4** (H4) predicted that there would be more significant within participant trial comparisons across the five COP parameters in HO participants compared to HY; it was expected that balance in the HO group would be more influenced by M421 VPT assessment due to reduced complexity and adaptability of balance associated with aging [46], [47].

Results

All participants scored within healthy criteria on the SWMF and TUG tests. Similar to SA1, the HY group ($\bar{x} = 0.561 \pm 0.019$ mG's) had significantly lower VPT than the HO group ($\bar{x} = 2.82 \pm 0.291$ mG's, p=0.0115). Repeated measures ANOVA of the effects of M421 on balance during threshold detection (BLM-THR) identified no significant differences across any of the five COP parameters analyzed (**Figure 14-Figure 15**). Similarly, no significant changes in balance were identified following the M421 assessment (BLO-PTO, BLC-PTC). MLW during VPT detection was the only parameter to approach significant effects (p=0.1124).

Within participant differences revealed some significant effects for the three sets of trial comparisons for SA2 (**Table 4**). One linear COP measure, MLW, and one nonlinear COP measure, APA, resulted in the highest number of significant trial comparisons. Across the five COP parameters, fewer significant differences were found after threshold assessment with EC than after assessment with EO or during threshold assessment. The combined total number of significant differences across the three sets of trial comparisons was equal between the HO and HY groups (i.e. 9), although a higher proportion of those outcomes were attributed to differences in COP parameters during VPT detection (BLM-THR) for HO and afterwards (BLO-PTO) for HY. Overall, 80% of the within participant trial differences were not significant.

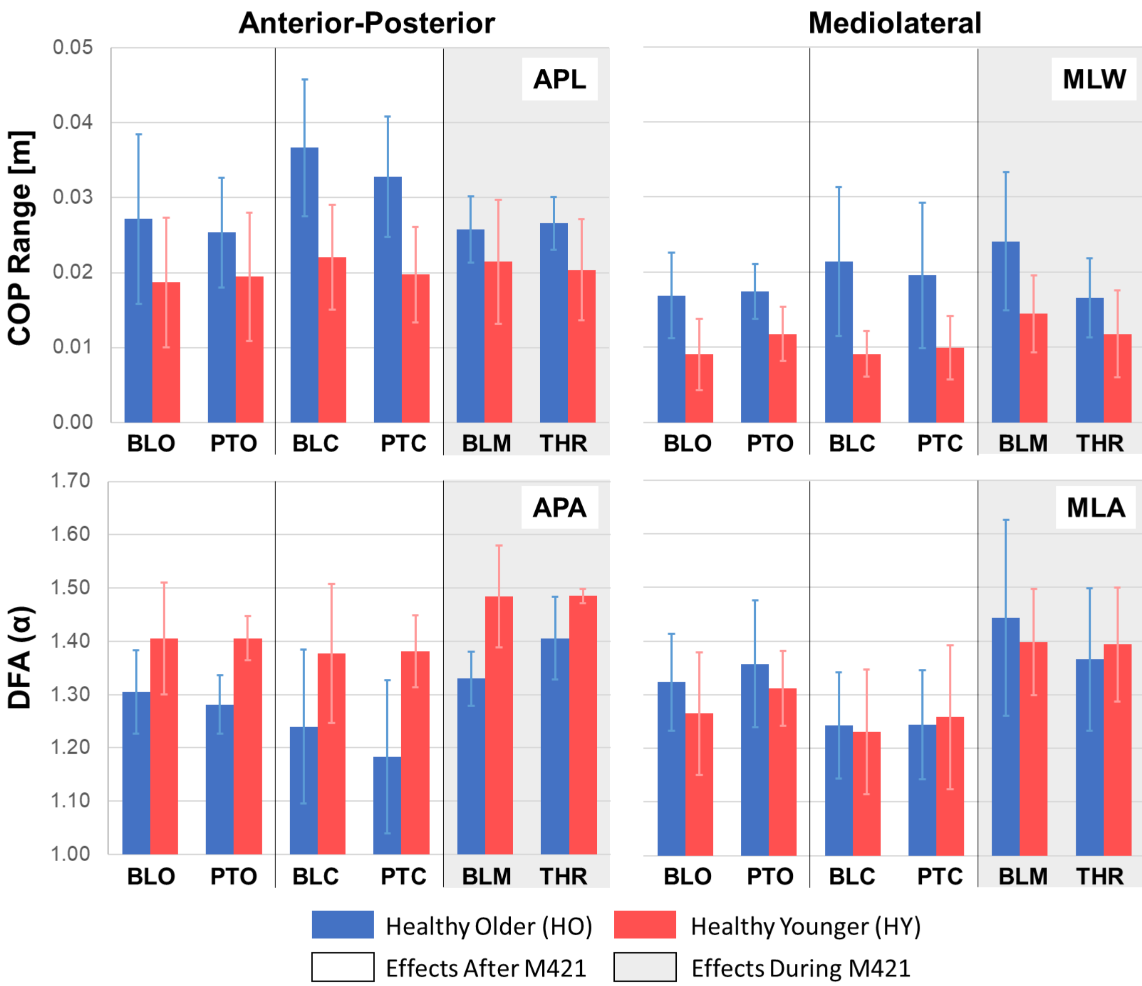

Figure 14. COP Ranges and DFA Values Across Trials

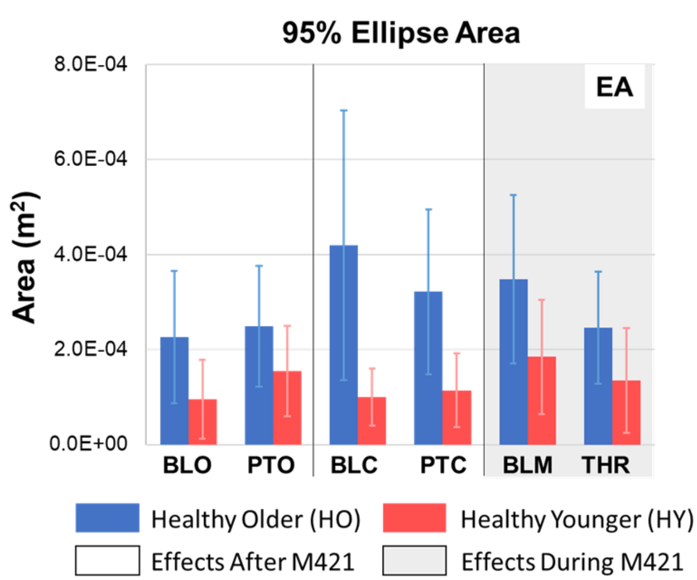

Figure 15. COP Ellipse Area Across Trials

Table 4. Counts of Significant Within-Participant Trial Differences

	BLO-PTO	BLC-PTC	BLM-THR	
APL	1/6	1/6	0/6	2/18
MLW	2/6	1/6	2/6	5/18
EA	2/6	1/6	1/6	4/18
APA	1/6	1/6	3/6	5/18
MLA	1/6	0/6	1/6	2/18
	7/30	4/30	7/30	**18/90**

Discussion

Support for H3. Results from SA2 fully supported H3. Repeated measures ANOVA concluded that balance is not significantly different during or following M421 VPT detection compared to pre-assessment conditions. Visual comparison of HO and HY group averages for the five COP parameters (**Figure 14**-**Figure 15**) makes it clear to see that there were only very small changes in balance during and following threshold detection. While individual subjects did demonstrate some significant differences between the three trial comparisons, an overwhelming majority of these comparisons were insignificant across the five COP parameters (**Table 4**). In only one instance were more than two of the five parameters significant within the same trial comparison (BLO-PTO) for a single participant (HY Participant #3). VPT detection tests inherently include both suprathreshold and subthreshold stimuli to identify sensory threshold level, so one may infer that intermittently administering brief suprathreshold stimuli may induce undesirable changes in balance during M421 assessments. However, our results suggest that the M421 method does not manipulate balance in undesirable manners neither during nor after VPT detection.

Opposition of H4. It was expected that due to the detrimental effects of aging on postural sway, HO participants would yield a greater number of significant within participant trial comparisons across the five COP parameters. SA2 results did not support H4. Overall similarity between HO and HY groups does not, however, suggest that the age groups responded to the M421 method equally. Analysis of the percent change between the three sets of trial comparisons provides a posteriori insight (**Table 5**). For example, HO subjects expressed 23% smaller EA on average following threshold detection (BLC-PTC) while HY group increased EA by 13%. Due to relatively large standard deviations though, neither change was a significant effect. Opposite but non-significant effects between age groups were also identified in MLW following M421 assessment with EC (BLC-PTC).

There were no consistent trends within individual parameters across the trial comparisons, suggesting insignificant mixed effects during and after threshold assessment. It is difficult to draw meaningful inferences on the effects of M421 VPT detection from percent changes for two reasons. First, the magnitude scale of each COP parameter varies; a 10% change in APL is not directly comparable to a 10% change in APA. Secondly, relatively large standard deviations were observed within each age group across all COP parameters.

Table 5. Average Group Percent Change Between Trials

	BLO-PTO		**BLC-PTC**		**BLM-THR**	
	HO	HY	HO	HY	HO	HY
APL	-6.8%	3.9%	-10%	-10%	3.1%	-5.0%
MLW	3.0%	30%	-8.5%	9.3%	-31%	-19%
EA	10%	62%	-23%	14%	-29%	-27%
APA	-1.8%	0.0%	-4.6%	0.3%	5.7%	0.0%
MLA	2.6%	3.7%	0.1%	2.2%	-5.4%	-0.3%

Limitations and Future Studies (Engineering Notes). High group variability within each parameter undoubtedly influenced overall SA2 findings. Retrospective power analysis revealed just 65% power under current statistical conditions. This outcome is largely due to the small sample size which was limited by lab access restrictions. Future studies should consider expanding the study to seek stronger statistical conclusions. Eight participants per age group (8 HY, 8 HO, N=16) would be required to achieve 95% power to detect an effect size of two standard deviations or greater between balance during or after M421 and baseline conditions. Nevertheless, overall SA2 results on the limited sample size available provide no reason to believe at this point that the M421 VPT detection method has significant impacts on balance during or following threshold assessment.

The absence of evidence to demonstrate that balance after threshold detection is any different than balance prior to assessment yields a significant benefit for future stochastic-resonance-based vibration intervention studies. Measuring balance before threshold detection is unnecessary with the M421 system, and post-threshold balance conditions (PTO, PTC) can effectively serve as the initial (baseline) conditions for analyzing the primary effects of the vibration intervention – which is what researchers are ultimately interested in. Because it is so critical that VPT is accurately detected before each stochastic resonance treatment for reasons previously discussed, threshold assessment cannot be eliminated from individual sessions. However, it would be highly advantageous if the selected VPT detection method could reduce the time length of each test session. M421 provides both an accurate physiology-based option and shorter testing times. In a practical sense, future vibratory devices with the M421 algorithm could administer treatment vibrations immediately after VPT is detected, reducing the amount of time a patient is required to stand for treatment. Shorter standing treatment times are expected to increase user compliance, reduce fatigue, and deter falling.

Although the novel M421 method has demonstrated reliability in detecting VPT and limited effects on balance during quiet standing, it would still be an incomplete argument at this point to assume that the method is superior to existing threshold detection methods (BSHB, UML, DML, MOL, SM). More information directly comparing VPT detection approaches is still needed [67]. The first step should be to conduct repeated threshold assessments on an age-diverse set of individuals using each of the VPT detection methods. Perhaps each participant would perform 2-3 threshold tests under each approach, and the reliability of each method would be analyzed. Once it is determined which, if any, existing methods demonstrate similar consistency to M421 over several trials, a second analysis should compare the effects of these methods on balance during and after VPT detection, as was conducted in SA2. These investigations could provide key information for identifying the optimal approach for detecting VPT prior to stochastic-resonance-based vibration interventions.

Limitations and Future Studies (Clinical Notes). As noted earlier, VPT detection tests should not be used in lieu of existing clinical tools for diagnosing neuropathies and other somatosensory deficiencies [58]. What threshold methods such as M421 can provide, though, is additional insight that existing screening tools may not be able to detect. All participants in SA2 are simply grouped into the "healthy" category based on their performance during SWMF and TUG tests; no clinical indicators of neuropathy were observed. Meanwhile, average VPT's between HY and HO groups were significantly different, indicating a clear decline in somatosensory abilities even among middle-aged and older adults who are typically considered "healthy." Therefore, clinical tools like SWMF and TUG could be considered tests of "unhealthiness" while M421 may be considered a test of "healthiness." Each provides separate but important outcomes for making informed clinical decisions to reduce risk of falling, which has shown to worsen as early as middle age [20].

VPT magnitudes remained fairly consistent across the four SA2 testing sessions. The average within participant standard deviation was 0.155mG’s, which equates to just 1% of the system’s vibration range. For patients without significant health history concerns, it is possible that VPT is not easily influenced from day to day by the physiological factors outlined in Chapter 2. Sensory abilities in healthy adults may be robust enough to maintain a relatively constant threshold over short time periods (days or weeks), which could imply that threshold would not need to be measured before each vibration treatment on healthy persons. However, due to the aforementioned implications of administering vibration that is misaligned with true VPT, careful consideration should be given before altering existing procedures and this assumption should not be made for fall-risk populations including the elderly or persons with foot neuropathies.

Chapter 4: Summary (Putting It All Together)

Primary Goal

Falls to the ground cause damaging consequences on an individual's health and lifestyle. There is a pressing need for affordable, home-based solutions to prevent fall incidents. Sensory deficiencies in the feet can be a key contributor to falling. Stochastic-resonance-based vibration therapies are one of the current modalities being investigated to potentially rehabilitate balance in persons with impaired somatosensory abilities. During vibration interventions, vibration amplitude must remain below sensory threshold to encourage beneficial responses in standing balance. It is therefore critical to accurately and reliably detect vibration perception threshold (VPT). Many methods have been developed for detecting VPT, but several concerns exist with these approaches. Very little attention has been given to the reliability of these methods or any effects they may have on standing balance. Instead, the primary focus of the field for nearly two decades has been understanding the effects of a single type of stochastic vibration intervention. Most studies simply select a VPT detection method out of necessity, and some seemingly at random, then perform a single threshold assessment on both feet simultaneously and forgo investigating potential effects of the threshold detection method on balance. We believed that it could not reasonably be assumed that threshold assessments have no impact on subsequent vibratory stimulations without further investigation. Our main goals were (1) to develop a new VPT detection method, the modified 4-2-1 method, based on the existing approaches and underlying physiological principles, (2) to determine the reliability of the M421 method, and (3) to investigate if the M421 method effects balance during or after threshold assessment.

Key Findings

A custom vibration system was developed that can output stochastic vibrations. The system consists of a vibrating rubber mat and the novel M421 VPT detection algorithm. M421 is a double-blind approach that blocks against the effects of reaction time through instantaneous automated feedback. To address the need for greater comparability between patient populations and across vibration systems, a common scale for expressing VPT, G-forces, was established. SA1 determined that conducting a single threshold test on both feet is not statistically different than two separate tests performed on each individual foot, allowing for quicker VPT detection times and reducing fatigue risk. SA2 analysis failed to identify any changes in balance either during or after the M421 assessment when compared to balance before threshold detection. While individual participants may experience slight manipulations in certain components of balance, there is no evidence to suggest that these effects are strong enough to increase fall risk. Future studies will seek to further validate the novel M421 method through direct comparisons against other existing threshold detection methods.

Implications of Findings

The work herein was conducted under the belief that it is essential to first understand the effects of VPT detection on balance before investigating the feasibility of stochastic-resonance-based vibrations for fall prevention. This thesis encompasses the development and preliminary validation of a robust VPT detection method. To the best of our knowledge, these steps represent the most comprehensive analysis to date of a threshold method for use in vibratory balance interventions. M421 has demonstrated the ability to reliably detect VPT across a wide age range without impacting standing balance in undesirable manners. The same cannot be said at this time for any other threshold detection method that we know of. M421 will be used to detect VPT during future investigations into the effects of various stochastic vibrations on standing balance. Positive results may lead to a revolutionary balance enhancement tool that is affordable, non-invasive, discrete, and personalized. This proactive solution could prevent the physical, emotional, and financial costs associated with falling while improving the quality of life for millions of fall-risk individuals.

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